Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

For

Copper-catalysed C(sp^3)–N coupling initiated by selective C–C bond cleavage of cyclobutanone oxime esters

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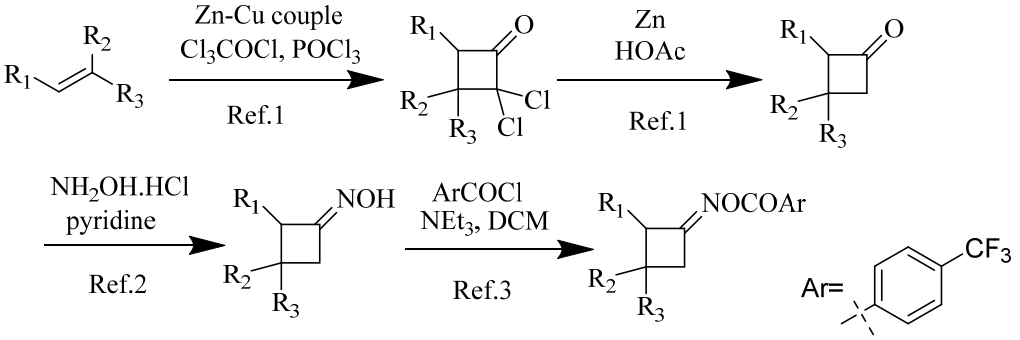
1. General remarks

^{1}H NMR spectra were recorded on 400 or 600 MHz (100 or 150 MHz for ^{13}C NMR) agilent NMR spectrometer with $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts were reported in parts per million (ppm, δ scale) downfield from TMS at 0.00 ppm and referenced to the $CDCl_3$ at 7.26 ppm (for ^{1}H NMR) or 77.16 ppm (for ^{13}C NMR); HRMS was recorded on a GCT Premier^{TM} (ESI) Mass Spectrometer. Infrared (FT-IR) spectra were recorded on a Varian 1000FT-IR, ν_{max} in cm^{-1}. Melting points were measured using SGW, X-4B and values are uncorrected. All commercially available reagents and solvents were used as received unless otherwise specified.

2. Preparation of cyclobutanone oxime esters



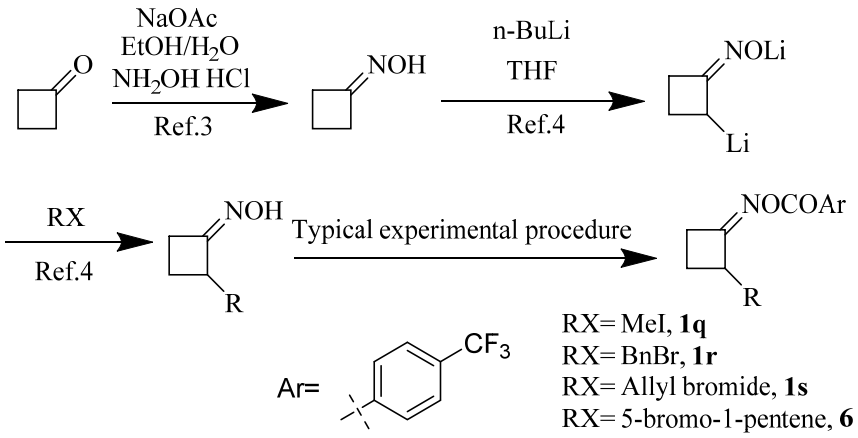
Cyclobutanone oxime esters were obtained from the correspounding cyclobutanones, which were commercial available or produced by the reduction of *α*,*α*-dichlorocyclobutanones synthesized from the corresponding alkenes by the reported procedure[1]. The following experimental procedure is typical: To a 50 mL three-necked flask under argon were added alkene derivative (5.0 mmol, 1.0 equiv), zinc-copper couple (960 mg, 15.0 mmol, 3.0 equiv), and anhydrous ether (10 mL). To the mixture was added a solution of trichloroacetyl chloride (1.12 mL, 10.0 mmol, 2.0 equiv) and phosphorus oxychloride (0.51 mL, 5.5 mmol, 1.1 equiv) in ether (10 mL) over 1 h through an addition funnel. The suspension was stirred overnight at reflux. The resulting mixture was filtered through a pad of Celite and was washed with ether (20 mL). The organic solution was successively washed with water (30 mL), a saturated aqueous solution of $NaHCO_3$ (30 mL) and brine (30 mL), and dried over $MgSO_4$. Then the solution was filtered, concentrated and used in the next step without further purification.

A mixture of 2,2-dichlorocyclobutanones (1.0 equiv) and zinc dust (4.0 equiv) in acetic acid (10 mL) was stirred at room temperature for 2 h and then heated at 80 °C for 5 h. The resulting mixture was allowed to cool to room temperature, followed by diluting with water (30 mL) and extracted with ether (3 × 20 mL). The organic phase was washed successively with a saturated solution of aqueous $NaHCO_3$ (3 × 30 mL), water (30 mL) and brine (30 mL), then dried over $MgSO_4$ and concentrated in vacuum. The residue was then purified by flash chromatography with a mixture of petroleum ether and ethyl acetate to afford various cyclobutanones.

To a stirred solution of cyclobutanones (1.0 equiv) in pyridine (0.5 M) was added hydroxylamine hydrochloride (2.0 equiv) at rt. After stirring for 2 h, pyridine was removed under reduced pressure. The residue was diluted with water and extracted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude material, which were used in the next step without further purification.

To a mixture of cyclobutanone oxime (1.0 equiv), triethylamine (2.0 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added 4-trifluoromethyl benzoyl chloride (1.5 equiv) at 0 °C. After 6 h, water was added to the above solution, and the mixture was diluted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO_2 with EtOAc–PE as an eluent to give cyclobutanone oxime esters.

General experimental procedure for the synthesis of *a*-substituted oximes



To a mixture of hydroxylamine hydrochloride (18.0 mmol), sodium acetate (22.5 mmol), ethanol (10.5 mL) and water (4.5 mL) in a 30-mL two-necked flask was added cyclobutanone (15 mmol) and the mixture was stirred at 100 °C for 12 h. The reaction mixture was cooled to room temperature and then ethanol was removed under reduced pressure and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography to give cyclobutanone oxime as a white solid (1.0 g, 78%).

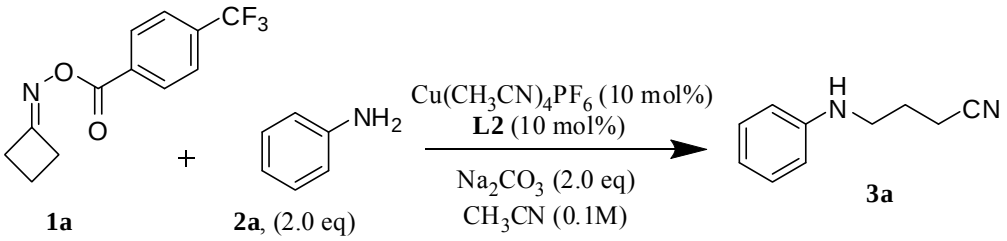
Cyclobutanone oxime (1.0 equiv) in absolute THF (0.5 M) was added *n*-BuLi (2.0 equiv) slowly at 0 °C, and the resulting mixture was stirred for another 15 min at this temperature for the formation of syn dianion. RX (1.0 equiv) was added dropwise at 0 °C and the mixture was warmed to RT for 2 h. Subsequently, the reaction was quenched by cold water, and the mixture was diluted with EA. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO_2 with EtOAc–PE as an eluent to give *a*-substituted oximes in quantively yield.

References

[1] Xu, H.-J.; Zhu, F.-F.; Shen, Y.-Y.; Wang, X.; Feng, Y.-S. *Tetrahedron.* **2012**, *68*, 4145.
[2] Cho, H.; Iwama, Y.; Sugimooto, K. J.; Mori, S.; Tokuyamma, H. *J. Org. Chem.* **2010**, *75*, 627.
[3] Nishimura, T.; Yoshinaka, T.; Nishiguchi, Y.; Maeda, Y.; Uemura. S. *Org. Lett.* **2005**, *7*, 2425.
[4] Zhao, B.-L.; Shi Z.-Z. *Angew. Chem. Int. Ed.* **2017**, 56, 12727.

3. Typical experimental procedures

Conditions A



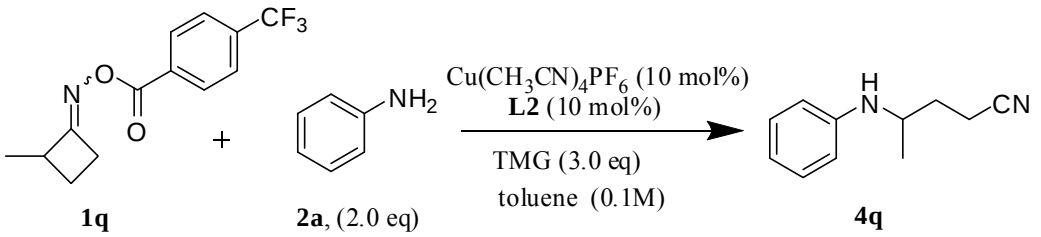
1a **2a**, (2.0 eq) **3a**

To a mixture of cyclobutanone oxime ester (**1a**, 51.4 mg, 0.2 mmol), aniline (**2a**, 37 μL, 0.4 mmol), Na_2CO_3 (43 mg, 2.0 eq), $Cu(CH_3CN)_4PF_6$ (7.5 mg, 10 mol%), 6,6'-dimethyl-2,2'-bipyridine (**L2**, 3.7 mg, 10 mol%) in flame-dried Schlenk tube was added degassed acetonitrile (2.0 mL) under Ar. The resulting mixture was stirred at room temperature for 6 h, and the solvent was then removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE : EA = 10 : 1) to afford 31.4 mg of **3a** as an oil (98% yield).

Gram-scale transformation

To a mixture of cyclobutanone oxime ester (**1a**, 1.028 g, 4.0 mmol), aniline (**2a**, 740 μL, 8.0 mmol), Na_2CO_3 (860 mg, 2.0 eq), $Cu(CH_3CN)_4PF_6$ (150 mg, 10 mol%), 6,6'-dimethyl-2,2'-bipyridine (**L2**, 74 mg, 10 mol%) in flame-dried Schlenk tube was added degassed acetonitrile (20 mL) under Ar. The resulting mixture was stirred at room temperature for 6 h, and the solvent was then removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE : EA = 10 : 1) to afford 555 mg of **3a** as an oil (87% yield).

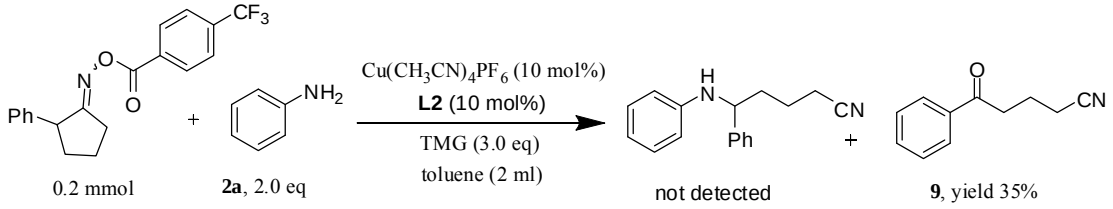
Conditions B



1q **2a**, (2.0 eq) **4q**

To a mixture of cyclobutanone oxime ester (**1q**, 54.2 mg, 0.2 mmol), aniline (**2a**, 37 μL, 0.4 mmol), TMG (75 μL, 3.0 eq), $Cu(CH_3CN)_4PF_6$ (7.5 mg, 10 mol%), 6,6'-dimethyl-2,2'-bipyridine (**L2**, 3.7 mg, 10 mol%) in flame-dried Schlenk tube was added degassed toluene (2.0 mL) under Ar. The resulting mixture was stirred at room temperature for 4 h, and the solvent was then removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE : EA = 10:1) to afford 27.8 mg of **4q** as an oil (80% yield).

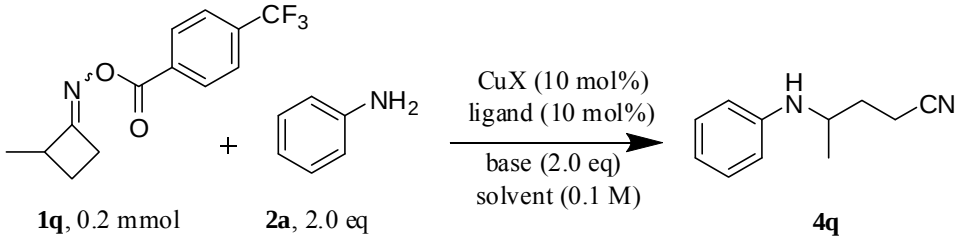
4. The reaction of the oxime ester derived from 2-phenyl cyclopentanone



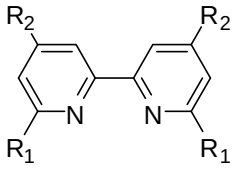
0.2 mmol **2a**, 2.0 eq not detected **9**, yield 35%

To a mixture of 2-phenylcyclopentan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (69.5 mg, 0.2 mmol), aniline (**2a**, 37 μL, 0.4 mmol), TMG (75 μL, 3.0 eq), $Cu(CH_3CN)_4PF_6$ (7.5 mg, 10 mol%), 6,6'-dimethyl-2,2'-bipyridine (**L2**, 3.7 mg, 10 mol%) in flame-dried Schlenk tube was added degassed toluene (2.0 mL) under Ar. The resulting mixture was stirred at room temperature for 12 h, and the solvent was then removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE : EA = 10:1) to afford 12.1 mg of **9** as an oil (35% yield).

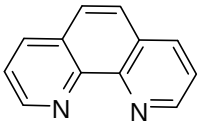
5. Optimization of reaction parameters for secondary carbons



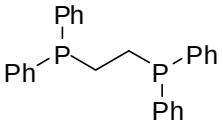
1q, 0.2 mmol **2a**, 2.0 eq **4q**



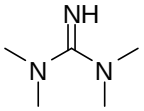
L1: R_1 = H, R_2 = H
L2: R_1 = CH_3, R_2 = H
L7: R_1 = H, R_2 = *t*-Bu



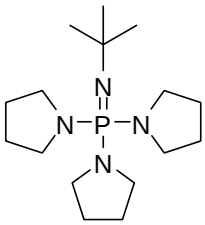
L8



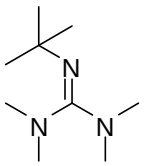
L9



TMG



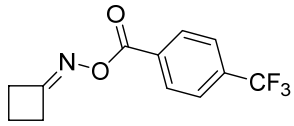
BTPP



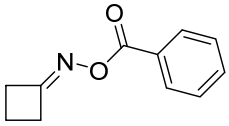
2-(*t*-Bu)-TMG

Entry	CuX	Base	Solvent	Ligand	Yield
1	$Cu(CH_3CN)_4PF_6$	Na_2CO_3	CH_3CN	**L2**	< 5%
2	$Cu(CH_3CN)_4PF_6$	KO^{t}Bu	CH_3CN	**L2**	< 5%
3	$Cu(CH_3CN)_4PF_6$	BTPP	CH_3CN	**L2**	< 5%
4	$Cu(CH_3CN)_4PF_6$	No base	CH_3CN	**L2**	< 5%
5	$Cu(CH_3CN)_4PF_6$	NEt_3	CH_3CN	**L2**	48%
6	$Cu(CH_3CN)_4PF_6$	TMG	CH_3CN	**L2**	55%
7	$Cu(CH_3CN)_4PF_6$	2-(*t*-Bu)-TMG	CH_3CN	**L2**	< 5%
8	CuI	TMG	CH_3CN	**L2**	52%
9	CuCl	TMG	CH_3CN	**L2**	45%
10	$Cu(CH_3CN)_4PF_6$	TMG	CH_3CN	**L1**	43%
11	$Cu(CH_3CN)_4PF_6$	TMG	CH_3CN	**L7**	45%
12	$Cu(CH_3CN)_4PF_6$	TMG	CH_3CN	**L8**	35%
13	$Cu(CH_3CN)_4PF_6$	TMG	CH_3CN	**L9**	40%
14	$Cu(CH_3CN)_4PF_6$	TMG	DMF	**L2**	20%
15	$Cu(CH_3CN)_4PF_6$	TMG	THF	**L2**	40%
16	$Cu(CH_3CN)_4PF_6$	TMG	Toluene	**L2**	70%
17	**$Cu(CH_3CN)_4PF_6$**	**TMG (3.0 eq)**	**Toluene**	**L2**	**80%**
18	$Cu(CH_3CN)_4PF_6$	TMG (4.0 eq)	Toluene	**L2**	68%

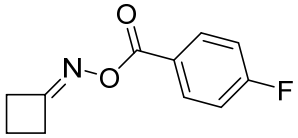
6. Characterization of the substrates and products



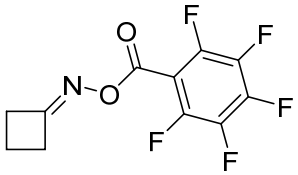
Cyclobutanone O-(4-(trifluoromethyl)benzoyl) oxime (1a): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 3.15 (t, *J* = 8.1 Hz, 4H), 2.13 (p, *J* = 8.1 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 170.1, 162.9, 134.8 (q, *J* = 32.7 Hz), 132.5, 130.1, 125.6 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 272.8 Hz), 32.1, 32.0, 14.4.



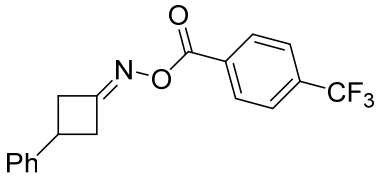
Cyclobutanone O-benzoyl oxime (1aa): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 3.14 (t, *J* = 8.0 Hz, 4H), 2.11 (p, *J* = 8.1 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.4, 164.1, 133.2, 129.6, 129.1, 128.5, 31.9, 31.8, 14.3.



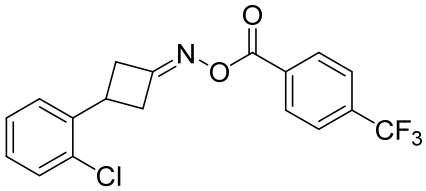
Cyclobutanone O-(4-fluorobenzoyl) oxime (1ab): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.6, 5.9 Hz, 2H), 7.12 (t, *J* = 8.4 Hz, 2H), 3.13 (t, *J* = 8.0 Hz, 4H), 2.12 (p, *J* = 8.0 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 169.5, 165.9 (d, *J* = 254.5 Hz), 163.2, 132.2 (d, *J* = 9.3 Hz), 125.4 (d, *J* = 2.8 Hz), 115.8 (d, *J* = 22.0 Hz), 32.0, 31.9, 14.4.



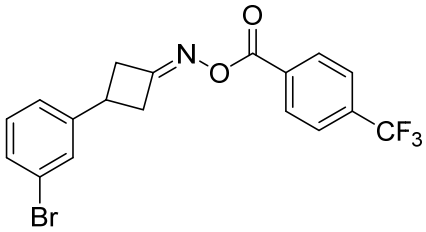
Cyclobutanone O-perfluorobenzoyl oxime (1ac): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (dt, *J* = 21.8, 8.0 Hz, 4H), 2.11 (p, *J* = 8.1 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 171.3, 156.7, 146.7 – 146.1 (m), 144.8 – 144.5 (m), 144.5 – 144.1 (m), 142.9 – 142.2 (m), 138.9 – 138.4 (m), 137.3 – 136.6 (m), 32.2, 31.7, 14.2.



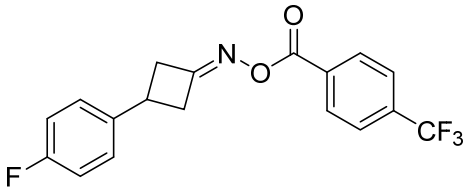
3-Phenylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.26 (m, 3H), 3.84 – 3.48 (m, 3H), 3.41 – 3.18 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 166.9, 162.9, 142.9, 134.9 (q, *J* = 32.8 Hz), 132.4, 130.2, 128.9, 127.1, 126.4, 125.71 (q, *J* = 3.5 Hz), 123.67 (q, *J* = 272.7 Hz), 39.7, 39.6, 32.6.



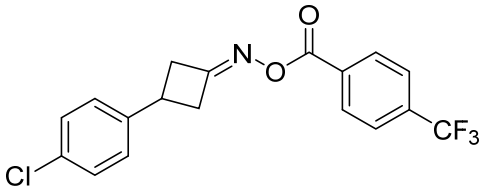
3-(2-Chlorophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.25 – 7.19 (m, 1H), 4.01 (p, *J* = 8.3 Hz, 1H), 3.81 – 3.53 (m, 2H), 3.37 – 3.19 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.5, 162.9, 139.3, 134.9 (q, *J* = 32.9 Hz), 134.1, 132.3, 130.2, 130.0, 128.5, 127.2, 126.7, 125.7 (q, *J* = 3.7 Hz)，123.6 (q, *J* = 272.8 Hz), 38.4, 37.9, 30.9.



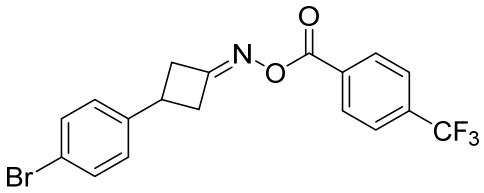
3-(3-Bromophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.9 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 2H), 7.57 – 7.34 (m, 2H), 7.34 – 7.14 (m, 2H), 3.67 (m, 3H), 3.26 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.1, 162.8, 145.2, 134.9 (q, *J* = 32.9 Hz), 132.3, 130.5, 130.3, 130.2, 129.7, 125.7 (q, *J* = 3.6 Hz), 125.1, 123.6 (q, *J* = 272.9 Hz), 123.0, 39.5, 39.4, 32.3.



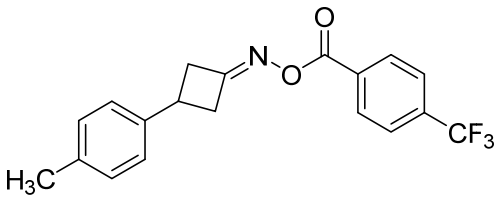
3-(4-Fluorophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.24 (m, 2H), 7.05 (t, *J* = 8.4 Hz, 2H), 3.85 – 3.48 (m, 3H), 3.28 – 3.17 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.5, 163.0, 161.9 (d, *J* = 245.6 Hz), 138.6 (d, *J* = 3.0 Hz), 134.9 (q, *J* = 32.8 Hz), 132.3, 130.2, 128.0 (d, *J* = 8.0 Hz), 125.7 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.7 Hz), 115.7 (d, *J* = 21.3 Hz), 39.9, 39.8, 32.1.



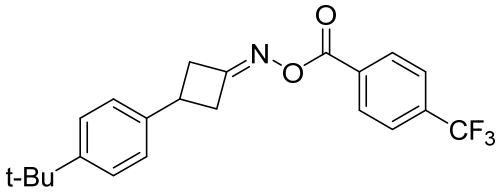
3-(4-Chlorophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1f): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 3.65 (m, 3H), 3.41 – 3.04 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 166.3, 162.8, 141.3, 134.9 (q, *J* = 32.7 Hz), 133.0, 132.3, 130.6, 130.2, 129.1, 127.9, 125.7 (q, *J* = 3.4 Hz), 123.6 (q, *J* = 272.9 Hz), 39.7, 39.6, 32.1.



3-(4-Bromophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 3.62 (m, 3H), 3.21 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.3, 162.9, 141.9, 134.9 (q, *J* = 32.9 Hz), 132.3, 132.0, 130.2, 128.2, 125.7 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.7 Hz), 120.9, 39.6, 39.5, 32.2.

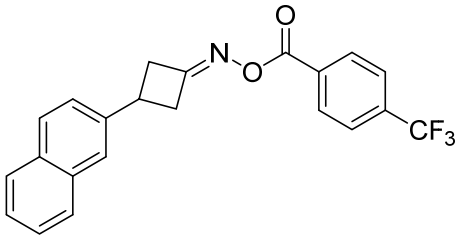


3-(P-tolyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.18 (m, 4H), 3.83 – 3.44 (m, 3H), 3.34 – 3.14 (m, 2H), 2.35 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.1, 162.9, 139.9, 136.7, 134.8 (q, *J* = 32.8 Hz), 132.4, 130.1, 129.5, 126.3, 125.6 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.8 Hz), 39.7, 39.6, 32.3, 21.1.

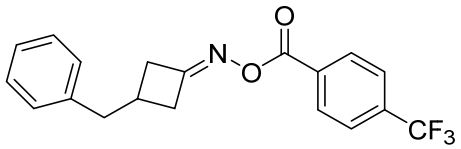


3-(4-(Tert-butyl)phenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1i): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 2H), 3.65 (m, 3H), 3.34 – 3.21 (m, 2H), 1.34 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 167.1, 162.9, 150.1, 139.9, 134.8 (q, *J* =

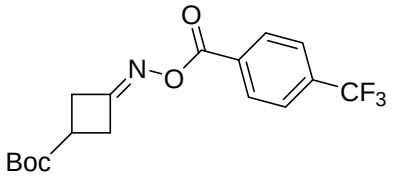
32.7 Hz), 132.4, 130.1, 126.1, 125.8, 125.6 (q, *J* = 3.2 Hz), 123.6 (q, *J* = 272.7 Hz), 39.7, 39.6, 34.6, 32.2, 31.4



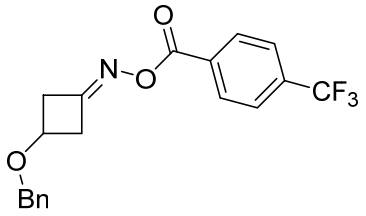
3-(Naphthalen-2-yl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1j): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.90 – 7.79 (m, 3H), 7.75 – 7.68 (m, 3H), 7.57 – 7.44 (m, 2H), 7.41 (d, *J* = 8.4 Hz, 1H), 4.04 – 3.80 (m, 1H), 3.77 – 3.57 (m, 2H), 3.44 – 3.19 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 166.8, 162.8, 140.1, 134.7 (q, *J* = 32.7 Hz), 133.4, 132.4, 132.3, 130.1, 128.8, 127.7, 127.6, 126.5, 126.0, 125.6 (q, *J* = 3.3 Hz), 124.8, 124.5, 123.6 (q, *J* = 272.8 Hz), 39.4, 32.7.



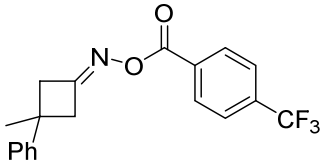
3-Benzylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1k): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.18 (d, *J* = 7.3 Hz, 2H), 3.29 – 3.19 (m, 2H), 2.93 – 2.78 (m, 5H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.7, 162.9, 139.3, 134.8 (q, *J* = 32.7 Hz), 132.5, 130.1, 128.8, 128.7, 126.7, 125.6 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.6 Hz), 41.8, 37.4, 37.3, 29.5.



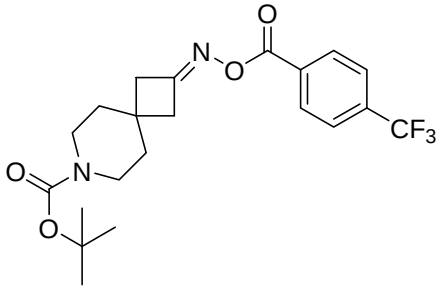
Tert-butyl-3-(((4-(trifluoromethyl)benzoyl)oxy)imino)cyclobutane-1-carboxylate (1l): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 3.35 (d, *J* = 7.8 Hz, 4H), 3.26 – 3.07 (m, 1H), 1.48 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 172.4, 165.7, 162.7, 134.9 (q, *J* = 32.8 Hz), 130.1, 125.7 (q, *J* = 3.3 Hz), 123.63 (q, *J* = 272.7 Hz), 81.8, 35.8, 35.6, 32.1, 28.1.



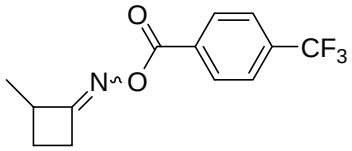
3-(Benzyloxy)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1m): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.9 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 2H), 7.37 (m, 5H), 4.64 – 4.45 (m, 2H), 4.36 – 4.21 (m, 1H), 3.47 – 3.33 (m, 2H), 3.21 – 3.07 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 164.0, 162.8, 137.2, 134.9 (q, *J* = 32.9 Hz), 132.3, 130.1, 128.7, 128.2, 128.0, 125.6 (q, *J* = 3.4 Hz), 123.6 (q, *J* = 272.8 Hz), 71.3, 66.6, 40.5, 40.4.



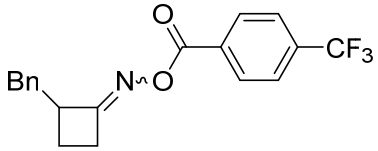
3-Methyl-3-phenylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1n): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.26 (m, 3H), 3.50 (t, *J* = 15.3 Hz, 2H), 3.34 – 3.20 (m, 2H), 1.62 (s, 3H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 166.1, 162.9, 147.9, 134.9 (q, *J* = 32.7 Hz), 132.4, 130.2, 128.8, 126.6, 125.6 (q, *J* = 3.3 Hz), 125.2, 123.6 (q, *J* = 272.7 Hz), 44.9, 44.8, 38.1, 30.9.



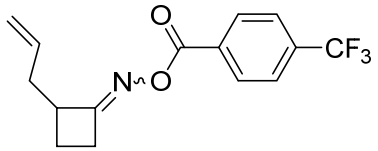
Tert-butyl-2-(((4-(trifluoromethyl)benzoyl)oxy)imino)-7-azaspiro[3.5]nonane-7-carboxylate (1p): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 3.40 (t, *J* = 5.3 Hz, 4H), 2.89 (s, 4H), 1.70 – 1.65 (m, 4H), 1.46 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 166.0, 162.8, 154.9, 134.9 (q, *J* = 32.8 Hz), 132.3, 130.1, 125.7 (q, *J* = 3.4 Hz), 123.65 (q, *J* = 273.2 Hz), 79.9, 42.04, 42.02, 36.4, 33.5, 28.5.



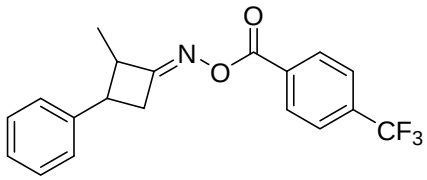
2-Methylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1q): Z/E mixture; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.15 (d, *J* = 7.9 Hz, 2H), 7.76 – 7.65 (m, 2H), 3.62 – 3.41 (m, 1H), 3.23 – 2.94 (m, 2H), 2.35 – 2.23 (m, 1H), 1.76 – 1.67 (m, 1H), 1.44 (d, *J* = 7.2 Hz, 1.4H)/1.38 (d, *J* = 7.1 Hz, 1.6H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 173.9/173.3, 163.1/163.0, 134.8 (q, *J* = 32.8 Hz)/134.7 (q, *J* = 32.7 Hz), 132.6/132.5, 130.1/130.0, 125.7/125.6 (q, *J* = 4.1 Hz), 123.7 (q, *J* = 272.7 Hz)/123.6 (q, *J* = 273.0 Hz), 41.2/40.7, 29.3/28.6, 22.9/22.0, 17.6/17.5.



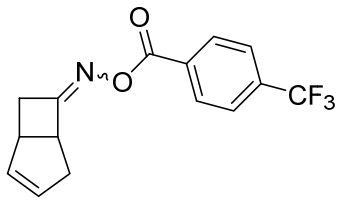
2-Benzylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1r): Z/E mixture; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.0 Hz, 1.3H)/8.01 (d, *J* = 8.0 Hz, 0.7H), 7.73 (d, *J* = 8.1 Hz, 1.3H)/7.69 (d, *J* = 8.1 Hz, 0.7H), 7.45 – 7.27 (m, 2H), 7.25 – 7.11 (m, 3H), 3.82 – 3.66 (m, 1H), 3.33 – 3.20 (m, 1H), 3.08 – 2.92 (m, 3H), 2.26 – 2.10 (m, 1H), 1.94 – 1.78 (m, 1H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 172.5/171.3, 163.0/163.0, 138.6/138.3, 134.9 (q, *J* = 32.6 Hz)/134.8 (q, *J* = 32.5 Hz), 132.5/132.3, 130.1/130.0, 129.0/128.9, 128.8/128.7, 126.8/126.6, 125.8 – 125.6 (m), 123.7 (q, *J* = 272.7 Hz)/123.6 (q, *J* = 271.2 Hz), 47.3/46.6, 38.0/37.6, 29.2/29.1, 20.7/19.9.



2-Allylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1s): Z/E mixture; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.13 (d, *J* = 8.0 Hz, 2H), 7.76 – 7.67 (m, 2H), 5.92 – 5.62 (m, 1H), 5.19 – 4.99 (m, 2H), 3.67 – 3.40 (m, 1H), 3.11 – 2.93 (m, 2H), 2.68 – 2.55 (m, 1H), 2.54 – 2.38 (m, 1H), 2.28 – 2.11 (m, 1H), 1.90 – 1.75 (m, 1H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 172.6/171.5, 162.9/162.8, 134.8 (q, *J* = 32.8 Hz)/134.7 (q, *J* = 32.7 Hz), 134.4/134.1, 132.5/132.4, 130.0, 125.6 (q, *J* = 3.4 Hz)/125.5 (q, *J* = 3.6 Hz), 123.7 (q, *J* = 272.8 Hz)/123.6 (q, *J* = 272.7 Hz), 117.7/117.2, 45.3/44.7, 36.1/35.4, 29.2/28.9, 20.3/19.2.

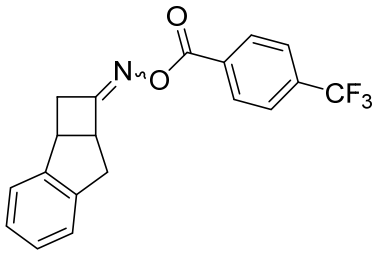


2-Methyl-3-phenylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime （1t）： **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 7.0 Hz, 3H), 3.82 – 3.40 (m, 2H), 8.23 – 8.14 (m, 2H), 1.51 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 170.8, 163.0, 142.2, 134.7 (q, *J* = 32.6 Hz), 132.5, 130.1, 128.9, 127.2, 126.5, 125.6 (q, *J* = 3.5 Hz), 123.6 (q, *J* = 272.8 Hz), 49.5, 41.6, 36.8, 16.4.

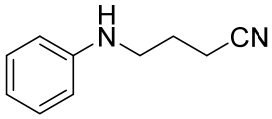


Bicyclo[3.2.0]hept-2-en-6-one O-(4-(trifluoromethyl)benzoyl) oxime (1u): Z/E mixture; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.2 Hz, 0.8H)/8.13 (d, *J* = 8.2 Hz,

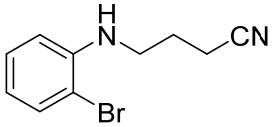
1.2H), 7.73 (d, *J* = 8.2 Hz, 0.8H)/7.70 (d, *J* = 8.2 Hz, 1.2H), 5.90 – 5.77 (m, 2H), 4.00 – 3.89 (m, 1H), 3.51 – 3.42 (m, 1H), 3.36 – 3.23 (m, 1H), 2.94 – 2.66 (m, 3H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 173.9/172.6, 162.9/162.7, 134.9 (q, *J* = 32.7 Hz)/ 134.8 (q, *J* = 32.7 Hz), 132.7/132.2, 132.5/132.4, 132.1/131.7, 130.1/130.0, 125.7 (q, *J* = 3.5 Hz)/125.6 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 272.9 Hz), 47.1/47.0, 40.9/40.1, 39.1/39.0, 37.8/35.9.



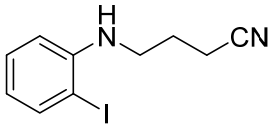
2,2a,7,7a-Tetrahydro-1H-cyclobuta[a]inden-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1v): Z/E mixture; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 (d, *J* = 8.0 Hz, 0.6H)/8.09 (d, *J* = 8.1 Hz, 1.4H), 7.77 (d, *J* = 8.1 Hz, 0.6H)/7.68 (d, *J* = 8.1 Hz, 1.4H), 7.32 – 7.20 (m, 4H), 4.24 – 4.12 (m, 1H), 4.09 – 3.98 (m, 1H), 3.69 – 3.27 (m, 3H), 3.12 – 2.88 (m, 1H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 172.7/171.7, 162.7/162.6, 144.0, 143.1, 142.4, 134.9 (q, *J* = 32.8 Hz)/134.7 (q, *J* = 32.7 Hz), 132.3, 130.5, 130.1, 130.0, 127.7, 127.6, 127.5, 125.7 (q, *J* = 3.1 Hz)/125.5 (q, *J* = 3.3 Hz), 125.4, 125.1, 125.0, 124.9, 123.7 (q, *J* = 272.8 Hz)/123.6 (q, *J* = 272.8 Hz), 48.0, 40.5, 40.2, 39.9, 39.7, 37.0, 35.3.



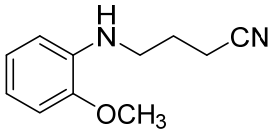
4-(Phenylamino)butanenitrile (3a): oil; 98% yield (31.4 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.20 (t, *J* = 7.5 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 2H), 3.72 (brs, 1H), 3.32 (t, *J* = 6.4 Hz, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.97 (p, *J* = 6.5 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.6, 129.5, 119.5, 117.9, 112.9, 42.3, 25.3, 14.9； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3395, 2931, 2246, 1601, 748; **HRMS (ESI)** calcd $C_{10}H_{13}N_2$ $[M + H]^+$: 161.1073, found: 161.1071.



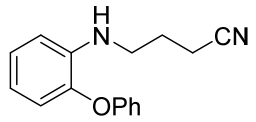
4-((2-Bromophenyl)amino)butanenitrile (3b): oil; 80% yield (38 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 (d, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 1H), 4.34 (brs, 1H), 3.38 (m, 2H), 2.49 (t, *J* = 7.0 Hz, 2H), 2.01 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 144.3, 132.7, 128.7, 119.3, 118.5, 111.3, 110.1, 42.2, 25.2, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3397, 2922, 2246, 1594, 740; **HRMS (ESI)** calcd $C_{10}H_{12}{}^{79}BrN_2$ $[M + H]^+$: 239.0178, found: 239.0182.



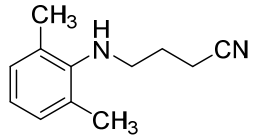
4-((2-Iodophenyl)amino)butanenitrile (3c): oil; 78% (44.3 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.48 (t, *J* = 7.5 Hz, 1H), 4.18 (brs, 1H), 3.40 – 3.34 (m, 2H), 2.49 (t, *J* = 7.0 Hz, 2H), 2.01 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 146.5, 139.3, 129.6, 119.4, 119.3, 110.7, 85.9, 42.6, 25.0, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3384, 2929, 2245, 1587, 740; **HRMS (ESI)** calcd $C_{10}H_{12}IN_2$ $[M + H]^+$: 287.0040, found: 287.0040.



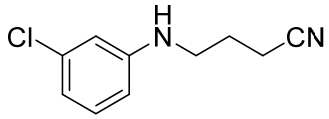
4-((2-Methoxyphenyl)amino)butanenitrile (3d): oil; 96% yield (36 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.88 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 4.28 (brs, 1H), 3.85 (s, 3H), 3.33 (t, *J* = 6.5 Hz, 2H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.00 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 146.9, 137.5, 121.4, 119.5, 117.0, 109.8, 109.6, 55.5, 42.1, 25.4, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3412, 2937, 2245, 1601, 735; **HRMS (ESI)** calcd $C_{11}H_{15}N_2O$ $[M + H]^+$: 191.1179, found: 191.1176.



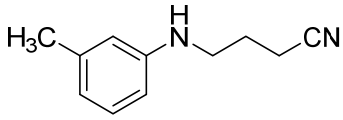
4-((2-Phenoxyphenyl)amino)butanenitrile (3e): oil; 97% yield (49.1 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (t, *J* = 7.5 Hz, 2H), 7.07 (dd, *J* = 12.8, 6.7 Hz, 2H), 6.97 (d, *J* = 7.8 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 4.22 (brs, 1H), 3.34 (t, *J* = 6.4 Hz, 2H), 2.39 (t, *J* = 6.9 Hz, 2H), 2.12 – 1.85 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 157.4, 143.2, 139.8, 129.9, 125.1, 123.0, 119.5, 119.3, 117.5, 117.4, 111.4, 41.9, 25.3, 14.8; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3358, 2948, 2249, 1608, 742; **HRMS (ESI)** calcd $C_{16}H_{17}N_2O$ $[M + H]^+$: 253.1335, found: 253.1333.



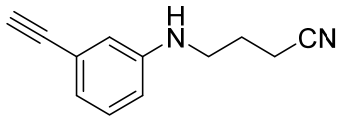
4-((2,6-Dimethylphenyl)amino)butanenitrile (3f): oil; 95% yield (35.6 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.01 (d, *J* = 7.2 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 3.10 (t, *J* = 6.6 Hz, 2H), 2.53 (t, *J* = 7.0 Hz, 2H), 2.29 (s, 6H), 1.96 – 1.90 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 145.2, 130.0, 129.0, 122.7, 119.5, 46.7, 26.9, 18.5, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 2928, 2245, 1594, 1506, 766; **HRMS (ESI)** calcd $C_{12}H_{17}N_2$ $[M + H]^+$: 189.1386, found: 189.1388.



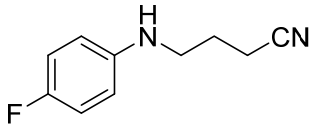
4-((3-Chlorophenyl)amino)butanenitrile (3g): oil; 85% yield (33 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.09 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 7.4 Hz, 1H), 6.58 (s, 1H), 6.48 (d, *J* = 7.7 Hz, 1H), 3.82 (brs, 1H), 3.30 (t, *J* = 5.8 Hz, 2H), 2.47 (t, *J* = 6.4 Hz, 2H), 2.00 – 1.92 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 148.7, 135.2, 130.5, 119.3, 117.8, 112.5, 111.3, 42.2, 25.1, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3391, 2933, 2247, 1597, 763; **HRMS (ESI)** calcd $C_{10}H_{12}{}^{35}ClN_2$ $[M + H]^+$: 195.0684, found: 195.0688.



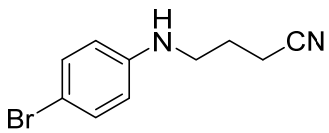
4-(m-Tolylamino)butanenitrile (3h): oil; 90% yield (32 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.08 (t, *J* = 7.1 Hz, 1H), 6.57 (d, *J* = 6.8 Hz, 1H), 6.51 – 6.37 (m, 2H), 3.66 (brs, 1H), 3.31 (t, *J* = 5.7 Hz, 2H), 2.47 (t, *J* = 6.5 Hz, 2H), 2.29 (s, 3H), 2.04 – 1.78 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.6, 139.3, 129.3, 119.5, 118.9, 113.7, 110.1, 42.4, 25.4, 21.7, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3395, 2924, 2246, 1605, 692; **HRMS (ESI)** calcd $C_{11}H_{15}N_2$ $[M + H]^+$: 175.1230, found: 175.1231.



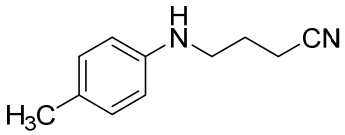
4-((3-Ethynylphenyl)amino)butanenitrile (3i): oil; 65% yield (24 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.12 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 6.71 (s, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 3.81 (s, 1H), 3.26 (t, *J* = 6.4 Hz, 2H), 3.04 (s, 1H), 2.44 (t, *J* = 7.0 Hz, 2H), 1.93 (p, *J* = 6.7 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.5, 129.4, 122.8, 121.7, 119.4, 115.8, 113.8, 84.1, 76.7, 42.2, 25.1, 14.8; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3394, 3286, 2933, 2105, 1598, 687; **HRMS (ESI)** calcd $C_{12}H_{13}N_2$ $[M + H]^+$: 185.1073, found: 185.1071.



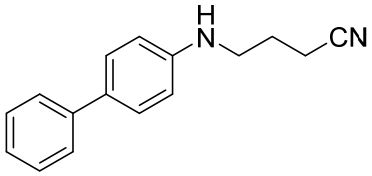
4-((4-Fluorophenyl)amino)butanenitrile (3j): oil; 85% yield (30.2 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.90 (t, *J* = 8.6 Hz, 2H), 6.67 – 6.47 (m, 2H), 3.58 (brs, 1H), 3.27 (t, *J* = 6.6 Hz, 2H), 2.48 (t, *J* = 7.0 Hz, 2H), 1.96 (p, *J* = 6.7 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 156.1 (d, *J* = 235.5 Hz), 143.9, 119.4, 115.9 (d, *J* = 22.4 Hz), 113.8 (d, *J* = 7.4 Hz), 43.1, 25.3, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3385, 2931, 2247, 1508, 819; HRMS (ESI) calcd $C_{10}H_{12}FN_2$ $[M + H]^+$: 179.0979, found: 179.0976.



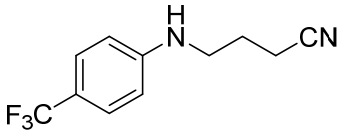
4-((4-Bromophenyl)amino)butanenitrile (3k): oil; 82% yield (39.4 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.26 (d, *J* = 8.5 Hz, 1H), 6.49 (d, *J* = 8.5 Hz, 2H), 3.75 (s, 1H), 3.28 (t, *J* = 6.3 Hz, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.95 (p, *J* = 6.7 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 146.6, 132.1, 119.3, 114.5, 109.6, 42.4, 25.1, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3361, 2939, 2245, 1589, 819; **HRMS (ESI)** calcd $C_{10}H_{12}{}^{79}BrN_2$ $[M + H]^+$: 239.0178, found: 239.0176.



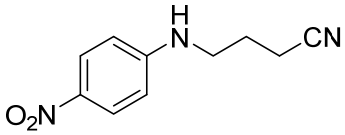
4-(p-Tolylamino)butanenitrile (3l): oil; 71% yield (25 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.01 (d, *J* = 8.0 Hz, 2H), 6.55 (d, *J* = 8.1 Hz, 2H), 3.58 (brs, 1H), 3.29 (t, *J* = 6.5 Hz, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 2.25 (s, 3H), 1.96 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 145.3, 130.0, 127.3, 119.5, 113.1, 42.7, 25.4, 20.5, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3358, 2918, 2236, 1612, 807; **HRMS (ESI)** calcd $C_{11}H_{15}N_2$ $[M + H]^+$: 175.1230, found: 175.1228.



4-([1,1'-Biphenyl]-4-ylamino)butanenitrile (3m): oil; 62% yield (29.1 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (d, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 2H), 7.28 – 7.23 (m, 1H), 6.68 (d, *J* = 7.8 Hz, 2H), 3.81 (brs, 1H), 3.35 (t, *J* = 6.2 Hz, 2H), 2.48 (t, *J* = 6.3 Hz, 2H), 2.14 – 1.78 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.0, 141.1, 131.0, 128.8, 128.2, 126.4, 126.3, 119.5, 113.2, 42.4, 25.3, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3378, 2922, 2249, 1608, 764; **HRMS (ESI)** calcd $C_{16}H_{17}N_2$ $[M + H]^+$:237.1386, found: 237.1388.

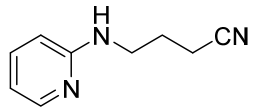


4-((4-(Trifluoromethyl)phenyl)amino)butanenitrile (3n): oil; 80% yield (35.4 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 2H), 4.10 (brs, 1H), 3.36 (t, *J* = 6.0 Hz, 2H), 2.48 (t, *J* = 6.7 Hz, 2H), 2.13 – 1.88 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 150.1, 126.8 (q, *J* = 3.7 Hz), 124.9 (q, *J* = 270.3 Hz), 119.5 (q, *J* = 32.6 Hz), 119.2, 112.0, 42.0, 25.0, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3385, 2967, 2249, 1615, 825; **HRMS (ESI)** calcd $C_{11}H_{12}F_3N_2$ $[M + H]^+$: 229.0947, found: 229.0950.

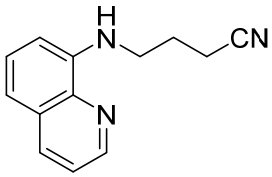


4-((4-Nitrophenyl)amino)butanenitrile (3o): oil; 64% yield (26 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.09 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 8.9 Hz, 2H), 4.69 (s, 1H), 3.47

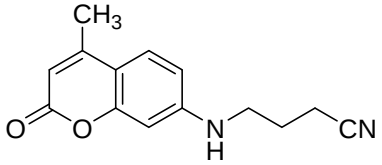
– 3.40 (m, 2H), 2.50 (t, *J* = 6.8 Hz, 2H), 2.26 – 1.90 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 152.9, 138.6, 126.6, 119.0, 111.3, 41.9, 24.9, 15.0; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3349, 2923, 2252, 1595, 827; **HRMS (ESI)** calcd $C_{10}H_{11}N_3O_2Na$ $[M + Na]^+$: 228.0743, found: 228.0742.



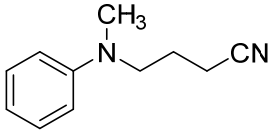
4-(Pyridin-2-ylamino)butanenitrile (3p): oil; 49% yield (15.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.07 (s, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 6.70 – 6.52 (m, 1H), 6.41 (d, *J* = 8.3 Hz, 1H), 4.59 (s, 1H), 3.48 (q, *J* = 6.2 Hz, 2H), 2.46 (t, *J* = 7.1 Hz, 2H), 2.00 (p, *J* = 6.7 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 158.3, 148.1, 137.7, 119.6, 113.5, 107.5, 40.6, 25.6, 14.9; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3392, 2930, 2246, 1600, 771; **HRMS (ESI)** calcd $C_9H_{12}N_3$ $[M + H]^+$: 162.1026, found: 162.1028.



4-(Quinolin-8-ylamino)butanenitrile (3q): oil; 83% yield (35 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.98 – 8.53 (m, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 6.21 (brs, 1H), 3.52 (t, *J* = 7.1 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.11 (p, *J* = 6.7 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.1, 144.2, 138.2, 136.2, 128.8, 127.8, 121.6, 119.5, 114.6, 104.8, 41.9, 25.3, 15.0; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3391, 2929, 2245, 1574, 790; **HRMS (ESI)** calcd $C_{13}H_{14}N_3$ $[M + H]^+$: 212.1182, found: 212.1183.

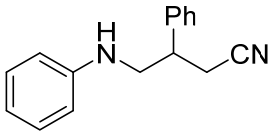


4-((4-Methyl-2-oxo-2H-chromen-7-yl)amino)butanenitrile (3r): oil; 55% yield (26.6 mg); **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.38 (d, *J* = 8.6 Hz, 1H), 6.54 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.50 (d, *J* = 2.1 Hz, 1H), 6.00 (s, 1H), 4.46 (s, 1H), 3.39 (dd, *J* = 10.5, 6.6 Hz, 2H), 2.50 (t, *J* = 7.0 Hz, 2H), 2.35 (s, 3H), 2.01 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 162.0, 156.0, 153.1, 151.0, 125.9, 119.2, 111.2, 110.3, 109.9, 98.6, 42.0, 24.9, 18.7, 15.0; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3336, 2920, 1617, 1505, 771; **HRMS (ESI)** calcd $C_{14}H_{14}N_2O_2Na$ $[M + Na]^+$: 265.0947, found: 265.0946.

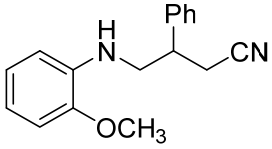


4-(Methyl(phenyl)amino)butanenitrile (3s): oil; 73% yield (25.2 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24 (t, *J* = 7.8 Hz, 2H), 6.85 – 6.62 (m, 3H), 3.45 (t, *J* = 6.9 Hz, 2H), 2.94 (s, 3H), 2.38 (t, *J* = 7.0 Hz, 2H), 1.94 (p, *J* = 6.9 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 149.1, 129.4, 119.5, 117.1, 112.7, 51.3, 38.9, 23.2, 14.9; **FT-IR** (thin

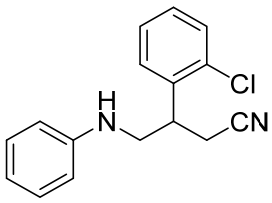
film, KBr): ν (cm^{-1}) 2935, 2244, 1598, 1505, 748; **HRMS (ESI)** calcd $C_{11}H_{15}N_2$ $[M + H]^+$: 175.1230, found: 175.1227.



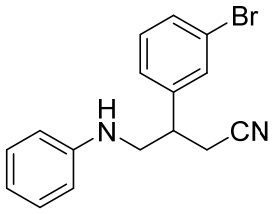
3-Phenyl-4-(phenylamino)butanenitrile (4a): oil; 80% yield (37.2 mg); **^{1}H NMR (400 MHz,$CDCl_3$)** δ 7.40 (t, *J* = 7.2 Hz, 2H), 7.37 – 7.31 (m, 1H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 3.68 (brs, 1H), 3.60 (dd, *J* = 13.1, 6.9 Hz, 1H), 3.45 (dd, *J* = 12.8, 7.4 Hz, 1H), 3.39 – 3.27 (m, 1H), 2.85 – 2.66 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.3, 139.4, 129.5, 129.3, 128.1, 127.4, 118.4, 118.3, 113.2, 48.1, 41.5, 22.3; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3400, 2920, 2246, 1601, 749; **HRMS (ESI)** calcd $C_{16}H_{17}N_2$ $[M + H]^+$: 237.1386 , found: 237.1383.



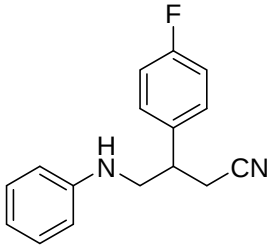
4-((2-Methoxyphenyl)amino)-3-phenylbutanenitrile (4b): oil; 75% yield (40 mg); **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.41 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.4 Hz, 2H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 4.37 (brs, 1H), 3.81 (s, 3H), 3.58 (dd, *J* = 13.3, 7.8 Hz, 1H), 3.48 (dd, *J* = 13.3, 6.5 Hz, 1H), 3.39 – 3.29 (m, 1H), 2.82 (dd, *J* = 16.8, 5.9 Hz, 1H), 2.77 – 2.70 (m, 1H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.0, 139.6, 137.3, 129.1, 127.9, 127.4, 121.4, 118.5, 117.3, 110.1, 109.9, 55.5, 48.0, 41.5, 22.1. **FT-IR** (thin film, KBr): ν (cm^{-1}) 3419, 2934, 2245, 1511, 734; **HRMS (ESI)** calcd $C_{17}H_{19}N_2O$ $[M + H]^+$: 267.1492 , found: 267.1493.



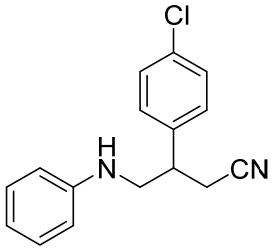
3-(2-Chlorophenyl)-4-(phenylamino)butanenitrile (4c): oil; 65% yield (35.2 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 (d, *J* = 7.6 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.31 – 7.26 (m, 1H), 7.24 – 7.15 (m, 3H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 2H), 3.69 (brs, 1H), 3.57 (dd, *J* = 13.2, 7.1 Hz, 1H), 3.44 (dd, *J* = 13.2, 7.1 Hz, 1H), 3.35 – 3.23 (m, 1H), 2.81 – 2.67 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.1, 141.8, 131.4, 130.9, 130.6, 129.6, 126.2, 123.4, 118.5, 118.0, 113.2, 48.1, 41.3, 22.1; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3399, 2922, 2248, 1601, 749; **HRMS (ESI)** calcd $C_{16}H_{16}{}^{35}ClN_2$ $[M + H]^+$: 271.0997, found: 271.0999.



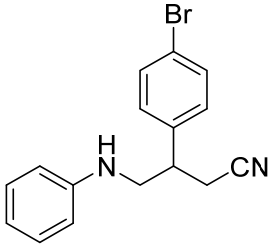
3-(3-Bromophenyl)-4-(phenylamino)butanenitrile (4d): oil; 60% yield (38.1mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (d, *J* = 7.6 Hz, 1H), 7.34 – 7.19 (m, 3H), 7.15 (t, *J* = 7.5 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 2H), 4.01 – 3.71 (m, 1H), 3.69 (brs, 1H), 3.51 (d, *J* = 7.0 Hz, 2H), 2.95 – 2.61 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.3, 136.7, 134.3, 130.4, 129.5, 129.2, 127.8, 127.7, 118.3, 118.1, 113.1, 46.7, 37.5, 21.0; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3401, 2925, 2247, 1602, 729; **HRMS (ESI)** calcd $C_{16}H_{16}{}^{79}BrN_2$ $[M + H]^+$: 315.0491, found: 315.0495.



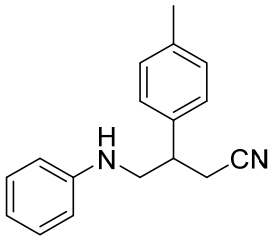
3-(4-Fluorophenyl)-4-(phenylamino)butanenitrile (4e): oil; 56% yield (28.5 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.25 – 7.16 (m, 4H), 7.09 (t, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 2H), 3.71 (brs, 1H), 3.57 (dd, *J* = 13.1, 7.0 Hz, 1H), 3.42 (dd, *J* = 13.0, 7.3 Hz, 1H), 3.37 – 3.25 (m, 1H), 2.83 – 2.64 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 162.4 (d, *J* = 247.0 Hz), 147.2, 135.2 (d, *J* = 3.1 Hz), 129.6, 129.1 (d, *J* = 8.1 Hz), 118.4, 118.2, 116.2 (d, *J* = 21.5 Hz), 113.2, 48.2, 40.9, 22.5; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3399, 2923, 2247, 1602, 750; **HRMS (ESI)** calcd $C_{16}H_{16}FN_2$ $[M + H]^+$: 255.1292, found: 255.1293.



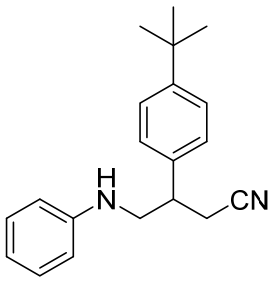
3-(4-Chlorophenyl)-4-(phenylamino)butanenitrile (4f): oil; 60% yield (32.5 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.16 (m, 4H), 6.77 (t, *J* = 7.1 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 2H), 3.68 (brs, 1H), 3.56 (dd, *J* = 13.0, 6.9 Hz, 1H), 3.42 (dd, *J* = 13.0, 7.1 Hz, 1H), 3.36 – 3.27 (m, 1H), 2.83 – 2.64 (m, 2H); **^{13}C NMR (150MHz, $CDCl_3$)** δ 147.1, 137.9, 134.0 129.6, 129.5, 128.8, 118.4, 118.1, 113.2, 48.1, 40.9, 22.2； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3399, 2923, 2246, 1601, 749; **HRMS (ESI)** calcd $C_{16}H_{16}{}^{35}ClN_2$ $[M + H]^+$: 271.0997, found: 271.0998.



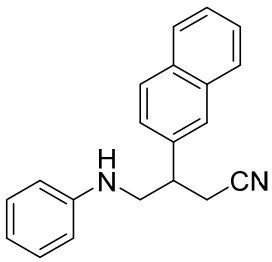
3-(4-Bromophenyl)-4-(phenylamino)butanenitrile (4g): oil; 62% yield (39.1 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 2H), 3.66 (s, 1H), 3.57 (dd, *J* = 13.2, 7.0 Hz, 1H), 3.42 (dd, *J* = 13.0, 7.3 Hz, 1H), 3.35 – 3.24 (m, 1H), 2.85 – 2.64 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.1, 138.5, 132.5, 129.6, 129.2, 122.1, 118.5, 118.1, 113.2, 48.1, 41.1, 22.2; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3395, 2920, 2246, 1601, 749; **HRMS (ESI)** calcd $C_{16}H_{16}{}^{79}BrN_2$ $[M + H]^+$: 315.0491, found: 315.0495.



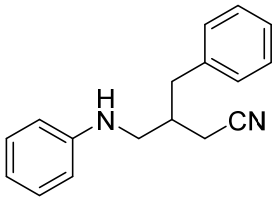
4-(Phenylamino)-3-(p-tolyl)butanenitrile (4h): oil; 82% yield (41.2 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.22 – 7.12 (m, 6H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 2H), 3.65 (brs, 1H), 3.57 (dd, *J* = 13.0, 6.8 Hz, 1H), 3.42 (dd, *J* = 12.6, 7.6 Hz, 1H), 3.34 – 3.22 (m, 1H), 2.83 – 2.63 (m, 2H), 2.36 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.4, 137.9, 136.4, 130.0, 129.5, 127.3, 118.5, 118.3, 113.3, 48.2, 41.1, 22.5, 21.2; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3398, 2923, 2248, 1602, 729; **HRMS (ESI)** calcd $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543, found: 251.1545.



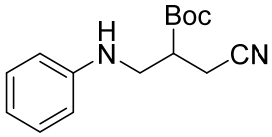
3-(4-(Tert-butyl)phenyl)-4-(phenylamino)butanenitrile (4i): oil; 80% yield (46.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (d, *J* = 7.9 Hz, 2H), 7.23 – 7.12 (m, 4H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 2H), 3.69 (brs, 1H), 3.58 (dd, *J* = 13.0, 6.9 Hz, 1H), 3.44 (dd, *J* = 12.9, 7.3 Hz, 1H), 3.35 – 3.24 (m, 1H), 2.89 – 2.64 (m, 2H), 1.33 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 151.1, 147.4, 136.3, 129.5, 127.1, 126.2, 118.6, 118.2, 113.3, 48.2, 41.0, 34.7, 31.4, 22.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3401, 2961, 2247, 1602, 748; **HRMS (ESI)** calcd $C_{20}H_{25}N_2$ $[M + H]^+$: 293.2012, found: 293.2014.



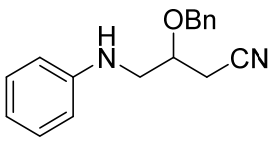
3-(Naphthalen-2-yl)-4-(phenylamino)butanenitrile (4j): oil; 42% yield (24 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 – 7.82 (m, 3H), 7.73 (s, 1H), 7.57 – 7.46 (m, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 2H), 3.77 – 3.63 (m, 2H), 3.60 – 3.43 (m, 2H), 3.00 – 2.69 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.3, 136.8, 133.6, 133.1, 129.6, 129.3, 128.0, 127.9, 126.8, 126.7, 126.5, 124.9, 118.4, 113.3, 48.1, 41.7, 22.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3396, 2921, 2245, 1601, 746; **HRMS (ESI)** calcd $C_{20}H_{19}N_2$ $[M + H]^+$: 287.1543, found: 287.1544.



3-Benzyl-4-(phenylamino)butanenitrile (4k): oil; 86% yield (42.9 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (t, *J* = 7.3 Hz, 2H), 7.26 (d, *J* = 7.0 Hz, 1H), 7.22 – 7.14 (m, 4H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.56 (d, *J* = 7.9 Hz, 2H), 3.29 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.19 (dd, *J* = 13.7, 7.9 Hz, 1H), 2.87 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.71 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.46 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.39 – 2.23 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.6, 138.3, 129.5, 129.1, 128.9, 126.9, 118.4, 118.0, 112.9, 46.8, 37.9, 37.4, 19.6; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3402, 2925, 2246, 1601, 747; **HRMS (ESI)** calcd $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543, found: 251.1540.

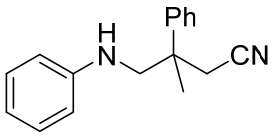


Tert-butyl 3-cyano-2-((phenylamino)methyl)propanoate (4l): oil; 40% yield (20.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.20 (t, *J* = 7.6 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 3.97 (brs, 1H), 3.64 – 3.51 (m, 1H), 3.50 – 3.37 (m, 1H), 2.97 (p, *J* = 6.3 Hz, 1H), 2.76 – 2.59 (m, 2H), 1.49 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 170.6, 147.1, 129.6, 118.5, 117.9, 113.2, 83.0, 44.7, 42.1, 28.1, 17.7; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3403, 2922, 1603, 1508, 748; **HRMS (ESI)** calcd $C_{15}H_{21}N_2O_2$ $[M + H]^+$: 261.1598 , found: 261.1597.

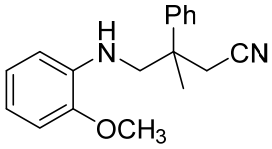


3-(Benzyloxy)-4-(phenylamino)butanenitrile (4m): oil; 55% yield (29.5 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 – 7.31 (m, 5H), 7.18 (t, *J* = 7.5 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 2H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.03 – 3.84 (m, 2H), 3.40 (dd, *J* = 13.3, 4.0 Hz, 1H), 3.31 (dd, *J* = 13.3, 5.1 Hz,

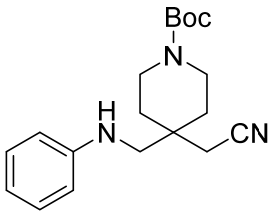
1H), 2.68 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.5, 137.2, 129.5, 128.8, 128.4, 128.2, 118.4, 117.4, 113.3, 73.1, 72.4, 46.4, 21.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3399, 2870, 2249, 1602, 746; **HRMS (ESI)** calcd $C_{17}H_{19}N_2O$ $[M + H]^+$: 267.1492 , found: 267.1495.



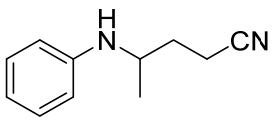
3-Methyl-3-phenyl-4-(phenylamino)butanenitrile (4n): oil; 87% yield (43.5 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.30 (m, 5H), 7.17 (t, *J* = 7.5 Hz, 2H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 7.9 Hz, 2H), 3.51 (d, *J* = 12.3 Hz, 1H), 3.42 (d, *J* = 12.5 Hz, 1H), 3.31 (s, 1H), 2.85 (s, 2H), 1.63 (s, 3H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 148.0, 142.2, 129.4, 129.2, 127.6, 126.0, 118.2, 118.1, 113.3, 53.7, 41.6, 28.5, 24.5; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3395, 2971, 2244, 1601, 735; **HRMS (ESI)** calcd $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543 , found: 251.1546.



4-((2-Methoxyphenyl)amino)-3-methyl-3-phenylbutanenitrile (4o): oil; 77% yield (43 mg); **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.45 – 7.37 (m, 4H), 7.35 – 7.30 (m, 1H), 6.86 (t, *J* = 8.2 Hz, 1H), 6.74 (d, *J* = 7.2 Hz, 1H), 6.68 (t, *J* = 7.7 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 4.06 (s, 1H), 3.74 (s, 3H), 3.48 (d, *J* = 12.7 Hz, 1H), 3.41 (d, *J* = 12.7 Hz, 1H), 2.87 (d, *J* = 4.2 Hz, 2H), 1.64 (s, 3H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 147.0, 142.5, 138.0, 129.1, 127.5, 126.0, 121.4, 118.2, 117.2, 110.4, 109.8, 55.6, 53.6, 41.8, 28.4, 24.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 2968, 1600, 1511, 734; **HRMS (ESI)** calcd $C_{18}H_{21}N_2O$ $[M + H]^+$: 281.1648 , found: 281.1652.

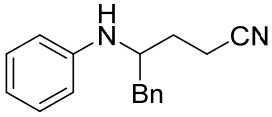


Tert-butyl 4-(cyanomethyl)-4-((phenylamino)methyl)piperidine-1-carboxylate (4p): oil; 82% yield (54 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.19 (t, *J* = 7.3 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 2H), 3.71 – 3.59 (m, 3H), 3.35 – 3.17 (m, 4H), 2.52 (s, 2H), 1.66 – 1.57 (m, 4H), 1.46 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 154.7, 148.2, 129.5, 118.3, 117.8, 113.3, 80.0, 50.6, 36.5, 32.4, 28.5, 23.8; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3377, 2920, 1602, 1500, 744; **HRMS (ESI)** calcd $C_{19}H_{28}N_3O_2$ $[M + H]^+$: 330.2176 , found: 330.2178.

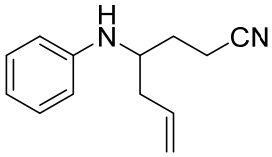


4-(Phenylamino)pentanenitrile (4q): oil; 80% yield (27.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.19 (t, *J* = 7.7 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 2H),

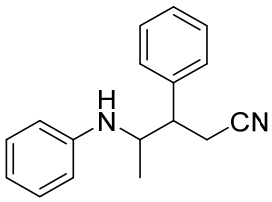
3.85 – 3.56 (m, 1H), 3.31 (brs, 1H), 2.48 (t, *J* = 7.2 Hz, 2H), 2.02 – 1.73 (m, 2H), 1.24 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR (150 MHz, CDCl$_3$)** δ 147.0, 129.5, 119.8, 118.0, 113.6, 47.8, 32.7, 20.8, 14.2； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3382, 2967, 2245, 1600, 748; **HRMS (ESI)** calcd $C_{11}H_{15}N_2$ $[M + H]^+$: 175.1230 , found: 175.1231.



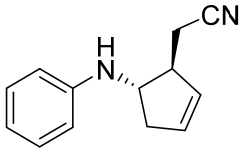
5-Phenyl-4-(phenylamino)pentanenitrile (4r): oil; 62% yield (31 mg); **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.32 (t, *J* = 7.1 Hz, 2H), 7.24 (m, 3H), 7.14 (d, *J* = 7.2 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 2H), 3.79 (m, 1H), 3.40 (brs, 1H), 2.94 (dd, *J* = 13.5, 3.9 Hz, 1H), 2.81 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.56 – 2.35 (m, 2H), 2.04 – 1.96 (m, 1H), 1.66 – 1.57 (m, 1H); **^{13}C NMR (150 MHz, CDCl$_3$)** δ 147.0, 137.2, 129.7, 129.6, 128.8, 126.9, 119.8, 118.4, 114.0, 53.0, 40.4, 30.2, 14.5； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3391, 2924, 2244, 1598, 694; **HRMS (ESI)** calcd $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543 , found: 251.1546.



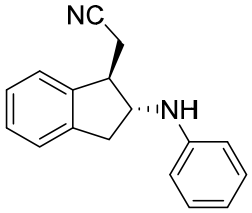
4-(Phenylamino)hept-6-enenitrile (4s): oil; 55% yield (22.3 mg); **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.19 (t, *J* = 7.7 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 7.9 Hz, 2H), 5.86 – 5.69 (m, 1H), 5.17 – 5.08 (m, 2H), 3.67 – 3.54 (m, 1H), 3.41 (brs, 1H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.38 – 2.28 (m, 2H), 2.07 – 1.97 (m, 1H), 1.74 (td, *J* = 14.7, 7.1 Hz, 1H); **^{13}C NMR (150 MHz, CDCl$_3$)** δ 147.1, 133.6, 129.6, 119.9, 119.0, 118.3, 113.9, 51.7, 38.8, 30.4, 14.2； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3379, 2926, 2245, 1601, 748; **HRMS (ESI)** calcd $C_{13}H_{17}N_2$ $[M + H]^+$: 201.1386, found: 201.1387.



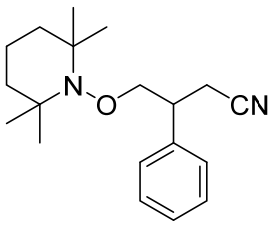
3-Phenyl-4-(phenylamino)pentanenitrile (4t): oil; 52% yield (26 mg); the title compound as a 5:1 mixture of inseparable diastereomers; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.43 – 7.29 (m, 3H), 7.25 – 7.17 (m, 4H), 6.76 (t, *J* = 7.1 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 2H), 4.01 – 3.82 (m, 1H), 3.37 – 3.23 (m, 1H), 3.06 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.97 (dd, *J* = 16.7, 6.0 Hz, 1H), 2.76 (dd, *J* = 16.7, 8.4 Hz, 1H), 1.12 (d, *J* = 6.4 Hz, 0.5H)/1.01 (d, *J* = 6.3 Hz, 2.5H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 147.1/146.9, 138.8/137.6, 129.7/129.6, 129.0/128.9, 128.4/128.2, 128.0/127.9, 119.3/119.0, 118.3, 114.0/113.9, 52.1/51.3, 48.1/47.1, 21.9/20.1, 19.0/18.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3369, 2971, 2247, 1599, 693; **HRMS (ESI)** calcd $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543, found: 251.1546.



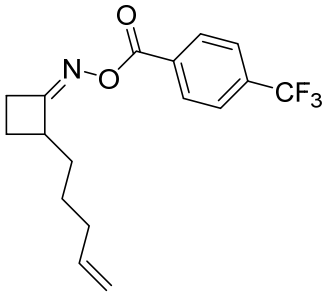
2-(5-(Phenylamino)cyclopent-2-en-1-yl)acetonitrile (4u): oil; 35% yield (14 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.20 (t, *J* = 7.4 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.7 Hz, 2H), 5.94 (d, *J* = 3.1 Hz, 1H), 5.80 – 5.69 (m, 1H), 4.09 – 3.81 (m, 1H), 3.11 – 2.84 (m, 2H), 2.59 (dd, *J* = 16.7, 5.5 Hz, 1H), 2.49 (dd, *J* = 16.7, 7.0 Hz, 1H), 2.27 (d, *J* = 17.3 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.9, 132.4, 130.3, 129.6, 118.4, 118.3, 113.8, 58.2, 49.2, 39.8, 21.9； **FT-IR** (thin film, KBr): ν (cm^{-1}) 3389, 2923, 2248, 1601, 727; **HRMS (ESI)** calcd $C_{13}H_{15}N_2$ $[M + H]^+$: 199.1230 , found: 199.1227.



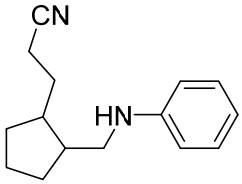
2-(2-(Phenylamino)-2,3-dihydro-1H-inden-1-yl)acetonitrile (4v): oil; 49% yield (24.2 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 – 7.33 (m, 1H), 7.31 – 7.26 (m, 3H), 7.22 (t, *J* = 7.6 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 2H), 4.27 – 4.08 (m, 1H), 3.85 (brs, 1H), 3.51 (dd, *J* = 16.3, 6.6 Hz, 1H), 3.39 (dd, *J* = 11.1, 5.4 Hz, 1H), 2.85 – 2.77 (m, 2H), 2.71 (dd, *J* = 16.9, 6.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.9, 141.1, 140.8, 129.7, 128.4, 127.5, 125.6, 124.3, 118.41, 118.39, 113.7, 59.6, 48.0, 38.5, 21.3; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3386, 2924, 2249, 1601, 726; **HRMS (ESI)** calcd $C_{18}H_{19}N_2$ $[M + H]^+$: 263.1543, found: 263.1542.



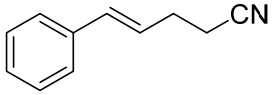
3-Phenyl-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanenitrile (5a): oil; 57% yield (34 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.19 (m, 5H), 3.98 (d, *J* = 6.3 Hz, 2H), 3.41 – 3.09 (m, 1H), 2.92 (dd, *J* = 16.7, 5.8 Hz, 1H), 2.74 (dd, *J* = 16.7, 7.9 Hz, 1H), 1.63 – 1.49 (m, 1H), 1.48 – 1.38 (m, 4H), 1.35 – 1.23 (m, 1H),1.11 (s, 3H), 1.09 (s, 6H), 1.07 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 139.3, 128.8, 127.7, 127.6, 118.7, 78.2, 60.0, 42.0, 39.74, 39.68, 33.1, 21.1, 20.3, 20.2, 17.1; **FT-IR** (thin film, KBr): ν (cm^{-1}) 2927, 2246, 1602, 1506, 696; **HRMS (ESI)** calcd $C_{19}H_{29}N_2O$ $[M + H]^+$: 301.2274, found: 301.2277.



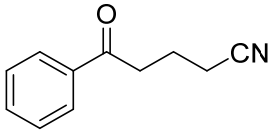
2-(Pent-4-en-1-yl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 5.80 (m, 1H), 4.99 (dd, *J* = 22.0, 13.6 Hz, 2H), 3.58 – 3.32 (m, 1H), 3.19 – 2.93 (m, 2H), 2.31 – 2.21 (m, 1H), 2.09 (dd, *J* = 13.7, 6.8 Hz, 2H), 1.97 – 1.61 (m, 3H), 1.56 – 1.47 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.4, 163.0, 138.5, 134.7 (q, *J* = 32.7 Hz), 132.7, 130.1, 125.6 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 272.9 Hz), 115.0, 45.7, 33.6, 31.9, 29.2, 26.2, 21.1.



3-(2-((Phenylamino)methyl)cyclopentyl)propanenitrile (7): oil; 77% yield (35 mg); the title compound as a 3.4:1 mixture of inseparable diastereomers; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.19 (t, *J* = 7.6 Hz, 2H), 6.71 (t, *J* = 7.1 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 2H), 3.59 (s, 1H), 3.20 – 3.07 (m, 1H), 3.01 – 2.88 (m, 1H), 2.54 – 2.30 (m, 2H), 2.29 – 2.18 (m, 1H), 2.18 – 2.05 (m, 1H), 1.98 – 1.79 (m, 3H), 1.78 – 1.45 (m, 4H), 1.42 – 1.32 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.48/148.46, 129.43/129.41, 120.0/119.9, 117.6/117.5, 112.85/112.83, 48.7, 45.0, 44.3, 43.0, 42.1, 40.8, 32.1, 31.2, 30.8, 30.0, 29.2, 25.7, 24.2, 22.6, 16.5, 16.4; **FT-IR** (thin film, KBr): ν (cm^{-1}) 3394, 2926, 2244, 1601, 748; **HRMS (CI)** calcd $C_{15}H_{21}N_2$ $[M + H]^+$: 229.1705, found: 229.1699.



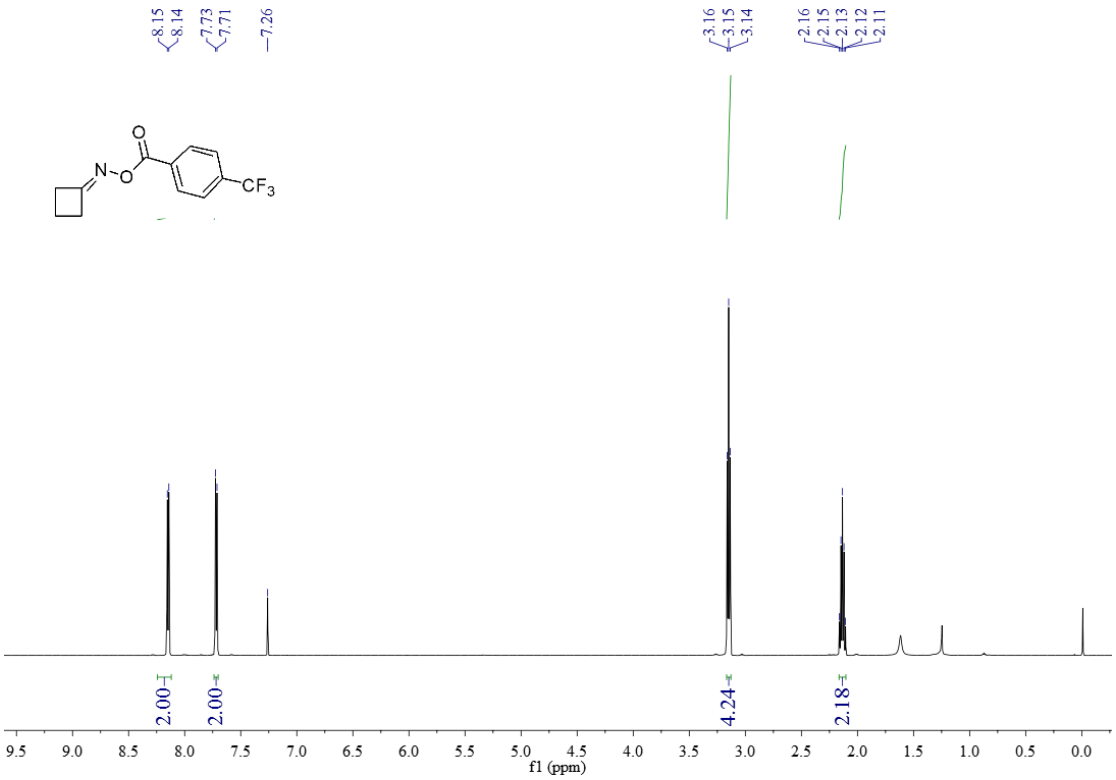
5-Phenylpent-4-enenitrile (8): oil; 63% yield (19.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** 7.41 – 7.30 (m, 4H), 7.29 – 7.22 (m, 1H), 6.54 (d, *J* = 15.8 Hz, 1H), 6.32 – 6.12 (m, 1H), 2.63 – 2.55 (m, 2H), 2.54 – 2.48 (m, 2H); **^{13}C NMR (150 MHz, $CDCl_3$)** δ 136.7, 133.1, 128.7, 127.8, 126.4, 125.6, 119.3, 28.9, 17.7.



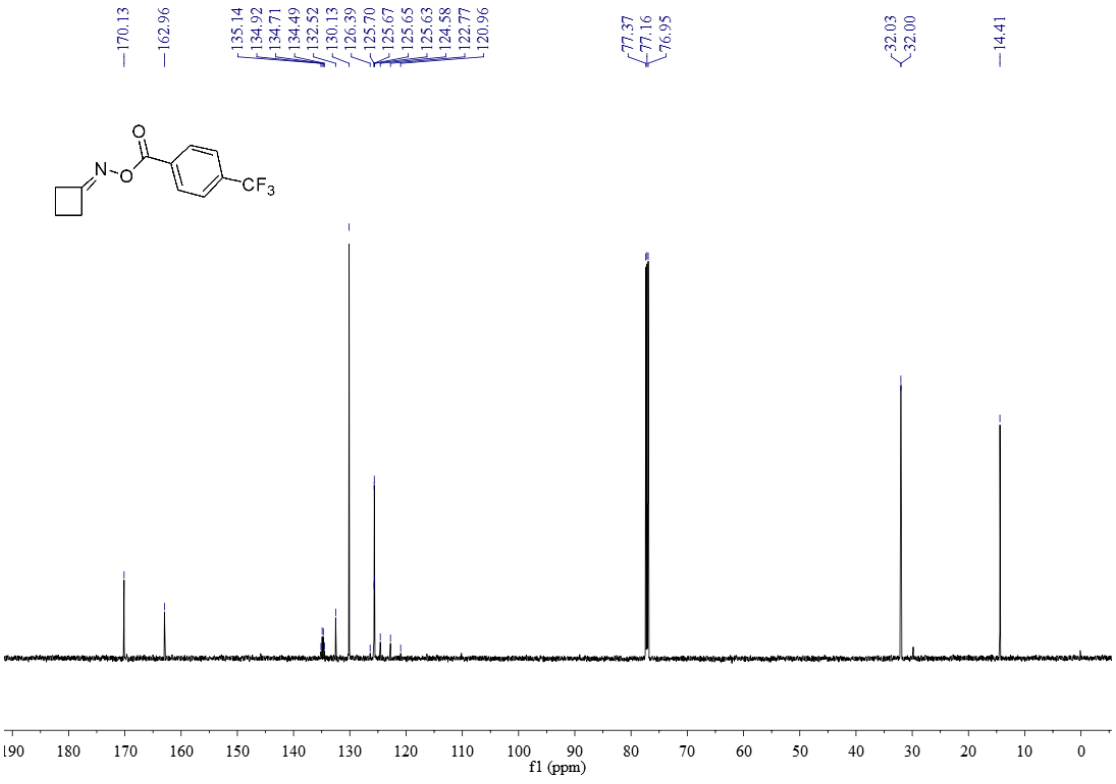
5-Oxo-5-phenylpentanenitrile (9): oil; 35% yield (12 mg); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 3.19 (t, *J* = 6.7 Hz, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 2.12 (p, *J* = 6.8 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.3, 136.6, 133.6, 128.9, 128.1, 119.6, 36.4, 19.9, 16.8.

7. NMR Spectra for the substrates and products

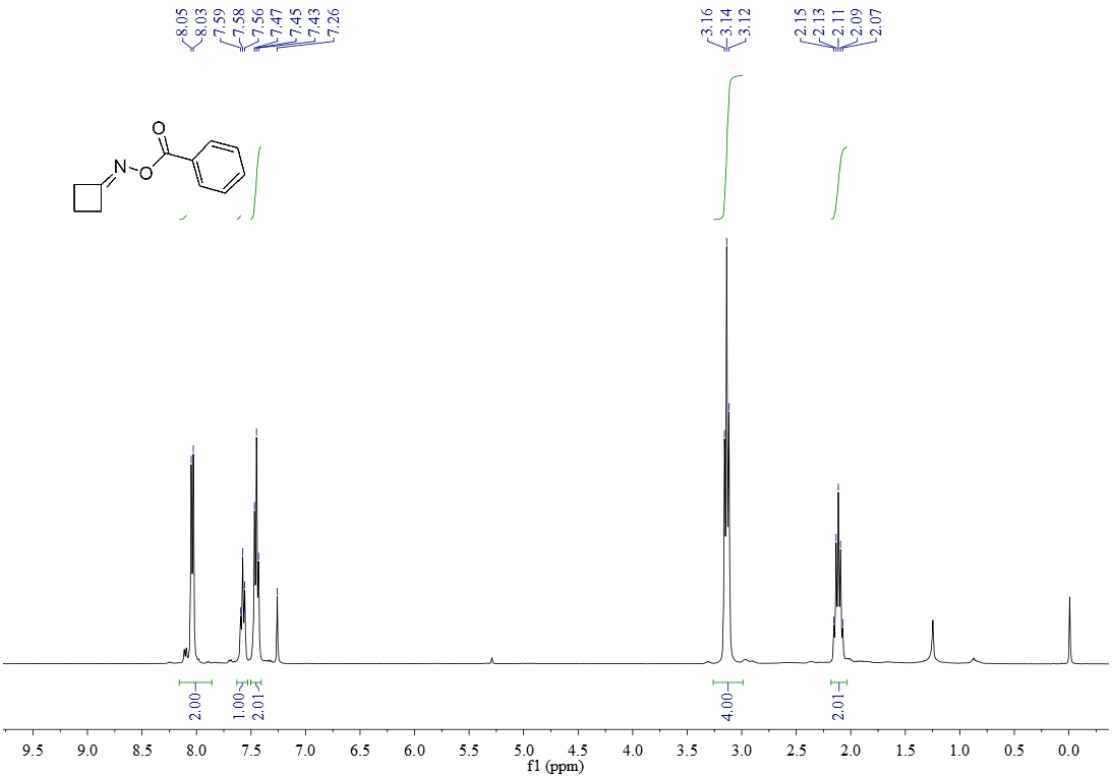
^{1}H NMR of **1a**



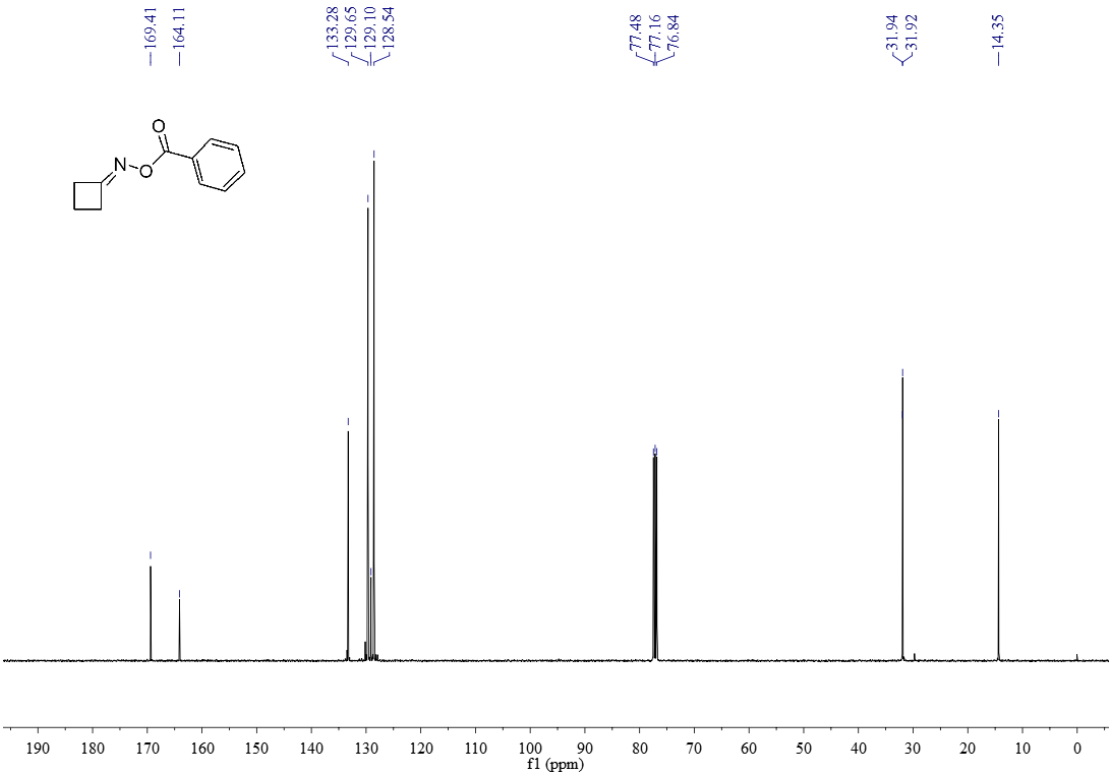
^{13}C NMR of **1a**



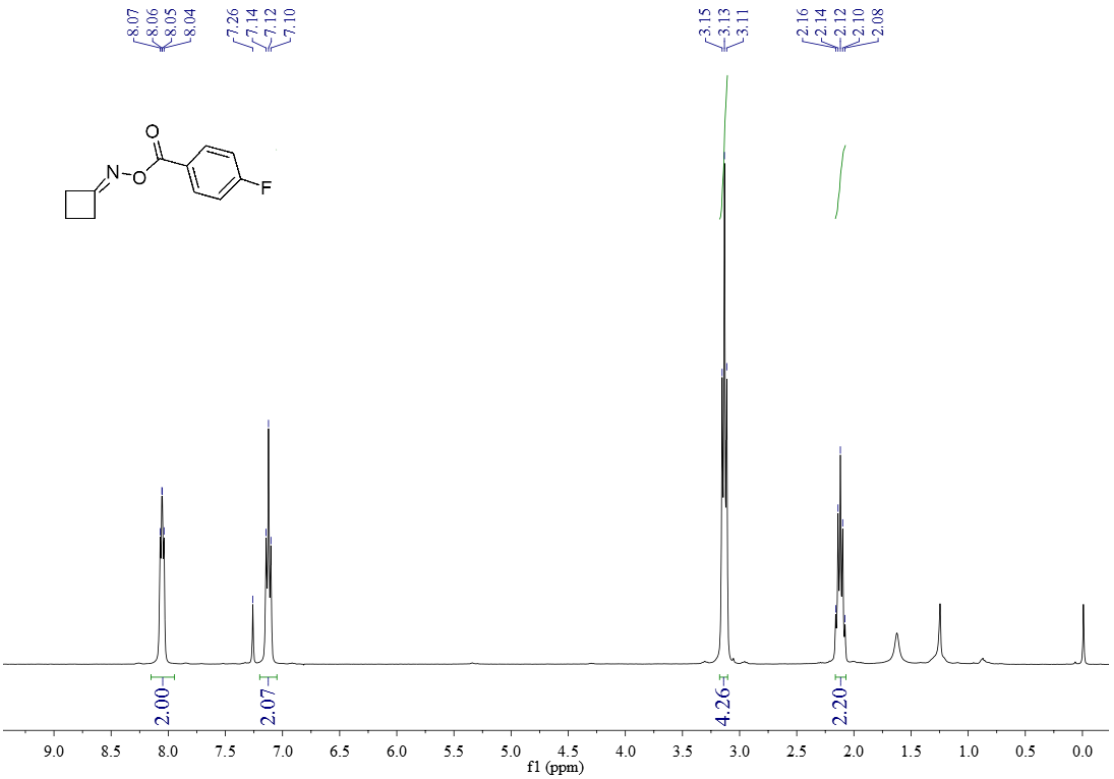
^{1}H NMR of **1aa**



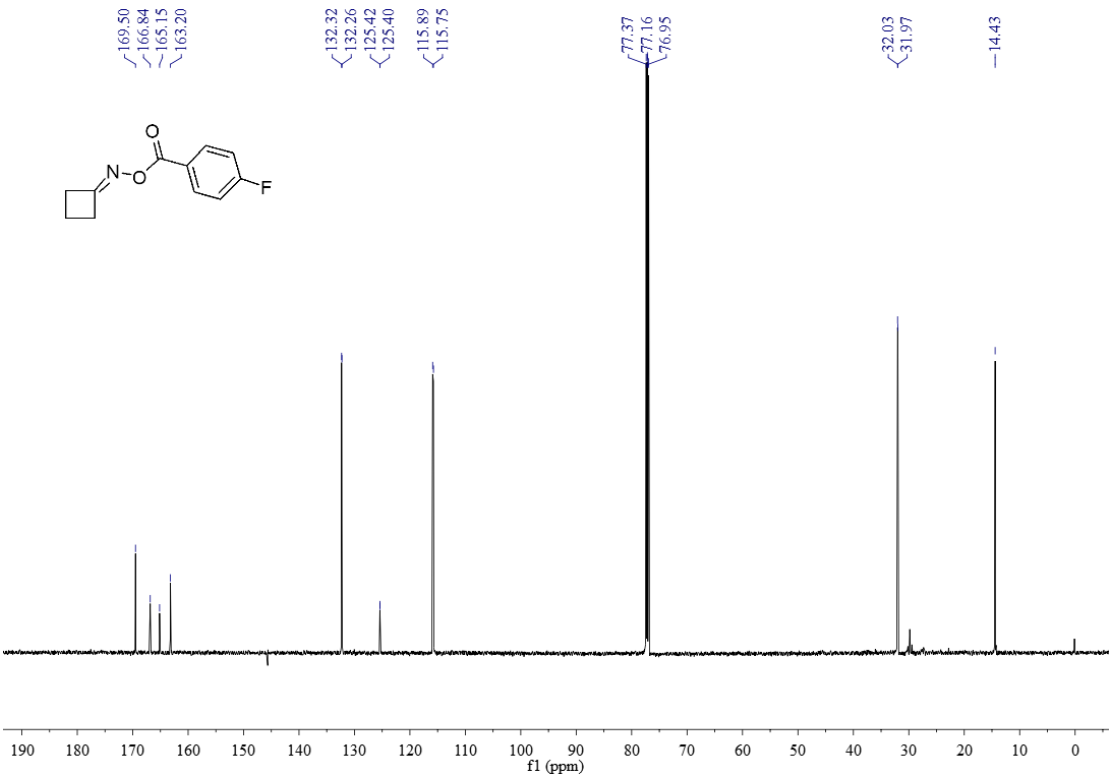
^{13}C NMR of **1aa**



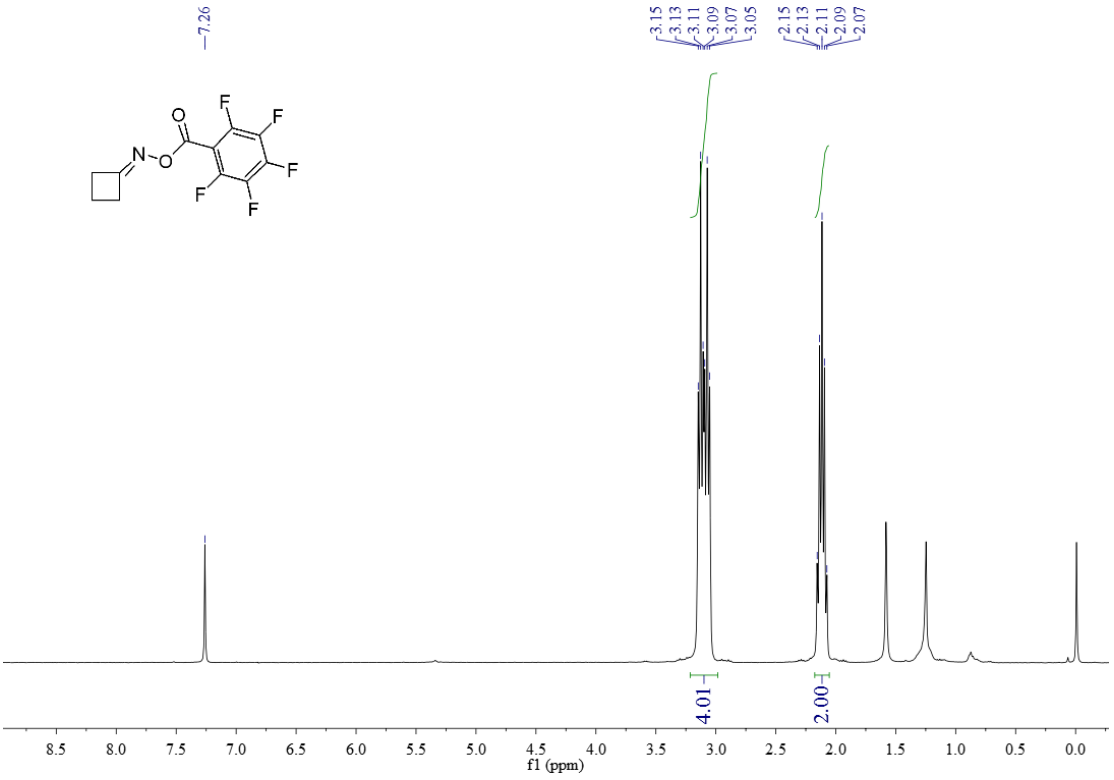
^{1}H NMR of **1ab**



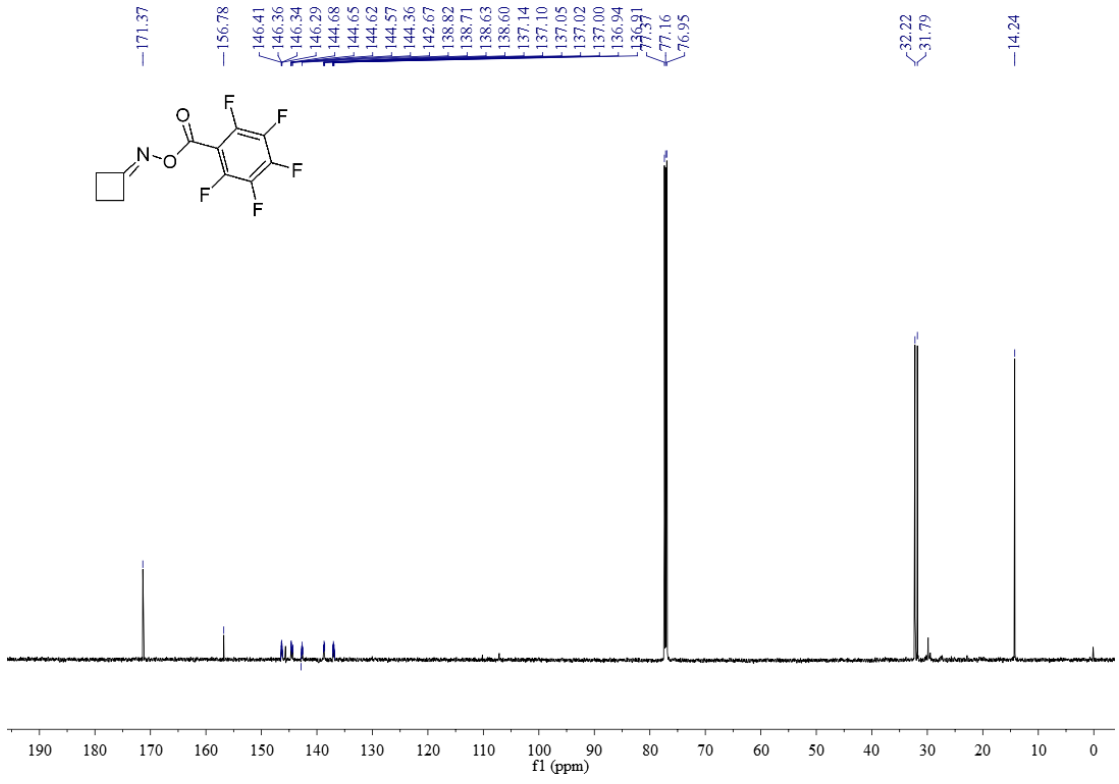
^{13}C NMR of **1ab**



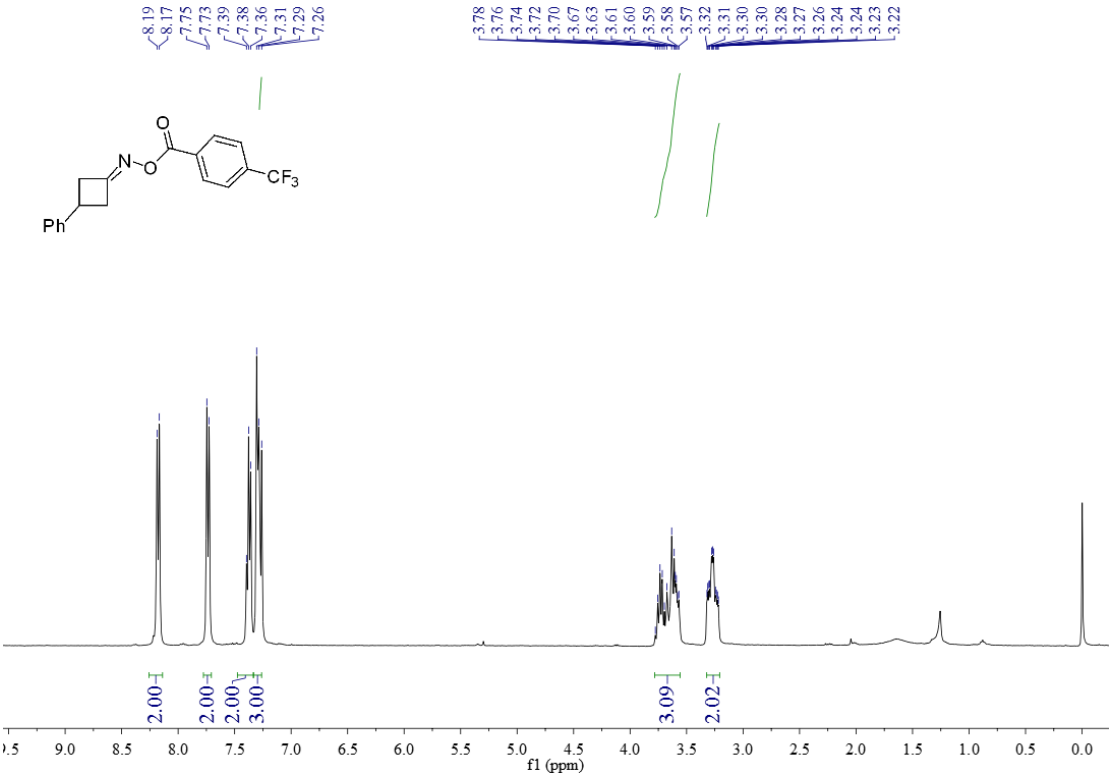
^{1}H NMR of **1ac**



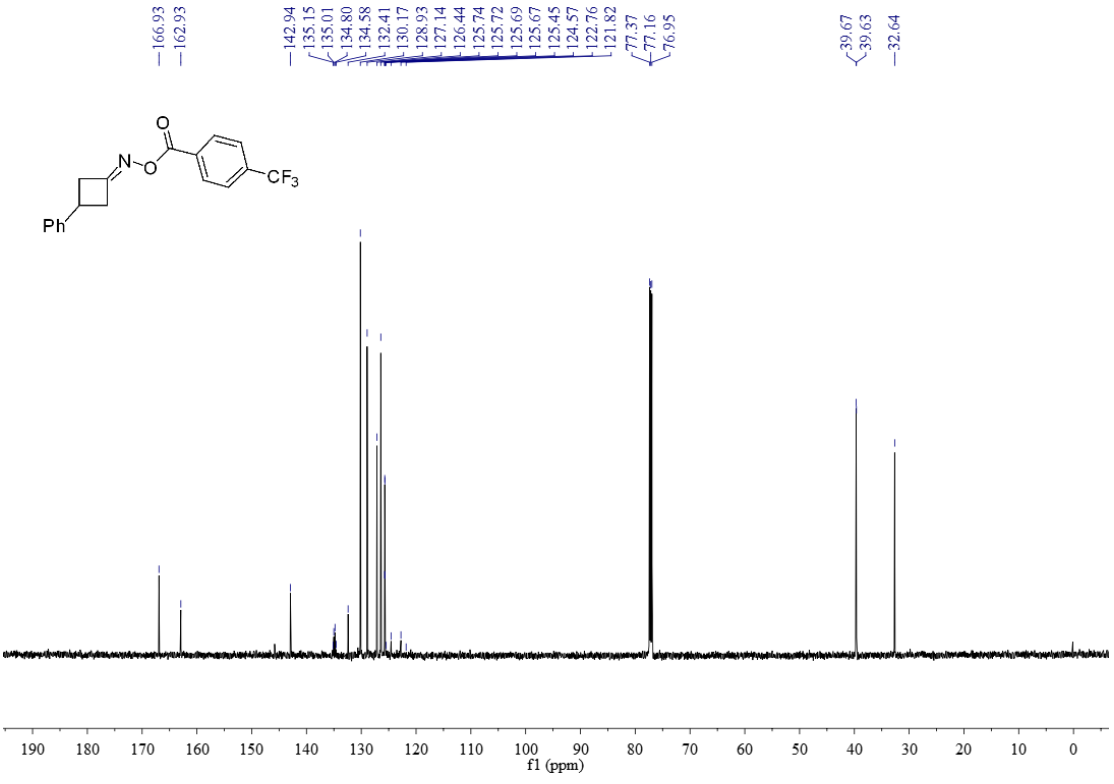
^{13}C NMR of **1ac**



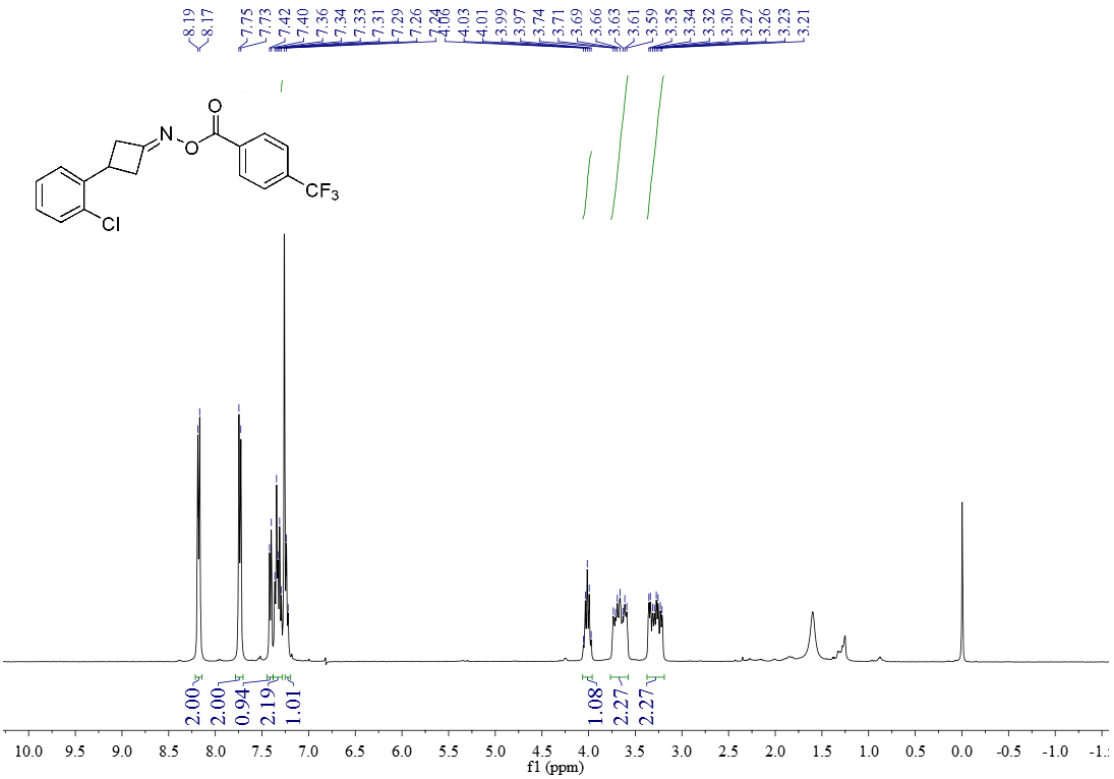
^{1}H NMR of **1b**



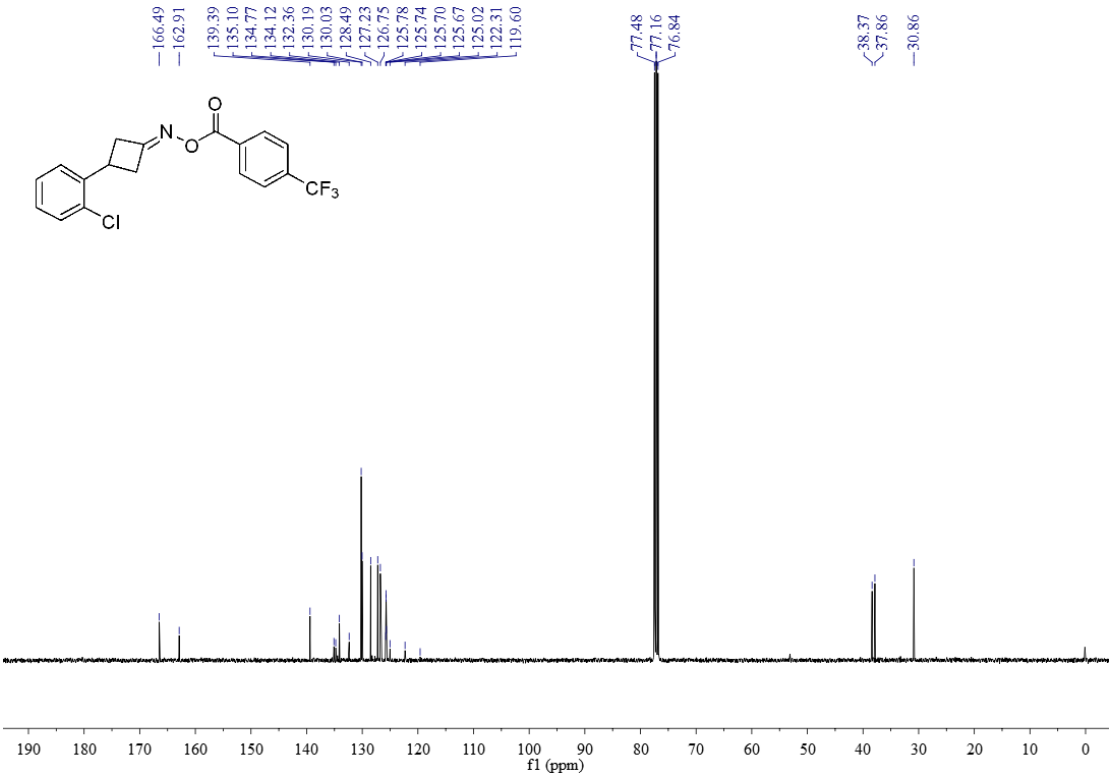
^{13}C NMR of **1b**



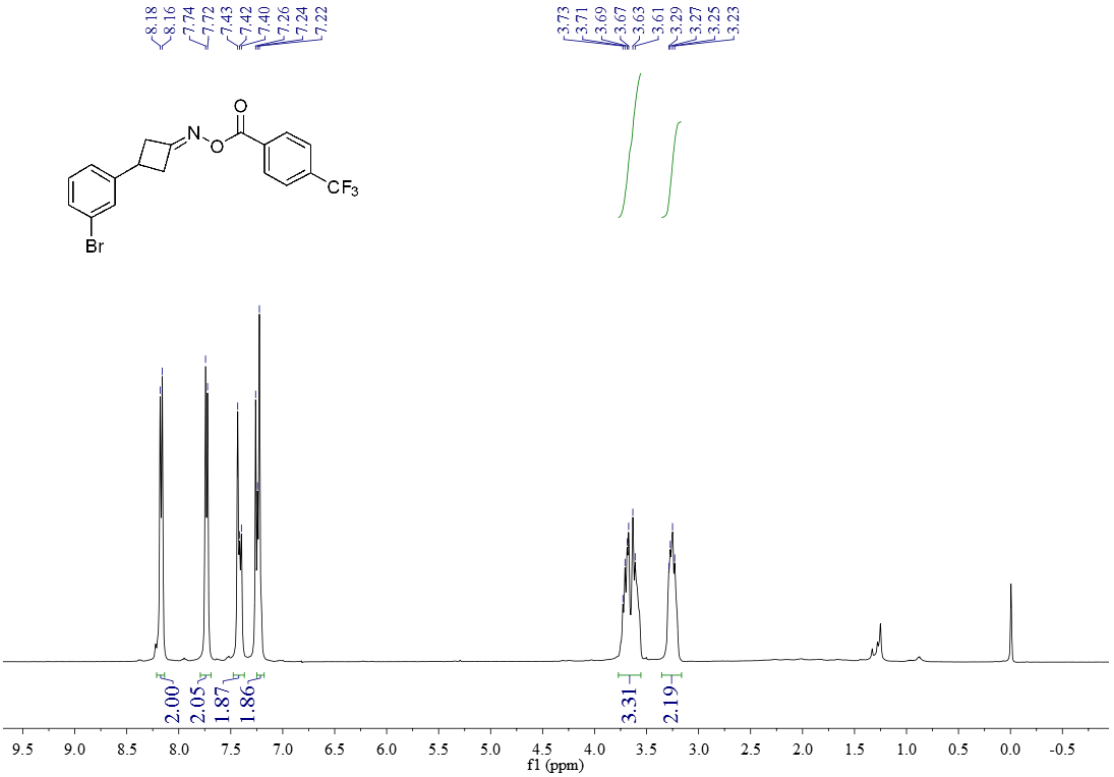
^{1}H NMR of **1c**



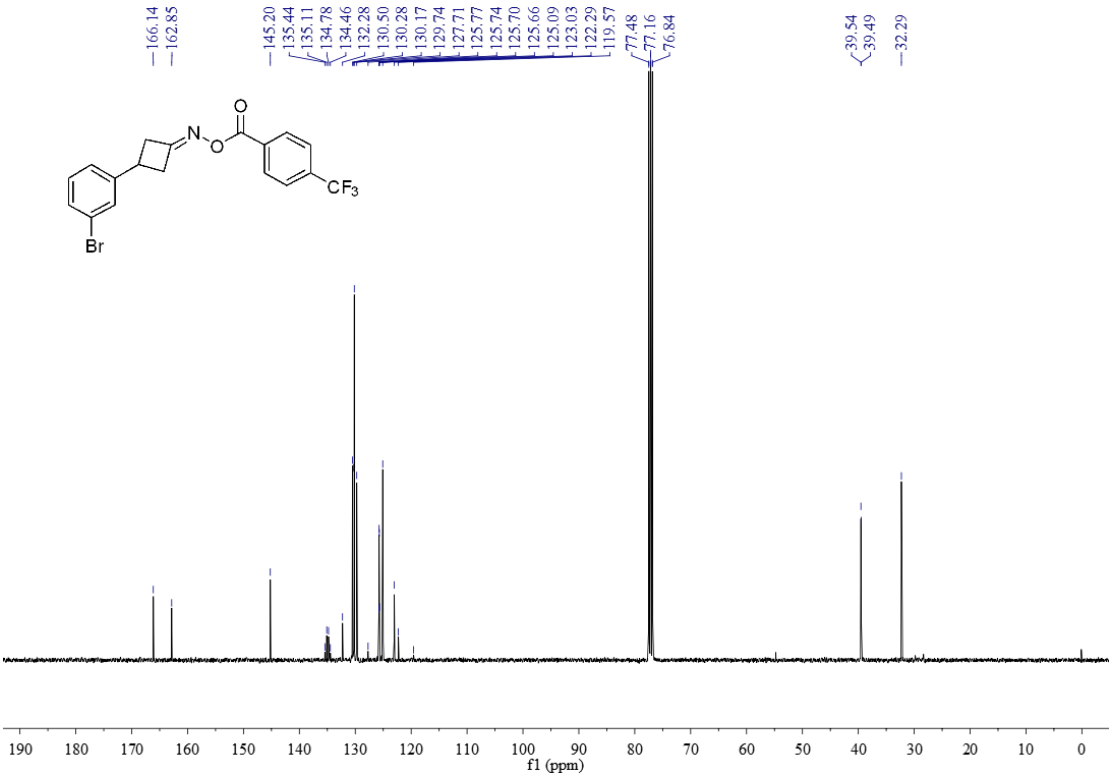
^{13}C NMR of **1c**



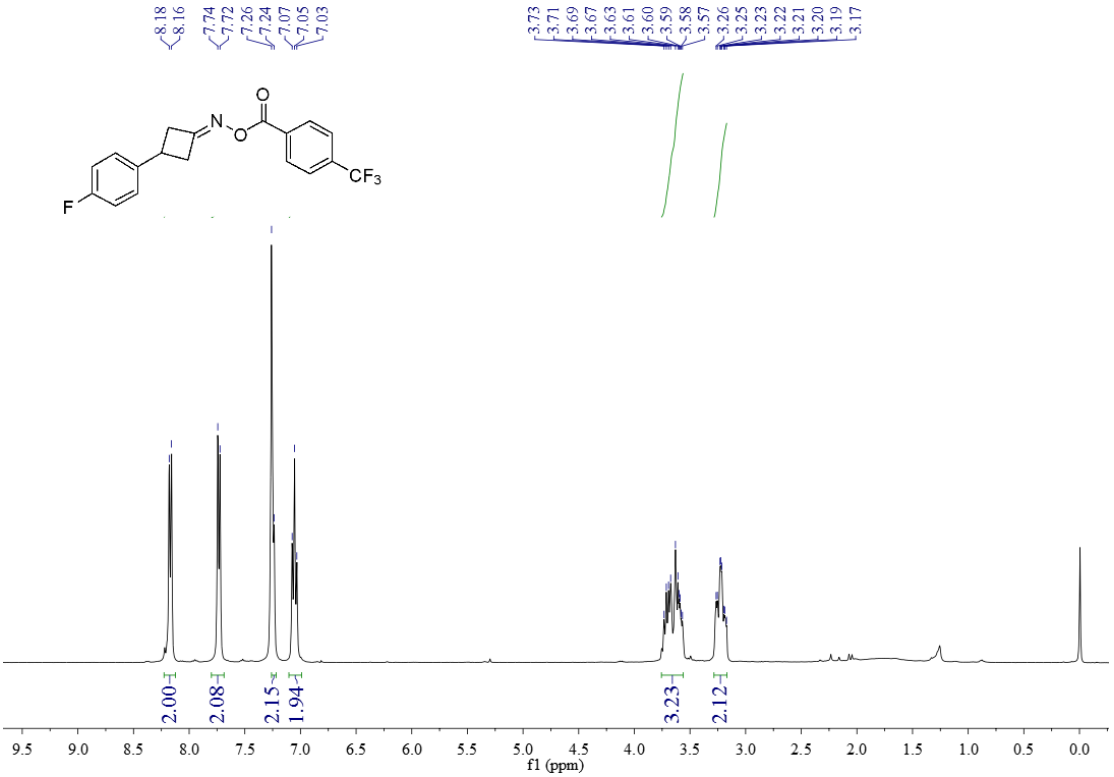
^{1}H NMR of **1d**



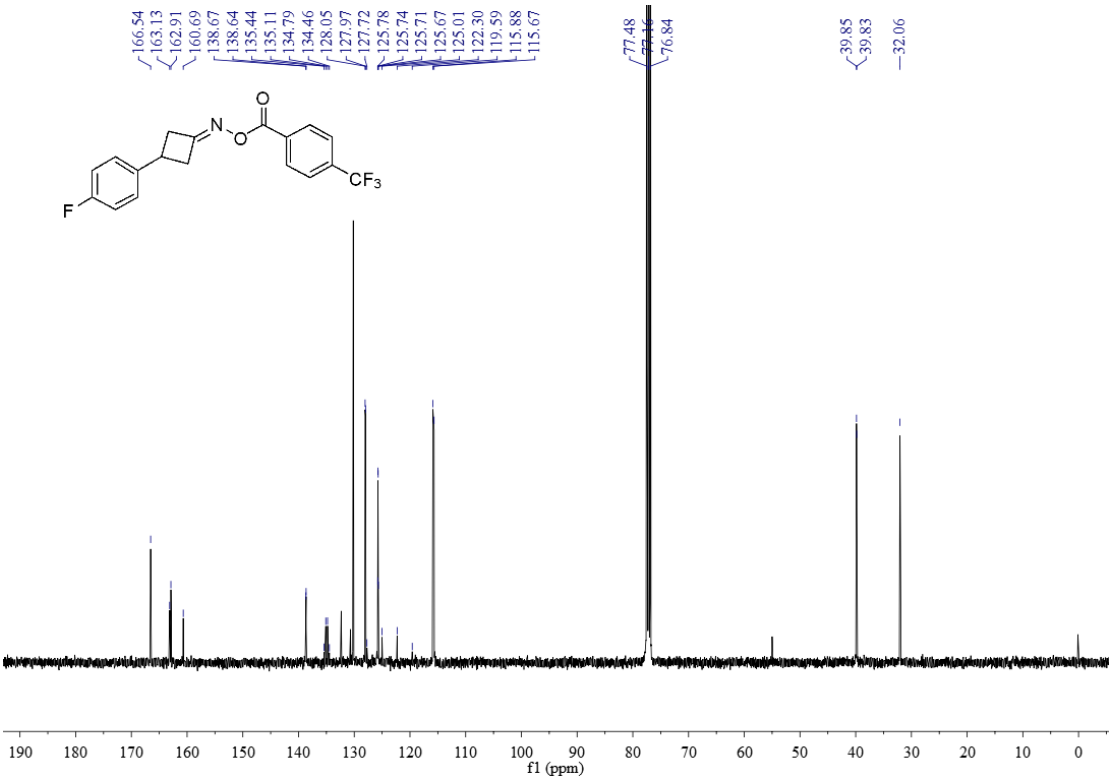
^{13}C NMR of **1d**



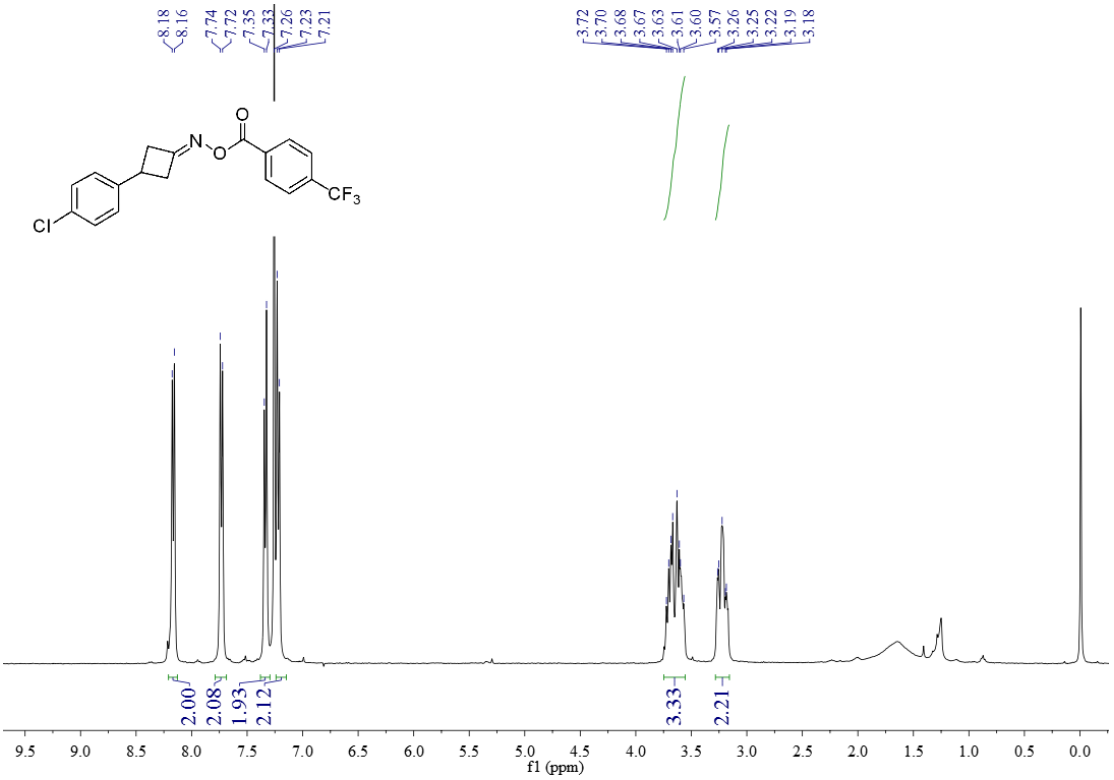
^{1}H NMR of **1e**



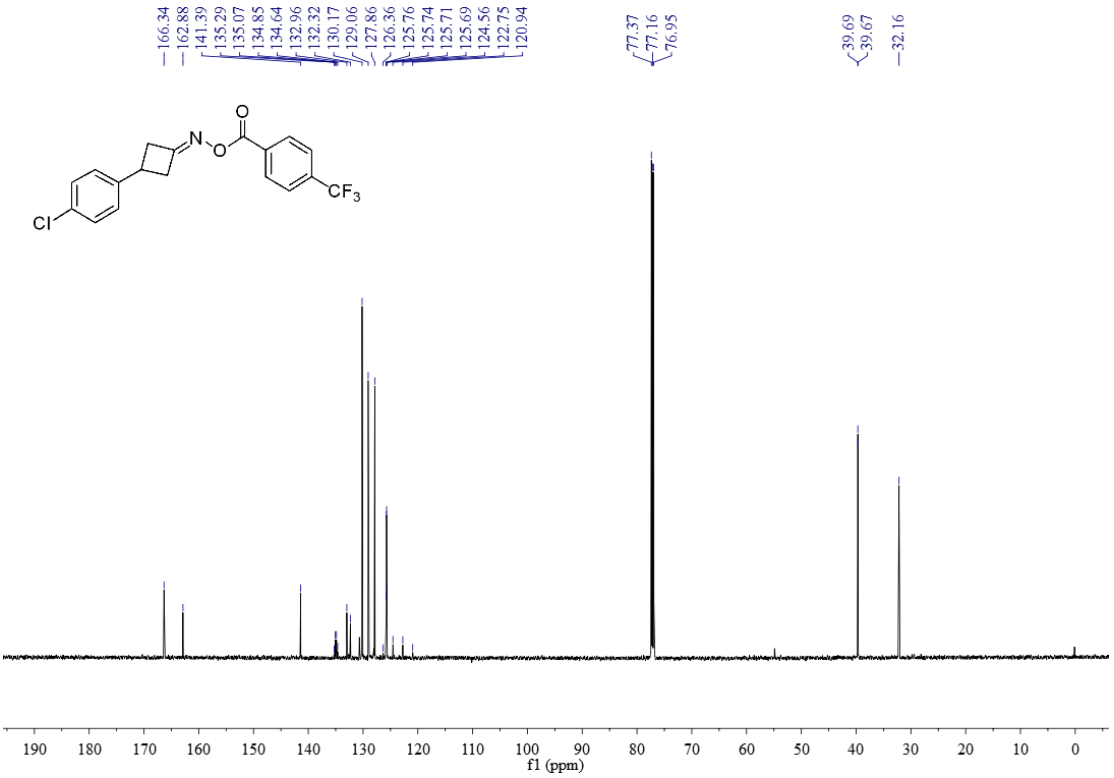
^{13}C NMR of **1e**



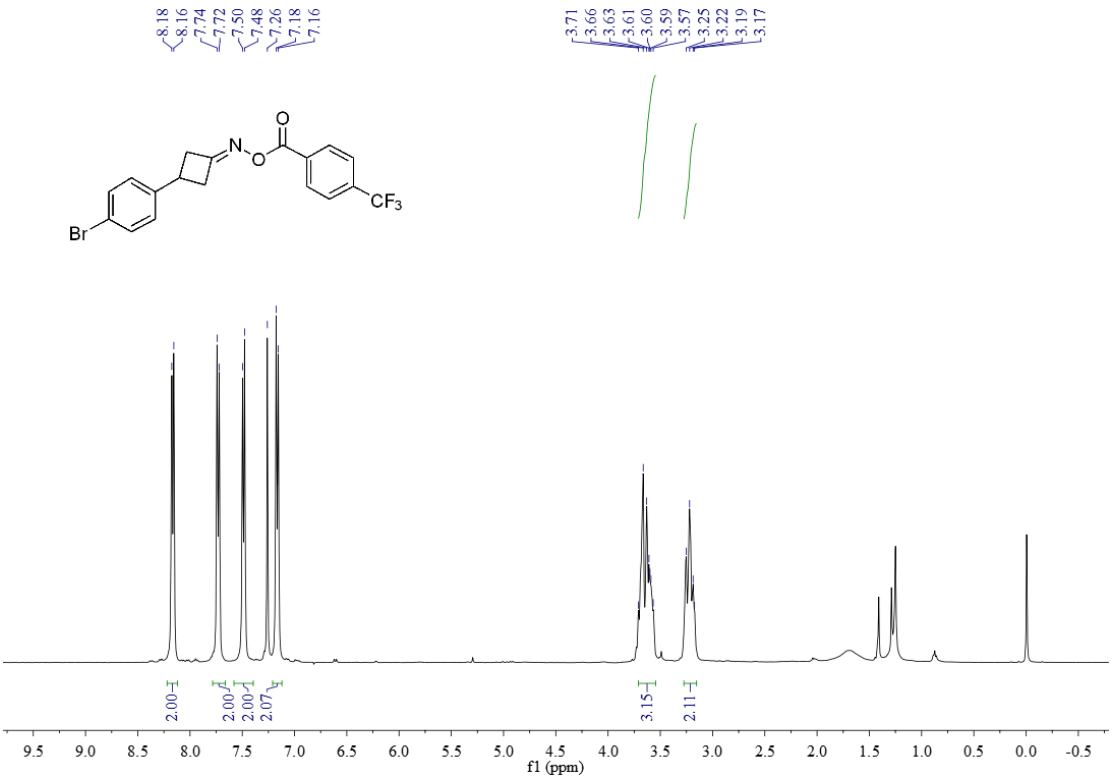
^{1}H NMR of **1f**



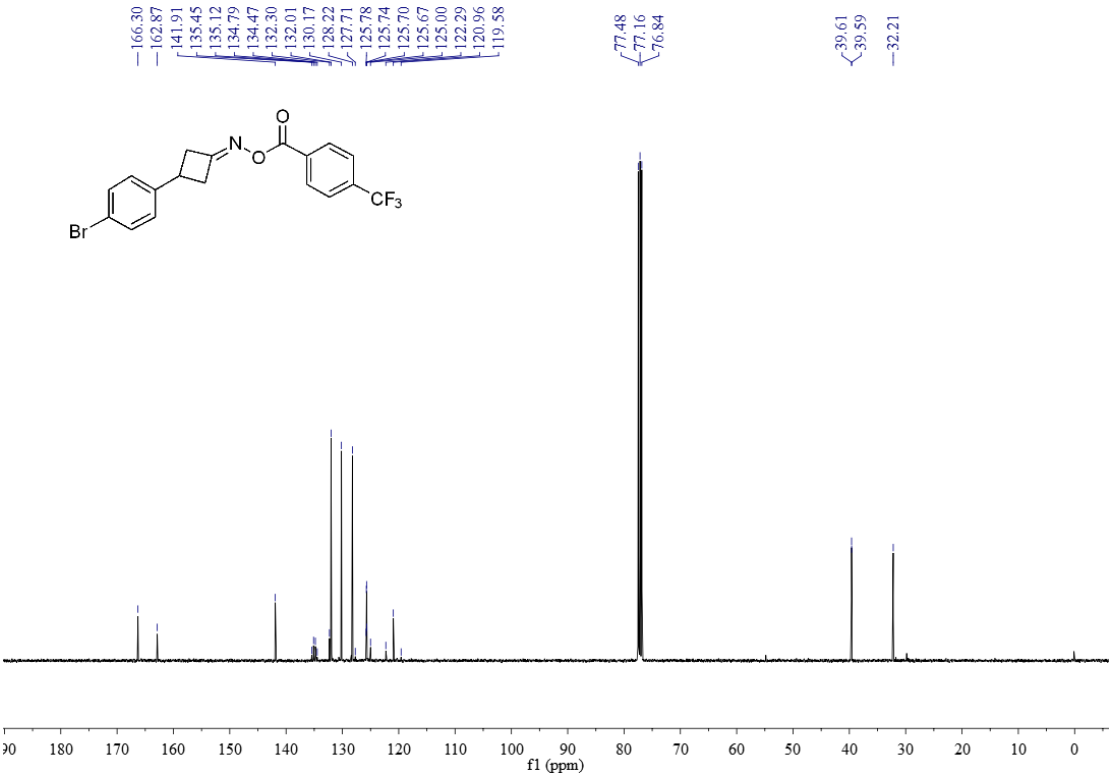
^{13}C NMR of **1f**



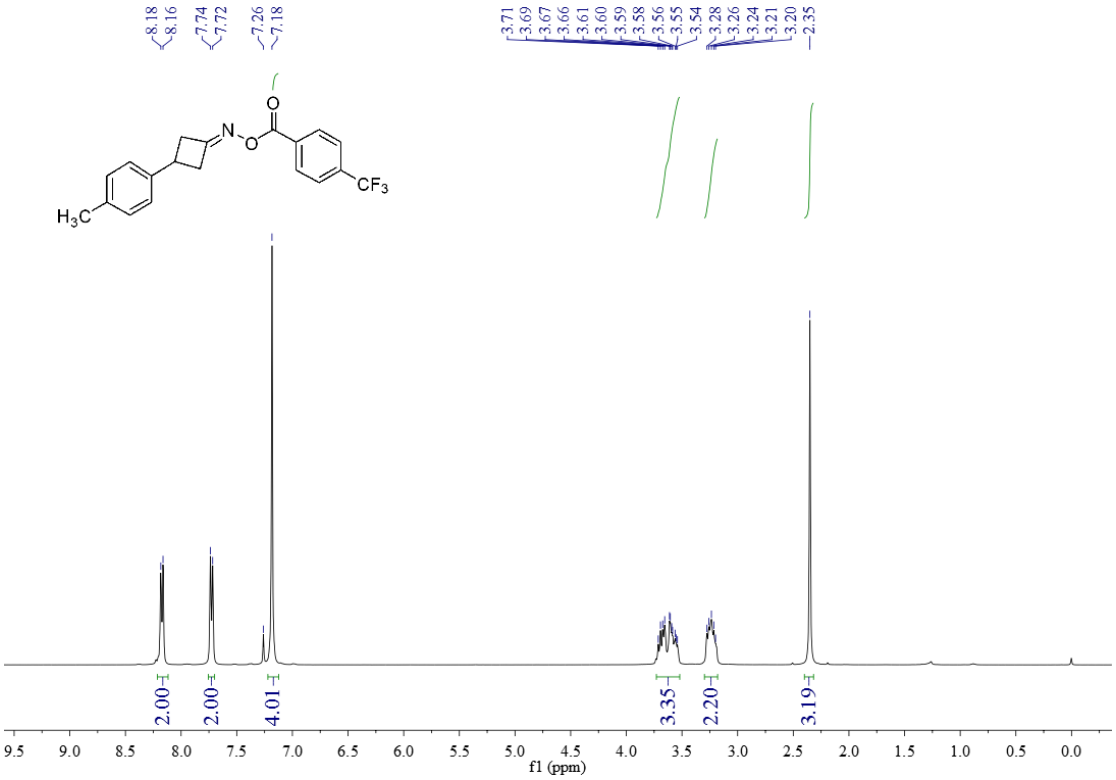
^{1}H NMR of **1g**



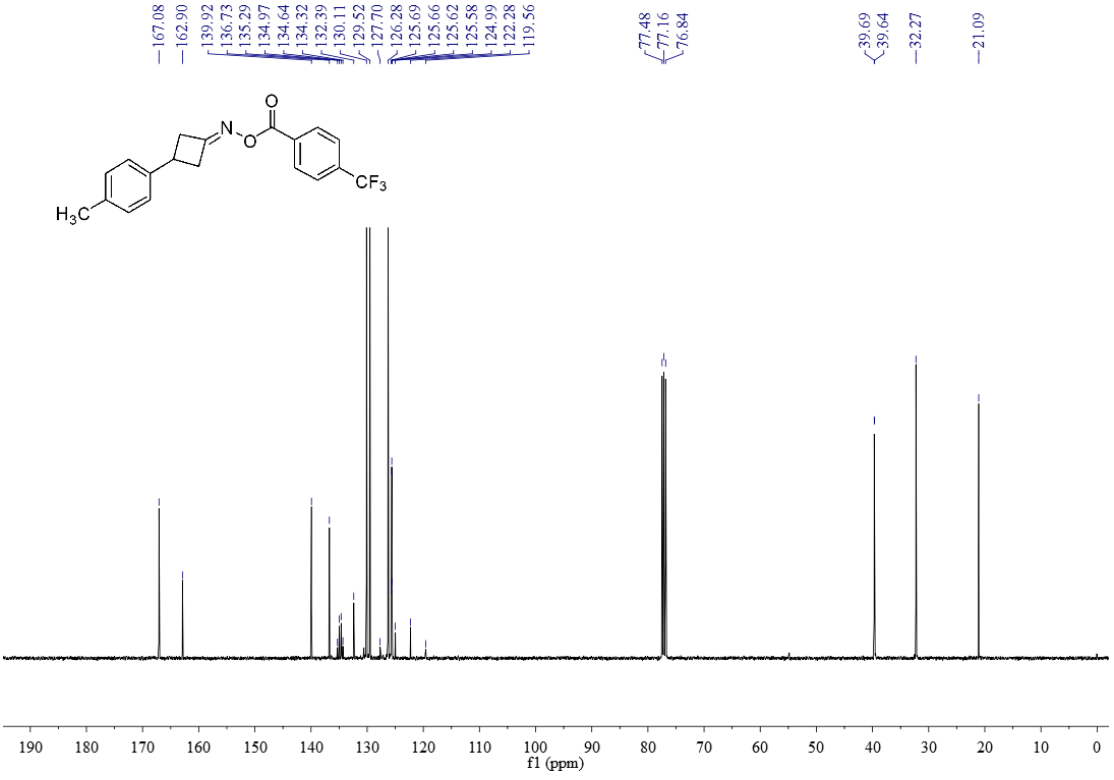
^{13}C NMR of **1g**



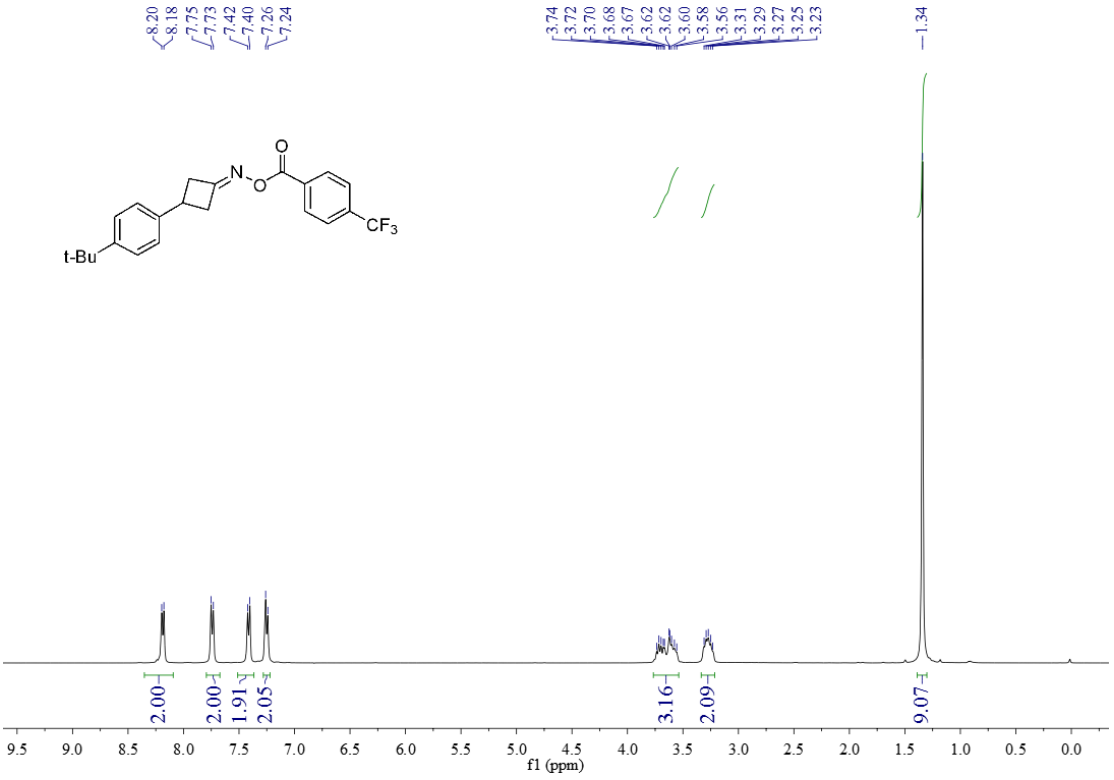
^{1}H NMR of **1h**



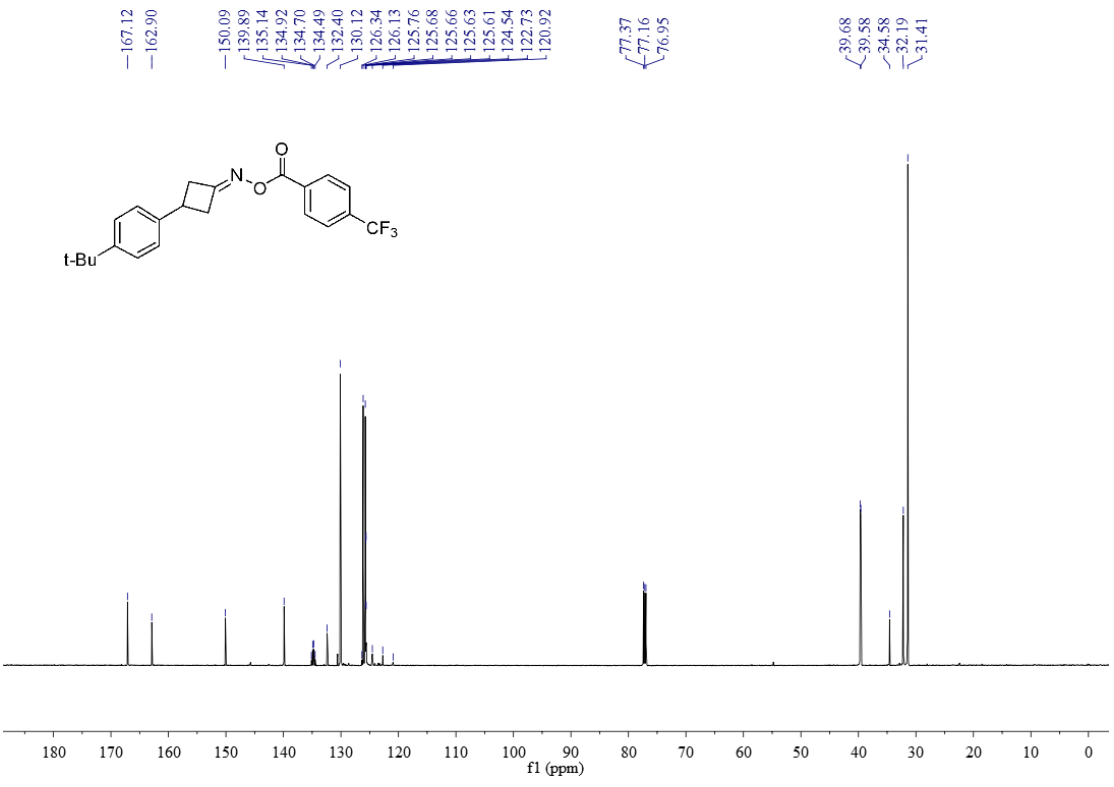
^{13}C NMR of **1h**



^{1}H NMR of **1i**



^{13}C NMR of **1i**



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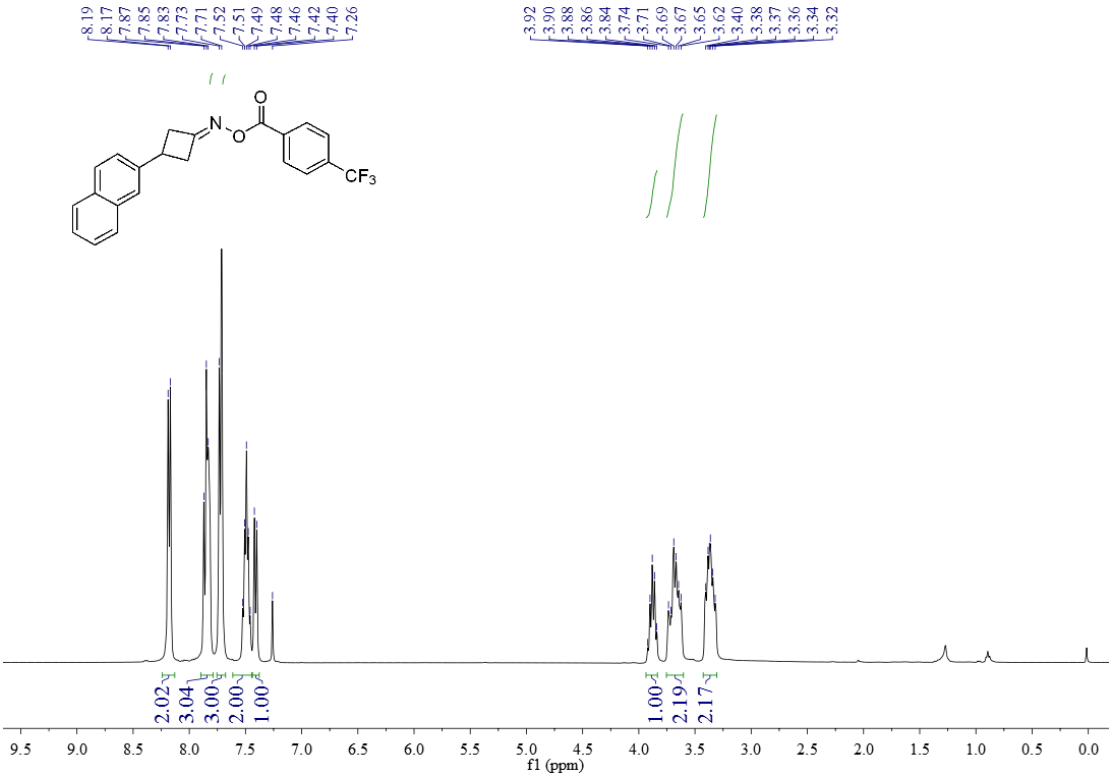

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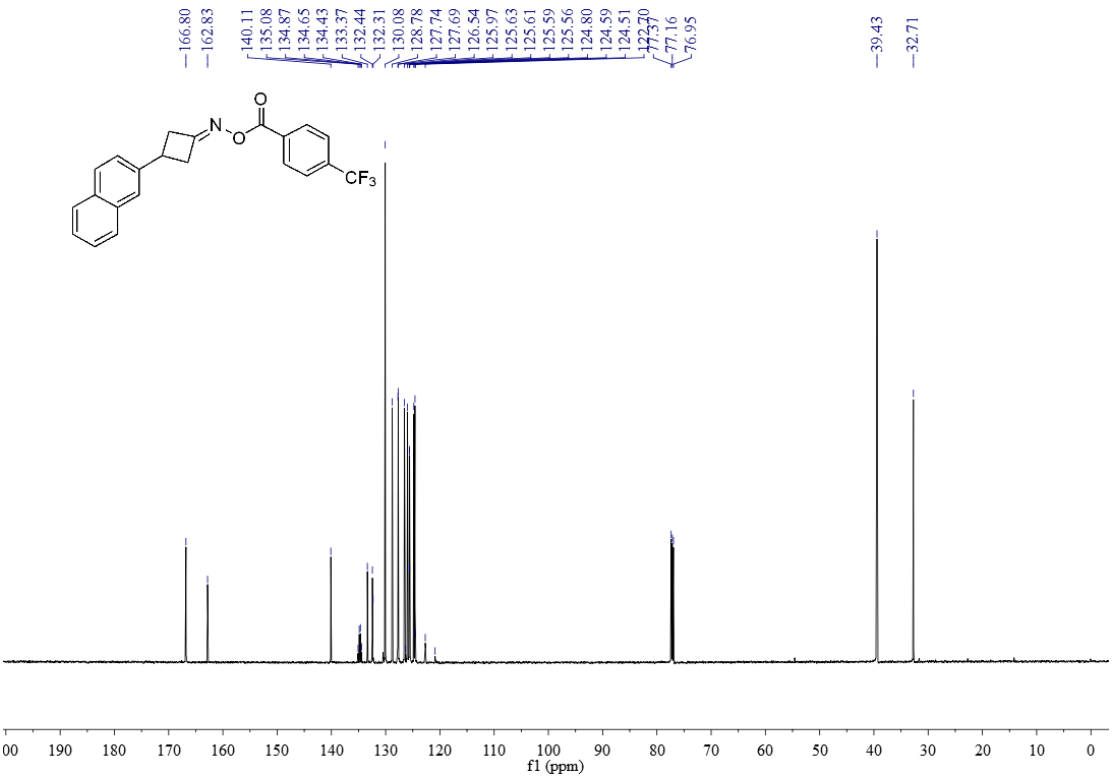
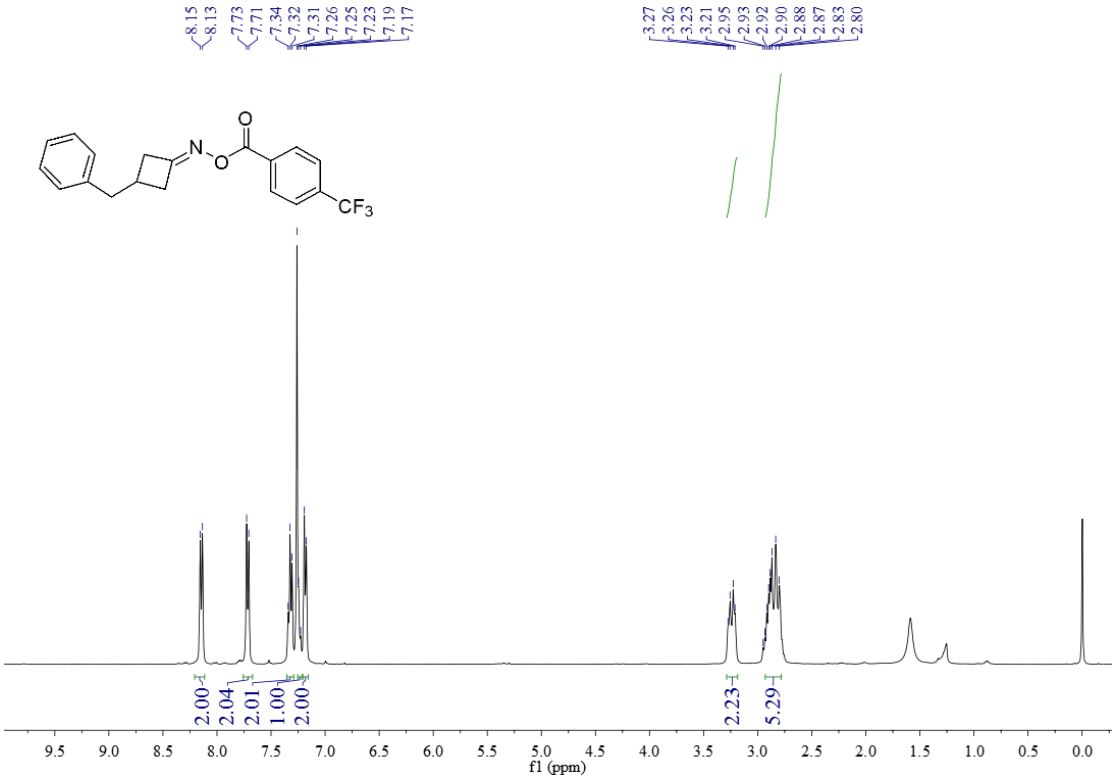


^{1}H NMR of **1k**



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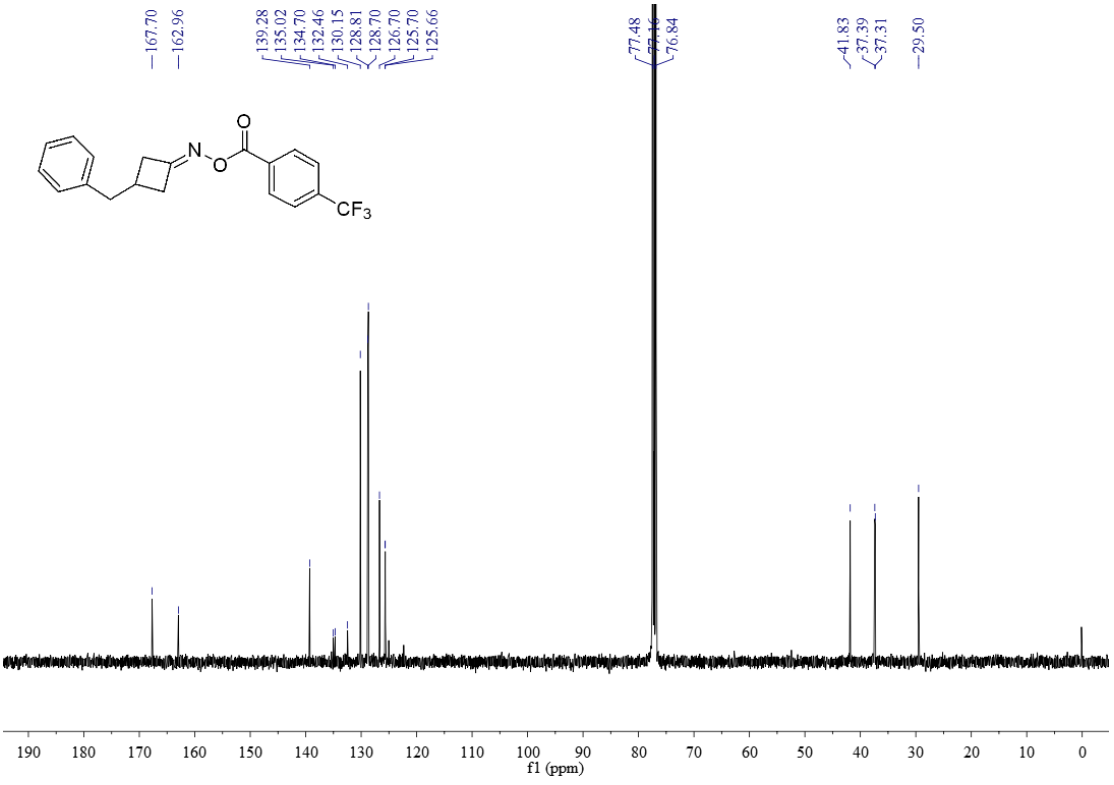

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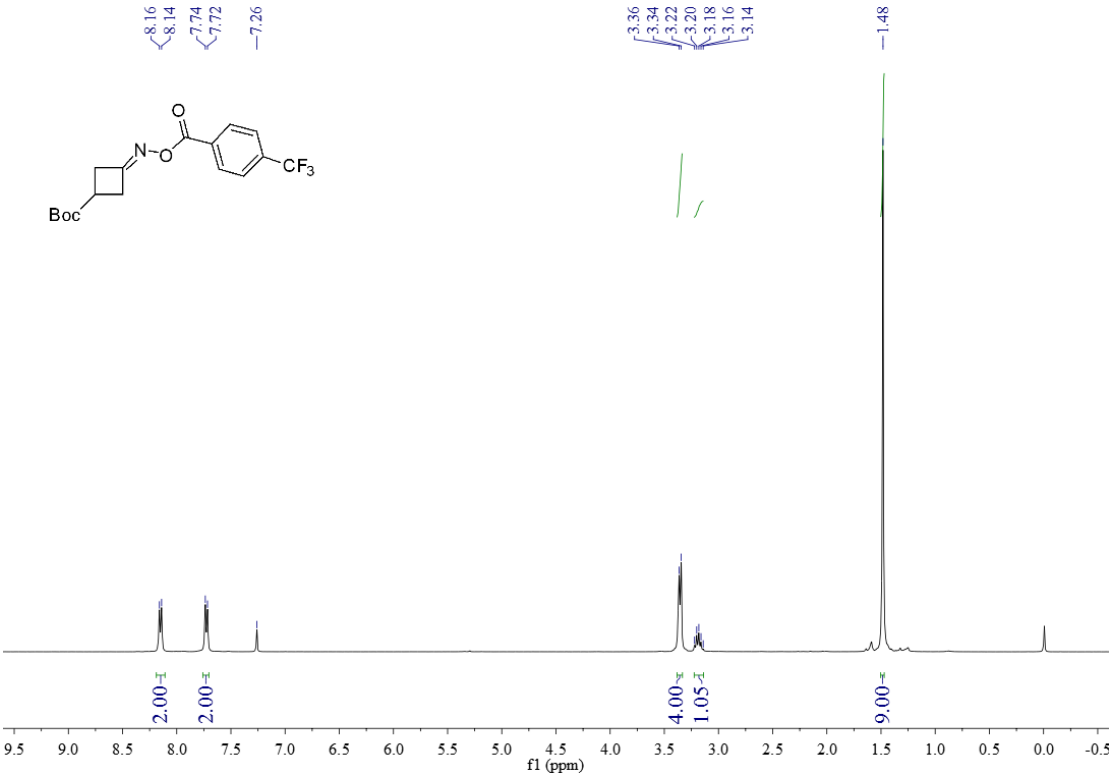
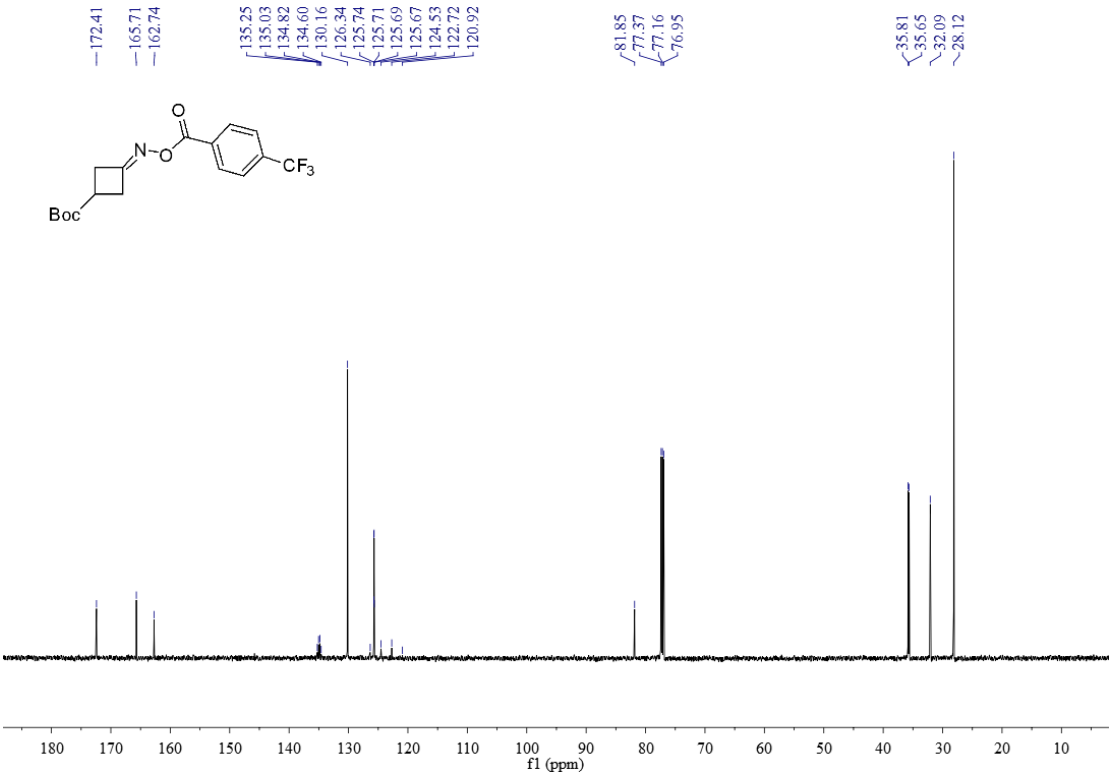
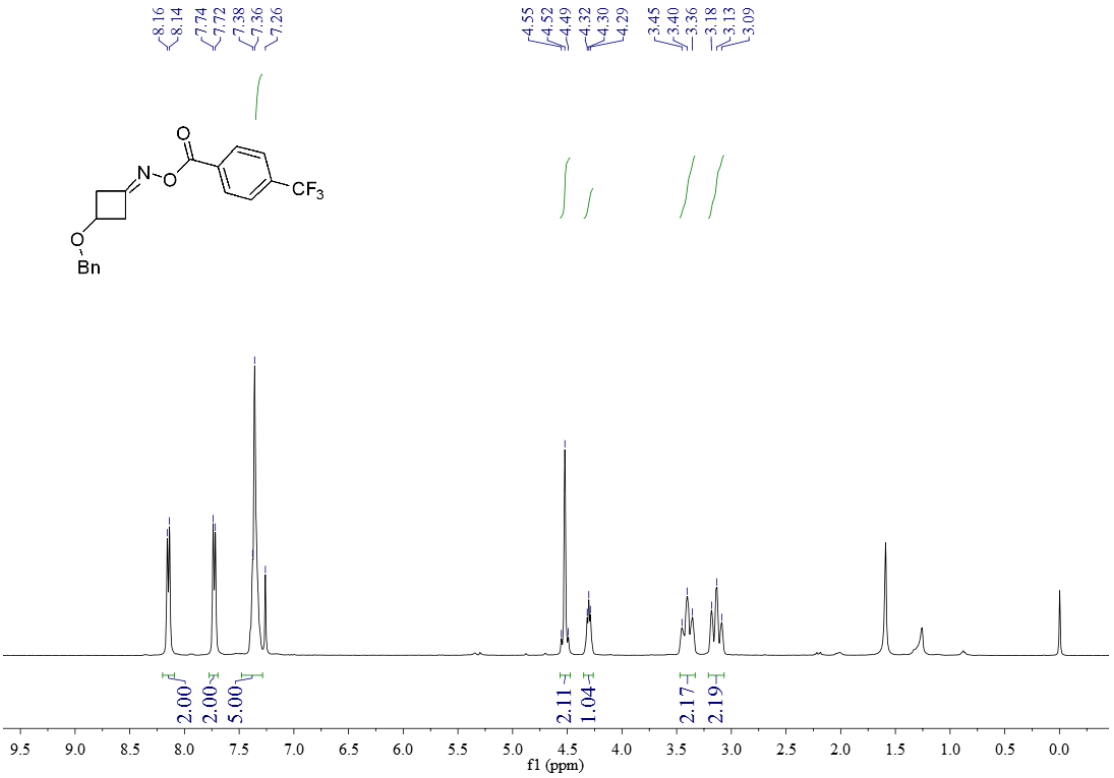


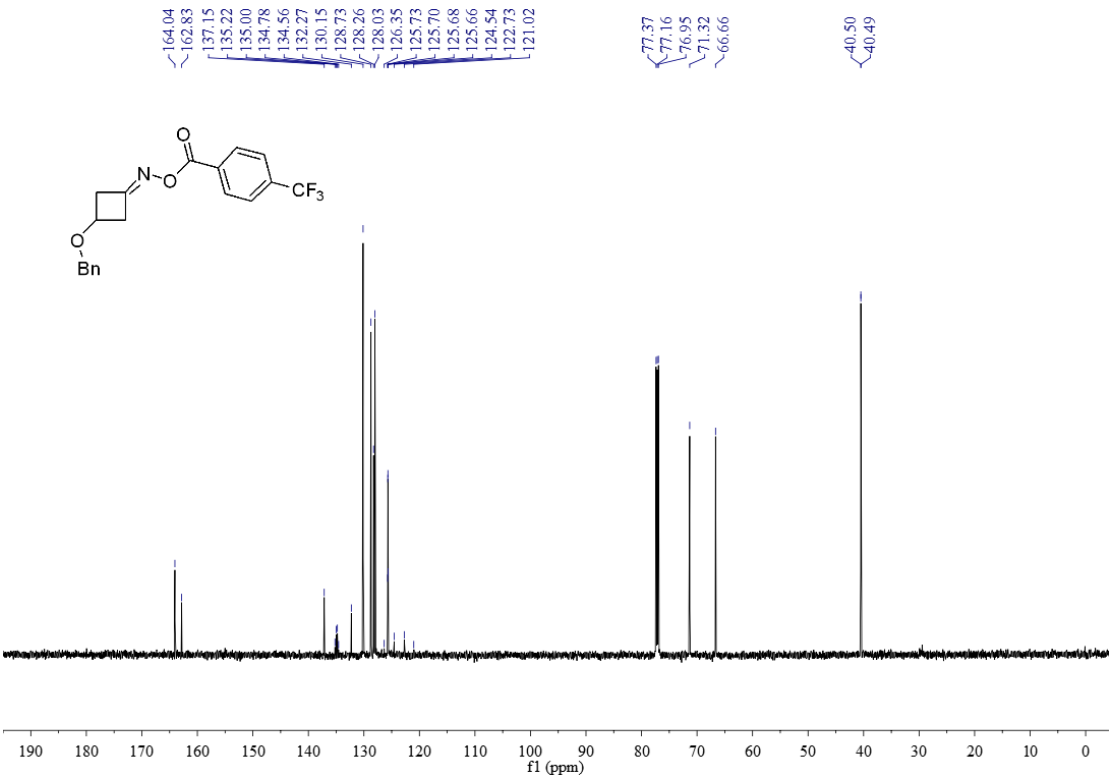
^{13}C NMR of **1l**



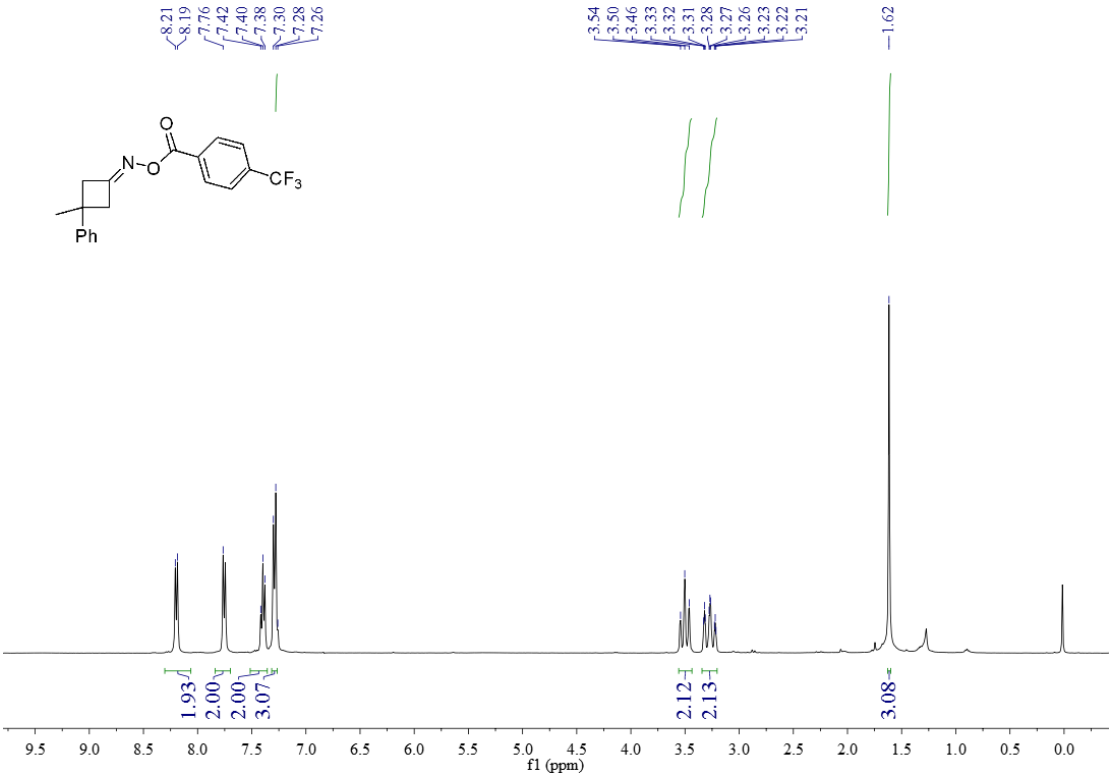
^{1}H NMR of **1m**



^{13}C NMR of **1m**



^{1}H NMR of **1n**



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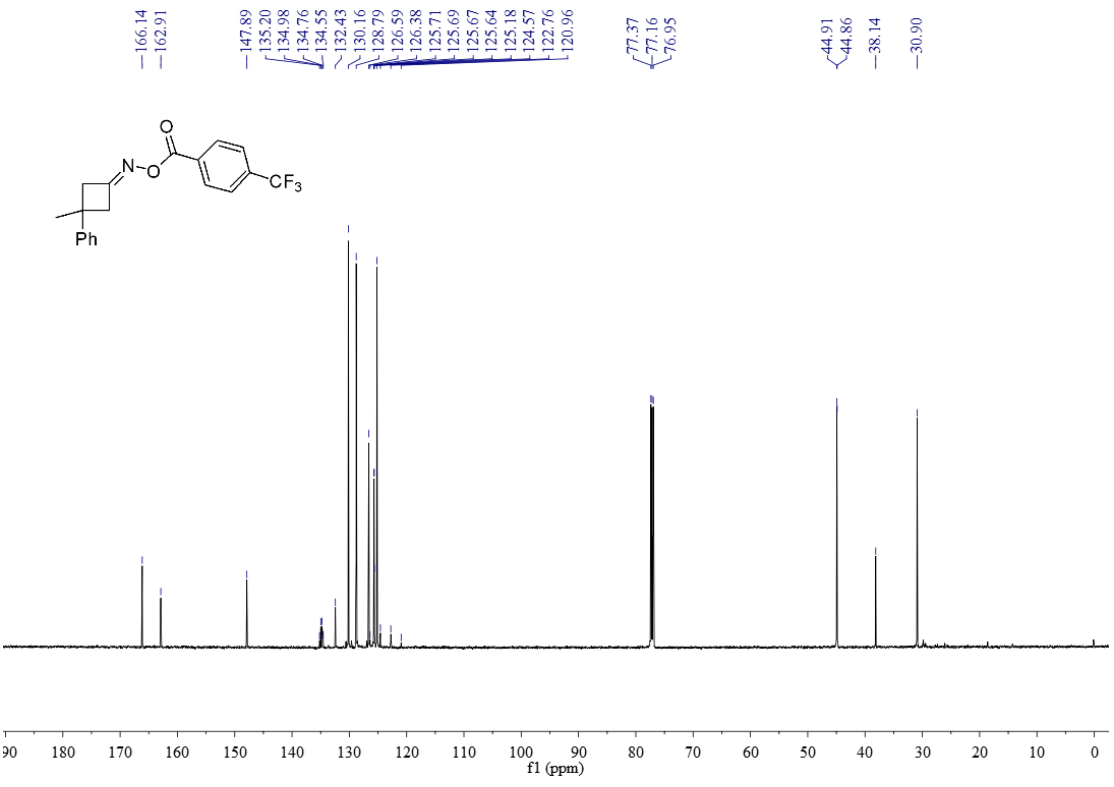
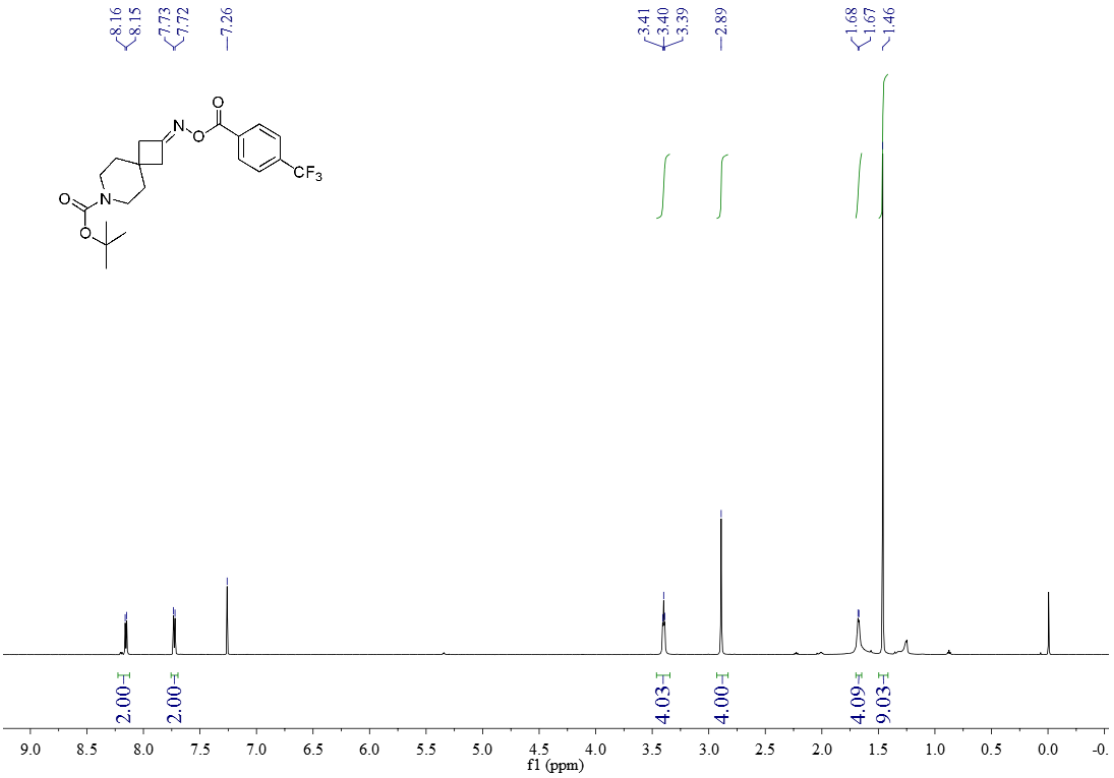
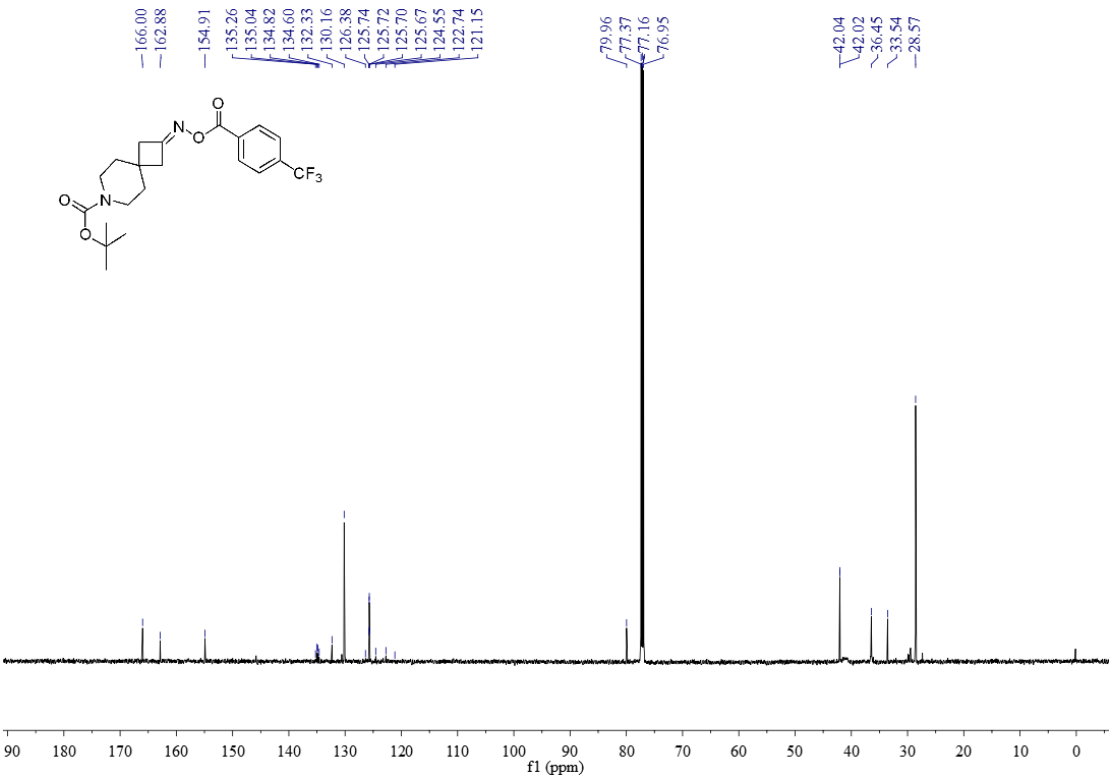


^{1}H NMR of **1p**



^{13}C NMR of **1p**



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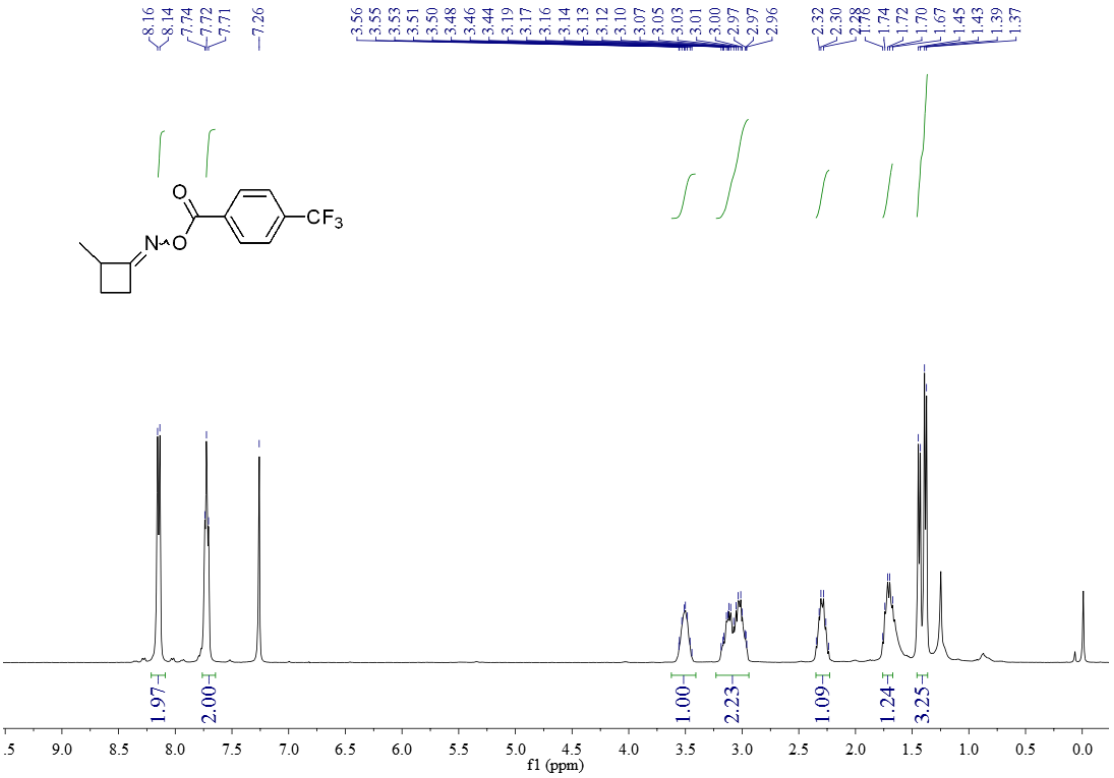
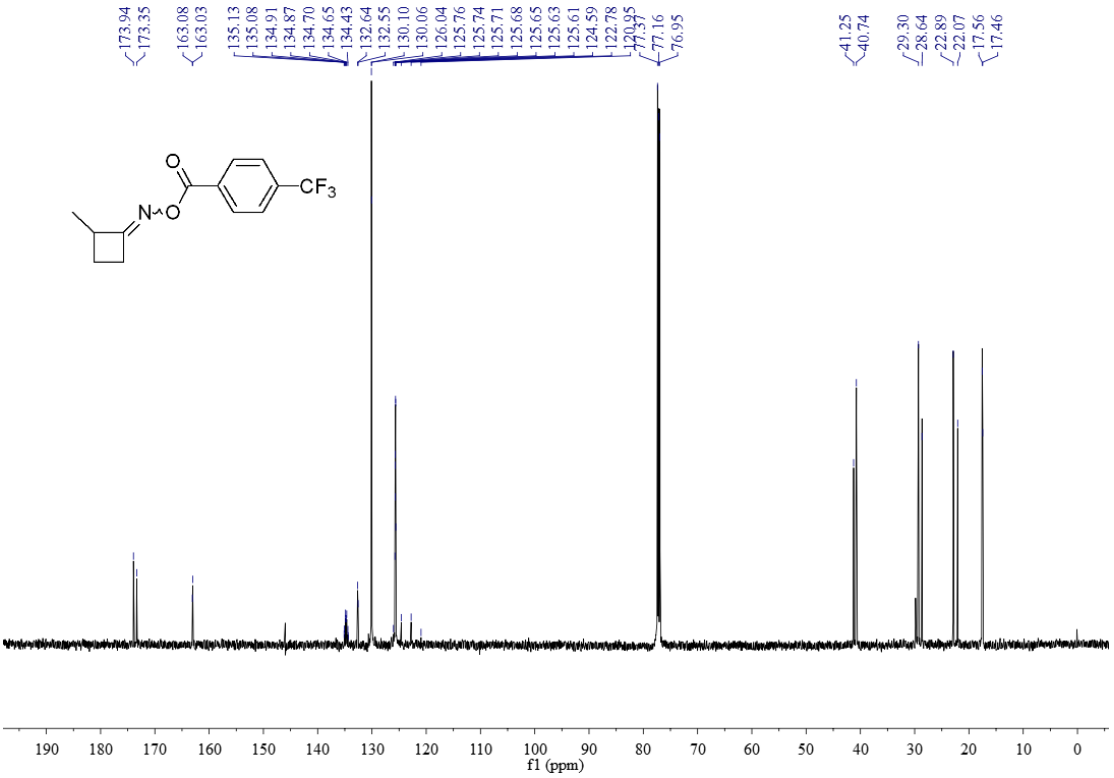
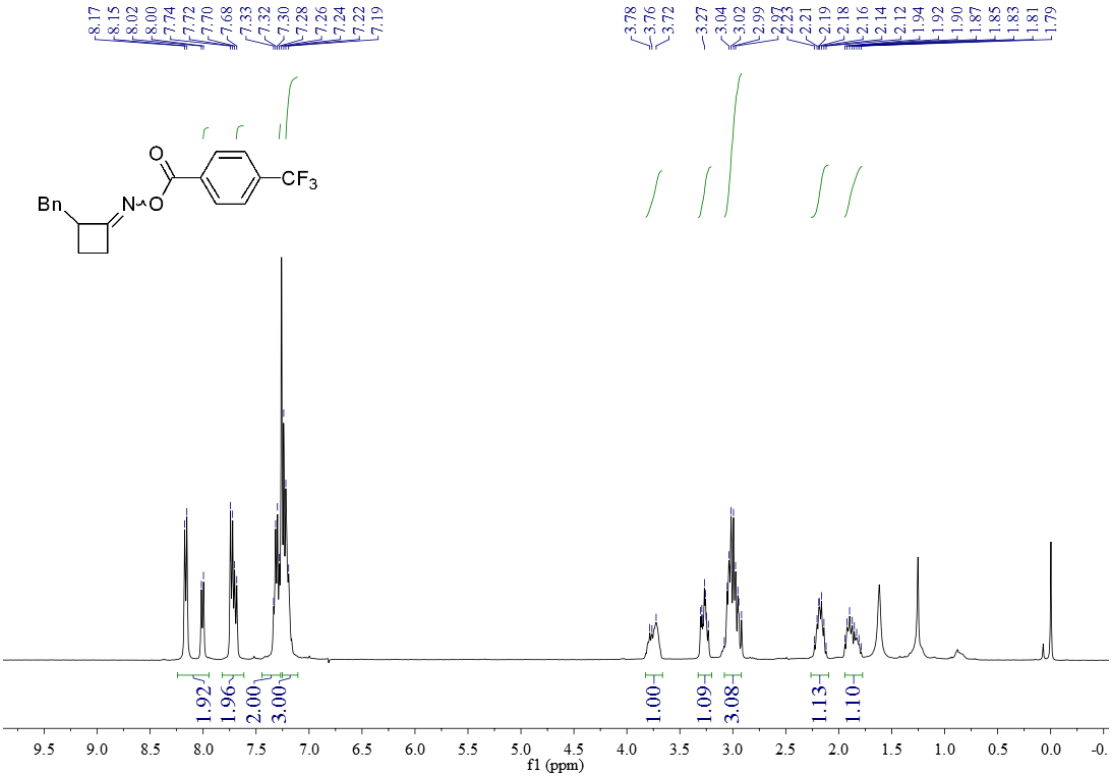


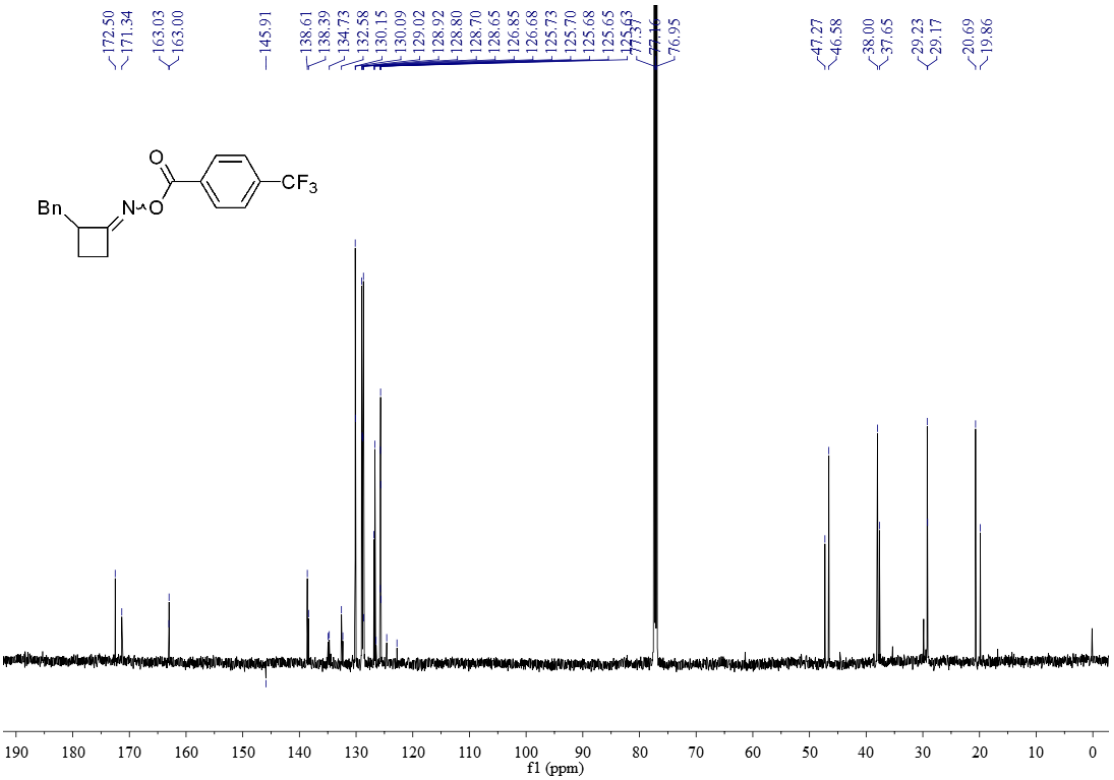
^{13}C NMR of **1q**



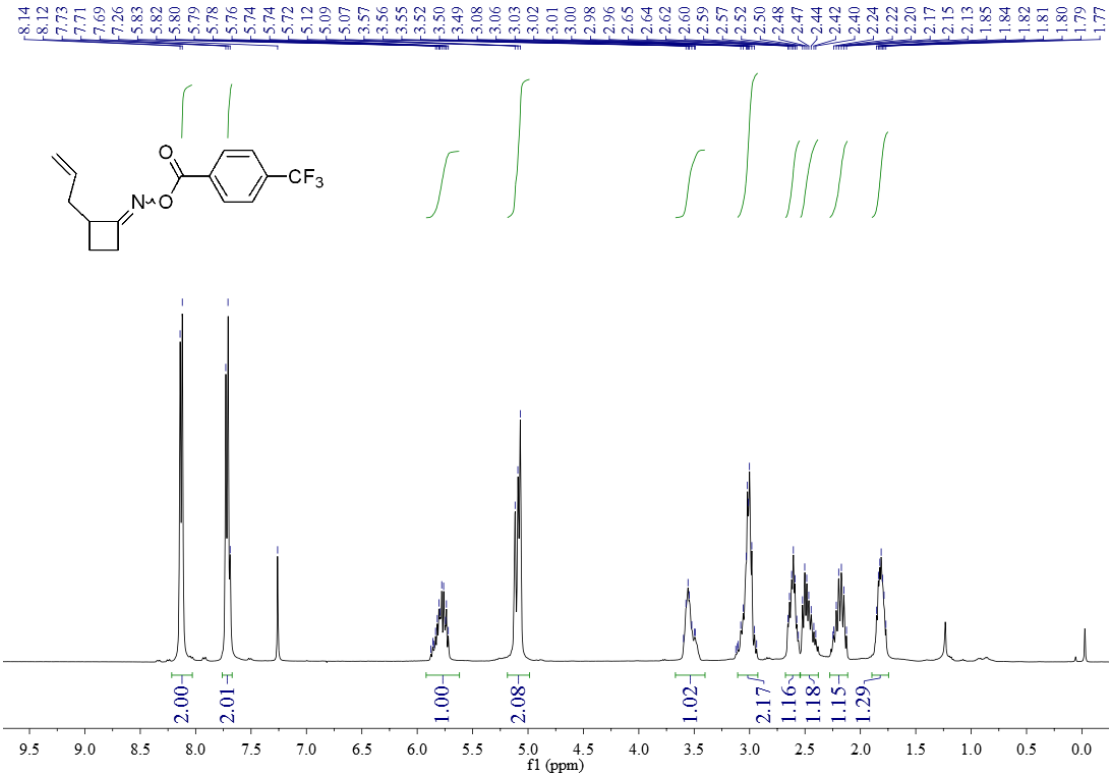
^{1}H NMR of **1r**



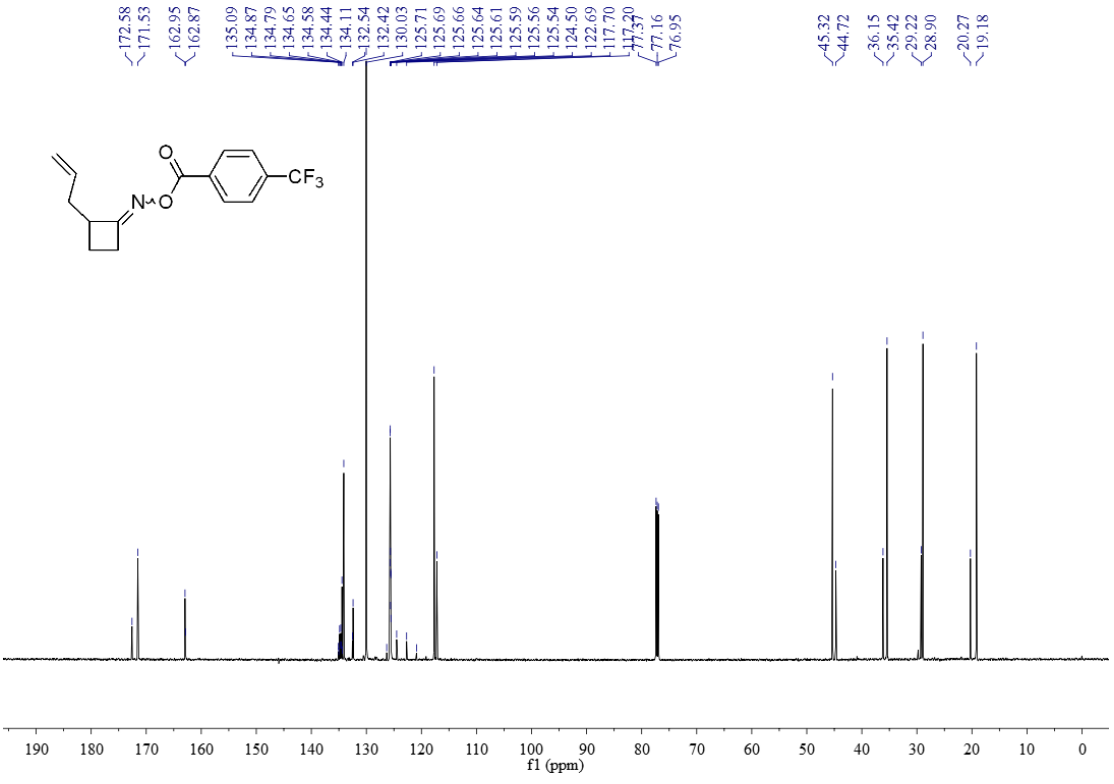
^{13}C NMR of **1r**



^{1}H NMR of **1s**



^{13}C NMR of **1s**



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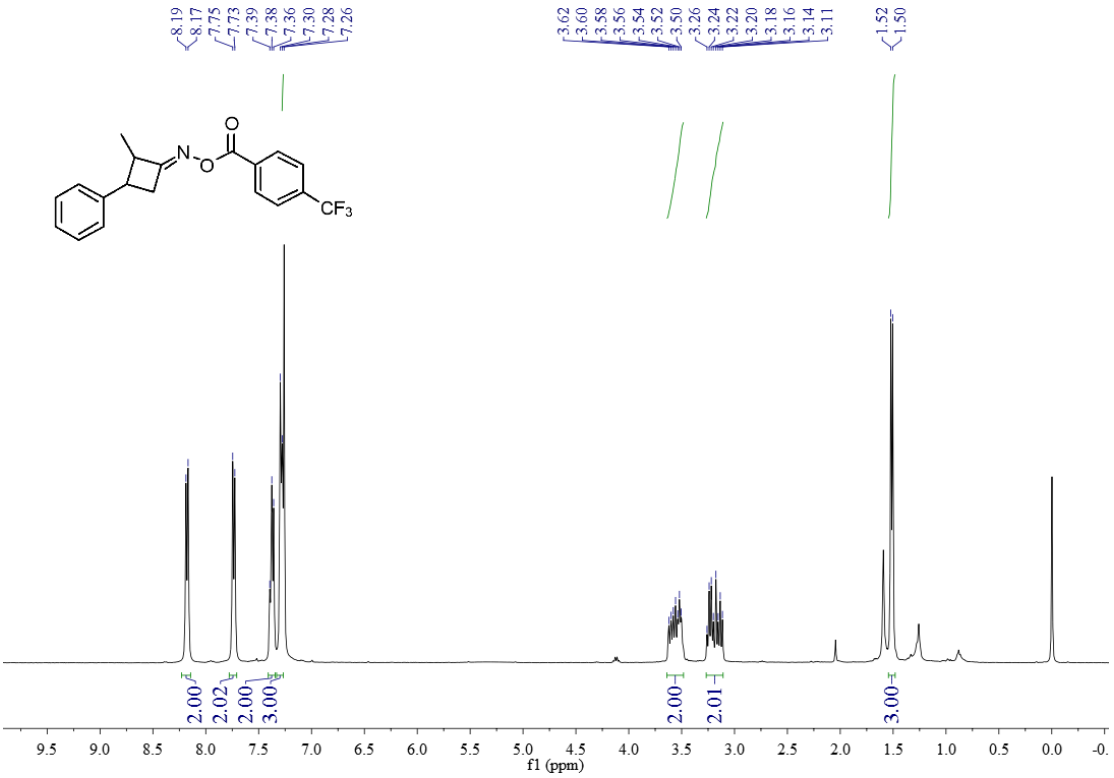
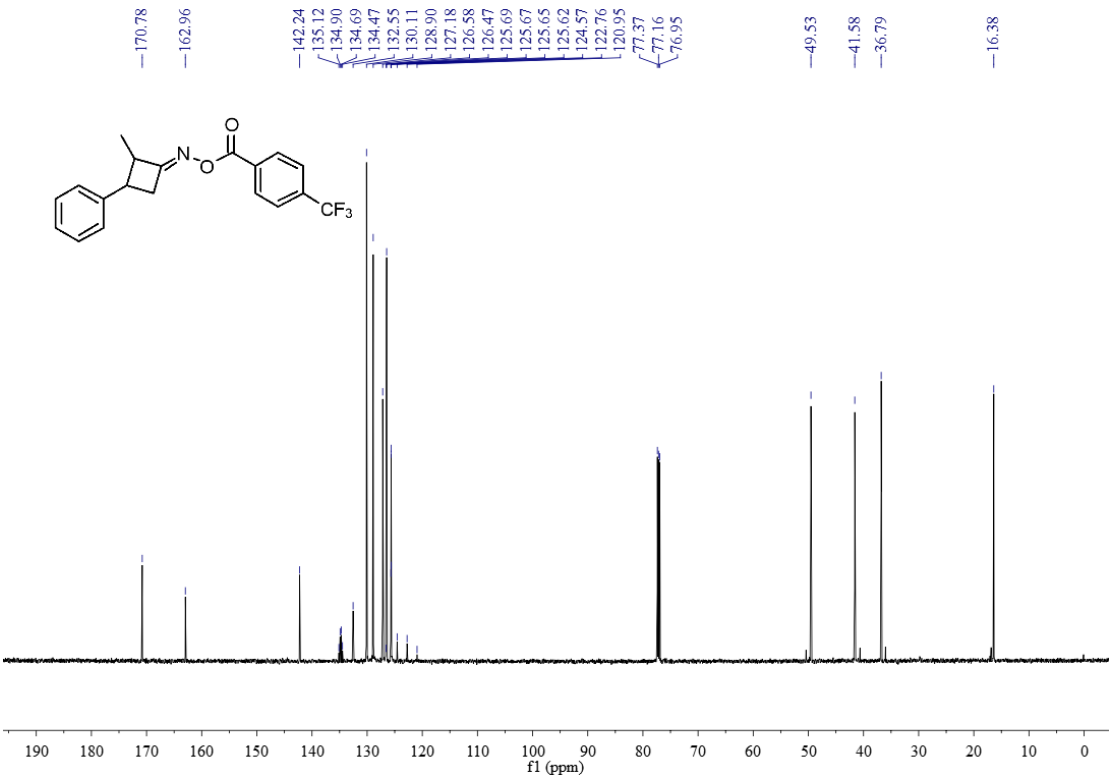


^{13}C NMR of **1t**



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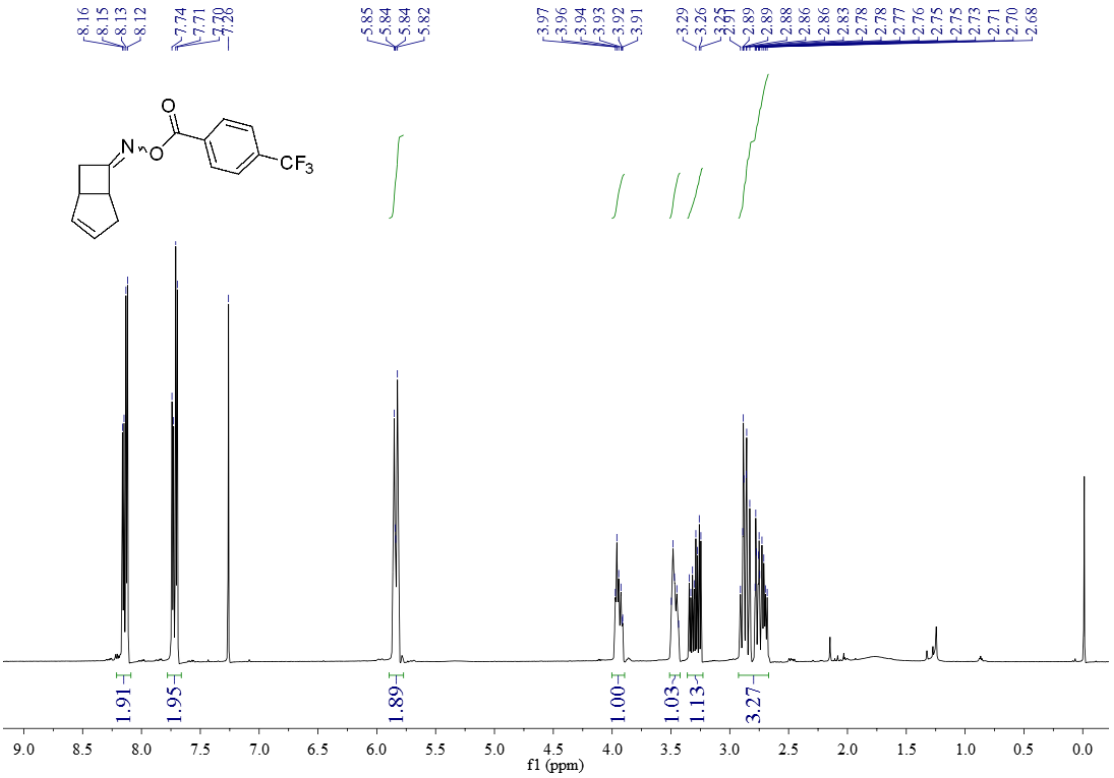
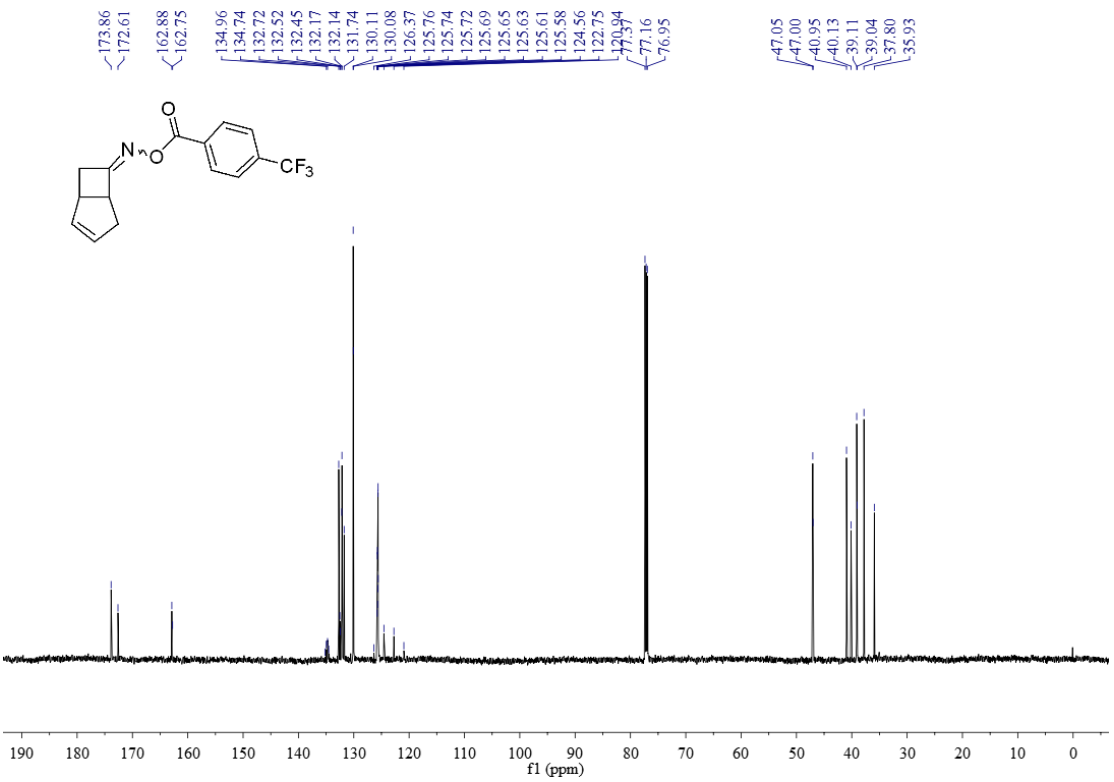
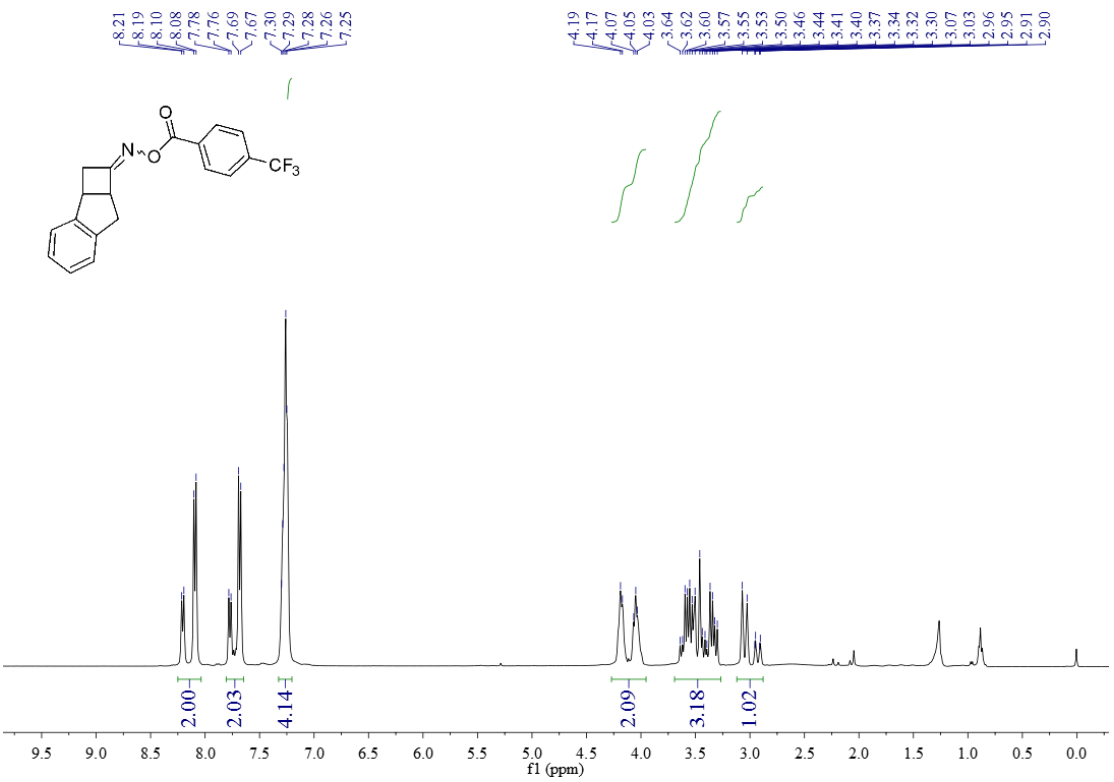


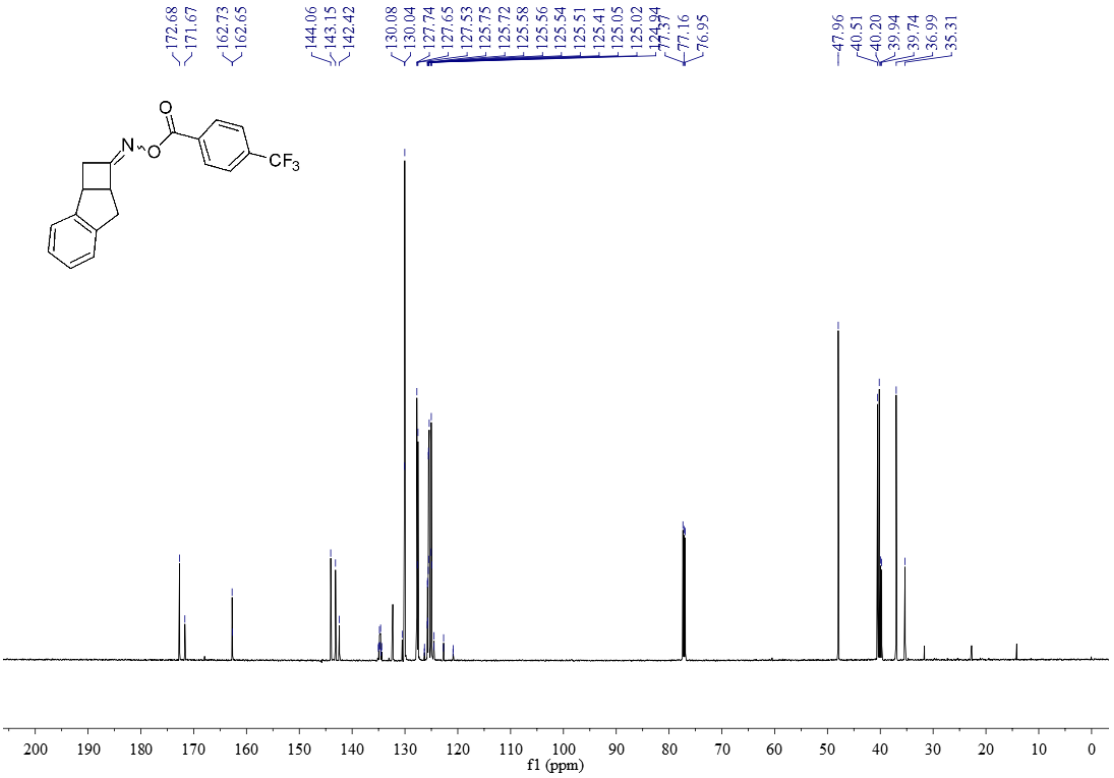
^{13}C NMR of **1u**



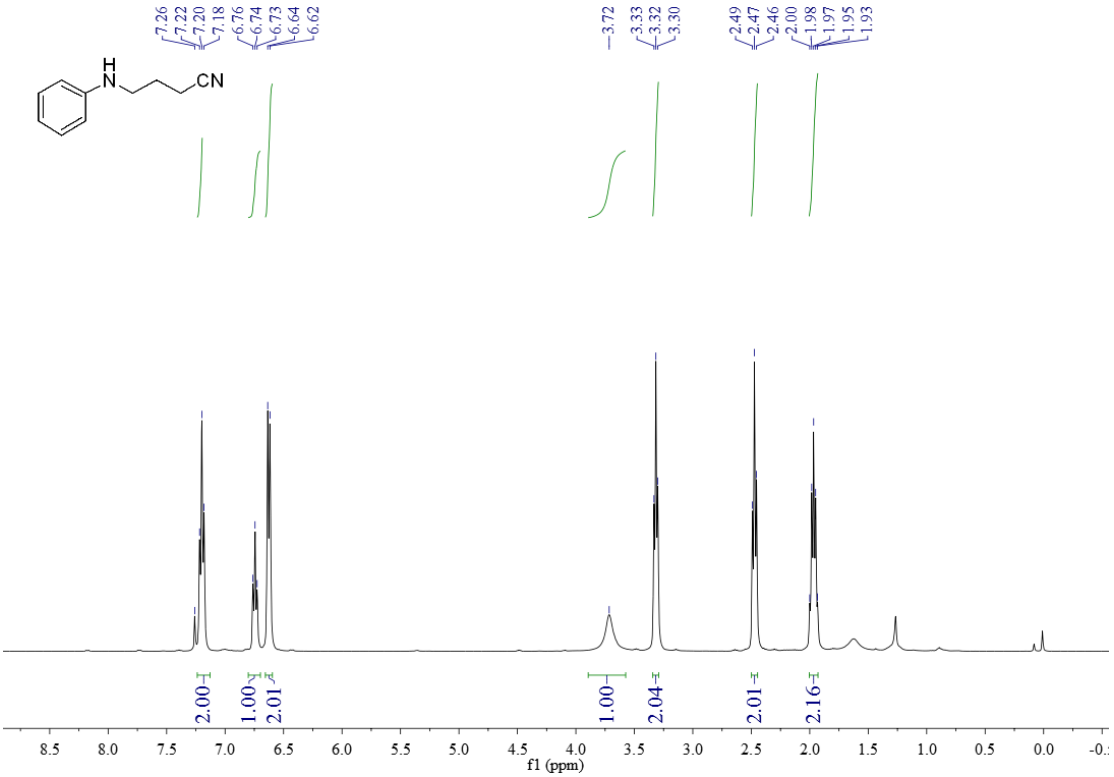
^{1}H NMR of **1v**



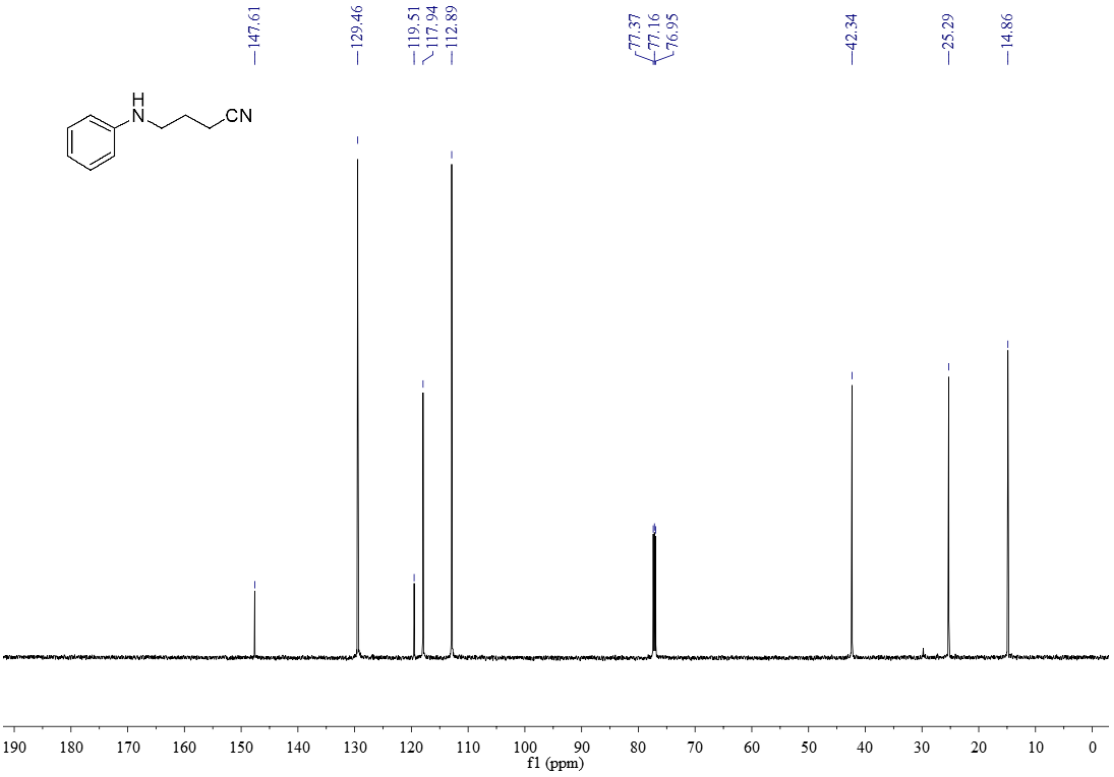
^{13}C NMR of **1v**



^{1}H NMR of **3a**



^{13}C NMR of **3a**



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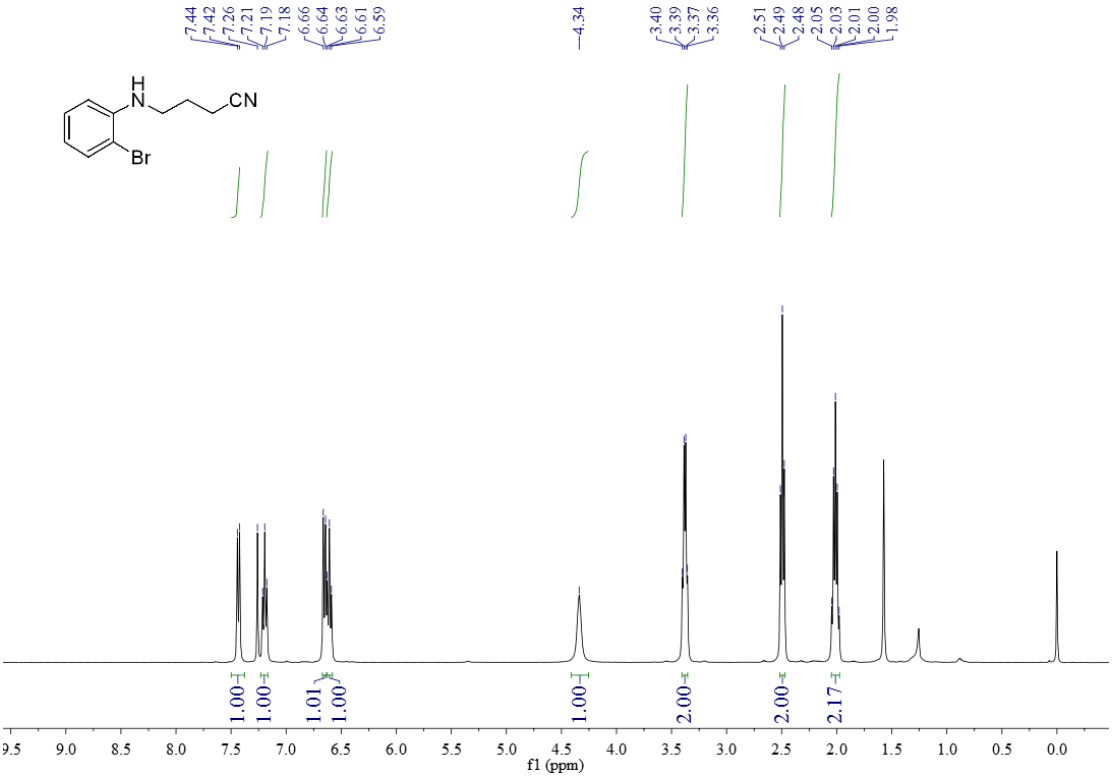
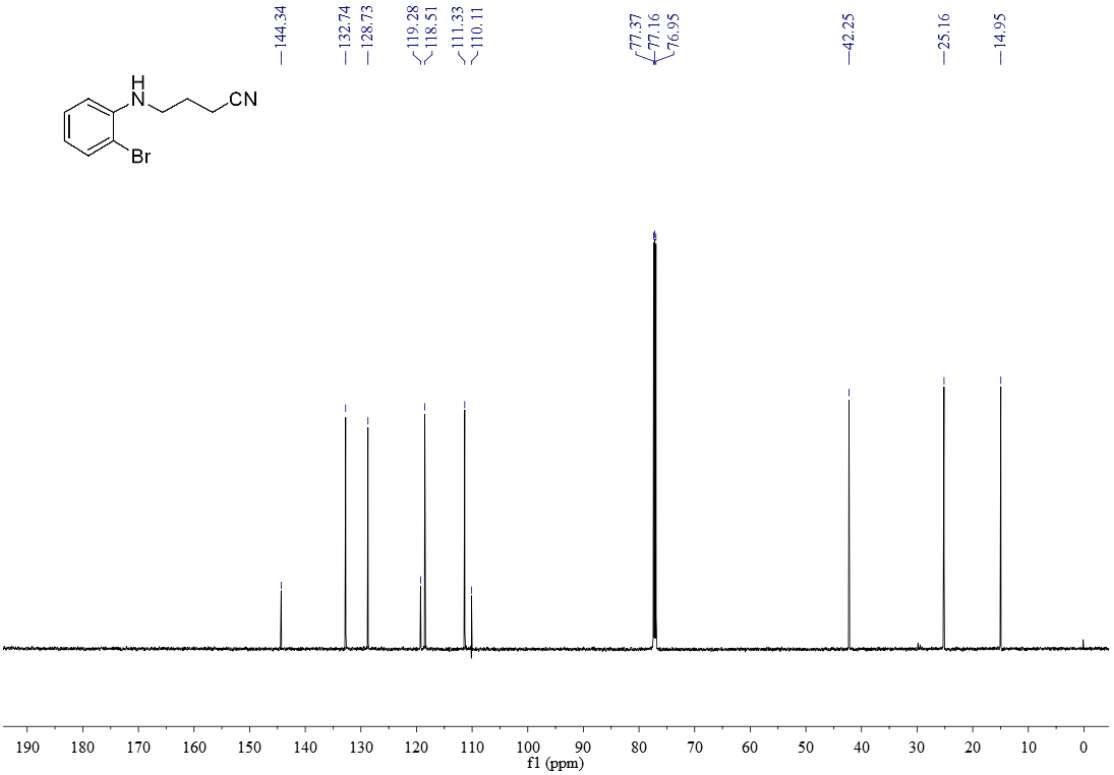


^{13}C NMR of **3b**



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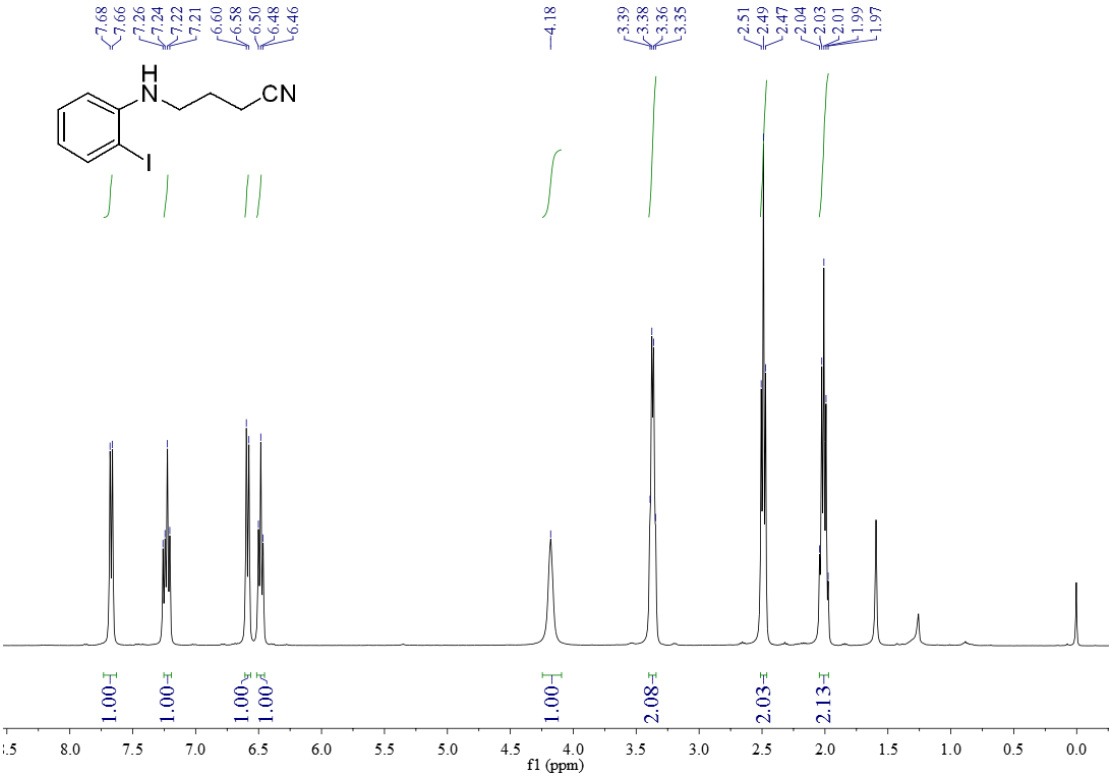
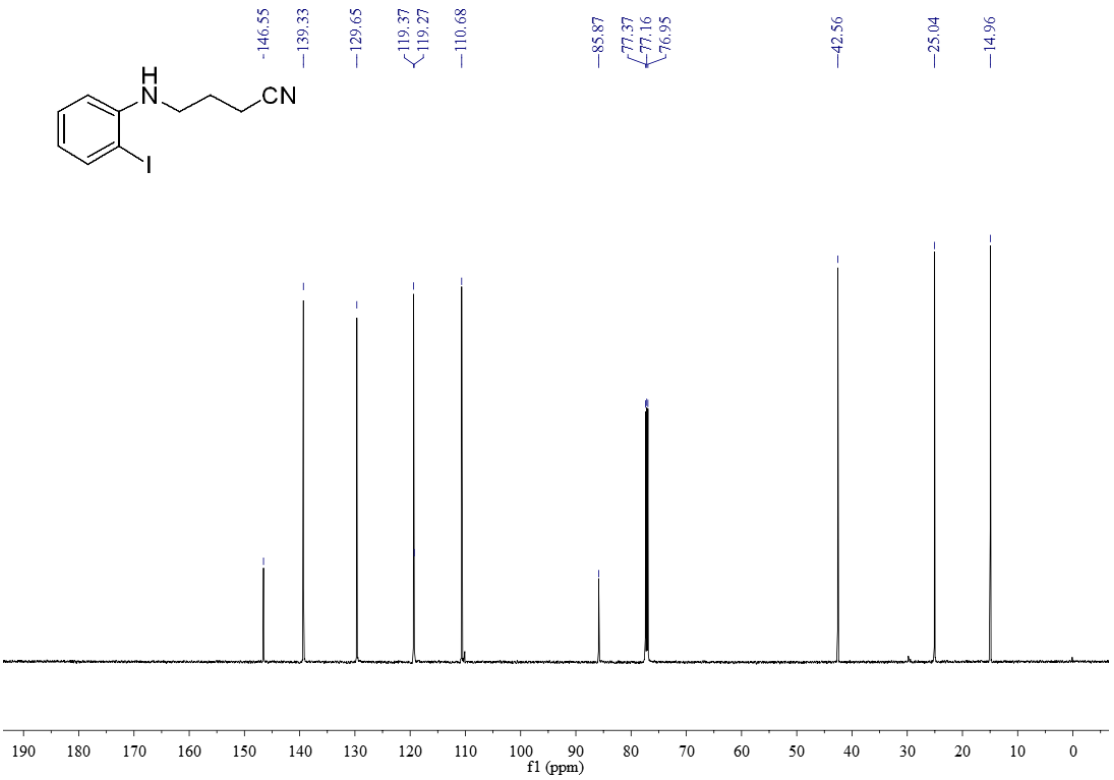
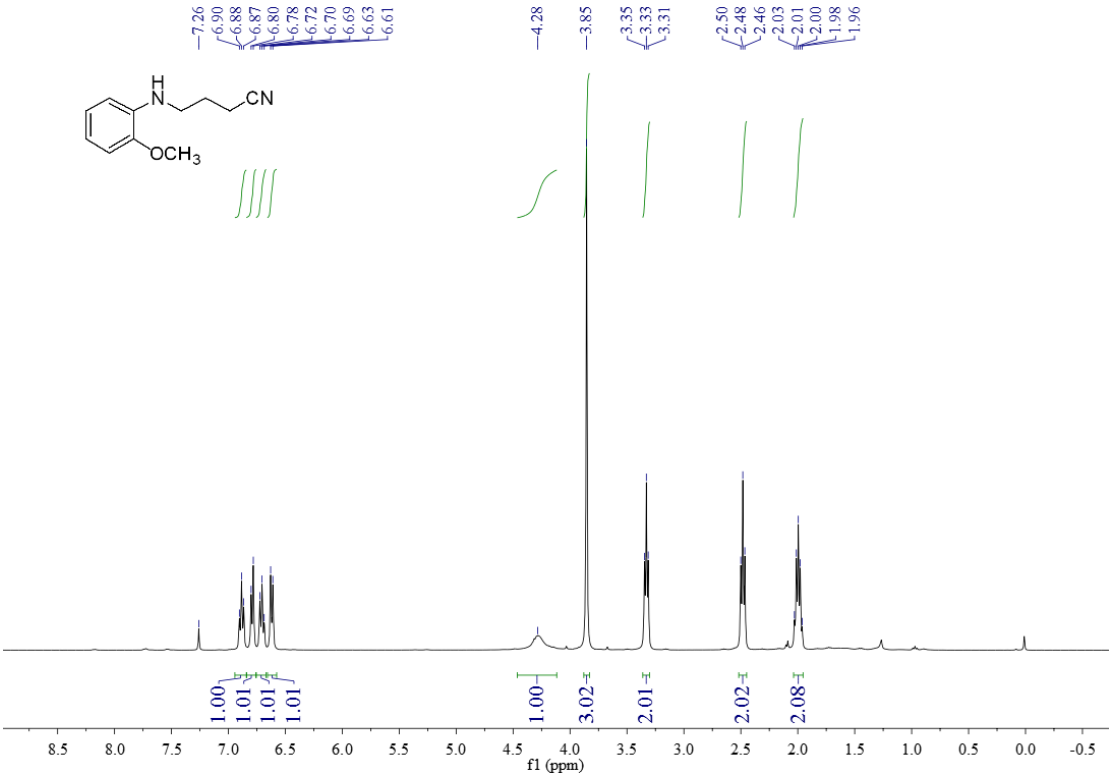


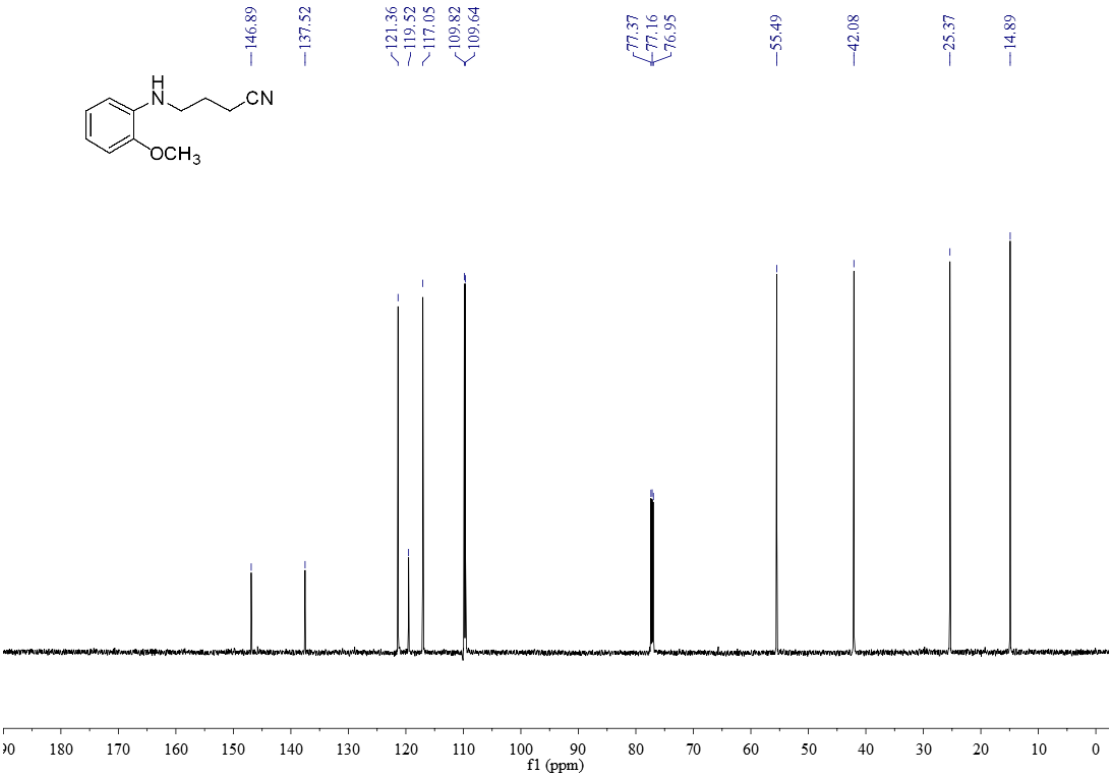
^{13}C NMR of **3c**



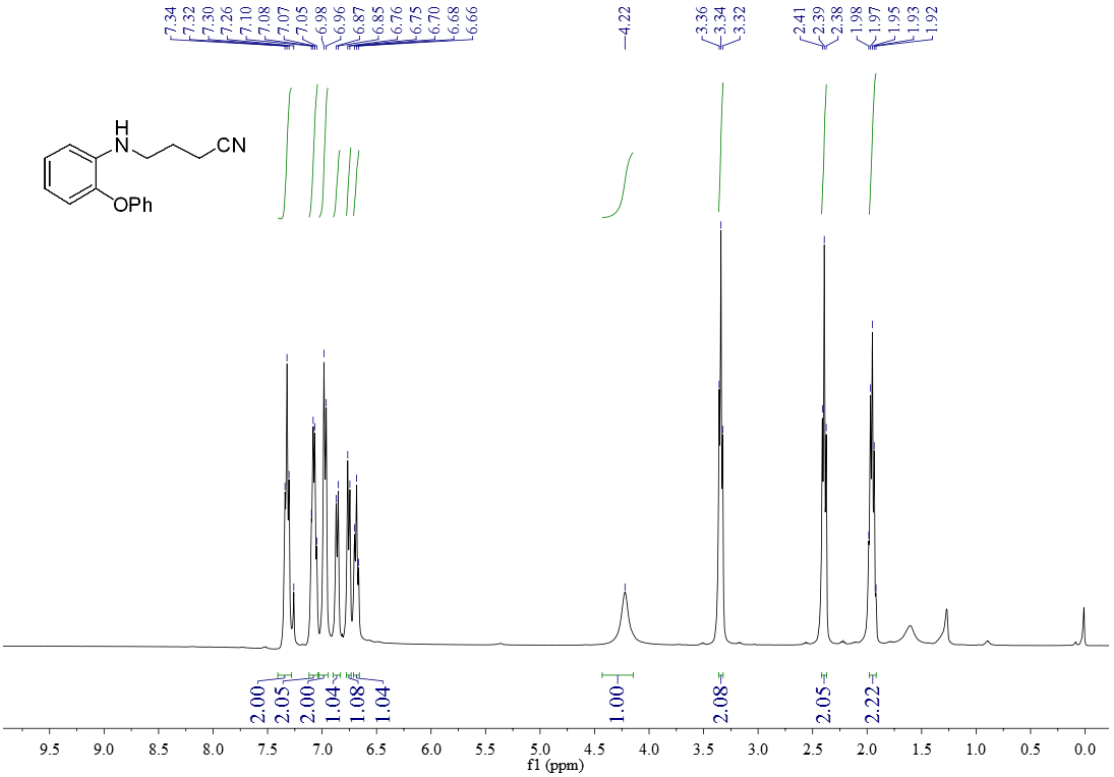
^{1}H NMR of **3d**



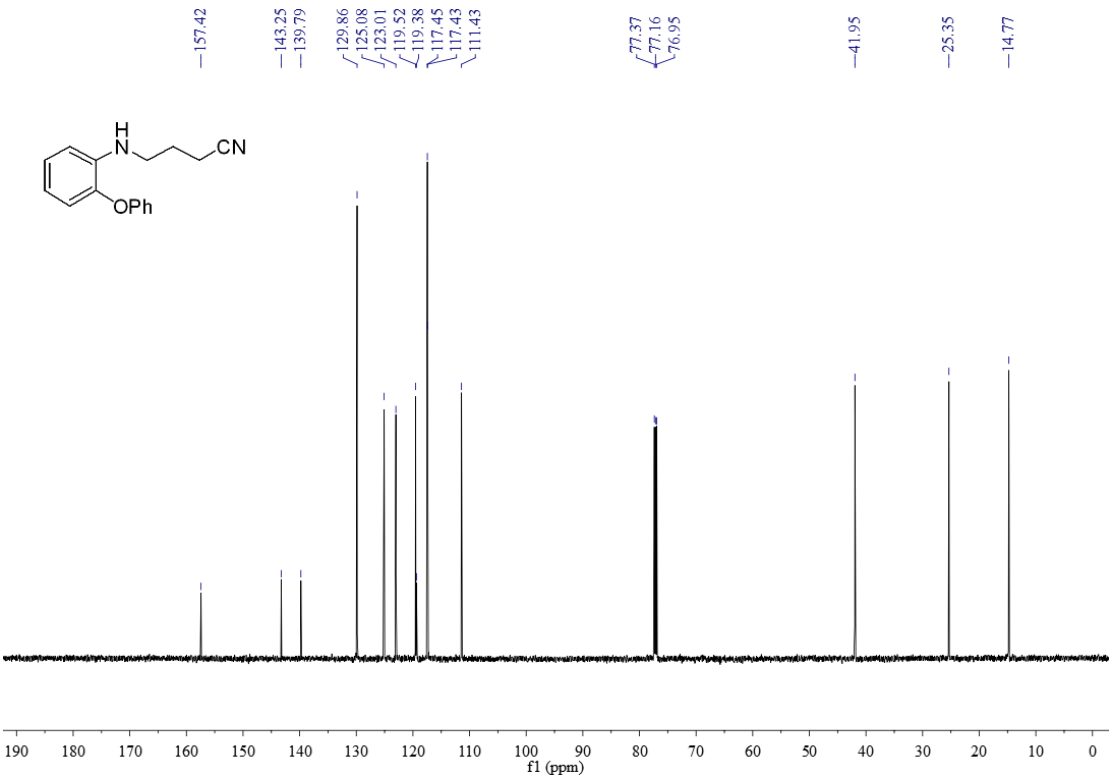
^{13}C NMR of **3d**



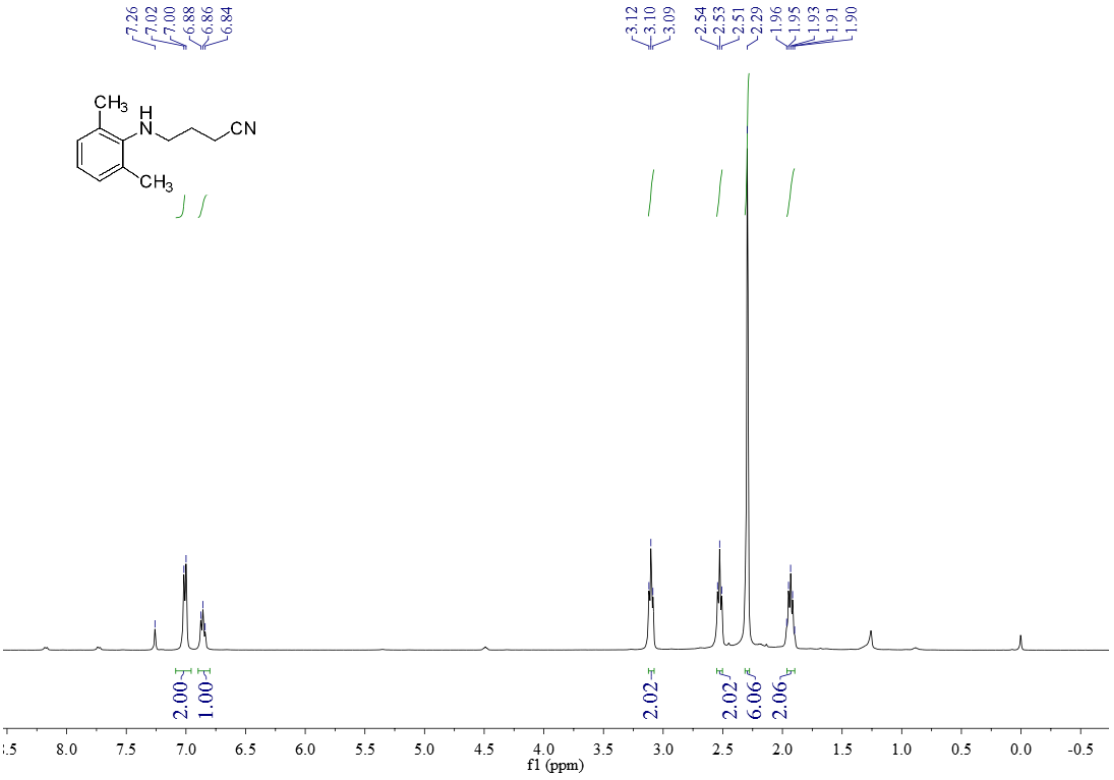
^{1}H NMR of **3e**



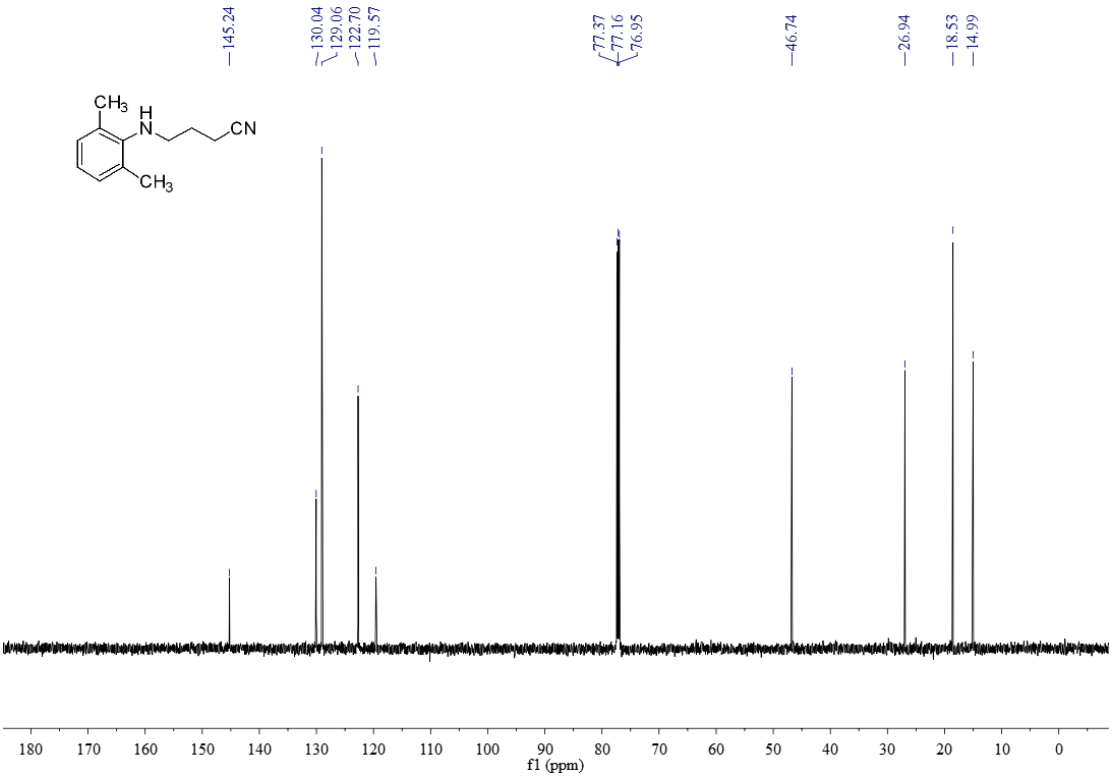
^{13}C NMR of **3e**



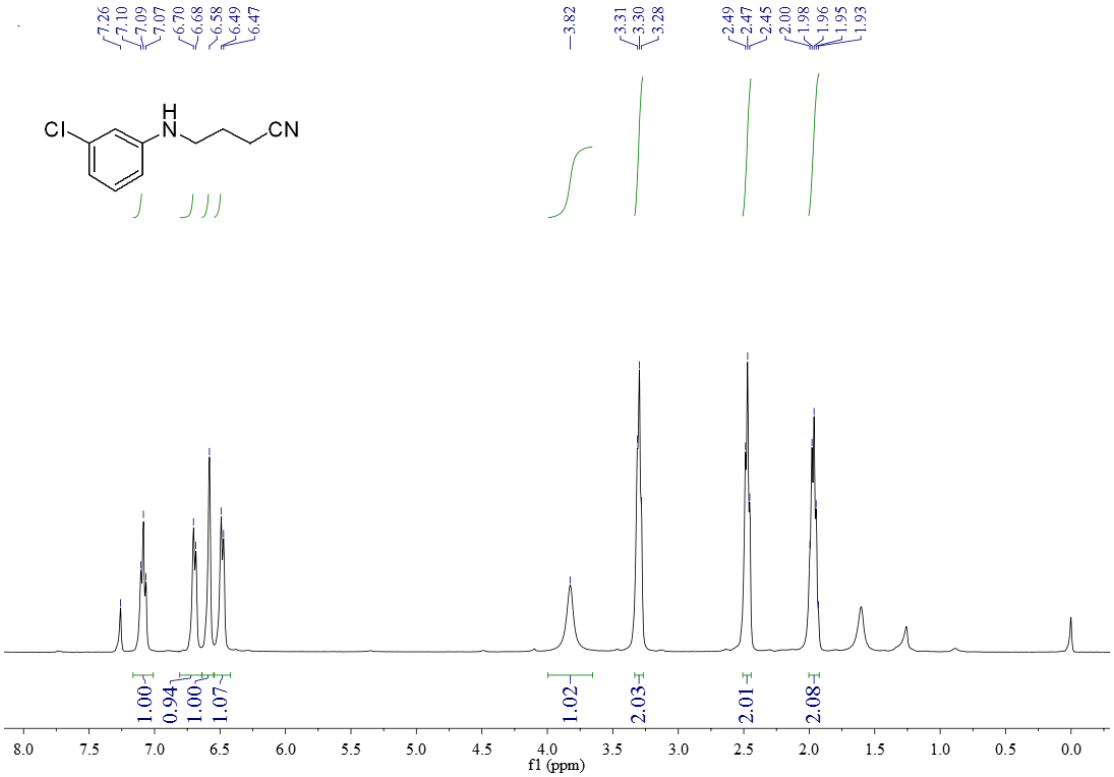
^{1}H NMR of **3f**



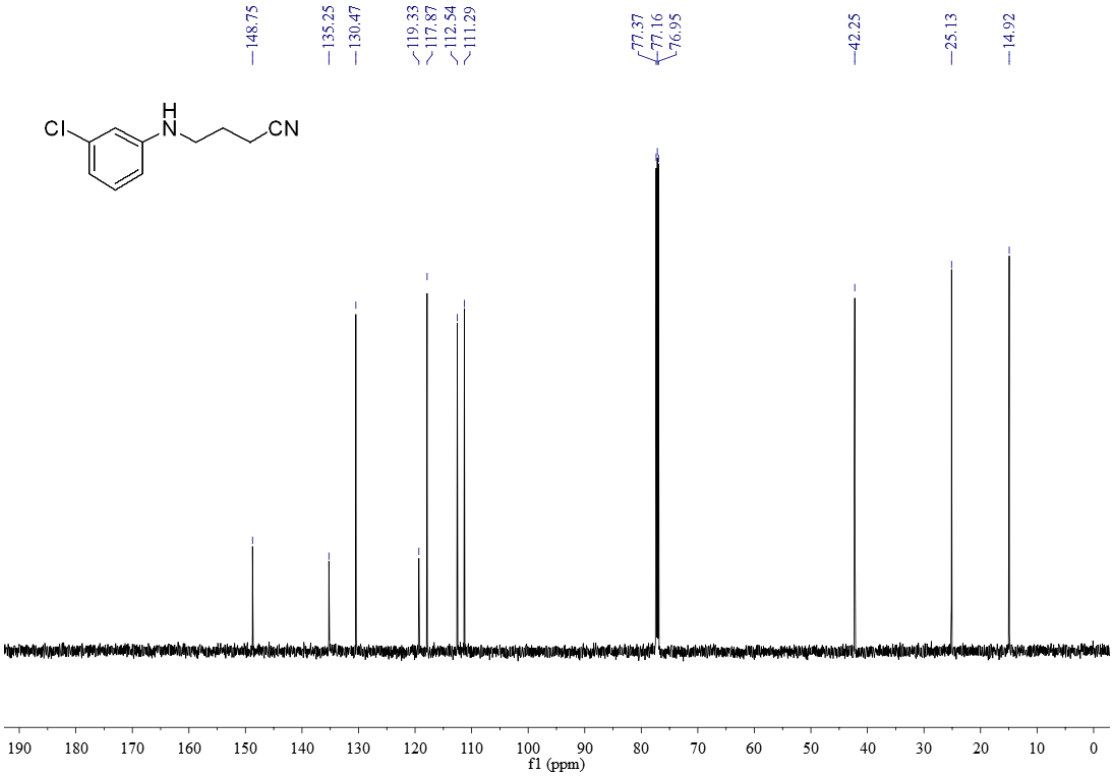
^{13}C NMR of **3f**



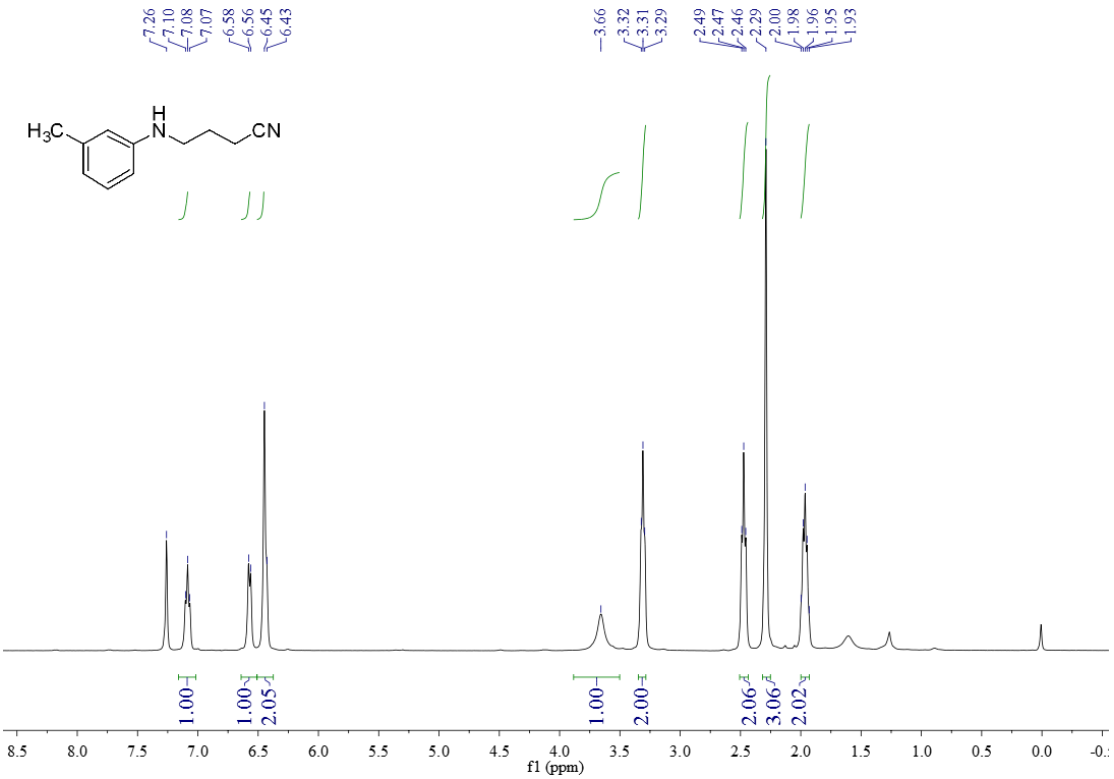
^{1}H NMR of **3g**



^{13}C NMR of **3g**



^{1}H NMR of **3h**



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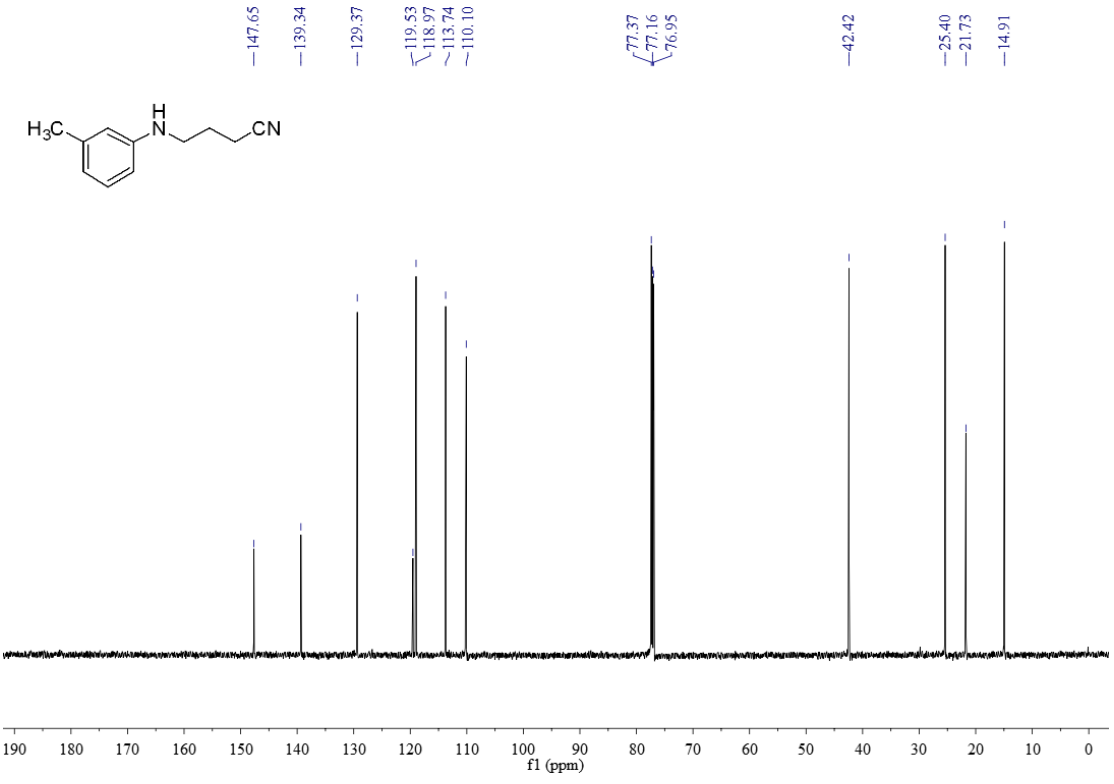
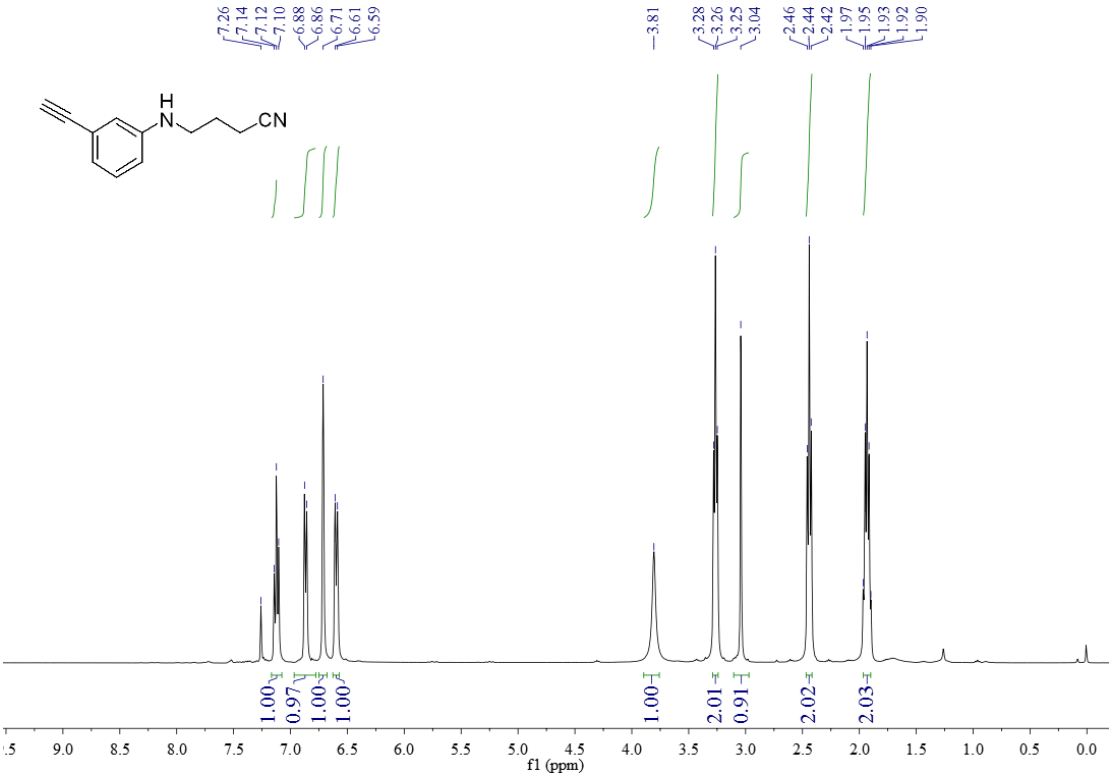
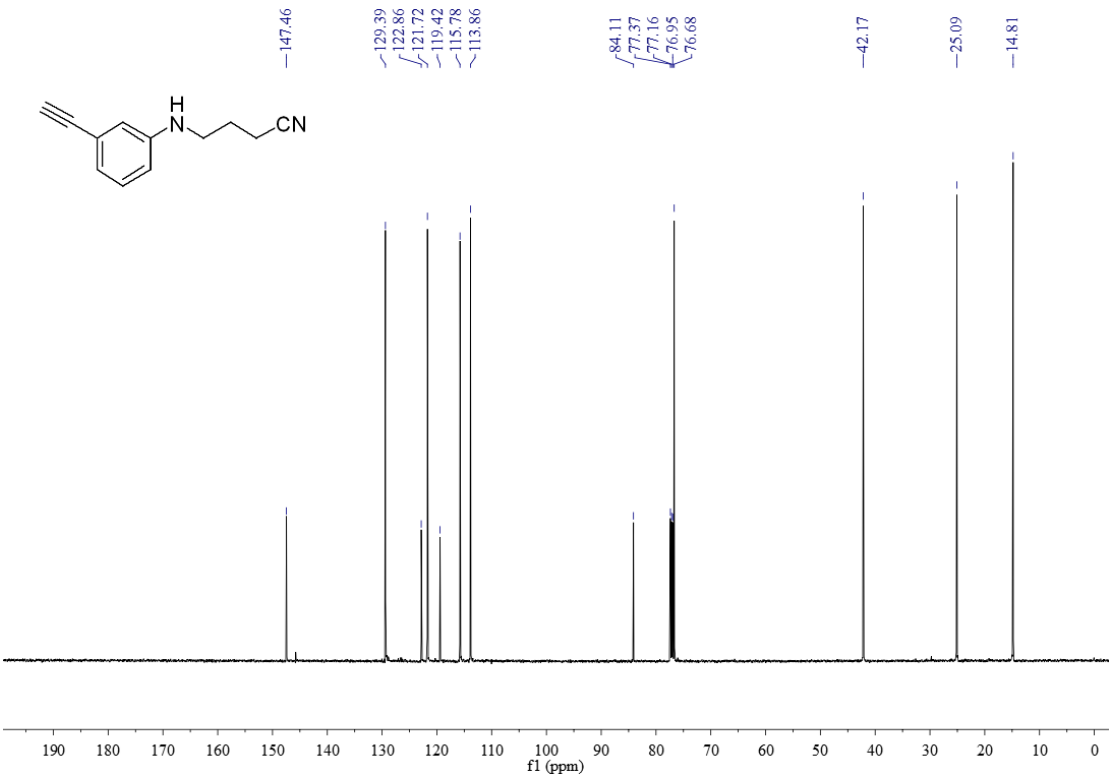


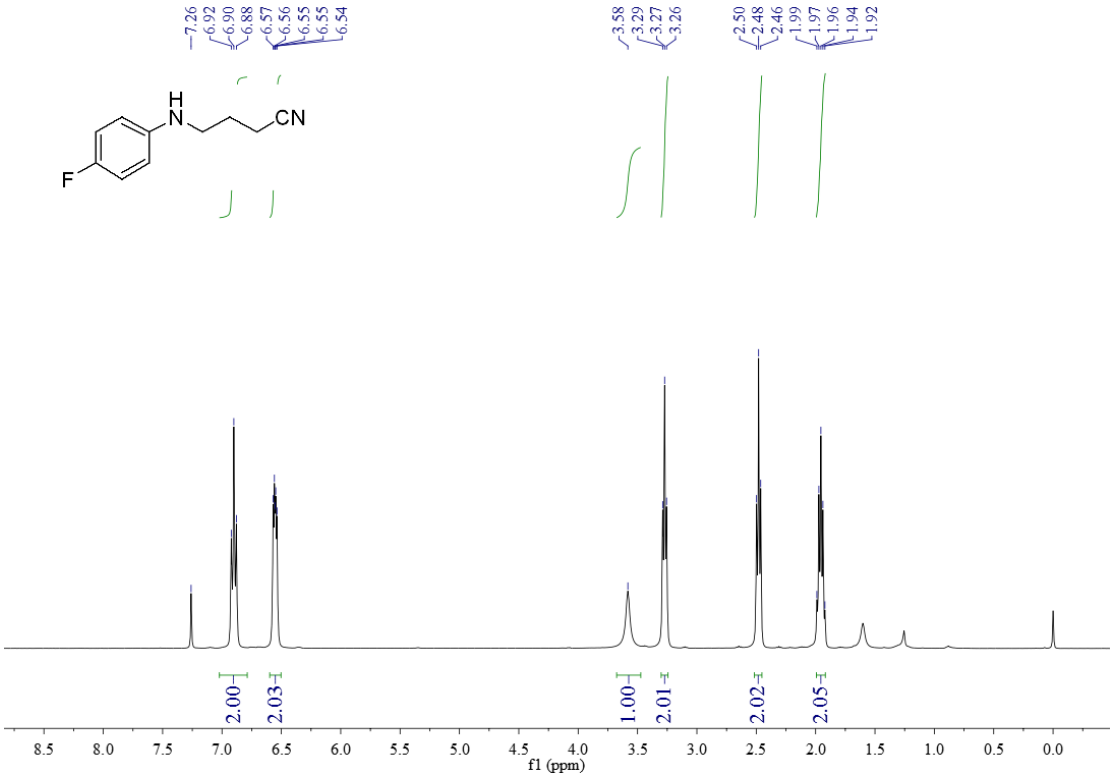
^{1}H NMR of **3i**



^{13}C NMR of **3i**



^{1}H NMR of **3j**



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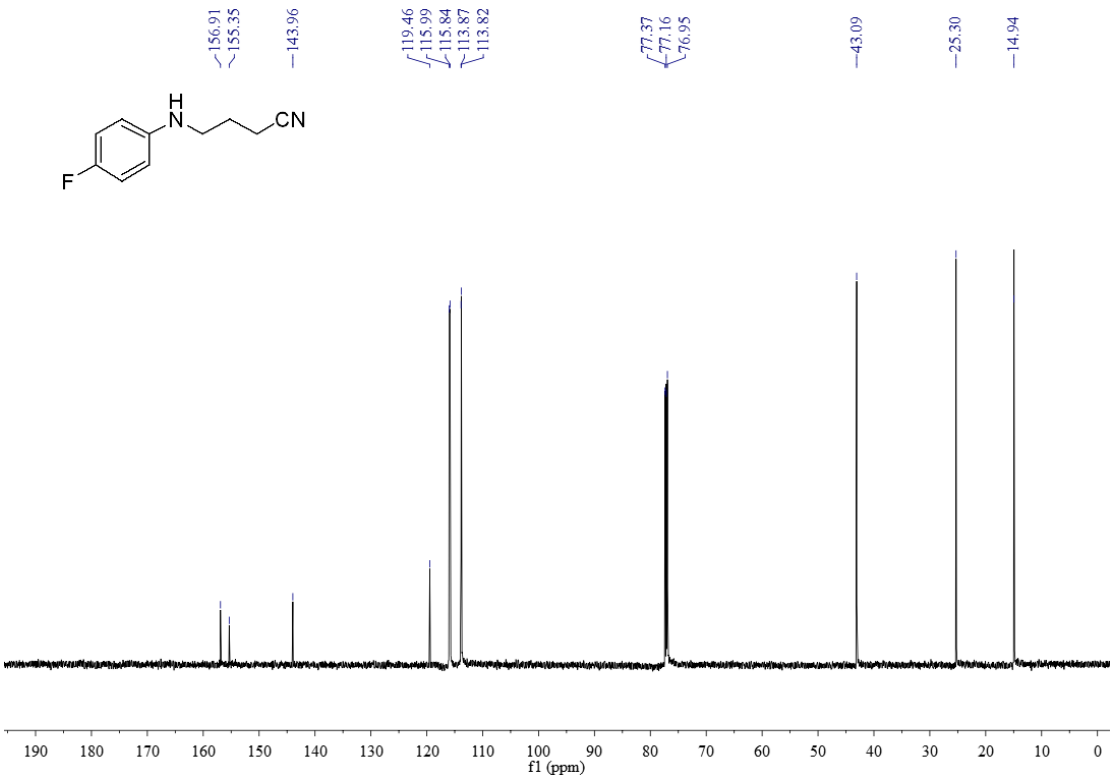
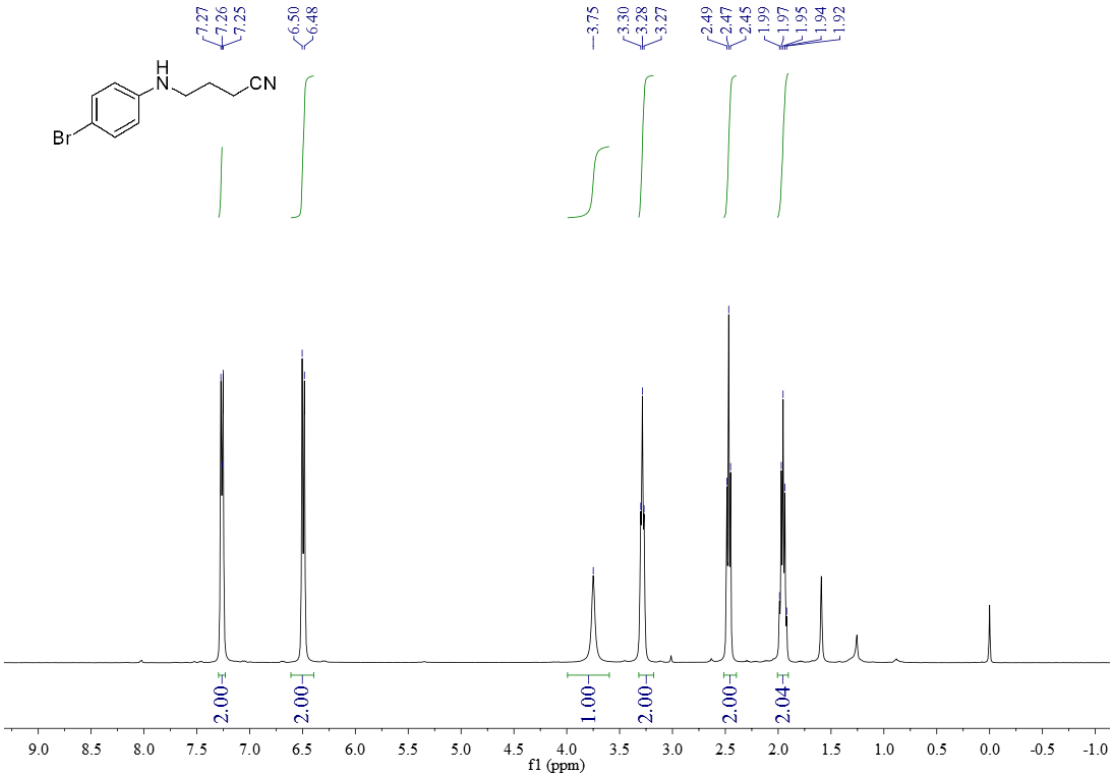


^{1}H NMR of **3k**



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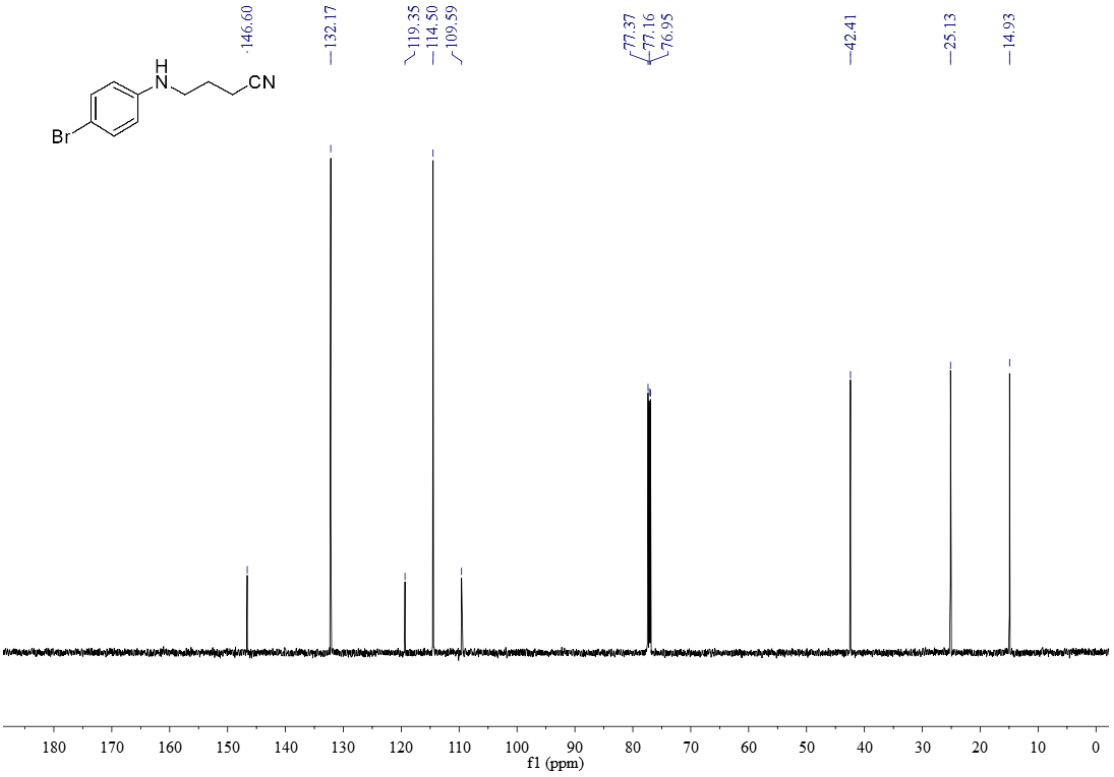
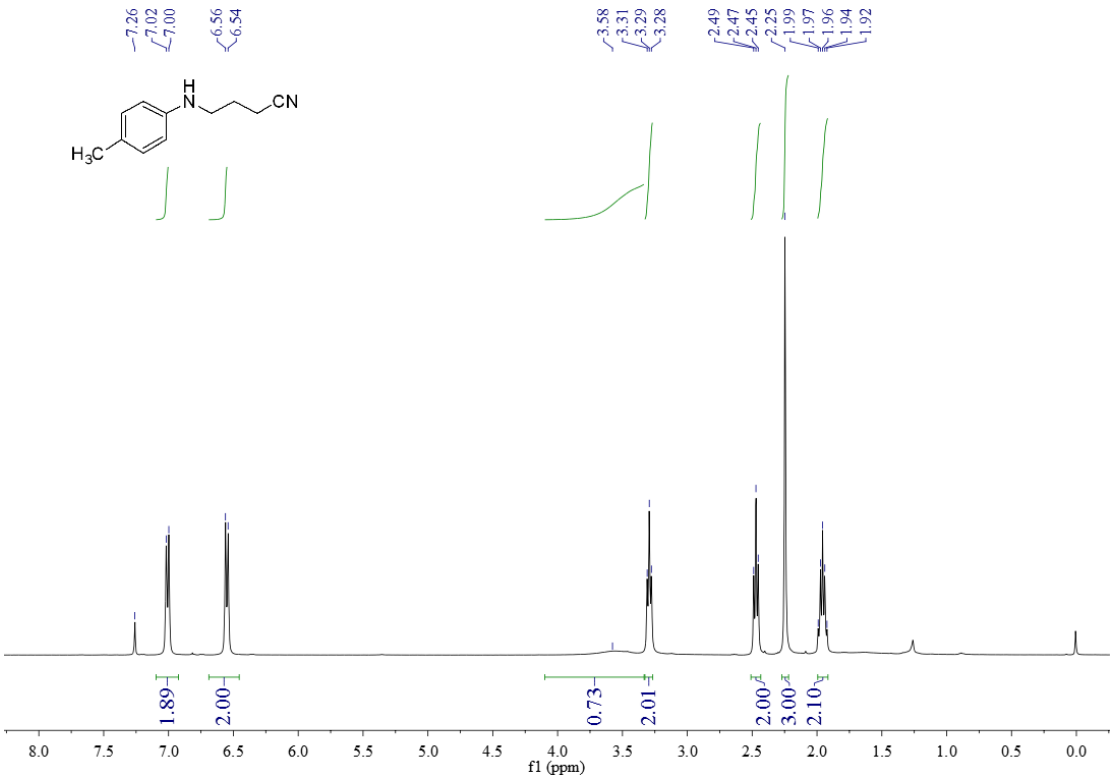
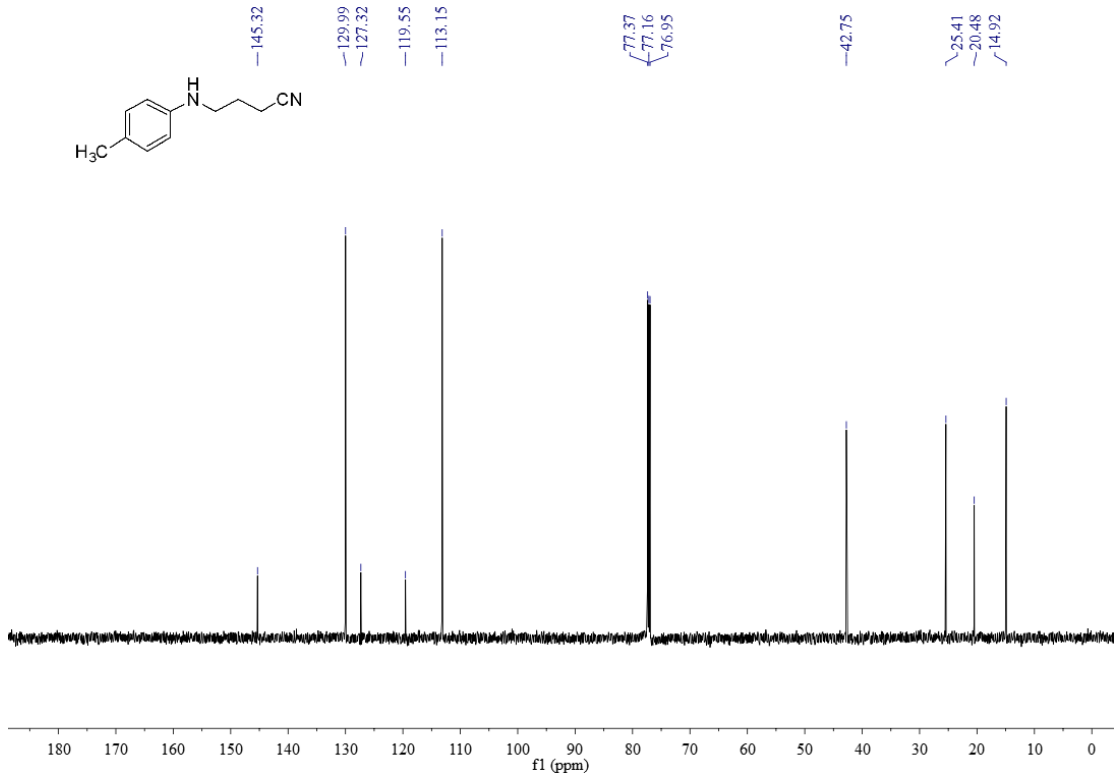


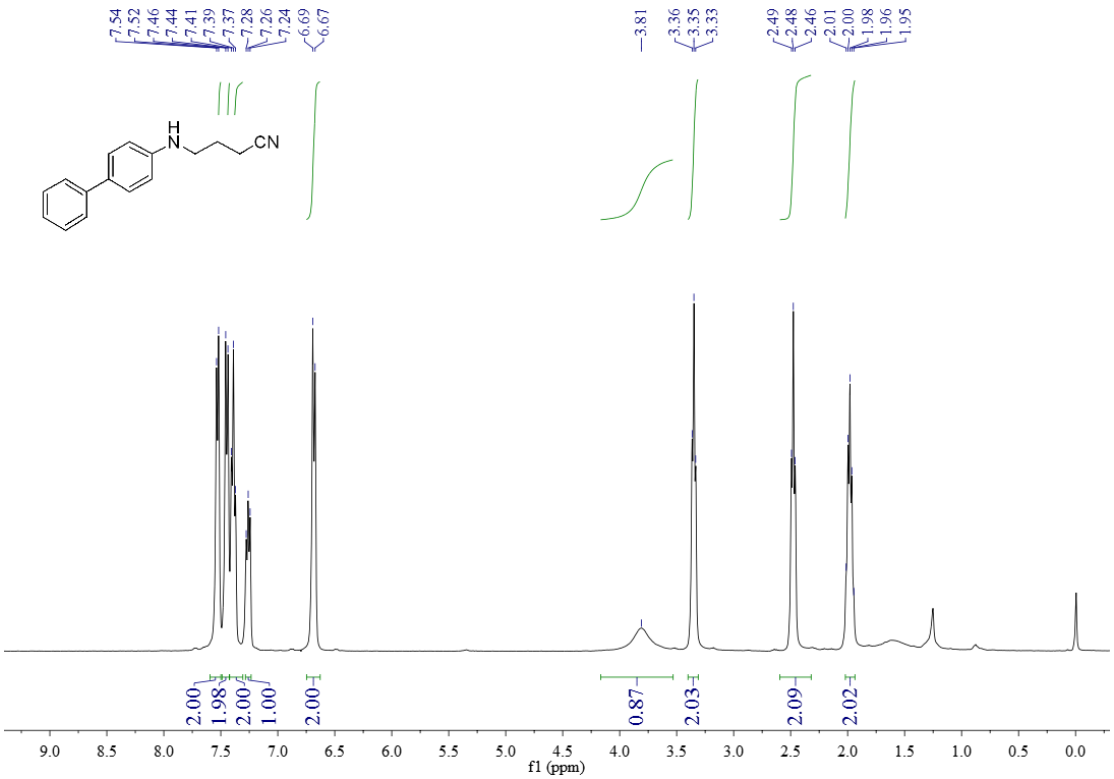
^{1}H NMR of **3l**



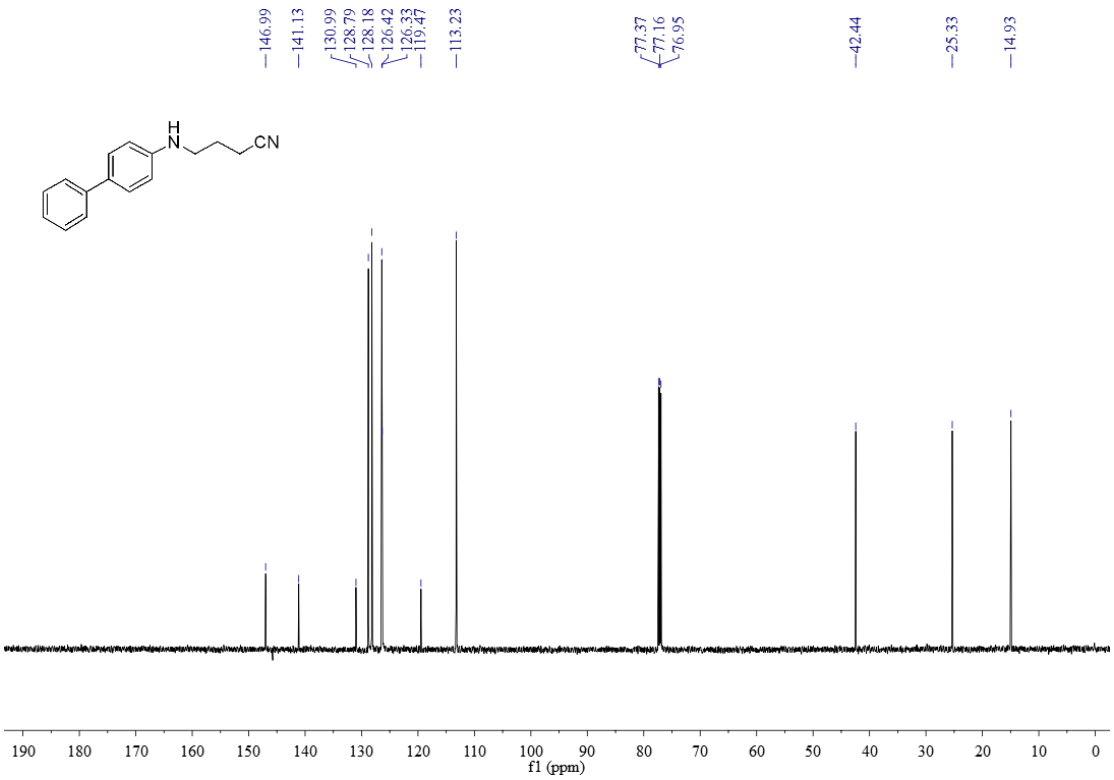
^{13}C NMR of **3l**



^{1}H NMR of **3m**



^{13}C NMR of **3m**



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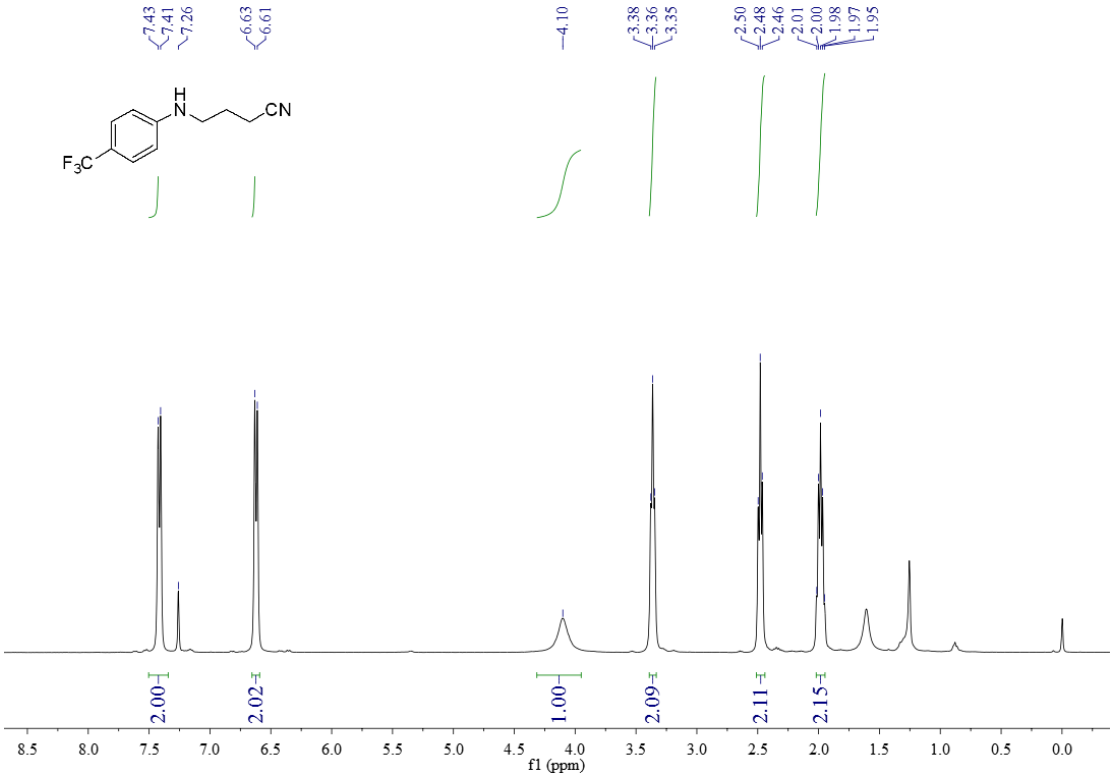

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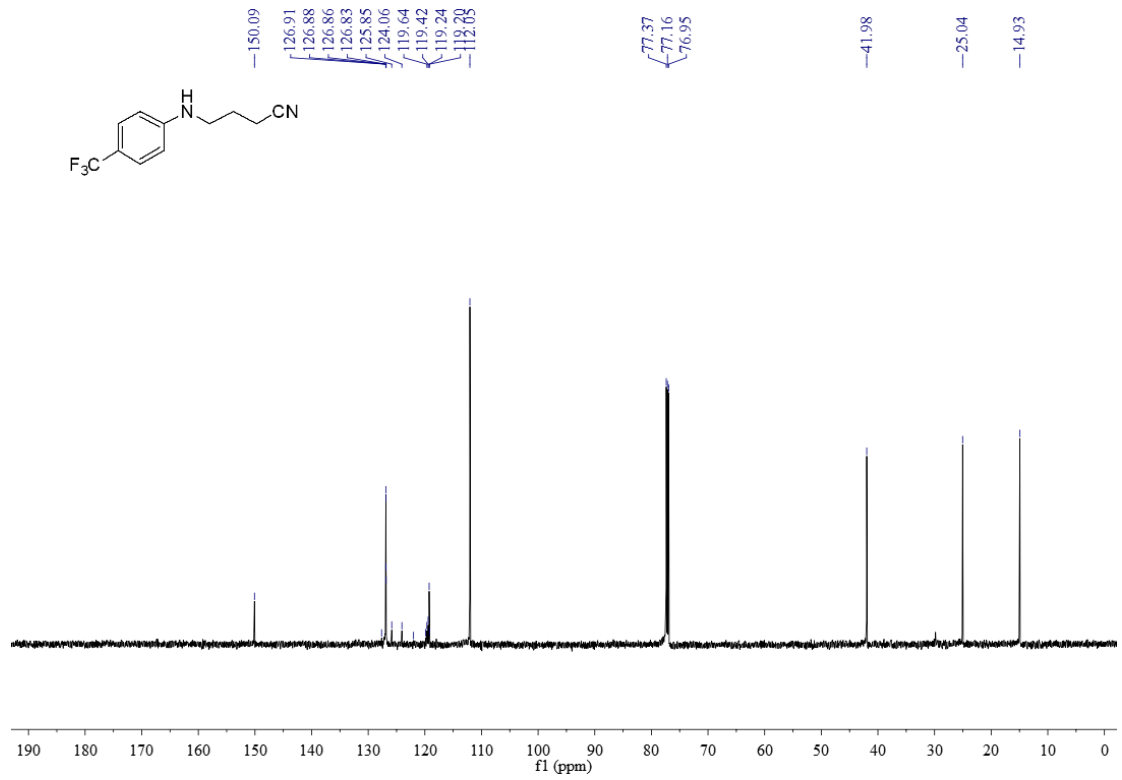

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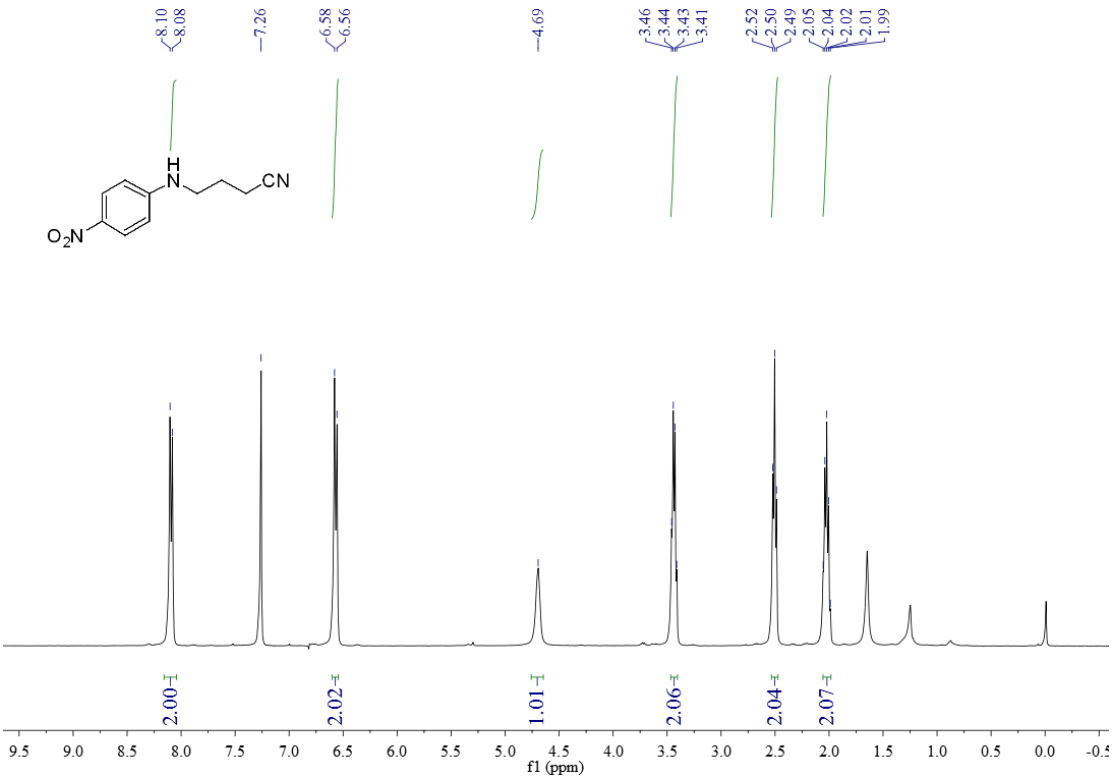
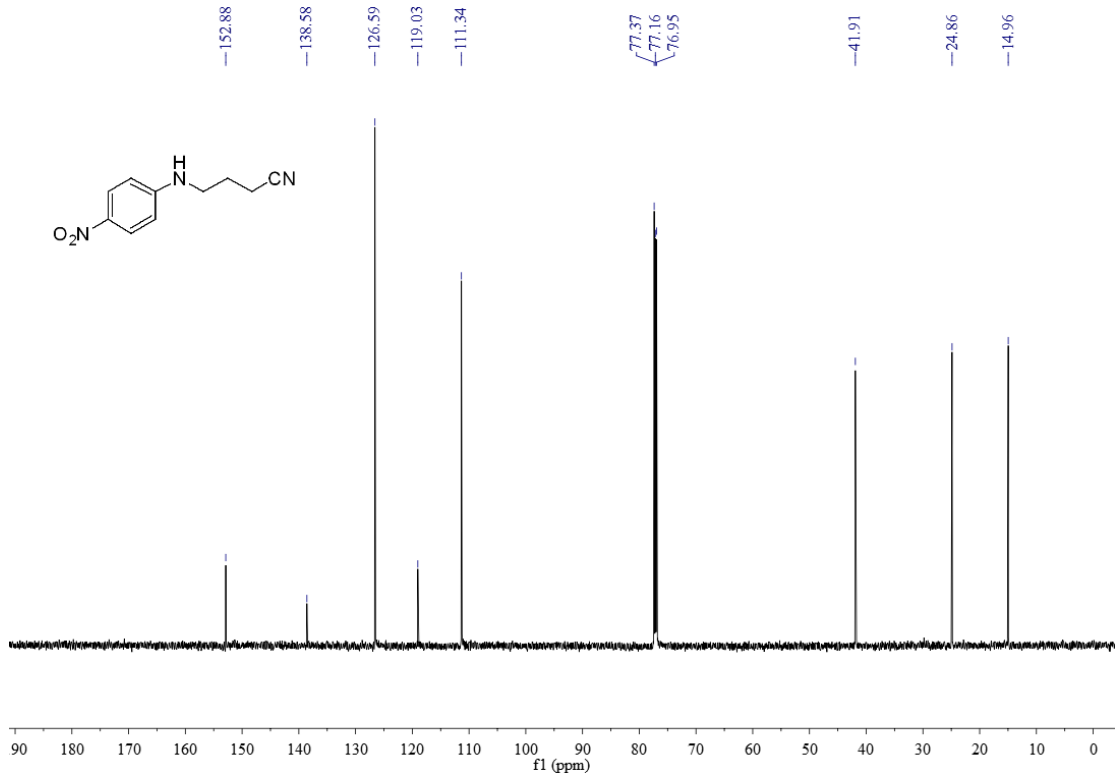


^{13}C NMR of **3o**



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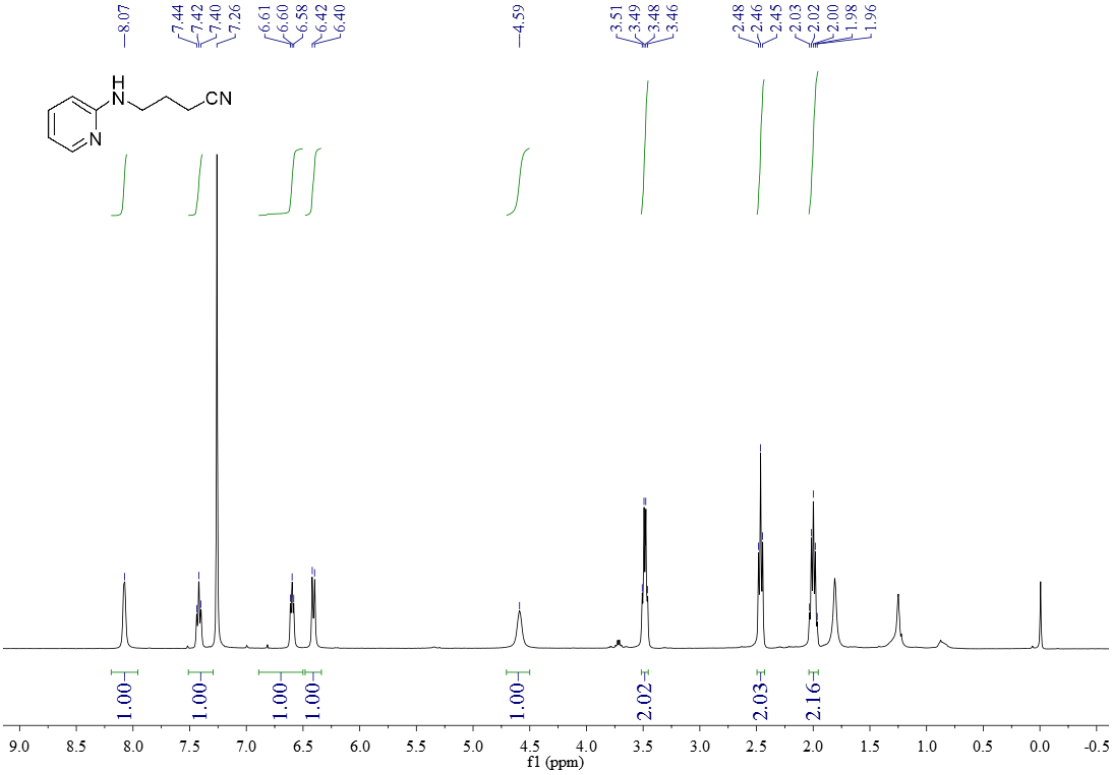
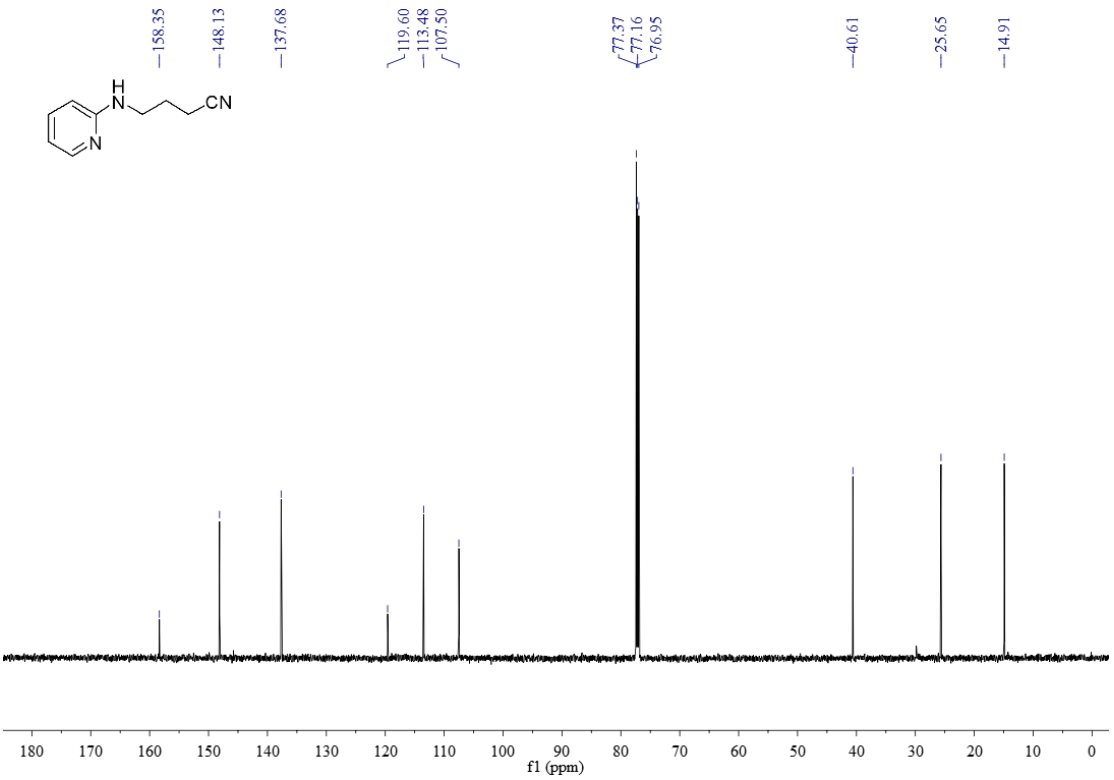
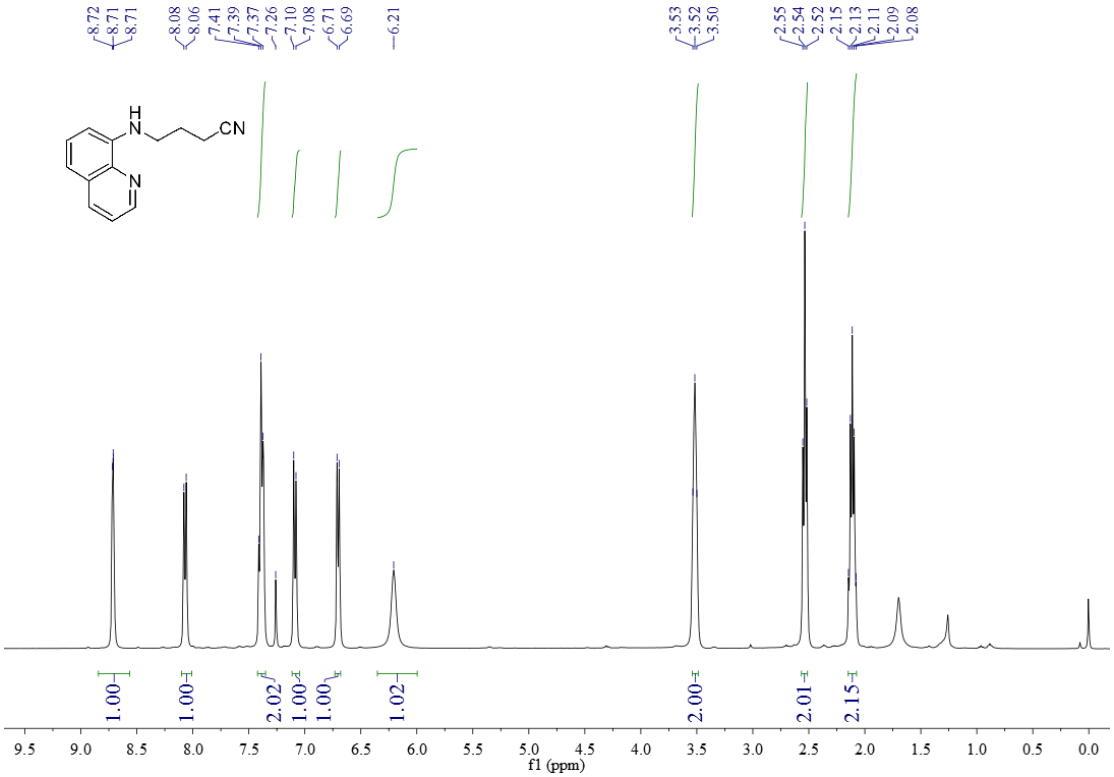


^{13}C NMR of **3p**



^{1}H NMR of **3q**



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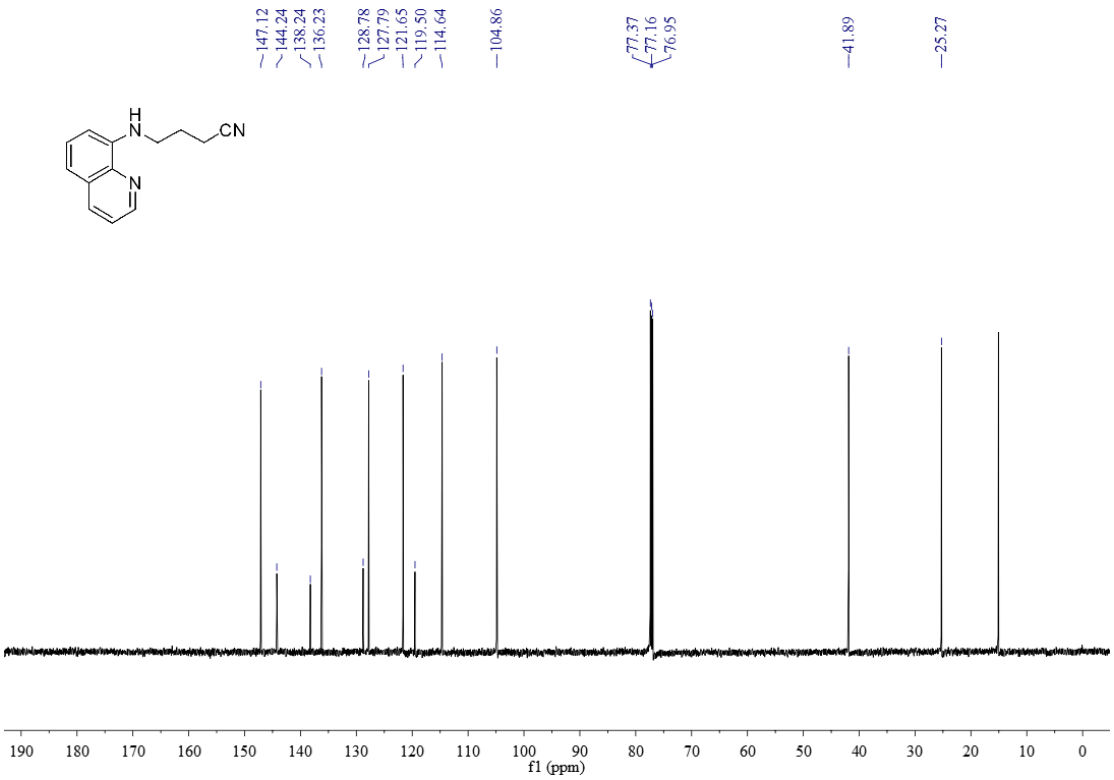

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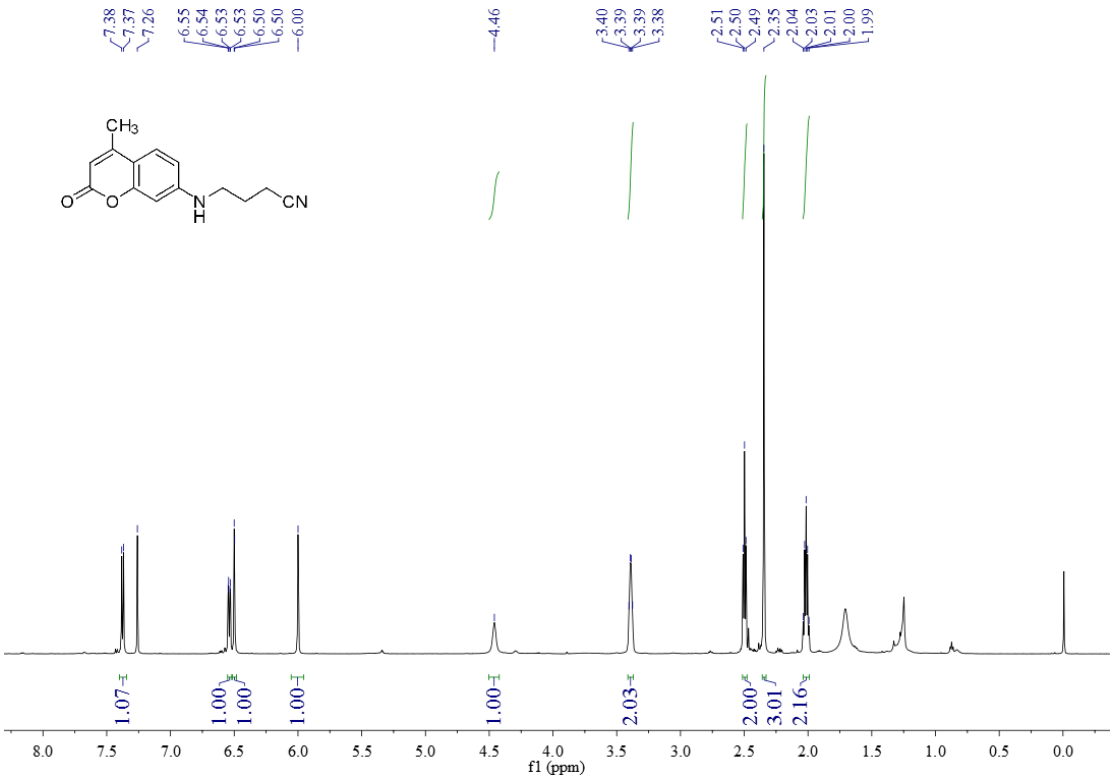

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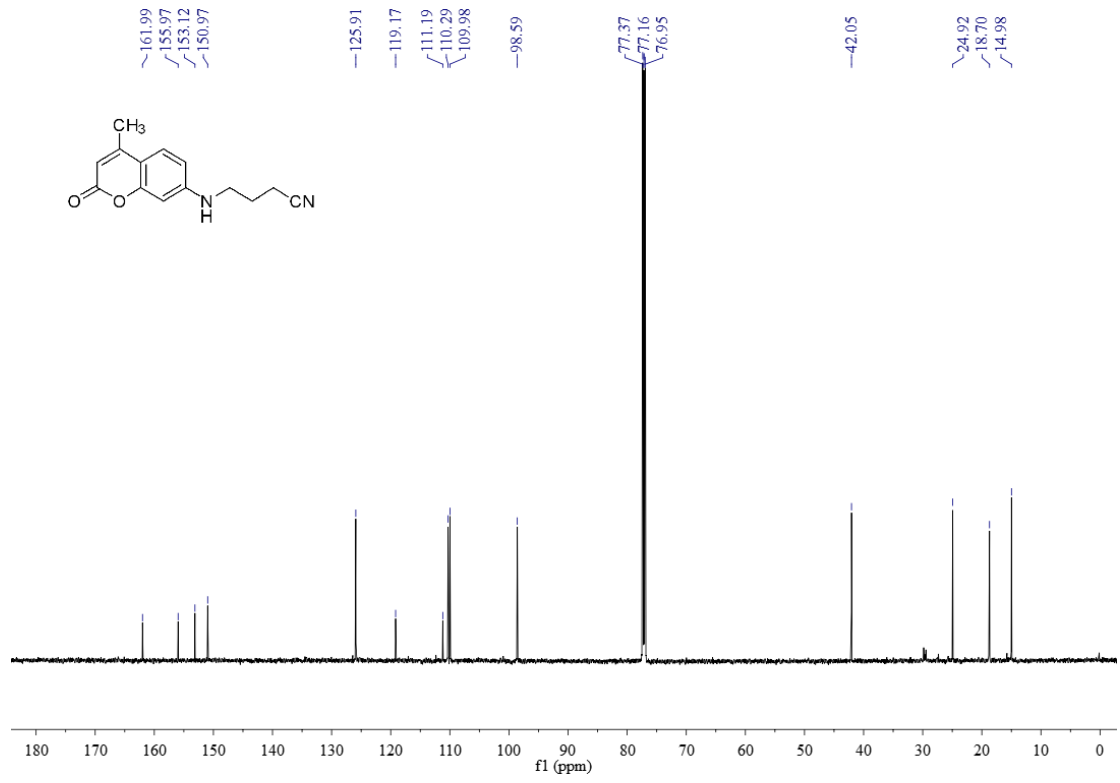

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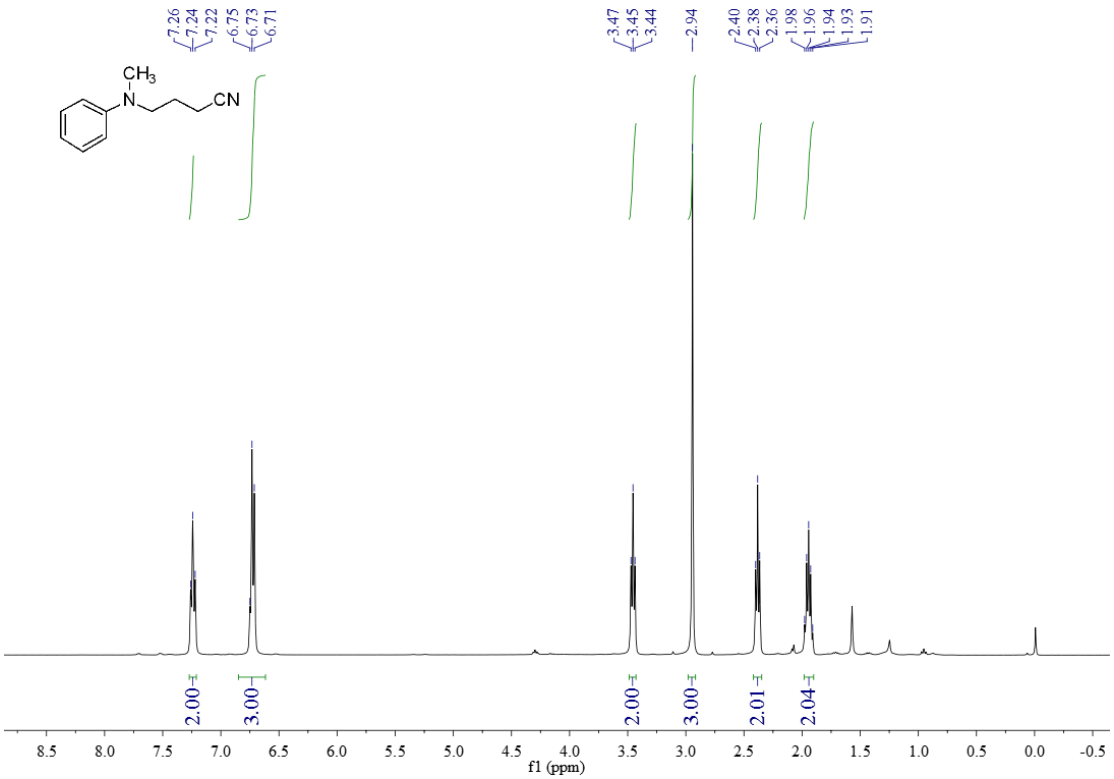

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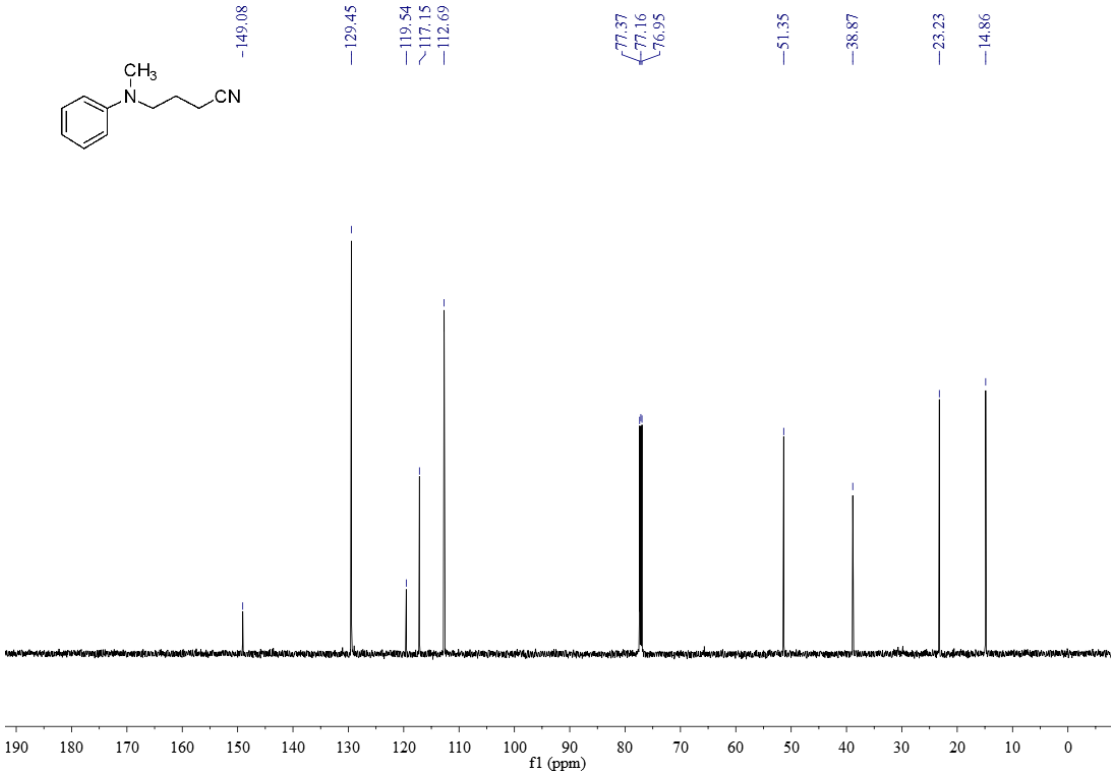
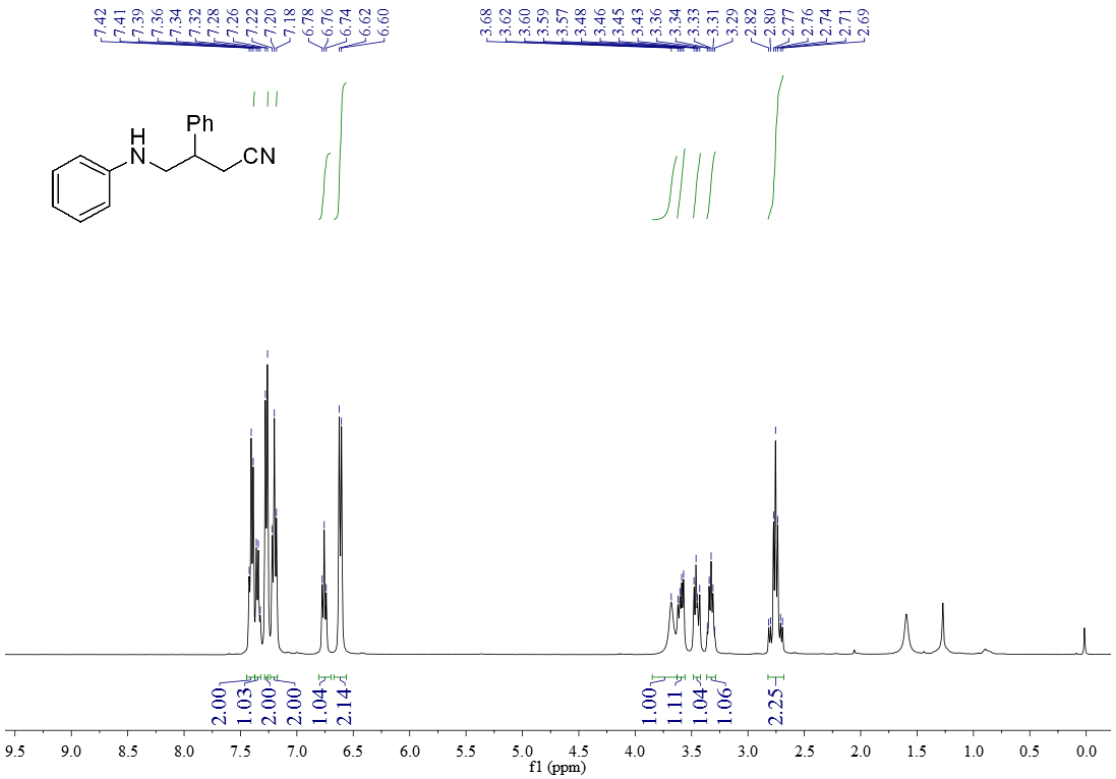
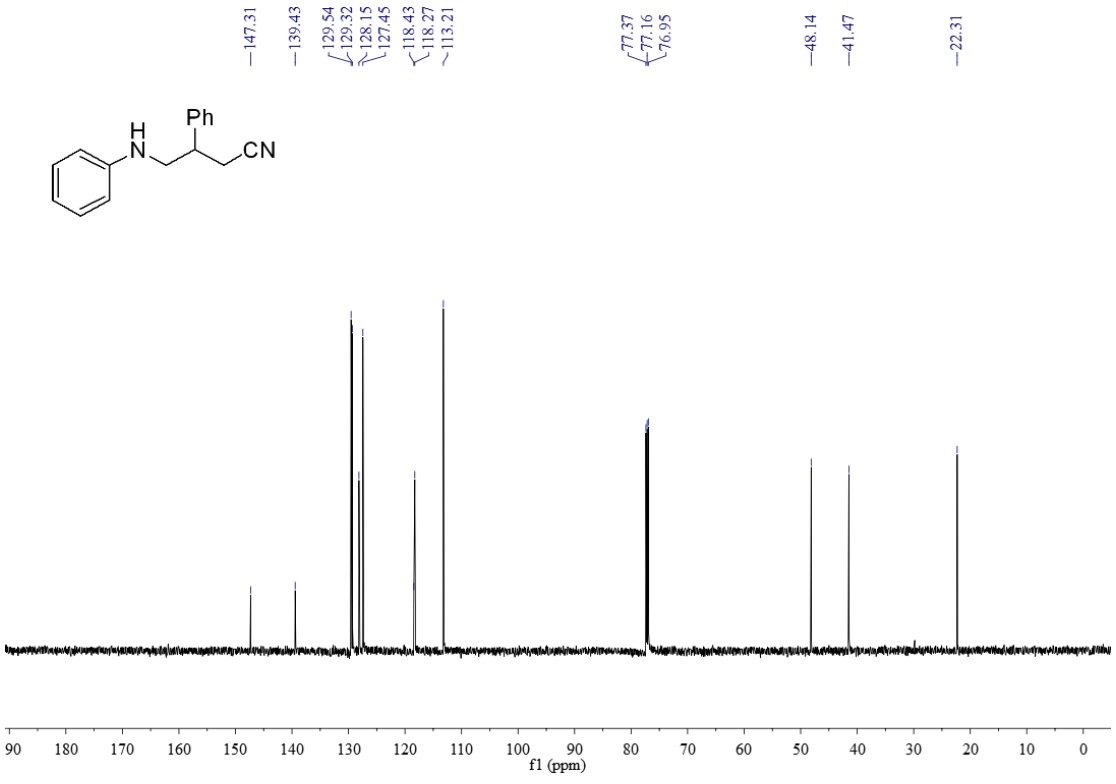


^{1}H NMR of **4a**



^{13}C NMR of **4a**



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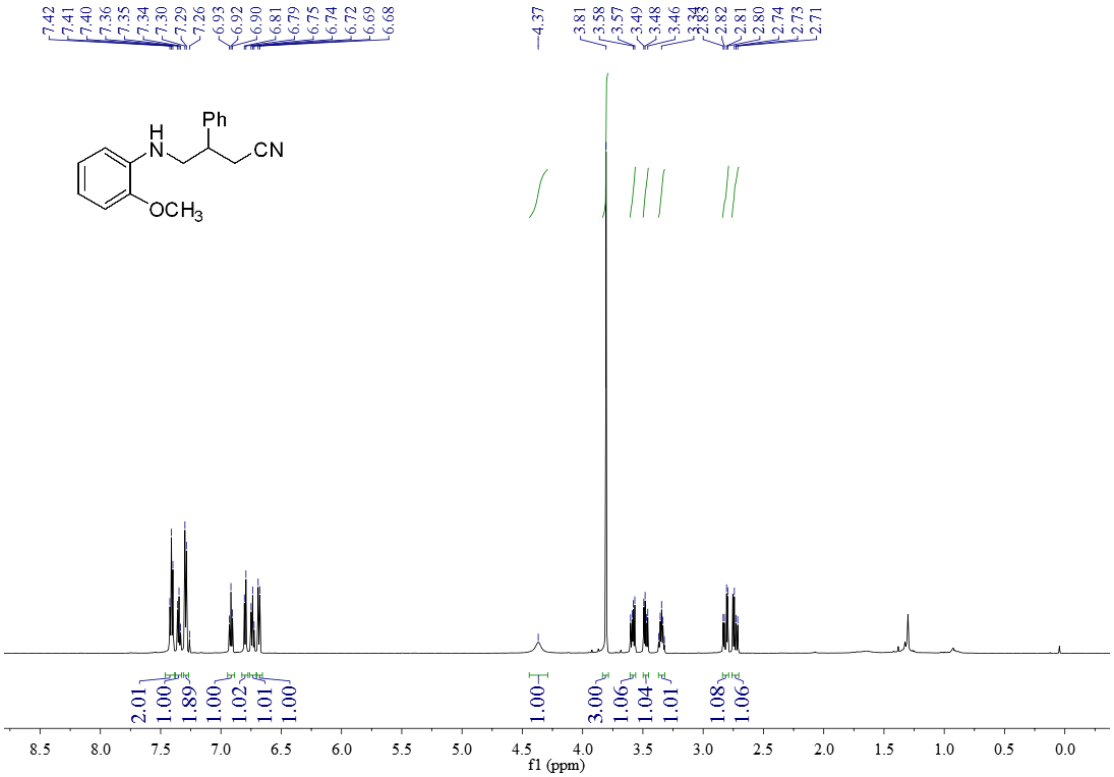
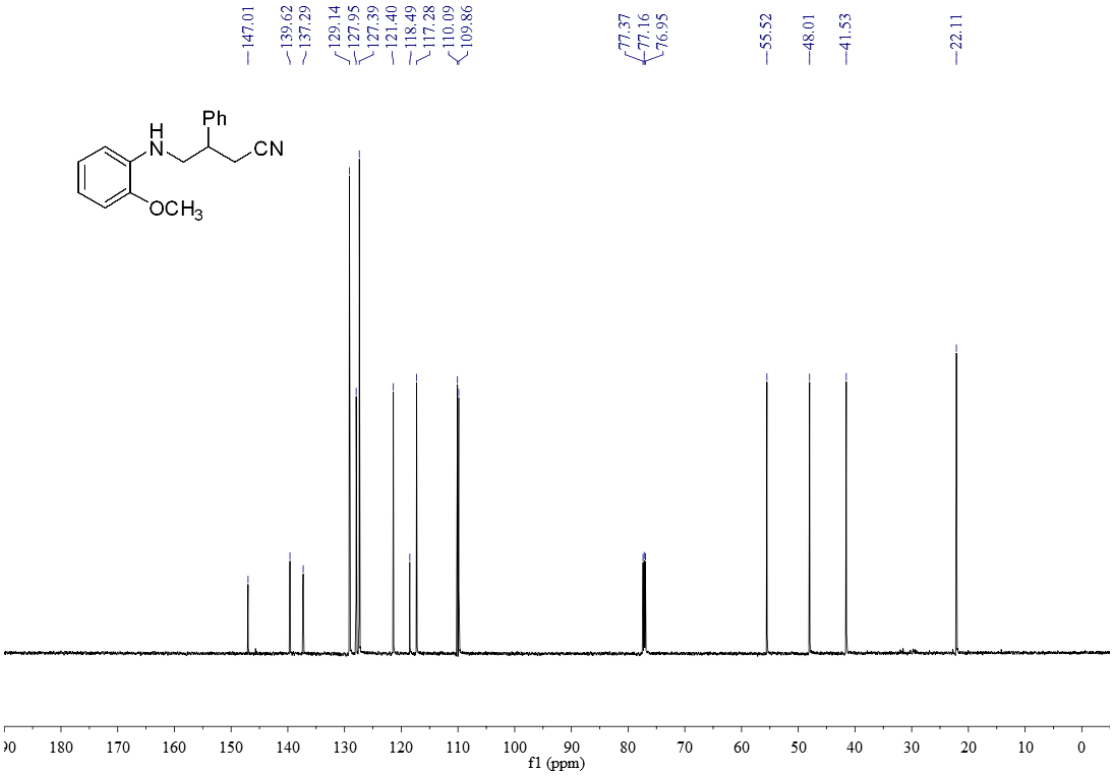
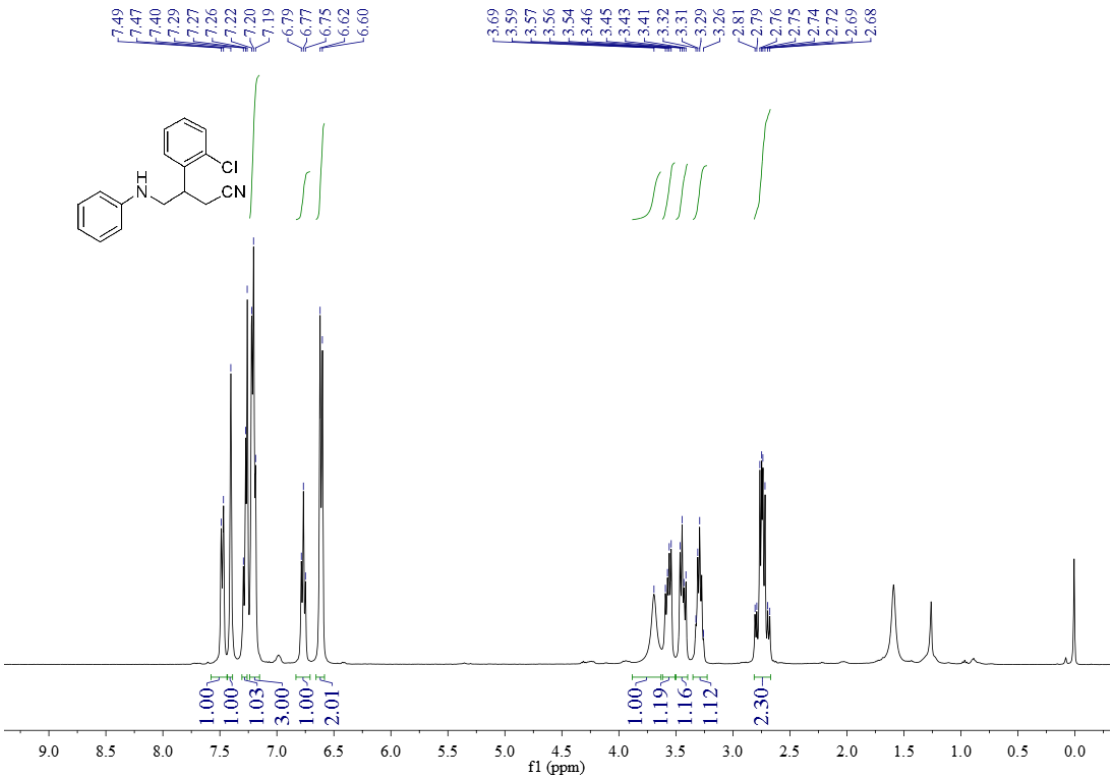


^{13}C NMR of **4b**



^{1}H NMR of **4c**



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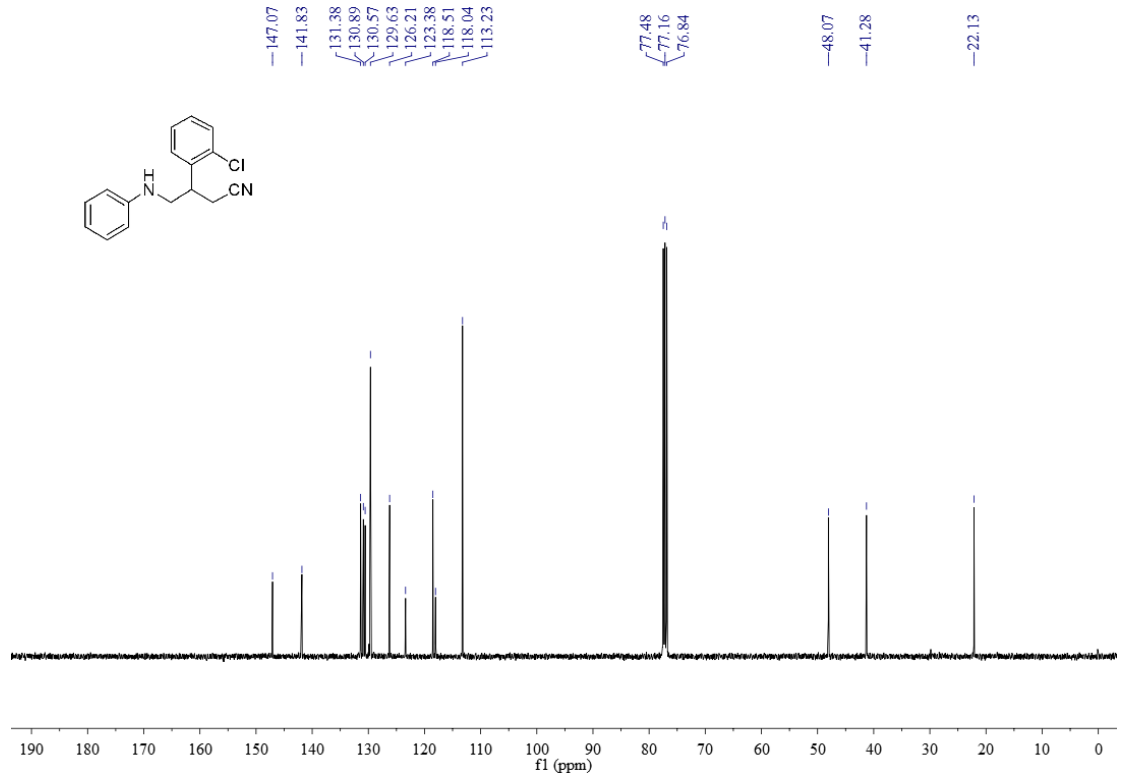

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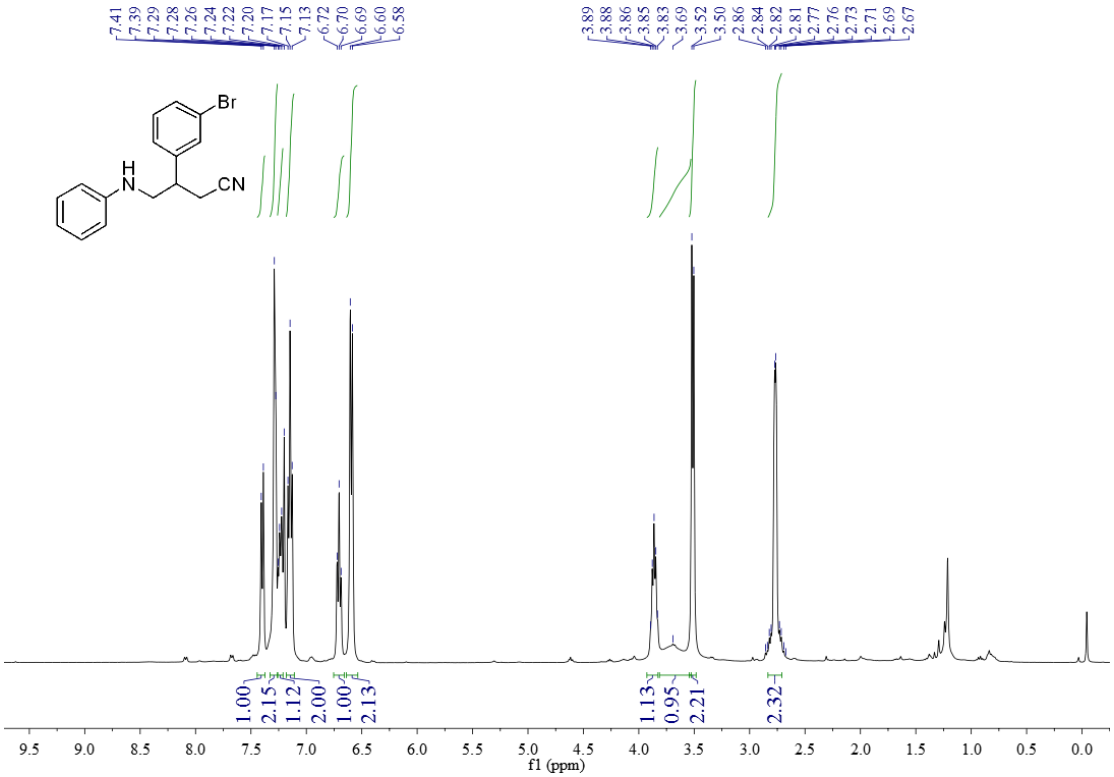
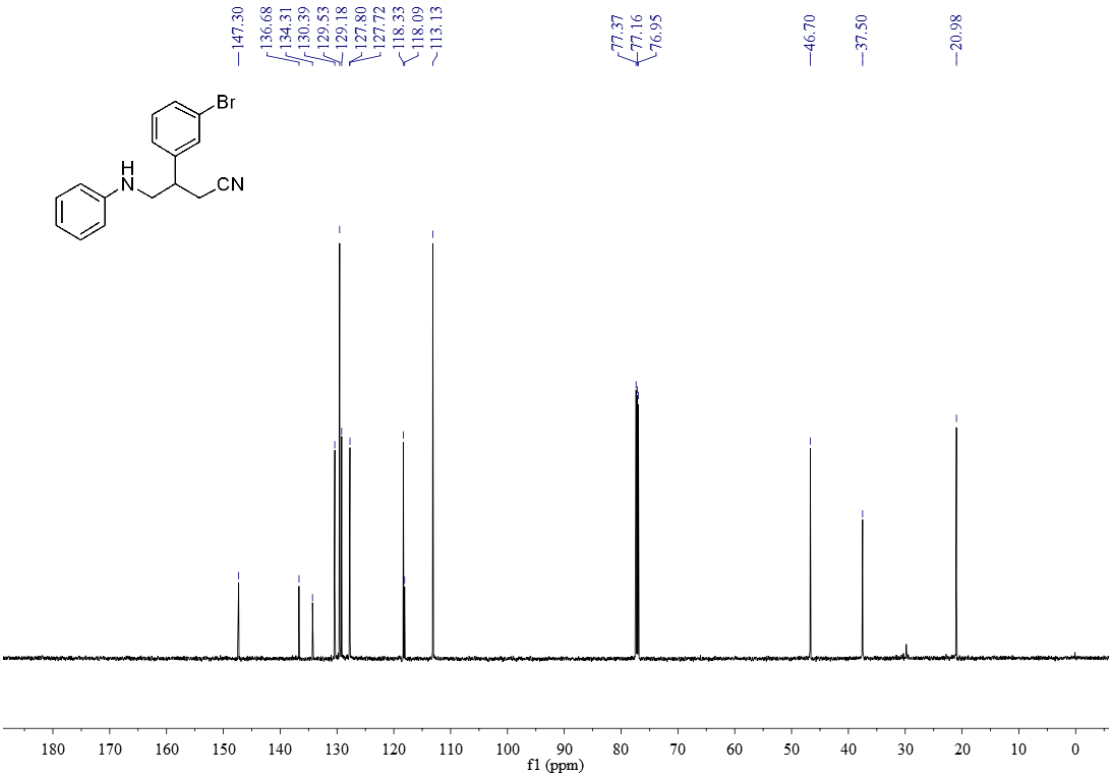


^{13}C NMR of **4d**



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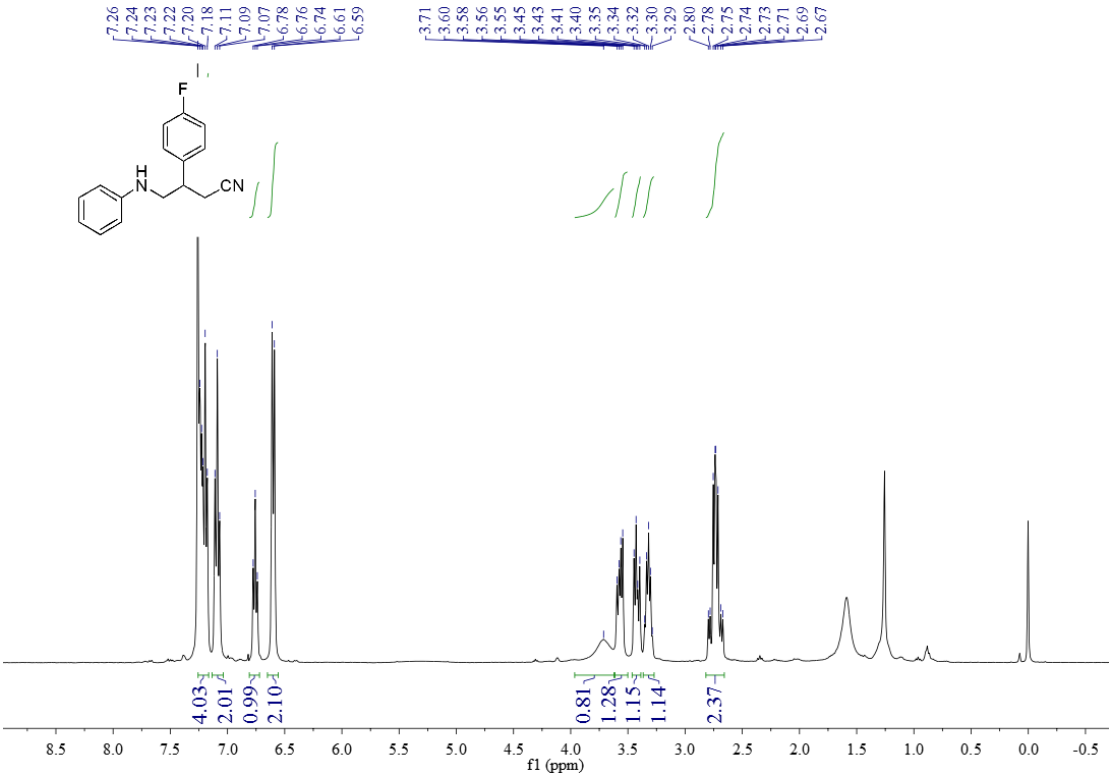
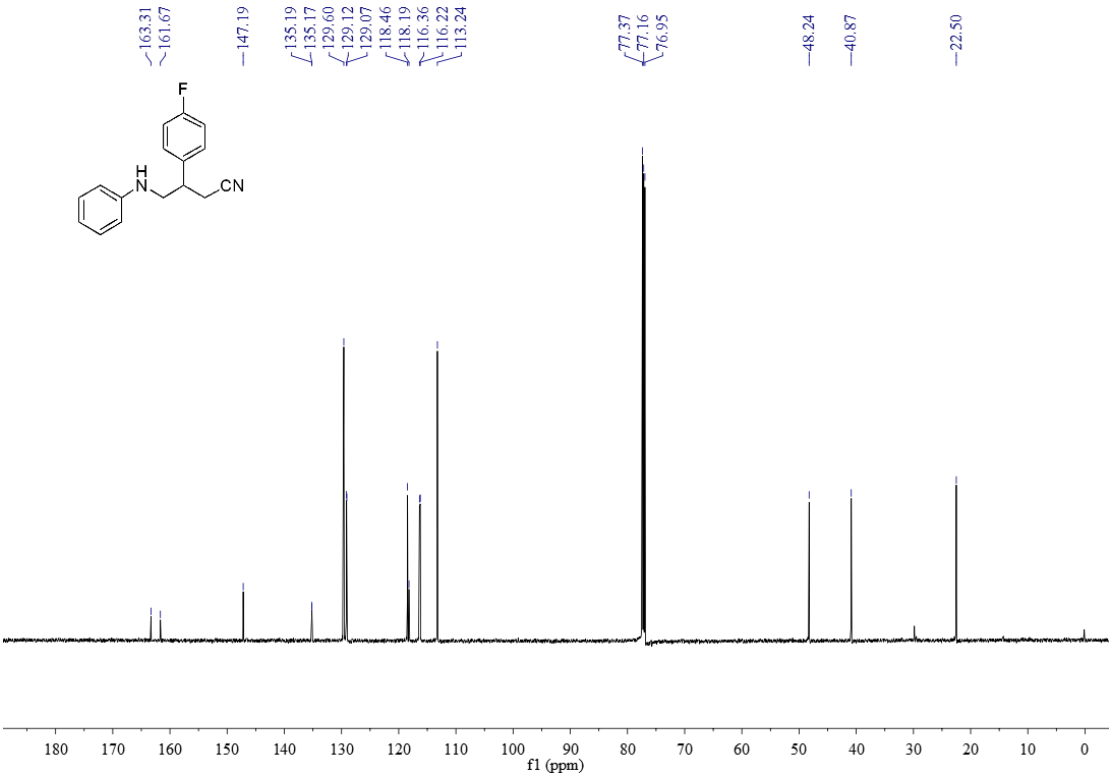
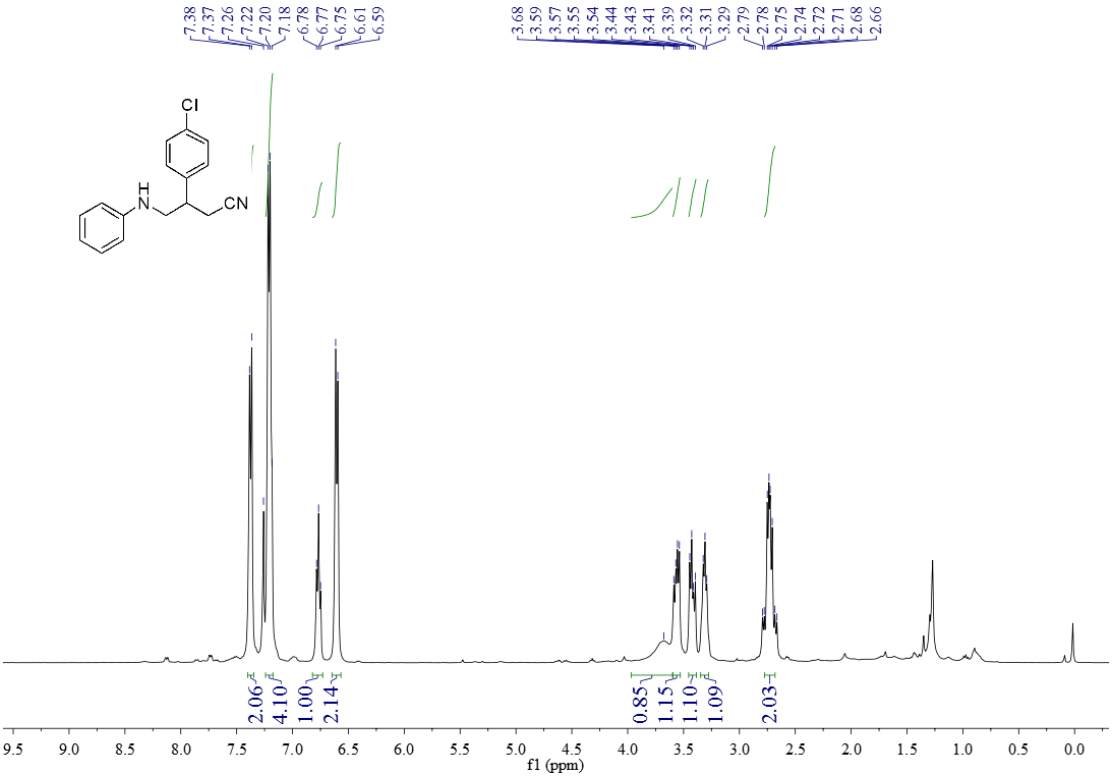


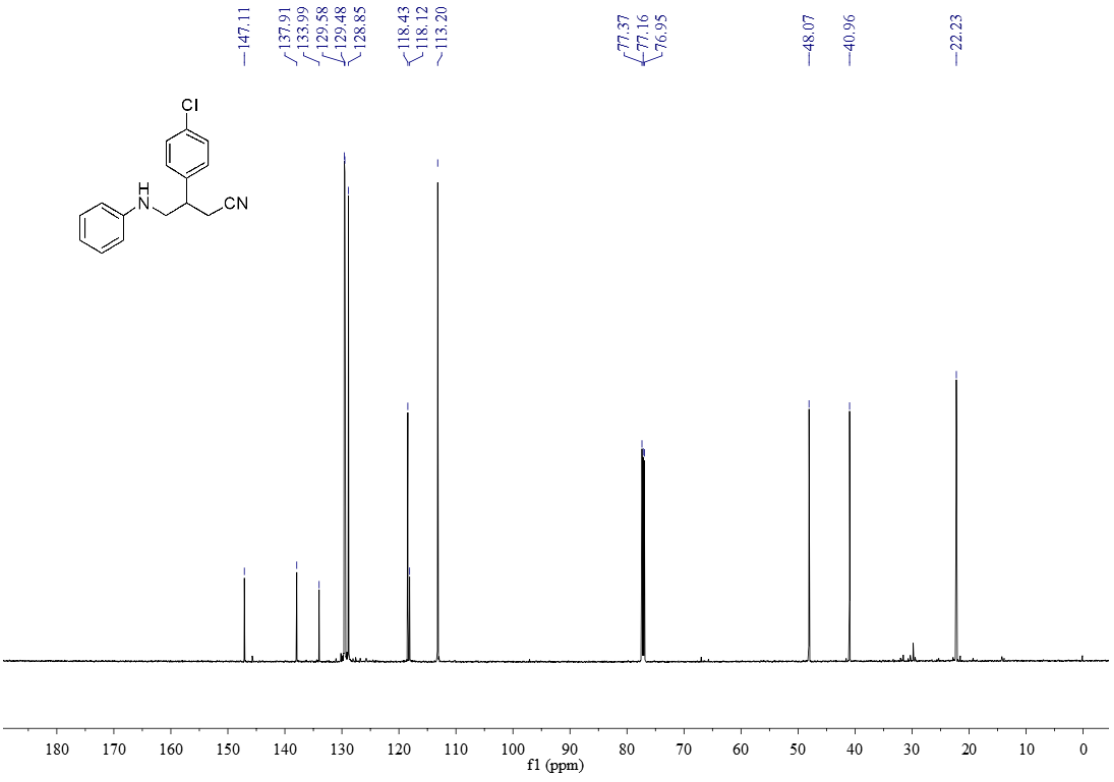
^{13}C NMR of **4e**



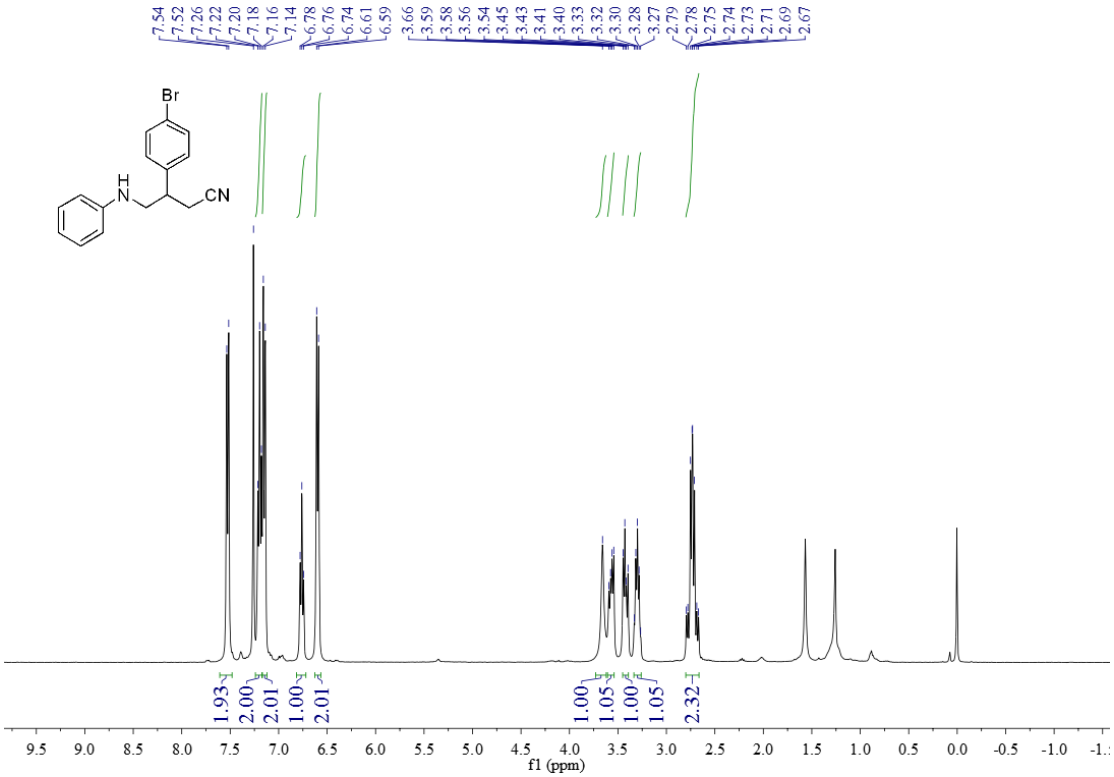
^{1}H NMR of **4f**



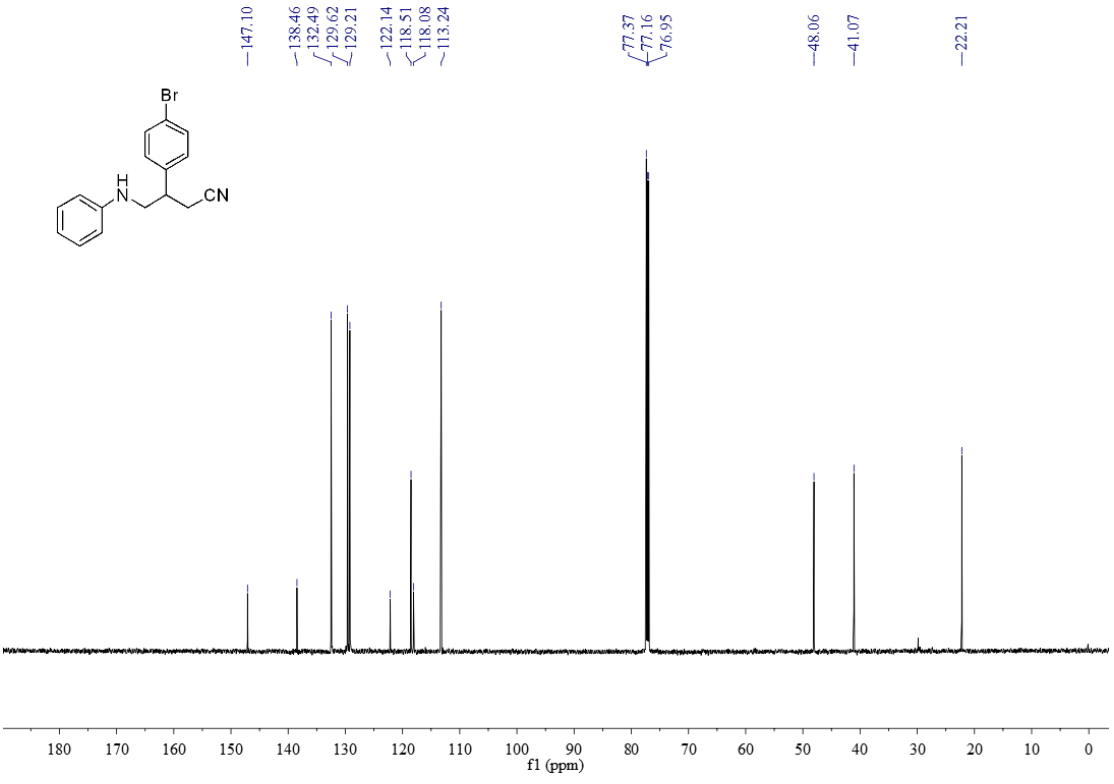
^{13}C NMR of **4f**



^{1}H NMR of **4g**



^{13}C NMR of **4g**



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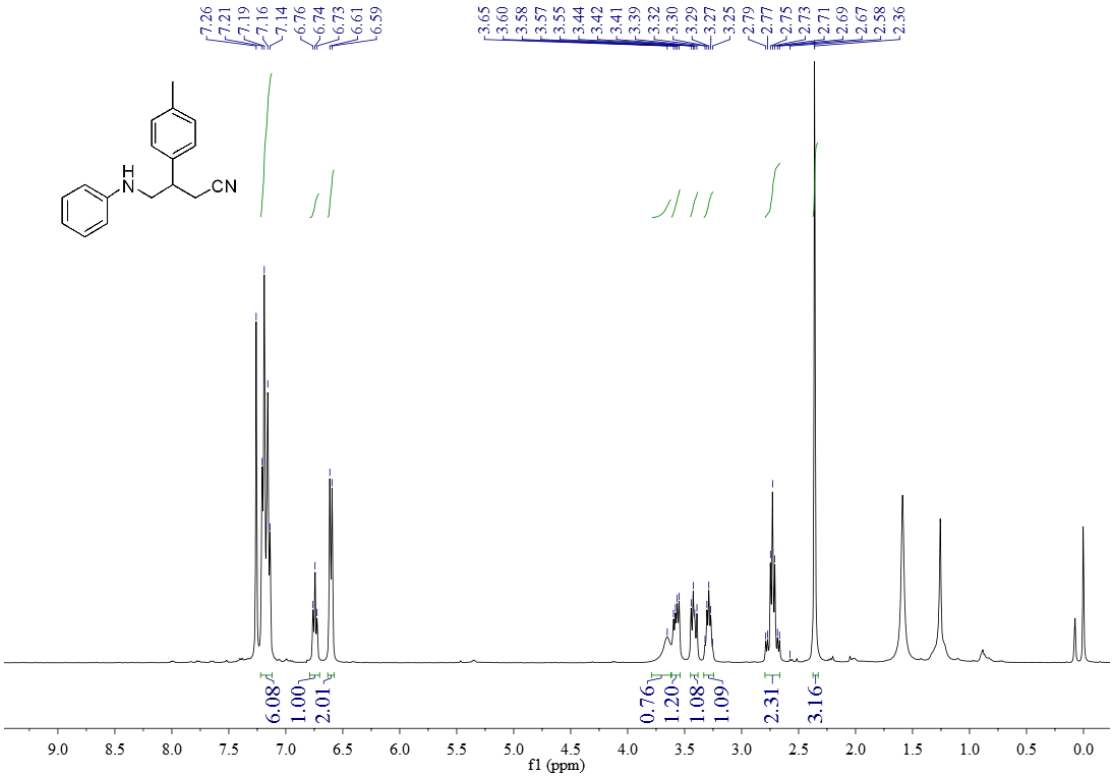

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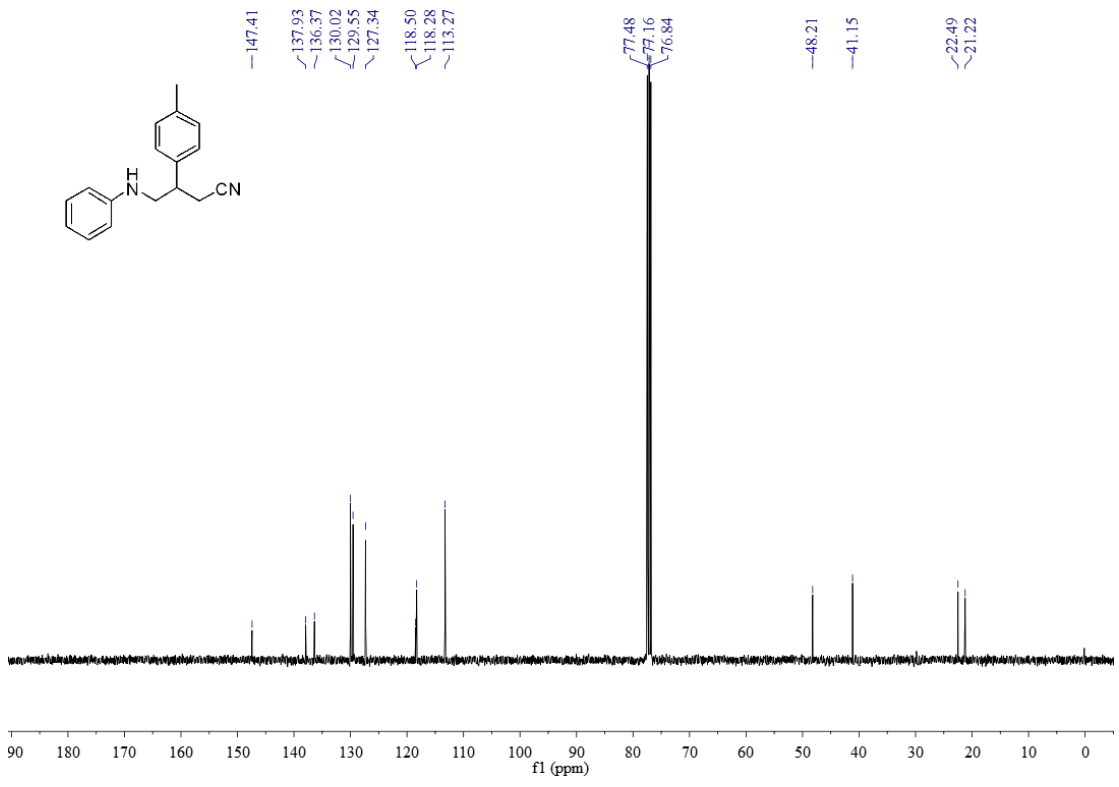
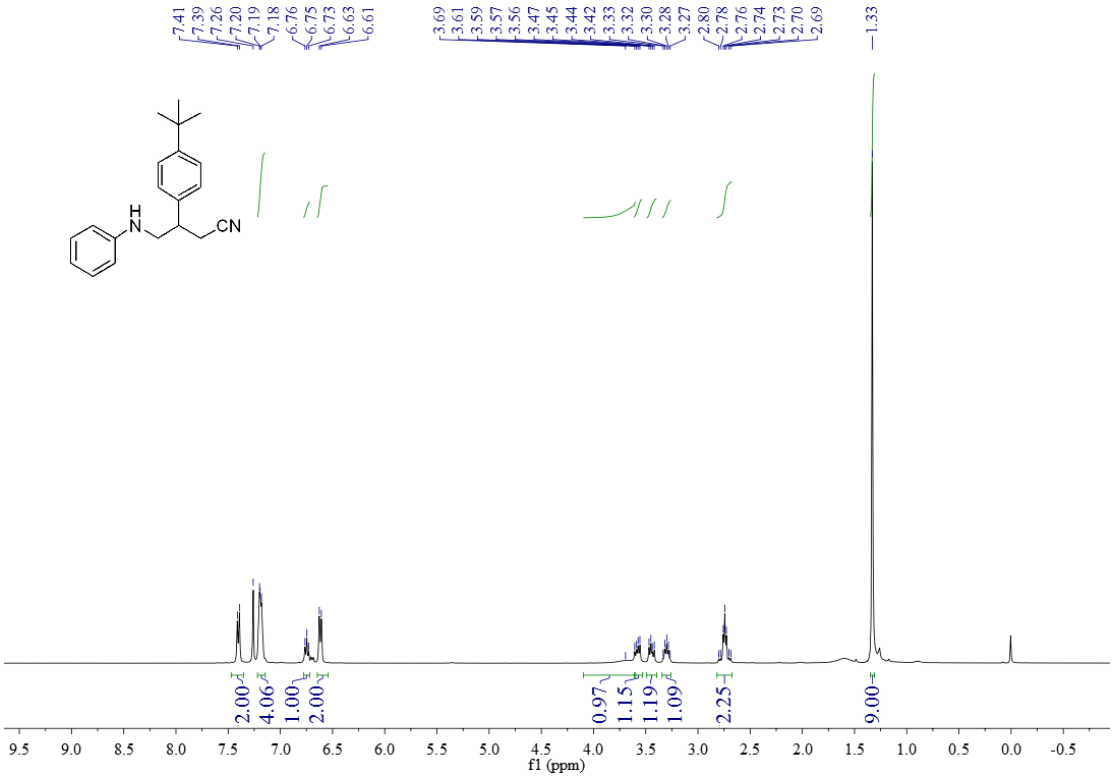
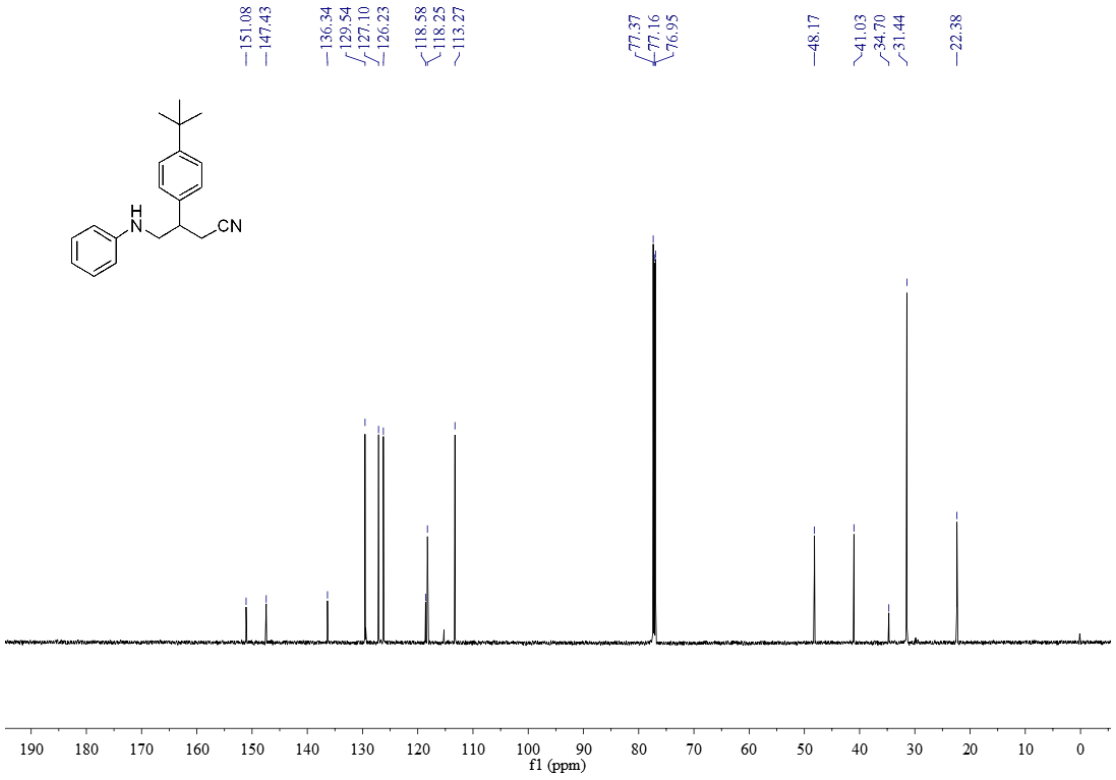


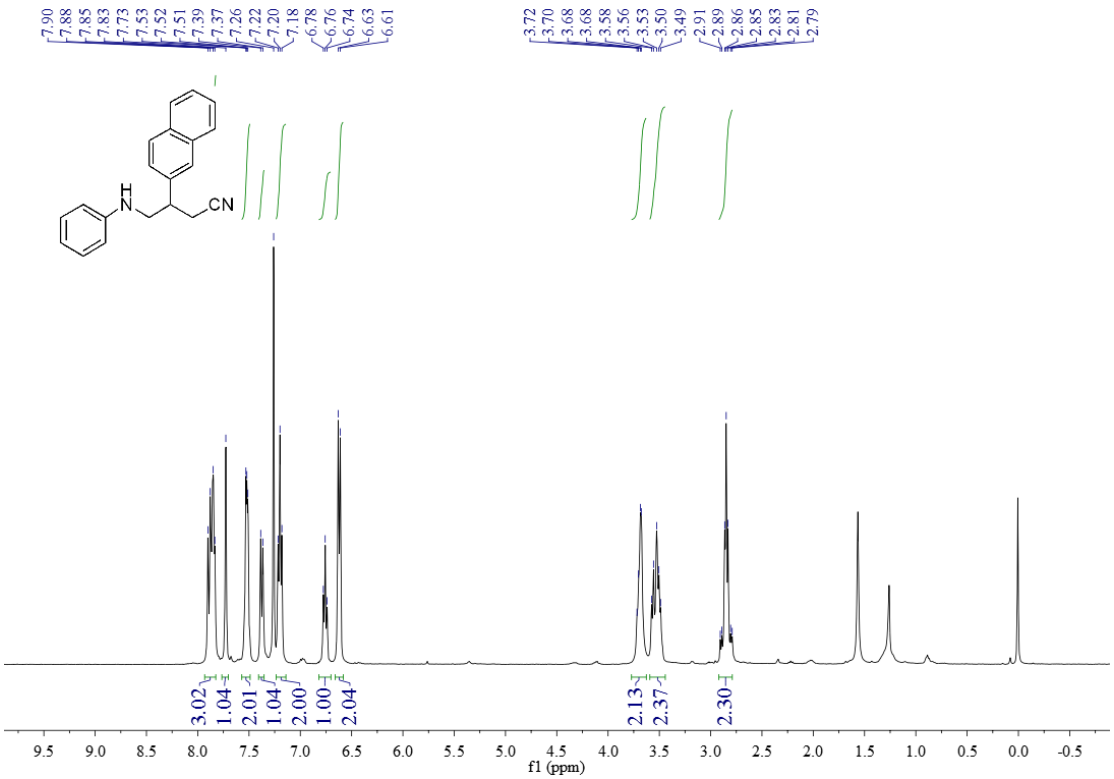
^{1}H NMR of **4i**



^{13}C NMR of **4i**



^{1}H NMR of **4j**



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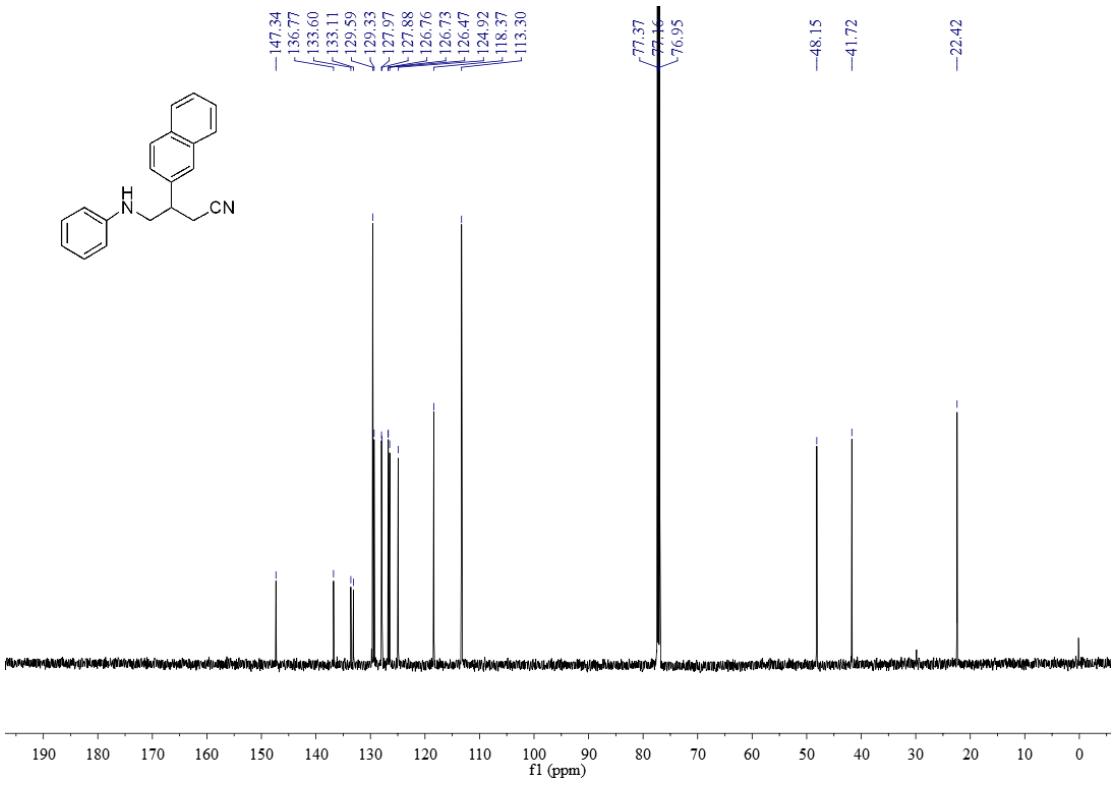
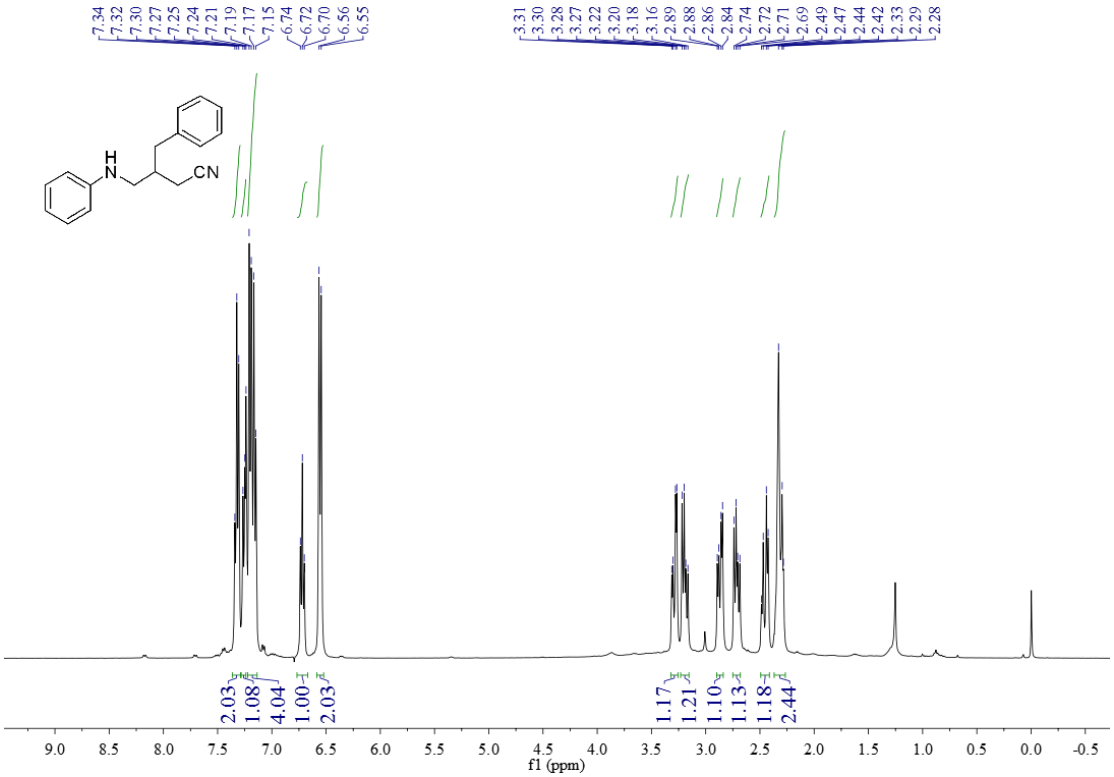


^{1}H NMR of **4k**



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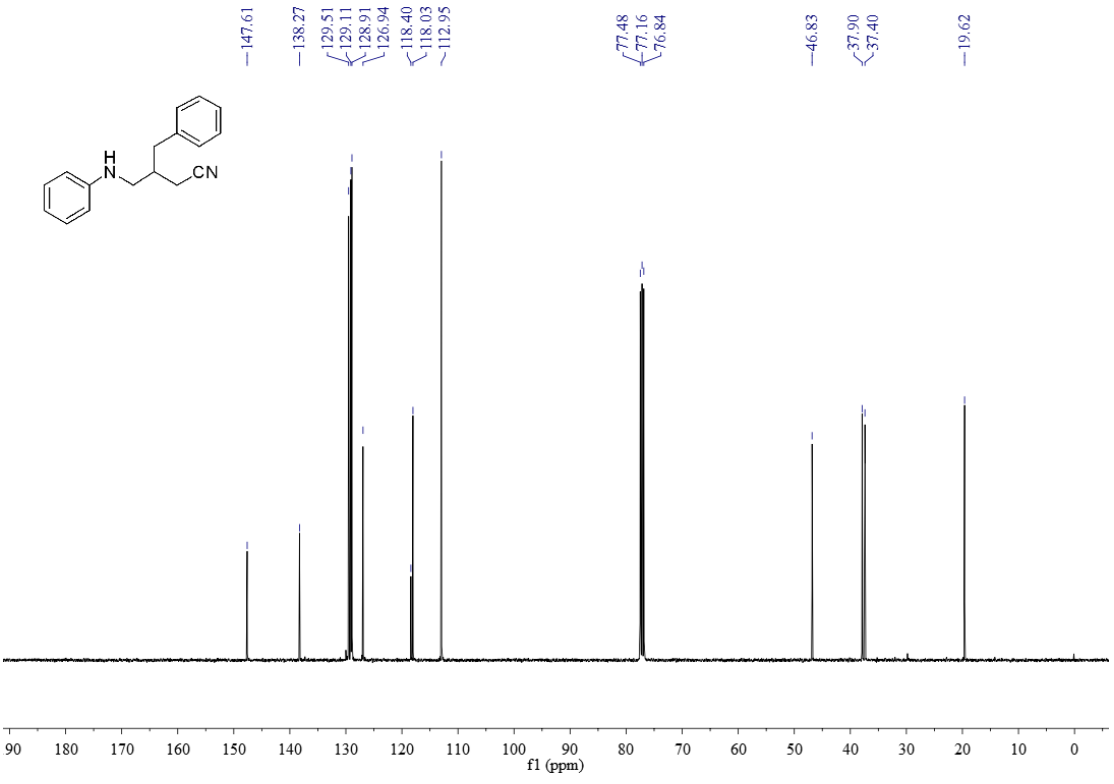
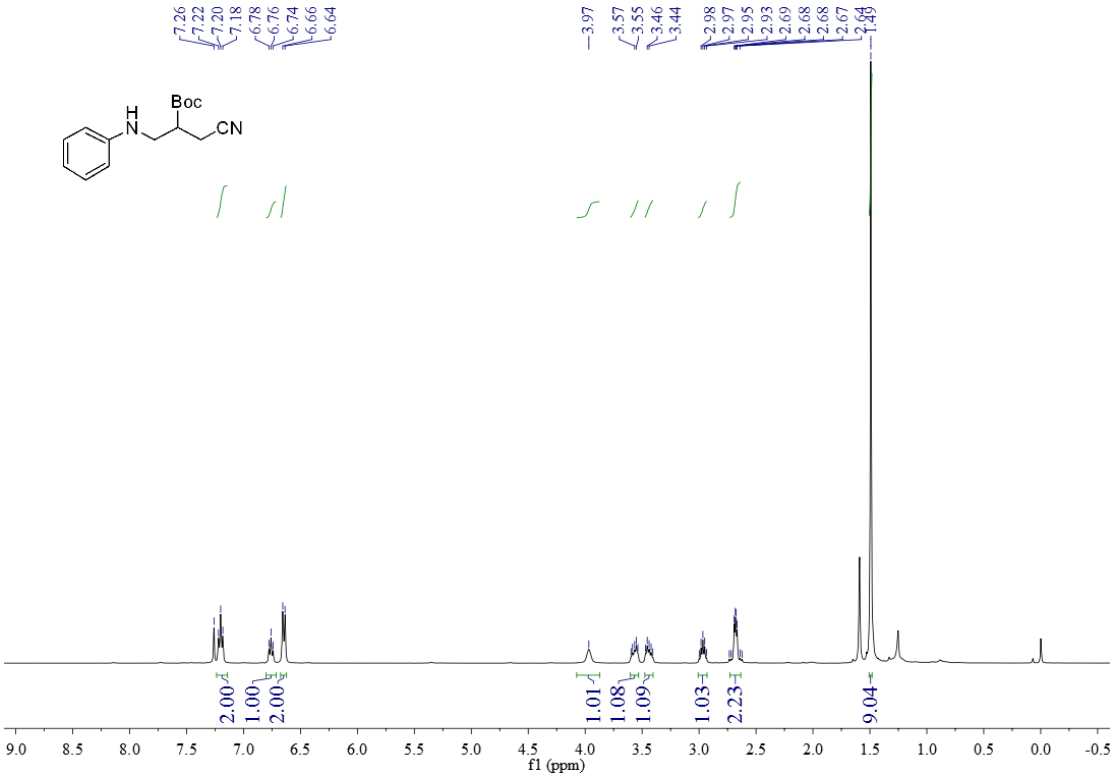
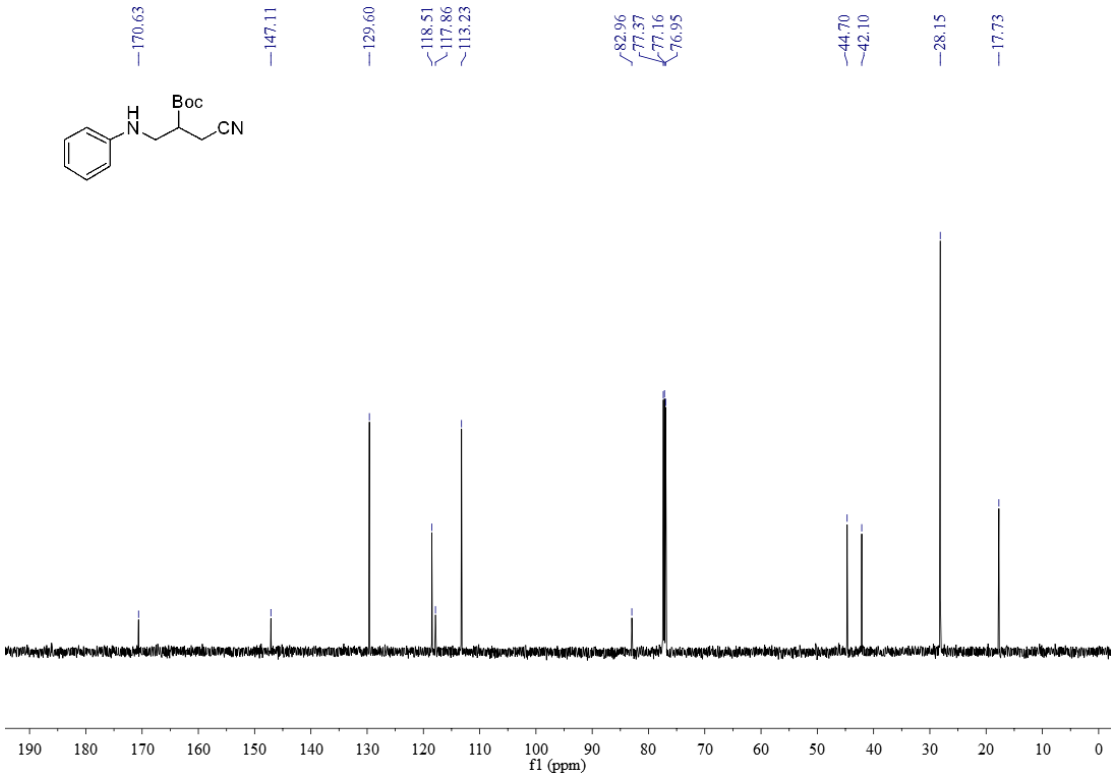


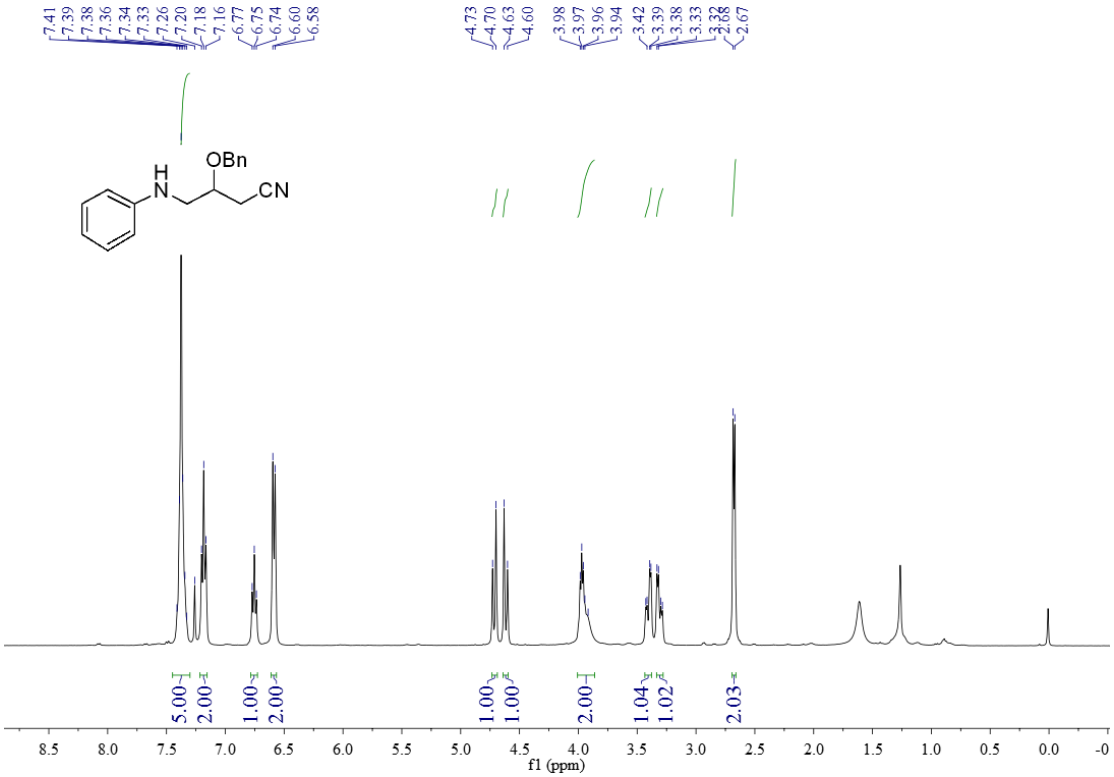
^{1}H NMR of **4l**



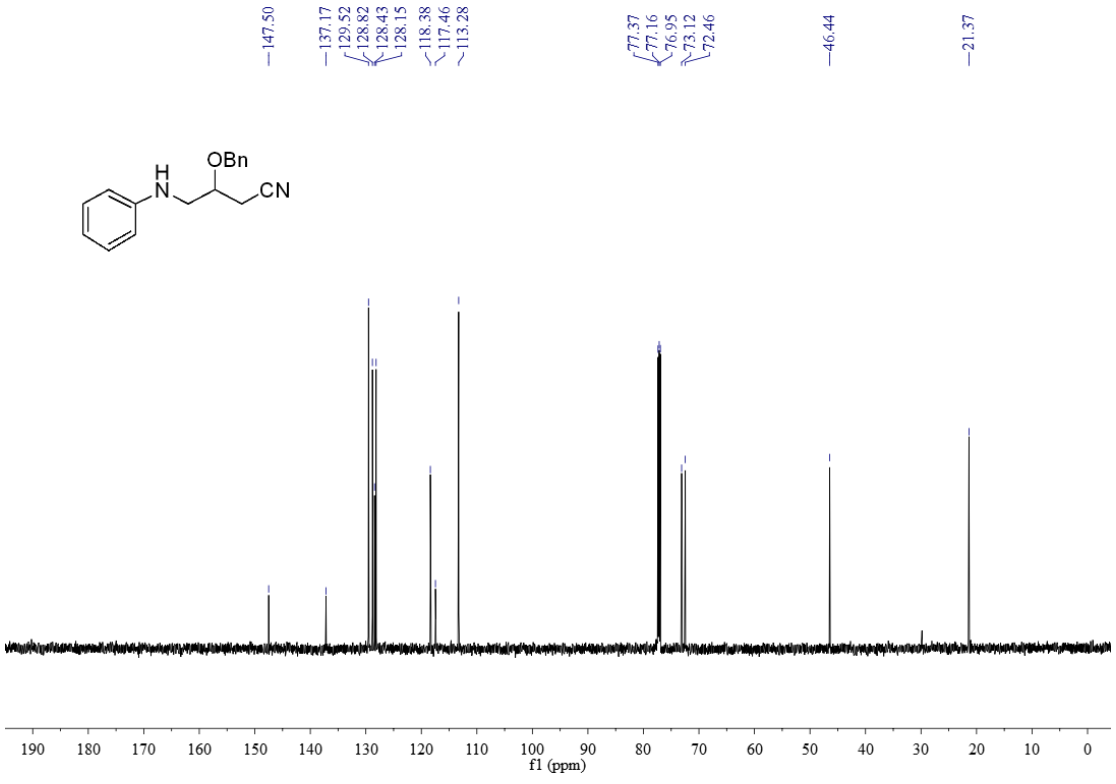
^{13}C NMR of **4l**



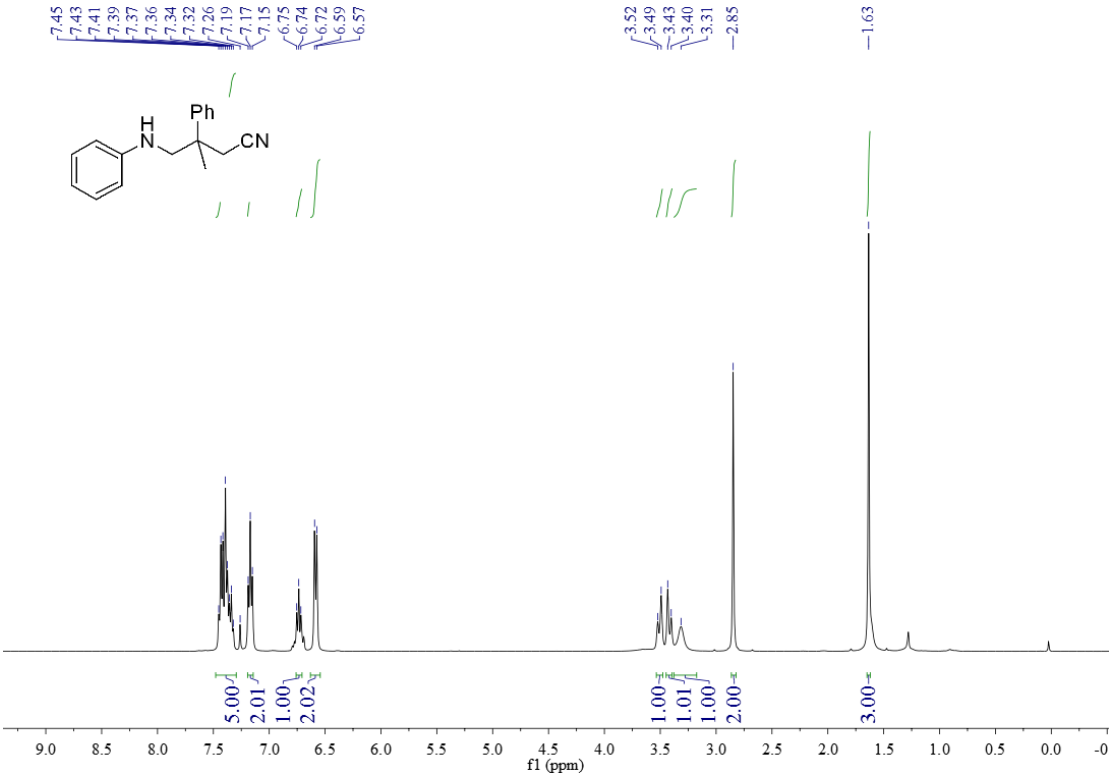
^{1}H NMR of **4m**



^{13}C NMR of **4m**



^{1}H NMR of **4n**



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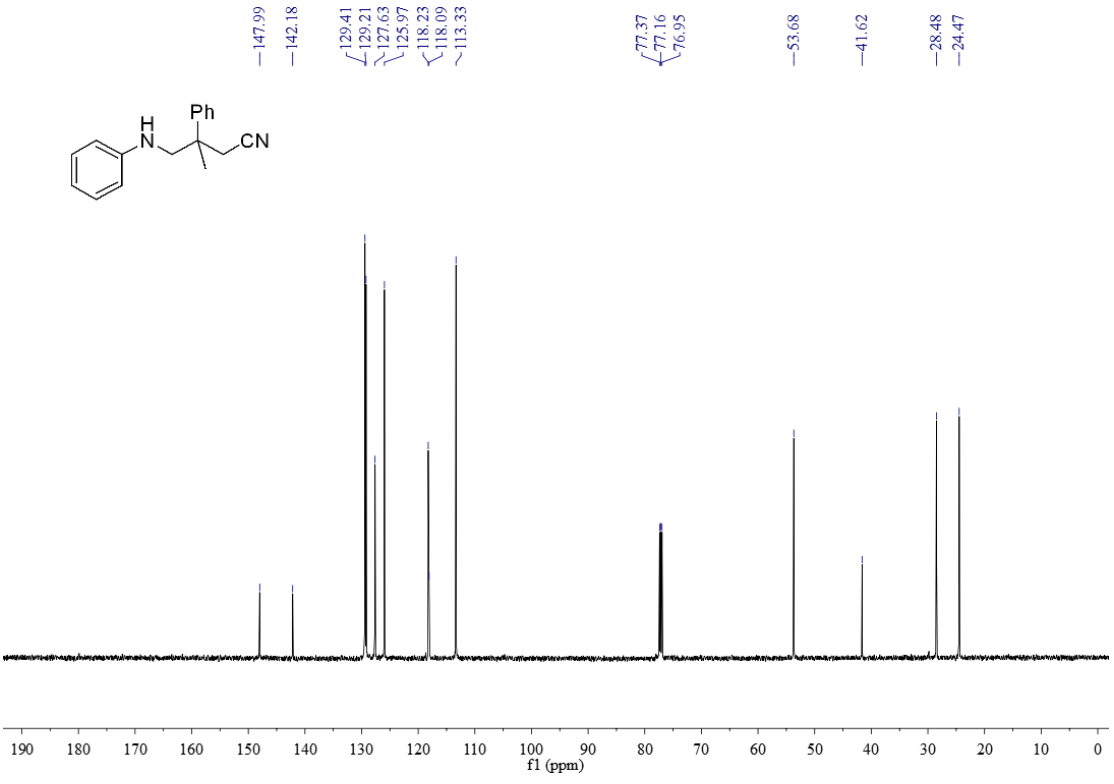

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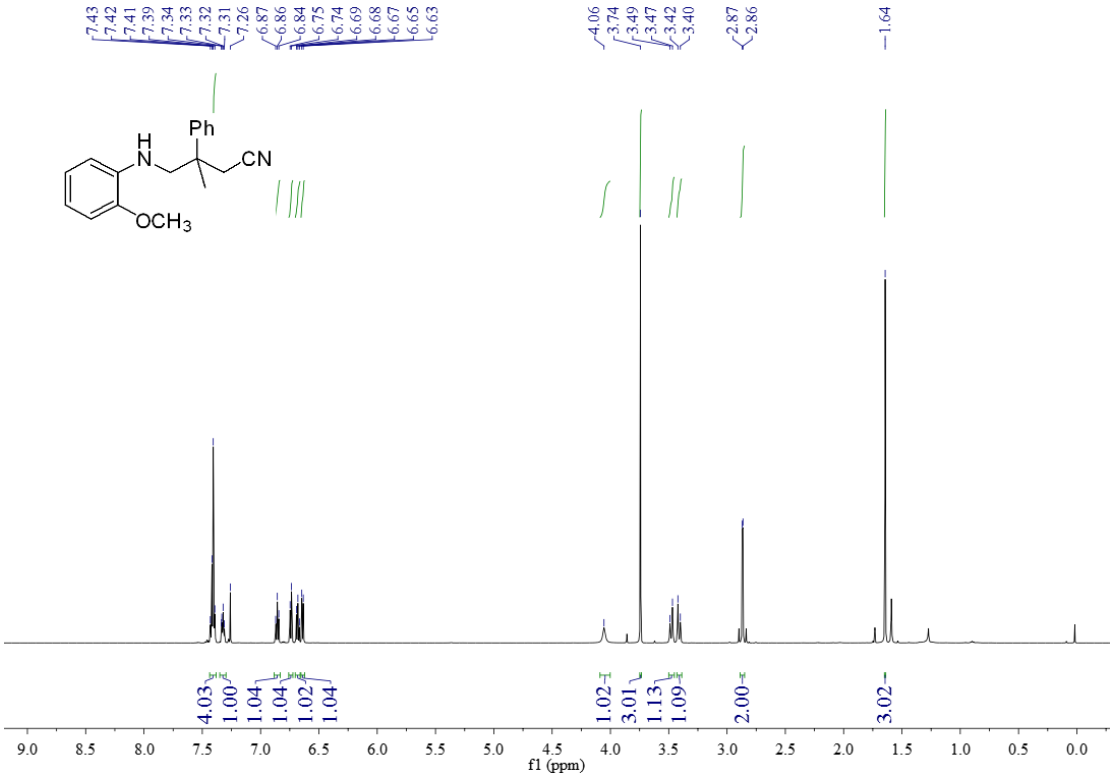
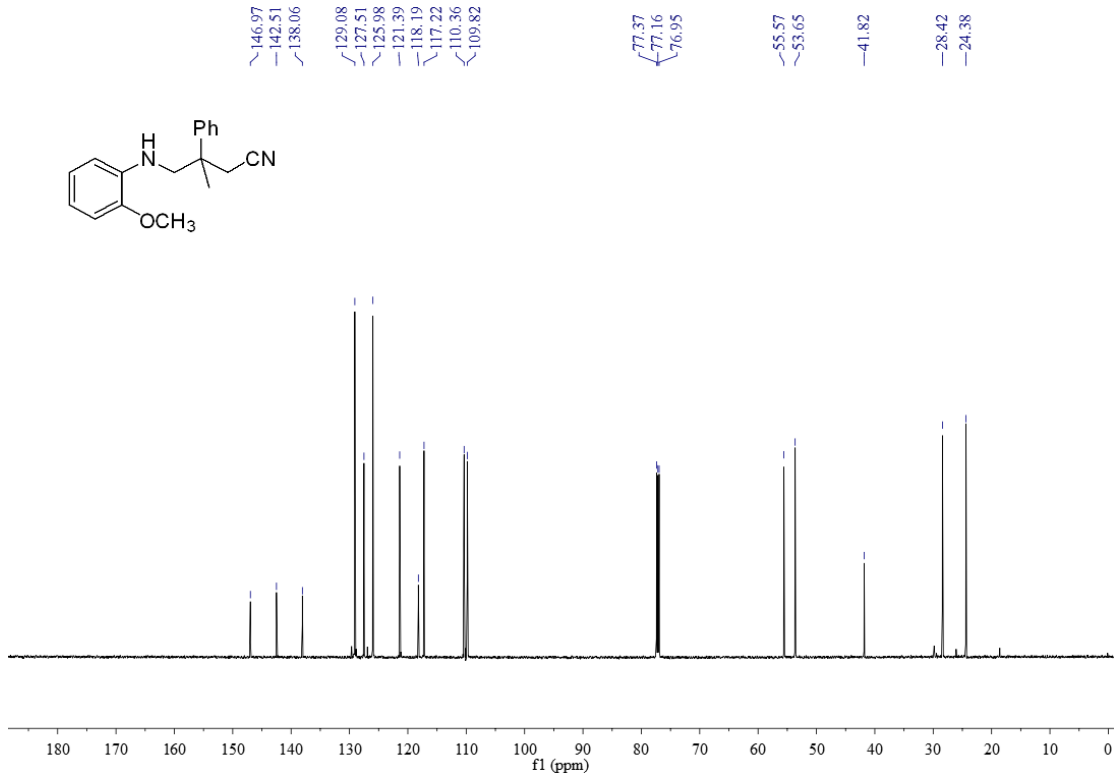


^{13}C NMR of **4o**



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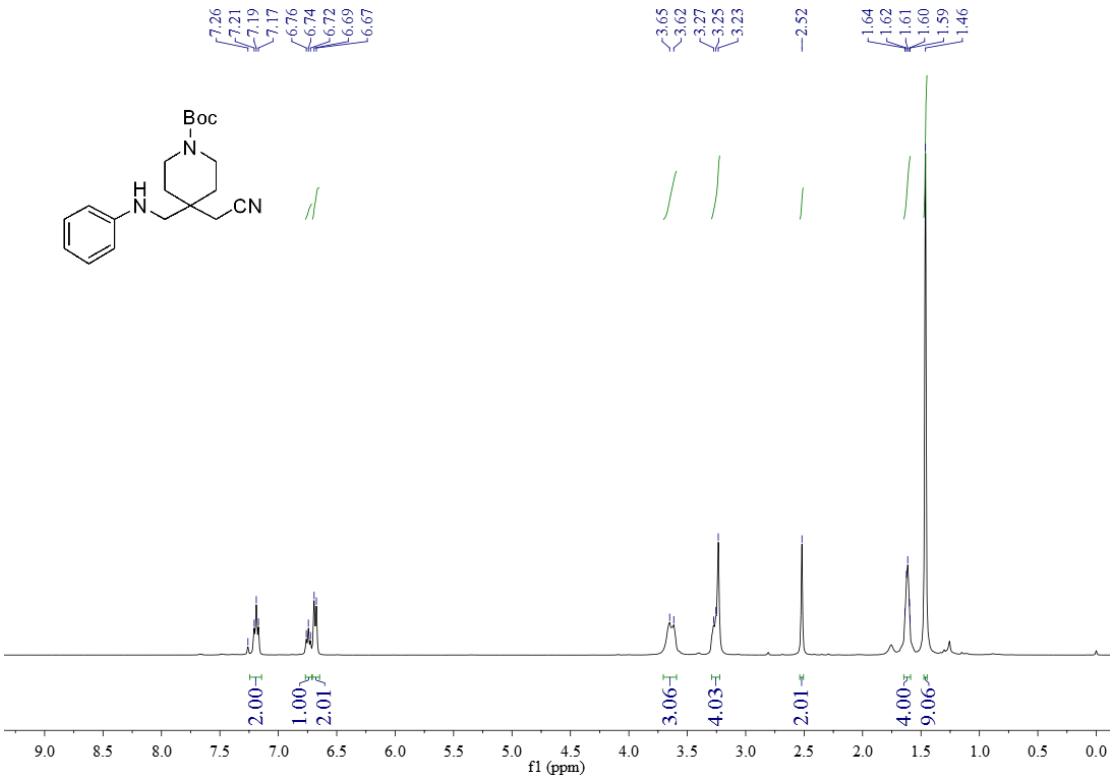

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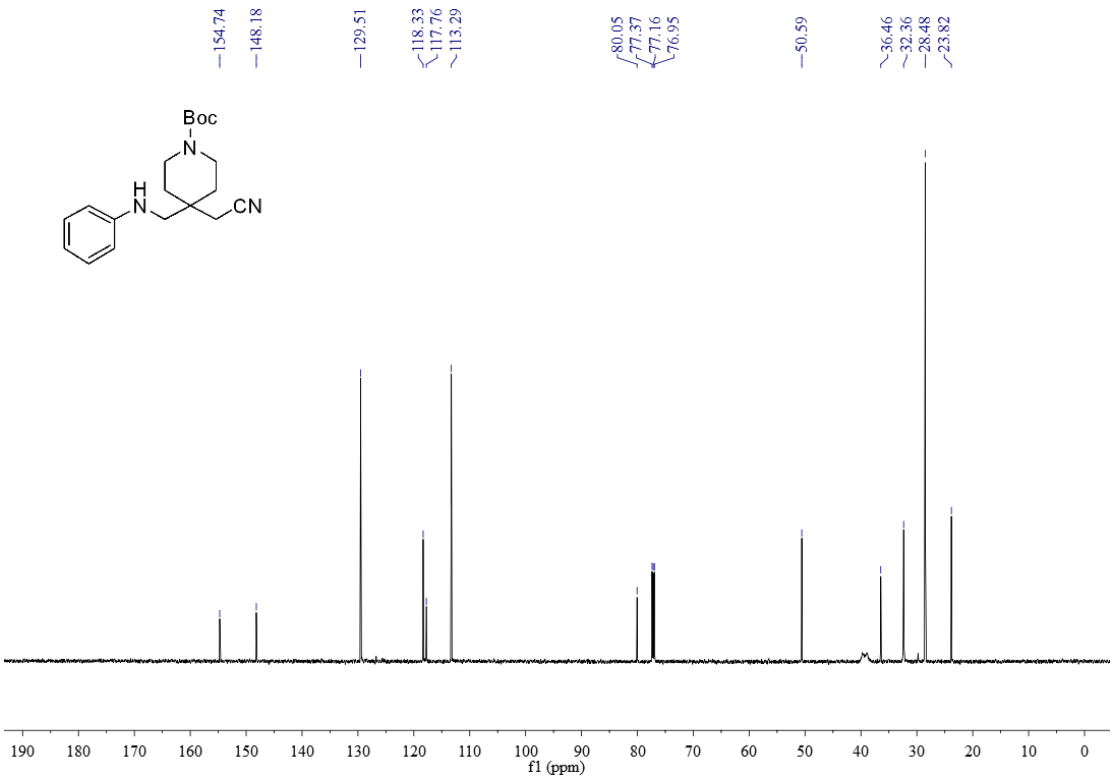

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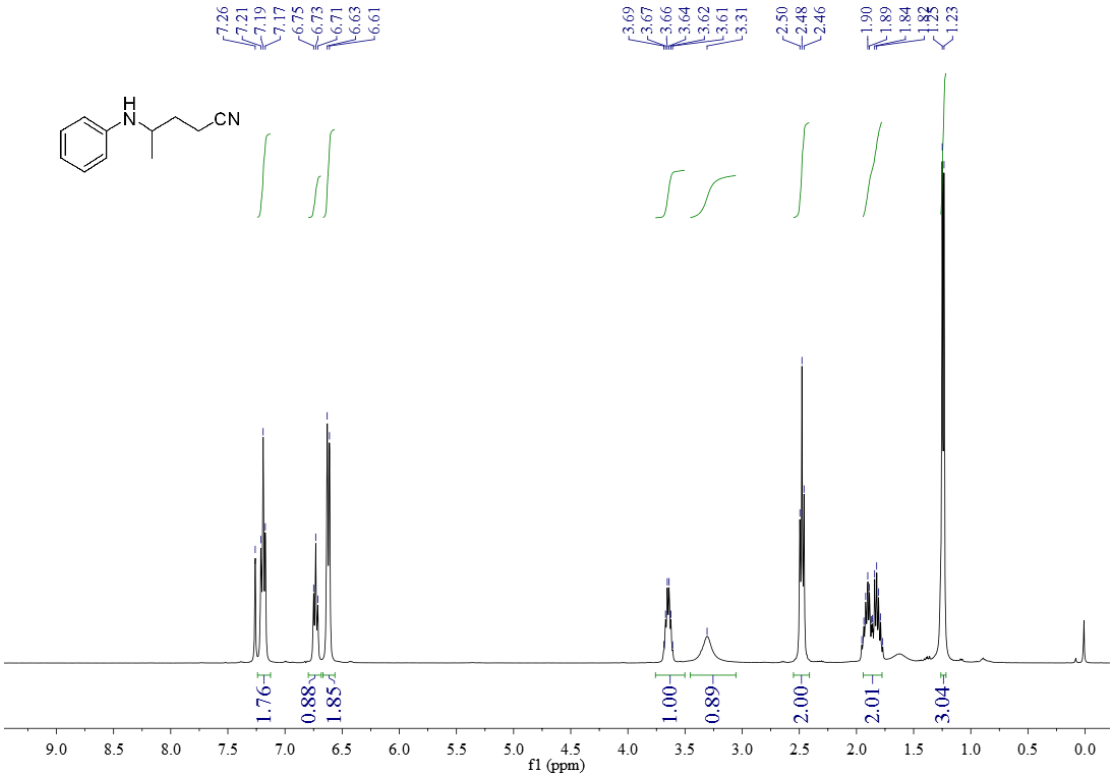

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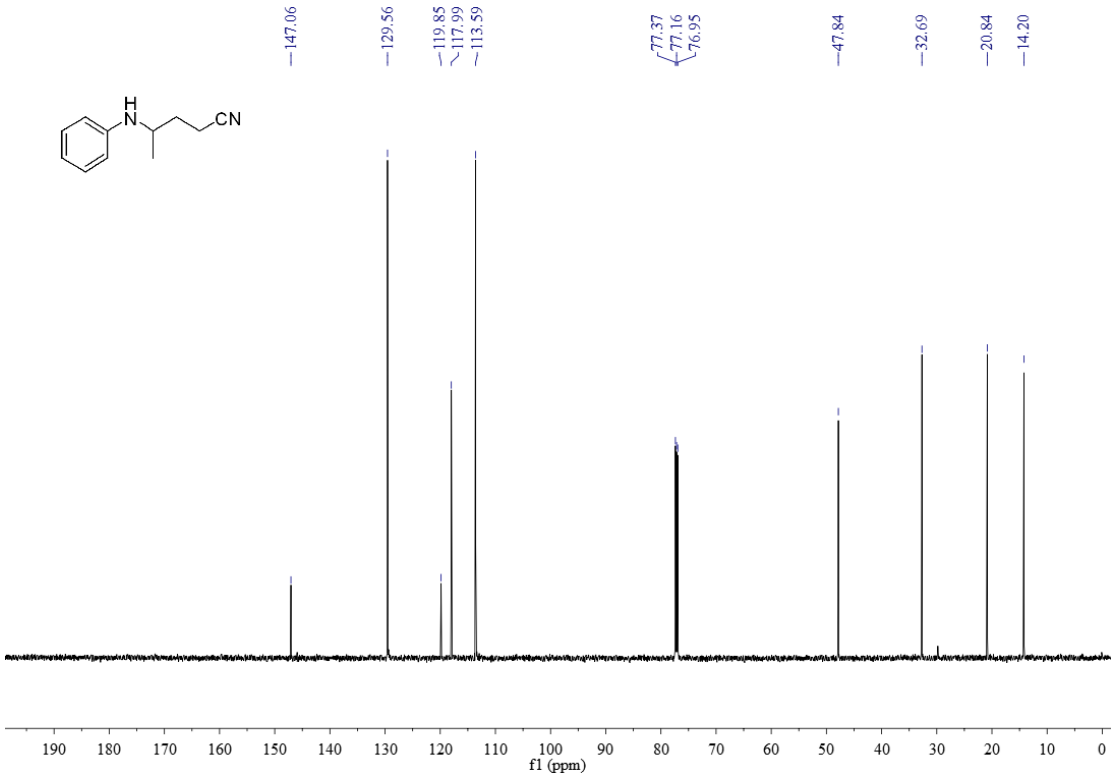
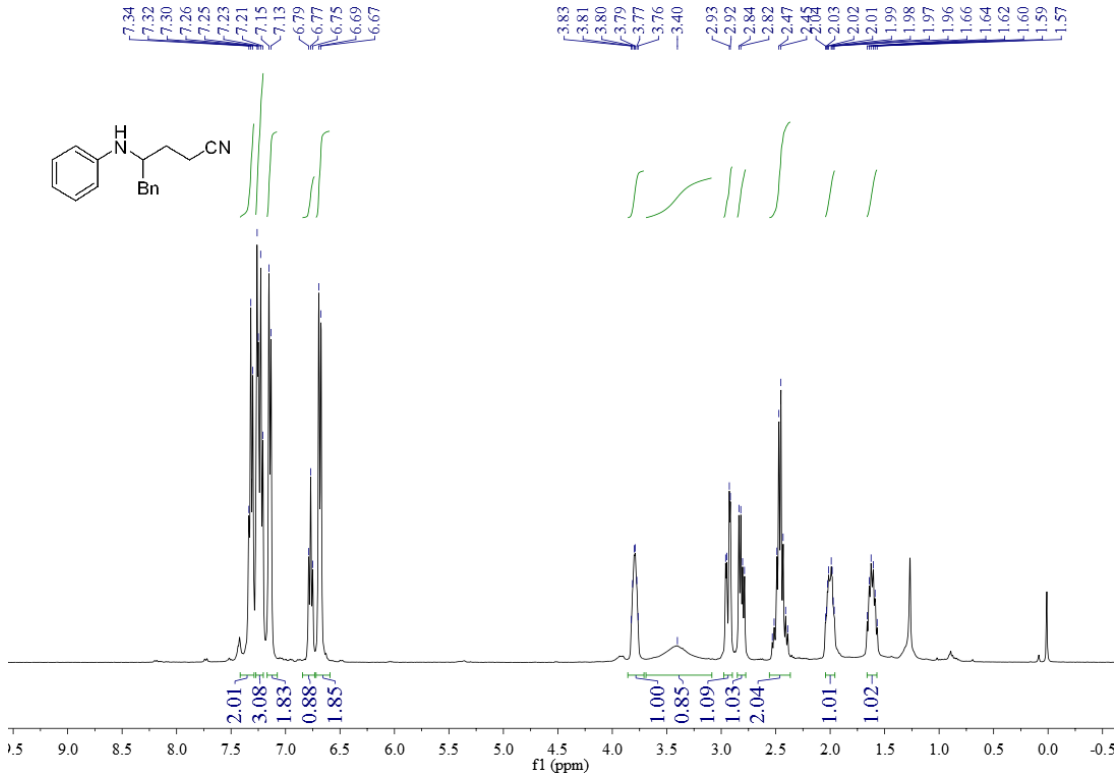
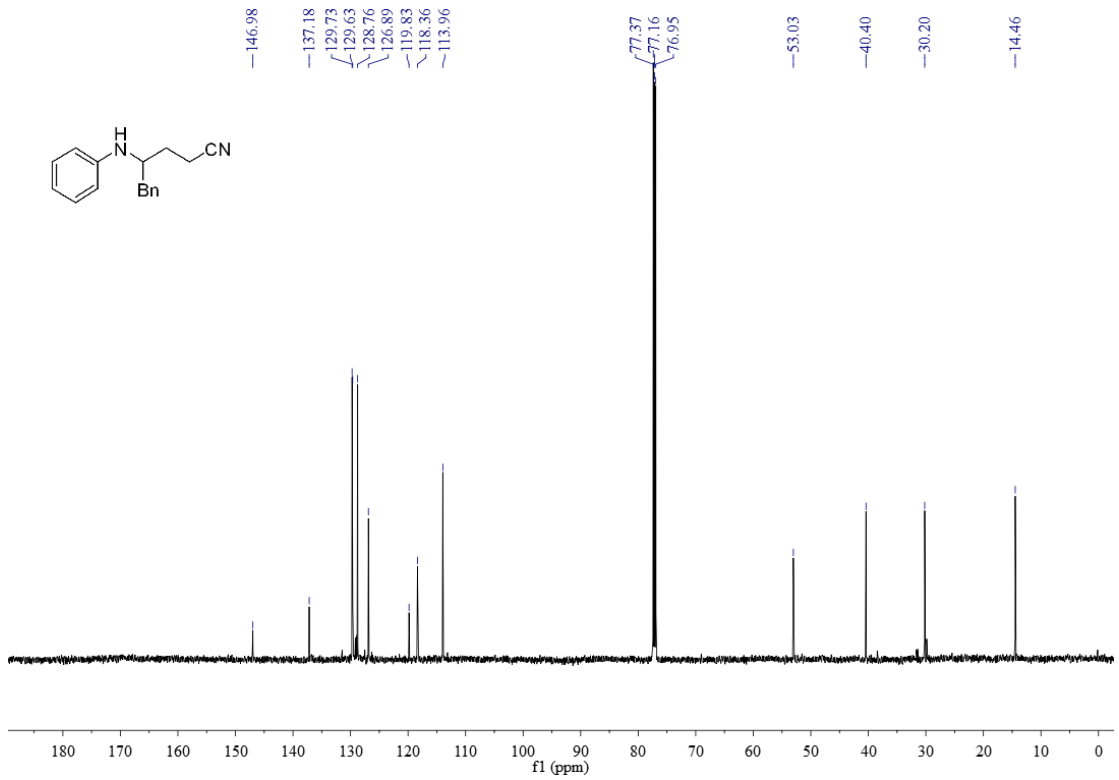


^{1}H NMR of **4r**



^{13}C NMR of **4r**



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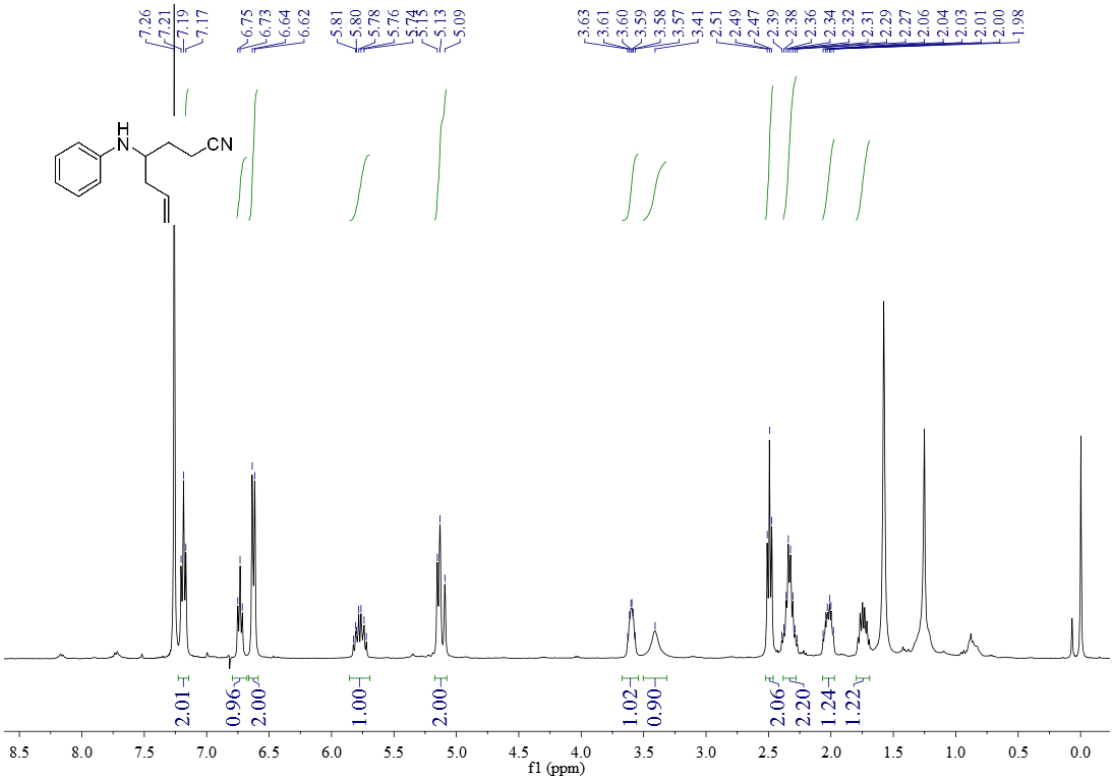

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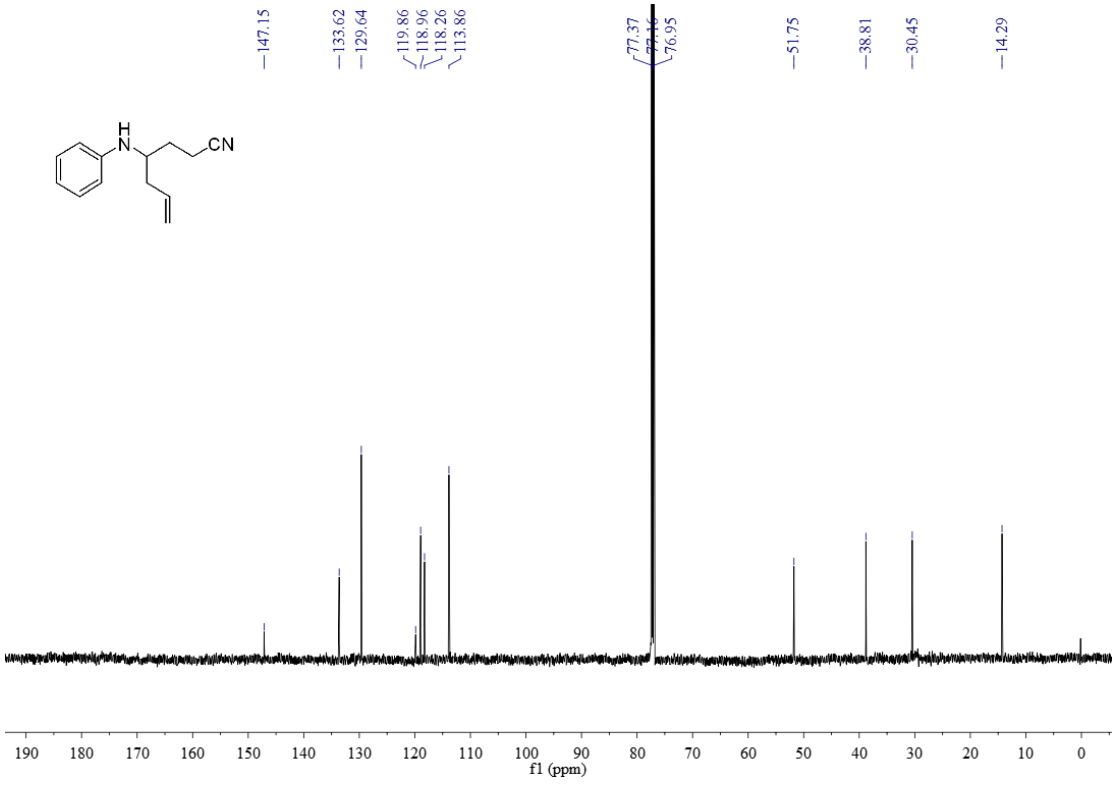
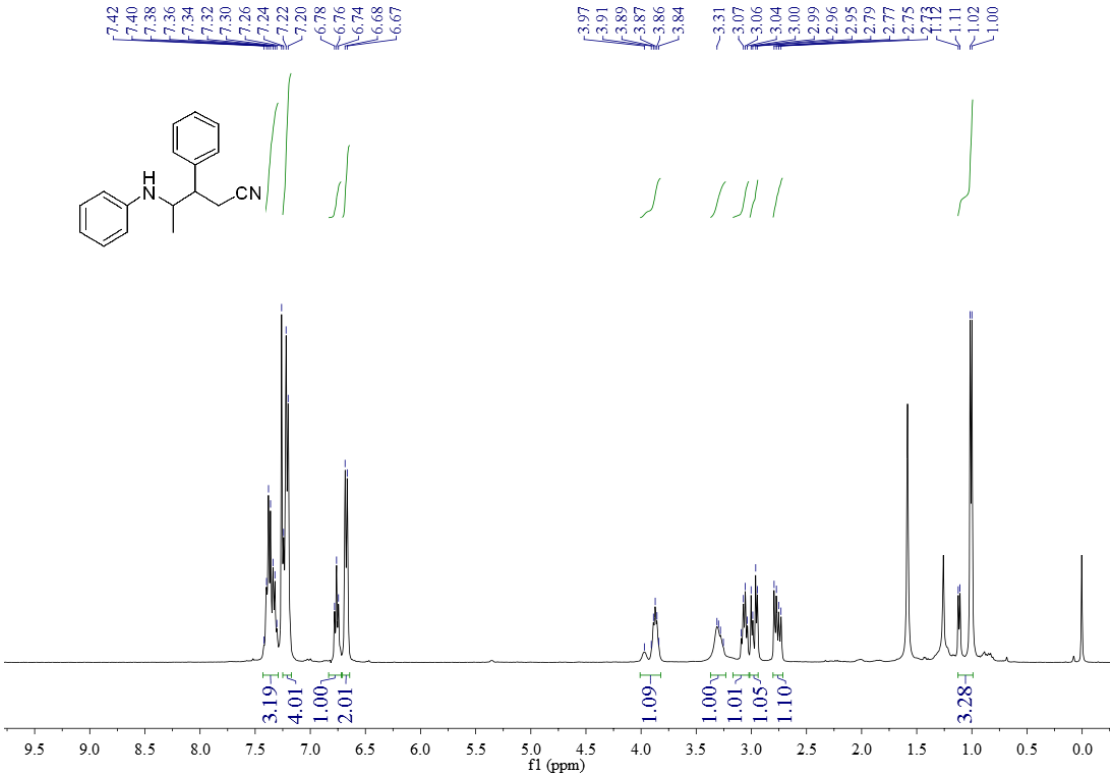
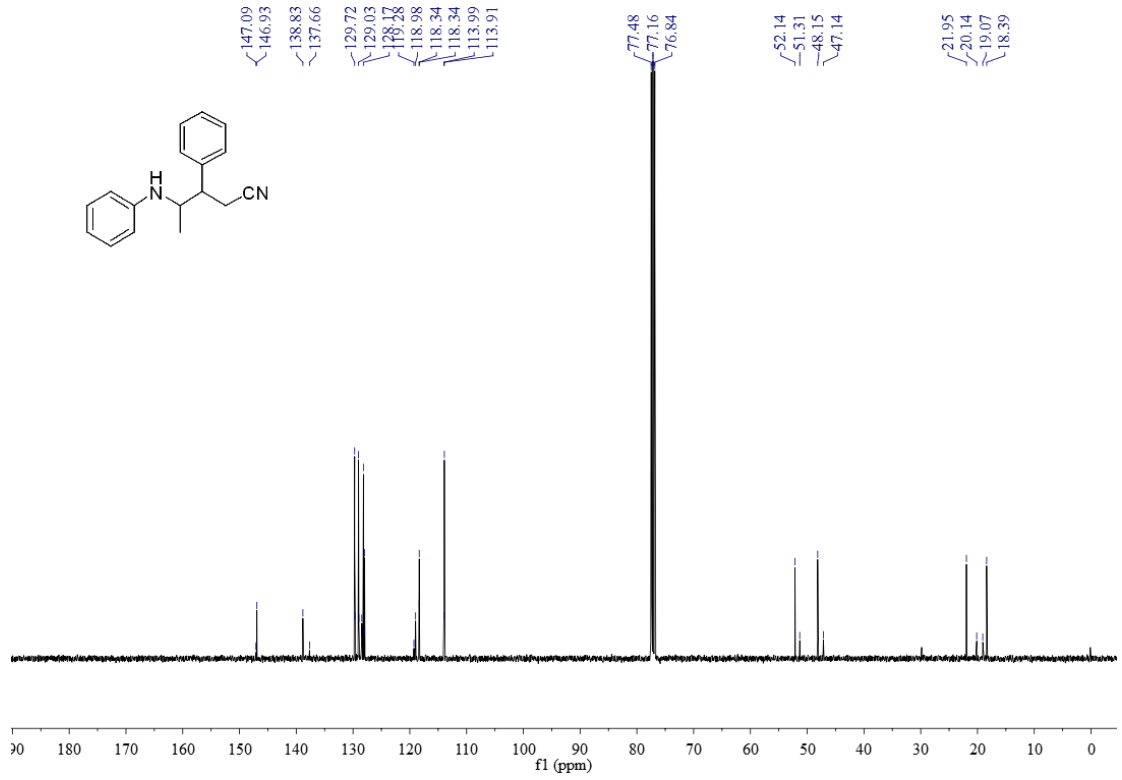


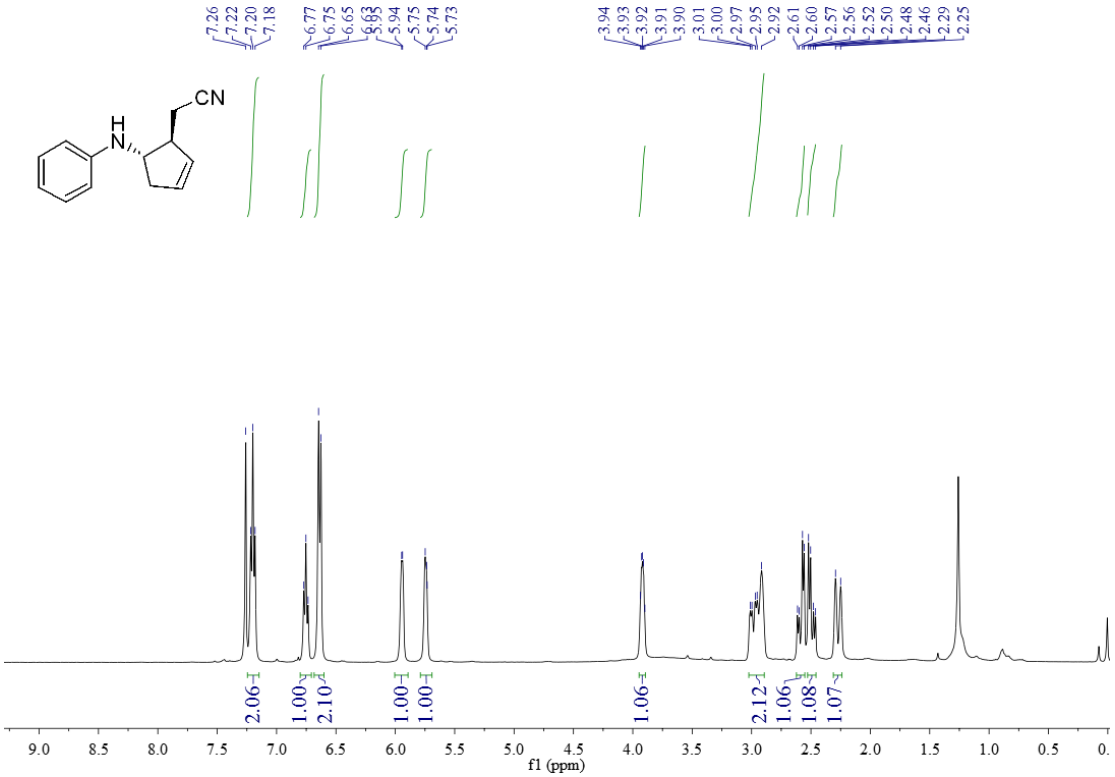
^{1}H NMR of **4t**



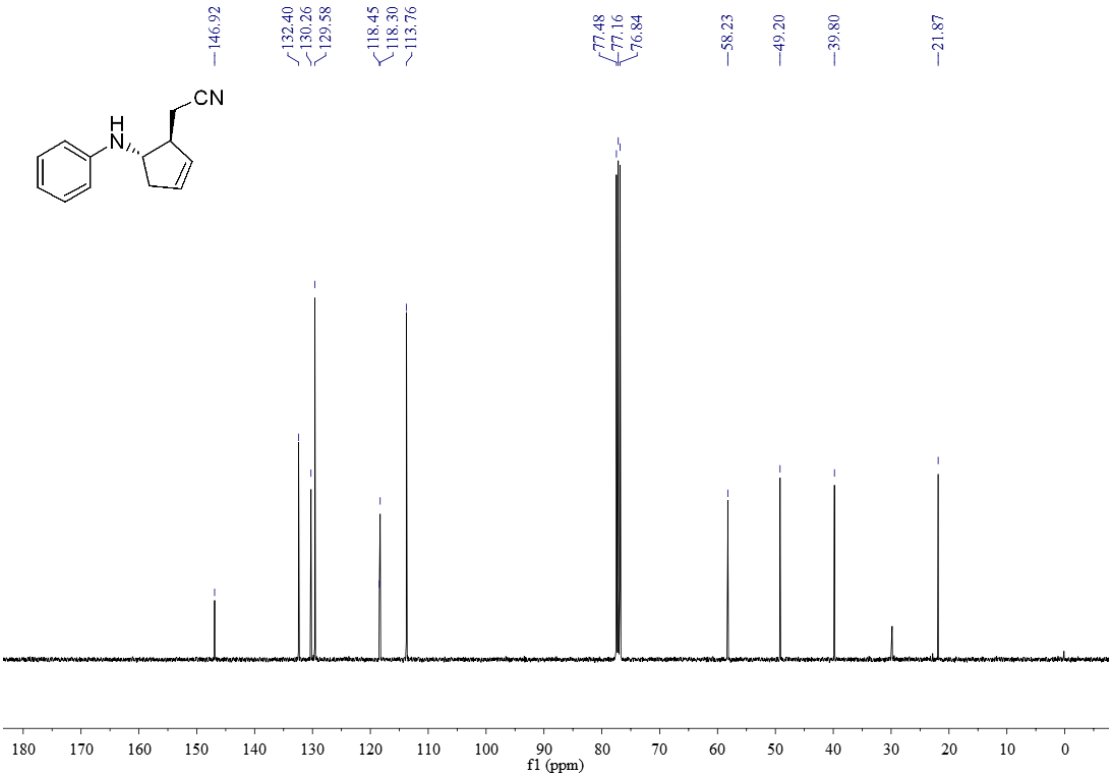
^{13}C NMR of **4t**



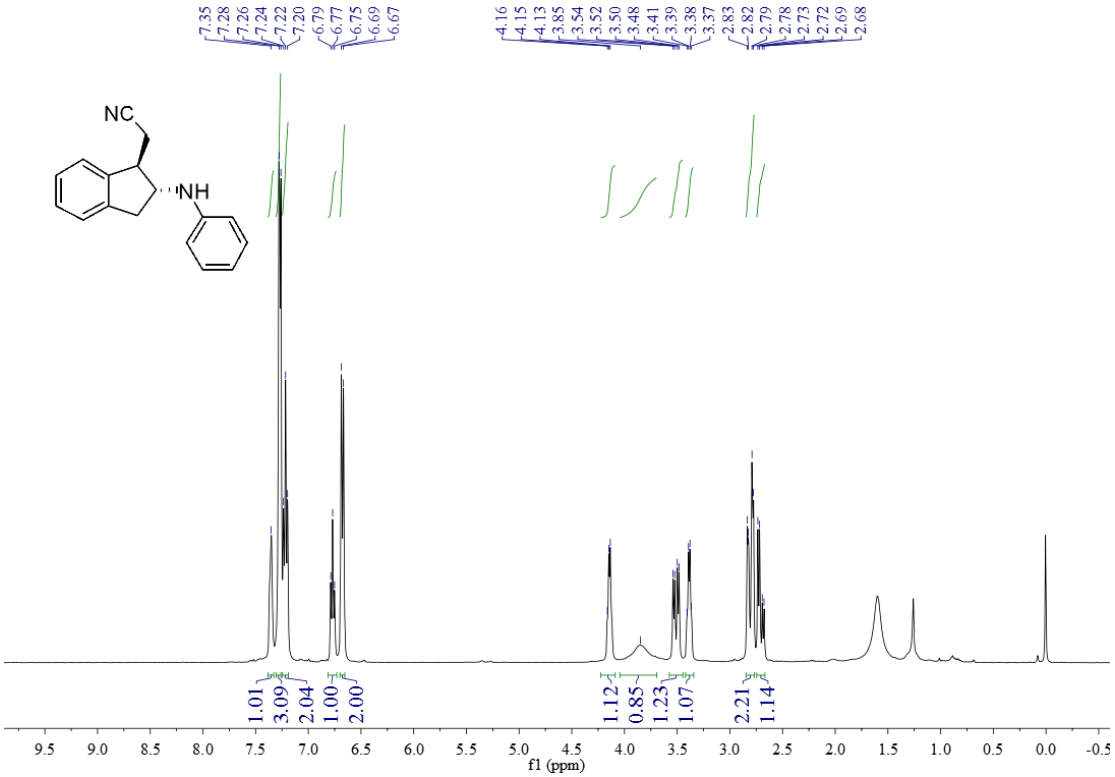
^{1}H NMR of **4u**



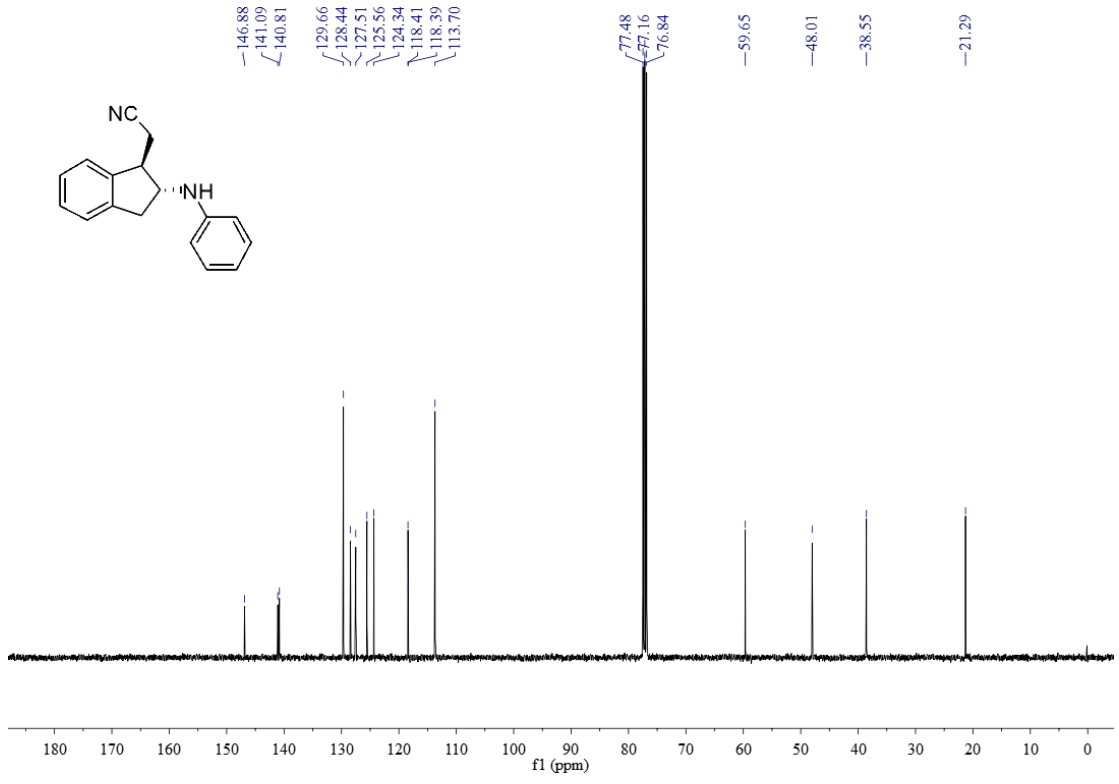
^{13}C NMR of **4u**



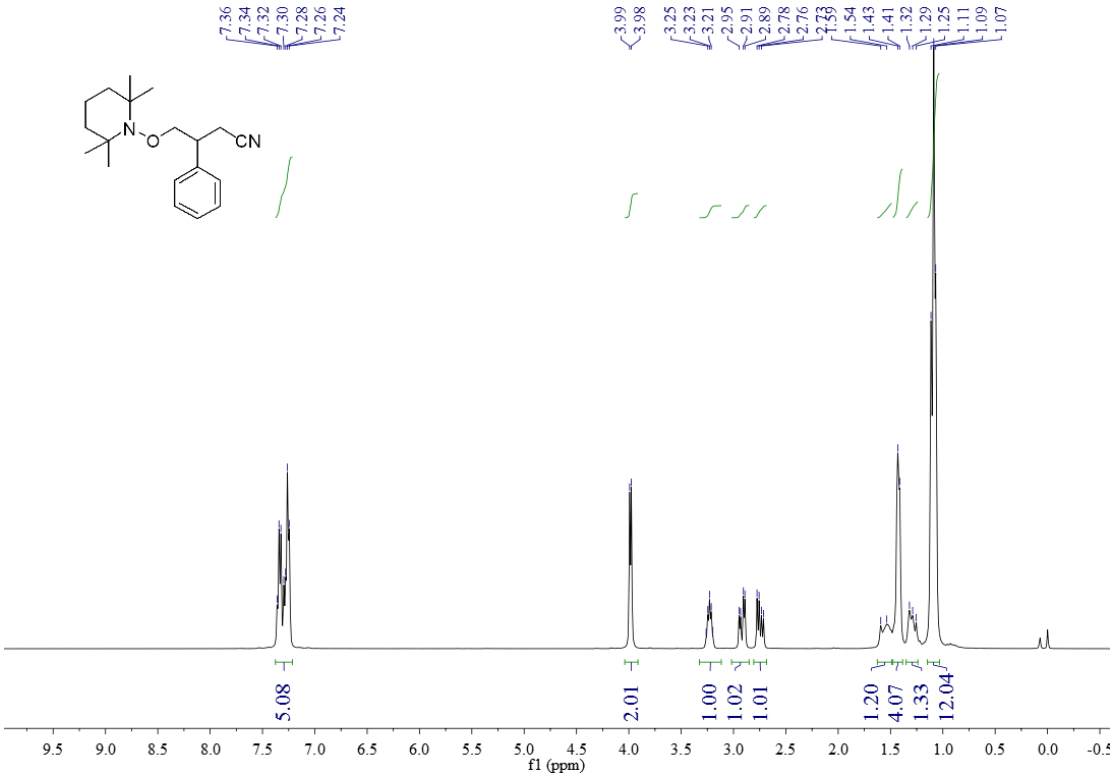
^{1}H NMR of **4v**



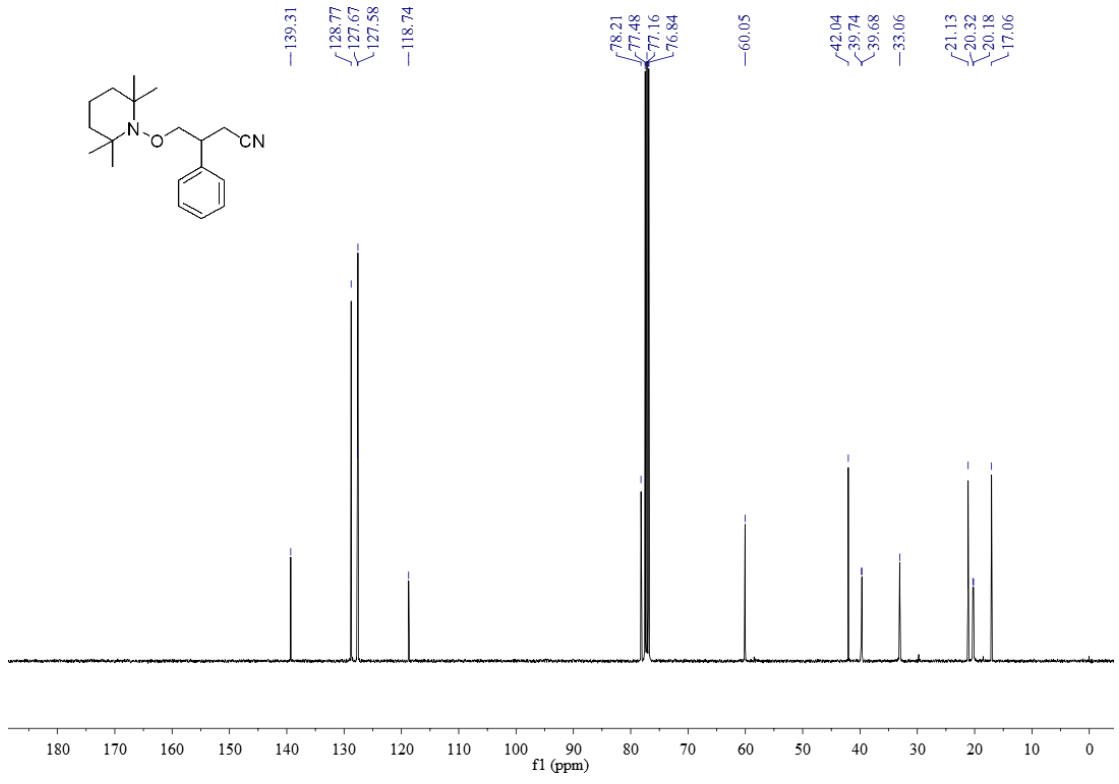
^{13}C NMR of **4v**



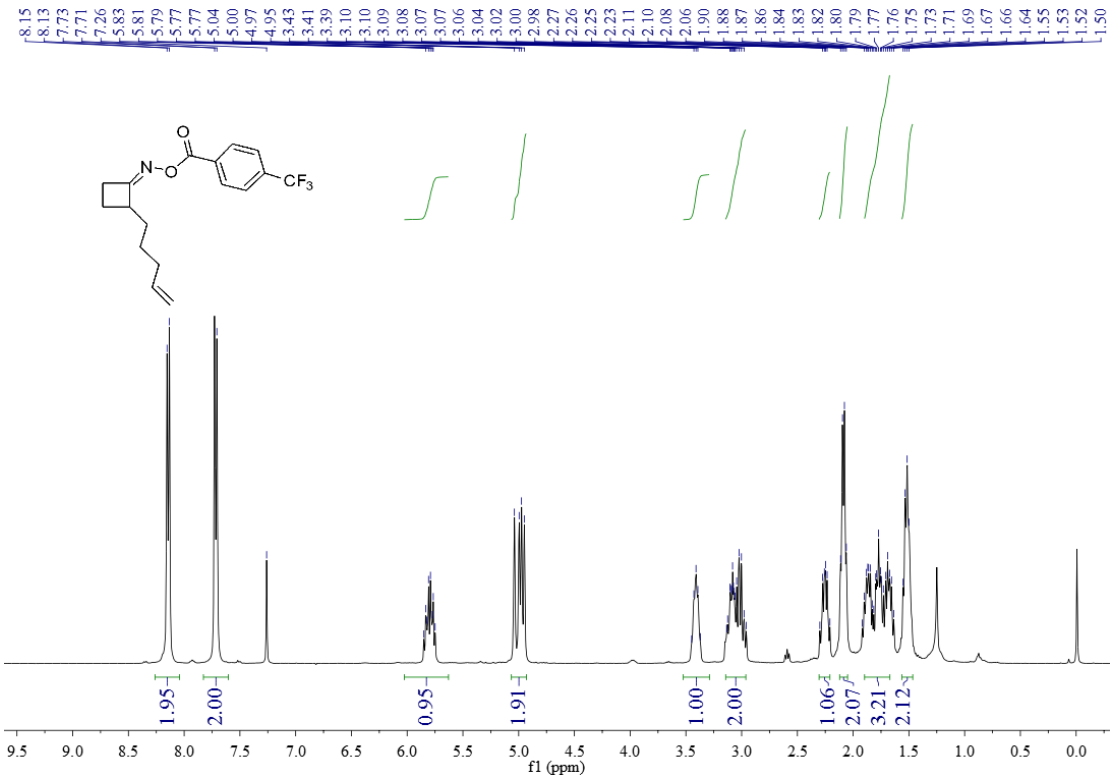
^{1}H NMR of **5a**



^{13}C NMR of **5a**



^{1}H NMR of **6**



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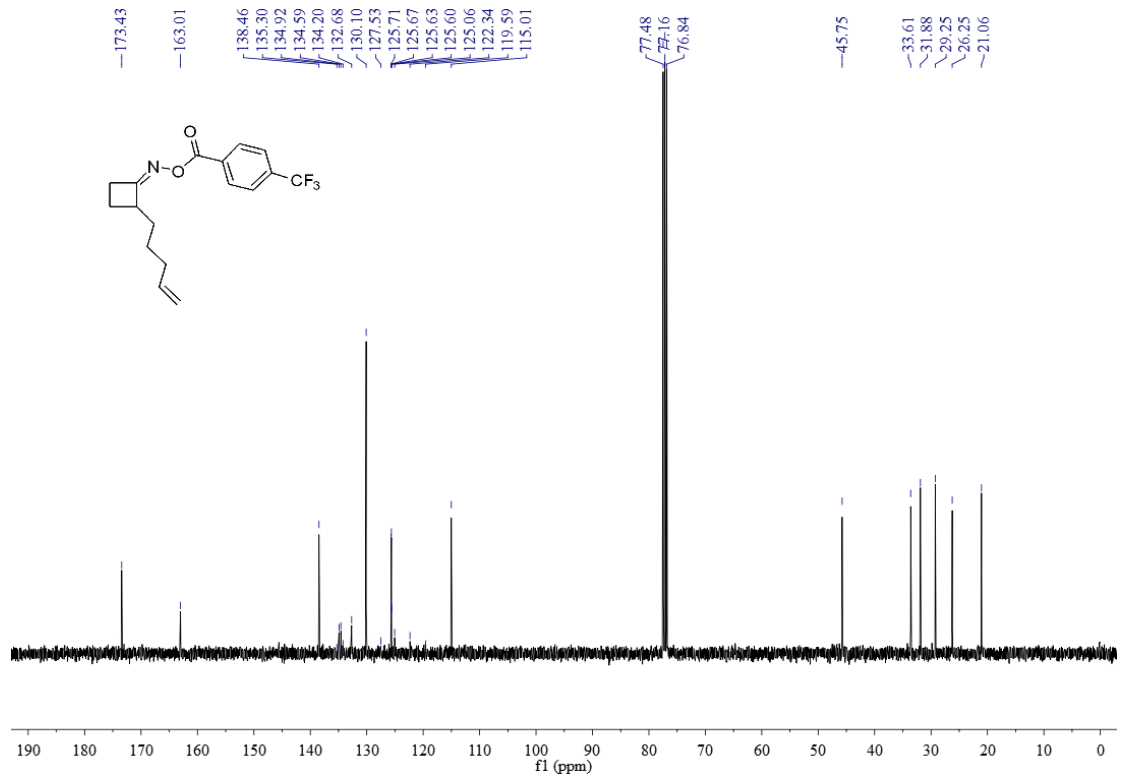
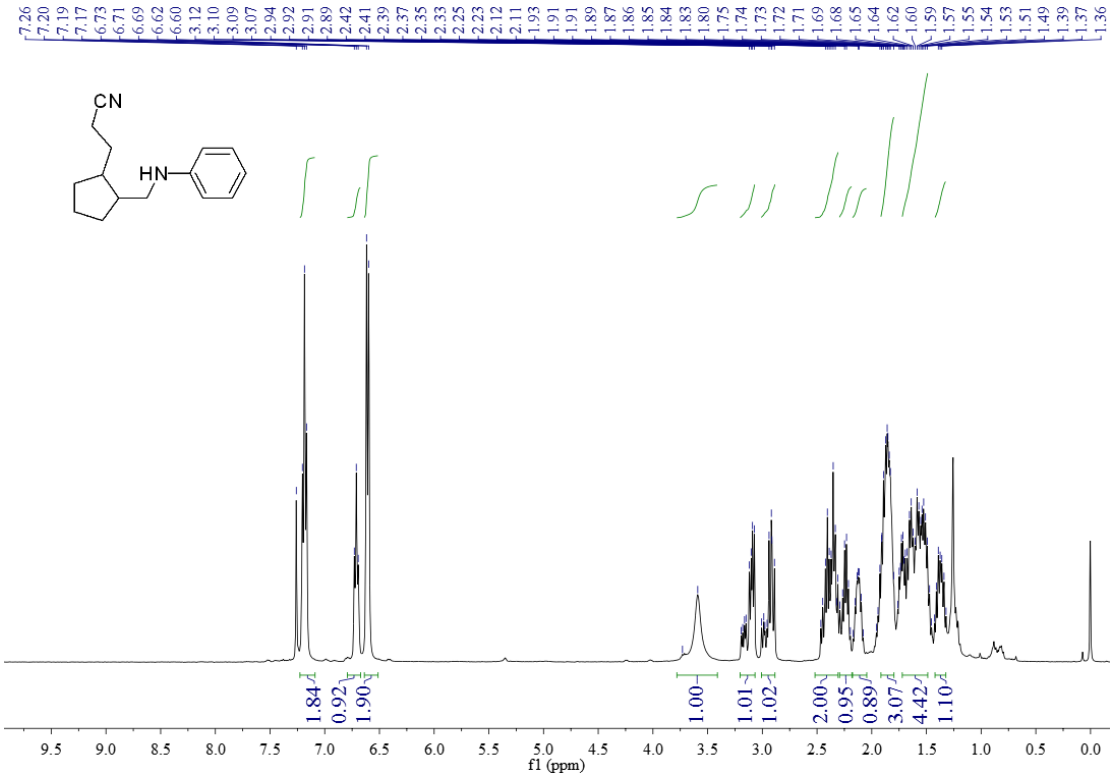


^{1}H NMR of **7**



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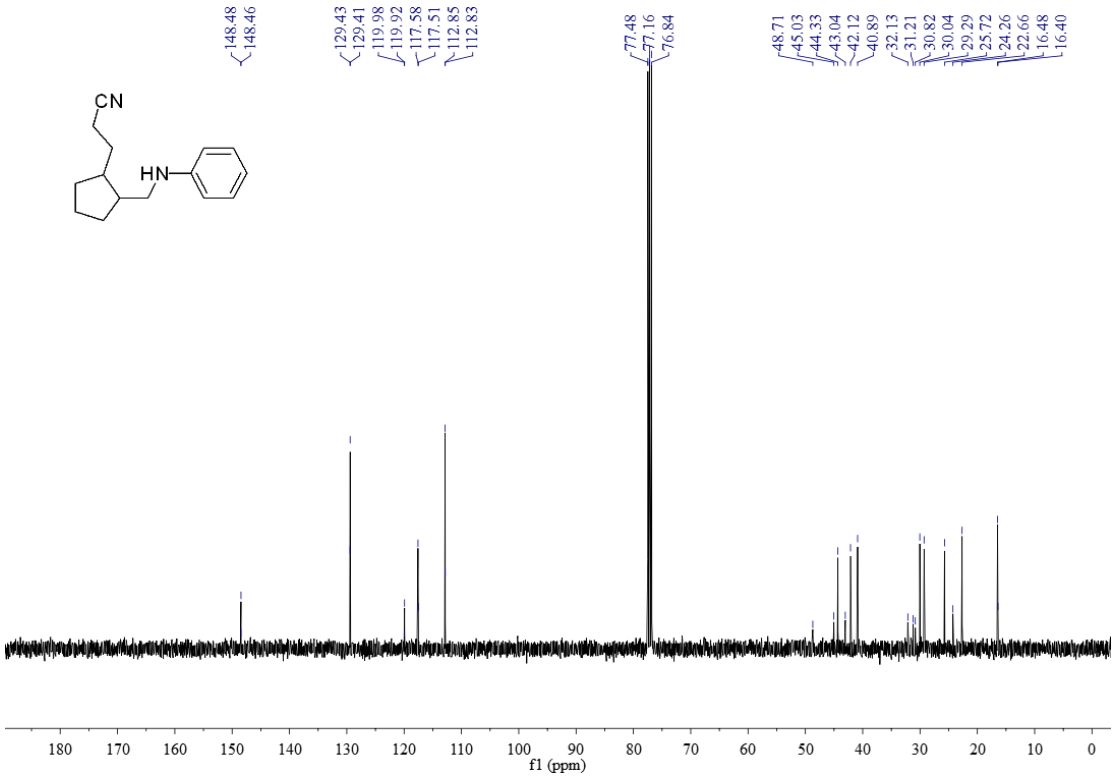
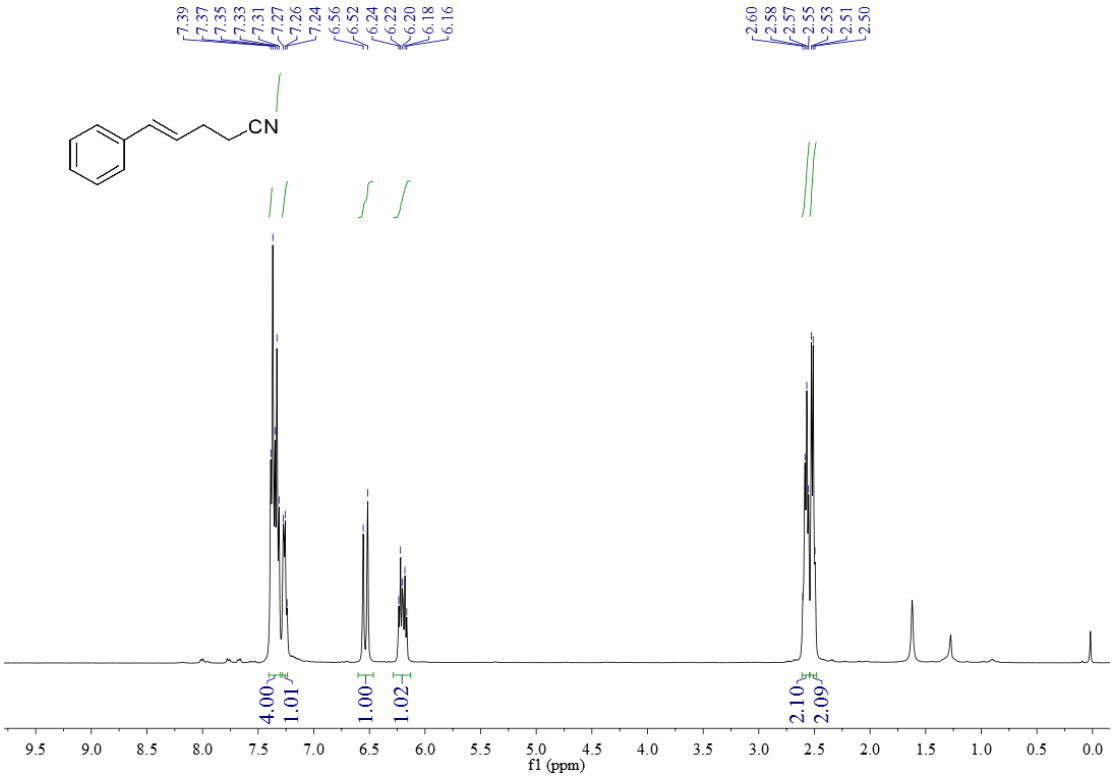
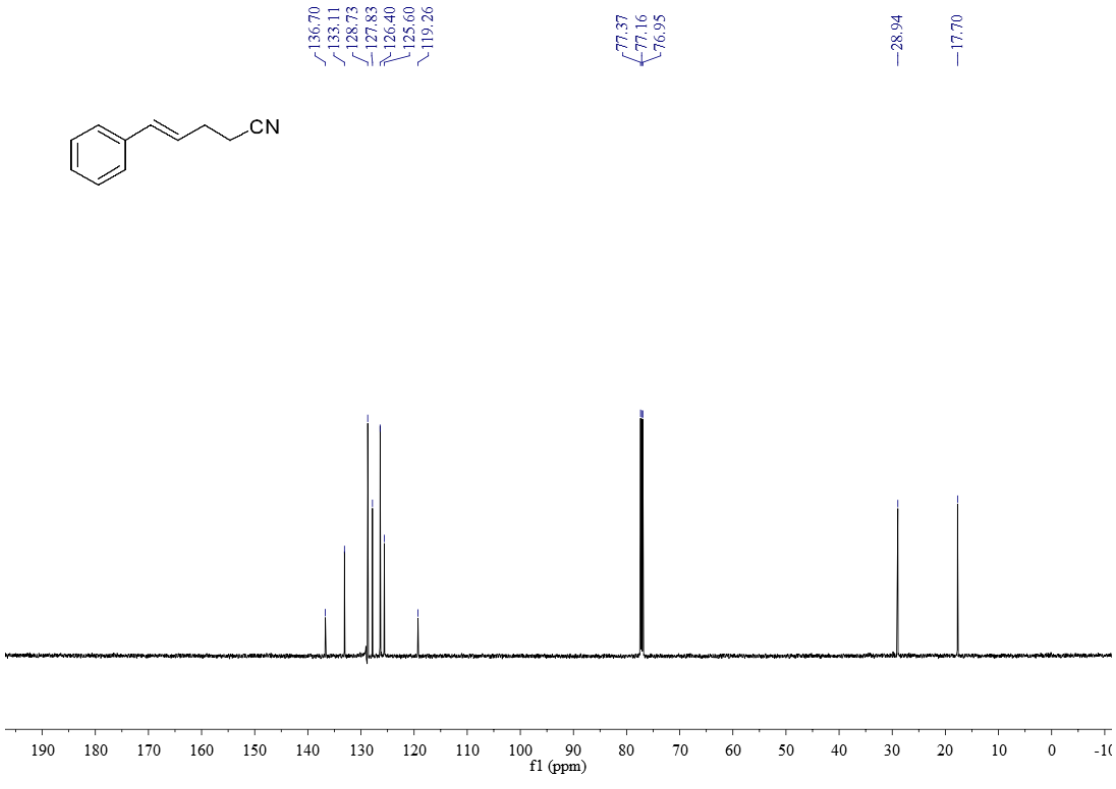


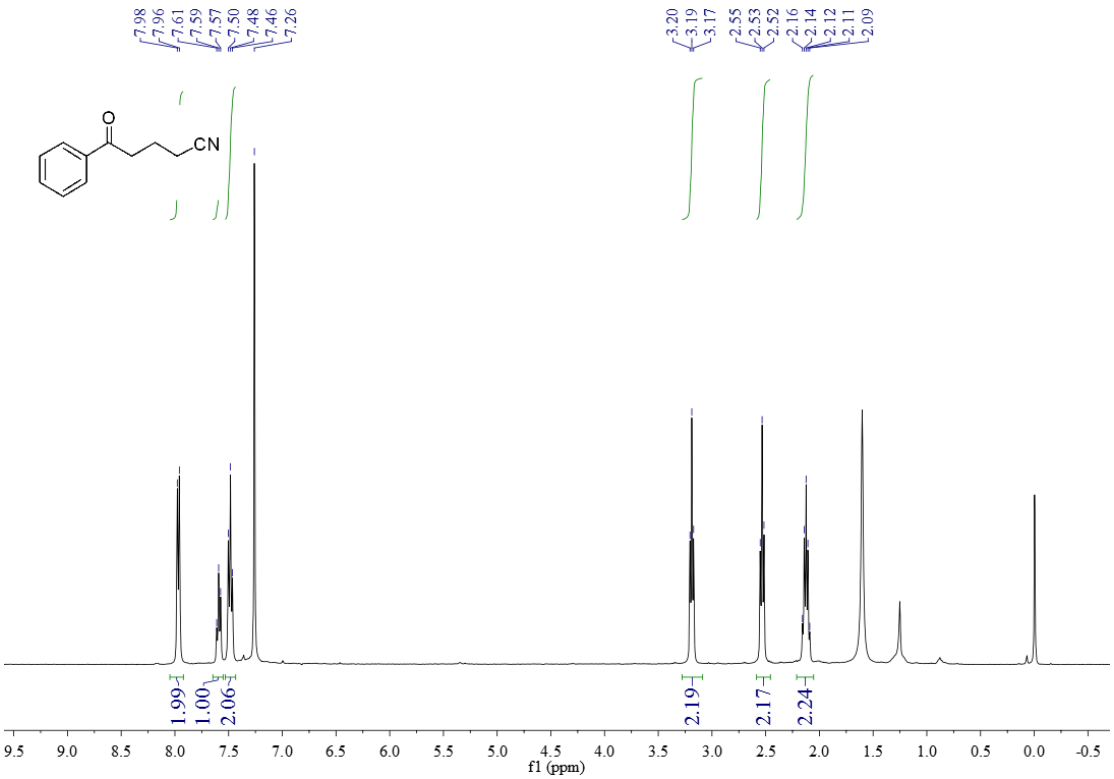
^{1}H NMR of **8**



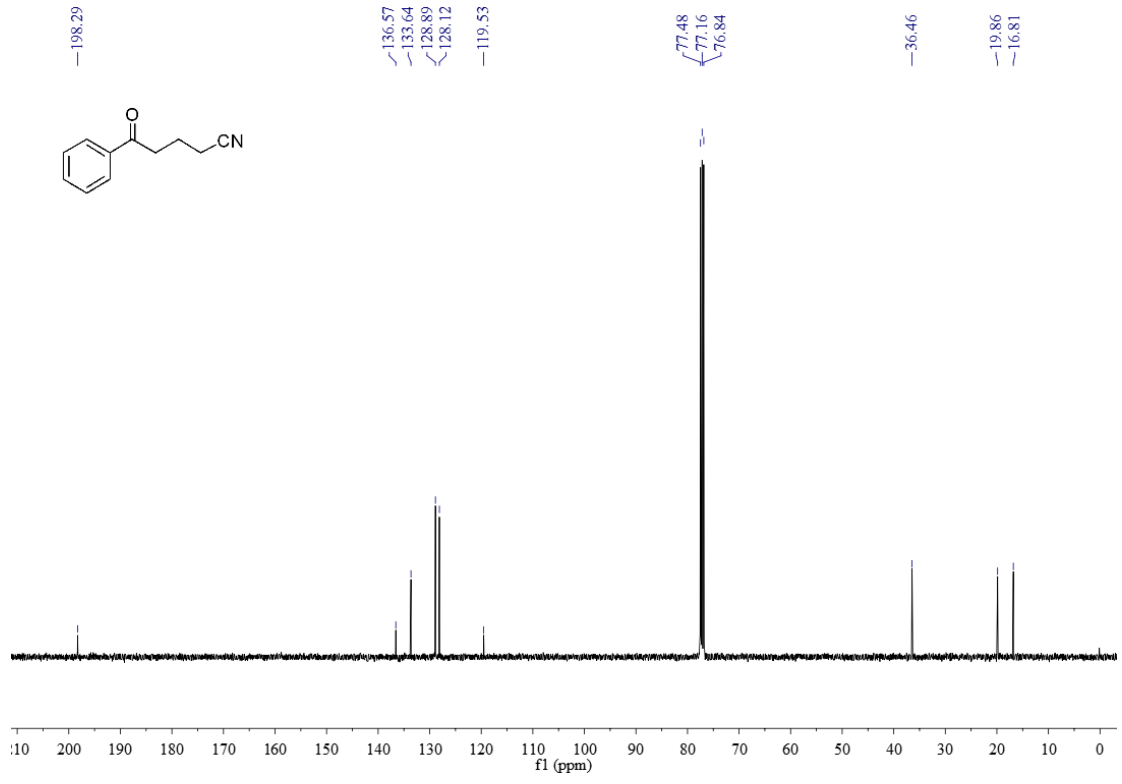
^{13}C NMR of **8**



^{1}H NMR of **9**

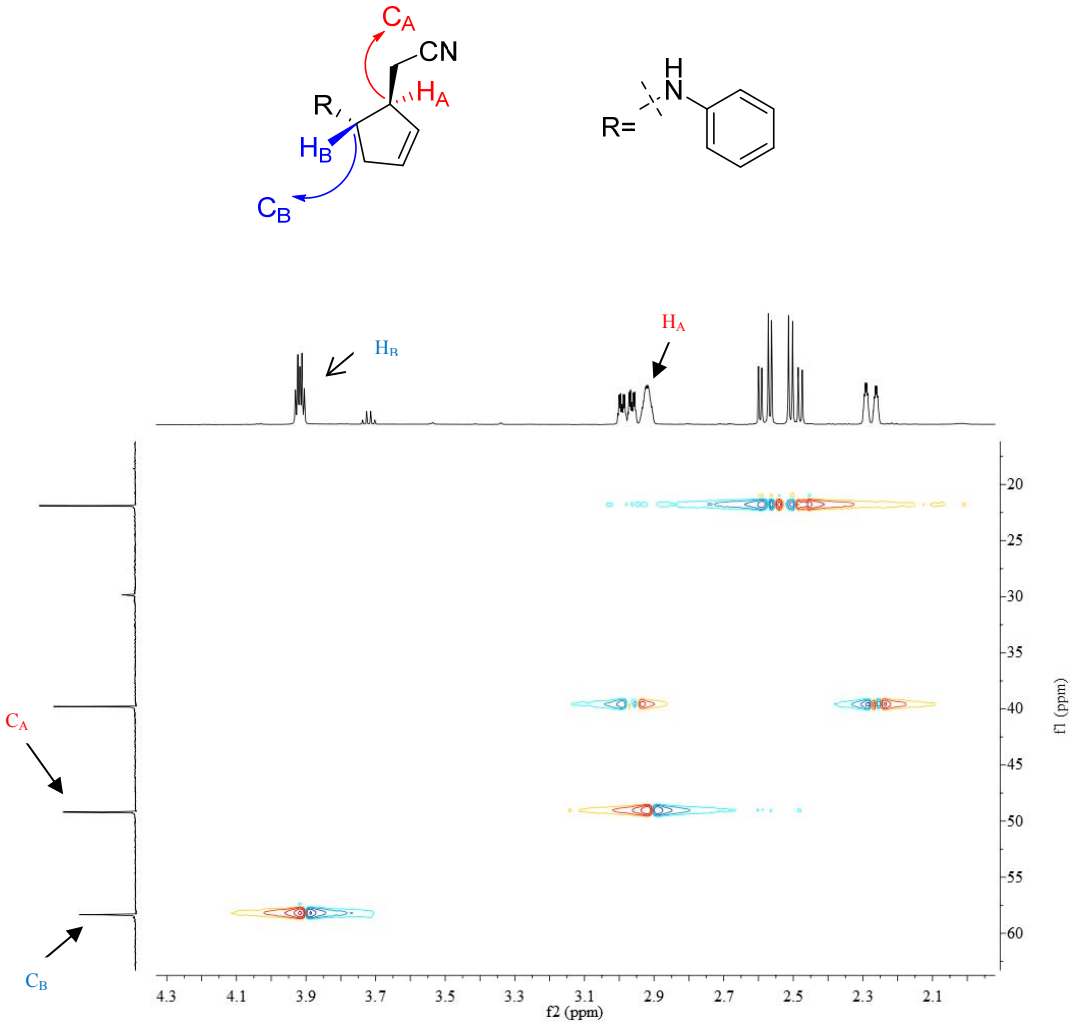


^{13}C NMR of **9**

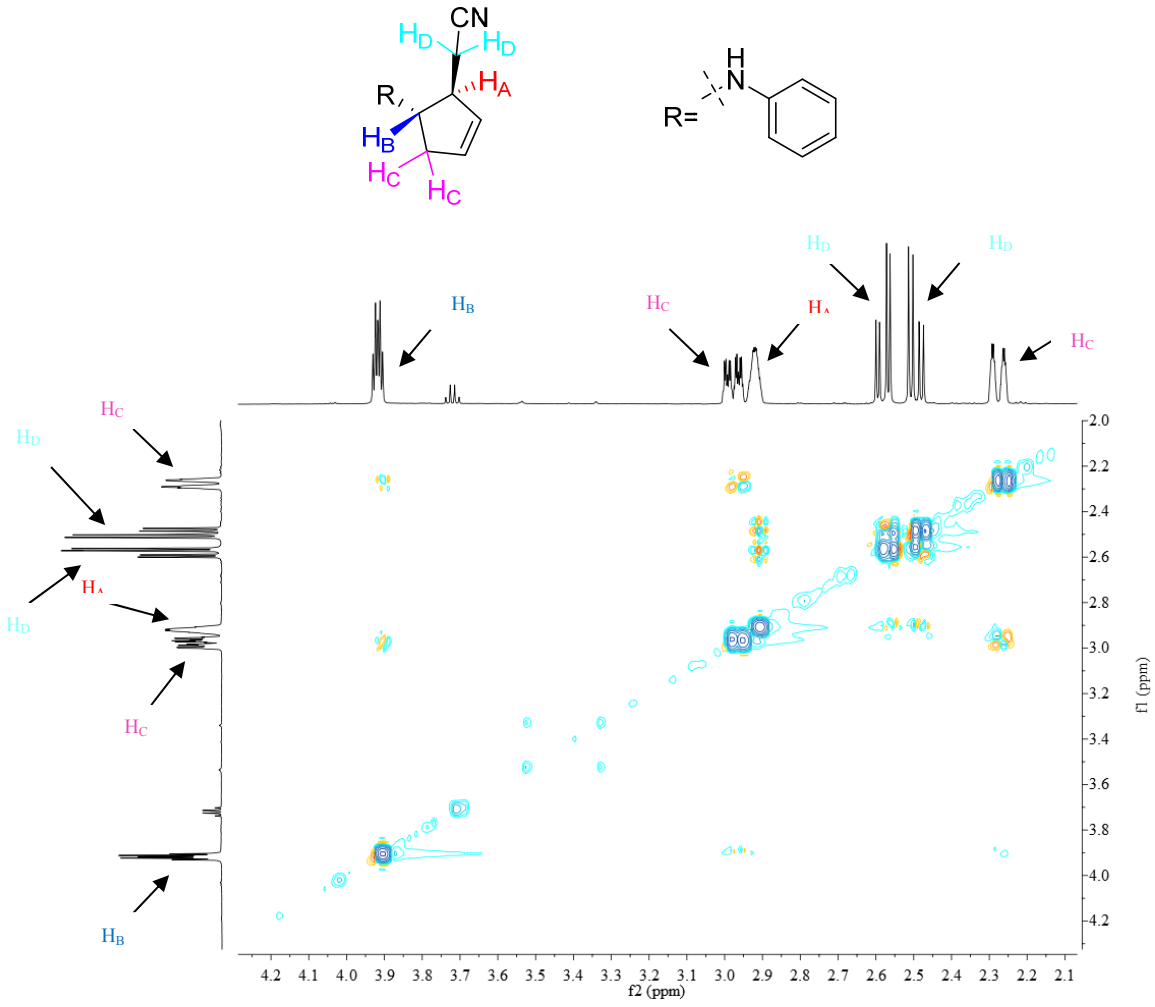


8. 2D NMR Spectra

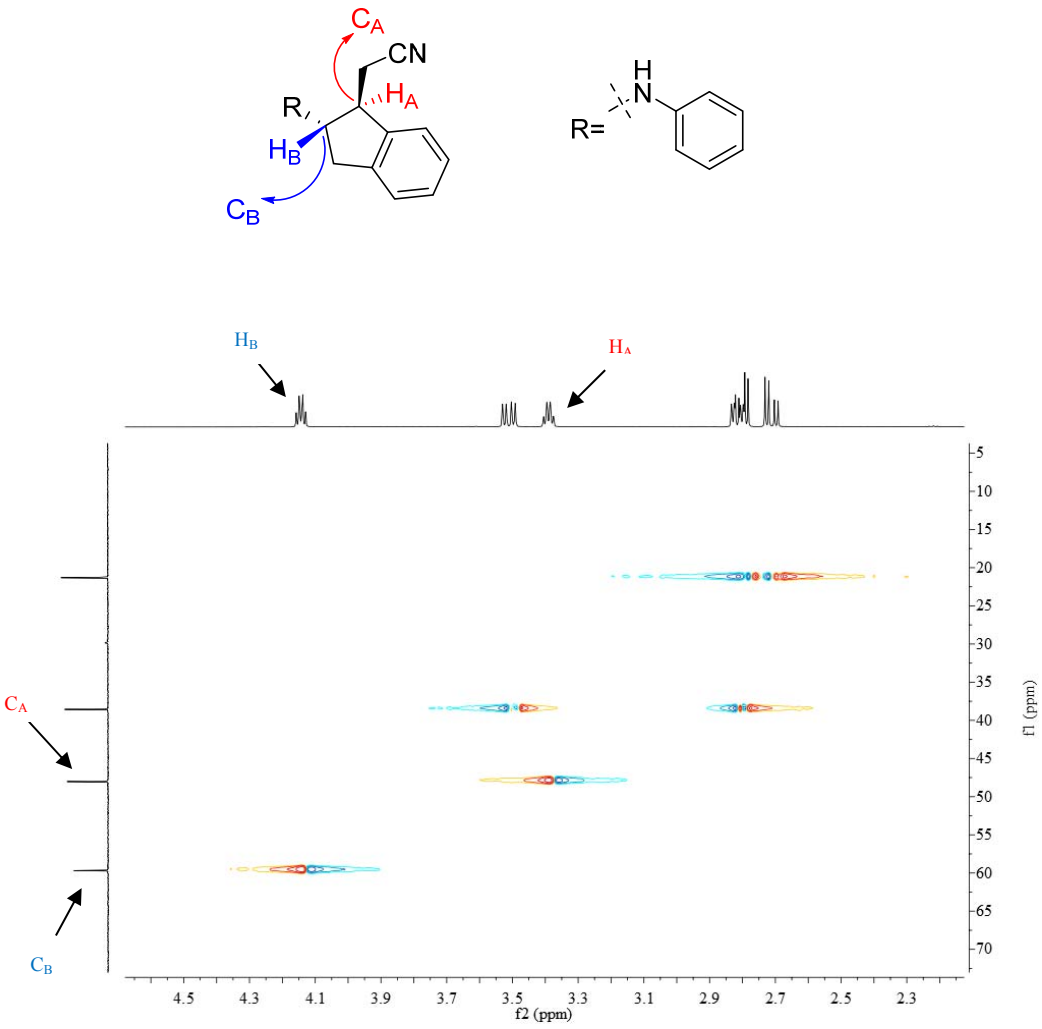
HSQC of spectrum of 4u



2D-NOE spectrum of 4u



HSQC of spectrum of 4v



2D-NOE spectrum of 4v