Supporting Information

Pd-Catalyzed Imine-Directed One-Pot Access to Polysubstituted Pyrroles via Tandem Triple Isocyanide Insertion/Aza-Nazarov Cyclization Reactions

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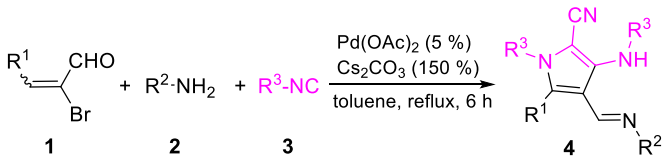
1. General Information

Unless otherwise noted, reactions were performed in Schlenk tube by oil bath under an atmosphere of N_2. Materials were purchased from commercial suppliers without further purification. Solvents were used with further distillation. Oil bath was used for all required reactions with magnetic stirring. Column chromatography purifications were performed under "flash" conditions using 200-300 mesh silica gel. Analytical TLC was carried out on silica gel 60 F254 plates which were visualized by exposure to ultraviolet light. Melting points were determined with an X-4 model apparatus. Crystal was tested on a Bruker APEX-II CCD diffractometer. HRMS was measured on an FT-ICR MS Bruker15TSolarix spectrometer. NMR spectra were recorded on a Bruker 400 spectrometer calibrated to $CDCl_3$ or DMSO-d_6 using tetramethylsilane (TMS) as internal standards. ^{1}H NMR spectral data are reported in terms of chemical shift (δ, ppm), multiplicity (s = single, d = doublet, t = triplet, q = quartet, m =multiplet), coupling constant (Hz), and integration. ^{13}C NMR spectral data are reported in terms of chemical shift.

2. General Procedure for the Preparation of 4, 5 and 6

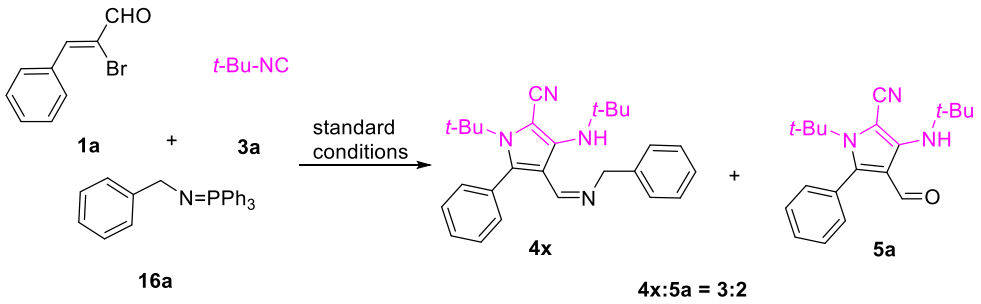
General procedure for the preparation of compounds 4a-w:

A mixture of aldehydes **1** (0.5 mmol) and anilines **2** (0.5 mmol, 1.0 equiv.) were stirred in toluene (0.1 M, 5 mL) at room temperature for 1 h. Then isocyanide **3** (1.8 mmol, 3.6 equiv.), Cs_2CO_3 (245mg, 0.75 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.05 equiv.) were added to an oven-dried Schlenk tube under N_2. The mixtures were allowed to stir at reflux temperature by oil bath for 5 h and monitored by TLC. After completion, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel with ethylacetate/petroleum ether (1:20-25) as the eluent to give **4a-w** in a yield of 54-81%.



General procedure for the preparation of compounds 4x:

A mixture of aldehyde **1a** (0.5 mmol) and benzylphosphonimide **16a** (0.5 mmol, 1.0 equiv.) was stirred in toluene (0.1 M, 5 mL) at room temperature for 1 h. Then isocyanide **3a** (1.8 mmol, 3.6 equiv.), Cs_2CO_3 (245mg, 0.75 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.05 equiv.) were added to an oven-dried Schlenk tube under N_2. The mixtures were allowed to stir at reflux temperature by oil bath for 5 h and monitored by TLC. After completion, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel with ethylacetate/petroleum ether (1: 25) as the eluent to give the mixture of **4x** and **5a** (3:2).



General procedure for the preparation of compounds 5:

To a stirred solution of compounds **4** (0.5 mmol) in THF (2 mL) was added dropwise of a solution of hydrochloric acid (2 M, 0.5 mL) in THF (2 mL) at room temperature. Then the reactions were heated to refluxing temperature by oil bath for 1 h and monitored by TLC. After completion, the reaction mixture was concentrated under reduced pressure and the residue was purified by silica flash chromatography with EtOAc/petroleum ether (1: 18) as the eluent to give products **5a-c** in a yield of 83-88%.

General procedure for the preparation of compounds 6:

To a stirred solution of $NaBH_3CN$ (37.8 mg, 0.6 mmol, 1.2 equiv.) in THF (3 mL) was added dropwise of a solution of compounds **4a** (216 mg, 0.5 mmol) in THF (2

mL) in an ice-bath. Then the reactions were carried out for 3 h and monitored by TLC. Upon completion, the reaction mixture was concentrated under reduced pressure and the residue was purified by silica flash chromatography with EtOAc/petroleum ether (1: 20) as the eluent to give products **6a** in a yield of 93%.

3. X-ray Crystallography Data of 4b

Crystal sample preparation of 4b: A solution of compound **4b** (0.03 g) in AcOEt (1.5 mL) was placed in a vial (10 mL). Then *n*-hexane (6 mL) was added to the solution with a dropper. The single crystal **4b** was obtained by slowly evaporating mixed solvent at room temperature under the air conditions. A suitable crystal was selected and tested on a Bruker APEX-II CCD diffractometer. The crystal was kept at 150.0 K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of [mo_1014_1_0m]

Crystal Data for $C_{27}H_{32}N_4$ (M =412.56 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 22.1822(6) Å, b = 11.9377(3) Å, c = 27.1989(8) Å, β = 95.1440(10)°, V = 7173.4(3) $Å^3$, Z = 12, T = 150.0 K, μ(MoKα) = 0.068 mm^{-1}, Dcalc = 1.146 g/cm^3, 97486 reflections measured ($3.728° \leqslant 2\Theta \leqslant 52.044°$), 14129 unique ($R_{int}$ = 0.1158, R_{sigma} = 0.0607) which were used in all calculations. The final R_1 was 0.0549 ($I > 2\sigma(I)$) and wR_2 was 0.1514 (all data).

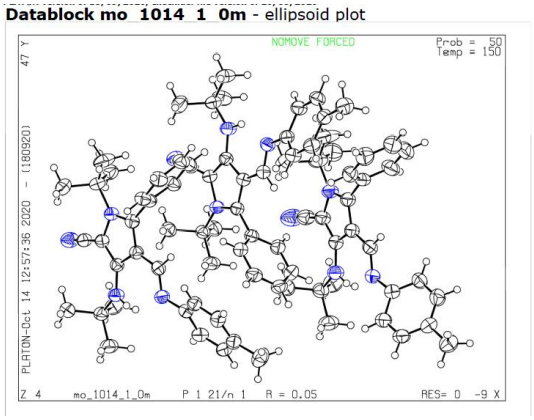


Figure S1. X-ray crystal structure of **4b** is drawn at the 50% probability.

Table 1 Crystal data and structure refinement for exp_1889.

Identification code	mo_1014_1_0m
Empirical formula	$C_{27}H_{32}N_4$
Formula weight	412.56
Temperature/K	150.0
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	22.1822(6)
b/Å	11.9377(3)
c/Å	27.1989(8)
α /°	90
β /°	95.1440(10)
γ /°	90
Volume/Å^3	7173.4(3)
Z	12
ρ calcg/cm^3	1.146
μ /mm^{-1}	0.068
F(000)	2664.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.728 to 52.044
Index ranges	-27 ⩽ h ⩽ 27, -14 ⩽ k ⩽ 14, -33 ⩽ l ⩽ 33
Reflections collected	97486
Independent reflections	14129 [R_{int} = 0.1158, R_{sigma} = 0.0607]
Data/restraints/parameters	14129/0/858
Goodness-of-fit on F^2	1.010
Final R indexes [I>=2σ (I)]	R_1 = 0.0549, wR_2 = 0.1216
Final R indexes [all data]	R_1 = 0.1120, wR_2 = 0.1514
Largest diff. peak/hole / e Å^{-3}	0.21/-0.18

4. HRMS Figures of 12a

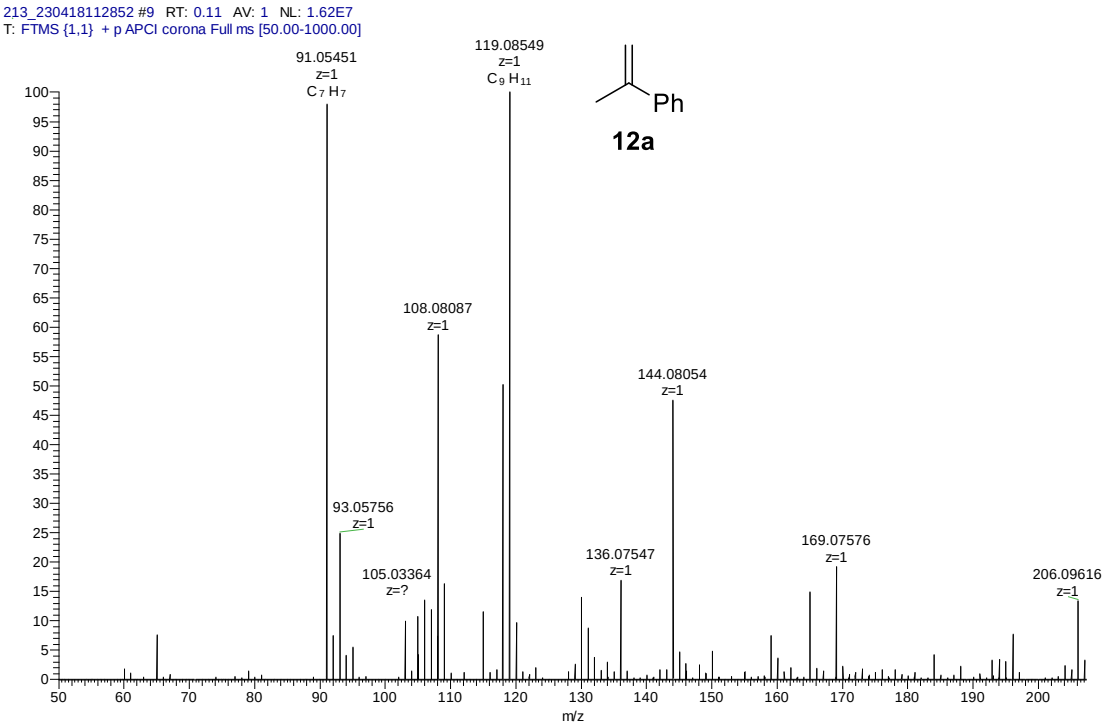


Figure S2. HRMS Figures of 12a.

5. Characterization Datas

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4a):

Bright yellow solid, yield: 0.168g (78%), ethylacetate/petroleum ether = 1: 20, mp 182–183 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.41 (s, 1H), 7.63-6.82 (m, 10H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.5, 150.3, 145.7, 143.2, 132.8, 130.7, 130.3, 129.2, 129.0, 128.0, 121.9, 121.1, 110.4, 86.7, 61.8, 52.1, 32.2, 30.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{30}ClN_4$ 433.2154; Found: 433.2155.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-phenyl-4-((p-tolylimino)methyl)-1*H*-pyrrole-2-carbonitrile (4b):

yellow solid, yield: 0.146g (71%), ethylacetate/petroleum ether = 1: 20, mp 194–195 ℃. ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm) 8.39 (s, 1H), 7.59-6.76 (m, 10H), 2.23 (s, 3H), 1.51-1.45 (m, 18H); ^{13}C {^{1}H} NMR (DMSO-d_6, 100 MHz) δ (ppm) 154.2, 148.7, 145.0, 143.3, 134.5, 132.2, 130.8, 129.7, 129.3, 128.7, 128.0, 120.8,

109.6, 85.7, 61.5, 51.5, 31.5, 30.4, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{33}N_4$ 413.2700; Found: 413.2698.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-fluorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4c):

yellow solid, yield: 0.150g (72%), ethylacetate/petroleum ether = 1: 25, mp 191–192 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.42 (s, 1H), 7.64-6.84 (m, 10H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 160.5 (d, J_{C-F} = 242.3 Hz), 155.1, 147.8 (d, J_{C-F} = 2.9 Hz), 145.7, 143.0, 132.9, 130.8, 129.1, 128.0, 121.8 (d, J_{C-F} = 8.1 Hz), 121.2, 115.6 (d, J_{C-F} = 22.3 Hz), 110.4, 86.7, 61.7, 52.1, 32.3, 30.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{29}FN_4Na$ 439.2268; Found: 439.2266.

(*E*)-4-(((4-Bromophenyl)imino)methyl)-1-(*tert*-butyl)-3-(*tert*-butylamino)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4d):

Orange solid, yield: 0.193g (81%), ethylacetate/petroleum ether = 1: 20, mp 205–207 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.38 (s, 1H), 7.62-6.76 (m, 10H), 2.23 (s, 3H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.6, 150.8, 145.7, 143.2, 132.8, 132.0, 130.8, 129.2, 128.1, 122.3, 121.2, 118.1, 110.4, 86.7, 61.8, 52.1, 32.3, 30.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{30}BrN_4$ 477.1648; Found: 477.1646.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chloro-3-methylphenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4e):

Light yellow solid, yield: 0.156g (70%), ethylacetate/petroleum ether = 1: 25, mp 179–181 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.40 (s, 1H), 7.63-6.63 (m, 9H), 2.30 (s, 3H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.4, 150.4, 145.7, 143.1, 136.5, 132.9, 130.8, 130.5, 129.4, 129.2, 128.0, 123.4, 121.2, 118.9, 110.4, 86.7, 61.8, 52.0, 32.3, 30.8, 20.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{31}ClN_4Na$ 469.2129; Found: 469.2127.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((2,5-dimethylphenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4f):

Light yellow solid, yield: 0.143g (67%), ethylacetate/petroleum ether = 1: 25, mp

202–203 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.47 (s, 1H), 7.57-6.34 (m, 9H), 2.25-2.21 (m, 6H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.1, 151.1, 145.6, 143.1, 136.3, 133.0, 130.8, 129.9, 129.1, 128.4, 128.0, 125.4, 121.4, 118.5, 110.5, 86.4, 61.6, 51.9, 32.3, 30.9, 20.9, 17.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{35}N_4$ 427.2856; Found: 427.2855.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((3,4-dichlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (4g):

Bright yellow solid, yield: 0.172g (74%), ethylacetate/petroleum ether = 1: 25, mp 198–199 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.28 (s, 1H), 7.60-6.71 (m, 9H), 1.57-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 156.2, 151.4, 145.8, 143.5, 132.7, 132.6, 130.7, 130.6, 129.3, 128.3, 128.1, 122.5, 121.1, 120.2, 110.3, 86.7, 62.0, 52.1, 32.2, 30.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{29}Cl_2N_4$ 467.1764; Found: 467.1761.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-phenyl-4-(((4-(trifluoromethyl)phenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4h):

yellow solid, yield: 0.175g (75%), ethylacetate/petroleum ether = 1: 20, mp 180–181 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.32 (s, 1H), 7.64-7.01 (m, 10H), 1.57-1.54 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 156.5, 152.4, 145.8, 143.5, 132.7, 130.7, 129.5, 129.3, 128.1, 123.6, 121.3 (d, $J_{C\text{-}F}$ = 3.7 Hz), 121.1, 117.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 110.4, 86.7, 61.9, 52.1, 32.3, 30.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{30}F_3N_4$ 467.2417; Found: 467.2418.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-(4-chlorophenyl)-4-(((2,5-dimethylphenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4i):

Light yellow solid, yield: 0.152g (66%), ethylacetate/petroleum ether = 1: 25, mp 209–210 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.48 (s, 1H), 7.55-6.35 (m, 8H), 2.25-2.24 (m, 6H), 1.57-1.52 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.6, 151.0, 145.6, 141.4, 136.4, 135.3, 132.1, 131.5, 129.9, 128.4, 125.6, 121.2, 118.4, 110.6, 86.6, 61.7, 51.9, 32.4, 30.9, 21.0, 17.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{33}ClN_4Na$ 483.2286; Found: 483.2284.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-(4-chlorophenyl)-4-((p-tolylimino)methyl

)-1*H*-pyrrole-2-carbonitrile (4j):

Light yellow solid, yield: 0.163g (73%), ethylacetate/petroleum ether = 1: 25, mp 249–251 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.51 (s, 1H), 7.66-6.82 (m, 9H), 2.30 (s, 3H), 1.56-1.52 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.2, 149.2, 145.7, 141.2, 135.3, 134.9, 132.1, 131.5, 129.6, 128.4, 121.1, 120.5, 110.6, 86.9, 61.7, 52.0, 32.4, 30.8, 20.9; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{31}ClN_4Na$ 469.2129; Found: 469.2127.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-(4-chlorophenyl)-4-(((4-methoxyphenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4k):

Light yellow solid, yield: 0.125g (54%), ethylacetate/petroleum ether = 1: 20, mp 211–212 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.52 (s, 1H), 7.67-6.80 (m, 9H), 3.77 (s, 3H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.5, 153.2, 145.6, 144.7, 141.0, 135.3, 132.1, 131.9, 131.6, 128.4, 121.5, 114.3, 110.6, 87.0, 61.7, 55.5, 52.0, 32.4, 30.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{32}ClN_4O$ 463.2259; Found: 463.2262.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chloro-3-methylphenyl)imino)methyl)-5-(4-chlorophenyl)-1*H*-pyrrole-2-carbonitrile (4l):

Light yellow solid, yield: 0.180g (75%), ethylacetate/petroleum ether = 1: 20, mp 234–235 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.41 (s, 1H), 7.61-6.65 (m, 8H), 2.32 (s, 3H), 1.56-1.52 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.9, 150.2, 145.7, 141.4, 136.6, 135.4, 132.0, 131.3, 130.7, 129.5, 128.4, 123.4, 121.0, 118.8, 110.5, 86.9, 6 1.9, 52.0, 32.4, 30.8, 20.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{31}Cl_2N_4$ 481.1920; Found: 481.1917.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-5-(4-fluorophenyl)-4-(((4-methoxyphenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4m):

Light yellow solid, yield: 0.134g (60%), ethylacetate/petroleum ether = 1: 25, mp 191–192 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.52 (s, 1H), 7.67-6.80 (m, 9H), 3.76 (s, 3H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 163.0 (d, J_{C-F} = 248.5 Hz), 157.5, 153.3, 145.6, 144.8, 141.3, 132.6 (d, J_{C-F} = 8.1 Hz), 129.0 (d, J_{C-F} = 3.7 Hz), 121.5, 121.2, 115.3 (d, J_{C-F} = 21.6 Hz), 114.3, 110.7, 86.8, 61.6, 55.5,

52.0, 32.3, 30.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{31}FN_4NaO$ 469.2374; Found: 469.2371.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chloro-3-methylphenyl)imino)methyl)-5-(4-fluorophenyl)-1*H*-pyrrole-2-carbonitrile (4n):

Light yellow solid, yield: 0.167g (72%), ethylacetate/petroleum ether = 1: 20, mp 202–204 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.40 (s, 1H), 7.62-6.65 (m, 8H), 2.31 (s, 3H), 1.56-1.53 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 163.0 (d, J_{C-F} = 248.8 Hz), 155.0, 150.2, 145.6, 141.7, 136.6, 132.5 (d, J_{C-F} = 8.2 Hz), 130.7, 129.4, 128.7 (d, J_{C-F} = 3.7 Hz), 123.3, 121.1, 118.9, 115.3 (d, J_{C-F} = 21.6 Hz), 110.5, 86.8, 61.8, 52.0, 32.3, 30.8, 20.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{31}{}^{37}ClFN_4$ 467.2186; Found: 467.2184.

1-((3R)-Adamantan-1-yl)-3-(((3S,5S,7S)-adamantan-1-yl)amino)-5-phenyl-4-((*E*)-(p-tolylimino)methyl)-1*H*-pyrrole-2-carbonitrile (4o):

Light yellow solid, yield: 0.207g (73%), ethylacetate/petroleum ether = 1: 25, mp 219–221 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.27 (s, 1H), 7.55-6.72 (m, 10H), 2.21-1.49 (m, 33H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.8, 149.3, 145.6, 142.6, 134.6, 133.4, 130.8, 129.5, 128.8, 127.8, 122.3, 120.5, 111.0, 86.7, 63.6, 52.8, 43.7, 43.3, 36.2, 35.6, 30.3, 29.9, 20.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{39}H_{45}N_4$ 569.3639; Found: 569.3635.

1-((3R)-Adamantan-1-yl)-3-(((3S,5S,7S)-adamantan-1-yl)amino)-4-((E)-((3,4-dichlorophenyl)imino)methyl)-5-phenyl-1H-pyrrole-2-carbonitrile (4p):

Light yellow solid, yield: 0.249g (80%), ethylacetate/petroleum ether = 1: 25, mp 285–287 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.12 (s, 1H), 7.54-6.70 (m, 9H), 2.24-1.60 (m, 30H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 156.2, 151.4, 145.7, 143.3, 133.0, 132.6, 130.8, 130.5, 129.1, 128.2, 127.9, 122.5, 122.1, 120.1, 110.8, 86.6, 64.0, 52.9, 43.7, 43.2, 36.2, 35.6, 30.3, 29.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{38}H_{41}Cl_2N_4$ 623.2703; Found: 623.2704.

1-((3R)-Adamantan-1-yl)-3-(((3S,5S,7S)-adamantan-1-yl)amino)-4-((E)-((2,5-dimethylphenyl)imino)methyl)-5-phenyl-1H-pyrrole-2-carbonitrile (4q):

Bright yellow solid, yield: 0.180g (62%), ethylacetate/petroleum ether = 1: 20, mp

205–207 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.31 (s, 1H), 7.52-6.32 (m, 9H), 2.25-1.59 (m, 36H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.1, 151.1, 145.5, 142.8, 136.3, 133.4, 130.8, 129.8, 128.9, 128.5, 127.8, 125.3, 122.5, 118.4, 111.0, 86.4, 63.6, 52.7, 43.7, 43.3, 36.2, 35.6, 30.3, 29.9, 21.0, 18.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{40}H_{47}N_4$ 583.3795; Found: 583.3792.

1-((3R)-Adamantan-1-yl)-3-(((3R)-adamantan-1-yl)amino)-5-(4-fluorophenyl)-4-((*E*)-((4-fluorophenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4r):

Light yellow solid, yield: 0.218g (74%), ethylacetate/petroleum ether = 1: 20, mp 293–295 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.27 (s, 1H), 7.59-6.87 (m, 9H), 2.23-1.62 (m, 30H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 162.9 (d, J_{C-F} = 231.6 Hz), 160.5 (d, J_{C-F} = 225.5 Hz), 154.7, 147.7 (d, J_{C-F} = 2.8 Hz), 145.5, 141.4, 132.5 (d, J_{C-F} = 8.2 Hz), 129.2 (d, J_{C-F} = 3.8 Hz), 128.6 (d, J_{C-F} = 81.0 Hz), 122.1, 121.7 (d, J_{C-F} = 8.1 Hz), 115.6 (d, J_{C-F} = 22.3 Hz), 115.1 (d, J_{C-F} = 21.6 Hz), 111.1, 86.9, 63.8, 52.8, 43.8, 43.2, 36.2, 35.6, 30.2, 29.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{38}H_{41}F_2N_4$ 591.3294; Found: 591.3289.

1-((3R)-Adamantan-1-yl)-3-(((3R)-adamantan-1-yl)amino)-4-((*E*)-((4-chloro-3-methylphenyl)imino)methyl)-5-(4-fluorophenyl)-1*H*-pyrrole-2-carbonitrile (4s):

Light yellow solid, yield: 0.239g (77%), ethylacetate/petroleum ether = 1: 25, mp 269–270 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.24 (s, 1H), 7.57-6.64 (m, 8H), 2.31-1.62 (m, 33H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 162.9 (d, J_{C-F} = 248.4 Hz), 155.1, 150.3, 145.6, 141.5, 136.6, 132.6 (d, J_{C-F} = 8.2 Hz), 130.7, 129.5, 129.2 (d, J_{C-F} = 3.7 Hz), 123.3, 122.1, 118.9, 115.2 (d, J_{C-F} = 21.5 Hz), 111.1, 86.9, 63.9, 52.9, 43.9, 43.3, 36.2, 35.6, 30.3, 29.9, 20.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{39}H_{43}ClFN_4$ 621.3155; Found: 621.3151.

1-((3R)-Adamantan-1-yl)-3-(((3R)-adamantan-1-yl)amino)-5-(4-fluorophenyl)-4-((*E*)-((4-methoxyphenyl)imino)methyl)-1*H*-pyrrole-2-carbonitrile (4t):

Light yellow solid, yield: 0.192g (64%), ethylacetate/petroleum ether = 1: 25, mp 295–297 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.36 (s, 1H), 7.62-6.79 (m, 9H), 3.76 (s, 3H), 2.22-1.62 (m, 30H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 162.8 (d, J_{C-F} = 248.1 Hz), 157.5, 153.3, 145.1 (d, J_{C-F} = 70.3 Hz), 141.0, 132.6 (d, J_{C-F} = 8.1

Hz), 129.4 (d, J_{C-F} = 3.7 Hz), 122.2 121.5, 115.1 (d, J_{C-F} = 21.5 Hz), 114.3, 111.2, 86.9, 63.7, 55.5, 52.8, 43.9, 43.3, 36.2, 35.6, 30.2, 29.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{39}H_{44}FN_4O$ 603.3494; Found: 603.3489.

(*E*)-4-(((4-Chlorophenyl)imino)methyl)-5-phenyl-1-(2-phenylpropan-2-yl)-3-((2-phenylpropan-2-yl)amino)-1*H*-pyrrole-2-carbonitrile (4u):

Light yellow solid, yield: 0.195g (70%), ethylacetate/petroleum ether = 1: 18, mp 180–182 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.68 (s, 1H), 7.72-6.82 (m, 20H), 1.66 (s, 6H), 1.53 (s, 6H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.6, 150.2, 147.0, 146.9, 143.6, 132.2, 131.0, 130.5, 129.3, 129.1, 128.4, 128.2, 128.0, 127.1, 126.4, 125.6, 124.8, 122.0, 116.8, 110.3, 89.0, 66.5, 57.1, 32.6, 31.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{36}H_{34}ClN_4$ 557.2467; Found: 557.2465.

(*E*)-5-Phenyl-1-(2-phenylpropan-2-yl)-3-((2-phenylpropan-2-yl)amino)-4-((p-tolylimino)methyl)-1*H*-pyrrole-2-carbonitrile (4v):

Light yellow solid, yield: 0.174g (65%), ethylacetate/petroleum ether = 1: 18, mp 138–139 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.68 (s, 1H), 7.72-6.82 (m, 20H), 1.66 (s, 6H), 1.53 (s, 6H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.8, 149.2, 147.1, 147.0, 143.7, 143.3, 134.8, 132.4, 131.0, 129.6, 129.1, 128.3, 128.2, 128.0, 127.0, 126.3, 125.7, 124.8, 120.6, 117.0, 110.4, 88.9, 66.3, 57.1, 32.6, 31.8, 20.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{37}H_{37}N_4$ 537.3013; Found: 537.3015.

(*E*)-4-(((4-Chlorophenyl)imino)methyl)-5-phenyl-1-(2,4,4-trimethylpentan-2-yl)-3-((2,4,4-trimethylpentan-2-yl)amino)-1*H*-pyrrole-2-carbonitrile (4w):

Light yellow solid, yield: 0.144g (53%), ethylacetate/petroleum ether = 1: 20, mp 158–160 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.68 (s, 1H), 7.72-6.82 (m, 20H), 1.66 (s, 6H), 1.53 (s, 6H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 155.6, 150.3, 145.9, 143.1, 133.2, 130.8, 130.3, 129.2, 129.0, 128.0, 121.9, 116.2, 111.0, 87.5, 65.5, 56.2, 56.0, 53.3, 33.4, 31.8, 31.7, 31.6, 31.1, 31.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{34}H_{46}ClN_4$ 545.3406; Found: 545.3407.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (5a):

White solid, yield: 0.137g (85%), ethylacetate/petroleum ether = 1: 18, mp 186–

188 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.89 (s, 1H), 7.46-7.26 (m, 6H), 1.57-1.50 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 187.1, 146.4, 146.2, 131.5, 130.6, 129.5, 128.0, 120.6, 113.6, 86.1, 62.5, 51.9, 32.1, 30.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}N_3O$ 324.2070; Found: 324.2069.

(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (5b):

White solid, yield: 0.148g (83%), ethylacetate/petroleum ether = 1: 18, mp 163–165 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.90 (s, 1H), 7.50-7.27 (m, 5H), 1.58-1.49 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 186.7, 146.4, 144.5, 135.9, 131.9, 130.0, 128.4, 120.4, 113.7, 86.4, 62.6, 51.9, 32.2, 30.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{25}ClN_3O$ 358.1681; Found: 358.1682.

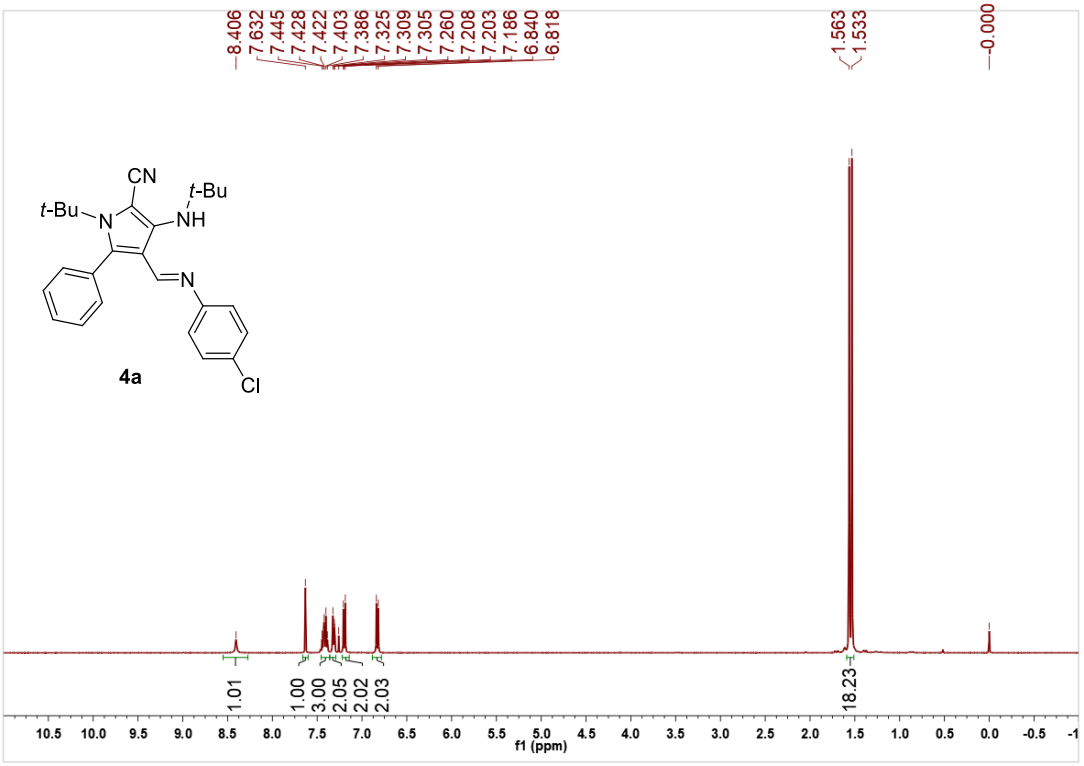
(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (5c):

White solid, yield: 0.219g (88%), ethylacetate/petroleum ether = 1: 18, mp 260–262 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.86 (s, 1H), 7.34-7.08 (m, 5H), 2.23-1.62 (m, 30H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 186.9, 146.3, 144.6, 132.5 (d, $J_{C\text{-}F}$ = 8.2 Hz), 127.8 (d, $J_{C\text{-}F}$ = 3.8 Hz), 121.5, 115.2, 115.0, 114.3, 86.5, 64.8, 52.7, 43.7, 43.0, 36.0, 35.5, 30.2, 29.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{37}FN_3O$ 498.2915; Found: 498.2917.

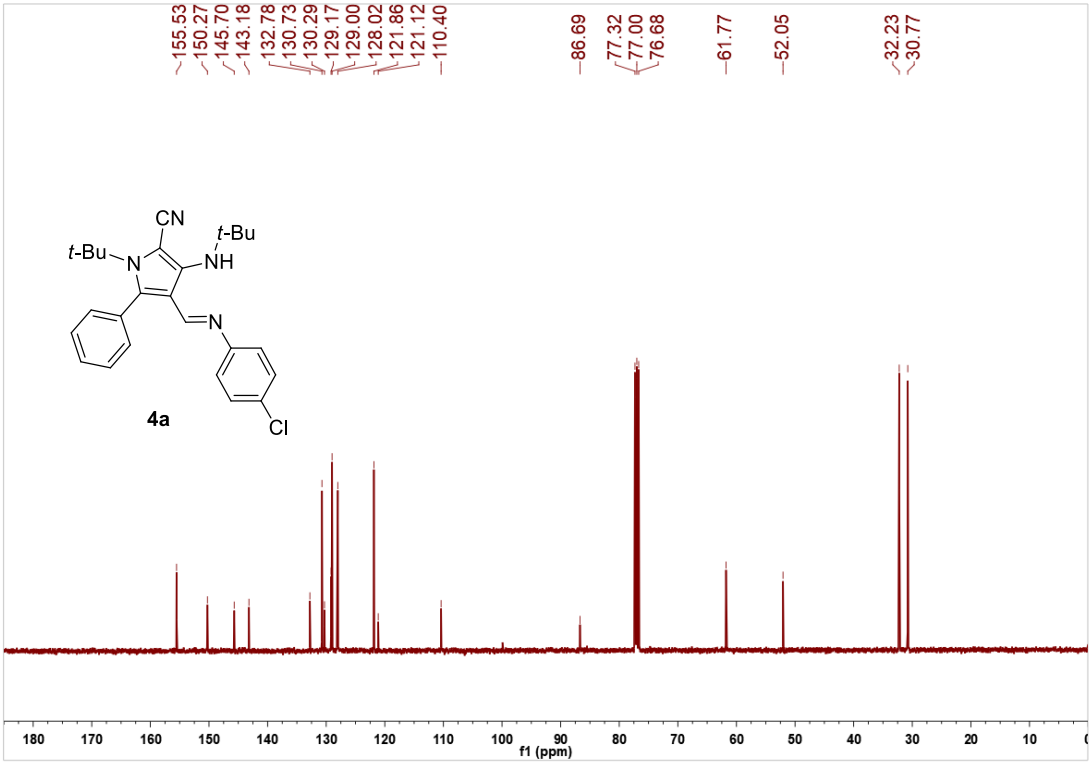
(*E*)-1-(*Tert*-butyl)-3-(*tert*-butylamino)-4-(((4-chlorophenyl)imino)methyl)-5-phenyl-1*H*-pyrrole-2-carbonitrile (6a):

White solid, yield: 0.202g (93%), ethylacetate/petroleum ether = 1: 20, mp 186–188 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.40-6.35 (m, 9H), 4.81 (s, 1H), 3.65 (s, 2H), 3.01 (s, 1H), 1.52-1.23 (m, 18H); ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 146.8, 141.8, 137.2, 134.3, 130.8, 128.8, 128.7, 128.1, 121.8, 117.2, 116.7, 114.0, 99.2, 61.1, 55.7, 40.1, 32.3, 30.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{32}ClN_4$ 435.2310; Found: 435.2312.

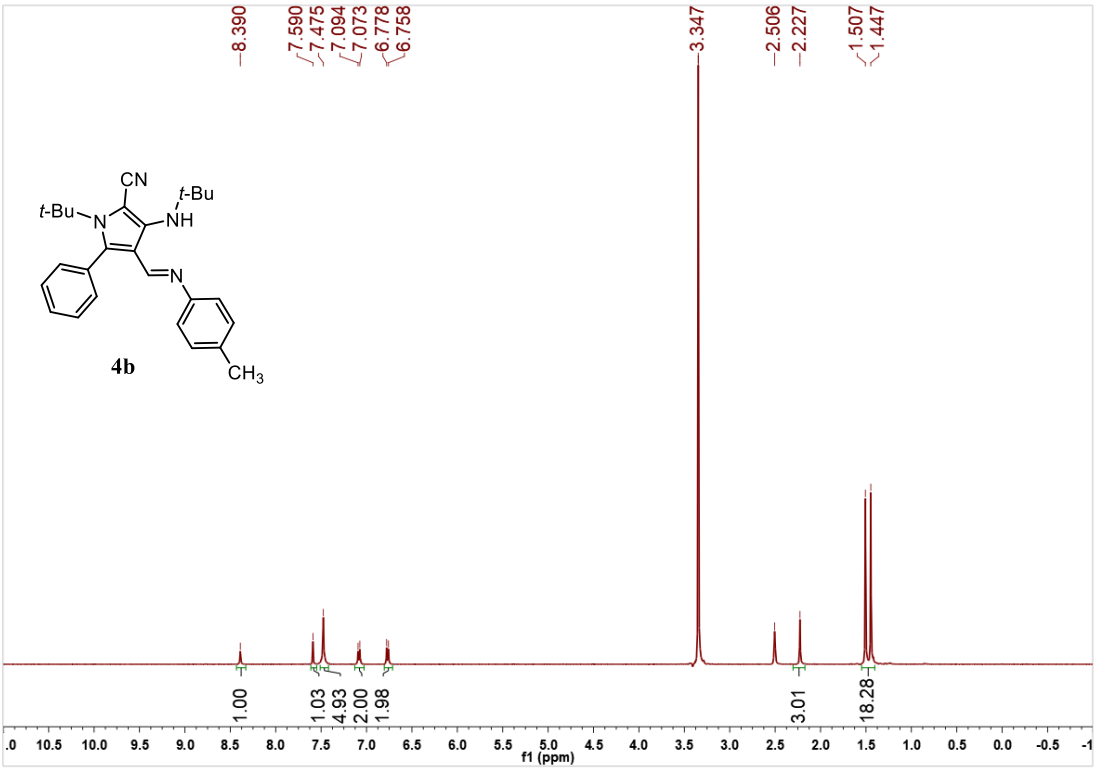
6. Copies of ^{1}H and ^{13}C NMR Spectrum



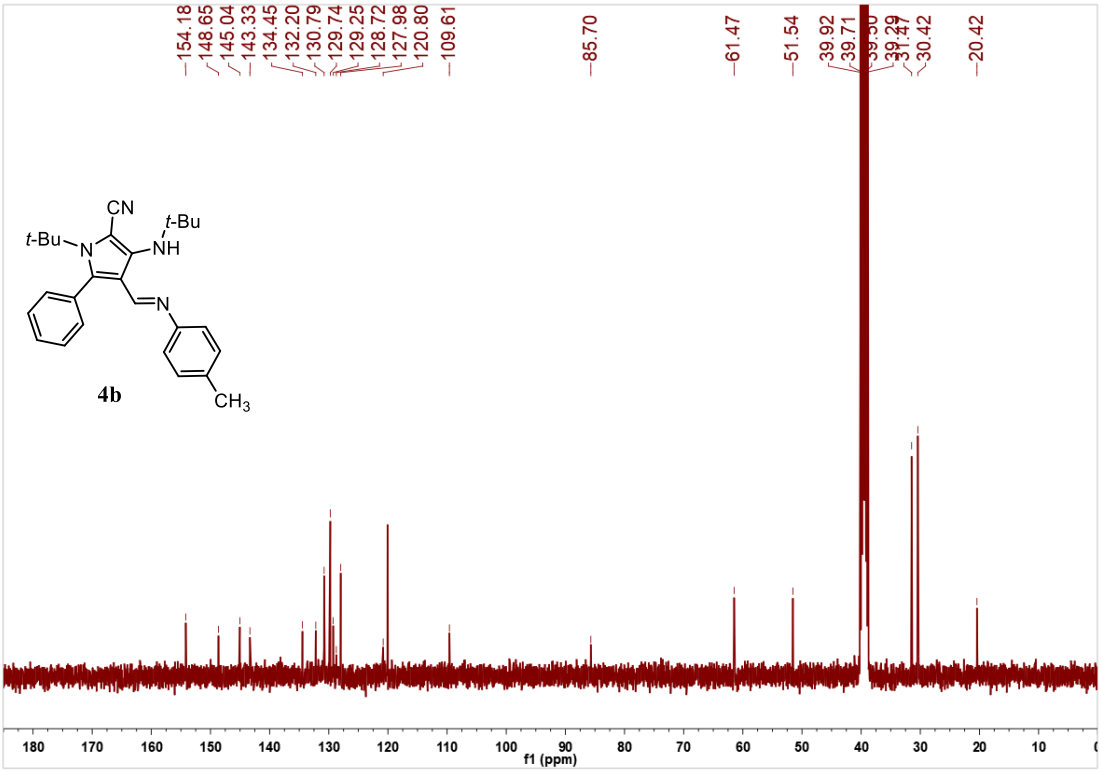
^{1}H NMR (400 MHz), $CDCl_3$



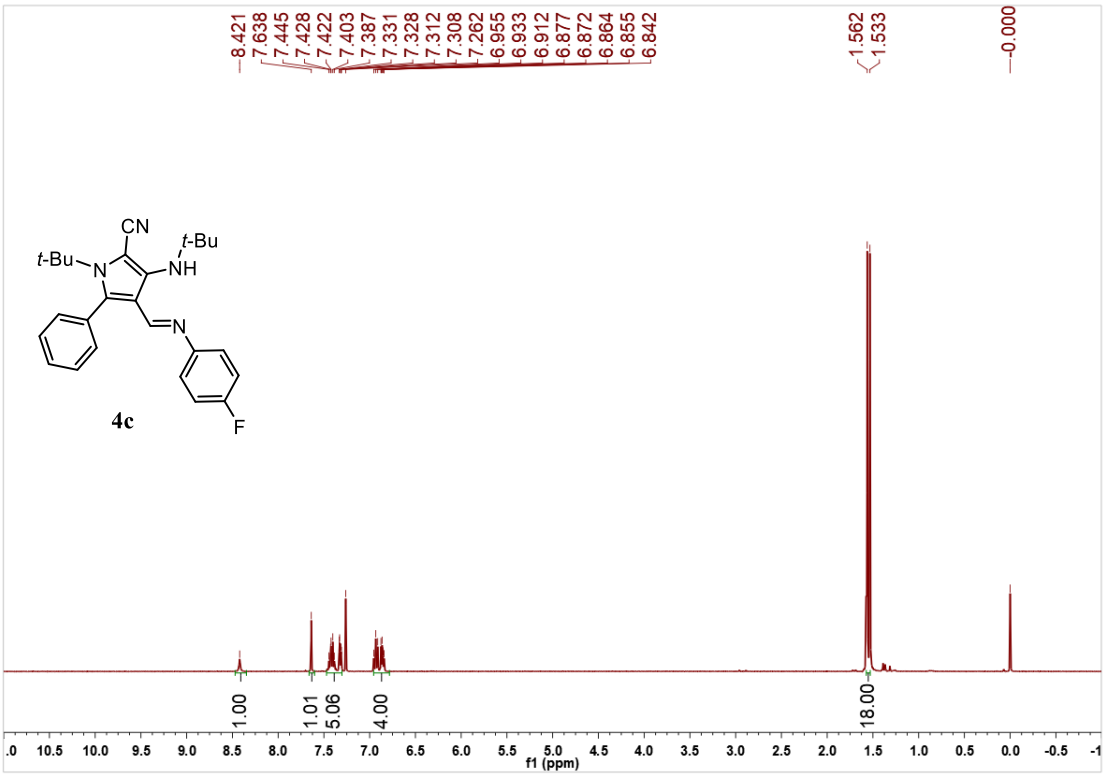
^{13}C NMR (100 MHz), $CDCl_3$



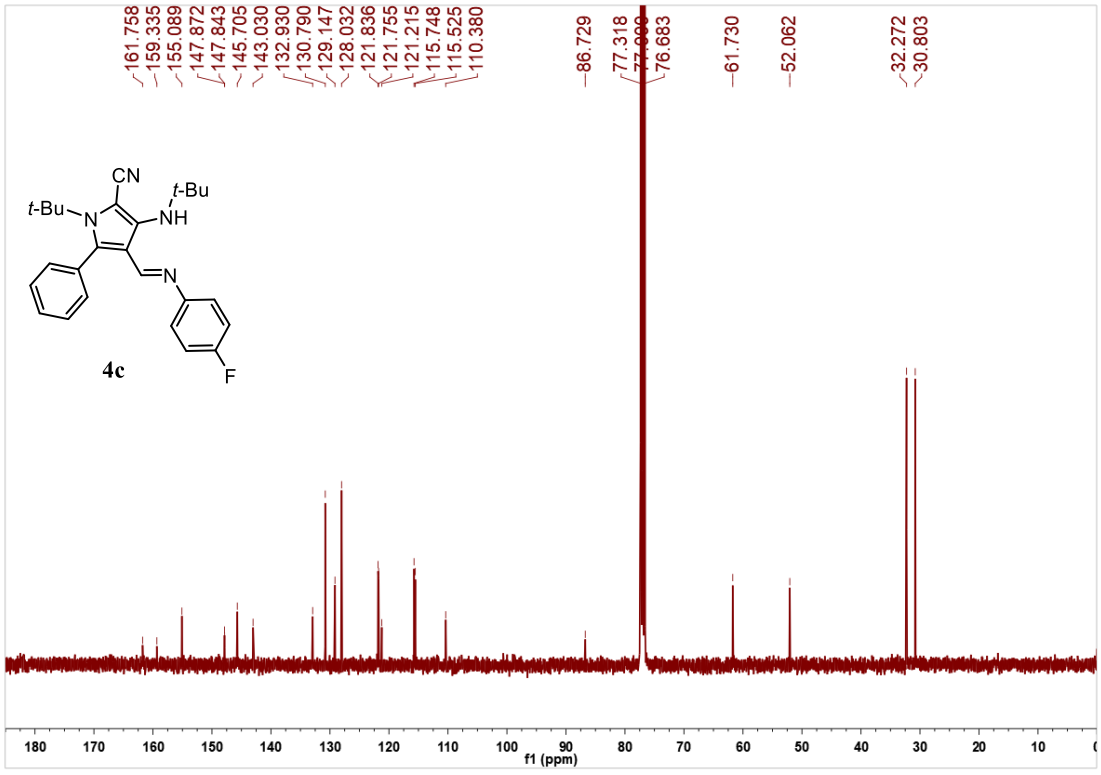
^{1}H NMR (400 MHz), DMSO-d_6



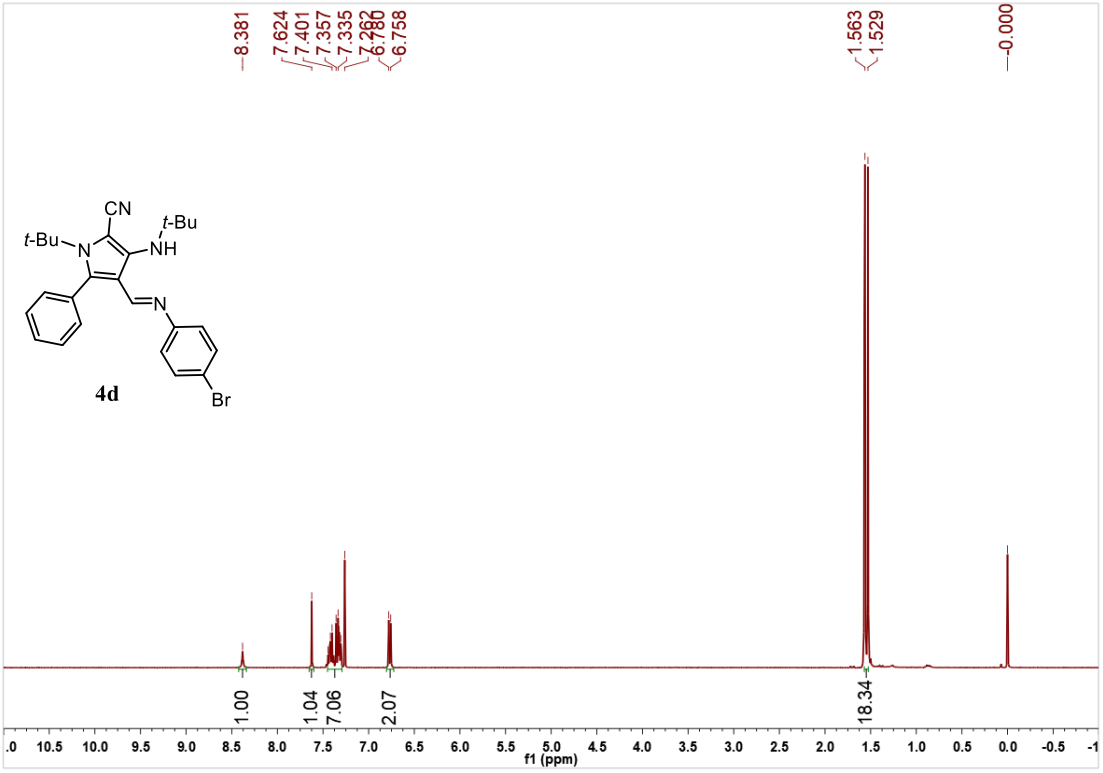
^{13}C NMR (100 MHz), DMSO-d_6



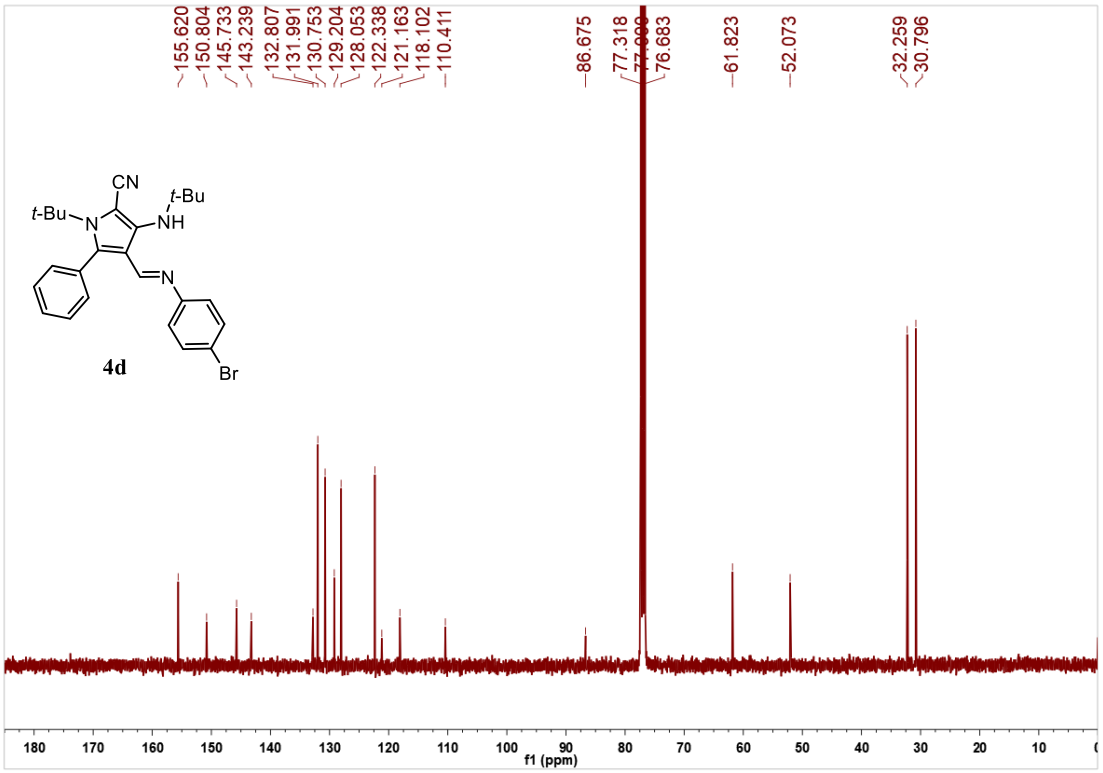
^{1}H NMR (400 MHz), $CDCl_3$



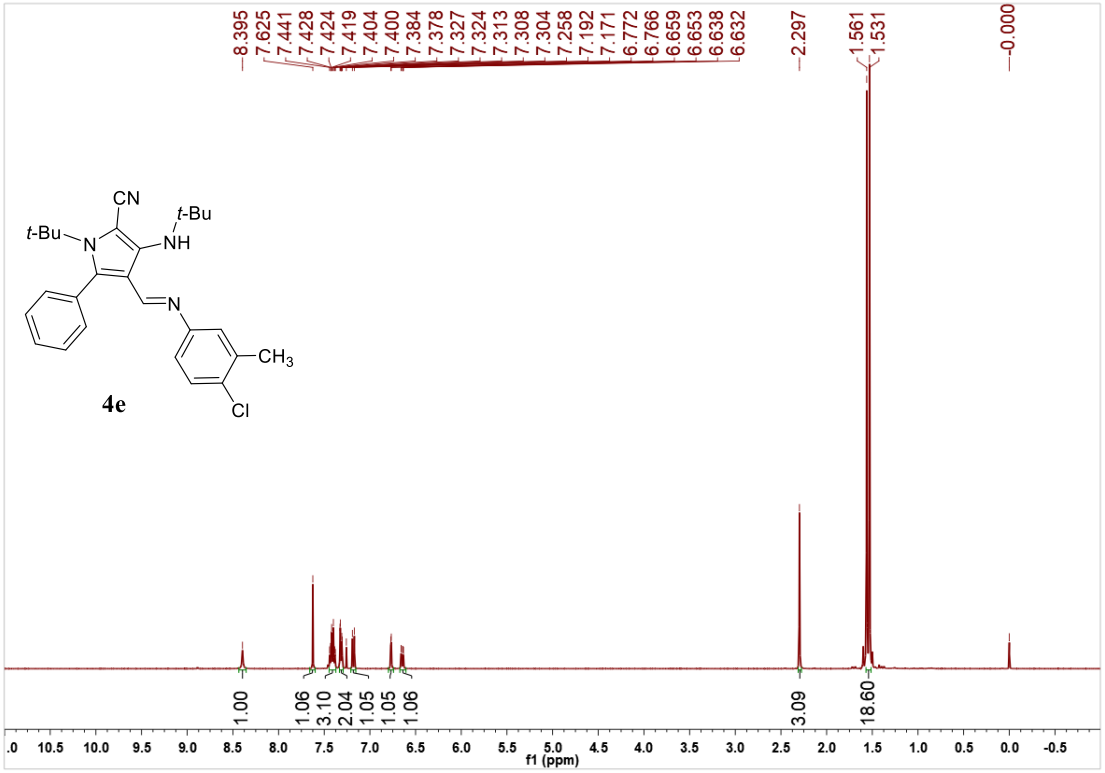
^{13}C NMR (100 MHz), $CDCl_3$



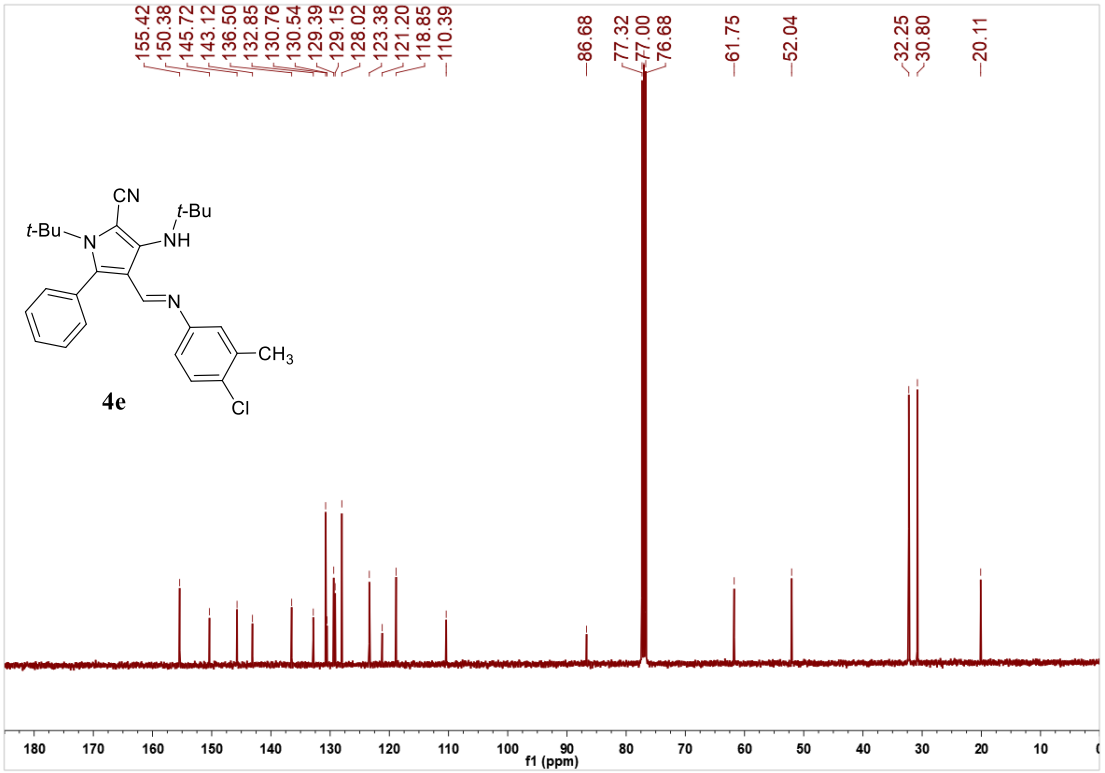
^{1}H NMR (400 MHz), $CDCl_3$



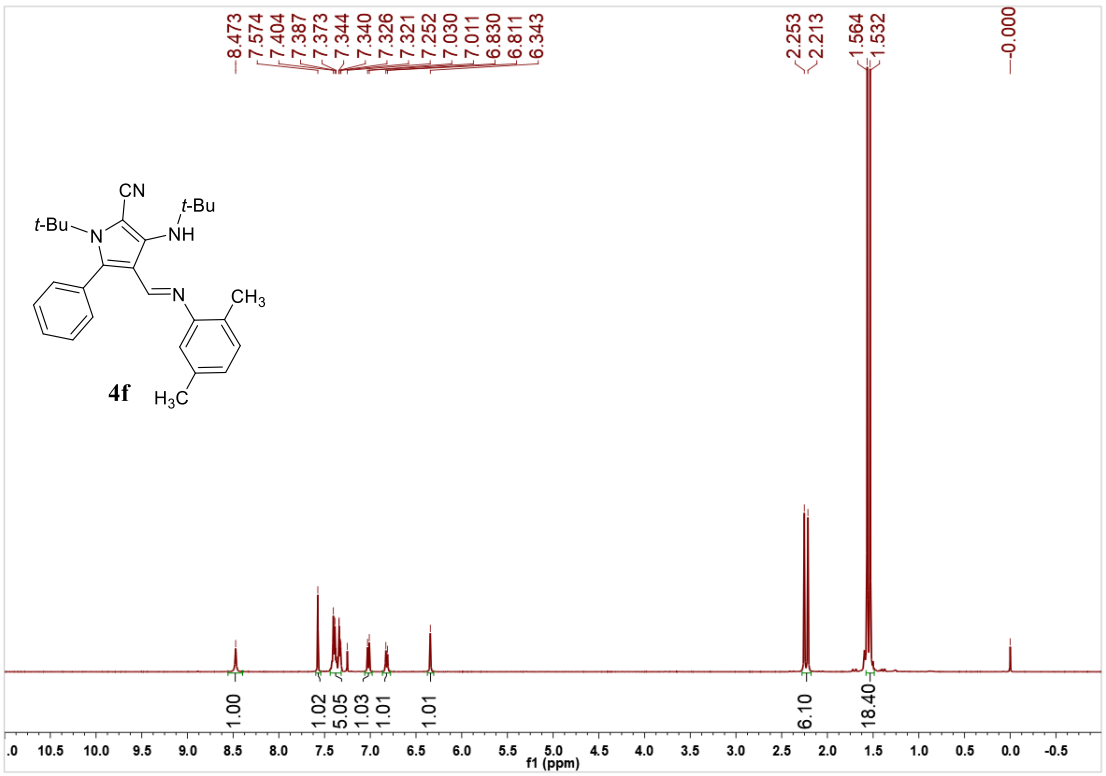
^{13}C NMR (100 MHz), $CDCl_3$



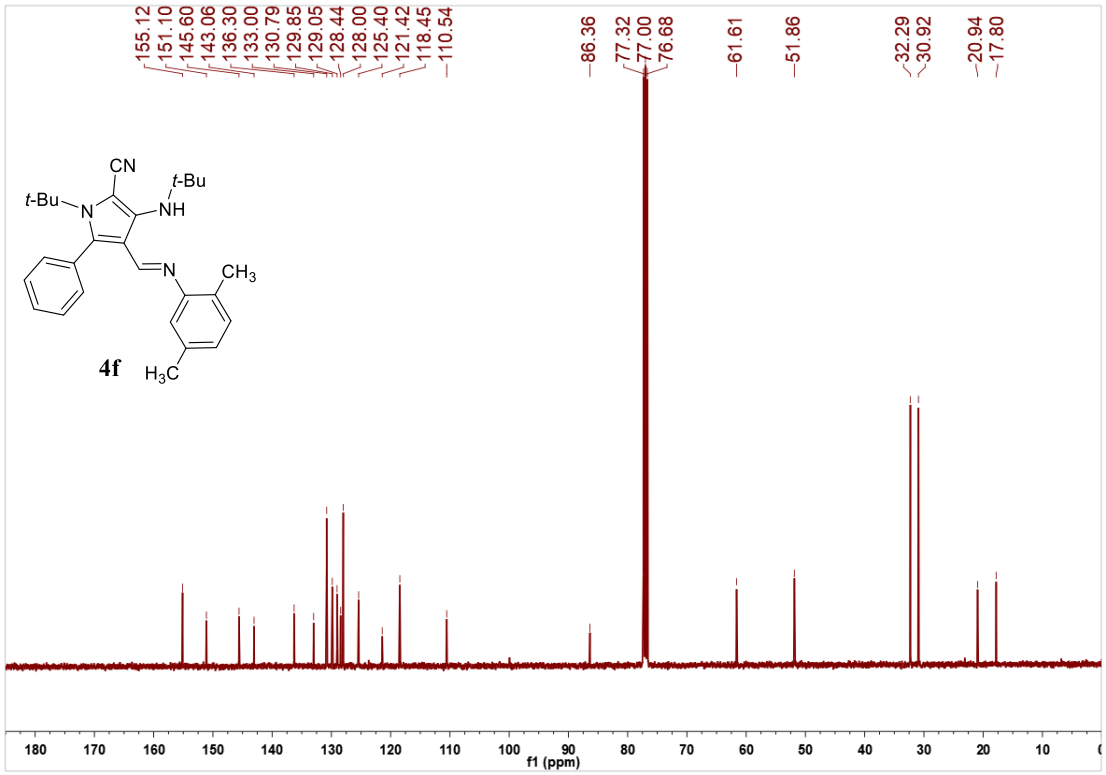
^{1}H NMR (400 MHz), $CDCl_3$



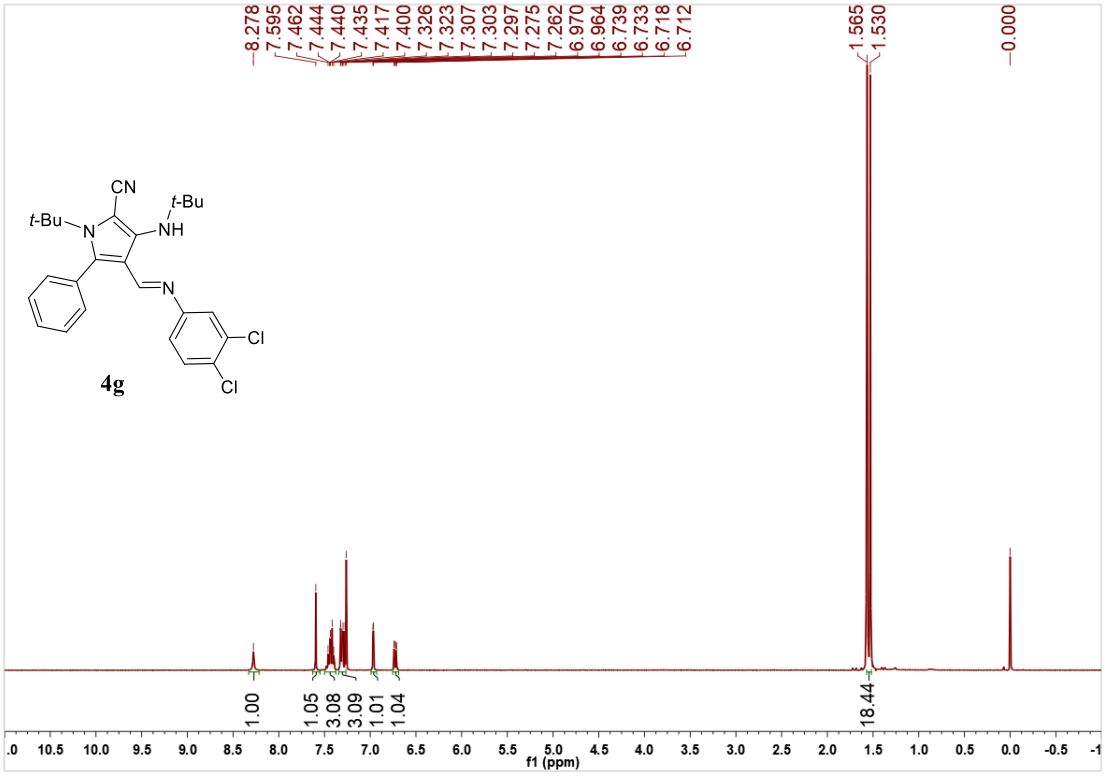
^{13}C NMR (100 MHz), $CDCl_3$



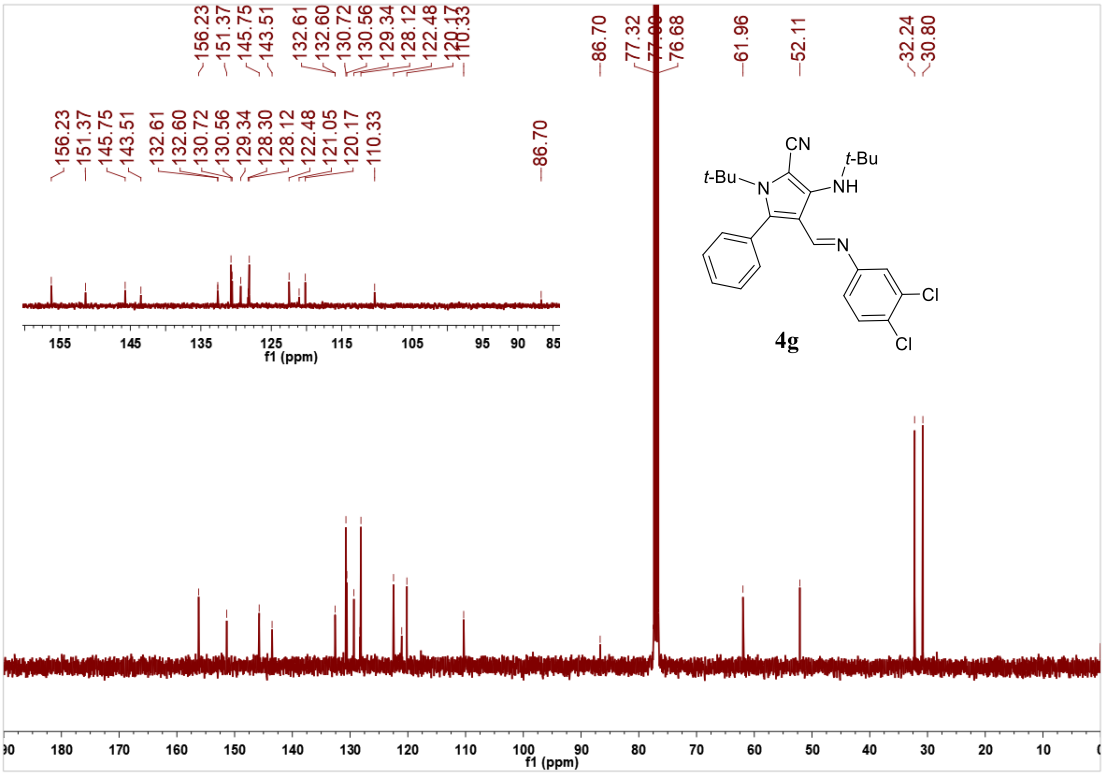
^{1}H NMR (400 MHz), $CDCl_3$



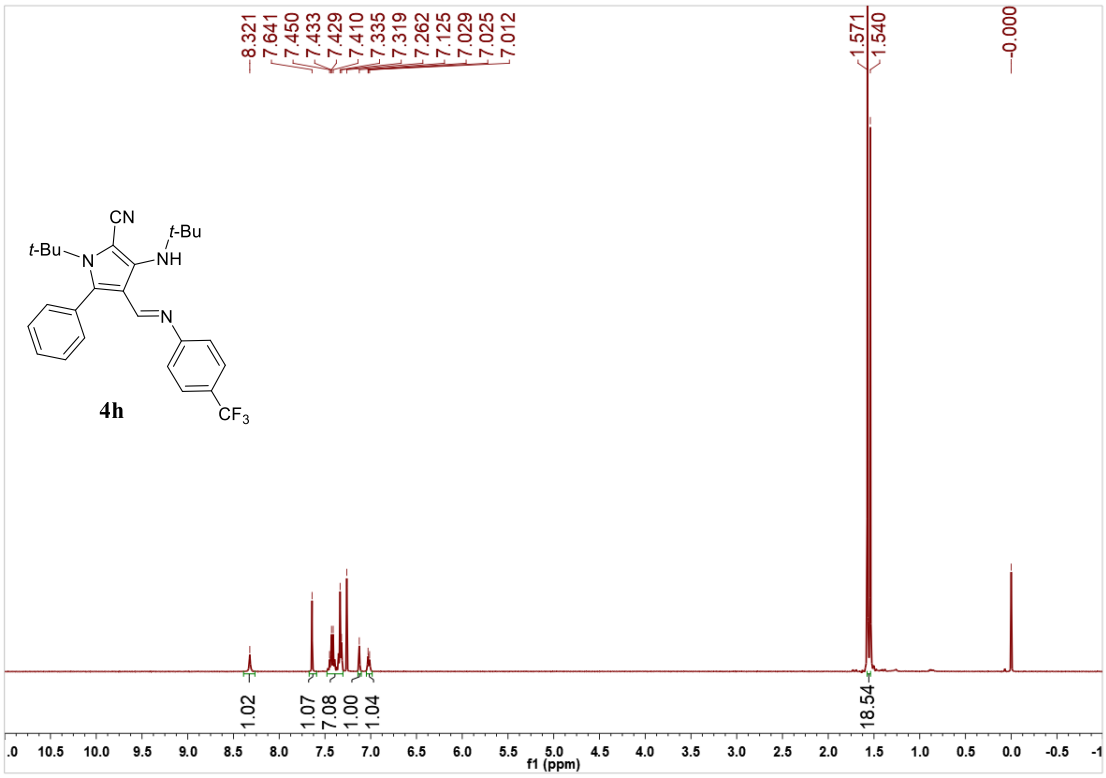
^{13}C NMR (100 MHz), $CDCl_3$



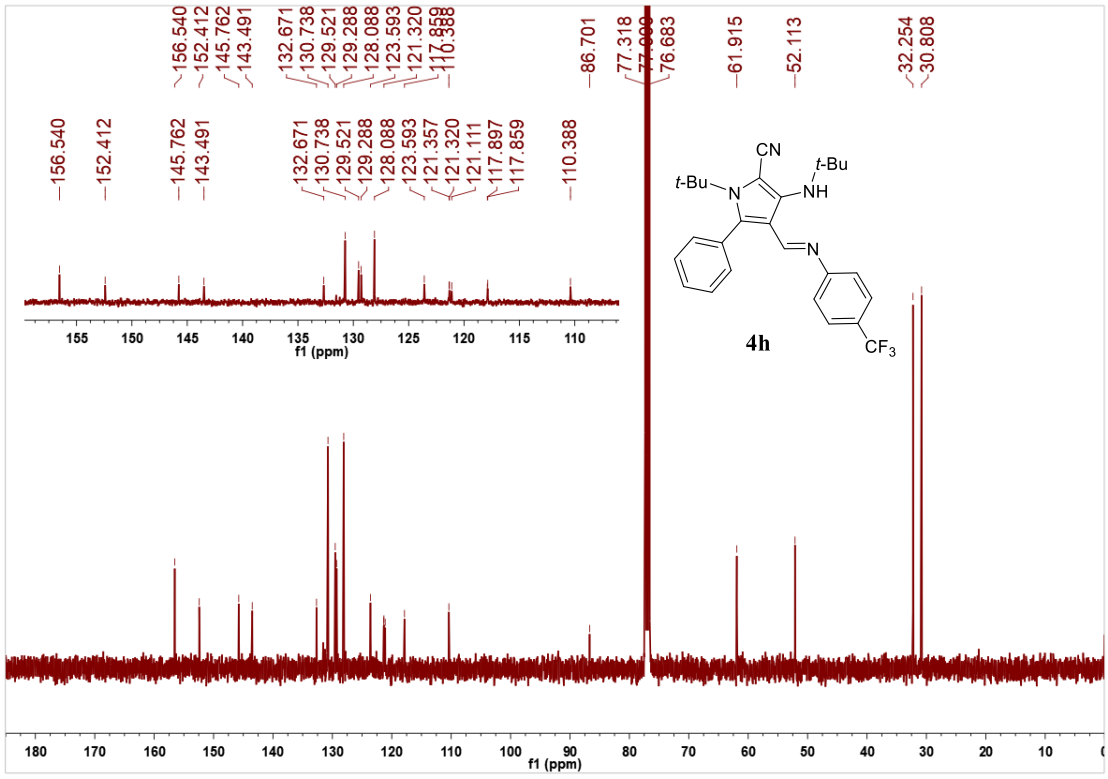
^{1}H NMR (400 MHz), $CDCl_3$



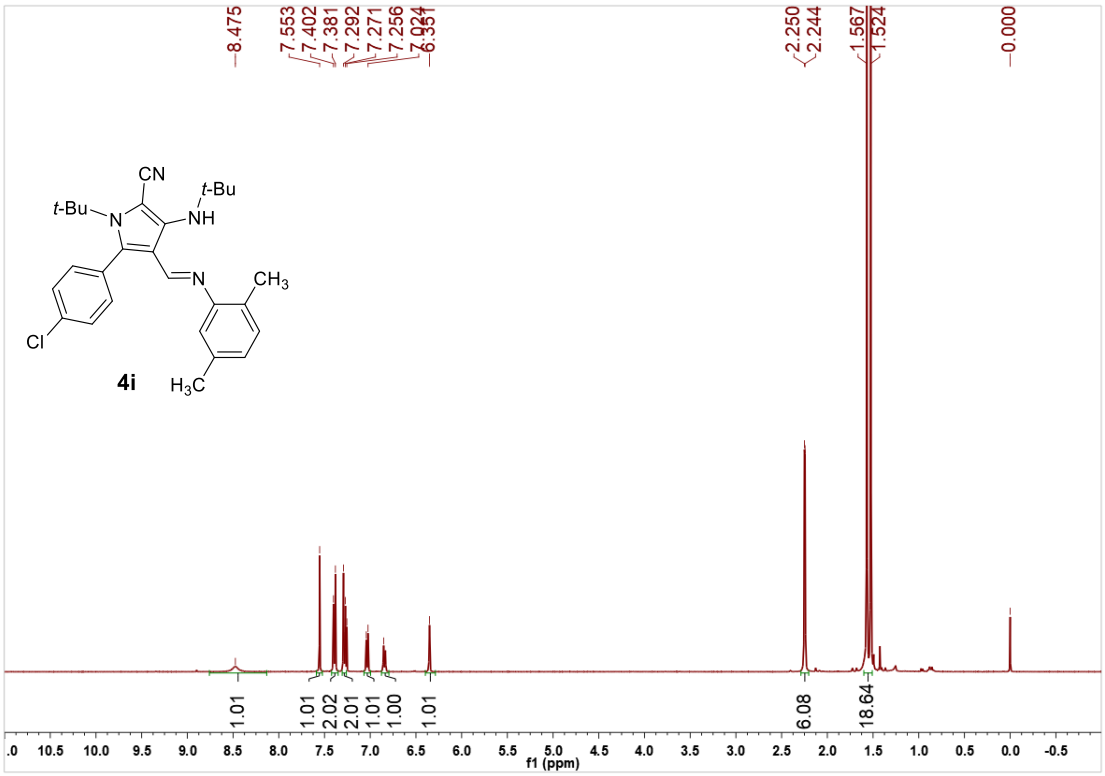
^{13}C NMR (100 MHz), $CDCl_3$



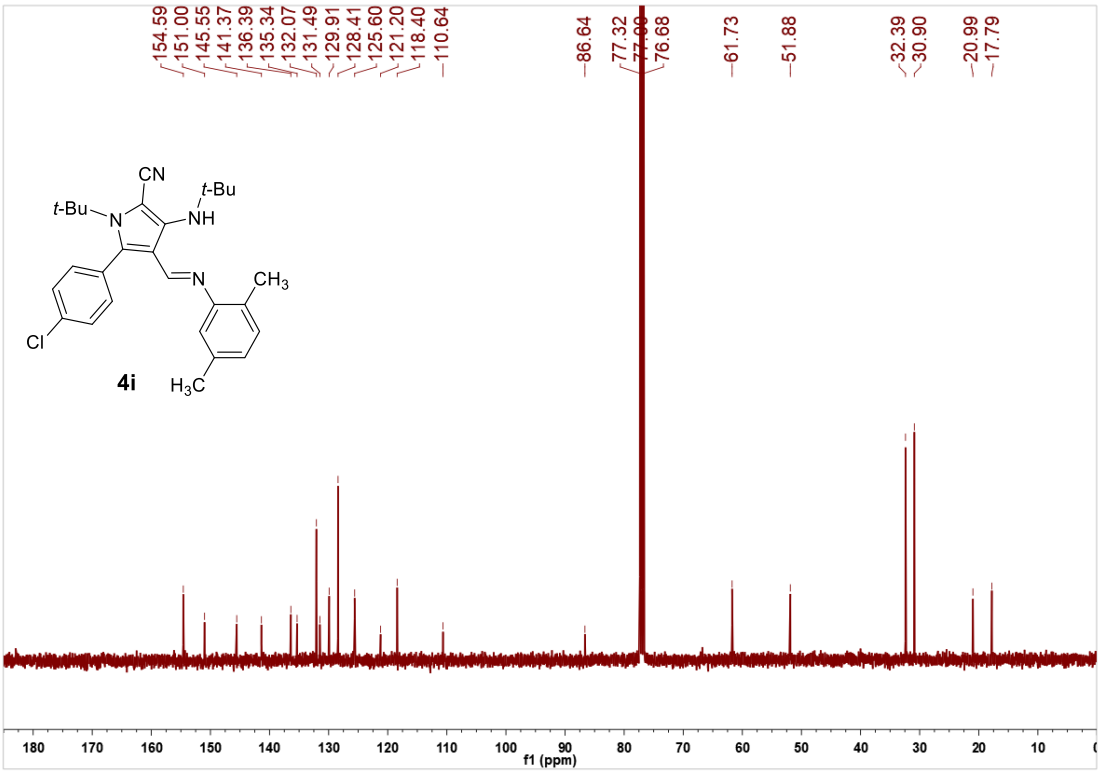
^{1}H NMR (400 MHz), $CDCl_3$



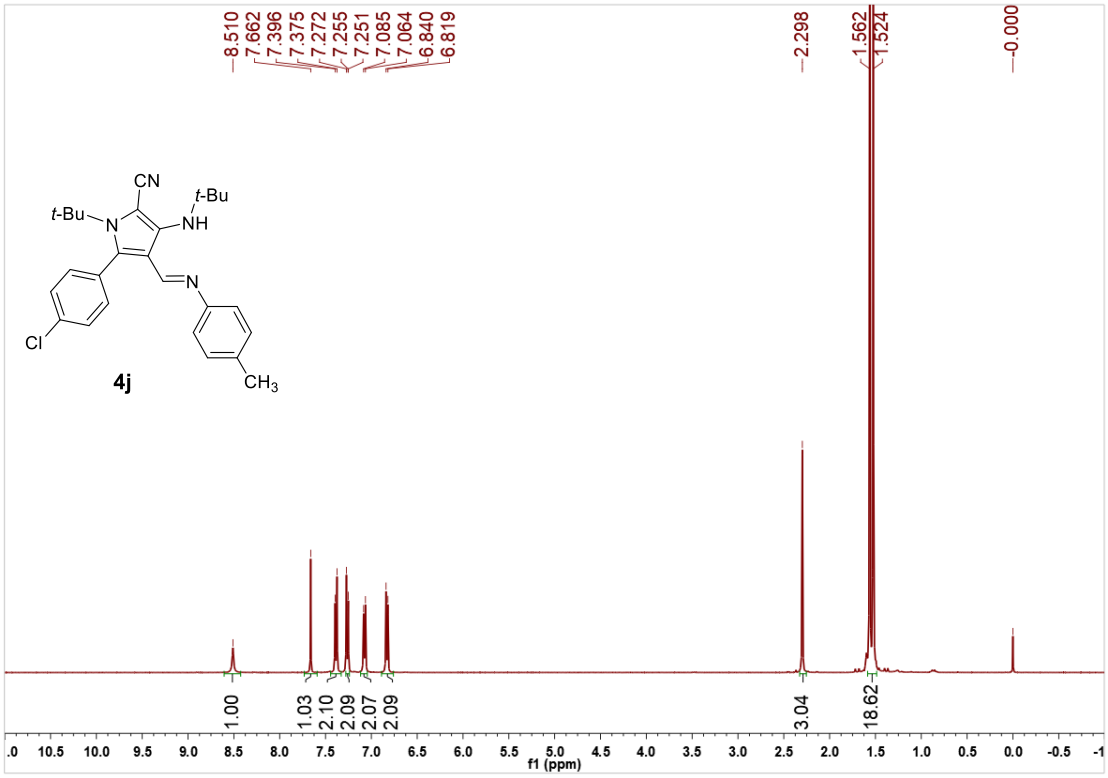
^{13}C NMR (100 MHz), $CDCl_3$



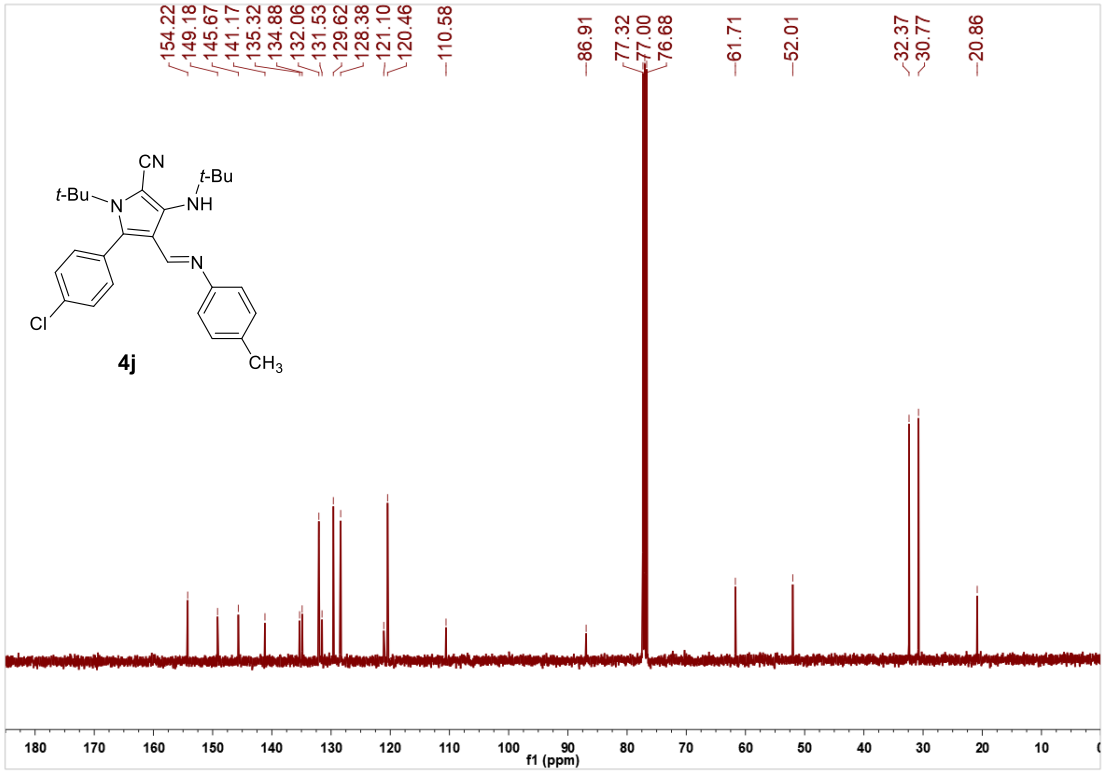
^{1}H NMR (400 MHz), $CDCl_3$



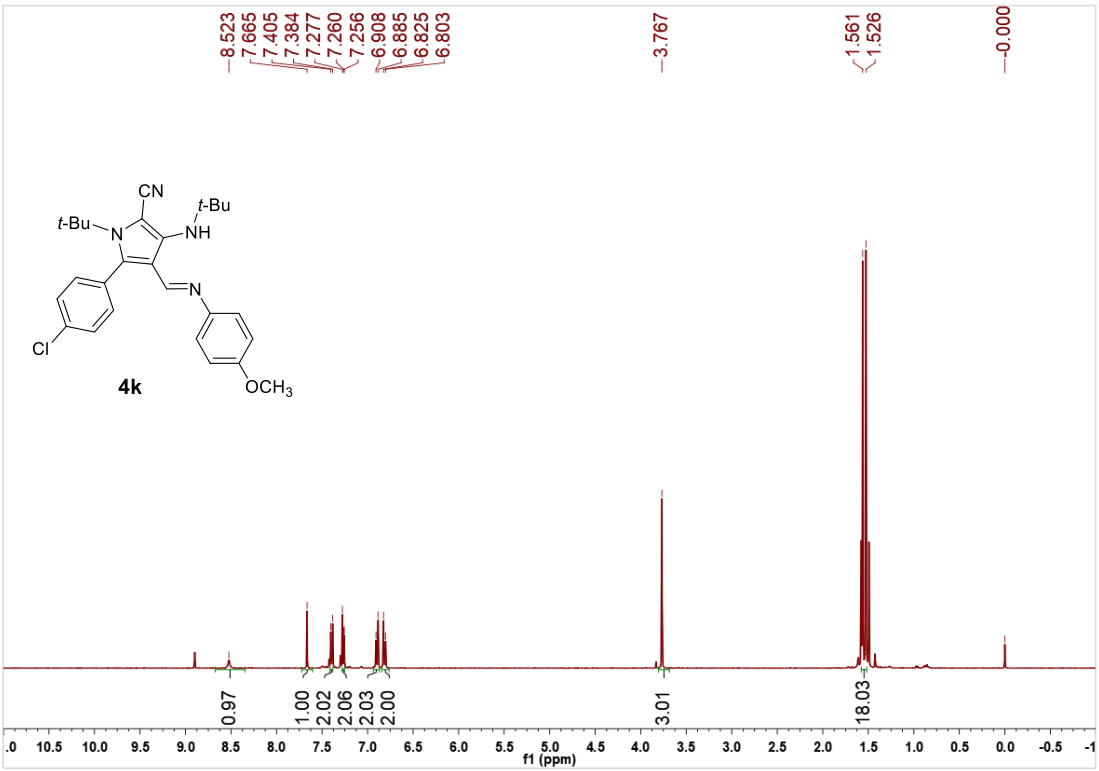
^{13}C NMR (100 MHz), $CDCl_3$



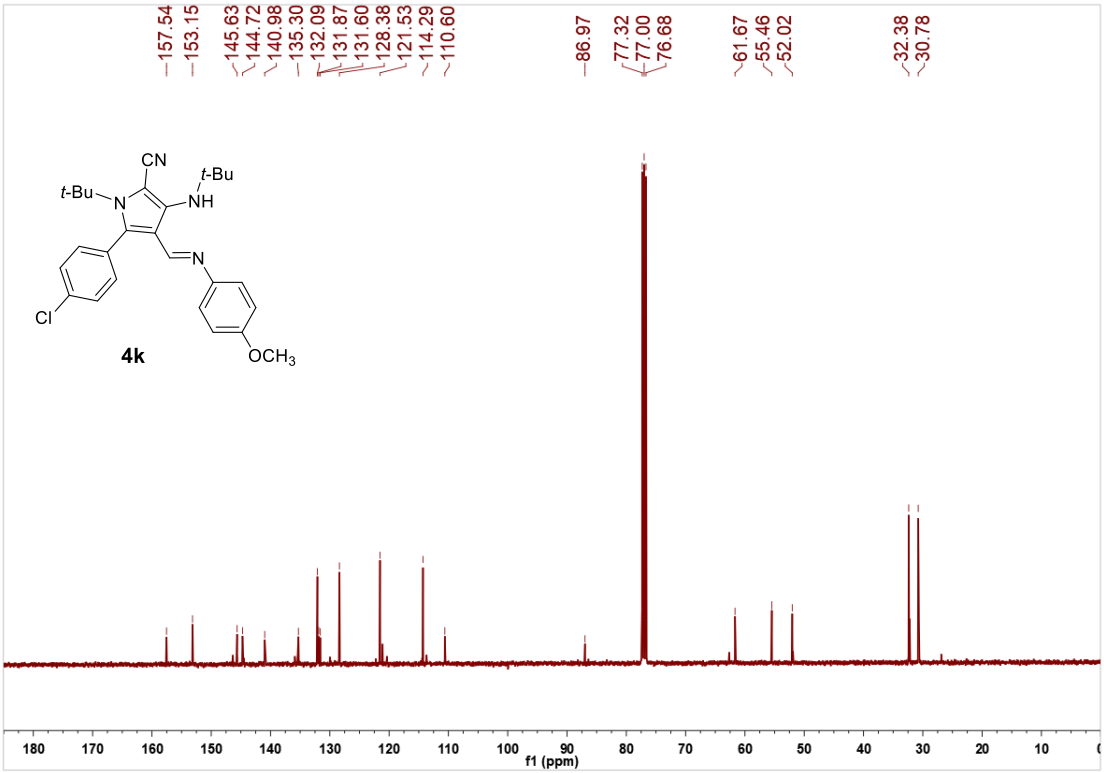
^{1}H NMR (400 MHz), $CDCl_3$



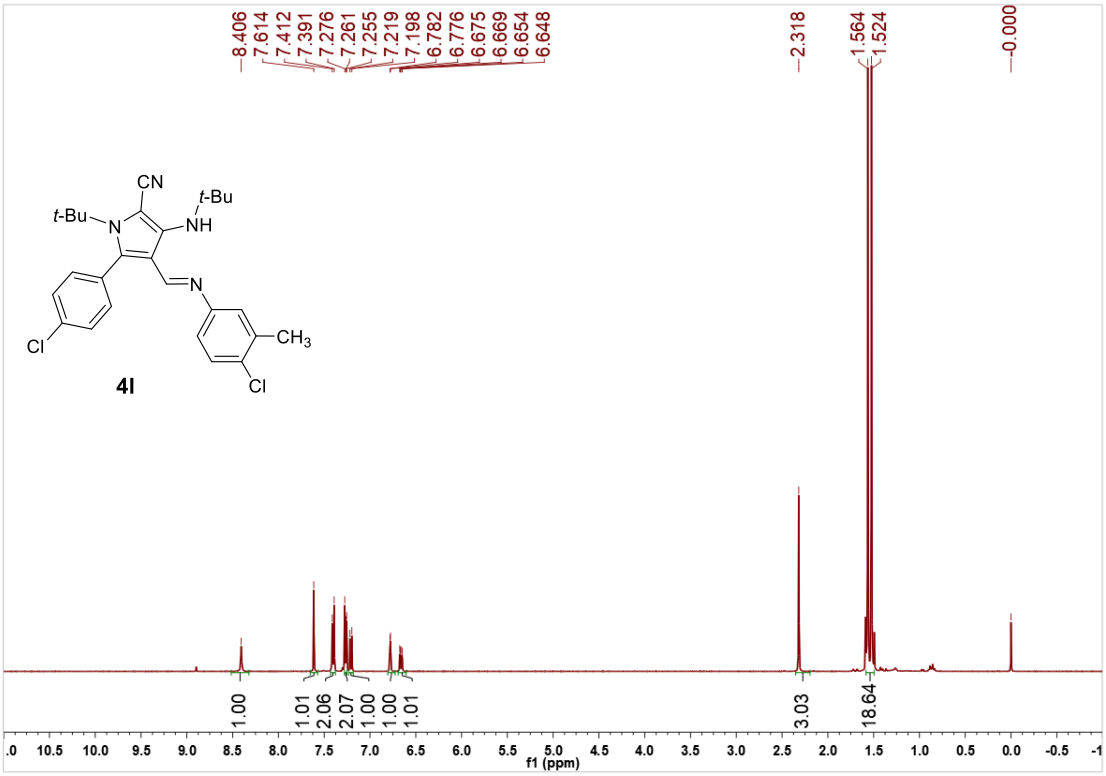
^{13}C NMR (100 MHz), $CDCl_3$



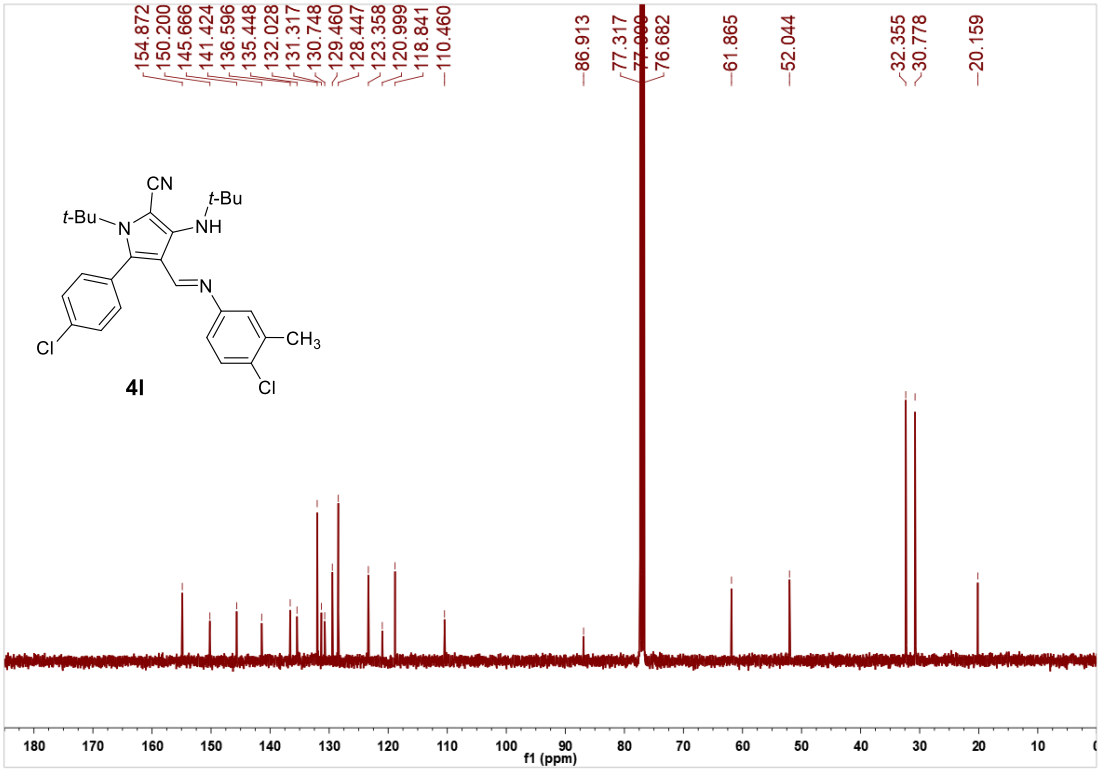
^{1}H NMR (400 MHz), $CDCl_3$



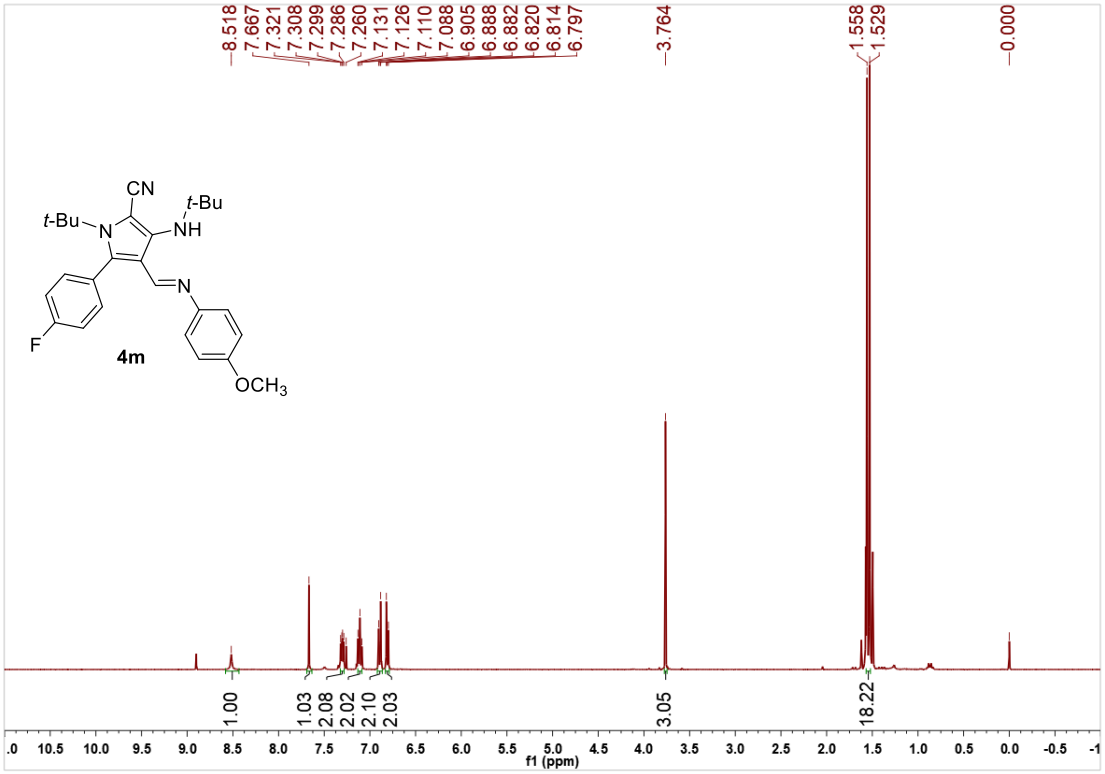
^{13}C NMR (100 MHz), $CDCl_3$



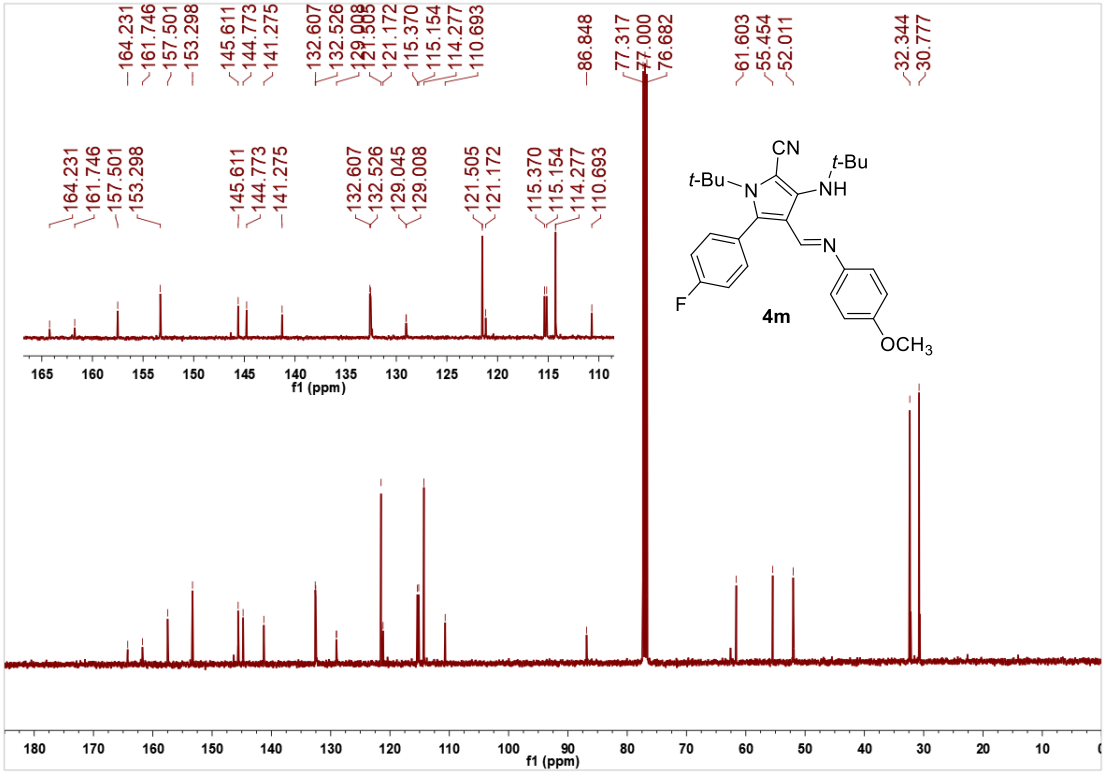
^{1}H NMR (400 MHz), $CDCl_3$



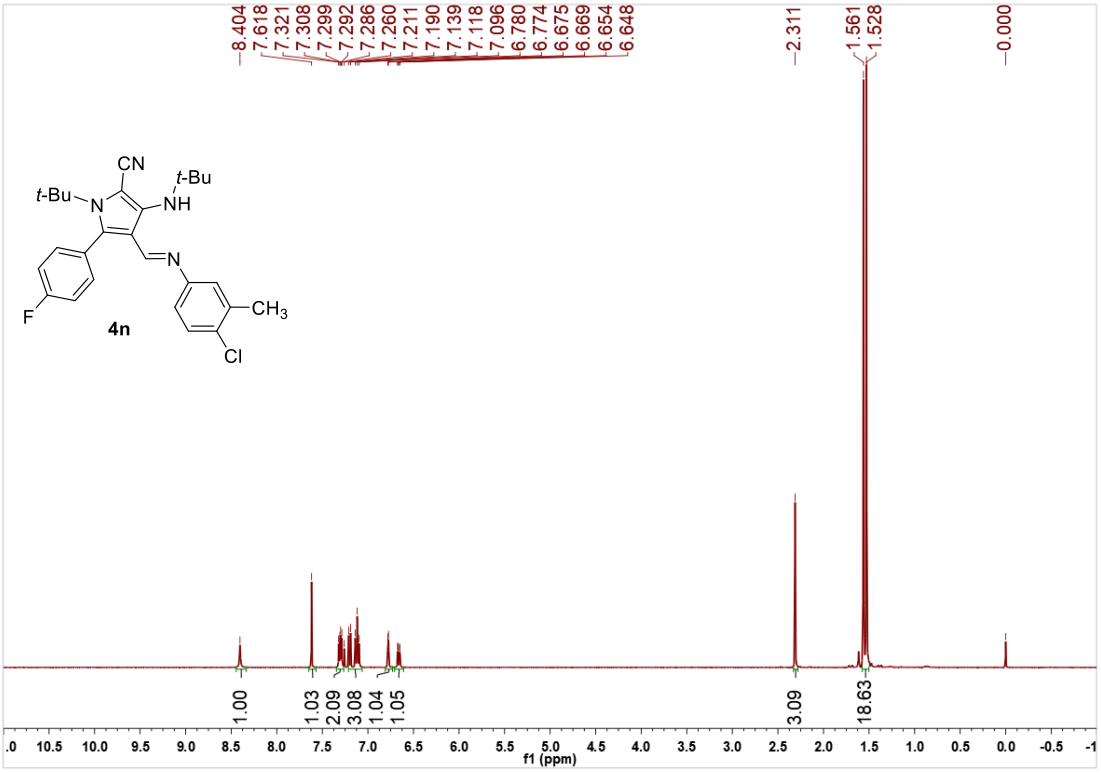
^{13}C NMR (100 MHz), $CDCl_3$



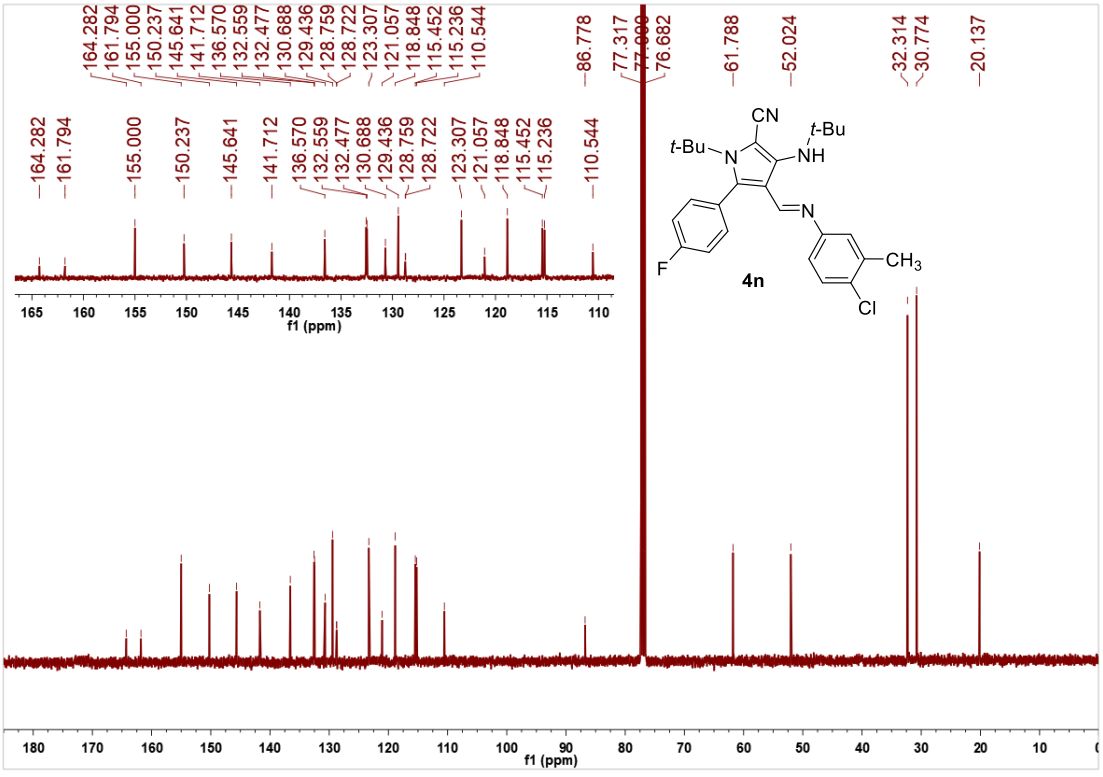
^{1}H NMR (400 MHz), $CDCl_3$



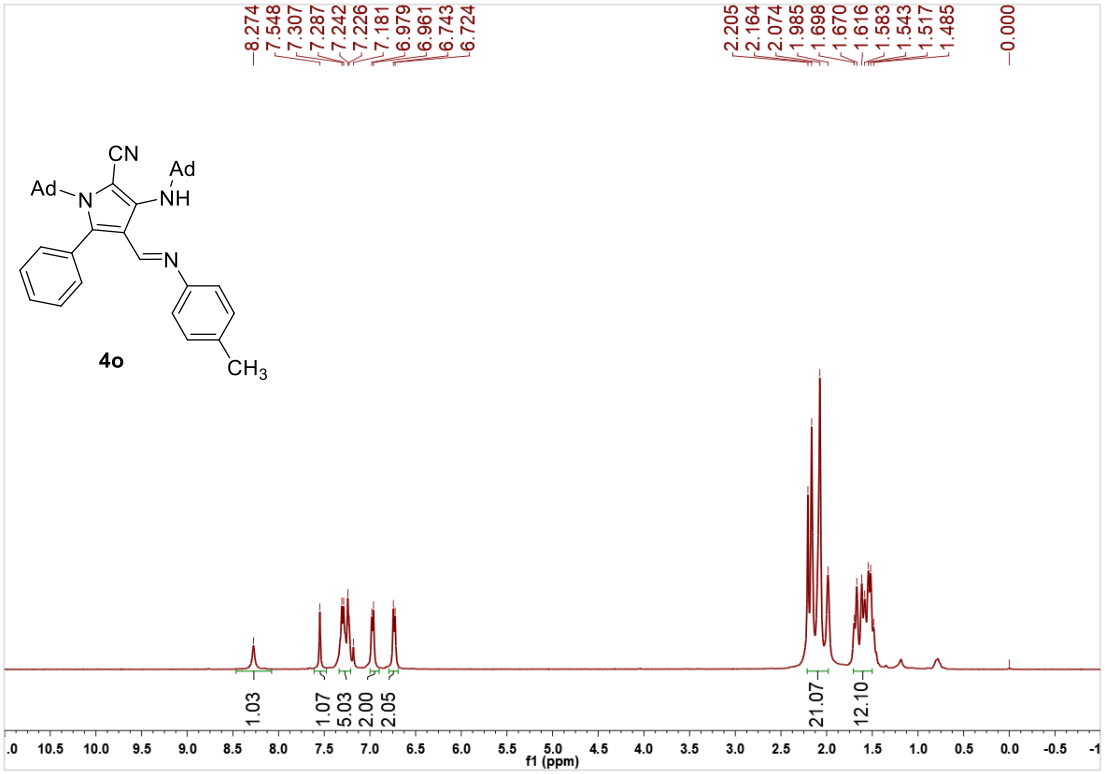
^{13}C NMR (100 MHz), $CDCl_3$



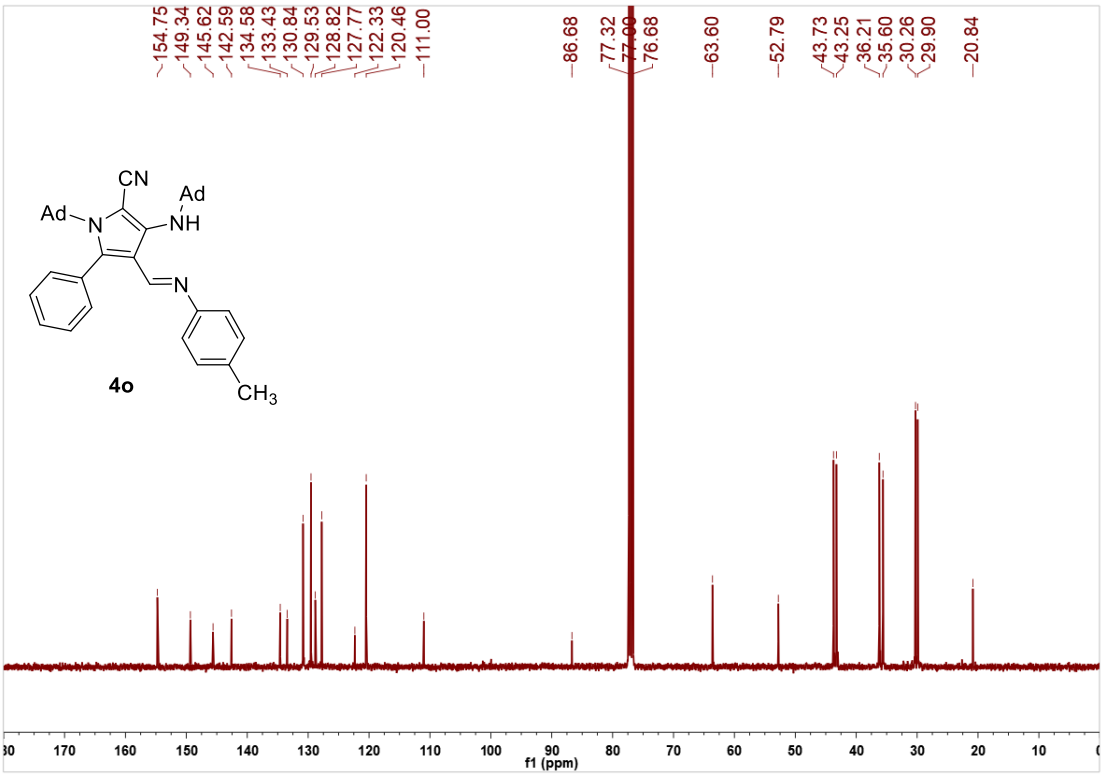
^{1}H NMR (400 MHz), $CDCl_3$



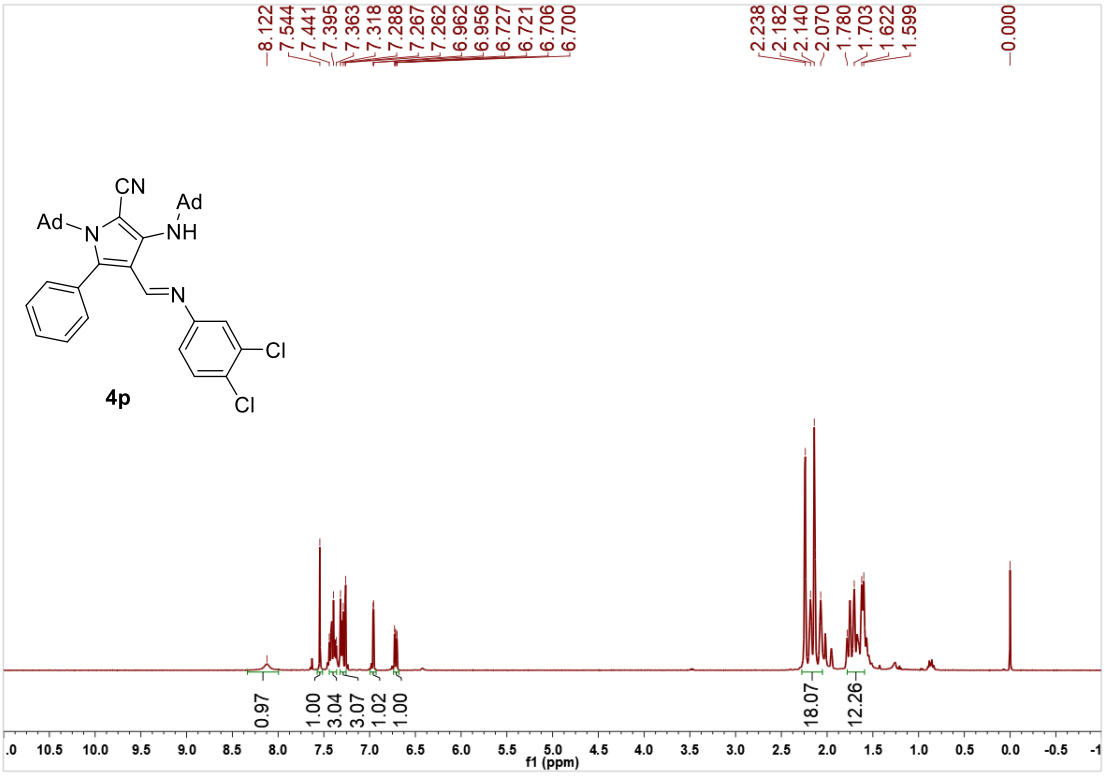
^{13}C NMR (100 MHz), $CDCl_3$



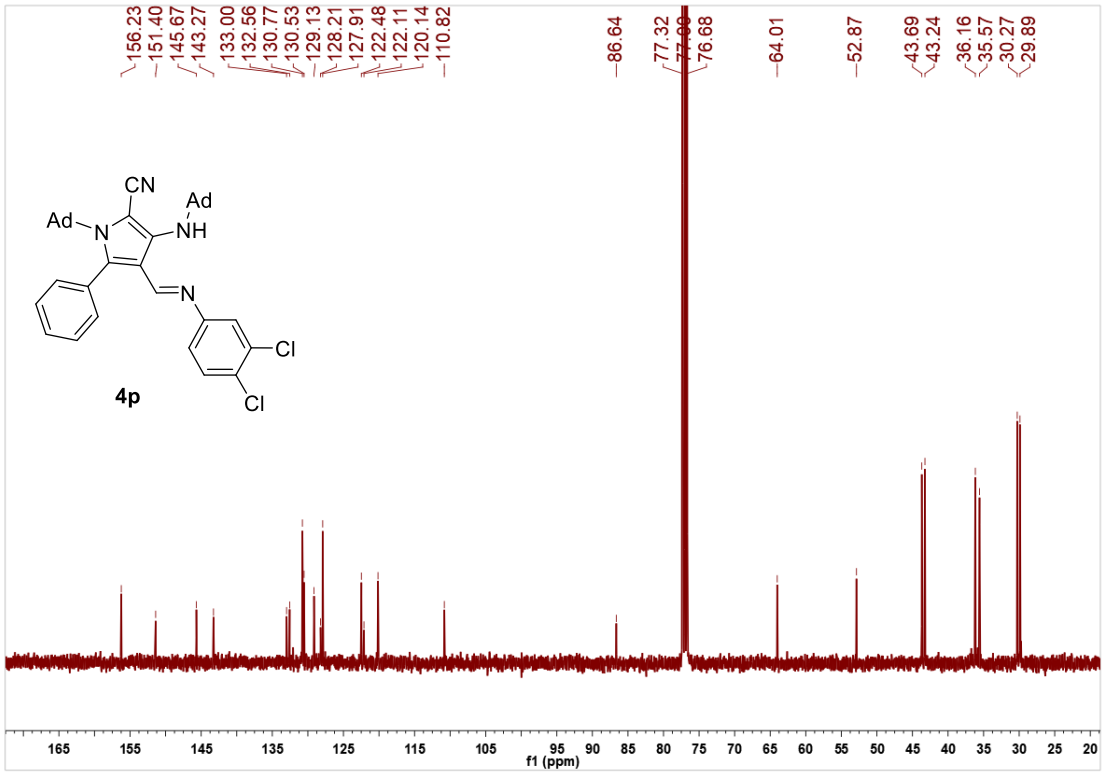
^{1}H NMR (400 MHz), $CDCl_3$



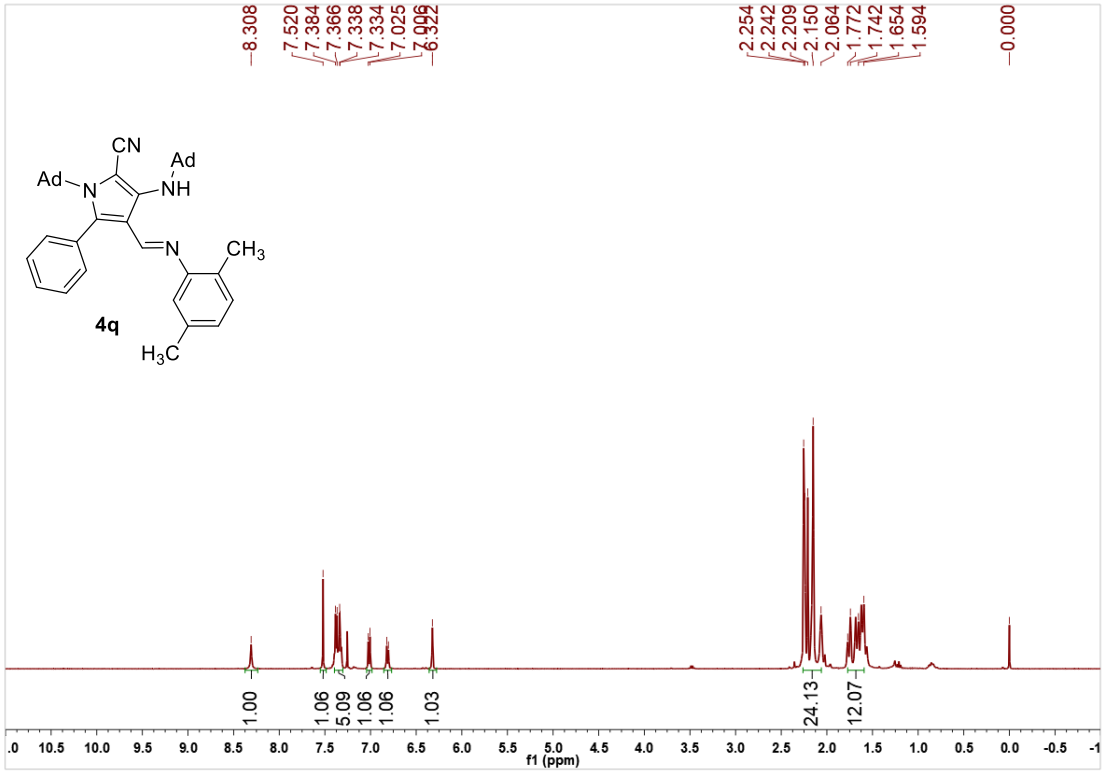
^{13}C NMR (100 MHz), $CDCl_3$



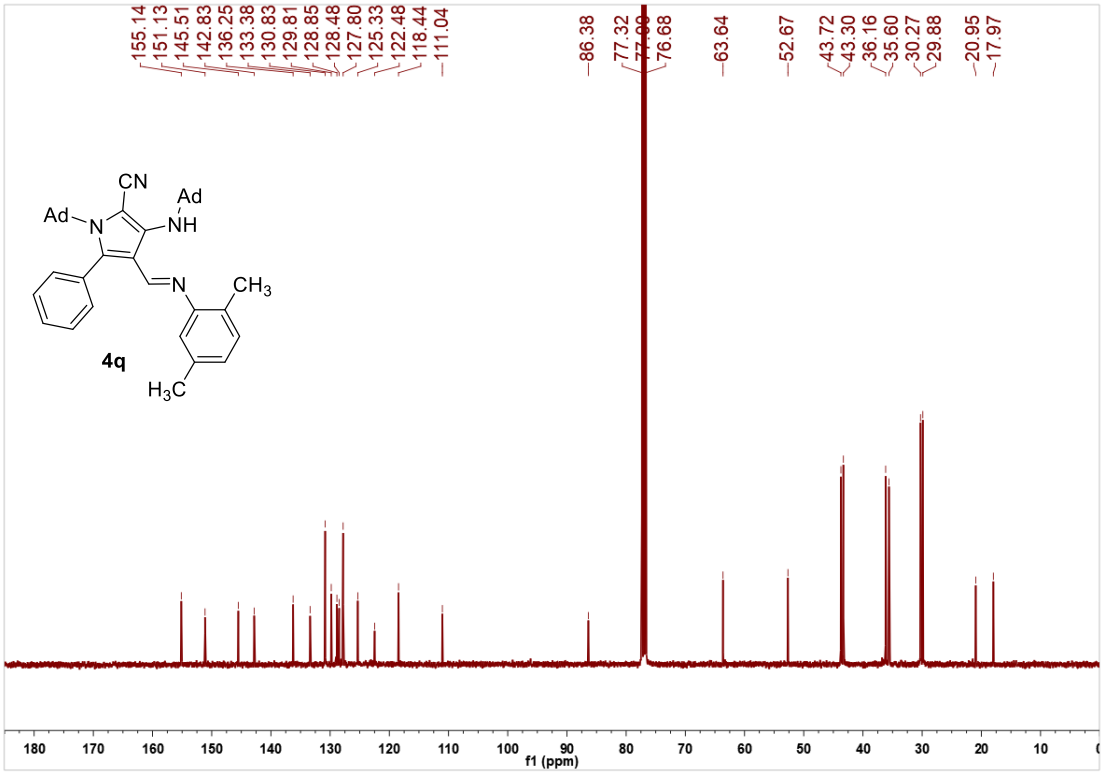
^{1}H NMR (400 MHz), $CDCl_3$



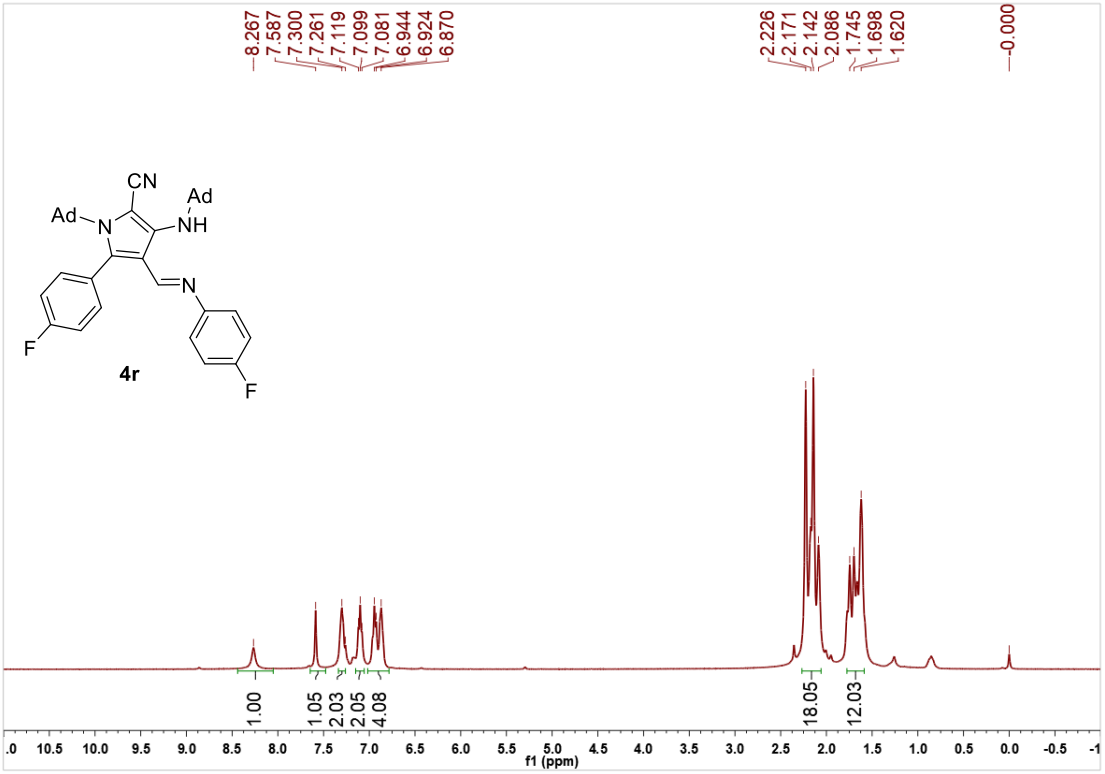
^{13}C NMR (100 MHz), $CDCl_3$



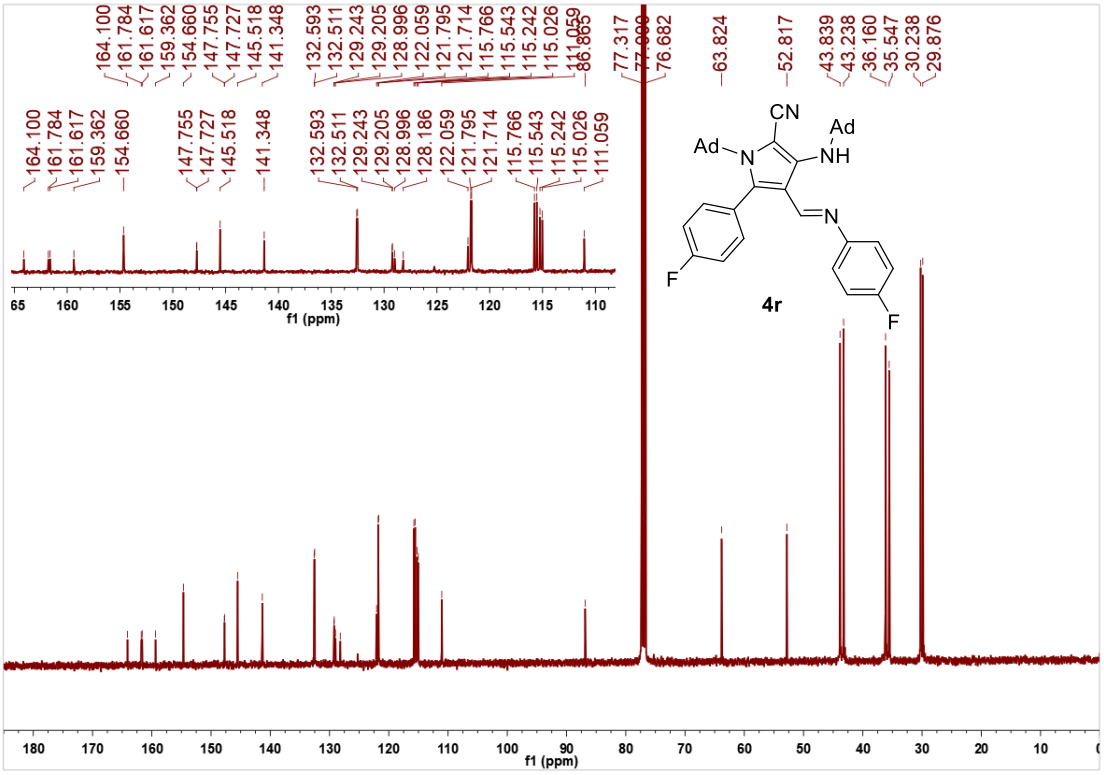
^{1}H NMR (400 MHz), $CDCl_3$



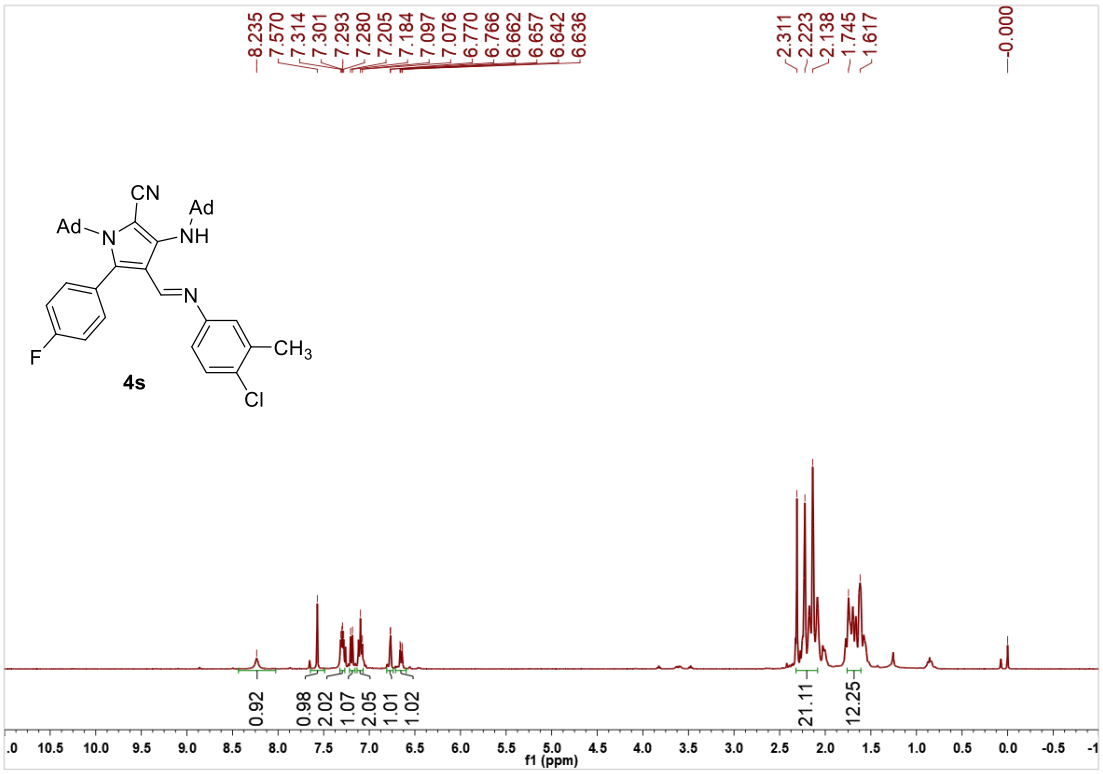
^{13}C NMR (100 MHz), $CDCl_3$



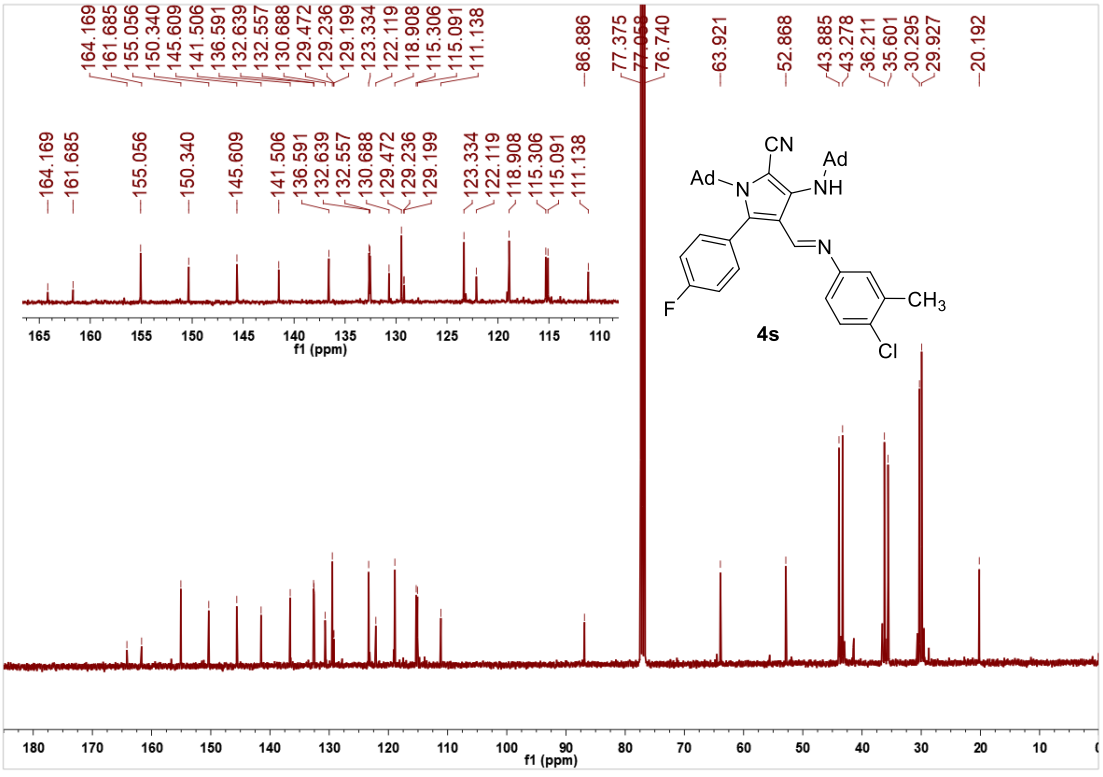
^{1}H NMR (400 MHz), $CDCl_3$



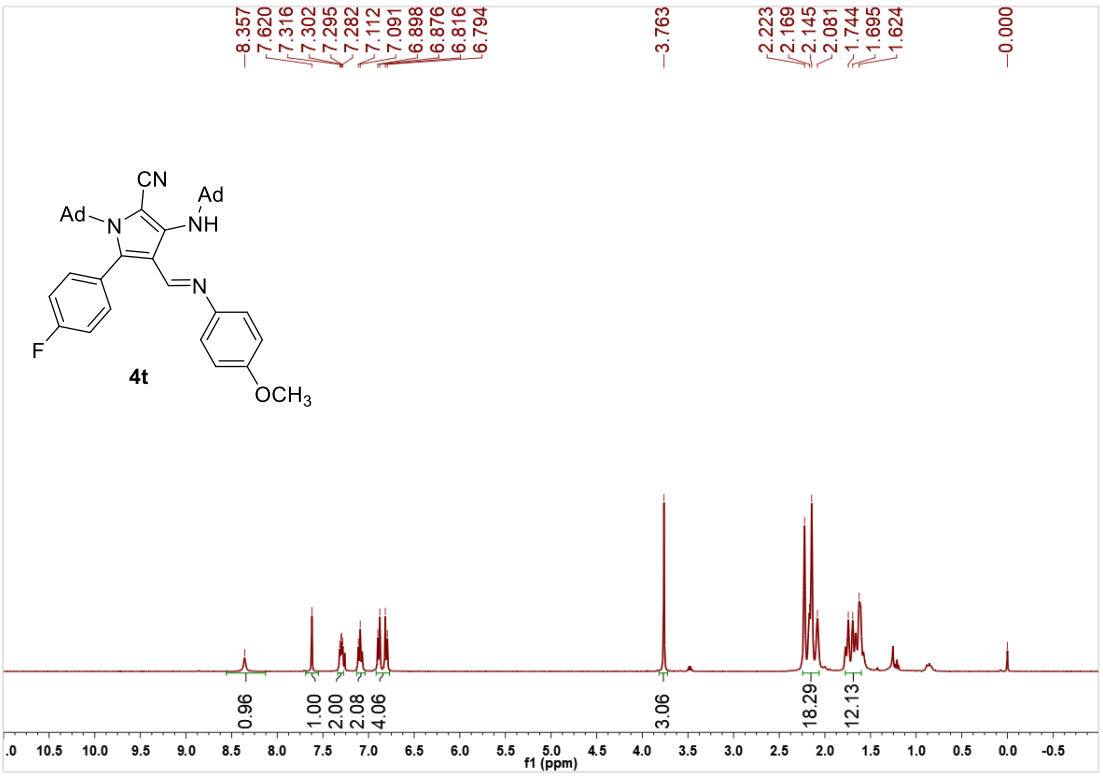
^{13}C NMR (100 MHz), $CDCl_3$



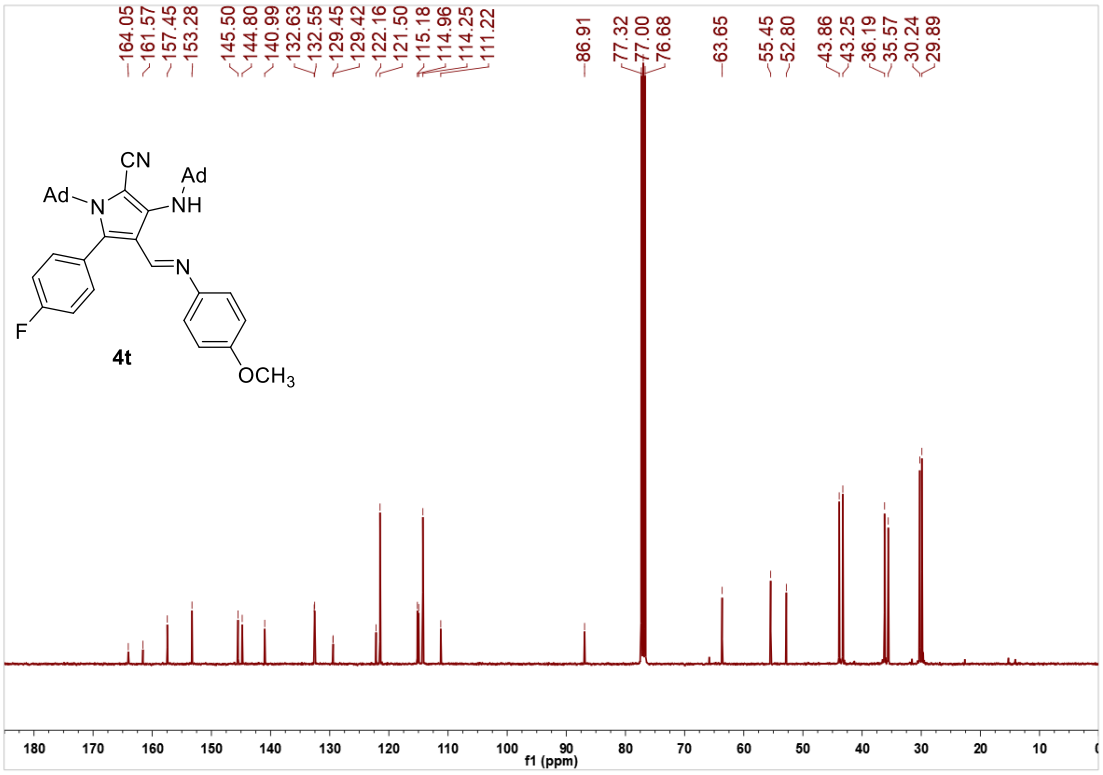
^{1}H NMR (400 MHz), $CDCl_3$



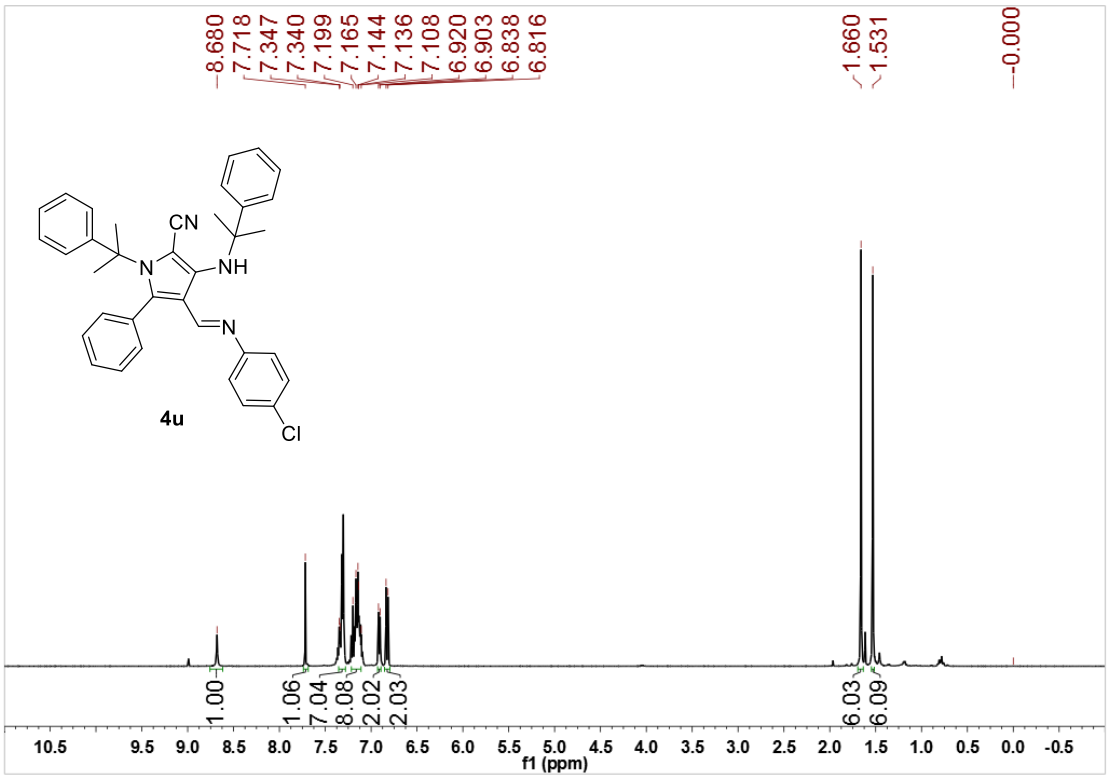
^{13}C NMR (100 MHz), $CDCl_3$



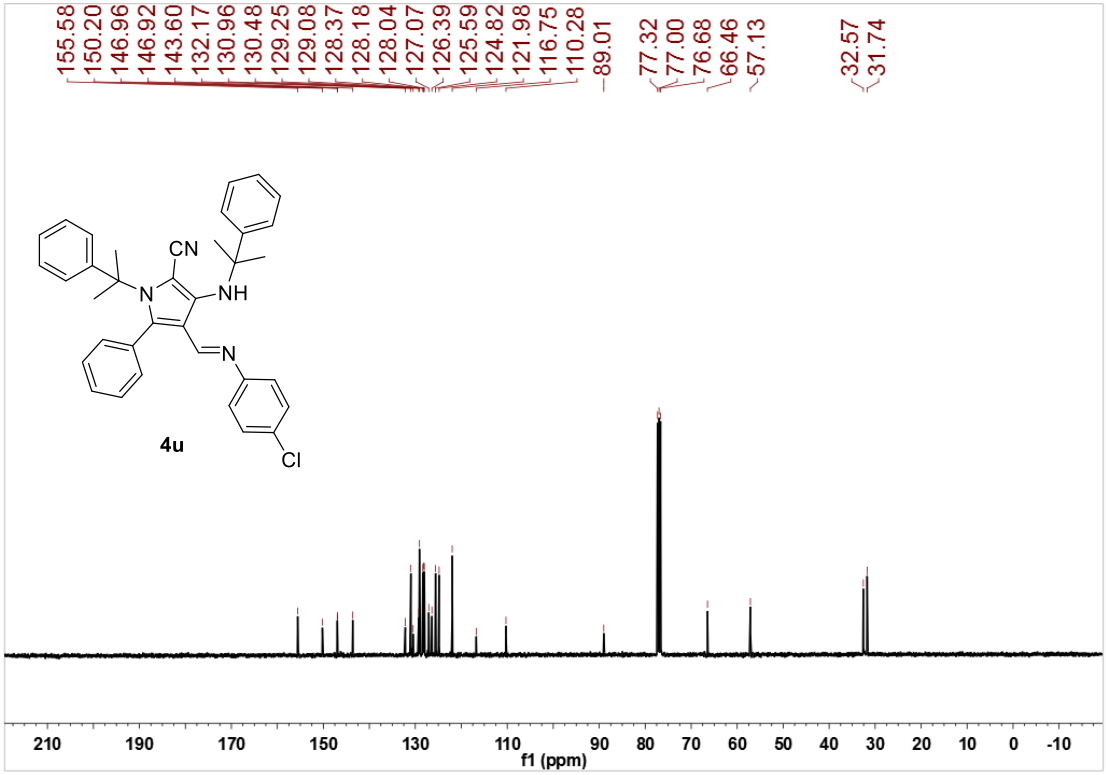
^{1}H NMR (400 MHz), $CDCl_3$



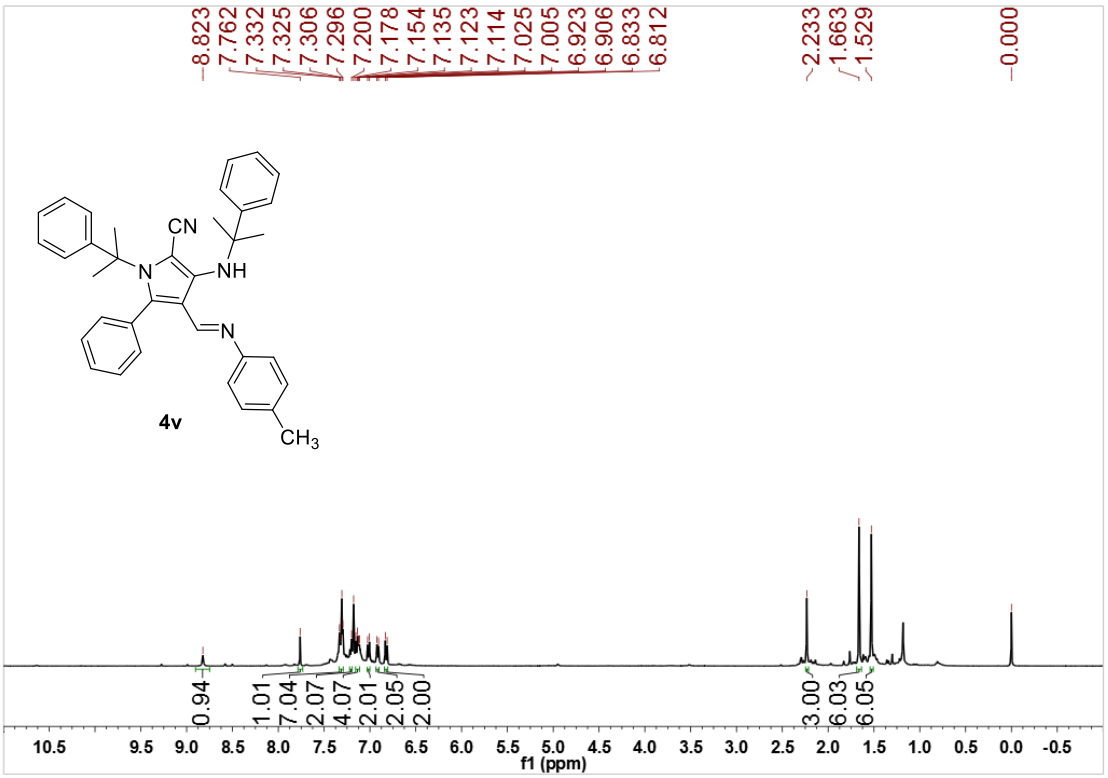
^{13}C NMR (100 MHz), $CDCl_3$



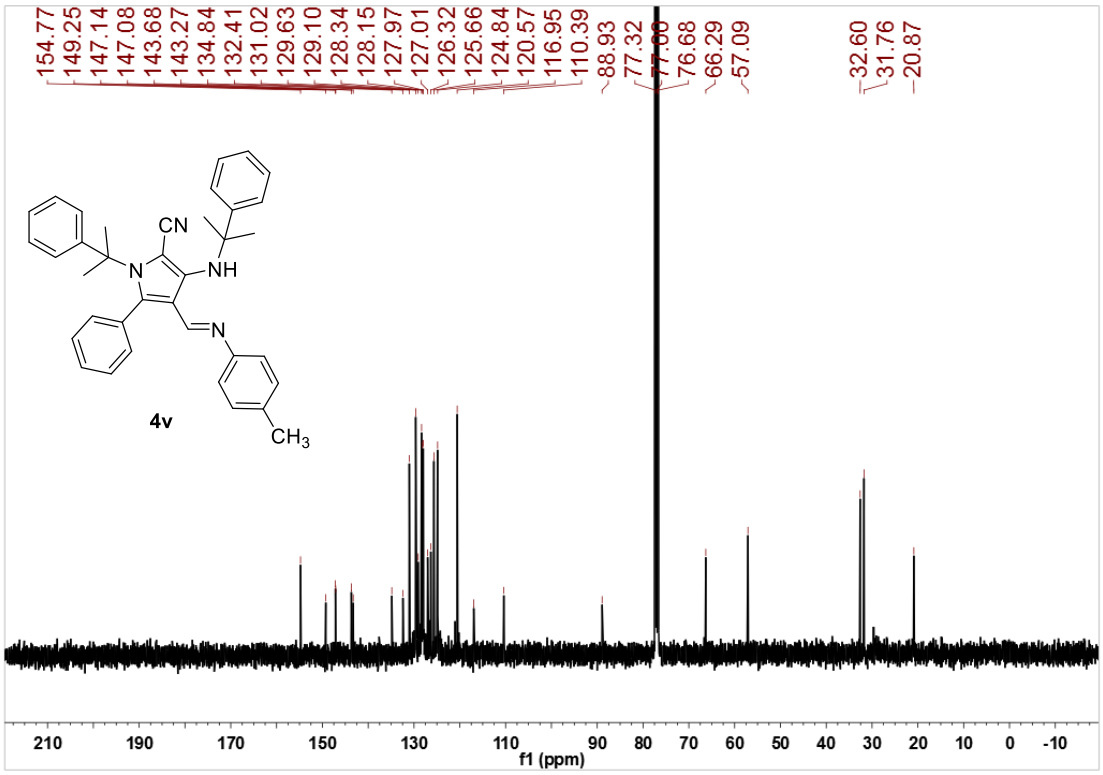
^{1}H NMR (400 MHz), $CDCl_3$



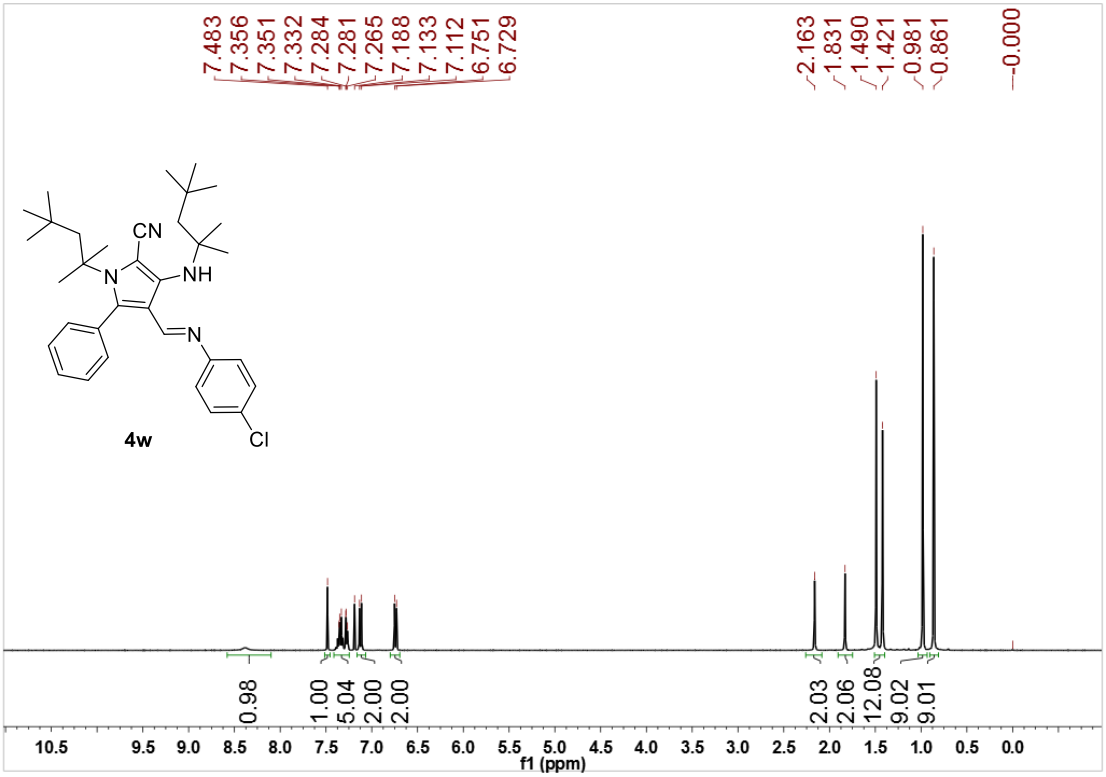
^{13}C NMR (100 MHz), $CDCl_3$



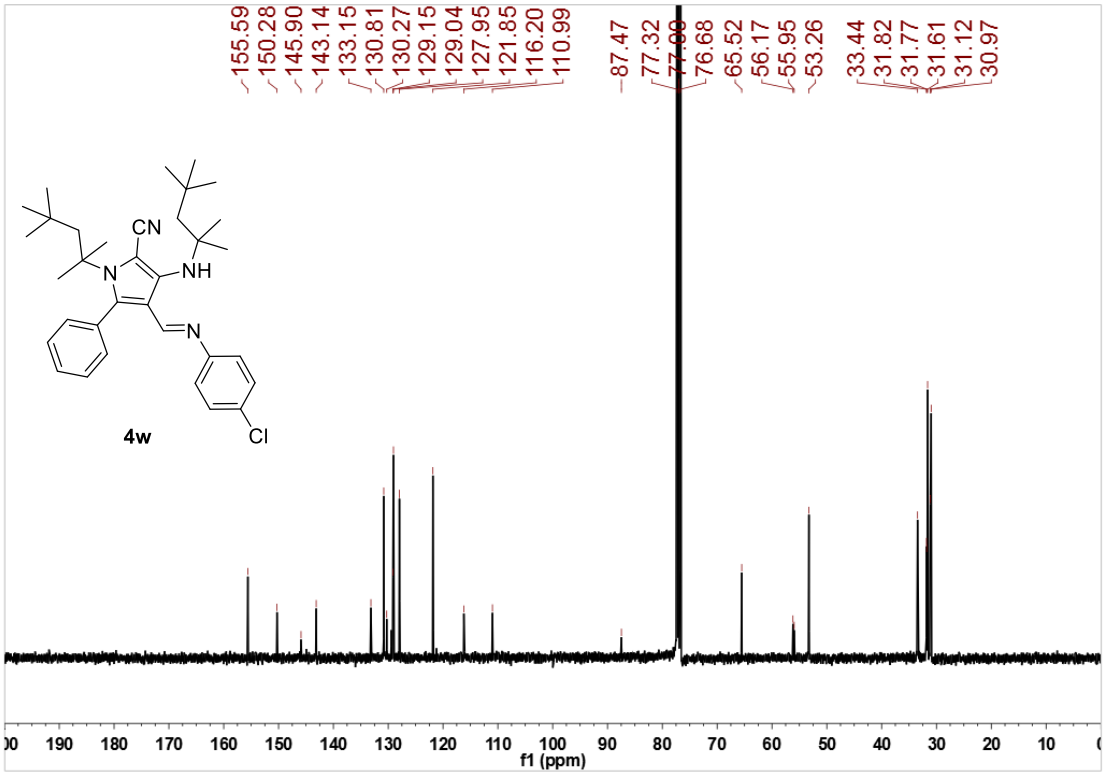
^{1}H NMR (400 MHz), $CDCl_3$



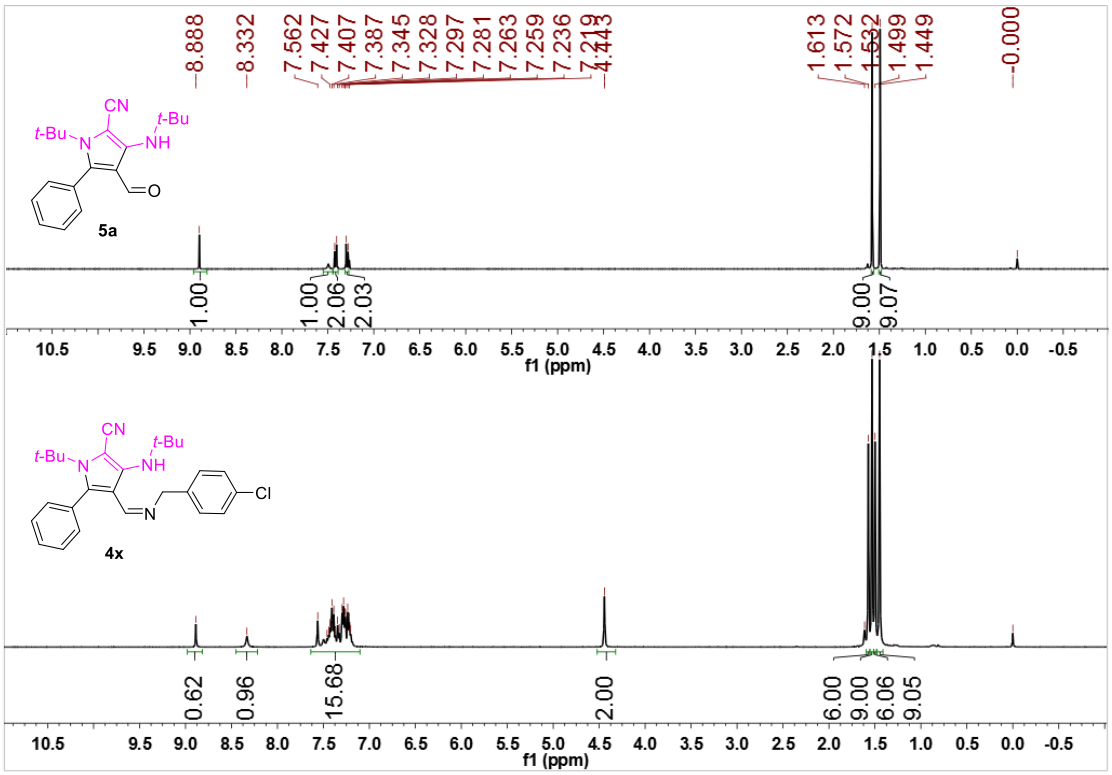
^{13}C NMR (100 MHz), $CDCl_3$



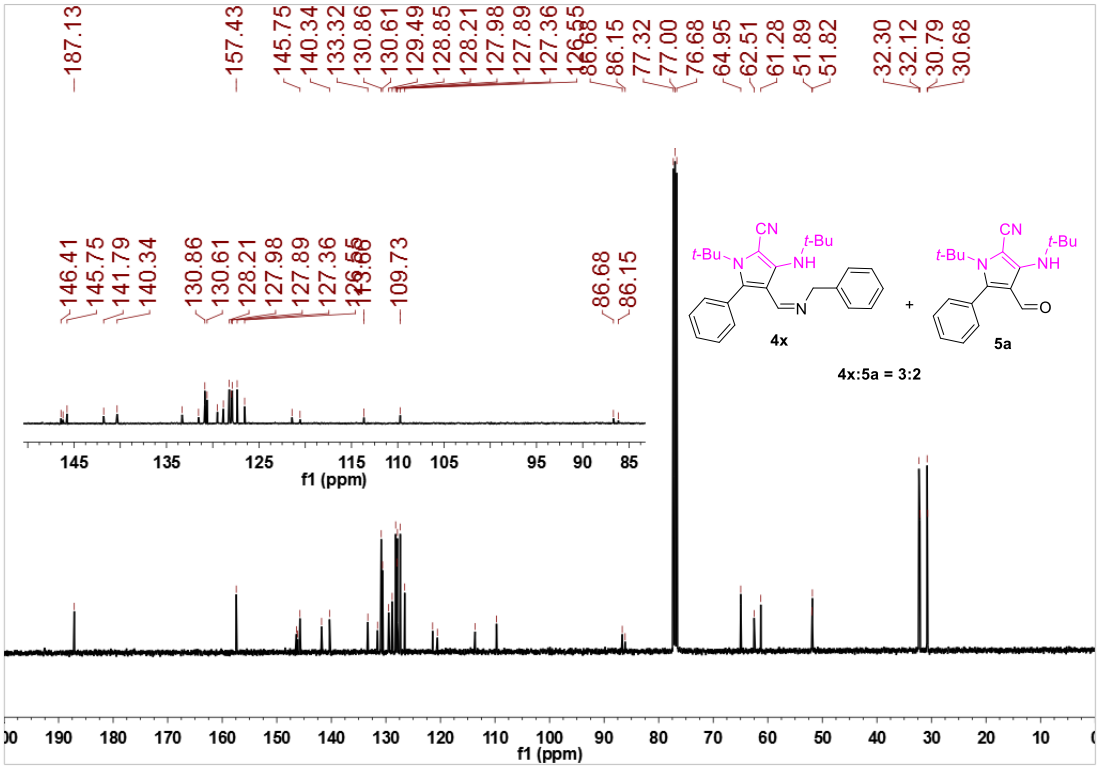
^{1}H NMR (400 MHz), $CDCl_3$



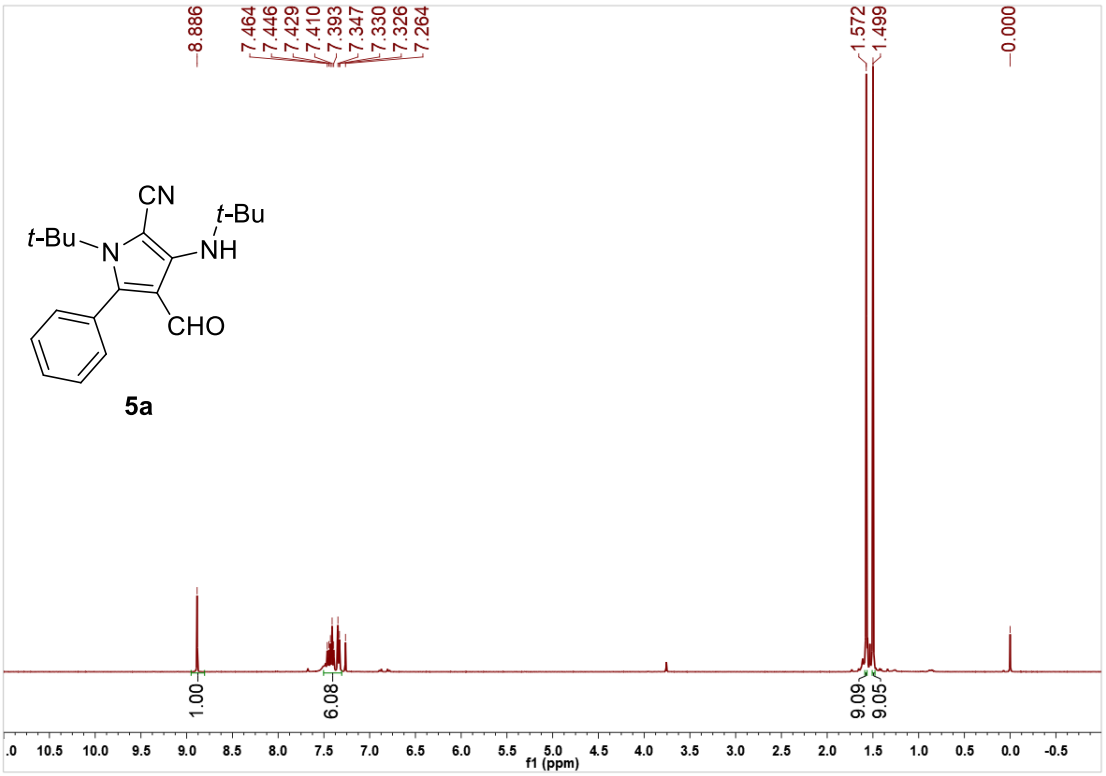
^{13}C NMR (100 MHz), $CDCl_3$



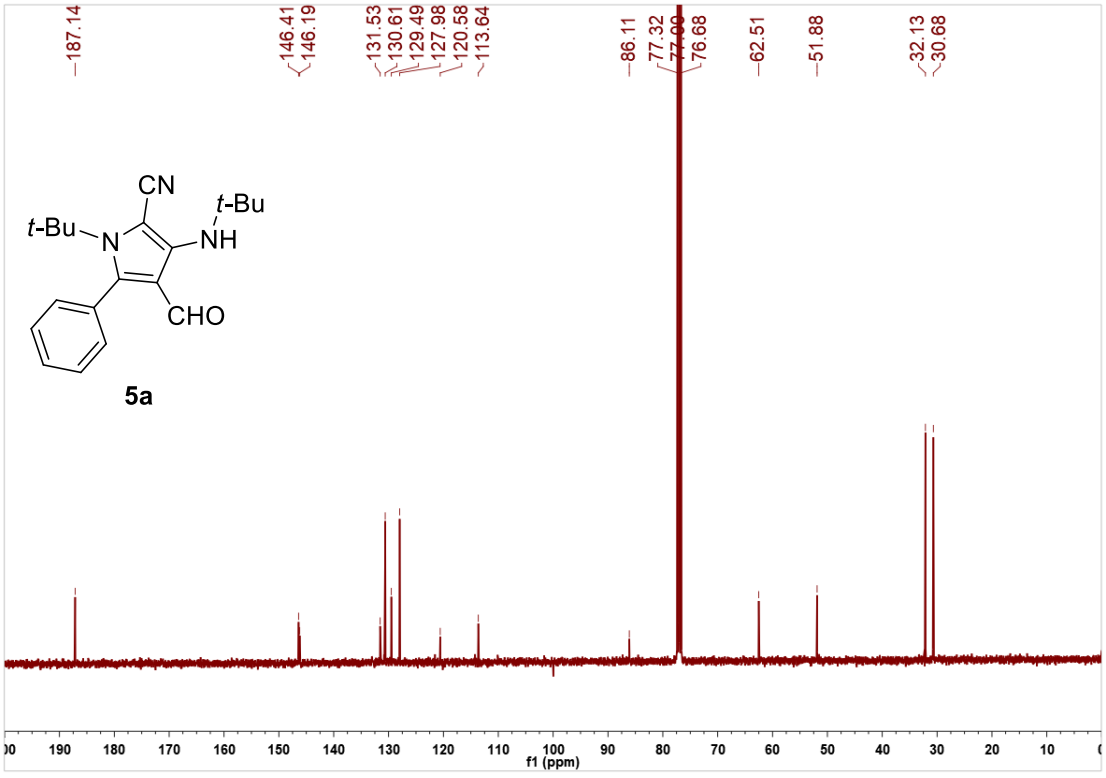
^{1}H NMR (400 MHz), $CDCl_3$



^{13}C NMR (100 MHz), $CDCl_3$



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



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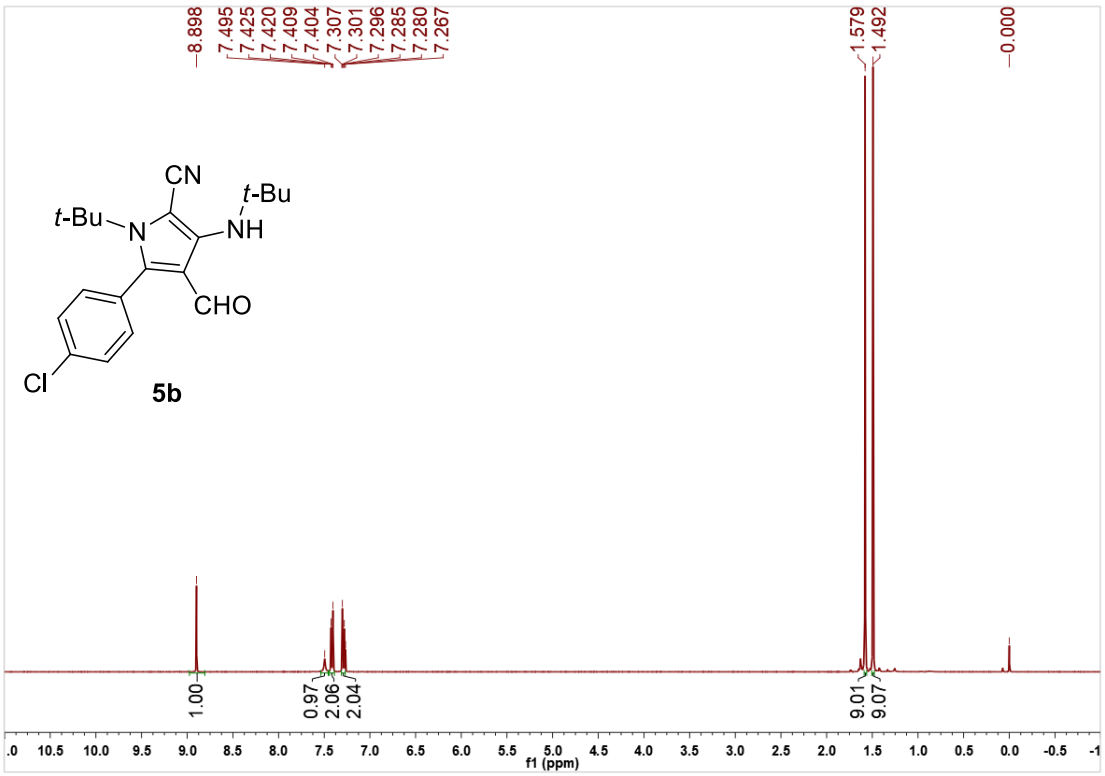
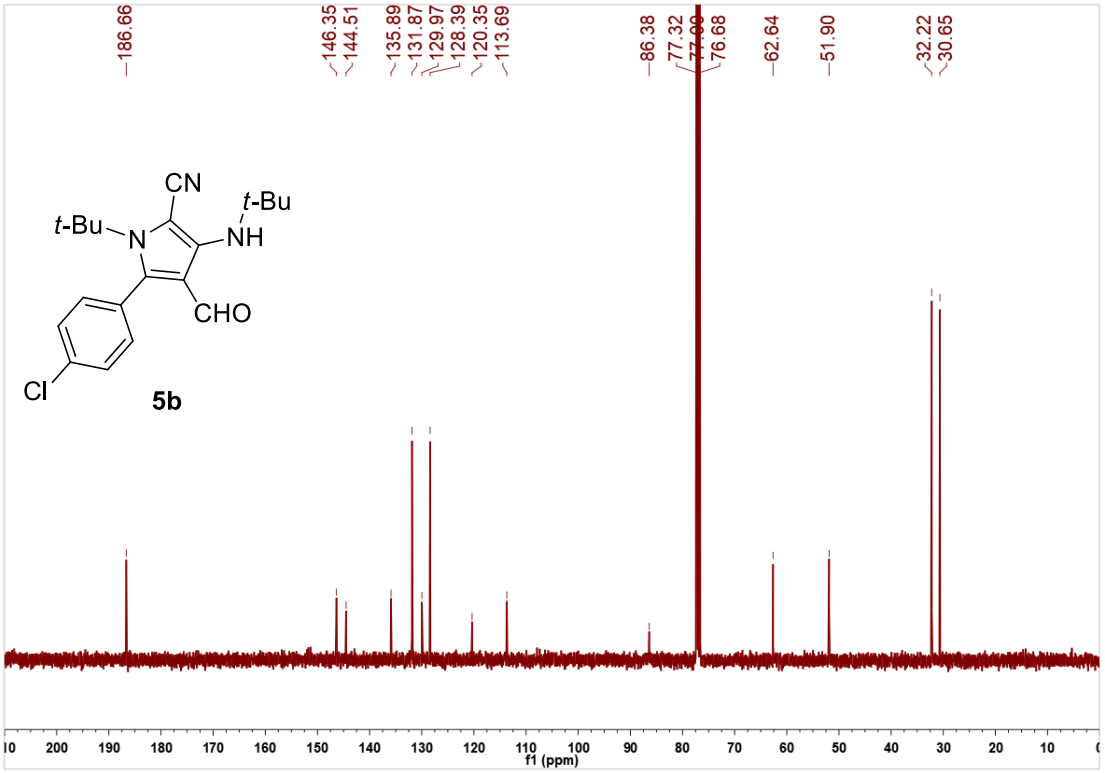
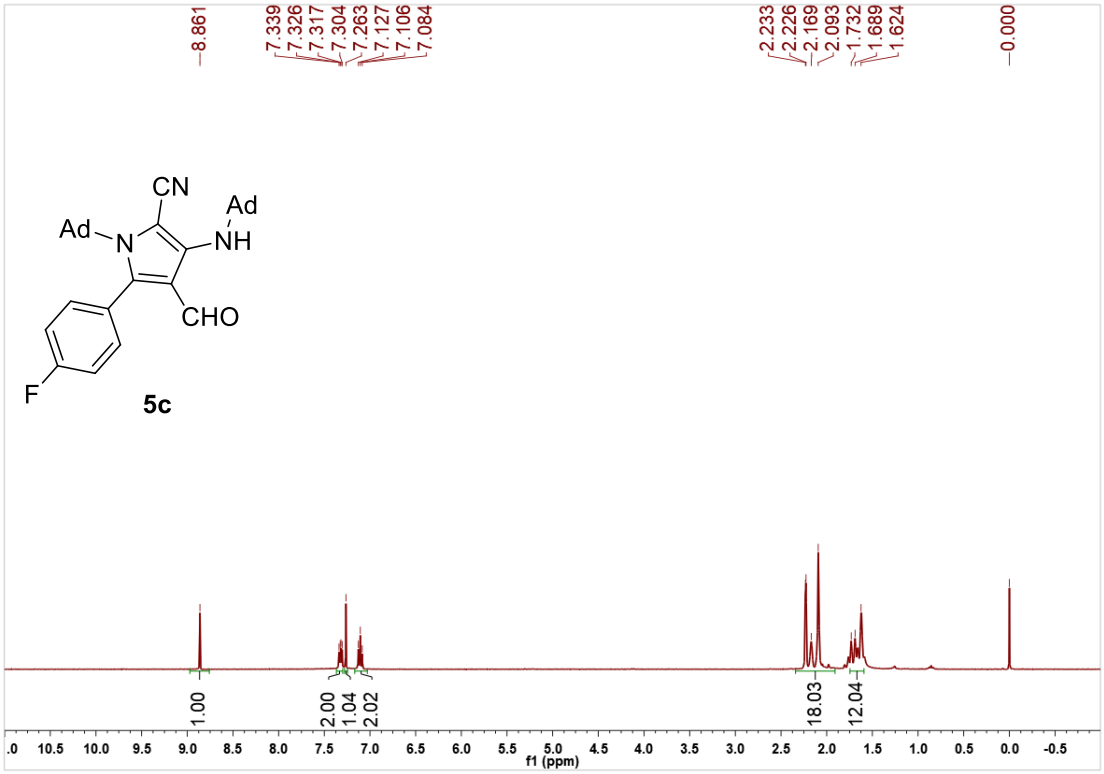


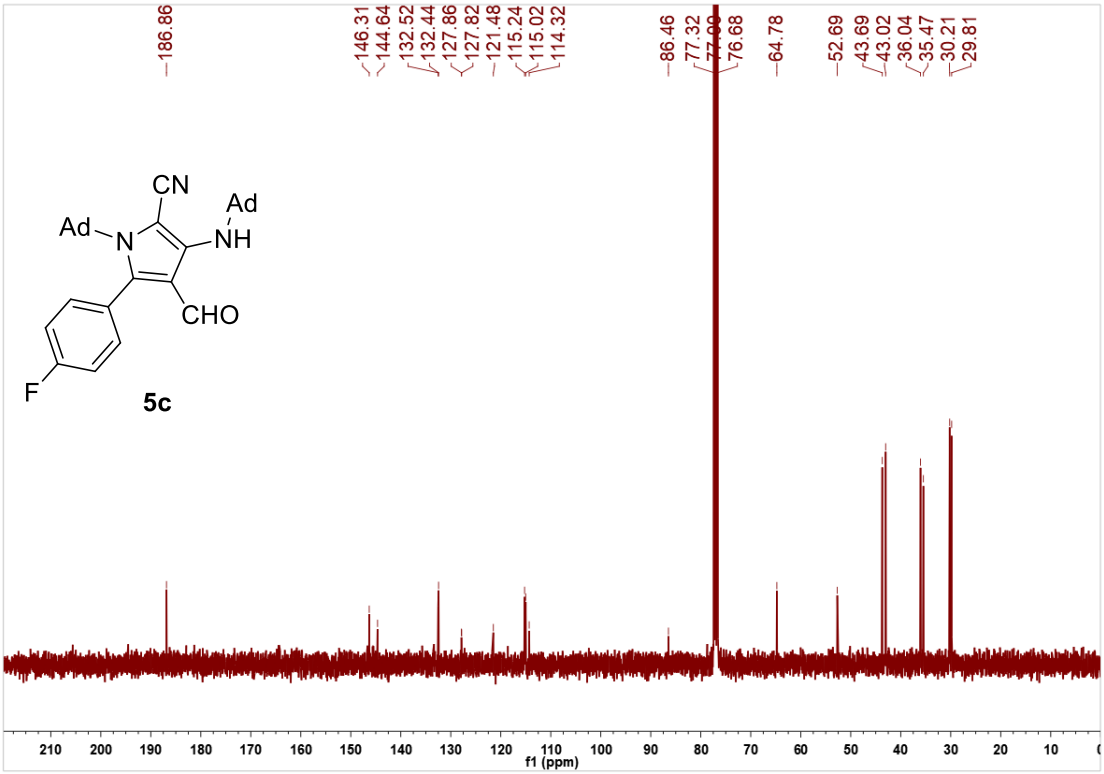
^{1}H NMR (400 MHz), $CDCl_3$



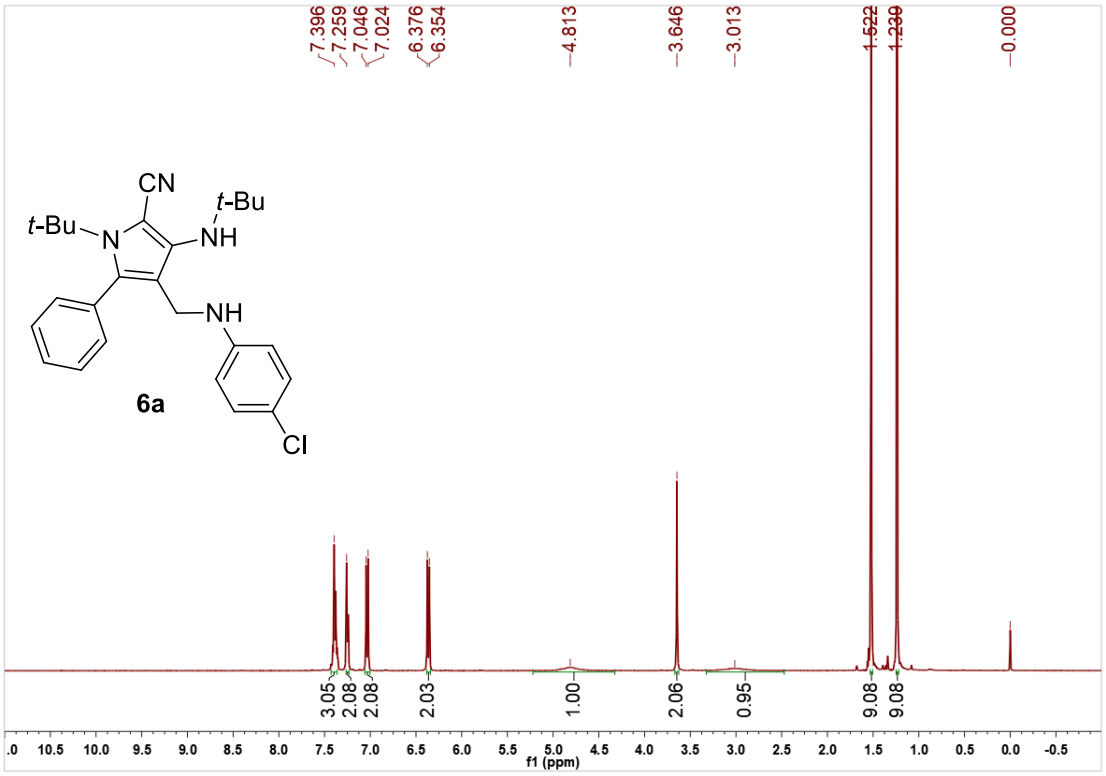
^{13}C NMR (100 MHz), $CDCl_3$



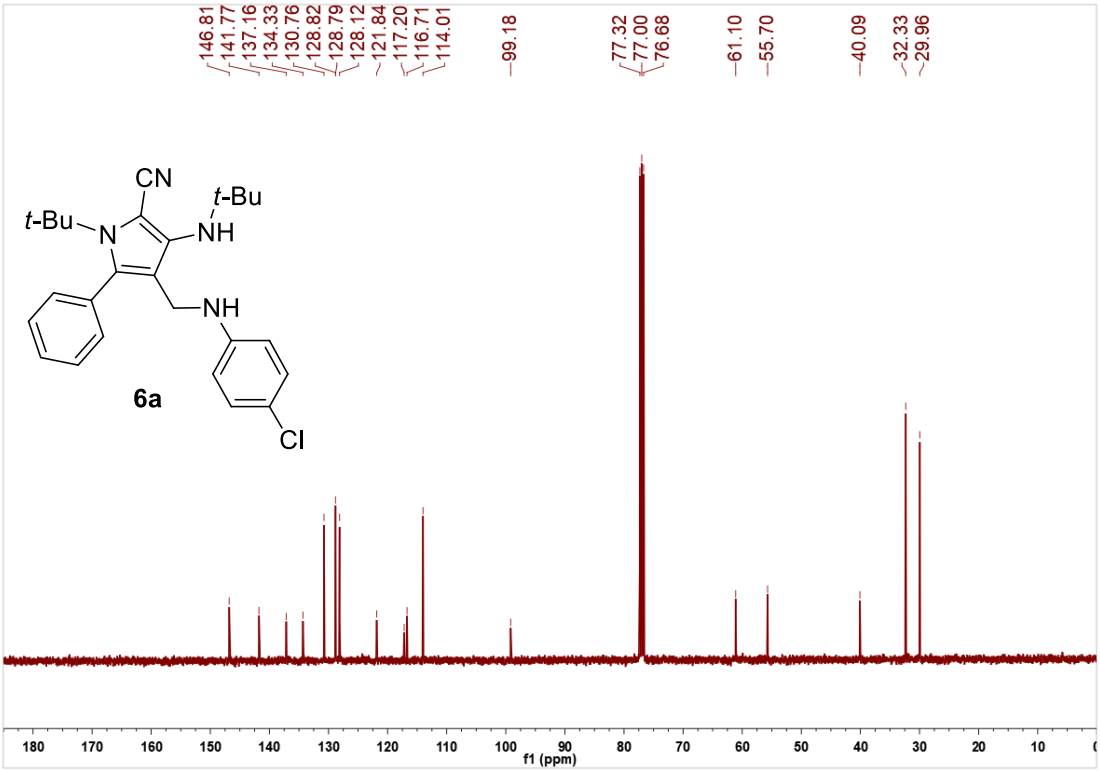
^{1}H NMR (400 MHz), $CDCl_3$



^{13}C NMR (100 MHz), $CDCl_3$



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



^{13}C NMR (100 MHz), $CDCl_3$