Access and Modulation of Substituted 1-Methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole

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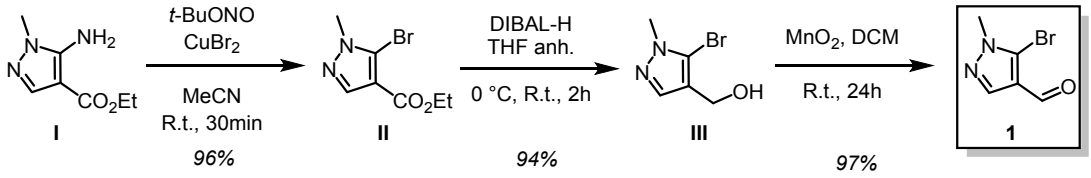
General Methods

All reagents and organic solvents were purchased from commercial suppliers and were used without further purification. Microwave assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by an IR sensor. Solvents mentioned as dry were purified with a dry station GT S100 immediately prior to use. The reactions were monitored by thin-layer chromatography (TLC) analysis using 0.2 mm precoated Kieselgel 60 F254 (Merck) silica gel plates visualized with a MACHEREY NAGEL UV_{254} lamp. Column chromatography was performed on silica gel 60 (230-400 mesh, 40 – 63 μm). Solvent ratios for chromatography and are reported as v/v ratios and are indicated for each compound. Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected on an IA9200 Thermo Scientific Electrothermal Melting Point apparatus/instrument. Infrared analyses were determined on a Thermo Scientific ATR Nicolet iS10 and interpreted using OMNIC software. ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker ULTRASHIELD® PLUS 400MHz spectrometer (^{13}C, 100 MHz) or on a Bruker AVANCE 250MHz (^{13}C, 62.9 MHz) spectrometer, as solutions in deuterated solvents. Unless otherwise indicated, chemical shifts (δ) are reported in parts per million (ppm) values, and coupling constants (J) are reported in Hertz. Peak multiplicities are designated by the following abbreviations: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; dd = double doublet, br = broadened. High-resolution mass spectrometry analyses (HRMS) were performed on a Maxis Bruker 4G Spectrometer. X-ray diffraction data were collected on Xcalibur CCD area detector diffractometer equipped with monochromatized Mo-Ka radiation (0.71073 Å) at 296 K. The data collection, unit cell refinement, and data reduction were performed using the CrysAlis Pro,[1] Oxford Diffraction Ltd. software package. Analytical numeric absorption correction using a multifaceted crystal model based on expressions derived was carried.[2] The positions of non-H atoms were determined and refinement by SHELXS-2014 program. Non-hydrogen atoms were first refined isotropically followed by anisotropic refinement by full matrix least-squares calculations based on F^2 using SHELXL-2014 program.

Compounds Described by the Literature

Starting material compound **1** was prepared as previously described in the literature and as follows:



Synthesis of Ethyl 5-bromo-1-methyl-1*H*-pyrazole-4-carboxylate[3] (II)

[1] A. T. CrysAlisPro, Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)(compiled Aug 13 2014, 18:06:01).
[2] R. C. Clark, J. S. Reid, *Acta Crystallogr. Sect. A* **1995**, *51*, 887-897.

Copper$^{(II)}$ bromide (6.3 g, 0.0283 moles) and *tert*-butyl nitrite (4.2 mL, 0.0354 moles) were combined in acetonitrile (50 mL). Commercial ethyl 5-amino-1-methyl-1*H*-pyrazole-4-carboxylate (**I**) (4.0 g, 0.0236 moles) was slowly added portionwise, and the reaction was maintained left at room temperature for 30 minutes. The mixture was cooled to room temperature, poured into aqueous hydrochloric acid (6 N, 160 mL), diluted with dichloromethane (150 mL), and stirred for 10 min. The aqueous layer was extracted with dichloromethane (3x100 mL), and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude obtained needed no further purification and was engaged in the next step. **Yield**: 96% (5.33 g). Light yellow solid. **M.p.**: 38 – 39 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.79 (s, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 161.4 (C=O), 141.6 (CH), 117.7 (C), 113.6 (C), 60.1 (CH_2), 37.8 (N-CH_3), 14.1 (CH_3). **IR *v* (cm^{-1})**: 2995, 2974, 2931, 2871, 1709, 1528, 1470, 1389, 1214, 1173, 1214, 1173, 1040, 770. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_7H_{10}{}^{79}BrN_2O_2]^+$ 232.9920; found 232.9917, calculated for $[C_7H_{10}{}^{81}BrN_2O_2]^+$ 234.9900; found 234.9897.

Synthesis of (5-bromo-1-methyl-1*H*-pyrazol-4-yl)methanol[4] (III)

A solution of ethyl 5-bromo-1-methyl-1*H*-pyrazole-4-carboxylate (**II)** (5.33 g, 0.0228 moles) in anhydrous tetrahydrofuran (75 mL) at 0°C was treated with diisobutylaluminum hydride (1 M solution in tetrahydrofuran, 58 mL, 0.0571 moles), and the mixture was allowed to warm to room temperature and stir for 2 hours. A cold saturated aqueous sodium potassium tartrate solution was added, and stirring was continued for 4 hours. The aqueous layer was extracted with dichloromethane, and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The resulted crude mixture needed no further purification and was engaged in the next step. **Yield**: 94% (4.14 g). Colorless solid. **M.p.**: 55 – 56 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.48 (s, 1H), 4.46 (s, 2H), 3.82 (s, 3H), 2.53 (s, 1H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 139.3 (CH), 120.9 (C), 113.7 (C), 55.6 (CH_2), 37.6 (N-CH_3). **IR *v* (cm^{-1})**: 3255, 2947, 2896, 2848, 2741, 1554, 1413, 1398, 1322, 1189, 1012, 995, 880. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_5H_8{}^{79}BrN_2O]^+$ 190.9815; found 190.9815, calculated for $[C_5H_8{}^{81}BrN_2O]^+$ 192.9794, found 192.9796.

Synthesis of 5-bromo-1-methyl-1*H*-pyrazole-4-carbaldehyde (1)

A solution of (5-bromo-1-methyl-1*H*-pyrazol-4-yl)methanol (**III**) (4.14 g, 0.0216 moles) in dichloromethane (25 mL) was treated with activated manganese$^{(IV)}$ oxide (18.8 g, 0.216 moles) and the mixture was stirred at room temperature for 24 hours. Afterwards, the reaction mixture was filtered on Celite® and the filter pad washed with dichloromethane. The recovered filtrates were then concentrated under reduced pressure to yield the crude compound that required no further purification. **Yield**: 97% (4.01 g). Light yellow solid. **M.p.**: 75 – 76 °C. **^{1}H NMR (400 MHz,**

[3] P. Gillespie, R. A. Goodnow, Q. Zhang, *US20060223852A1* **2006**, *Chem. Abstr.* **2006***, 145*, 397512.
[4] C. J. Helal, T. A. Chappie, J. M. Humphrey, *WO2012168817A1* **2012**, *Chem. Abstr.* **2012***, 158*, 56278.

Chloroform-*d*): δ 9.78 (s, 1H), 7.97 (s, 1H), 3.94 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 183.4 (C=O), 141.0 (CH), 121.7 (C), 119.7 (C), 37.6 (N-CH_3). **IR *v* (cm^{-1}):** 2953, 2920, 2852, 1655, 1524, 1501, 1454, 1419, 1388, 1368, 1190, 1094, 763. **HRMS (ESI):** (*m/z*) $[M+H]^+$ calculated for $[C_5H_6{}^{79}BrN_2O]^+$ 188.9658; found 188.9653, calculated for $[C_5H_6{}^{81}BrN_2O]^+$ 190.9638, found 190.9634.

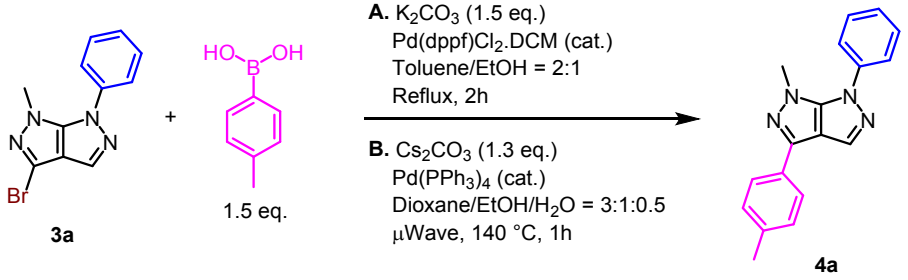
Optimization for the Suzuki-Miyaura Cross-Coupling Reaction

The first optimization conditions make use of a palladium$^{(II)}$ catalyst, a mixture of two solvents and conventional heating (Conditions A).[5] The second approach relies on palladium$^{(0)}$ catalyst, three solvents

and microwave irradiation (Conditions B).[6] In order to discriminate the best option for our substrate (3-bromo-1-methyl-6-phenyl-pyrazolo[3,4-*c*]pyrazole **3a**), comparative trials were performed, targeting the amount of catalyst loading (Table 1).

Initials results indicated that Conditions B are slightly superior to the Conditions A (Table 1, entry 1). The same pattern was noticed with catalyst amount ranging from 5 mol% to 2.5 mol% (Table 1, entries 2 and 3). The decisive result came when the palladium charge diminished again by half (1.25 mol%) as total conversion was only seen when applying Conditions B (Table 1, entry 5). The latter became obviously the most adapted choice for performing this transformation.

Table 1. Optimization for the Suzuki-Miyaura Cross-Coupling Reaction



Entry	Method	Catalyst (mol%)	Yield (%)[a]	SM (%)
1	A	10	69	0
	B	10	84	0
2	A	5	72	0
	B	5	81	0
3	A	2.5	72	0
	B	2.5	79	0
4	A	1.25	77	Traces
	B	1.25	83	0
5	B	0	0	83[a]

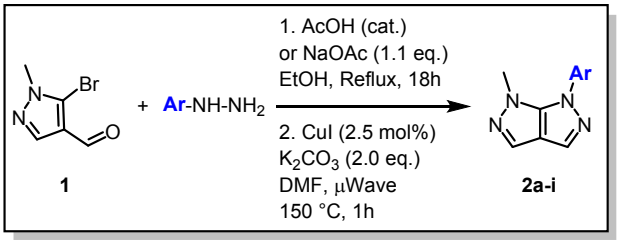
[a] Isolated yield after silica gel chromatography purification

General Procedures

A) Synthesis of 1-methyl-6-arylpyrazolo[3,4-*c*]pyrazoles 2a-i

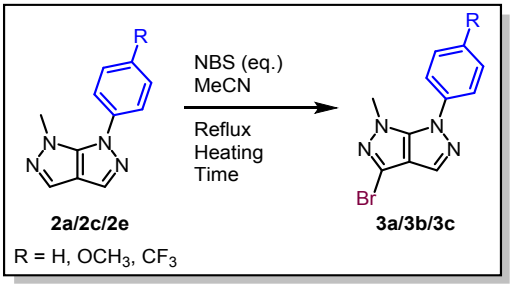
[5] M. Naas, Ph.D. Dissertation, Université d'Orléans, **2016**.
[6] S. Grosse, C. Pillard, F. Himbert, S. Massip, J. M. Léger, C. Jarry, P. Bernard, G. Guillaumet, *Eur. J. Org. Chem.* **2013**, 4146-4155.

To a stirred solution of 5-bromo-1-methyl-1*H*-pyrazole-4-carbaldehyde **1** (100 mg, 0.529 mmoles, 1.0 eq.) in ethanol (2 mL) a few drops of glacial acetic acid and the desired hydrazine (1.1 eq., 0.58 mmoles) were added. If the hydrazine is found under its hydrochloric form salt, a stoichiometric amount of sodium acetate (1.1 eq., 0.58 mmoles) is added to the mixture instead of the glacial acetic acid. This mixture was refluxed for 18 h and afterwards concentrated under reduced pressure. The crude was solubilized in DMF (3 mL), transferred to a dry tube and then potassium carbonate (146 mg, 1.06 mmoles, 2.0 eq.) and copper iodide (2.5 mg, 0.013 mmoles, 2.5 mol%) were added to the mixture. The tube was evacuated, backfilled with dry argon three times and then sealed. The reaction mixture was then heated at 150 °C for 1 hour under microwave irradiation. Solvent removal and purification by silica gel column chromatography using appropriate solvents afforded the expected bicyclic compound.



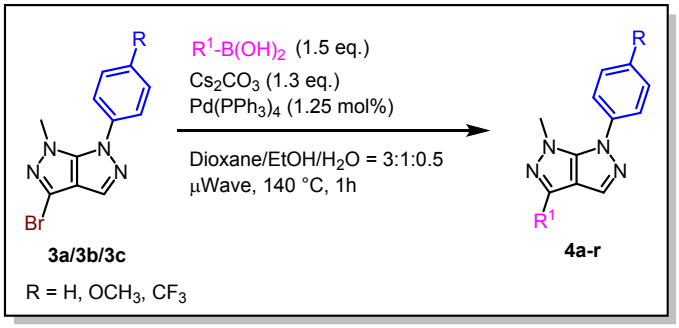
B) Synthesis of 3-bromo-1-methyl-6-arylpyrazolo[3,4-*c*]pyrazoles 3a, 3b and 3c

To a stirred solution of 1-methyl-6-arylpyrazolo[3,4-*c*]pyrazole (**2a, 2c, or 2e**) (100 mg, 1.0 eq.) in acetonitrile (2 mL) the correspondent amount of NBS is added. Depending on the nature of the substituent, the mixture is left under stirring at reflux or under microwave irradiation (sealed tube) for the given time. The reaction mixture is afterwards extracted with dichloromethane (3 x 10 mL) and water. The organic layers collected were washed with a saturated solution of $Na_2S_2O_3$, dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using appropriate solvents.



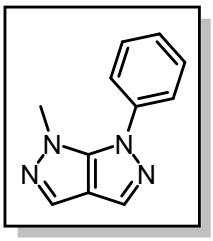
C) Synthesis of 1-methyl-3-aryl-6-arylpyrazolo[3,4-*c*]pyrazoles 4a-r

To a stirred solution of 3-bromo-1-methyl-6-arylpyrazolo[3,4-*c*]pyrazoles (**3a, 3b or 3c**) (100 mg, 1.0 eq.) and corresponding boronic acid (1.5 eq.) in a mixture (3 mL) of dioxane, ethanol and water (3:1:0.5), a solution of cesium carbonate (1.3 eq.) in 0.5 mL of water was added. The tube was argon flushed three times and then $Pd(PPh_3)_4$ (1.25 mol%) was added. The tube was again argon flushed, sealed and microwave irradiated at 140 °C for 1 h. The reaction mixture was then filtrated on Celite®, rinsed and extracted with EtOAc (3 x 10 mL). The organic layers collected were washed, dried on $MgSO_4$, filtered and evaporated. The crude obtained was purified by silica gel column chromatography using appropriate solvents, affording the desired compound.



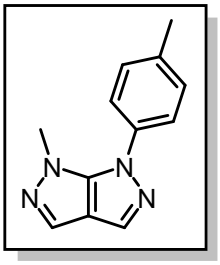
Characterization Data for the Newly Synthesized Compounds

1-Methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2a)



Prepared as described in the general procedure **A** (phenylhydrazine: 63 mg, 57 µL, 0.58 mmoles, CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 76% (80 mg). Orange oil. **Column chromatography eluents**: PE/EtOAc = 8/2. **^{1}H NMR (400 MHz, Acetone-*d*$_6$)**: δ 7.67 (d, J = 7.9 Hz, 2H), 7.62 (s, 1H), 7.58 (t, J = 7.9 Hz, 2H), 7.45 (s, 1H), 7.43 (t, J = 7.9 Hz, 1H), 3.85 (s, 3H). **^{13}C NMR (101 MHz, Acetone-*d*$_6$)**: δ 149.1 (C), 139.8 (C), 130.2 (2xCH), 130.0 (CH), 128.0 (CH), 127.6 (CH), 124.1 (2XCH), 121.0 (C), 37.7 (N-CH_3). **IR *v* (cm^{-1})**: 3056, 2942, 1682, 1595, 1508, 1457, 1436, 1372, 1189, 1112, 1034, 1004, 990, 969, 844, 759, 715, 696. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{11}H_{11}N_4]^+$ 199.0978; found 199.0978.

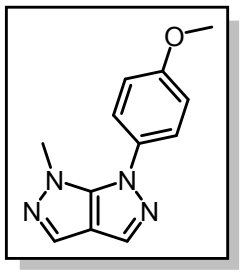
1-Methyl-6-(*p*-tolyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2b)



Prepared as described in the general procedure **A** (4-methylphenylhydrazine hydrochloride: 92 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 64% (72 mg). Beige solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 88 – 89 °C. **^{1}H NMR (400 MHz, Acetone-*d*$_6$)**: δ 7.59 (s, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.44 (s, 1H), 7.37 (d, J = 8.2 Hz, 2H), 3.81 (s, 3H), 2.41 (s, 3H). **^{13}C NMR (101 MHz, Acetone-*d*$_6$)**: δ 149.1 (C), 137.9 (C), 137.4 (C), 130.6 (2xCH), 129.6 (CH), 127.5 (CH), 124.2 (2xCH), 120.8 (C), 37.5

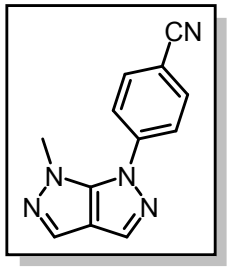
(N-CH_3), 21.0 (CH_3). **IR *v* (cm^{-1})**: 3108, 3041, 2918, 2854, 1711, 1604, 1583, 1515, 1436, 1416, 1376, 1365, 1216, 1198, 1108, 1036, 999, 977, 843, 819, 720. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_{13}N_4]^+$ 213.1134; found 213.1136.

1-(4-Methoxyphenyl)-6-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2c)



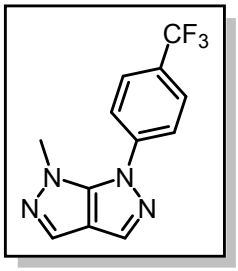
Prepared as described in the general procedure **A** (4-methoxyphenylhydrazine hydrochloride: 102 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 46% (56 mg). Light orange oil. **Column chromatography eluents**: PE/EtOAc = 8/2. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.57 (s, 1H), 7.46 (s, 1H), 7.44 (d, J = 8.9 Hz, 2H), 7.01 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H), 3.77 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 159.3 (C), 148.7 (C), 131.6 (C), 129.1 (CH), 127.6 (CH), 125.7 (2xCH), 119.4 (C), 114.6 (2xCH), 55.7 (O-CH_3), 36.9 (N-CH_3). **IR *v* (cm^{-1})**: 3001, 2935, 2837, 1600, 1585, 1514, 1444, 1421, 1370, 1299, 1246, 1182, 1137, 1109, 1035, 1013, 994, 969, 832, 718, 704. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_{13}N_4O]^+$ 229.1083; found 229.1085.

4-(6-Methylpyrazolo[3,4-*c*]pyrazol-1(6*H*)-yl)benzonitrile (2d)



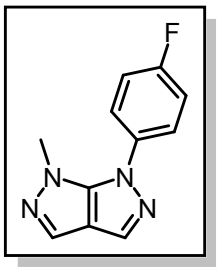
Prepared as described in the general procedure **A** (4-cyanophenylhydrazine hydrochloride: 99 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 76% (90 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 7/3. **M.p.**: 154 – 155 °C. **^{1}H NMR (250 MHz, Chloroform-*d*)**: δ 7.82 (d, J = 8.9 Hz, 2H), 7.72 – 7.67 (m, 3H), 7.52 (s, 1H), 3.94 (s, 3H). **^{13}C NMR (63 MHz, Chloroform-*d*)**: δ 148.1 (C), 142.1 (C), 133.7 (2xCH), 131.6 (CH), 128.3 (CH), 122.8 (2xCH), 121.0 (C), 118.2 (CN), 110.6 (C), 38.1 (N-CH_3). **IR *v* (cm^{-1})**: 3133, 3104, 2924, 2853, 2224, 1605, 1591, 1512, 1438, 1411, 1378, 1344, 1287, 1185, 1172, 1110, 1032, 996, 967, 837, 711, 704. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_{10}N_5]^+$ 224.0930; found 224.0930.

1-Methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2e)



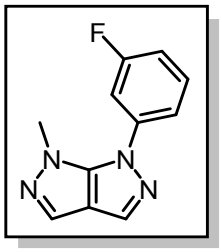
Prepared as described in the general procedure **A** (4-(trifluoromethyl)-phenylhydrazine: 103 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 54% (77 mg). Light yellow solid. **Column chromatography eluents**: DCM/EtOAc = 95/5. **M.p.:** 89 – 90 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.78 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.66 (s, 1H), 7.50 (s, 1H), 3.90 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 148.2 (C), 141.4 (C), 130.9 (CH), 129.2 (q, $^2J_{C\text{-}F}$ = 33.0 Hz, C), 128.1 (CH), 126.8 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, 2xCH), 123.8 (q, $^1J_{C\text{-}F}$ = 272.1 Hz, CF_3), 122.9 (2xCH), 120.6 (C), 37.8 (N-CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*)**: δ -62.4. **IR *v* (cm^{-1})**: 3106, 2923, 2854, 1616, 1597, 1523, 1507, 1143, 1318, 1193, 1180, 1157, 1118, 1107, 1065, 1031, 999, 970, 872, 839, 823, 714, 690. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_{10}F_3N_4]^+$ 267.0852; found 267.0852.

1-(4-Fluorophenyl)-6-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2f)



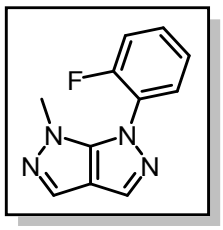
Prepared as described in the general procedure **A** (4-fluorophenylhydrazine hydrochloride: 95 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 62% (71 mg). Colorless oil. **Column chromatography eluents**: PE/EtOAc = 8/2. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.60 (s, 1H), 7.51 (dd, J = 8.9, 4.7 Hz, 2H), 7.48 (s, 1H), 7.24 – 7.16 (dd, J = 8.9, 8.8 Hz, 2H), 3.80 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 161.9 (d, $^1J_{C\text{-}F}$ = 248.0 Hz, C), 148.5 (C), 134.7 (d, $^4J_{C\text{-}F}$ = 3.1 Hz, C), 129.8 (CH), 127.8 (CH), 125.7 (d, $^3J_{C\text{-}F}$ = 8.6 Hz, 2xCH), 119.8 (C), 116.5 (d, $^2J_{C\text{-}F}$ = 23.1 Hz, 2xCH), 37.1 (N-CH_3). **IR ν (cm^{-1})**: 3111, 3066, 2943, 1701, 607, 1594, 1513, 1443, 1417, 1371, 1218, 1190, 1218, 1190, 1152, 1033, 999, 969, 838, 815, 718, 701. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{11}H_{10}FN_4]^+$ 217.0884; found 217.0884.

1-(3-Fluorophenyl)-6-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2g)



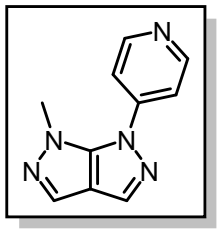
Prepared as described in the general procedure **A** (3-fluorophenylhydrazine hydrochloride: 95 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 85% (98 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 103 – 104 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.62 (s, 1H), 7.51 – 7.42 (m, 2H), 7.36 – 7.29 (m, 2H), 7.09 (d, J = 8.8 Hz, 1H), 3.88 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 163.0 (d, $^1J_{C\text{-}F}$ = 248.4 Hz, C), 148.2 (C), 140.0 (d, $^3J_{C\text{-}F}$ = 10.2 Hz, CH), 130.7 (d, $^3J_{C\text{-}F}$ = 9.2 Hz, C), 130.2 (CH), 127.9 (CH), 120.2 (C), 118.6 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, CH), 114.4 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, CH), 110.9 (d, $^2J_{C\text{-}F}$ = 24.7 Hz, CH), 37.5 (N-CH_3). **IR ν (cm^{-1})**: 3091, 2992, 2934, 2853, 1161, 1595, 1509, 1464, 1429, 1414, 1379, 1199, 1171, 1148, 1113, 1081, 1030, 970, 869, 784, 712. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{11}H_{10}FN_4]^+$ 217.0884; found 217.0883.

1-(2-Fluorophenyl)-6-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2h)



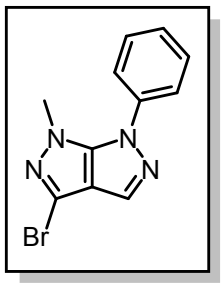
Prepared as described in the general procedure **A** (2-fluorophenylhydrazine hydrochloride: 95 mg, 0.58 mmoles; NaOAc: 48 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 46% (53 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 57 – 58 °C. **^{1}H NMR (400 MHz, Acetone-d_6)**: δ 7.72 – 7.67 (m, 2H), 7.61 – 7.53 (ddd, J = 8.2, 8.1, 4.7 Hz, 1H), 7.48 – 7.40 (m, 3H), 3.71 (s, 3H). **^{13}C NMR (101 MHz, Acetone-d_6)**: δ 157.1 (d, $^1J_{C\text{-}F}$ = 248.7 Hz, C), 150.1 (C), 131.0 (d, $^3J_{C\text{-}F}$ = 7.8 Hz, CH), 130.8 (CH), 129.2 (C), 127.6 (CH), 127.5 (CH), 126.1 (d, $^3J_{C\text{-}F}$ = 3.9 Hz, CH), 120.1 (C), 117.4 (d, $^2J_{C\text{-}F}$ = 19.5 Hz, CH), 36.2 (s, N-CH_3). **IR ν (cm^{-1})**: 3113, 3075, 2924, 2852, 1607, 1515, 1494, 1479, 1463, 1445, 1432, 1417, 1370, 1260, 1216, 1187, 1103, 1025, 1000, 972, 846, 836, 755, 725, 717, 704. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{11}H_{10}FN_4]^+$ 217.0884; found 217.0882.

1-Methyl-6-(pyridin-4-yl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (2i)



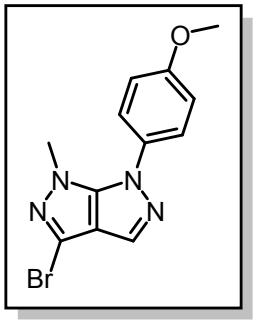
Prepared as described in the general procedure **A** (4-hydrazinopyridine: 64 mg, 0.58 mmoles; CuI: 2.5 mg, 0.013 mmoles; K_2CO_3: 146 mg, 1.06 mmoles). **Yield**: 46% (49 mg). White yellow solid. **Column chromatography eluents**: EtOAc/MeOH = 95/5. **M.p.**: 105 – 106 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.75 (br s, 2H), 7.68 (s, 1H), 7.53 (br s, 2H), 7.50 (s, 1H), 4.00 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 151.2 (2xCH), 147.9 (C), 145.3 (C), 131.8 (CH), 128.3 (CH), 121.2 (C), 116.1 (2xCH), 38.5 (N-CH_3). **IR *v* (cm^{-1})**: 3088, 3036, 2943, 1682, 1647, 1587, 1569, 1508, 1440, 1417, 1381, 1191, 1115, 1030, 1009, 993, 696, 842, 820, 715. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{10}H_{10}N_5]^+$ 200.0930; found 200.0930.

3-Bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (3a)



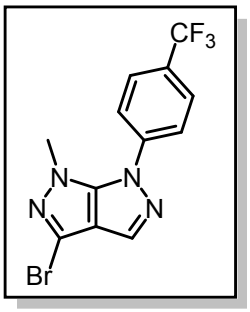
Prepared as described in the general procedure **B** (1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **2a**: 100 mg, 0.5 mmoles; NBS: 1.5 eq, 135 mg, 0.75 mmoles; MeCN: 2 mL; microwave irradiation at 100 °C for 2h). **Yield**: 77% (108 mg). Light orange oil. **Column chromatography eluents**: PE/EtOAc = 95/5. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.60 (s, 1H), 7.55 – 7.50 (m, 4H), 7.41 (t, J = 8.6 Hz, 1H), 3.79 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 148.8 (C), 138.1 (C), 129.6 (2xCH), 129.1 (CH), 128.1 (CH), 123.8 (2xCH), 119.9 (C), 113.1 (C-Br), 37.6 (N-CH_3). **IR *v* (cm^{-1})**: 3066, 2928, 1726, 1594, 1506, 1457, 1431, 1367, 1238, 1148, 1079, 1038, 1008, 983, 905, 840, 759, 715, 696. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{11}H_{10}{}^{79}BrN_4]^+$ 277.0083; found 277.0084, calculated for $[C_{11}H_{10}{}^{81}BrN_4]^+$ 279.0064, found 279.0065.

3-Bromo-6-(4-methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (3b)



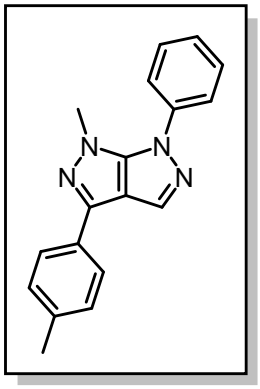
Prepared as described in the general procedure **B** (1-(4-methoxyphenyl)-6-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **2c**: 100 mg, 0.43 mmoles; NBS: 78 mg, 0.43 mmoles, 1.0 eq.; MeCN: 2 mL; conventional heating at reflux for 4h). **Yield**: 55% (74 mg). Colorless oil. **Column chromatography eluents:** PE/EtOAc = 9/1. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.54 (s, 1H), 7.41 (d, J = 8.9 Hz, 2H), 7.00 (d, J = 8.9 Hz, 2H), 3.85 (s, 3H), 3.71 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 159.5 (C), 149.0 (C), 131.0 (C), 128.5 (CH), 125.8 (2xCH), 119.4 (C), 114.7 (2xCH), 112.8 (C-Br), 55.7 (O-CH_3), 37.2 (N-CH_3). **IR *v* (cm^{-1})**: 3107, 2936, 2836, 1600, 1585, 1514, 1462, 1366, 1299, 1246, 1150, 1040, 904, 832, 716. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_{12}{}^{79}BrN_4O]^+$ 307.0189; found 307.0189, calculated for $[C_{12}H_{12}{}^{81}BrN_4O]^+$ 309.0169, found 309.0168.

3-Bromo-1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (3c)



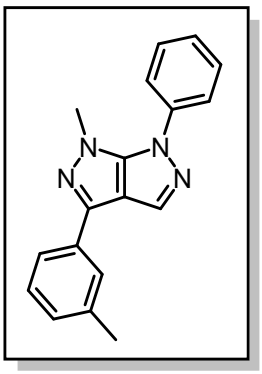
Prepared as described in the general procedure **B** (1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole 2**e**: 100 mg, 0.37 mmoles; NBS: 101 mg, 0.56 mmoles, 1.5 eq.; MeCN: 2 mL; microwave irradiation at 100 °C for 4h). **Yield**: 92% (120 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 7/3. **M.p.**: 132 – 133 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.79 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.62 (s, 1H), 3.85 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 148.5 (C), 140.9 (C), 130.2 (CH), 129.7 (q, $^2J_{C\text{-}F}$ = 33.2 Hz, C), 126.9 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, 2xCH), 123.7 (q, $^1J_{C\text{-}F}$ = 272.2 Hz, CF_3), 123.1 (2xCH), 120.6 (C), 113.4 (C-Br), 38.1 (N-CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*)**: -62.5. **IR *v* (cm^{-1})**: 3108, 2924, 2853, 1613, 1596, 1583, 1523, 1500, 1438, 1416, 1320, 1249, 1151, 1107, 1065, 1034, 1009, 904, 838. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{12}H_9{}^{79}BrF_3N_4]^+$ 344.9957; found 344.9958, calculated for $[C_{12}H_9{}^{81}BrF_3N_4]^+$ 346.9937, found 346.9938.

1-Methyl-6-phenyl-3-(*p*-tolyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4a)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 4-methylphenylboronic acid: 74 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 83% (87 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 126 – 127 °C. **^{1}H NMR (400 MHz, Acetone-*d*$_6$)**: δ 7.98 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 3.88 (s, 3H), 2.37 (s, 3H). **^{13}C NMR (101 MHz, Acetone-*d*$_6$)**: δ 150.1 (C), 139.6 (C), 139.3 (C), 138.5 (C), 131.0 (C), 130.6 (CH), 130.3 (2xCH), 130.2 (2xCH), 128.1 (CH), 126.6 (2xCH), 124.3 (2xCH), 118.0 (C), 37.8 (N-CH_3), 21.3 (CH_3). **IR *v* (cm^{-1})**: 3013, 2919, 1854, 1596, 1510, 1496, 1459, 1416, 1310, 1295, 1278, 1206, 1087, 1040, 1017, 1002, 990, 909, 820, 766, 753, 724, 696. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{18}H_{17}N_4]^+$ 289.1447; found 289.1446.

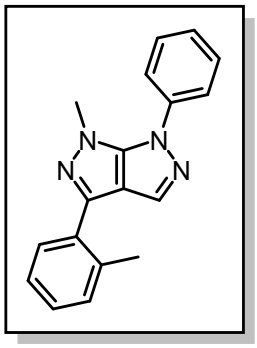
1-Methyl-6-phenyl-3-(*m*-tolyl)-1,6-dihydropyrazolopyrazolo[3,4-*c*]pyrazole (4b)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmol; 3-methylphenyl- boronic acid: 74 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 89% (93 mg). White yellow solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 137 – 138 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.85 (s, 1H), 7.75 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.36 (t, J = 7.7 Hz, 1H), 7.19 (d, J = 7.7 Hz, 1H), 3.88 (s, 3H), 2.44 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.4 (C), 139.9 (C), 138.6 (C), 138.5 (C), 132.5 (C), 130.3 (CH), 129.6 (2xCH), 129.2 (CH), 128.8 (CH), 127.8 (CH), 126.6

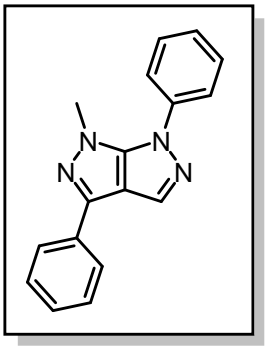
(CH), 123.8 (2xCH), 123.5 (CH), 117.4 (C), 37.5 (N-CH_3), 21.6 (CH_3). **IR *v* (cm^{-1})**: 3059, 2920, 2851, 1596, 1579, 1505, 1456, 1417, 1315, 1196, 1172, 1081, 1039, 1025, 1014, 939, 825, 838, 796, 762. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{18}H_{17}N_4]^+$ 289.1447; found 289.1447.

1-Methyl-6-phenyl-3-(*o*-tolyl)-1,6-dihydropyrazolopyrazolo[3,4-*c*]pyrazole (4c)



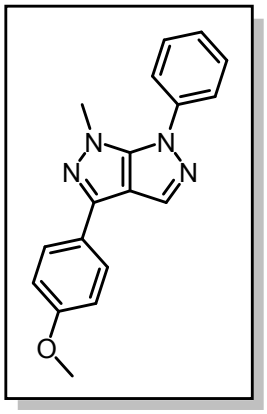
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 2-methylphenylboronic acid: 74 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 86% (90 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 134 – 135 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.71 – 7.66 (m, 2H), 7.59 (d, J = 7.3 Hz, 2H), 7.53 (t, J = 7.3 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 7.32 – 7.28 (m, 3H), 3.88 (s, 3H), 2.61 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.1 (C), 140.6 (C), 138.9 (C), 136.7 (C), 132.2 (C), 131.5 (CH), 131.0 (CH), 129.9 (CH), 129.8 (2xCH), 128.5 (CH), 128.0 (CH), 126.3 (CH), 124.1 (2xCH), 119.5 (C), 37.8 (N-CH_3), 21.7 (CH_3). **IR *v* (cm^{-1})**: 3059, 3039, 2953, 2923, 1597, 1526, 1507, 1457, 1414, 1379, 1302, 1270, 1206, 1074, 1041, 1010, 989, 908, 846, 760. **HRMS (ESI)**: *(m/z)* [M+H]+ calculated for $[C_{18}H_{17}N_4]^+$ 289.1447; found 289.1447.

1-Methyl-3,6-diphenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4d)



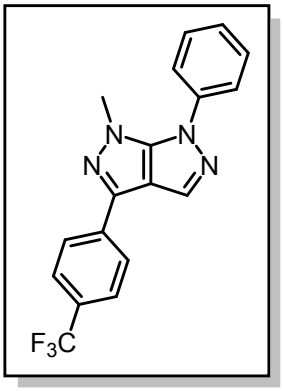
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmol; phenylboronic acid: 66 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 92% (91 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 133 – 135 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.92 (d, J = 8.3 Hz, 2H), 7.85 (s, 1H), 7.58 (d, J = 7.3 Hz, 2H), 7.52 (t, J = 8.3 Hz, 2H), 7.46 (t, J = 7.3 Hz, 2H), 7.43 – 7.33 (m, 2H), 3.86 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.3 (C), 139.6 (C), 138.4 (C), 132.5 (C), 130.1 (CH), 129.5 (2xCH), 128.8 (2xCH), 128.3 (CH), 127.7 (CH), 126.1 (2xCH), 123.7 (2xCH), 117.3 (C), 37.4 (N-CH_3). **IR *v* (cm^{-1})**: 3089, 3056, 2923, 2852, 1595, 1504, 1455, 1418, 1208, 1081, 1016, 988, 907, 758. 694. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{17}H_{15}N_4]^+$ 275.1291; found 275.1289.

3-(4-Methoxyphenyl)-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4e)



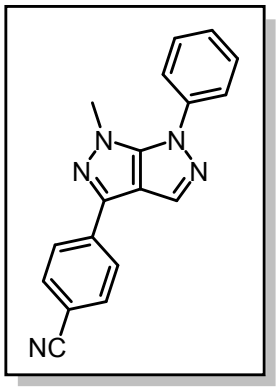
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmol; 4-methoxyphenylboronic acid: 83 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 90% (99 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 108 – 109 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.84 (d, J = 8.8 Hz, 2H), 7.82 (s, 1H), 7.57 (d, J = 8.0, 2H), 7.54 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 8.0, 1H), 6.99 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 159.9 (C), 149.4 (C), 139.6 (C), 138.5 (C), 130.2 (CH), 129.5 (2xCH), 127.7(CH), 127.5 (2xCH), 125.4 (C), 123.7 (2xCH), 117.1 (C), 114.3 (2xCH), 55.4 (O-CH_3), 37.4 (N-CH_3). **IR *v* (cm^{-1})**: 3052, 2999, 2941, 2837, 1596, 1538, 1506, 1458, 1439, 1417, 1245, 1173, 1109, 1087, 1024, 1011, 989, 908, 827, 841, 792. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{18}H_{17}N_4O]^+$ 305.1396; found 305.1396.

1-Methyl-6-phenyl-3-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4f)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 4-trifluoromethylphenylboronic acid: 103 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 86% (107 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 136 – 137 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.01 (d, J = 8.1 Hz, 2H), 7.85 (s, 1H), 7.71 (d, J = 8.1 Hz, 2H), 7.61 – 7.51 (m, 4H), 7.43 (t, J = 8.1 Hz, 1H), 3.89 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.4 (C), 138.3 (C), 138.0 (C), 136.0 (C), 130.3 (q, $^2J_{C\text{-}F}$ = 32.5 Hz, C), 129.8 (CH), 129.6 (2xCH), 128.0 (CH), 126.2 (2xCH), 125.9 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, 2xCH), 124.3 (q, $^1J_{C\text{-}F}$ = 272.0 Hz, CF_3), 123.9 (2xCH), 117.4 (C), 37.6 (N-CH_3).). **^{19}F NMR (235 MHz, Chloroform-*d*)**: δ -62.5; **IR *v* (cm^{-1})**: 3113, 3063, 2950, 1616, 1590, 1590, 1575, 1540, 1495, 1169, 1110, 1082, 1041, 1010, 990, 955, 854, 845. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{18}H_{14}F_3N_4]^+$ 343.1165; found 343.1166.

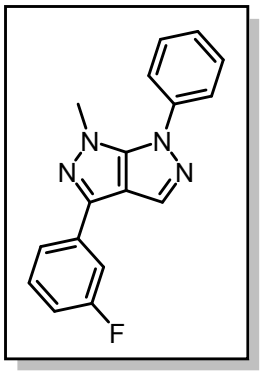
4-(1-Methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazol-3-yl)benzonitrile (4g)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmol; 4-cyanophenylboronic acid: 80 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 72% (78 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 7/3. **M.p.:** 203 – 204 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.00 (d, J = 8.4 Hz, 2H), 7.85 (s, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.61 – 7.52 (m, 4H), 7.44 (t, J = 8.0 Hz, 1H), 3.90 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.5 (C), 138.2 (C),

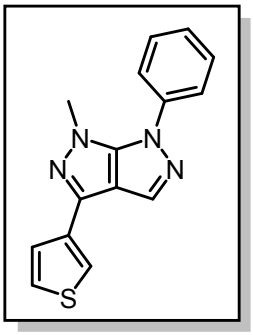
137.4 (C), 137.0 (C), 132.8 (2xCH), 129.7 (2xCH), 129.7 (CH), 128.1 (CH), 126.5 (2xCH), 124.0 (2xCH), 119.0 (CN), 117.4 (C), 111.5 (C), 37.7 (N-CH_3). **IR *v* (cm^{-1})**: 3056, 2943, 2226, 1592, 1581, 1502, 1435, 1417, 1296, 1281, 1206, 1081, 1041, 1019, 990, 908, 844. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{18}H_{14}N_5]^+$ 300.1243; found 300.1244.

3-(3-Fluorophenyl)-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4h)



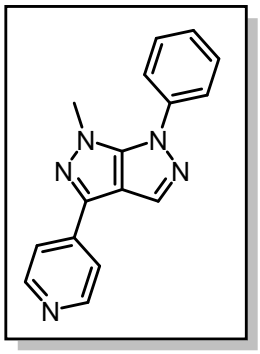
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 3-fluorophenylboronic acid: 76 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield:** 90% (95 mg). Beige solid. **Column chromatography eluents:** PE/EtOAc = 8/2. **M.p.:** 97 – 98 °C. **^{1}H NMR (400 MHz, Chloroform-*d*):** δ 7.83 (s, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 9.8 Hz, 1H), 7.59 – 7.50 (m, 4H), 7.45 – 7.39 (m, 2H), 7.04 (dd, J = 8.5, 8.2 Hz, 1H), 3.87 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 163.3 (d, $^1J_{C\text{-}F}$ = 245.5 Hz, C), 149.4 (C), 138.4 (C), 138.3 (C), 134.8 (d, $^3J_{C\text{-}F}$ = 8.3 Hz, C), 130.4 (d, $^3J_{C\text{-}F}$ = 8.4 Hz, CH), 129.9 (CH), 129.6 (2xCH), 127.9 (CH), 123.8 (2xCH), 121.9 (d, $^4J_{C\text{-}F}$ = 2.8 Hz, CH), 117.3 (C), 115.1 (d, $^2J_{C\text{-}F}$ = 21.3 Hz, CH), 112.8 (d, $^2J_{C\text{-}F}$ = 22.8 Hz, CH), 37.5 (N-CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*):** δ -112.9. **IR *v* (cm^{-1}):** 3054, 2931, 2850, 1595, 1580, 1507, 1481, 1449, 1411, 1297, 1183, 1082, 1018, 990, 881, 831. **HRMS (ESI):** (*m/z*) $[M+H]^+$ calculated for $[C_{17}H_{14}FN_4]^+$ 293.1197; found 293.1197.

1-Methyl-6-phenyl-3-(thiophen-3-yl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4i)



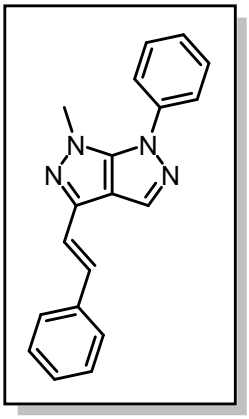
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 3-thienylboronic acid: 70 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 85% (86 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 100 – 101 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.78 (s, 1H), 7.68 (s, 1H), 7.61 – 7.50 (m, 5H), 7.43 – 7.38 (m, 2H), 3.84 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.1 (C), 138.5 (C), 136.0 (C), 134.2 (C), 129.8 (CH), 129.5 (2xCH), 127.7 (CH), 126.4 (CH), 125.9 (CH), 123.7 (2xCH), 122.0 (CH), 117.4 (C), 37.3 (N-CH_3). **IR *v* (cm^{-1})**: 3095, 3061, 2947, 1596, 1510, 1460, 1413, 1282, 1211, 1188, 1038, 1013, 1001, 951, 870, 793, 779. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{15}H_{13}N_4S]^+$ 281.0855; found 281.0858.

1-Methyl-6-phenyl-3-(pyridin-4-yl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4j)



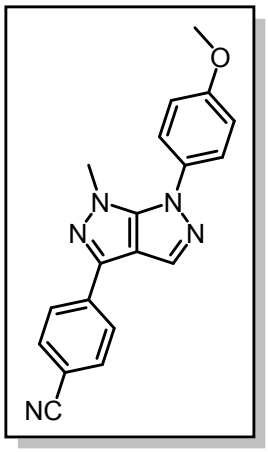
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; 4-pyridinylboronic acid: 67 mg, 0.54 mmoles 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 78% (78 mg). Beige solid. **Column chromatography eluents**: PE/EtOAc = 1/9. **M.p.**: 158 – 159 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.68 (br s, 2H), 7.84 (s, 1H), 7.75 (br s, 2H), 7.58 – 7.47 (m, 4H), 7.41 (t, J = 6.8 Hz, 1H), 3.86 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 150.3 (2xCH), 149.3 (C), 139.8 (C), 138.1 (C), 136.7 (C), 129.6 (2xCH), 129.5 (CH), 128.0 (CH), 123.8 (2xCH), 120.3 (2xCH), 117.5 (C), 37.7 (N-CH_3). **IR *v* (cm^{-1})**: 3034, 2925, 1609, 1594, 1556, 1506, 1432, 1407, 1388, 1323, 1291, 1204, 1094, 1019, 1002, 992, 917, 826. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{16}H_{14}N_5]^+$ 276.1243; found 276.1244.

(*E*)-1-Methyl-6-phenyl-3-styryl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4k)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-phenyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3a**: 100 mg, 0.36 mmoles; *trans*-2-phenylvinylboronic acid: 81 mg, 0.54 mmoles, 1.5 eq.; Cs_2CO_3: 153 mg, 0.47 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5.5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 64% (70 mg). Light brown solid. **Column chromatography eluents**: PE/EtOAc = 8/2. **M.p.**: 140 – 141 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.84 (s, 1H), 7.60 – 7.47 (m, 6H), 7.37 (q, J = 7.8 Hz, 3H), 7.27 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 18.5 Hz, 1H), 7.14 (d, J = 18.5 Hz, 1H), 3.79 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.0 (C), 139.9 (C), 138.3 (C), 136.7 (C), 132.8 (CH), 130.0 (CH), 129.5 (2xCH), 128.8 (2xCH), 128.1 (CH), 127.7 (CH), 126.6 (2xCH), 123.7 (2xCH), 120.2 (CH), 116.6 (C), 37.3 (N-CH_3). **IR *v* (cm^{-1})**: 3100, 3061, 3030, 2946, 1591, 1580, 1505, 1494, 1429, 1304, 1261, 1201, 1046, 1013, 1001, 989, 961, 906, 874, 852, 744. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{17}N_4]^+$ 301.1447; found 301.1449.

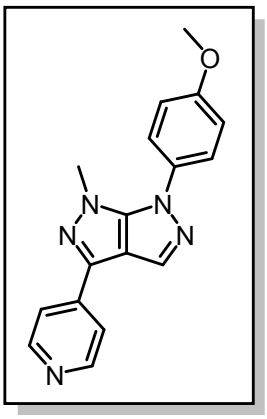
4-(6-(4-Methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazol-3-yl)benzonitrile (4l)



Prepared as described in the general procedure **C** (3-bromo-6-(4-methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3b**: 100 mg, 0.32 mmoles; 4-cyanophenylboronic acid: 72 mg, 0.48 mmoles, 1.5 eq.; Cs_2CO_3: 138 mg, 0.42 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 75% (81 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 7/3. **M.p.**: 186 – 187 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.99 (d, J = 8.3 Hz, 2H), 7.81 (s, 1H), 7.73 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.9 Hz, 2H), 7.04 (d, J = 8.9 Hz, 2H), 3.88 (s, 3H), 3.83 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 159.6 (C), 149.7 (C), 137.3 (C), 137.1 (C), 132.7 (2xCH), 131.1 (C), 129.1 (CH), 126.4 (2xCH), 126.0 (2xCH), 119.0 (CN), 116.9 (C), 114.7 (2xCH), 111.3 (C), 55.7 (O-CH_3), 37.3 (N-CH_3). **IR *v* (cm^{-}**

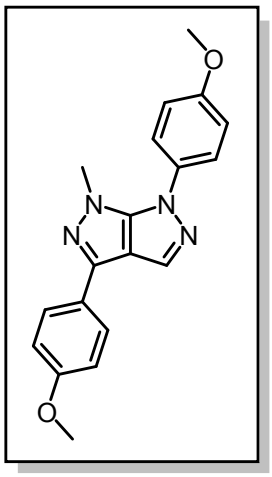
[1]): 3105, 3082, 3012, 2942, 2842, 2221, 1610, 1593, 1580, 1517, 1439, 1299, 1253, 1203, 1110, 1086, 1045, 1017, 989, 910, 841, 826. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{16}N_5O]^+$ 330.1349; found 330.1353.

6-(4-Methoxyphenyl)-1-methyl-3-(pyridin-4-yl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4m)



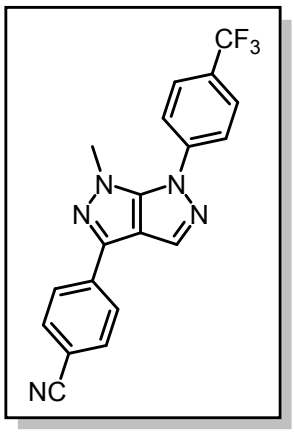
Prepared as described in the general procedure **C** (3-bromo-6-(4-methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3b**: 100 mg, 0.32 mmol; 4-pyridinylboronic acid: 61 mg, 0.48 mmoles, 1.5 eq.; Cs_2CO_3: 138 mg, 0.42 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 76% (76 mg). Colorless solid. **Column chromatography eluents**: DCM/EtOAc = 5/5. **M.p.**: 198 – 199 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.68 (d, J = 6.2 Hz, 2H), 7.83 (s, 1H), 7.76 (d, J = 6.2 Hz, 2H), 7.47 (d, J = 8.9 Hz, 2H), 7.04 (d, J = 8.9 Hz, 2H), 3.88 (s, 3H), 3.83 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 159.6 (C), 150.5 (2xCH), 149.7 (C), 140.0 (C), 136.7 (C), 131.1 (C), 129.1 (CH), 126.0 (2xCH), 120.3 (2xCH), 117.0 (C), 114.7 (2xCH), 55.7 (O-CH_3), 37.3 (N-CH_3). **IR *v* (cm^{-1})**: 3067, 2951, 2847, 1593, 1556, 1518, 1455, 1438, 1409, 1298, 1255, 1208, 1166, 1108, 1094, 1017, 991, 917, 821. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{17}H_{16}N_5O]^+$ 306.1349; found 306.1349.

3,6-Bis(4-methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4n)



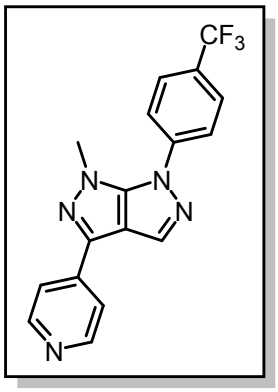
Prepared as described in the general procedure **C** (3-bromo-6-(4-methoxyphenyl)-1-methyl-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3b**: 100 mg, 0.32 mmoles; 4-methoxyphenylboronic acid: 75 mg, 0.48 mmoles, 1.5 eq.; Cs_2CO_3: 138 mg, 0.42 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 5 mg, 0.004 mmoles, 1.25 mol%). **Yield**: 80% (88 mg). Colorless solid. **Column chromatography eluent**: DCM. **M.p.**: 212 – 213 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.84 (d, J = 8.7 Hz, 2H), 7.78 (s, 1H), 7.47 (d, J = 8.9 Hz, 2H), 7.02 (d, J = 8.9 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.78 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 160.1 (C), 159.6 (C), 150.0 (C), 139.8 (C), 131.8 (C), 129.9 (CH), 127.7 (2xCH), 126.1 (2xCH), 125.8 (C), 116.9 (C), 114.9 (2xCH), 114.6 (2xCH), 56.0 (O-CH_3), 55.7 (O-CH_3), 37.2 (N-CH_3). **IR *v* (cm^{-1})**: 3105, 3002, 2974, 2941, 1840, 1596, 1537, 1513, 1500, 1452, 1438, 1302, 1244, 1168, 1106, 1043, 1024, 1013, 907, 839, 824. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{19}N_4O_2]^+$ 335.1502; found 335.1505.

4-(1-Methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazol-3-yl)benzonitrile (4o)



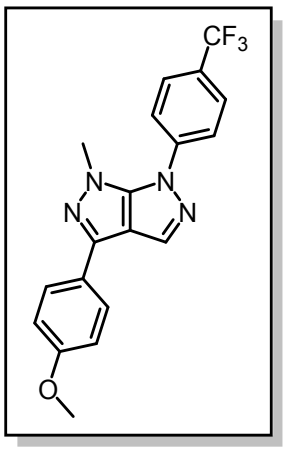
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3c**: 100 mg, 0.28 mmoles; 4-cyanophenylboronic acid: 64 mg, 0.43 mmoles, 1.5 eq.; Cs_2CO_3: 123 mg, 0.37 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 4.5 mg, 0.003 mmoles, 1.25 mol%). **Yield**: 68% (73 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 226 – 227 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.98 (d, J = 8.4 Hz, 2H), 7.88 (s, 1H), 7.82 (d, J = 8.6 Hz, 2H), 7.76 – 7.69 (m, 4H), 3.96 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.2 (C), 141.0 (C), 137.7 (C), 136.6 (C), 132.7 (2xCH), 130.7 (CH), 129.7 (q, $^2J_{C\text{-}F}$ = 33.1 Hz, C), 126.9 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, 2xCH), 126.5 (2xCH), 123.8 (d, $^1J_{C\text{-}F}$ = 272.2 Hz, CF_3), 123.3 (2xCH), 118.9 (CN), 118.0 (C), 111.7 (C), 38.2 (N-CH_3). **IR *v* (cm^{-1})**: 3343, 2923, 1852, 2225, 1616, 1579, 1522, 1541, 1421, 1384, 1315, 1168, 1103, 1038, 1013, 989, 955, 909, 839. **^{19}F NMR (235 MHz, Chloroform-*d*)** : δ -62.5; **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{13}F_3N_5]^+$ 368.1117; found 368.1116.

1-Methyl-3-(pyridin-4-yl)-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4p)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-(4-(trifluoromethyl)phenyl)pyrazolo[3,4-*c*]pyrazole **3e**: 100 mg, 0.28 mmoles; 4-pyridinylboronic acid: 54 mg, 0.43 mmoles, 1.5 eq.; Cs_2CO_3: 123 mg, 0.37 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 4.5 mg, 0.003 mmoles, 1.25 mol%). **Yield**: 79% (79 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 5/5. **M.p.**: 196 – 197 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 8.69 (d, J = 5.4 Hz, 2H), 7.90 (s, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 5.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 3.96 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 150.5 (2xCH), 149.2 (C), 141.0 (C), 139.5 (C), 137.2 (C), 130.7 (CH), 129.7 (q, $^2J_{C\text{-}F}$ = 33.1 Hz, C), 127.0 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, 2xCH), 123.8 (q, $^1J_{C\text{-}F}$ = 272.2 Hz, CF_3), 123.3 (2xCH), 120.3 (2xCH), 118.2 (C), 38.2 (N-CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*)**: δ -62.5; **IR *v* (cm^{-1})**: 3067, 2952, 1614, 1581, 1556, 1526, 1420, 1324, 1219, 1184, 1113, 1094, 1016, 992, 917, 846, 739. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{17}H_{13}F_3N_5]^+$ 344.1117; found 344.1118.

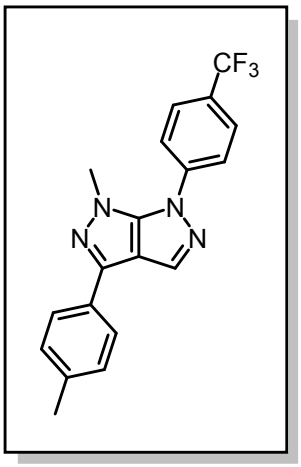
3-(4-Methoxyphenyl)-1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4q)



Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3c**: 100 mg, 0.28 mmoles; 4-methoxyphenylboronic acid: 67 mg, 0.43 mmoles, 1.5 eq.; Cs_2CO_3: 123 mg, 0.37 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 4.5 mg, 0.003 mmoles, 1.25 mol%). **Yield**: 94% (102 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 205 – 206 °C. **^{1}H NMR (400 MHz,**

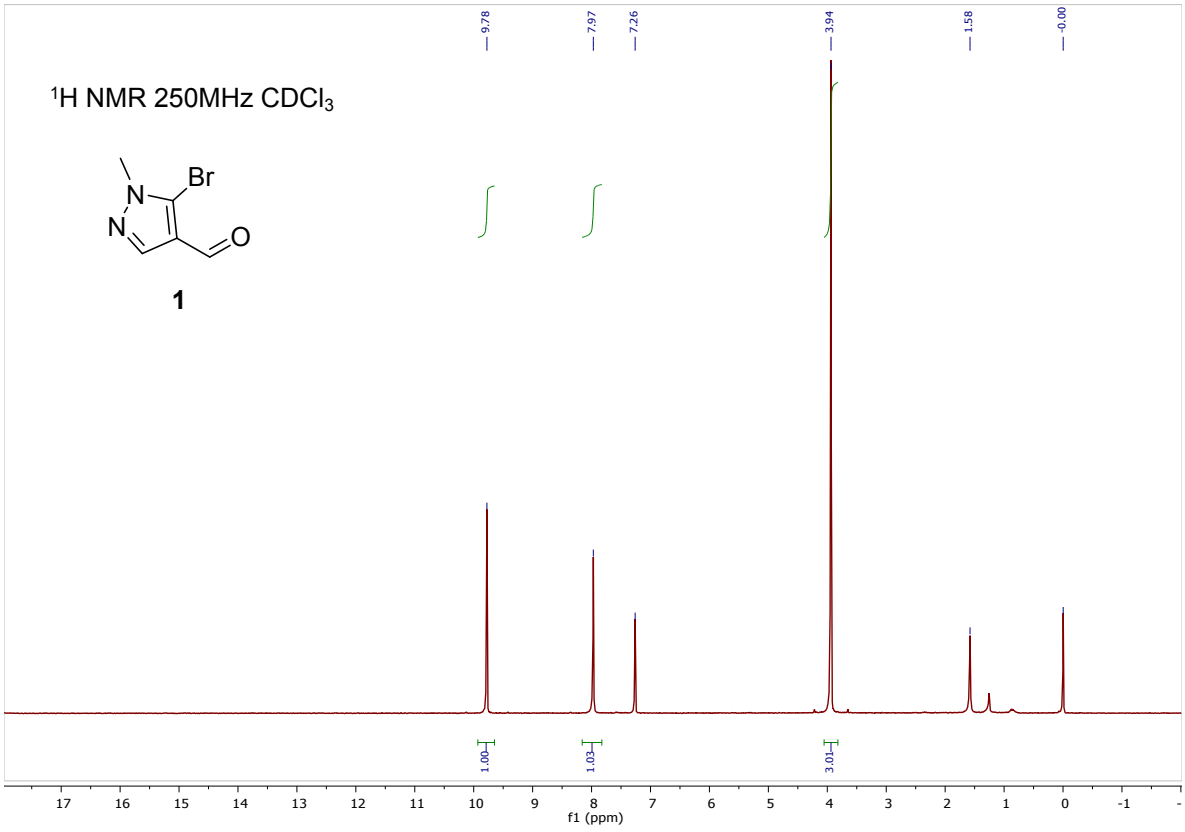
Chloroform-*d*): δ 7.88 – 7.77 (m, 5H), 7.71 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 3.91 (s, 3H), 3.86 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 160.0 (C), 149.2 (C), 141.4 (C), 140.0 (C), 131.4 (CH), 129.3 (q, $^{2}J_{C\text{-}F}$ = 33.1 Hz, C), 127.5 (2xCH), 126.8 (q, $^{3}J_{C\text{-}F}$ = 3.7 Hz, 2xCH), 125.0 (C), 123.0 (2xCH), 121.2 (d, $^{1}J_{C\text{-}F}$ = 272.1 Hz, CF_3), 117.8 (C), 114.4 (2xCH), 55.4 (O-CH_3), 37.8 (N-CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*)**: δ -62.4; **IR *v* (cm^{-1})**: 3338, 3057, 2937, 2845, 1596, 1614, 1540, 1425, 1323, 1251, 1107, 1088, 1031, 1007, 858, 832, 721, 715. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{16}F_3N_4O]^+$ 373.1270; found 373.1268.

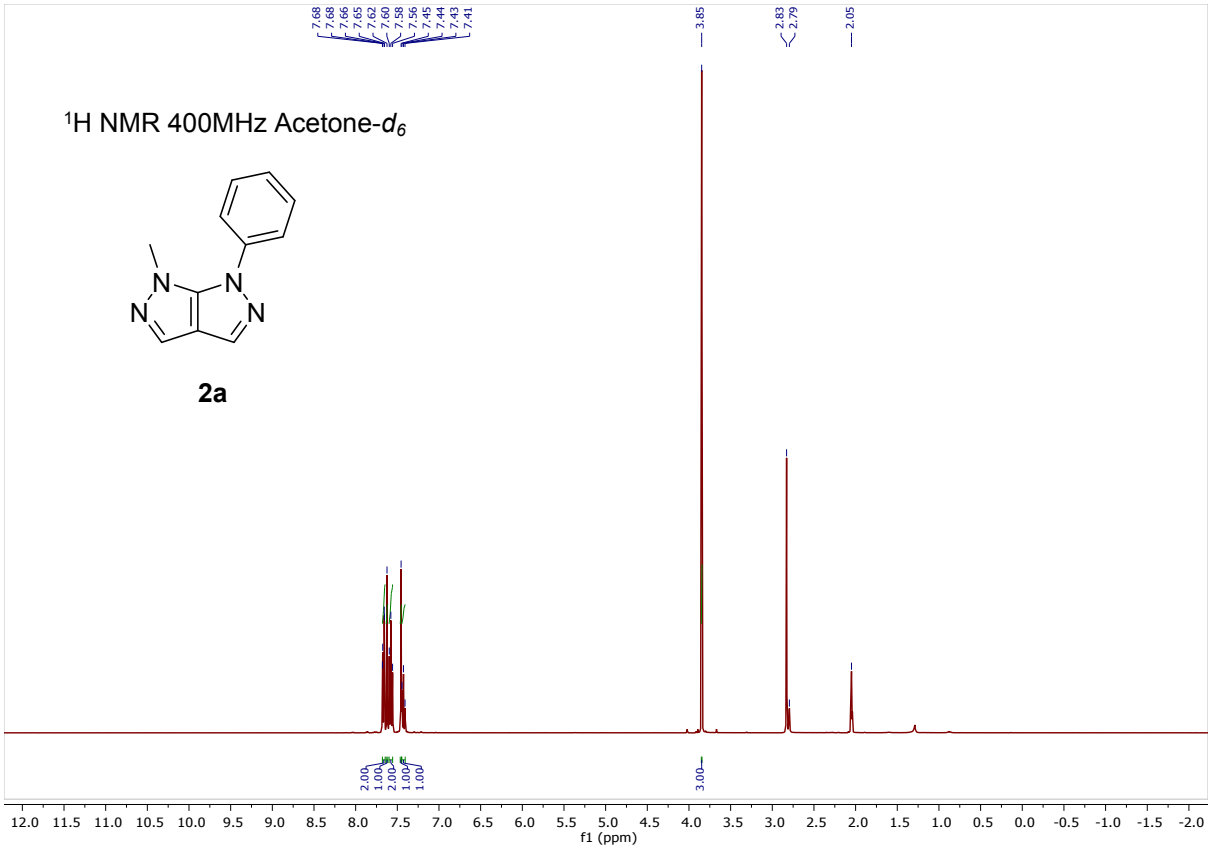
1-Methyl-3-(*p*-tolyl)-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole (4r)

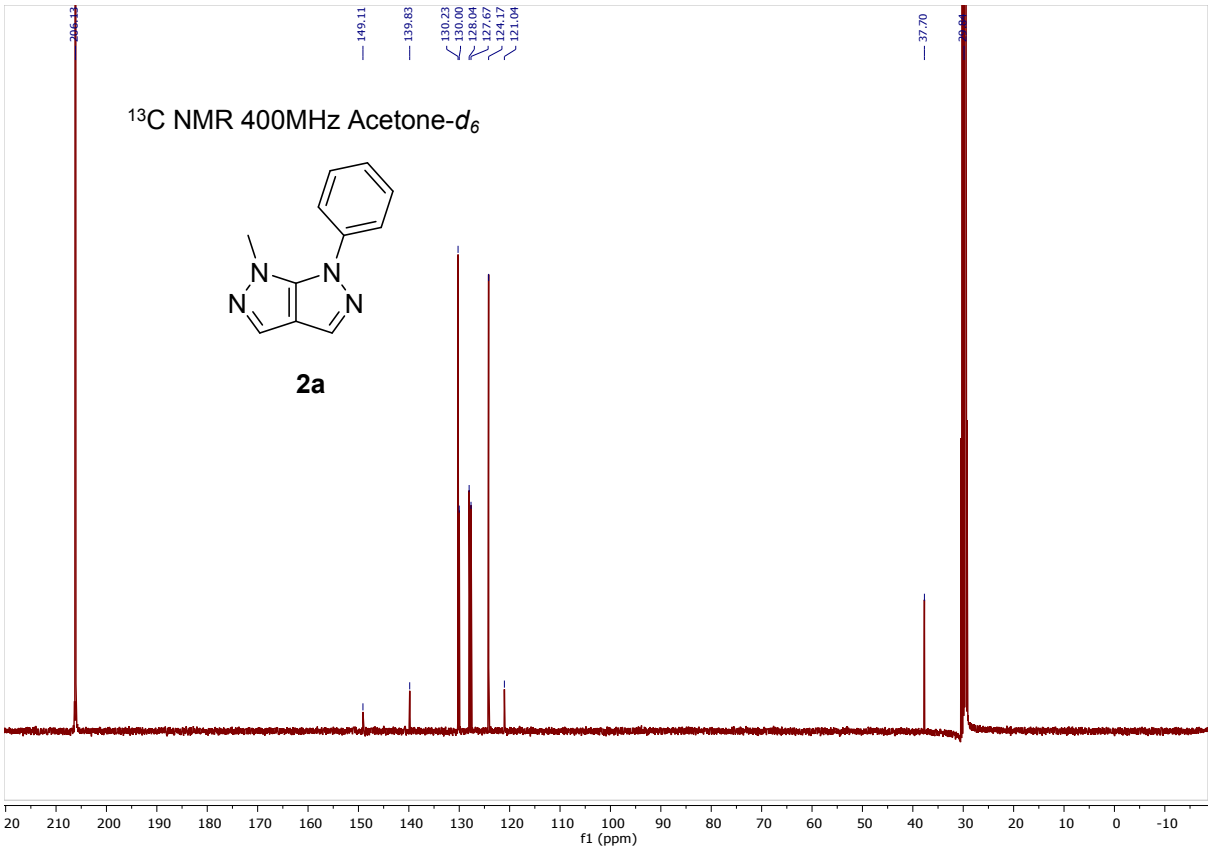


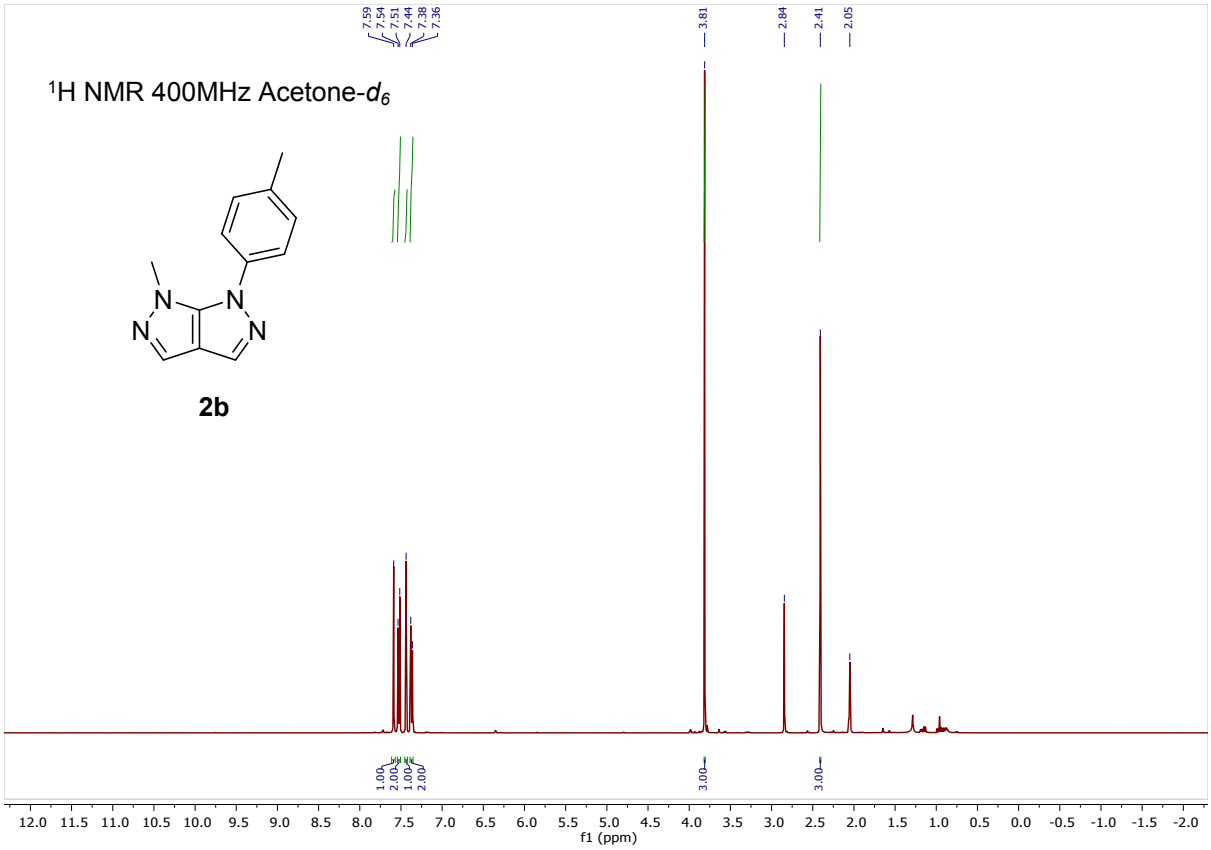
Prepared as described in the general procedure **C** (3-bromo-1-methyl-6-(4-(trifluoromethyl)phenyl)-1,6-dihydropyrazolo[3,4-*c*]pyrazole **3c**: 100 mg, 0.28 mmoles; 4-methylphenylboronic acid: 60 mg, 0.43 mmoles, 1.5 eq.; Cs_2CO_3: 123 mg, 0.37 mmoles, 1.3 eq.; $Pd(PPh_3)_4$: 4.5 mg, 0.003 mmoles, 1.25 mol%). **Yield**: 86% (89 mg). Colorless solid. **Column chromatography eluents**: PE/EtOAc = 9/1. **M.p.**: 204 – 205 °C. **^{1}H NMR (400 MHz, Chloroform-*d*)**: δ 7.87 (s, 1H), 7.79 (d, J = 7.8 Hz, 4H), 7.70 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 3.92 (s, 3H), 2.40 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)**: δ 149.2 (C), 141.4 (C), 140.2 (C), 138.6 (C), 131.4 (CH), 129.6 (2xCH), 129.5 (C), 129.3 (q, $^{2}J_{C\text{-}F}$ = 33.0 Hz, C), 126.9 (q, $^{3}J_{C\text{-}F}$ = 3.7 Hz, 2xCH), 126.1 (2xCH), 123.9 (q, $^{1}J_{C\text{-}F}$ = 272.1 Hz, CF_3), 123.1 (2xCH), 118.0 (C), 37.9 (N-CH_3), 21.5 (CH_3). **^{19}F NMR (235 MHz, Chloroform-*d*)**: δ -62.4; **IR *v* (cm^{-1})**: 2926, 1614, 1594, 1582, 1522, 1504, 1424, 1317, 1162, 1110, 1085, 1066, 1039, 1014, 990, 965, 952, 909, 842, 825, 737. **HRMS (ESI)**: (*m/z*) $[M+H]^+$ calculated for $[C_{19}H_{16}F_3N_4]^+$ 357.1249; found 357.1247.

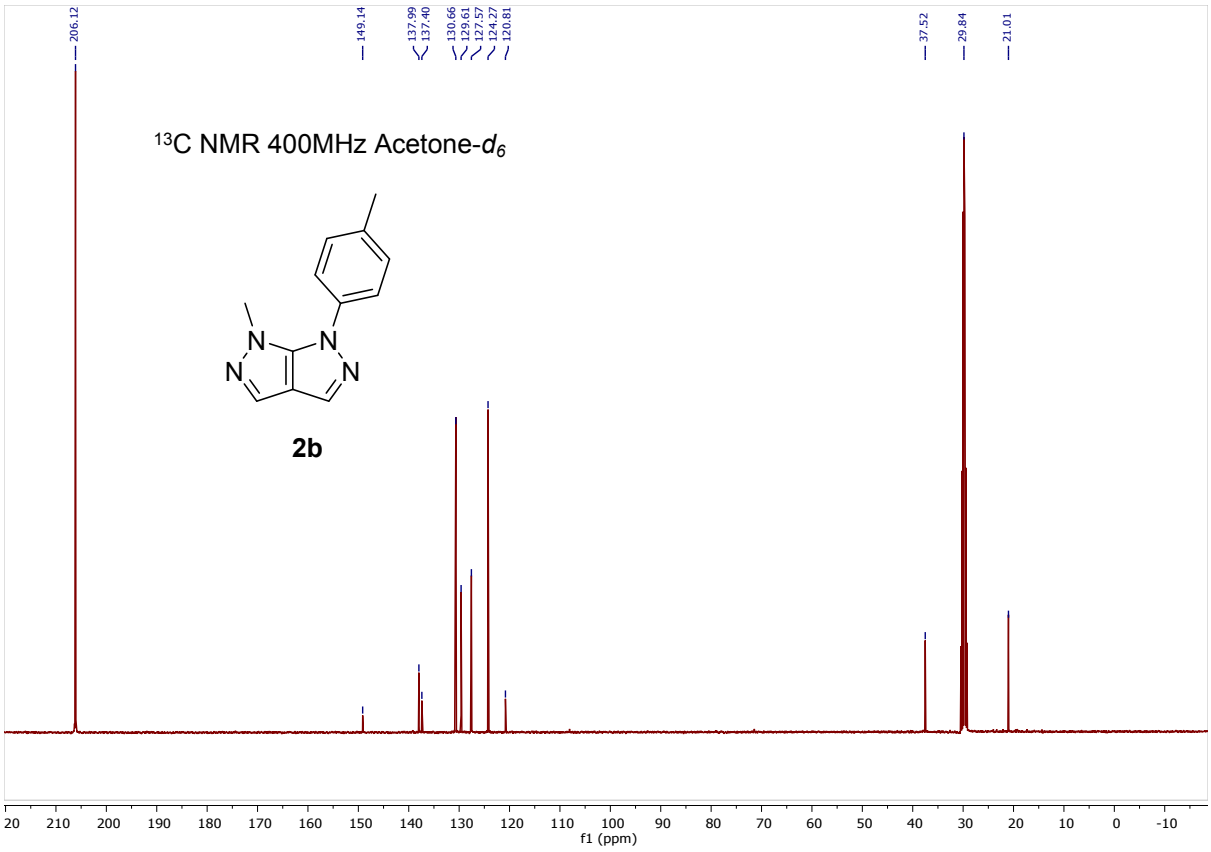
^{1}H and ^{13}C NMR Spectra

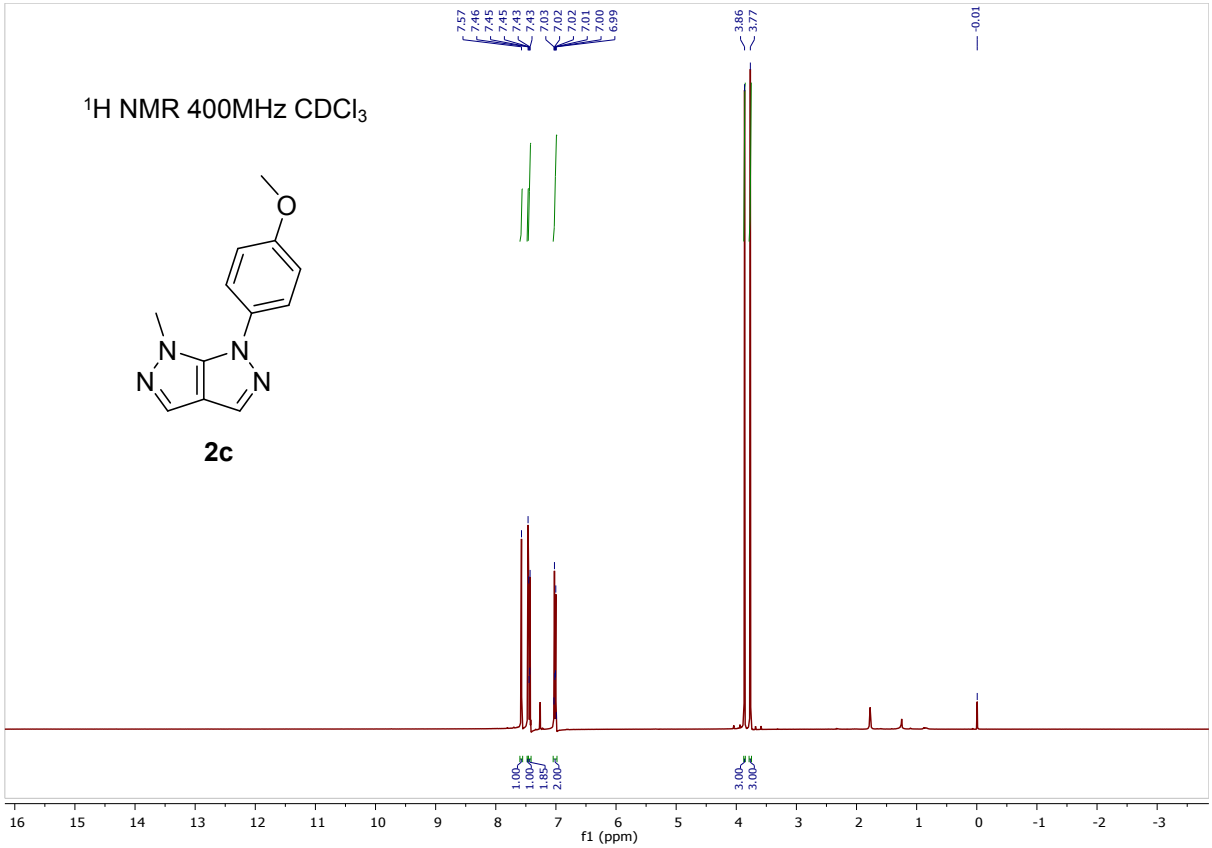


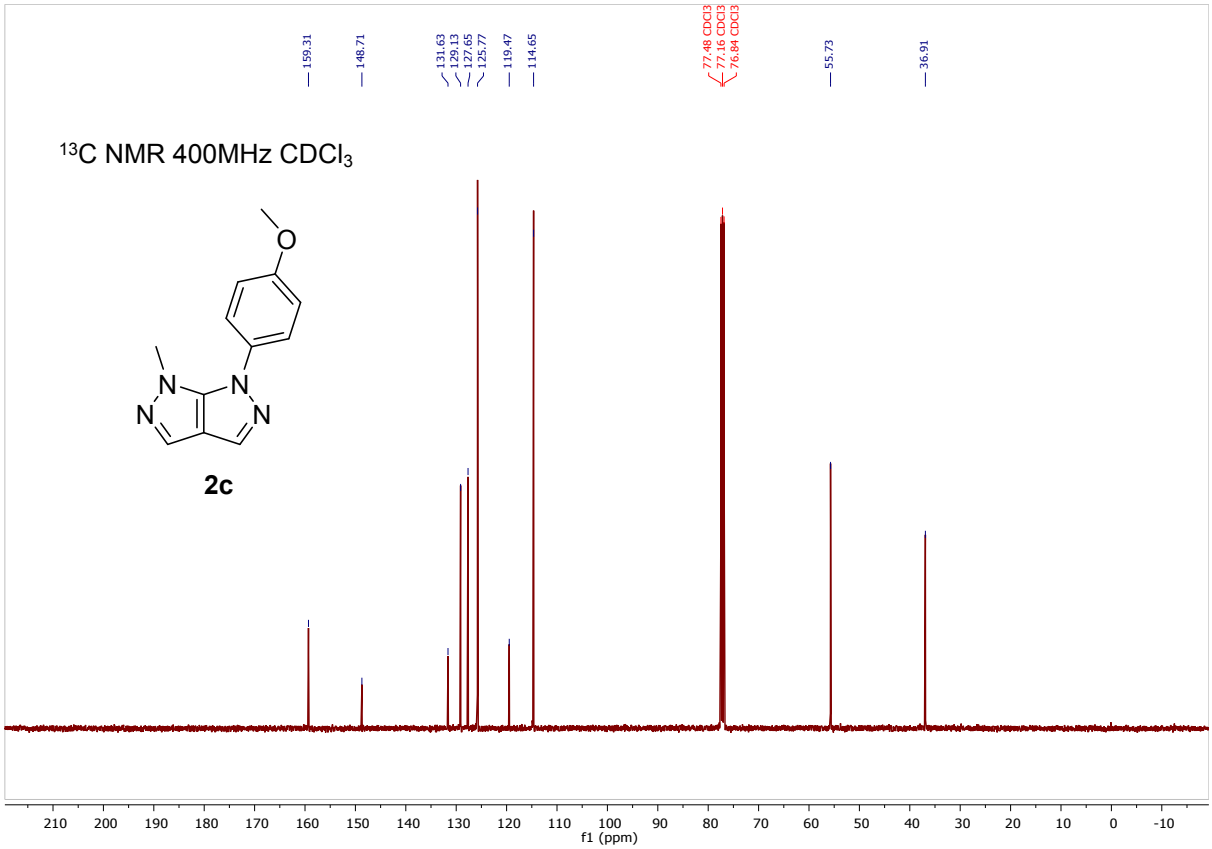

7.68
7.68
7.66
7.65
7.62
7.60
7.58
7.56
7.45
7.44
7.43
7.41
3.85
2.83
2.79
2.05
^{1}H NMR 400MHz Acetone-d_6
N
N
N
N
2a
2.00
1.00
2.00
1.00
1.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

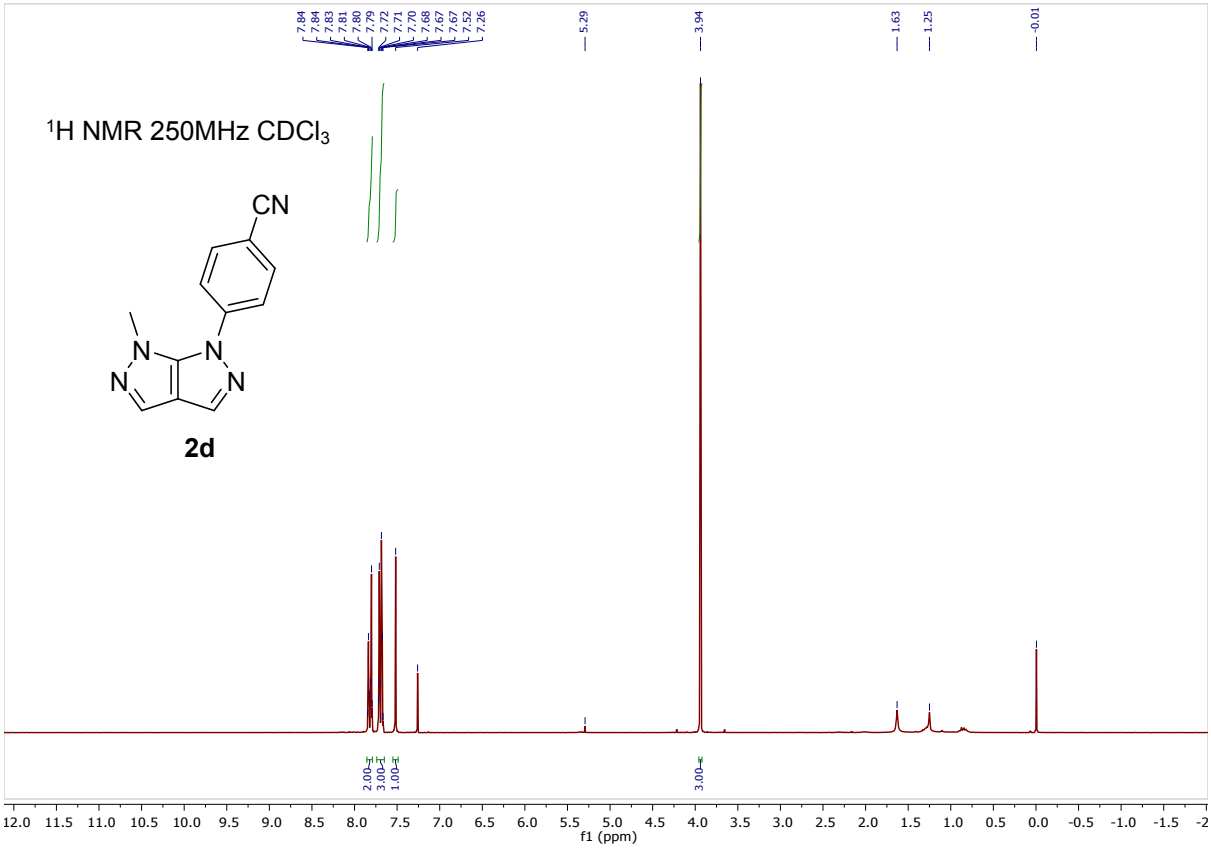

206.13
149.11
139.83
130.23
130.00
128.04
127.67
124.17
121.04
37.70
^{13}C NMR 400MHz Acetone-d_6
N
N
N
N
2a
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

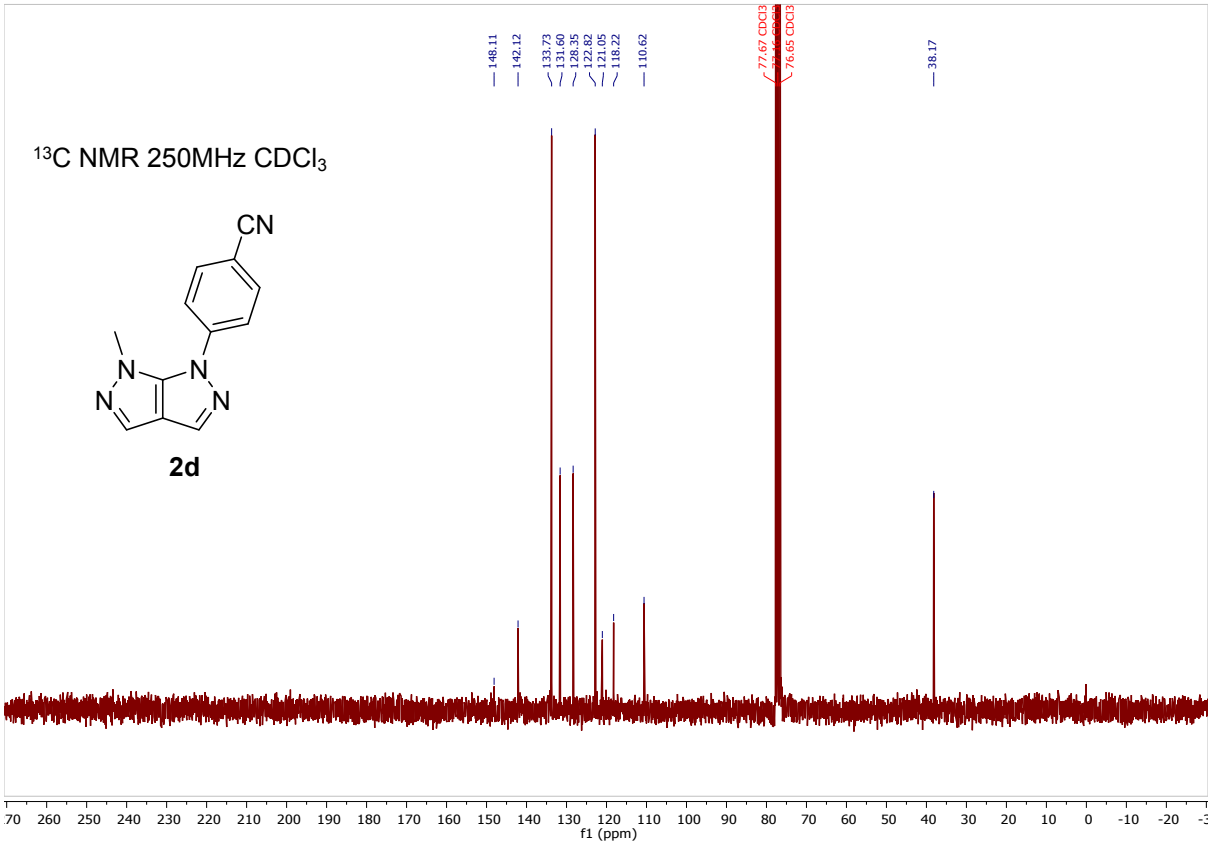

7.59
7.54
7.51
7.44
7.38
7.36
3.81
2.84
2.41
2.05
1H NMR 400MHz Acetone-d6
2b
1.00
2.00
1.00
2.00
3.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

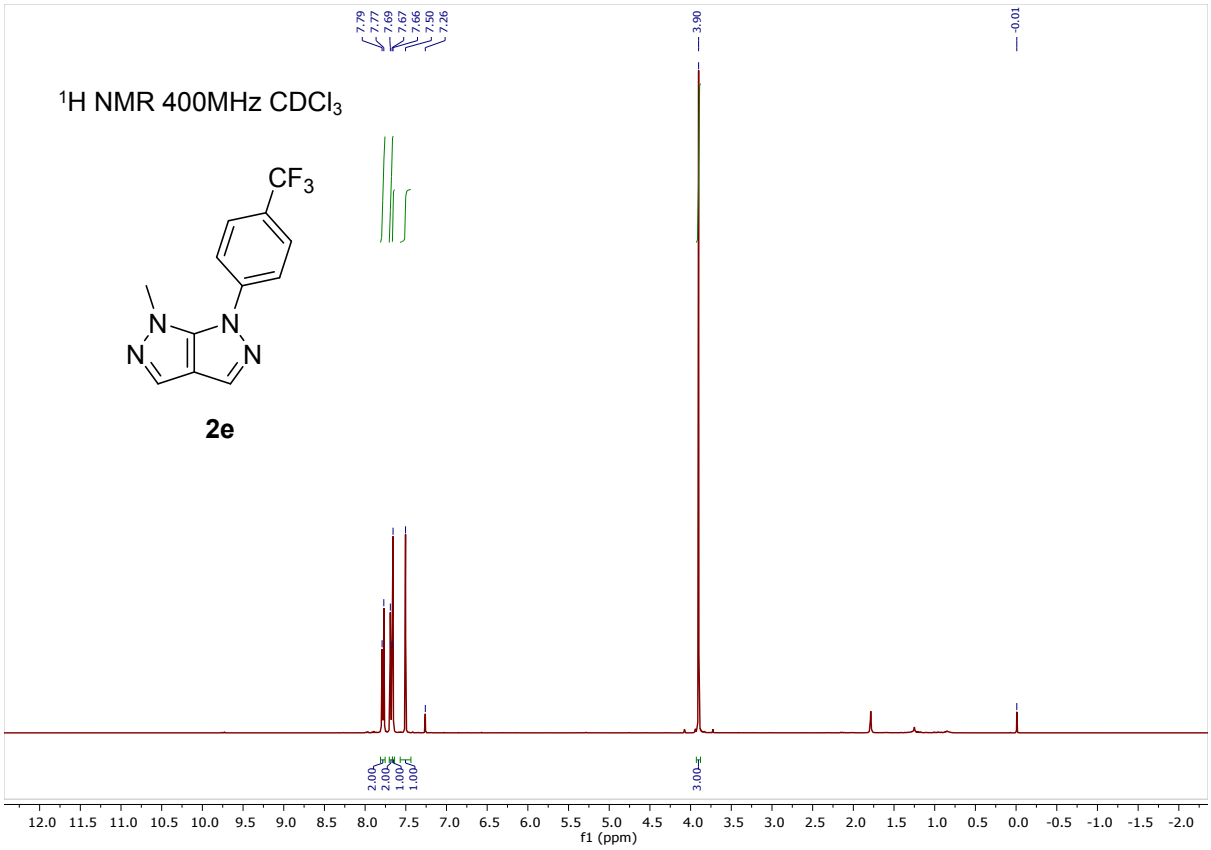

206.12
149.14
137.99
137.40
130.66
129.61
127.57
124.27
120.81
37.52
29.84
21.01
13C NMR 400MHz Acetone-d6
2b
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

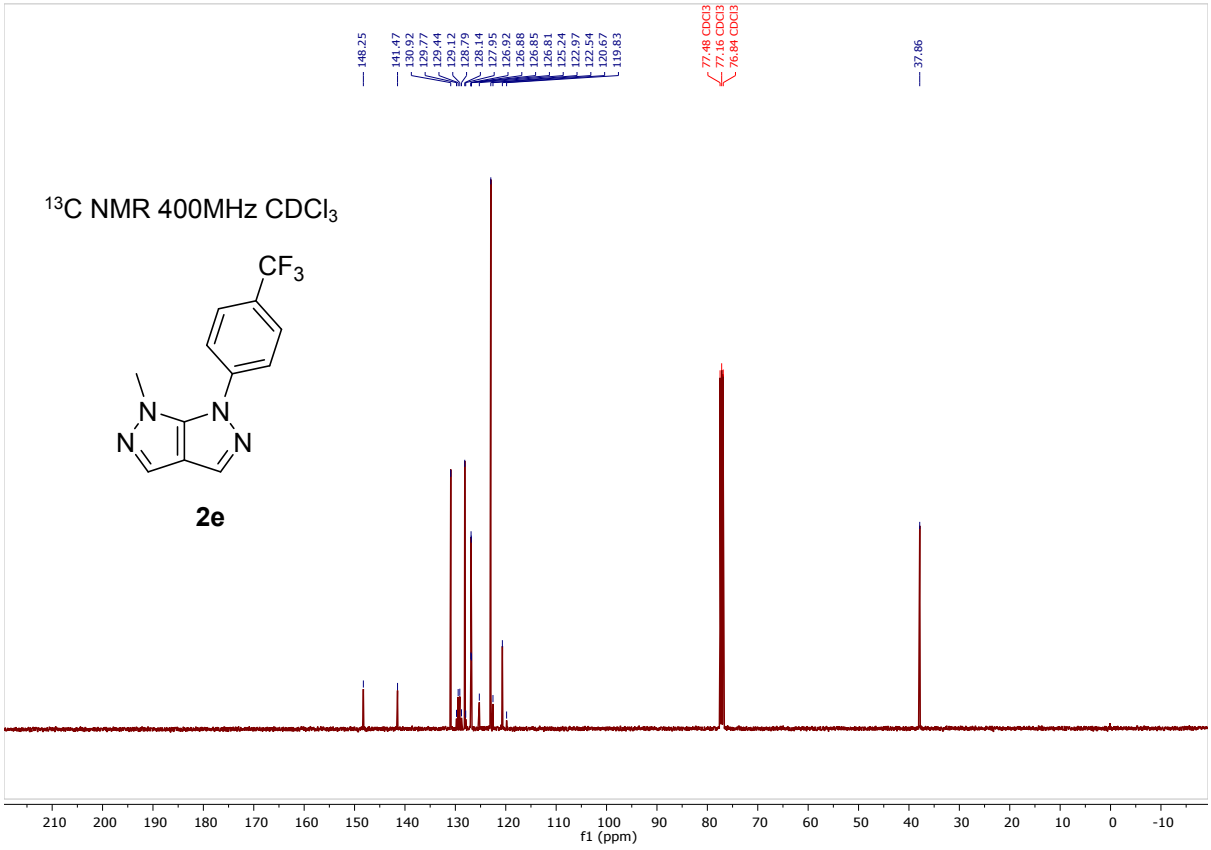

7.57
7.46
7.45
7.45
7.43
7.43
7.03
7.02
7.02
7.01
7.00
6.99
3.86
3.77
-0.01
1H NMR 400MHz CDCl3
O
N
N
N
N
2c
1.00
1.00
1.85
2.00
3.00
3.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)


159.31
148.71
131.63
129.13
127.65
125.77
119.47
114.65
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.73
36.91
13C NMR 400MHz CDCl3
O
N
N
N
N
2c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.84
7.84
7.83
7.81
7.80
7.79
7.72
7.71
7.70
7.68
7.67
7.67
7.52
7.26
5.29
3.94
1.63
1.25
-0.01
^{1}H NMR 250MHz $CDCl_3$
CN
N
N
N
N
2d
2.00
3.00
1.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2
f1 (ppm)


148.11
142.12
133.73
131.60
128.35
122.82
121.65
118.22
110.62
77.67 CDCl3
76.65 CDCl3
38.17
^{13}C NMR 250MHz $CDCl_3$
CN
N
N
N
N
2d
70 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


7.79
7.77
7.69
7.67
7.66
7.50
7.26
3.90
-0.01
^{1}H NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
2e
2.00
2.00
1.00
1.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


148.25
141.47
130.92
129.77
129.44
129.12
128.79
128.14
127.95
126.92
126.88
126.85
126.81
125.24
122.97
122.54
120.67
119.83
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.86
^{13}C NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
2e
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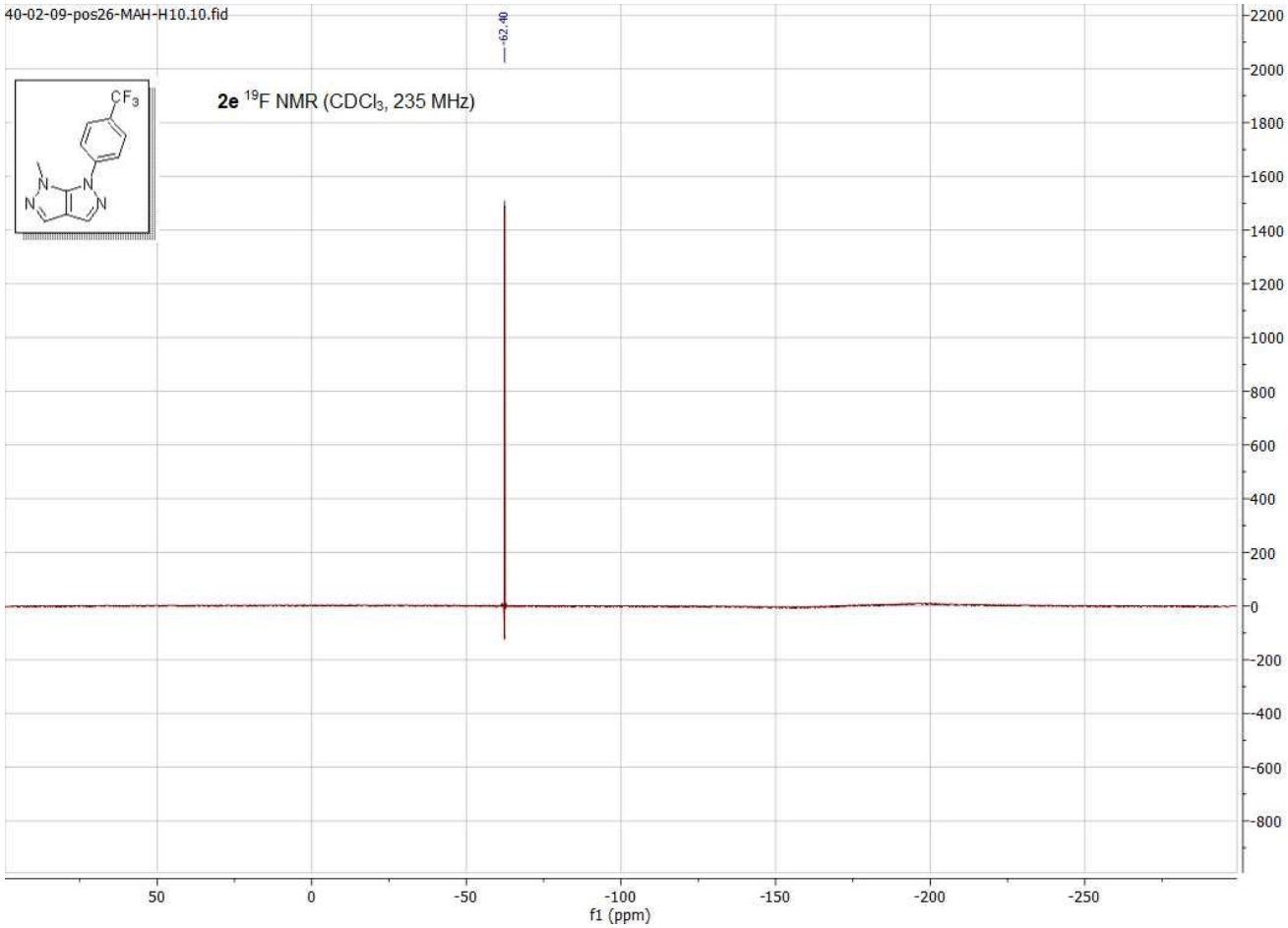
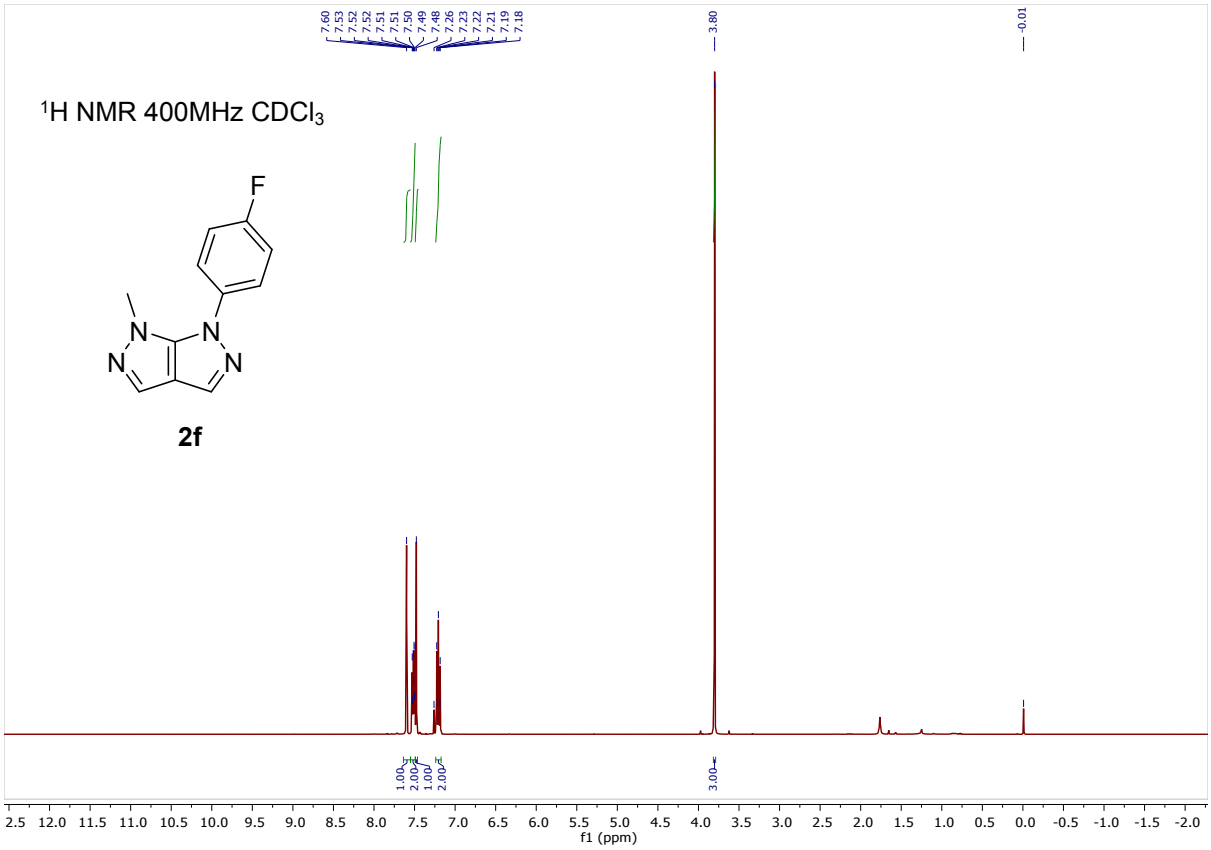
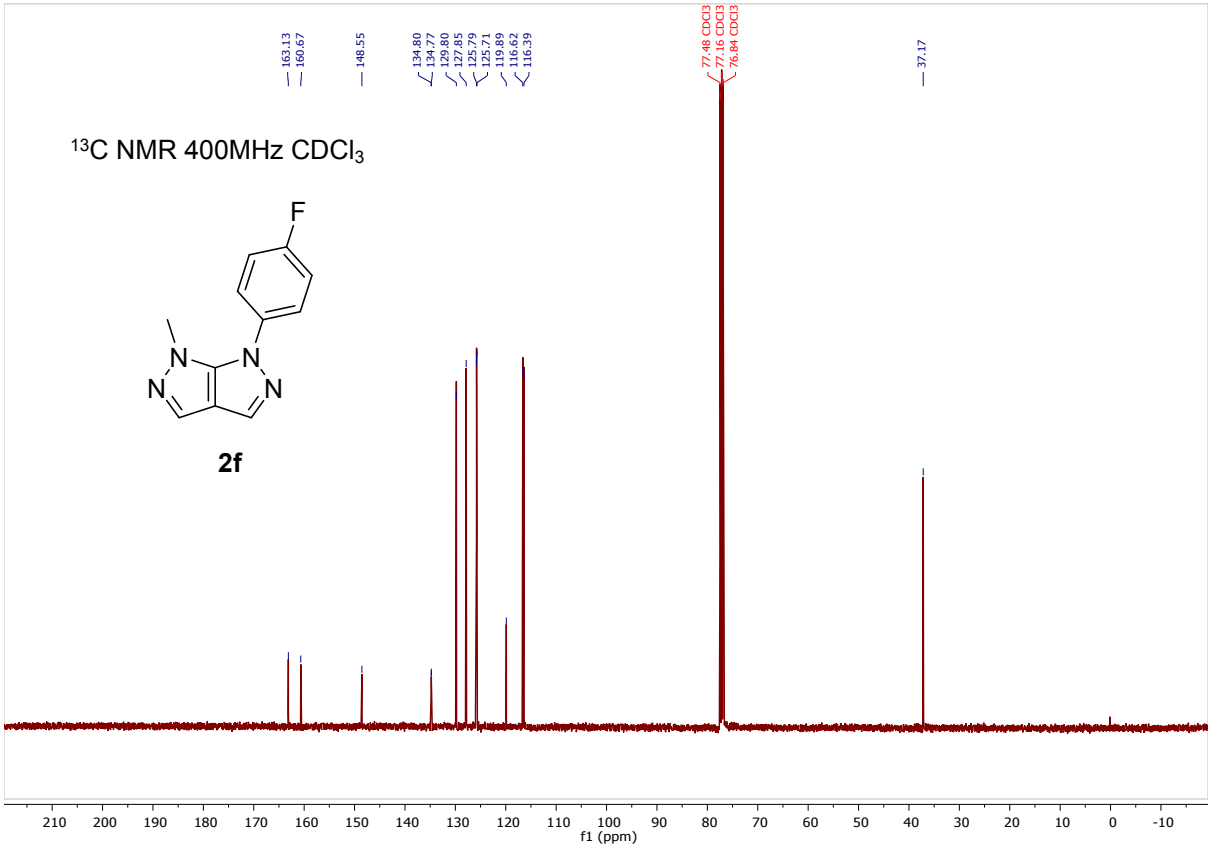
f1 (ppm)


40-02-09-pos26-MAH-H10.10.fid
-62.40
2e ^{19}F NMR ($CDCl_3$, 235 MHz)
CF_3
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400
-600
-800
50
0
-50
-100
-150
-200
-250
f1 (ppm)


7.60
7.53
7.52
7.52
7.51
7.51
7.50
7.49
7.48
7.26
7.23
7.22
7.21
7.19
7.18
3.80
-0.01
1H NMR 400MHz CDCl3
F
N
N
N
N
2f
1.00
2.00
1.00
2.00
3.00
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)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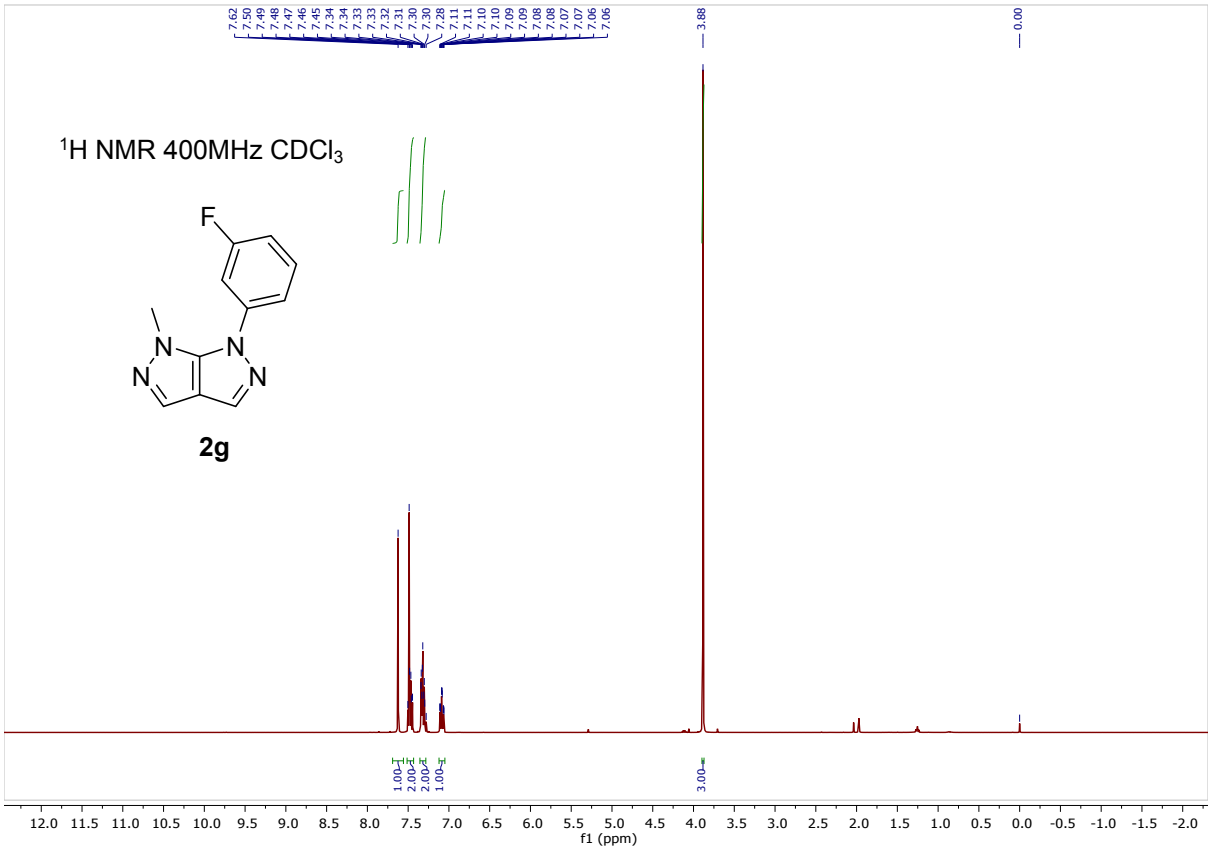
134.80
134.77
129.80
127.85
125.79
125.71
119.89
116.62
116.39
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.17
13C NMR 400MHz CDCl3
F
N
N
N
N
2f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.62
7.50
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7.48
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7.46
7.45
7.34
7.34
7.33
7.33
7.32
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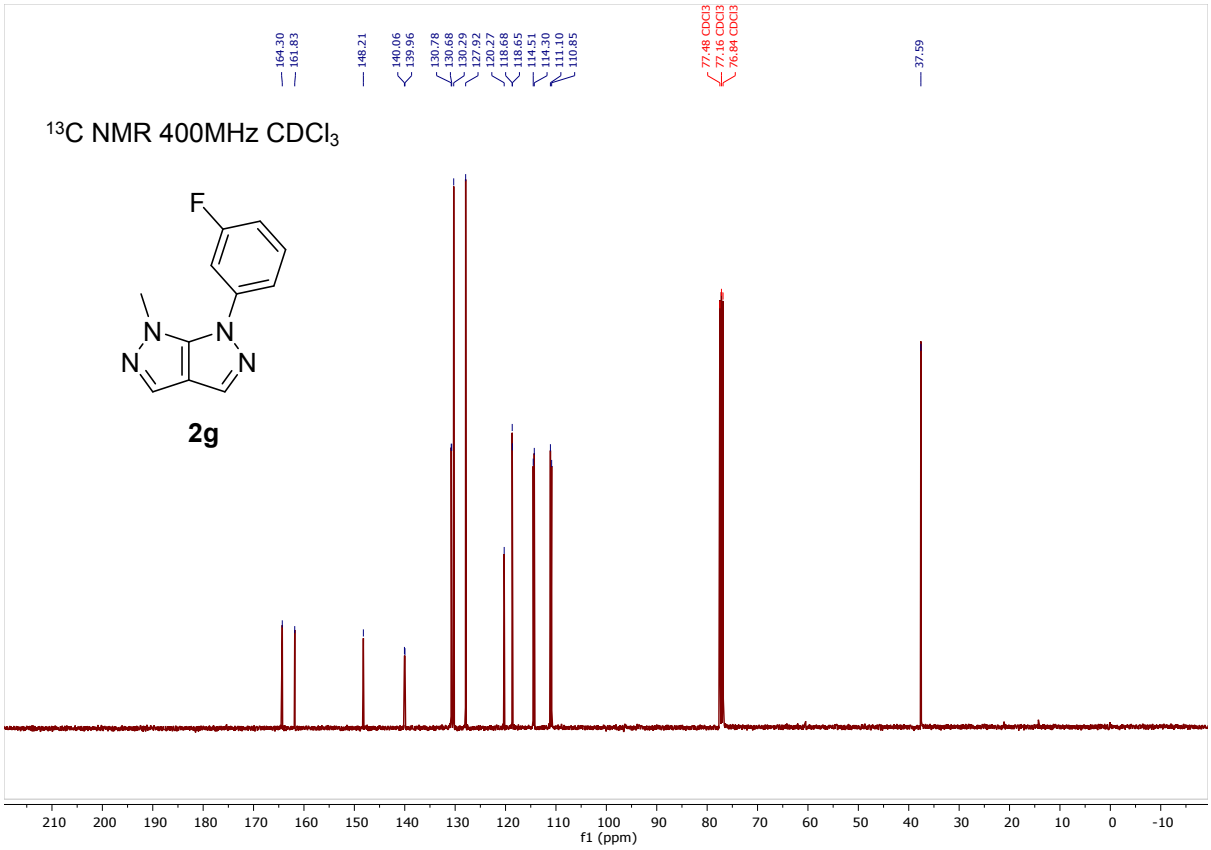
7.30
7.30
7.28
7.11
7.11
7.10
7.10
7.09
7.09
7.08
7.08
7.07
7.07
7.06
7.06
7.06
3.88
0.00
1H NMR 400MHz CDCl3
F
N
N
N
N
2g
1.00
2.00
2.00
1.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


164.30
161.83
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140.06
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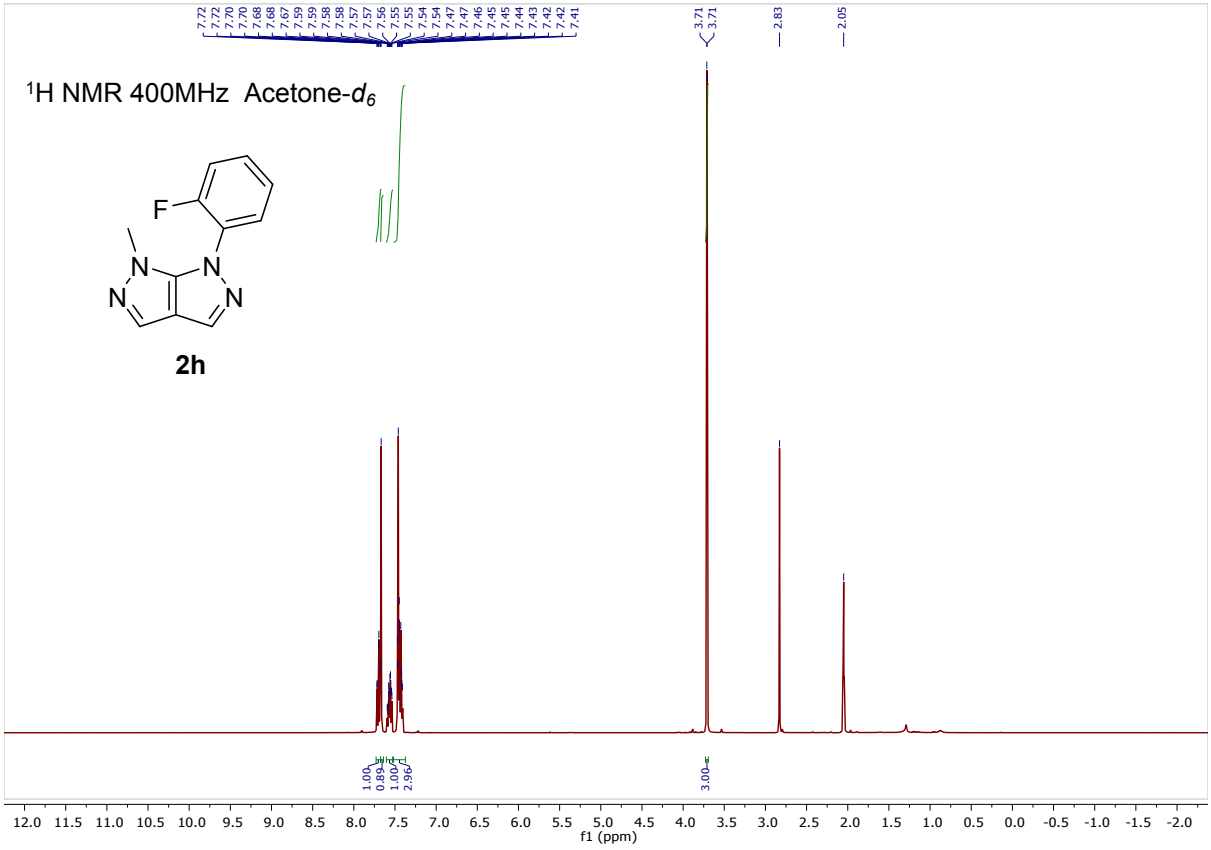
130.78
130.68
130.29
127.92
120.27
118.68
116.65
114.51
114.30
111.10
110.85
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.59
13C NMR 400MHz CDCl3
F
N
N
N
N
2g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.72
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7.68
7.67
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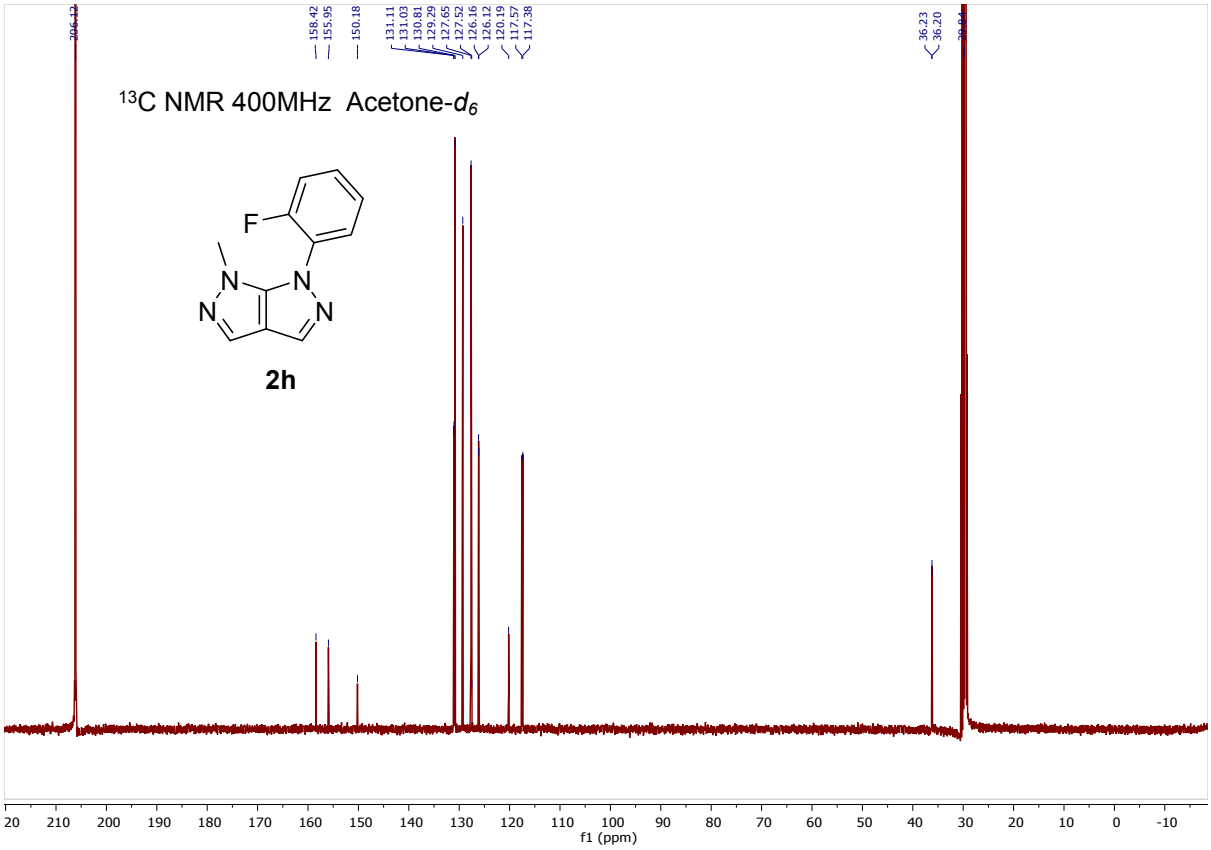
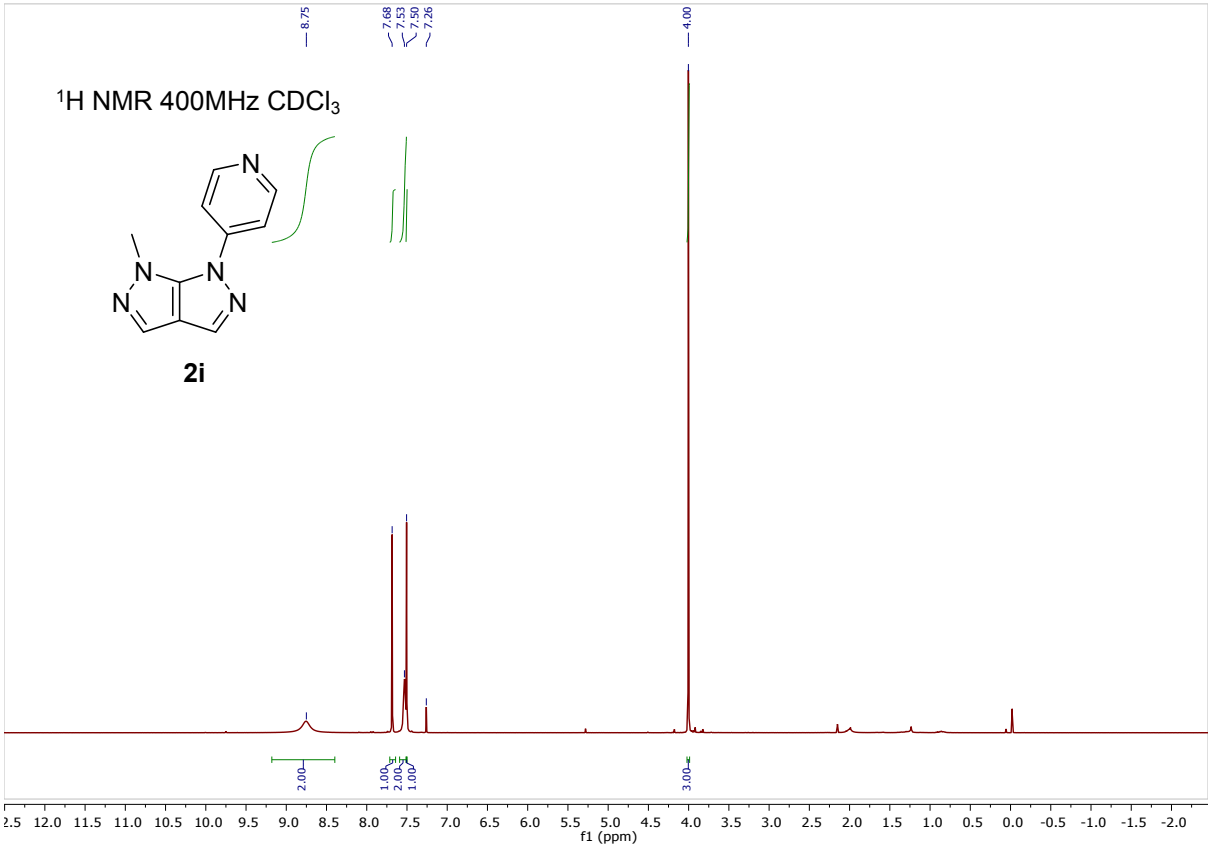
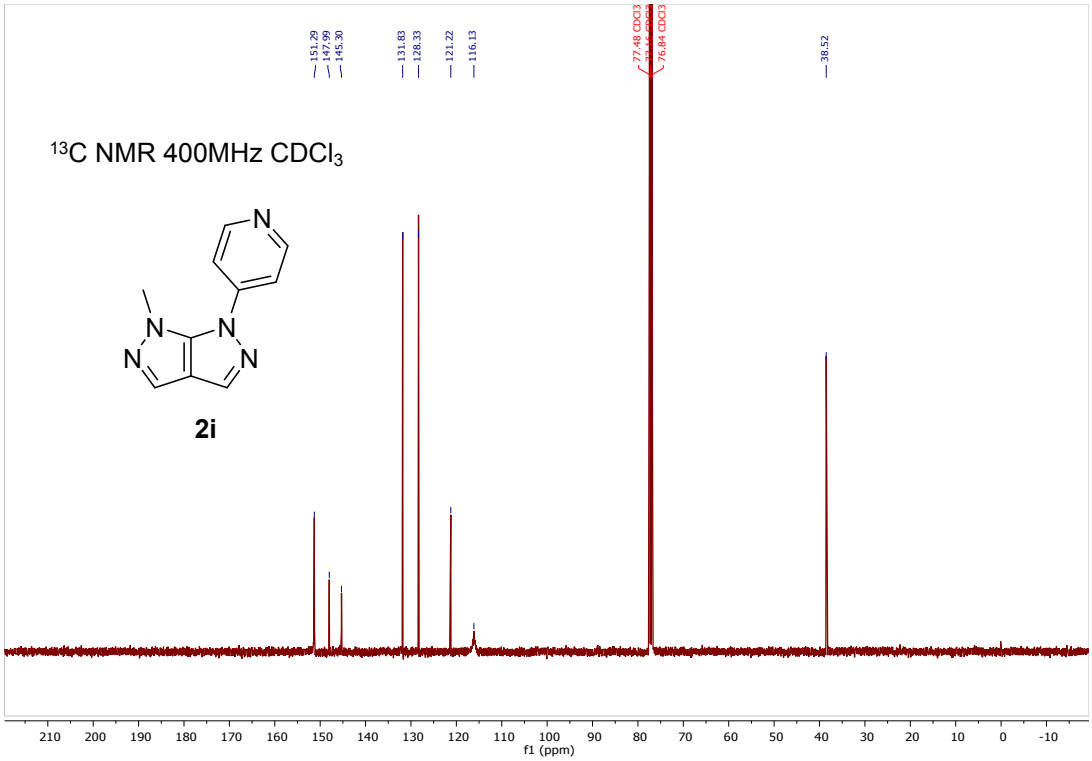
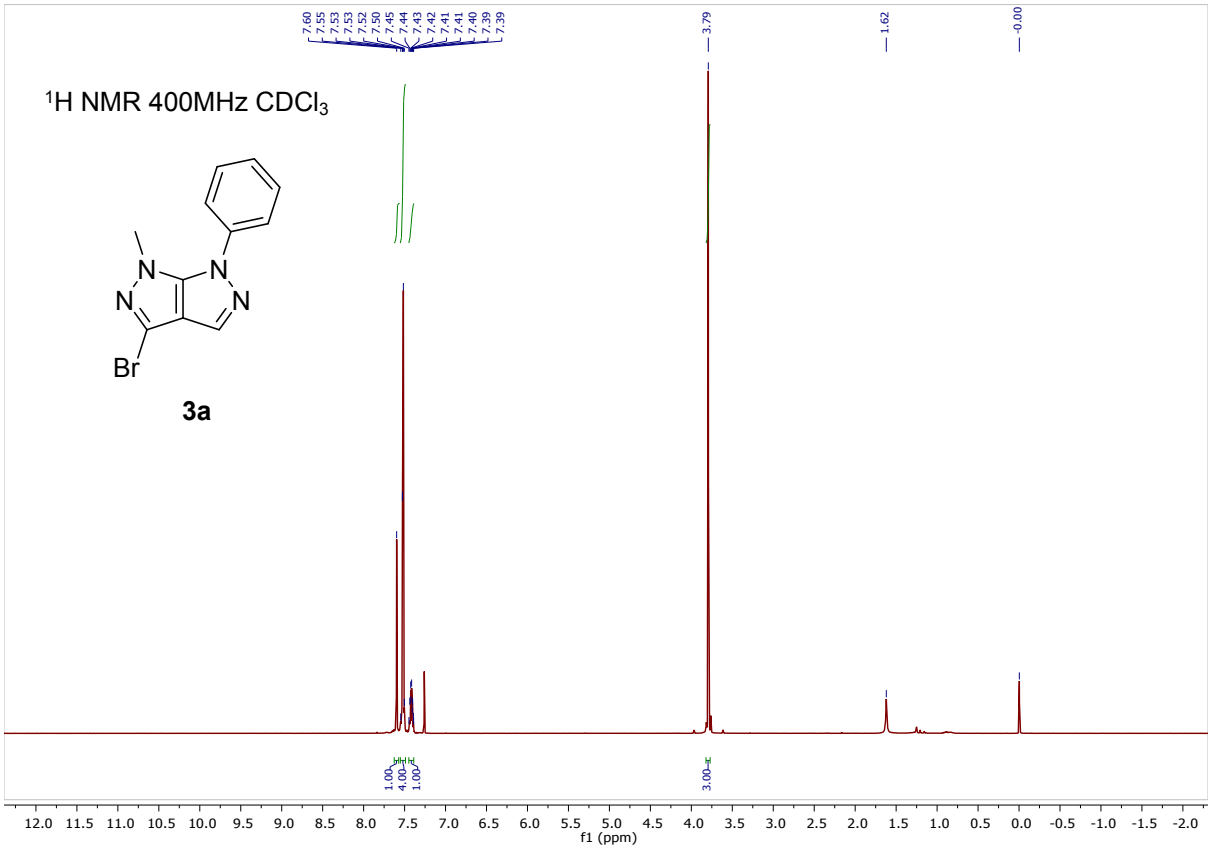
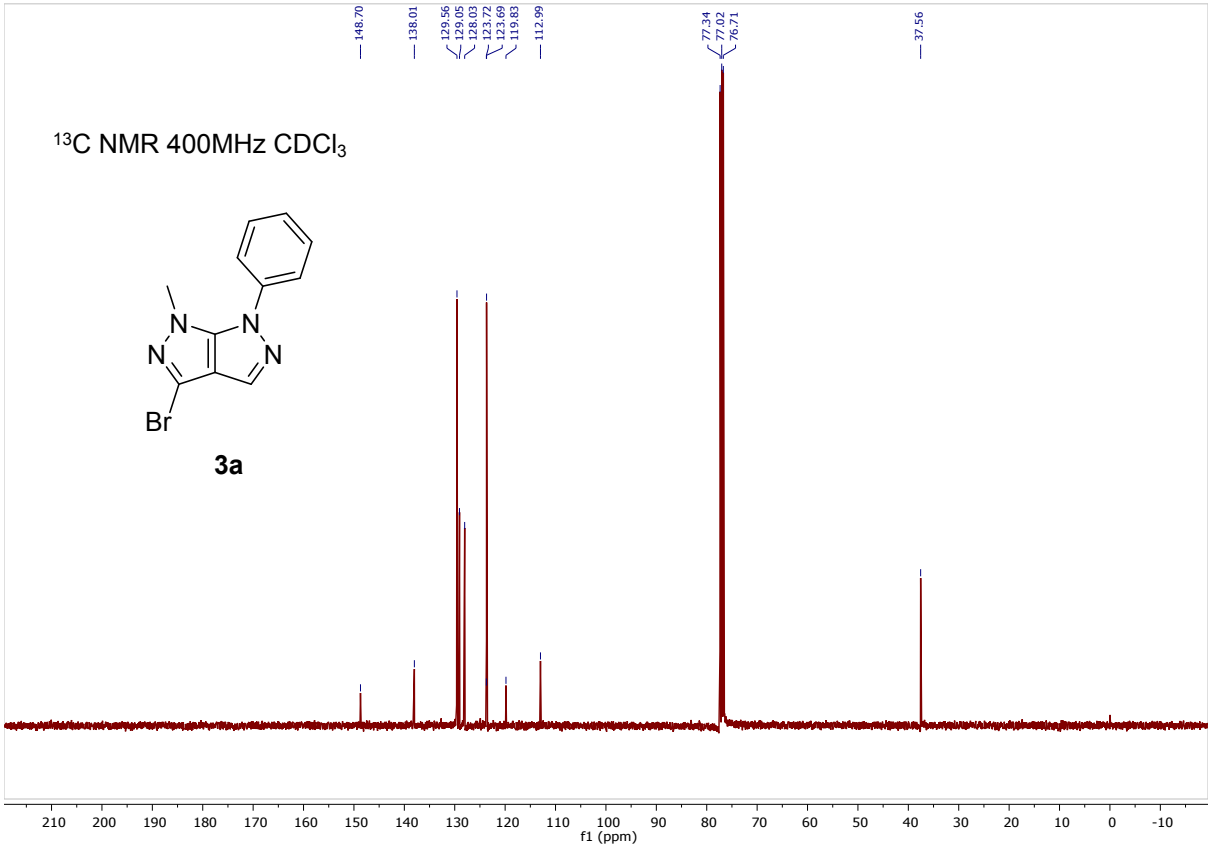
7.41
3.71
3.71
2.83
2.05
1H NMR 400MHz Acetone-d6
F
N
N
N
N
2h
1.00
0.89
1.00
2.96
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


206.12
158.42
155.95
150.18
131.11
131.03
130.81
129.29
127.65
127.52
126.16
126.12
120.19
117.57
117.38
36.23
36.20
^{13}C NMR 400MHz Acetone-d_6
F
N
N
N
N
2h
f1 (ppm)


8.75
7.68
7.53
7.50
7.26
4.00
^{1}H NMR 400MHz $CDCl_3$
N
N
N
N
2i
2.00
1.00
2.00
1.00
3.00
f1 (ppm)


151.29
147.99
145.30
131.83
128.33
121.22
116.13
77.48 CDCl3
76.84 CDCl3
38.52
13C NMR 400MHz CDCl3
2i
f1 (ppm)


7.60
7.55
7.53
7.53
7.52
7.50
7.45
7.44
7.43
7.42
7.41
7.41
7.40
7.39
7.39
3.79
1.62
-0.00
1H NMR 400MHz CDCl3
Br
3a
1.00
4.00
1.00
3.00
f1 (ppm)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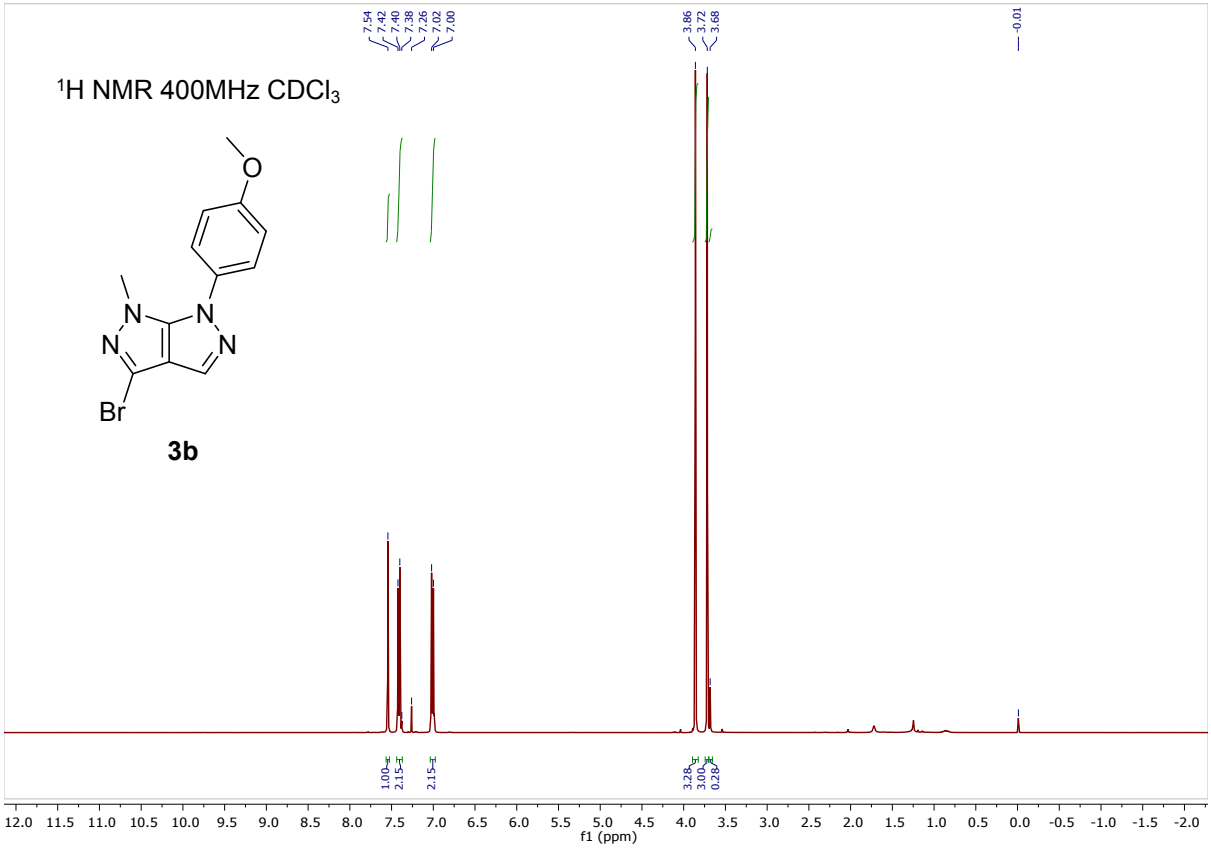
129.56
129.05
128.03
123.72
123.69
119.83
112.99
77.34
77.02
76.71
37.56
^{13}C NMR 400MHz $CDCl_3$
N
N
N
N
Br
3a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.42
7.40
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7.00
3.86
3.72
3.68
-0.01
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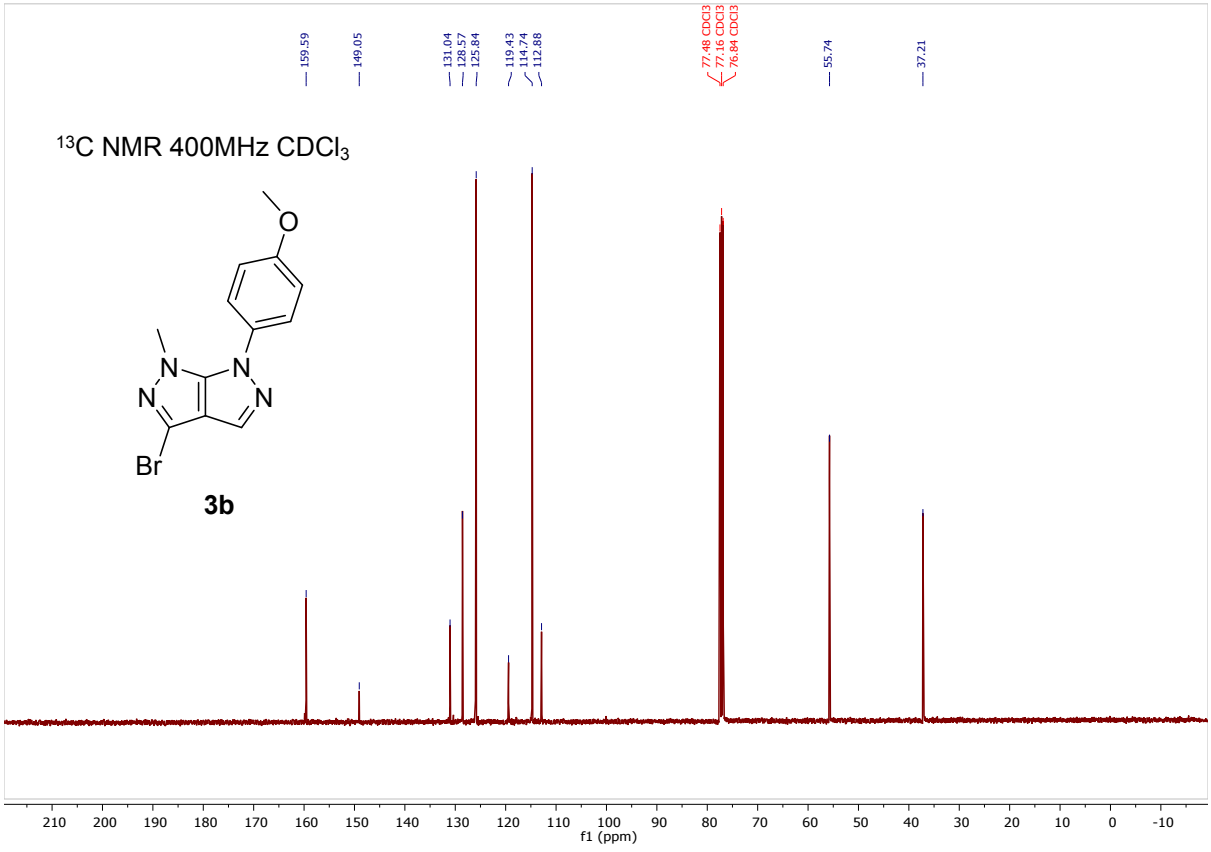
O
N
N
N
N
Br
3b
1.00
2.15
2.15
3.28
3.00
0.28
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)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128.57
125.84
119.43
114.74
112.88
77.48 CDCl3
77.16 CDCl3
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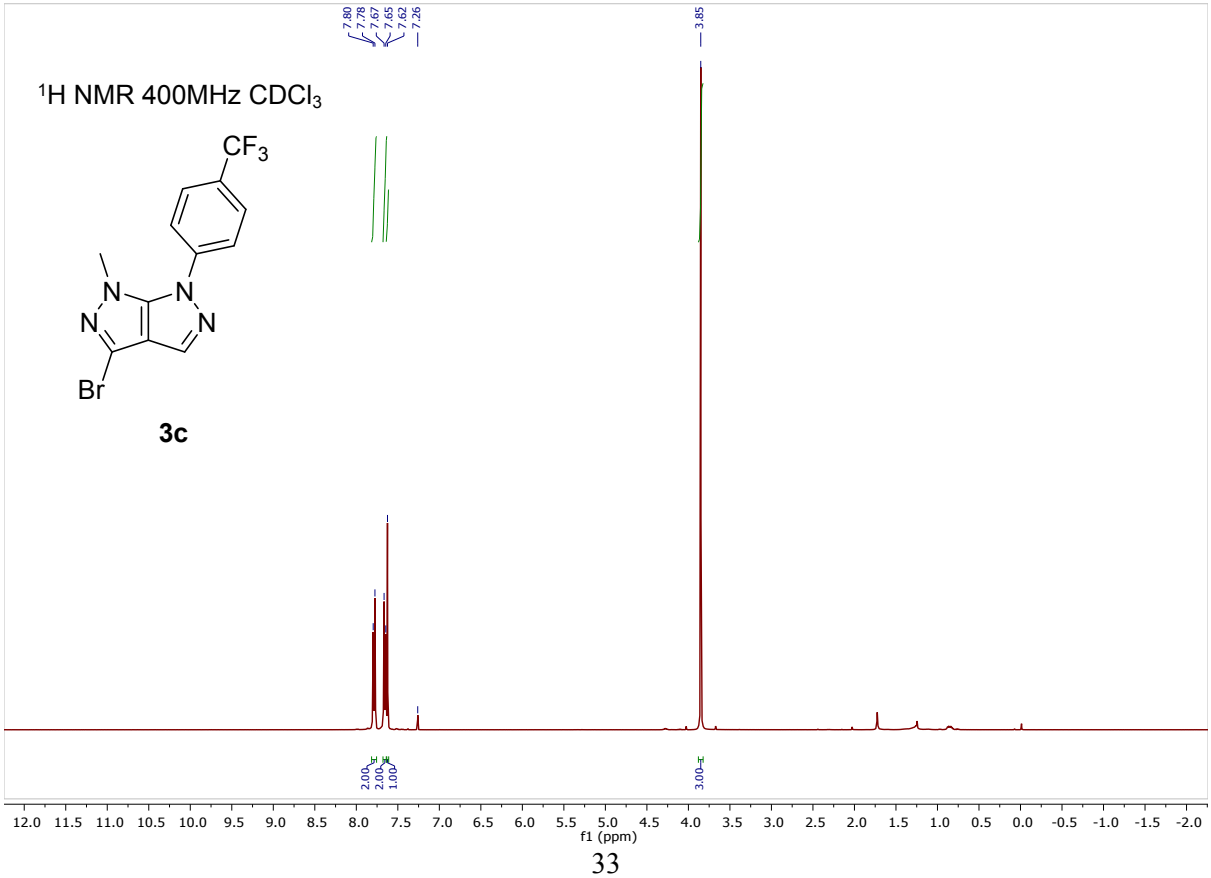
55.74
37.21
13C NMR 400MHz CDCl3
O
N
N
N
N
Br
3b
f1 (ppm)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CF3
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N
Br
3c
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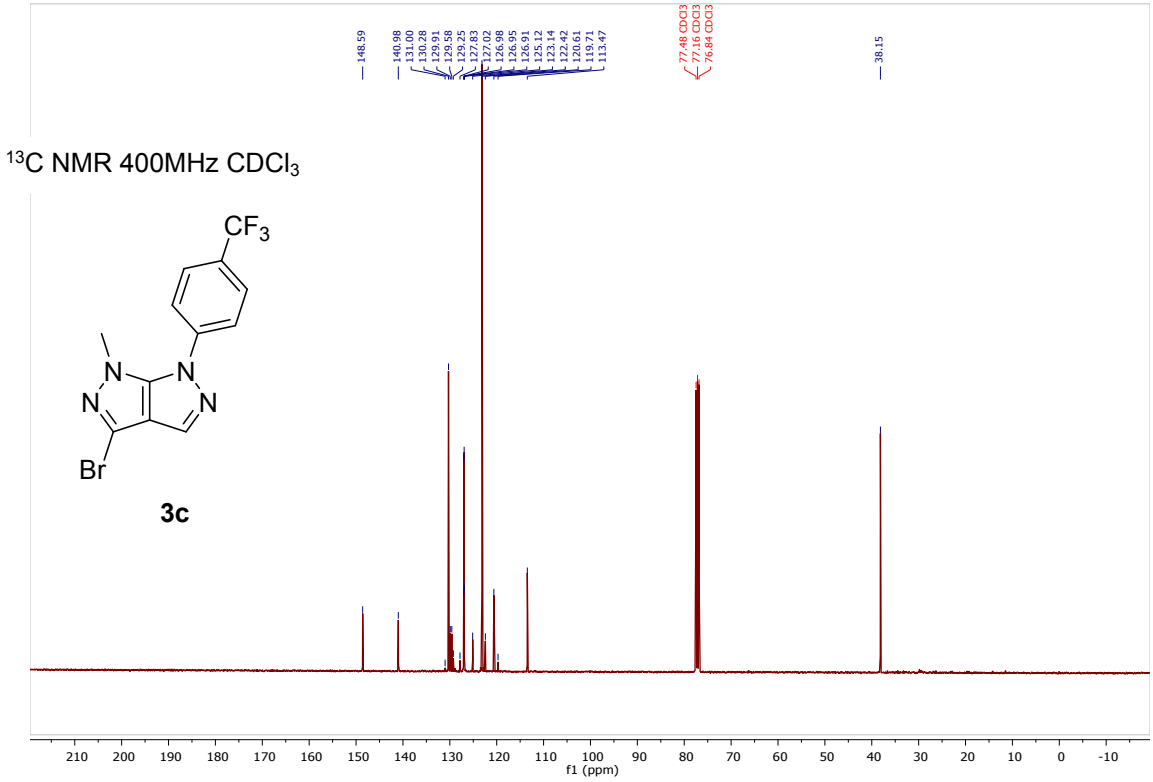
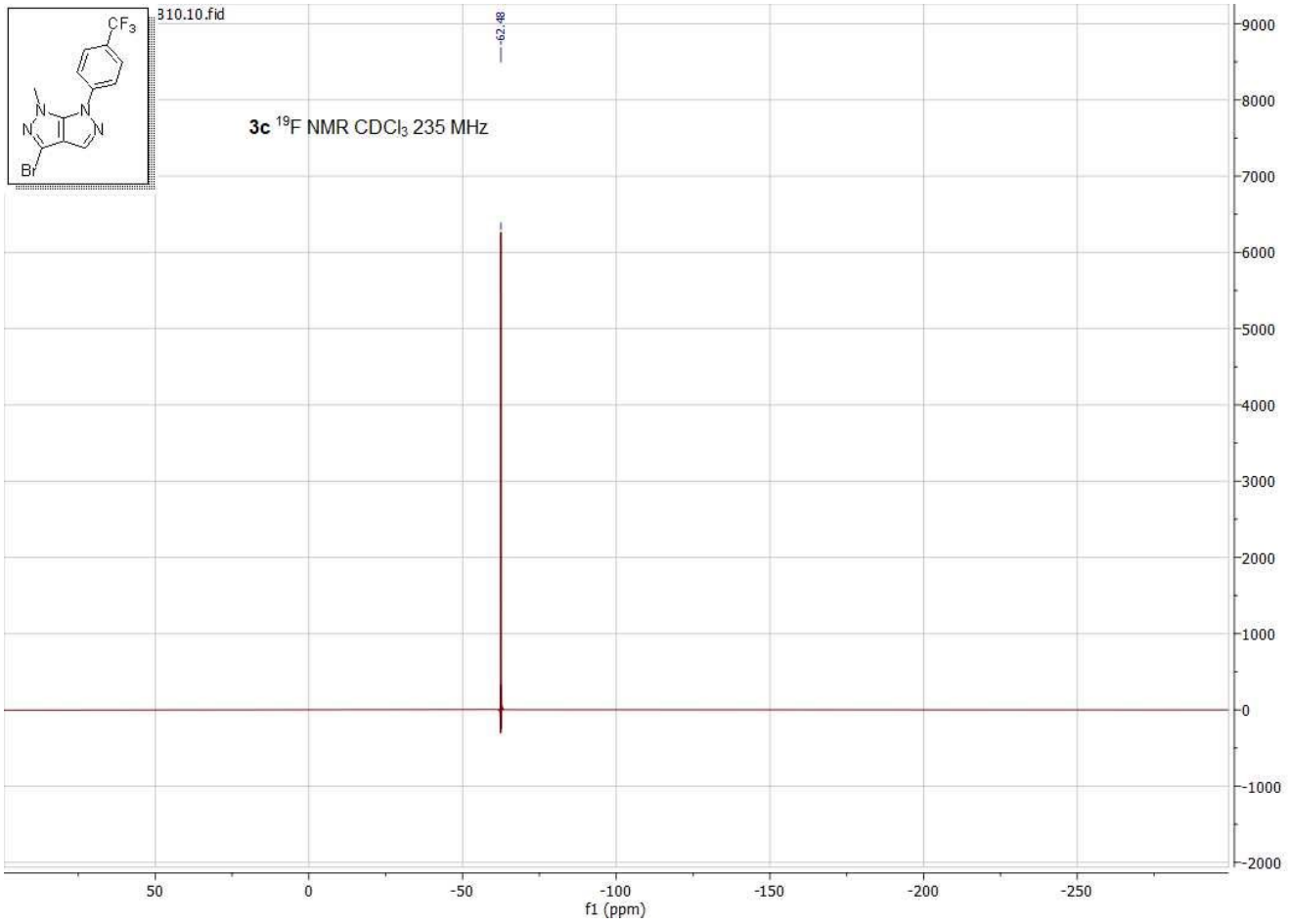
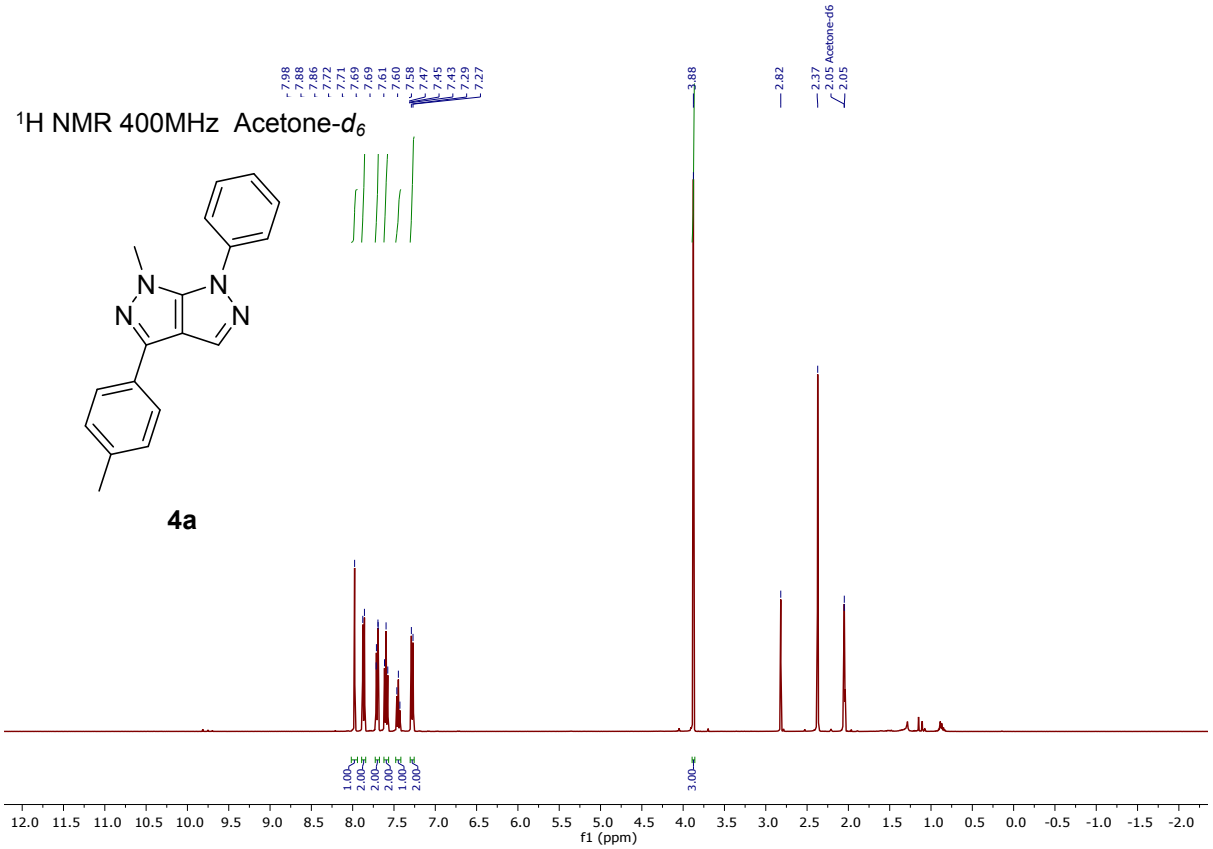
2.00
1.00
3.00
f1 (ppm)



^{13}C NMR 400MHz $CDCl_3$

3c


310.10.fid
-62.48
3c ^{19}F NMR $CDCl_3$ 235 MHz
f1 (ppm)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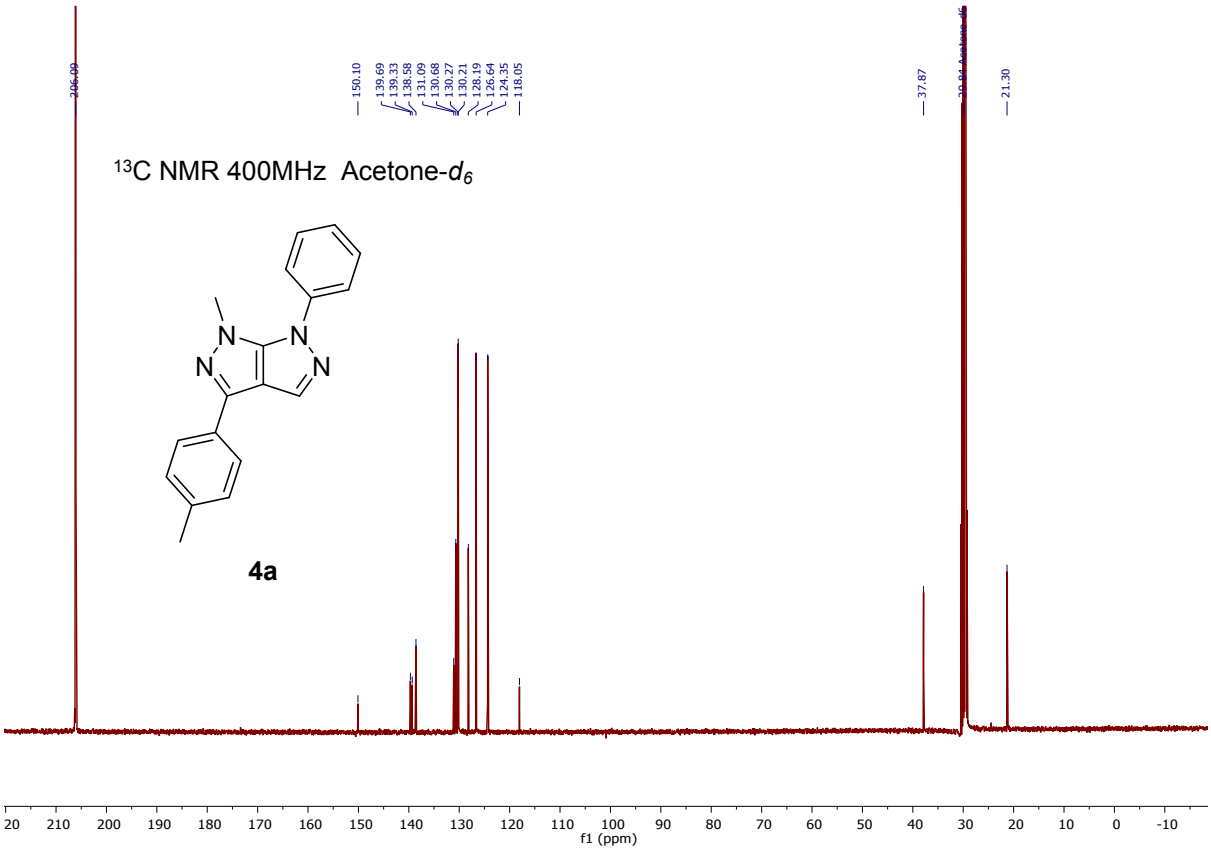
4a
f1 (ppm)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130.27
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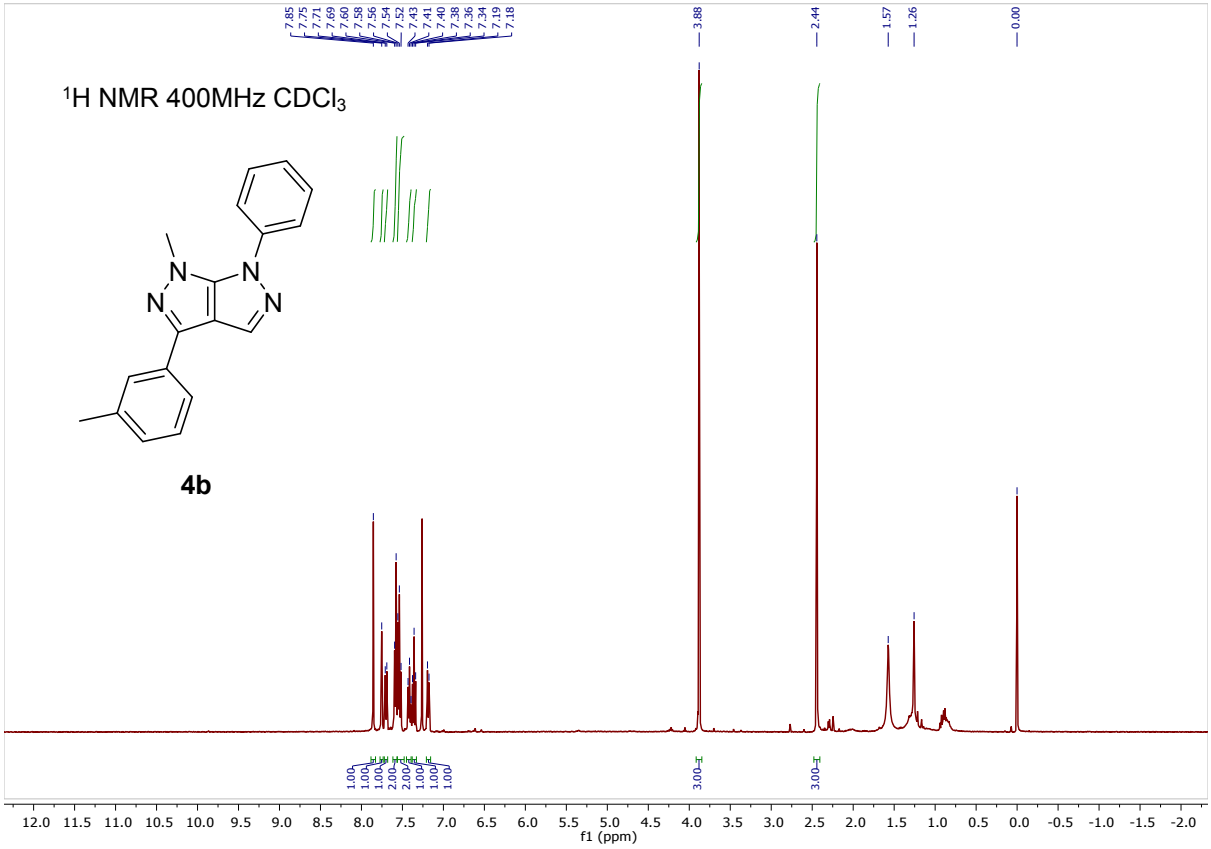
118.05
37.87
30.84
21.30
^{13}C NMR 400MHz Acetone-d_6
4a
f1 (ppm)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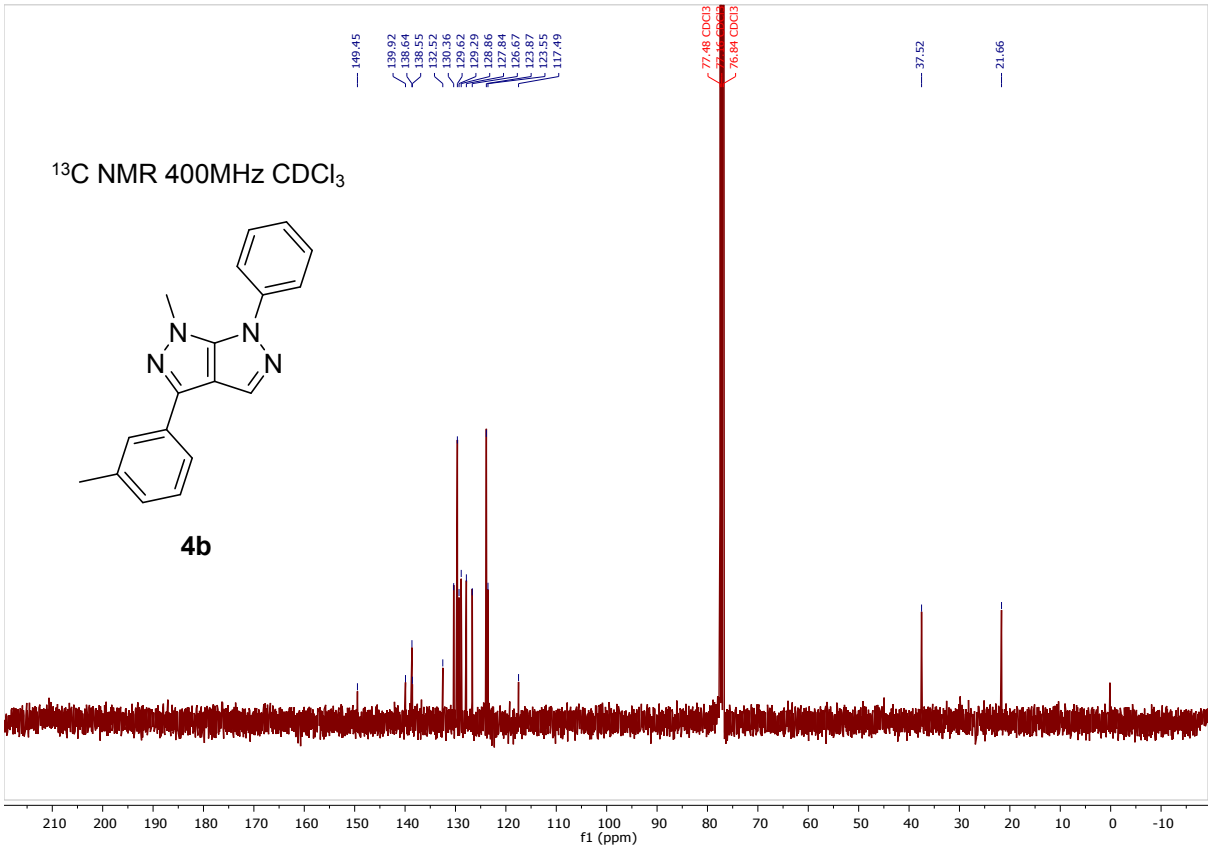
7.40
7.38
7.36
7.34
7.19
7.18
3.88
2.44
1.57
1.26
0.00
^{1}H NMR 400MHz $CDCl_3$
4b
f1 (ppm)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123.55
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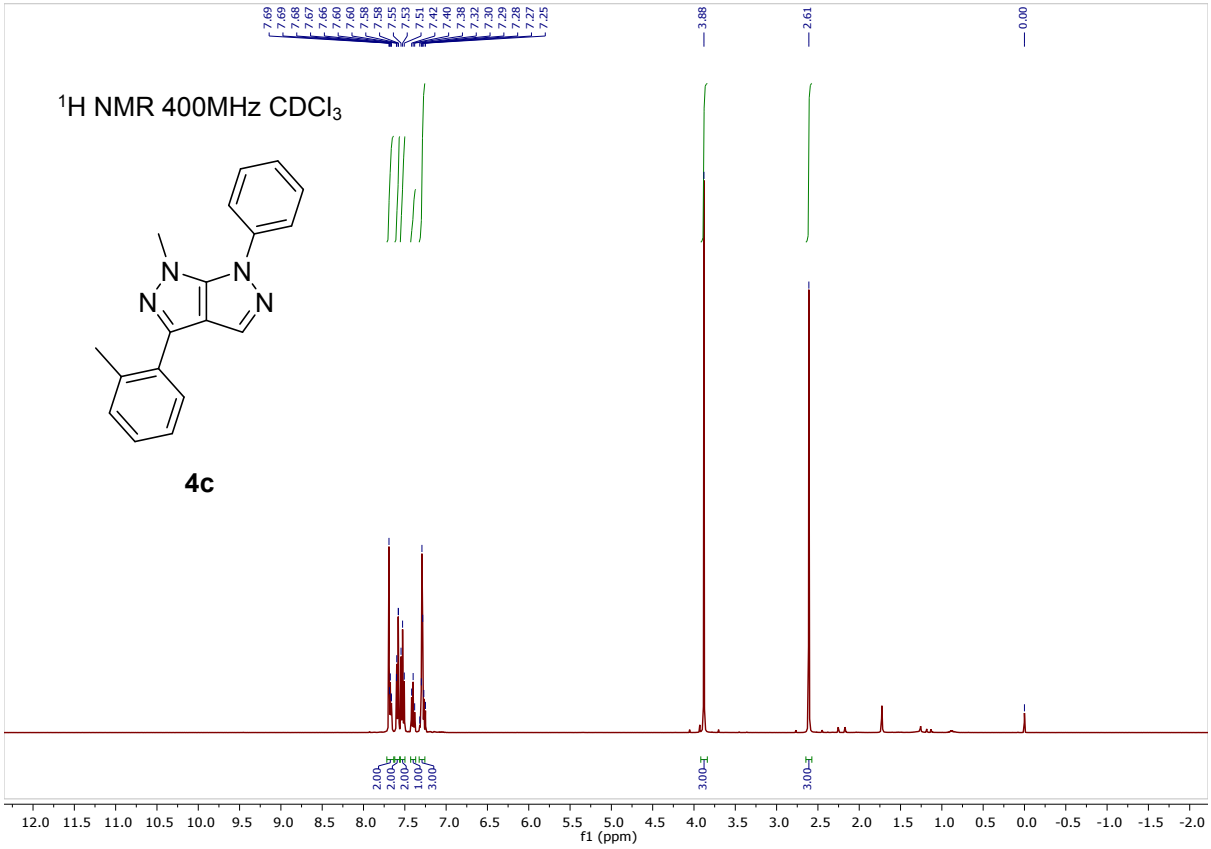
77.16 CDCl3
76.84 CDCl3
37.52
21.66
13C NMR 400MHz CDCl3
4b
f1 (ppm)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7.40
7.38
7.32
7.30
7.29
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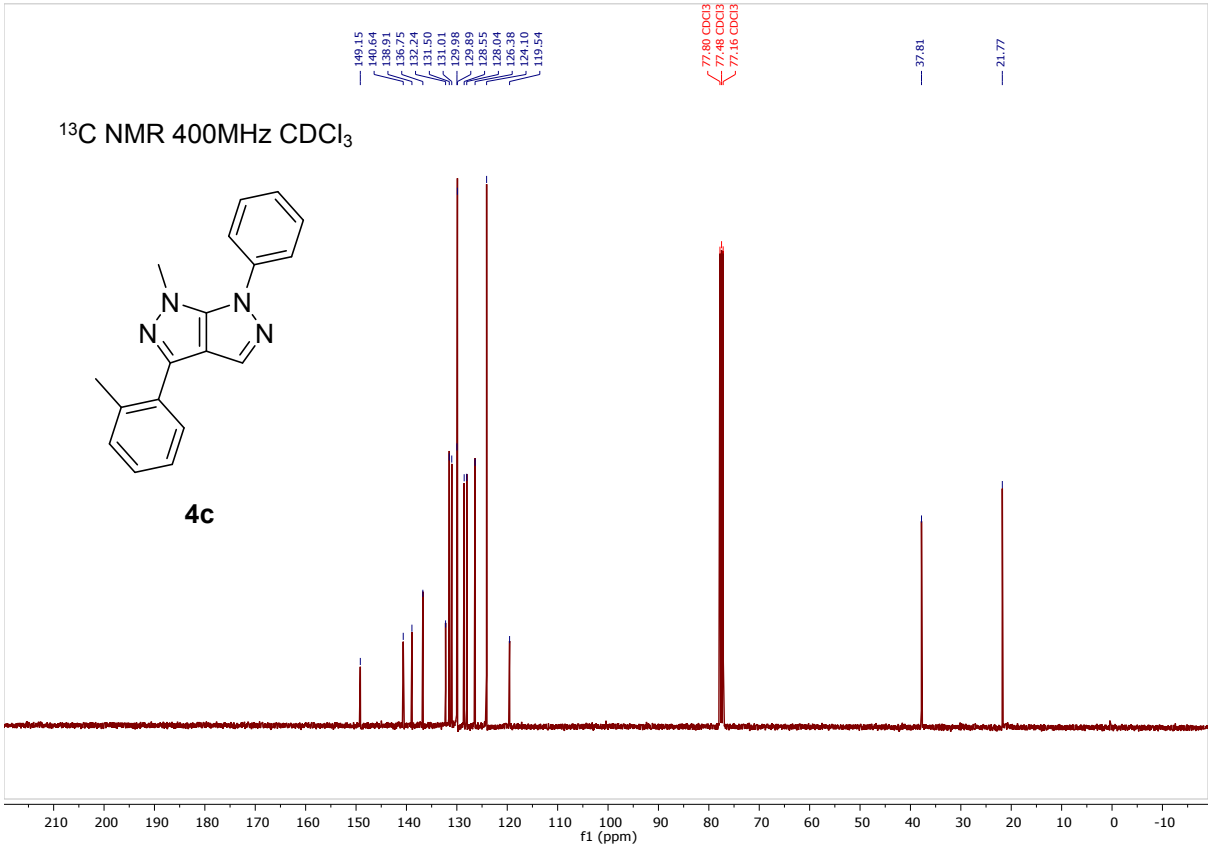
7.27
7.25
3.88
2.61
0.00
1H NMR 400MHz CDCl3
4c
f1 (ppm)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128.04
126.38
124.10
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77.48 CDCl3
77.16 CDCl3
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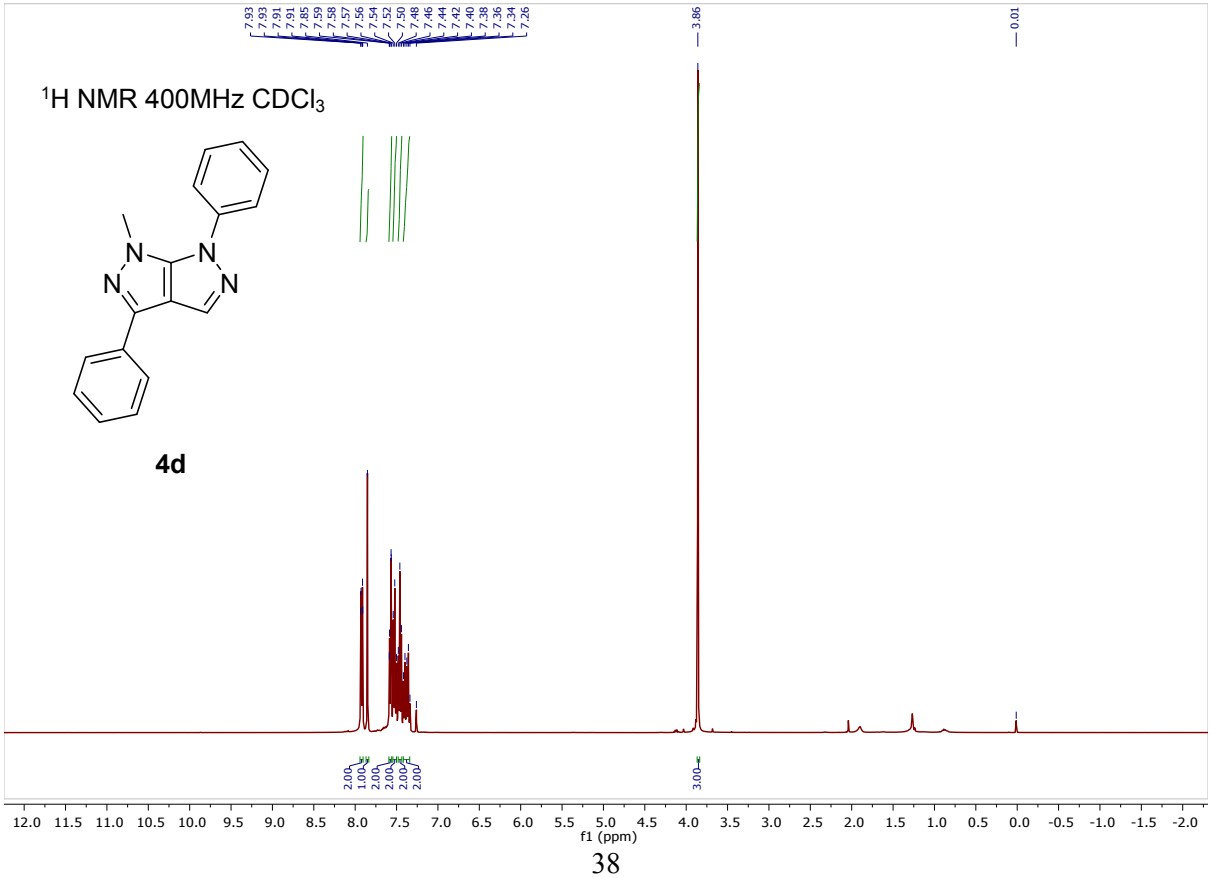
4c
f1 (ppm)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7.44
7.42
7.40
7.38
7.36
7.34
7.26
3.86
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4d
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1.00
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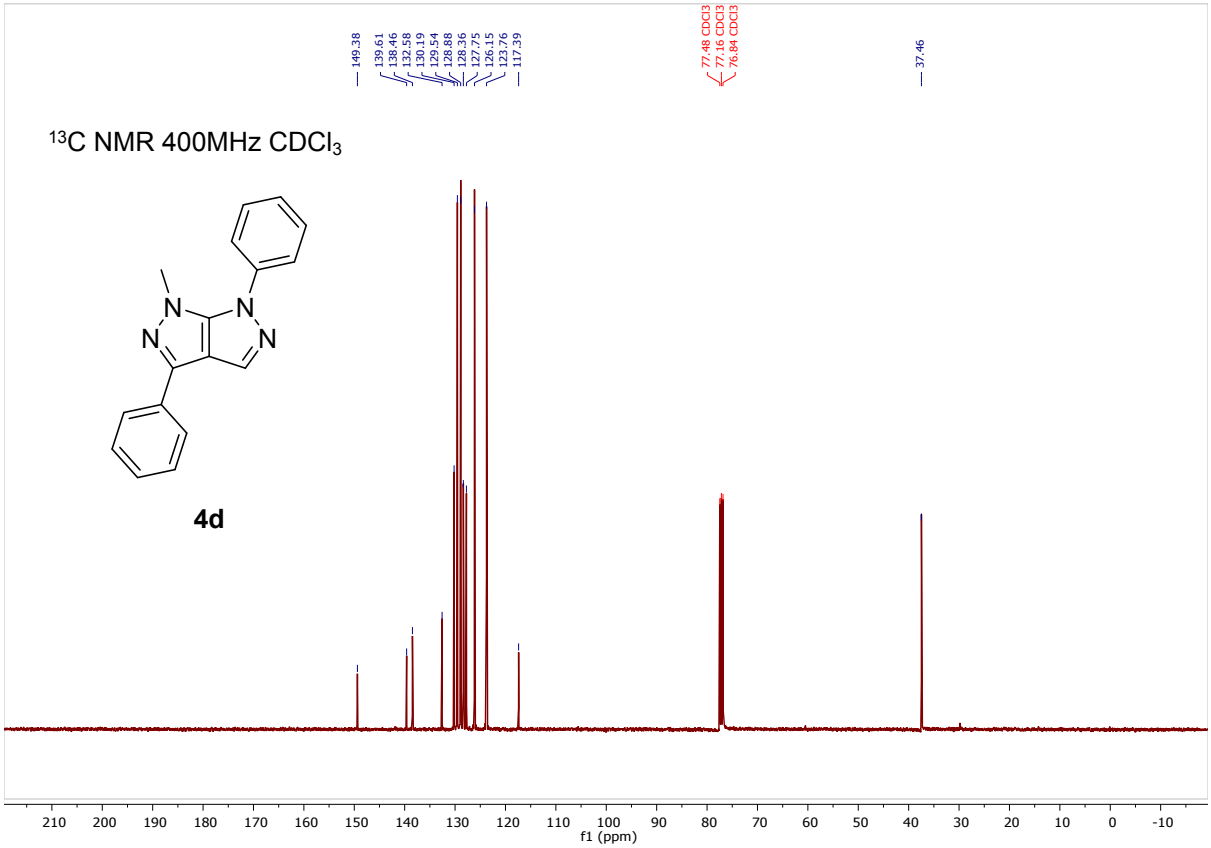
2.00
2.00
3.00
f1 (ppm)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117.39
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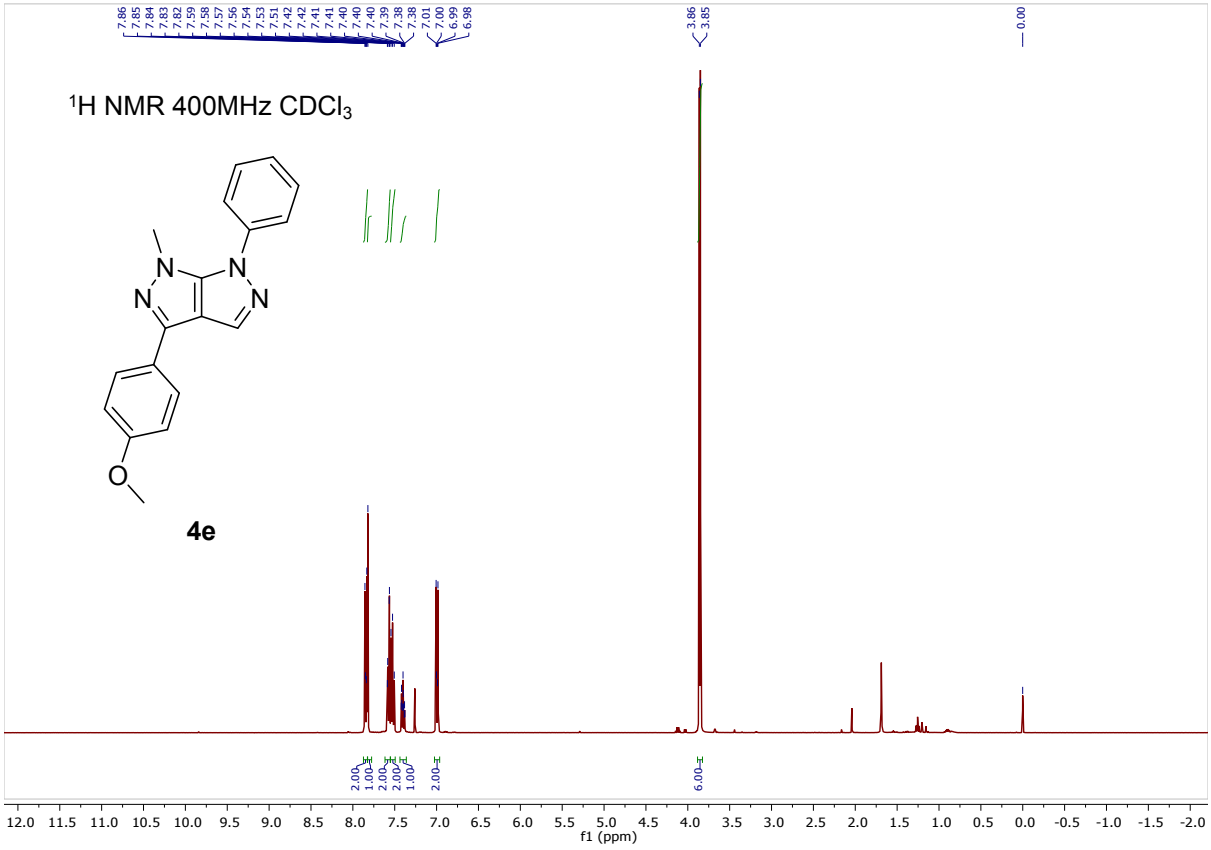
37.46
13C NMR 400MHz CDCl3
4d
f1 (ppm)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7.40
7.40
7.39
7.38
7.38
7.01
7.00
6.99
6.98
3.86
3.85
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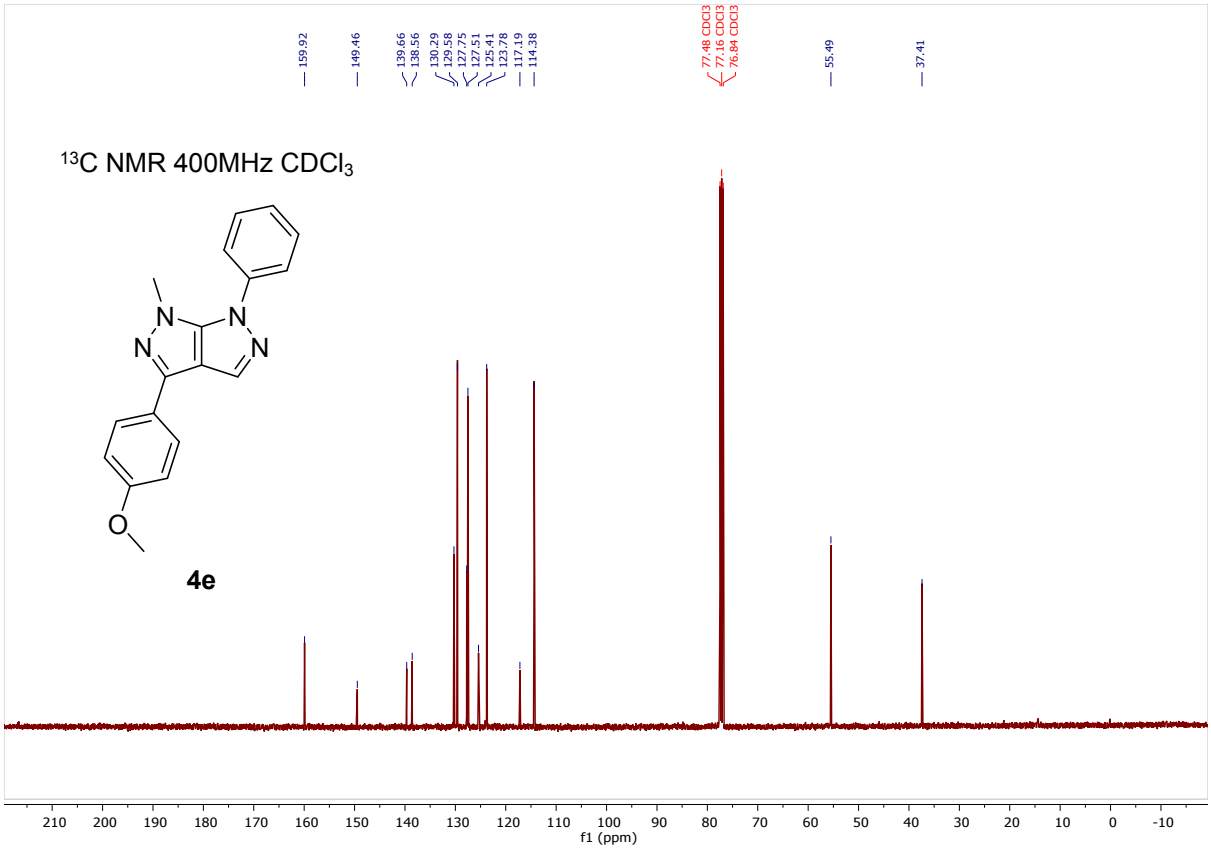
4e
2.00
1.00
2.00
2.00
1.00
2.00
6.00
f1 (ppm)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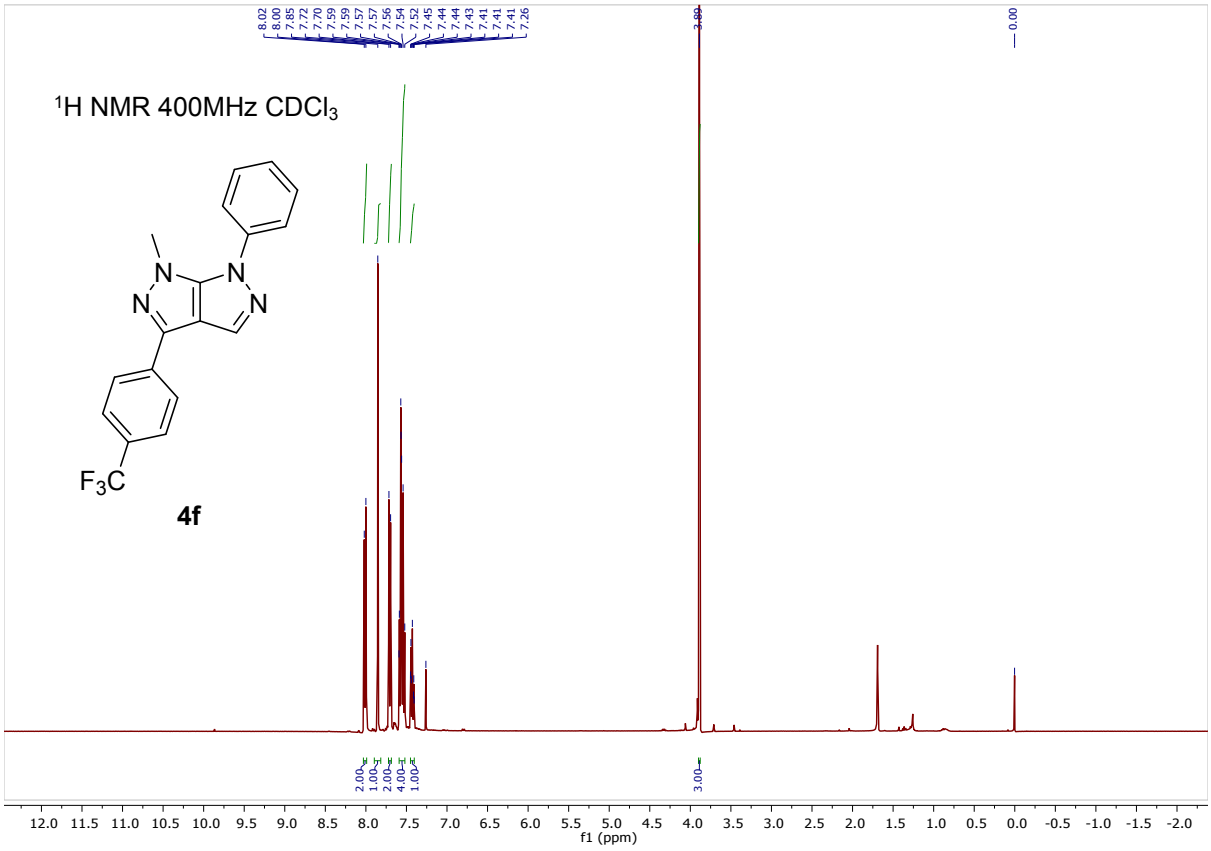
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.49
37.41
13C NMR 400MHz CDCl3
4e
f1 (ppm)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7.44
7.43
7.41
7.41
7.41
7.26
3.99
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F3C
4f
2.00
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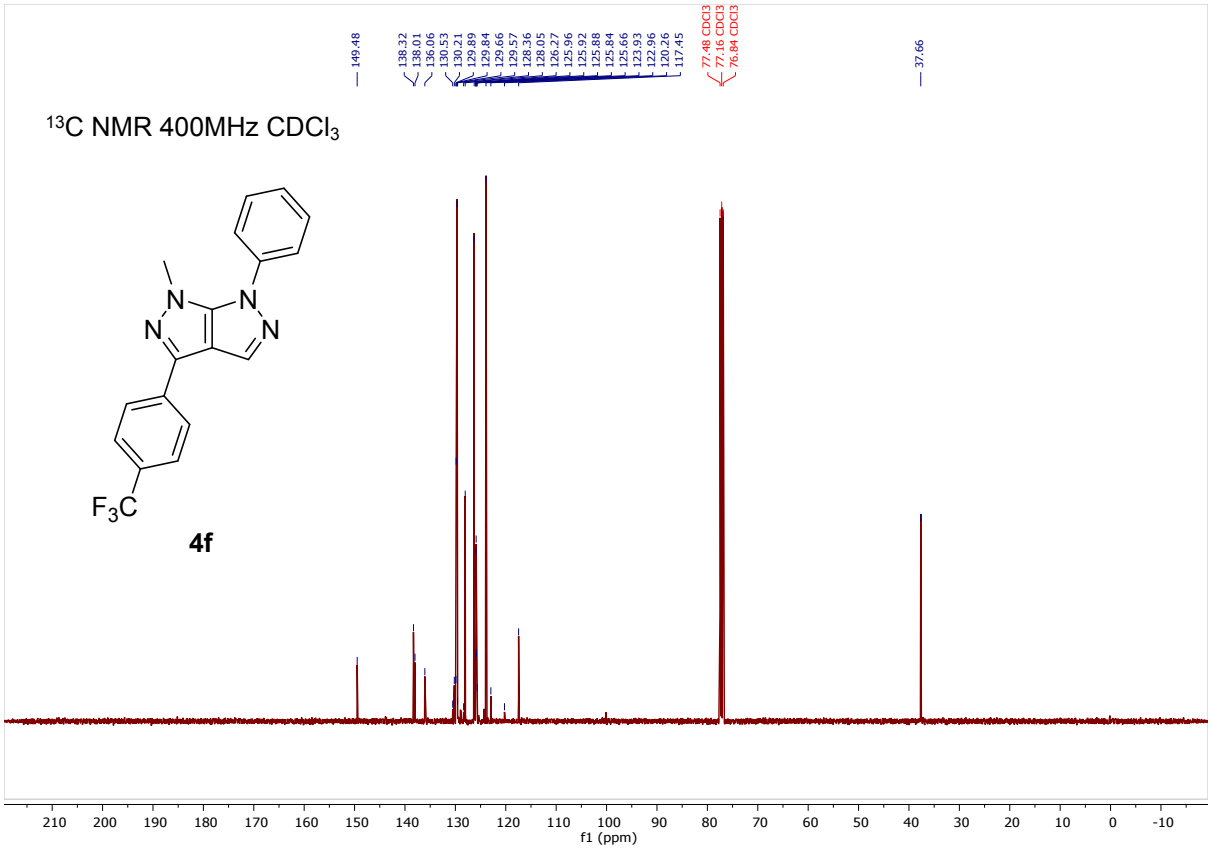
3.00
f1 (ppm)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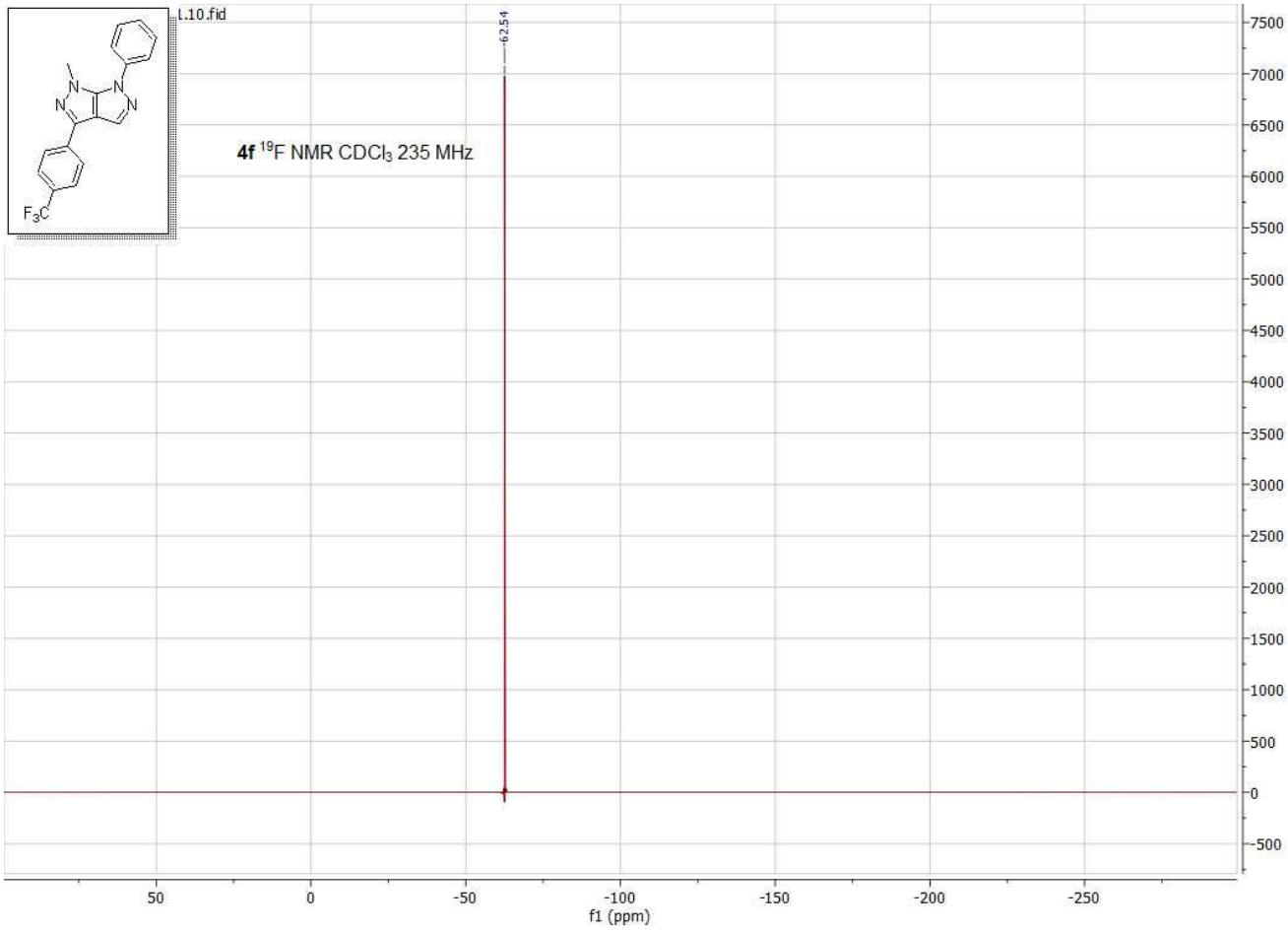
125.84
125.66
123.93
122.96
120.26
117.45
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.66
13C NMR 400MHz CDCl3
F3C
4f
f1 (ppm)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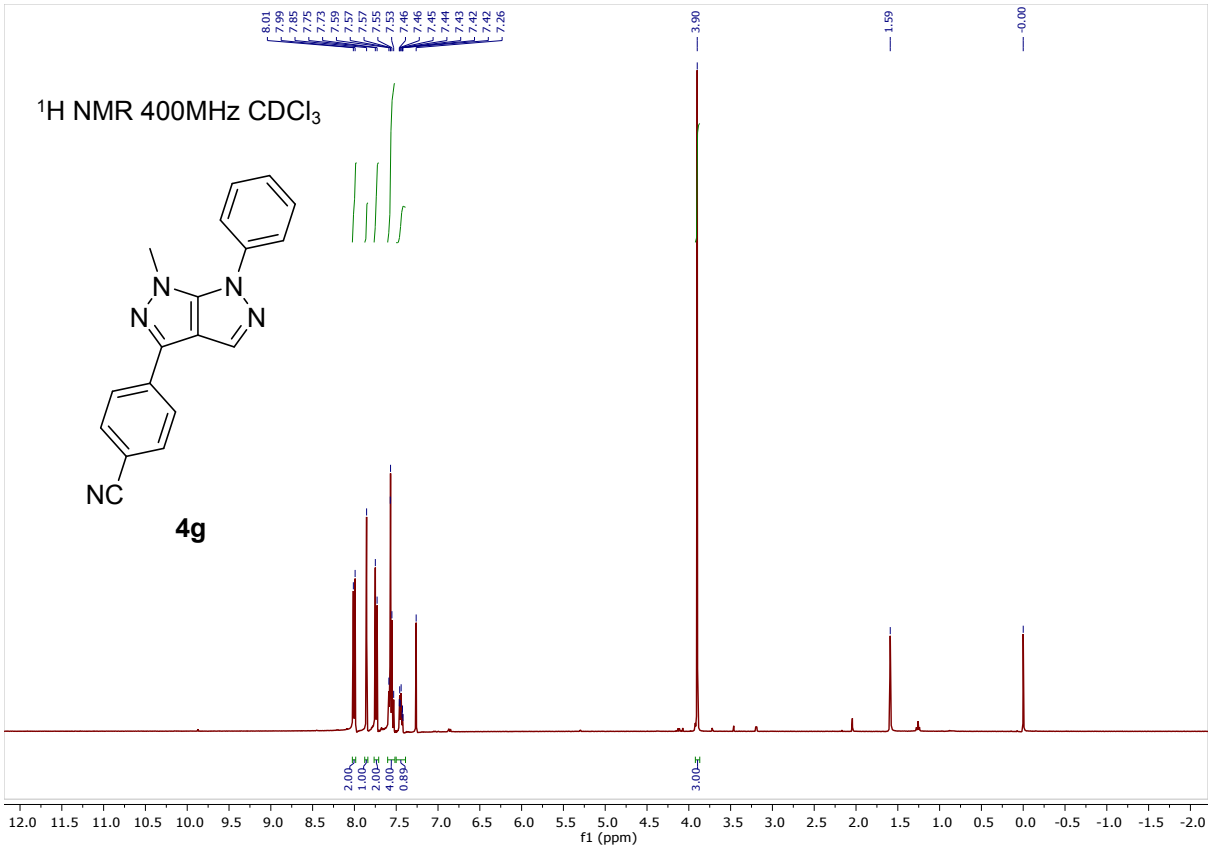
4f 19F NMR CDCl3 235 MHz
F3C
f1 (ppm)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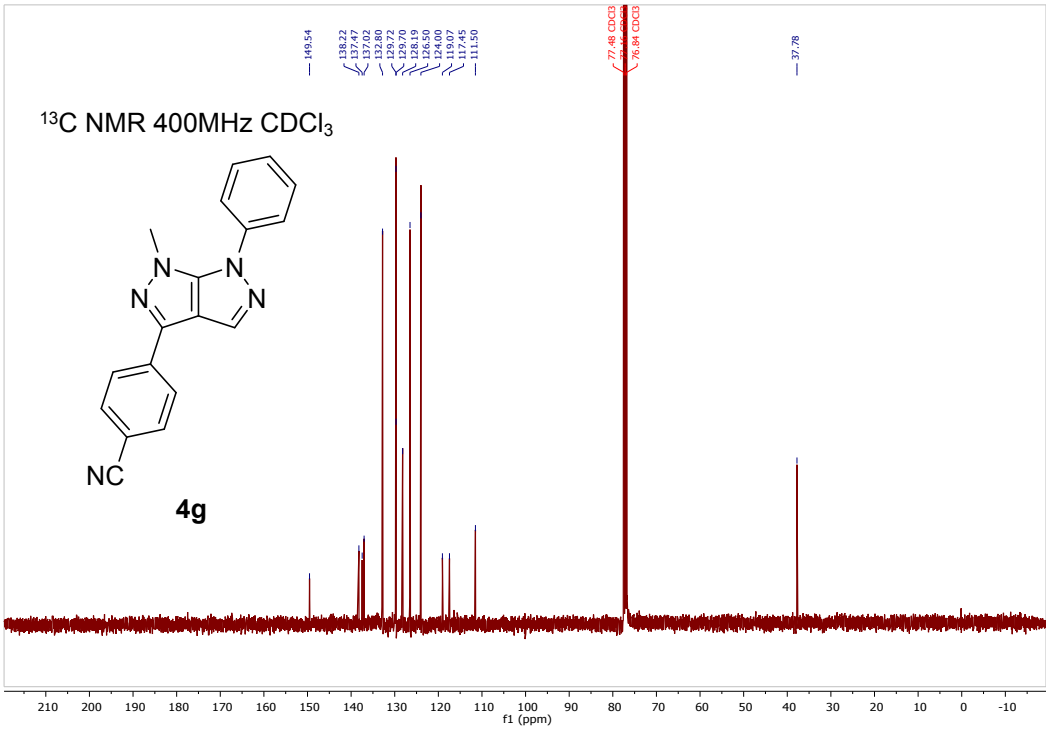
4g
f1 (ppm)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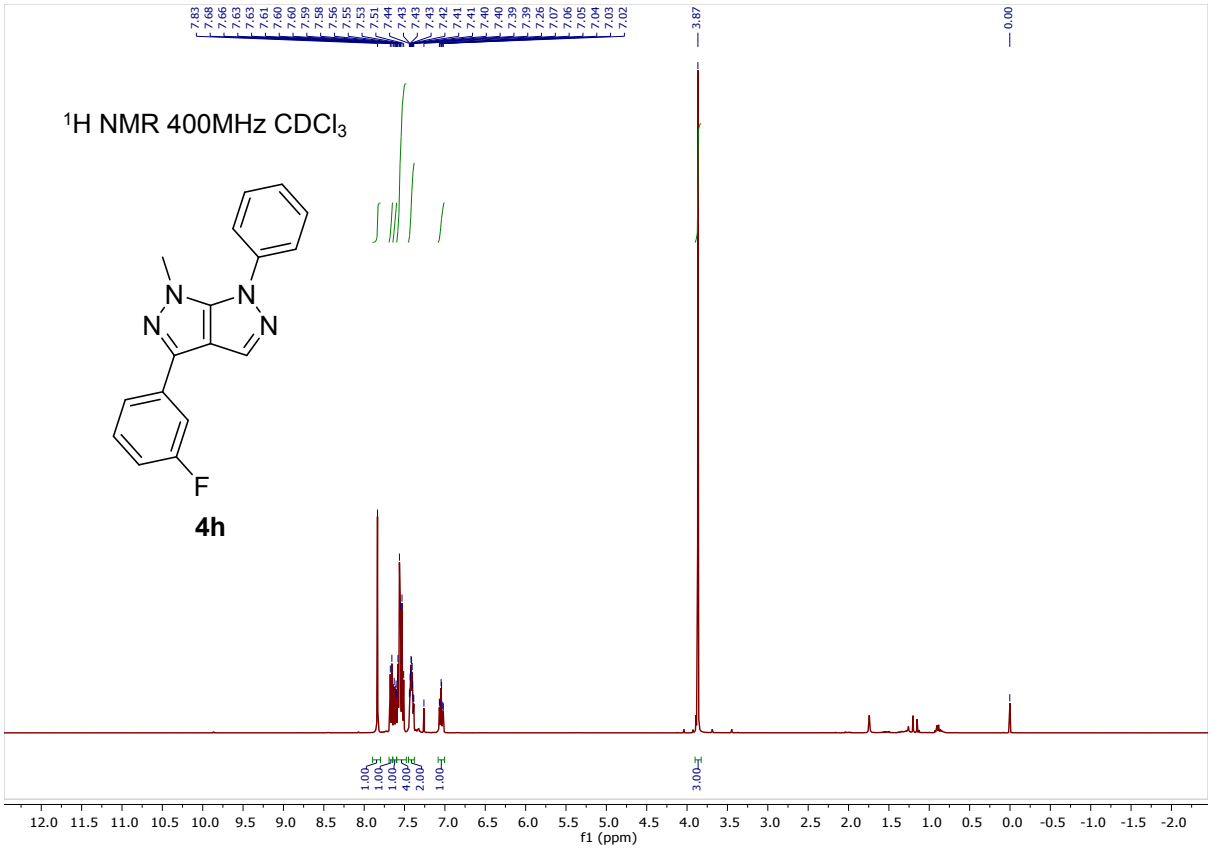
4g
f1 (ppm)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7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.39
7.26
7.07
7.06
7.05
7.04
7.03
7.02
3.87
0.00
1H NMR 400MHz CDCl3
N
N
N
N
F
4h
1.00
1.00
1.00
4.00
2.00
1.00
3.00
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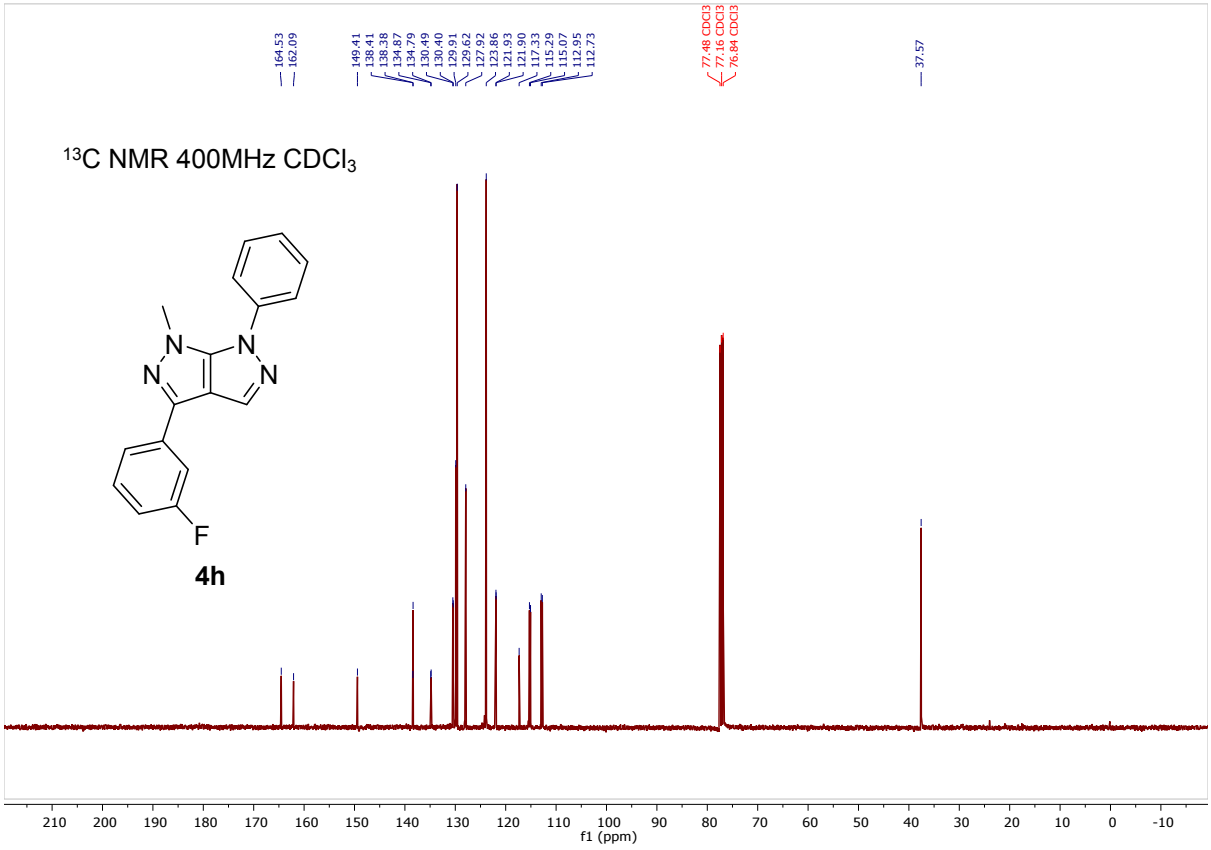
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121.90
117.33
115.29
115.07
112.95
112.73
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.57
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N
N
N
F
4h
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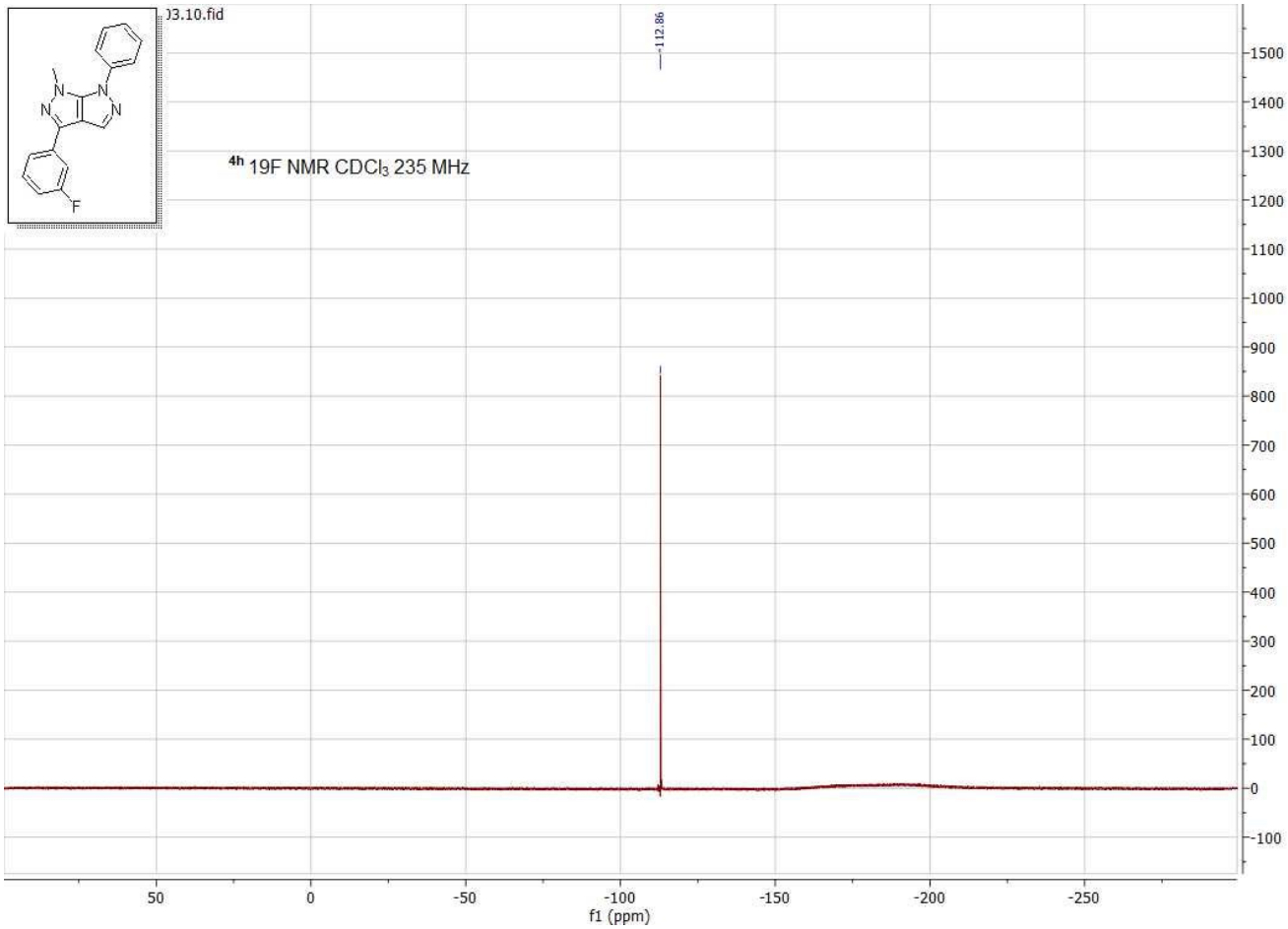
f1 (ppm)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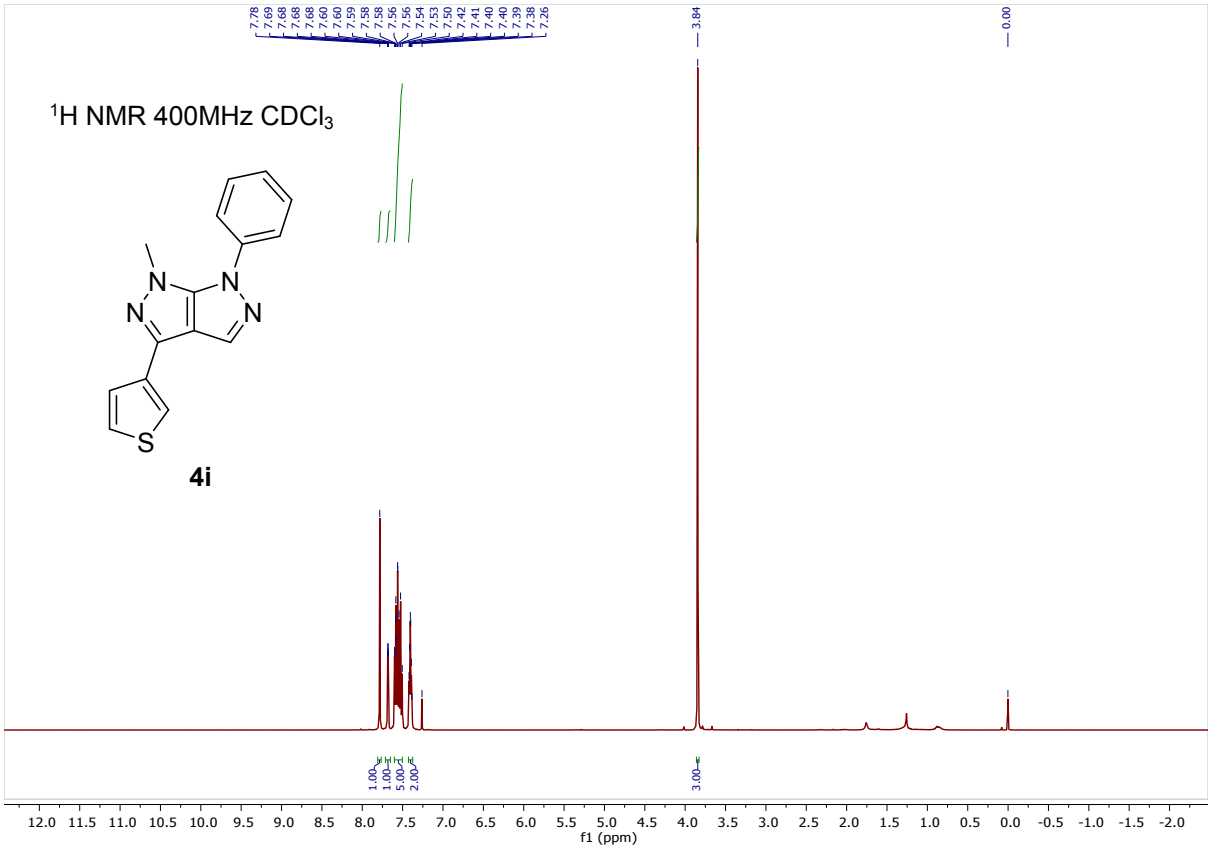
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7.54
7.53
7.50
7.42
7.41
7.40
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7.26
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5.00
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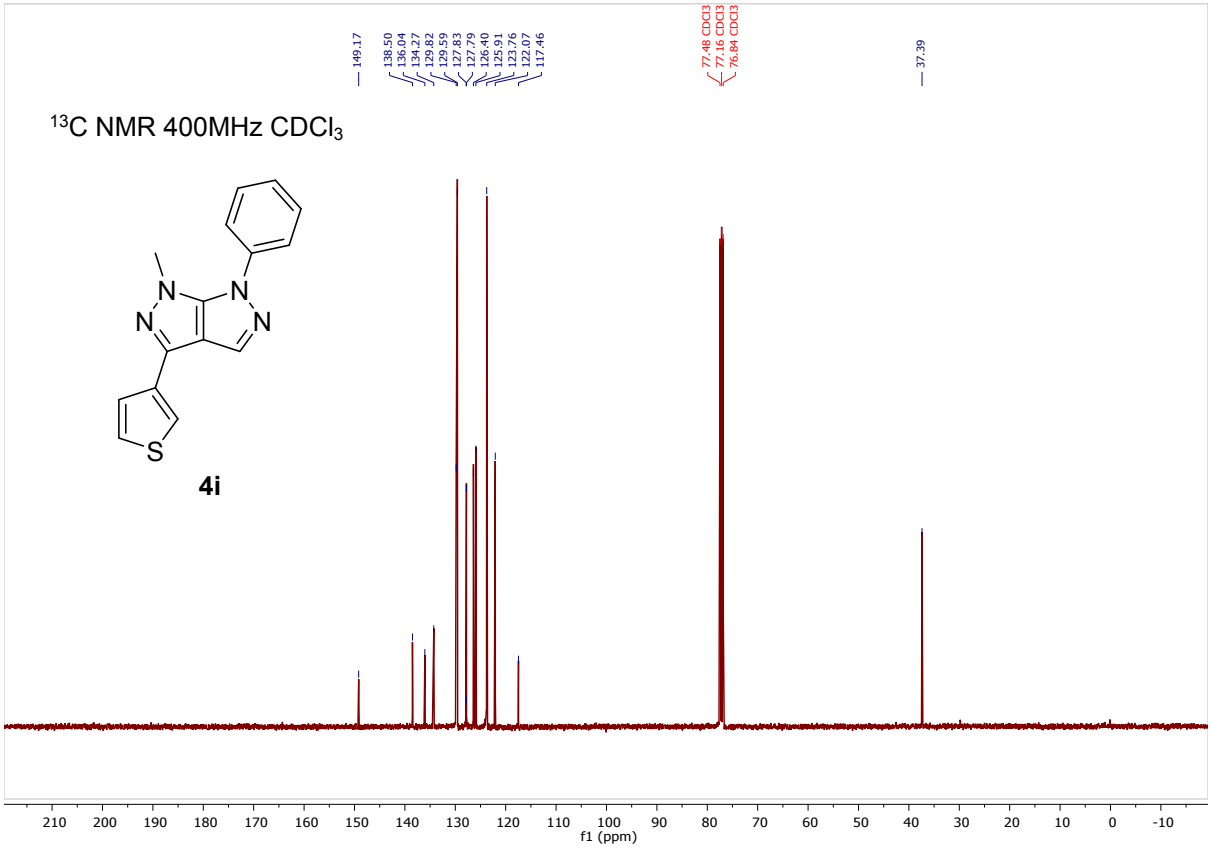
3.00
f1 (ppm)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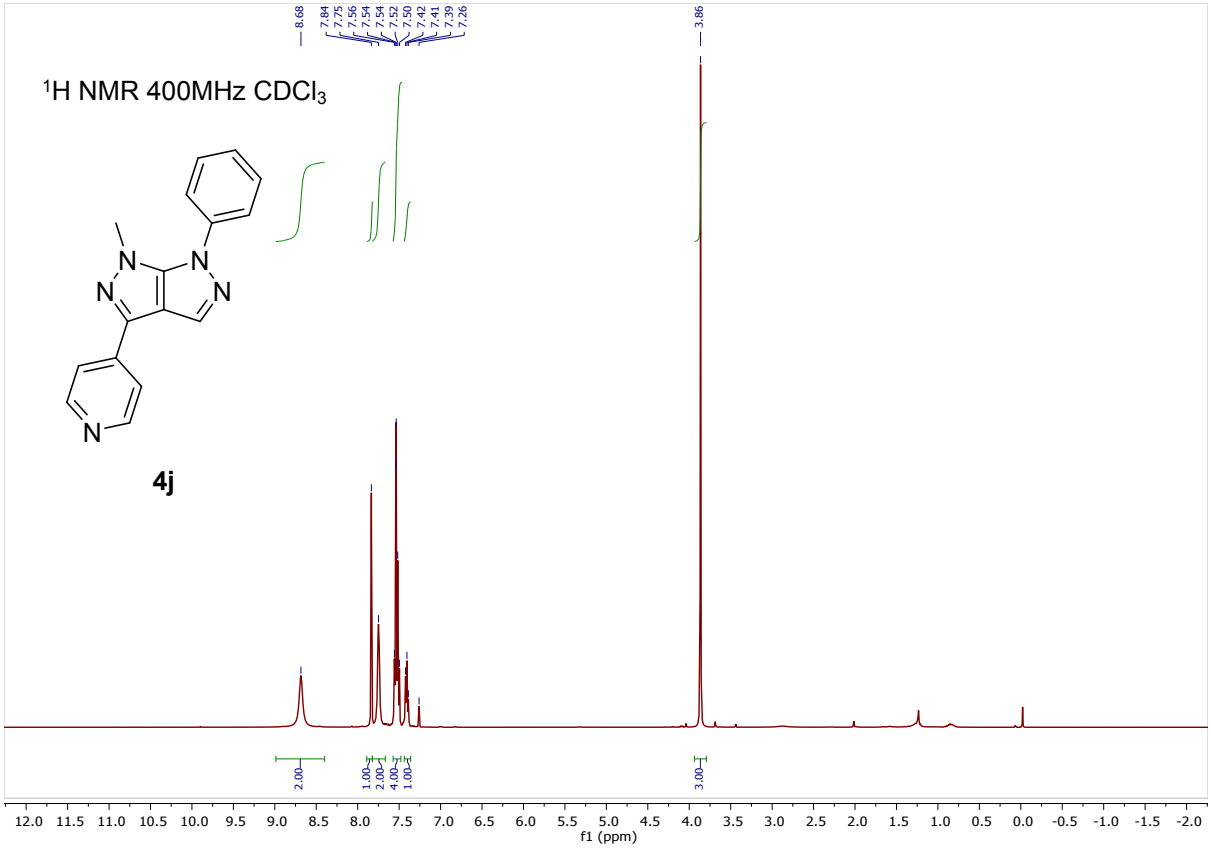
37.39
13C NMR 400MHz CDCl3
4i
f1 (ppm)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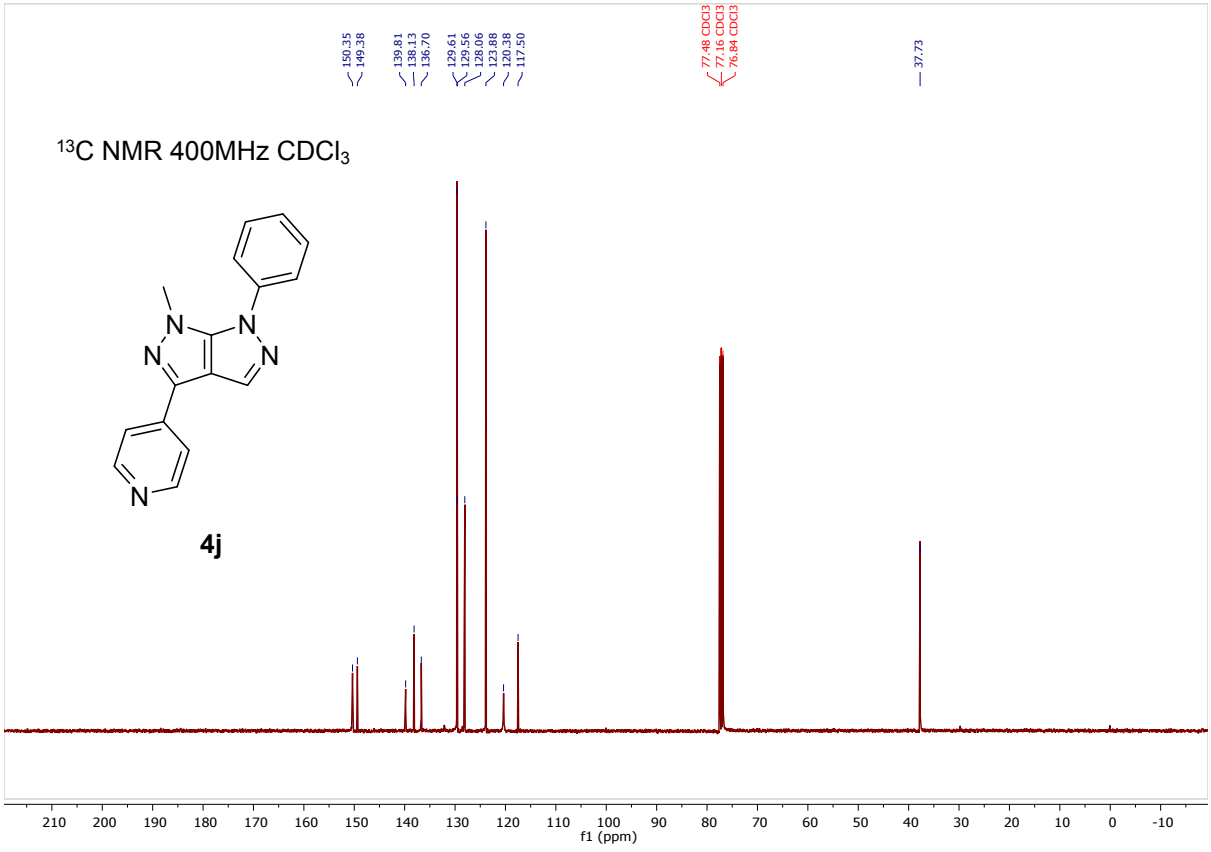
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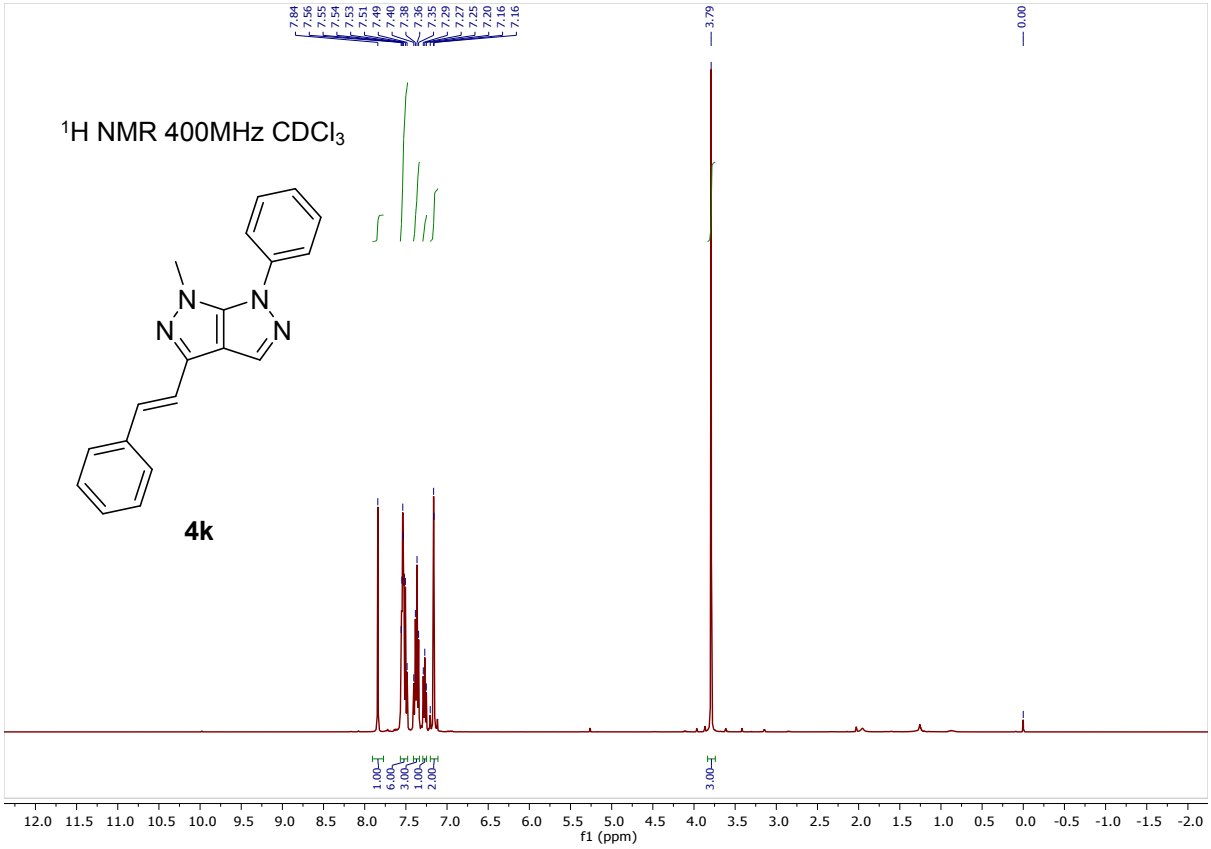
f1 (ppm)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7.25
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7.16
7.16
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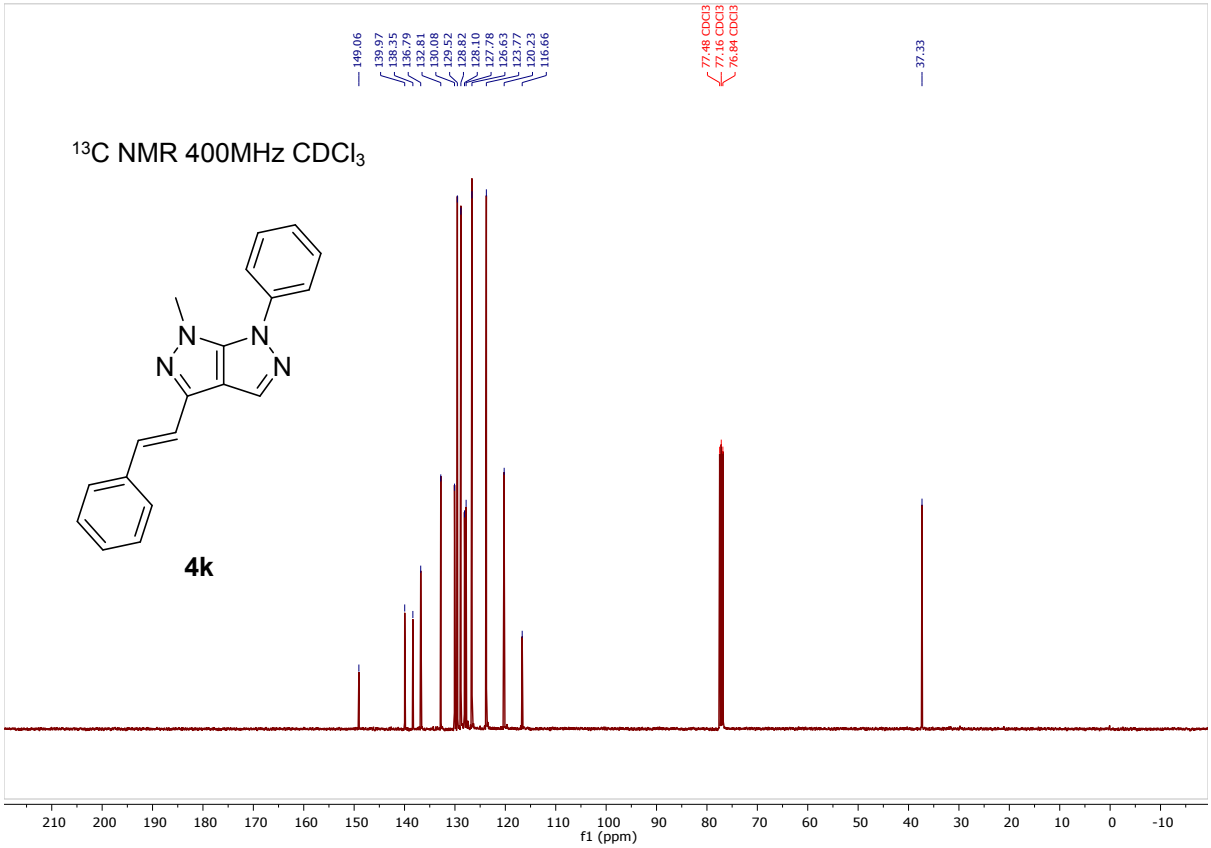
3.00
f1 (ppm)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37.33
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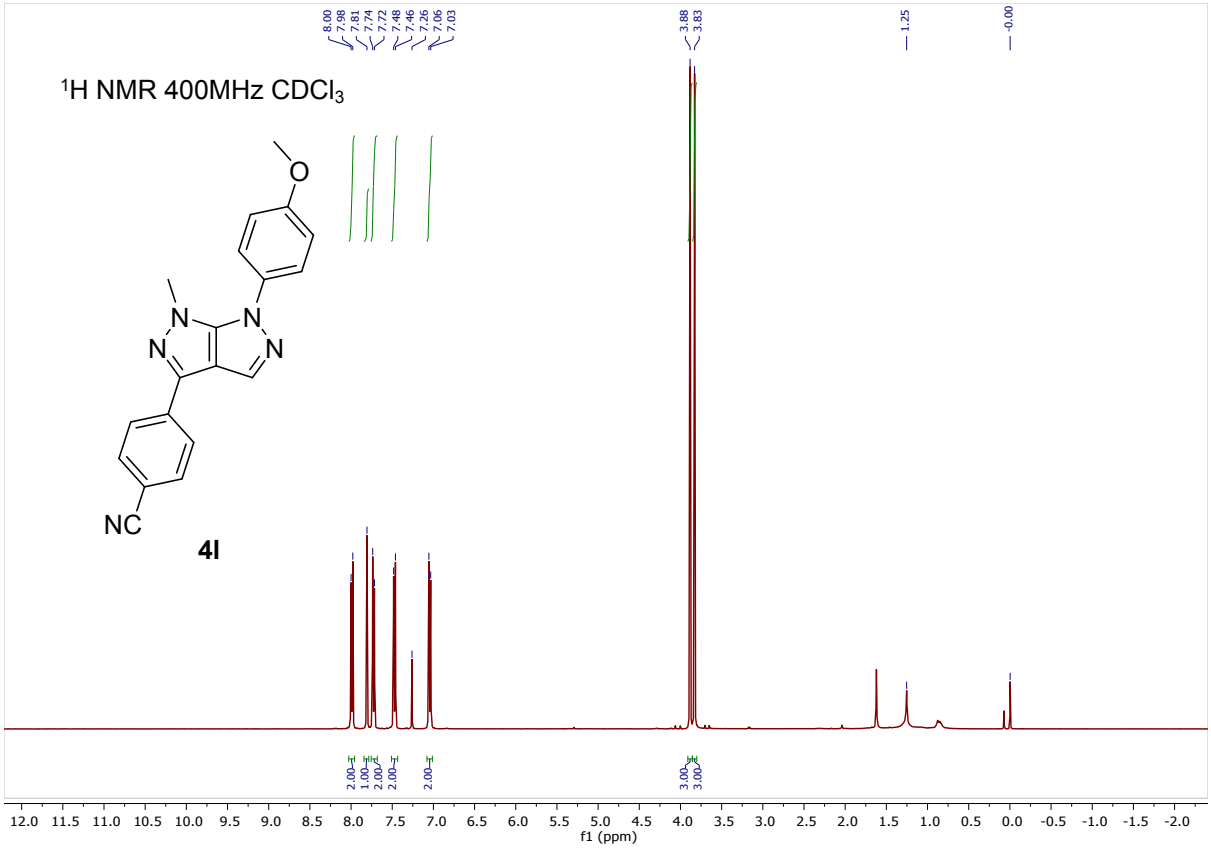
4k
f1 (ppm)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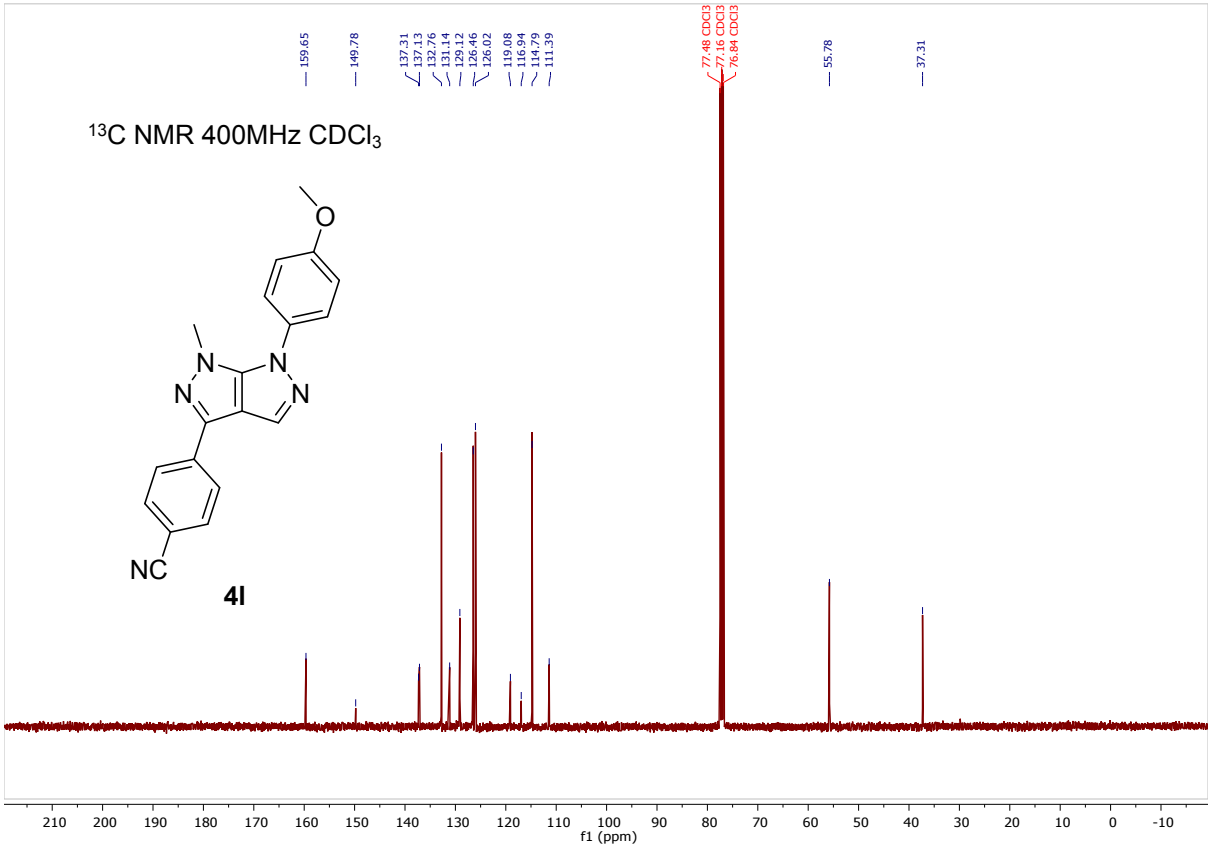
4l
f1 (ppm)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111.39
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
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37.31
13C NMR 400MHz CDCl3
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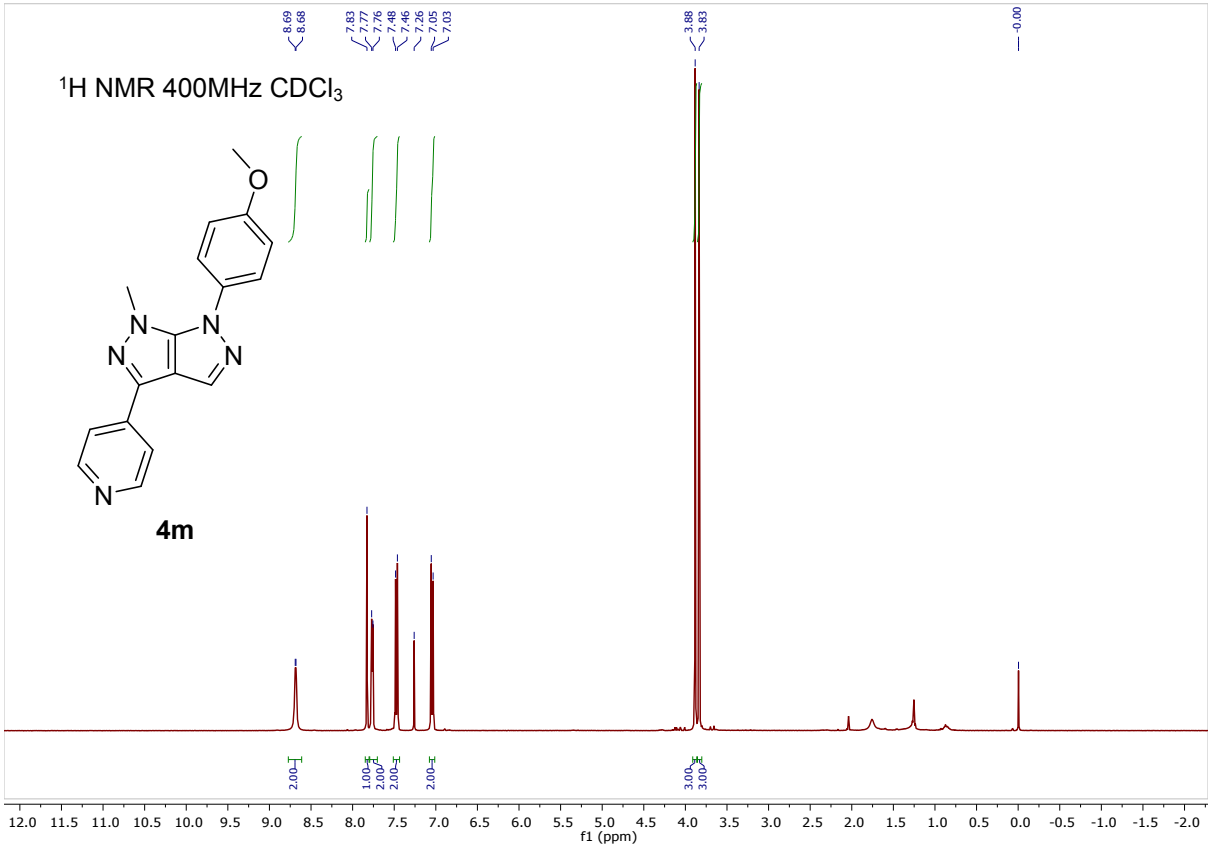
f1 (ppm)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3.88
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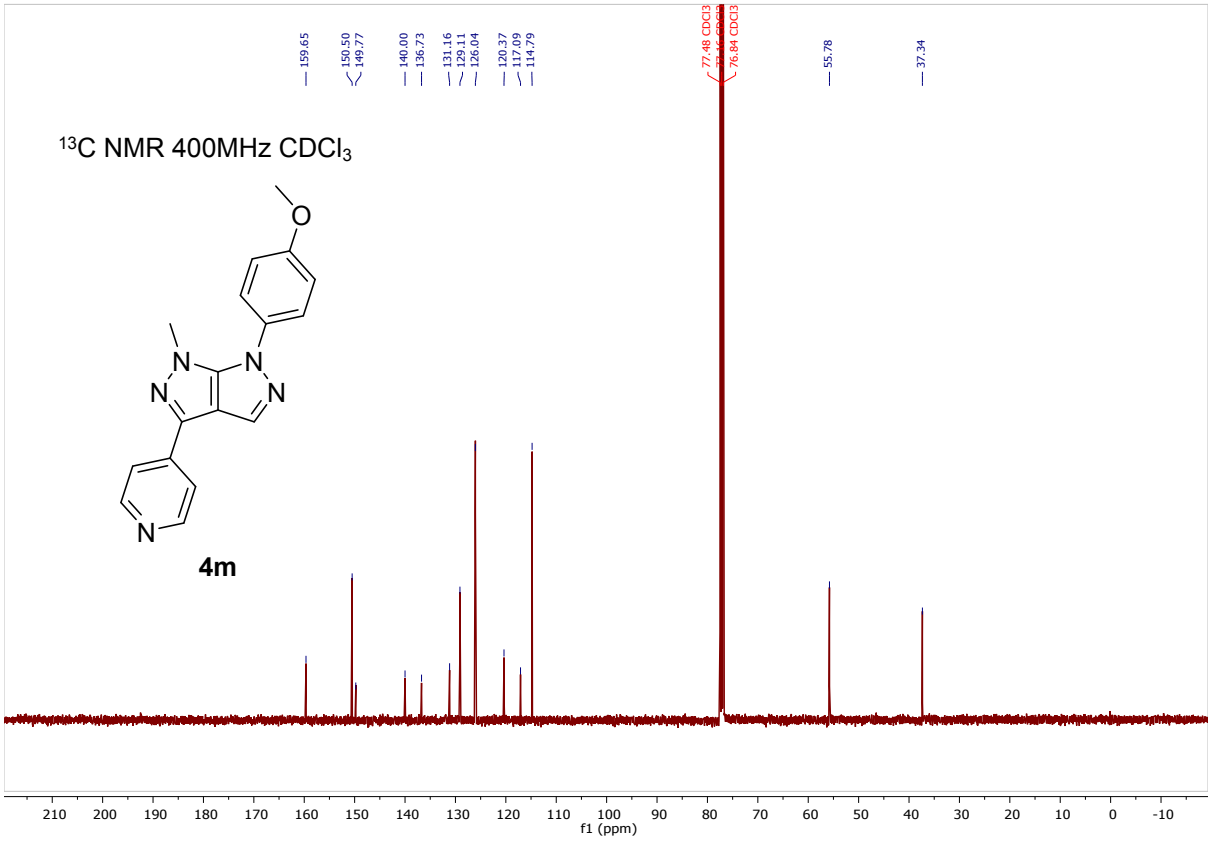
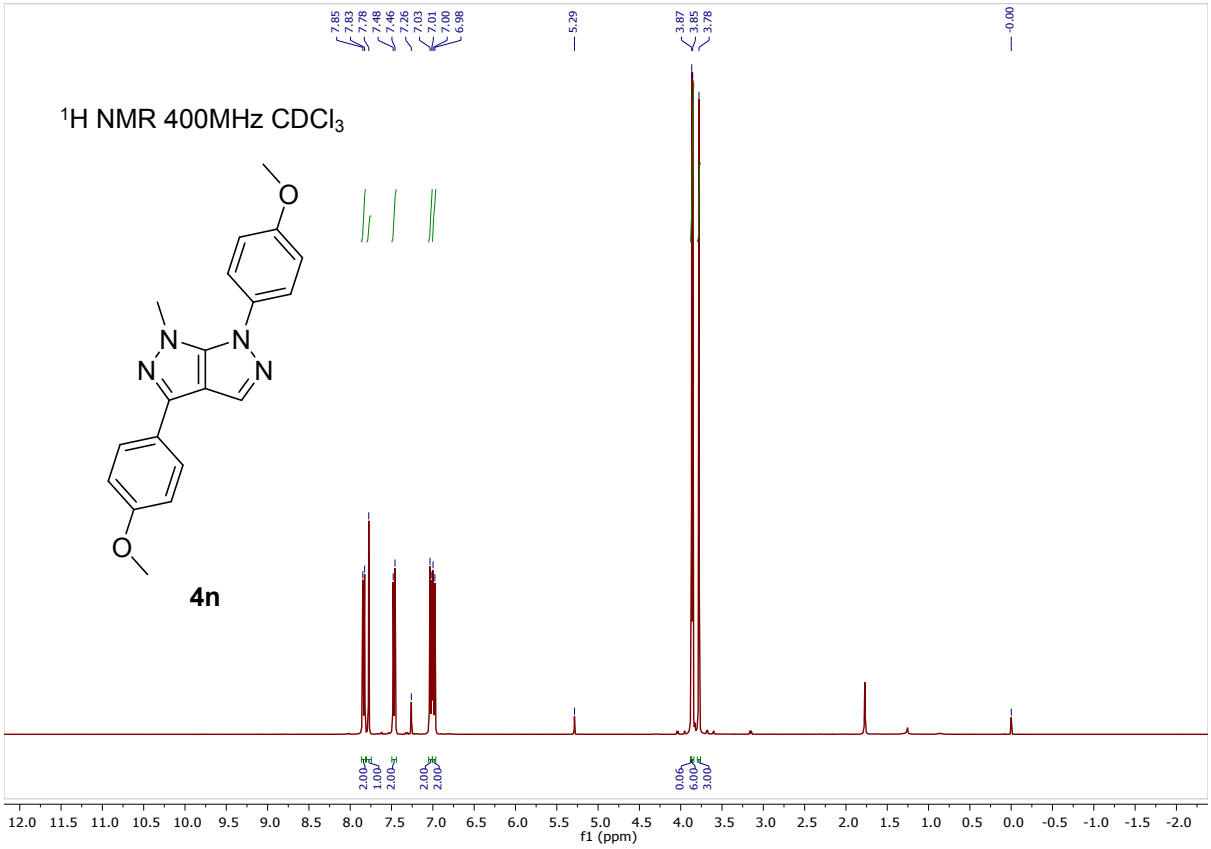
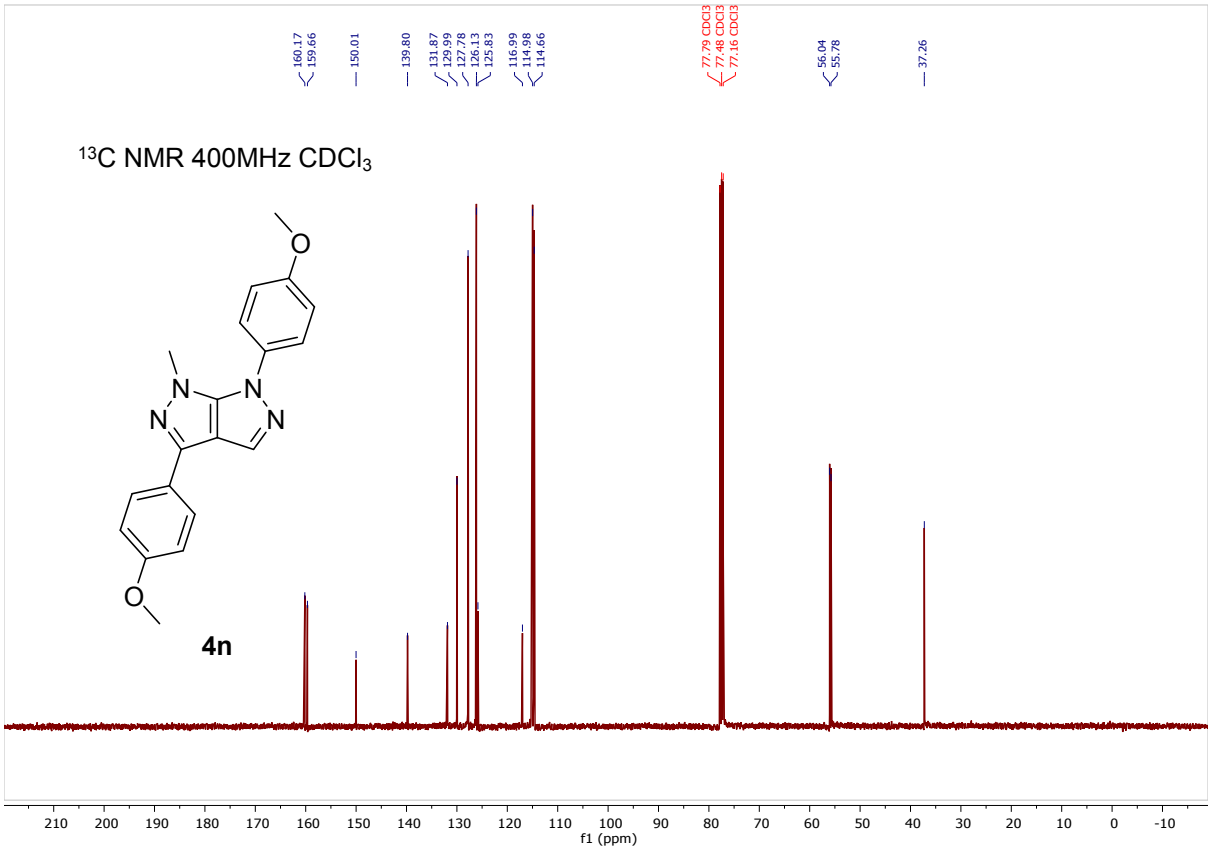
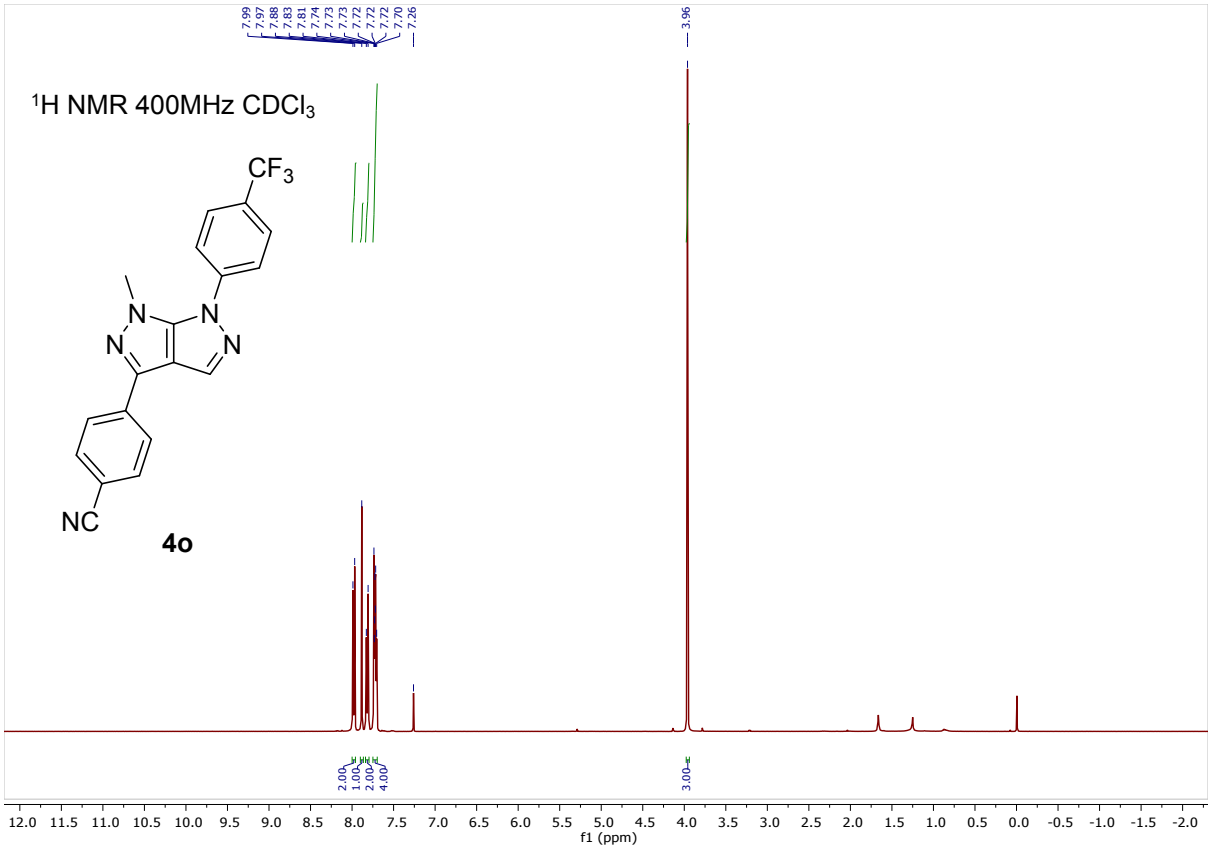
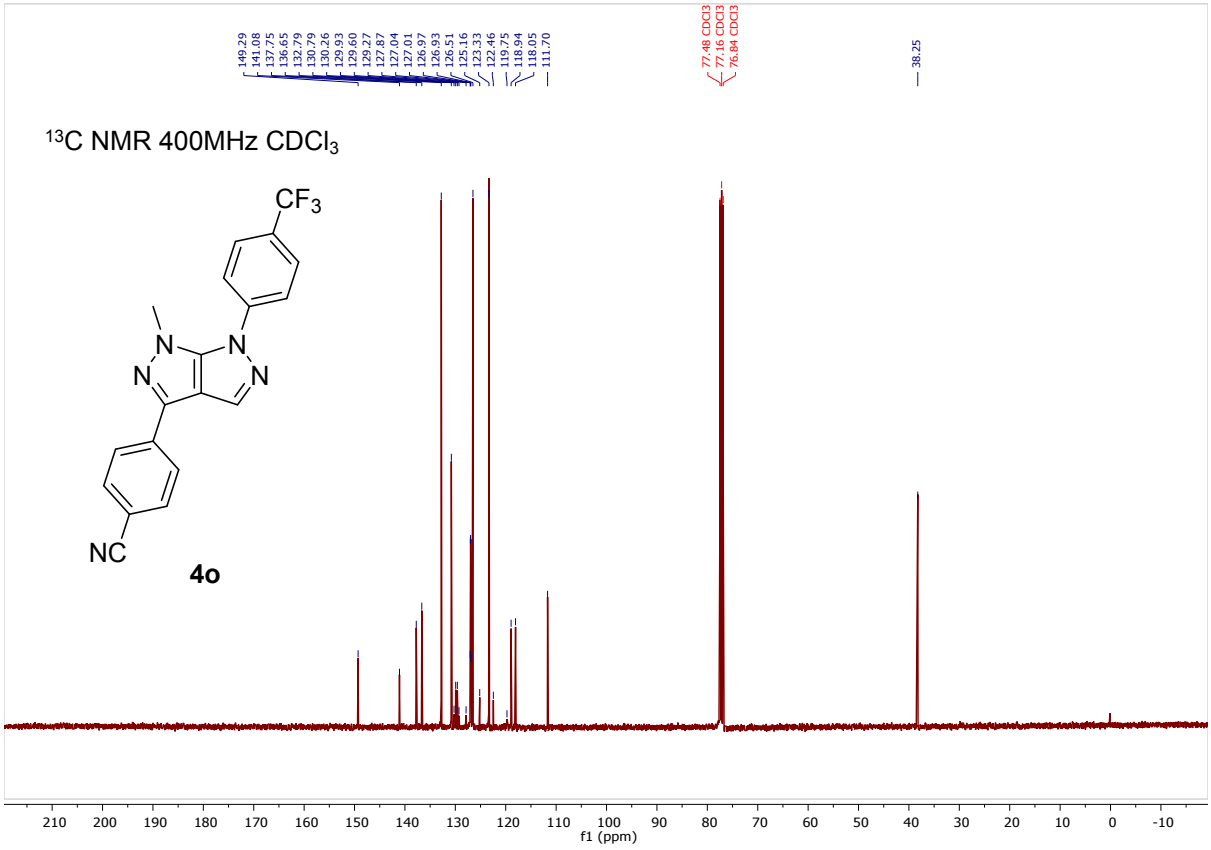
-0.00
1H NMR 400MHz CDCl3
O
N
N
N
N
N
4m
2.00
1.00
2.00
2.00
2.00
3.00
3.00
f1 (ppm)

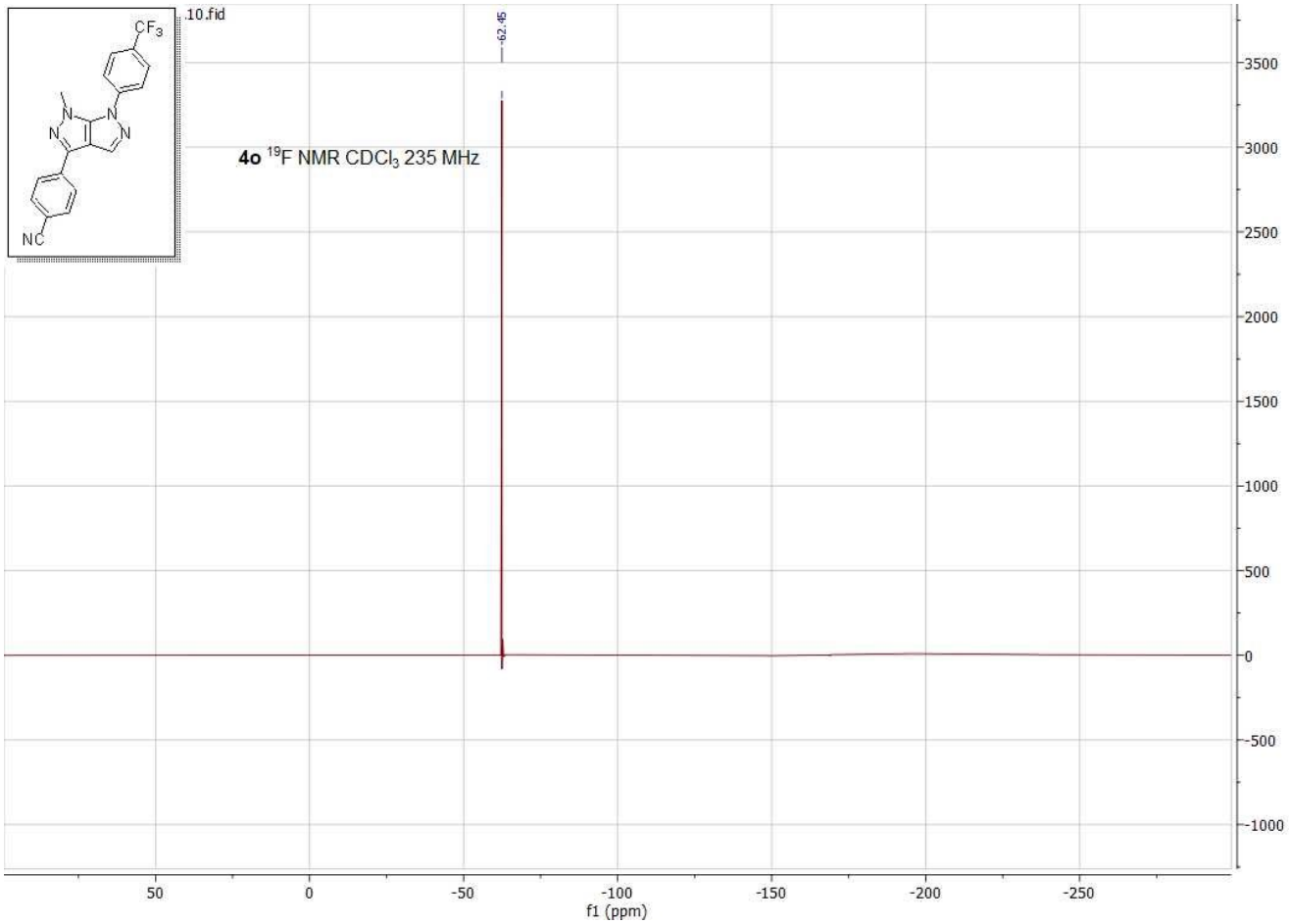

159.65
150.50
149.77
140.00
136.73
131.16
129.11
126.04
120.37
117.09
114.79
77.48 CDCl3
76.84 CDCl3
55.78
37.34
13C NMR 400MHz CDCl3
4m
f1 (ppm)

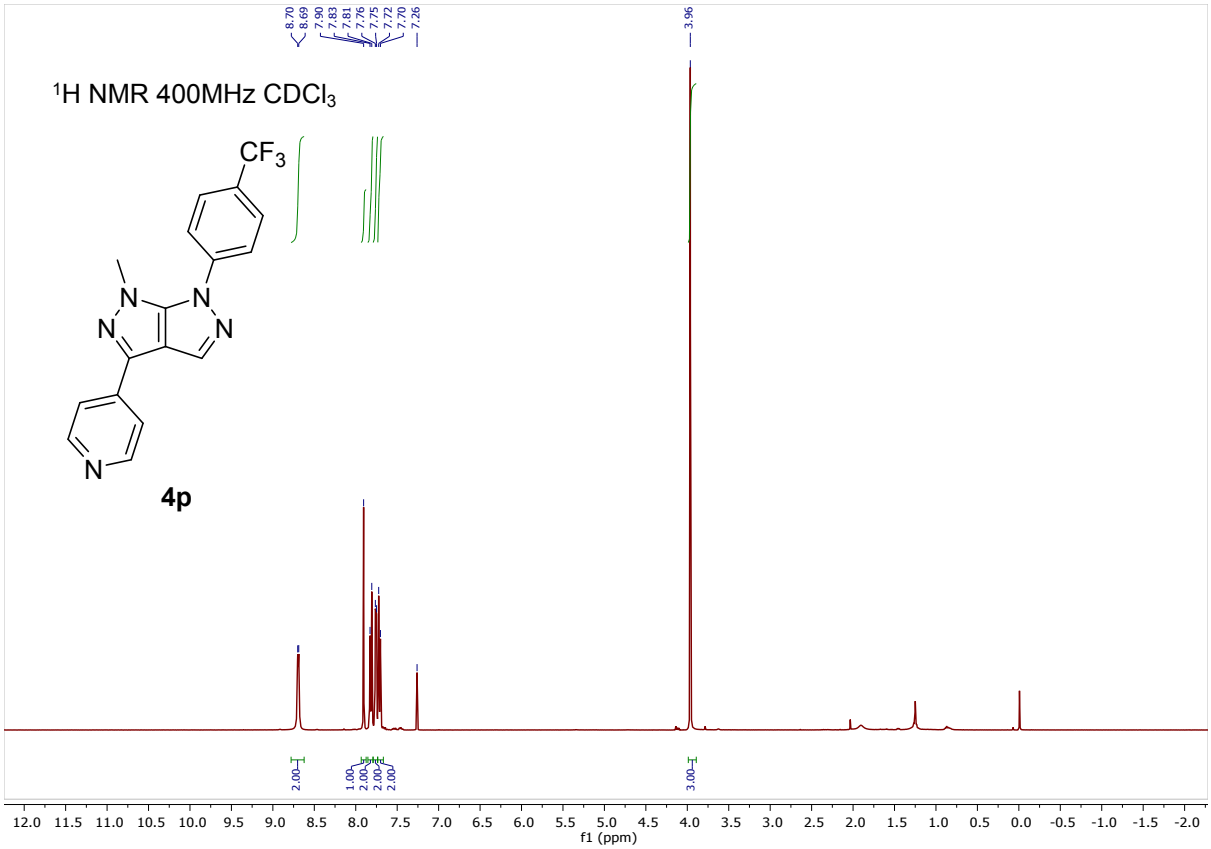

7.85
7.83
7.78
7.48
7.46
7.26
7.03
7.01
7.00
6.98
5.29
3.87
3.85
3.78
-0.00
1H NMR 400MHz CDCl3
4n
f1 (ppm)

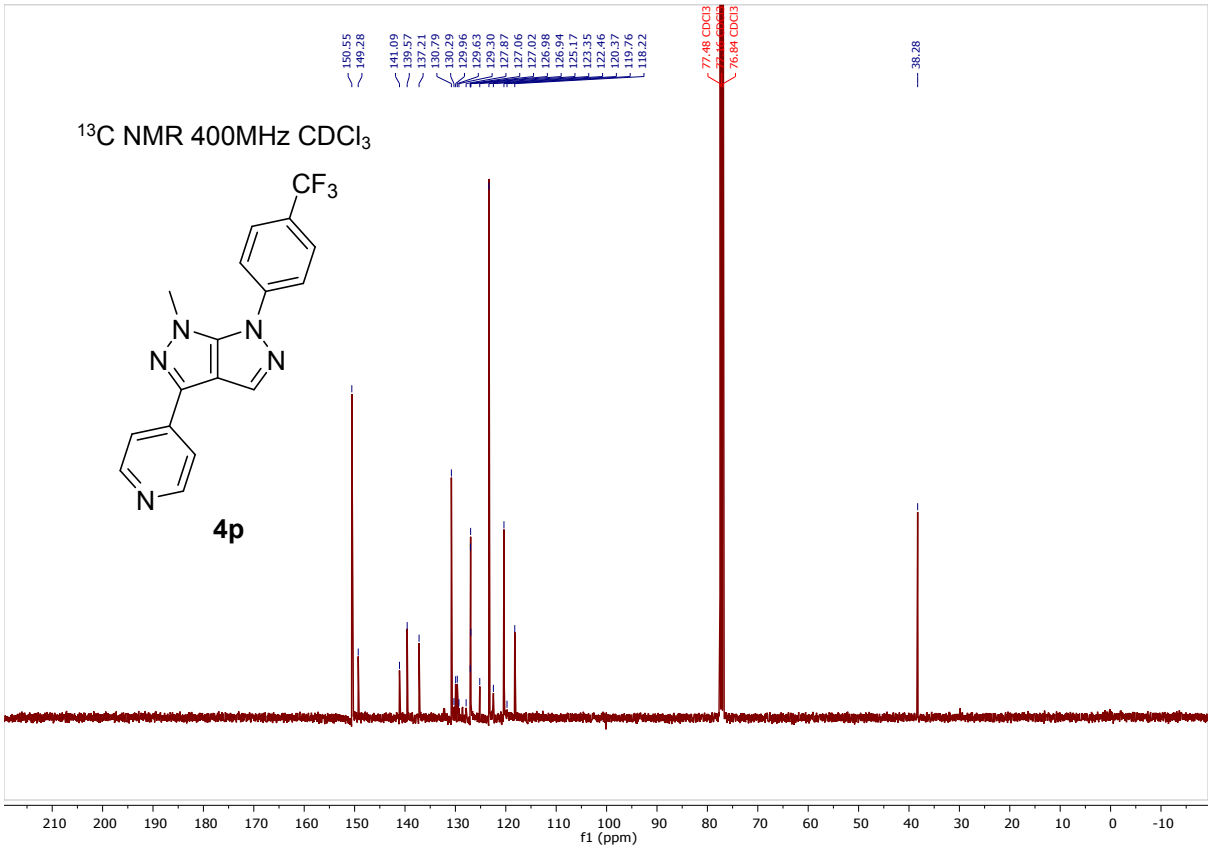

160.17
159.66
150.01
139.80
131.87
129.99
127.78
126.13
125.83
116.99
114.98
114.66
77.79 CDCl3
77.48 CDCl3
77.16 CDCl3
56.04
55.78
37.26
13C NMR 400MHz CDCl3
O
N
N
N
N
O
4n
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

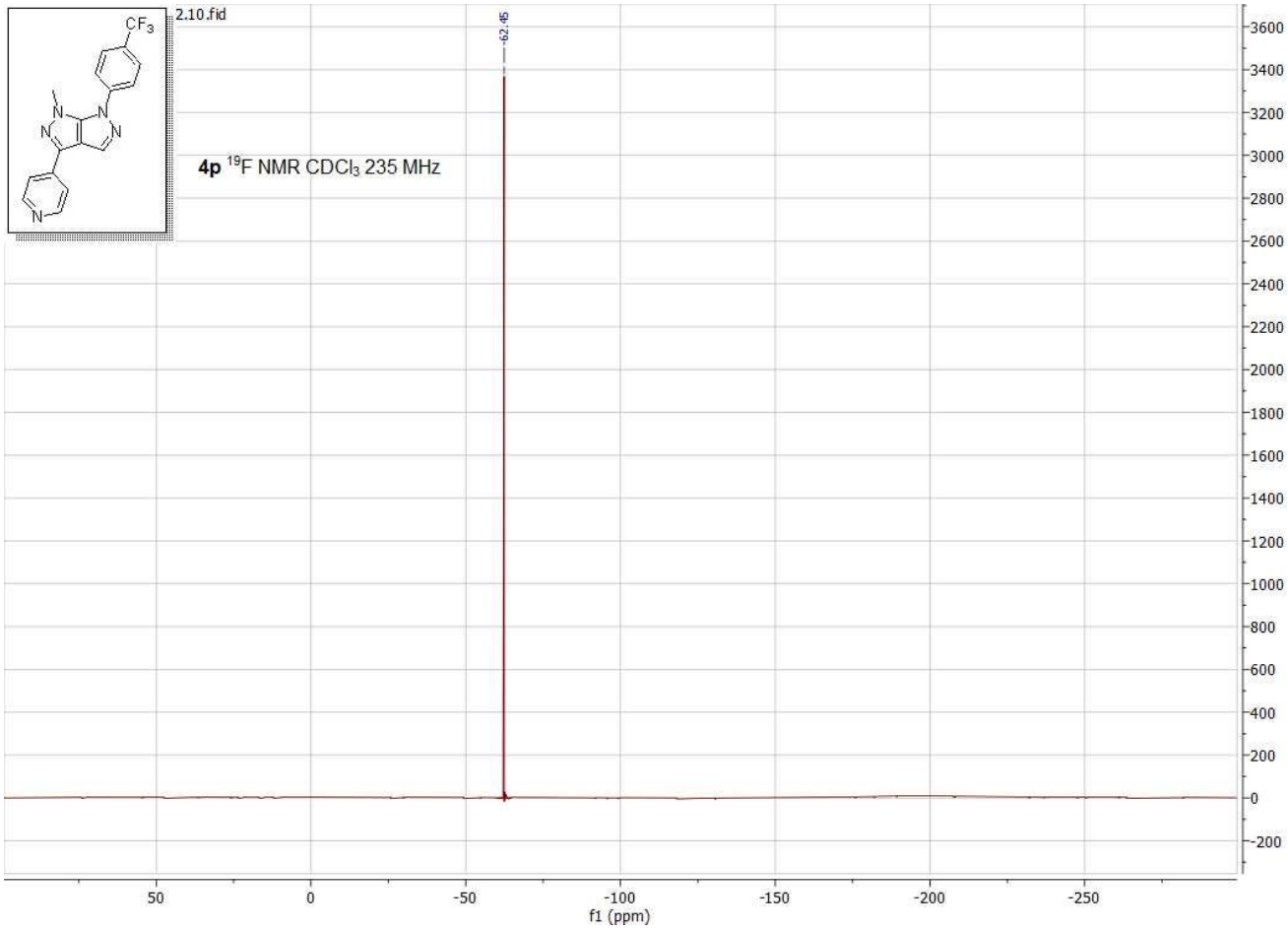

7.99
7.97
7.88
7.83
7.81
7.74
7.73
7.73
7.72
7.72
7.72
7.72
7.70
7.26
3.96
^{1}H NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
NC
4o
2.00
1.00
2.00
4.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

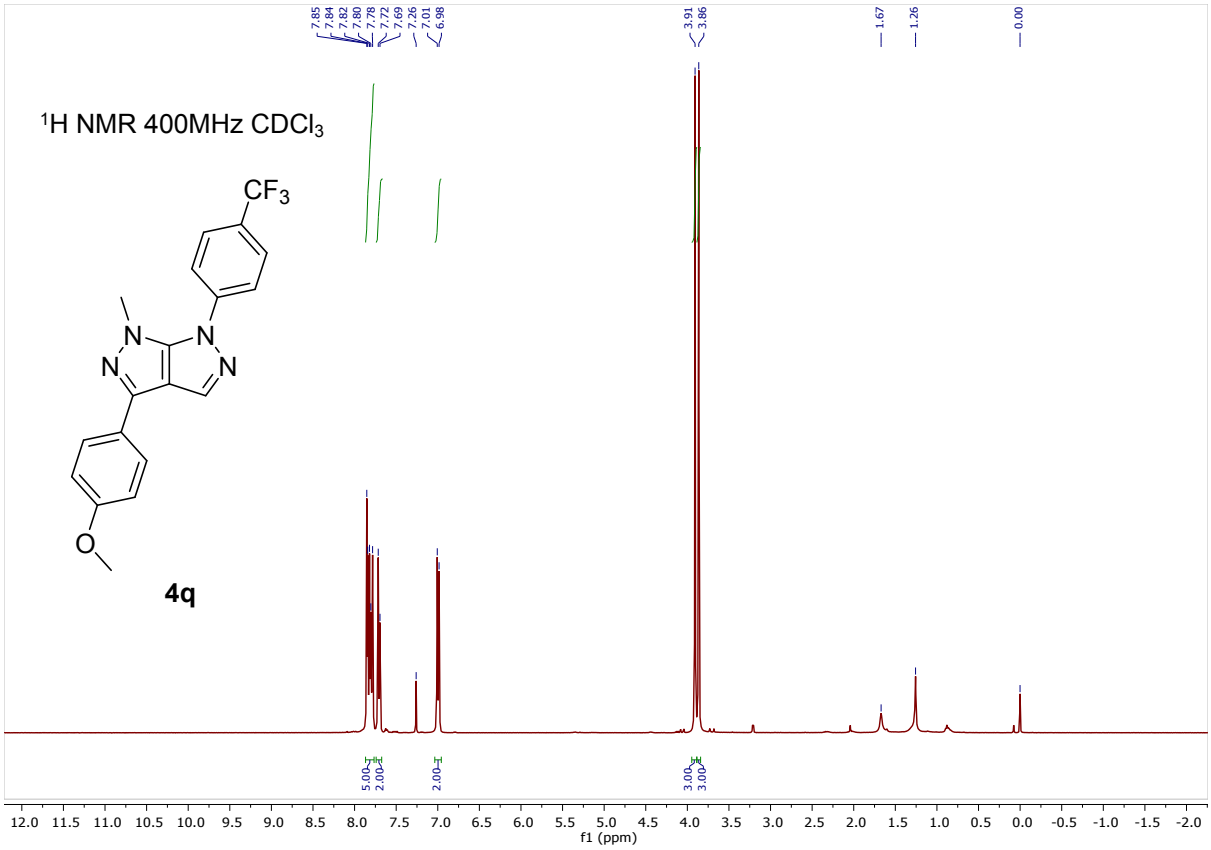

149.29
141.08
137.75
136.65
132.79
130.79
130.26
129.93
129.60
129.27
127.87
127.04
127.01
126.97
126.93
126.51
125.16
123.33
122.46
119.75
118.94
118.05
111.70
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
38.25
^{13}C NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
NC
4o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

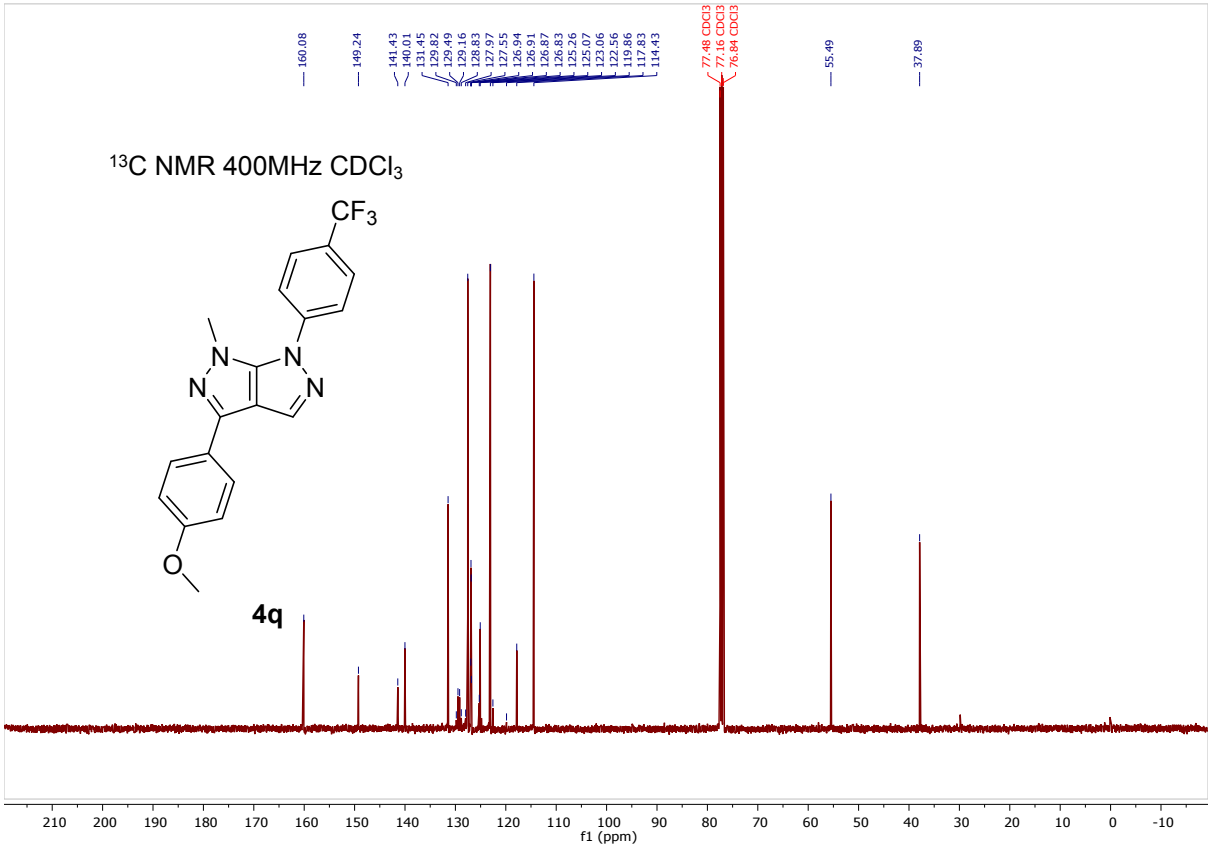

10.fid
CF3
NC
4o 19F NMR CDCl3 235 MHz
-62.45
f1 (ppm)

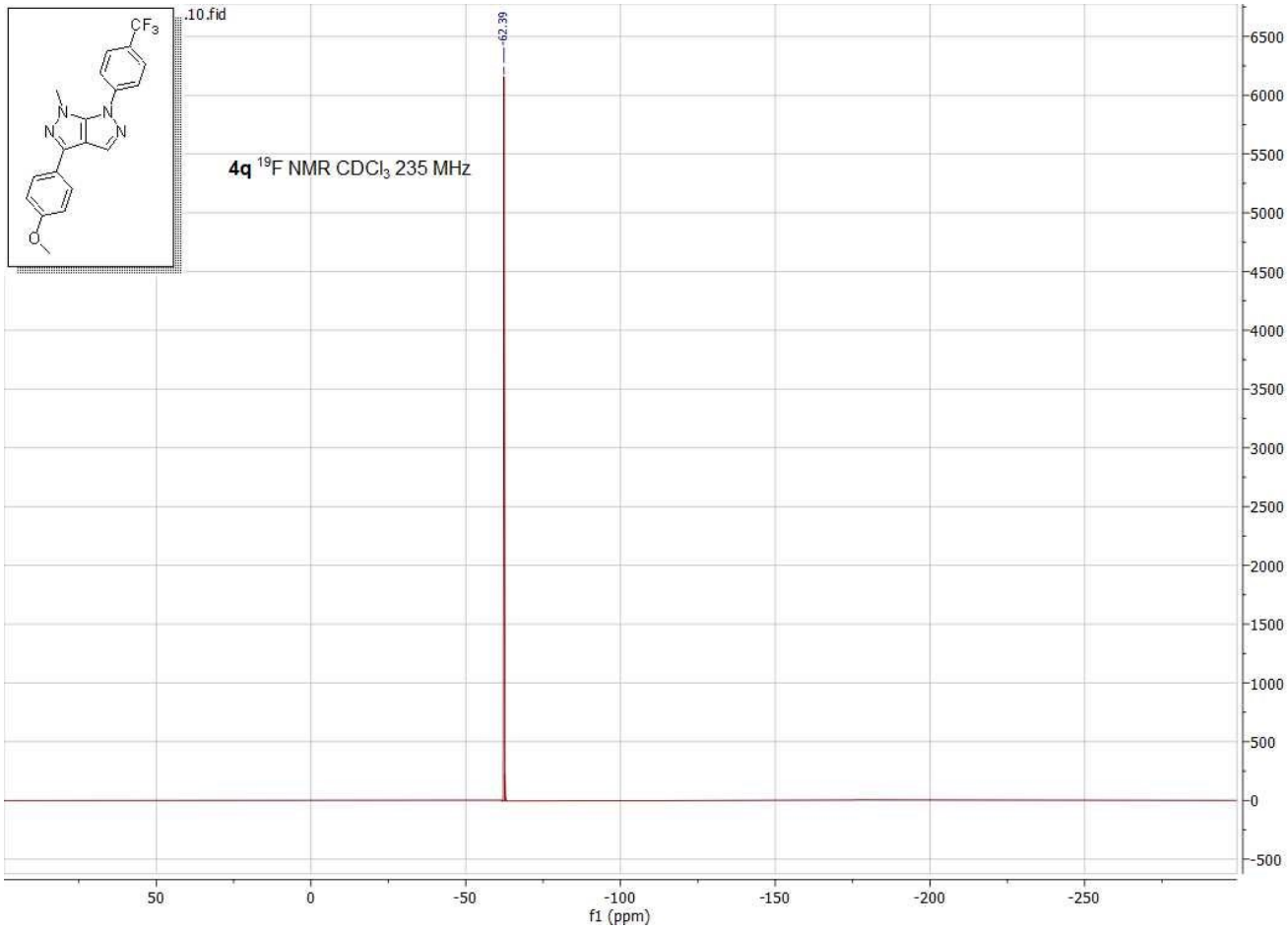

1H NMR 400MHz CDCl3
CF3
N
N
N
N
N
4p
8.70
8.69
7.90
7.83
7.81
7.76
7.75
7.72
7.70
7.26
3.96
2.00
1.00
2.00
2.00
2.00
3.00
f1 (ppm)

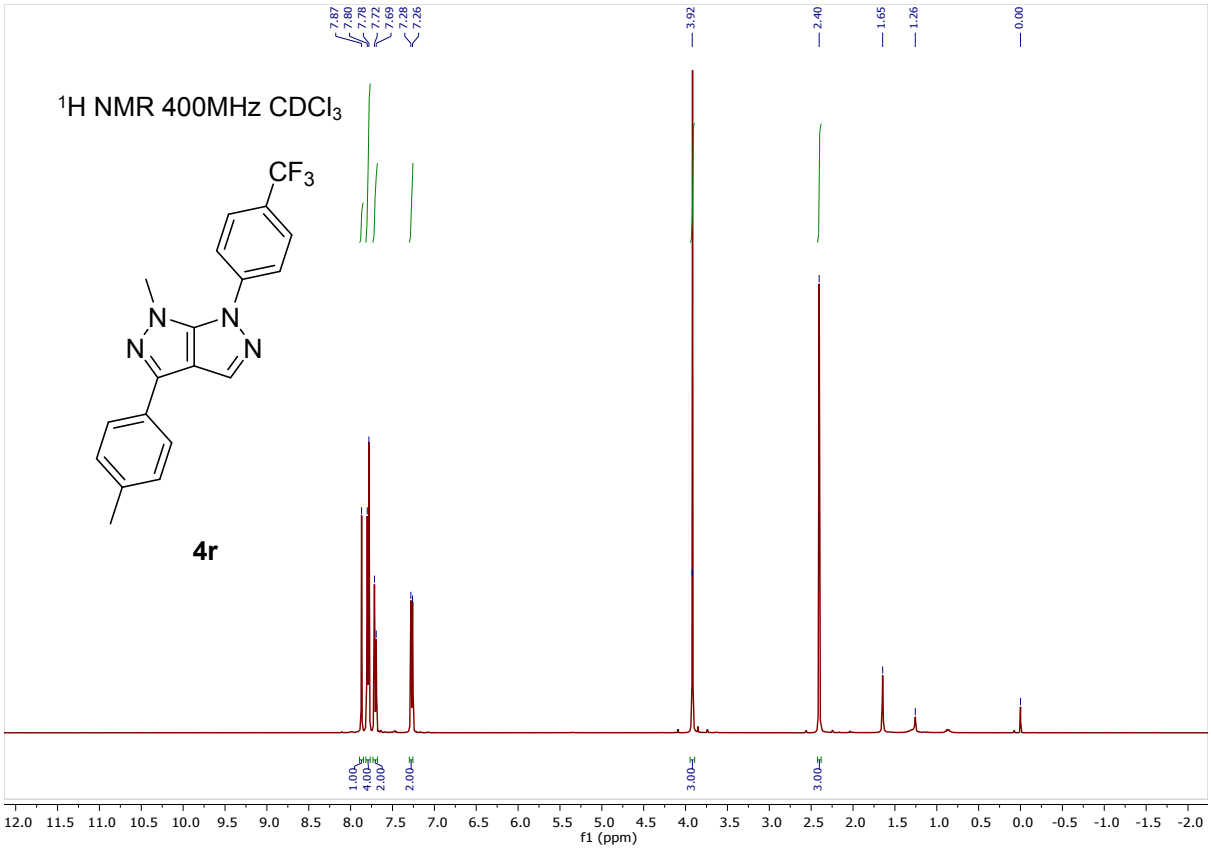

150.55
149.28
141.09
139.57
137.21
130.79
130.29
129.96
129.63
129.30
127.87
127.06
127.02
126.98
126.94
125.17
123.35
122.46
120.37
119.76
118.22
77.48 CDCl3
76.84 CDCl3
38.28
13C NMR 400MHz CDCl3
CF3
N
N
N
N
N
4p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

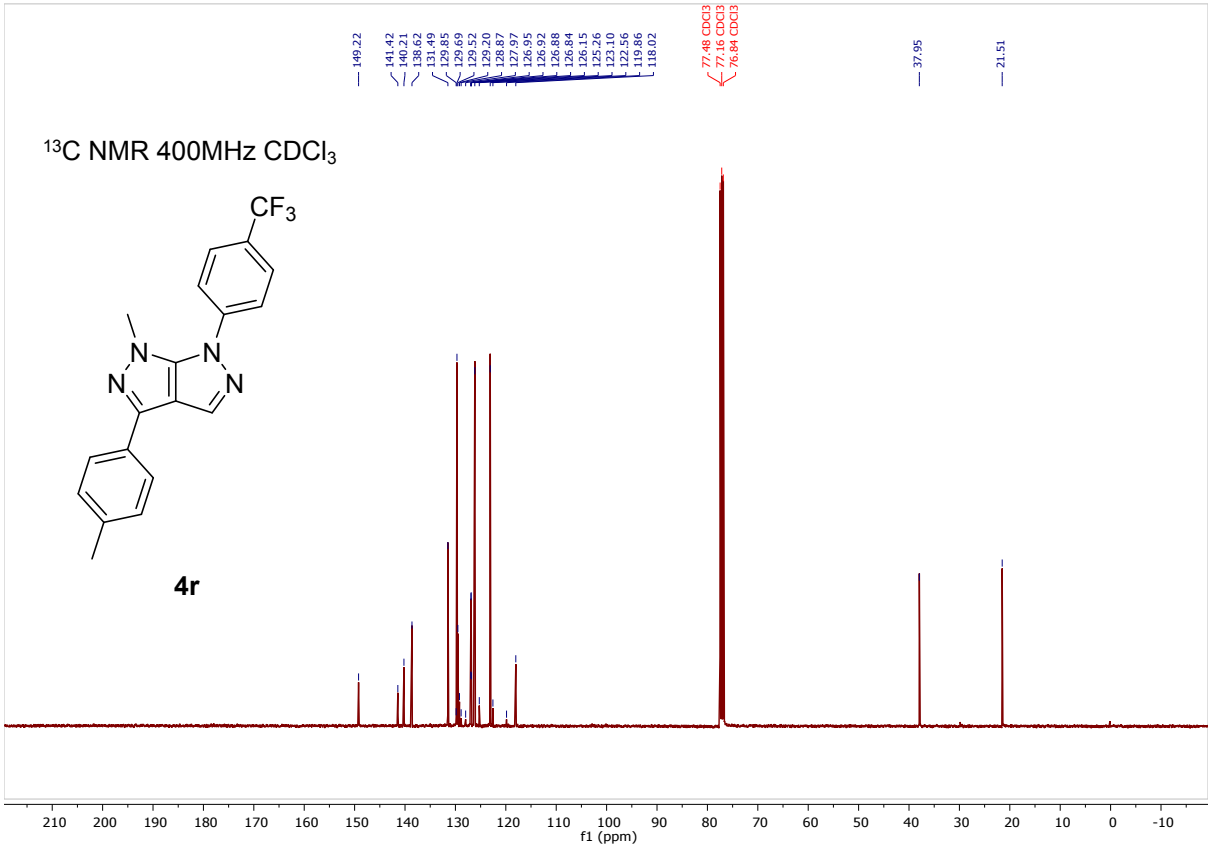

2.10.fid
-62.45
4p ^{19}F NMR $CDCl_3$ 235 MHz
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
50
0
-50
-100
-150
-200
-250
f1 (ppm)

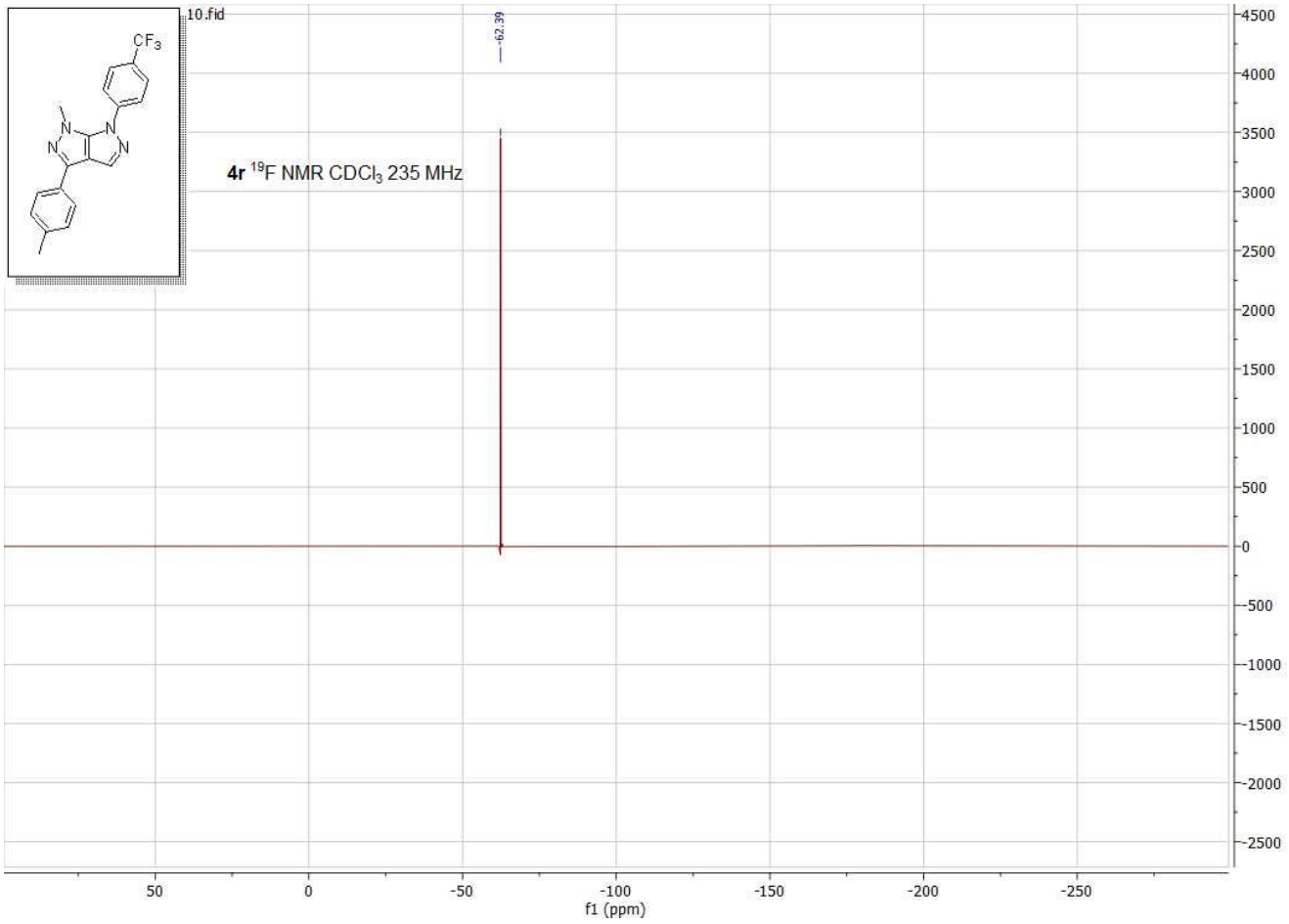

7.85
7.84
7.82
7.80
7.78
7.72
7.69
7.26
7.01
6.98
3.91
3.86
1.67
1.26
0.00
^{1}H NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
O
4q
5.00
2.00
2.00
3.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


160.08
149.24
141.43
140.01
131.45
129.82
129.49
129.16
128.83
127.97
127.55
126.94
126.91
126.87
126.83
125.26
125.07
123.06
122.56
119.86
117.83
114.43
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.49
37.89
^{13}C NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
O
4q
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


.10.fid
62.39
4q ^{19}F NMR $CDCl_3$ 235 MHz
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
50
0
-50
-100
-150
-200
-250
f1 (ppm)


7.87
7.80
7.78
7.72
7.69
7.28
7.26
3.92
2.40
1.65
1.26
0.00
^{1}H NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
4r
1.00
4.00
2.00
2.00
3.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


149.22
141.42
140.21
138.62
131.49
129.85
129.69
129.52
129.20
128.87
127.97
126.95
126.92
126.88
126.84
126.15
125.26
123.10
122.56
119.86
118.02
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
37.95
21.51
^{13}C NMR 400MHz $CDCl_3$
CF_3
N
N
N
N
4r
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


10.fid
CF3
N
N
N
N
-62.39
4r 19F NMR CDCl3 235 MHz
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
-1000
-1500
-2000
-2500
50
0
-50
-100
-150
-200
-250
f1 (ppm)