Electronic Supplementary Material (ESI) for ChemComm.

Sequential [3+2] annulation reaction of prop-2-ynylsulfonium salts and hydrazonyl chlorides: synthesis of pyrazoles containing functional motifs

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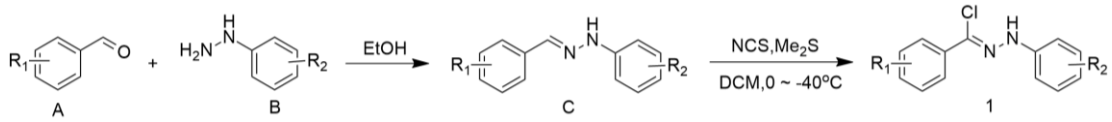
Supporting Information

Contents

1. General information

All the solvents were used from commercially available sources without any purification. White solid, yield referred to isolated compounds, unless noted otherwise. Reactions were monitored by TLC using a UV lamp as a visualizing agent. Low temperature conditions require the use of cryostat. The ^{1}H NMR and ^{13}C NMR spectra were recorded at 400, 500 MHz and 100,125 MHz, respectively, in $CDCl_3$/*d*6-DMSO solutions with shifts referenced to tetramethylsilane (TMS). All *J* values are in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet: t, triplet; q, quartet; m, multiplet. LC-MS equipment was used to record mass spectra for isolated compounds where appropriate.

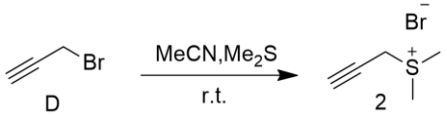
2. General procedure for the synthesis of 1



A (20 mmol) and **B** (20 mmol) were dissolved in 50 mL EtOH and the reaction mixture was stirred at room temperature until consumption of **A** (about need 5-30 min, monitored by TLC,). Then, by concentrating the reaction system under reduced pressure the solid product **C** was obtained.

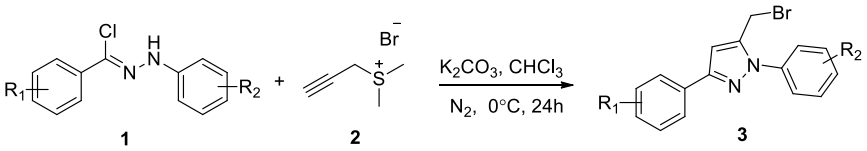
Dissolve NCS (15 mmol) in 100 mL DCM and stir at 0 °C for 5 minutes. A solution of Me_2S (20 mmol) in DCM (20 mL) was added dropwise until the white precipitate suddenly appeared. After stirring for 15 minutes, the reaction mixture was cooled to -40 ℃. Add solution of **C** (10 mmol) in DCM (30 mL) dropwise to the above reaction system. After the addition, react at -40 ℃ for 1 hour and then raise the temperature to 0 ℃. After the reaction is complete, the solvent was evaporated and through column chromatography to obtain the solid **1**.[1]

3. General procedure for the synthesis of 2



D (20 mmol) and Me_2S (40 mmol) were dissolved in 50 mL MeCN and the reaction mixture was stirred at room temperature overnight. The reaction mixture was filtrated and the filter residue was washed with 30 ml petroleum ether and dried under vacuum to obtain **2** as white solid.

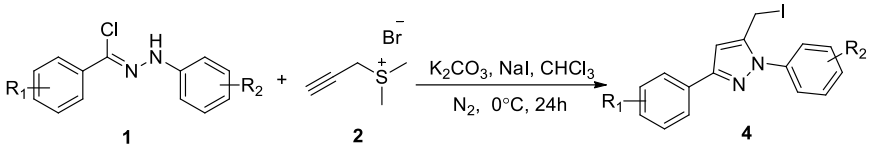
4. General procedure for the synthesis of 3



1 2 3

1 (1 mmol), **2** (2 mmol) and K_2CO_3 (2 mmol) were added in 10 mL $CHCl_3$ under N_2, then the reaction mixture was stirred at 0 ℃ for 24 h. After the completion of the reaction, the reaction mixture was filtrated. The filtrate was concentrated and purified by flash column chromatography (petroleum ether: ethyl acetate = 80:1) to obtain the product **3**.

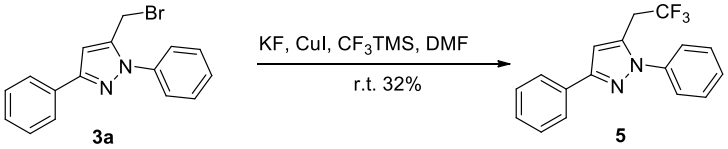
5. General procedure for the synthesis of 4



1 2 4

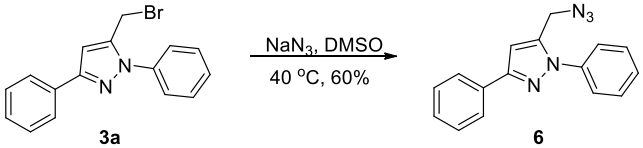
1 (1 mmol), **2** (2 mmol), NaI (5.0 eq) and K_2CO_3 (2 mmol) were added in 10 mL $CHCl_3$ under N_2, then the reaction mixture was stirred at 0 ℃ for 24 h. After the completion of the reaction, the reaction mixture was filtrated. The filtrate was concentrated and purified by flash column chromatography (petroleum ether: ethyl acetate = 80:1) to obtain the product **4**.

6. Synthesis of 5, 6, 7, 8, 9



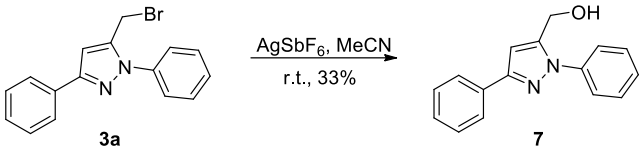
3a 5

3a (0.3 mmol), KF (0.6 mmol), CuI (0.45 mmol) and Trifluoromethyltrimethylsilane (0.6 mmol) were dissolved in DMF (2 mL). Reaction mixture was stirred at room temperature for 12 h. Then concentrate the reaction mixture and obtain **5** by column chromatography (petroleum ether: ethyl acetate = 50:1)[2].

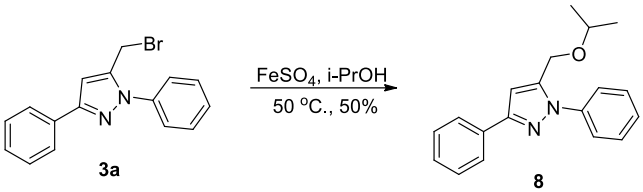


3a 6

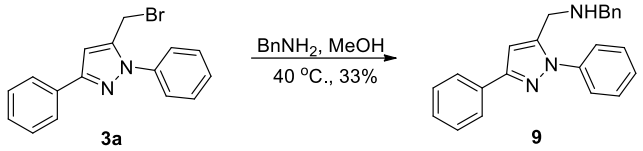
Dissolve **3a** (0.3 mmol) in 2 mL DMSO, NaN_3 (0.33 mmol) was added, then the reaction mixture was stirred at room temperature for 12h. After completion of the reaction as monitored by TLC, the reaction mixture was extracted by DCM. The DCM layer was concentrated and purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the **6**[3].



$AgSbF_6$ (0.5 mmol) was added to the solution of **3a** in CH_3CN (2 mL) and the reaction mixture was stirred at room temperature for 12h. After completion of the reaction as monitored by TLC, the reaction mixture was filtered and the filtrate was concentrated. Then the concentrate was purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the **7**[4].



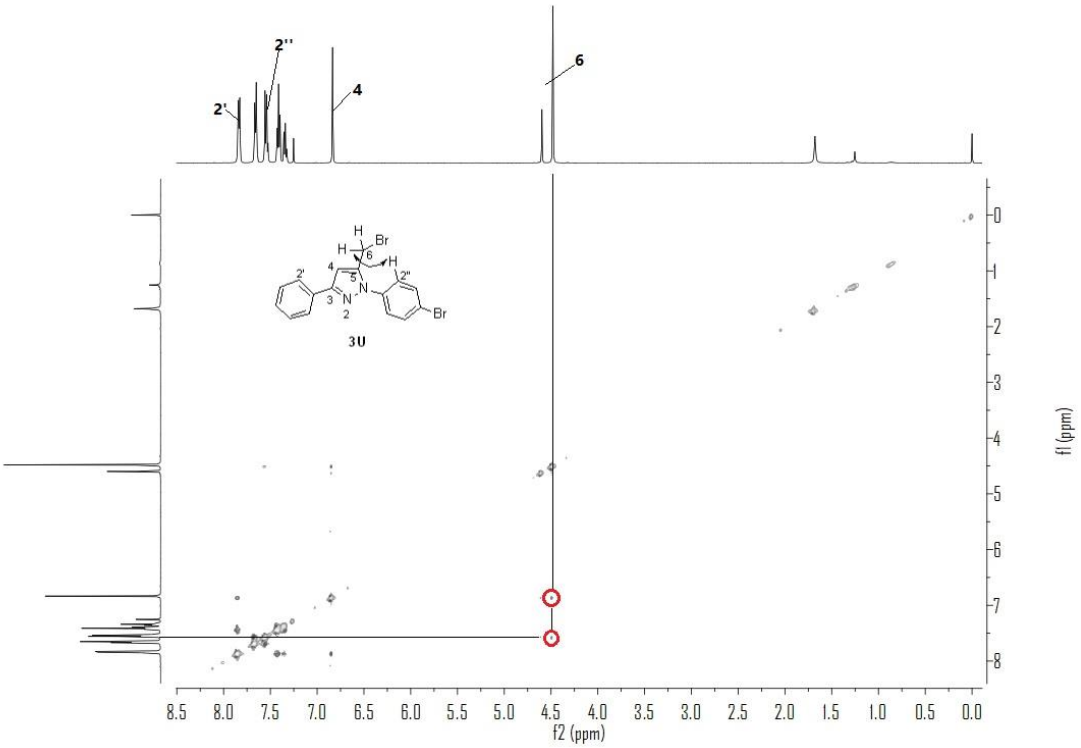
Isopropanol (1mL) was added to the mixture of **3a**(0.3 mmol) and $FeSO_4$ (0.3 mmol). Reaction mixture was stirred at 50 ℃ for 4h. After the completion of the reaction, the mixture was filtered. The filtrates was concentrated and the residue was purified by column chromatography (petroleum ether: ethyl acetate = 50:1) to obtain the **8**[5].



3a (0.3 mmol) and benzylamine (0.3 mmol) were dissolved in CH_3OH (2 mL). Reaction mixture was stirred at 40 ℃ for 4h. Then concentrate the reaction mixture and obtain **9** by column chromatography (petroleum ether: ethyl acetate = 50:1)[6].

7. The structure of 3u (NOESY)

According to the chemical shifts and the coupling constants in ^1H NMR spectra, the signals of the key H-6, H-4, H-2' and H-2'' can be identify. Then as shown in NOESY of **3u**, there are no correlations between H-6 and H-2' which indicated that the structure can not be **3u'**. Instead, we can find that there have correlations of H-6 with H-2'' and H-4. Therefore, the structure of product should be **3u**.



8. References

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2. Ribeiro, C. J. A.; Nunes, R. C.; Amaral, J. D.; Goncalves, L. M.; Rodrigues, C. M. P.; Moreira, R.; Santos, M. M. M., Spirotriazoline oxindoles: A novel chemical scaffold with in vitro anticancer properties. European Journal of Medicinal Chemistry 2017, 140, 494-509.

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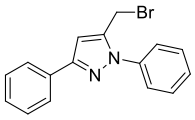
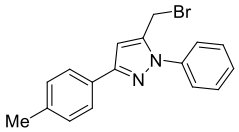
9. Analytical Data



5-(bromomethyl)-1,3-diphenyl-1*H*-pyrazole (3a)

White solid, yield: 65%, melting point: 95.3~96.2 ºC.

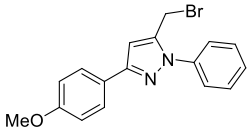
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, J = 7.2, 1.6 Hz, 2H), 7.67-7.63 (m, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 6.85 (s, 1H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 140.3, 139.3, 132.8, 129.6, 128.9, 128.8, 128.4, 126.0, 125.5, 106.2, 21.3; HRMS calcd for $C_{16}H_{13}BrN_2$+H^+: 313.0335, found: 313.0335.



5-(bromomethyl)-1-phenyl-3-(p-tolyl)-1*H*-pyrazole (3b)

White solid, yield: 64%, melting point: 100.1~100.5 ºC.

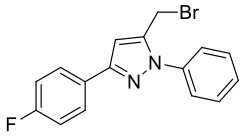
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.0 Hz, 2H), 7.68-7.62 (m, 2H), 7.57-7.50 (m, 2H), 7.50-7.43 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 6.82 (s, 1H), 4.50 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 140.2, 139.3, 138.2, 130.0, 129.6, 129.5, 128.7, 125.9, 125.4, 106.0, 21.5, 21.4; HRMS calcd for $C_{17}H_{15}BrN_2$+H^+: 327.0491, found: 327.0488.



5-(bromomethyl)-3-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazole (3c)

White solid, yield: 62%, melting point: 108.8~109.2 ºC.

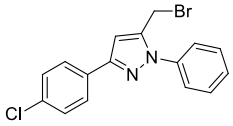
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.81-7.78 (m, 2H), 7.66-7.62 (m, 2H), 7,55-7.51 (m, 2H), 7.47-7.43 (m, 1H), 6.95 (d, J = 8.8 Hz, 2H), 6.77 (s, 1H), 4.50 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 152.0, 140.2, 139.3, 129.6, 128.7, 127.2, 125.6, 125.4, 114.3, 105.7, 55.5, 21.4; HRMS calcd for $C_{17}H_{15}BrN_2O$+H^+: 343.0441, found: 343.0443.



5-(bromomethyl)-3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazole (3d)

White solid, yield: 61%, melting point: 109.5~110.4 ºC.

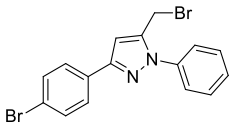
^{1}H-NMR (400 MHz, $CDCl_3$):δ 7.85-7.81 (m, 2H), 7.63 (m, 2H), 7.56-7.52 (m, 2H), 7.49-7.45 (m, 1H), 7.10 (t, *J* = 8.8 Hz, 2H), 6.79 (s, 1H), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1 (d, *J* = 246 Hz), 151.3, 140.5, 139.2, 129.7, 128.9, 127.6 (d, *J* = 8 Hz), 125.4, 125.3, 115.8 (d, *J* = 21 Hz), 105.9, 21.2; HRMS calcd for $C_{16}H_{12}BrFN_2$+H^+: 331.0241, found: 331.0238.



5-(bromomethyl)-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole (3e)

White solid, yield: 66%, melting point: 103.2~104.0 ºC.

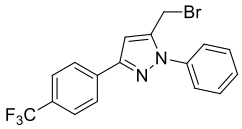
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.2 Hz, 2H), 7.67-7.60 (m, 2H), 7.58-7.51 (m, 2H), 7.50-7.44 (m, 1H), 7.38 (d, *J* = 7.2 Hz, 2H), 6.81 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1, 140.6, 139.1, 134.2, 131.4, 129.7, 129.1, 129.0, 127.2, 125.4, 106.1, 21.1; HRMS calcd for $C_{16}H_{12}BrClN_2$+H^+: 346.9945, found: 346.9941.



5-(bromomethyl)-3-(4-bromophenyl)-1-phenyl-1*H*-pyrazole (3f)

White solid, yield: 61%, melting point: 103.2~103.9 ºC.

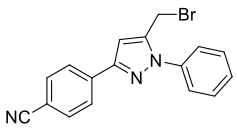
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.66-7.60 (m, 2H), 7.54 (m, 4H), 7.47 (t, *J* = 7.3 Hz, 1H), 6.82 (s, 1H), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1, 140.6, 139.1, 132.0, 131.9, 129.7, 129.0, 127.5, 125.4, 122.3, 106.0, 21.1; HRMS calcd for $C_{16}H_{12}Br_2N_2$+H^+: 390.9440, found: 390.9435.



5-(bromomethyl)-1-phenyl-3-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3g)

White solid, yield: 67%, melting point: 114.2~115.7 ºC.

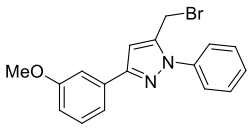
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.68-7.64 (m, 4H), 7.58-7.54 (m, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 6.89 (s, 1H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 140.8., 139.1, 129.7, 129.4 (q, *J* = 32 Hz), 129.1, 126.1, 125.9 (q, *J* = 4 Hz), 125.5, 124.1 (q, *J* = 270 Hz), 106.4, 21.0; HRMS calcd for $C_{17}H_{12}BrF_3N_2$+H^+: 381.0209, found: 381.0207.



4-(5-(bromomethyl)-1-phenyl-1*H*-pyrazol-3-yl)benzonitrile (3h)

White solid, yield: 65%, melting point: 137.5~138.3ºC.

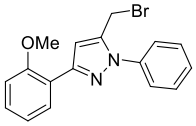
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.6 Hz, 2H), 7,69 (d, J = 8.0 Hz, 2H), 7.66-7.60 (m, 2H), 7.59-7.53 (m, 1H), 7.53-7.46, 6.89 (s, 1H), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 141.1, 138.9, 137.3, 132.8, 129.8, 129.3, 126.3, 125.4, 119.2, 111.7, 106.6, 20.8; HRMS calcd for $C_{17}H_{12}BrN_3$+H^+: 338.0287, found: 338.0288.



5-(bromomethyl)-3-(3-methoxyphenyl)-1-phenyl-1*H*-pyrazole (3i)

White solid, yield: 65%, melting point: 103.2~103.9 °C.

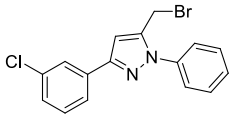
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.67-7.63 (m, 2H), 7.56-7.51 (m, 2H), 7.49-7.46 (m, 1H), 7.45-7.42 (m, 2H), 7.33 (t, J = 7.8 Hz, 1H), 6.91-6.87 (m, 1H), 6.83 (s, 1H), 4.50 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 152.1, 140.3, 139.3, 134.2, 129.9, 129.6, 128.8, 125.5, 118.6, 114.5, 111.0, 106.3, 55.6, 21.3; HRMS calcd for $C_{17}H_{15}BrN_2O$+H^+: 343.0441, found: 343.0444.



5-(bromomethyl)-3-(2-methoxyphenyl)-1-phenyl-1*H*-pyrazole (3j)

White solid, yield: 49%, melting point: 117.1~118.1 °C.

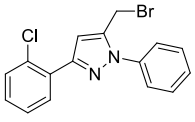
^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, J = 7.6, 1.6 Hz, 1H), 7.68-7.65 (m, 2H), 7,55-7.51 (m, 2H), 7.47-7.43 (m, 1H), 7.36-7.30 (m, 1H), 7.12 (d, J = 2.4 Hz, 1H), 7.04 (dd, J = 7.6, 1.2 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 4.59 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 149.1, 139.4, 139.2, 129.5, 129.4, 128.9, 128.6, 125.4, 121.7, 121.1, 111.5, 110.4, 55.7, 21.7; HRMS calcd for $C_{17}H_{15}BrN_2O$+H^+: 343.0441, found: 343.0448.



5-(bromomethyl)-3-(3-chlorophenyl)-1-phenyl-1*H*-pyrazole (3k)

White solid, yield: 72%, melting point: 108.5~109.1 °C.

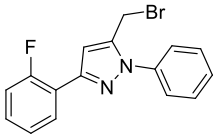
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.72 (d, J = 6.0 Hz, 1H), 7.69-7.60 (m, 2H), 7.55 (s, 2H), 7.49 (d, J = 6.0 Hz, 1H), 7.35-7.27 (m, 2H), 6.83 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 140.6, 139.1, 134.9, 134.7, 130.2, 129.7, 129.0, 128.3, 126.1, 125.4, 124.1, 106.2, 21.1; HRMS calcd for $C_{16}H_{12}BrClN_2$+H^+: 346.9945, found: 346.9944.



5-(bromomethyl)-3-(2-chlorophenyl)-1-phenyl-1*H*-pyrazole (3l)

White solid, yield: 51%, melting point: 119.8~120.1 ºC.

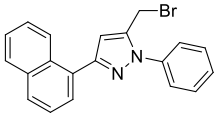
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.91 (dd, J = 7.6, 2.4 Hz, 1H), 7.68-7.64 (m, 2H), 7.56-7.52 (m,2H), 7.49-7.45 (m, 2H), 7.33-7.27 (m, 2H), 7.10 (s, 1H), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 139.5, 139.2, 132.5, 131.8, 130.8, 130.6, 129.6, 129.4, 128.9, 127.1, 125.4, 110.1, 21.3; HRMS calcd for $C_{16}H_{12}BrClN_2$+H^+: 346.9945, found: 346.9941.



5-(bromomethyl)-3-(2-fluorophenyl)-1-phenyl-1H-pyrazole(3m)

Pink solid, yield: 35%, melting point: 103.1~103.8 ºC

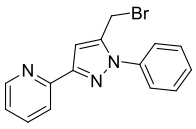
1H-NMR (500 MHz, CDCl3): δ 8.08 (m, 1H), 7.65 (m, 2H), 7.54 (m, 2H), 7.48 (m, 1H), 7.30 (m, 1H), 7.16 (m, 2H), 7.01(d, J = 4 Hz, 1H), 4.52 (s, 2H); 13C NMR (125 MHz, CDCl3): δ 159.8(d, J = 248 Hz), 146.6, 139.8, 139.0, 129.6, 129.5, 129.4, 128.7, 128.4(d, J = 3 Hz), 125.3, 125.2, 124.3(d, J = 3 Hz), 120.5(d, J = 12 Hz), 116.1(d, J = 22 Hz), 109.4(d, J = 10 Hz), 21.0; HRMS calcd for C16H12BrClN2+H+: 331.0241, found: 331.0244.



5-(bromomethyl)-3-(naphthalen-1-yl)-1-phenyl-1*H*-pyrazole (3n)

White solid, yield: 41%, melting point: 98.8~99.3ºC.

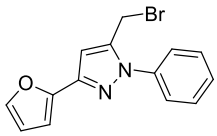
^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.63-8.57 (m, 1H), 7,92-7.88 (m, 2H), 7.78 (dd, J = 7.2, 1.2 Hz, 1H), 7.75-7.71 (m, 2H), 7.59-7.53 (m, 4H), 7.52 (t, J = 2.0 Hz, 1H), 7.50-7.46 (m, 1H), 6.87 (s, 1H), 4.59 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 139.6, 139.3, 134.2, 131.5, 130.9, 129.6, 128.9, 128.8, 128.6, 127.5, 126.7, 126.2, 126.1, 125.6, 125.4, 110.0, 21.3; HRMS calcd for $C_{20}H_{15}BrN_2$+H^+: 363.0491, found: 363.0489.



2-(5-(bromomethyl)-1-phenyl-1*H*-pyrazol-3-yl)pyridine (3o)

White solid, yield: 32%, melting point: 94.2~95.4ºC.

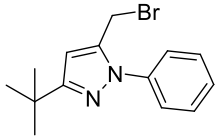
^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.64 (d, J = 4.8 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.73 (td, J = 8.0, 1.6 Hz, 1H), 7.67-7.63 (m, 2H), 7.56-7.51 (m, 2H), 7.49-7.46 (m, 1H), 7.25-7.22 (m, 1H), 7.19 (s, 1H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.4, 151.8, 149.6, 140.7, 139.2, 136.9, 129.6, 129.0, 125.6, 123.1, 120.4, 107.6, 21.2; HRMS calcd for $C_{15}H_{12}BrN_3$+H^+: 314.0287, found: 314.0288.



5-(bromomethyl)-3-(furan-2-yl)-1-phenyl-1*H*-pyrazole (3p)

White solid, yield: 40%, melting point: 76.6~76.9ºC.

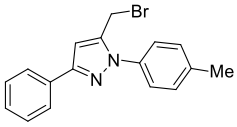
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.63-7.60 (m, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.47-7.44 (m, 2H), 6.77 (s, 1H), 6.75 (d, J = 2.8 Hz, 1H), 6.48-6.47 (m, 1H), 4.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 144.8, 142.4, 140.2, 139.0, 129.6, 129.0, 125.6, 111.6, 106.7, 105.8, 21.0; HRMS calcd for $C_{14}H_{11}BrN_2$+H^+: 303.0128, found: 303.0122.



5-(bromomethyl)-3-(tert-butyl)-1-phenyl-1*H*-pyrazole (3q)

White solid, yield: 65%, melting point: 71.9~72.7ºC.

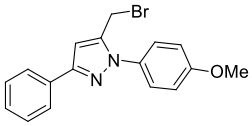
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 7.2 Hz, 2H), 7.49 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 6.39 (s, 1H), 4.46 (s, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 139.6, 138.8, 129.5, 128.3, 125.3, 105.7, 32.4, 30.7, 21.9; HRMS calcd for $C_{14}H_{17}BrN_2$+H^+: 293.0648, found: 293.0644.



5-(bromomethyl)-3-phenyl-1-(p-tolyl)-1*H*-pyrazole (3r)

White solid, yield: 57%, melting point: 88.0~88.8 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.89-7.82 (m, 2H), 7.53-7.49 (m, 2H), 7.45-7.37 (m, 2H), 7.35-7.32 (m, 3H), 6.83 (s, 1H), 4.49 (s, 2H), 2.44(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 140.3, 138.9, 136.8, 132.9, 130.2, 128.9, 128.3, 126.0, 125.4, 105.9, 21.4, 21.3; HRMS calcd for $C_{17}H_{15}BrN_2$+H^+: 327.0491, found: 327.0487.

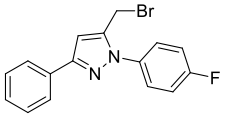


5-(bromomethyl)-1-(4-methoxyphenyl)-3-phenyl-1*H*-pyrazole (3s)

White solid, yield: 47%, melting point: 117.4~118.5 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 6.8 Hz, 2H), 7.59-7.50 (m, 2H), 7.45-7.37 (m, 2H), 7.33 (t, J = 6.8 Hz, 1H), 7.03 (d, J = 8.4 Hz, 2H), 6.81 (s, 1H), 4.46 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 151.9, 140.4, 133.0, 132.2, 128.9,

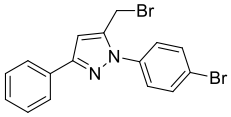
128.3, 127.1, 125.9, 114.7, 105.6, 55.8, 21.3; HRMS calcd for $C_{17}H_{15}BrN_2O+H^+$: 343.0441, found: 343.0443.



5-(bromomethyl)-1-(4-fluorophenyl)-3-phenyl-1*H*-pyrazole (3t)

White solid, yield: 75%, melting point: 103.7~104.3 ºC.

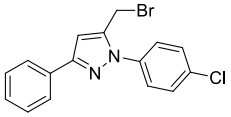
^{1}H-NMR (400 MHz, $CDCl_3$):δ 7.84 (dd, *J* = 7.2, 1.6 Hz, 2H), 7,65-7.60 (m, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.25-7.20 (m, 2H), 6.83 (s, 1H), 4.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7 (d, *J* = 247 Hz), 152.3, 140.5, 135.4, 132.7, 128.9, 128.5, 127.5 (d, *J* = 9 Hz), 126.0, 116.6 (d, *J* = 23 Hz), 106.1, 21.1; HRMS calcd for $C_{16}H_{12}BrFN_2+H^+$: 331.0241, found: 331.0244.



5-(bromomethyl)-1-(4-bromophenyl)-3-phenyl-1*H*-pyrazole (3u)

White solid, yield: 66%, melting point: 84.6~85.4 ºC.

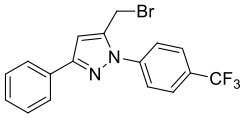
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 6.8 Hz, 2H), 7,67 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 6.4 Hz, 2H), 7.35 (d, J = 7.2, 1H), 6.84 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 140.4, 138.3, 132.8, 132.6, 129.0, 128.6, 126.8, 126.0, 122.6, 106.6, 21.1; HRMS calcd for $C_{16}H_{12}Br_2N_2+H^+$: 390.9440, found: 390.9447.



5-(bromomethyl)-1-(4-chlorophenyl)-3-phenyl-1*H*-pyrazole (3v)

White solid, yield: 63%, melting point: 92.6~93.4 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.2 Hz, 2H), 7.66-7.57 (m, 2H), 7.51 (d, *J* = 8.4Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 6.84 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, CDCl3): δ 152.5, 140.4, 137.8, 134.6, 132.6, 129.8, 128.9, 128.6, 126.6, 126.0, 106.5, 21.1; HRMS calcd for $C_{16}H_{12}BrClN_2+H^+$: 346.9945, found: 346.9941.

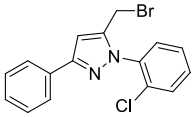


5-(bromomethyl)-3-phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3w)

White solid, yield: 70%, melting point: 99.7~100.3 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.86-7.80 (m, 6H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 6.88 (s, 1H), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 142.2 (q, *J* = 1.6 Hz), 140.5, 132.4, 129.0, 128.7, 126.9 (q, *J* = 3.6 Hz), 126.0, 125.2,

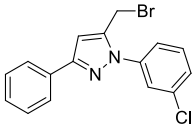
123.8 (q, J = 240.0 Hz), 107.2, 21.0; HRMS calcd for $C_{17}H_{12}BrF_3N_2$+H^+: 381.0209, found: 381.0204.



5-(bromomethyl)-1-(2-chlorophenyl)-3-phenyl-1*H*-pyrazole (3x)

White solid, yield: 47%, melting point: 99.3~100.2 ºC.

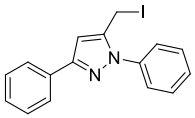
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 7.2 Hz, 2H), 7.62 (dd, J = 7.2, 1.6 Hz, 1H), 7.60-7.55 (m, 1H), 7.51-7.46 (m, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 6.83 (s, 1H), 4.36 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 141.6, 136.7, 132.8, 132.7, 131.3, 130.7, 130.5, 128.9, 128.5, 128.0, 126.1, 105.1, 20.5; HRMS calcd for $C_{16}H_{12}BrClN_2$+H^+: 346.9945, found: 346.9944.



5-(bromomethyl)-1-(3-chlorophenyl)-3-phenyl-1*H*-pyrazole (3y)

White solid, yield: 78%, melting point: 79.5~80.5 ºC.

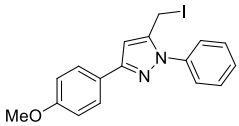
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 6.0 Hz, 2H), 7.71 (s, 1H), 7.63-7.53 (m, 1H), 7.47-7.41 (m, 4H), 7.38-7.33 (m, 1H), 6.85 (s, 1H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 140.4, 140.3, 135.4, 132.6, 130.6, 129.0, 128.9, 128.6, 126.0, 125.7, 123.2, 106.7, 21.0; HRMS calcd for $C_{16}H_{12}BrClN_2$+H^+: 346.9945, found: 346.9939.



5-(iodomethyl)-1,3-diphenyl-1*H*-pyrazole (4a)

White solid, yield: 75%.

^{1}H-NMR (400 MHz, *d*6-DMSO): δ 7.85 (dd, J = 7.2, 1.6 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 6.4 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.07 (s, 1H), 4.65 (s, 2H); ^{13}C NMR (100 MHz, *d*6-DMSO): δ 150.6, 141.9, 139.2, 132.5, 129.5, 128.8, 128.4, 128.2, 125.3, 124.8, 105.3, -6.4; HRMS calcd for $C_{16}H_{13}IN_2$+H^+: 361.0196, found: 361.0195.

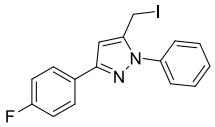


5-(iodomethyl)-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole(4b)

White solid, yield: 41%.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J = 8.8 Hz, 2H), 7.64-7.62 (m, 2H), 7.56-7.52 (m, 2H), 7.48-7.44 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.75 (s, 1H), 4.43 (s, 2H), 3.84(s,

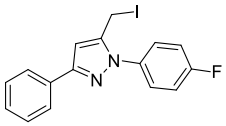
3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 152.0, 141.4, 139.4, 129.6, 128.7, 127.2, 125.7, 125.5, 114.3, 105.5, 55.6, -8.2 ; HRMS calcd for $C_{17}H_{15}IN_2O+H^+$: 391.0302, found: 391.0310.



3-(4-fluorophenyl)-5-(iodomethyl)-1-phenyl-1H-pyrazole(4c)

White solid, yield: 35%.

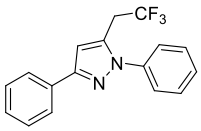
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, J = 8.8, 5.6 Hz, 2H), 7.62 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.6 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.09 (t, J = 8.8 Hz, 2H), 6.77 (s, 1H), 4.43 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1 (d, J = 250.0 Hz), 151.2, 141.7, 139.3, 129.7, 129.1, 129.1, 128.9, 127.7(d, J = 8.1 Hz), 125.5, 115.8 (d, J = 21.5 Hz), 105.2, -8.6 ; HRMS calcd for $C_{16}H_{12}FIN_2+H^+$: 379.0102, found: 379.0109.



1-(4-fluorophenyl)-5-(iodomethyl)-3-phenyl-1H-pyrazole(4d)

White solid, yield: 45%

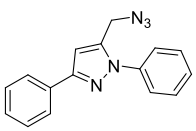
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.84-7.82 (m, 2H), 7.62 (dd, J = 8.8, 4.8 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.24-7.21 (m, 2H), 6.81 (s, 1H), 4.40 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 161.5, 152.2, 141.7, 135.4(d, J = 3.1 Hz), 132.7, 128.9, 128.5, 127.6 (d, J = 8.7 Hz), 125.9, 116.7 (d, J = 22.8 Hz), 105.3, -8.8 ; HRMS calcd for $C_{16}H_{12}FIN_2+H^+$: 379.0102, found: 379.0101.



1,3-diphenyl-5-(2,2,2-trifluoroethyl)-1H-pyrazole (5)

White solid, yield: 32%.

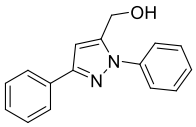
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.90-7.84 (m, 2H), δ 7.56-7.50 (m, 2H), δ 7.50-7.44 (m, 3H), 7.42 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 6.82 (s, 1H), 3.52 (q, J = 6.0 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 138.9, 133.3, 132.7, 129.5, 128.9, 128.7, 128.2, 126.2, 125.8, 123.3 (q, J = 273 Hz) , 105.4, 31.6(q, J = 32 Hz) ; HRMS calcd for $C_{27}H_{13}F_3N_2+H^+$: 302.1031, found: 302.1033.



5-(azidomethyl)-1,3-diphenyl-1*H*-pyrazole (6)

White solid, yield: 65%.

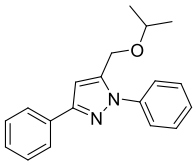
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 7.2 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.52 (t, J = 7.6 Hz, 2H), 7.46-7.41 (m, 3H), 7.35 (t, J = 7.2 Hz, 1H), 6.82 (s, 1H), 4.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 139.3, 138.1, 132.9, 129.7, 128.9, 128.6, 128.4, 126.0, 125.2, 105.9, 45.5; HRMS calcd for $C_{16}H_{13}N_5$+H^+: 276.1244, found: 276.1243.



(1,3-diphenyl-1*H*-pyrazol-5-yl)methanol (7)

Green solid, yield: 35%.

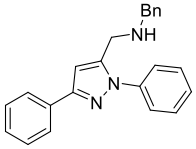
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.2 Hz, 2H), 7.60 (d, J = 7.6 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.43-7.37 (m, 3H), 7.34 (t, J = 7.2 Hz, 1H), 6.73 (s, 1H), 4.65 (s, 2H), 2.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 143.9, 139.6, 132.9, 129.6, 129.0, 128.5, 126.1, 124.8, 105.3, 56.1; HRMS calcd for $C_{16}H_{14}N_2O$+H^+: 251.1179, found: 251.1172.



5-(isopropoxymethyl)-1,3-diphenyl-1H-pyrazole (8)

White oil, yield: 50%.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J = 7.6, 1.2 Hz, 2H), 7.72-7.69 (m, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.43-7.38 (m, 3H), 7.32 (t, J = 7.6 Hz, 1H), 6.79 (s, 1H), 4.49 (s, 2H), 3.74-3.68 (m, 1H), 1.21 (d, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 141.3, 140.0, 133.4, 129.3, 128.8, 128.1, 128.0, 126.0, 124.9, 106.2, 71.5, 60.7, 22.2; HRMS calcd for $C_{19}H_{20}N_2O$+H^+: 293.1648, found: 293.1655.

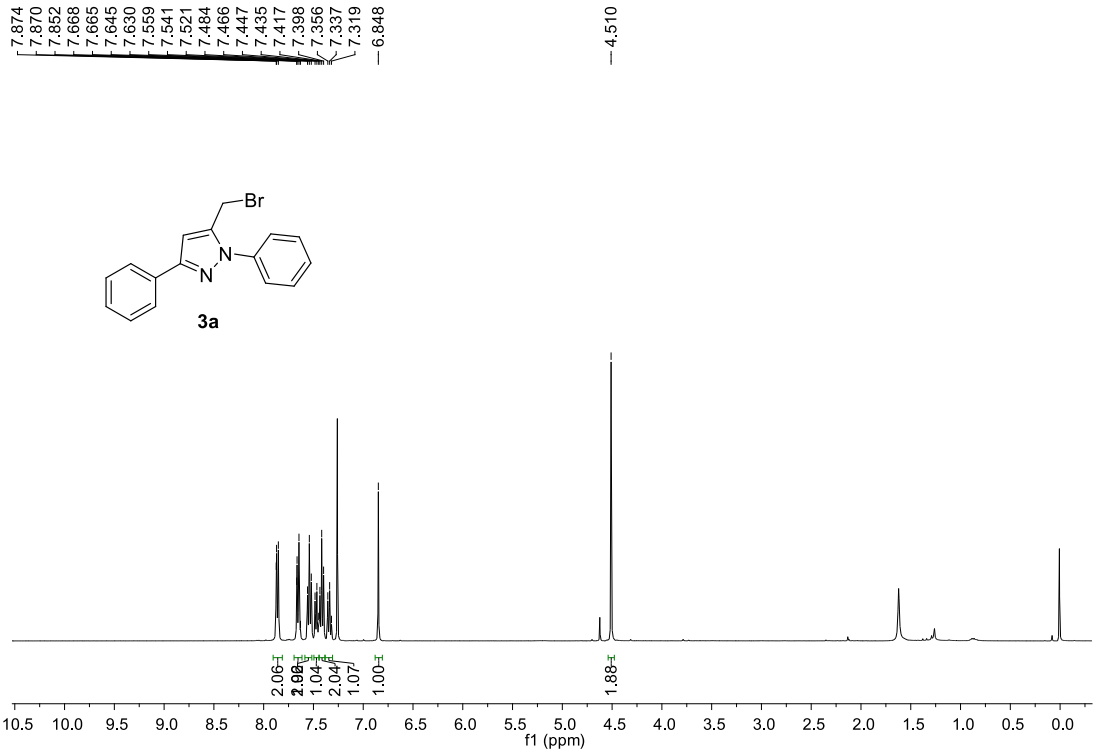


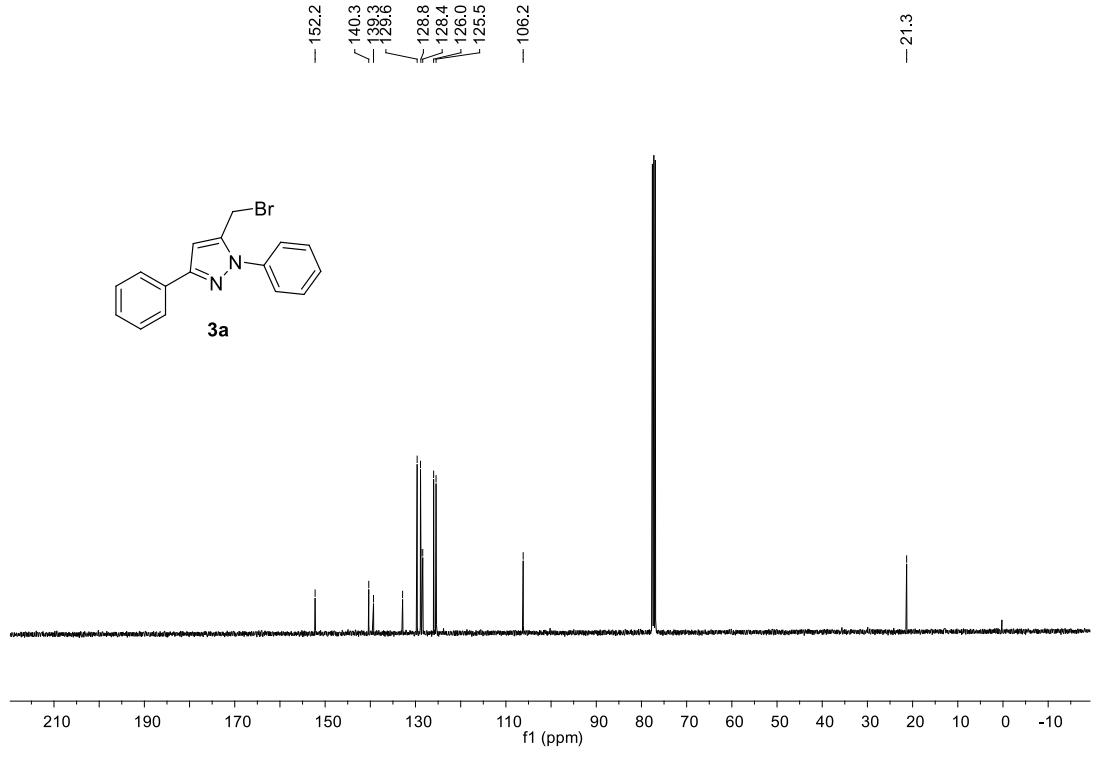
***N*-benzyl-1-(1,3-diphenyl-1*H*-pyrazol-5-yl)methanamine (9)**

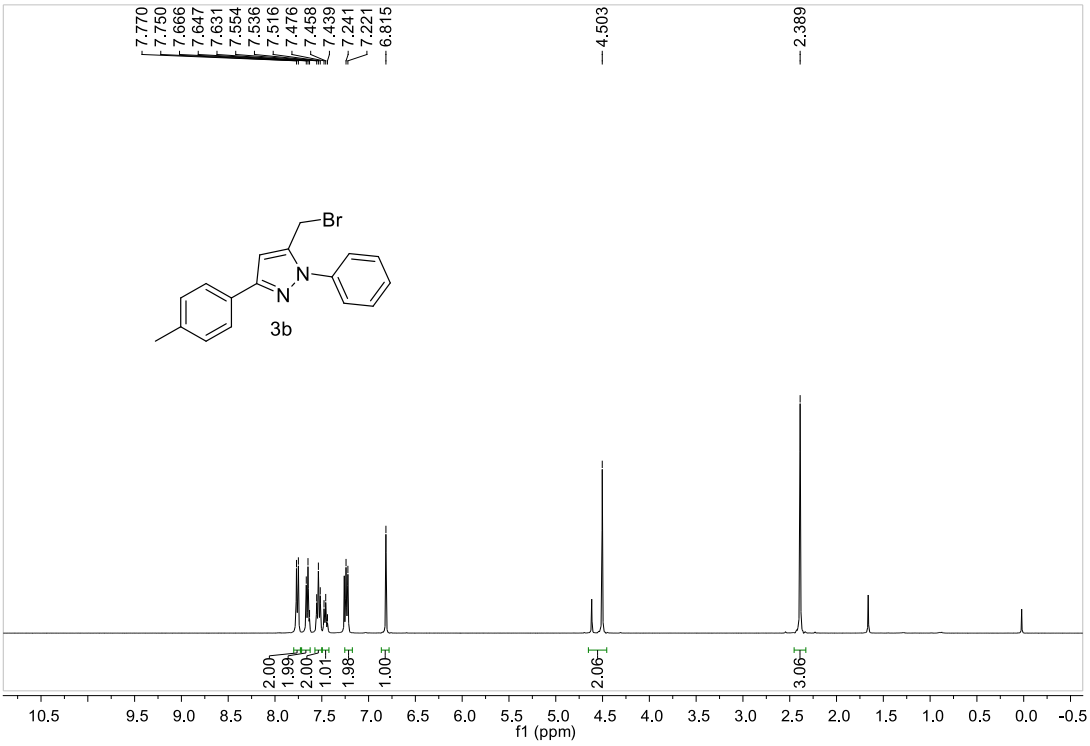
White solid, yield: 33%.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.2 Hz, 2H), 7.55 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 2H), 7.35-7.29 (m, 3H), 7.24-7.18 (m, 6H), 6.67 (s, 1H), 3.80 (s, 2H), 3.75 (s, 2H), 1.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 143.1, 140.1, 133.4, 129.4, 128.8, 128.7, 128.4, 128.1, 128.0, 127.4, 126.0, 125.1, 104.8, 100.2, 53.4, 44.3; HRMS calcd for $C_{23}H_{21}N_3$+H^+: 340.1808, found: 340.1801.

10. ^{1}H and ^{13}C NMR Spectra



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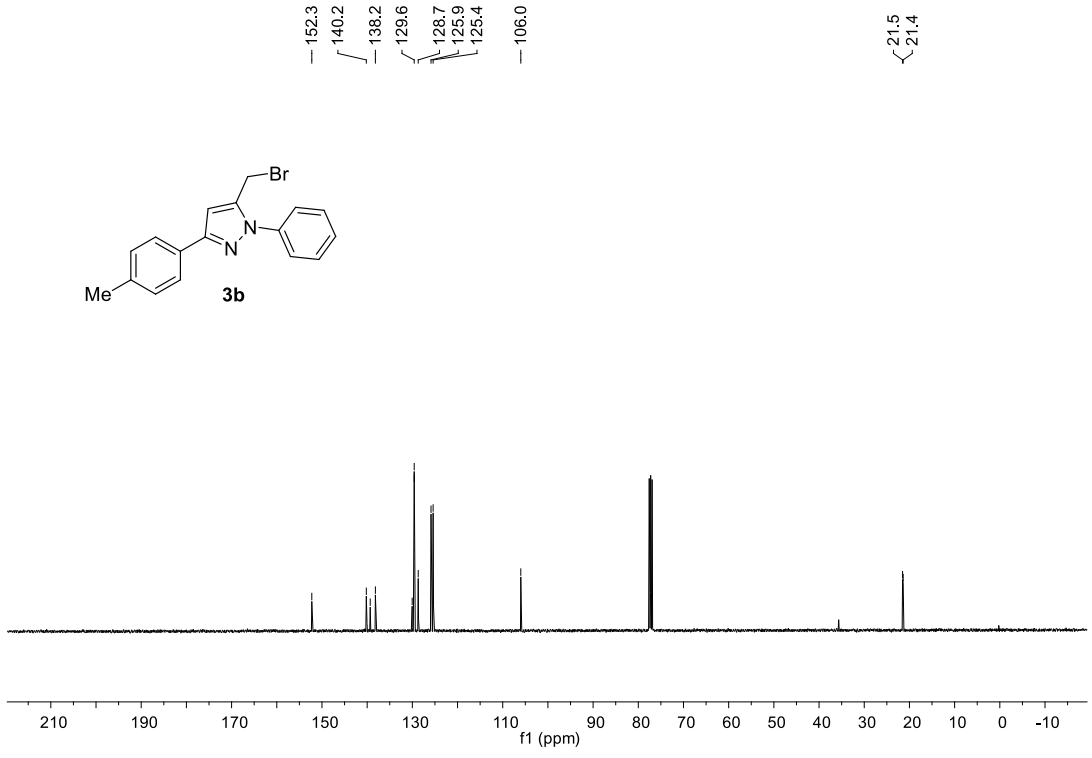
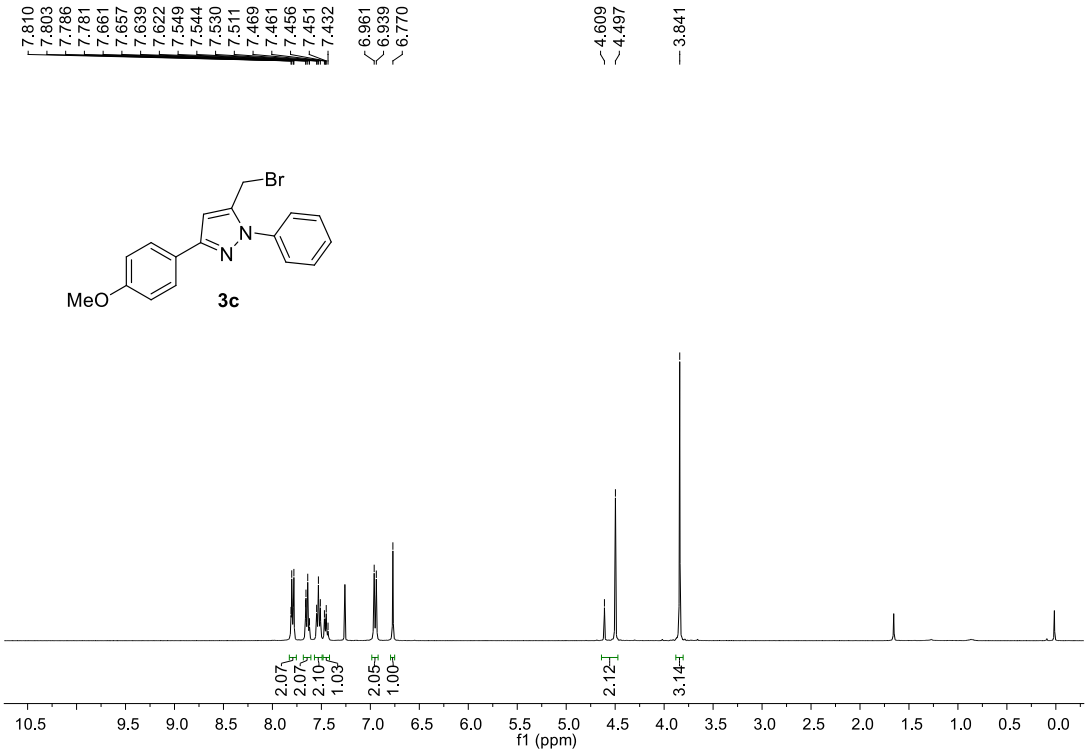
7.666
7.647
7.631
7.554
7.536
7.516
7.476
7.458
7.439
7.241
7.221
6.815
4.503
2.389
Br
N
N
3b
2.00
1.99
2.00
1.01
1.98
1.00
2.06
3.06
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


152.3
140.2
138.2
129.6
128.7
125.9
125.4
106.0
21.5
21.4
Br
N
N
Me
3b
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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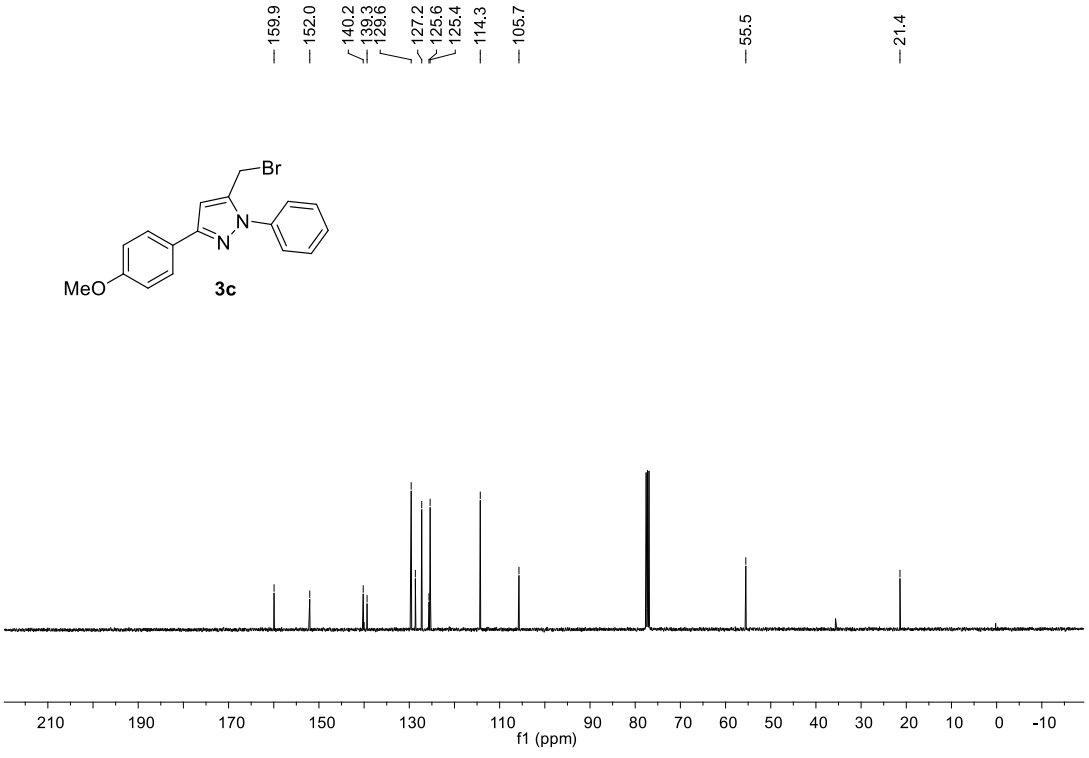
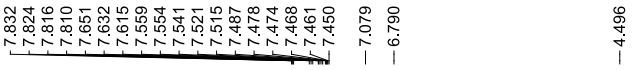
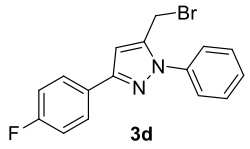
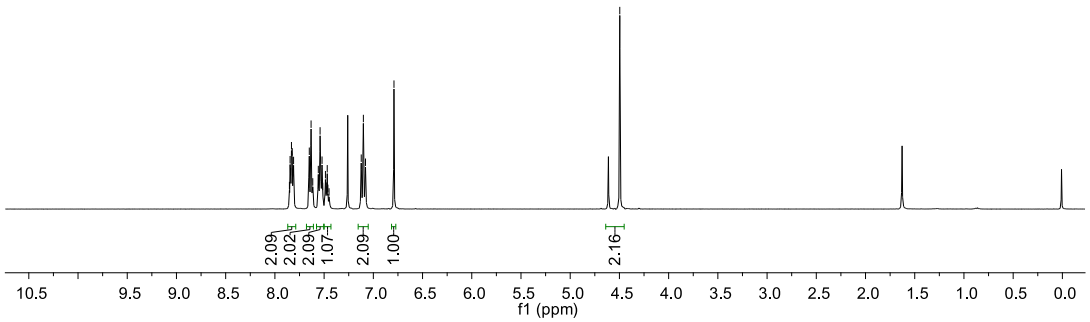
7.803
7.786
7.781
7.661
7.657
7.639
7.622
7.549
7.544
7.530
7.511
7.469
7.461
7.456
7.451
7.432
6.961
6.939
6.770
4.609
4.497
3.841
Br
N
N
MeO
3c
2.07
2.07
2.10
1.03
2.05
1.00
2.12
3.14
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


159.9
152.0
140.2
139.3
129.6
127.2
125.6
125.4
114.3
105.7
55.5
21.4
Br
N
N
MeO
3c
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.832
7.824
7.816
7.810
7.651
7.632
7.615
7.559
7.554
7.541
7.521
7.515
7.487
7.478
7.474
7.468
7.461
7.450
7.079
6.790
4.496


Br
N
N
F

3d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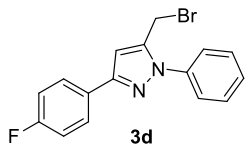
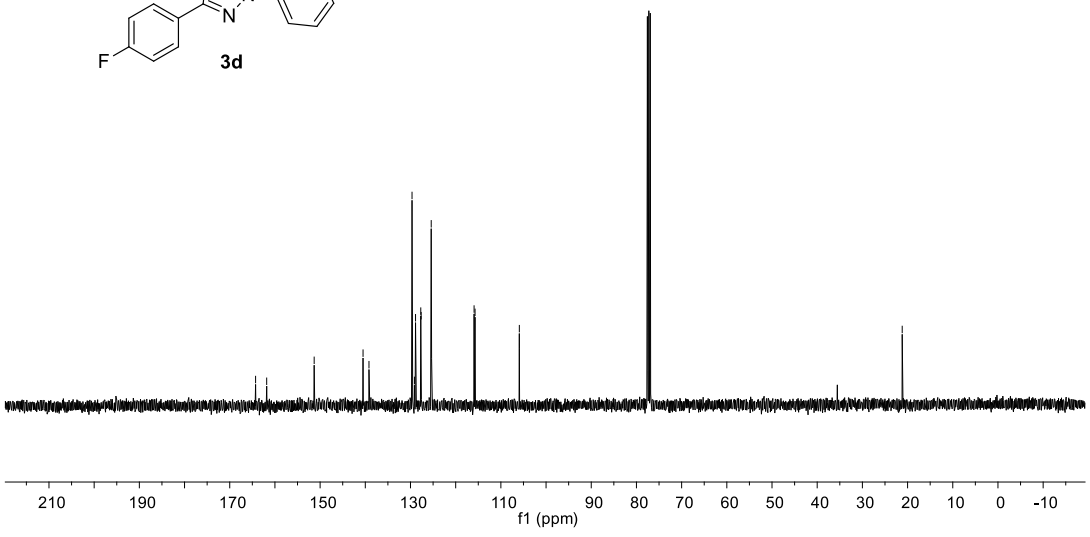
2.02
2.09
1.07
2.09
1.00
2.16
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.3
161.8
151.3
140.5
139.2
129.1
127.7
125.4
115.9
115.7
105.9
21.2


Br
N
N
F

3d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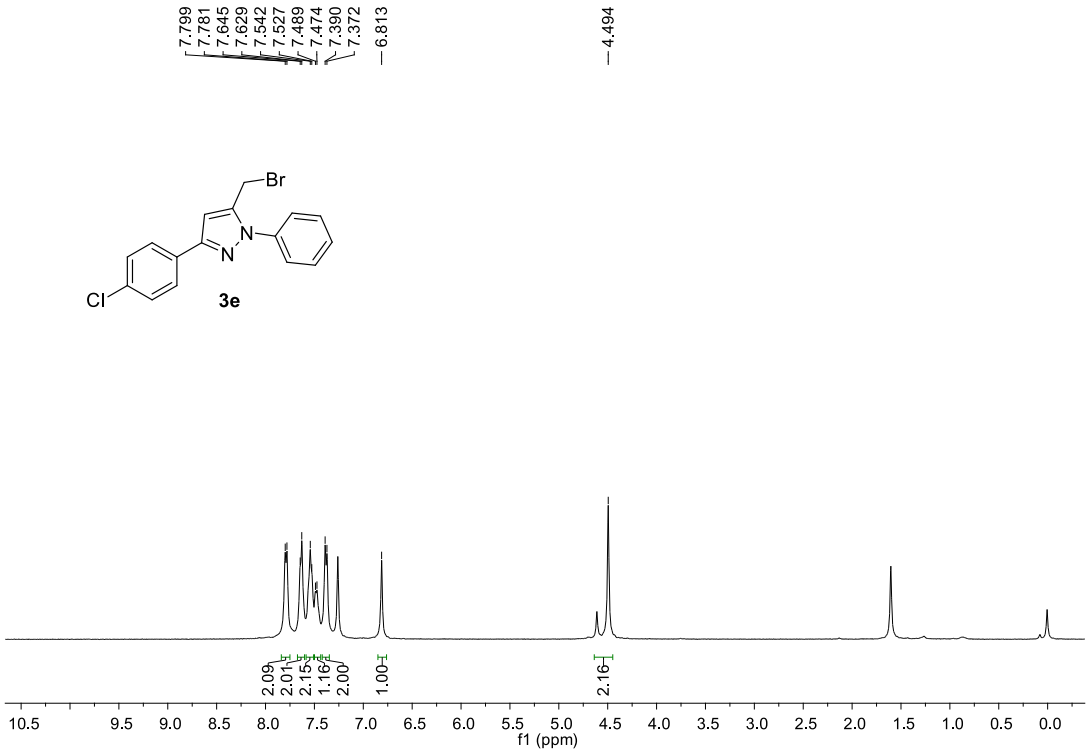
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.781
7.645
7.629
7.542
7.527
7.489
7.474
7.390
7.372
6.813
4.494
Br
N
N
Cl
3e
2.09
2.01
2.15
1.16
2.00
1.00
2.16
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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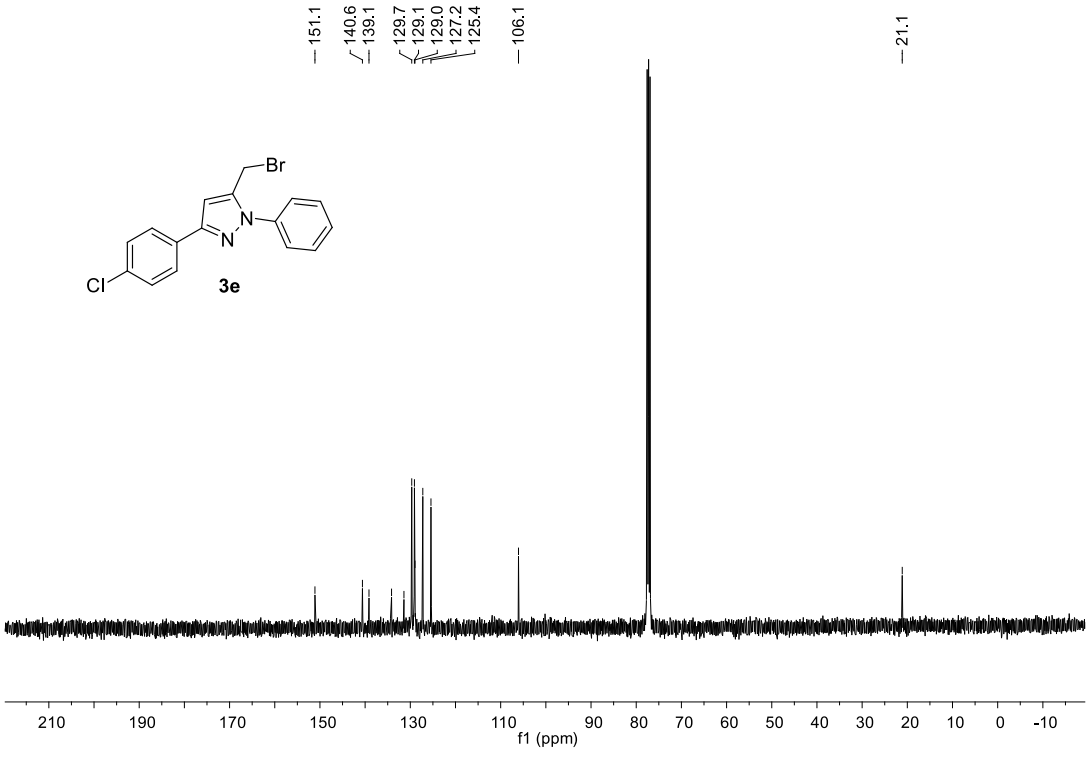
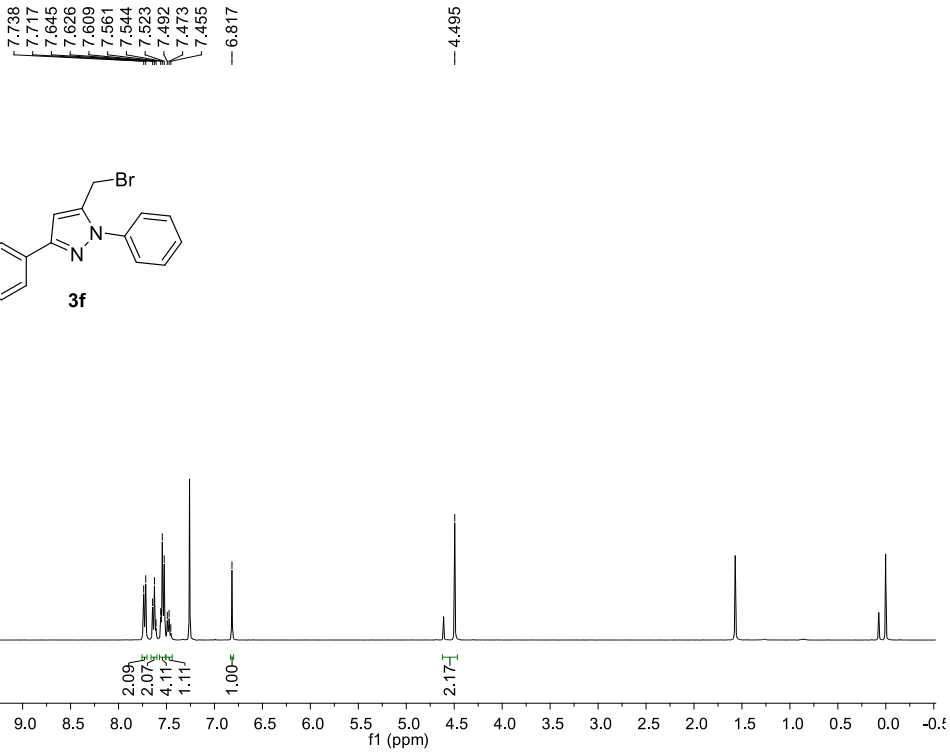
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


151.1
140.6
139.1
129.7
129.1
129.0
127.2
125.4
106.1
21.1
Br
N
N
Cl
3e
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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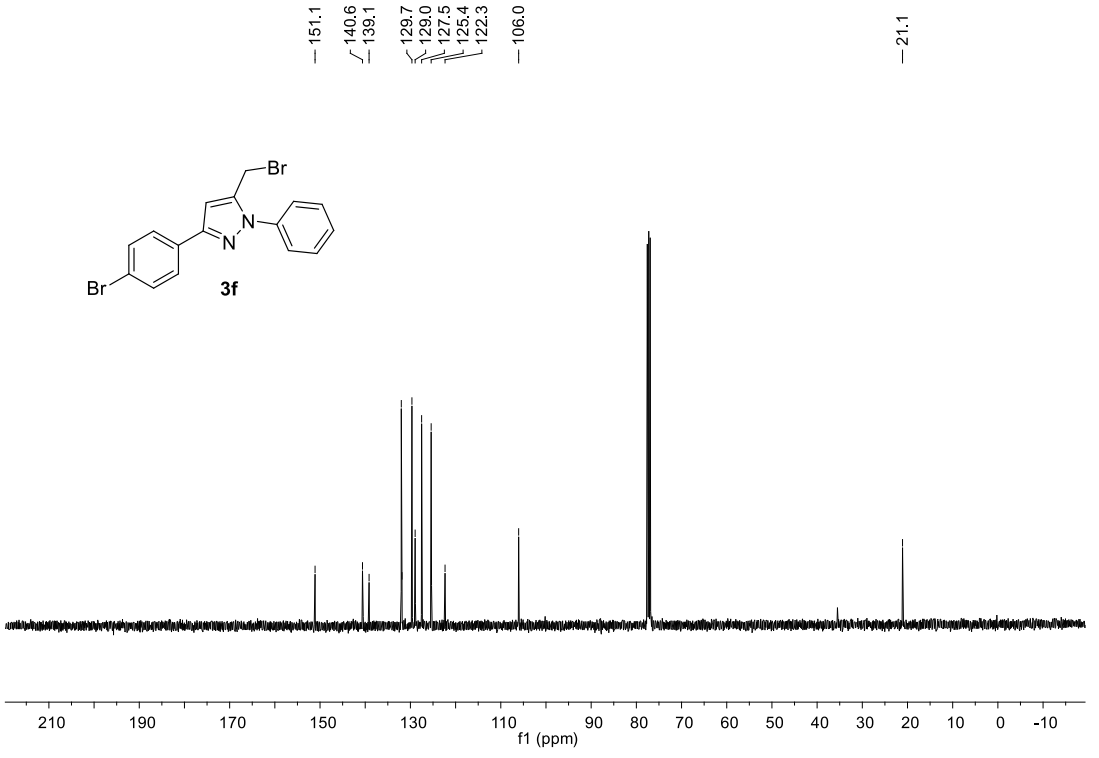
7.645
7.626
7.609
7.561
7.544
7.523
7.492
7.473
7.455
6.817
4.495
Br
N
N
Br
3f
2.09
2.07
4.11
1.11
1.00
2.17
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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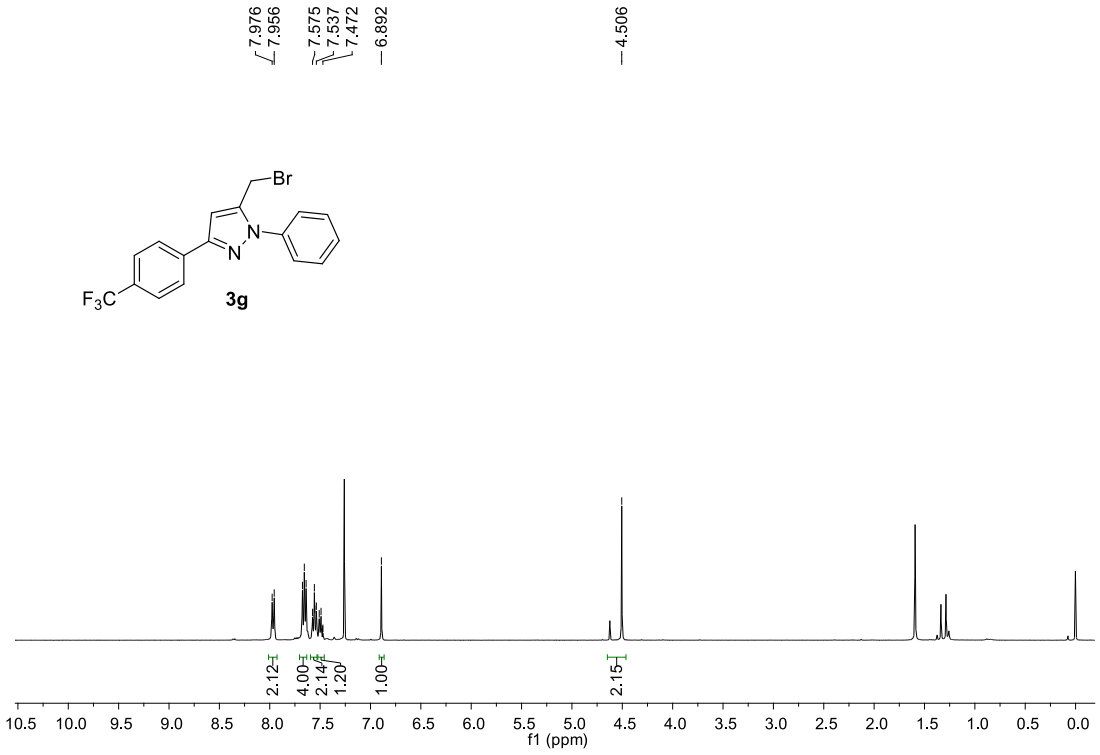
140.6
139.1
129.7
129.0
127.5
125.4
122.3
106.0
21.1
Br
N
N
Br
3f
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.537
7.472
6.892
4.506
Br
N
N
F3C
3g
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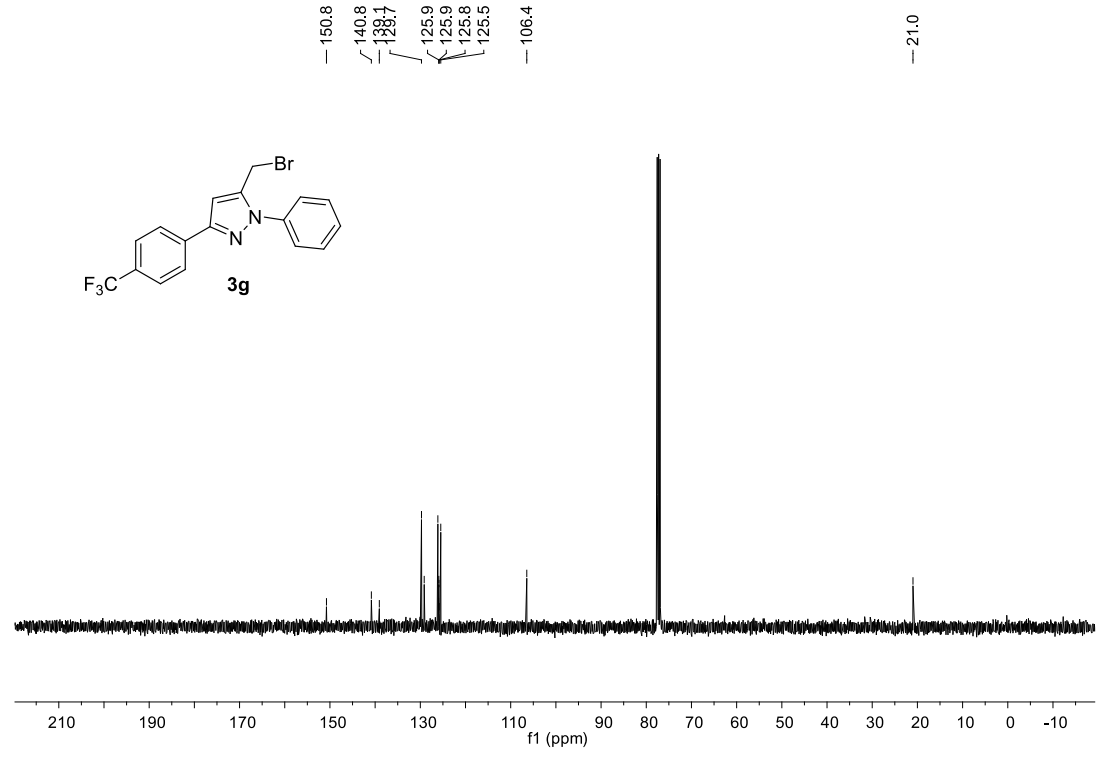
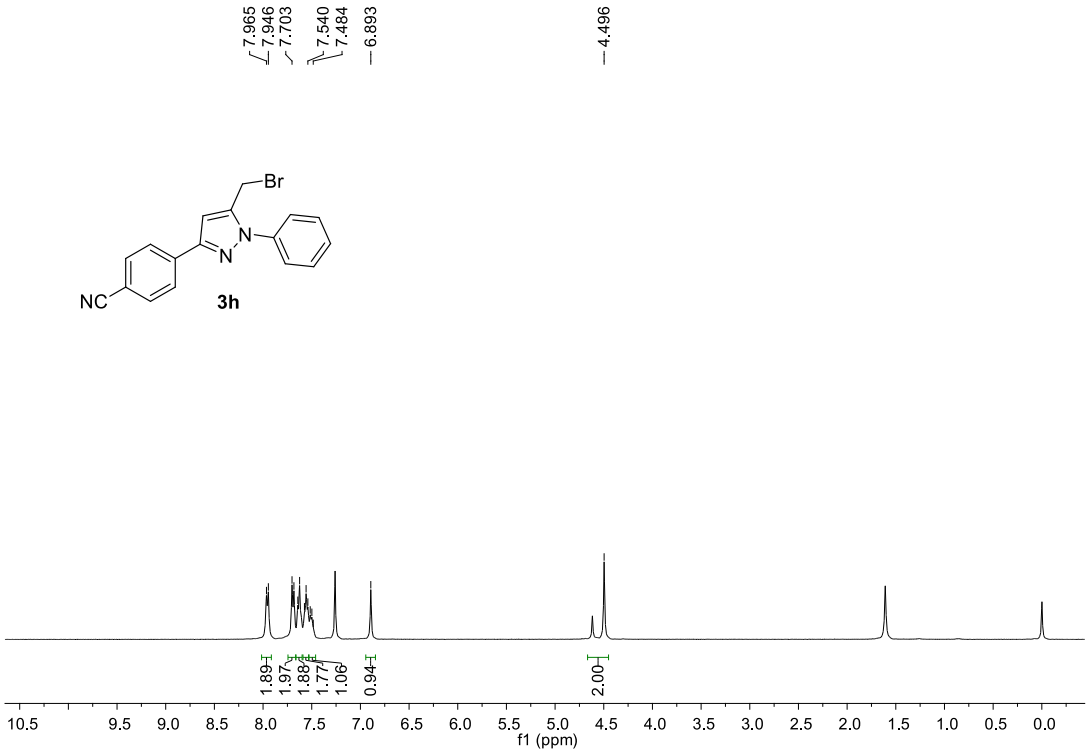
4.00
2.14
1.20
1.00
2.15
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


150.8
140.8
138.1
129.7
125.9
125.9
125.8
125.5
106.4
21.0
Br
N
N
F3C
3g
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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Br
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N
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3h
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1.77
1.06
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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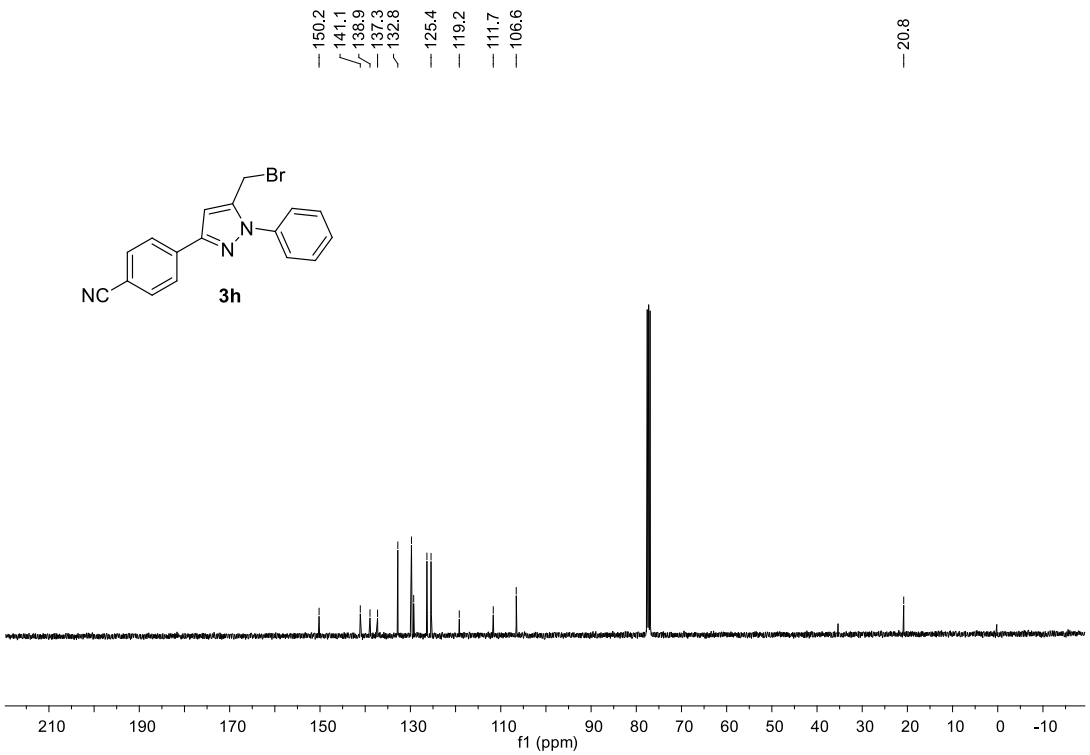
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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138.9
137.3
132.8
125.4
119.2
111.7
106.6
20.8
Br
N
N
NC
3h
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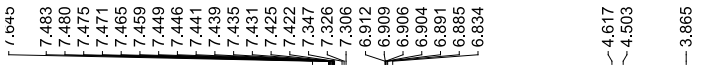
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.439
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7.425
7.422
7.347
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6.906
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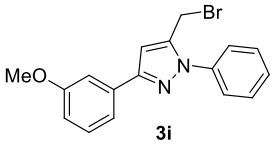
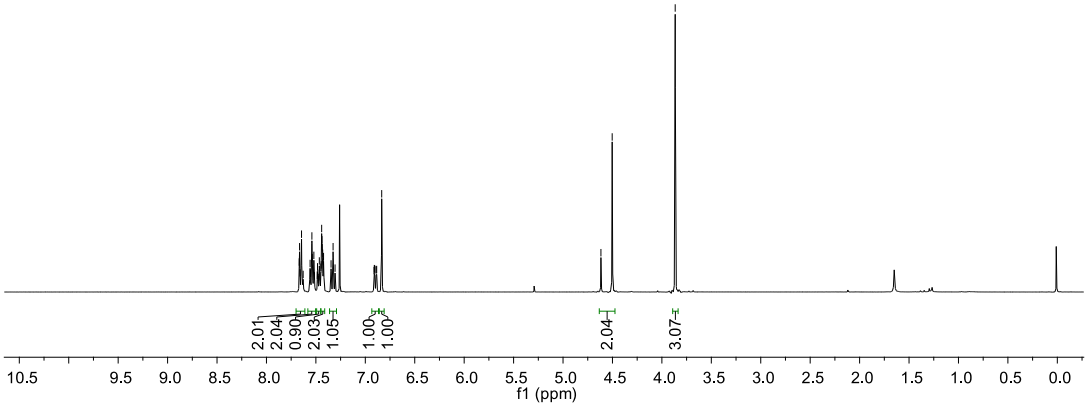
6.834
4.617
4.503
3.865


Br
MeO
N
N

3i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1.00
1.00
2.04
3.07
10.5
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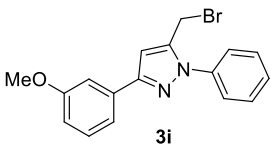
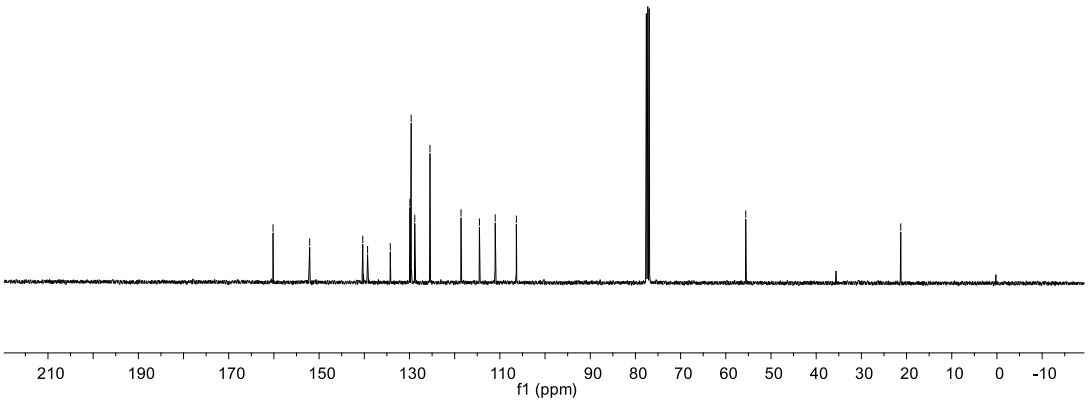
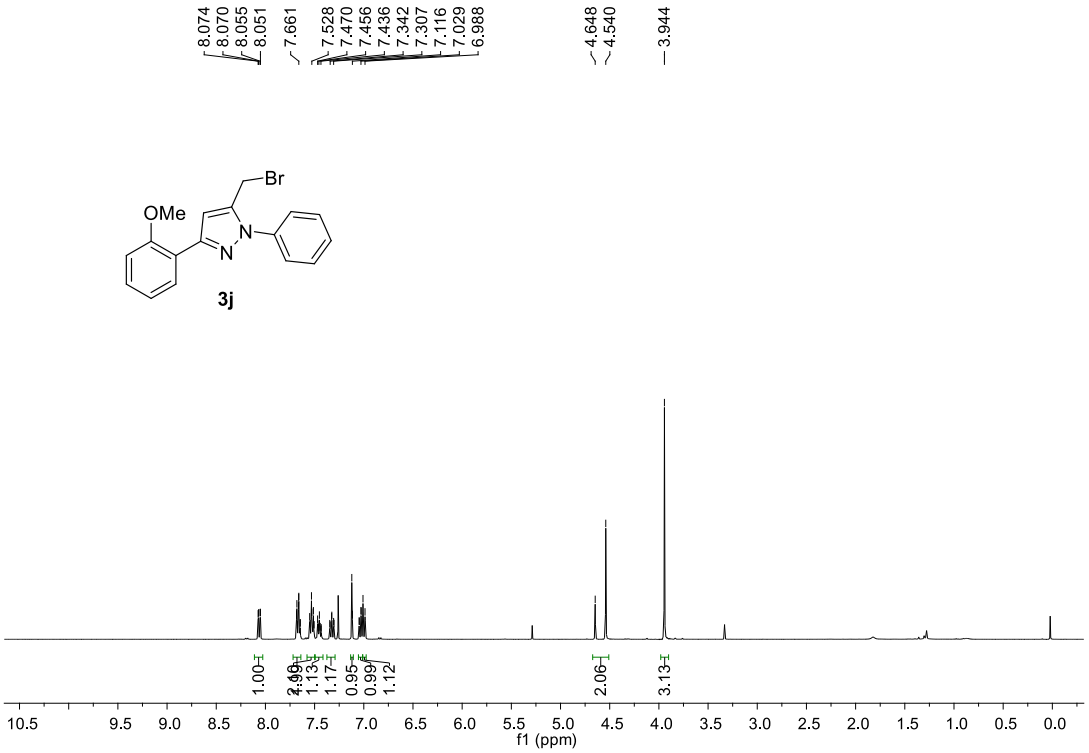
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


160.2
152.1
140.3
139.3
134.2
129.6
125.5
118.6
111.0
106.3
55.6
21.3


Br
MeO
N
N

3i


210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.307
7.116
7.029
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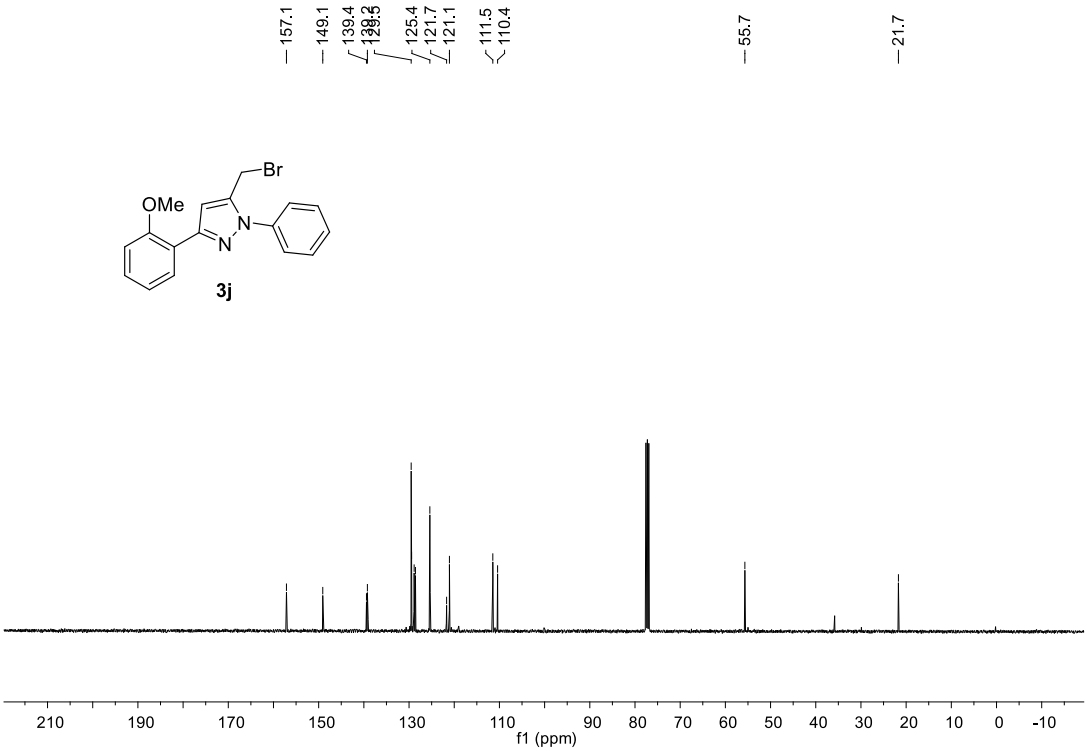
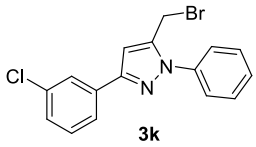
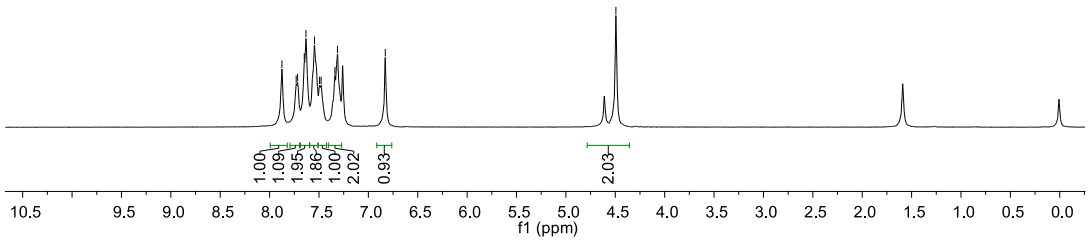
4.540
3.944
Br
OMe
N
N
3j
1.00
2.06
3.13
f1 (ppm)


157.1
149.1
139.4
125.4
121.7
121.1
111.5
110.4
55.7
21.7
Br
OMe
N
N
3j
f1 (ppm)

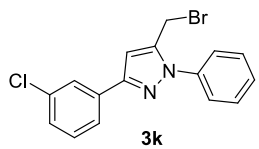

7.875
7.731
7.716
7.649
7.632
7.545
7.494
7.479
7.339
7.313
6.829
4.494


Br
Cl
N
N

3k

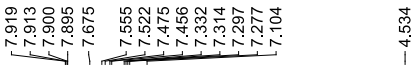

1.00
1.09
1.95
1.86
1.00
2.02
0.93
2.03
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

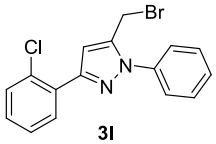

150.9
140.6
139.1
134.7
129.7
126.1
125.4
124.1
106.2
21.1


Br
Cl
N
N

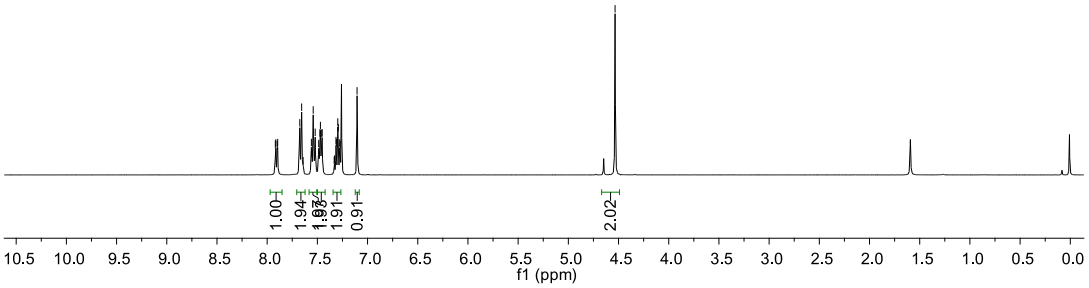
3k

210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

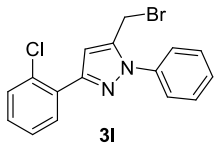

7.919
7.913
7.900
7.895
7.675
7.555
7.522
7.475
7.456
7.332
7.314
7.297
7.277
7.104
4.534


Br
Cl
N
N

3l

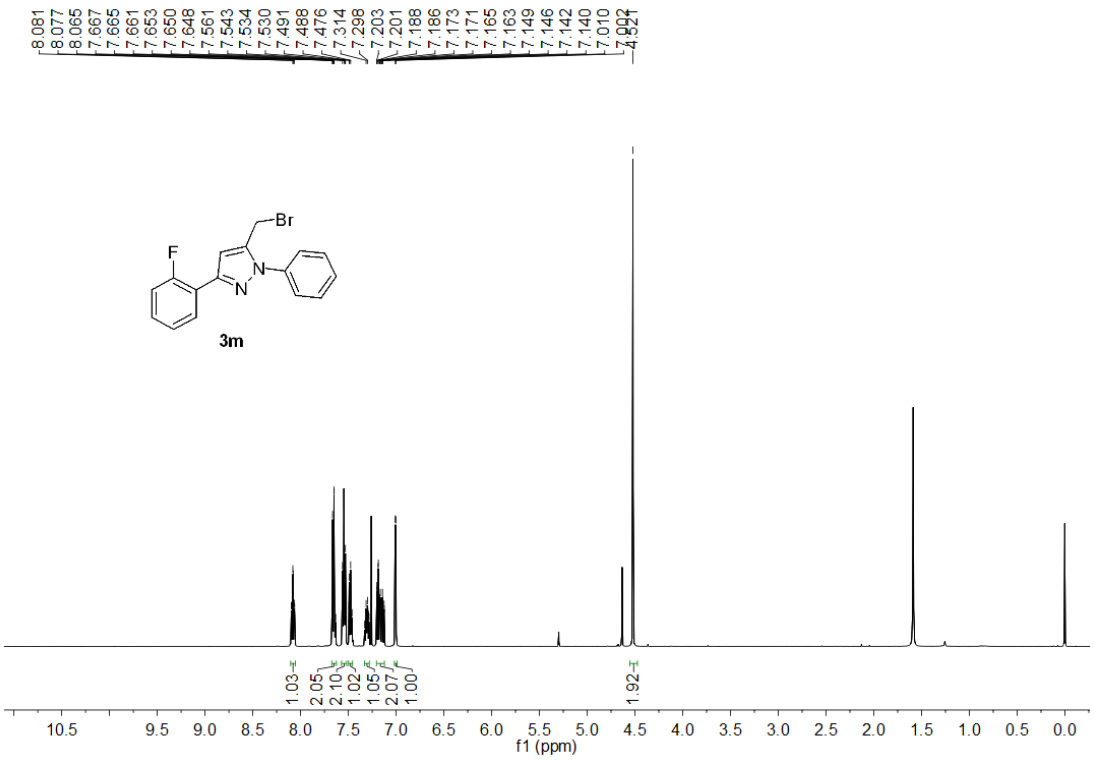

1.00
1.94
1.91
0.91
2.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

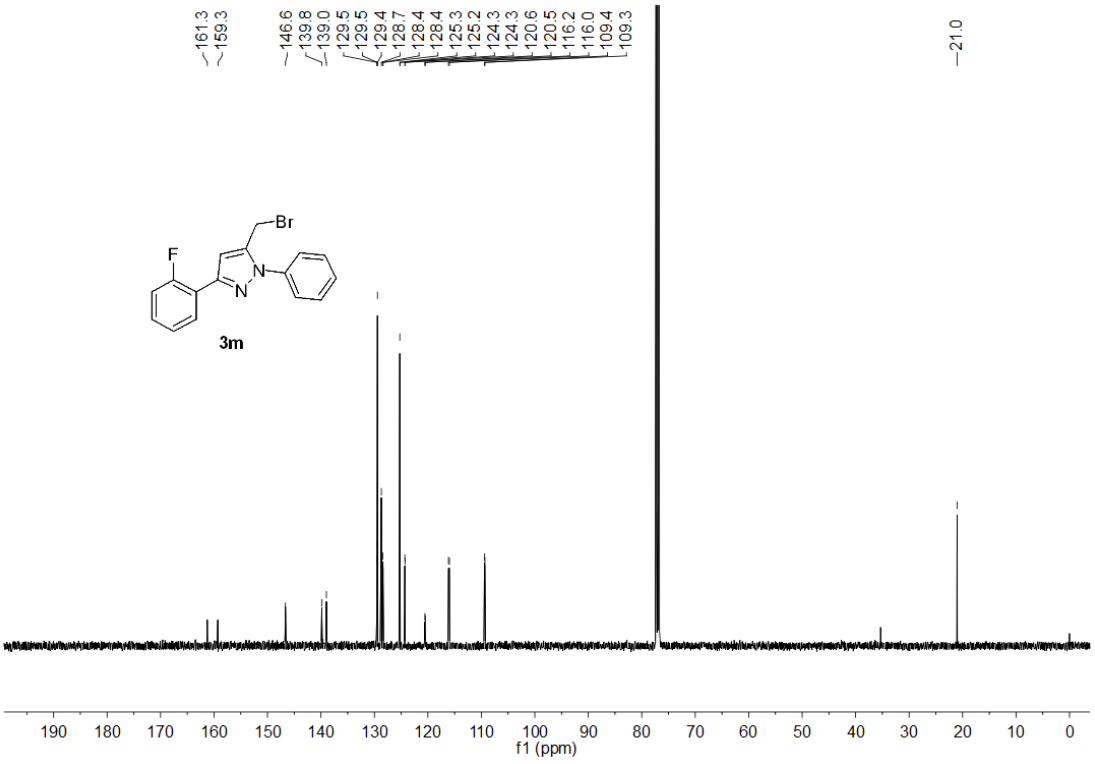

149.8
139.5
139.2
130.8
129.6
128.9
125.4
110.1
21.3

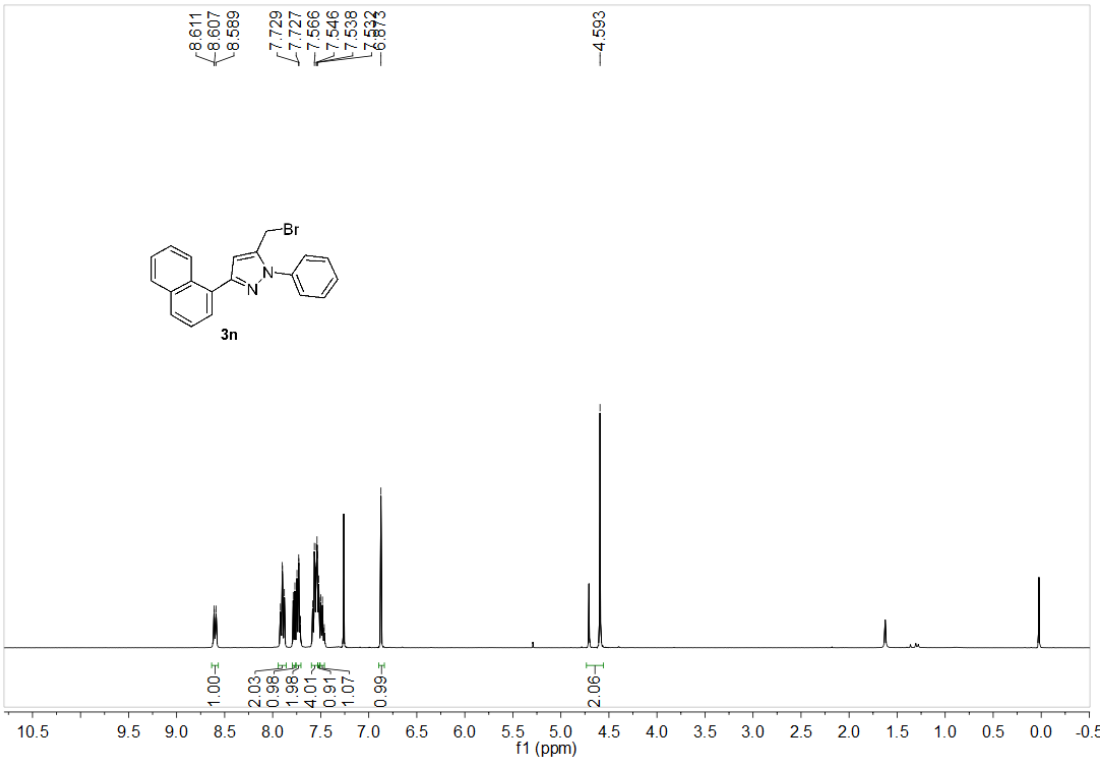

Br
Cl
N
N

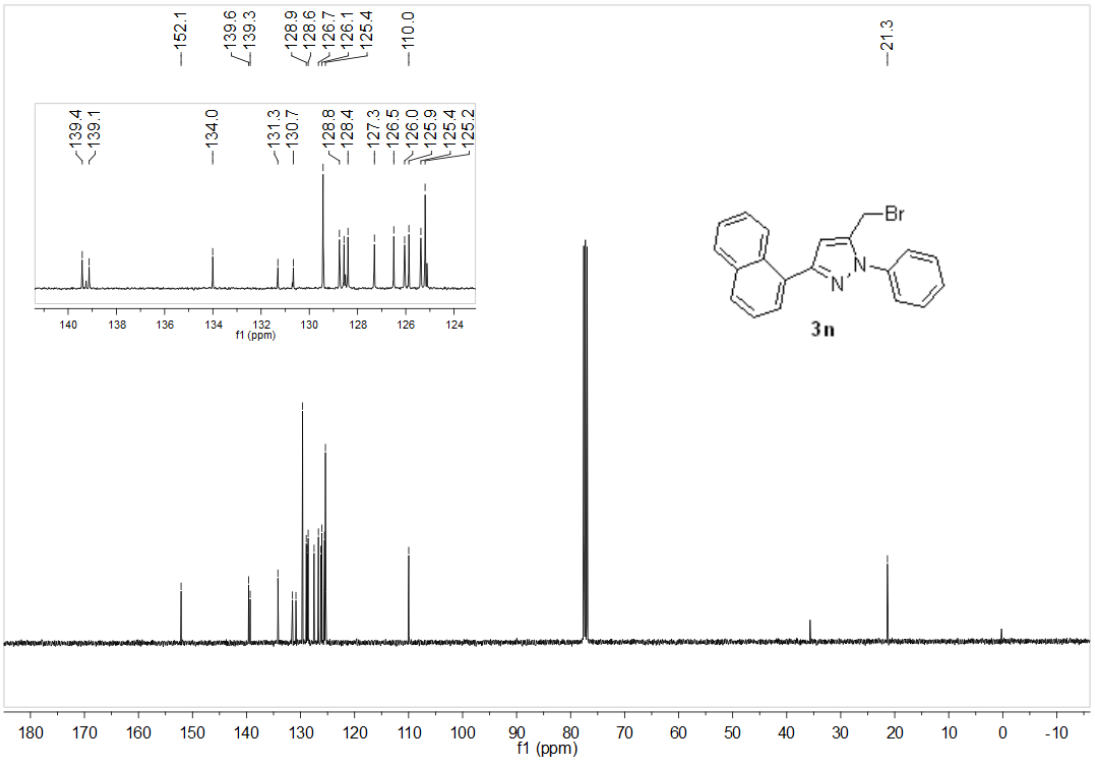
3l

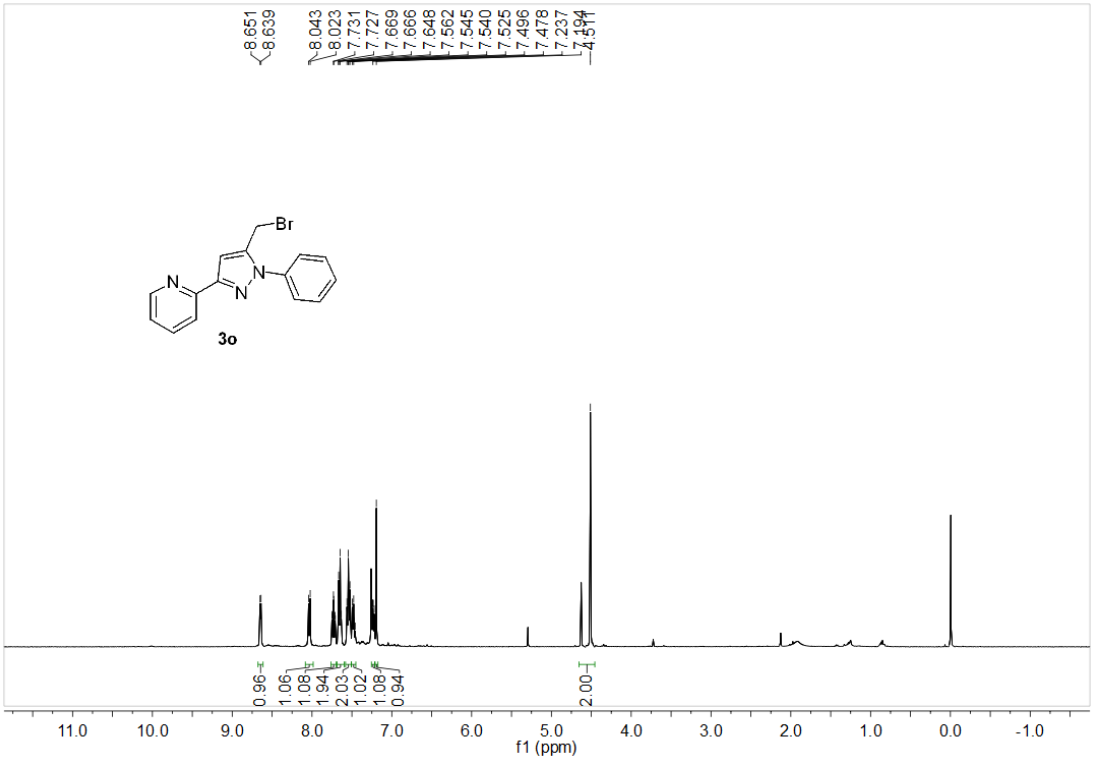
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

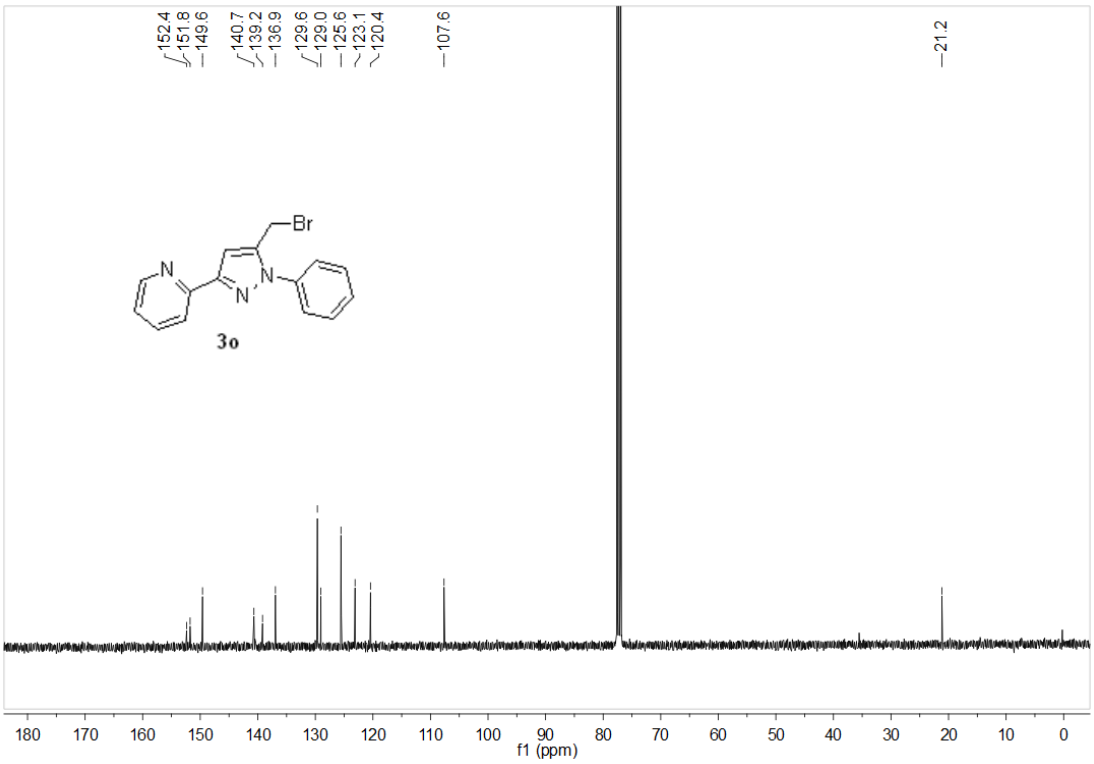

8.081
8.077
8.065
7.667
7.665
7.661
7.653
7.650
7.648
7.561
7.543
7.534
7.530
7.491
7.488
7.476
7.314
7.298
7.203
7.201
7.188
7.186
7.173
7.171
7.165
7.163
7.149
7.146
7.142
7.140
7.010
7.002
4.921
Br
F
N
N
3m
1.03
2.05
2.10
1.02
1.05
2.07
1.00
1.92
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

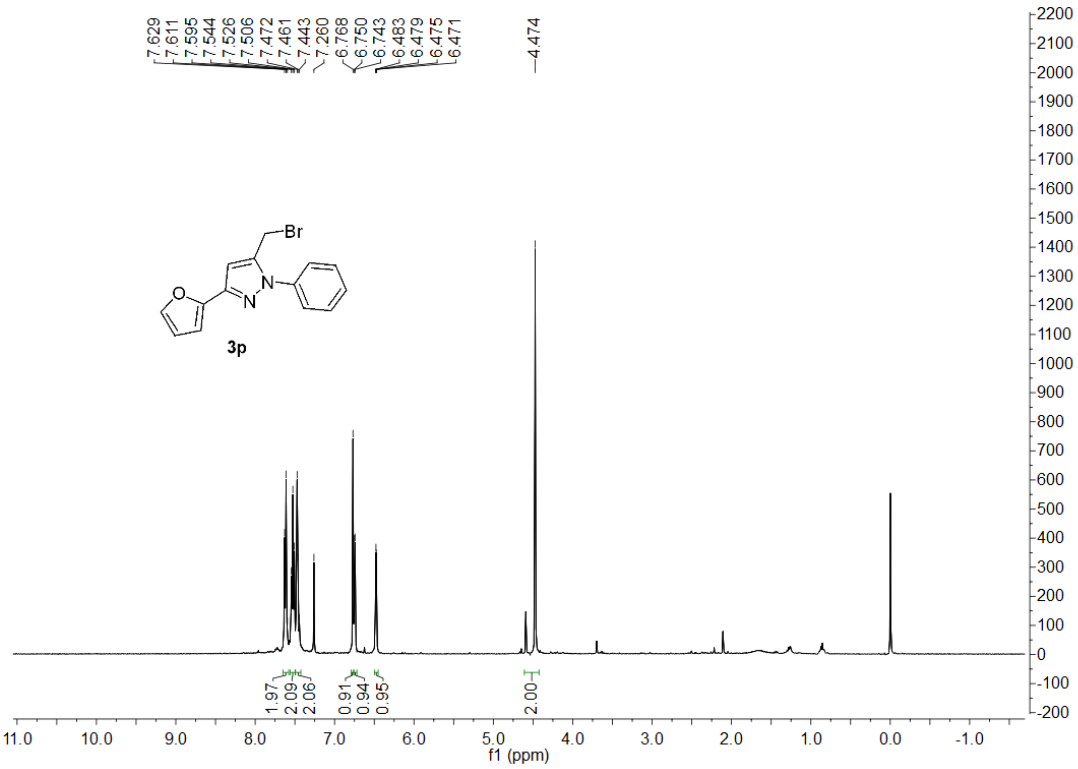

161.3
159.3
146.6
139.8
139.0
129.5
129.5
129.4
128.7
128.4
128.4
125.3
125.2
124.3
124.3
120.6
120.5
116.2
116.0
109.4
109.3
21.0
Br
F
N
N
3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

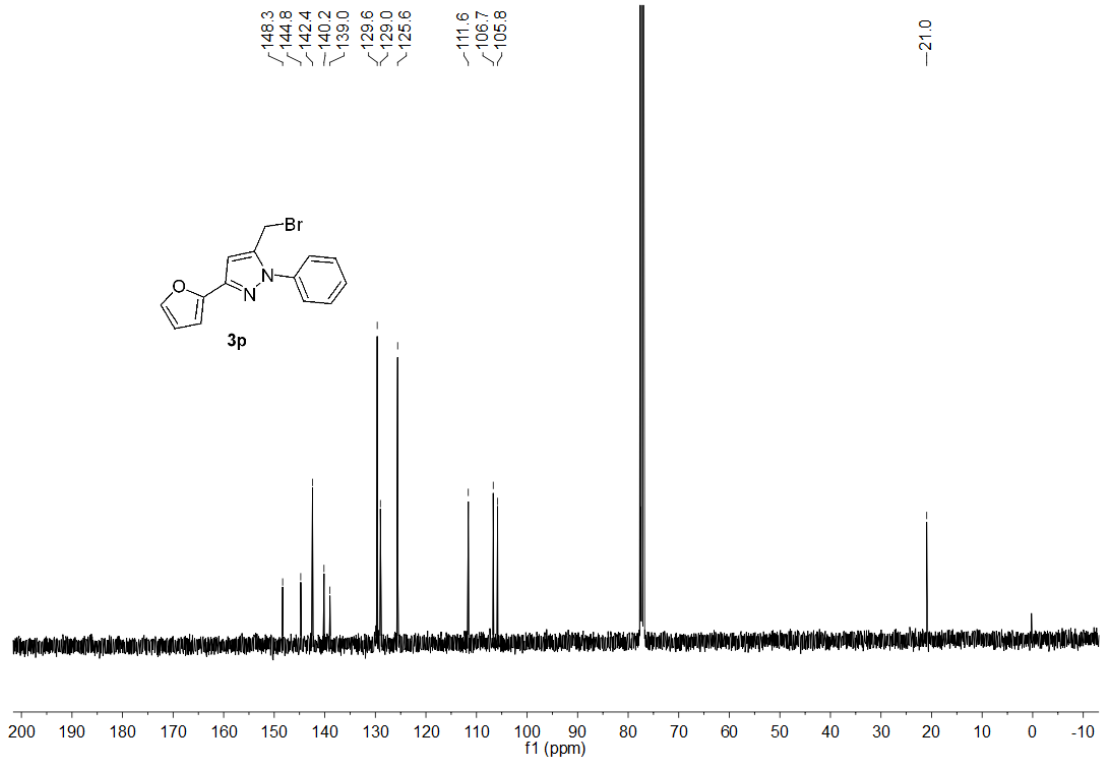

8.611
8.607
8.589
7.729
7.727
7.566
7.546
7.538
4.593
Br
N
N
3n
1.00
2.03
0.98
1.98
4.01
0.91
1.07
0.99
2.06
f1 (ppm)

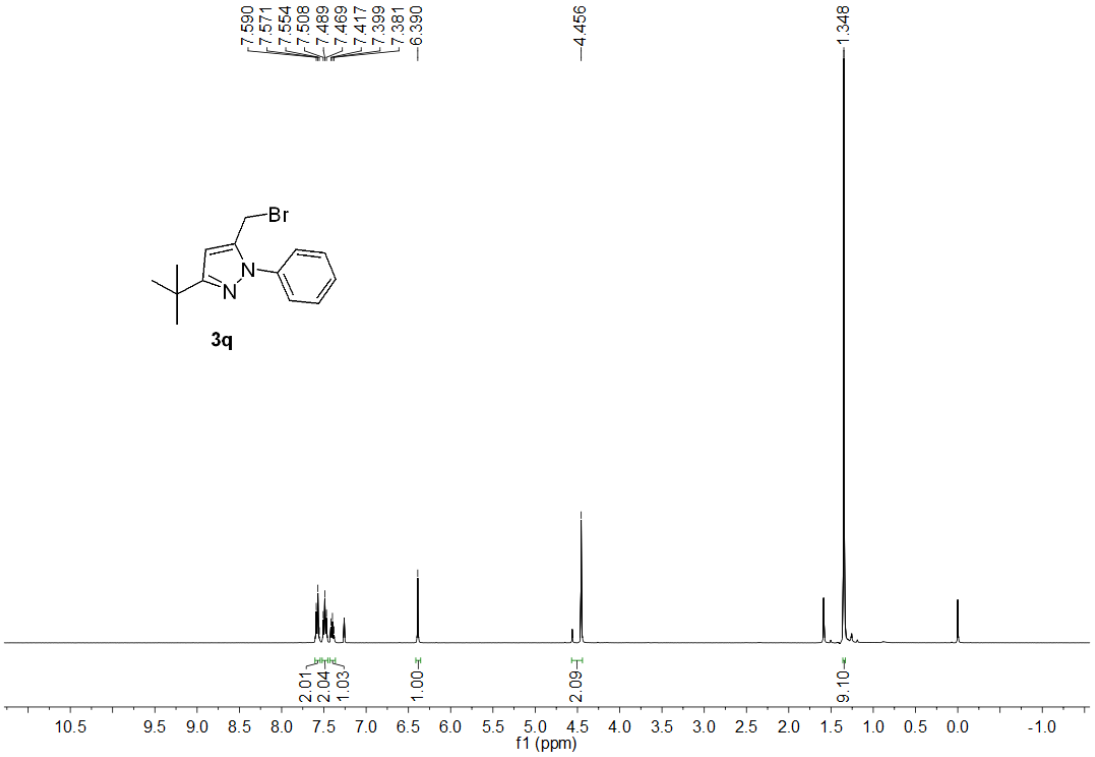

152.1
139.6
139.3
128.9
128.6
126.7
126.1
125.4
110.0
21.3
139.4
139.1
134.0
131.3
130.7
128.8
128.4
127.3
126.5
126.0
125.9
125.4
125.2
f1 (ppm)
Br
N
N
3n
f1 (ppm)

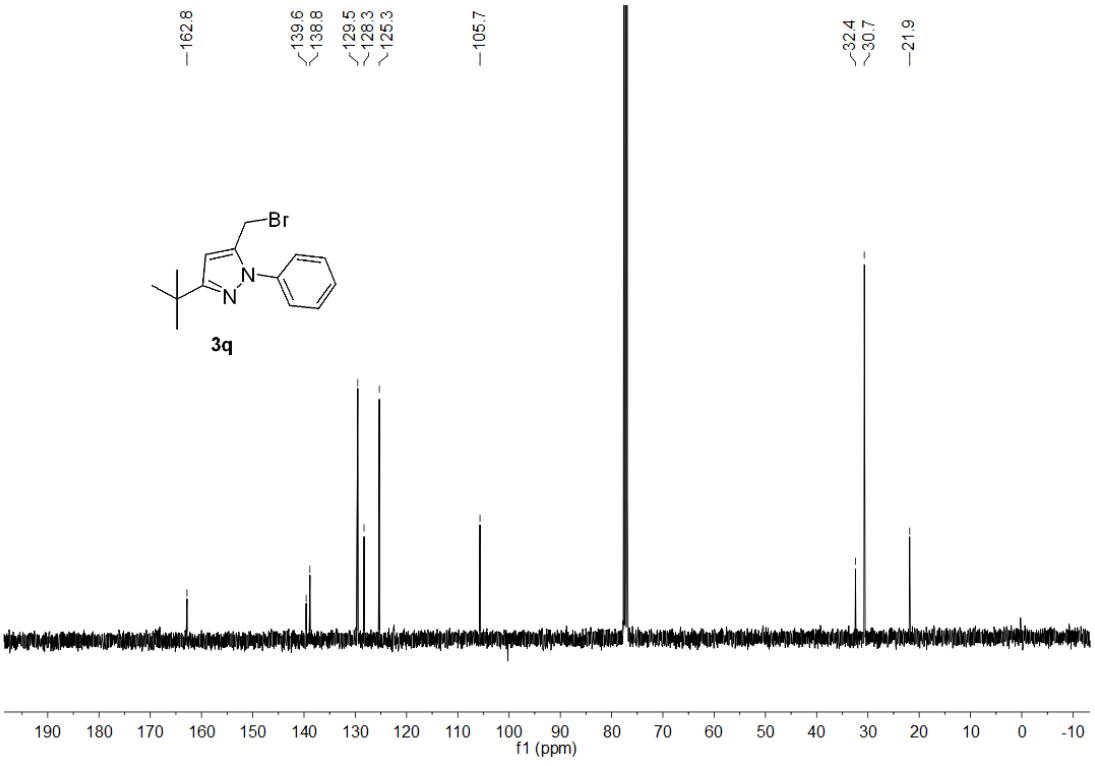

8.651
8.639
8.043
8.023
7.731
7.727
7.669
7.666
7.648
7.562
7.545
7.540
7.525
7.496
7.478
7.237
7.194
4.511
Br
N
N
3o
0.96
1.06
1.08
1.94
2.03
1.02
1.08
0.94
2.00
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

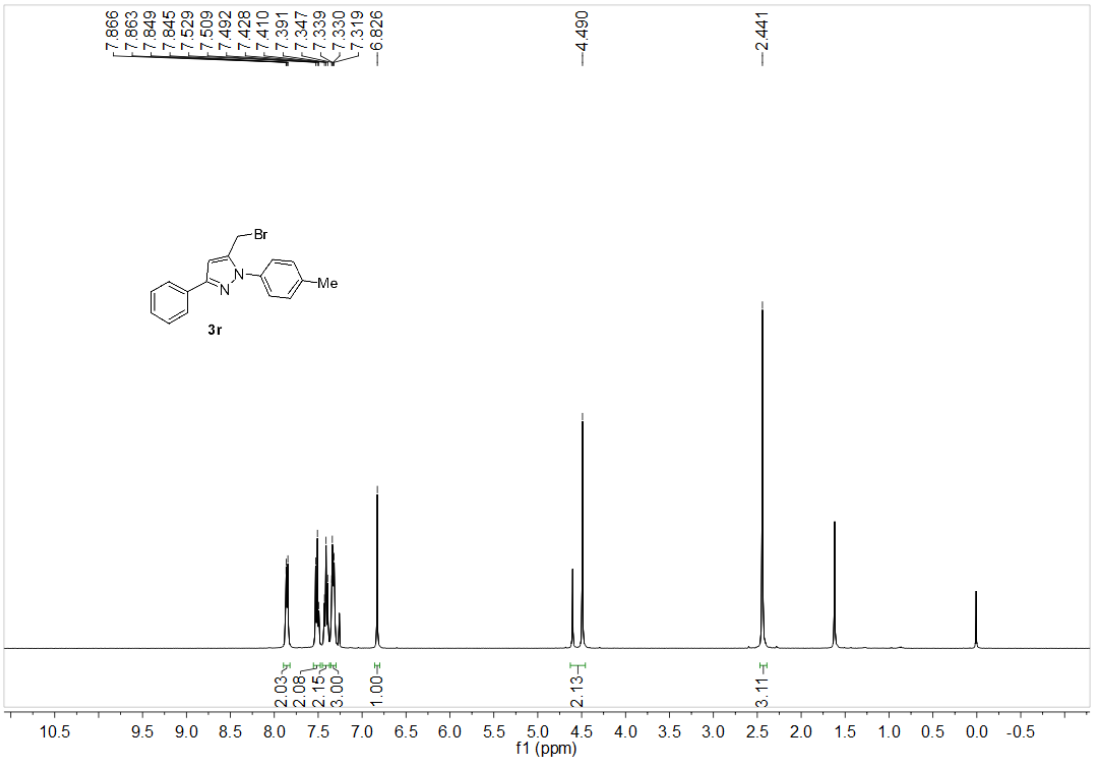

152.4
151.8
149.6
140.7
139.2
136.9
129.6
129.0
125.6
123.1
120.4
107.6
21.2
Br
N
N
3o
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.629
7.611
7.595
7.544
7.526
7.506
7.472
7.461
7.443
7.260
6.768
6.750
6.743
6.483
6.479
6.475
6.471
4.474
Br
O
N
N
3p
1.97
2.09
2.06
0.91
0.94
0.95
2.00
f1 (ppm)


148.3
144.8
142.4
140.2
139.0
129.6
129.0
125.6
111.6
106.7
105.8
21.0
Br
O
N
N
3p
f1 (ppm)


7.590
7.571
7.554
7.508
7.489
7.469
7.417
7.399
7.381
6.390
4.456
1.348
Br
N
N
3q
2.01
2.04
1.03
1.00
2.09
9.10
10.5 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 -1.0
f1 (ppm)


162.8
139.6
138.8
129.5
128.3
125.3
105.7
32.4
30.7
21.9
Br
N
N
3q
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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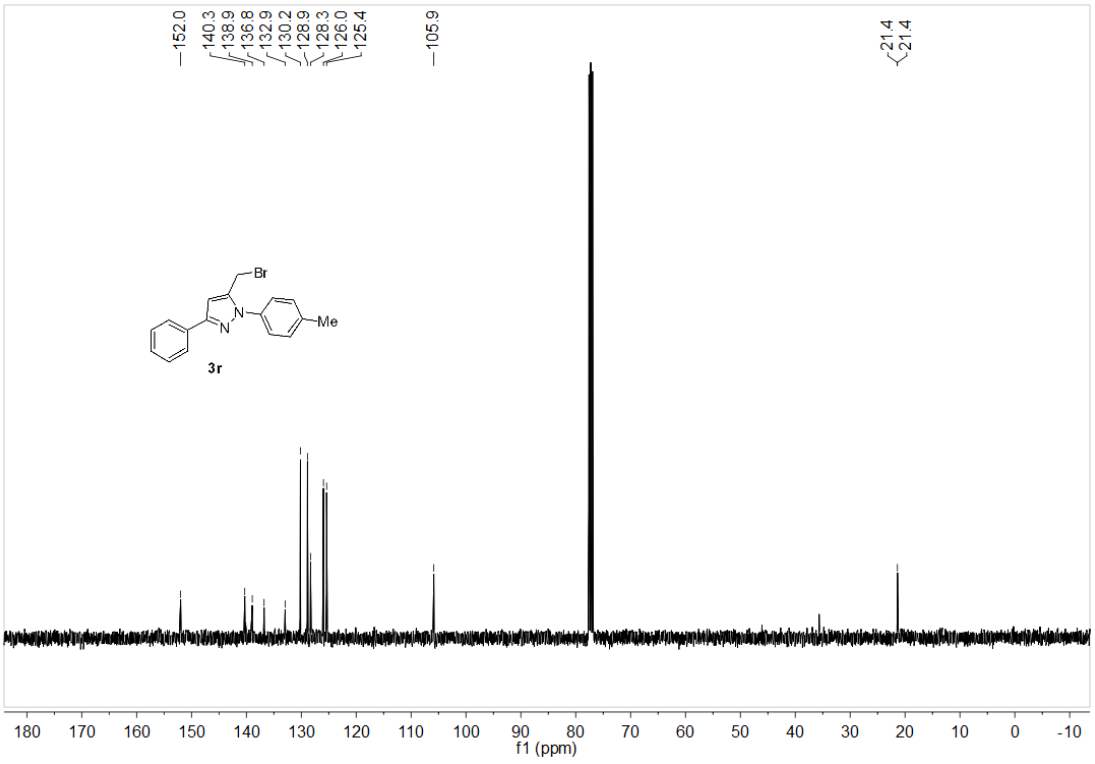
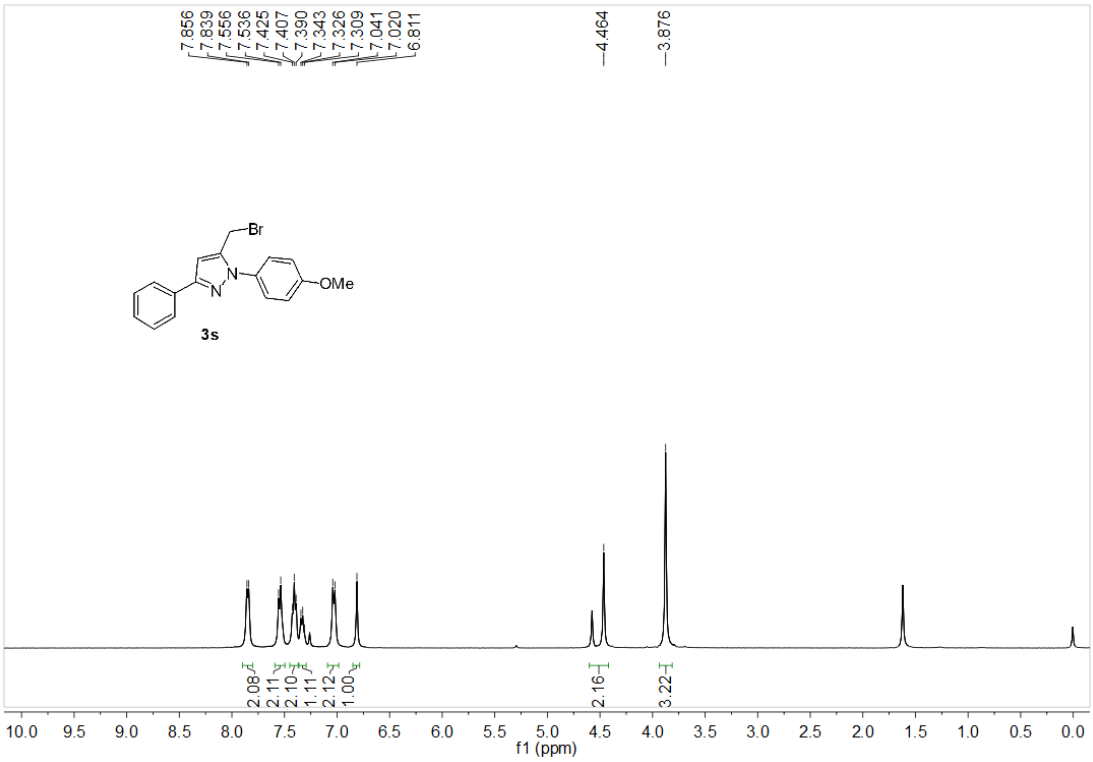
7.863
7.849
7.845
7.529
7.509
7.492
7.428
7.410
7.391
7.347
7.339
7.330
7.319
6.826
4.490
2.441
Br
N
N
Me
3r
2.03
2.08
2.15
3.00
1.00
2.13
3.11
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


152.0
140.3
138.9
136.8
132.9
130.2
128.9
128.3
126.0
125.4
105.9
21.4
21.4
Br
N
N
Me
3r
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.856
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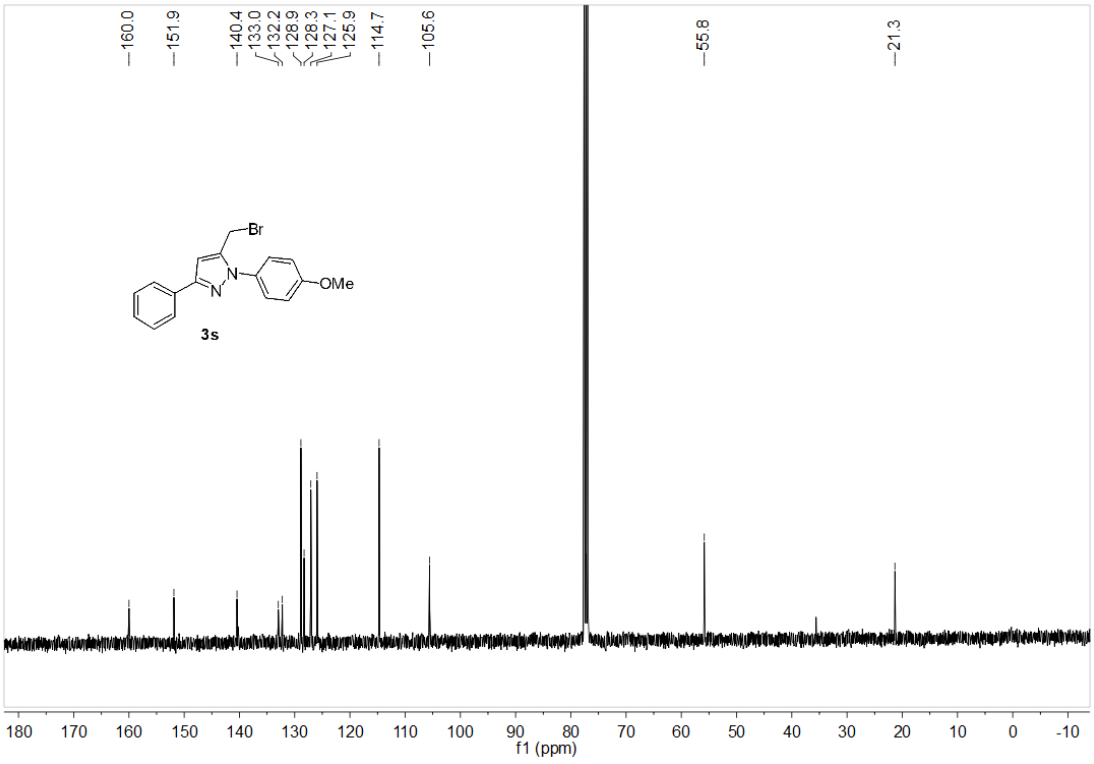
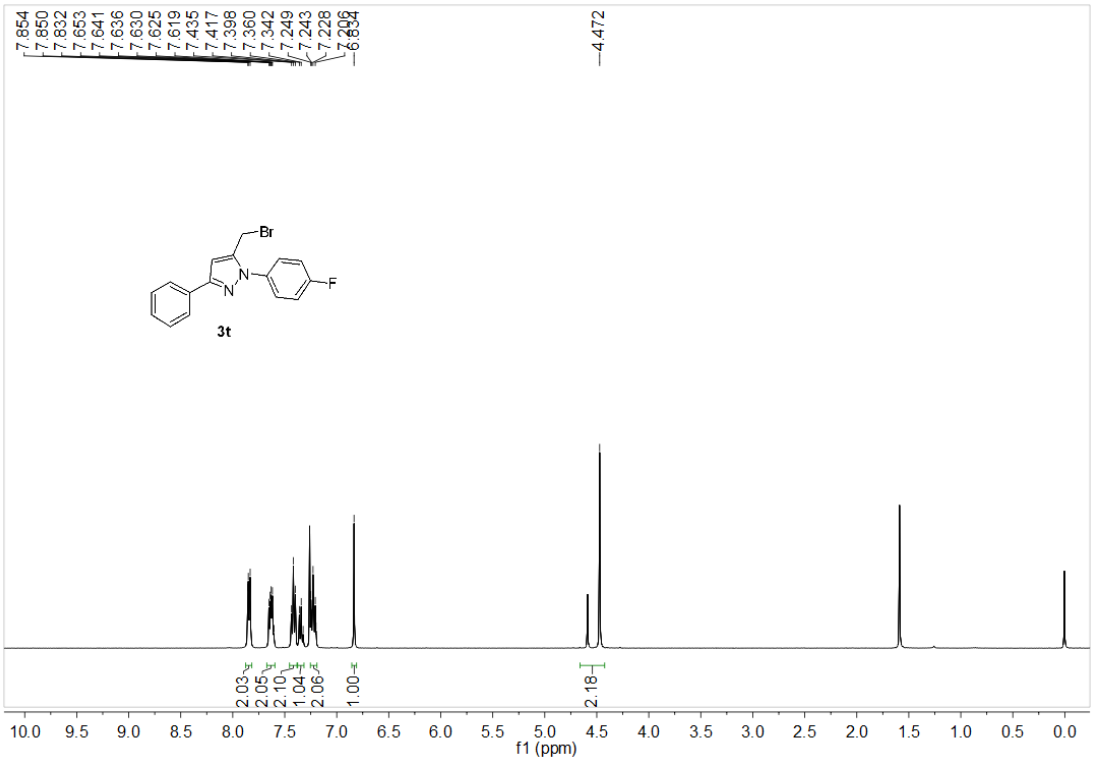
7.556
7.536
7.425
7.407
7.390
7.343
7.326
7.309
7.041
7.020
6.811
4.464
3.876
Br
N
N
OMe
3s
2.08
2.11
2.10
1.11
2.12
1.00
2.16
3.22
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


160.0
151.9
140.4
133.0
132.2
128.9
128.3
127.1
125.9
114.7
105.6
55.8
21.3
Br
N
N
OMe
3s
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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7.850
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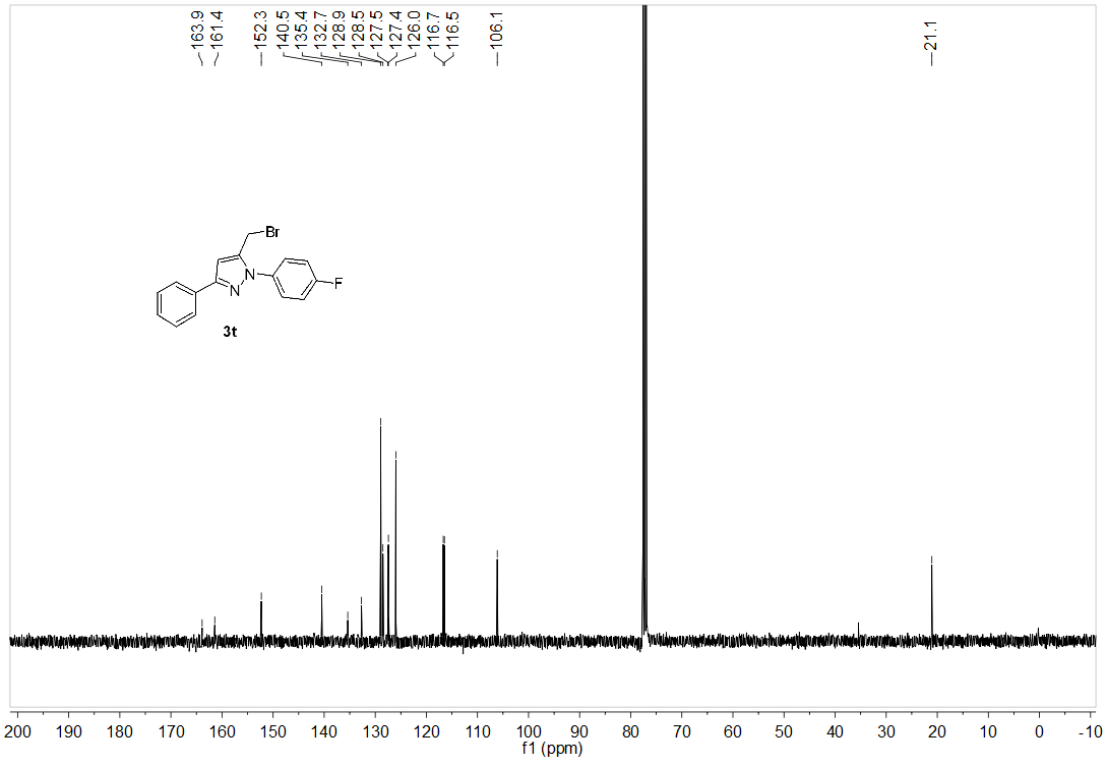
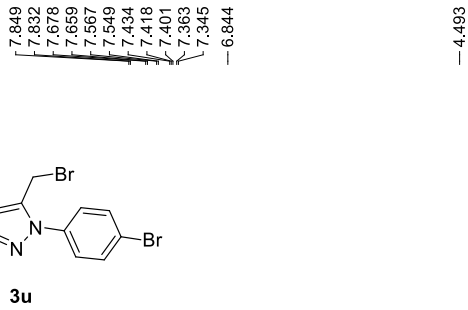
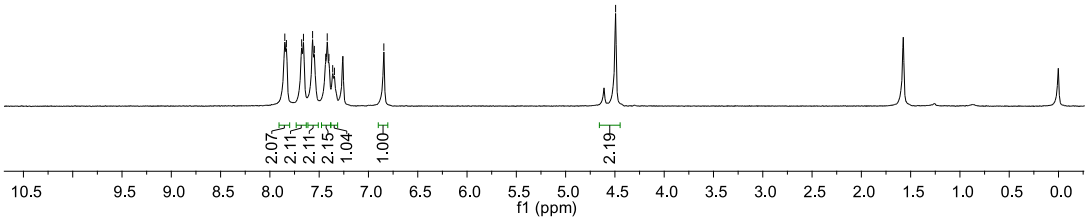
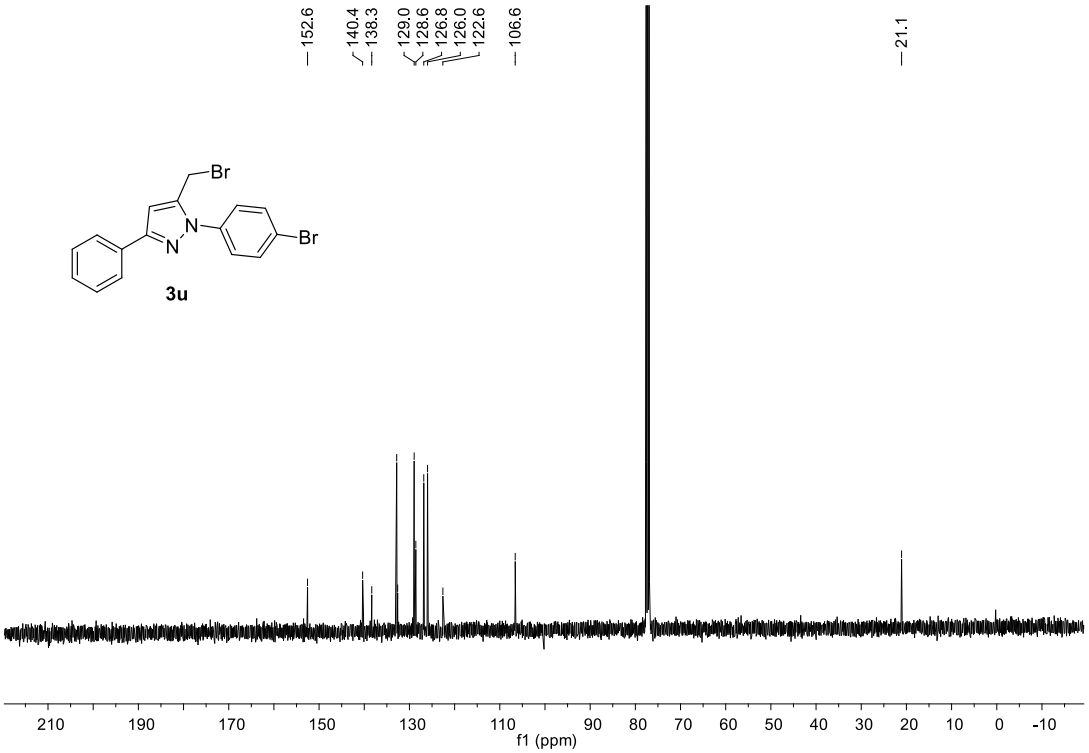
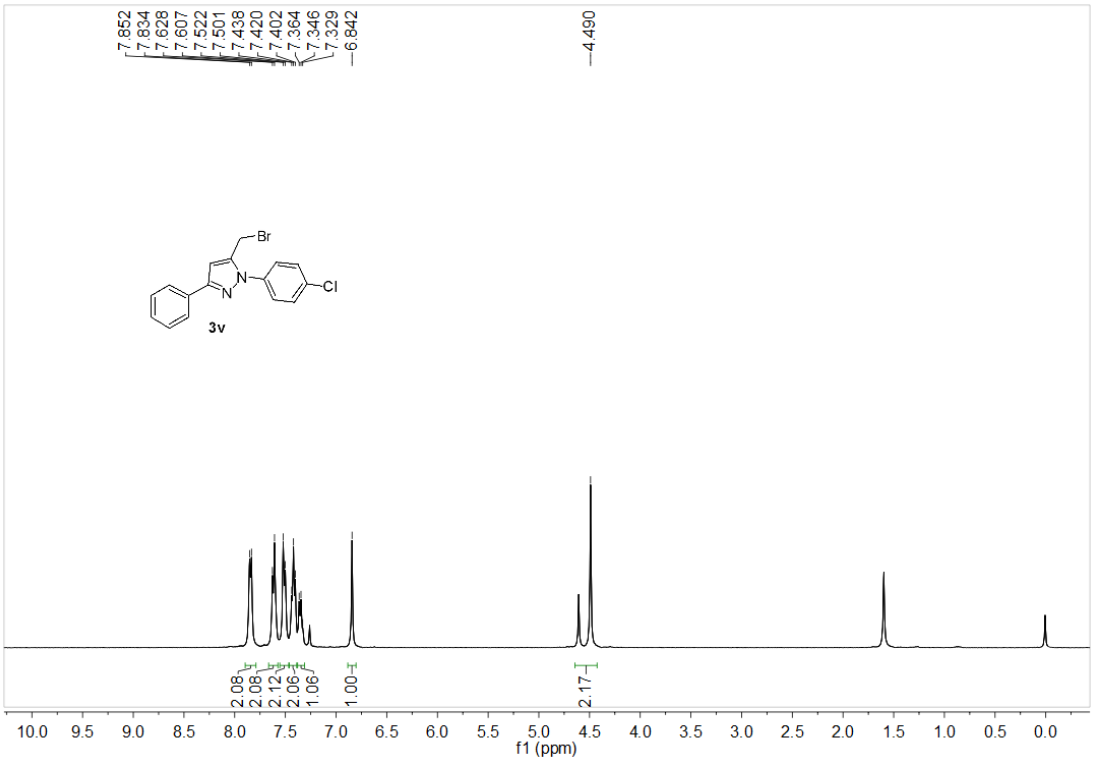
7.641
7.636
7.630
7.625
7.619
7.435
7.417
7.398
7.360
7.342
7.249
7.243
7.228
4.472
Br
N
N
F
3t
2.03
2.05
2.10
1.04
2.06
1.00
2.18
f1 (ppm)

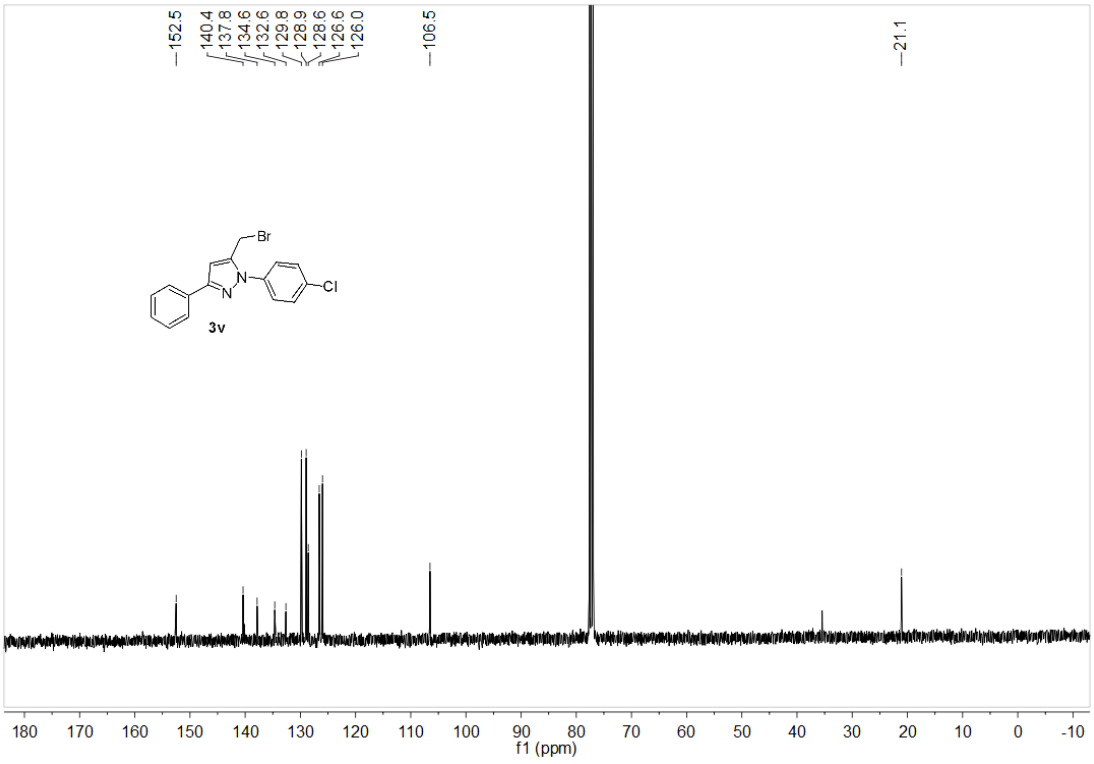

163.9
161.4
152.3
140.5
135.4
132.7
128.9
128.5
127.5
127.4
126.0
116.7
116.5
106.1
21.1
Br
N
N
F
3t
f1 (ppm)

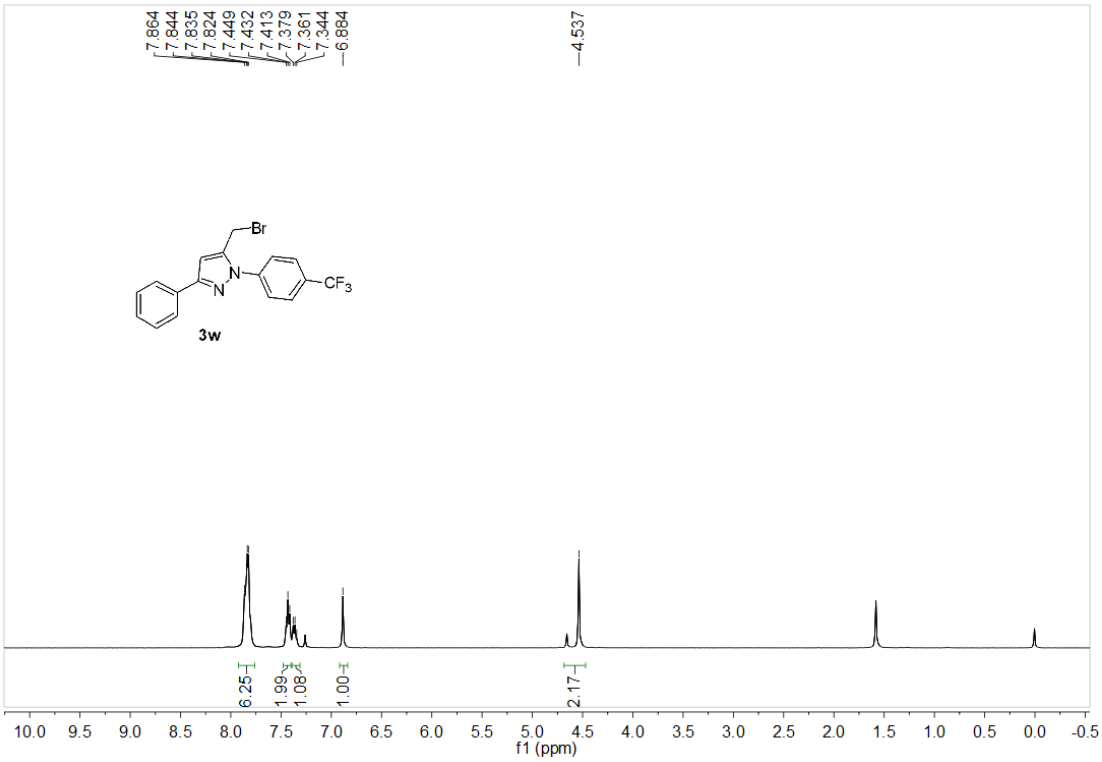

7.849
7.832
7.678
7.659
7.567
7.549
7.434
7.418
7.401
7.363
7.345
6.844
4.493
Br
N
N
Br
3u

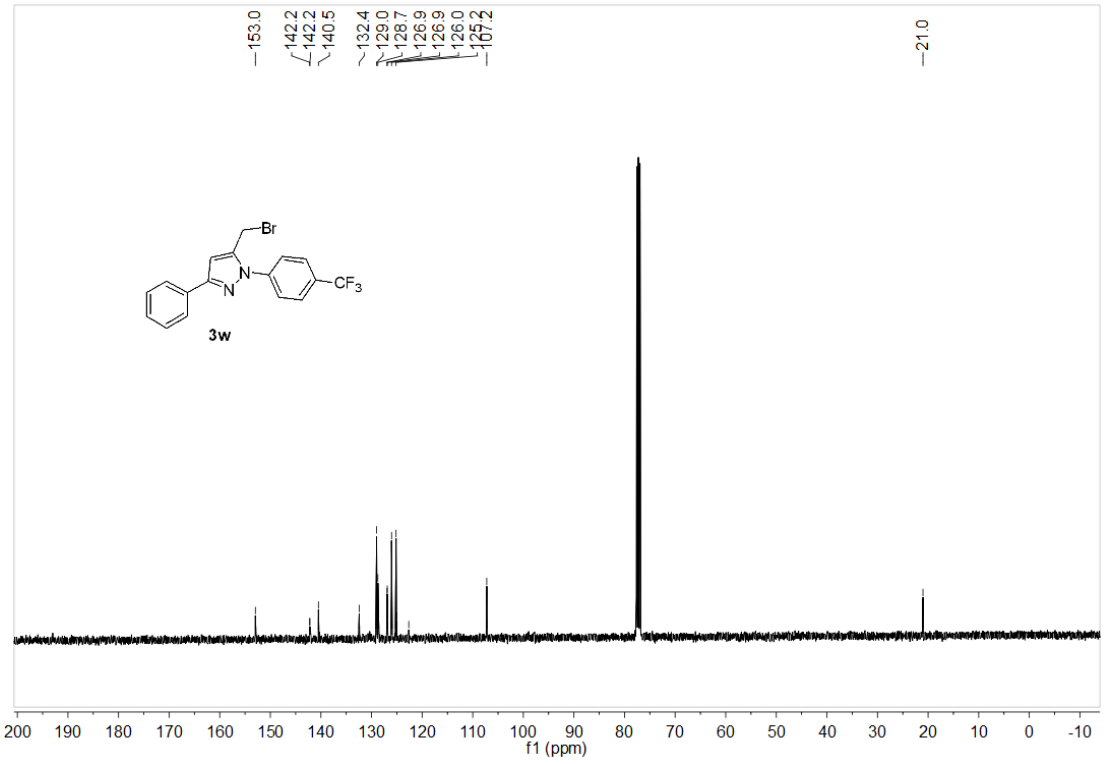

2.07
2.11
2.11
2.15
1.04
1.00
2.19
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

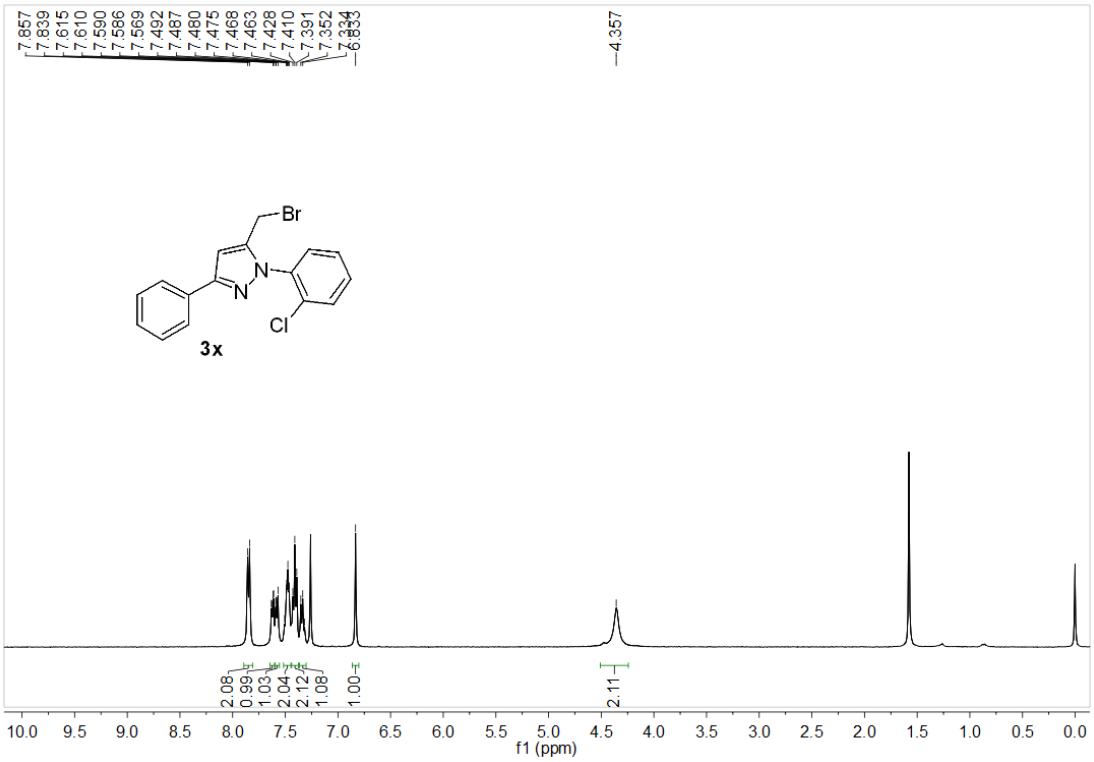

152.6
140.4
138.3
129.0
128.6
126.8
126.0
122.6
106.6
21.1
Br
N
N
Br
3u
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

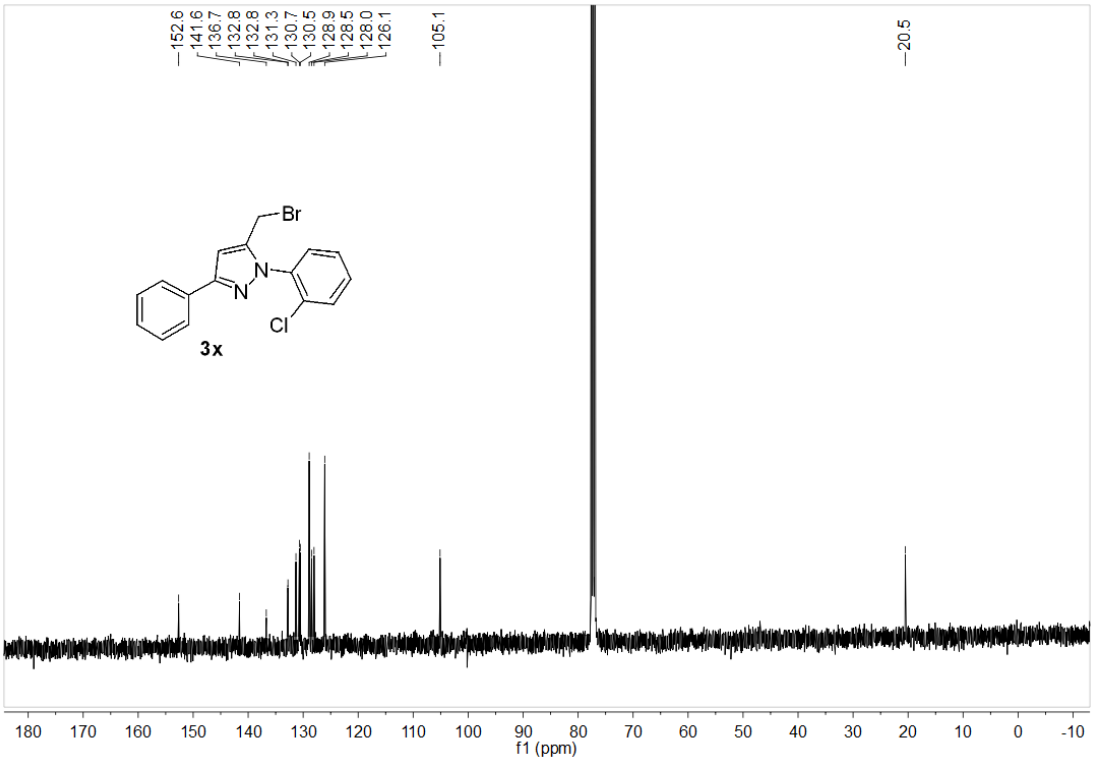

7.852
7.834
7.628
7.607
7.522
7.501
7.438
7.420
7.402
7.364
7.346
7.329
6.842
4.490
Br
N
N
Cl
3v
2.08
2.08
2.12
2.06
1.06
1.00
2.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

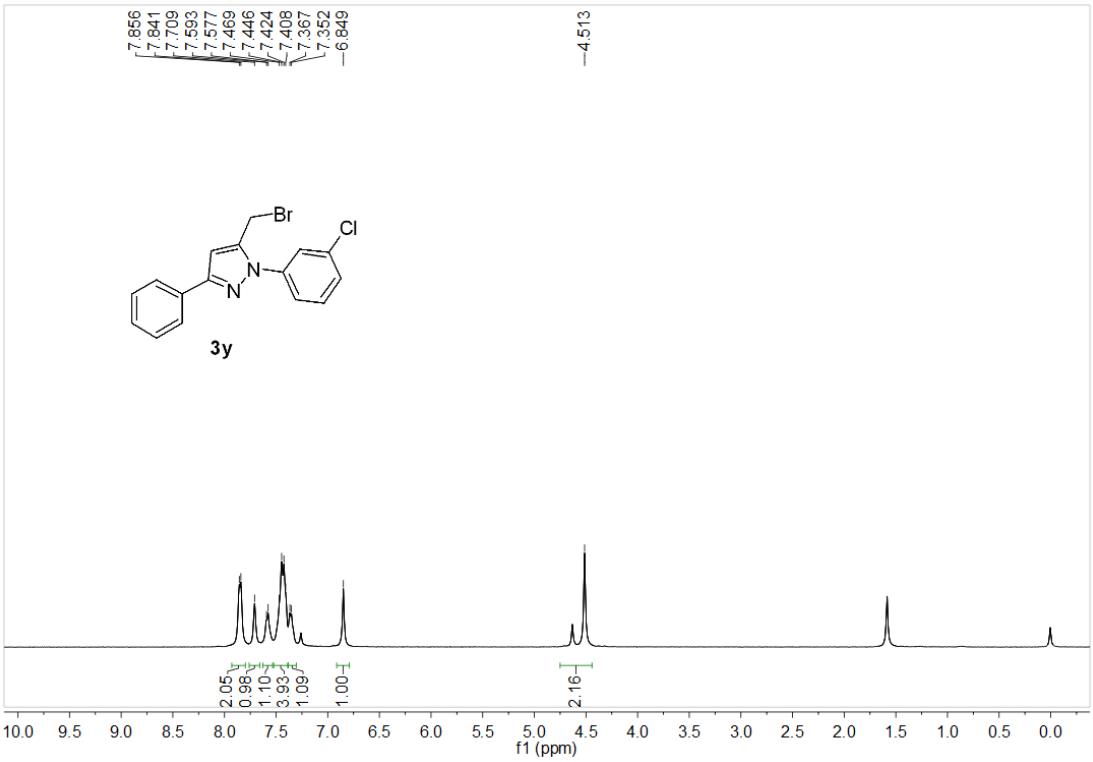

152.5
140.4
137.8
134.6
132.6
129.8
128.9
128.6
126.6
126.0
106.5
21.1
Br
N
N
Cl
3v
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

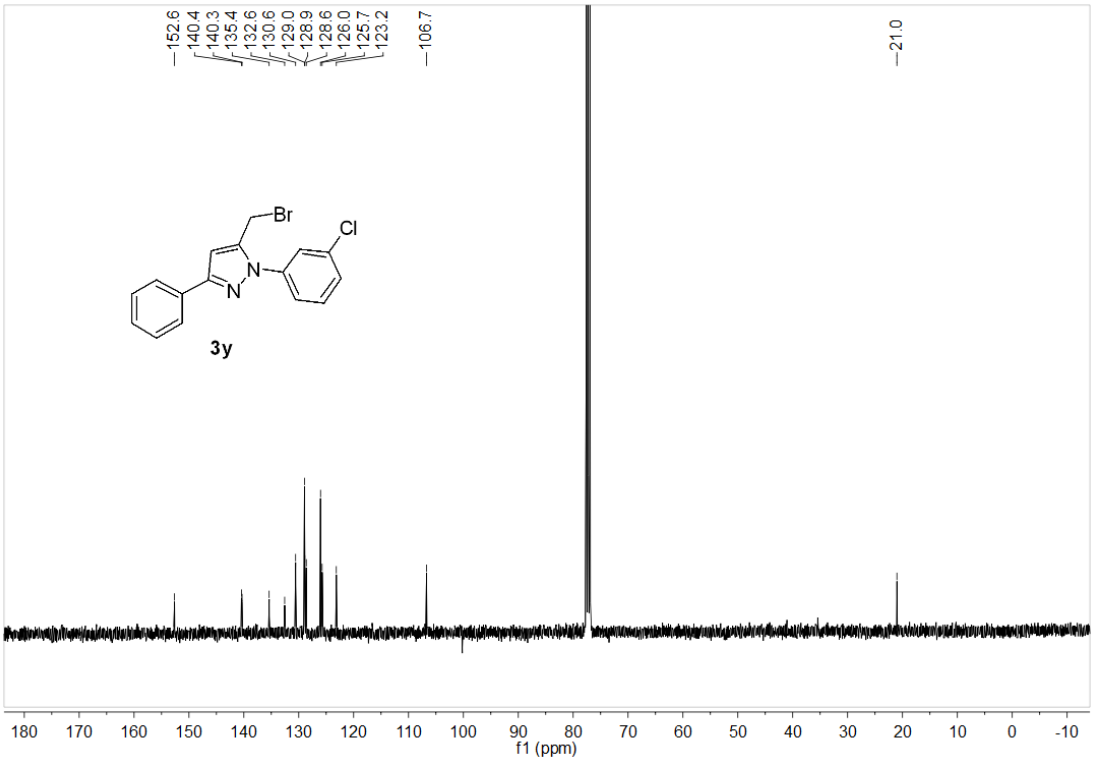

7.864
7.844
7.835
7.824
7.449
7.432
7.413
7.379
7.361
7.344
6.884
4.537
Br
N
N
CF3
3w
6.25
1.99
1.08
1.00
2.17
f1 (ppm)

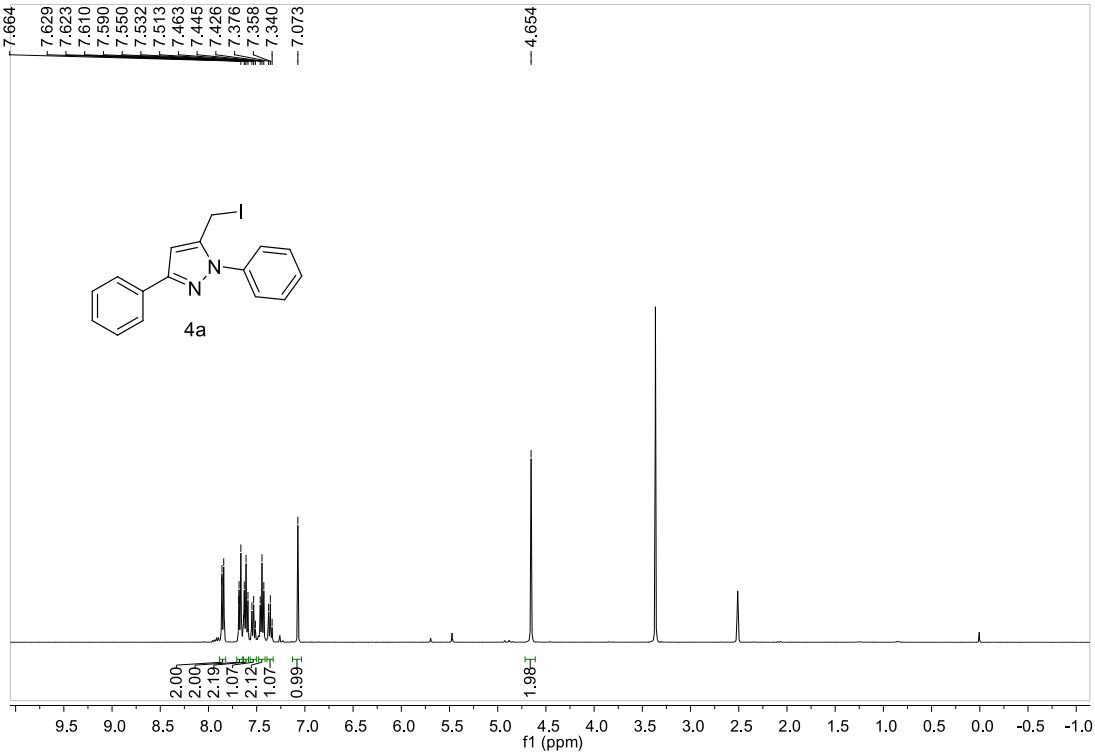

153.0
142.2
142.2
140.5
132.4
129.0
128.7
126.9
126.9
126.0
125.2
107.2
21.0
Br
N
N
CF3
3w
f1 (ppm)

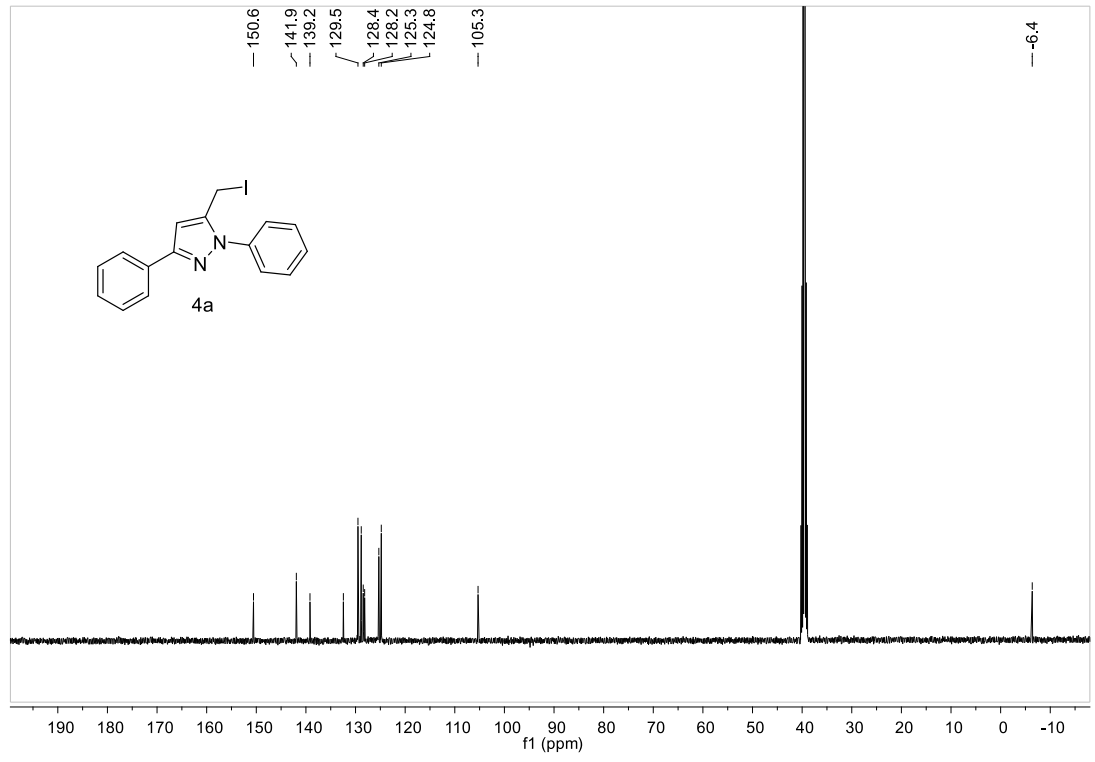

7.857
7.839
7.615
7.610
7.590
7.586
7.569
7.492
7.487
7.480
7.475
7.468
7.463
7.428
7.410
7.391
7.352
6.833
4.357
Br
N
N
Cl
3x
2.08
0.99
1.03
2.04
2.12
1.08
1.00
2.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

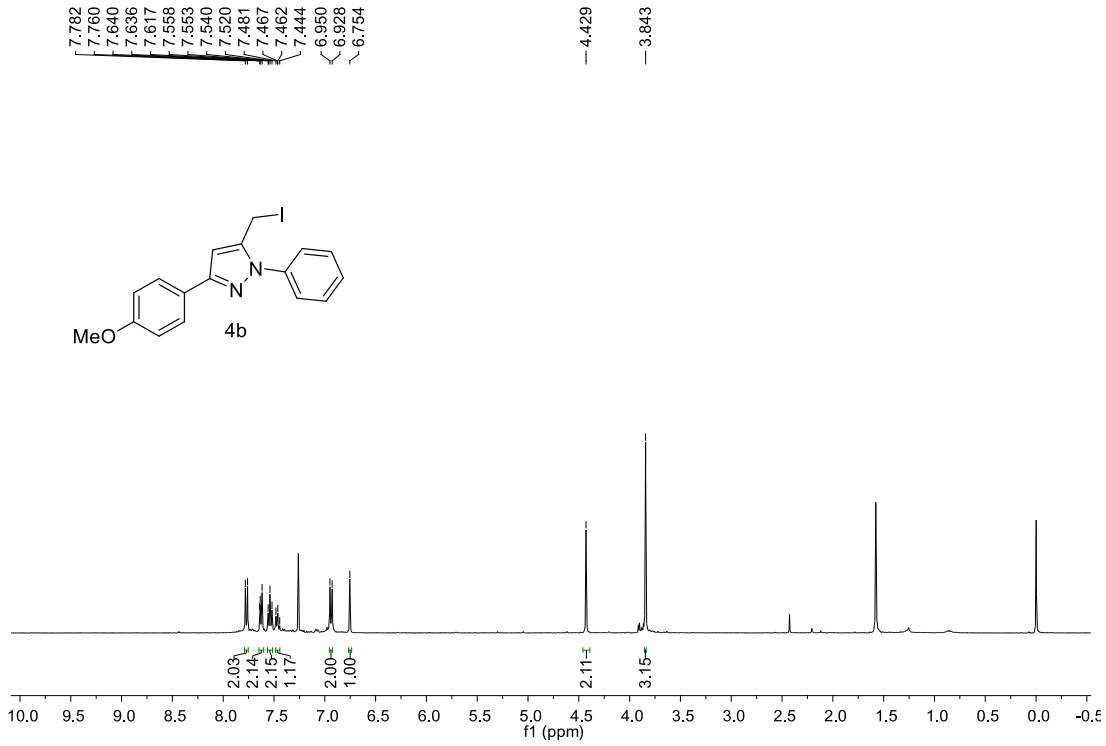

152.6
141.6
136.7
132.8
132.8
131.3
130.7
130.5
128.9
128.5
128.0
126.1
105.1
20.5
Br
N
N
Cl
3x
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

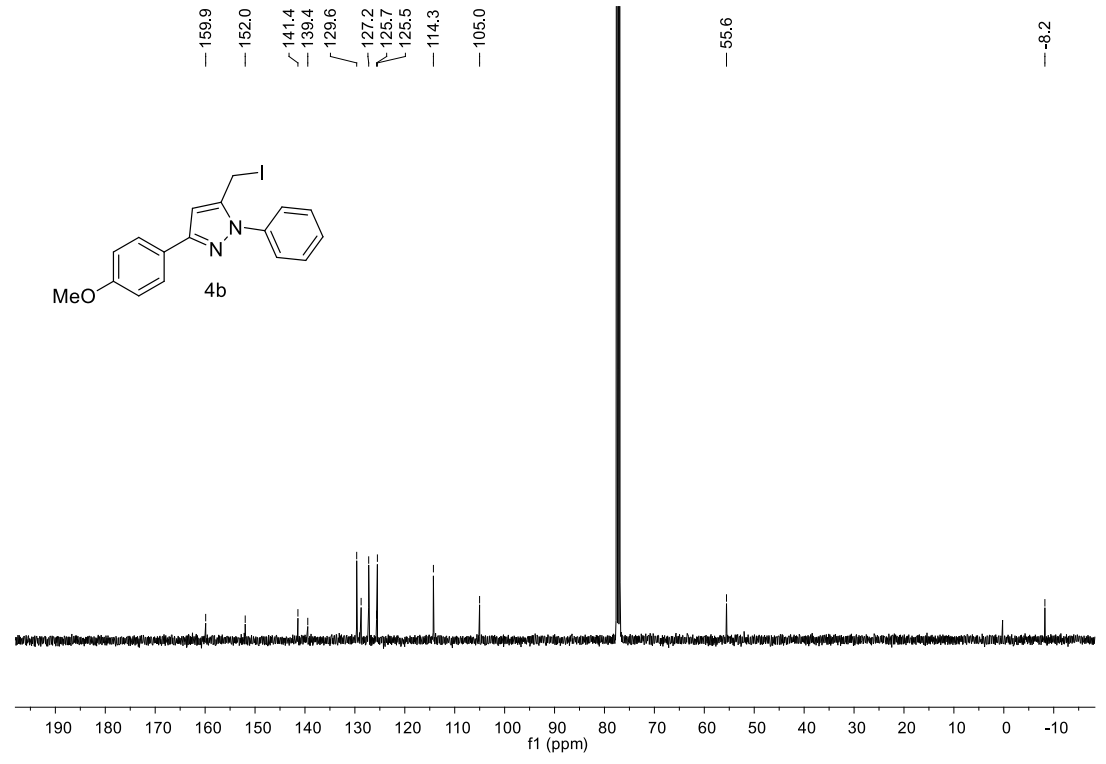

7.856
7.841
7.709
7.593
7.577
7.469
7.446
7.424
7.408
7.367
7.352
6.849
4.513
Br
Cl
N
N
3y
2.05
0.98
1.10
3.93
1.09
1.00
2.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

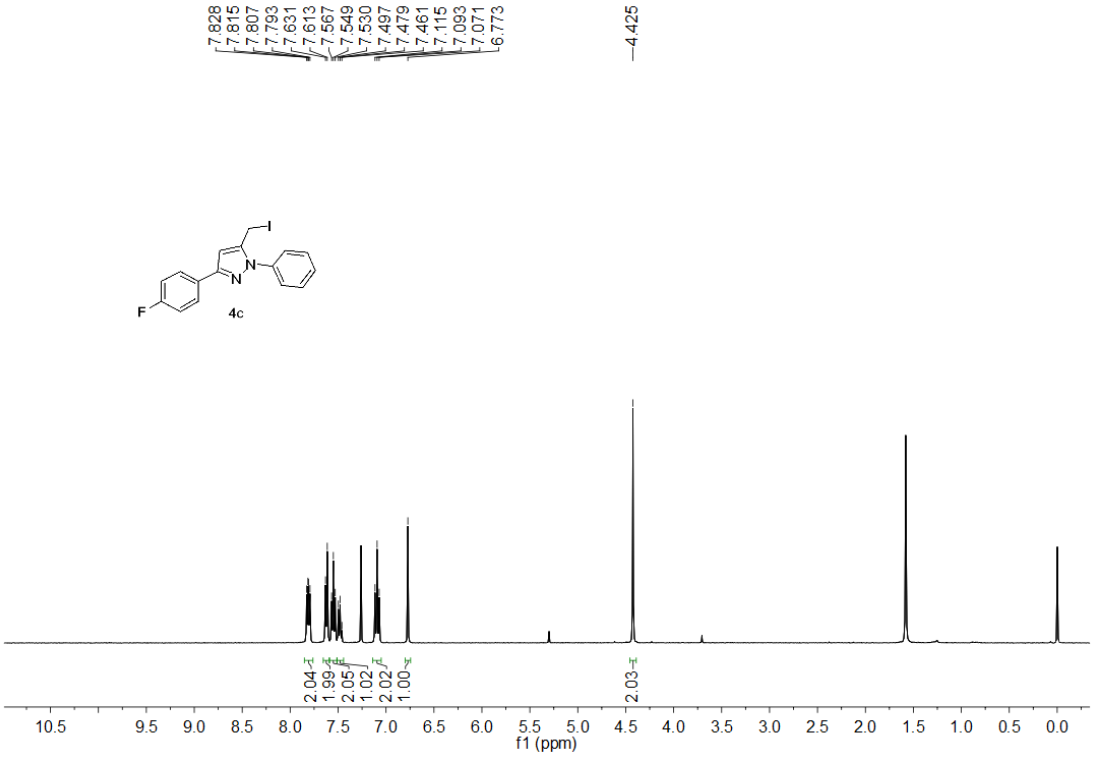

152.6
140.4
140.3
135.4
132.6
130.6
129.0
128.9
128.6
126.0
125.7
123.2
106.7
21.0
Br
Cl
N
N
3y
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

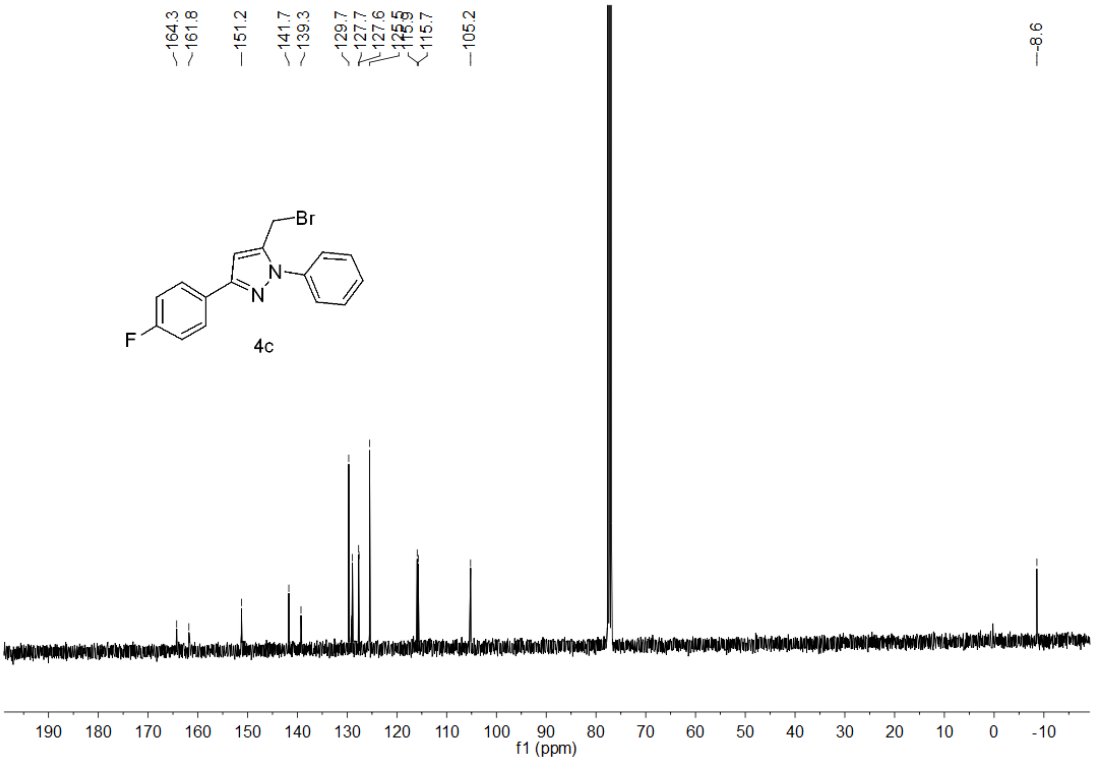

7.664
7.629
7.623
7.610
7.590
7.550
7.532
7.513
7.463
7.445
7.426
7.376
7.358
7.340
7.073
4.654
I
N
N
4a
2.00
2.00
2.19
1.07
2.12
1.07
0.99
1.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

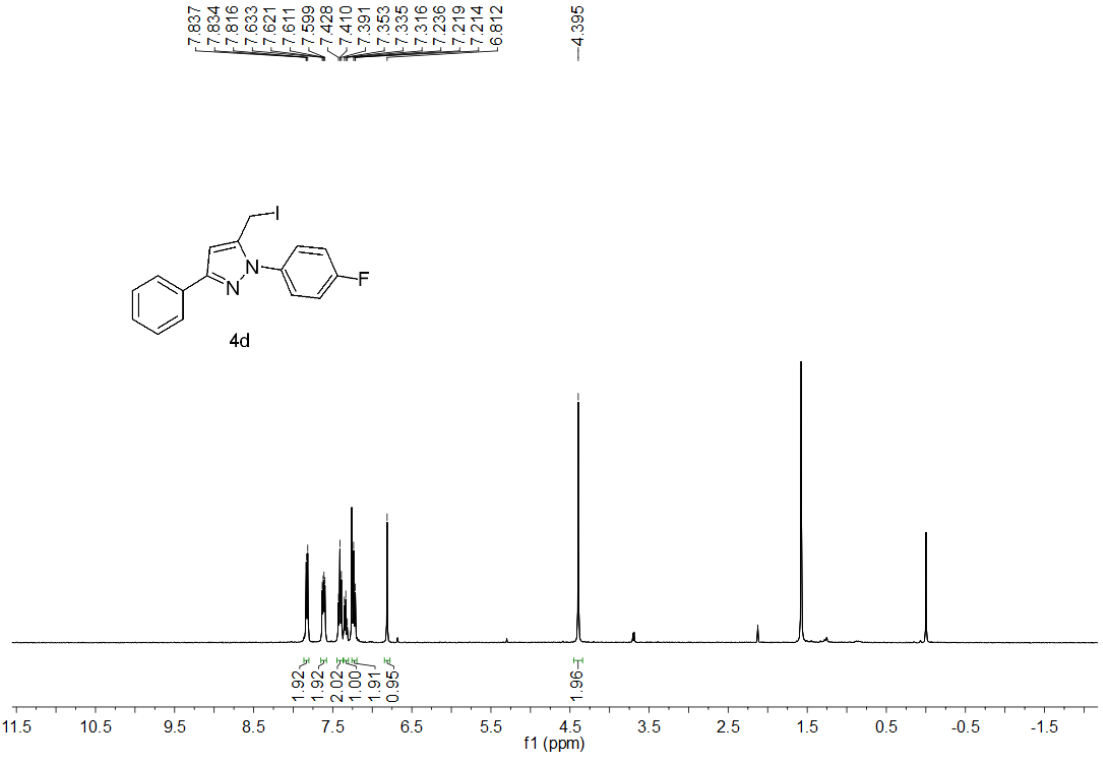

150.6
141.9
139.2
129.5
128.4
128.2
125.3
124.8
105.3
-6.4
I
N
N
4a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

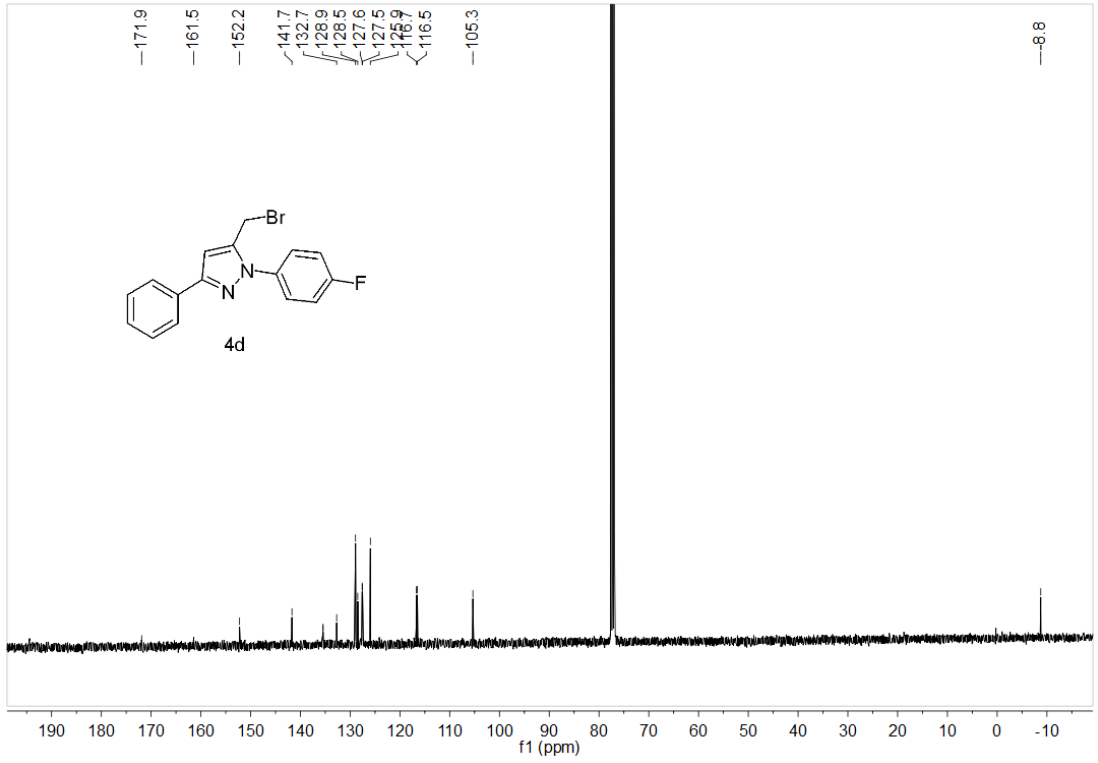

7.782
7.760
7.640
7.636
7.617
7.558
7.553
7.540
7.520
7.481
7.467
7.462
7.444
6.950
6.928
6.754
4.429
3.843
I
N
N
MeO
4b
2.03
2.14
2.15
1.17
2.00
1.00
2.11
3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

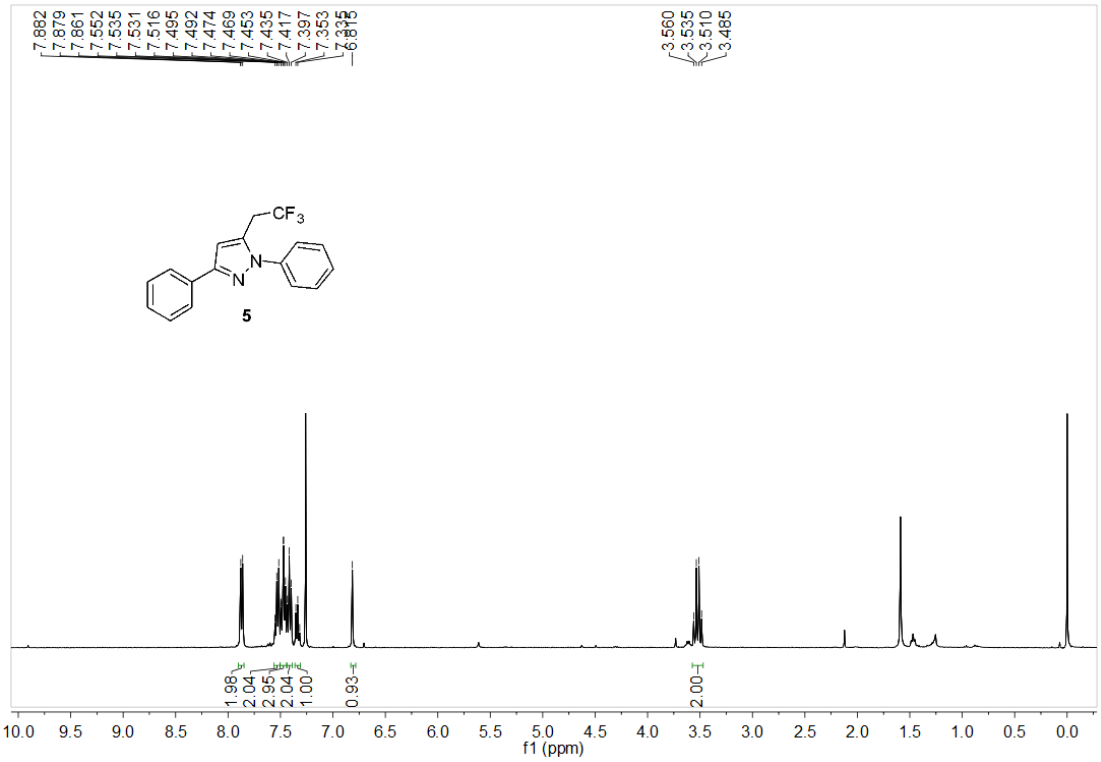

159.9
152.0
141.4
139.4
129.6
127.2
125.7
125.5
114.3
105.0
55.6
-8.2
I
N
N
MeO
4b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

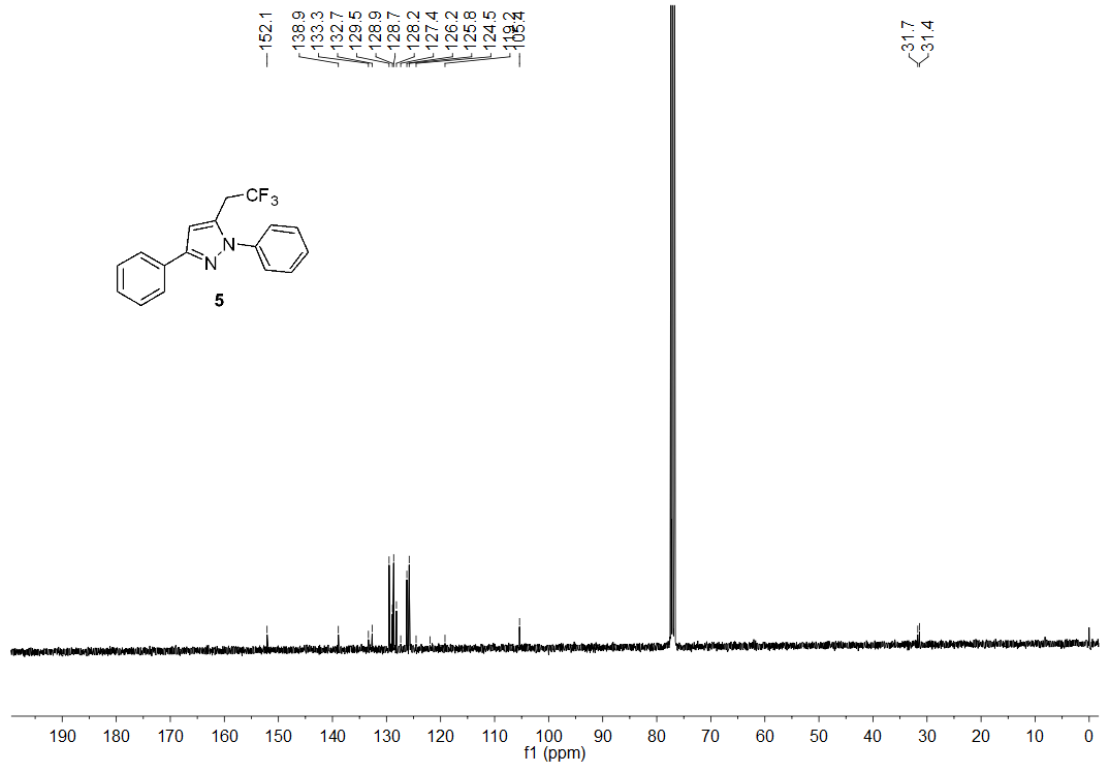

7.828
7.815
7.807
7.793
7.631
7.613
7.567
7.549
7.530
7.497
7.479
7.461
7.115
7.093
7.071
6.773
4.425
I
N
N
F
4c
2.04
1.99
2.05
1.02
2.02
1.00
2.03
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

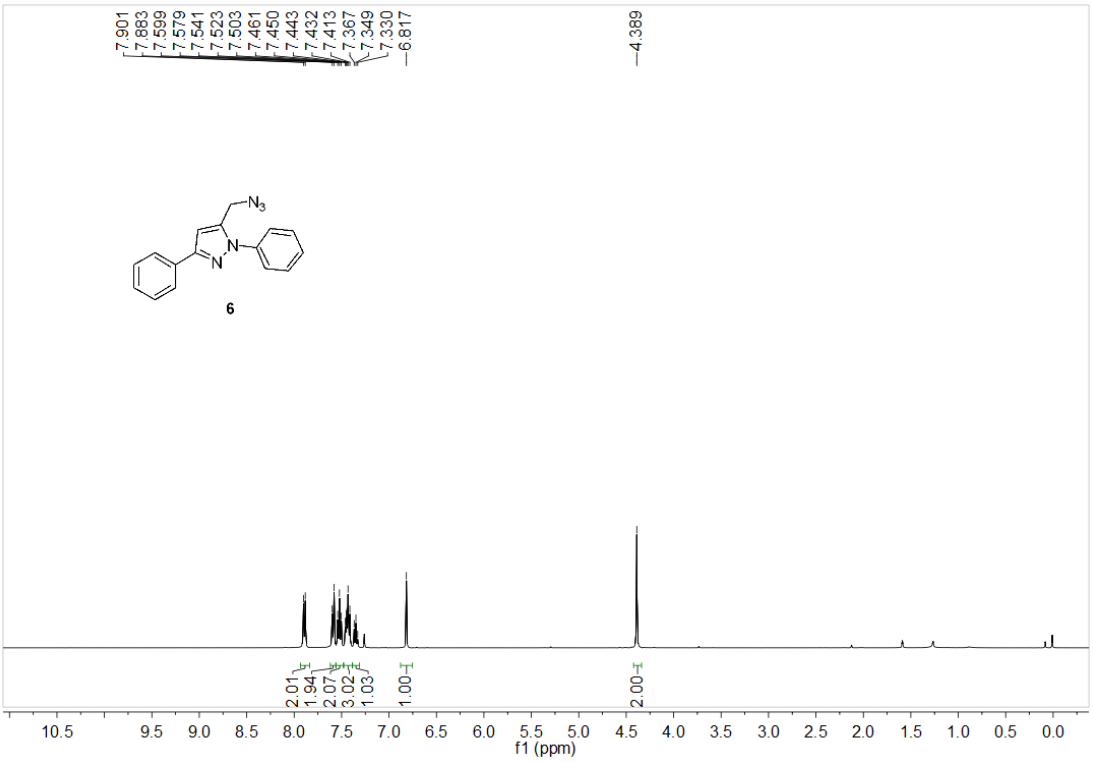

164.3
161.8
151.2
141.7
139.3
129.7
127.7
127.6
115.7
105.2
8.6
Br
N
N
F
4c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

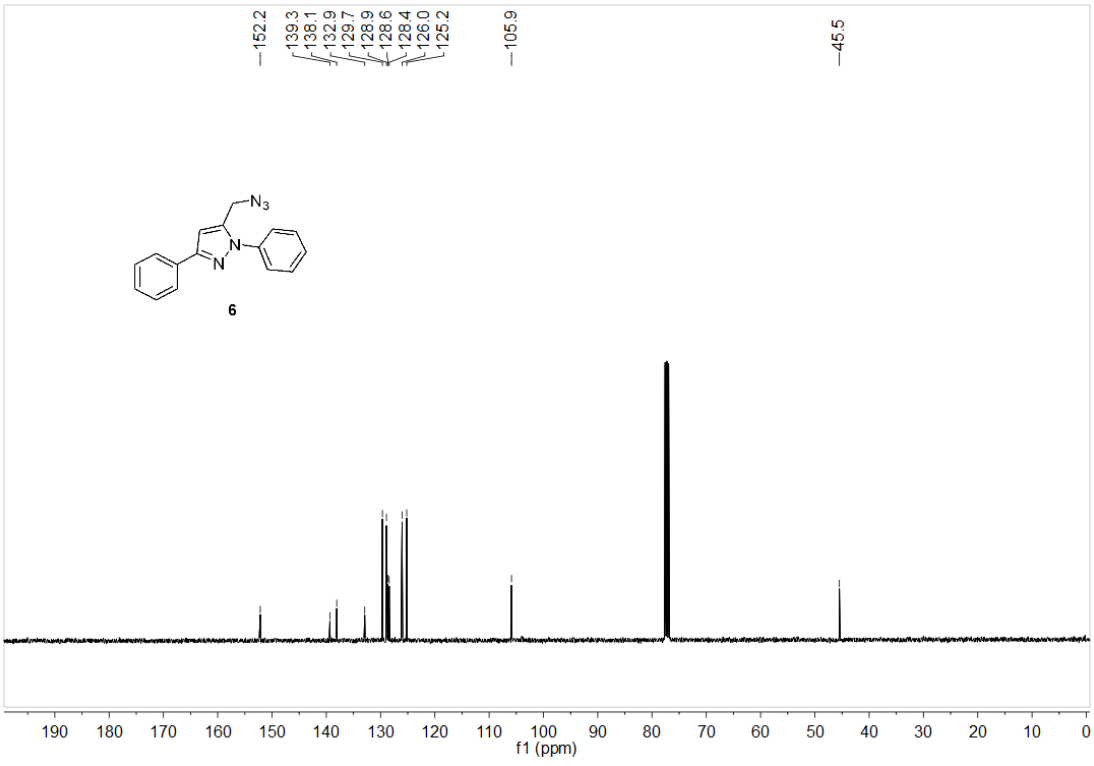

7.837
7.834
7.816
7.633
7.621
7.611
7.599
7.428
7.410
7.391
7.353
7.335
7.316
7.236
7.219
7.214
6.812
4.395
I
N
N
F
4d
1.92
1.92
2.02
1.00
1.91
0.95
1.96
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
f1 (ppm)

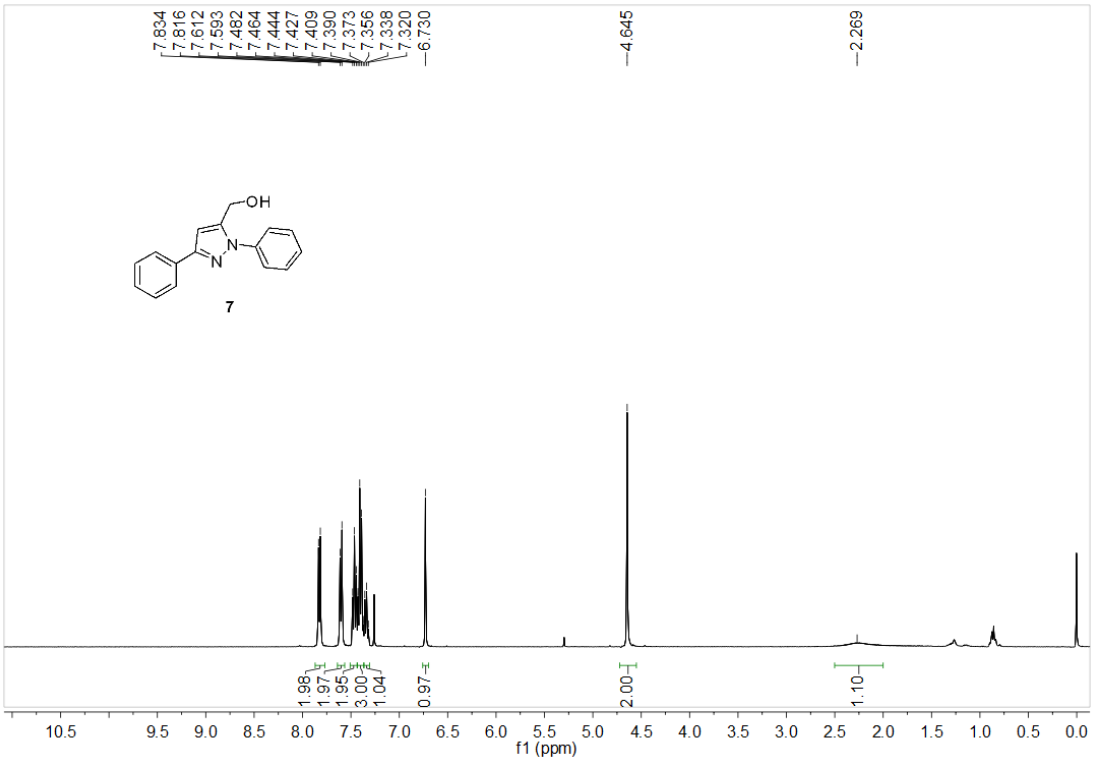

171.9
161.5
152.2
141.7
132.7
128.9
128.5
127.6
127.5
116.7
116.5
105.3
8.8
Br
N
N
F
4d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

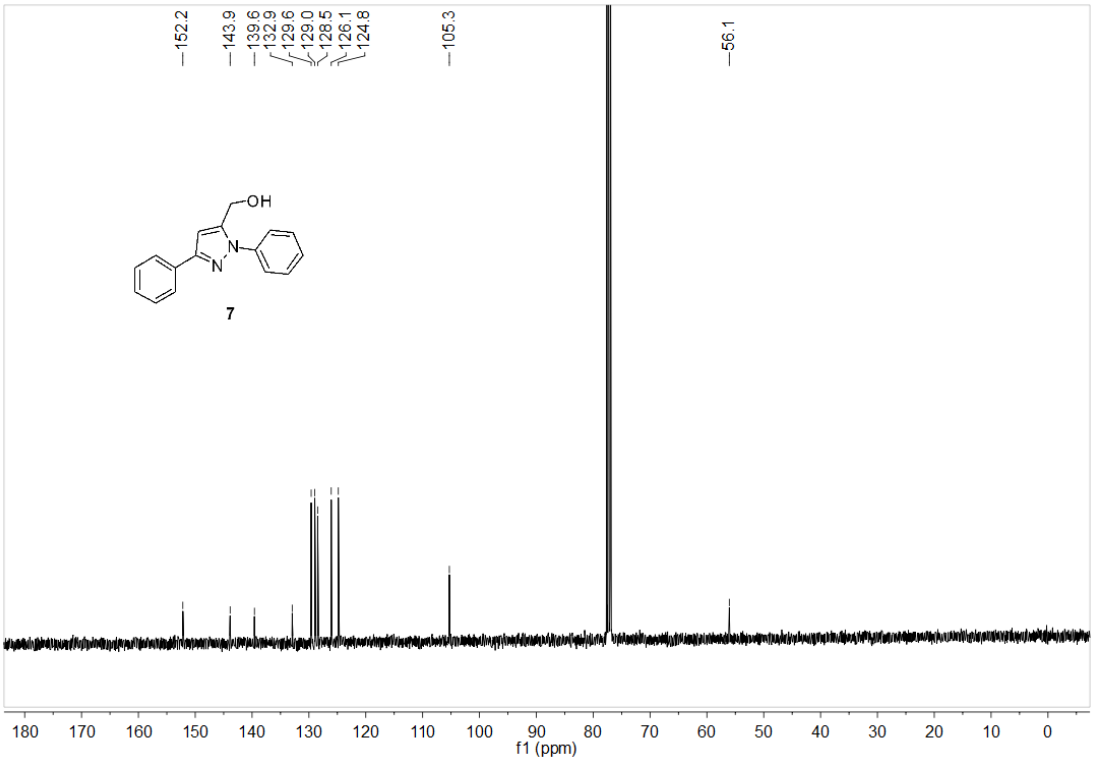

7.882
7.879
7.861
7.552
7.535
7.531
7.516
7.495
7.492
7.474
7.469
7.453
7.435
7.417
7.397
7.353
3.560
3.535
3.510
3.485
CF3
N
N
5
1.98
2.04
2.95
2.04
1.00
0.93
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

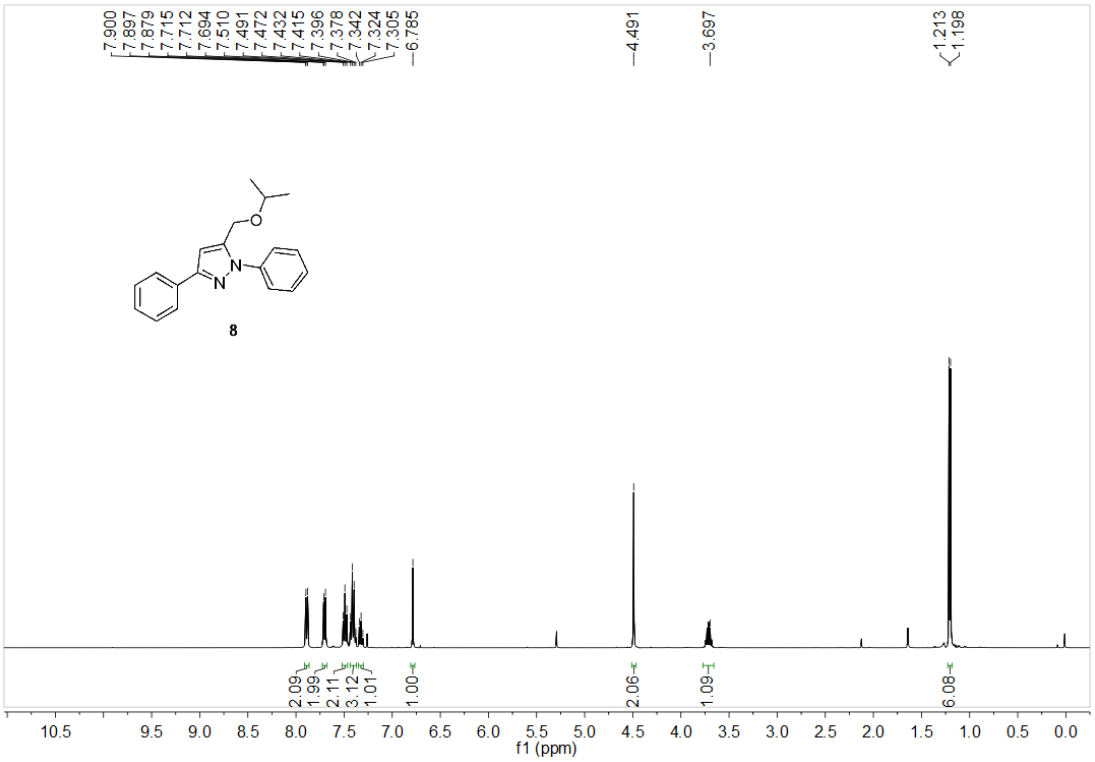

152.1
138.9
133.3
132.7
129.5
128.9
128.7
128.2
127.4
126.2
125.8
124.5
31.7
31.4
CF3
N
N
5
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

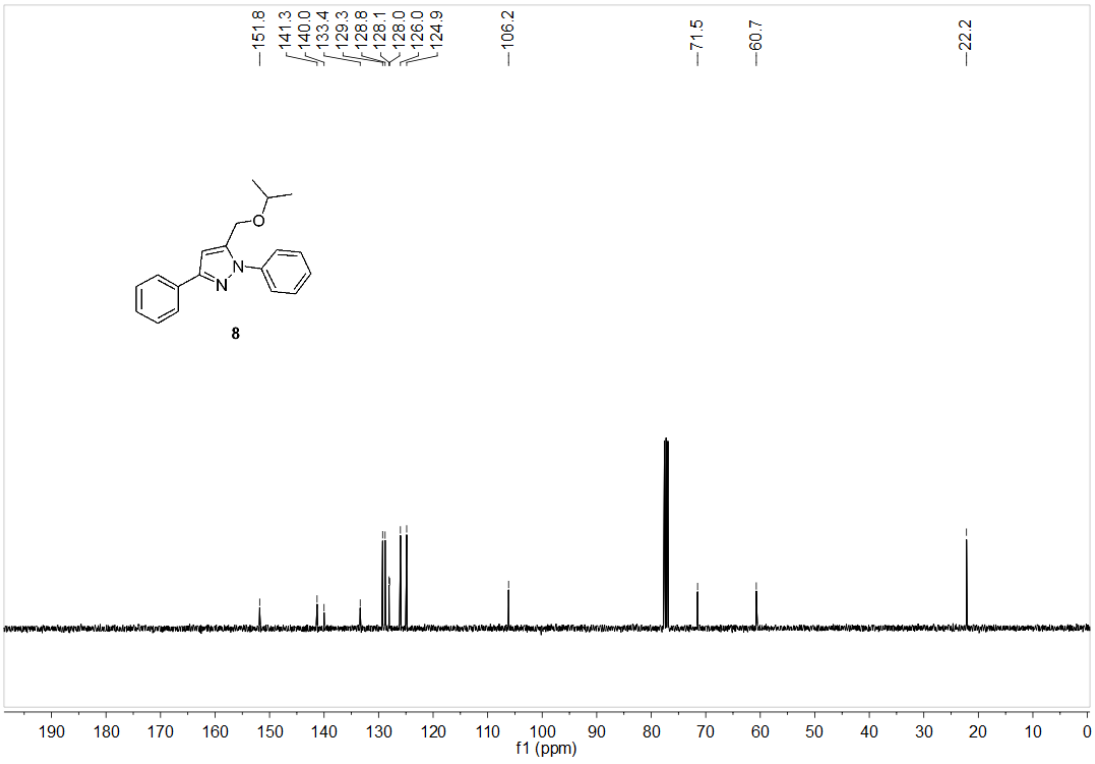

7.901
7.883
7.599
7.579
7.541
7.523
7.503
7.461
7.450
7.443
7.432
7.413
7.367
7.349
7.330
6.817
4.389
N3
N
N
6
2.01
1.94
2.07
3.02
1.03
1.00
2.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

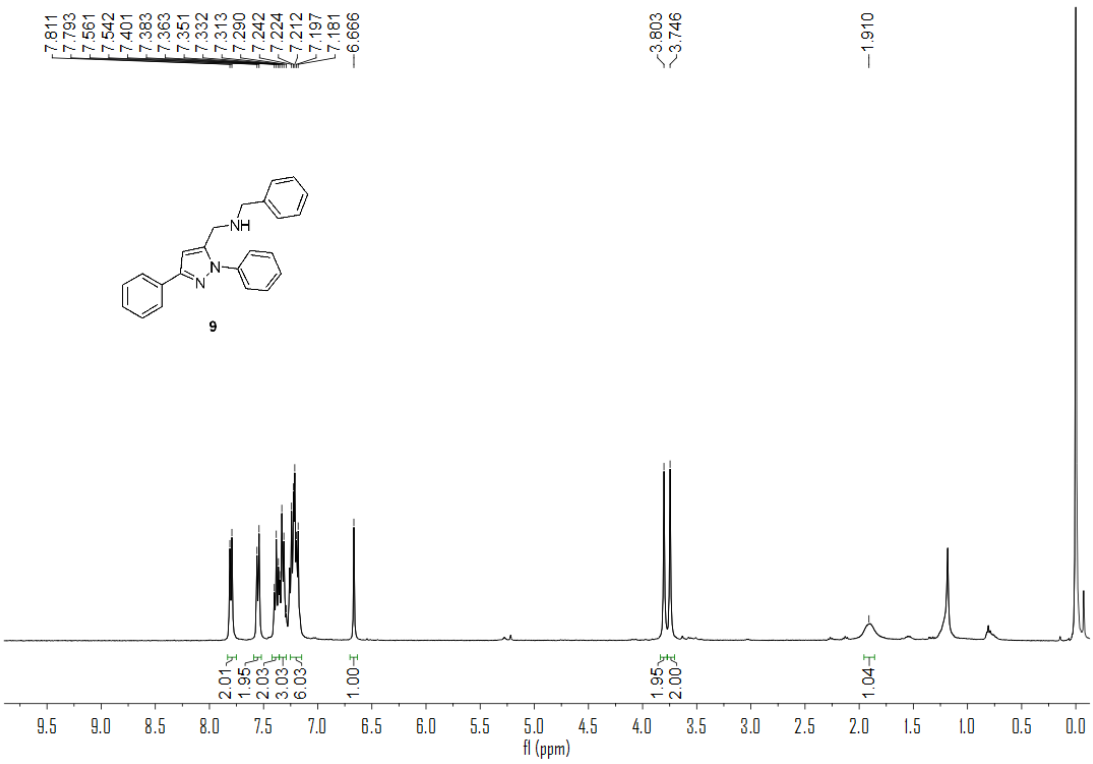

152.2
139.3
138.1
132.9
129.7
128.9
128.6
128.4
126.0
125.2
105.9
45.5
N3
N
N
6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

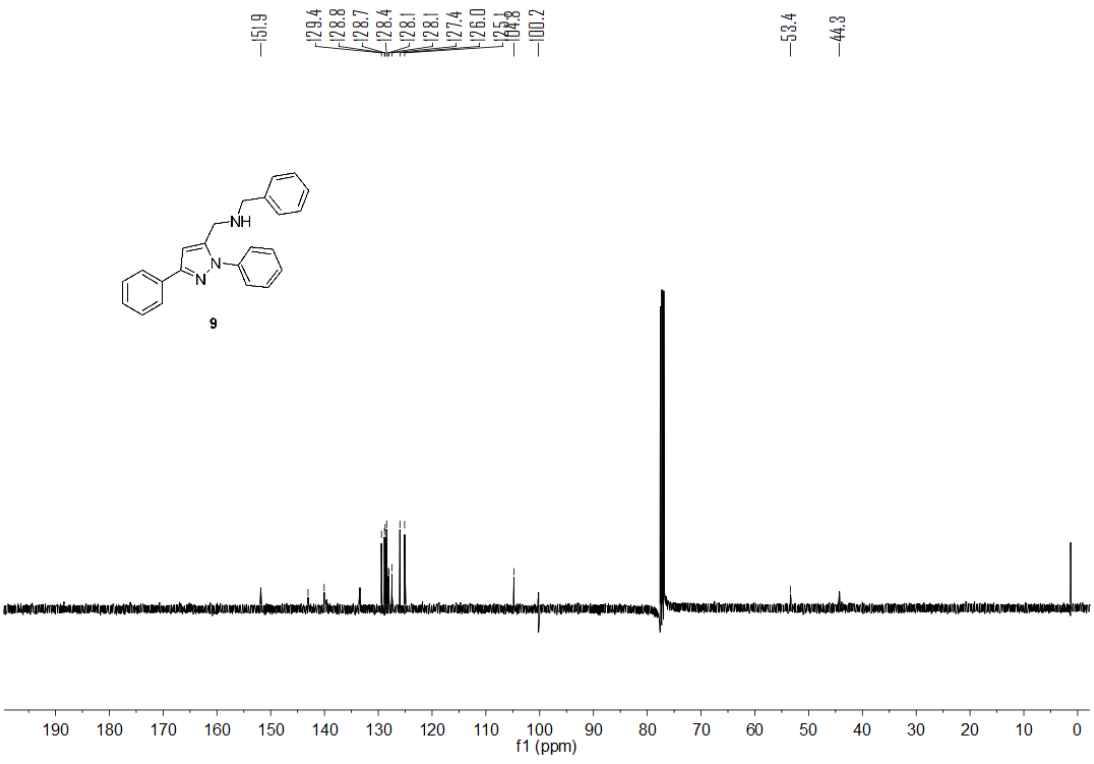

7.834
7.816
7.612
7.593
7.482
7.464
7.444
7.427
7.409
7.390
7.373
7.356
7.338
7.320
6.730
4.645
2.269
OH
N
N
7
1.98
1.97
1.95
3.00
1.04
0.97
2.00
1.10
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


152.2
143.9
139.6
132.9
129.6
129.0
128.5
126.1
124.8
105.3
56.1
OH
N
N
7
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.900
7.897
7.879
7.715
7.712
7.694
7.510
7.491
7.472
7.432
7.415
7.396
7.378
7.342
7.324
7.305
6.785
4.491
3.697
1.213
1.198
8
2.09
1.99
2.11
3.12
1.01
1.00
2.06
1.09
6.08
f1 (ppm)


151.8
141.3
140.0
133.4
129.3
128.8
128.1
128.0
126.0
124.9
106.2
71.5
60.7
22.2
8
f1 (ppm)


7.811
7.793
7.561
7.542
7.401
7.383
7.363
7.351
7.332
7.313
7.290
7.242
7.224
7.212
7.197
7.181
6.666
3.803
3.746
1.910
NH
N
N
9
2.01
1.95
2.03
3.03
6.03
1.00
1.95
2.00
1.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


151.9
129.4
128.8
128.7
128.4
128.1
128.1
127.4
126.0
105.1
104.8
100.2
53.4
44.3
NH
N
N
9
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)