Supporting Information

A Novel Methodology for Synthesis of Dihydropyrazole Derivatives as Potential Anticancer Agents

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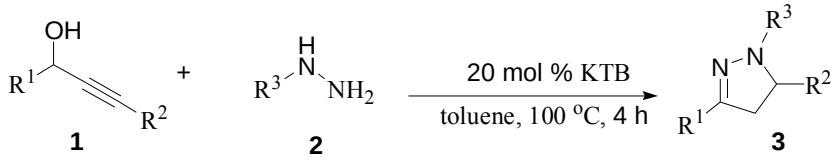
1 General Information Methods.

All manipulations were performed under an air atmosphere unless otherwise statement. Column chromatography was performed on silica gel (300−400 mesh). NMR spectra were obtained using a Bruker Avance 500 and 400 spectrometer (^{1}H at 500 MHz, 400 MHz and ^{13}C at 125 MHz, 100 MHz). Chemical shifts for ^{1}H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0 ppm).

Materials. Unless stated otherwise, commercial reagents were used without further purification. All reagents were weighed and handled in air at room temperature.

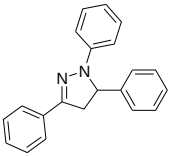
2 General Experimental Procedure



1 2 3

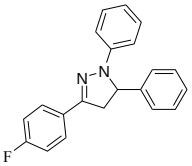
The reaction mixture of propargyl alcohols **1** (0.5 mmol), hydrazines **2** (0.6 mmol), KTB (20 mol %), and toluene (2 mL) was stirred at 100 °C for 4 h. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford dihydropyrazoles **3**.

3 Characterization of the Compounds



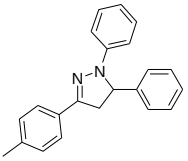
1,3,5-Triphenyl-4,5-dihydro-1*H*-pyrazole (**3aa**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 92% (137 mg, 0.46 mmol) as a yellow solid: 138-139 ^{o}C (Lit[1] 134-136 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.77-7.71 (m, 2H), 7.43-7.37 (m, 3H), 7.35 (dd, *J* = 3.2, 2.0 Hz, 5H), 7.23-7.16 (m, 2H), 7.12-7.07 (m, 2H), 6.83-6.76 (m, 1H), 5.28 (dd, *J* = 12.4, 7.3 Hz, 1H), 3.85 (dd, *J* = 17.1, 12.4 Hz, 1H), 3.15 (dd, *J* = 17.1, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 146.7, 144.9, 142.6, 132.7, 129.1, 128.9,128.6, 128.5, 127.5, 125.9, 125.7,119.0, 113.4, 64.5, 43.6. MS: m/z = 299 [M+H^{+}].

The spectral data showed good agreement with the literature data.[1]



3-(4-Fluoro-phenyl)-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole (**3ba**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 87% (137 mg, 0.435 mmol) as a yellow solid: 125-126 ^{o}C (Lit[2] 124-126 ^{o}C); ^{1}H NMR (400 MHz, CDCl3, δ ppm) 7.76-7.64 (m, 2H), 7.39-7.32 (m, 5H), 7.29 (dd, *J* = 6.1, 2.5 Hz, 1H), 7.19 (dd, *J* = 8.8, 7.3 Hz, 2H), 7.09-7.06 (m, 3H), 6.83-6.76 (m, 1H), 5.27 (dd, *J* = 12.4, 7.3 Hz, 1H), 3.82 (dd, *J* = 17.0, 12.4 Hz, 1H), 3.12 (dd, *J* = 17.0, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)164.2, 161.7, 145.8, 144.8, 142.5, 129.2, 128.9, 127.6, 127.5 ,127.4, 125.8, 119.1, 115.7, 115.5, 113.4, 64.6, 43.6. MS: m/z = 317 [M+H^{+}].

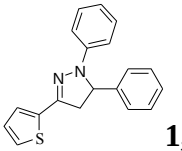
The spectral data showed good agreement with the literature data.[2]



1,5-Diphenyl-3-p-tolyl-4,5-dihydro-1*H*-pyrazole (**3ca**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 93% (145 mg, 0.465 mmol) as a yellow solid: 137-138 ^{o}C (Lit[3] 137-139 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm)7.66 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 4.2 Hz, 4H), 7.30 (dd, *J* = 4.8, 3.8

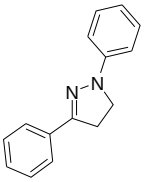
Hz, 1H), 7.22 (dd, *J* = 8.7, 7.3 Hz, 4H), 7.14-7.09 (m, 2H), 6.85-6.79 (m, 1H), 5.26 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.83 (dd, *J* = 17.1, 12.3 Hz, 1H), 3.14 (dd, *J* = 17.1, 7.3 Hz, 1H), 2.41 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 146.9, 145.0, 142.7, 138.6, 129.9, 129.2, 129.1, 128.8, 127.5, 125.8, 125.7, 118.9, 113.3, 64.4, 43.6, 21.4. MS: m/z = 313 [M+H$^+$].

The spectral data showed good agreement with the literature data.[3]

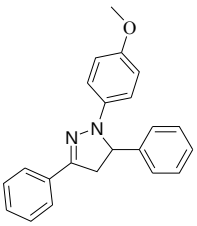


1,5-Diphenyl-3-thiophen-2-yl-4,5-dihydro-1*H*-pyrazole (**3da**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 88% (134 mg, 0.44 mmol) as a yellow solid: 127-128 ^{o}C (Lit[4] 128-129 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.41-7.38 (m, 1H), 7.38-7.35 (m, 3H), 7.34-7.29 (m, 2H), 7.25-7.18 (m, 2H), 7.14-7.09 (m, 2H), 7.06 (ddd, *J* = 8.5, 4.3, 2.5 Hz, 2H), 6.84 (tt, *J* = 7.4, 1.1 Hz, 1H), 5.27 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.84 (dd, *J* = 16.9, 12.3 Hz, 1H), 3.15 (dd, *J* = 16.9, 7.3 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 144.6, 142.8, 142.3, 136.5, 129.0, 128.8, 127.6, 127.3, 126.4, 125.9, 125.8, 119.1, 113.4, 64.5, 44.2. MS: m/z = 305 [M+H$^+$].

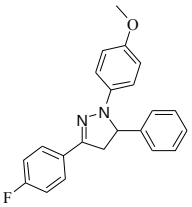
The spectral data showed good agreement with the literature data.[4]



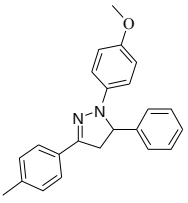
1,3-Diphenyl-4,5-dihydro-1*H*-pyrazole (**3ea**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 85% (94 mg, 0.425 mmol) as a yellow solid (mp 148-150 ^{o}C). 1H NMR (400 MHz, CDCl3, δ ppm) 7.81-7.73 (m, 2H), 7.44-7.37 (m, 2H), 7.37-7.29 (m, 3H), 7.20-7.11 (m, 2H), 6.88 (tt, *J* = 7.4, 1.1 Hz, 1H), 3.89 (t, J = 10.5 Hz, 2H), 3.25 (t, *J* = 10.5 Hz, 2H); 13C NMR (100 MHz, CDCl3, δ ppm) 149.0, 145.9, 133.0, 129.4, 129.1, 128.5, 125.7, 119.1, 113.0, 48.3, 32.0. MS: m/z = 223 [M+H+]. Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.36. Found: C, 80.86; H, 6.51.



1-(4-Methoxy-phenyl)-3,5-diphenyl-4,5-dihydro-1*H*-pyrazole (**3ab**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 95% (156 mg, 0.475 mmol) as a yellow solid (mp 145-157 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.74 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.38-7.28 (m, 6H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.82-6.77 (m, 2H), 5.24-5.12 (m, 1H), 3.87-3.78 (m, 1H), 3.75 (s, 3H), 3.14 (dd, *J* = 16.9, 8.3 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 153.3, 146.2, 142.7, 139.7, 132.9, 129.1, 128.5,128.3, 127.5, 126.1, 125.6, 114.9, 114.4, 65.7, 55.6, 43.7. MS: m/z = 329 [M+H$^+$]. Anal. Calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14. Found: C, 80.33; H, 6.31.

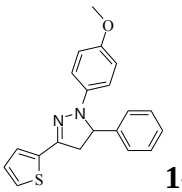


3-(4-Fluoro-phenyl)-1-(4-methoxy-phenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazole (**3bb**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 89% (154 mg, 0.445 mmol) as a yellow solid (mp 125-127 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.74-7.69 (m, 2H), 7.43-7.36 (m, 4H), 7.34-7.30 (m, 1H), 7.14-7.05 (m, 4H), 6.85-6.78 (m, 2H), 5.17 (dd, *J* = 12.2, 8.5 Hz, 1H), 3.80-3.73 (m, 4H), 3.10 (dd, *J* = 16.9, 8.5 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 163.7, 161.8, 153.3, 145.3, 142.5, 139.6, 129.0, 127.5, 127.2, 126.0, 115.5, 115.4, 114.8, 114.3, 65.7, 55.4, 43.6. MS: m/z = 347 [M+H$^+$]. Anal. Calcd for $C_{22}H_{19}FN_2O$: C, 76.28; H, 5.53. Found: C, 76.43; H, 5.30.

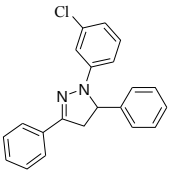


1-(4-Methoxy-phenyl)-5-phenyl-3-p-tolyl-4,5-dihydro-1*H*-pyrazole (**3cb**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 94% (161 mg, 0.47 mmol) as a yellow solid (mp 157-158 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.63 (d, *J* = 8.1 Hz, 2H), 7.39-7.33 (m, 4H), 7.29-7.28 (m, 1H),

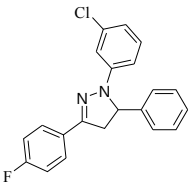
7.21 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 2H), 6.81-6.76 (m, 2H), 5.15 (dd, *J* = 12.1, 8.5 Hz, 1H), 3.80 (dd, *J* = 16.9, 12.2 Hz, 1H), 3.74 (s, 3H), 3.12 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.39 (s, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm)153.2, 146.5, 142.8, 139.9, 138.4, 130.1, 129.2, 129.0, 127.5, 126.1, 125.6, 114.8, 114.4, 65.7, 55.6, 43.8, 21.3. MS: m/z = 343 [M+H$^+$]. Anal. Calcd for $C_{23}H_{22}N_2O$: C, 80.67; H, 6.48. Found: C, 80.41; H, 6.67.



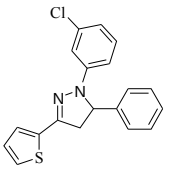
1-(4-Methoxy-phenyl)-5-phenyl-3-thiophen-2-yl-4,5-dihydro-1*H*-pyrazole (**3db**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 92% (154 mg, 0.46 mmol) as a yellow solid (mp 151-152 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.37 (d, *J* = 4.3 Hz, 4H), 7.30 (d, *J* = 4.6 Hz, 2H), 7.06-6.98 (m, 4H), 6.78 (d, *J* = 9.0 Hz, 2H), 5.16 (dd, *J* = 12.1, 8.4 Hz, 1H), 3.80 (dd, *J* = 16.8, 12.2 Hz, 1H), 3.74 (s, 3H), 3.13 (dd, *J* = 16.8, 8.4 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 153.3,142.4,142.3, 139.4, 136.7, 129.1, 127.6, 127.2, 126.2, 126.0,125.5, 115.0, 114.3, 65.8, 55.5, 44.4. MS: m/z = 335 [M+H$^+$]. Anal. Calcd for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42. Found: C, 71.59; H, 5.68.



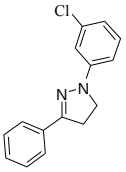
1-(3-Chloro-phenyl)-3,5-diphenyl-4,5-dihydro-1*H*-pyrazole (**3ac**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 87% (144 mg, 0.435 mmol) as a yellow solid (mp 148-150 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.79-7.72 (m, 2H), 7.46-7.34 (m, 5H), 7.34-7.27 (m, 4H), 7.07 (t, *J* = 8.1 Hz, 1H), 6.80-6.75 (m, 2H), 5.24 (dd, *J* = 12.3, 6.8 Hz, 1H), 3.84 (dd, *J* = 17.1, 12.3 Hz, 1H), 3.16 (dd, *J* = 17.1, 6.8 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 147.7, 145.7, 141.9, 134.79, 132.3, 129.8, 129.2, 128.9, 128.5, 127.7, 125.8,125.7, 118.7, 113.4, 111.1, 64.1, 43.6. MS: m/z = 333 [M+H$^+$]. Anal. Calcd for $C_{21}H_{17}ClN_2$: C, 75.78; H, 5.15. Found: C, 75.53; H, 5.34.



1-(3-Chloro-phenyl)-3-(4-fluoro-phenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazole (**3bc**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 85% (149 mg, 0.425 mmol) as a yellow solid (mp 143-145 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm)7.64 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.34-7.15 (m, 6H), 7.07-6.94 (m, 3H), 6.71 (dd, *J* = 11.5, 4.4 Hz, 2H), 5.15 (dd, *J* = 12.2, 6.8 Hz, 1H), 3.72 (dd, *J* = 17.1, 12.3 Hz, 1H), 3.04 (dd, *J* = 17.1, 6.8 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm)164.1, 162.1, 146.7, 145.7, 141.8, 134.7, 129.8, 129.2, 127.8, 127.6,127.5, 125.7, 118.8, 115.7, 115.5, 113.4, 111.1, 64.2, 43.6. MS: m/z = 351 [M+H^{+}]. Anal. Calcd for $C_{21}H_{16}ClFN_2$: C, 71.90; H, 4.60. Found: C, 71.69; H, 4.78.

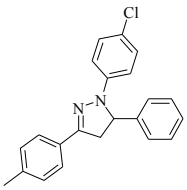


1-(3-Chloro-phenyl)-5-phenyl-3-thiophen-2-yl-4,5-dihydro-1*H*-pyrazole (**3dc**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 84% (142 mg, 0.42 mmol) as a yellow solid (mp 127-128 ^{o}C). ^{1}H NMR **(**500 MHz, $CDCl_3$, δ ppm) 7.39-7.32 (m, 3H), 7.30 (d, *J* = 6.5 Hz, 3H), 7.19 (t, *J* = 2.1 Hz, 1H), 7.05-7.02 (m, 3H), 6.82-6.71 (m, 2H), 5.23 (dd, *J* = 12.2, 6.8 Hz, 1H), 3.84 (dd, *J* = 17.0, 12.3 Hz, 1H), 3.15 (dd, *J* = 17.0, 6.8 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 145.5, 143.8, 141.6, 136.1, 134.7, 129.8, 129.2, 127.8, 127.4, 126.9, 126.4, 125.7, 118.9, 113.5, 111.2, 64.2, 44.3. MS: m/z = 339 [M+H^{+}]. Anal. Calcd for $C_{19}H_{15}ClN_2S$: C, 67.35; H, 4.46. Found: C, 67.18; H, 4.62.



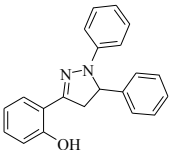
1-(3-Chloro-phenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (**3ec**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 79% (101 mg, 0.395 mmol) as a yellow solid (mp 107-108 ^{o}C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.73 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.44-7.35 (m, 3H), 7.22-7.14 (m, 2H), 6.94-6.93

(m, 1H), 6.82-6.81 (m, 1H), 3.81 (t, *J* = 10.5 Hz, 2H), 3.22 (t, *J* = 10.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 149.8, 146.6, 134.8, 132.5, 130.0, 128.7, 128.5, 125.8, 118.6, 112.8, 110.8, 47.8, 31.9. MS: m/z = 257 [M+H$^+$]. Anal. Calcd for $C_{15}H_{13}ClN_2$: C, 70.18; H, 5.10. Found: C, 70.04; H, 5.31.



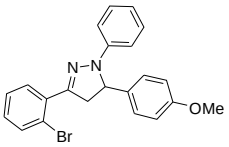
1-(4-Chlorophenyl)-3-(4-methylphenyl)-5-phenyl-4,5-dihydropyrazole (3cd): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 82% (142 mg, 0.41 mmol) as a pink solid 152-153 ^{o}C (Lit[1] 152-153 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) δ 7.59 (d, *J* = 7.2 Hz, 2H), 7.34 - 7.23 (m, 5H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.09 (d, *J* = 7.6 Hz, 2H), 6.96 (d, *J* = 7.7 Hz, 2H), 5.18 (dd, *J* = 11.2, 7.5 Hz, 1H), 3.80 (dd, *J* = 15.9, 13.4 Hz, 1H), 3.11 (dd, *J* = 17.1, 6.7 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 147.5, 143.5, 142.1, 138.9, 129.7, 129.2, 129.1, 128.7, 127.7, 125.8, 125.7, 123.6, 114.4, 64.4, 43.8, 21.4. MS: m/z = 347 [M+H$^+$]. Anal. Calcd for $C_{22}H_{19}ClN_2$: C, 76.18; H, 5.52. Found: C, 76.01; H, 5.70.

The spectral data showed good agreement with the literature data.[1]



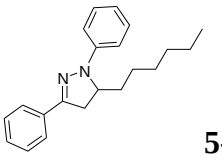
3-(2-Hydroxyphenyl)-1,5-diphenyl-4,5-dihydropyrazole (3ha): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 89% (140 mg, 0.445 mmol) as a white solid 178-180 ^{o}C (Lit[1] 178-180 ^{o}C); ^{1} H NMR (400 MHz, $CDCl_3$, δ ppm) 10.66 (s, 1H), 7.38 (dd, *J* = 8.8, 5.7 Hz, 2H), 7.32 (dd, *J* = 8.9, 4.8 Hz, 4H), 7.28 (d, *J* = 1.8 Hz, 1H), 7.17-7.12 (m, 3H), 7.08 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.90-6.80 (m, 3H), 5.21 (dd, *J* = 12.2, 7.4 Hz, 1H), 3.98 (dd, *J* = 17.3, 12.2 Hz, 1H), 3.29 (dd, *J* = 17.3, 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 157.2, 150.2, 142.6, 141.4, 130.7, 129.4, 129.0, 128.1, 127.2, 125.9, 124.8, 119.5, 116.7, 116.1, 114.5, 63.4, 44.1. MS: m/z = 315 [M+H$^+$].

The spectral data showed good agreement with the literature data.[5]

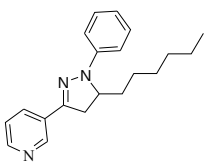


3-(2-Bromophenyl)-5-(4-methoxyphenyl)-1-phenyl-4,5-dihydropyrazole (3ga): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 94% (191 mg, 0.47 mmol) as a yellow solid (mp 154-156 ^{o}C) (Lit[1] 154-156 ^{o}C); ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.67 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.38-7.37 (m, 1H), 7.35-7.29 (m, 2H), 7.26-7.20 (m, 3H), 7.09-7.05 (m, 2H), 6.87-6.84 (m, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 5.23 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.99 (dd, *J* = 17.3, 12.1 Hz, 1H), 3.76 (s, 3H), 3.30 (dd, *J* = 17.3, 7.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 159.0, 146.7, 144.7, 134.2, 134.1, 133.5, 130.4, 129.5, 128.7, 127.2, 127.1, 121.1, 119.4, 114.5, 113.7, 64.5, 55.2, 46.1. MS: m/z = 407 and 409 [M+H$^+$]. Anal. Calcd for $C_{22}H_{19}BrN_2O$: C, 64.87; H, 4.70. Found: C, 64.62; H, 4.91.

The spectral data showed good agreement with the literature data.[1]

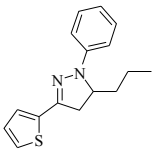


5-Hexyl-1,3-diphenyl-4,5-dihydro-1*H*-pyrazole (**3ia**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 87% (133 mg, 0.435 mmol) as a black oil. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.73 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.41-7.37 (m, 2H), 7.34-7.27 (m, 3H), 7.16 (dd, *J* = 8.7, 1.0 Hz, 2H), 6.84-6.81 (m, 1H), 4.40-4.36 (m, 1H), 3.42 (dd, *J* = 16.8, 11.3 Hz, 1H), 2.99 (dd, *J* = 16.8, 5.0 Hz, 1H), 1.91-1.81 (m, 1H), 1.58-1.50 (m, 1H), 1.32 (d, *J* = 6.1 Hz, 4H), 1.27 (d, *J* = 5.8 Hz, 4H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 147.2, 144.4, 133.1, 129.1, 128.4, 128.3, 125.6, 118.7, 113.3, 59.9, 38.1, 32.3, 31.8, 29.2, 24.9, 22.6, 14.0. MS: m/z = 307 [M+H$^+$]. Anal. Calcd for $C_{21}H_{26}N_2$: C, 82.31; H, 8.55. Found: C, 82.54; H, 8.39.

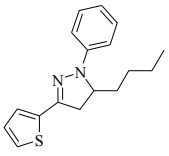


3-(5-Hexyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-pyridine(**3ja**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding

87% (130 mg, 0.425 mmol) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 8.85 (s, 1H), 8.52 (d, *J* = 4.7 Hz, 1H), 8.05 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.29 (m, 3H), 7.17 (d, *J* = 8.3 Hz, 2H), 6.87 (t, *J* = 7.3 Hz, 1H), 4.39 (dd, *J* = 4.8, 2.4 Hz, 1H), 3.37 (dd, *J* = 16.7, 11.5 Hz, 1H), 2.95 (dd, *J* = 16.7, 3.9 Hz, 1H), 1.92-1.78 (m, 1H), 1.55 (dd, *J* = 8.9, 4.3 Hz, 1H), 1.32 (dd, *J* = 15.7, 8.2 Hz, 8H), 0.89 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 148.7, 146.7, 143.9, 143.7, 132.1, 129.0, 123.2, 119.1, 113.3, 59.8, 37.4, 32.1, 31.6, 28.9, 24.6, 22.4, 13.9.MS: m/z = 308 [M+H$^+$]. Anal. Calcd for $C_{20}H_{25}N_3$: C, 78.14; H, 8.20. Found: C, 78.42; H, 8.09.

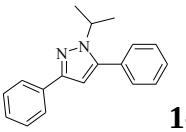


1-Phenyl-5-propyl-3-thiophen-2-yl-4,5-dihydro-1*H*-pyrazole (**3ka**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 82% (110.7 mg, 0.410 mmol) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.32-7.26 (m, 3H), 7.18-7.13 (m, 2H), 7.10 (d, *J* = 3.3 Hz, 1H), 7.05 (t, *J* = 4.3 Hz, 1H), 6.86 (t, *J* = 6.9 Hz, 1H), 4.40-4.36 (m, 1H), 3.42 (dd, *J* = 16.6, 11.3 Hz, 1H), 2.99 (dd, *J* = 16.6, 4.9 Hz, 1H), 1.89-1.79 (m, 1H), 1.60-1.53 (m, 1H), 1.44-1.36 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 144.1, 143.3, 137.1, 129.0, 127.2, 126.1, 125.4, 118.8, 113.3, 59.8, 38.9, 34.4, 18.1, 13.9. MS: m/z = 271 [M+H+]. Anal. Calcd for $C_{16}H_{18}N_2S$: C, 71.07; H, 6.71. Found: C, 71.32; H, 6.69.



5-Butyl-1-phenyl-3-thiophen-2-yl-4,5-dihydro-1*H*-pyrazole (**3la**): Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 80% (113.6 mg, 0.400 mmol) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.31-7.25 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 2.6 Hz, 1H), 7.04 (t, *J* = 4.2 Hz, 1H), 6.85 (t, *J* = 7.3 Hz, 1H), 4.38-4.34 (m, 1H), 3.42 (dd, *J* = 16.6, 11.3 Hz, 1H), 2.99 (dd, *J* = 16.6, 4.9 Hz, 1H), 1.92-1.82 (m, 1H), 1.60-1.55 (m, 1H), 1.39-1.28 (m, 4H), 0.92(t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 144.1, 143.3, 137.1,

129.0, 127.2, 126.1, 125.4, 118.8, 113.3, 60.0, 38.9, 32.0, 27.0, 22.5, 14.0. MS: m/z = 285 [M+H$^+$]. Anal. Calcd for $C_{17}H_{20}N_2S$: C, 71.79; H, 7.09. Found: C, 71.42; H, 7.32.



1-Isopropyl-3,5-diphenyl-1*H*-pyrazole (**3ae**): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 56% (73.4 mg, 0.280 mmol) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 7.90 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 6.6 Hz, 2H), 7.46-7.42 (m, 4H), 7.35-7.29 (m, 2H), 6.56 (s, 1H), 4.61-4.56 (m, 1H), 1.55 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 150.2, 143.9, 133.9, 131.2, 129.0, 128.6, 128.5, 128.4,127.3, 125.6, 102.9, 50.2, 23.0. MS: m/z = 263 [M+H$^+$]. Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92. Found: C, 82.57; H, 6.79.

4 References

(1) Wu, Q.; Liu, P.; Pan, Y.-M.; Xu, Y.-L.; Wang, H.-S. *RSC Adv.* **2012**, *2*, 10167-10170.

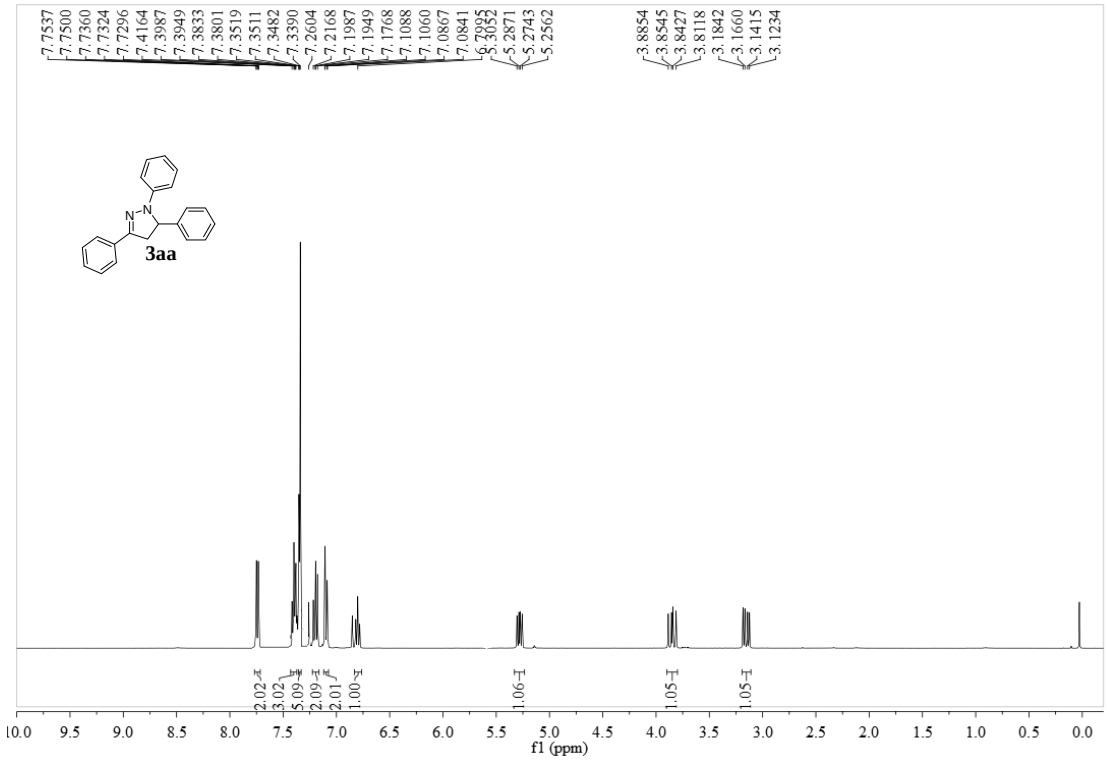
(2) Verma, M.; Chaudhry A. F.; Fahrni, C. *J. Org. Biomol. Chem.* **2009**, 7, 1536-1546.

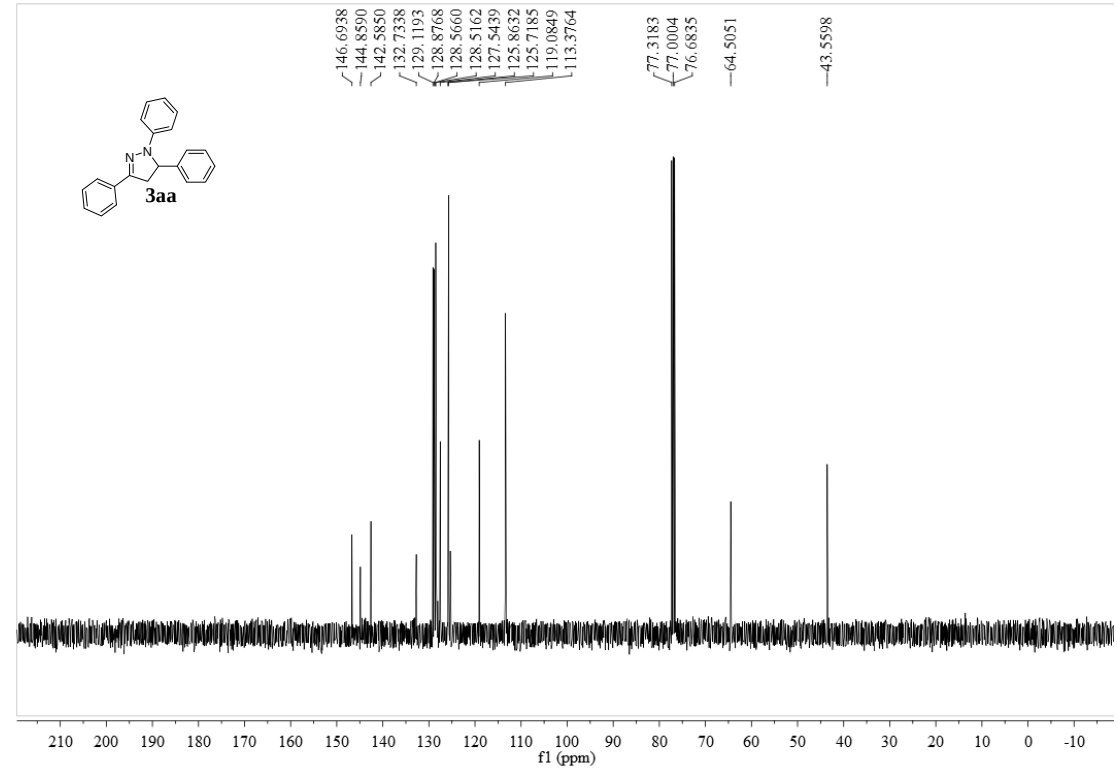
(3) Fazaeli, R.; Aliyan, H.; Mallakpour, S.; Rafiee, Z.; Bordbar, M.; *Chinese Journal of Catalysis*. **2011**, 32: 582-588.

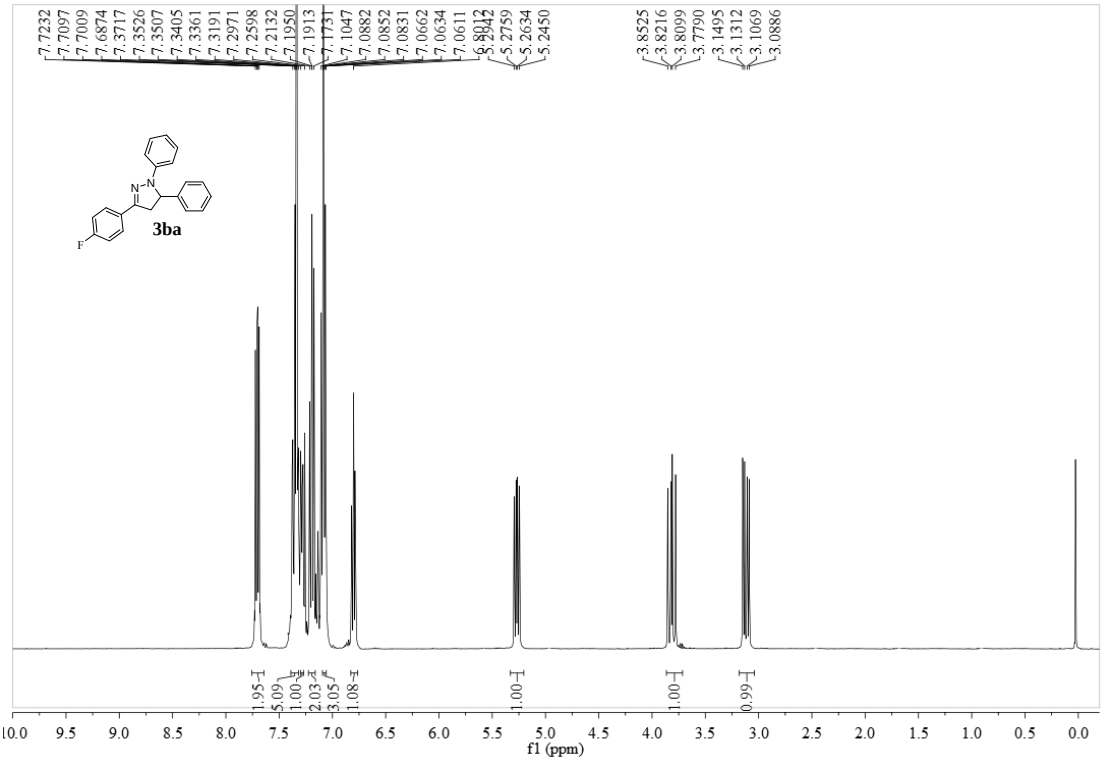
(4) Ozdemir1, Z.; Kandilci, H. B.; Gumusel, B.; Calis, U.; Bilgin, A. A. *Arch. Pharm. Chem. Life Sci*. **2008**, 341, 701-707.

(5) Lokhande, P. D.; Hasanzadeh, K. *J. Chem. Pharm. Res.* **2011**, 3(2):105-112.

5 Copies of ^{1}H NMR and ^{13}C NMR Spectra of Products



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3.1312
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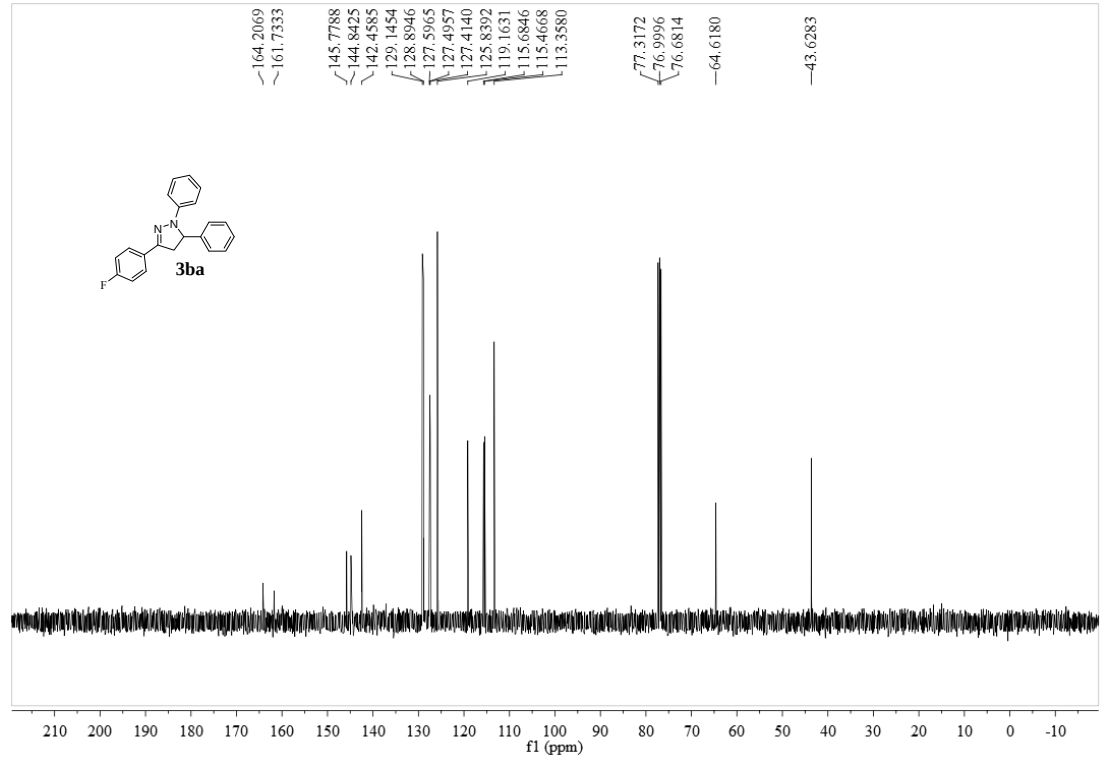
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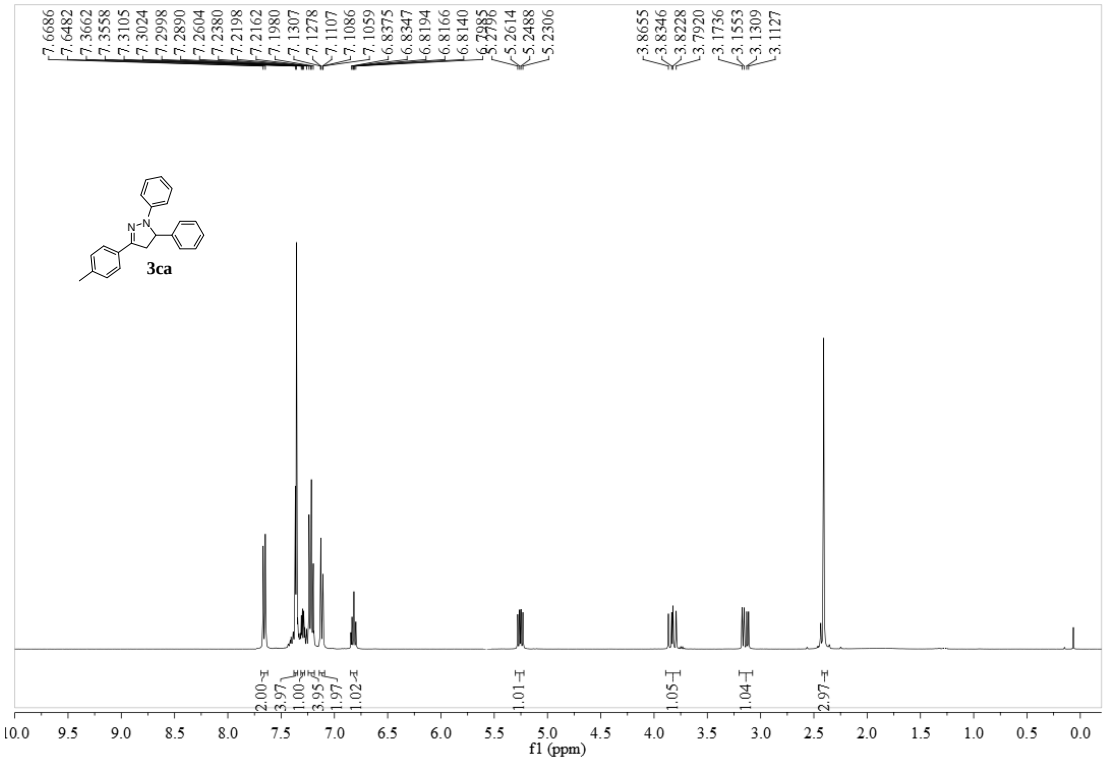
3ba
f1 (ppm)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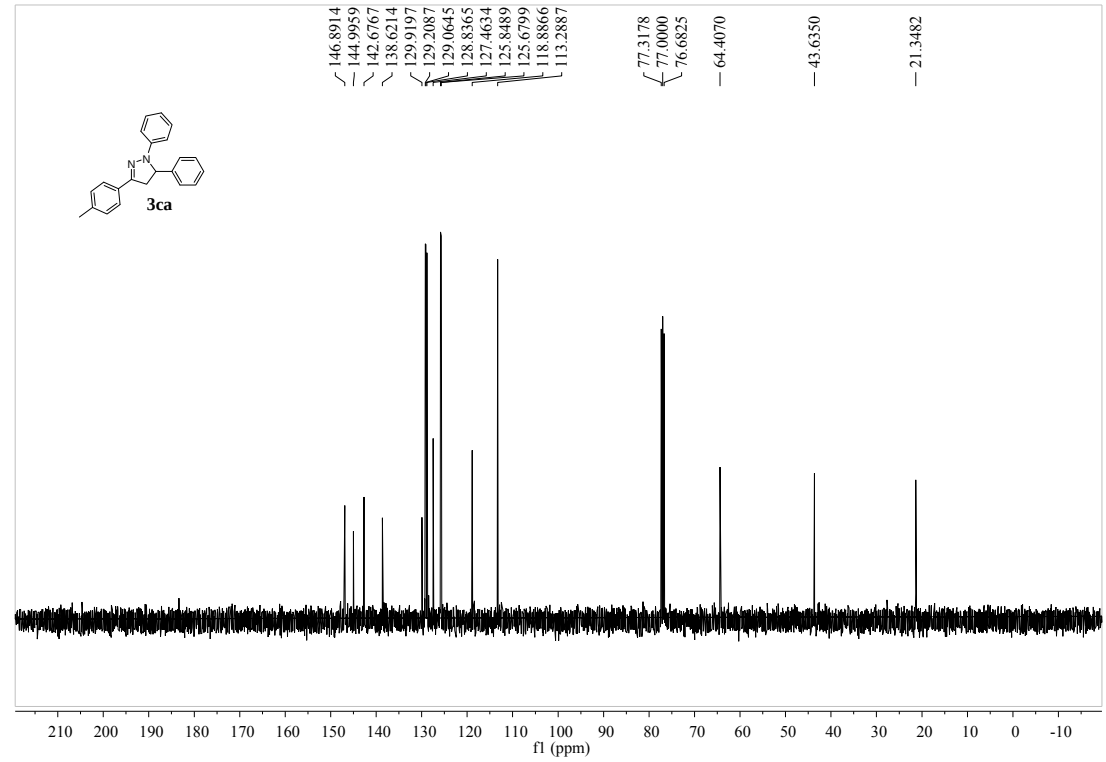
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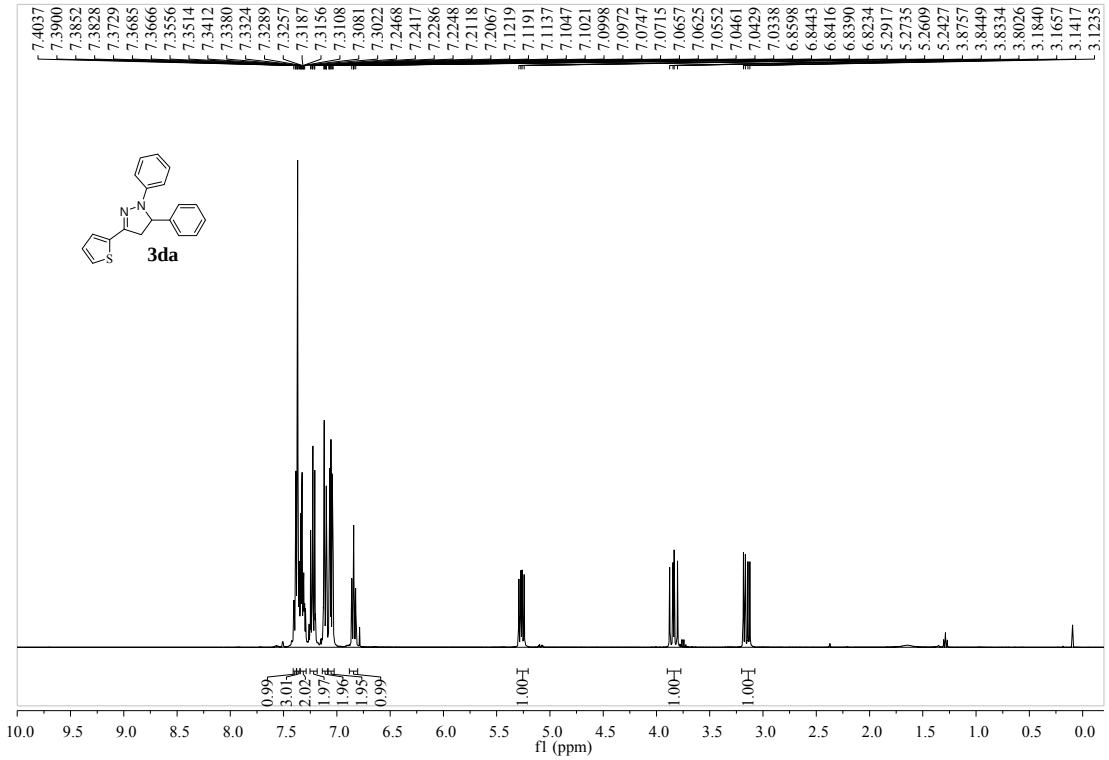
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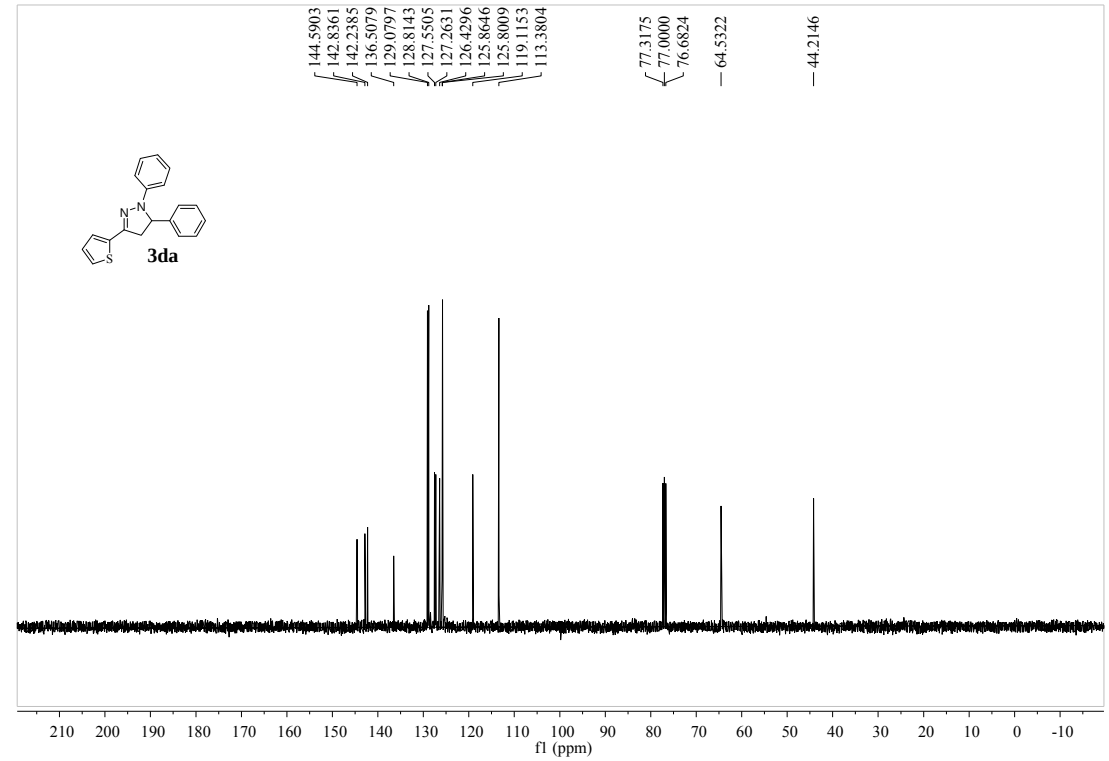
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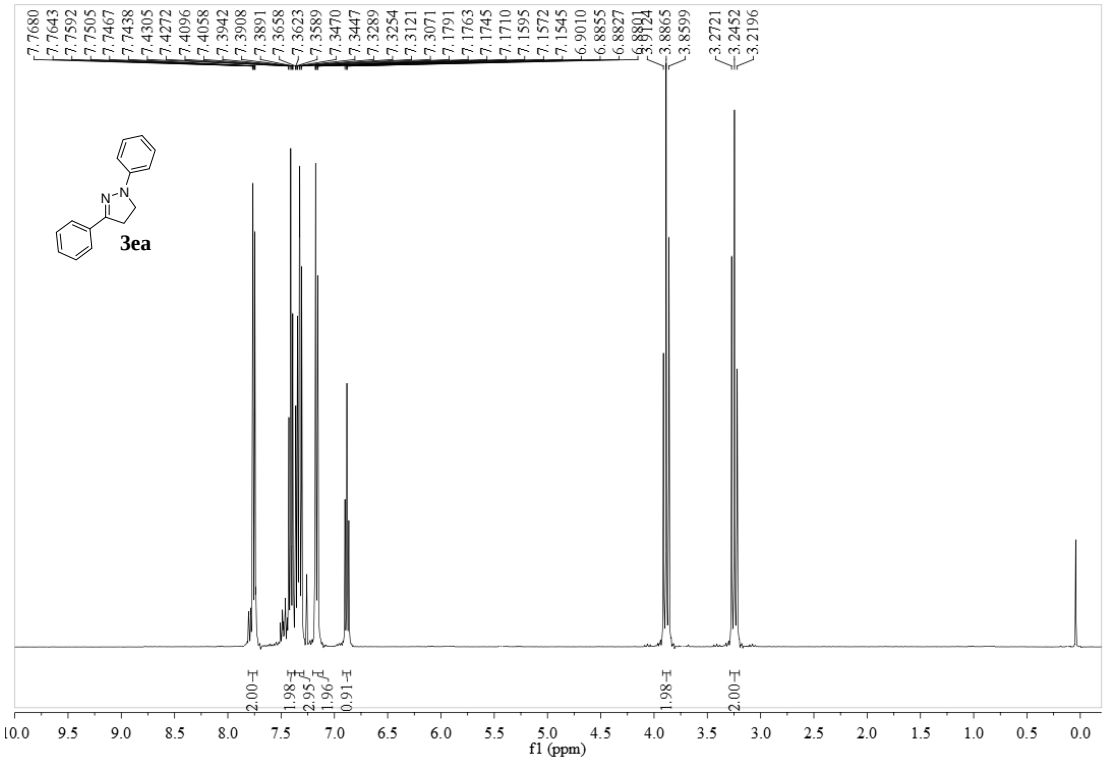
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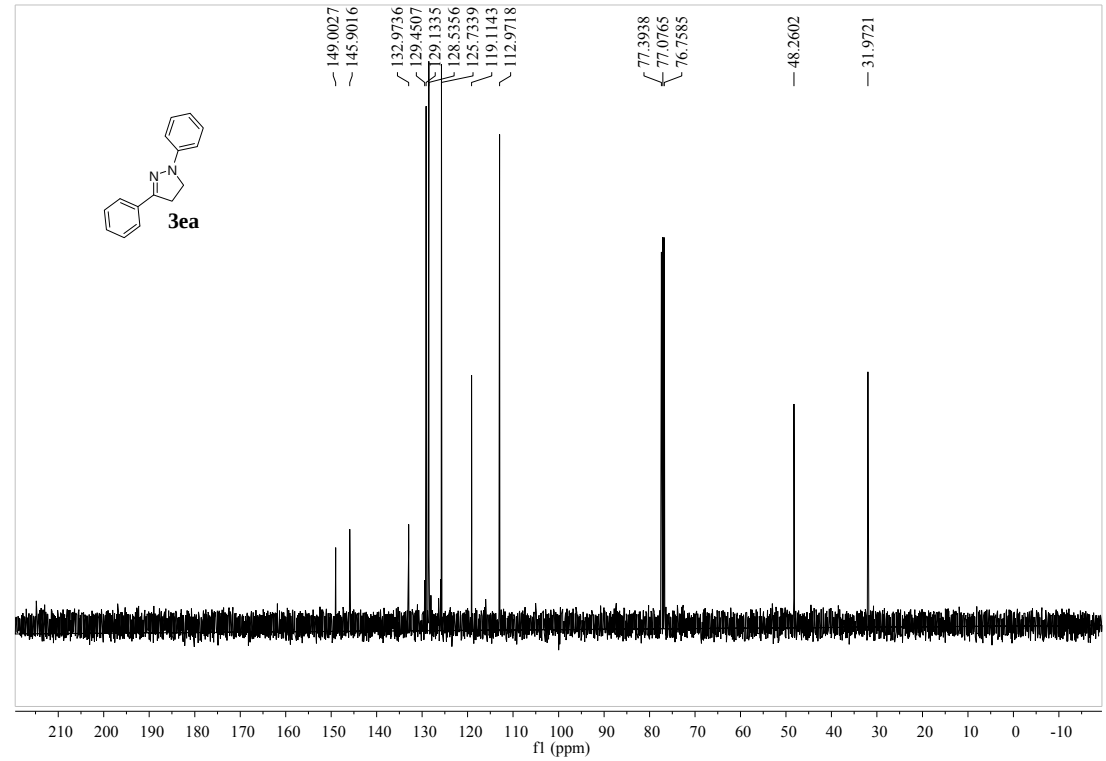
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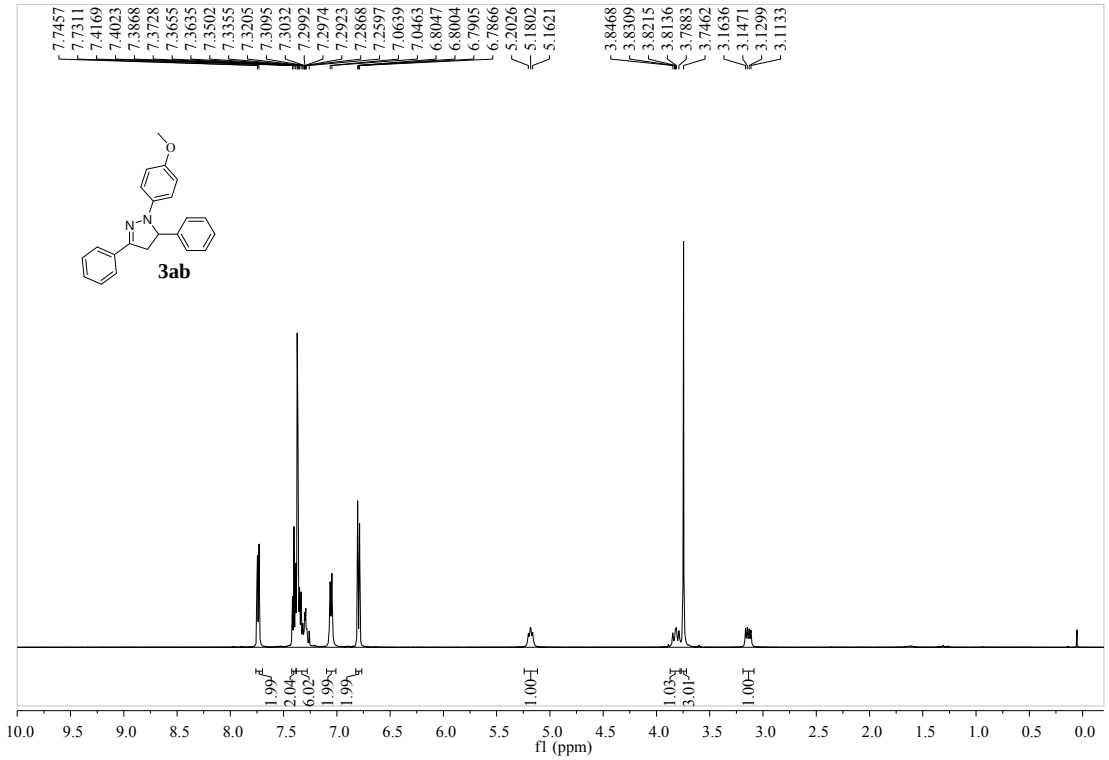
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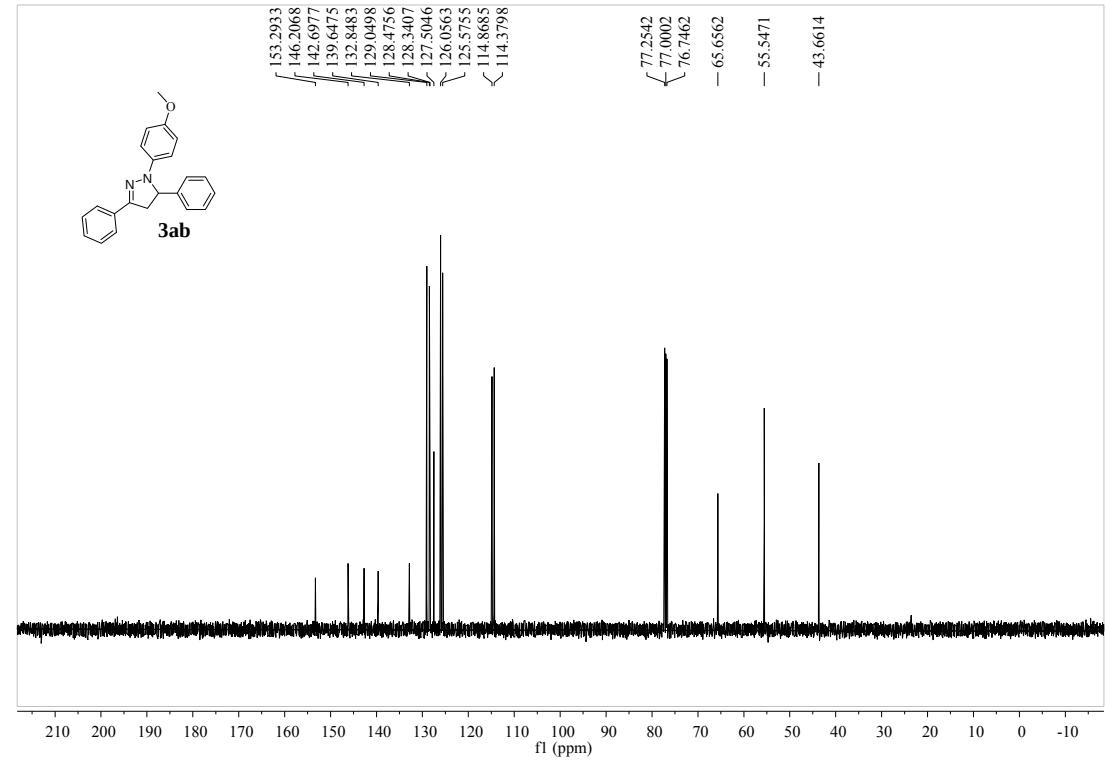
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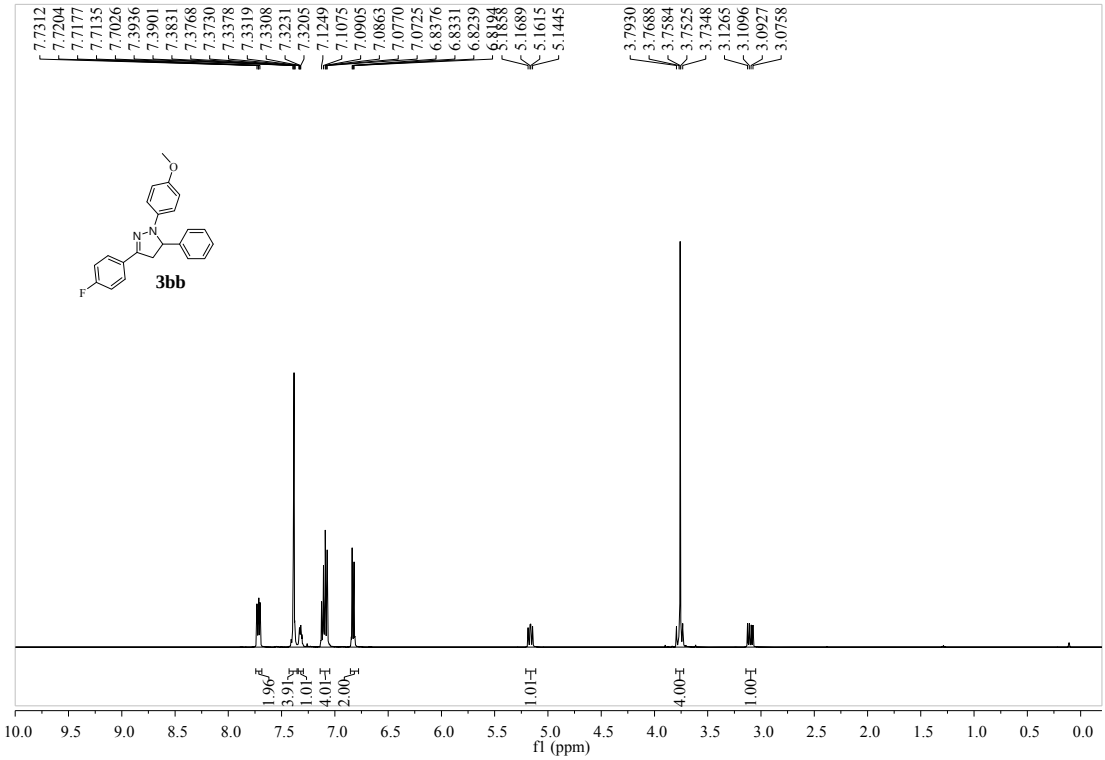
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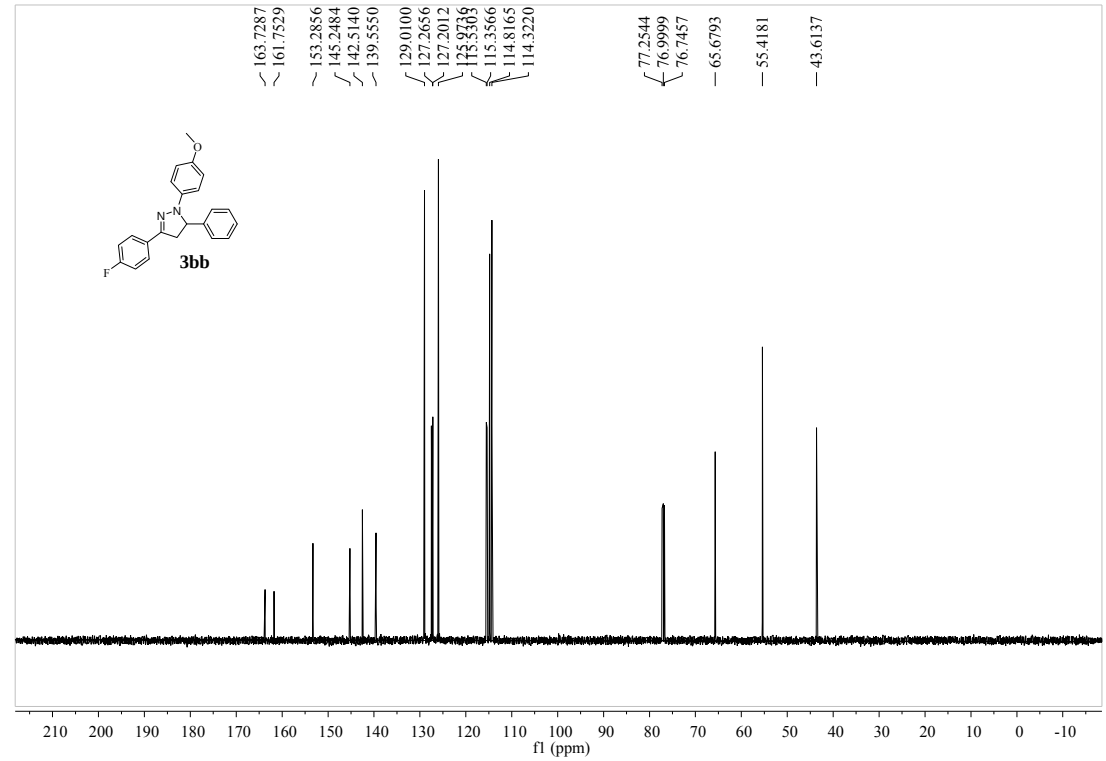
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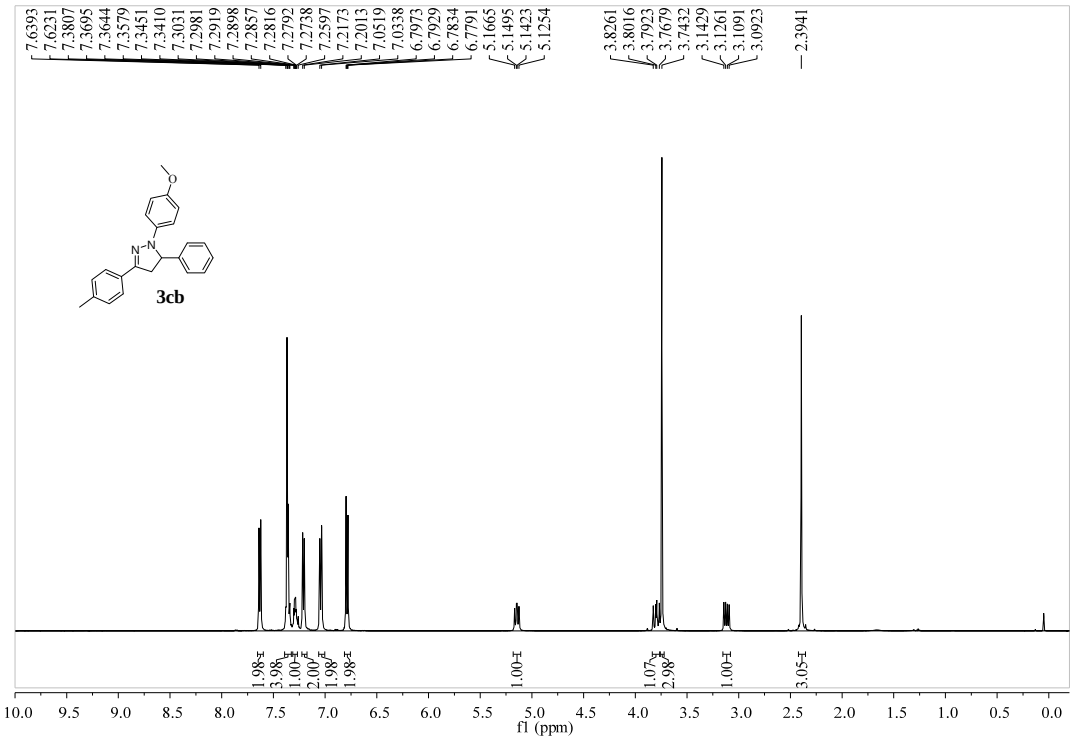
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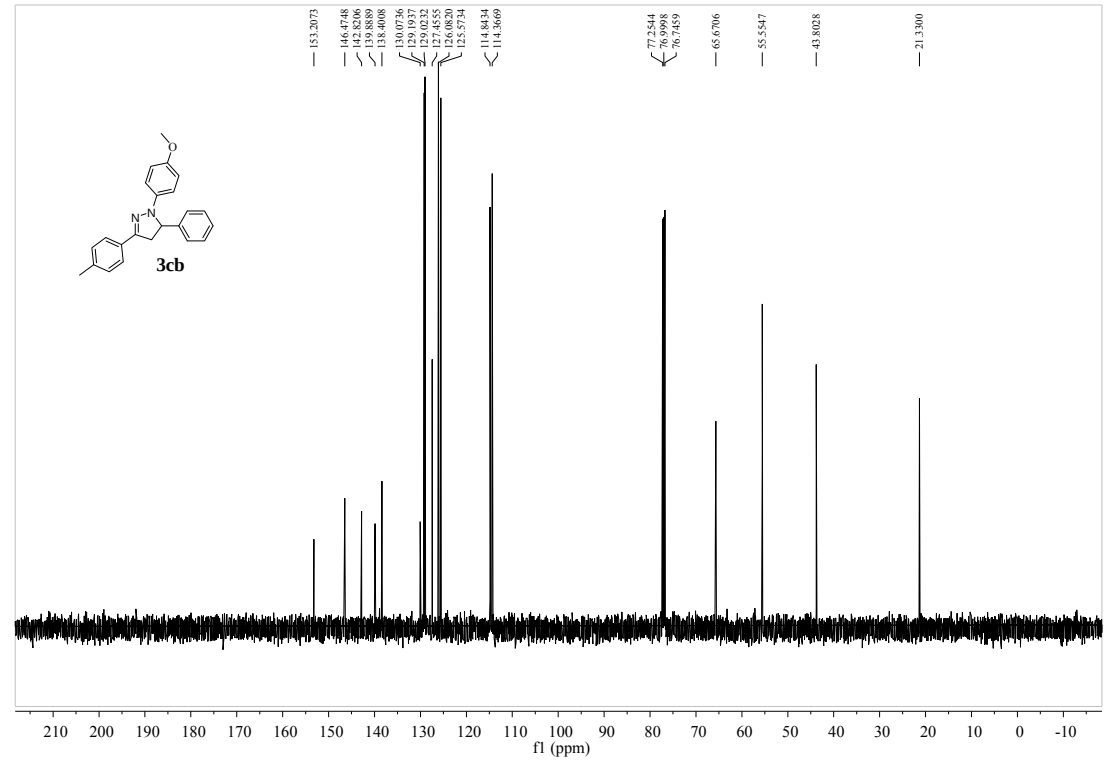
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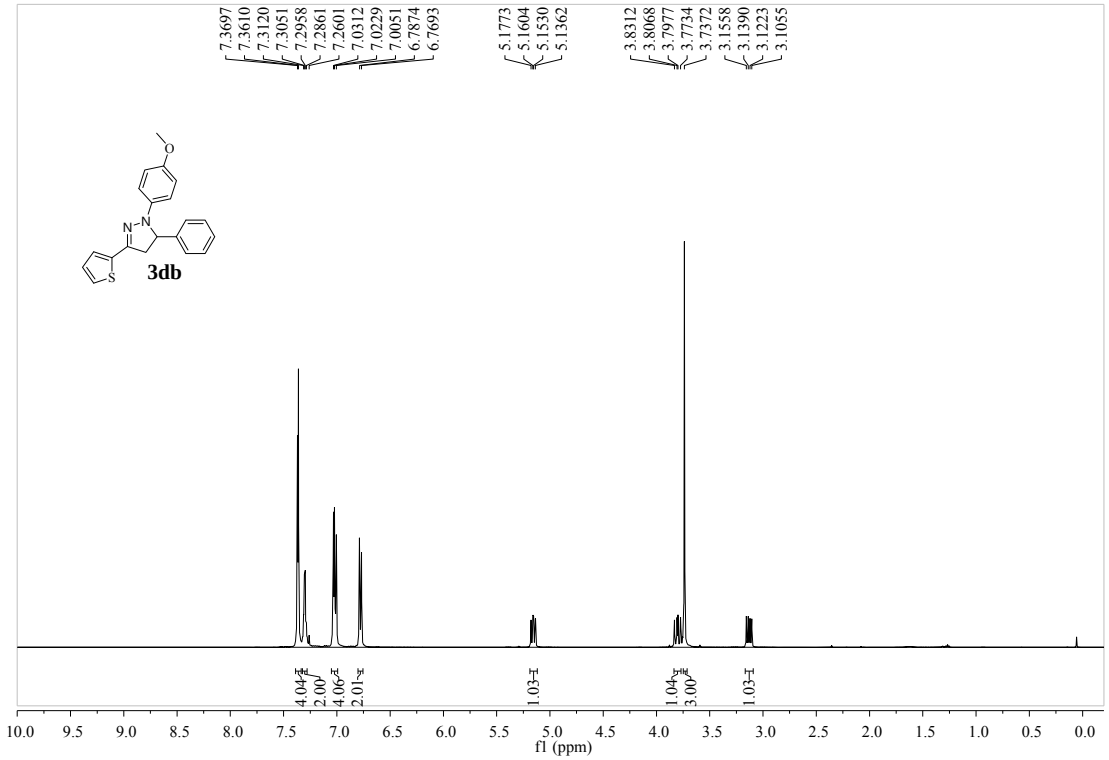
f1 (ppm)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3.7977
3.7734
3.7372
3.1558
3.1390
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4.06
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1.04
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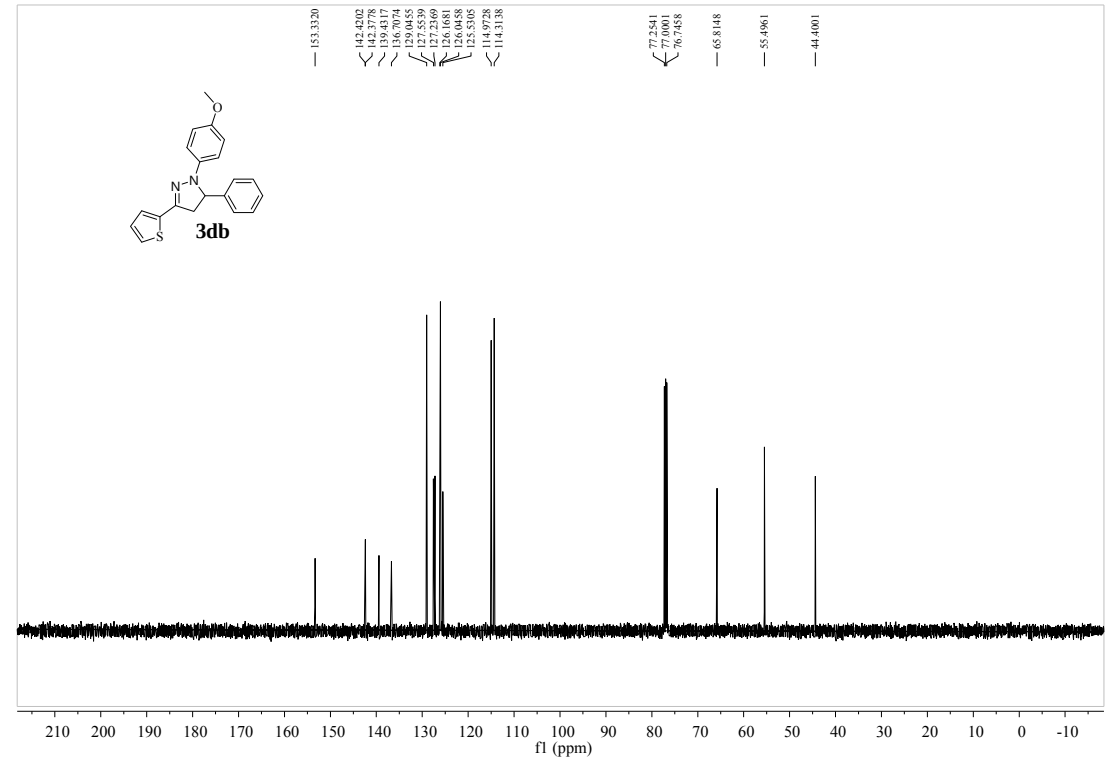
1.03
f1 (ppm)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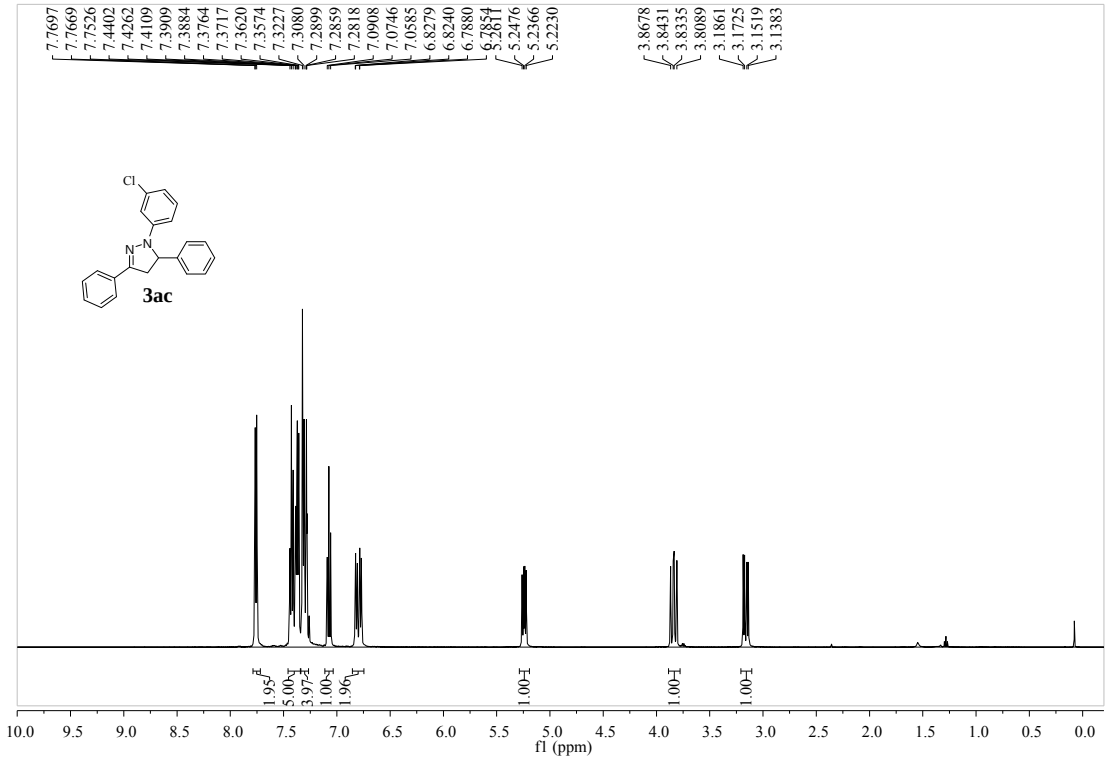
f1 (ppm)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3.1383
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5.00
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1.96
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1.00
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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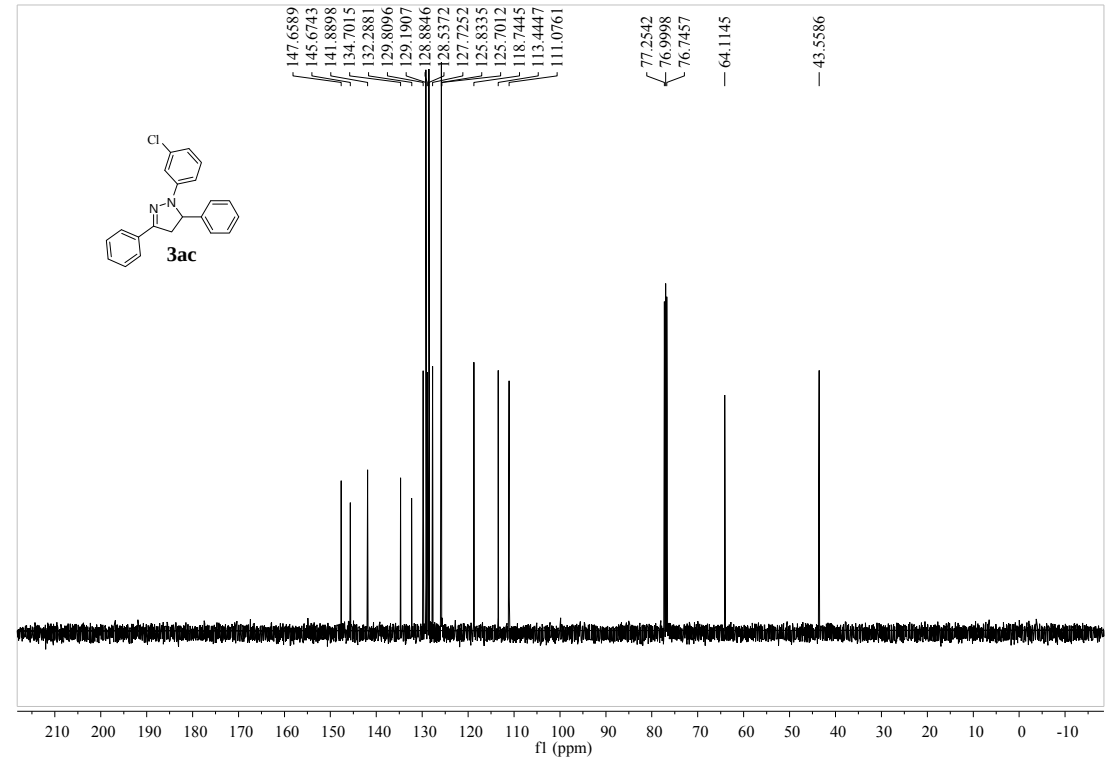
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111.0761
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76.9998
76.7457
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N
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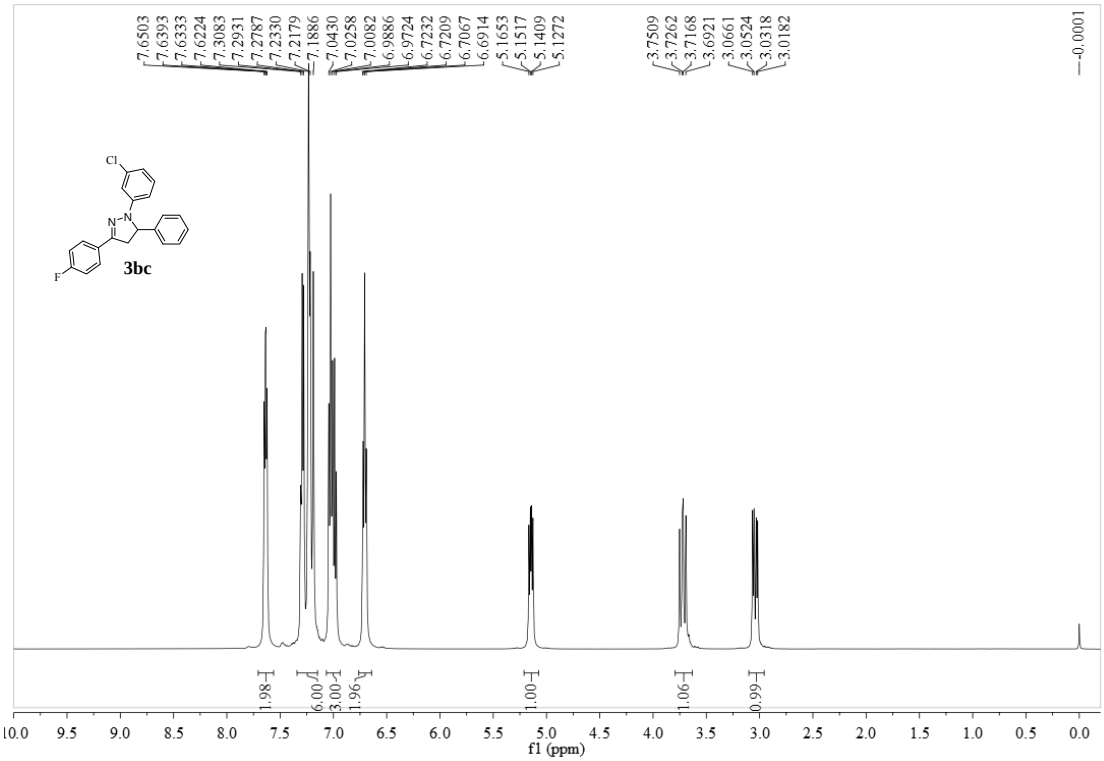
f1 (ppm)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7.0082
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6.9724
6.7232
6.7209
6.7067
6.6914
5.1653
5.1517
5.1409
5.1272
3.7509
3.7262
3.7168
3.6921
3.0661
3.0524
3.0318
3.0182
-0.0001
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N
F
3bc
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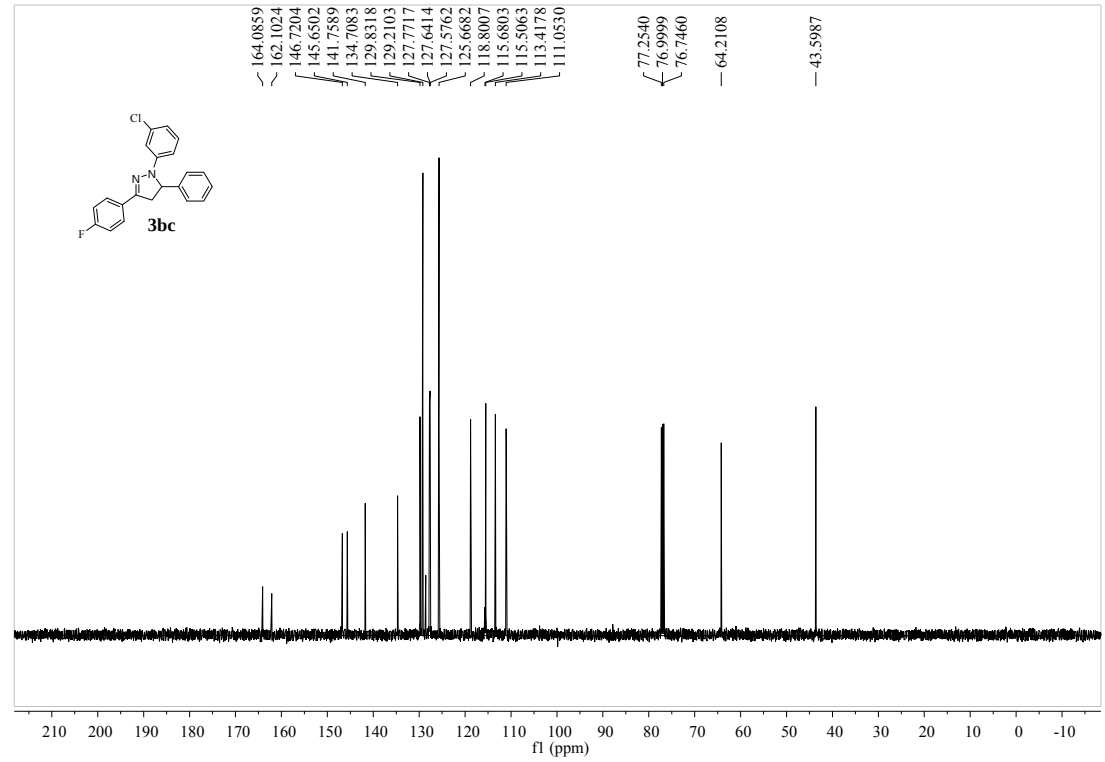
6.00
3.00
1.96
1.00
1.06
0.99
f1 (ppm)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Cl
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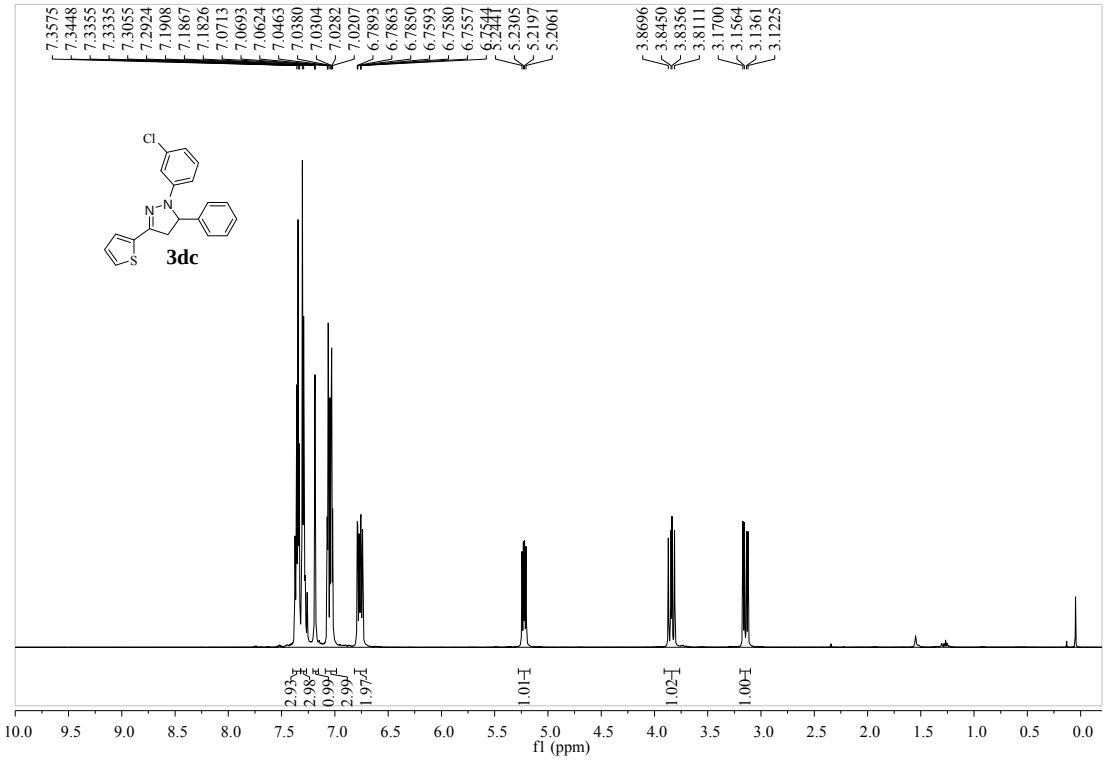
N
F
3bc
f1 (ppm)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3.1225
Cl
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S
3dc
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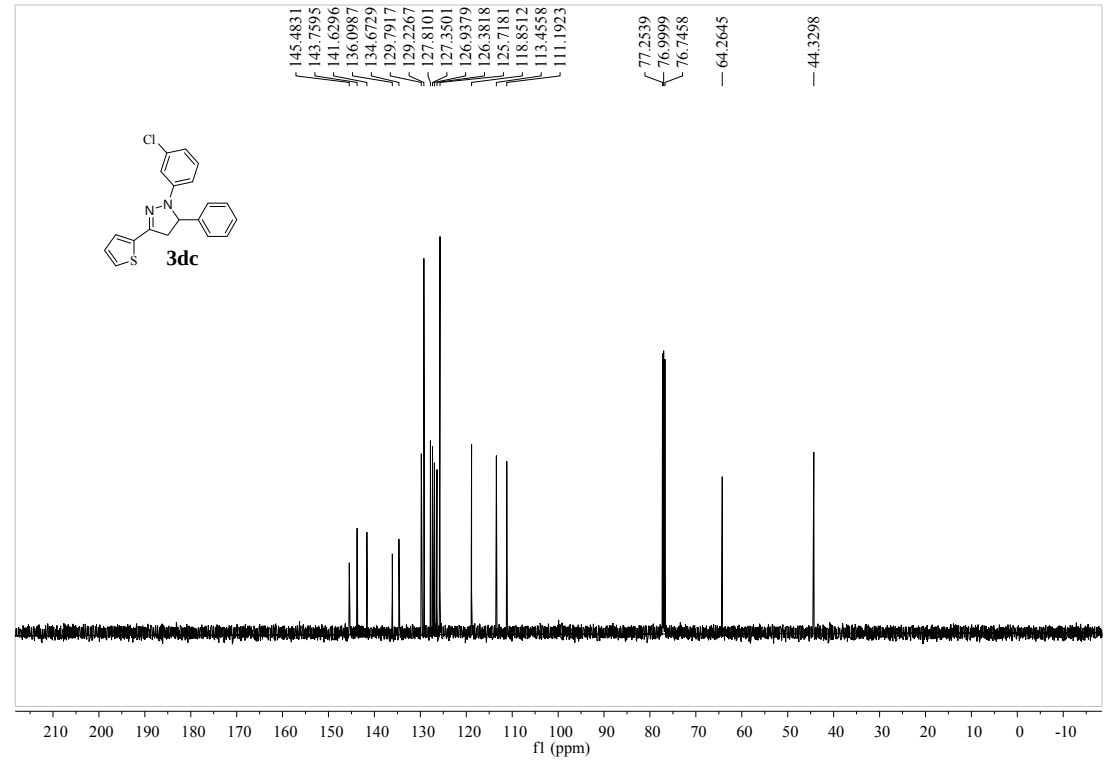
2.98
0.99
2.99
1.97
1.01
1.02
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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113.4558
111.1923
77.2539
76.9999
76.7458
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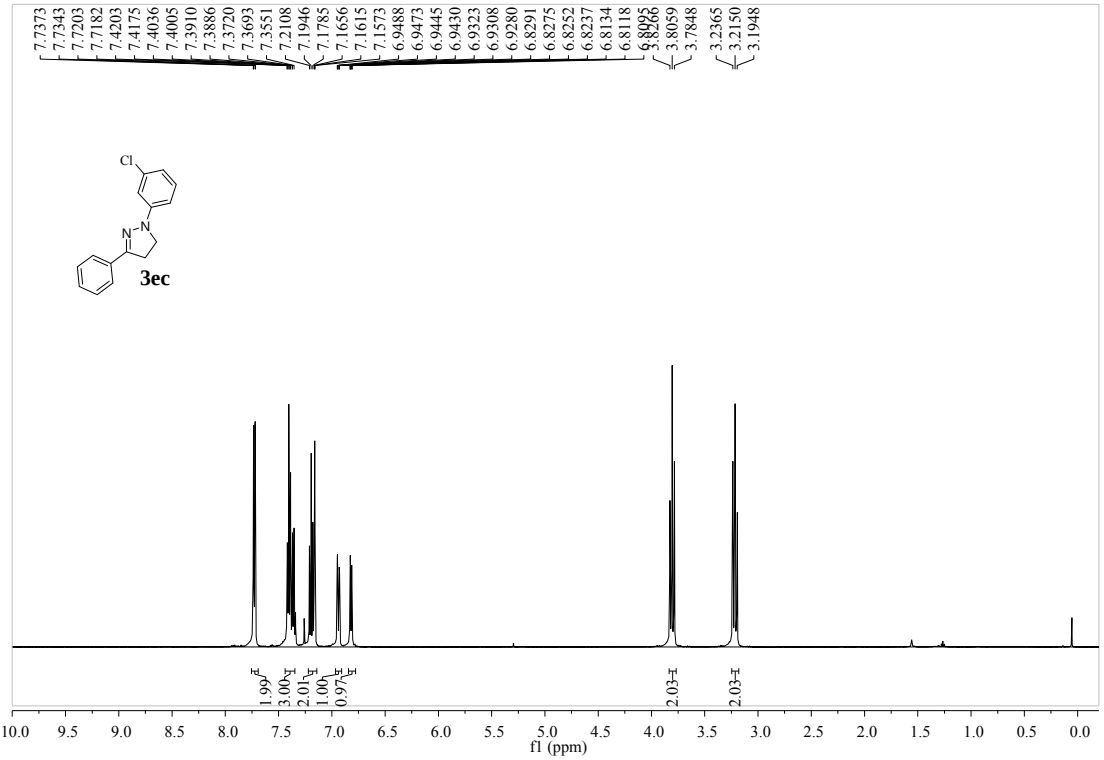
S
3dc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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3.2150
3.1948
Cl
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N
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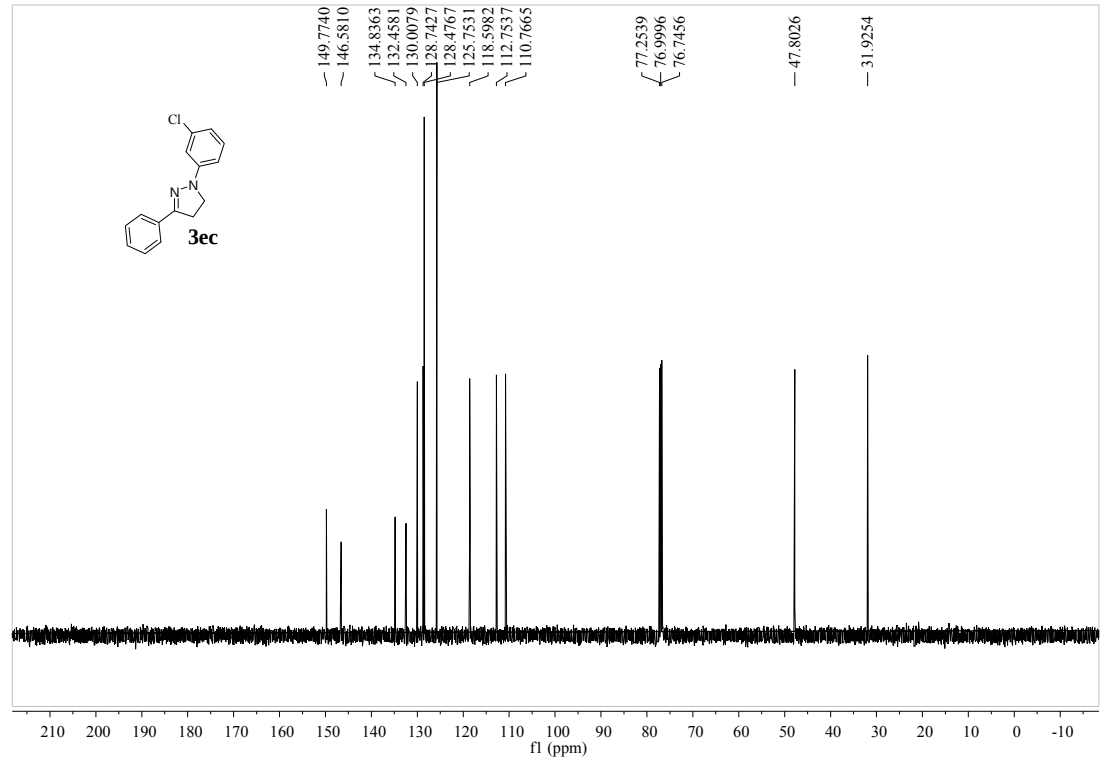
1.99
3.00
2.01
1.00
0.97
2.03
2.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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76.9996
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N
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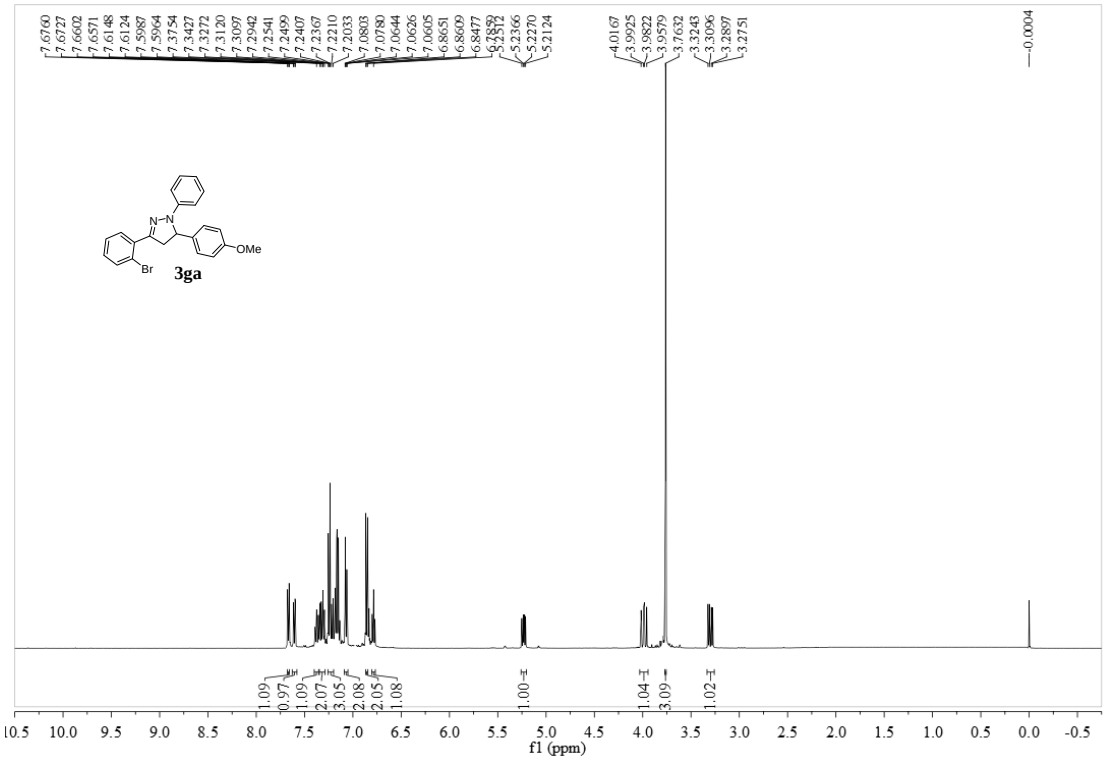
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.2942
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7.2499
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7.2210
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3.2897
3.2751
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OMe
Br
3ga
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3.05
2.08
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1.04
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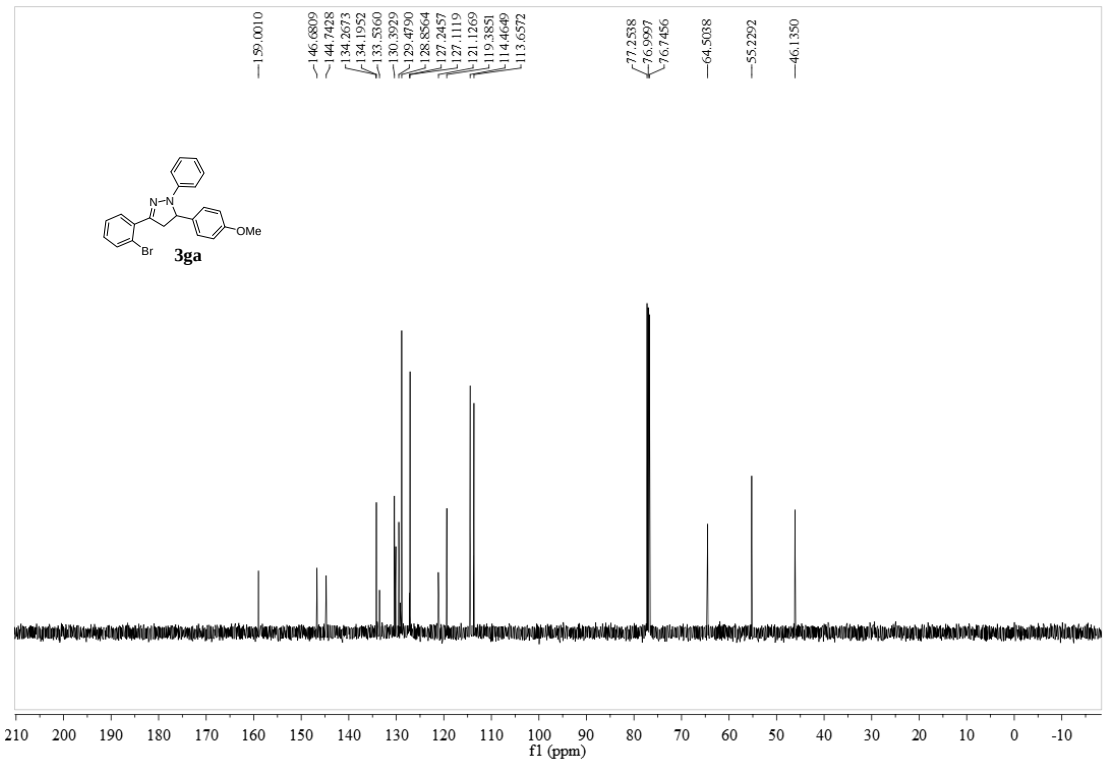
1.02
f1 (ppm)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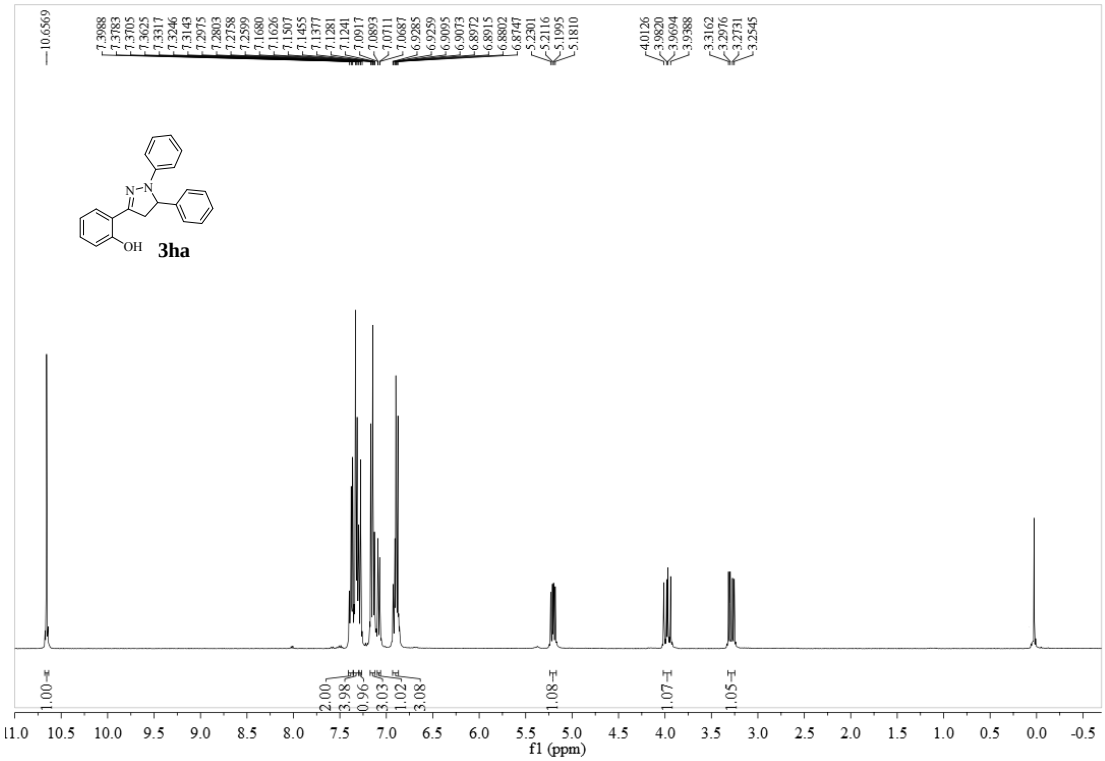
OMe
Br
3ga
f1 (ppm)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5.1995
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OH
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1.08
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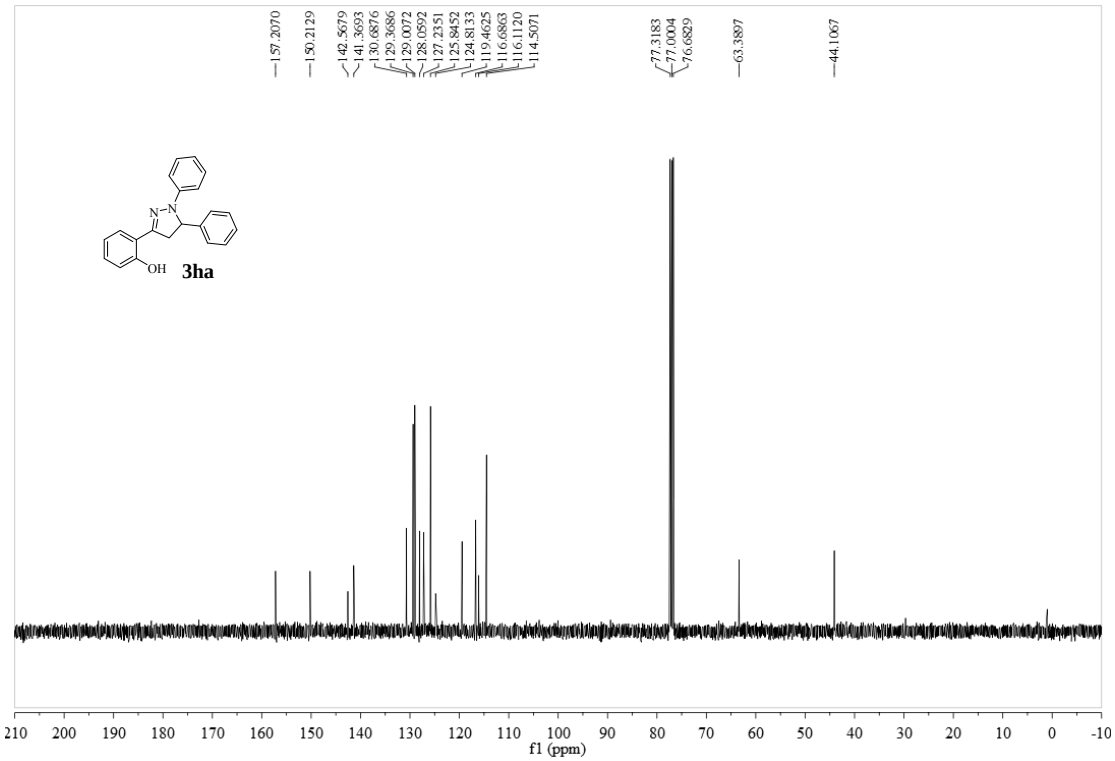
1.05
f1 (ppm)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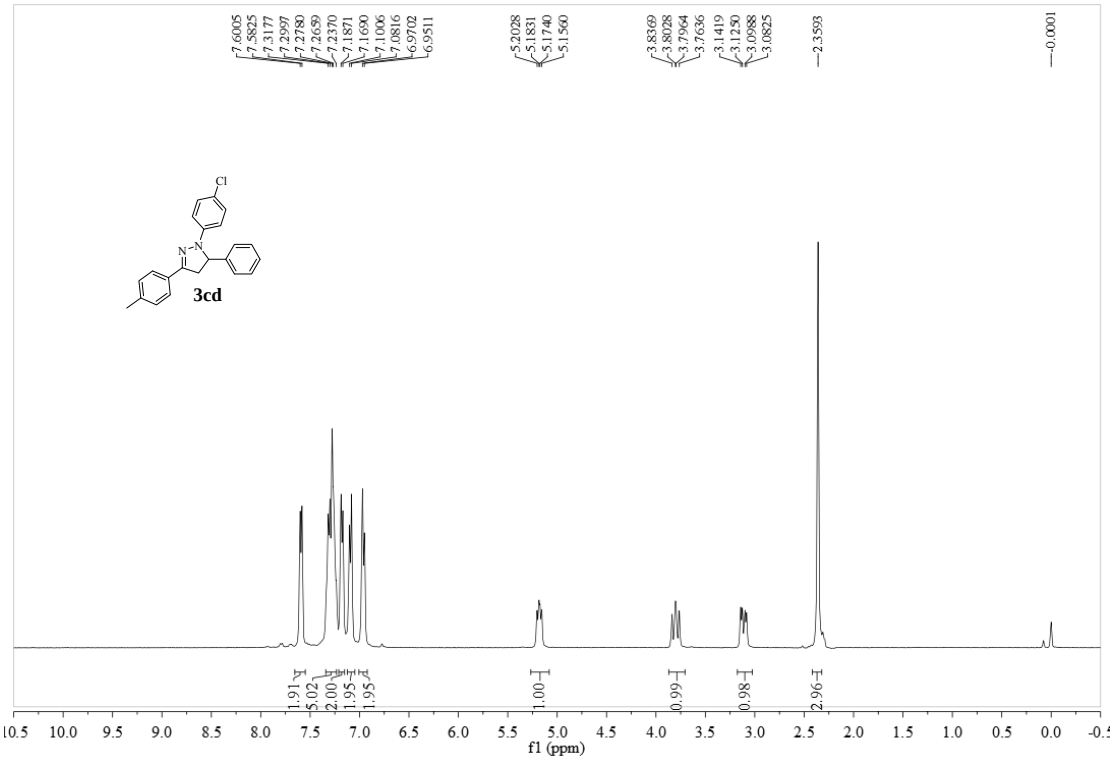
3ha
f1 (ppm)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3.1419
3.1250
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3.0825
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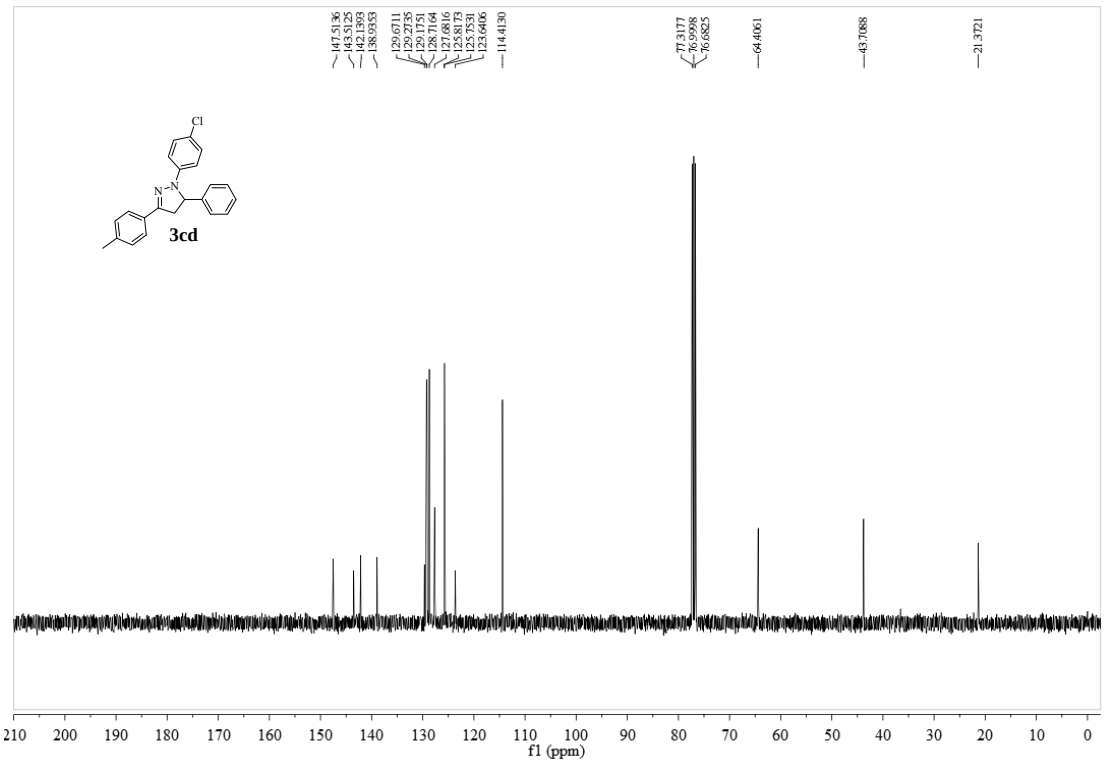
2.96
f1 (ppm)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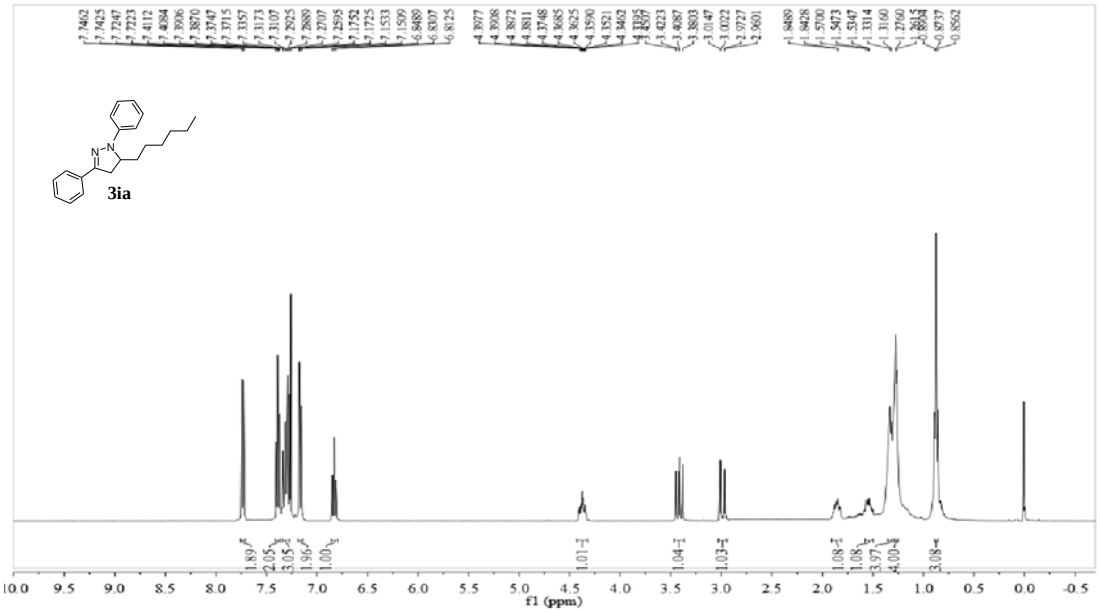
Cl
3cd
f1 (ppm)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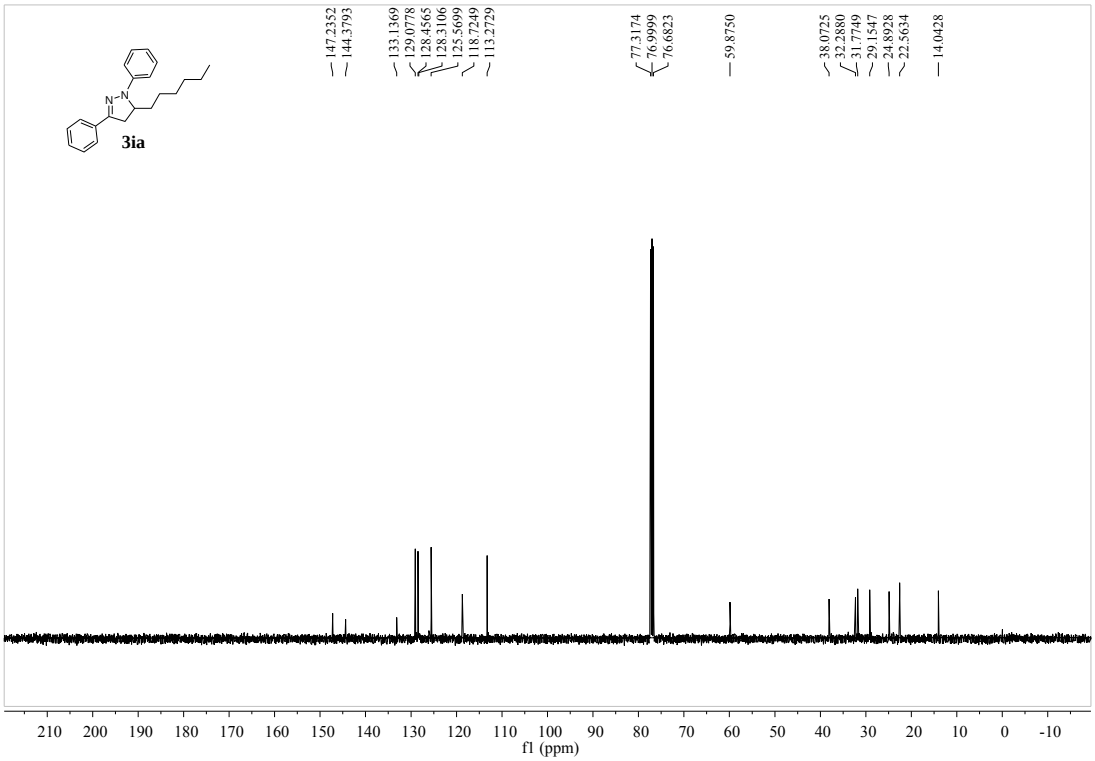
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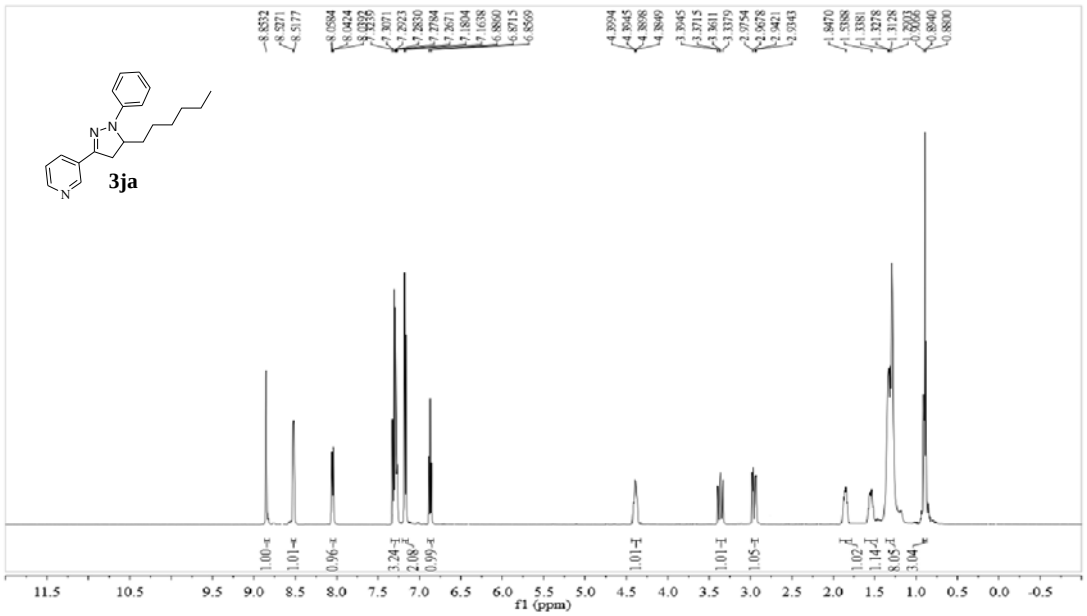
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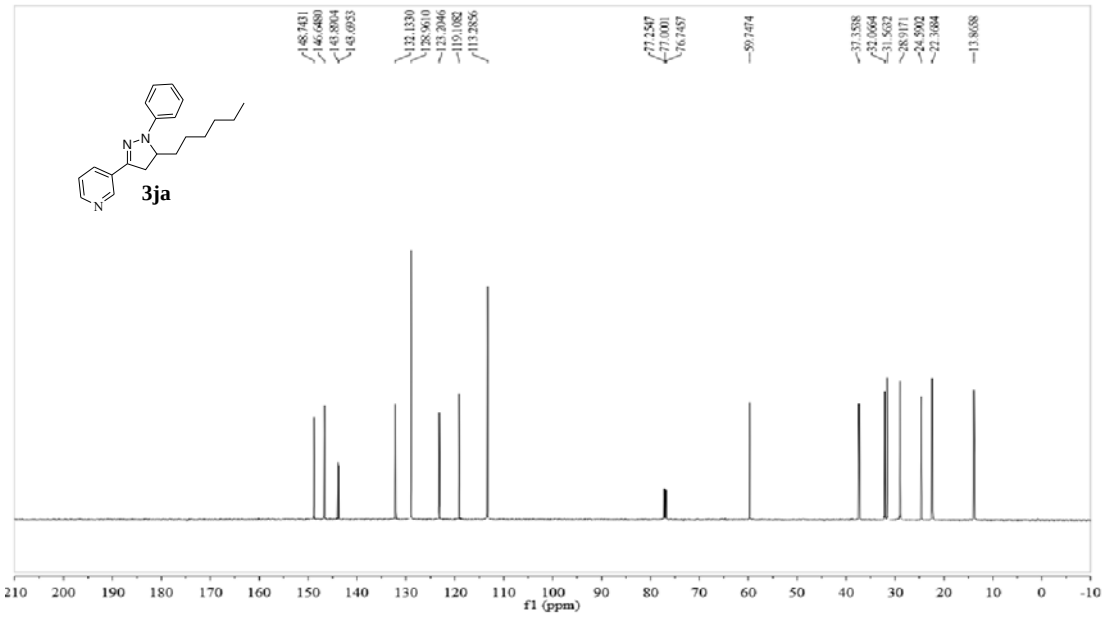
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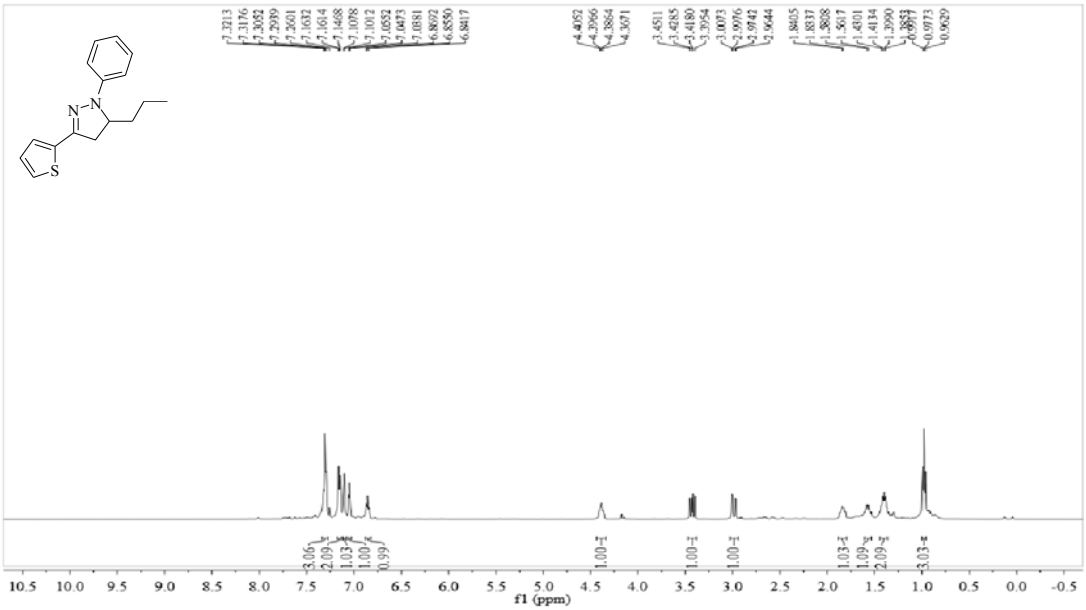
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1.00
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1.09
2.09
3.03
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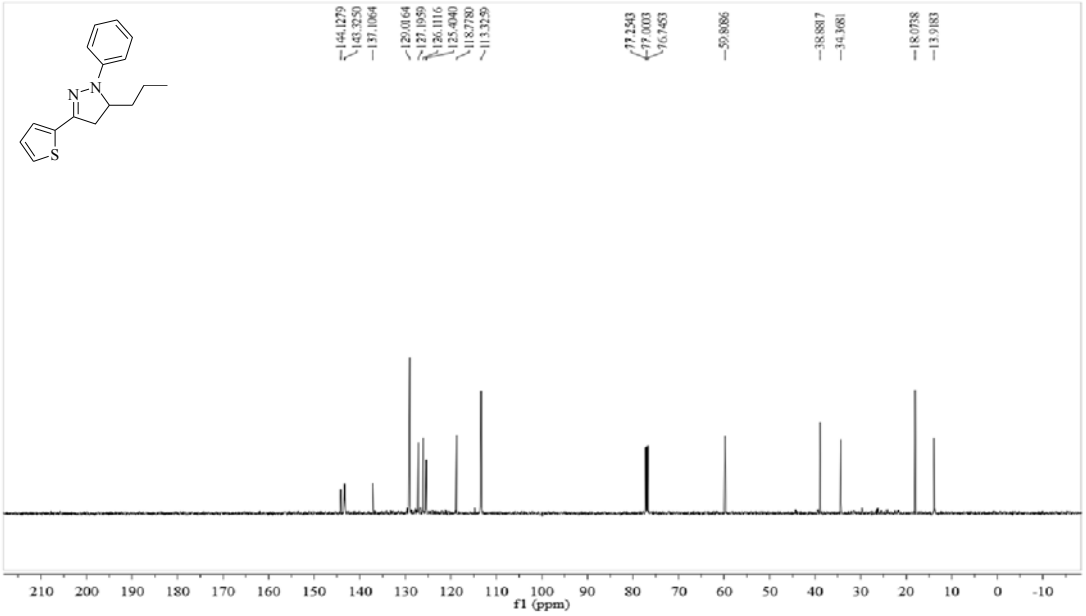
f1 (ppm)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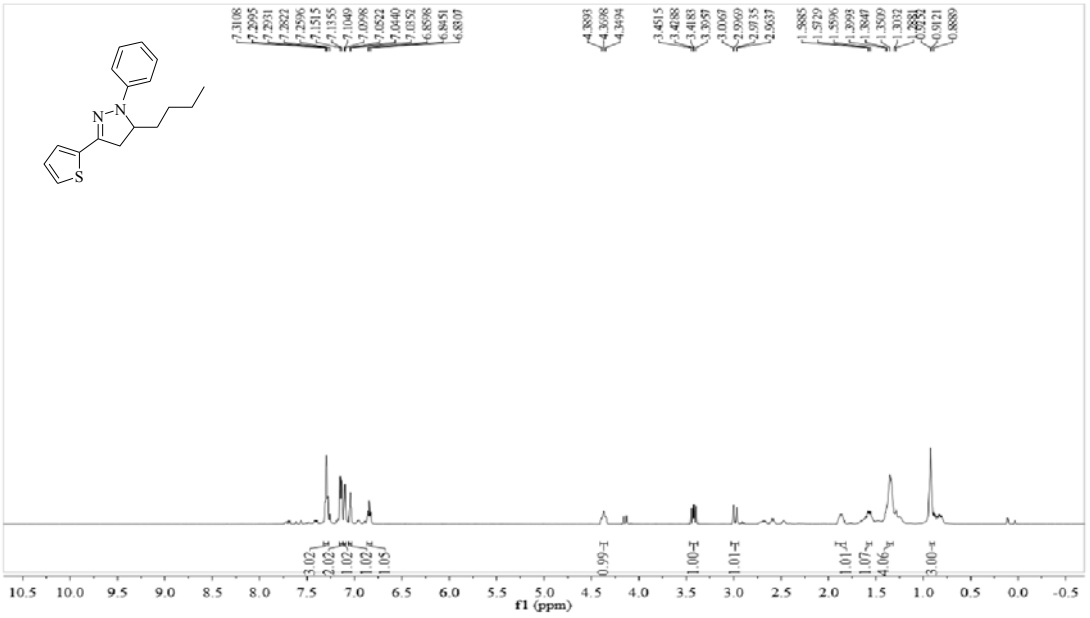
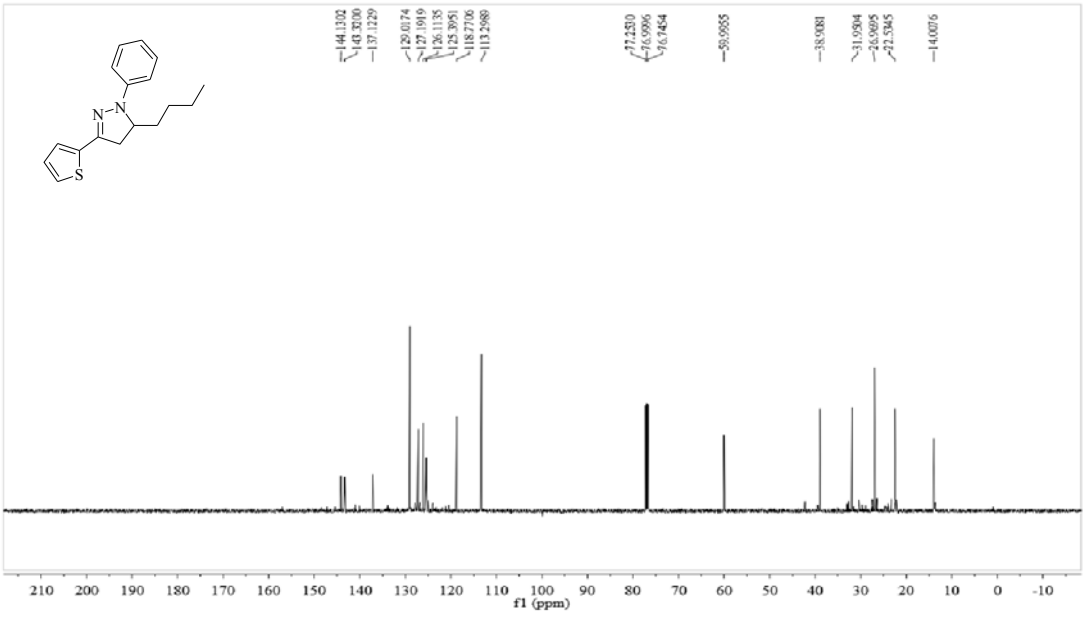
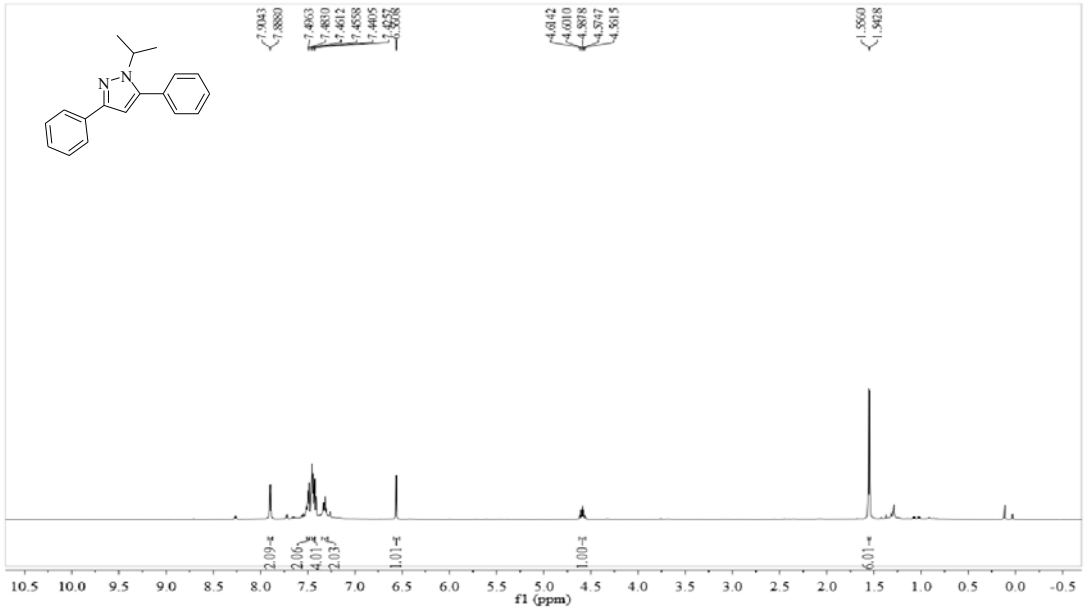

f1 (ppm)


f1 (ppm)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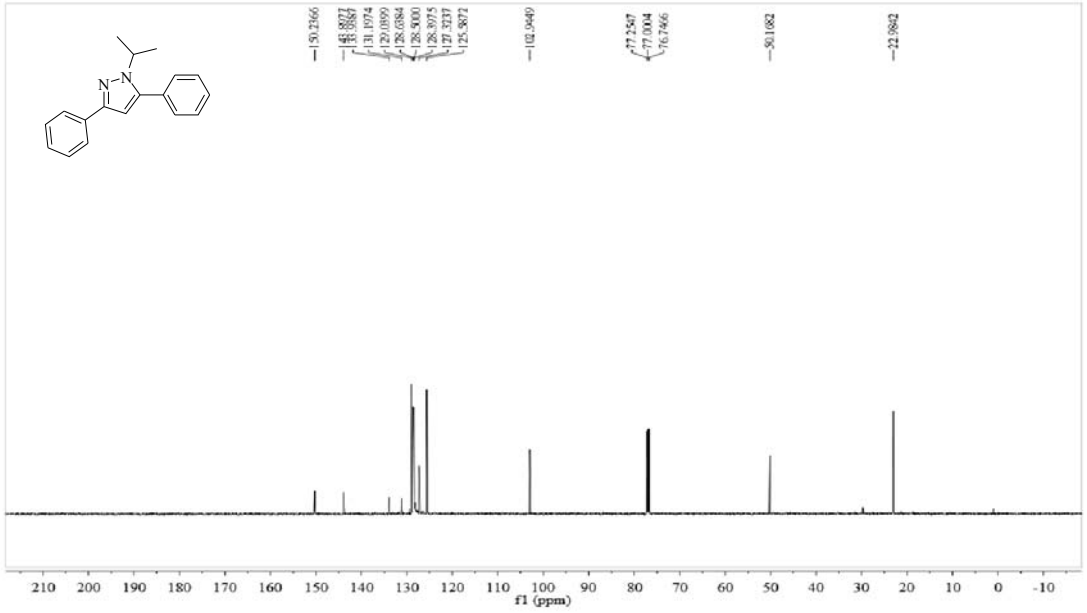
7.8880
7.4863
7.4830
7.4612
7.4588
7.4405
6.8842
6.8610
4.8818
4.5747
4.5615
1.5560
1.5428
2.09
2.05
4.01
2.03
1.01
1.00
6.01
f1 (ppm)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141.8077
131.1974
129.0899
128.6584
128.5000
128.3975
127.3237
125.9872
102.9449
77.2567
77.0004
76.7466
50.1082
22.2842
f1 (ppm)