Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Electronic Supplementary Information

The use of Enaminones and Enamines as effective synthons for MSA-catalyzed regioselective synthesis of 1,3,4-Tri- and 1,3,4,5-Tetrasubstituted Pyrazoles

Liancheng Duan, Hui Zhou, Yucheng Gu, Ping Gong*, Mingze Qin*

Key Laboratory of Structure-based Drug Design and Discovery (Shenyang Pharmaceutical University), Ministry of Education, 103 Wenhua Road, Shenhe District, Shenyang 110016, People's Republic of China

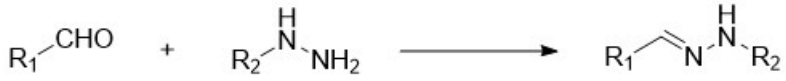
Syngenta Jealott's Hill International Research Center, Bracknell, Berkshire RG42 6EY, U.K.

1. General Information

Unless otherwise noted, all reagents and solvents were obtained from commercial sources and used without further purification. Solvents were dried using standard methods and distilled before use. Reactions were monitored by thin-layer chromatography (TLC) on silica plates (F-254) and visualized under UV light. All ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker ARX-400, 400 MHz spectrometers with TMS as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in hertz (Hz). HRMS analysis was performed on a Q-TOF mass analyzer using the ESI ionization method. Column chromatography was run on silica gel (200-300 mesh) from Qingdao Ocean Chemicals (Qingdao, Shandong, China).

2. General Procedure and Product Characterization

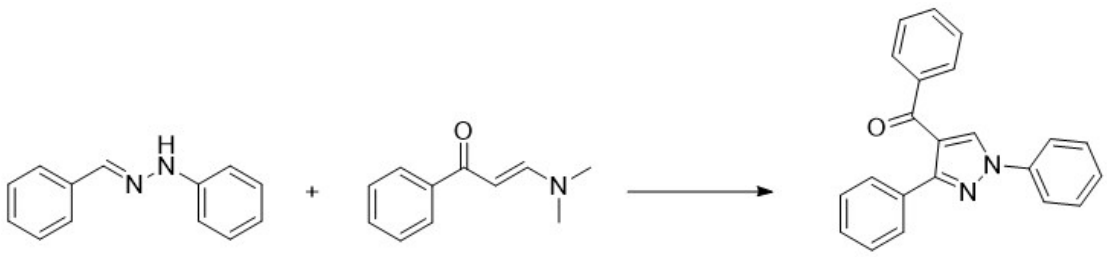
2.1 General procedure for the synthesis of 1 and 2



Typical Procedure for the Synthesis of **1**: Aldehyde (1.0 equiv.) was added to an ethanol solution of Hydrazine (1.0 equiv.). After the reaction mixture was heated under reflux for 6 hours. The precipitate was collected on a Büchner funnel. The crude product was purified by recrystallization from ethanol and washed with diethyl ether[1].

Typical Procedure for the Synthesis of **2**: Aryl ketones (1.0 equiv.) and N,N-dimethylformamide dimethyl acetal (DMF-DMA) (2.0 equiv.) were refluxed until the starting materials were consumed, as determined by thin-layer chromatography (TLC), then left to cool to room temperature, the precipitate was collected by filtration, and recrystallized from ethanol. Compounds 2m–2p were prepared by literature procedures[2-6].

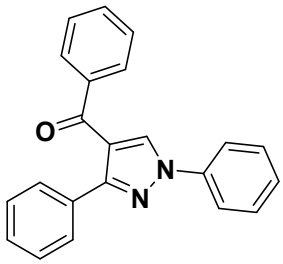
2.2 The Optimal Experimental Conditions



1a **2a** **3aa**

Representative procedure for the synthesis of (1,3-diphenyl-1H-pyrazol-4-yl)(phenyl)methanone (**3aa**): Corresponding Hydrazones **1a** (0.1 mmol, 1.0 equiv.), (E)-3-(dimethylamino)-1-phenylprop-2-en-1-one **2a** (0.1 mmol, 1.0 equiv.) were added to a 10 mL round-bottom flask followed by the adding of MSA (1.0 equiv.) in DCM (3 mL), and the reaction mixture was stirred at room temperature in air for 5 h. After the reaction was complete (monitored by TLC), the solvent was removed to give the crude product, which was purified by column chromatography on silica gel with a mixture of hexane/dichloromethane (1:1, v/v) to afford the desired product **3aa**.

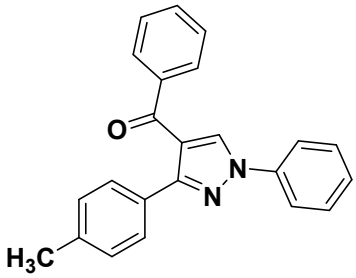
2.3 Product Characterization



3aa, 73 %

(1,3-diphenyl-1*H*-pyrazol-4-yl)(phenyl)methanone(3aa)

Yield: 73% (white solid); mp 143–145℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.01 (d, J = 7.8 Hz, 2H), 7.89 (d, J = 7.4 Hz, 2H), 7.73 – 7.62 (m, 3H), 7.60 – 7.49 (m, 4H), 7.45 – 7.34 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.64, 153.26, 139.32, 138.75, 133.89, 133.36, 132.56, 130.04, 129.88, 129.07, 128.98, 128.92, 128.57, 127.76, 120.76, 119.69. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{16}N_2O$ $[M + H]^+$: 325.3830, found $[M + H]^+$: 325.3836.

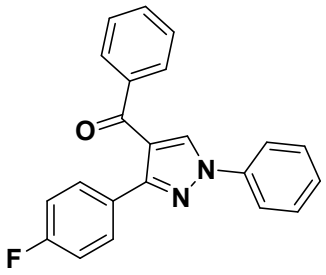


3ab, 70%

Phenyl(1-phenyl-3-(p-tolyl)-1*H*-pyrazol-4-yl)methanone(3ab)

Yield: 70% (white solid); mp 145–147℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 7.99 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 7.4 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.60 – 7.50 (m, 6H), 7.39 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.69, 153.21, 139.34, 138.81, 138.33, 133.83, 133.34, 130.02, 129.88, 129.71, 129.15, 129.08, 128.85, 127.68,

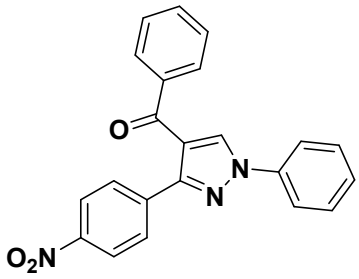
120.63, 119.64, 21.33. HRMS (ESI-Q-TOF, m/z) calcd for $C_{23}H_{18}N_2O$ [M + H]$^+$: 339.1430, found [M + H]$^+$: 339.3214.



3ac, 63%

(3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3ac)

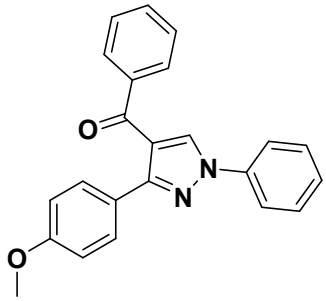
Yield: 63% (white solid); mp 153–155℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.00 (d, J = 7.9 Hz, 2H), 7.89 (d, J = 7.3 Hz, 2H), 7.75 (dd, J = 8.6, 5.6 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.54 (q, J = 7.8 Hz, 4H), 7.41 (t, J = 7.4 Hz, 1H), 7.24 (t, J = 8.9 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.53, 152.38, 139.26, 138.78, 134.14, 133.34, 131.23, 131.15, 130.04, 129.88, 129.08, 127.83, 120.61, 119.74, 115.60, 115.38. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{15}FN_2O$ [M + H]$^+$: 343.1268, found [M + H]$^+$: 343.3736.



3ad, 54%

(3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3ad)

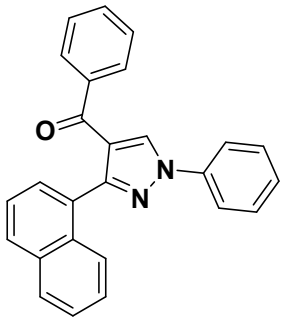
Yield: 54% (yellow solid); mp 169–172℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.27 (d, J = 8.8 Hz, 2H), 8.01 (dd, J = 14.2, 8.3 Hz, 4H), 7.95 (d, J = 7.3 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.57 (td, J = 7.6, 3.0 Hz, 4H), 7.43 (t, J = 7.4 Hz, 1H).^{13}C NMR (151 MHz, DMSO-d_6) δ 189.27, 151.26, 147.70, 139.14, 139.07, 138.56, 134.59, 133.53, 130.14, 130.06, 129.95, 129.14, 128.14, 123.79, 121.24, 119.95. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{15}N_3O_3$ [M + H]$^+$: 370.1223, found [M + H]$^+$: 370.3800.



3ae, 64%

(3-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3ae)

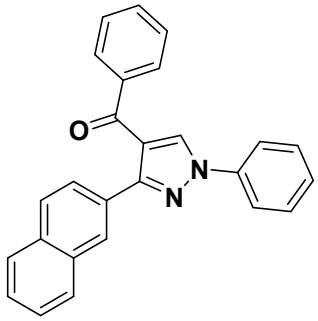
Yield: 64% (white solid); mp 131−133℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 (s, 1H), 7.99 (d, J = 7.8 Hz, 2H), 7.89 (d, J = 7.2 Hz, 2H), 7.65 (dt, J = 7.3, 2.7 Hz, 3H), 7.53 (q, J = 7.3 Hz, 4H), 7.39 (t, J = 7.4 Hz, 1H), 6.99 – 6.93 (m, 2H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.73, 159.97,153.01, 139.34, 138.90, 133.89, 133.29, 130.32, 130.01, 129.87, 129.07, 127.64, 124.92, 120.43, 119.61, 114.01, 55.62. HRMS (ESI-Q-TOF, m/z) calcd for $C_{23}H_{18}N_2O_2$ $[M + H]^+$: 355.1268, found $[M + H]^+$: 355.4090.



3af, 68%

(3-(naphthalen-1-yl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3af)

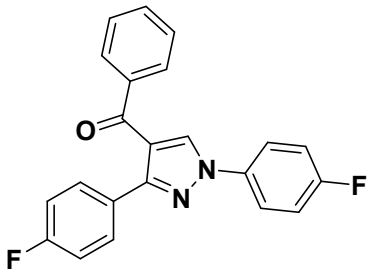
Yield: 68% (white solid); mp 134−136℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (s, 1H), 8.05 (d, J = 8.0 Hz, 2H), 7.97 (d, J = 7.8 Hz, 2H), 7.90 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.60 – 7.47 (m, 6H), 7.43 (q, J = 7.4 Hz, 4H).^{13}C NMR (101 MHz, DMSO-d_6) δ 188.82, 152.80, 139.40, 138.66, 133.51, 133.26, 133.01, 131.94, 130.86, 130.08, 129.47, 129.10, 128.87, 128.63, 128.53, 127.83, 126.83, 126.28, 125.73, 125.58, 122.70, 119.78. HRMS (ESI-Q-TOF, m/z) calcd for $C_{26}H_{18}N_2O$ $[M + H]^+$: 375.1419, found $[M + H]^+$: 375.4340.



3ag, 70%

(3-(naphthalen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3ag)

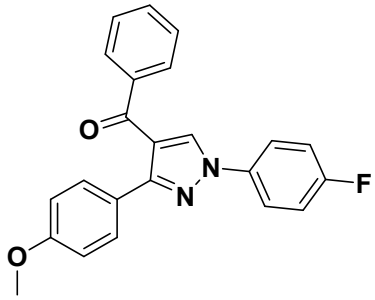
Yield: 70% (white solid); mp 133–135℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (s, 1H), 8.27 (s, 1H), 8.05 (d, J = 7.9 Hz, 2H), 7.98 – 7.89 (m, 5H), 7.81 (dd, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.60 – 7.49 (m, 6H), 7.42 (t, J = 7.4 Hz, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 189.66, 153.23, 139.34, 138.84, 134.16, 133.35, 133.20, 133.09, 130.07, 129.91, 129.09, 128.68, 128.07, 127.99, 127.94, 127.83, 126.99, 126.91, 126.81, 121.00, 119.77. HRMS (ESI-Q-TOF, m/z) calcd for $C_{26}H_{18}N_2O$ [M + H]$^+$: 375.1428, found [M + H]$^+$: 375.4490.



3ah, 57%

(1,3-bis(4-fluorophenyl)-1*H*-pyrazol-4-yl)(phenyl)methanone (3ah)

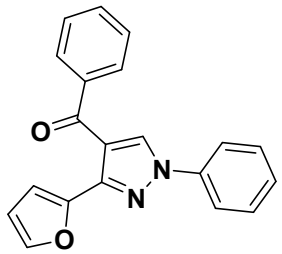
Yield: 57% (white solid); mp 146–148℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.08 – 8.01 (m, 2H), 7.93 – 7.87 (m, 2H), 7.78 – 7.72 (m, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.7 Hz, 2H), 7.44 – 7.36 (m, 2H), 7.27 – 7.19 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.46, 152.43, 138.76, 134.38, 133.34, 131.24, 131.15, 129.87, 129.07, 121.98, 121.90, 120.60, 116.90, 116.67, 115.59, 115.37. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{14}F_2N_2O$ [M + H]$^+$: 361.1074, found [M + H]$^+$: 361.3438.



3ai, 59%

(1-(4-fluorophenyl)-3-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)(phenyl)methanone (3ai)

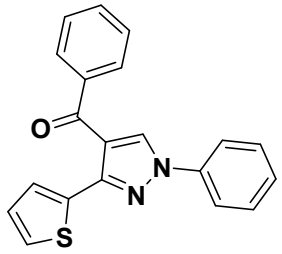
Yield: 59% (white solid); mp 158–161℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.91 (s, 1H), 8.03 (ddt, J = 8.2, 5.5, 2.8 Hz, 2H), 7.92 – 7.86 (m, 2H), 7.65 (d, J = 8.6 Hz, 3H), 7.53 (t, J = 7.7 Hz, 2H), 7.43 – 7.35 (m, 2H), 6.98 – 6.92 (m, 2H), 3.78 (s, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ189.67, 159.99, 153.07, 138.88, 134.14, 133.29, 130.32, 129.86, 129.06, 124.84, 121.83, 121.75, 120.42, 116.87, 116.64, 114.00, 55.62. HRMS (ESI-Q-TOF, m/z) calcd for $C_{23}H_{17}FN_2O_2$ $[M + H]^+$: 373.1374, found $[M + H]^+$: 373.3996.



3aj, 76%

(3-(furan-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3aj)

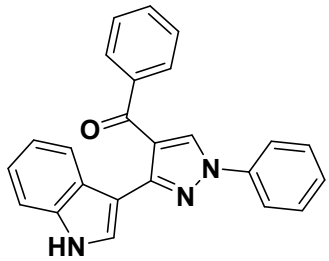
Yield: 76% (brown solid); mp 119–121℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.03 – 7.97 (m, 2H), 7.95 – 7.88 (m, 2H), 7.77 (d, J = 1.0 Hz, 1H), 7.72 – 7.63 (m, 1H), 7.60 – 7.51 (m, 4H), 7.41 (t, J = 7.4 Hz, 1H), 7.22 (dd, J = 3.4, 0.5 Hz, 1H), 6.61 (dd, J = 3.4, 1.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 188.99, 146.65, 144.12, 144.02, 139.19, 138.9, 133.93, 133.27, 130.03, 129.73, 129.12, 127.90, 120.06, 119.78, 111.94, 111.79. HRMS (ESI-Q-TOF, m/z) calcd for $C_{20}H_{14}N_2O_2$ $[M + H]^+$: 315.1155, found $[M + H]^+$: 315.3440.



3ak, 74%

Phenyl(1-phenyl-3-(thiophen-2-yl)-1*H*-pyrazol-4-yl)methanone (3ak)

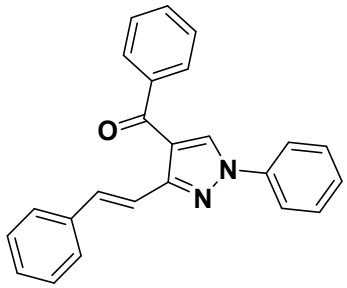
Yield: 74% (brown solid); mp 98–100℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.02 – 7.92 (m, 4H), 7.88 (dd, J = 3.7, 1.0 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.62 (dd, J = 5.1, 1.0 Hz, 1H), 7.60 – 7.53 (m, 4H), 7.41 (t, J = 7.4 Hz, 1H), 7.13 (dd, J = 5.0, 3.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 189.36, 147.48, 139.11, 139.04, 134.63, 134.37, 133.30, 130.03, 129.85, 129.14, 128.73, 127.97, 127.90, 127.80, 119.90, 119.77. HRMS (ESI-Q-TOF, m/z) calcd for $C_{20}H_{14}N_2OS$ [M + H]$^+$: 331.1127, found [M + H]$^+$: 315.4064.



3al, 62%

(3-(1*H*-indol-3-yl)-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3al)

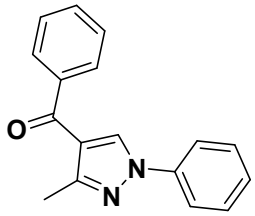
Yield:62% (yellow solid); mp 209–211℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.44 (s, 1H), 8.89 (s, 1H), 8.43 (d, J = 8.3 Hz, 1H), 8.38 (d, J = 2.5 Hz, 1H), 8.07 (d, J = 7.8 Hz, 2H), 7.93 (d, J = 7.3 Hz, 2H), 7.67 (t, J = 7.3 Hz, 1H), 7.57 (q, J = 7.4 Hz, 4H), 7.48 (d, J = 6.7 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.24 – 7.12 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.88, 149.56, 139.94, 139.46, 136.64, 134.09, 132.91, 130.07, 129.80, 129.07, 128.36, 127.36, 126.32, 122.26, 122.18, 120.40, 120.22, 119.33, 112.09, 107.46. HRMS (ESI-Q-TOF, m/z) calcd for $C_{24}H_{17}N_3O$ [M + H]$^+$: 364.1427, found [M + H]$^+$: 364.4240.



3am, 64%

(E)-phenyl(1-phenyl-3-styryl-1*H*-pyrazol-4-yl)methanone (3am)

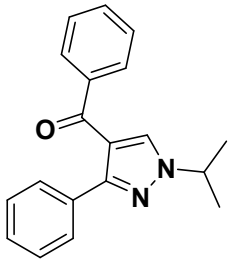
Yield:64% (light yellow solid); mp 150–152℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 (s, 1H), 8.03 (d, J = 7.7 Hz, 2H), 7.97 – 7.91 (m, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.65 – 7.50 (m, 8H), 7.46 – 7.38 (m, 3H), 7.33 (t, J = 7.3 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 189.65, 151.28, 139.41, 139.31, 136.93, 133.98, 132.99, 132.59, 129.98, 129.50, 129.33, 129.15, 128.79, 127.88, 127.20, 120.59, 119.95, 118.90. HRMS (ESI-Q-TOF, m/z) calcd for $C_{24}H_{18}N_2O$ $[M + H]^+$: 351.1429, found $[M + H]^+$: 351.4210.



3an, 76%

(3-methyl-1-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3an)

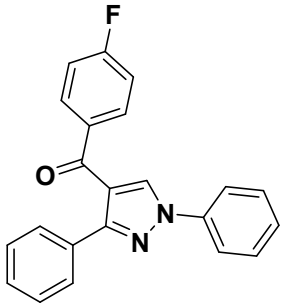
Yield:76% (yellow solid); mp 80–82℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 7.93 (d, J = 7.9 Hz, 2H), 7.88 (d, J = 7.4 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.51 (t, J = 7.9 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 2.51 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 189.49, 152.37, 139.53 , 139.33, 133.38, 132.70, 129.91, 129.28, 129.09, 127.42, 120.60, 119.55, 14.31. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{14}N_2O$ $[M + H]^+$: 263.1216, found $[M + H]^+$: 263.3127.



3ao, 72%

(1-isopropyl-3-phenyl-1*H*-pyrazol-4-yl)(phenyl)methanone (3ao)

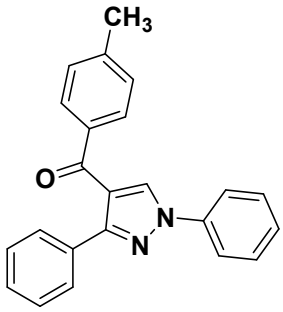
Yield:72% (yellow solid); mp 72–75℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (s, 1H), 7.78 (d, J = 7.2 Hz, 2H), 7.61 (dd, J = 8.5, 4.9 Hz, 3H), 7.49 (t, J = 7.6 Hz, 2H), 7.38 – 7.29 (m, 3H), 4.62 (hept, J = 6.6 Hz, 1H), 1.50 (d, J = 6.7 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 189.51, 151.69, 139.47, 134.86, 133.40, 132.76, 129.68, 129.46, 128.95, 128.89, 128.31, 118.25, 54.14, 22.82. HRMS (ESI-Q-TOF, m/z) calcd for $C_{19}H_{18}N_2O$ $[M + H]^+$: 291.1429, found $[M + H]^+$: 291.3764.



3ap, 70%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(4-fluorophenyl)methanone (3ap)

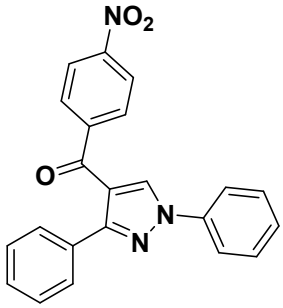
Yield:70% (white solid); mp 131–133℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (s, 1H), 8.07 – 7.91 (m, 4H), 7.71 – 7.63 (m, 2H), 7.56 (t, J = 7.8 Hz, 2H), 7.45 – 7.28 (m, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 188.23, 153.22, 139.31, 135.46, 133.92, 132.78, 132.72, 132.51, 130.03, 128.99, 128.93, 128.56, 127.78, 120.65, 119.69, 116.10, 115.95. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{15}FN_2O$ $[M + H]^+$: 343.1266, found $[M + H]^+$:343.4224.



3aq, 66%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(p-tolyl)methanone (3aq)

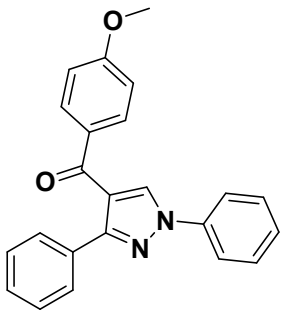
Yield:66% (white solid); mp 117–119℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.00 (d, J = 7.8 Hz, 2H), 7.81 (d, J = 8.1 Hz, 2H), 7.68 (dd, J = 7.3, 2.2 Hz, 2H), 7.55 (t, J = 7.9 Hz, 2H), 7.40 (dd, J = 9.4, 4.4 Hz, 4H), 7.33 (d, J = 8.0 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 189.33, 153.03, 143.77, 139.36, 136.19, 133.50, 132.61, 130.05, 130.02, 129.63, 128.87, 128.58, 127.68, 120.91, 119.63, 21.60. HRMS (ESI-Q-TOF, m/z) calcd for $C_{23}H_{18}N_2O$ $[M + H]^+$: 339.1429, found $[M + H]^+$:339.4221.



3ar, 82%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(4-nitrophenyl)methanone (3ar)

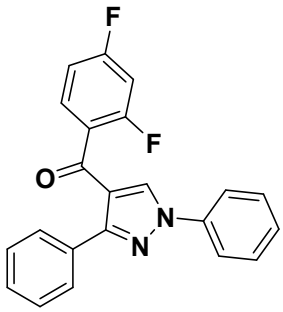
Yield:82% (yellow solid); mp 178–181℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (s, 1H), 8.32 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 8.8 Hz,2H), 8.00 (d, J = 7.7 Hz, 2H), 7.73 (dd, J = 6.7, 3.0 Hz, 2H), 7.56 (t, J = 7.9 Hz, 2H), 7.42 (dd, J = 8.7, 4.8 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.09, 153.36, 149.90, 144.28, 139.14, 135.17, 132.30, 130.98, 130.06, 129.27, 129.15, 128.53, 128.01, 124.08, 120.32, 119.79. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{15}N_3O_3$ $[M + H]^+$: 370.1123, found $[M + H]^+$:370.3820.



3as, 66%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(4-methoxyphenyl)methanone (3as)

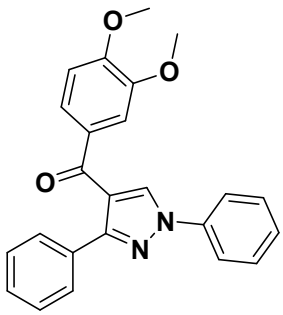
Yield:66% (white solid); mp 112–114℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.00 (d, J = 7.7 Hz, 2H), 7.90 (d, J = 8.8 Hz, 2H), 7.70 – 7.64 (m, 2H), 7.55 (t, J = 7.9 Hz, 2H), 7.43 – 7.35 (m, 4H), 7.05 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.40, 163.63, 152.80, 139.39, 133.07, 132.62, 132.34, 131.34, 130.04, 128.84, 128.77, 128.64, 127.63, 120.99, 119.55, 114.37, 56.04. HRMS (ESI-Q-TOF, m/z) calcd for $C_{23}H_{18}N_2O_2$ $[M + H]^+$: 355.1388, found $[M + H]^+$:355.4282.



3at, 64%

(2,4-difluorophenyl)(1,3-diphenyl-1*H*-pyrazol-4-yl)methanone (3at)

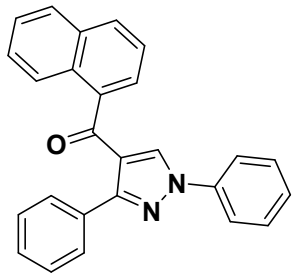
Yield:64% (white solid); mp 102–104℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 1H), 7.99 (d, J = 8.1 Hz, 2H), 7.80 – 7.63 (m, 3H), 7.55 (t, J = 7.6 Hz, 2H), 7.40 (dd, J = 8.1, 7.0 Hz, 4H), 7.29 (t, J = 10.0 Hz, 1H), 7.17 (t, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.01, 153.35, 139.07, 135.09, 133.02, 132.92, 132.19, 130.06, 129.30, 129.10, 128.40, 128.00, 125.35, 122.18, 119.68, 112.47, 112.25, 105.21. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{14}F_2N_2O$ $[M + H]^+$: 361.1074, found $[M + H]^+$:361.3648.



3au, 62%

(3,4-dimethoxyphenyl)(1,3-diphenyl-1*H*-pyrazol-4-yl)methanone (3au)

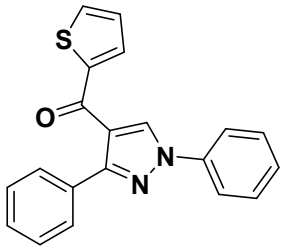
Yield:62% (white solid); mp 224–226℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.01 (d, J = 7.9 Hz, 2H), 7.70 – 7.61 (m, 2H), 7.56 (t, J = 6.7 Hz, 3H), 7.48 – 7.30 (m, 5H), 7.06 (d, J = 8.4 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.38, 153.58, 152.75, 149.02, 139.40, 133.06, 132.66, 131.21, 130.06, 128.84, 128.77, 128.64, 127.62, 125.04, 121.05, 119.52, 112.09, 111.35, 56.26, 55.95. HRMS (ESI-Q-TOF, m/z) calcd for $C_{24}H_{20}N_2O_3$ $[M + H]^+$: 385.1474, found $[M + H]^+$:385.4353.



3av, 71%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(naphthalen-1-yl)methanone (3av)

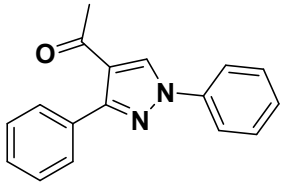
Yield:71% (white solid); mp 119–121℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 8.26 (dd, J = 8.2, 4.9 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.05 – 8.00 (m, 1H), 7.98 – 7.93 (m, 2H), 7.84 (dd, J = 7.1, 0.9 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.63 – 7.57 (m, 2H), 7.56 – 7.47 (m, 3H), 7.41 – 7.32 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 190.8, 153.68, 139.1 , 137.29, 135.22, 133.84, 132.58, 131.97, 130.55, 130.01, 129.27, 128.98, 128.93, 128.88, 128.34, 127.87, 127.80, 126.86, 125.57, 125.29, 122.99, 119.70. HRMS (ESI-Q-TOF, m/z) calcd for $C_{26}H_{18}N_2O$ $[M + H]^+$: 375.1439, found $[M + H]^+$:375.4430.



3aw, 81%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(thiophen-2-yl)methanone (3aw)

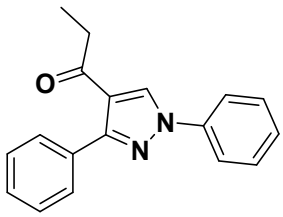
Yield:81% (brown solid); mp 187–189℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (s, 1H), 8.09 (dd, J = 4.9, 1.0 Hz, 1H), 8.03 (d, J = 7.7 Hz, 2H), 7.97 (dd, J = 3.8, 1.0 Hz, 1H), 7.72 (dd, J = 7.7, 1.8 Hz, 2H), 7.57 (t, J = 8.0 Hz, 2H), 7.47 – 7.38 (m, 4H), 7.28 (dd, J = 4.9, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.19, 152.72, 145.02, 139.35, 135.95, 135.65, 133.24, 132.48, 130.04, 129.34, 128.99, 128.86, 128.67, 127.78, 120.31, 119.75. HRMS (ESI-Q-TOF, m/z) calcd for $C_{20}H_{14}N_2OS$ $[M + H]^+$: 331.0827, found $[M + H]^+$:331.4050.



3ax, 43%

1-(1,3-diphenyl-1*H*-pyrazol-4-yl)ethan-1-one (3ax)

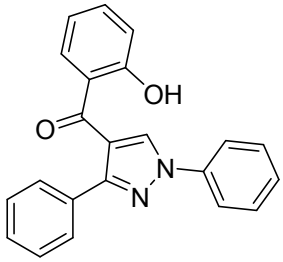
Yield:43% (white solid); mp 100–103℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.35 (s, 1H), 8.05 – 7.95 (m, 2H), 7.82 – 7.73 (m, 2H), 7.58 (t, J = 8.0 Hz, 2H), 7.49 – 7.36 (m, 4H), 2.51 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 192.31, 152.53, 139.25, 134.84, 132.82, 130.09, 129.57, 128.98, 128.23, 127.79, 122.18, 119.47, 29.74. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{14}N_2O$ $[M + H]^+$: 263.1106, found $[M + H]^+$:263.3120..



3ay, 41%

1-(1,3-diphenyl-1*H*-pyrazol-4-yl)propan-1-one (3ay)

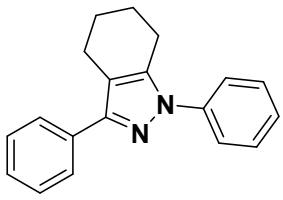
Yield:41% (white solid); mp 98–100℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (s, 1H), 8.03 – 7.96 (m, 2H), 7.81 – 7.74 (m, 2H), 7.58 (dd, J = 10.8, 5.1 Hz, 2H), 7.48 – 7.37 (m, 4H), 2.94 (q, J = 7.3 Hz, 2H), 1.08 (t, J = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 195.41, 152.59, 139.30, 134.03, 132.93, 130.07, 129.54, 128.93, 128.22, 127.73, 121.70, 119.46, 34.30, 8.72. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{16}N_2O$ $[M + H]^+$: 277.1263, found $[M + H]^+$:277.3390.



3az, 70-80%

(1,3-diphenyl-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (3az)

Yield:70-80% (white solid); mp 169–171℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 8.97 (s, 1H), 8.00 (d, J = 7.8 Hz, 2H), 7.69 (dd, J = 16.0, 6.6 Hz, 3H), 7.53 (dt, J = 15.5, 7.5 Hz, 3H), 7.45 – 7.33 (m, 4H), 7.04 – 6.84 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 188.23, 153.22, 139.31, 133.92, 132.78, 132.72, 132.51, 130.03, 128.99, 128.93, 128.56, 127.78, 120.65, 119.69, 116.10, 115.95. HRMS (ESI-Q-TOF, m/z) calcd for $C_{22}H_{16}N_2O_2$ $[M + H]^+$: 341.1225, found $[M + H]^+$:341.3820.

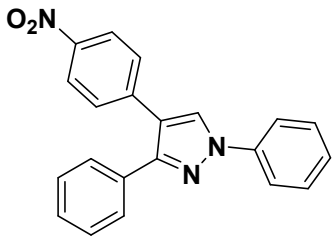


3ba, 68%

1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-indazole (3ba)

Yield:68% (light yellow solid); mp 131–134℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 – 7.75 (m, 2H), 7.61 (dd, J = 8.5, 1.0 Hz, 2H), 7.52 (dd, J = 10.6, 5.2 Hz, 2H), 7.45 (dd, J = 10.4, 4.7 Hz, 2H), 7.41 – 7.31 (m, 2H), 2.75 (d, J = 12.6 Hz, 4H), 1.77 (s, 4H).^{13}C NMR (151 MHz, DMSO-d_6) δ 148.44, 140.09, 134.28, 129.63, 128.99, 127.81, 127.16, 126.89, 123.29, 115.56, 23.71, 23.02, 22.71, 22.50.

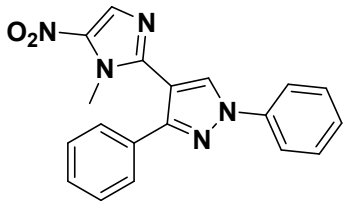
HRMS (ESI-Q-TOF, m/z) calcd for $C_{19}H_{18}N_2$ [M + H]$^+$: 275.1671, found [M + H]$^+$:275.3670.



3bb, 72%

4-(4-nitrophenyl)-1,3-diphenyl-1*H*-pyrazole (3bb)

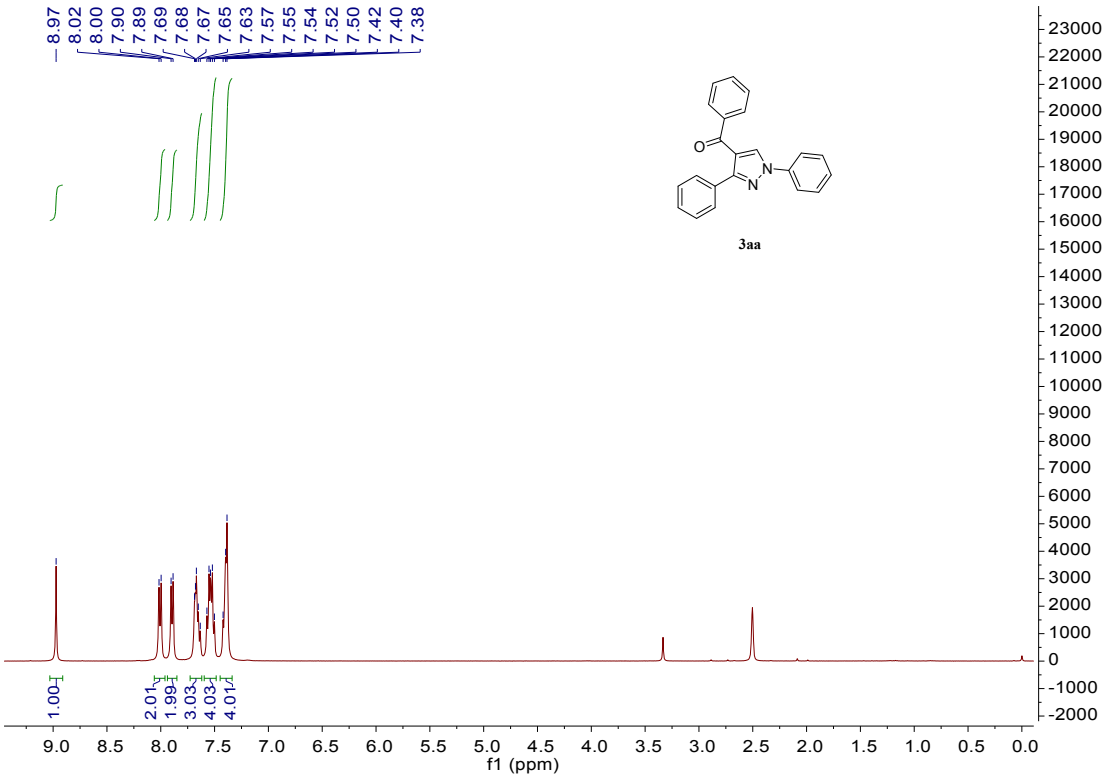
Yield:72% (red solid); mp 163–165℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (s, 1H), 8.22 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 7.7 Hz, 2H), 7.65 – 7.48 (m, 6H), 7.48 – 7.41 (m, 3H), 7.38 (t, J = 7.4 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.46, 146.42, 140.07, 139.60, 132.91, 130.06, 129.59, 129.23, 129.10, 128.92, 128.81, 127.26, 124.29, 120.55, 119.00. HRMS (ESI-Q-TOF, m/z) calcd for $C_{21}H_{15}N_3O_2$ [M + H]$^+$: 342.2166, found [M + H]$^+$:342.3728.



3bc, 64%

4-(1-methyl-5-nitro-1*H*-imidazol-2-yl)-1,3-diphenyl-1*H*-pyrazole (3bc)

Yield:64% (yellow solid); mp 177–179℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 1H), 8.25 (s, 1H), 8.00 (d, J = 7.9 Hz, 2H), 7.64 – 7.52 (m, 4H), 7.46 – 7.36 (m, 4H), 3.72 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 151.58, 145.83, 140.04, 139.43, 133.33, 132.21, 132.05, 130.14, 129.11, 127.72, 119.35, 109.72, 35.05. HRMS (ESI-Q-TOF, m/z) calcd for $C_{19}H_{15}N_5O_2$ [M + H]$^+$: 346.2131, found [M + H]$^+$:346.4620.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7.52
7.50
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N
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1.99
3.03
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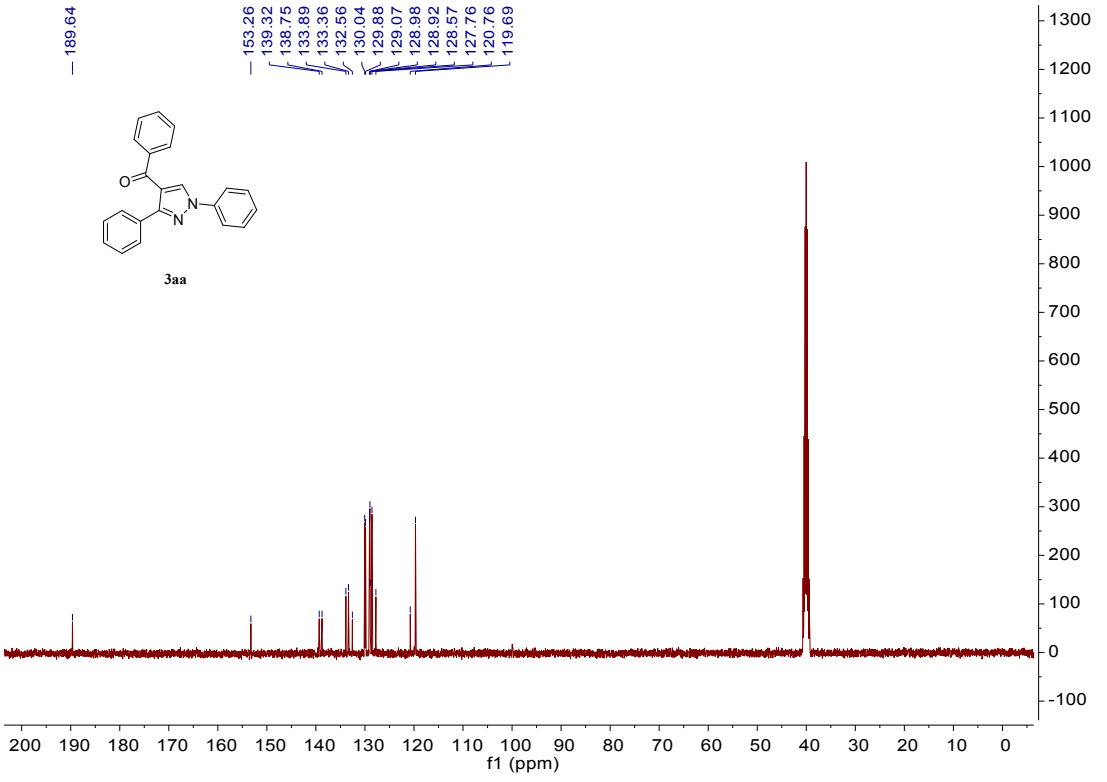
4.01
f1 (ppm)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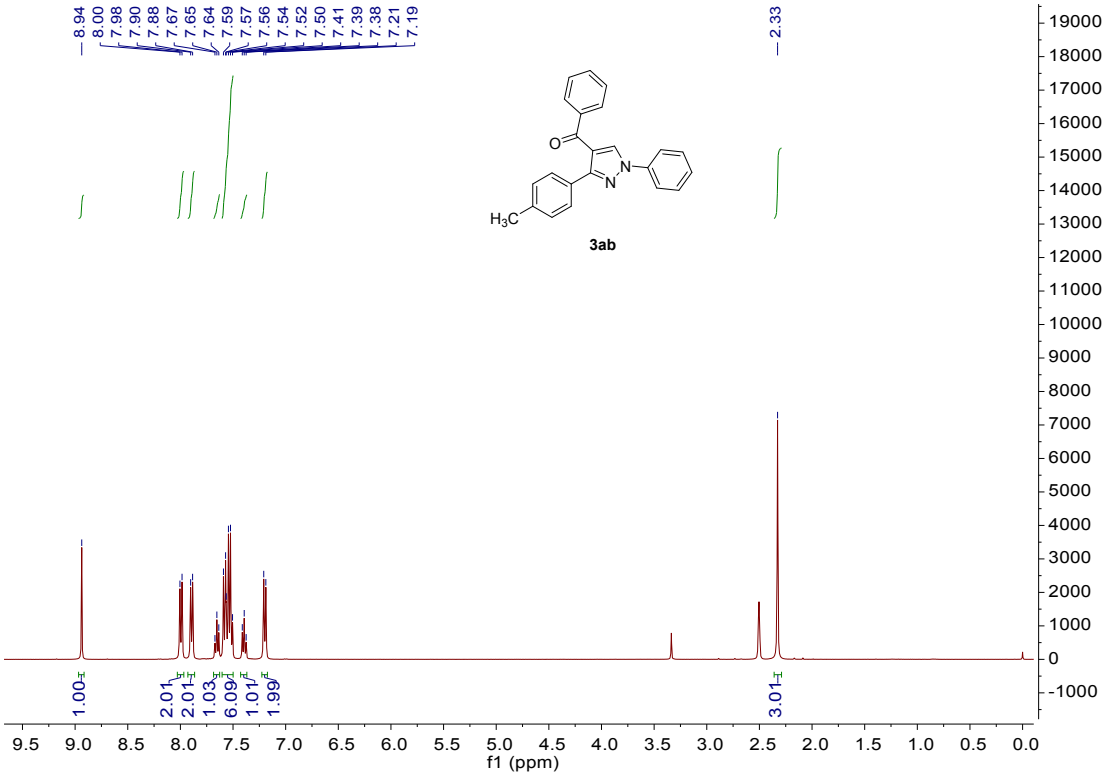
f1 (ppm)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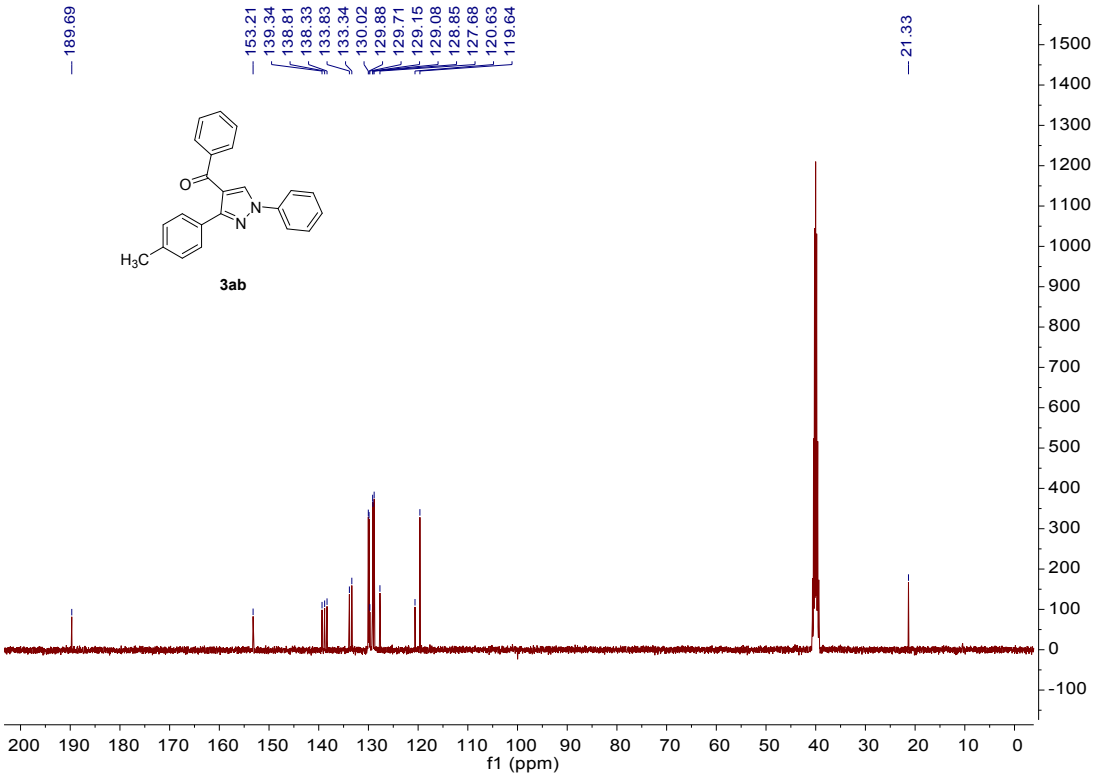
3.01
f1 (ppm)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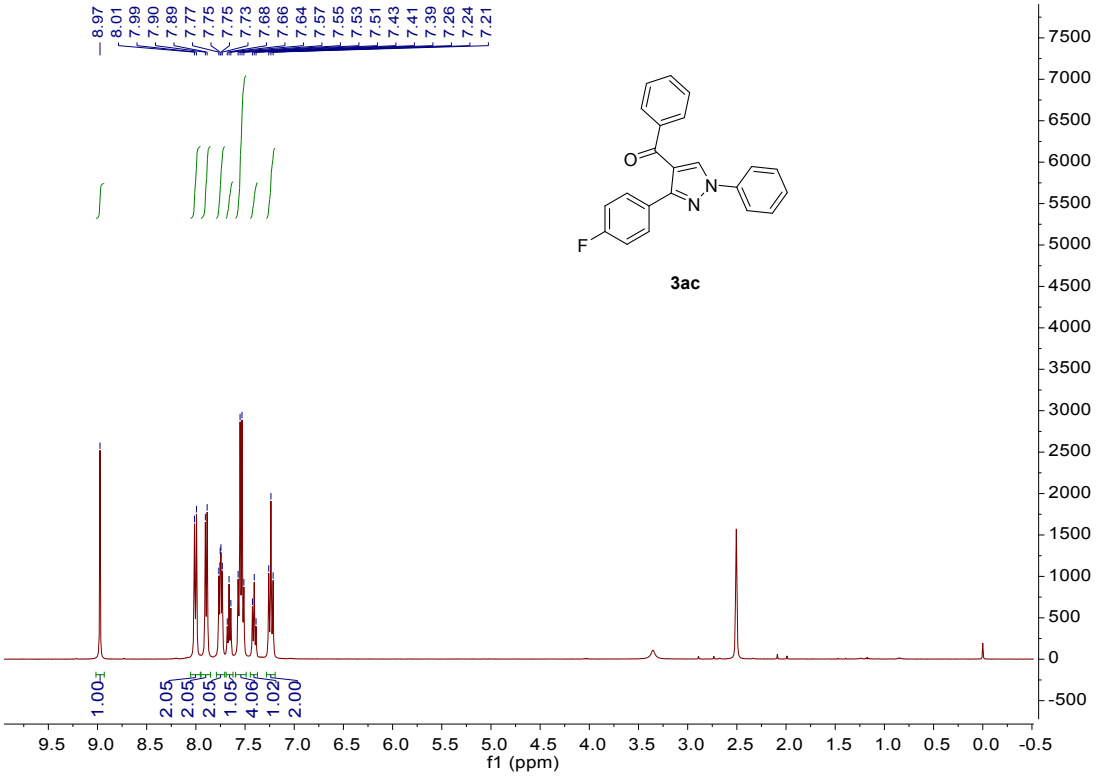
H3C
3ab
f1 (ppm)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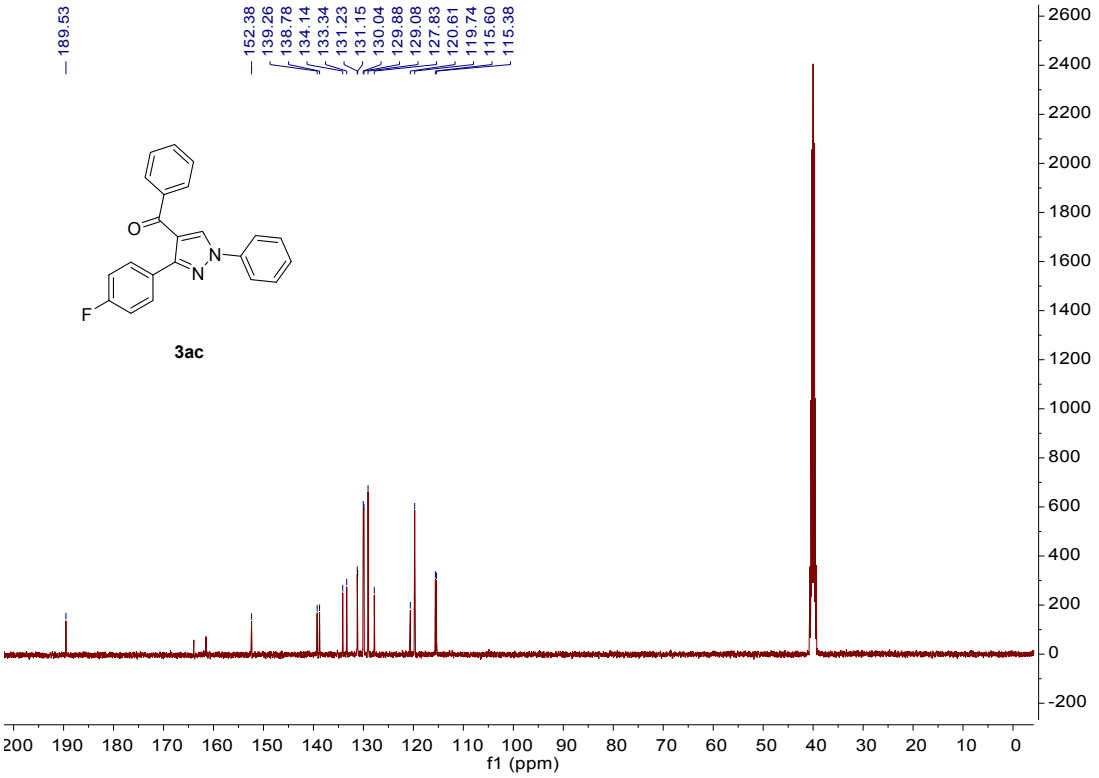
2.00
f1 (ppm)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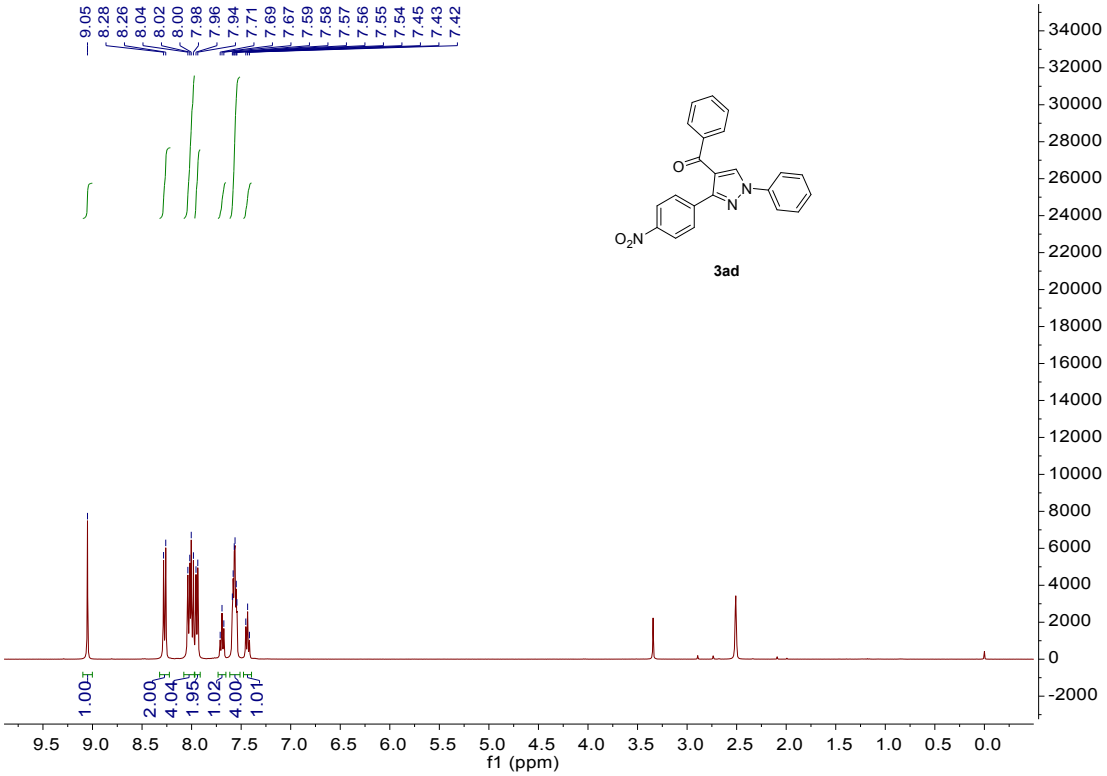
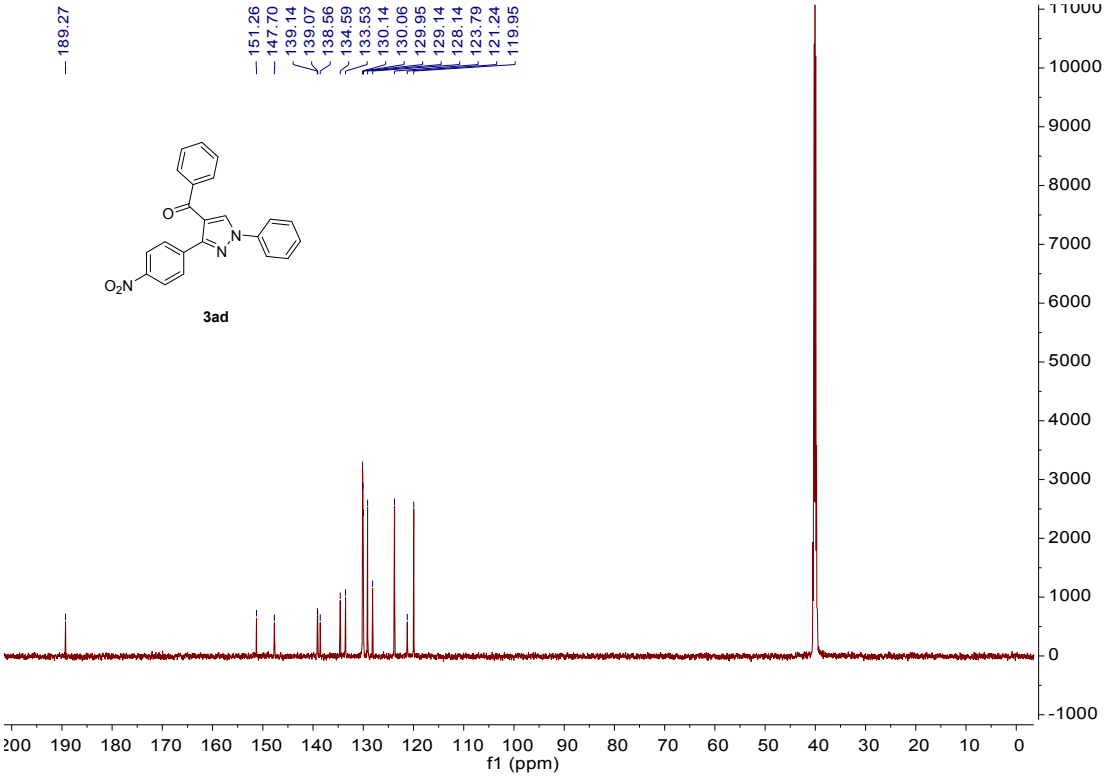
N
N
F
3ac
f1 (ppm)


9.05
8.28
8.26
8.04
8.02
8.00
7.98
7.96
7.94
7.71
7.69
7.67
7.59
7.58
7.57
7.56
7.55
7.54
7.45
7.43
7.42
O
N
N
O2N
3ad
1.00
2.00
4.04
1.95
1.02
4.00
1.01
f1 (ppm)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138.56
134.59
133.53
130.14
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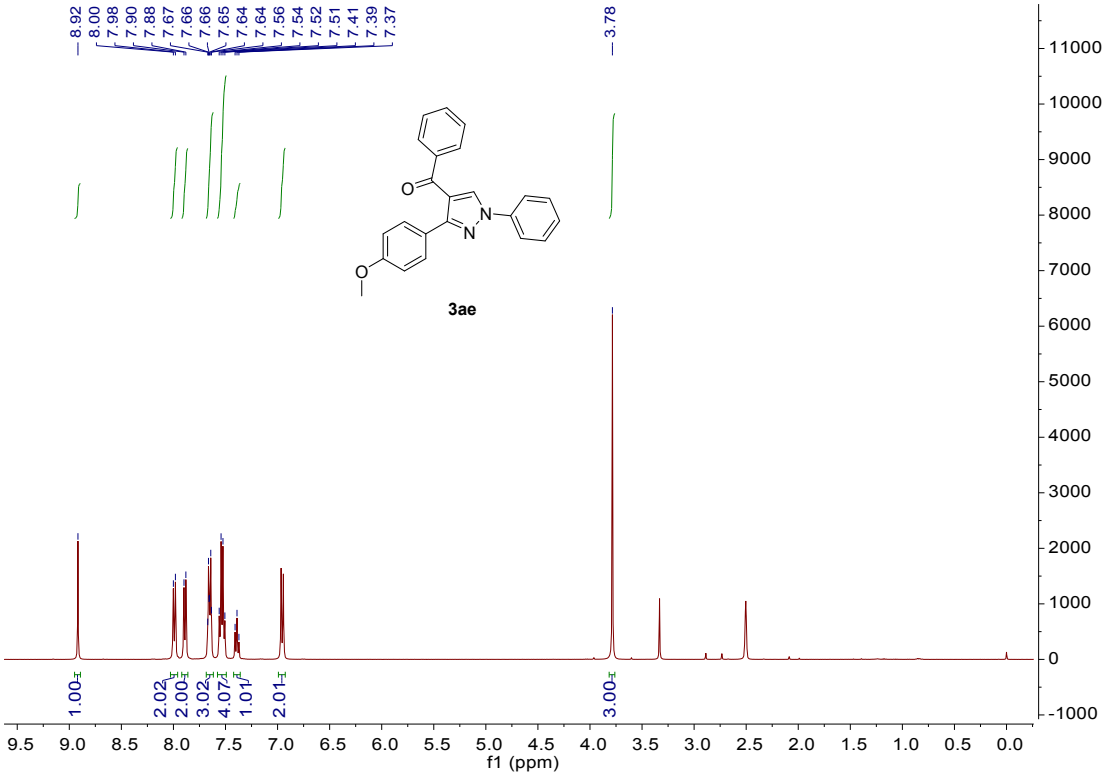
129.14
128.14
123.79
121.24
119.95
O
N
N
O2N
3ad
f1 (ppm)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7.66
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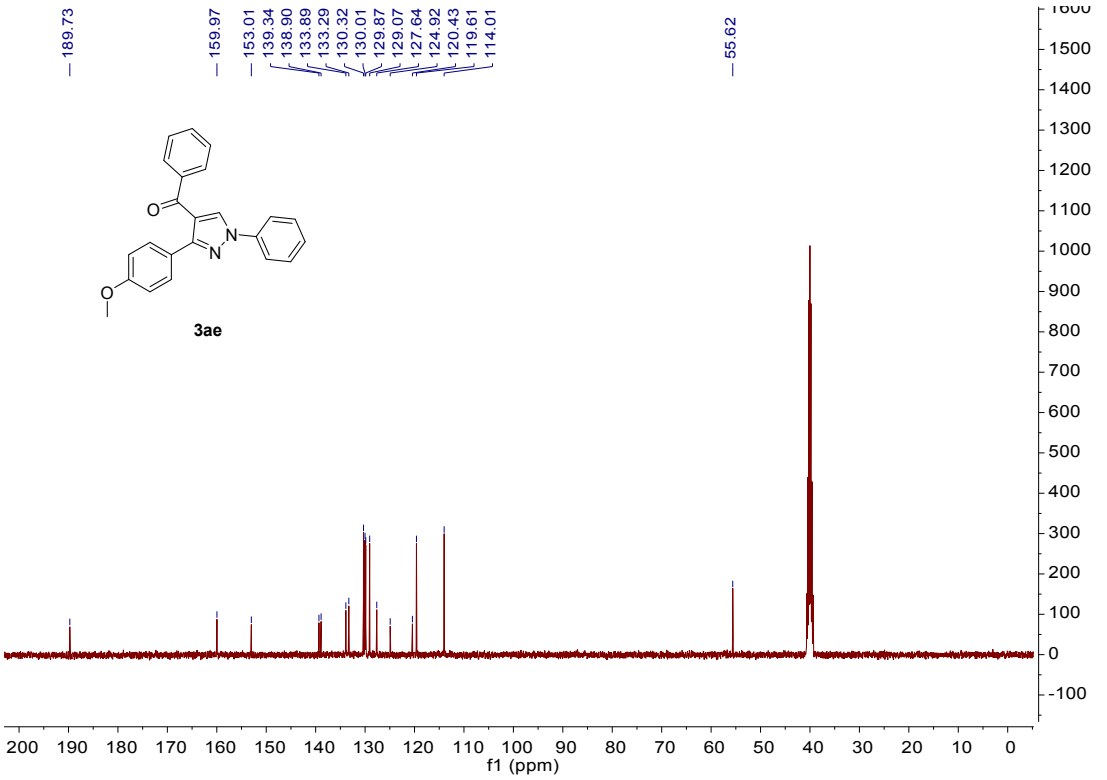
7.64
7.64
7.56
7.54
7.52
7.51
7.41
7.39
7.37
3.78
O
N
N
O
3ae
1.00
2.02
2.00
3.02
4.07
1.01
2.01
3.00
f1 (ppm)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133.89
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130.32
130.01
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129.07
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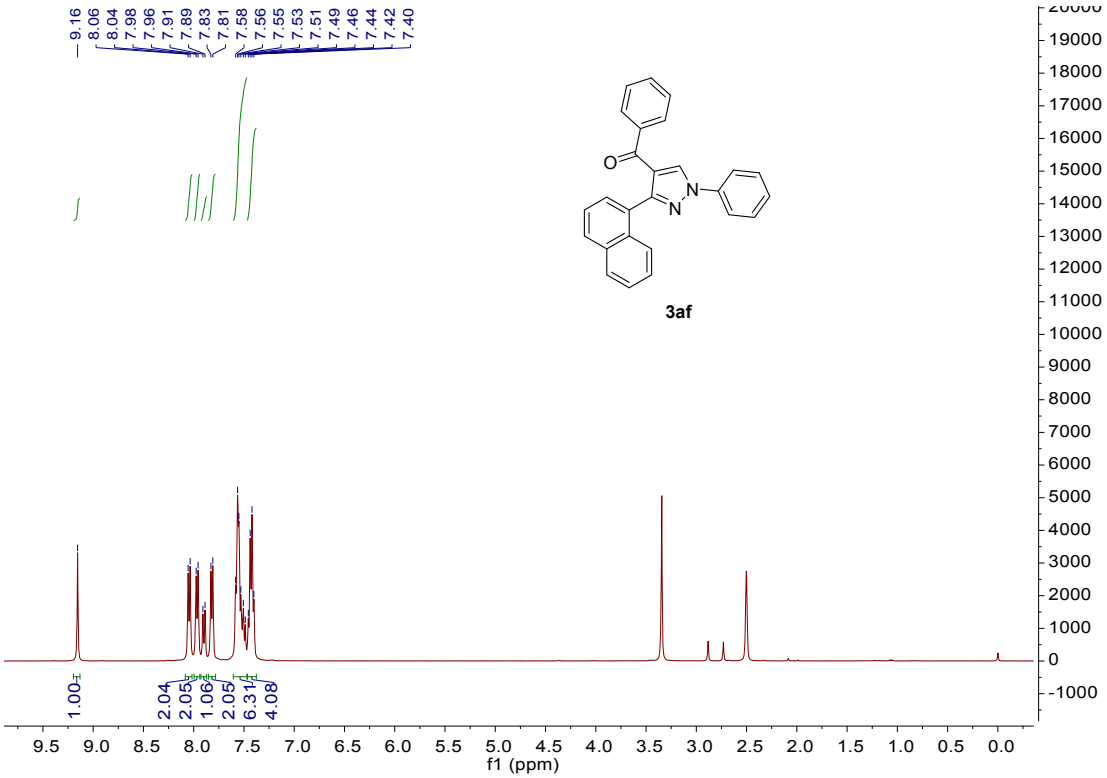
124.92
120.43
119.61
114.01
55.62
O
N
N
O
3ae
f1 (ppm)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7.91
7.89
7.83
7.81
7.58
7.56
7.55
7.53
7.51
7.49
7.46
7.44
7.42
7.40
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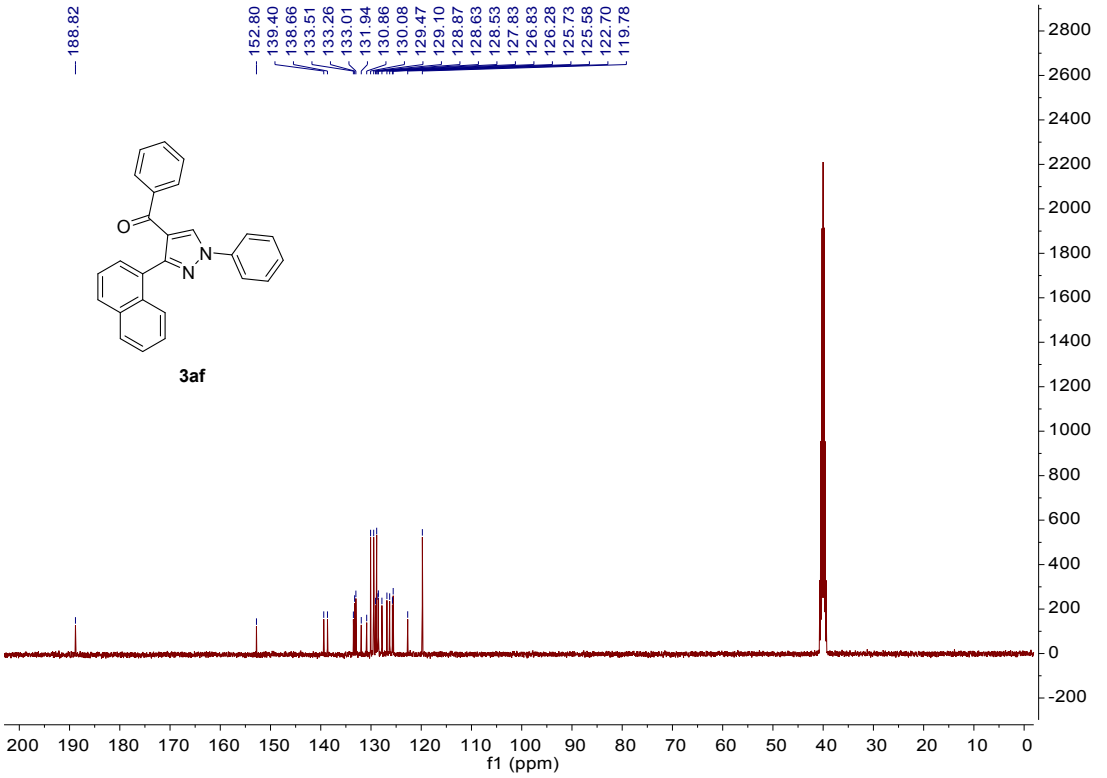
N
3af
1.00
2.04
2.05
1.06
2.05
6.31
4.08
f1 (ppm)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130.08
129.47
129.10
128.87
128.63
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126.83
126.28
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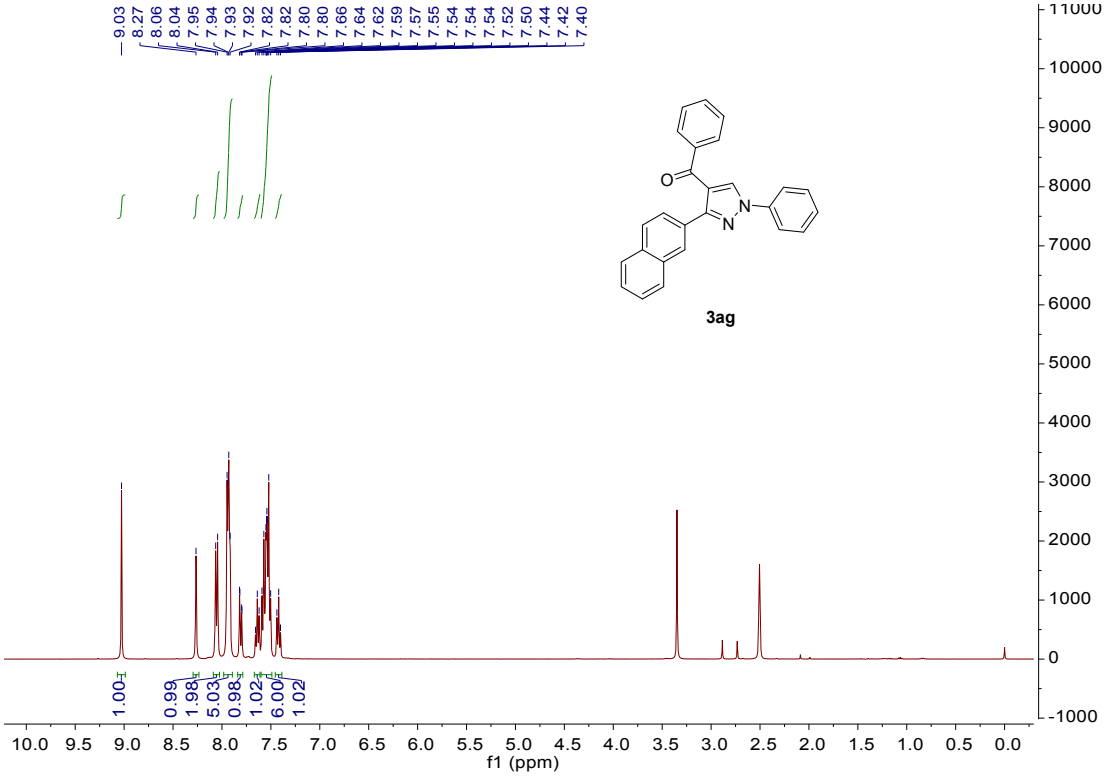
125.58
122.70
119.78
O
N
N
3af
f1 (ppm)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7.94
7.93
7.92
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7.82
7.80
7.80
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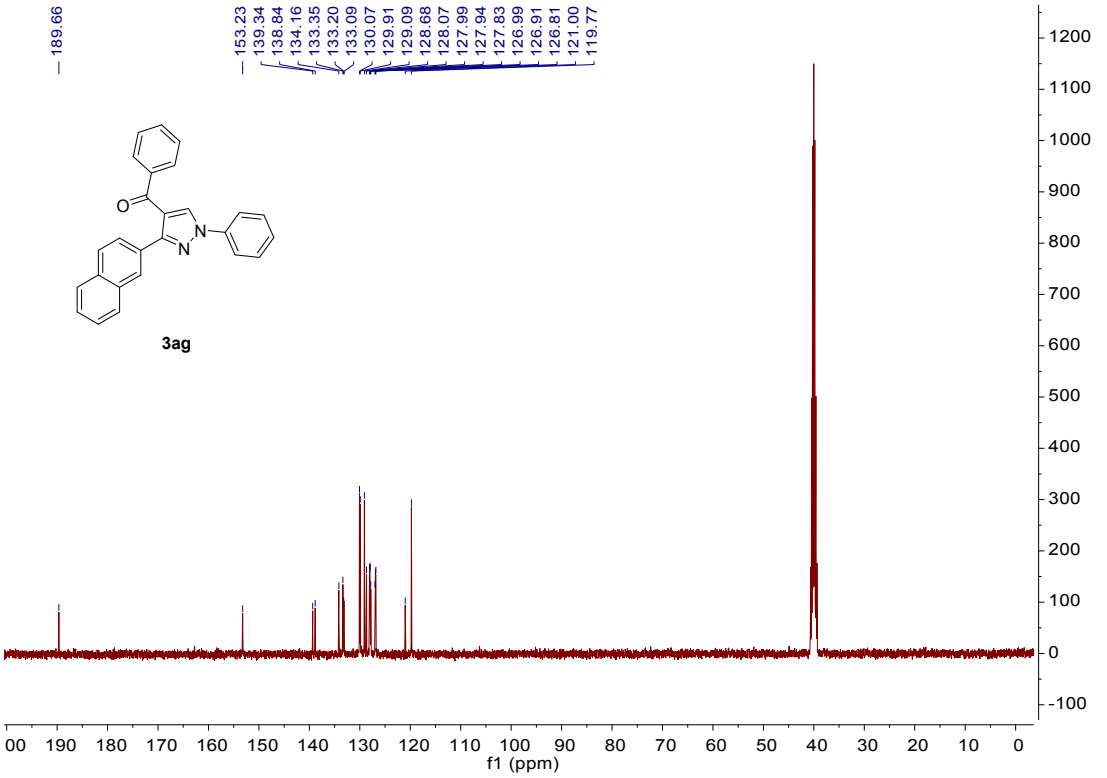
7.64
7.62
7.59
7.57
7.55
7.54
7.54
7.54
7.52
7.50
7.44
7.42
7.40
3ag
1.00
0.99
1.98
5.03
0.98
1.02
6.00
1.02
f1 (ppm)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133.35
133.20
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130.07
129.91
129.09
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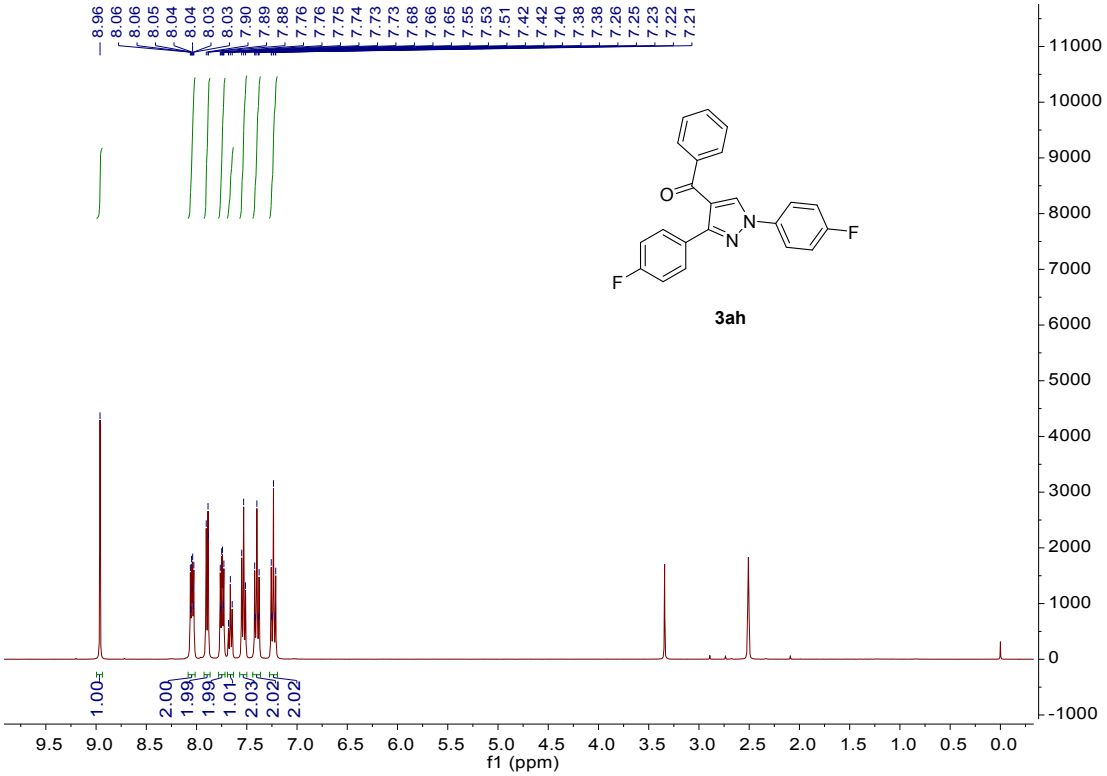
126.81
121.00
119.77
3ag
f1 (ppm)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8.06
8.06
8.05
8.04
8.04
8.03
8.03
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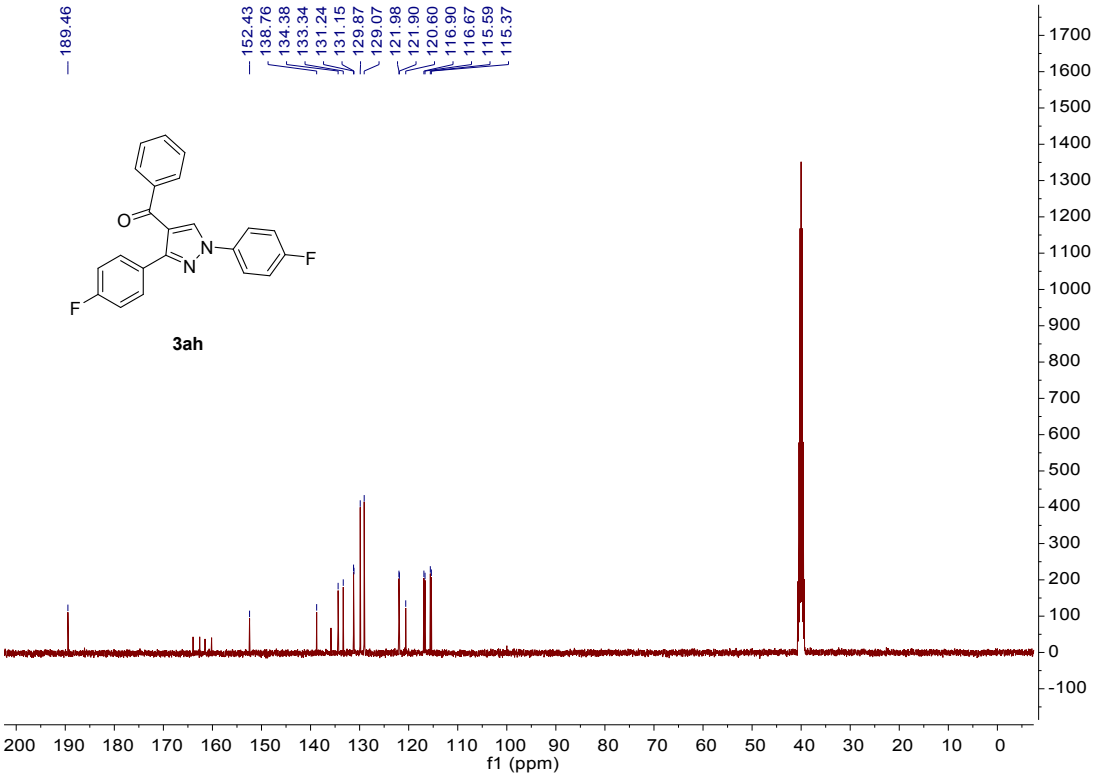
7.89
7.88
7.76
7.76
7.75
7.74
7.73
7.73
7.68
7.66
7.65
7.55
7.53
7.51
7.42
7.42
7.40
7.38
7.38
7.26
7.25
7.23
7.22
7.21
O
N
N
F
F
3ah
1.00
2.00
1.99
1.99
1.01
2.03
2.02
2.02
f1 (ppm)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131.24
131.15
129.87
129.07
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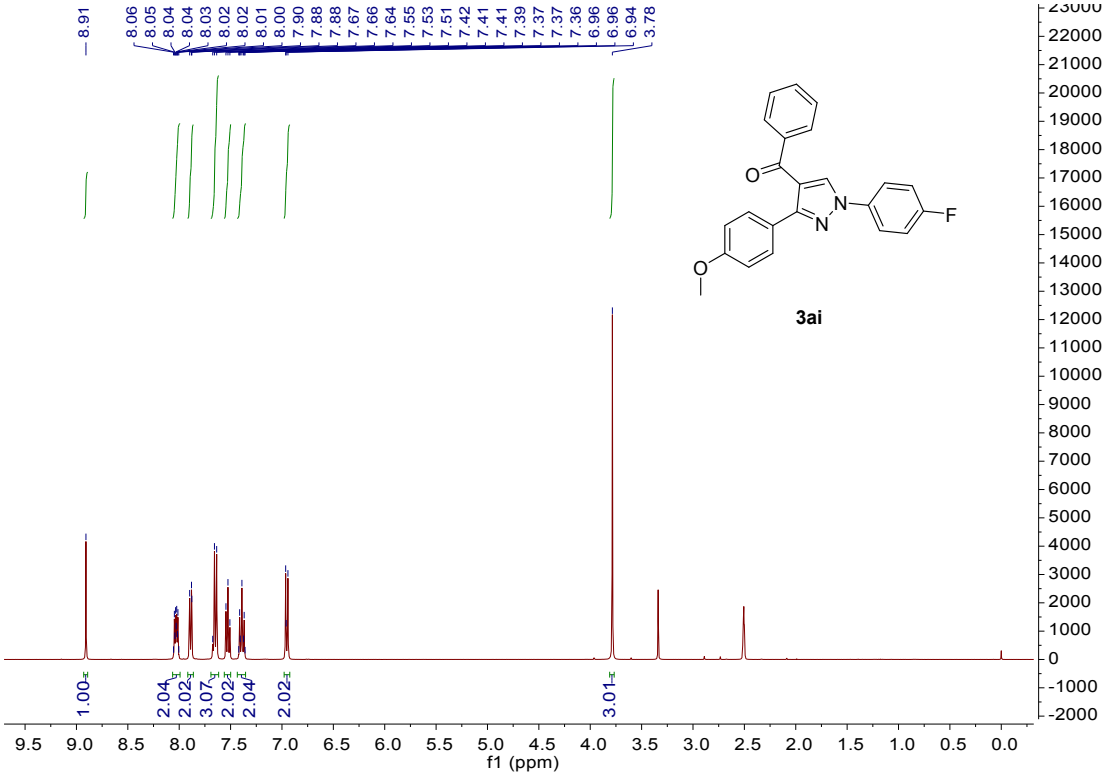
116.90
116.67
115.59
115.37
O
N
N
F
F
3ah
f1 (ppm)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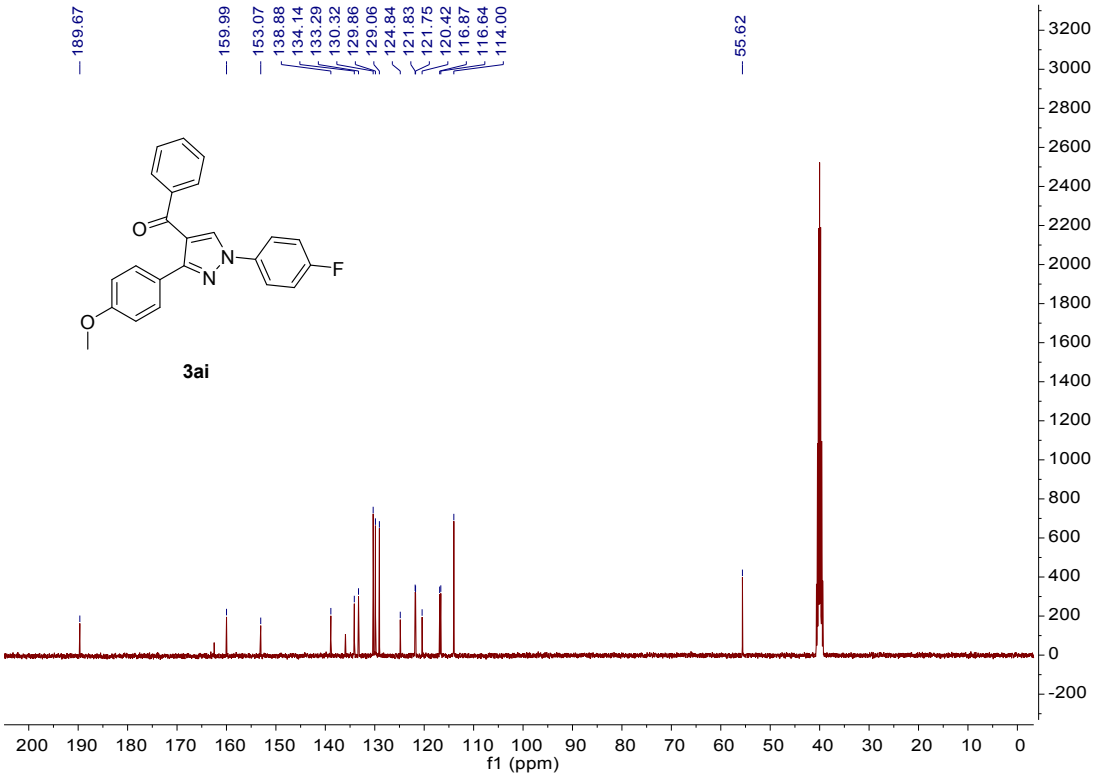
8.04
8.03
8.02
8.02
8.01
8.00
7.90
7.88
7.88
7.67
7.66
7.64
7.55
7.53
7.51
7.42
7.41
7.41
7.39
7.37
7.37
7.36
6.96
6.96
6.94
3.78
1.00
2.04
2.02
3.07
2.02
2.04
2.02
3.01
f1 (ppm)
3ai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133.29
130.32
129.86
129.06
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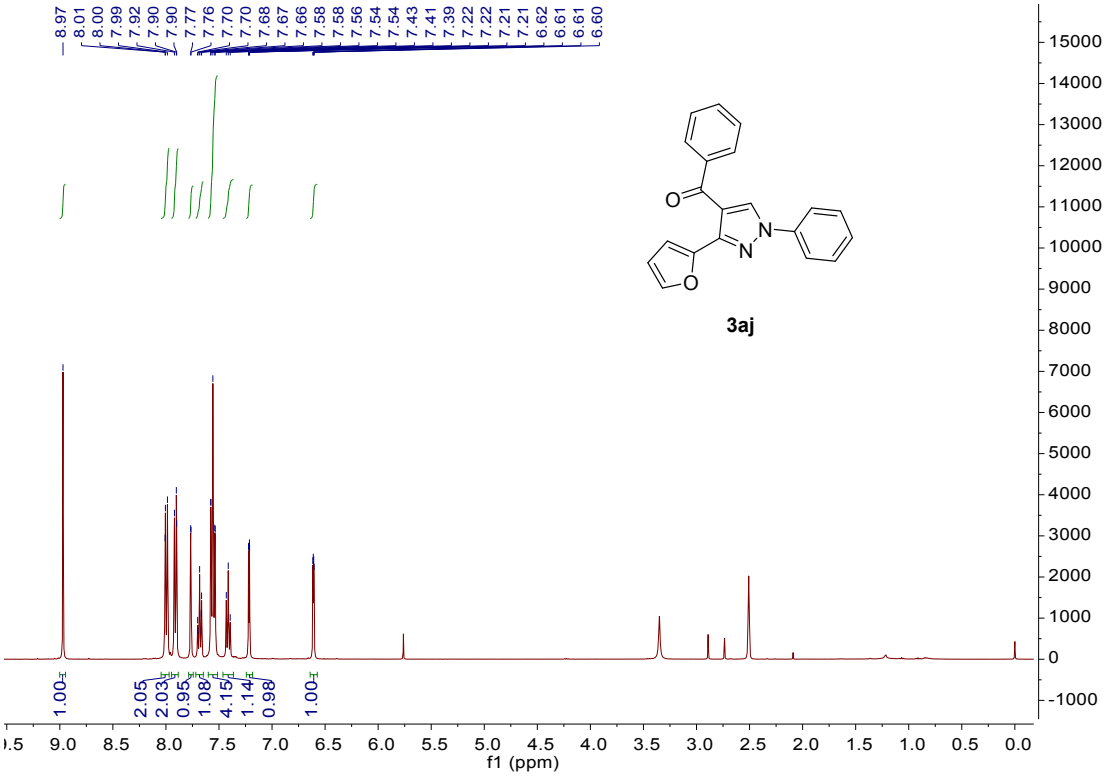
121.83
121.75
120.42
116.87
116.64
114.00
55.62
f1 (ppm)
3ai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7.99
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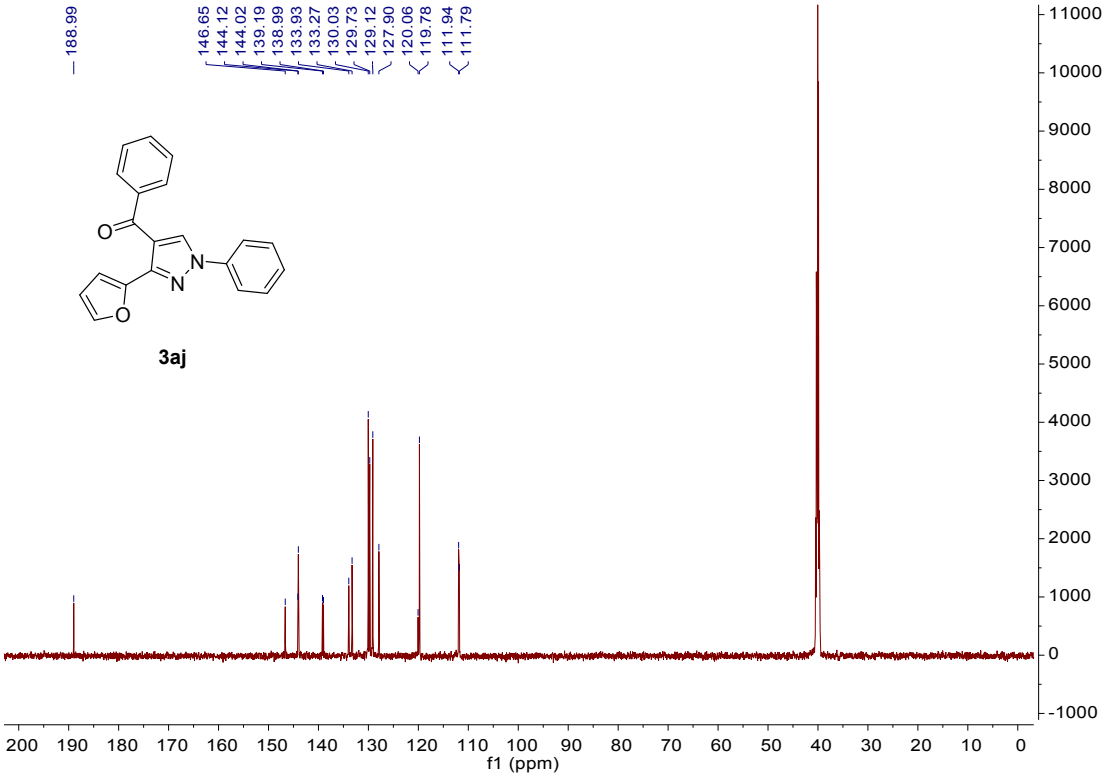
7.90
7.90
7.77
7.76
7.70
7.70
7.68
7.67
7.66
7.58
7.58
7.56
7.54
7.54
7.43
7.41
7.39
7.22
7.22
7.21
7.21
6.62
6.61
6.61
6.60
O
N
N
O
3aj
1.00
2.05
2.03
0.95
1.08
4.15
1.14
0.98
1.00
f1 (ppm)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144.02
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138.99
133.93
133.27
130.03
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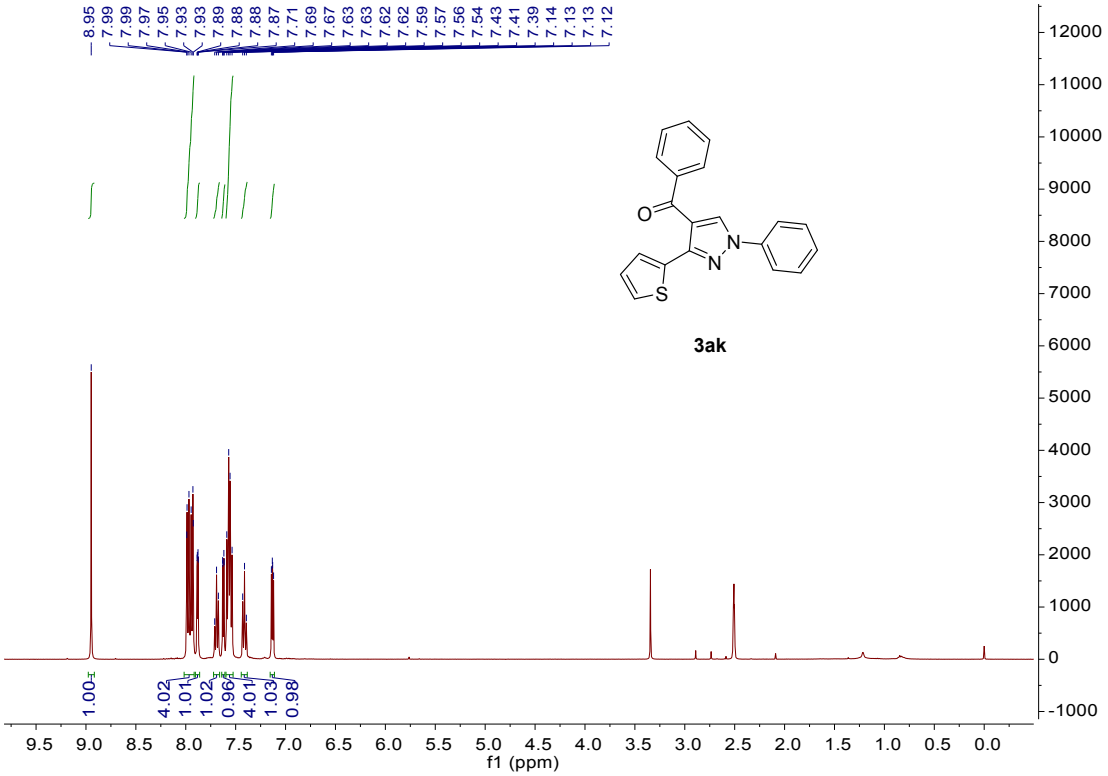
127.90
120.06
119.78
111.94
111.79
O
N
N
O
3aj
f1 (ppm)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7.99
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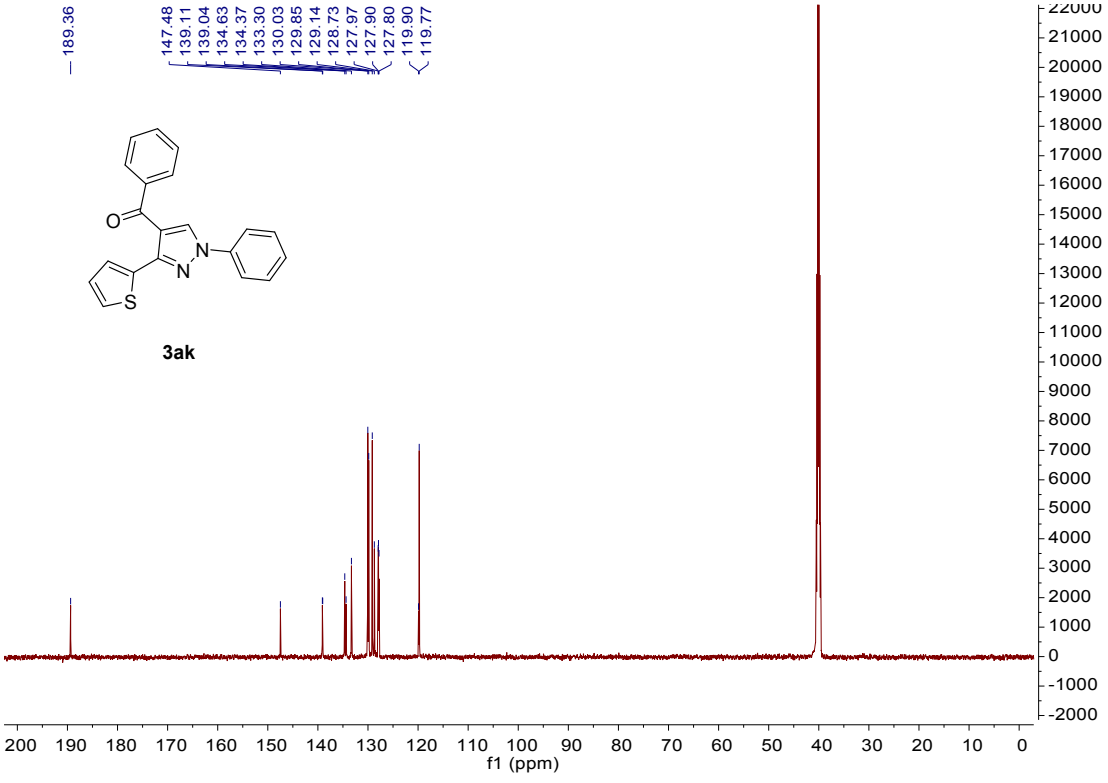
7.93
7.89
7.88
7.88
7.87
7.71
7.69
7.67
7.63
7.63
7.62
7.62
7.59
7.57
7.56
7.54
7.43
7.41
7.39
7.14
7.13
7.13
7.12
O
N
N
S
3ak
1.00
4.02
1.01
1.02
0.96
4.01
1.03
0.98
f1 (ppm)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130.03
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127.90
127.80
119.90
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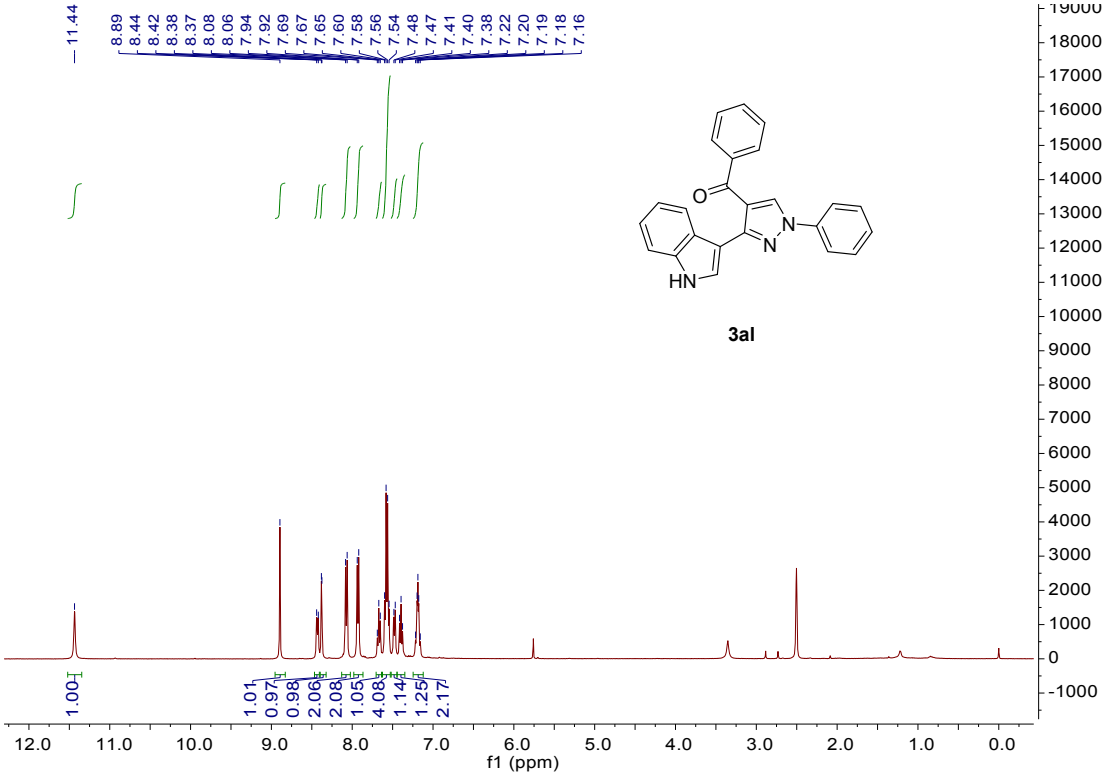
O
N
N
S
3ak
f1 (ppm)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8.37
8.08
8.06
7.94
7.92
7.69
7.67
7.65
7.60
7.58
7.56
7.54
7.48
7.47
7.41
7.40
7.38
7.22
7.20
7.19
7.18
7.16
O
N
N
HN
1.00
1.01
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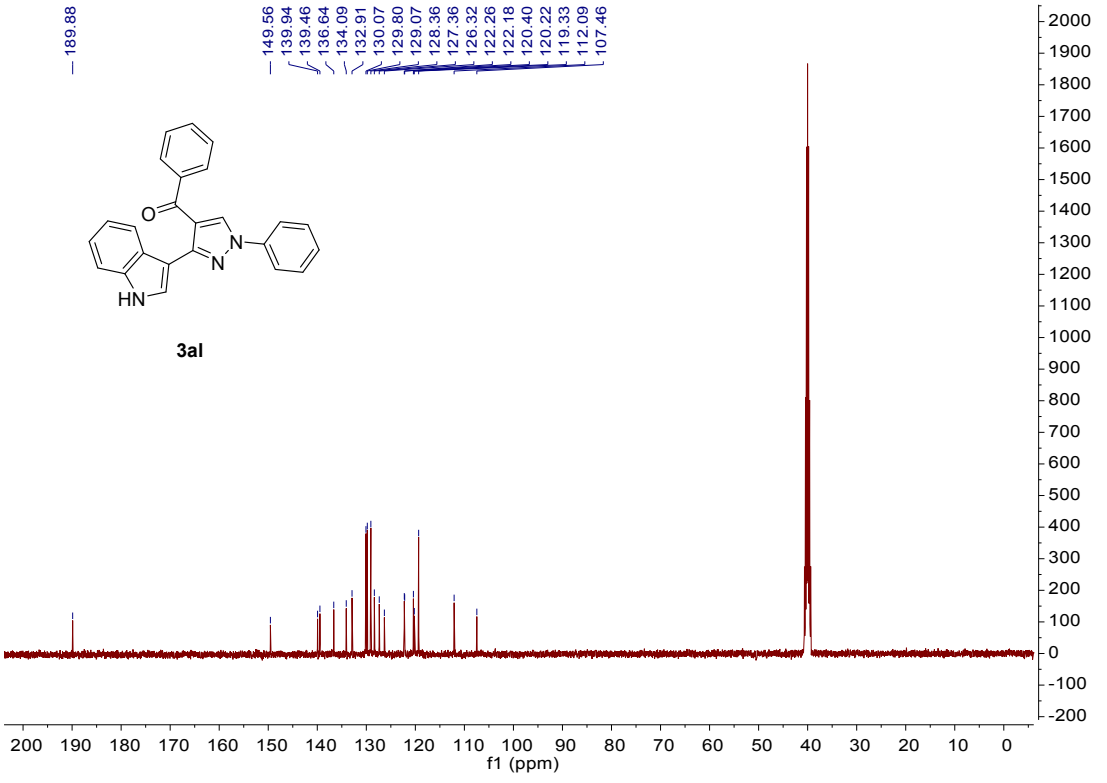
2.06
2.08
1.05
4.08
1.14
1.25
2.17
f1 (ppm)

3al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132.91
130.07
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129.07
128.36
127.36
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120.40
120.22
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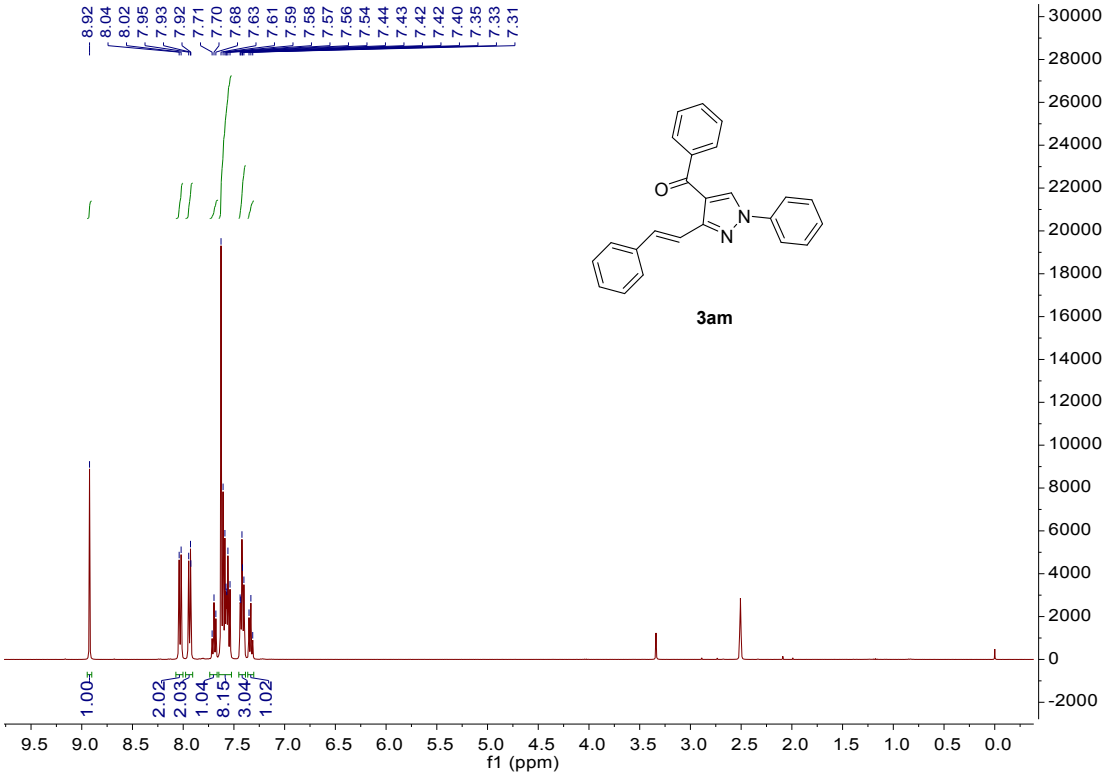
112.09
107.46
O
N
N
HN
f1 (ppm)

3al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7.63
7.61
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7.58
7.57
7.56
7.54
7.44
7.43
7.42
7.42
7.40
7.35
7.33
7.31
O
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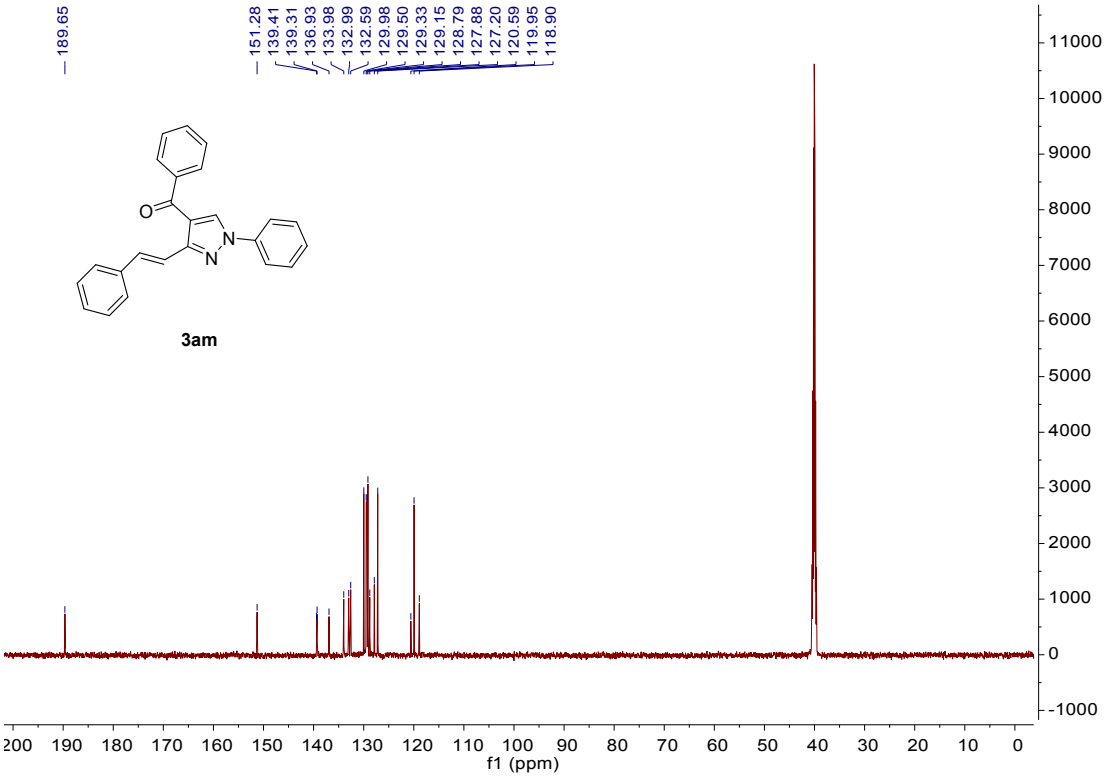
N
3am
1.00
2.02
2.03
1.04
8.15
3.04
1.02
f1 (ppm)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129.50
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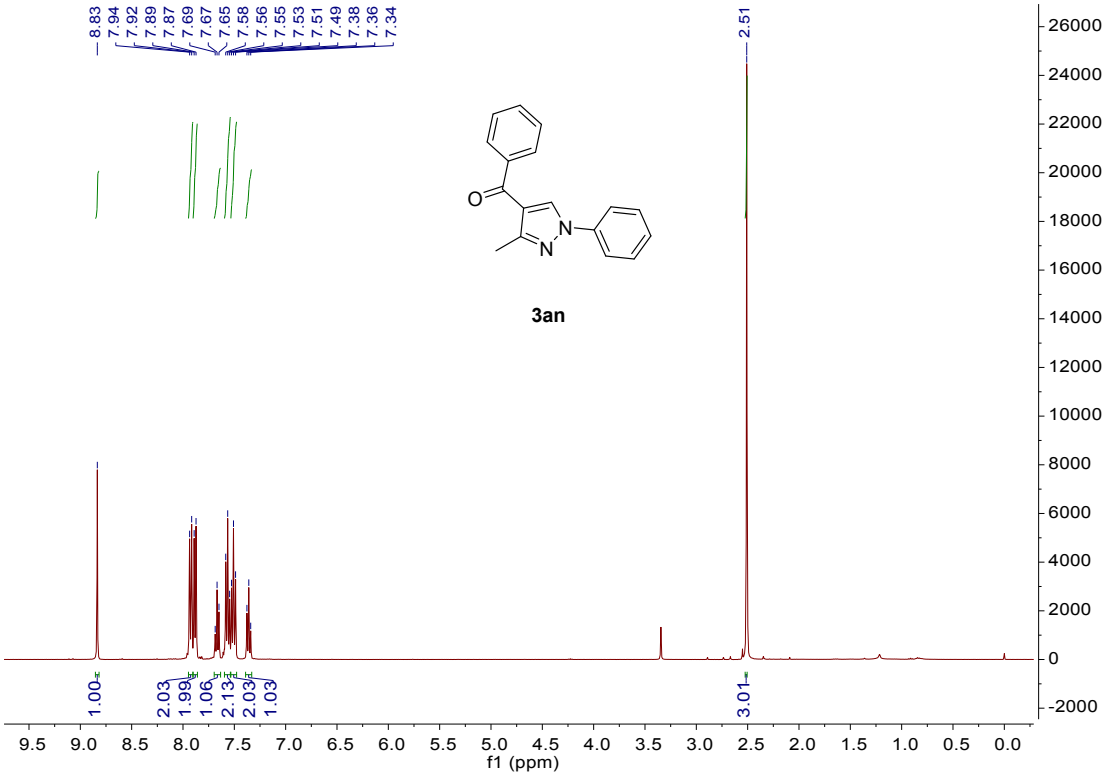
127.88
127.20
120.59
119.95
118.90
O
N
N
3am
f1 (ppm)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7.53
7.51
7.49
7.38
7.36
7.34
2.51
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N
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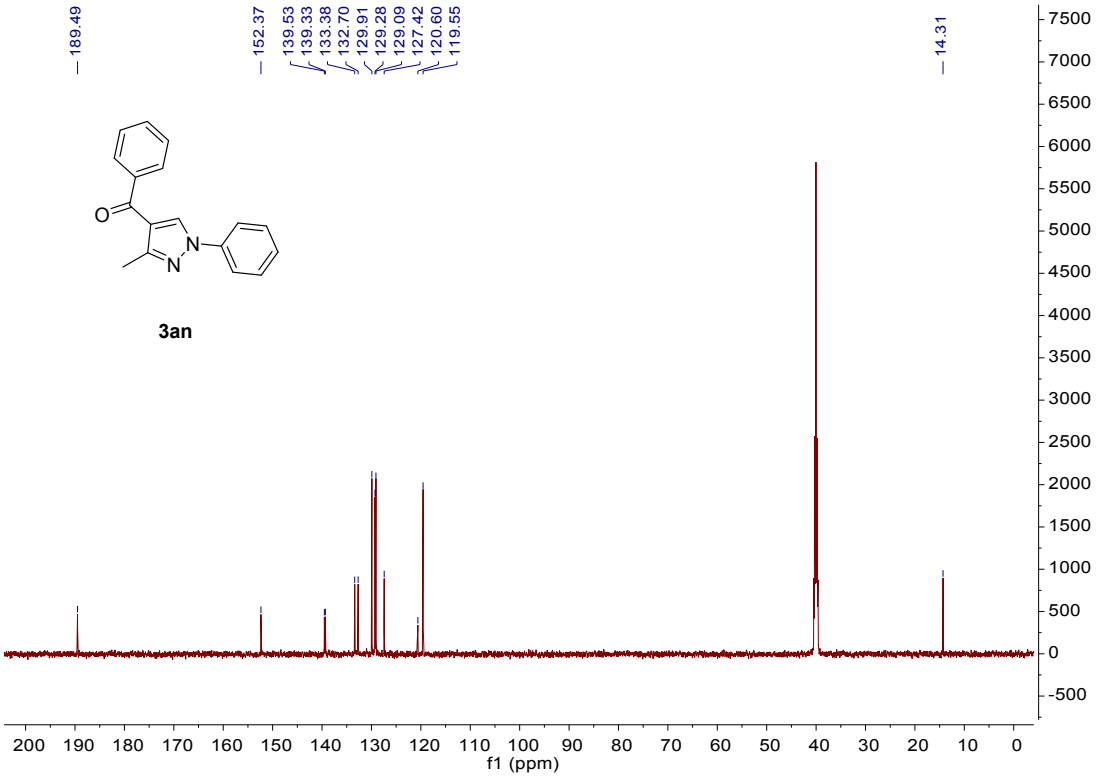
2.03
1.99
1.06
2.13
2.03
1.03
3.01
f1 (ppm)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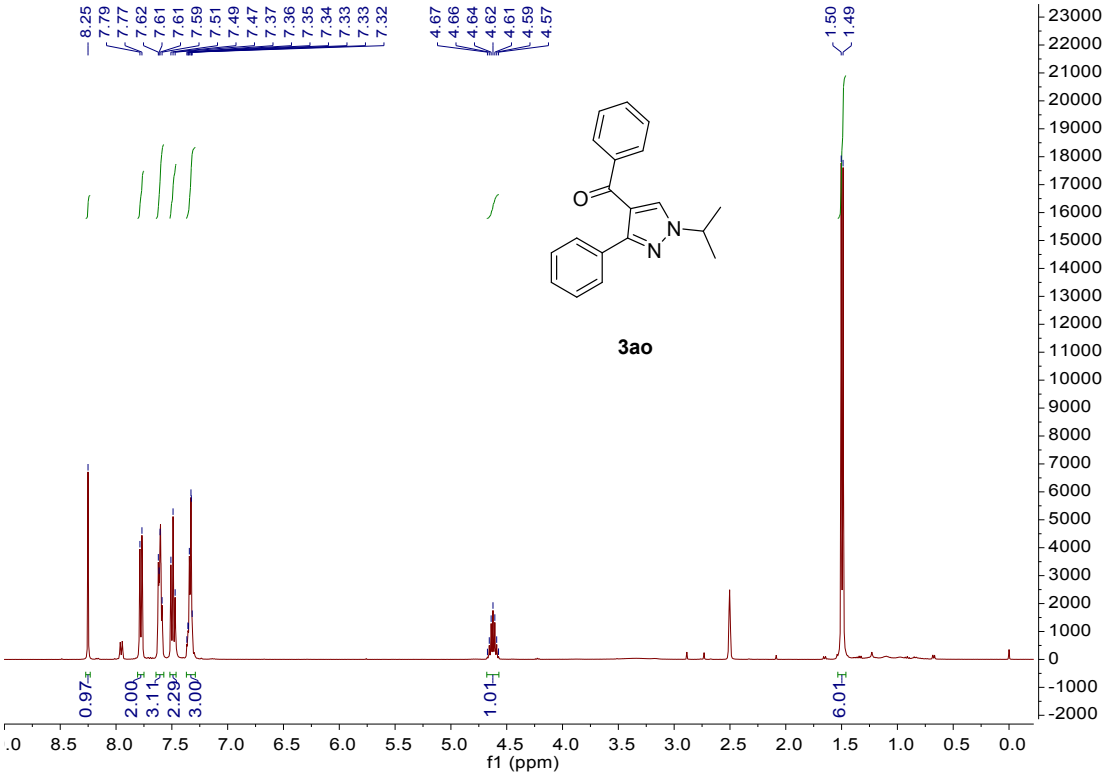
120.60
119.55
14.31
O
N
N
3an
f1 (ppm)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7.51
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7.37
7.36
7.35
7.34
7.33
7.33
7.32
4.67
4.66
4.64
4.62
4.61
4.59
4.57
1.50
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O
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N
3ao
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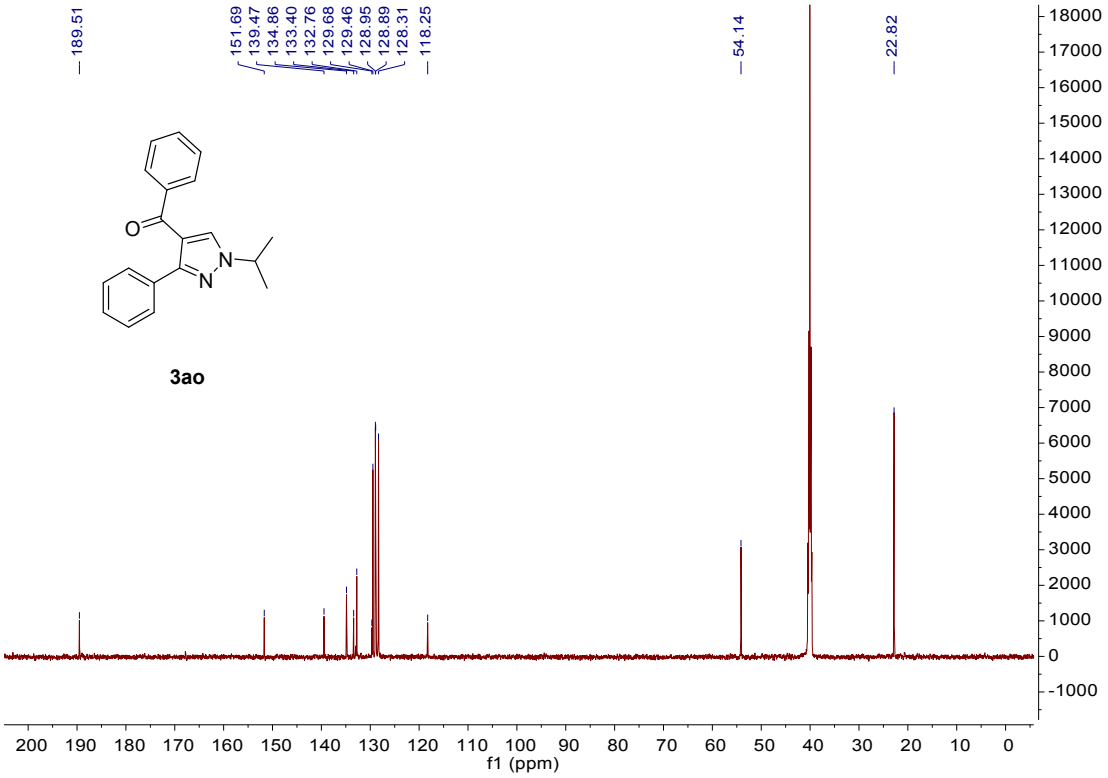
3.11
2.29
3.00
1.01
6.01
f1 (ppm)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132.76
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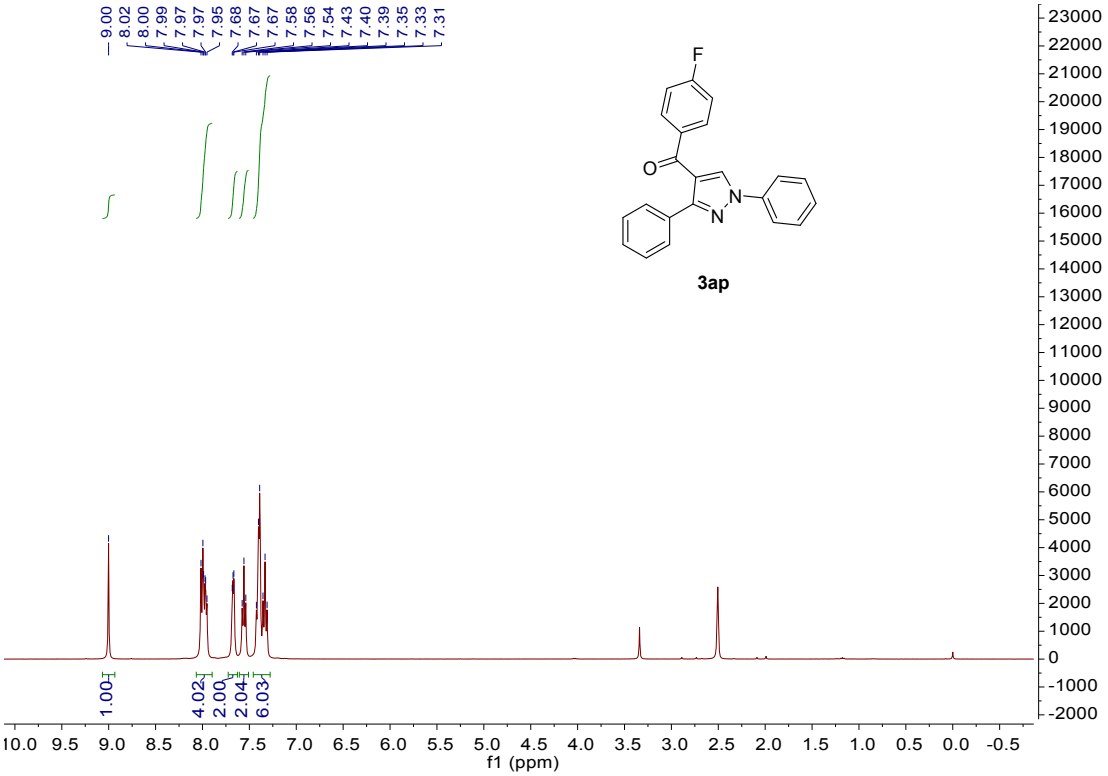
128.89
128.31
118.25
54.14
22.82
O
N
N
3ao
f1 (ppm)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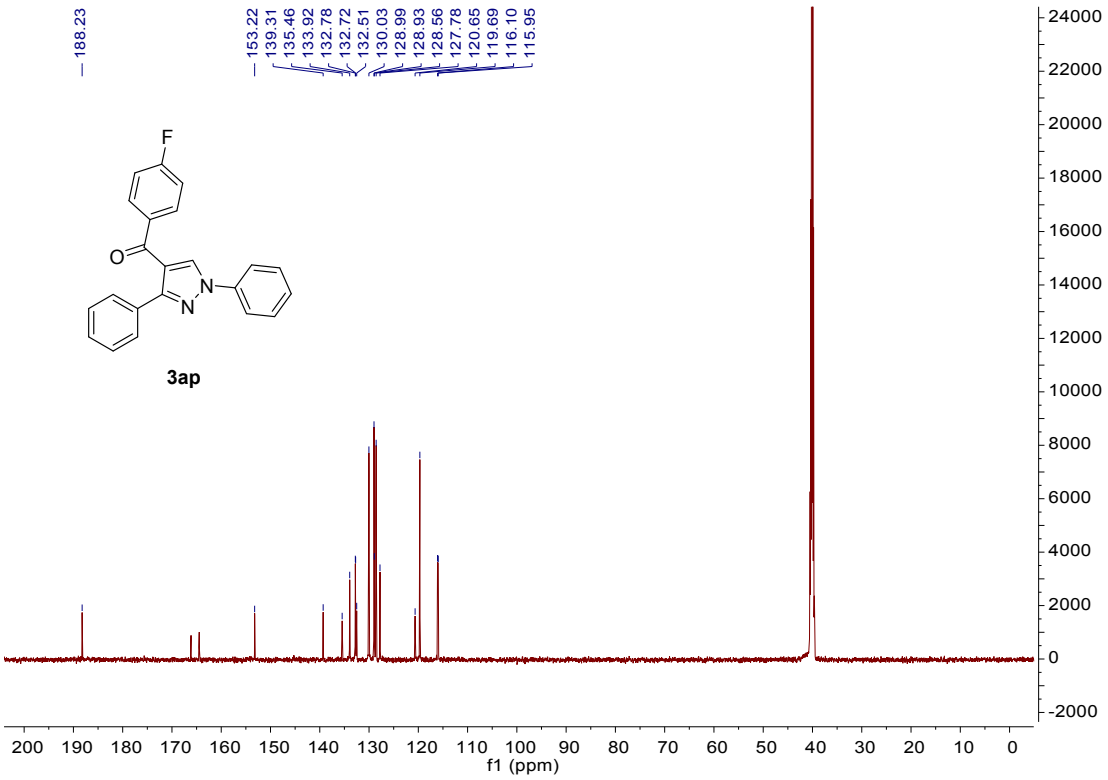
7.97
7.95
7.68
7.67
7.67
7.58
7.56
7.54
7.43
7.40
7.39
7.35
7.33
7.31
F
O
N
N
3ap
1.00
4.02
2.00
2.04
6.03
f1 (ppm)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132.78
132.72
132.51
130.03
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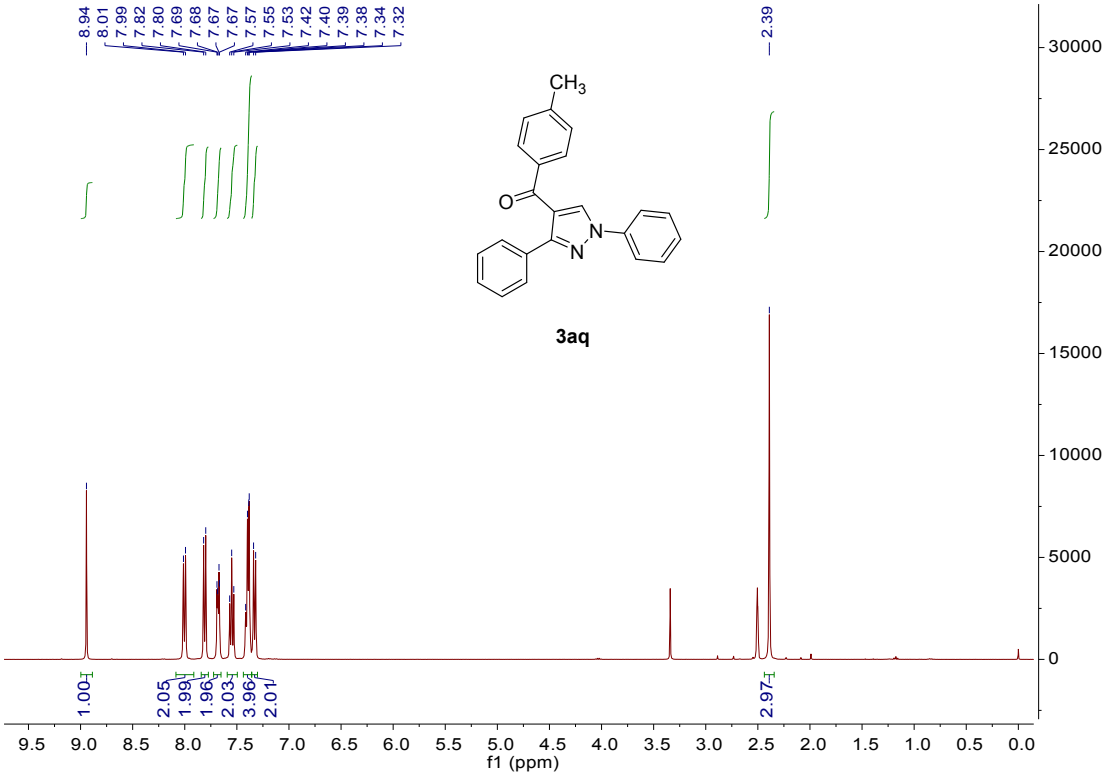
127.78
120.65
119.69
116.10
115.95
F
O
N
N
3ap
f1 (ppm)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7.69
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7.67
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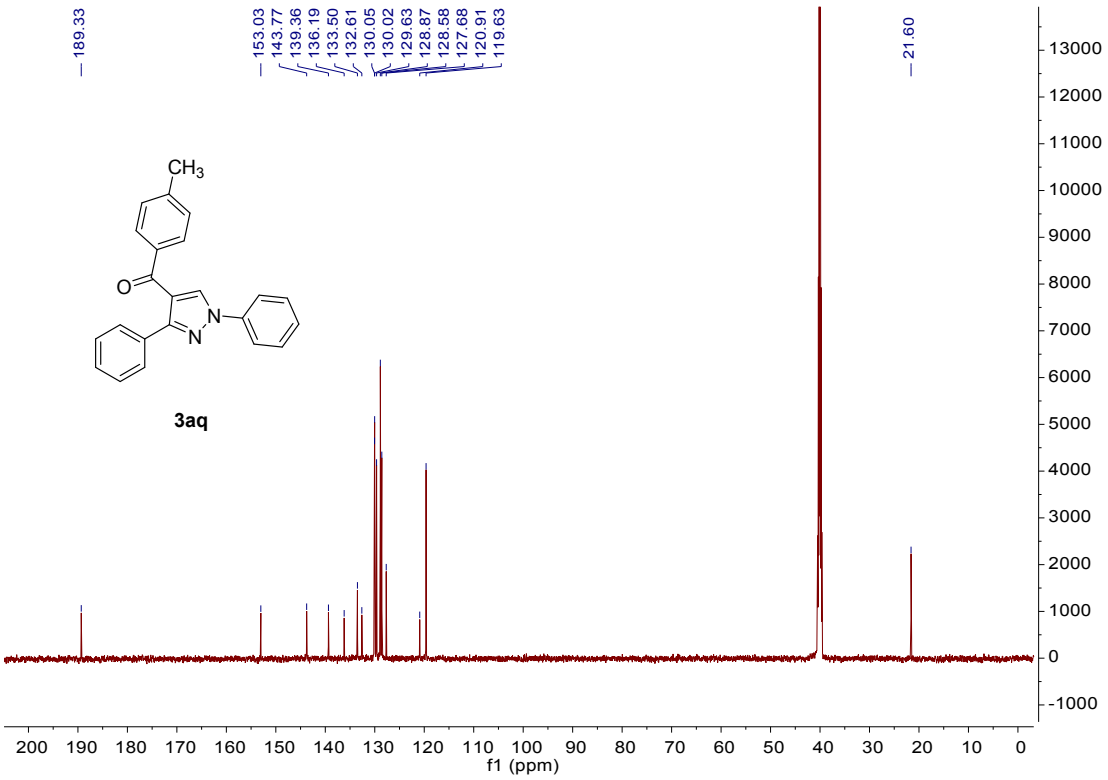
7.57
7.55
7.53
7.42
7.40
7.39
7.38
7.34
7.32
2.39
CH3
O
N
N
3aq
1.00
2.05
1.99
1.96
2.03
3.96
2.01
2.97
f1 (ppm)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133.50
132.61
130.05
130.02
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128.58
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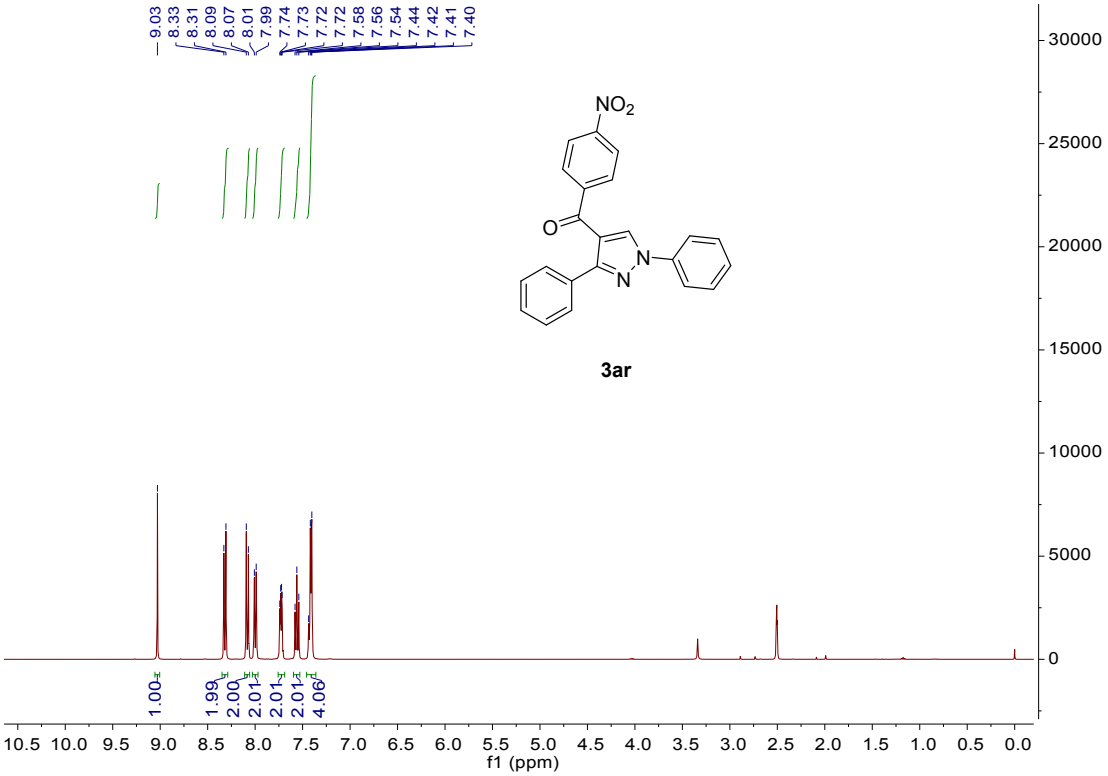
21.60
CH3
O
N
N
3aq
f1 (ppm)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7.74
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7.72
7.58
7.56
7.54
7.44
7.42
7.41
7.40
NO2
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N
3ar
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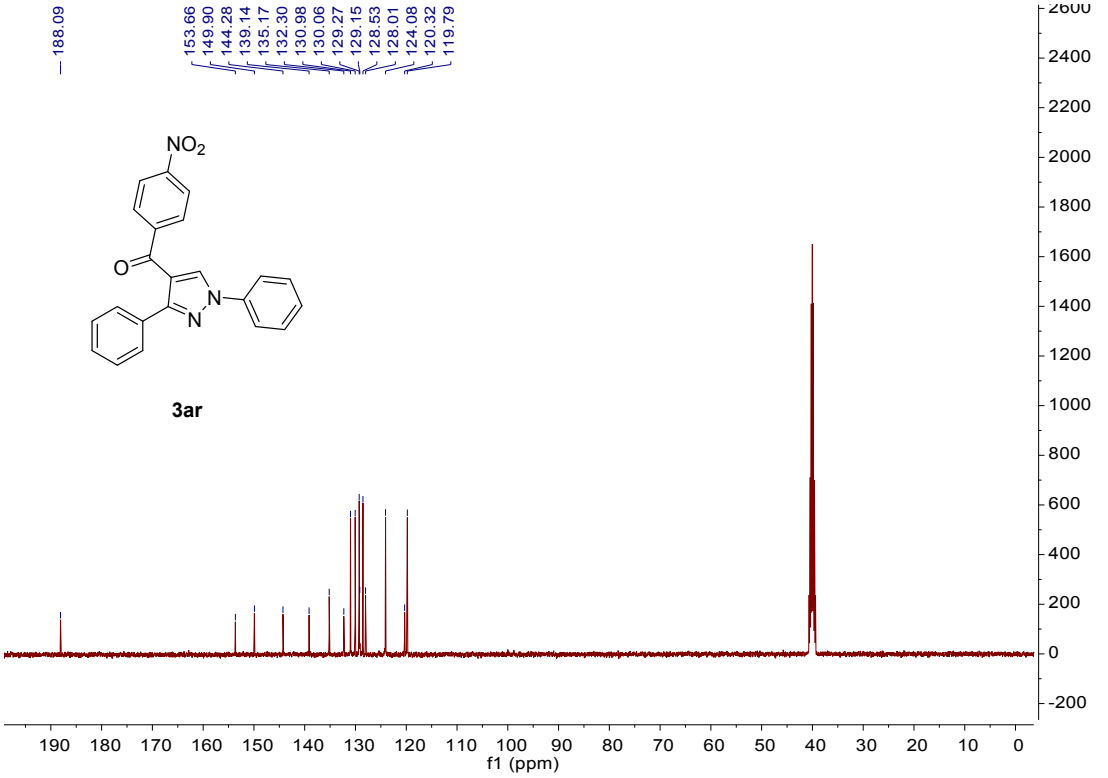
1.99
2.00
2.01
2.01
2.01
4.06
f1 (ppm)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129.27
129.15
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128.01
124.08
120.32
119.79
NO2
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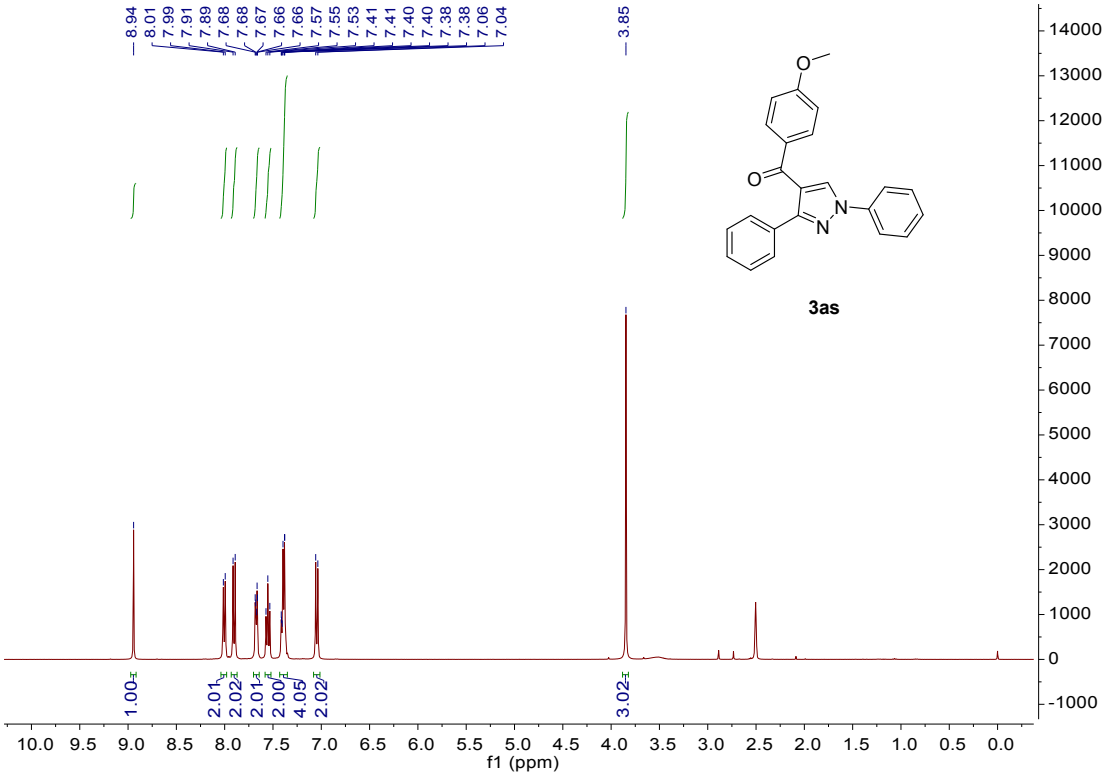
N
N
3ar
f1 (ppm)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8.01
7.99
7.91
7.89
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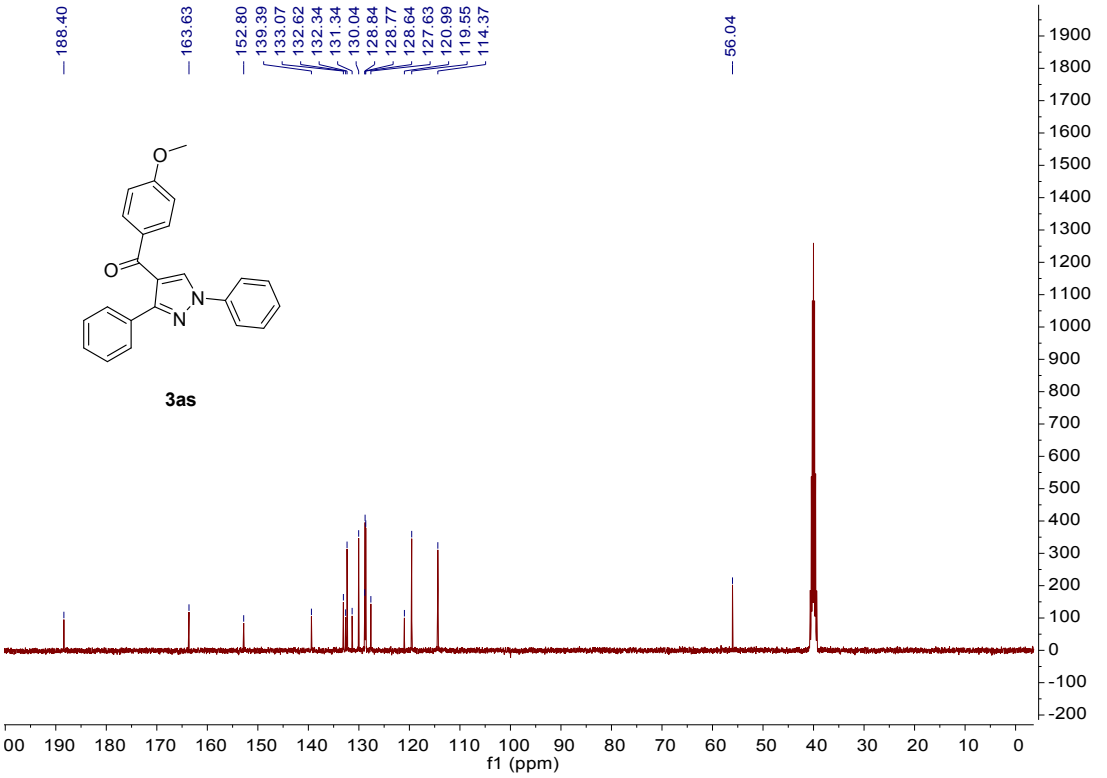
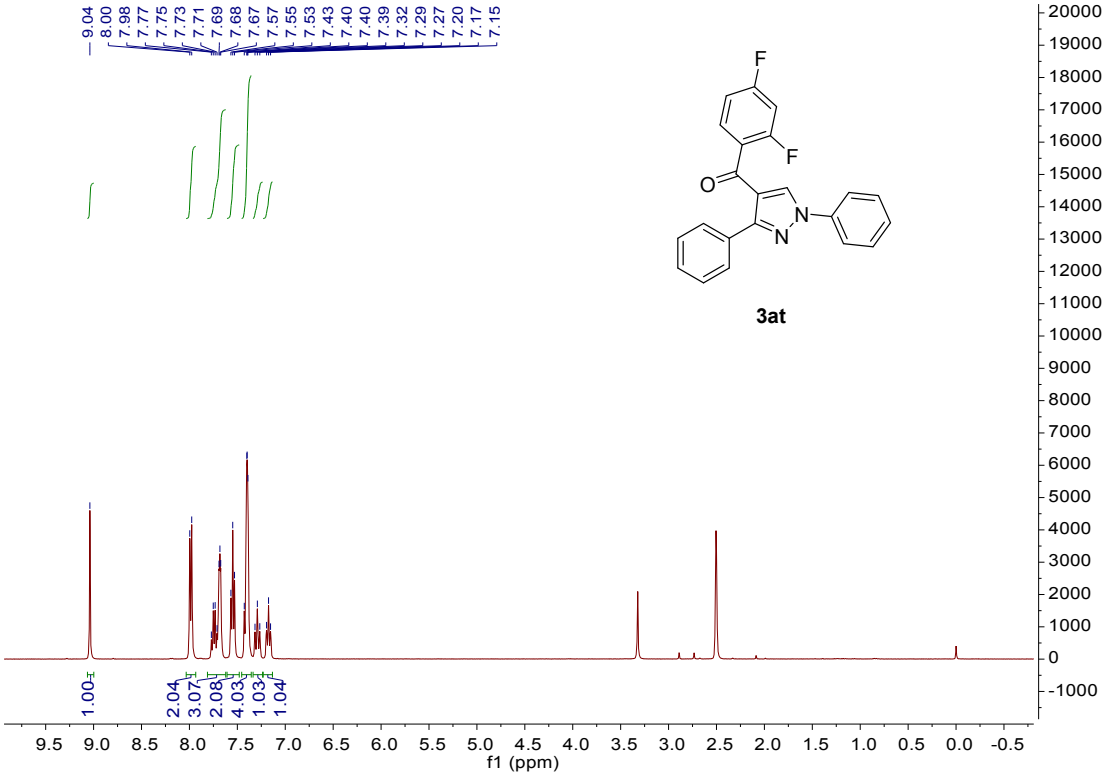
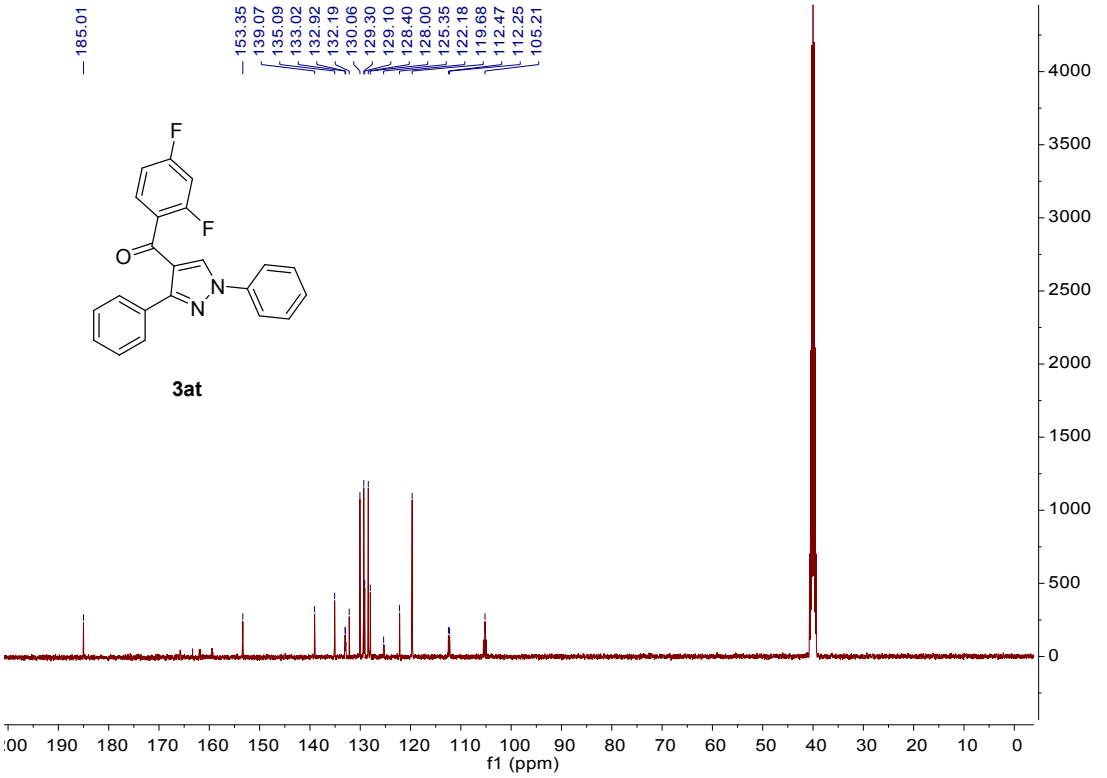
7.68
7.67
7.66
7.66
7.57
7.55
7.53
7.41
7.41
7.40
7.40
7.38
7.06
7.04
3.85
1.00
2.01
2.02
2.01
2.00
4.05
2.02
3.02
O
O
N
N
3as
f1 (ppm)


188.40
163.63
152.80
139.39
133.07
132.62
132.34
131.34
130.04
128.84
128.77
128.64
127.63
120.99
119.55
114.37
56.04
O
O
N
N
3as
f1 (ppm)


9.04
8.00
7.98
7.77
7.75
7.73
7.71
7.69
7.68
7.67
7.57
7.55
7.53
7.43
7.40
7.40
7.39
7.32
7.29
7.27
7.20
7.17
7.15
F
F
O
N
N
1.00
2.04
3.07
2.08
4.03
1.03
1.04
f1 (ppm)

3at


185.01
153.35
139.07
135.09
133.02
132.92
132.19
130.06
129.30
129.10
128.40
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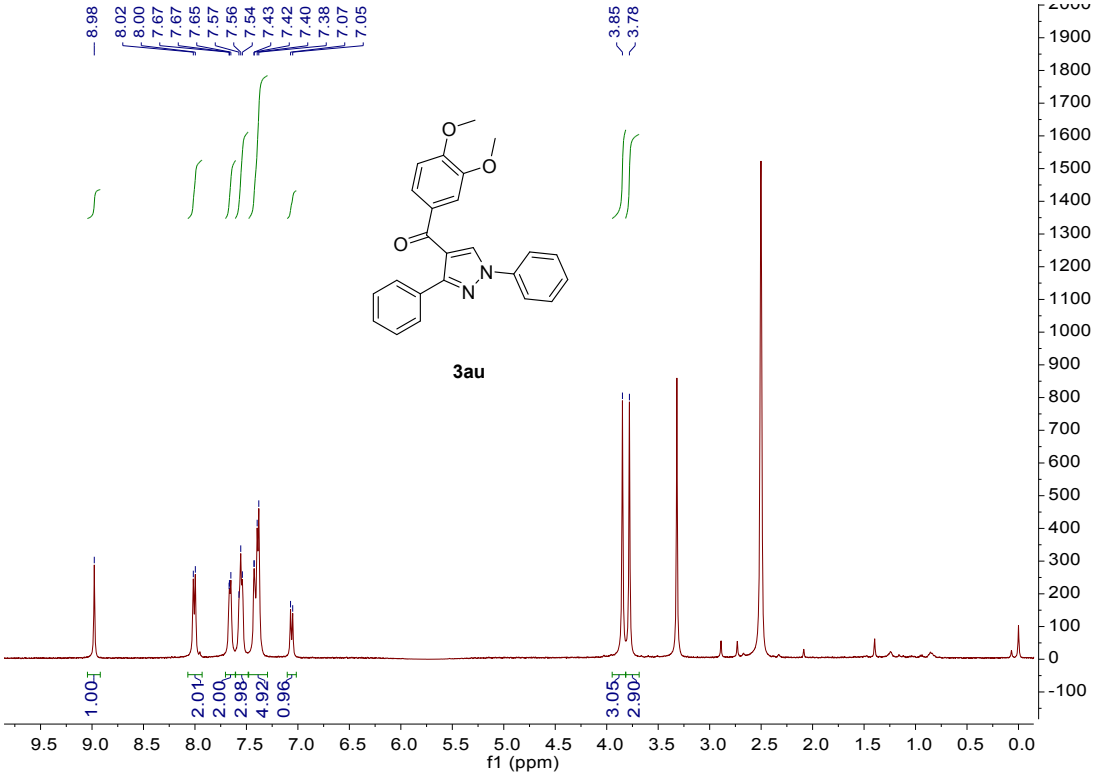
125.35
122.18
119.68
112.47
112.25
105.21
F
F
O
N
N
f1 (ppm)

3at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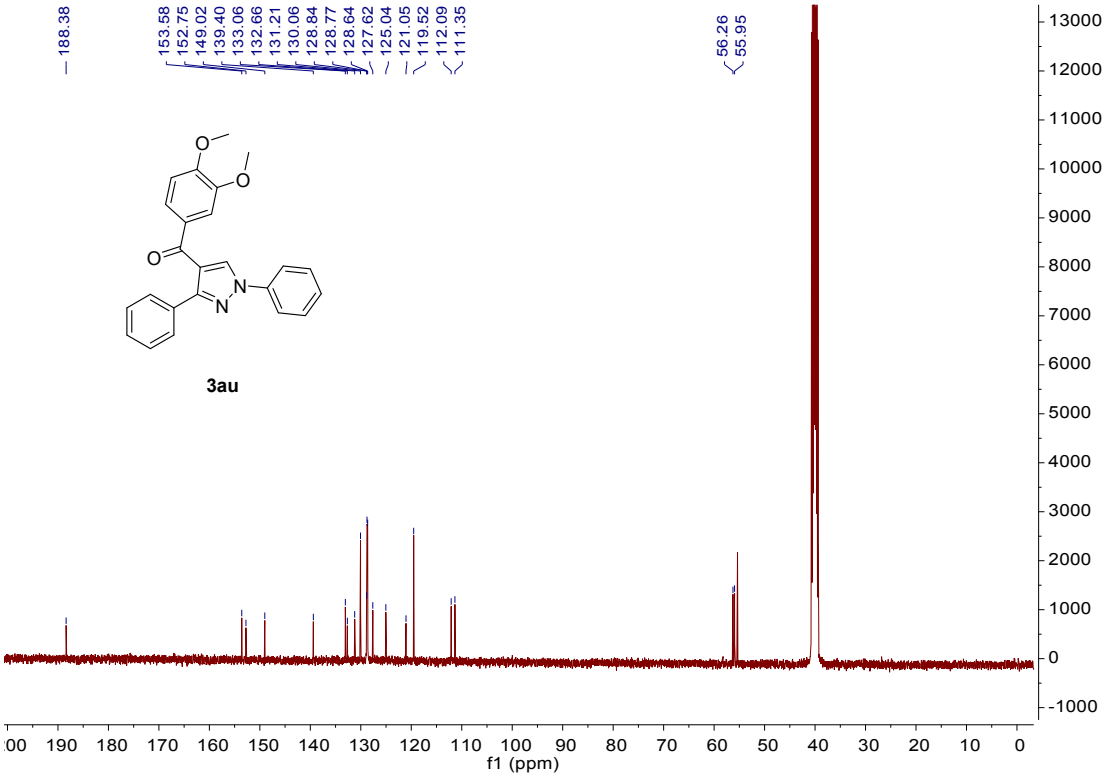
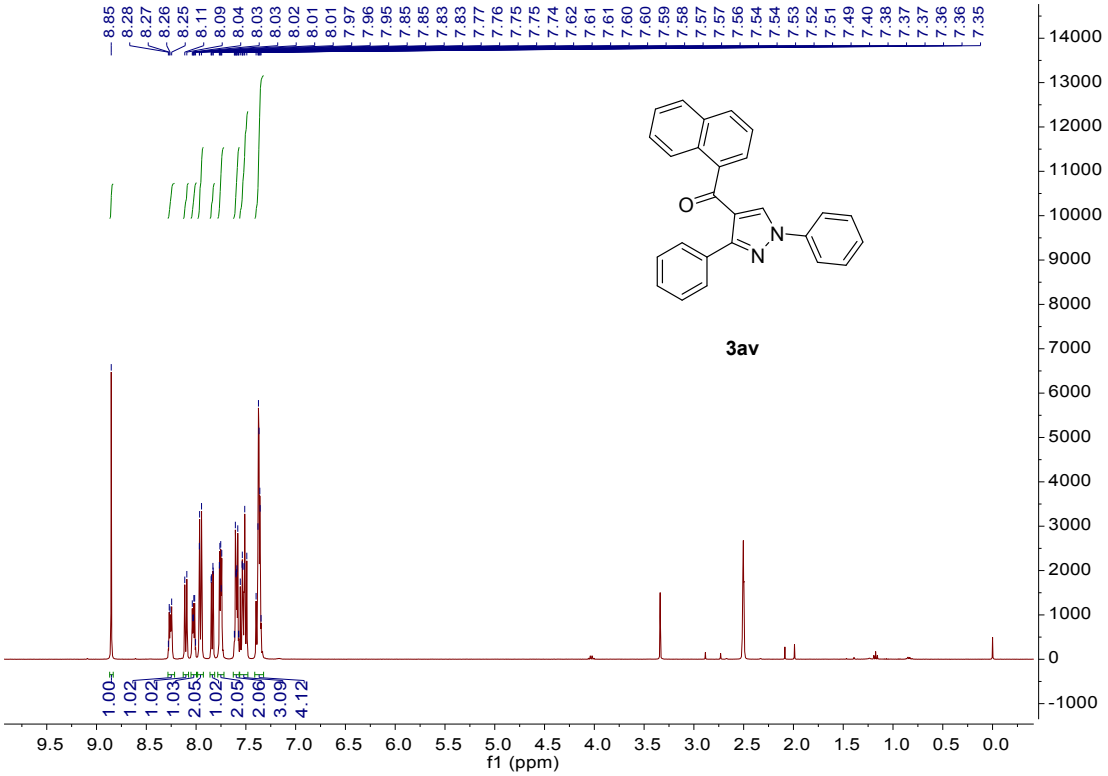
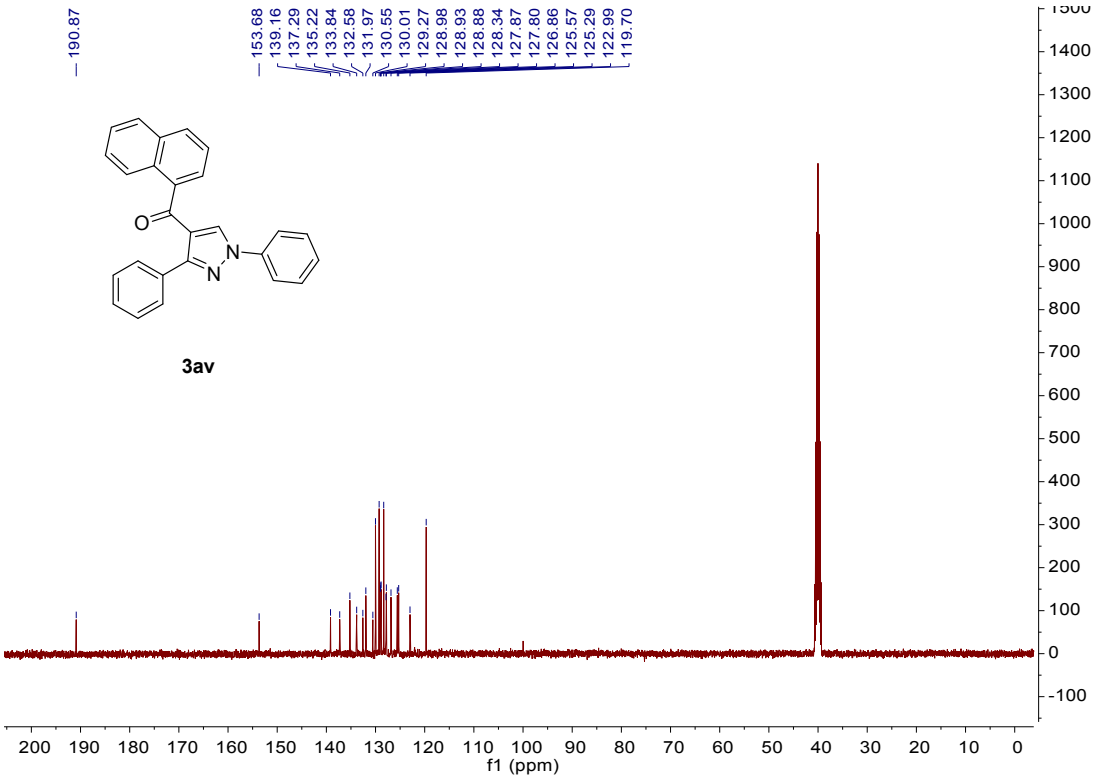
8.02
8.00
7.67
7.67
7.65
7.57
7.56
7.54
7.43
7.42
7.40
7.38
7.07
7.05
3.85
3.78
O
O
O
N
N
1.00
2.01
2.00
2.98
4.92
0.96
3.05
2.90
f1 (ppm)

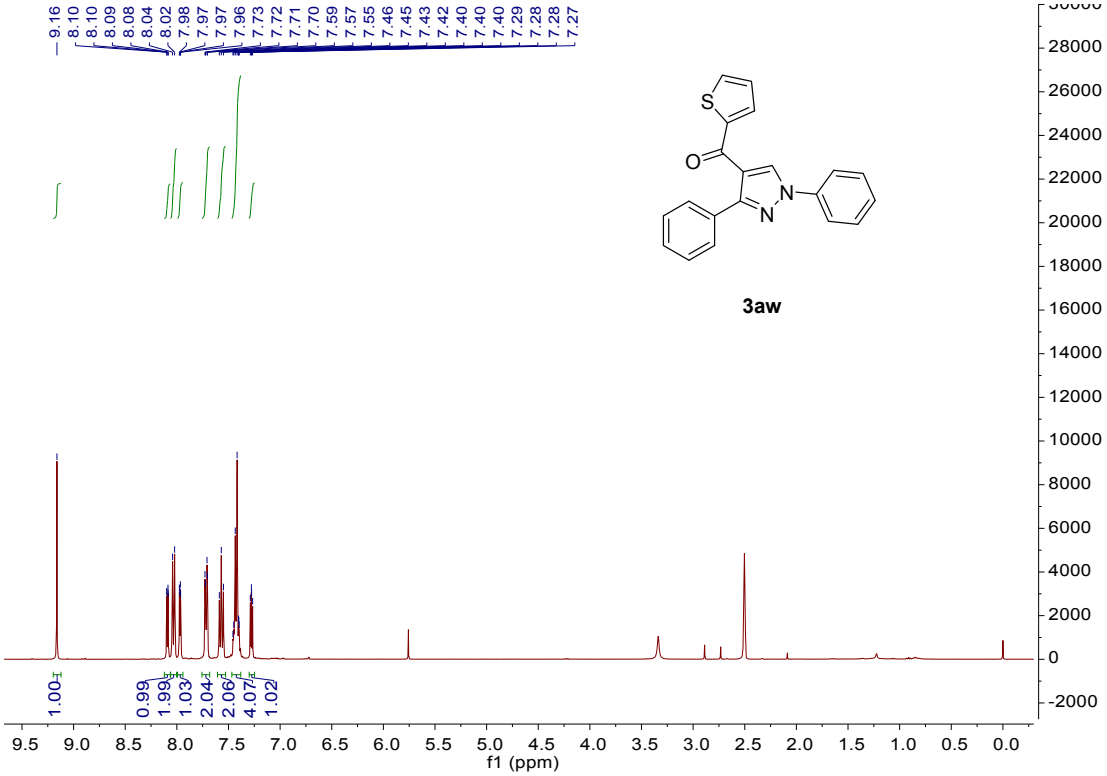
3au

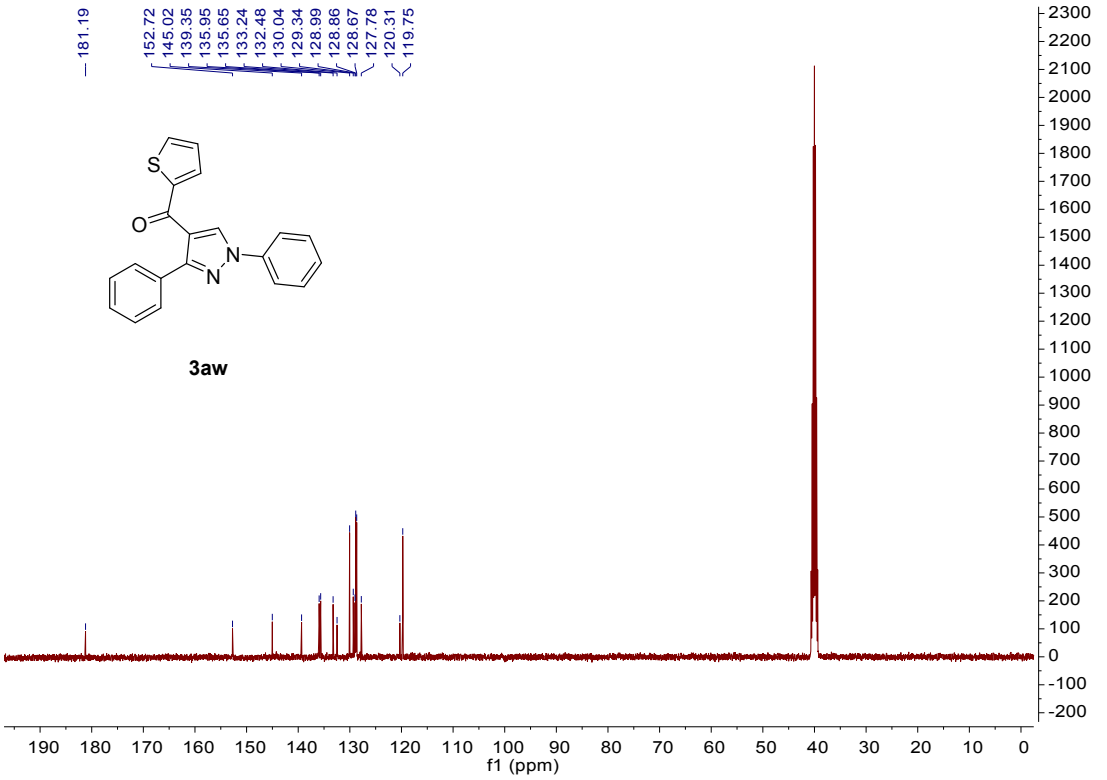

188.38
153.58
152.75
149.02
139.40
133.06
132.66
131.21
130.06
128.84
128.77
128.64
127.62
125.04
121.05
119.52
112.09
111.35
56.26
55.95
O
O
O
N
N
f1 (ppm)

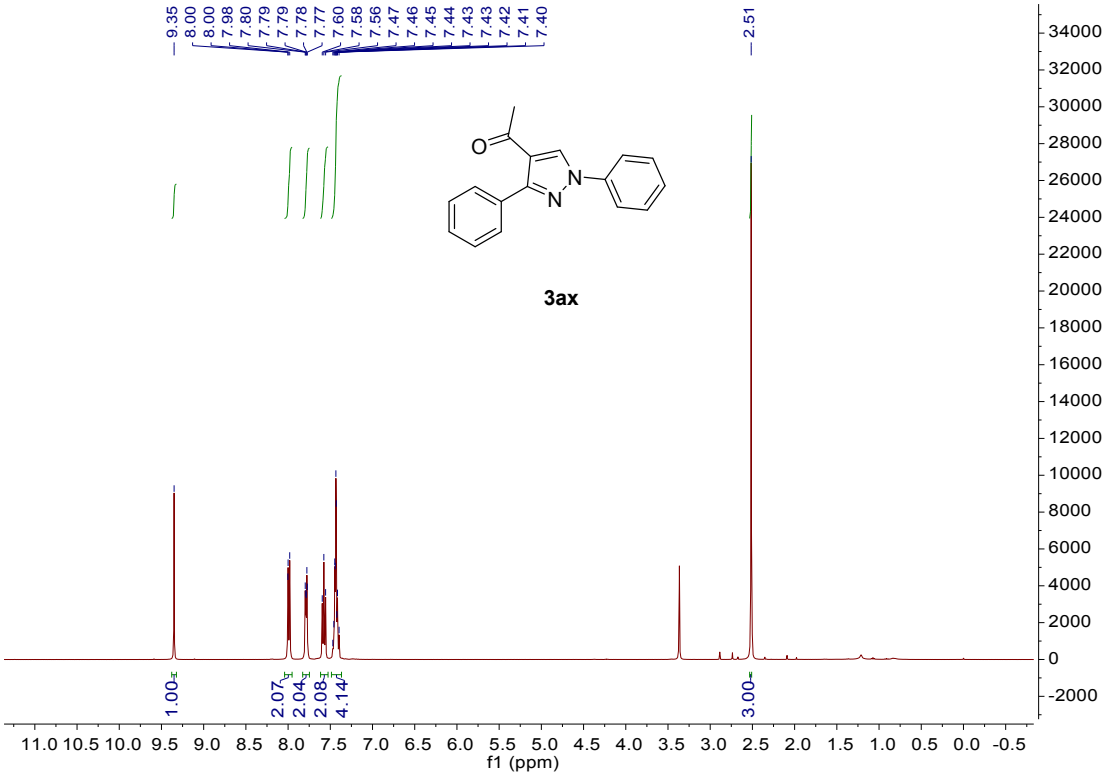
3au


8.85 8.28 8.27 8.26 8.25 8.11 8.09 8.04 8.03 8.03 8.02 8.01 8.01 7.97 7.96 7.95 7.85 7.85 7.83 7.83 7.77 7.76 7.75 7.75 7.74 7.62 7.61 7.61 7.60 7.60 7.59 7.58 7.57 7.57 7.56 7.54 7.54 7.53 7.52 7.51 7.49 7.40 7.38 7.37 7.37 7.36 7.36 7.35
O
N
N
3av
1.00 1.02 1.02 1.03 2.05 1.02 2.05 2.06 3.09 4.12
f1 (ppm)


190.87
153.68 139.16 137.29 135.22 133.84 132.58 131.97 130.55 130.01 129.27 128.98 128.93 128.88 128.34 127.87 127.80 126.86 125.57 125.29 122.99 119.70
O
N
N
3av
f1 (ppm)


9.16
8.10
8.10
8.09
8.08
8.04
8.02
7.98
7.97
7.97
7.96
7.73
7.72
7.71
7.70
7.59
7.57
7.55
7.46
7.45
7.43
7.42
7.40
7.40
7.29
7.28
7.28
7.27
S
O
N
N
3aw
1.00
0.99
1.99
1.03
2.04
2.06
4.07
1.02
f1 (ppm)


181.19
152.72
145.02
139.35
135.95
135.65
133.24
132.48
130.04
129.34
128.99
128.86
128.67
127.78
120.31
119.75
S
O
N
N
3aw
f1 (ppm)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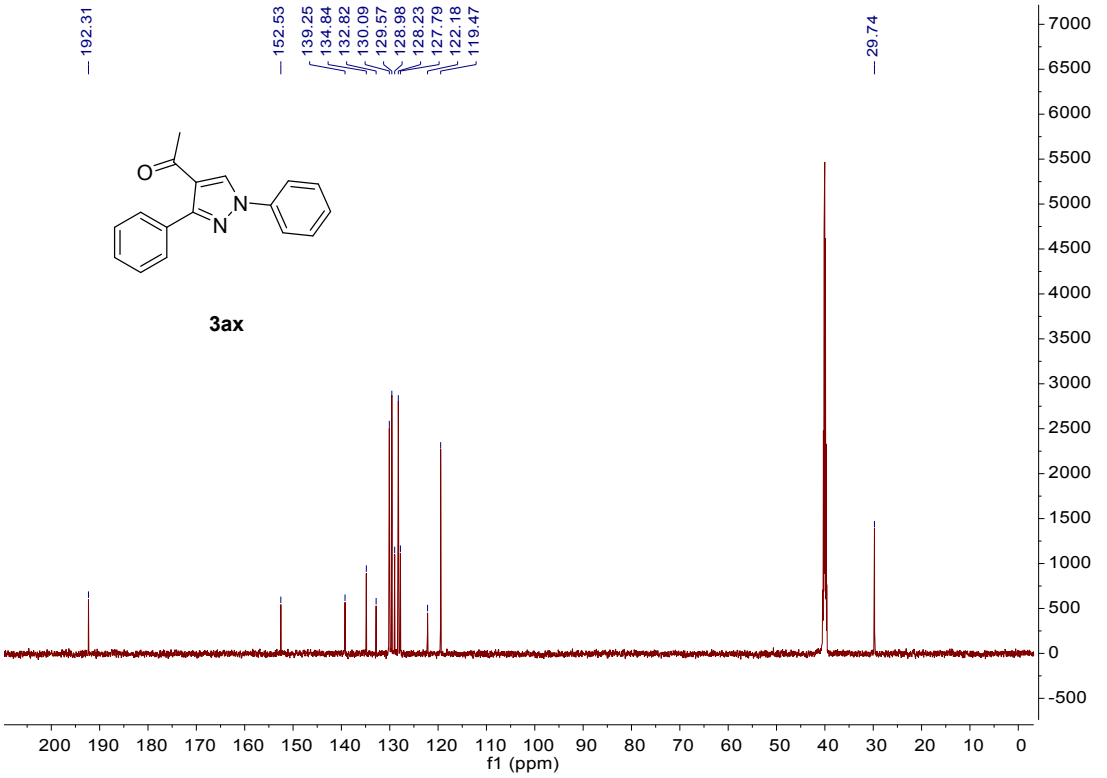
8.00
8.00
7.98
7.80
7.79
7.79
7.78
7.77
7.60
7.58
7.56
7.47
7.46
7.45
7.44
7.43
7.43
7.42
7.41
7.40
2.51
O
N
N
3ax
1.00
2.07
2.04
2.08
4.14
3.00
f1 (ppm)


192.31
152.53
139.25
134.84
132.82
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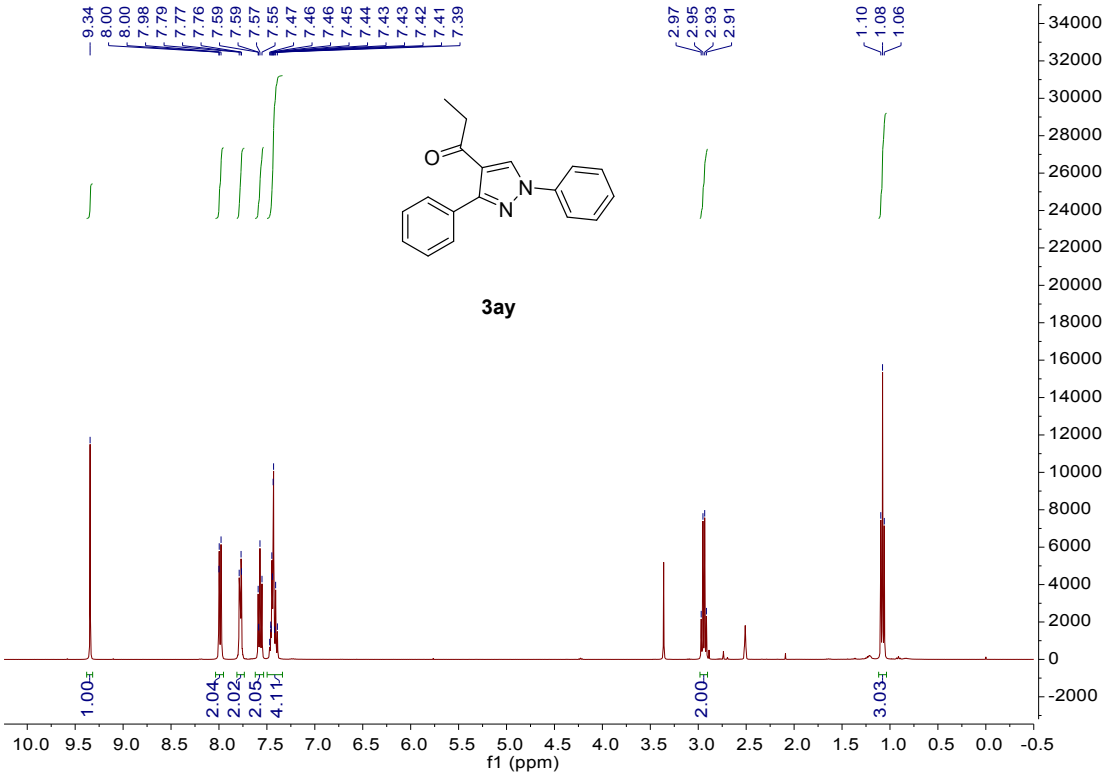
128.98
128.23
127.79
122.18
119.47
29.74
O
N
N
3ax
f1 (ppm)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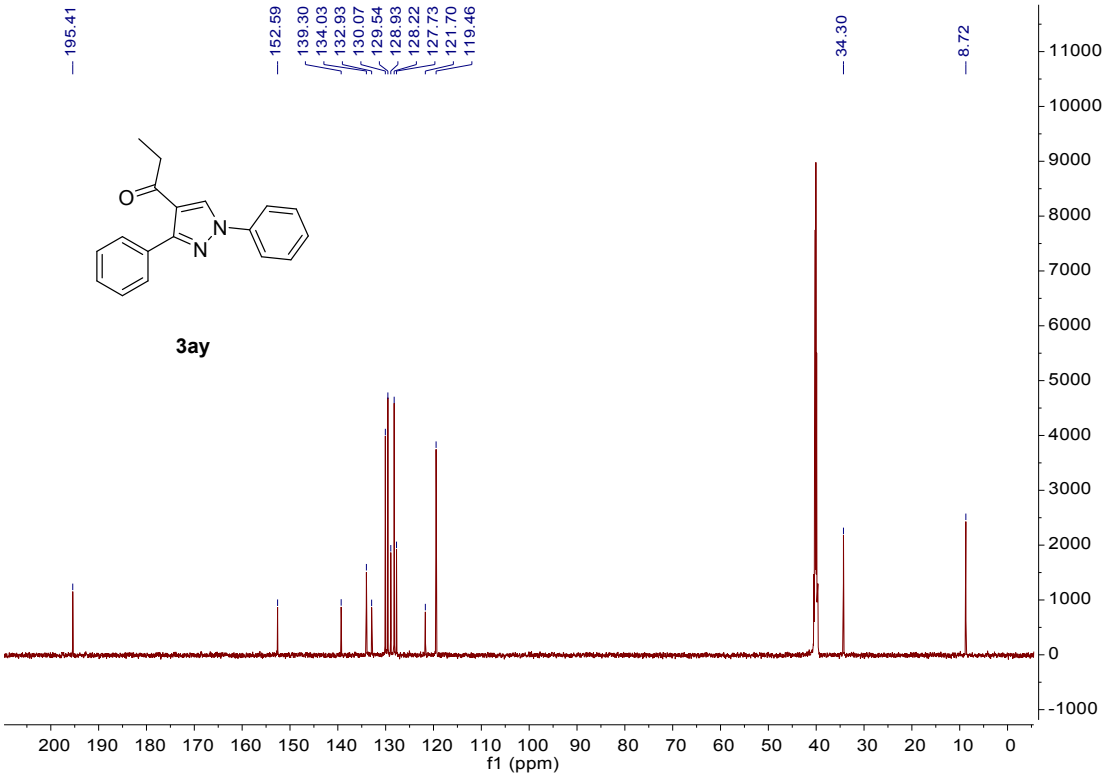
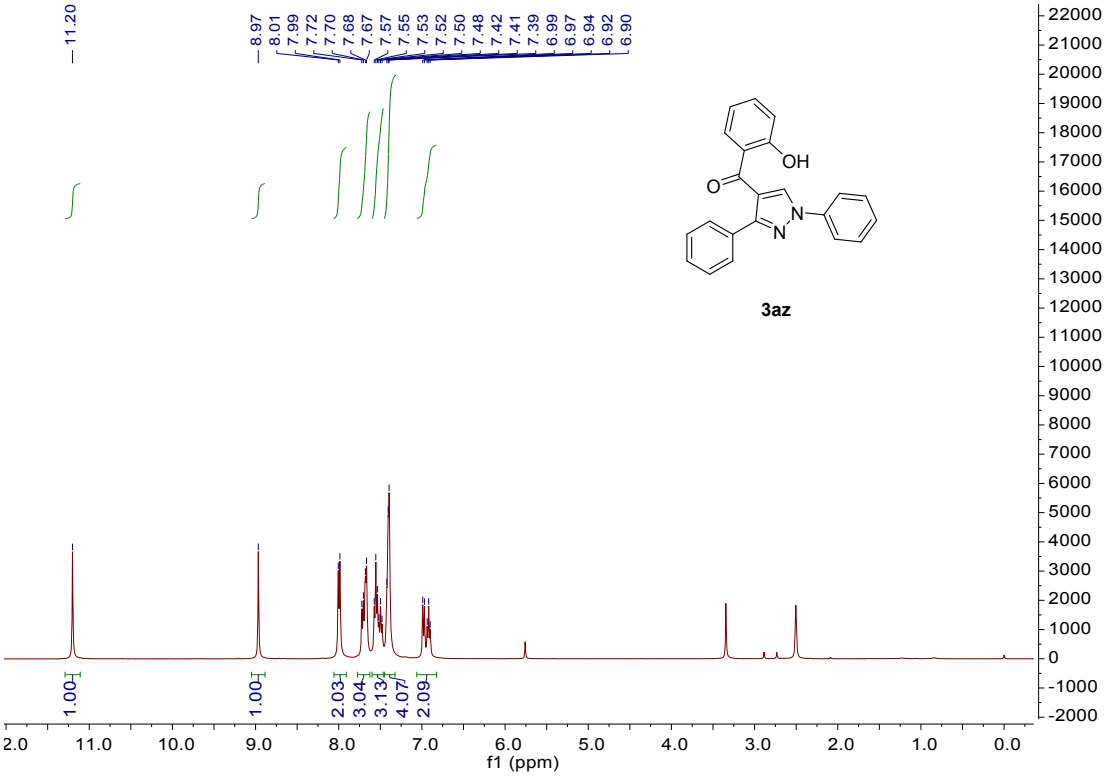
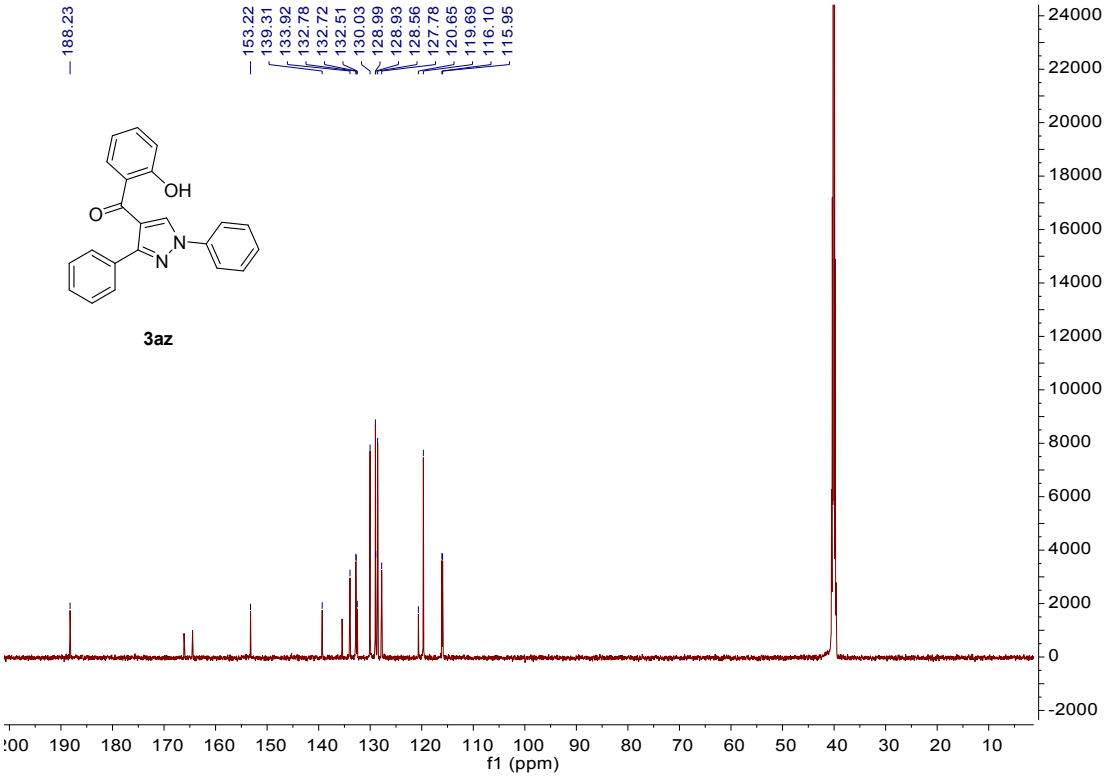
8.00
8.00
7.98
7.79
7.77
7.76
7.59
7.59
7.57
7.55
7.47
7.46
7.46
7.45
7.44
7.43
7.43
7.42
7.41
7.39
2.97
2.95
2.93
2.91
1.10
1.08
1.06
O
N
N
3ay
1.00
2.04
2.02
2.05
4.11
2.00
3.03
f1 (ppm)


195.41
152.59
139.30
134.03
132.93
130.07
129.54
128.93
128.22
127.73
121.70
119.46
34.30
8.72
O
N
N
3ay
f1 (ppm)


11.20
8.97
8.01
7.99
7.72
7.70
7.68
7.67
7.57
7.55
7.53
7.52
7.50
7.48
7.42
7.41
7.39
6.99
6.97
6.94
6.92
6.90
OH
O
N
N
3az
1.00
1.00
2.03
3.04
3.13
4.07
2.09
f1 (ppm)


188.23
153.22
139.31
133.92
132.78
132.72
132.51
130.03
128.99
128.93
128.56
127.78
120.65
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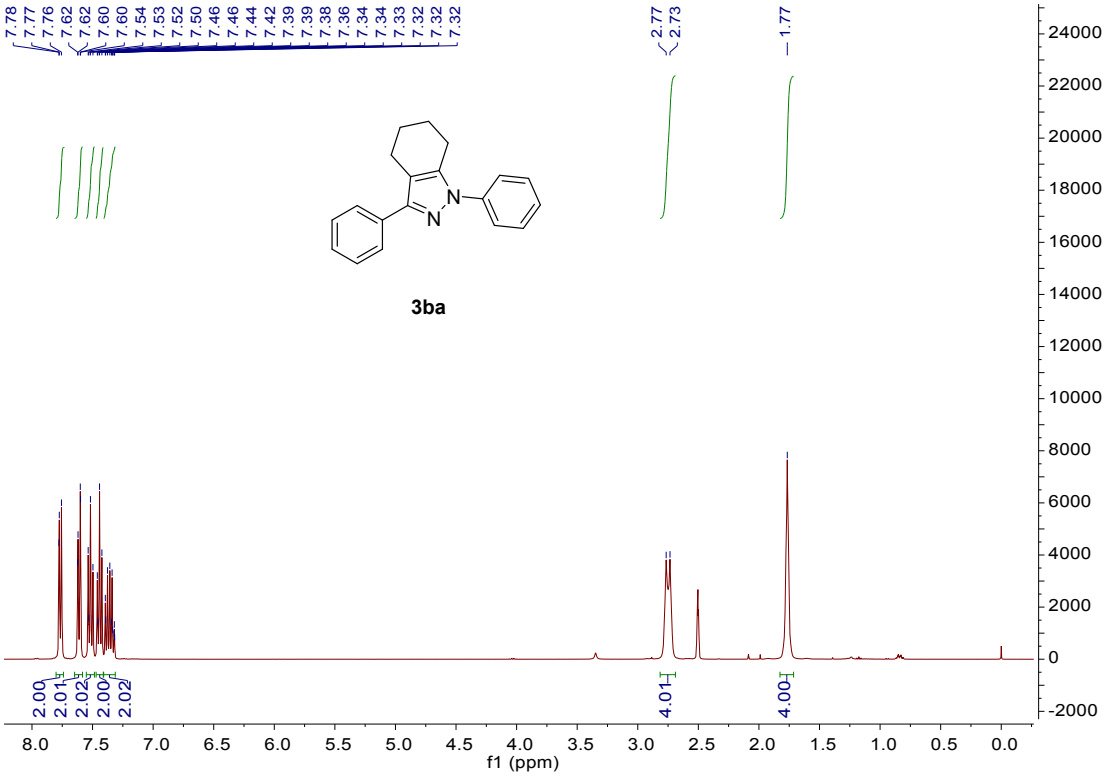
115.95
OH
O
N
N
3az
f1 (ppm)


7.78
7.77
7.76
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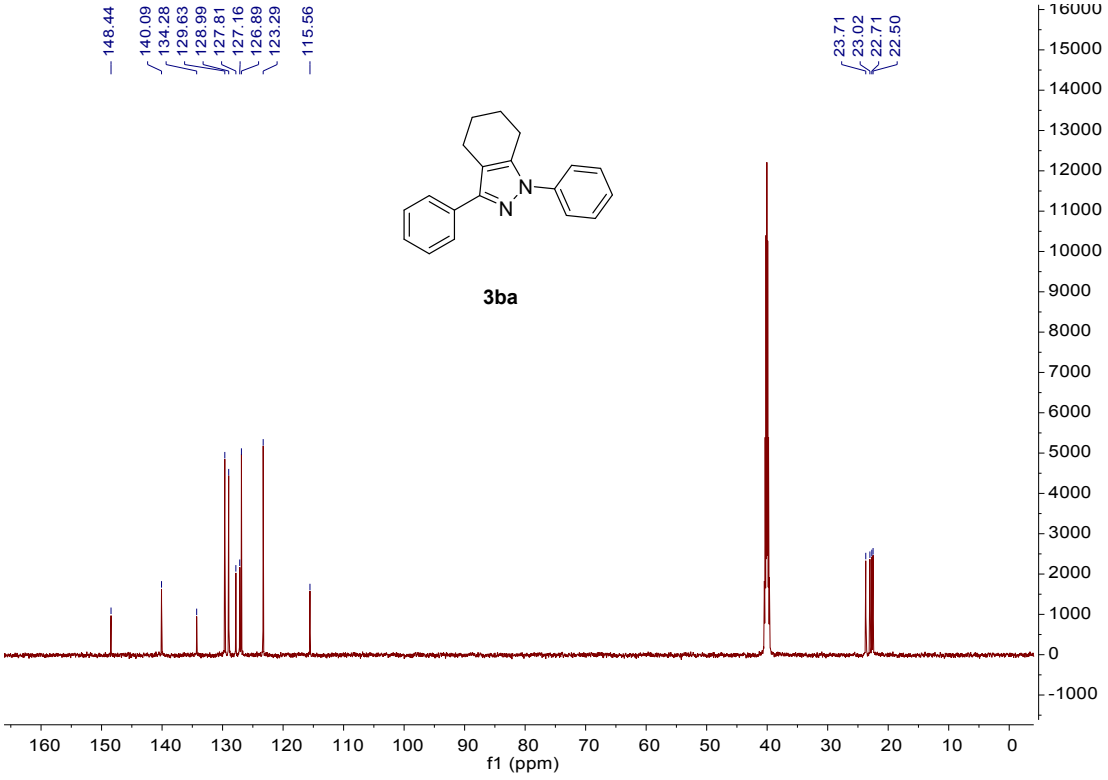
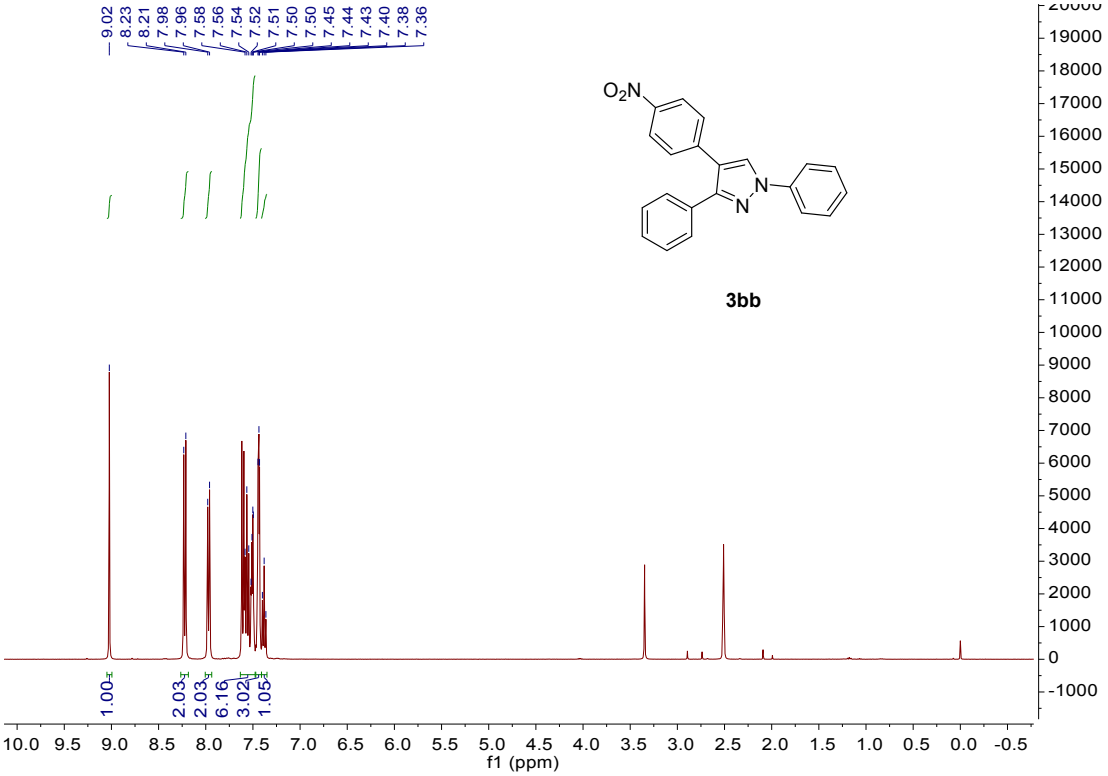
7.62
7.60
7.60
7.54
7.53
7.52
7.50
7.46
7.46
7.44
7.42
7.39
7.39
7.38
7.36
7.34
7.34
7.33
7.32
7.32
7.32
2.77
2.73
1.77
N
N
3ba
2.00
2.01
2.02
2.02
2.00
2.02
4.01
4.00
f1 (ppm)


148.44
140.09
134.28
129.63
128.99
127.81
127.16
126.89
123.29
115.56
23.71
23.02
22.71
22.50
N
N
3ba
f1 (ppm)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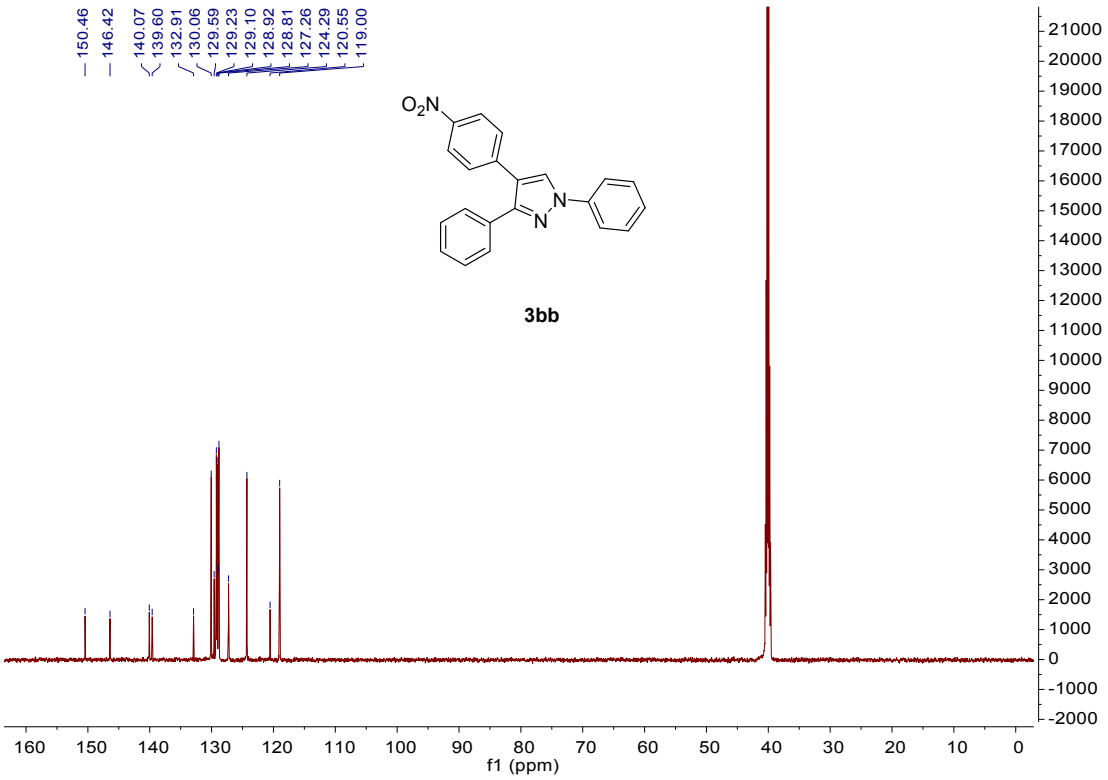
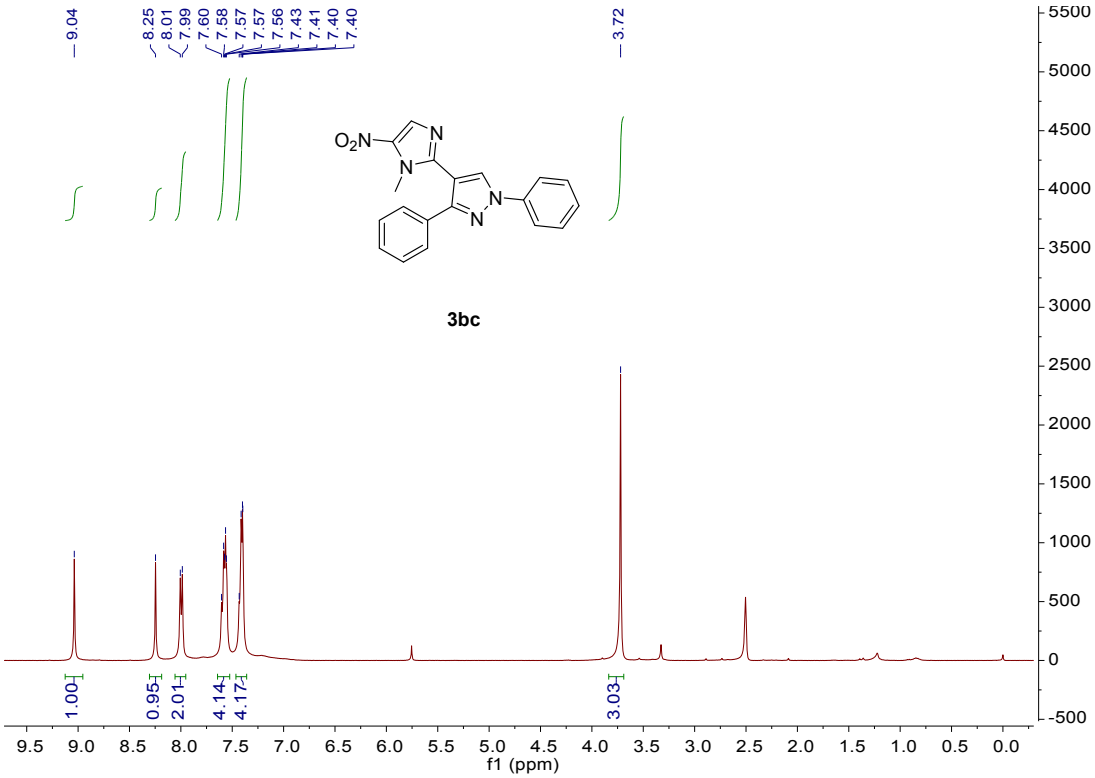
8.23
8.21
7.98
7.96
7.58
7.56
7.54
7.52
7.51
7.50
7.50
7.45
7.44
7.43
7.40
7.38
7.36
O2N
N
N
1.00
2.03
2.03
6.16
3.02
1.05
f1 (ppm)

3bb


150.46
146.42
140.07
139.60
132.91
130.06
129.59
129.23
129.10
128.92
128.81
127.26
124.29
120.55
119.00
O2N
N
N
f1 (ppm)

3bb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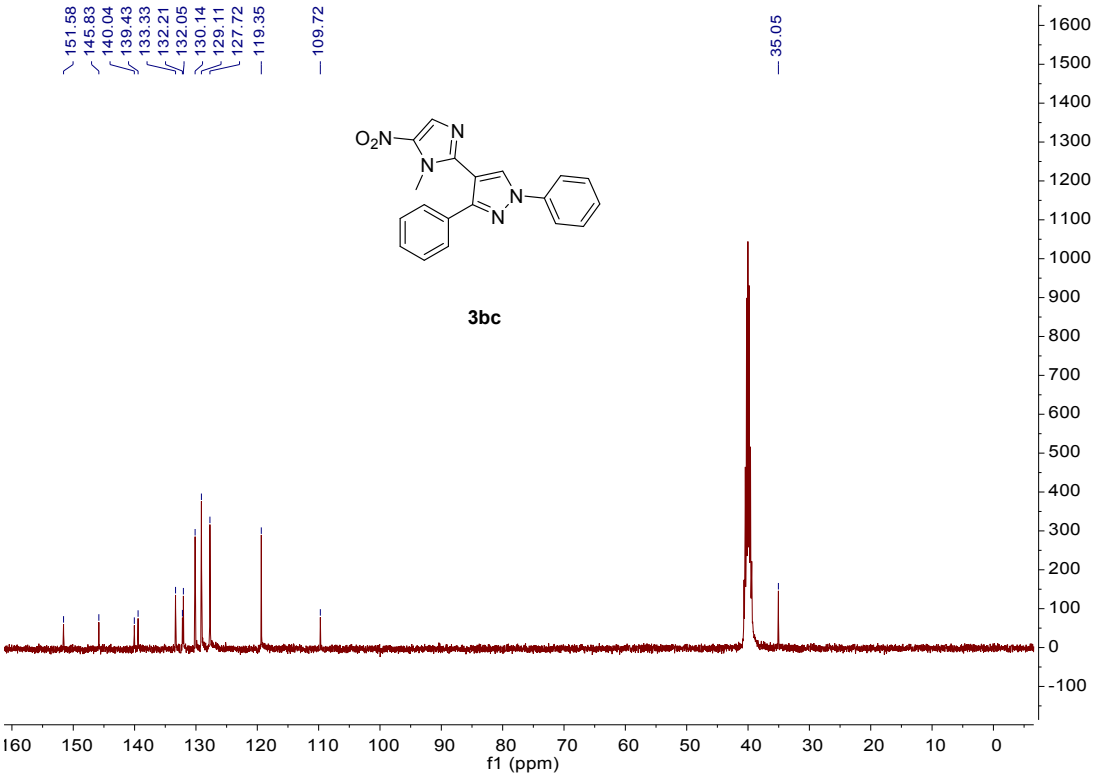
8.25
8.01
7.99
7.60
7.58
7.57
7.57
7.56
7.43
7.41
7.40
7.40
3.72
O2N
N
N
N
N
1.00
0.95
2.01
4.14
4.17
3.03
f1 (ppm)

3bc


151.58
145.83
140.04
139.43
133.33
132.21
132.05
130.14
129.11
127.72
119.35
109.72
35.05
O2N
N
N
N
N
f1 (ppm)

3bc

Notes and references

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