Transition-Metal-Free Synthesis of Polysubstituted Pyrrole Derivatives *via* Cyclization of Methyl Isocyanoacetate with Aurone Analogues

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Electronic Supplementary Information

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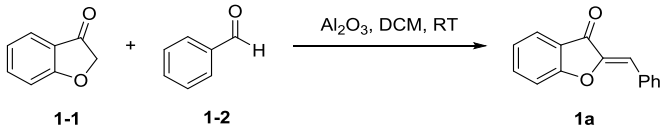
I. General Information

^{1}H and **^{13}C NMR** spectra were recorded on an Agilent 400M NMR spectrometer at ambient temperature. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: ^{1}H (chloroform δ 7.26, DMSO-d_6 δ 2.50), ^{13}C (chloroform δ 77.0, DMSO-d_6 δ 39.52). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz) and integration. Melting point (**M.P.**) was obtained on SGW X-4A. For thin layer chromatography (**TLC**), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. High resolution mass spectra (**HRMS**) were obtained on a Bruker SolariX 7.0T spectrometer.

Unless otherwise noted, all the reactions were carried out in air. Dichloromethane (DCM) and acetonitrile (ACN) were distilled from calcium hydride. Deuterated solvents were purchased from Cambridge Isotope Laboratories and used as received without further purification. Other chemicals were purchased from commercial suppliers and used as received without further purification.

II. Synthesis of Aurones

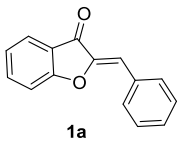


1-1 1-2 1a

General procedure:[1] To a solution of benzofuran-3(2*H*)-one **1-1** (1.0 mmol) and benzaldehyde **1-2** (1.0 mmol) in dichloromethane (10 mL) was added activated basic aluminum oxide (5.0 mmol) at room temperature with vigorously stirring. After reaction completion, aluminum oxide was filtered and washed abundantly with dichloromethane, the filtrate was concentrated to afford crude product, which was purified by flash chromatography on silica gel (hexanes/ethyl acetate, 20:1) to afford the product **1a** 17.8 mg as pale yellow solid.

III. Characterization of Aurones

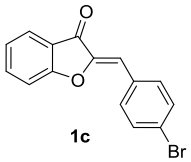
(*Z*)-2-Benzylidenebenzofuran-3(2*H*)-one (1a)[1]



1a

80% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 89-90 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.93 (d, *J* = 7.3 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.1 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.90 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.78, 166.16, 146.89, 136.89, 132.30, 131.53, 129.89, 128.89, 124.67, 123.47, 121.64, 113.03, 112.94.

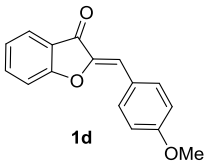
(*Z*)-2-(4-Bromobenzylidene)benzofuran-3(2*H*)-one (1c)[2]



1c

57% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 170-171 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.79 (dd, *J* = 12.4, 8.1 Hz, 3H), 7.69 – 7.65 (m, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.81 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.59, 166.08, 147.08, 137.04, 132.77, 132.15, 131.21, 124.74, 124.30, 123.66, 121.50, 112.93, 111.54.

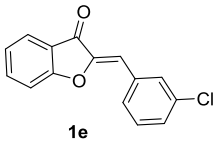
(*Z*)-2-(4-Methoxybenzylidene)benzofuran-3(2*H*)-one (1d)[3]



1d

91% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 133-134 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.91 – 7.87 (m, 2H), 7.81 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.64 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.00 – 6.98 (m, 2H), 6.89 (s, 1H), 3.87 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.54, 165.84, 161.07, 145.88, 136.50, 133.43, 125.06, 124.55, 123.25, 121.95, 114.50, 113.39, 112.86, 55.38.

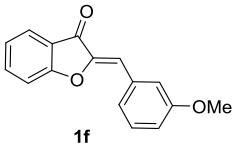
(*Z*)-2-(3-Chlorobenzylidene)benzofuran-3(2*H*)-one (1e)[4]



1e

86% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 96-97 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.91 (s, 1H), 7.78 (t, *J* = 12.5 Hz, 1H), 7.72 – 7.70 (m, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.38 – 7.32 (m, 3H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.76 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.55, 166.16, 147.28, 137.13, 134.80, 134.02, 130.87, 130.02, 129.70, 129.56, 124.73, 123.70, 121.37, 113.00, 111.07.

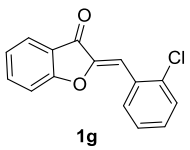
(*Z*)-2-(3-Methoxybenzylidene)benzofuran-3(2*H*)-one (1f)[2]



1f

85% yield, R_f = 0.4, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 116-117 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.81 (d, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 6.7 Hz, 2H), 7.40 – 7.32 (m, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.98 – 6.96 (m, 1H), 6.87 (s, 1H), 3.89 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.77, 166.15, 159.77, 146.97, 136.92, 133.50, 129.83, 124.68, 124.30, 123.50, 121.61, 116.51, 115.74, 112.95, 112.93, 55.34.

(*Z*)-2-(2-Chlorobenzylidene)benzofuran-3(2*H*)-one (1g)[2]

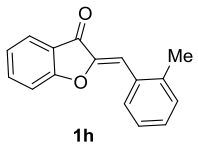


1g

86% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 133-134 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.35 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.46 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.38 (dd, *J* = 8.7, 7.6 Hz, 2H), 7.32 – 7.29 (m, 2H), 7.23 (t, *J* = 7.5 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.53, 166.17,

147.59, 137.06, 135.94, 132.23, 130.58, 130.39, 130.00, 127.04, 124.83, 123.69, 121.49, 112.91, 107.98.

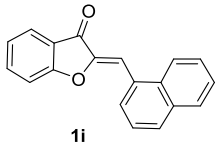
(*Z*)-2-(2-Methylbenzylidene)benzofuran-3(2*H*)-one (1h)[4]



1h

82% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 101-102 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.27 – 8.25 (m, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.34 – 7.20 (m, 5H), 7.14 (s, 1H), 2.52 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.76, 166.22, 146.99, 139.20, 136.84, 131.17, 130.81, 130.68, 129.83, 126.39, 124.70, 123.41, 121.73, 112.96, 109.87, 20.22.

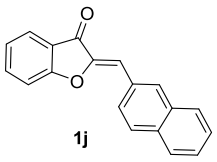
(*Z*)-2-(Naphthalen-1-ylmethylene)benzofuran-3(2*H*)-one (1i)[2]



1i

70% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 132-133 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.47 (d, *J* = 7.3 Hz, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.92 – 7.84 (m, 3H), 7.72 (s, 1H), 7.61 (qdd, *J* = 14.9, 11.2, 4.1 Hz, 4H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.24 (dd, *J* = 11.9, 4.1 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.61, 166.27, 147.71, 136.87, 133.73, 132.32, 130.57, 130.26, 128.96, 128.24, 127.08, 126.19, 125.58, 124.77, 123.52, 123.36, 121.80, 112.99, 108.57.

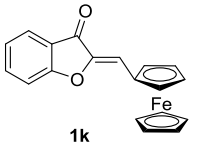
(*Z*)-2-(Naphthalen-2-ylmethylene)benzofuran-3(2*H*)-one (1j)



1j

78% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, **M.P.** 120-121 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.30 (s, 1H), 8.06 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.85 (ddd, *J* = 14.1, 9.3, 3.4 Hz, 4H), 7.67 – 7.63 (m, 1H), 7.54 – 7.49 (m, 2H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.03 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.63, 166.10, 147.06, 136.80, 133.72, 133.32, 132.33, 129.92, 128.73, 128.54, 127.72, 127.66, 127.47, 126.59, 124.66, 123.46, 121.70, 113.21, 112.97; **HRMS** (ESI): m/z calcd. for $[C_{19}H_{13}O_2, M+H]^+$: 273.0910; found: 273.0916.

[(*Z*)-(3-Oxo-2(3*H*)-benzofuranylidene)methyl]ferrocene (1k)[5]

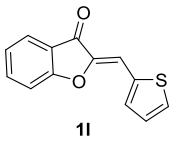


1k

74% yield, R_f = 0.4, (silica gel, petroleum ether:EtOAc = 10:1), purple solid, **M.P.** 150-151 °C. **^{1}H NMR** (400 MHz, Chloroform-d)

δ 7.80 (d, *J* = 7.5 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.89 (s, 1H), 4.86 (s, 2H), 4.54 (s, 2H), 4.17 (s, 5H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 182.87, 165.36, 145.98, 136.08, 124.45, 123.04, 122.60, 116.42, 112.91, 75.05, 71.79, 71.47, 69.93.

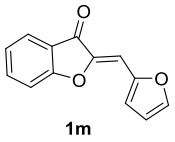
(*Z*)-2-(Thiophen-2-ylmethylene)benzofuran-3(2*H*)-one (1l)[6]



1l

90% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 102-103 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.79 (ddd, *J* = 7.6, 1.3, 0.5 Hz, 1H), 7.64 (ddd, *J* = 8.6, 7.3, 1.4 Hz, 1H), 7.61 – 7.60 (m, 1H), 7.55 – 7.54 (m, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.17 (s, 1H), 7.14 (dd, *J* = 5.1, 3.7 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.84, 165.62, 145.32, 136.64, 135.55, 133.08, 131.71, 128.05, 124.53, 123.47, 122.24, 113.00, 107.00.

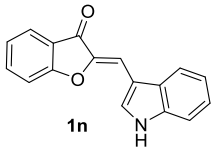
(*Z*)-2-(Furan-2-ylmethylene)benzofuran-3(2*H*)-one (1m)[6]



1m

84% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, **M.P.** 119-120 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 3.3 Hz, 1H), 6.89 (s, 1H), 6.60 (d, *J* = 1.4 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.95, 165.72, 148.79, 145.38, 145.00, 136.65, 124.51, 123.47, 122.02, 117.24, 113.13, 112.89, 101.57.

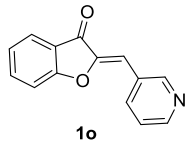
(*Z*)-2-((1*H*-Indol-3-yl)methylene)benzofuran-3(2*H*)-one (1n)



1n

48% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 3:1), orange solid, **M.P.** 232-233 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.11 (br, 1H), 8.26 (d, *J* = 2.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.75 (t, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.36 (s, 1H), 7.23 (ddd, *J* = 25.2, 15.5, 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 182.15, 164.58, 144.58, 136.83, 136.82, 132.68, 127.12, 124.26, 123.80, 123.28, 122.70, 121.45, 119.51, 113.55, 112.81, 108.92, 107.96; **HRMS** (ESI): m/z calcd. for $[C_{17}H_{11}NNaO_2, M+Na]^+$: 284.0682; found: 284.0682.

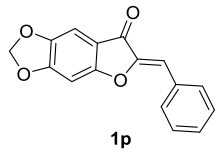
(*Z*)-2-(Pyridin-3-ylmethylene)benzofuran-3(2*H*)-one (1o)[7]



1o

73% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, **M.P.** 111-112 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 9.05 (s, 1H), 8.61 (d, *J* = 4.1 Hz, 1H), 8.29 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 6.85 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 184.31, 166.15, 152.21, 150.06, 148.00, 137.65, 137.28, 128.55, 124.83, 123.83, 123.73, 121.31, 112.96, 108.83.

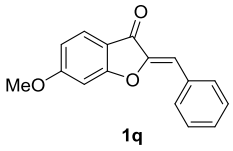
(*Z*)-6-Benzylidene-[1,3]dioxolo[4,5-*f*]benzofuran-7(6*H*)-one (1p)



1p

94% yield, R_f = 0.6, (silica gel, petroleum ether:EtOAc = 10:1), yellow solid, **M.P.** 189-191 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.86 (d, *J* = 7.3 Hz, 2H), 7.41 (dt, *J* = 23.3, 7.2 Hz, 3H), 7.09 (s, 1H), 6.80 (s, 1H), 6.76 (s, 1H), 6.09 (s, 2H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.13, 164.65, 155.84, 148.00, 145.05, 132.28, 131.40, 129.75, 128.87, 114.75, 112.35, 102.72, 101.81, 94.41. **HRMS** (ESI): m/z calcd. for $[C_{16}H_{10}NaO_4, M+Na]^+$: 289.0471; found: 289.0471.

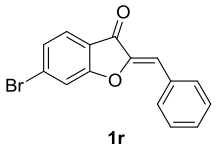
(*Z*)-2-Benzylidene-6-methoxybenzofuran-3(2*H*)-one (1q)[8]



1q

85% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), white scaly solid, **M.P.** 132-133 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.90 – 7.88 (m, 2H), 7.69 (t, *J* = 5.9 Hz, 1H), 7.45 (dd, *J* = 10.1, 4.6 Hz, 2H), 7.40 – 7.36 (m, 1H), 6.81 (s, 1H), 6.76 (dt, *J* = 8.4, 2.0 Hz, 2H), 3.92 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.02, 168.58, 167.45, 147.83, 132.43, 131.30, 129.59, 128.83, 125.83, 114.84, 112.18, 111.85, 96.65, 56.02.

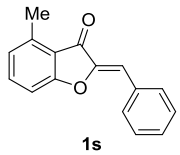
(*Z*)-2-Benzylidene-6-bromobenzofuran-3(2*H*)-one (1r)[9]



1r

95% yield, R_f = 0.3, (silica gel, petroleum ether:EtOAc = 10:1), pale yellow solid, **M.P.** 168-170 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.88 (d, *J* = 7.1 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.54 (s, 1H), 7.43 (dq, *J* = 14.3, 7.0 Hz, 3H), 7.35 (d, *J* = 8.1 Hz, 1H), 6.90 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.48, 166.08, 146.76, 131.93, 131.64, 131.34, 130.23, 128.97, 127.20, 125.51, 120.65, 116.62, 113.99.

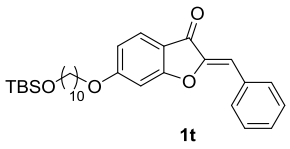
(*Z*)-2-Benzylidene-4-methylbenzofuran-3(2*H*)-one (1s)



1s

84% yield, R_f = 0.3, (silica gel, petroleum ether:EtOAc = 40:1), white solid, **M.P.** 108-109 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.45 (dq, *J* = 14.8, 7.5 Hz, 3H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.81 (s, 1H), 2.68 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 185.54, 166.43, 146.99, 140.15, 136.25, 132.49, 131.36, 129.59, 128.82, 124.86, 119.71, 111.90, 109.89, 17.79; **HRMS** (ESI): m/z calcd. for $[C_{16}H_{12}NaO_2, M+Na]^+$: 259.0730; found: 259.0731.

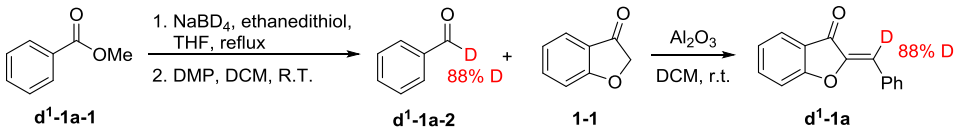
(*Z*)-2-Benzylidene-6-((10-((*tert*-butyldimethylsilyl)oxy)decyl)oxy)benzofuran-3(2*H*)-one (1t)



1t

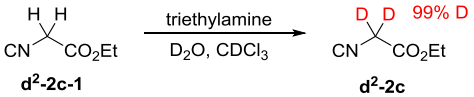
90% yield, R_f = 0.6, (silica gel, petroleum ether:EtOAc = 10:1), white solid, **M.P.** 58-59 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.88 (d, *J* = 7.8 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 6.80 (s, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 4.05 (t, *J* = 6.5 Hz, 2H), 3.59 (t, *J* = 6.6 Hz, 2H), 1.86 – 1.79 (m, 2H), 1.47 (dt, *J* = 15.2, 6.6 Hz, 4H), 1.40 – 1.25 (m, 10H), 0.88 (s, 9H), 0.04 (s, 6H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 183.07, 168.63, 167.09, 147.89, 132.46, 131.29, 129.55, 128.83, 125.78, 114.54, 112.66, 111.74, 96.95, 68.98, 63.31, 32.86, 29.53, 29.47, 29.41, 29.29, 28.91, 25.98, 25.92, 25.78, 18.38, -5.26. **HRMS** (ESI): m/z calcd. for $[C_{31}H_{45}O_4Si, M+H]^+$: 509.3082; found: 509.3079.

IV. Preparetion of d^1-1a and d^2-2c



Procedure:[10] To a flame-dried reaction tube equipped with a condenser was added $NaBD_4$ 126.0 mg (3.0 equiv.) and 10 mL anhydrous THF, then 1,2-ethanedithiol 376.0 mg (4.0 equiv.) and methyl benzoate 136.0 mg (1.0 equiv.) were added sequentially, then this mixture was refluxed at 80 °C overnight. After the reaction

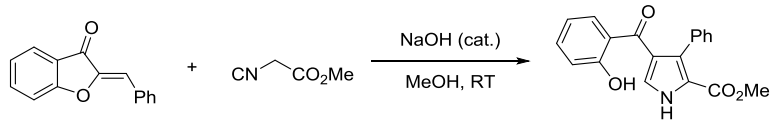
completion, qunched with 10 mL saturated NH_4Cl solution, and the aqueous phase was extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over sodium sulfate. The solvent was evaporated, and the residue was purified by a flash silica gel column chromatography (eluent: PE/EtOAc = 5:1) to give *d*-benzyl alcohol in 95% yield. The product was then dissolved in a 10 ml flask with 3 mL DCM, 2.5 equivalents of Dess-Martin periodinane was added and the reaction was stirred at r.t. for 5 hrs. After reaction completion, sodium thiosulfate aqueous solution was added to quench the reaction, the aqueous layer was extracted with CH_2Cl_2 (10 mL×3), and then the organic layers were combined, dried over sodium sulfate, and washed with saturated aq. $NaHCO_3$ (10 mL). Flash column chromatography (silica gel, PE/EtOAc = 50:1) yielded *d*-benzaldehyde **d^1-1a-2** in 90% yield with 88% deuterium labeling. To a round-bottom flask was added the obtained aldehyde and 5.0 equivalents of Al_2O_3 (basic), dissovled in 5.0 mL DCM, then the benzofuranone **1-1** (1.0 equiv.) was added, and the mixture was stirred at r.t.. After 10 h the reaction was diluted with CH_2Cl_2 and filtered through a short pad of celite and washed with CH_2Cl_2, the solvent was concentrated and the residue was purified by flash column chromatography (silica gel, PE/EtOAc = 20:1) to give product **d^1-1a** in 90% yield with 88% deuterium labeling. R_f = 0.3, (silica gel, petroleum ether:EtOAc = 20:1), pale yellow solid, **M.P.** 105-107 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.93 – 7.91 (m, 2H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.65 (dd, *J* = 11.3, 4.3 Hz, 1H), 7.46 (dd, *J* = 11.4, 4.4 Hz, 2H), 7.39 (dd, *J* = 8.7, 5.8 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.89 (s, 0.12H); **^{13}C NMR** (101 MHz, Chloroform-d) δ184.78, 166.14, 146.84, 136.88, 132.23, 131.51, 129.89, 128.88, 124.65, 123.45, 121.63, 112.96, 112.93; **HRMS** (ESI): m/z calcd. for $[C1_5H_9DNaO_2, M+Na]^+$: 246.0636; found: 246.0629.



Procedure:[11] To 20 mL of deuterium oxide in a Schlenk tube, which was previously rinsed with deuterium oxide and dried, was added sequentially a solution of 1.1 mL (10 mmol) of **d^2-2c-1** in 10 mL of deuteriochloroform and 50 μL

triethylamine. The reaction mixture was stirred at room temperature, and the exchange reaction was monitored by the disappearance of the methylene group protons at 4.18 in the ^{1}H NMR spectrum. After the exchange reaction was complete, the organic phase was separated and then was stirred for an additional 1 h with 20 mL of fresh deuterium oxide. The aqueous phase was separated, and the organic phase was dried over anhydrous sodium sulfate. The solvent was removed in vacuo, and the residue was distilled, to give 0.87 g of a colorless liquid with 99% deuterium labeling of α protons. **^{1}H NMR** (400 MHz, Chloroform-d) δ 4.20 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 163.98, 160.86, 62.65, 43.25, 13.90.

V. Synthesis of Pyrrole Derivatives with Isocyanoacetate and Aurores

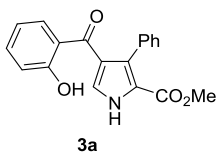


1a 2a 3a

General procedure: To a solution of aurone **1a** (22.2 mg, 0.1 mmol) in 1.0 mL MeOH was added isocyanoacetate **2a** (11.9 mg, 0.12 mmol), and then a solution of NaOH (1.0 M in MeOH) 20 μL (20 mol%) was added. The reaction was stirred at ambient temperature for 12h. After completion, the reaction was quenched with 20 μL HCl solution (1.0 N in MeOH), the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate, 5:1) to afford the product **3a** 31.8 mg.

VI. Characterization of Pyrroles

Methyl 4-(2-hydroxybenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3a)

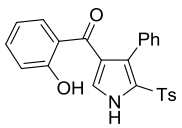


3a

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 53-54 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.89 (s, 1H), 9.70 (br, 1H), 7.64 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.42 –

7.38 (m, 1H), 7.35 – 7.26 (m, 6H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.78 – 6.74 (m, 1H), 3.75 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.54, 162.52, 161.23, 135.78, 132.80, 132.69, 132.08, 130.20, 127.57, 127.49, 126.28, 124.46, 120.41, 118.49, 117.98, 51.76. **HRMS** (ESI): m/z calcd. for $[C_{19}H_{15}NNaO_4, M+Na]^+$: 344.0893; found: 344.0894.

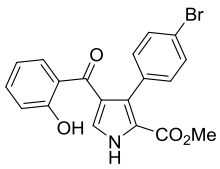
(2-Hydroxyphenyl)(4-phenyl-5-tosyl-1*H*-pyrrol-3-yl)methanone (3b)



3b

94% yield, R_f = 0.1, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 179-181 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.77 (s, 1H), 10.21 (br, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.27 (dt, *J* = 12.9, 6.7 Hz, 5H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.72 (t, *J* = 7.6 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.91, 162.47, 144.50, 137.72, 135.96, 132.70, 131.00, 130.48, 130.31, 129.46, 128.02, 127.76, 127.69, 127.21, 125.48, 124.82, 120.03, 118.56, 117.97, 21.54. **HRMS** (ESI): m/z calcd. for $[C_{24}H_{19}NNaO_4S, M+Na]^+$: 440.0927; found: 440.0926.

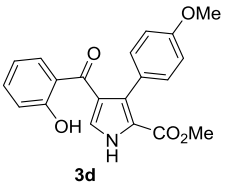
Methyl 3-(4-bromophenyl)-4-(2-hydroxybenzoyl)-1*H*-pyrrole-2-carboxylate (3c)



3c

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 80-81 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.81 (s, 1H), 9.62 (br, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 3H), 7.33 (d, *J* = 2.5 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 3.76 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.19, 162.56, 161.05, 135.97, 132.52, 131.86, 131.82, 130.83, 130.75, 126.55, 124.16, 121.79, 120.58, 120.36, 118.63, 118.15, 51.86. **HRMS** (ESI): m/z calcd. for $[C_{19}H_{14}BrNNaO_4, M+Na]^+$: 421.9998; found: 421.9998.

Methyl 4-(2-hydroxybenzoyl)-3-(4-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (3d)

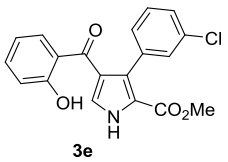


3d

91% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 65-67 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.93 (s, 1H), 9.68 (br, 1H), 7.64 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.40

(t, *J* = 7.8 Hz, 1H), 7.29 (dd, *J* = 9.7, 6.0 Hz, 3H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.76 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.79, 162.53, 161.30, 158.97, 135.78, 132.77, 132.00, 131.43, 126.54, 124.95, 124.22, 120.47, 120.23, 118.55, 117.97, 113.11, 55.13, 51.73. **HRMS** (ESI): m/z calcd. for $[C_{20}H_{17}NNaO_5, M+Na]^+$: 374.0999; found: 374.0998.

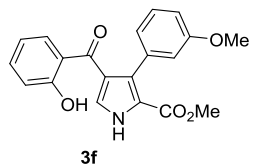
Methyl 3-(3-chlorophenyl)-4-(2-hydroxybenzoyl)-1*H*-pyrrole-2-carboxylate (3e)



3e

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 57-59 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.80 (s, 1H), 9.69 (br, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.27 – 7.18 (m, 3H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 3.76 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.00, 162.56, 160.96, 135.93, 134.67, 133.33, 132.45, 130.41, 130.27, 128.73, 128.45, 127.58, 126.39, 124.30, 120.78, 120.33, 118.57, 118.13, 51.89. **HRMS** (ESI): m/z calcd. for $[C_{19}H_{14}ClNNaO_4, M+Na]^+$: 378.0504; found: 378.0500.

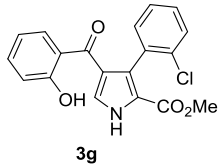
Methyl 4-(2-hydroxybenzoyl)-3-(3-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (3f)



3f

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 4:1), white solid, **M.P.** 50-52 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.89 (s, 1H), 9.77 (br, 1H), 7.62 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.30 (d, *J* = 3.2 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 6.95 – 6.89 (m, 3H), 6.82 – 6.80 (m, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.61, 162.46, 161.21, 158.80, 135.80, 134.08, 132.66, 131.73, 128.52, 126.21, 124.46, 122.81, 120.44, 120.39, 118.50, 117.94, 115.97, 113.11, 55.17, 51.78. **HRMS** (ESI): m/z calcd. for $[C_{20}H_{17}NNaO_5, M+Na]^+$: 374.0999; found: 374.1001.

Methyl 3-(2-chlorophenyl)-4-(2-hydroxybenzoyl)-1*H*-pyrrole-2-carboxylate (3g)

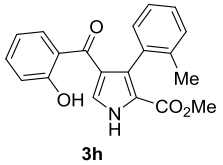


3g

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 163-165 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.67 (s, 1H), 9.67 (br, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 22.9, 14.9 Hz, 4H), 7.25 (s, 2H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H),

3.72 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.62, 162.32, 161.02, 135.64, 133.67, 132.54, 132.44, 131.98, 129.04, 128.90, 128.48, 126.40, 126.05, 124.59, 121.50, 120.25, 118.53, 117.99, 51.87. **HRMS** (ESI): m/z calcd. for [$C_{19}H_{14}ClNNaO_4$, M+Na]$^+$: 378.0504; found: 378.0501.

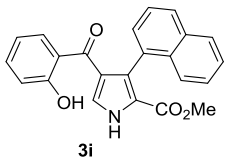
Methyl 4-(2-hydroxybenzoyl)-3-(*o*-tolyl)-1*H*-pyrrole-2-carboxylate (3h)



3h

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 65-66 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.75 (s, 1H), 9.61 (br, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 15.7, 8.0 Hz, 2H), 7.17 (d, *J* = 17.6 Hz, 4H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.81 (t, *J* = 7.3 Hz, 1H), 3.68 (s, 3H), 2.13 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.73, 162.37, 161.27, 136.58, 135.58, 133.08, 132.28, 131.50, 130.02, 129.38, 127.61, 126.67, 124.97, 124.36, 121.08, 120.43, 118.47, 118.07, 51.78, 20.19. **HRMS** (ESI): m/z calcd. for [$C_{20}H_{17}NNaO_4$, M+Na]$^+$: 358.1050; found: 358.1051.

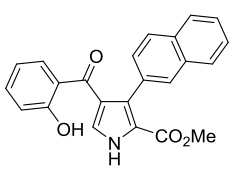
Methyl 4-(2-hydroxybenzoyl)-3-(naphthalen-1-yl)-1*H*-pyrrole-2-carboxylate (3i)



3i

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 57-59 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.62 (s, 1H), 9.94 (br, 1H), 7.82 (t, *J* = 8.8 Hz, 2H), 7.70 (t, *J* = 8.7 Hz, 2H), 7.44 (dd, *J* = 16.1, 6.6 Hz, 4H), 7.33 (dd, *J* = 21.2, 12.7 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 3.51 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.81, 162.19, 161.29, 135.55, 133.24, 132.56, 132.25, 131.23, 129.69, 128.28, 128.00, 127.94, 126.62, 125.89, 125.45, 125.41, 125.39, 124.88, 121.99, 120.36, 118.35, 117.89, 51.70. **HRMS** (ESI): m/z calcd. for [$C_{23}H_{17}NNaO_4$, M+Na]$^+$: 394.1050; found: 394.1047.

Methyl 4-(2-hydroxybenzoyl)-3-(naphthalen-2-yl)-1*H*-pyrrole-2-carboxylate (3j)

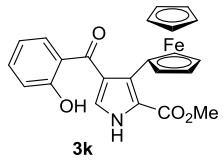


3j

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, **M.P.** 63-64 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.85 (s, 1H), 9.71 (br, 1H), 7.79 (dd, *J* = 13.7, 4.6 Hz, 4H), 7.71 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.38 (dd, *J* = 13.4, 6.1 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.76 (t, *J* = 7.6 Hz, 1H), 3.72 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.41, 162.55, 161.27, 135.80, 132.94, 132.63,

132.60, 132.03, 130.36, 129.17, 128.40, 128.10, 127.65, 126.95, 126.48, 125.96, 125.88, 124.51, 120.76, 120.47, 118.52, 118.05, 51.79. **HRMS** (ESI): m/z calcd. for $[C_{23}H_{17}NNaO_4, M+Na]^+$: 394.1050; found: 394.1049.

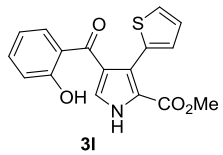
Methyl 4-(2-hydroxybenzoyl)-3-ferrocene-1*H*-pyrrole-2-carboxylate (3k)



3k

90% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 58-59 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.41 (s, 1H), 9.49 (br, 1H), 7.63 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.45 (dd, *J* = 11.3, 4.2 Hz, 1H), 7.11 (s, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 4.74 – 4.73 (m, 2H), 4.20 – 4.19 (m, 2H), 3.94 (s, 5H), 3.89 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 197.06, 162.97, 160.75, 136.18, 133.16, 129.73, 125.17, 125.03, 120.68, 120.46, 118.66, 118.19, 71.76, 69.33, 68.07, 51.72. **HRMS** (ESI): m/z calcd. for $[C_{23}H_{19}FeNNaO_4, M+Na]^+$: 452.0556; found: 452.0557.

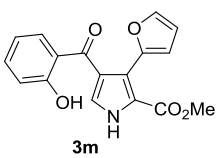
Methyl 4-(2-hydroxybenzoyl)-3-(thiophen-2-yl)-1*H*-pyrrole-2-carboxylate (3l)



3l

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 107-109 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.92 (s, 1H), 9.65 (br, 1H), 7.58 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.31 – 7.27 (m, 2H), 7.07 (dd, *J* = 3.5, 1.0 Hz, 1H), 6.96 – 6.94 (m, 2H), 6.76 – 6.72 (m, 1H), 3.81 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.65, 162.53, 160.87, 135.91, 132.86, 132.61, 129.06, 126.57, 126.49, 125.67, 125.26, 123.55, 120.97, 120.41, 118.54, 117.96, 51.87. **HRMS** (ESI): m/z calcd. for $[C_{17}H_{13}NNaO_4S, M+Na]^+$: 350.0457; found: 350.0458.

Methyl 3-(furan-2-yl)-4-(2-hydroxybenzoyl)-1*H*-pyrrole-2-carboxylate (3m)

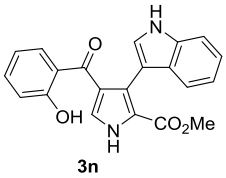


3m

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 48-50 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.04 (s, 1H), 9.55 (br, 1H), 7.50 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.42 – 7.38 (m, 1H), 7.29 (d, *J* = 3.2 Hz, 1H), 7.25 – 7.24 (m, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 3.4 Hz, 1H), 6.73 – 6.70 (m, 1H), 6.39 (dd, *J* = 3.3, 1.8 Hz, 1H), 3.89 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 196.11, 162.46, 160.53, 145.69, 142.28, 135.78, 132.40, 125.24, 124.00, 120.45, 120.31, 119.57, 118.57, 117.93, 111.42, 111.22, 51.94. **HRMS** (ESI): m/z calcd. for $[C_{17}H_{13}NNaO_5, M+Na]^+$: 334.0686;

found: 334.0685.

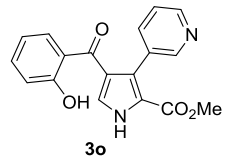
Methyl 4-(2-hydroxybenzoyl)-3-(1*H*-indol-3-yl)-1*H*-pyrrole-2-carboxylate (3n)



3n

95% yield, R_f = 0.3, (silica gel, petroleum ether:EtOAc = 2:1), orange solid, **M.P.** 232-233 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.45 (br, 1H), 11.37 (br, 1H), 11.04 (s, 1H), 7.56 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.39 (s, 1H), 7.37 – 7.36 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.1 Hz, 2H), 6.74 (t, *J* = 7.5 Hz, 1H), 3.60 (s, 3H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 194.74, 161.11, 160.33, 136.11, 134.92, 132.27, 129.13, 127.56, 126.44, 124.58, 124.13, 122.77, 120.93, 120.56, 119.44, 119.05, 118.97, 117.43, 111.77, 107.40, 51.49. **HRMS** (ESI): m/z calcd. for $[C_{21}H_{16}N_2NaO_4, M+Na]^+$: 383.1002; found: 383.1005.

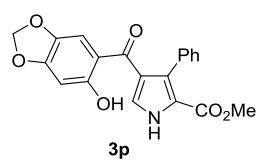
Methyl 4-(2-hydroxybenzoyl)-3-(pyridin-3-yl)-1*H*-pyrrole-2-carboxylate (3o)



3o

81% yield, R_f = 0.1, (silica gel, petroleum ether:EtOAc = 1:1), pale yellow solid, **M.P.** 88-90 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.77 (s, 1H), 10.56 (br, 1H), 8.59 (s, 1H), 8.53 (d, *J* = 4.3 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.41 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.28 (dd, *J* = 7.7, 5.0 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 3.72 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.77, 162.59, 160.90, 150.34, 147.88, 138.06, 135.97, 132.38, 129.46, 127.96, 126.99, 124.18, 122.55, 121.36, 120.26, 118.66, 118.21, 51.87. **HRMS** (ESI): m/z calcd. for $[C_{18}H_{14}N_2NaO_4, M+Na]^+$: 345.0846; found: 345.0843.

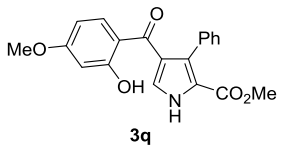
Methyl 4-(6-hydroxybenzo[*d*][1,3]dioxole-5-carbonyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3p)



3p

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 4:1), pale yellow solid, **M.P.** 172-173 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.82 (s, 1H), 9.60 (br, 1H), 7.34 – 7.27 (m, 6H), 6.95 (s, 1H), 6.42 (s, 1H), 5.90 (s, 2H), 3.75 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 193.88, 162.39, 161.23, 154.05, 140.01, 132.87, 131.63, 130.21, 127.59, 127.42, 125.12, 124.61, 120.07, 112.90, 109.52, 101.76, 98.48, 51.71. **HRMS** (ESI): m/z calcd. for $[C_{20}H_{15}NNaO_6, M+Na]^+$: 388.0792; found: 388.0787.

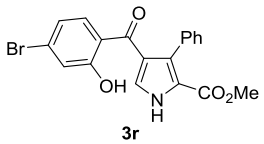
Methyl 4-(2-hydroxy-4-methoxybenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3q)



3q

93% yield, R_f = 0.3, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 61-63 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.59 (s, 1H), 9.84 (br, 1H), 7.53 (d, *J* = 8.9 Hz, 1H), 7.35 – 7.24 (m, 6H), 6.41 (d, *J* = 2.3 Hz, 1H), 6.28 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.27, 165.81, 165.58, 161.33, 134.50, 132.94, 131.79, 130.23, 127.56, 127.42, 125.62, 124.55, 120.10, 114.37, 107.06, 100.78, 55.55 51.70. **HRMS** (ESI): m/z calcd. for $[C_{20}H_{17}NNaO_5, M+Na]^+$: 374.0999; found: 374.1000.

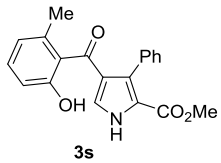
Methyl 4-(4-bromo-2-hydroxybenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3r)



3r

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 64-66 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.00 (s, 1H), 9.67 (br, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.32 – 7.30 (m, 6H), 7.12 (d, *J* = 1.9 Hz, 1H), 6.85 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.74 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.95, 162.95, 161.12, 133.57, 132.57, 131.88, 130.18, 130.14, 127.64, 127.62, 126.11, 124.29, 121.95, 121.16, 120.51, 119.17, 51.81. **HRMS** (ESI): m/z calcd. for $[C_{19}H_{14}BrNNaO_4, M+Na]^+$: 421.9998; found: 421.9996.

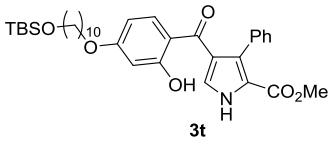
Methyl 4-(2-hydroxy-6-methylbenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3s)



3s

90% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 2:1), white solid, **M.P.** 62-63 °C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 9.71 (br, 1H), 8.60 (s, 1H), 7.30 – 7.20 (m, 6H), 7.09 (t, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.52 (d, *J* = 7.5 Hz, 1H), 3.70 (s, 3H), 2.14 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.86, 161.25, 157.45, 137.66, 132.54, 132.29, 131.42, 130.00, 127.56, 127.47, 127.38, 127.28, 124.99, 122.59, 120.77, 114.51, 51.71, 21.79; **HRMS** (ESI): m/z calcd. for $[C_{20}H_{17}NNaO_4, M+Na]^+$: 358.1050; found: 358.1053.

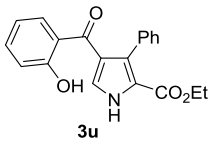
Methyl 4-(4-((10-((*tert*-butyldimethylsilyl)oxy)decyl)oxy)-2-hydroxybenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3t)



3t

91% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), colorless oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 12.56 (s, 1H), 9.61 (br, 2H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.35 – 7.26 (m, 6H), 6.38 (d, *J* = 2.3 Hz, 1H), 6.27 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.95 (t, *J* = 6.5 Hz, 2H), 3.74 (s, 3H), 3.60 (t, *J* = 6.6 Hz, 2H), 1.78 – 1.72 (m, 2H), 1.52 – 1.49 (m, 2H), 1.42 (dt, *J* = 14.2, 7.2 Hz, 2H), 1.34 – 1.26 (m, 10H), 0.90 (s, 9H), 0.05 (s, 6H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 194.13, 165.61, 165.44, 161.23, 134.40, 132.89, 131.72, 130.21, 127.55, 127.42, 125.30, 124.70, 120.09, 114.19, 107.45, 101.22, 68.36, 63.32, 51.67, 32.86, 29.53, 29.46, 29.40, 29.29, 28.93, 25.98, 25.91, 25.78, 18.37, -5.26. **HRMS** (ESI): m/z calcd. for $[C_{35}H_{49}NNaO_6Si, M+Na]^+$: 630.3221; found: 630.3218.

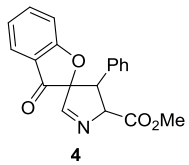
Ethyl 4-(2-hydroxybenzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3u)



3u

93% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P.** 53-55 ^{o}C. **^{1}H NMR** (400 MHz, Chloroform-d) δ 11.90 (s, 1H), 9.74 (br, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.35 – 7.28 (m, 6H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.76 (t, *J* = 7.6 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 195.49, 162.50, 160.90, 135.74, 132.94, 132.68, 131.95, 130.27, 127.45, 127.42, 126.23, 124.34, 120.85, 120.43, 118.49, 117.98, 60.88, 13.94. **HRMS** (ESI): m/z calcd. for $[C_{20}H_{17}NNaO_4, M+Na]^+$: 358.1050; found: 358.1041.

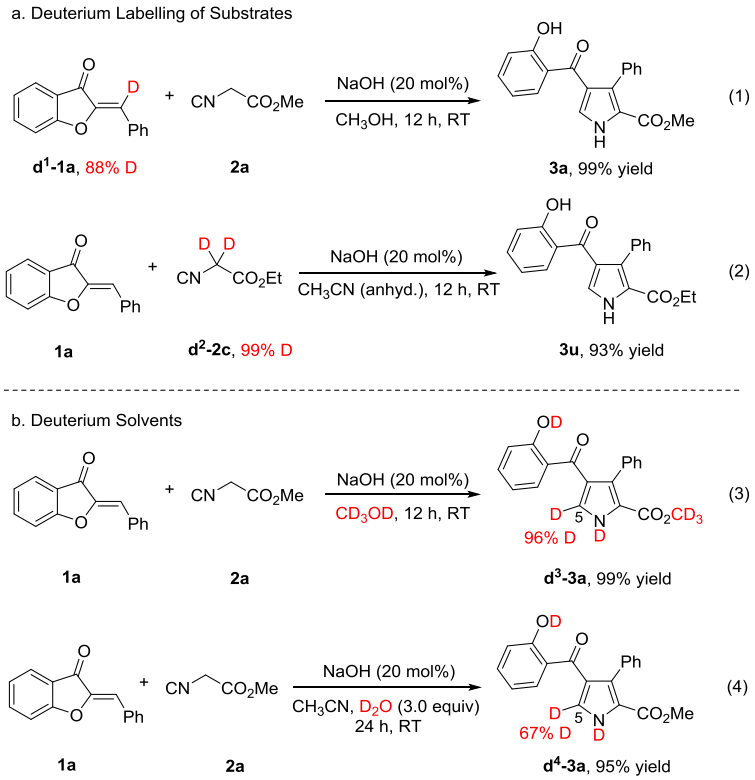
Mmethyl 3-oxo-4'-phenyl-4',5'-dihydro-3H-spiro[benzofuran-2,3'-pyrrole]-5'-carboxylate (4)



4

Colorless oil, R_f = 0.2 (silica gel, petroleum ether: EtOAc = 5:1). 31% yield. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.50 (dd, *J* = 9.2, 5.1 Hz, 2H), 7.19 – 7.16 (m, 5H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 5.22 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.12 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 197.47, 171.28, 170.06, 161.65, 138.72, 132.08, 129.21, 128.33, 127.93, 124.53, 122.78, 120.40, 113.27, 98.01, 79.65, 54.38, 52.73; **HRMS** (ESI): m/z calcd. for $[C_{19}H_{15}NNaO_4, M+Na]^+$: 344.0893; found: 344.0892.

VII. Deuterium Labelling Experiments



Procedure for eq. (1): To a solution of aurone **d^1-1a** (22.3 mg, 0.1 mmol) in 1.0 mL MeOH was added isocyanoacetate **2a** (11.9 mg, 0.12 mmol), then a solution of NaOH (1.0 M in MeOH) 20 μL (20 mol%) was added. The reaction was stirred at ambient temperature for 12h. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product **3a**.

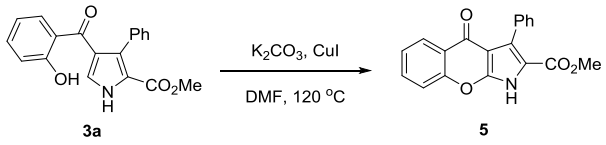
Procedure for eq. (2): To a flame-dried flask was added aurone **1a** (22.2 mg, 0.1 mmol), anhydrous MeCN 1.0 mL, and NaOH solid (0.8 mg, 20 mol%), then isocyanoacetate **d^2-2c** (13.8 mg, 0.12 mmol) was added dropwise, the reaction was stirred under argon atmosphere for 12h at room temperature. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product **3u**.

Procedure for eq. (3): To a solution of aurone **1a** (22.2 mg, 0.1 mmol) in 1.0 mL MeOD was added isocyanoacetate **2a** (11.9 mg, 0.12 mmol), and then NaOH solid (0.8 mg, 20 mol%) was added. The reaction was stirred at ambient temperature for

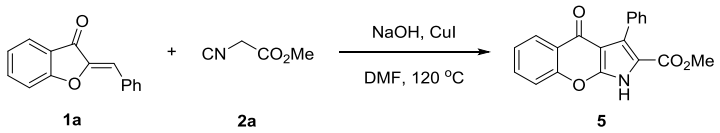
12h. After completion, monitoring the deuterium labeling percentage by NMR directly, the pure product was obtained by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1).

Procedure for eq. (4): To a flame-dried flask was added aurone **1a** (22.2 mg, 0.1 mmol), anhydrous MeCN 1.0 mL, and NaOH solid (0.8 mg, 20 mol%), then 3.0 equivalents of D_2O and isocyanoacetate **d^2-2c** (13.8 mg, 0.12 mmol) were added sequentially, the reaction was stirred under argon atmosphere for 12h at room temperature. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product **d^4-3a**.

VIII. Synthesis of Chromanone Fused Pyrrole 5



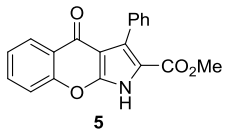
Procedure A:[12] To a 50 mL sealed tube was added the phenol derivative **3a** (642.6 mg, 2.0 mmol), potassium carbonate (276.4 mg, 2.0 mmol), CuI (38.1 mg, 0.2 mmol), DMF (10 mL) in sequence. This mixture was heated to 120 ^oC with stirring. After the reaction finished, the mixture was cooled down to ambient temperature, and concentrated in vacuo. This residue was diluted with 50 mL water, extracted with ethyl acetate (10 mL×3), washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give the crude product, which was further purified by flash chromatography on silica gel (hexanes/ethyl acetate, 2:1) to afford the product **5** 434.2 mg (68% yield).



Procedure B: To a 50mL sealed tube was added the aurone **1a** (88.8 mg, 0.4 mmol), sodium hydroxide (32.0 mg, 0.8 mmol), CuI (22.9 mg, 0.12 mmol), DMF (8 mL) and

isocyanoacetate **2a** (79.2 mg, 0.8 mmol) in sequence. This mixture was heated to 120 ^{o}C with stirring. After the reaction finished, the mixture was cooled down to ambient temperature, and concentrated in vacuo. This residue was diluted with water 30 mL, extracted with ethyl acetate (50 mL×3), washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give the crude product, which was further purified by flash chromatography on silica gel (hexanes/ethyl acetate = 2:1) to afford the product **5** 99.6 mg (78% yield).

Methyl 4-oxo-3-phenyl-1,4-dihydrochromeno[2,3-*b*]pyrrole-2-carboxylate (5)

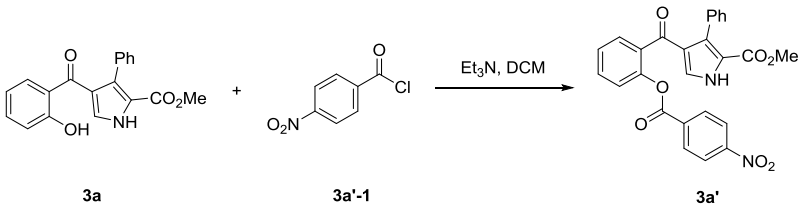


5

White solid, **M.P.** 263-265 ^{o}C, R_f = 0.2 (silica gel, petroleum ether: EtOAc = 2 : 1). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 13.34 (br, 1H), 8.03 (t, *J* = 28.8 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.46 – 7.42 (m, 3H), 7.34 (s, 3H), 3.65 (s, 3H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 172.78, 161.05, 153.99, 151.15, 134.05, 132.56, 131.33, 127.71, 127.65, 127.21, 126.41, 125.16, 123.30, 117.98, 114.73, 105.51, 51.87; **HRMS** (ESI): m/z calcd. for $[C_{19}H_{13}NNaO_4, M+Na]^+$: 342.0737; found: 342.0738.

IX. Preparation of the Single Crystal Compounds

Methyl 4-(2-((4-nitrobenzoyl)oxy)benzoyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (3a')



3a **3a'-1** **3a'**

To a solution of phenol derivative **3a** (160.5 mg, 0.5mmol) in dry DCM was added 4-nitrobenzoyl chloride (101.8 mg, 0.55 mmol) in 2 mL DCM dropwise, and then triethylamine (101.2 mg, 1.0 mmol) was added at room temperature. The reaction was stirred at room temperature until the phenol was completed, then quenched with aqueous NH_4Cl solution, the aqueous layer was extracted with CH_2Cl_2 (3×20 mL), the combined organic layers were washed with brine, dried over sodium sulfate and

concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford pure product **3a´** as pale yellow solid. **M.P.** 193-194 ^{o}C, R_f = 0.2 (silica gel, petroleum ether: EtOAc = 5 : 1). 81% yield. **^{1}H NMR** (400 MHz, Chloroform-d) δ 9.58 (br, 1H), 8.27 (d, *J* = 8.8 Hz, 2H), 8.19 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.43 (td, *J* = 7.9, 1.4 Hz, 1H), 7.31 (d, *J* = 3.5 Hz, 1H), 7.21 (ddd, *J* = 20.9, 9.7, 4.8 Hz, 7H), 3.67 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 188.66, 163.11, 161.08, 150.81, 147.95, 134.55, 132.57, 132.33, 131.93, 131.88, 131.23, 130.44, 130.25, 128.30, 127.36, 127.21, 125.91, 125.70, 123.57, 122.65, 120.58, 51.69; **HRMS** (ESI): m/z calcd. for [$C_{26}H_{18}N_2NaO_7$, M+Na]$^{+}$: 493.1006; found: 493.1005.

X. X-ray Crystallographic Analysis

The crystal **3a´** was prepared from a solution of ethyl acetate/hexane at ambient temperature.

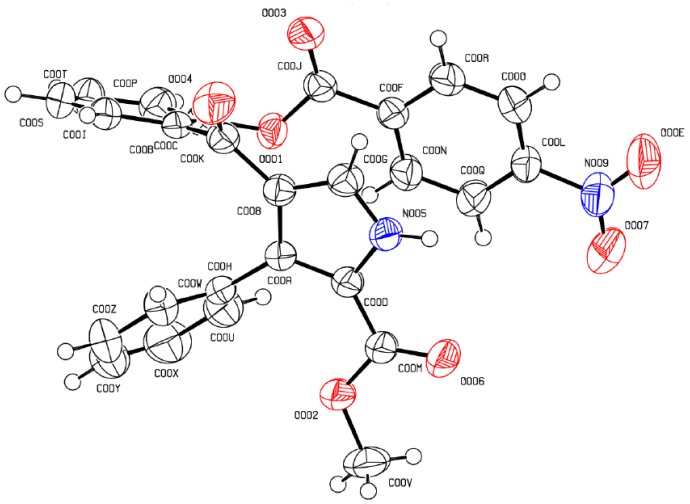


Figure 1. X-ray structure of **3a´**

Table 1. Crystal data and structure refinement for **$C_{26}H_{18}N_2O_7$** (CCDC 1833509)

Identification code	WZP
Empirical formula	$C_{26}H_{18}N_2O_7$
Formula weight	470.42
Temperature/K	293(2)

Crystal system	triclinic
Space group	P-1
a/Å	7.4307(5)
b/Å	10.8091(7)
c/Å	14.3220(8)
α/°	88.506(5)
β/°	89.846(5)
γ/°	83.022(5)
Volume/$Å^3$	1141.42(12)
Z	2
$\rho_{calc}g/cm^3$	1.369
μ/mm^{-1}	0.101
F(000)	488.0
Crystal size/mm^3	0.35 × 0.25 × 0.23
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.76 to 52.734
Index ranges	$-9 \leq h \leq 9$, $-13 \leq k \leq 12$, $-16 \leq l \leq 17$
Reflections collected	8044
Independent reflections	4665 [R_{int} = 0.0188, R_{sigma} = 0.0395]
Data/restraints/parameters	4665/0/317
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0525, wR_2 = 0.1201
Final R indexes [all data]	R_1 = 0.0776, wR_2 = 0.1387
Largest diff. peak/hole / e $Å^{-3}$	0.19/-0.25

XI. References

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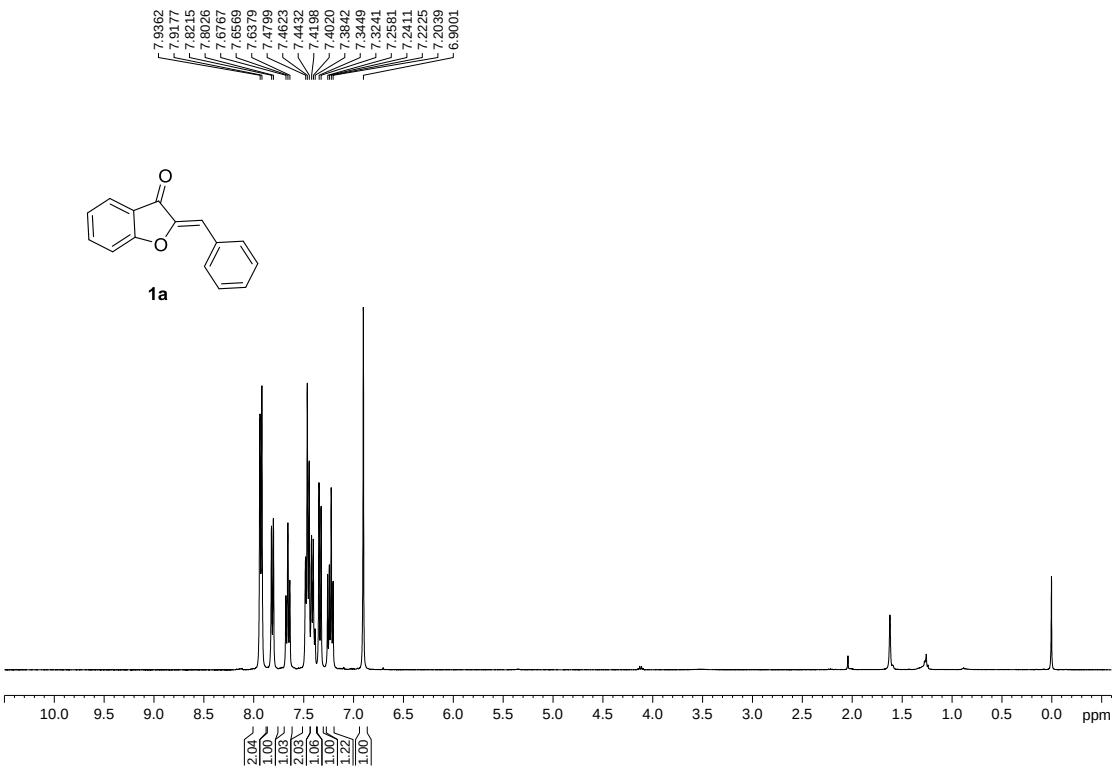
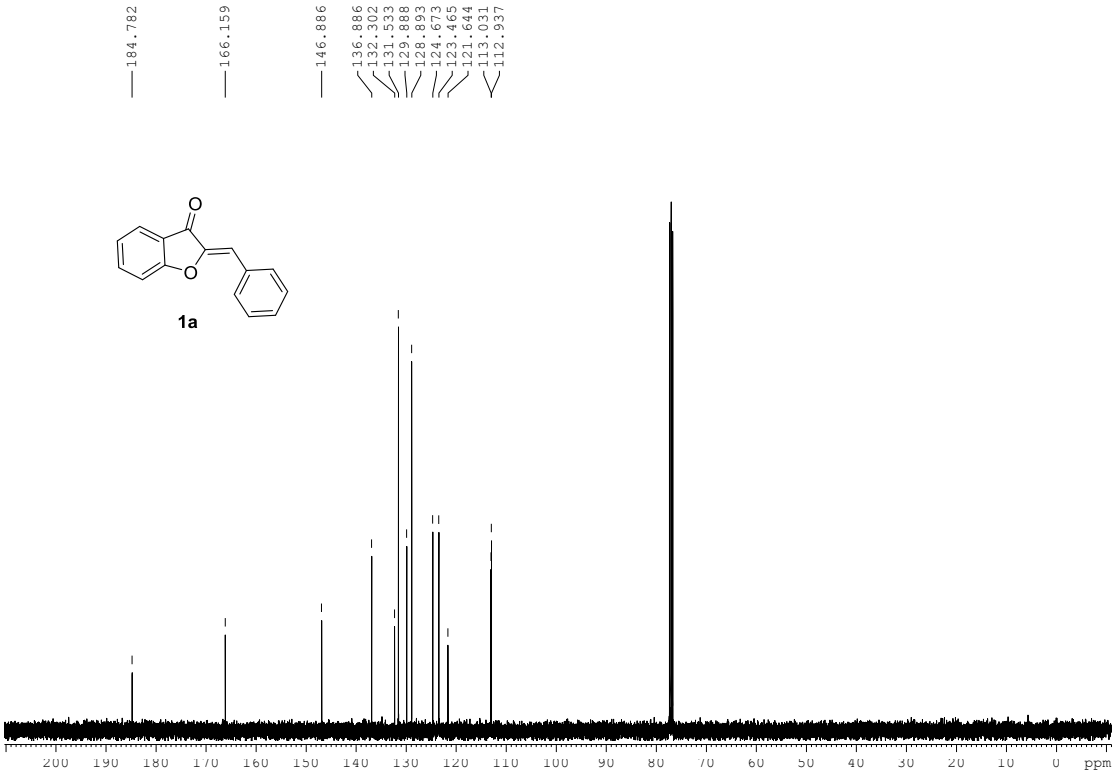
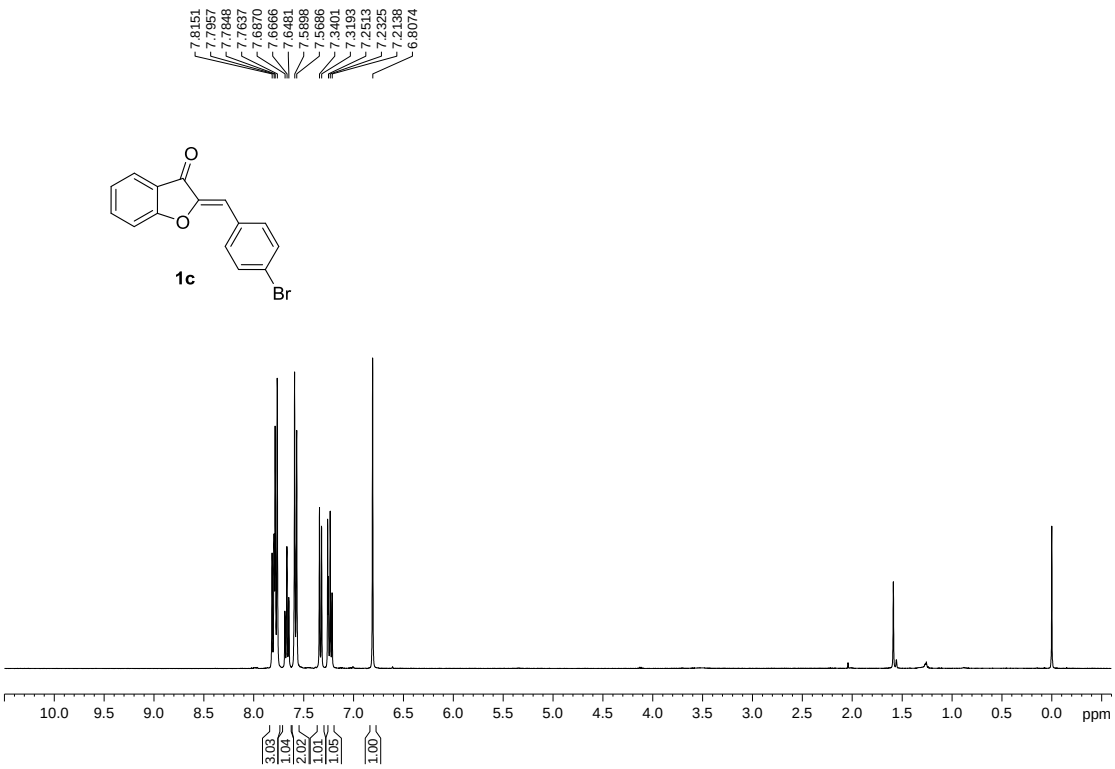
11. A. Togni, and S. D. Pastor, *J. Org. Chem.*, 1990, **55**, 1649-1664.

12. J. Sheng, B. Chao, H. Chen, and Y. Hu, *Org. Lett.*, **2013**, *15*, 4508-4511.

XII. NMR Spectra of the Products



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7.7637
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7.6666
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7.5898
7.5686
7.3401
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7.2513
7.2325
7.2138
6.8074
O
O
1c
Br
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 ppm
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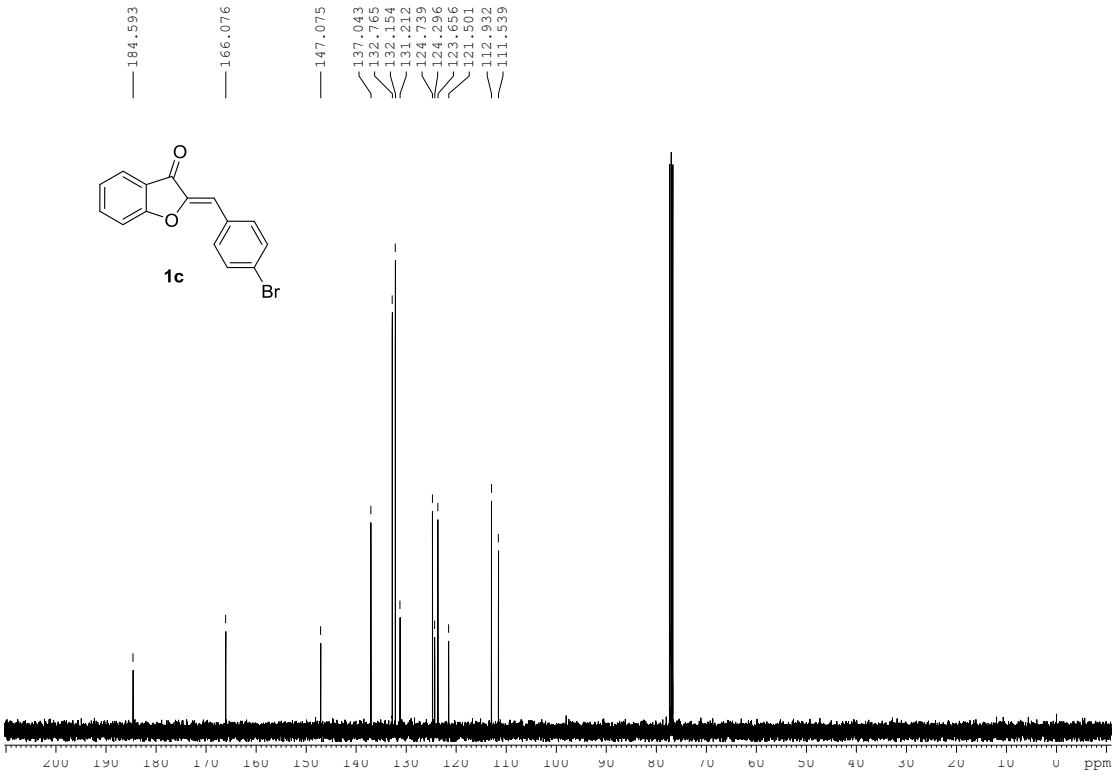
1.04
2.02
1.01
1.05
1.00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O
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1c
Br
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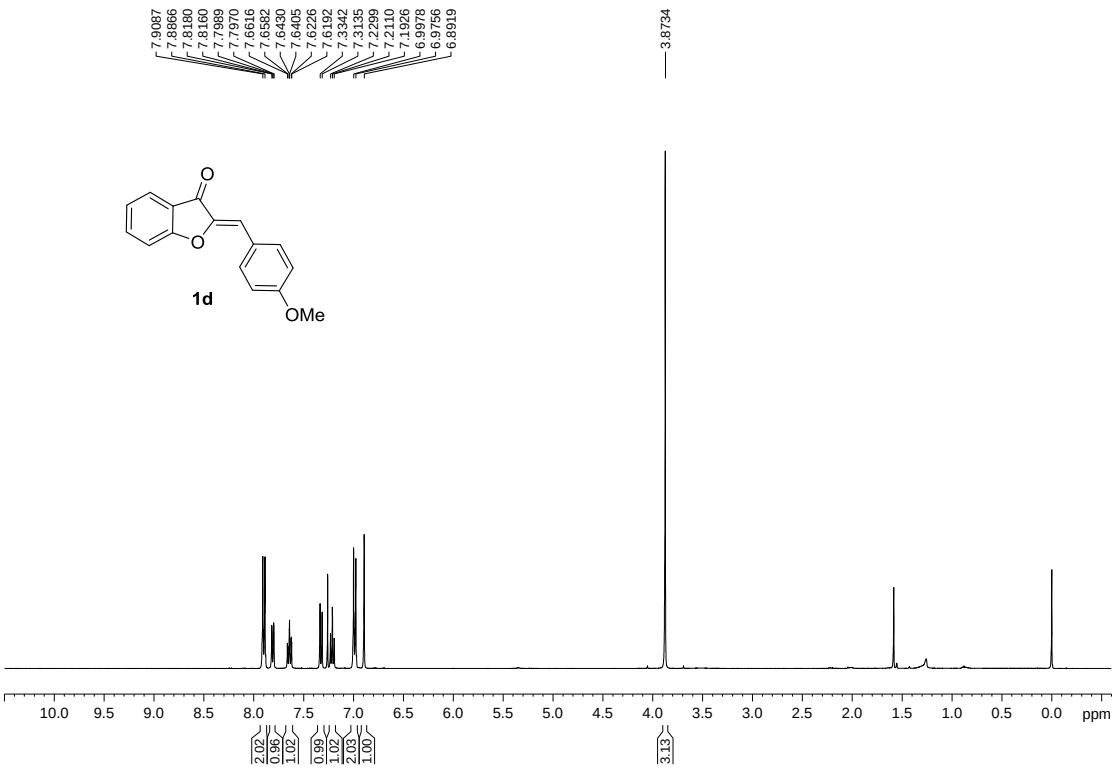
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7.6616
7.6582
7.6430
7.6405
7.6226
7.6192
7.3342
7.3135
7.2299
7.2110
7.1926
6.9978
6.9756
6.8919
3.8734
1d
OMe
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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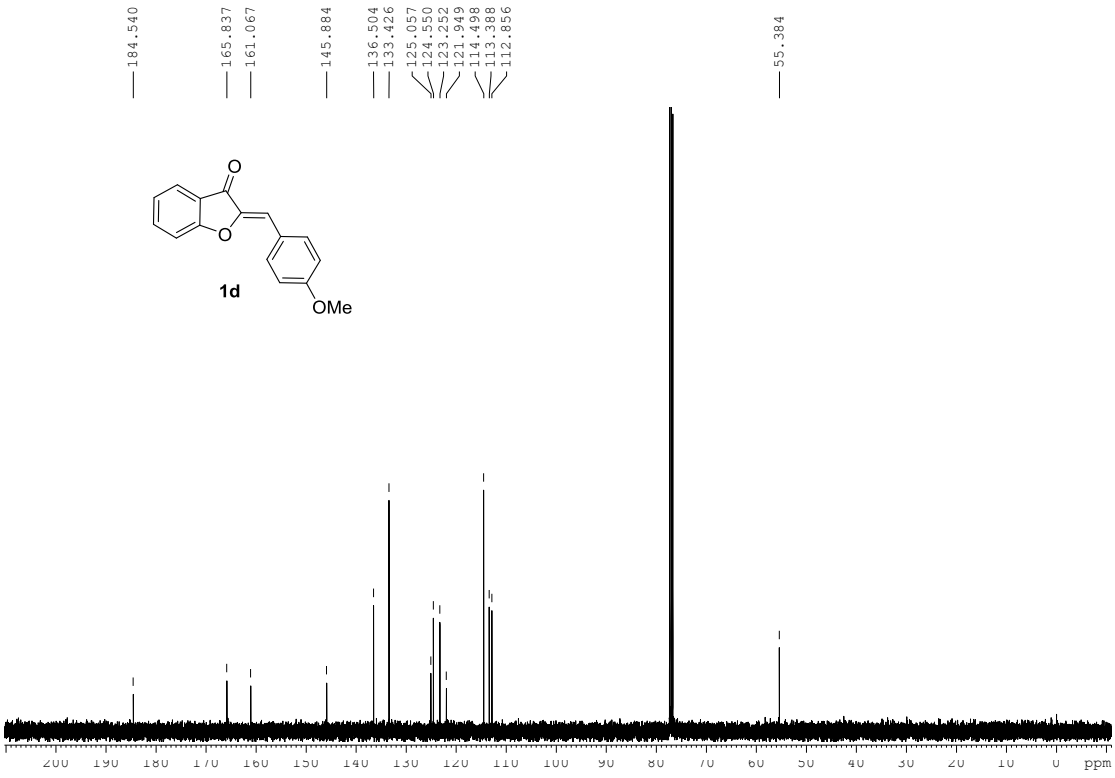
0.96
1.02
0.99
1.02
2.03
1.00
3.13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124.550
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55.384
1d
OMe
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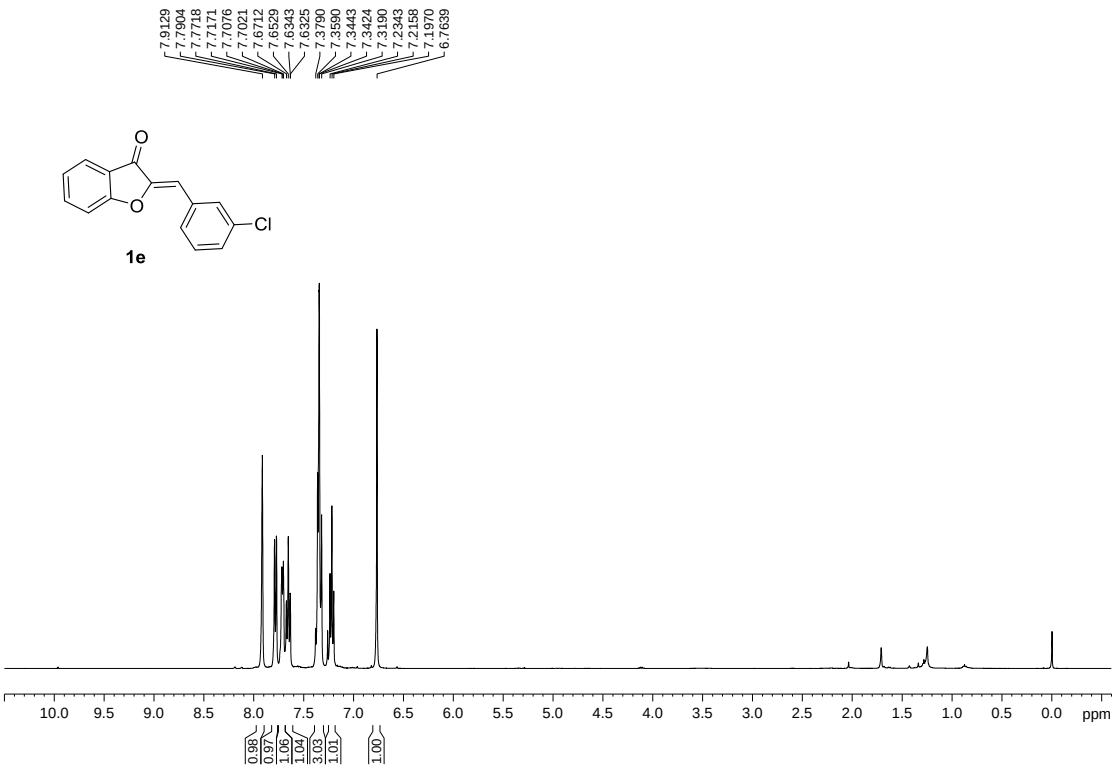
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7.6343
7.6325
7.3790
7.3590
7.3443
7.3424
7.3190
7.2343
7.2158
7.1970
6.7639
O
O
Cl
1e
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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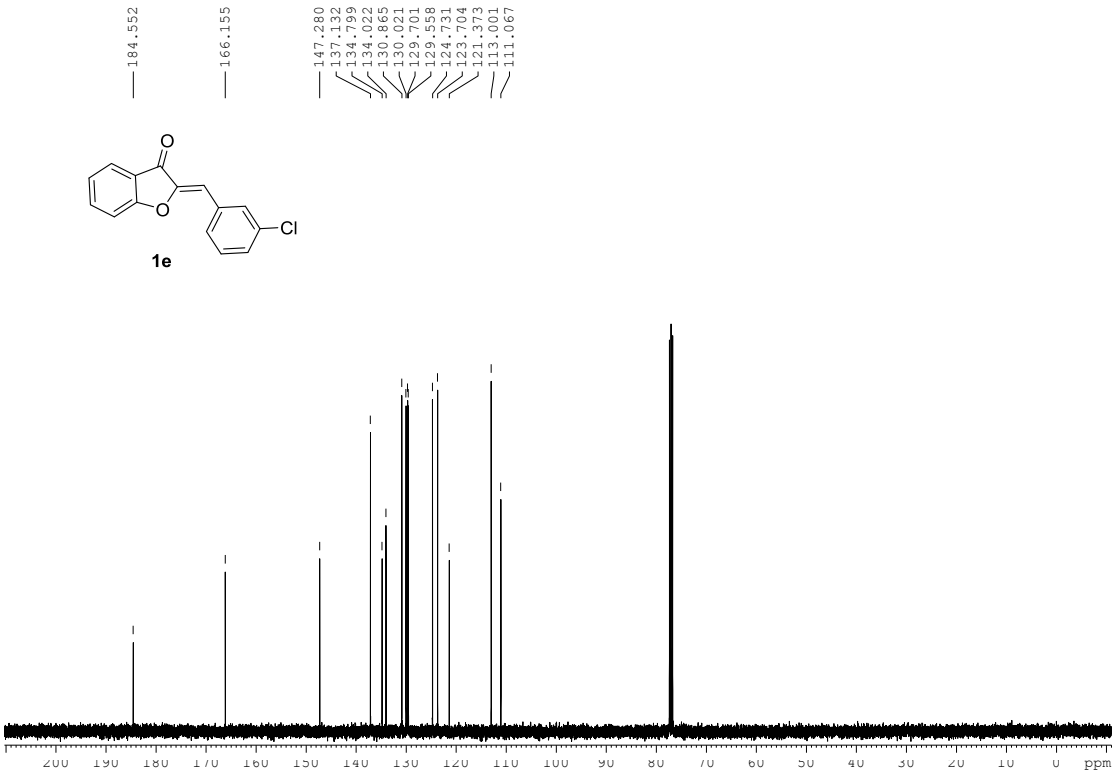
1.06
1.04
3.03
1.01
1.00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Cl
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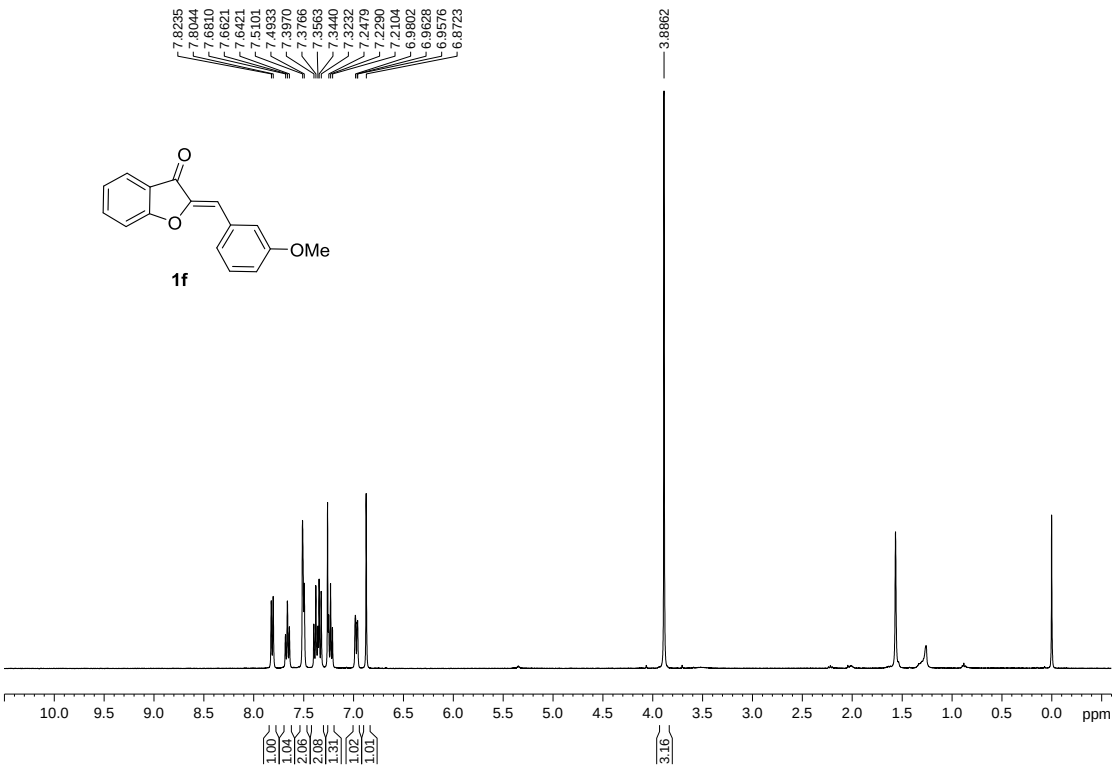
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7.3440
7.3232
7.2479
7.2290
7.2104
6.9802
6.9628
6.9576
6.8723
3.8862
O
O
OMe
1f
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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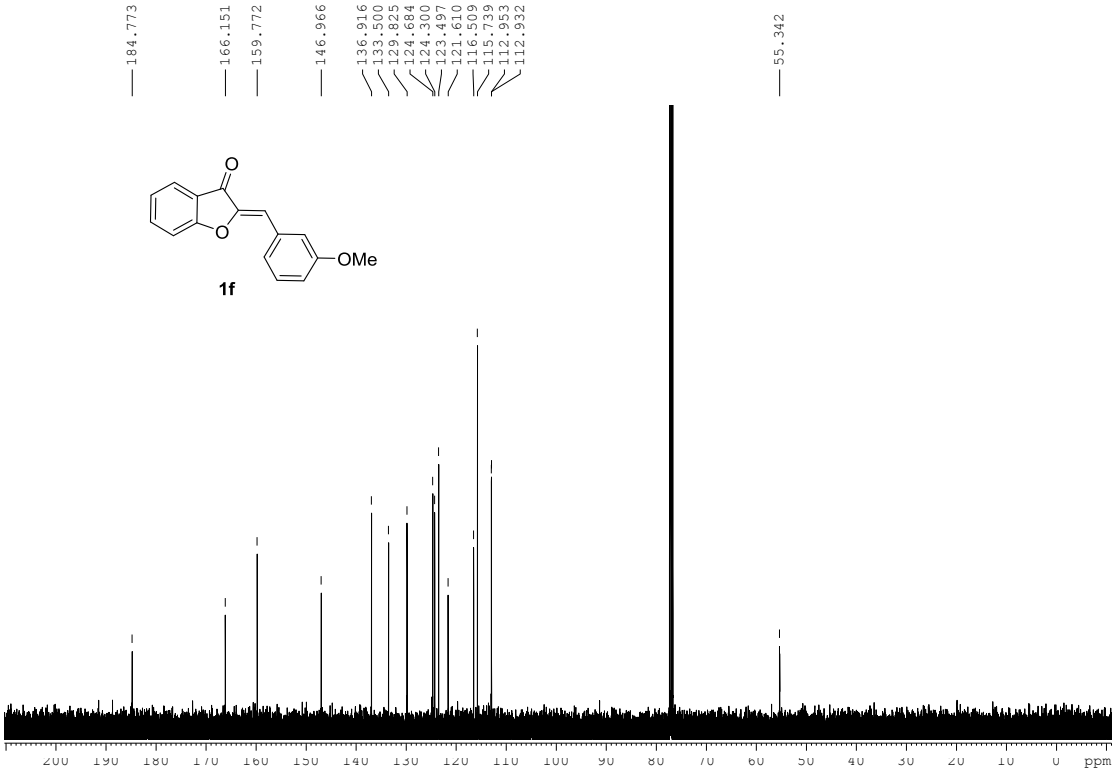
2.08
1.31
1.02
1.01
3.16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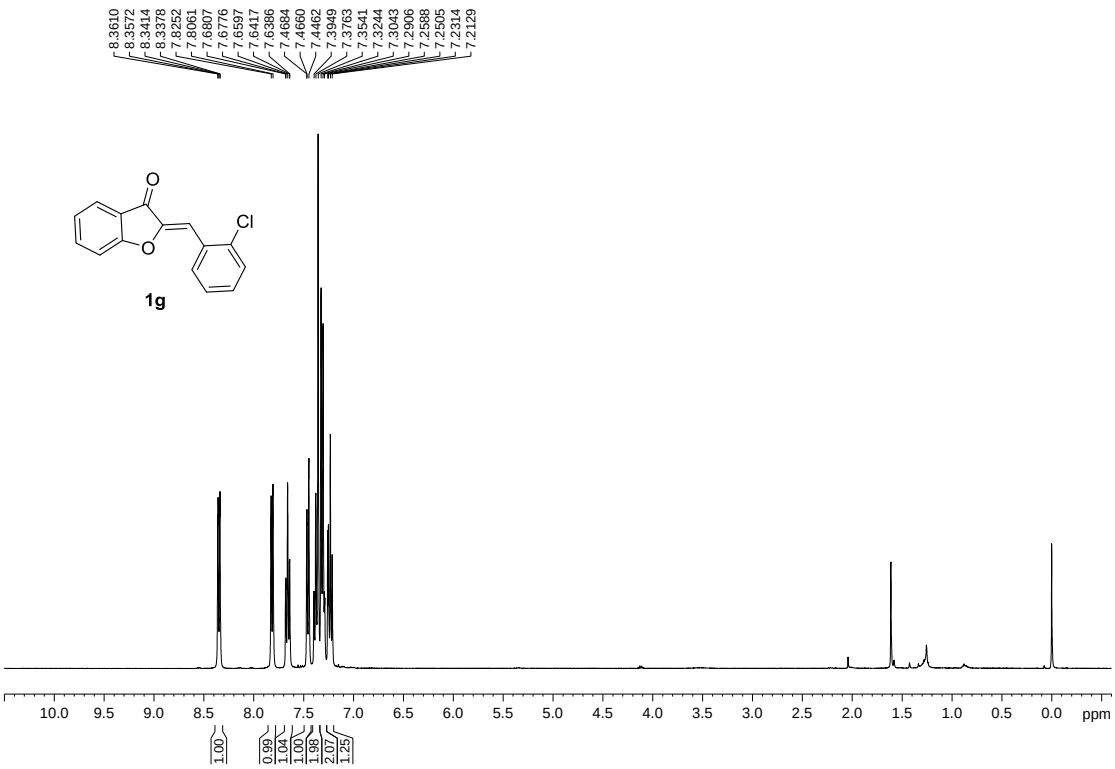
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7.4660
7.4462
7.3949
7.3763
7.3541
7.3244
7.3043
7.2906
7.2588
7.2505
7.2314
7.2129
O
O
Cl
1g
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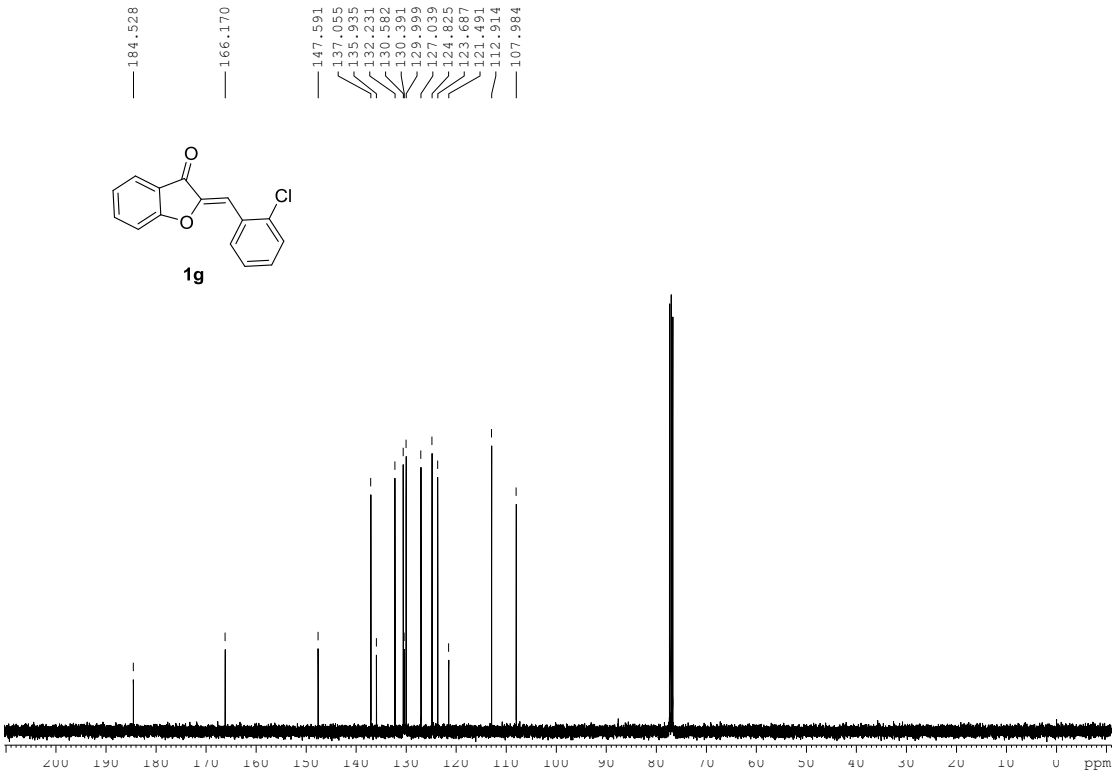
1.00
1.98
2.07
1.25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112.914
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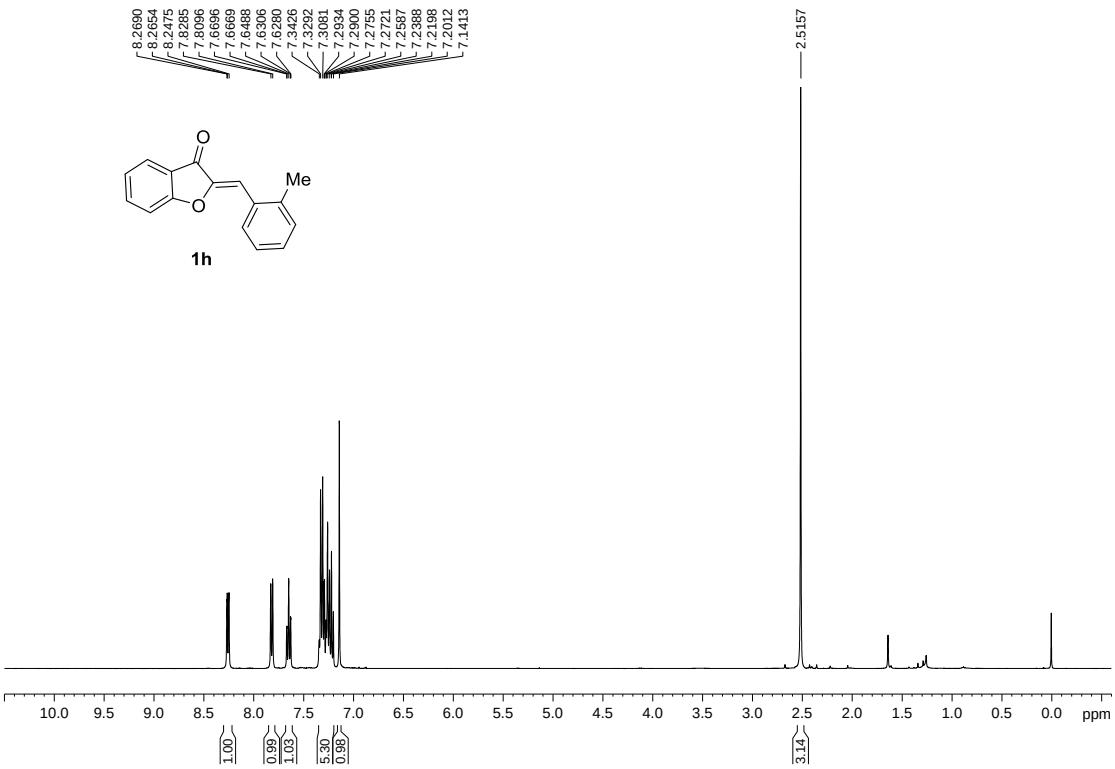
O
O
Cl
1g
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.2900
7.2755
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7.2587
7.2388
7.2198
7.2012
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O
Me
1h
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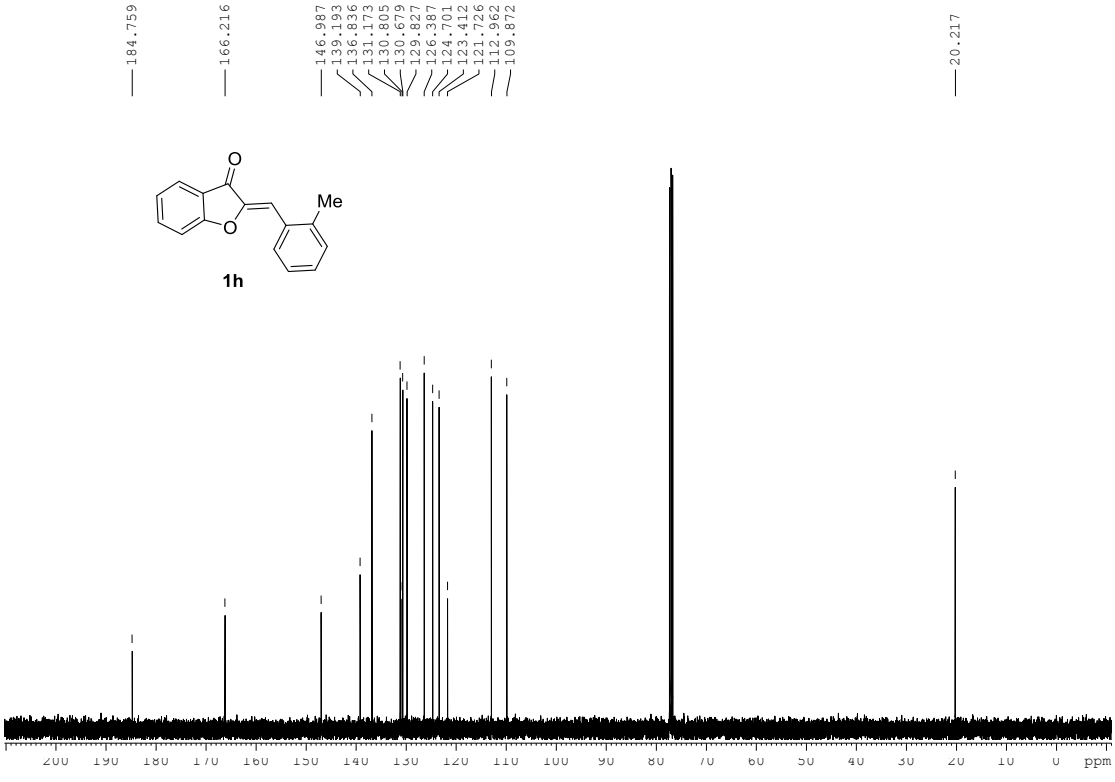
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O
Me
1h
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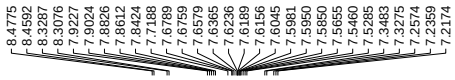
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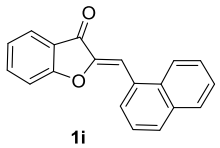
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O

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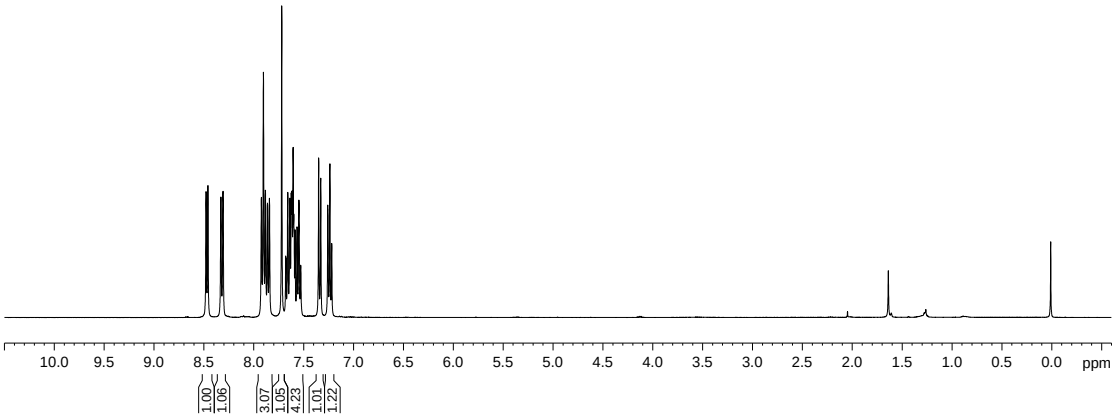
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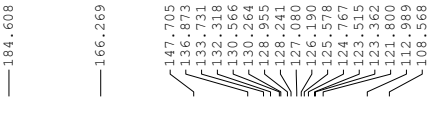
1.06
3.07
1.05
4.23
1.01
1.22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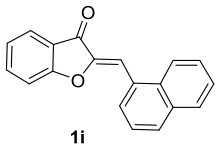
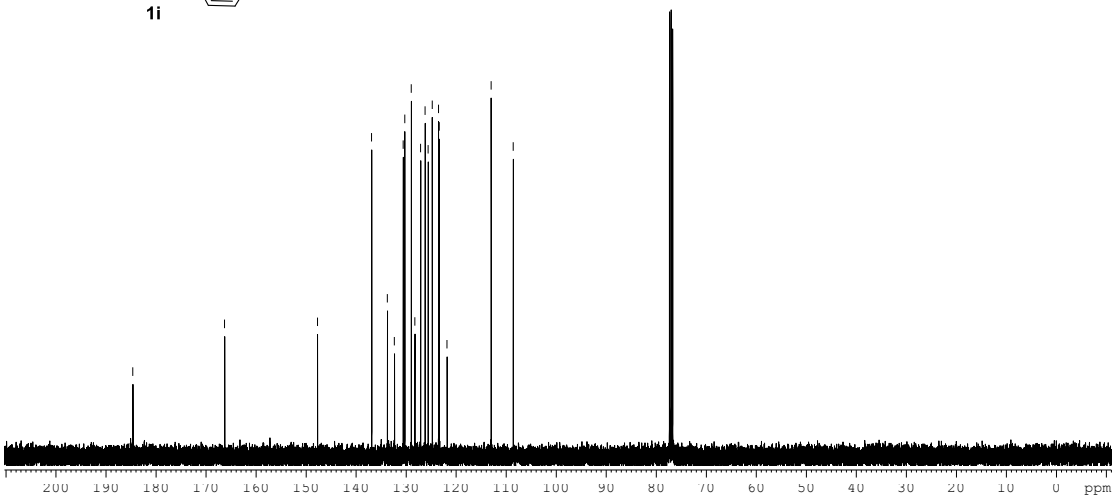

O
O

1i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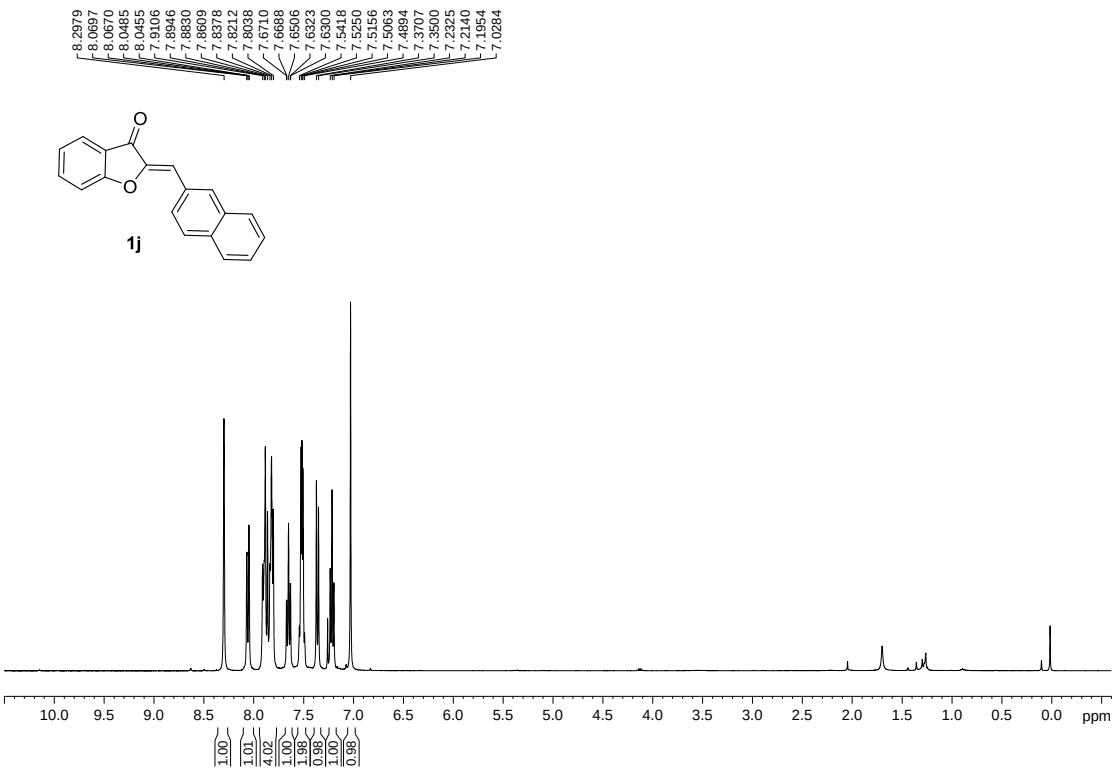
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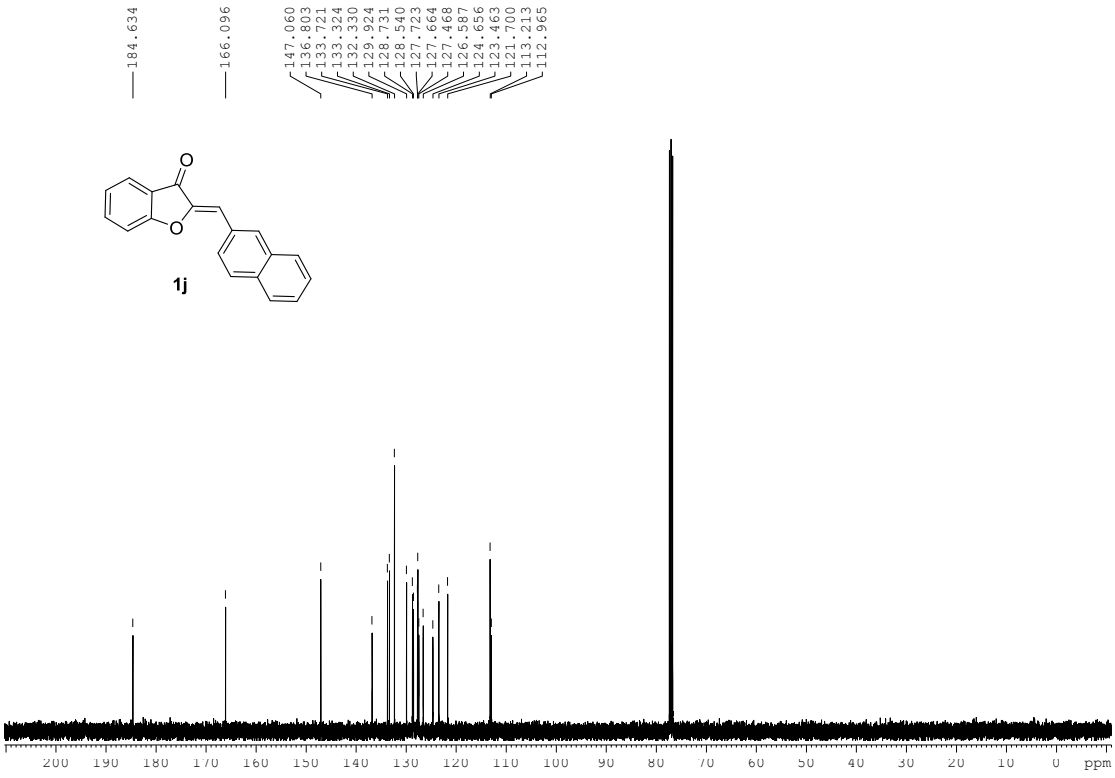
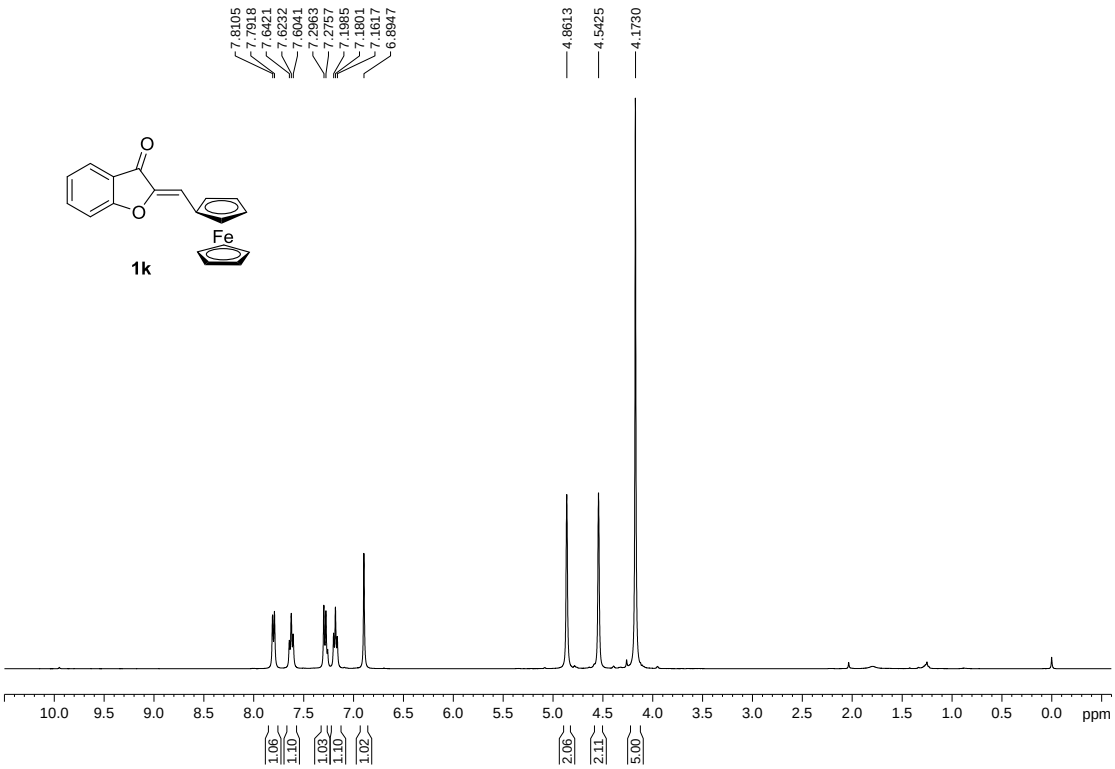
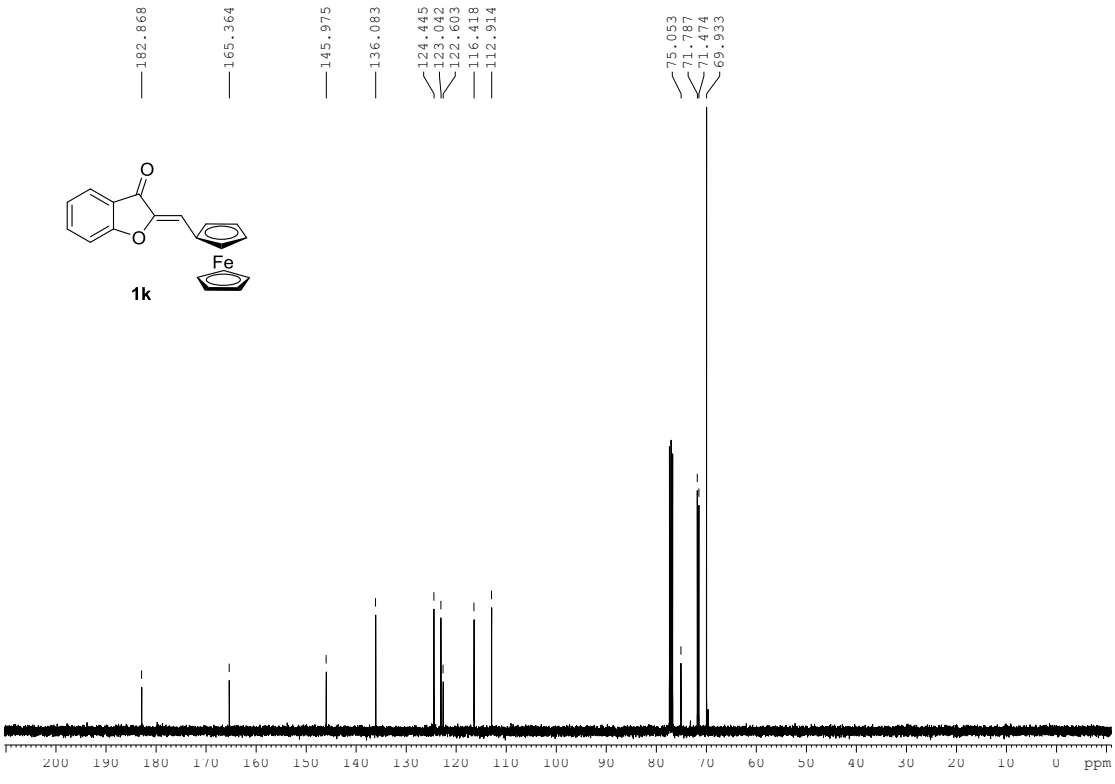
O
1j
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.01
4.02
1.00
1.98
0.98
1.00
0.98


184.634
166.096
147.060
136.803
133.721
133.324
132.330
129.924
128.731
128.540
127.723
127.664
127.468
126.587
124.656
123.463
121.700
113.213
112.965
O
O
1j
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.8105
7.7918
7.6421
7.6232
7.6041
7.2963
7.2757
7.1985
7.1801
7.1617
6.8947
4.8613
4.5425
4.1730
O
O
Fe
1k
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 ppm
1.06
1.10
1.03
1.10
1.02
2.06
2.11
5.00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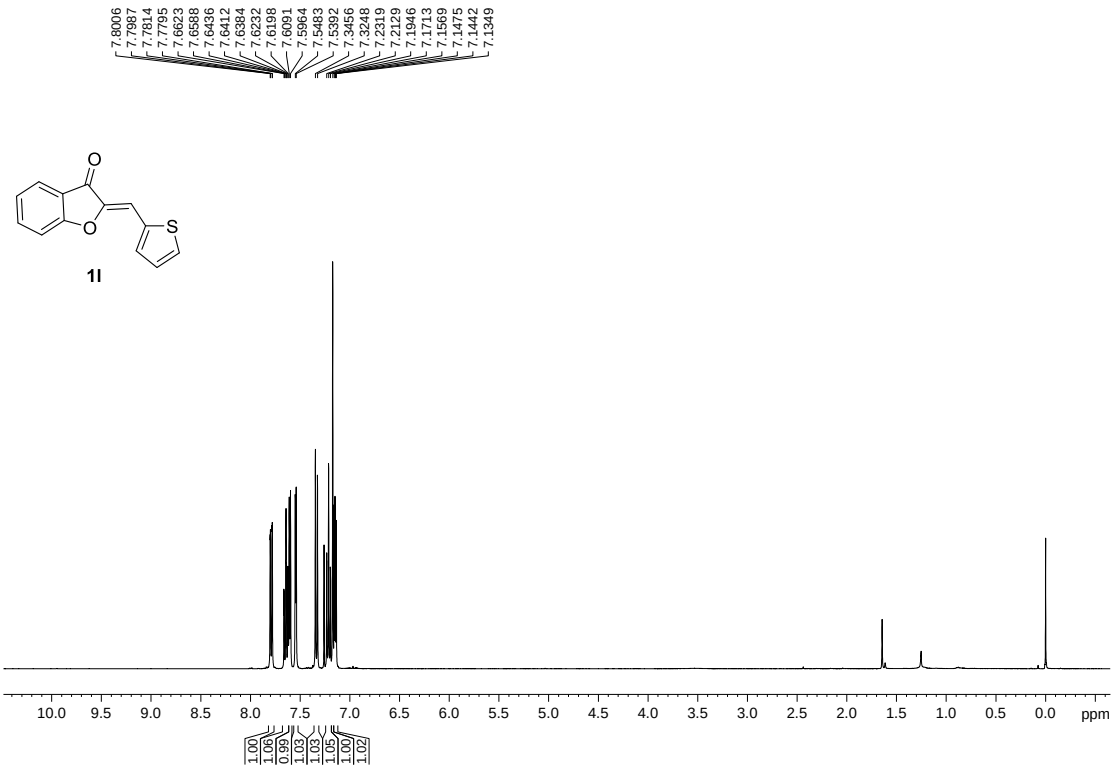
165.364
145.975
136.083
124.445
123.042
122.603
116.418
112.914
75.053
71.787
71.474
69.933
O
O
Fe
1k
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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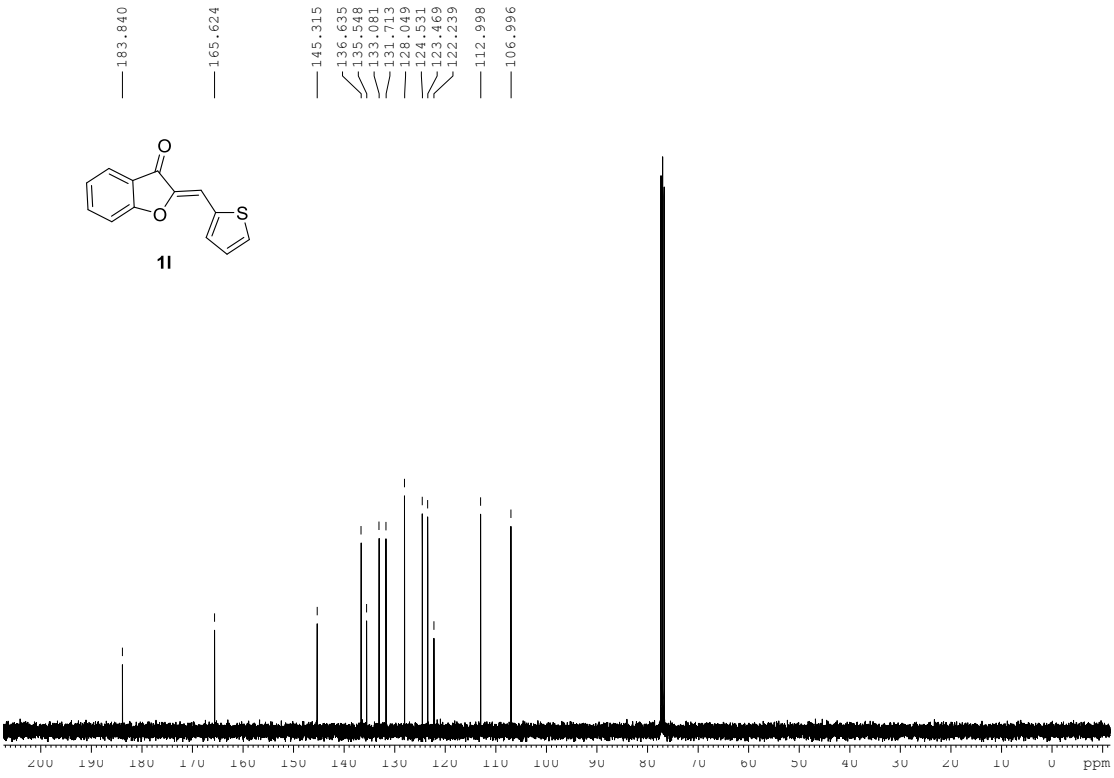
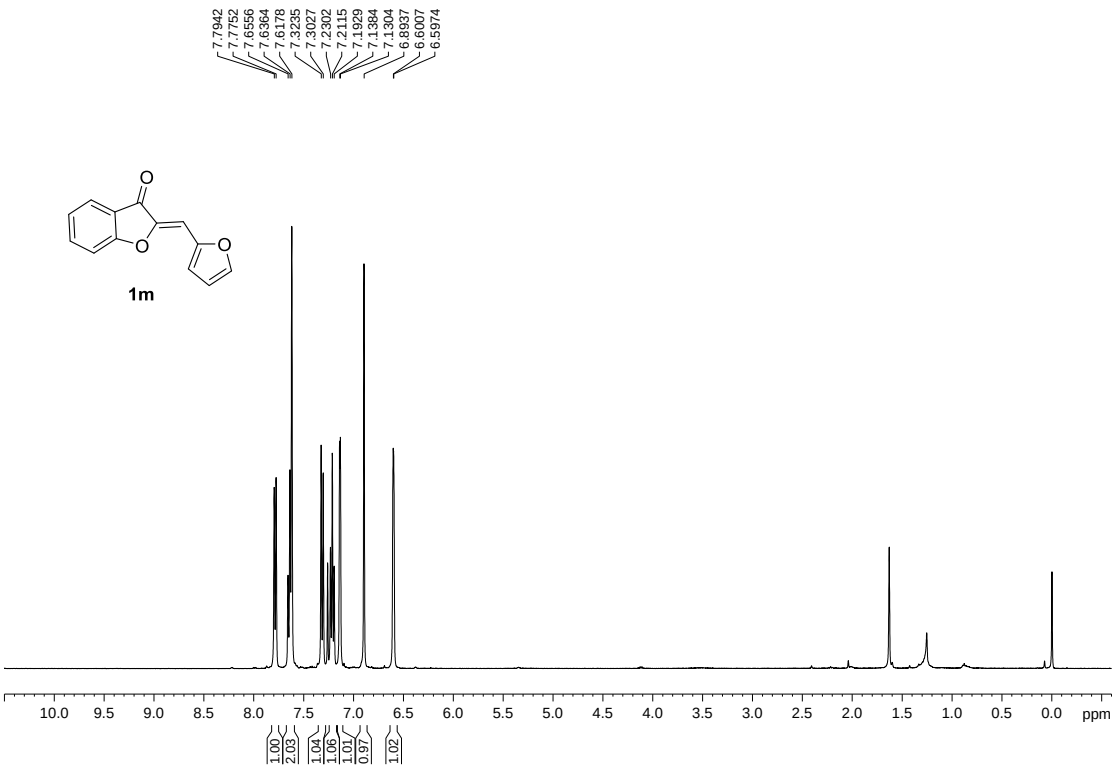
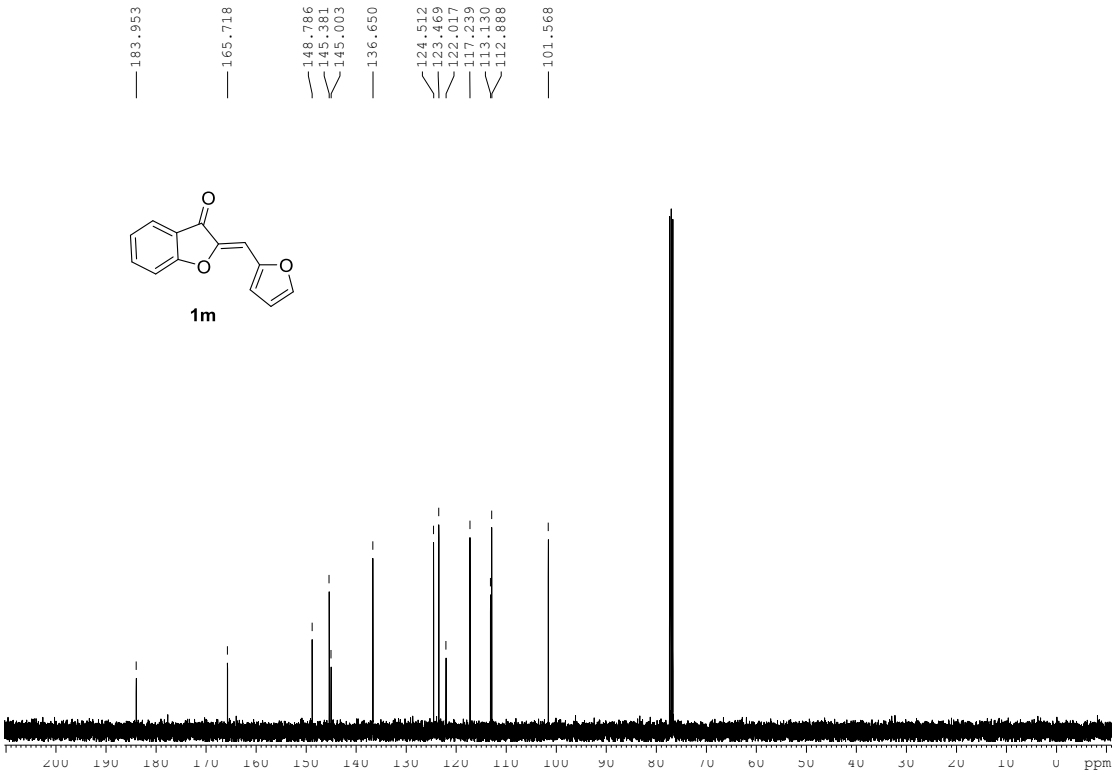
7.7987
7.7814
7.7795
7.6623
7.6588
7.6436
7.6412
7.6384
7.6232
7.6198
7.6091
7.5964
7.5483
7.5392
7.3456
7.3248
7.2319
7.2129
7.1946
7.1713
7.1569
7.1475
7.1442
7.1349
O
O
S
1l
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 1.06 0.99 1.03 1.03 1.05 1.00 1.02


183.840
165.624
145.315
136.635
135.548
133.081
131.713
128.049
124.531
123.469
122.239
112.998
106.996
O
O
S
1l
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.7942
7.7752
7.6556
7.6364
7.6178
7.3235
7.3027
7.2302
7.2115
7.1929
7.1384
7.1304
6.8937
6.6007
6.5974
1m
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 ppm
1.00
2.03
1.04
1.06
1.01
0.97
1.02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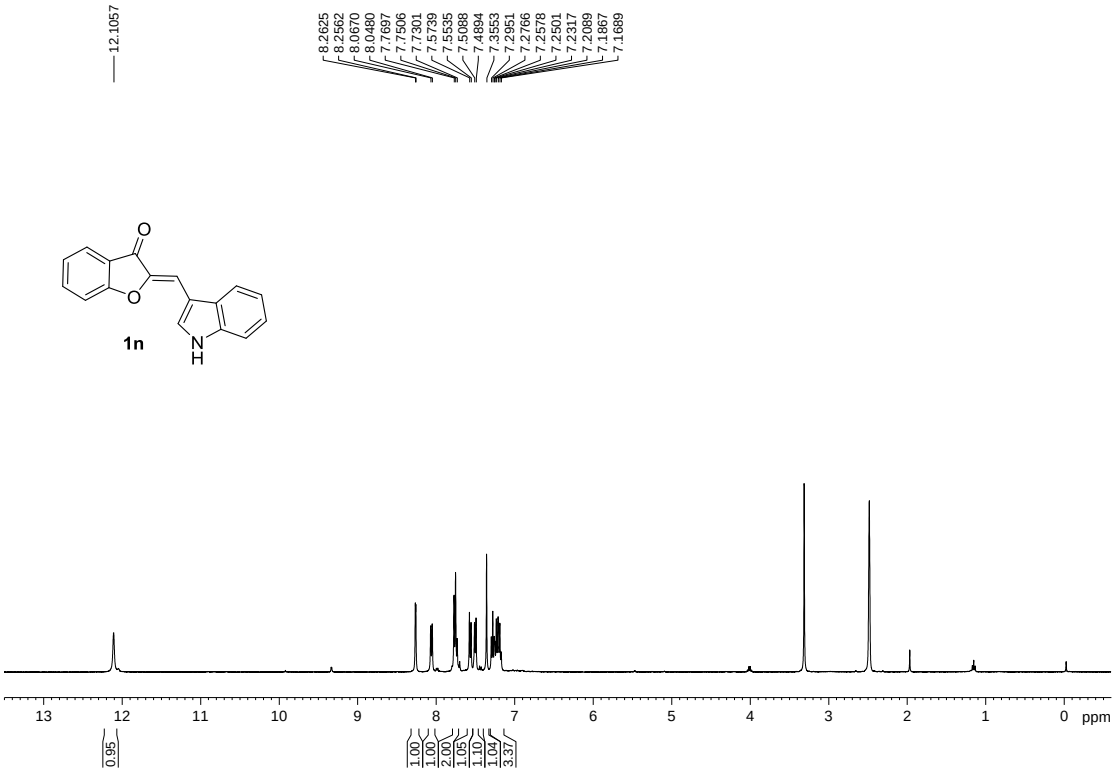
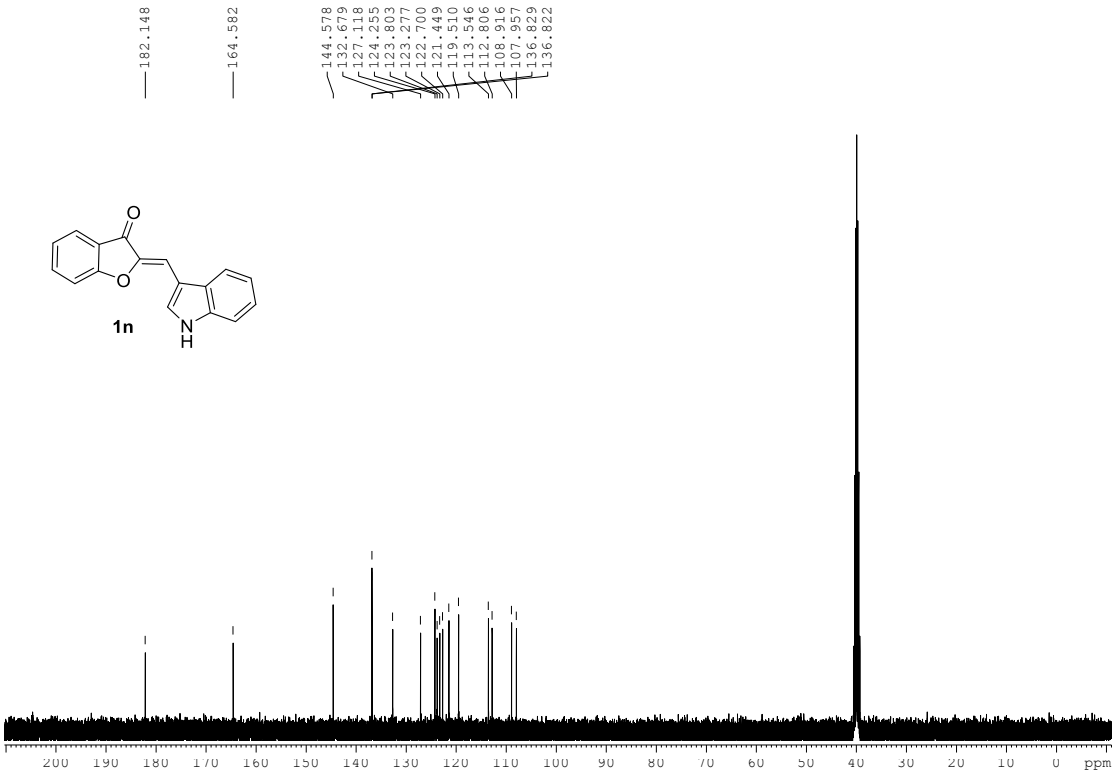
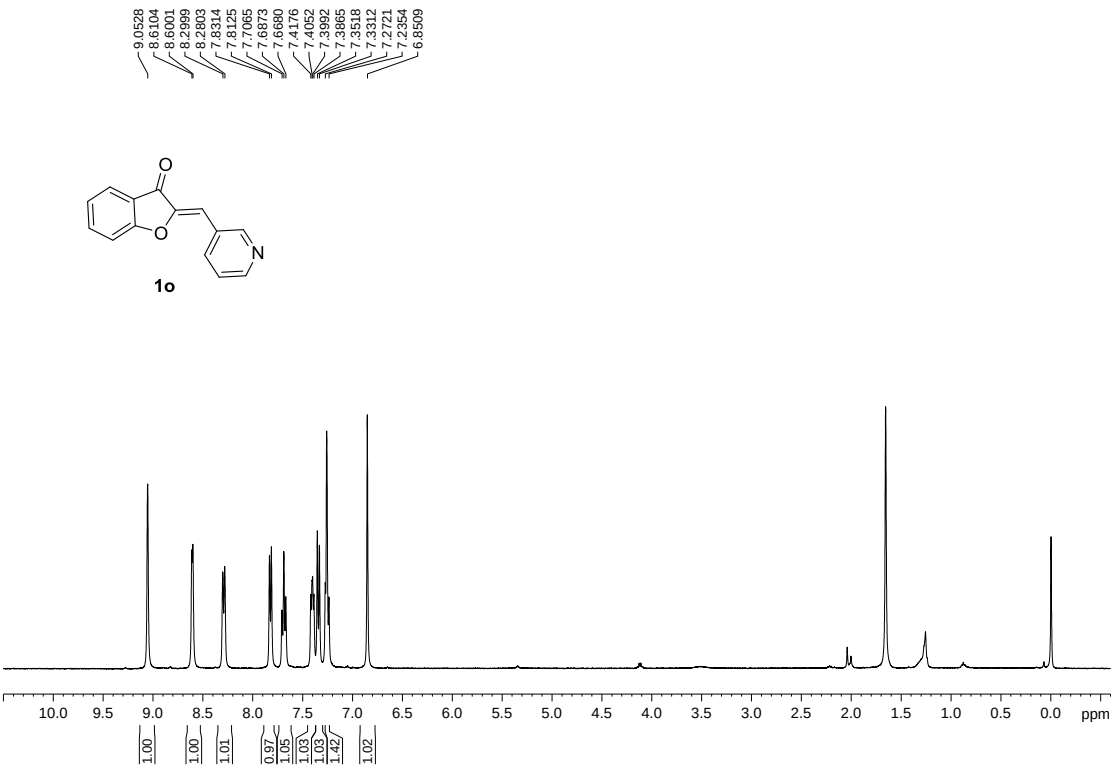
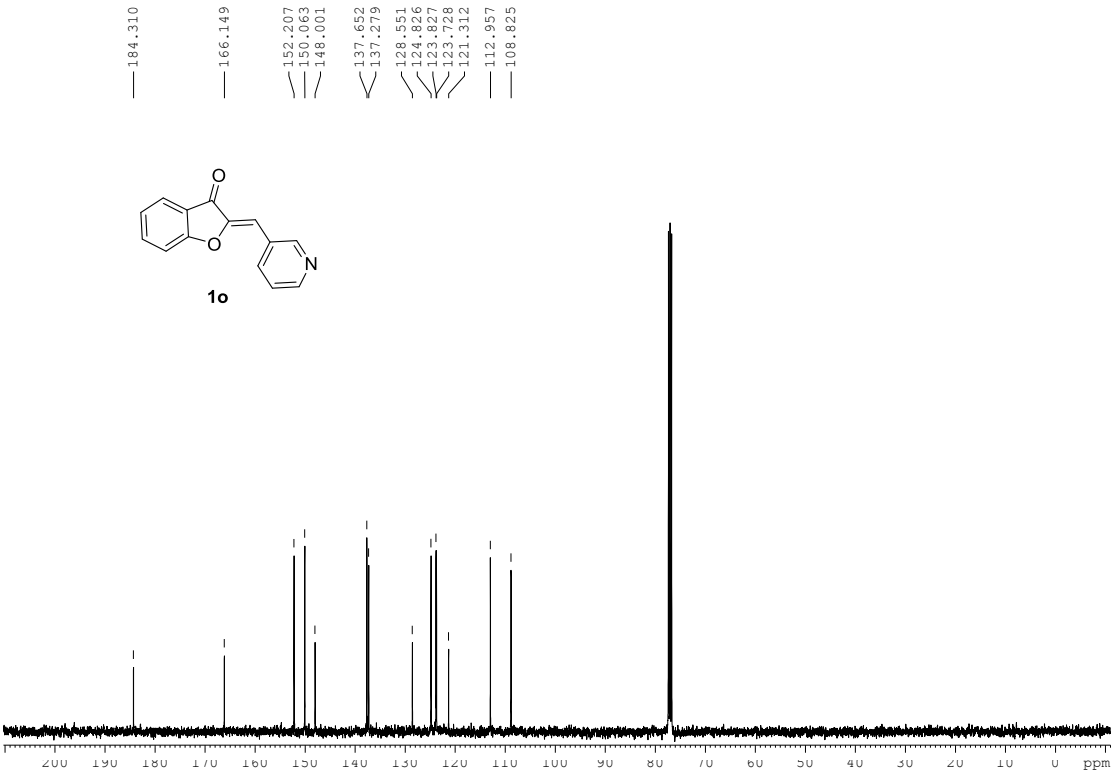
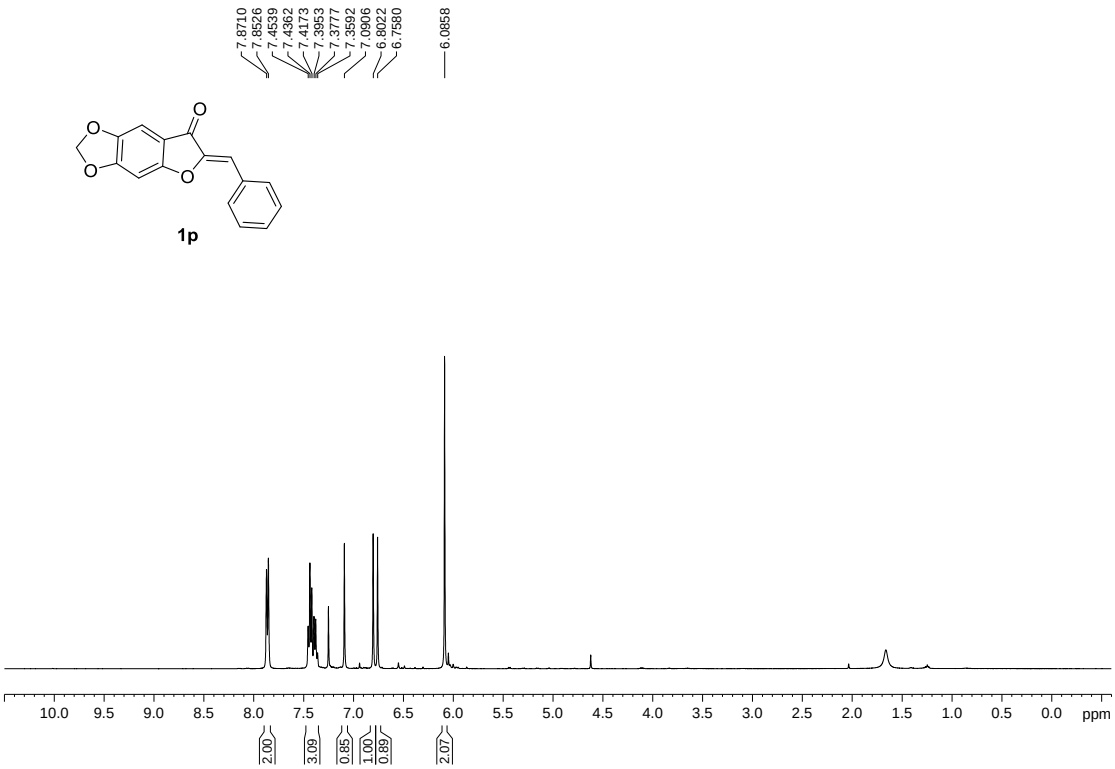
165.718
148.786
145.381
145.003
136.650
124.512
123.469
122.017
117.239
113.130
112.888
101.568
1m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

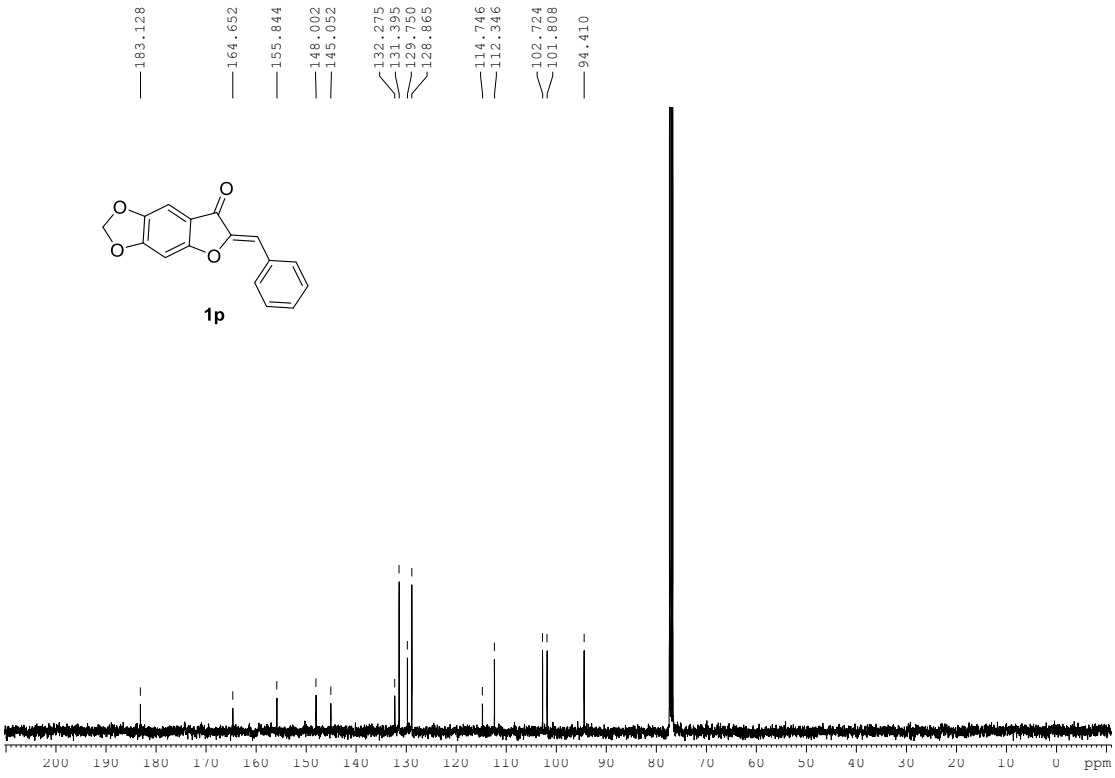

12.1057
8.2625
8.2562
8.0670
8.0480
7.7697
7.7506
7.7301
7.5739
7.5535
7.5088
7.4894
7.3553
7.2961
7.2766
7.2578
7.2501
7.2317
7.2089
7.1867
7.1689
O
O
N
H
1n
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
1.00
1.00
2.00
1.05
1.10
1.04
3.37


182.148
164.582
144.578
132.679
127.118
124.255
123.803
123.277
122.700
121.449
119.510
113.546
112.806
108.916
107.957
136.829
136.822
O
O
N
H
1n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


9.0528
8.6104
8.6001
8.2999
8.2803
7.8314
7.8125
7.7065
7.6873
7.6680
7.4176
7.4052
7.3992
7.3865
7.3518
7.3312
7.2721
7.2354
6.8509
O
O
N
1o
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 ppm
1.00
1.00
1.01
0.97
1.05
1.03
1.03
1.42
1.02


184.310
166.149
152.207
150.063
148.001
137.652
137.279
128.551
124.826
123.827
123.728
121.312
112.957
108.825
O
O
N
1o
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.8710
7.8526
7.4539
7.4362
7.4173
7.3953
7.3777
7.3592
7.0906
6.8022
6.7580
6.0858
1p
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 ppm
2.00
3.09
0.85
1.00
0.89
2.07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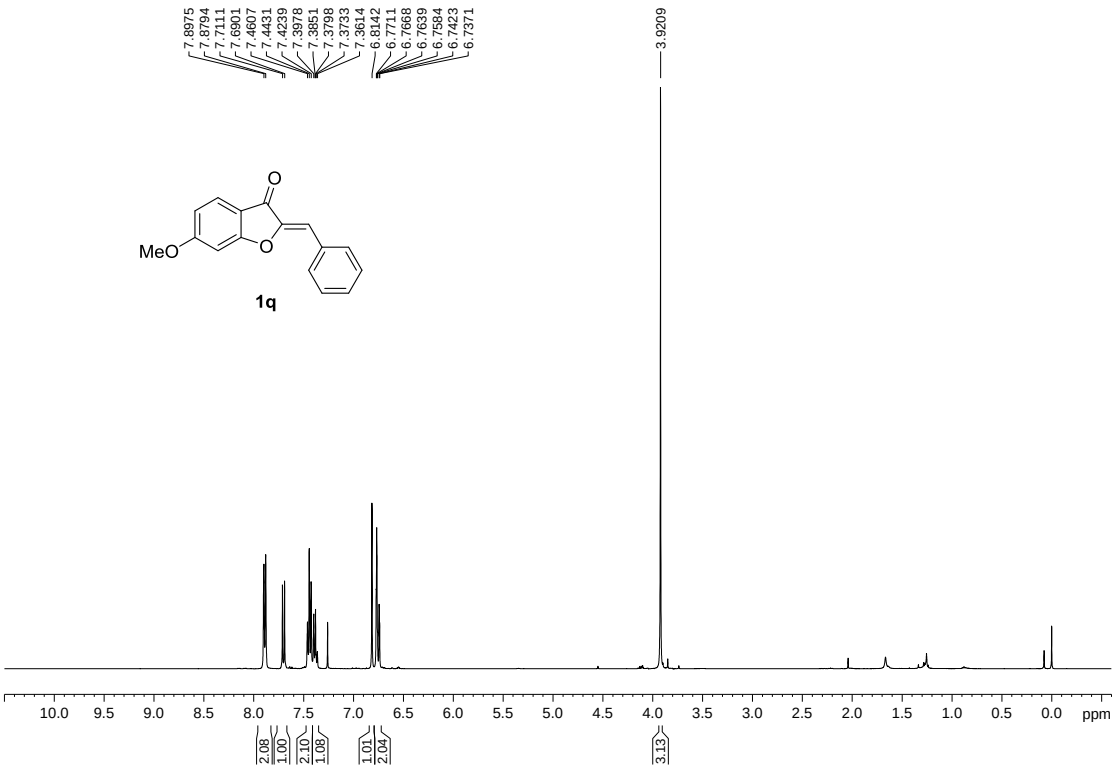
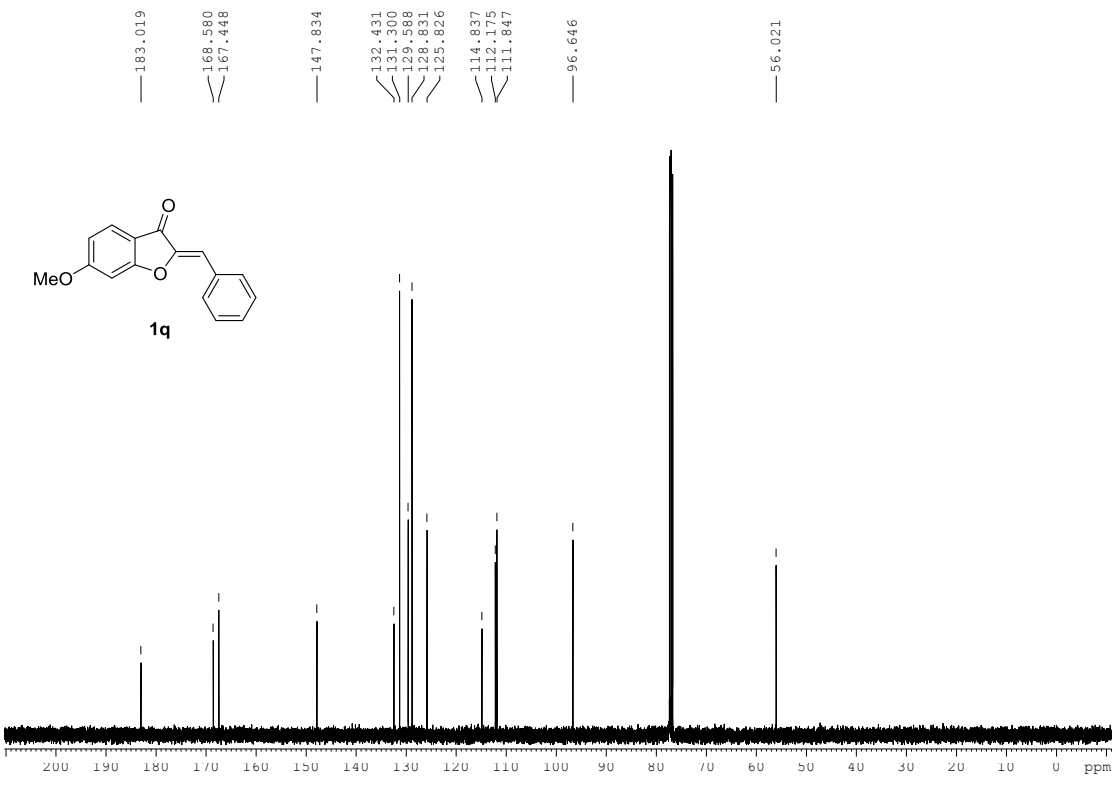
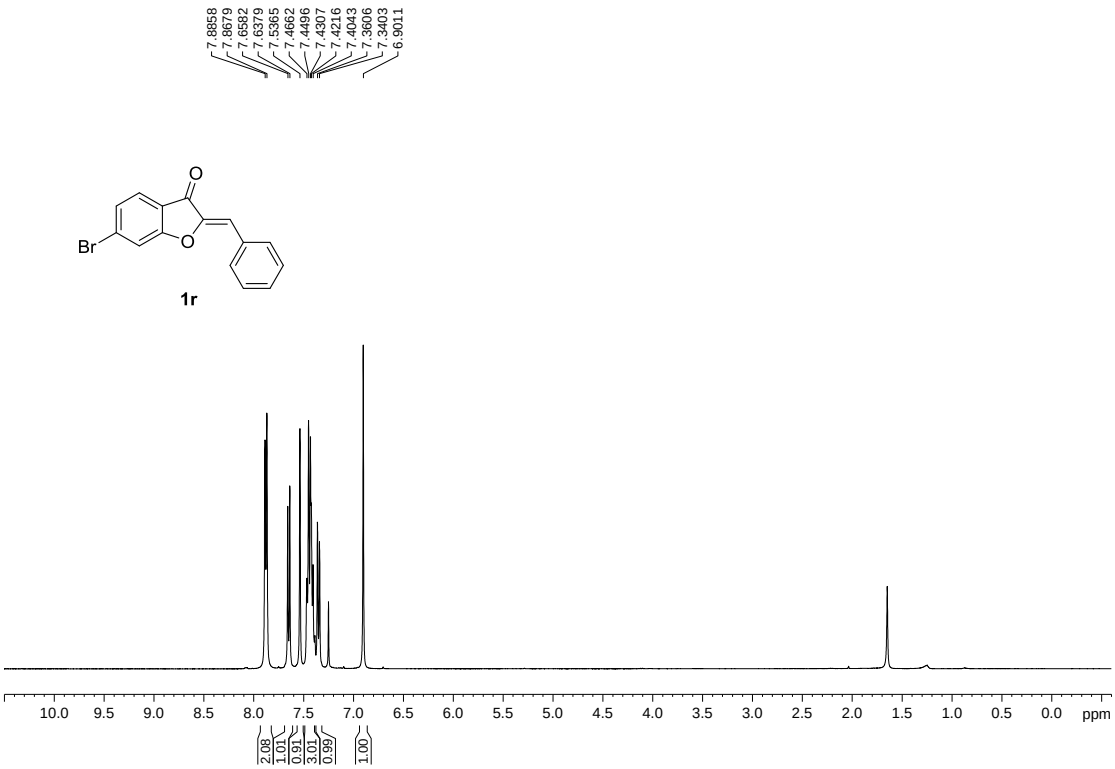
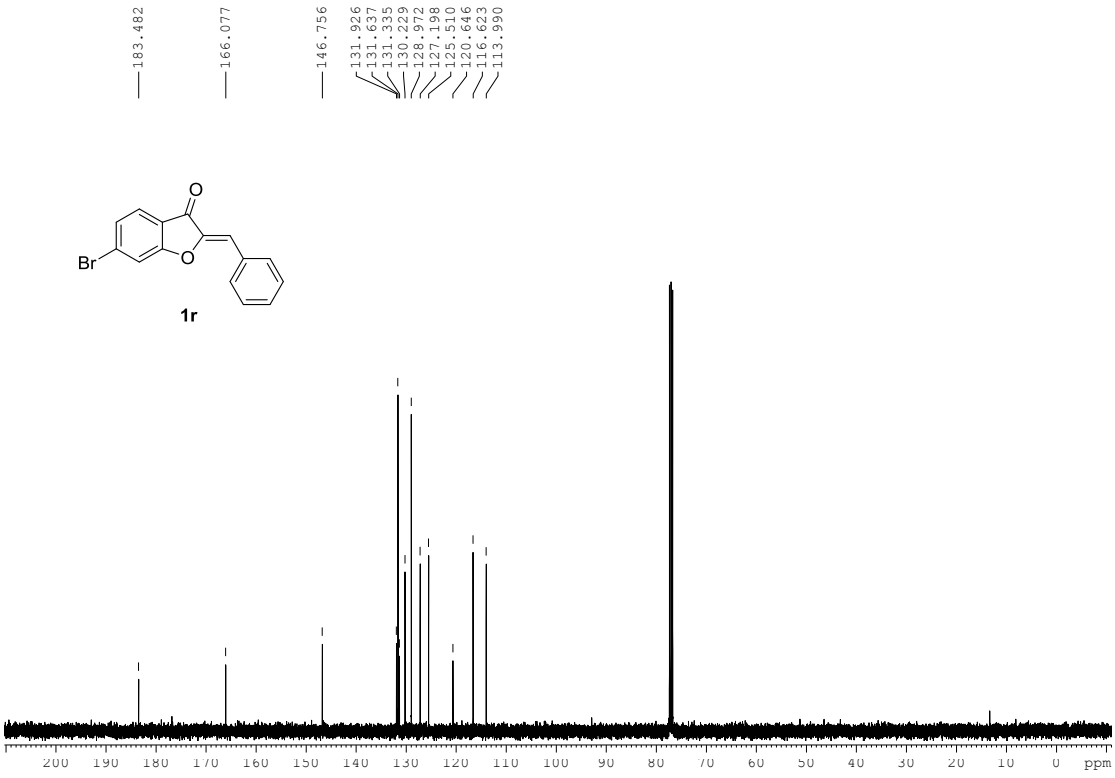
155.844
148.002
145.052
132.275
131.395
129.750
128.865
114.746
112.346
102.724
101.808
94.410
1p
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.8975
7.8794
7.7111
7.6901
7.4607
7.4431
7.4239
7.3978
7.3851
7.3798
7.3733
7.3614
6.8142
6.7711
6.7668
6.7639
6.7584
6.7423
6.7371
3.9209
O
MeO
O
1q
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 ppm
2.08
1.00
2.10
1.08
1.01
2.04
3.13


183.019
168.580
167.448
147.834
132.431
131.300
129.588
128.831
125.826
114.837
112.175
111.847
96.646
56.021
O
MeO
O
1q
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.8858
7.8679
7.6582
7.6379
7.5365
7.4662
7.4496
7.4307
7.4216
7.4043
7.3606
7.3403
6.9011
O
Br
O
1r
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 ppm
2.08
1.01
0.91
3.01
0.99
1.00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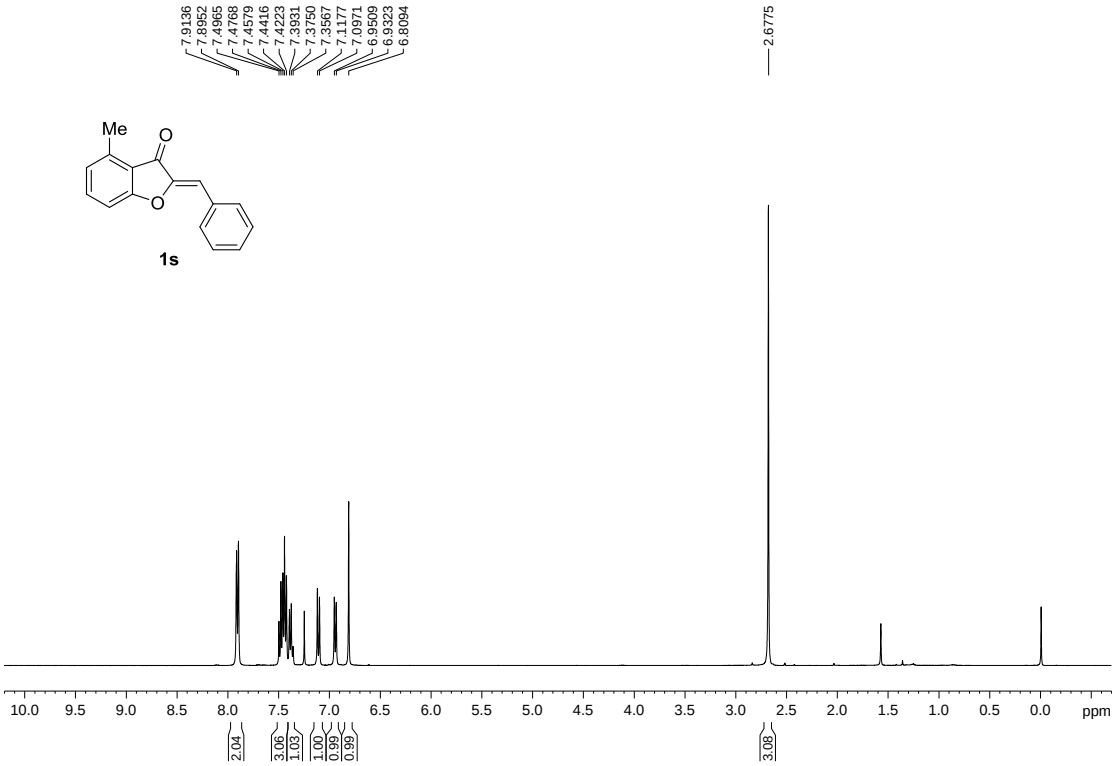
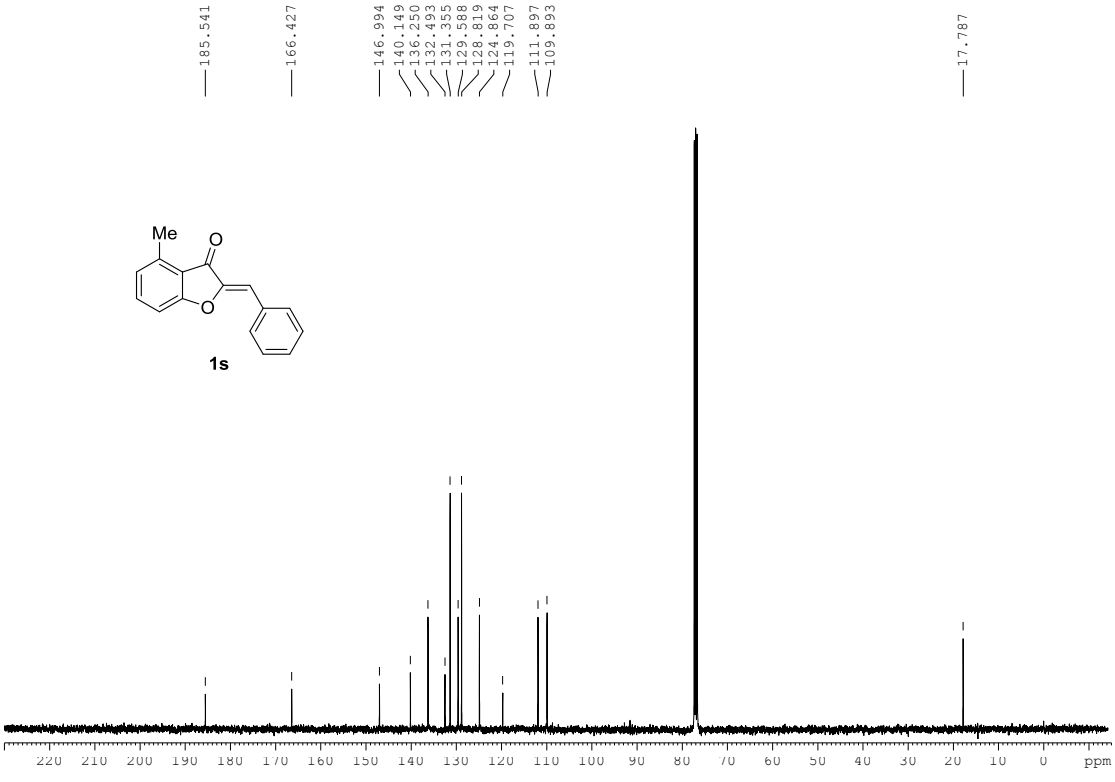
166.077
146.756
131.926
131.637
131.335
130.229
128.972
127.198
125.510
120.646
116.623
113.990
O
Br
O
1r
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.9136
7.8952
7.4965
7.4768
7.4579
7.4416
7.4223
7.3931
7.3750
7.3567
7.1177
7.0971
6.9509
6.9323
6.8094
2.6775
Me
O
O
1s
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 ppm
2.04
3.06
1.03
1.00
0.99
0.99
3.08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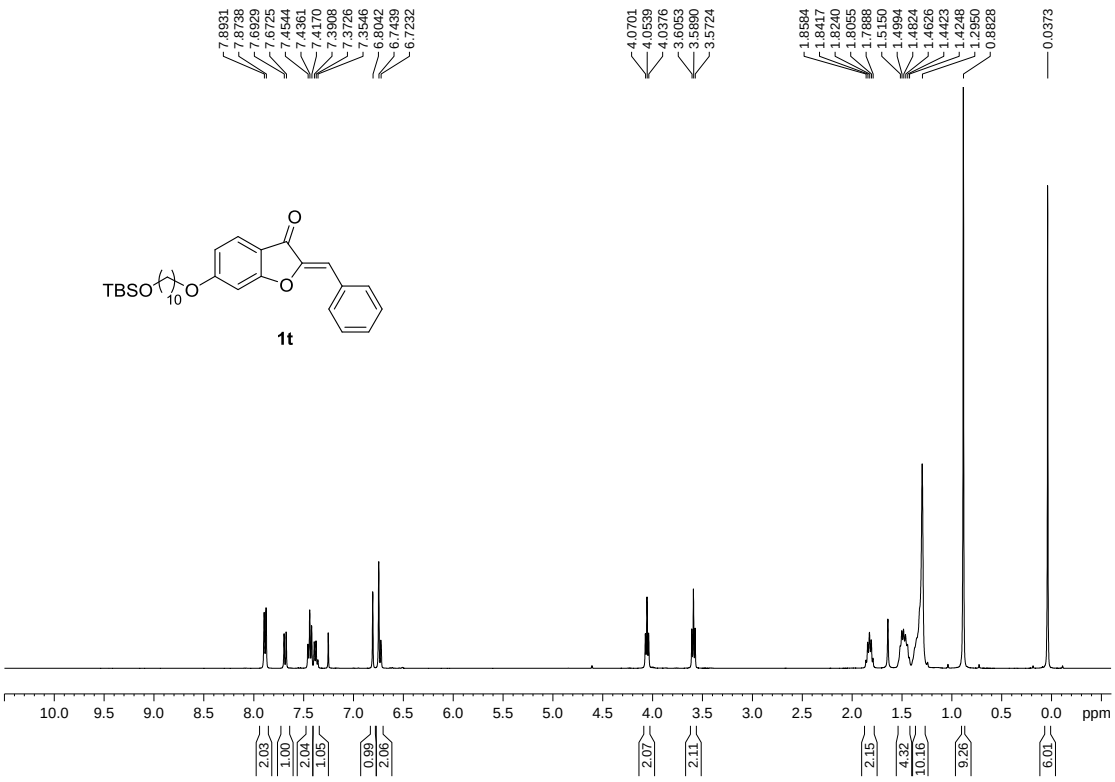
146.994
140.149
136.250
132.493
131.355
129.588
128.819
124.864
119.707
111.897
109.893
17.787
Me
O
O
1s
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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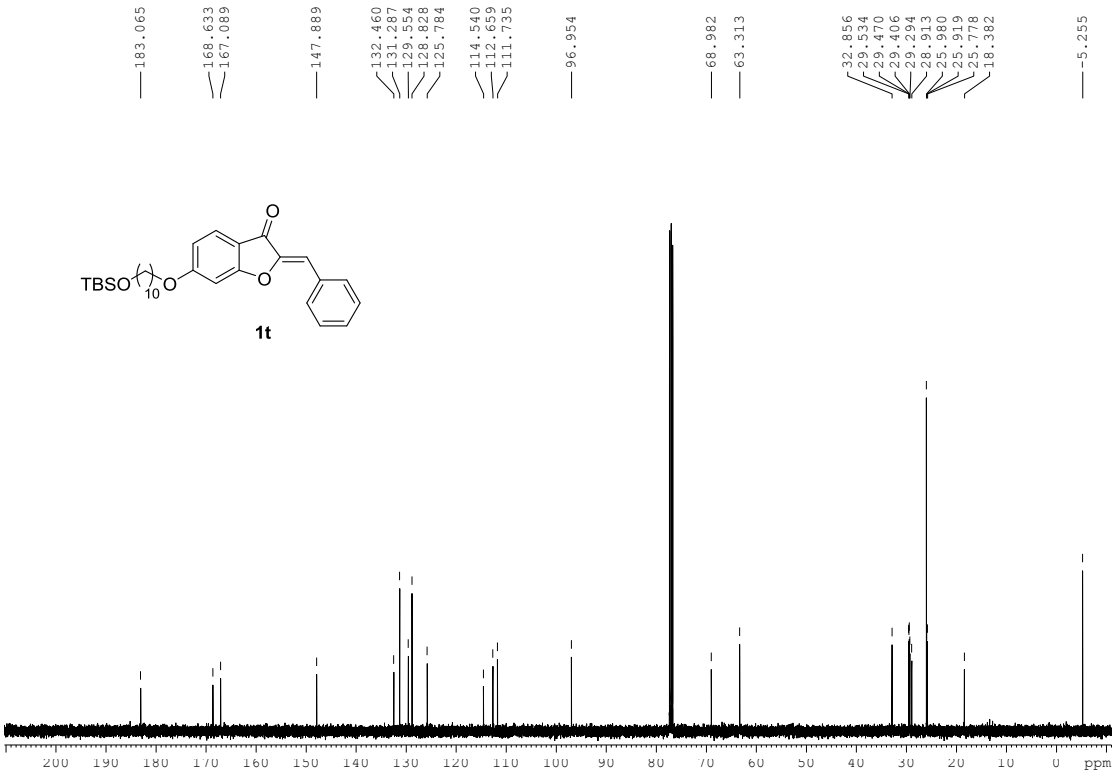
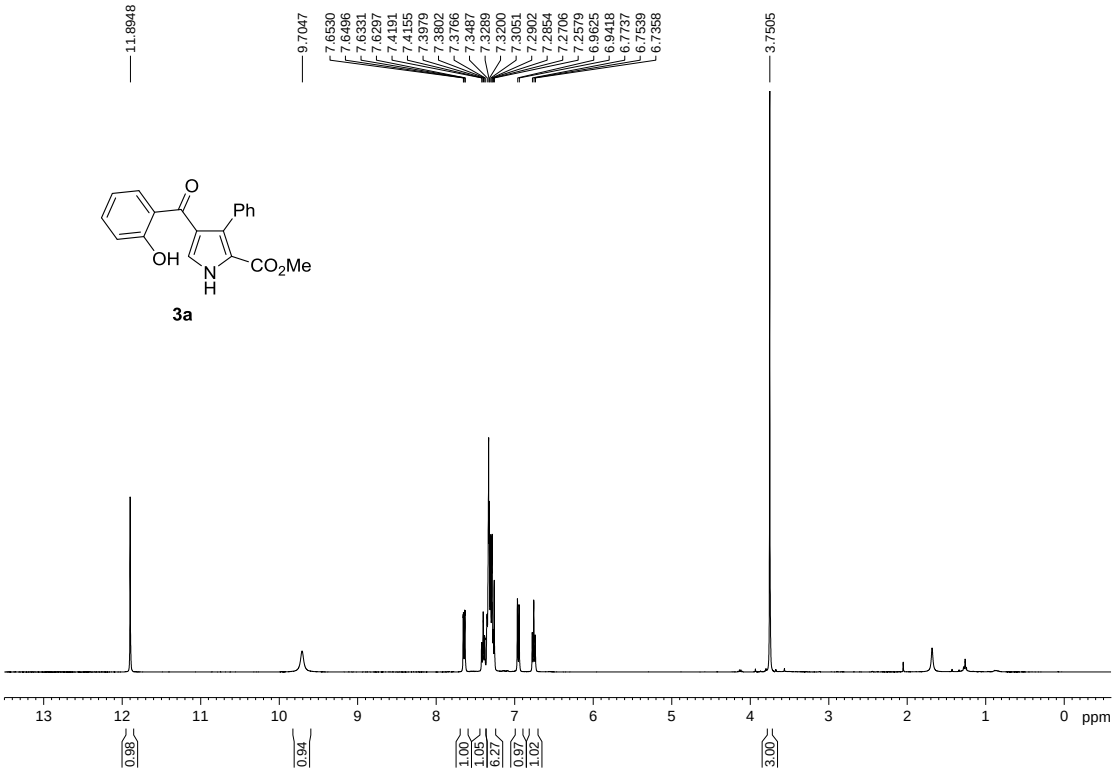
7.8738
7.6929
7.6725
7.4544
7.4361
7.4170
7.3908
7.3726
7.3546
6.8042
6.7439
6.7232
4.0701
4.0539
4.0376
3.6053
3.5890
3.5724
1.8584
1.8417
1.8240
1.8055
1.7888
1.5150
1.4994
1.4824
1.4626
1.4423
1.4248
1.2950
0.8828
0.0373
TBSO
10
O
O
O
1t
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.03
1.00
2.04
1.05
0.99
2.06
2.07
2.11
2.15
4.32
10.16
9.26
6.01


183.065
168.633
167.089
147.889
132.460
131.287
129.554
128.828
125.784
114.540
112.659
111.735
96.954
68.982
63.313
32.856
29.534
29.470
29.406
29.294
28.913
25.980
25.919
25.778
18.382
-5.255
TBSO
10
O
O
O
1t
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.6530
7.6496
7.6331
7.6297
7.4191
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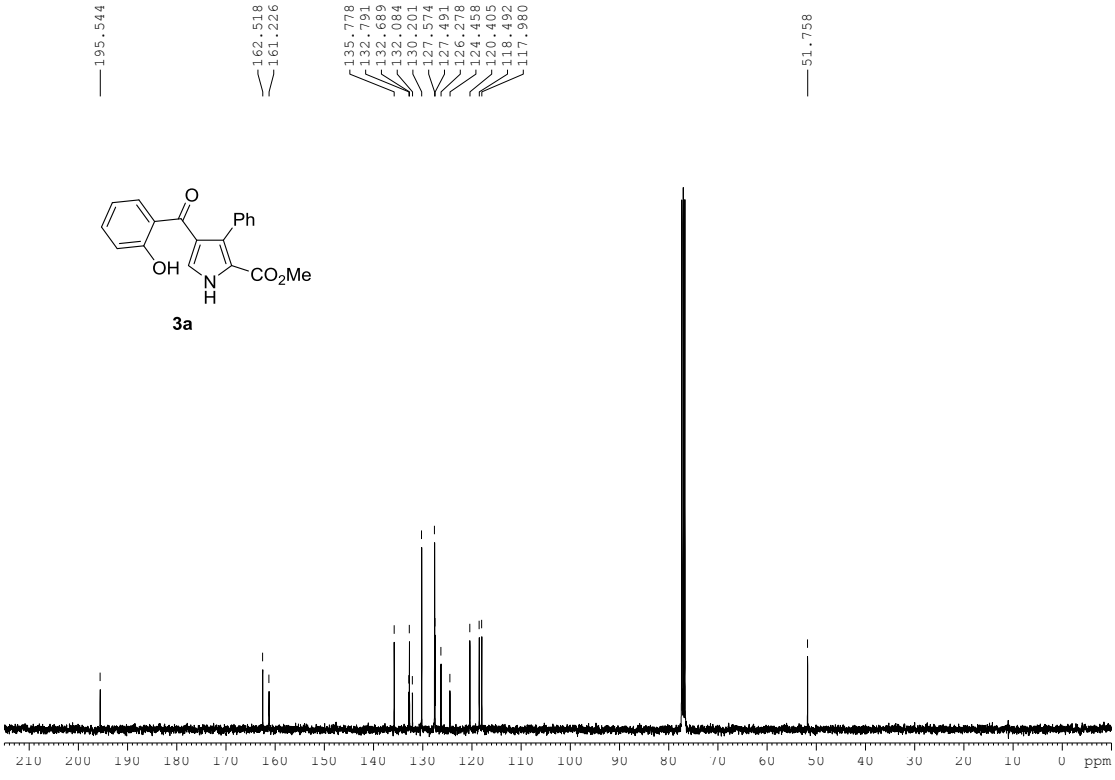
7.3979
7.3802
7.3766
7.3487
7.3289
7.3200
7.3051
7.2902
7.2854
7.2706
7.2579
6.9625
6.9418
6.7737
6.7539
6.7358
3.7505
O
Ph
OH
N
H
CO2Me
3a
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
0.94
1.00
1.05
6.27
0.97
1.02
3.00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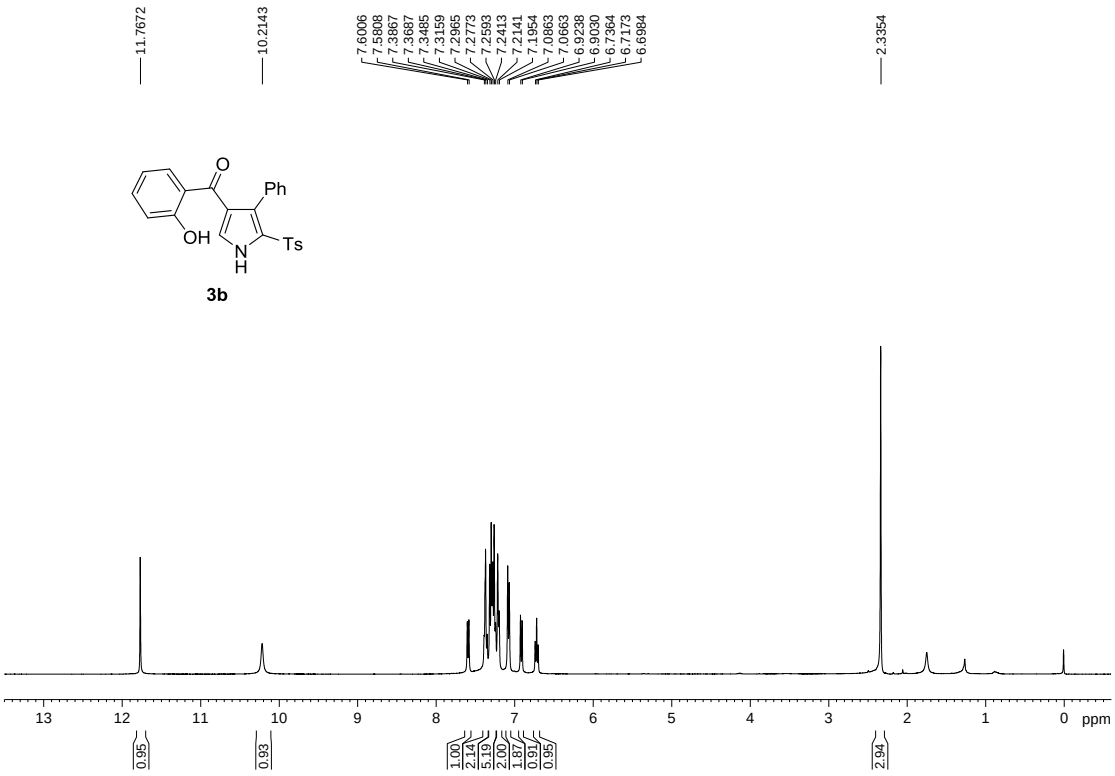
162.518
161.226
135.778
132.791
132.689
132.084
130.201
127.574
127.491
126.278
124.458
120.405
118.492
117.980
51.758
O
Ph
OH
N
H
CO2Me
3a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.6006
7.5808
7.3867
7.3687
7.3485
7.3159
7.2965
7.2773
7.2593
7.2413
7.2141
7.1954
7.0863
7.0663
6.9238
6.9030
6.7364
6.7173
6.6984
2.3354
O
Ph
OH
N
H
Ts
3b
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
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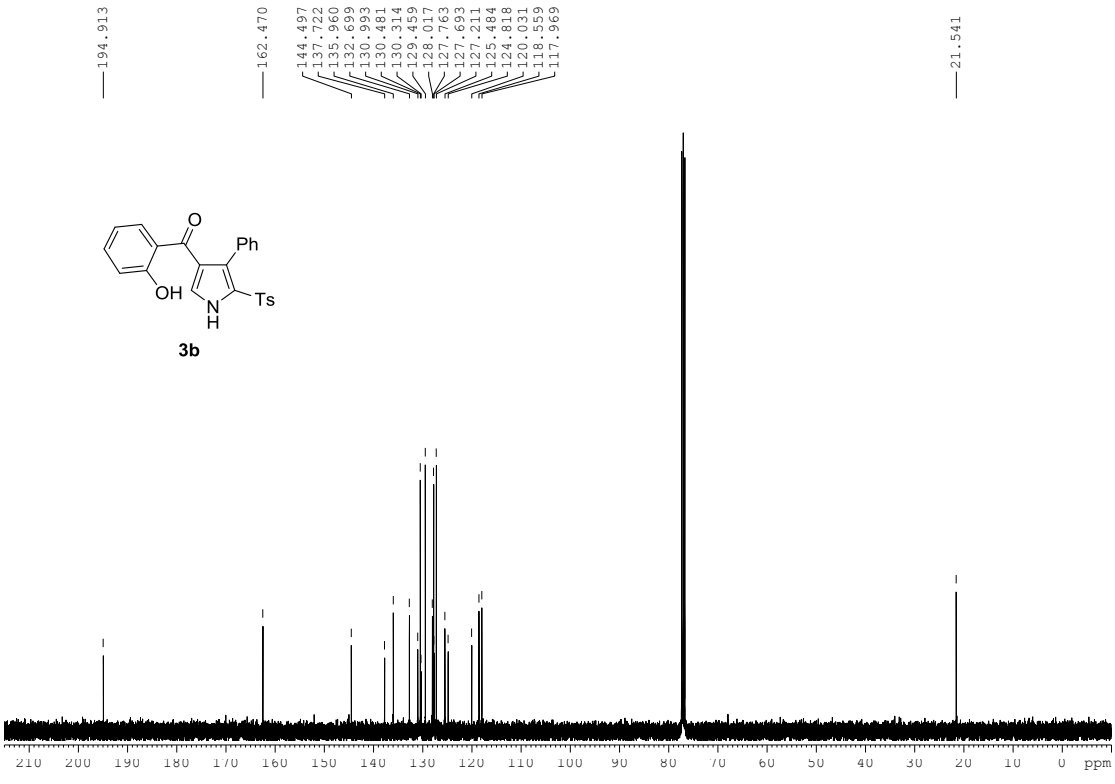
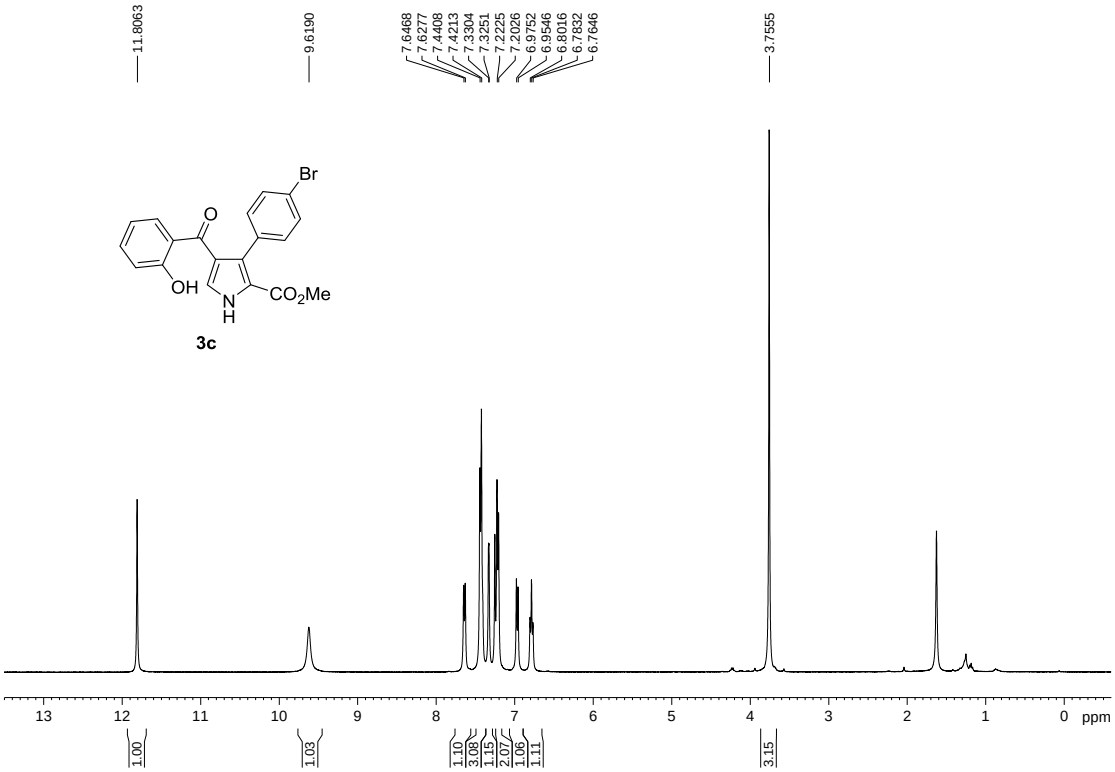
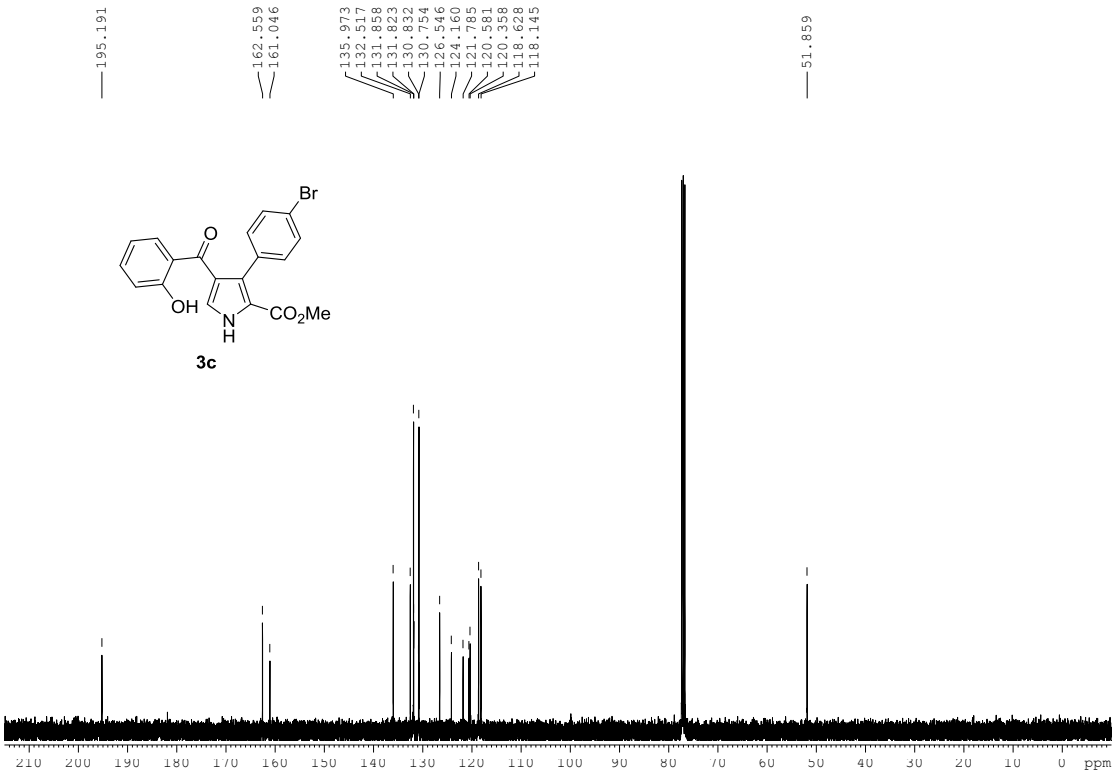
0.93
1.00
2.14
5.19
2.00
1.87
0.91
0.95
2.94


194.913
162.470
144.497
137.722
135.960
132.699
130.993
130.481
130.314
129.459
128.017
127.763
127.693
127.211
125.484
124.818
120.031
118.559
117.969
21.541
O
Ph
OH
N
H
Ts
3b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


11.8063
9.6190
7.6468
7.6277
7.4408
7.4213
7.3304
7.3251
7.2225
7.2026
6.9752
6.9546
6.8016
6.7832
6.7646
3.7555
Br
O
OH
N
H
CO2Me
3c
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.03
1.10
3.08
1.15
2.07
1.06
1.11
3.15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118.628
118.145
51.859
Br
O
OH
N
H
CO2Me
3c
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200
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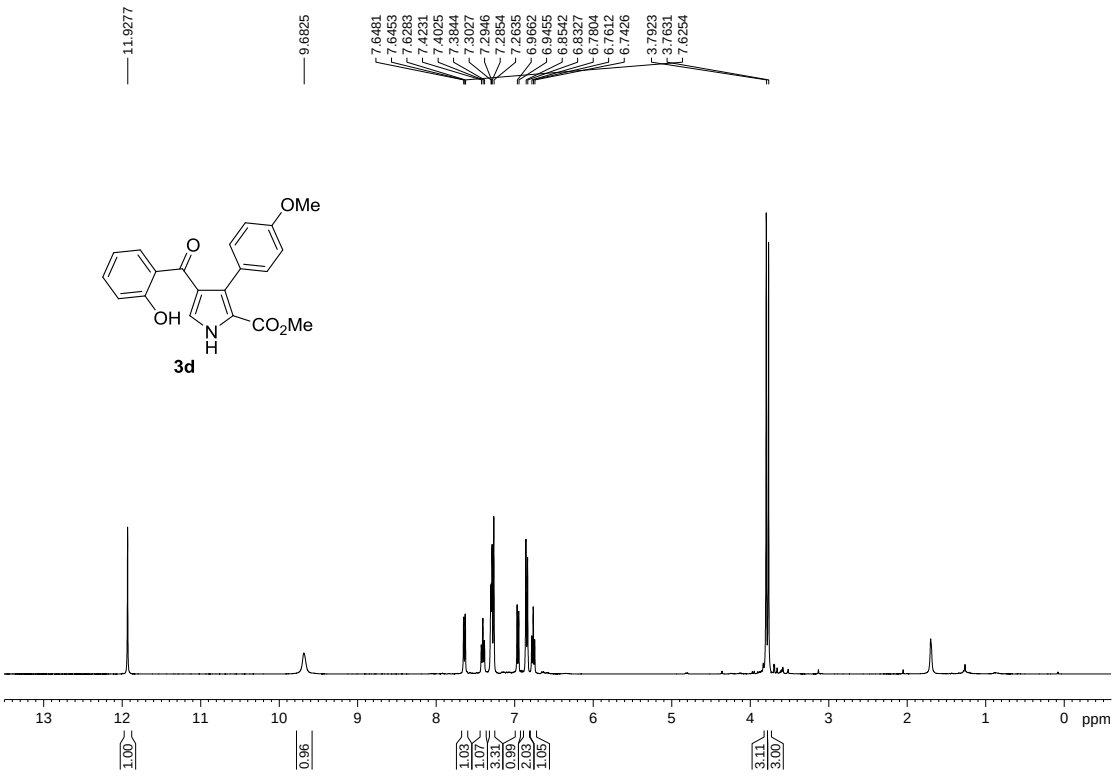
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7.2854
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6.9455
6.8542
6.8327
6.7804
6.7612
6.7426
3.7923
3.7631
7.6254
OMe
O
OH
N
H
CO2Me
3d
13
12
11
10
9
8
7
6
5
4
3
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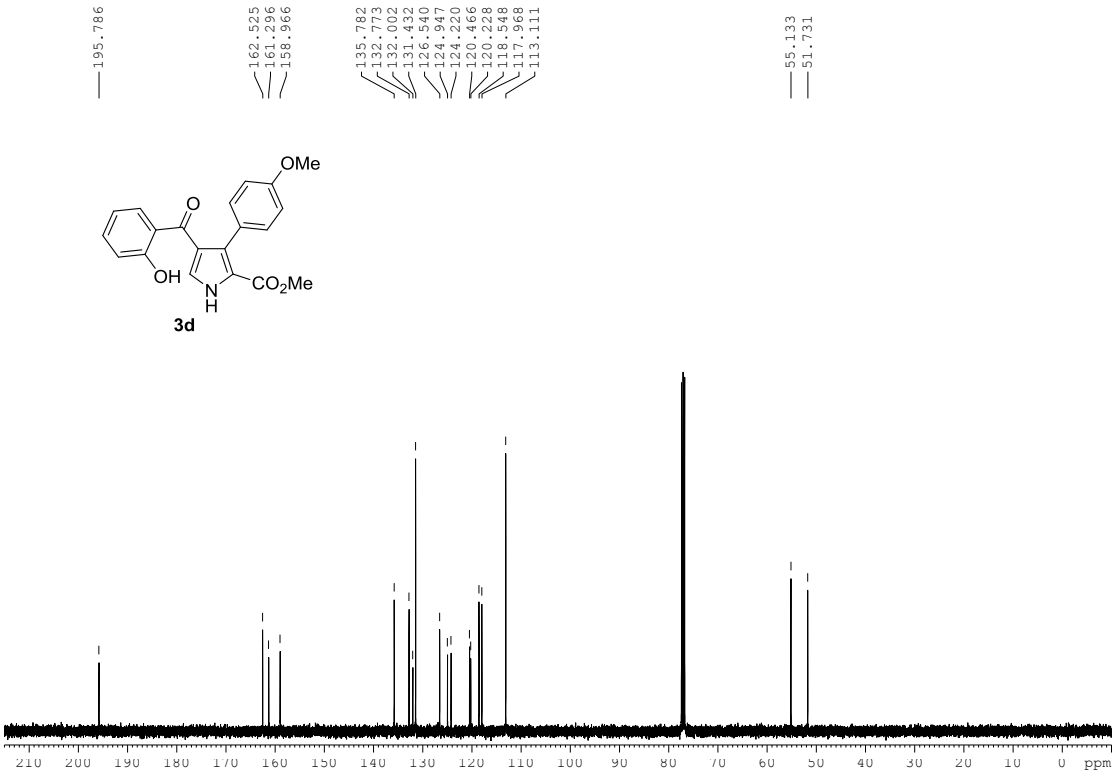
3.00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O
OH
N
H
CO2Me
3d
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200
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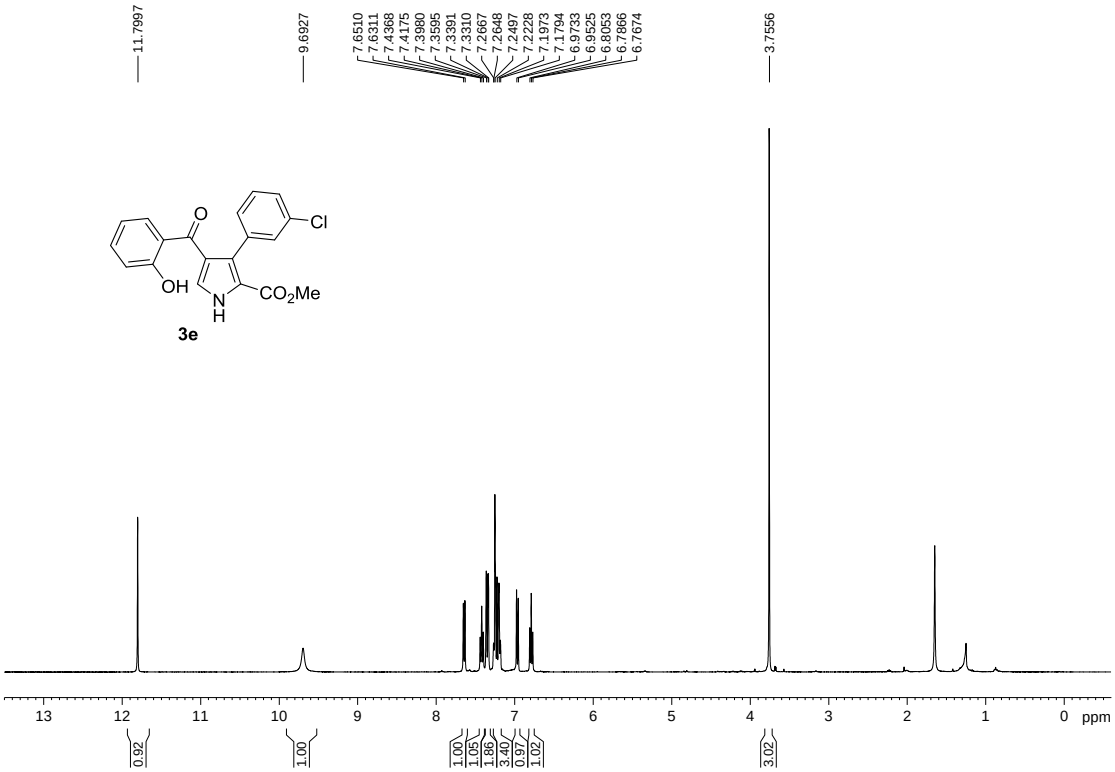
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7.2228
7.1973
7.1794
6.9733
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6.8053
6.7866
6.7674
3.7556
O
Cl
OH
N
H
CO2Me
3e
13
12
11
10
9
8
7
6
5
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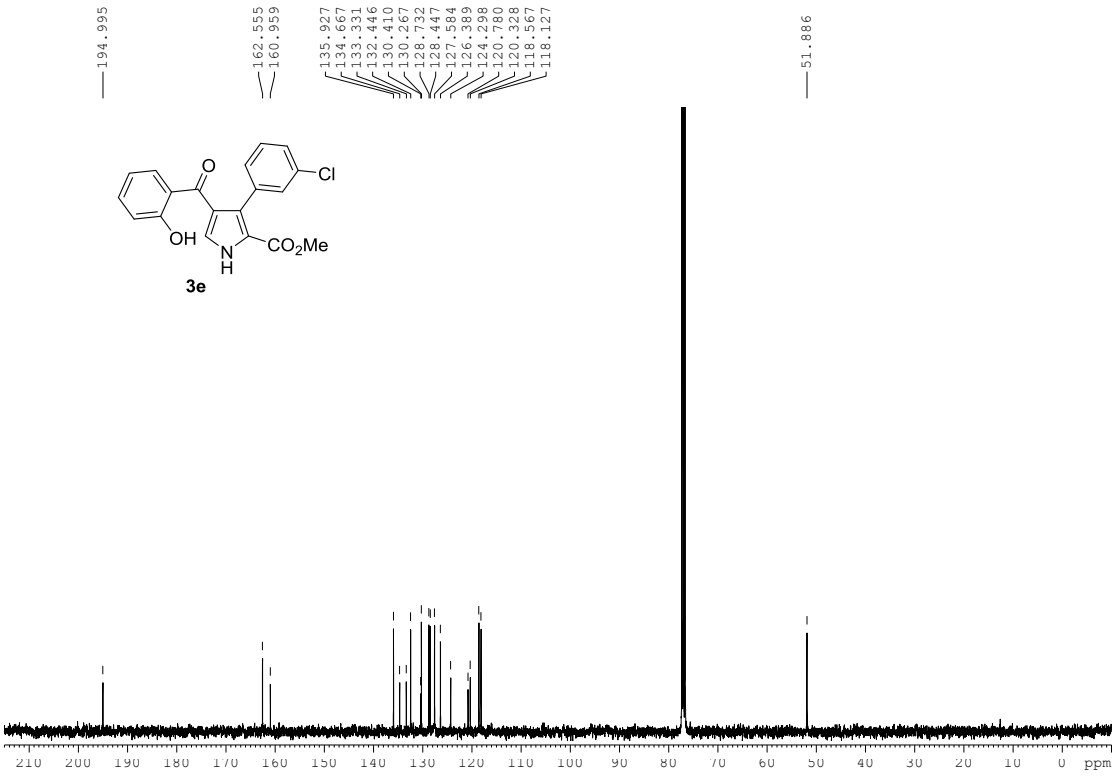
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120.780
120.328
118.567
118.127
51.886
O
Cl
OH
N
H
CO2Me
3e
210
200
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140
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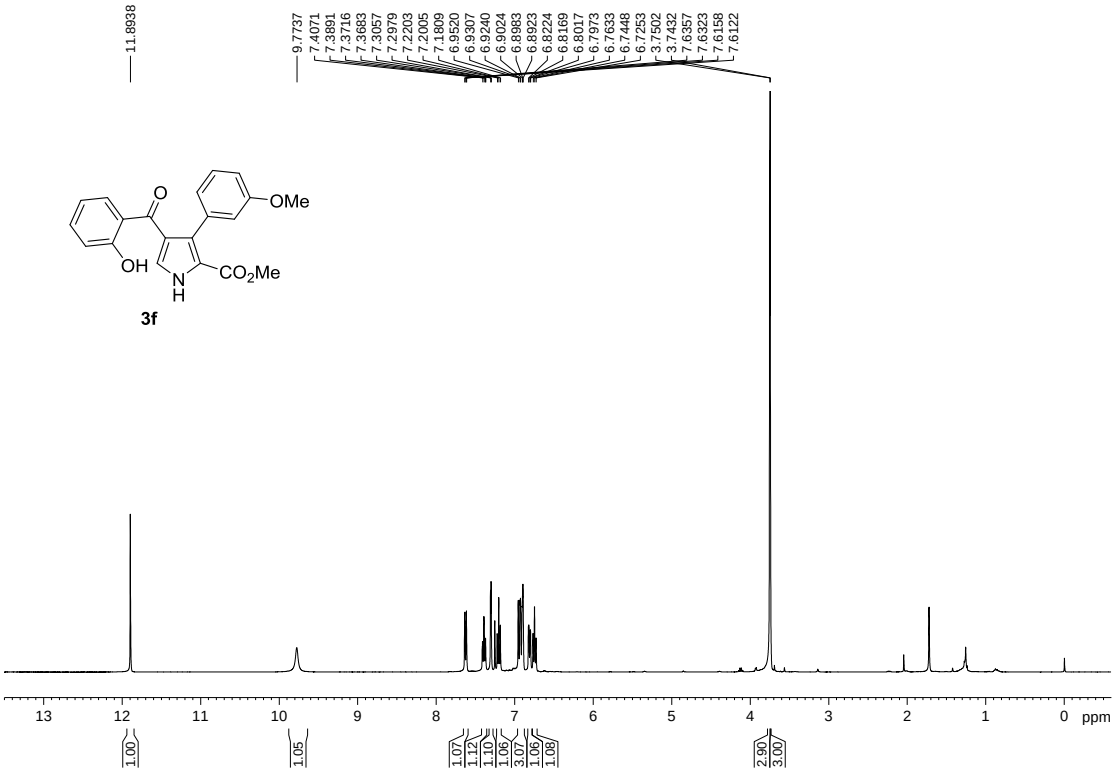
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6.9240
6.9024
6.8983
6.8923
6.8224
6.8169
6.8017
6.7973
6.7633
6.7448
6.7253
3.7502
3.7432
7.6357
7.6323
7.6158
7.6122
O
OMe
OH
N
H
CO2Me
3f
13
12
11
10
9
8
7
6
5
4
3
2
1
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1.07
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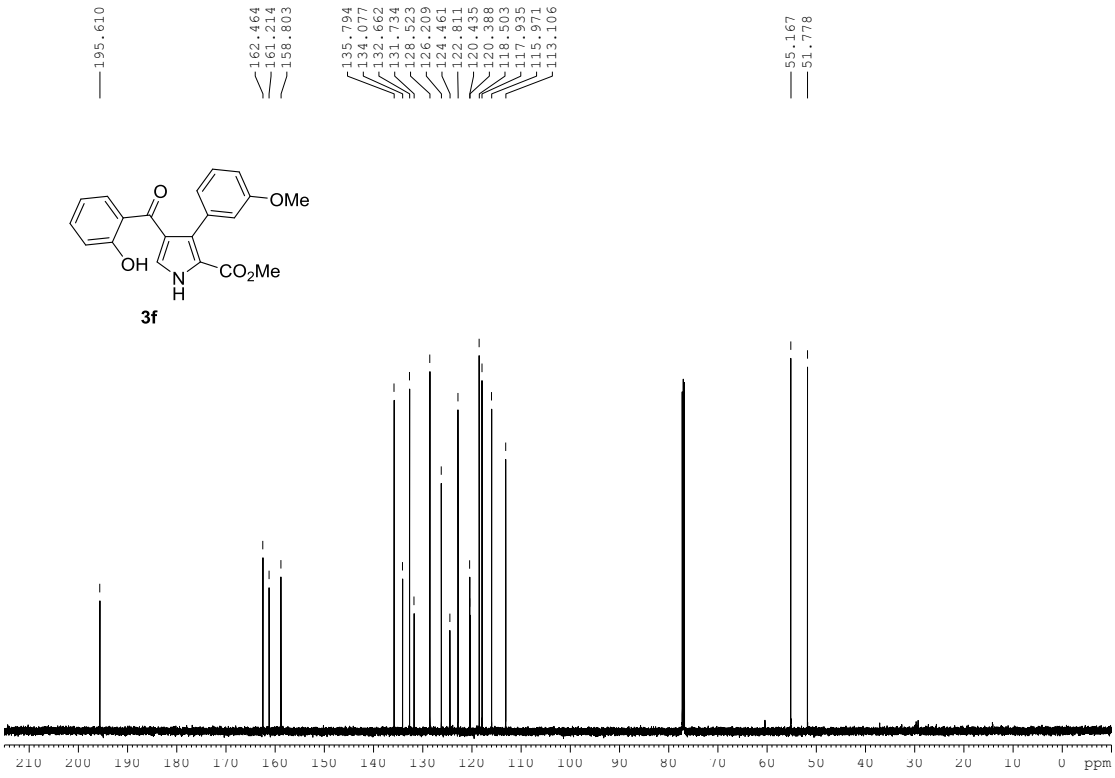
3.00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120.435
120.388
118.503
117.935
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113.106
55.167
51.778
O
OMe
OH
N
H
CO2Me
3f
210
200
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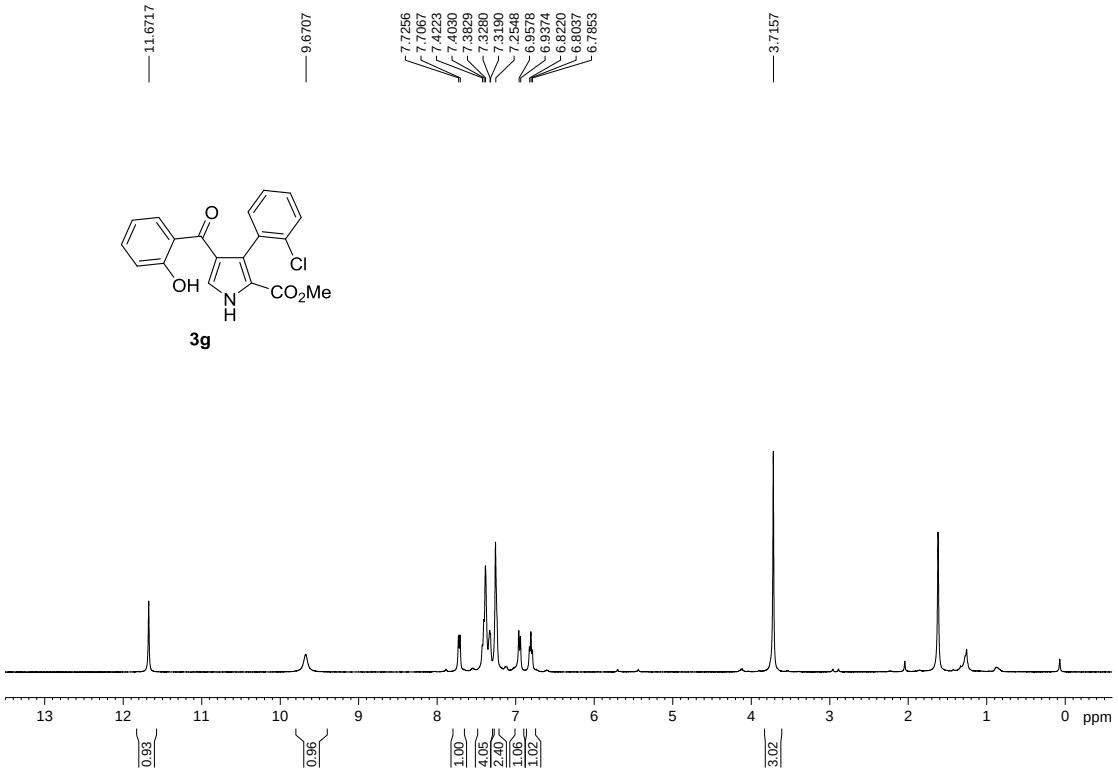
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6.9578
6.9374
6.8220
6.8037
6.7853
3.7157
O
OH
N
H
Cl
CO2Me
3g
13
12
11
10
9
8
7
6
5
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3
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ppm
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4.05
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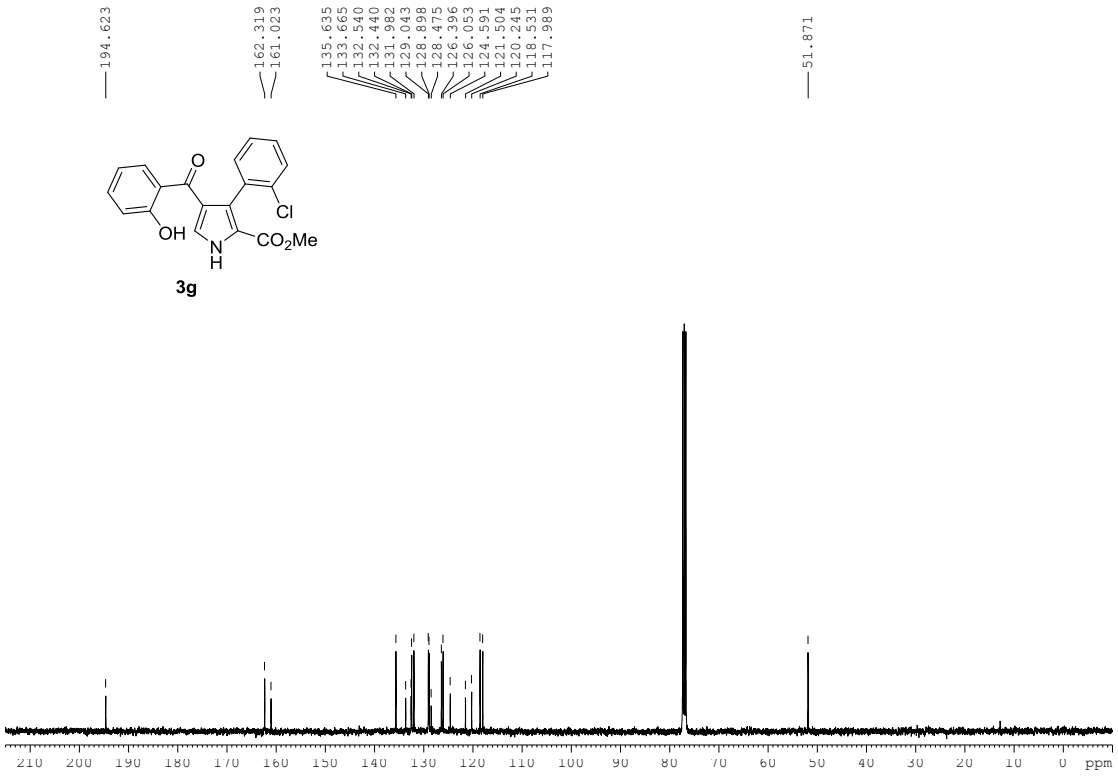
3.02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126.053
124.591
121.504
120.245
118.531
117.989
51.871
O
OH
N
H
Cl
CO2Me
3g
210
200
190
180
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150
140
130
120
110
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80
70
60
50
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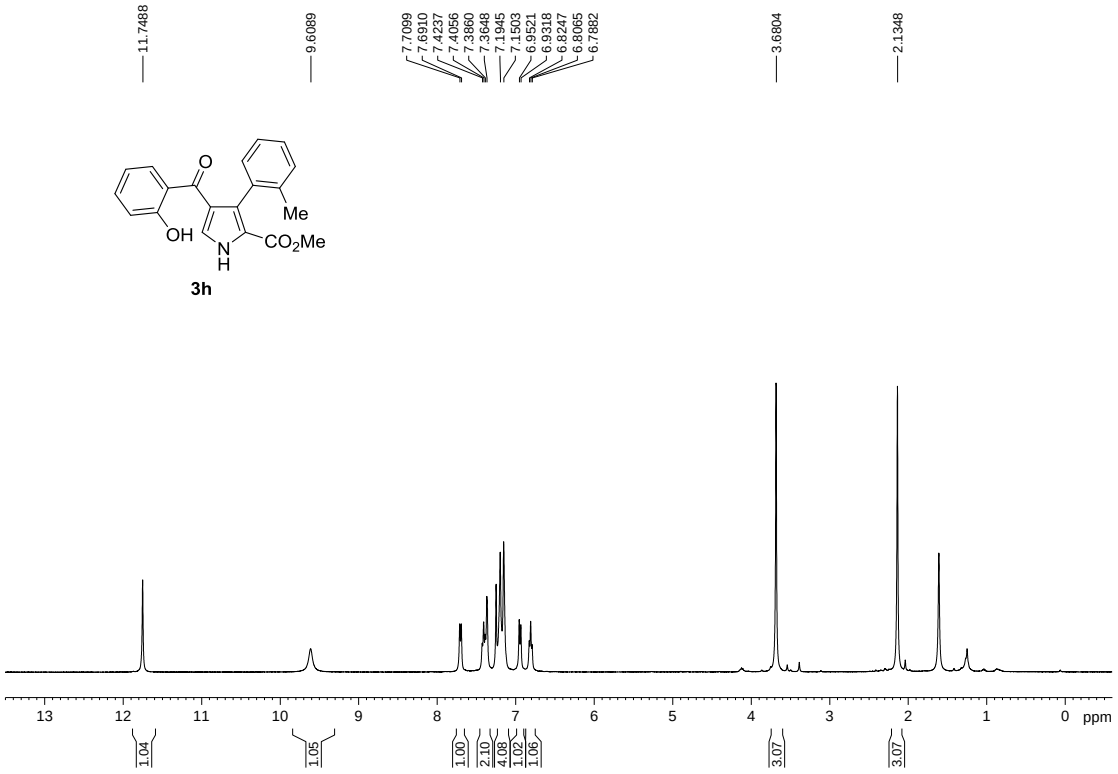
10
0
ppm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6.8247
6.8065
6.7882
3.6804
2.1348
O
OH
N
H
Me
CO2Me
3h
13
12
11
10
9
8
7
6
5
4
3
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1
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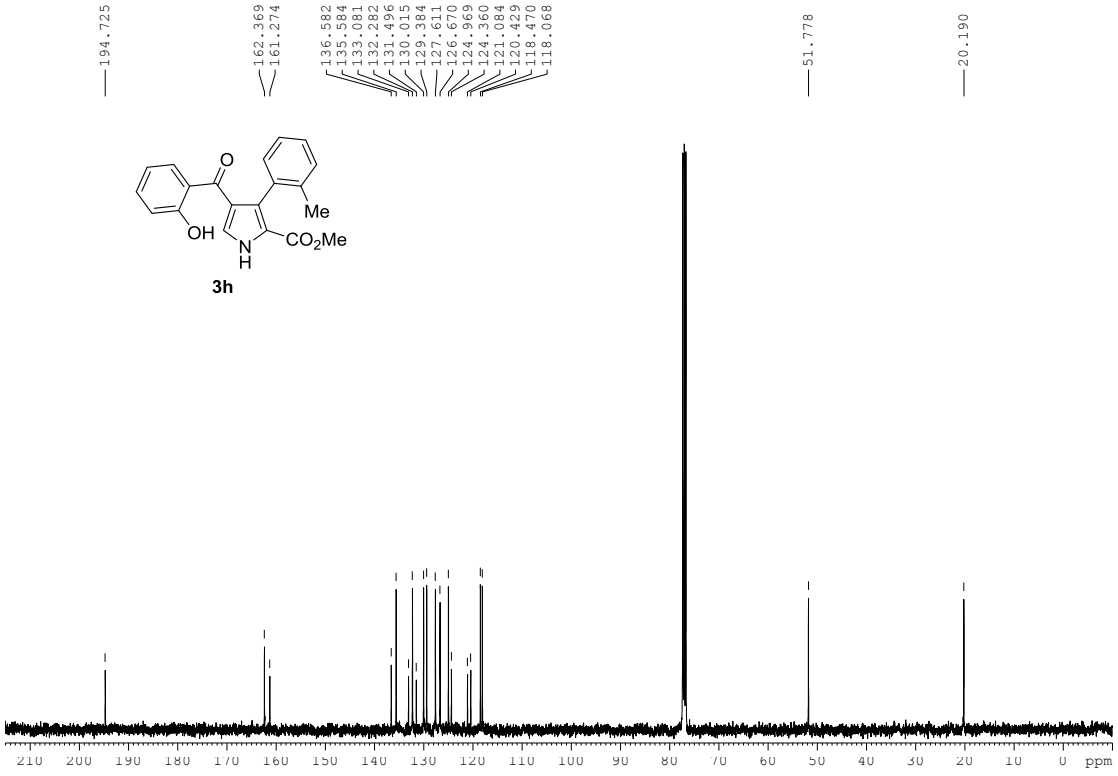
ppm
1.04
1.05
1.00
2.10
4.08
1.02
1.06
3.07
3.07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121.084
120.429
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20.190
O
OH
N
H
Me
CO2Me
3h
210
200
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150
140
130
120
110
100
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80
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60
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30
20
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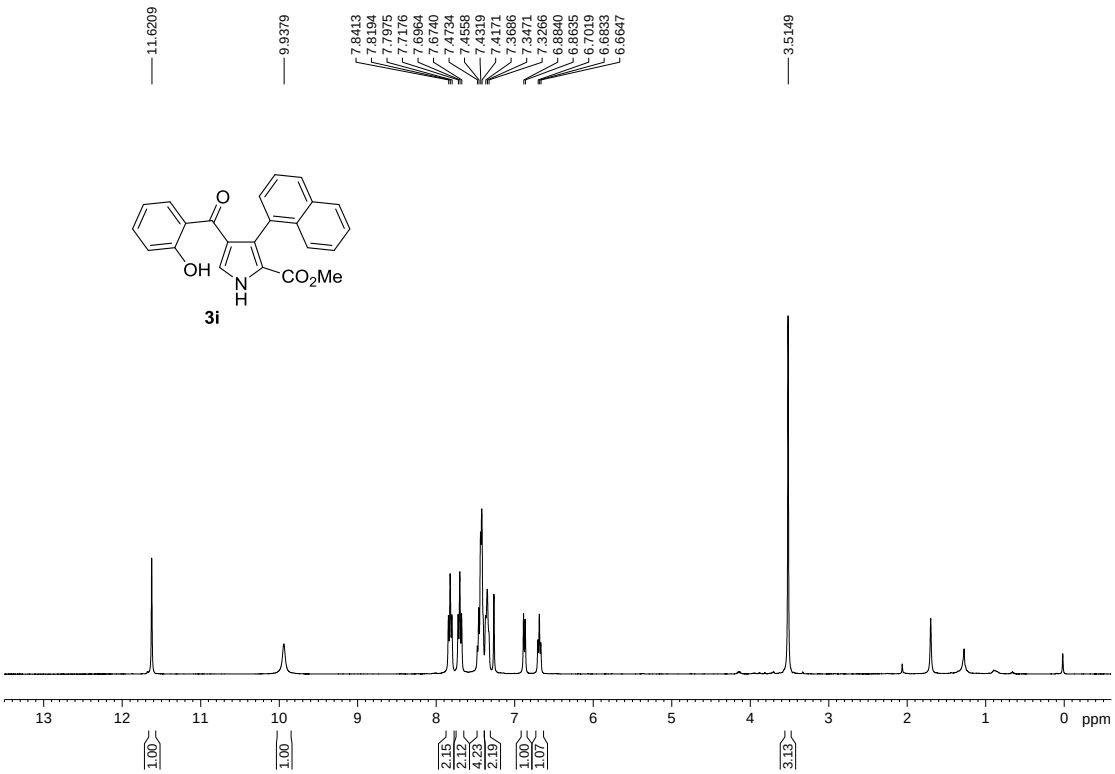
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7.4171
7.3686
7.3471
7.3266
6.8840
6.8635
6.7019
6.6833
6.6647
3.5149
O
OH
N
H
CO2Me
3i
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4.23
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1.00
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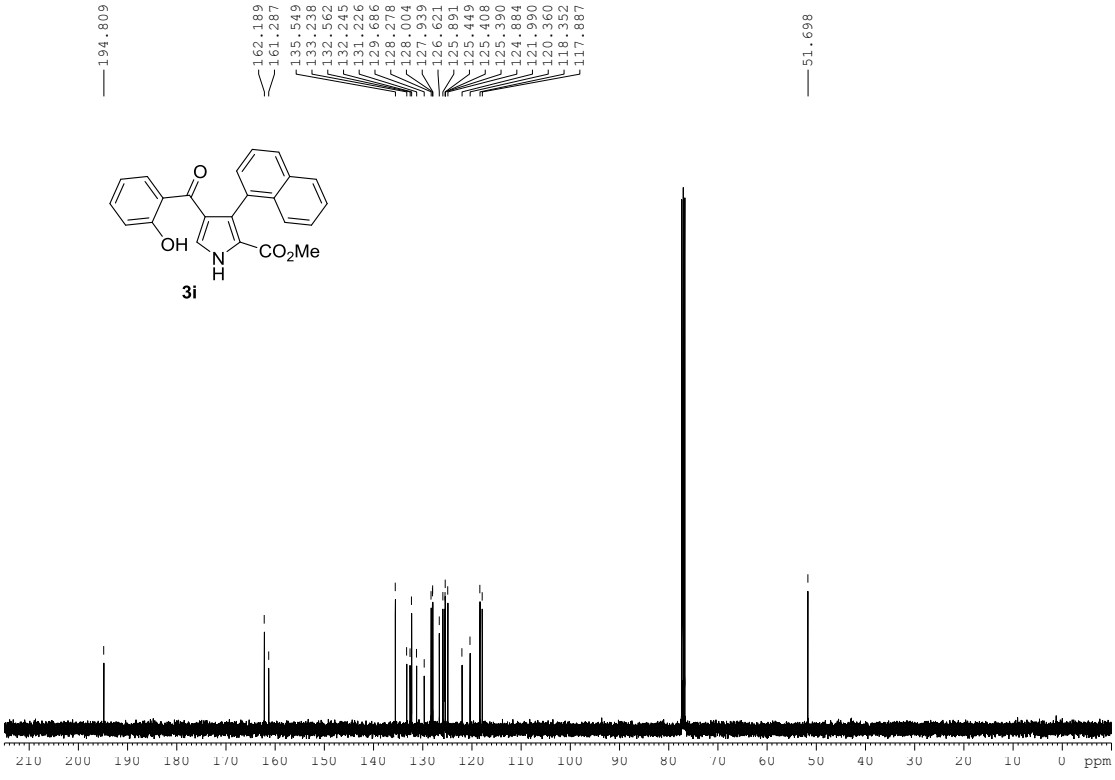
3.13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125.891
125.449
125.408
125.390
124.884
121.990
120.360
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O
OH
N
H
CO2Me
3i
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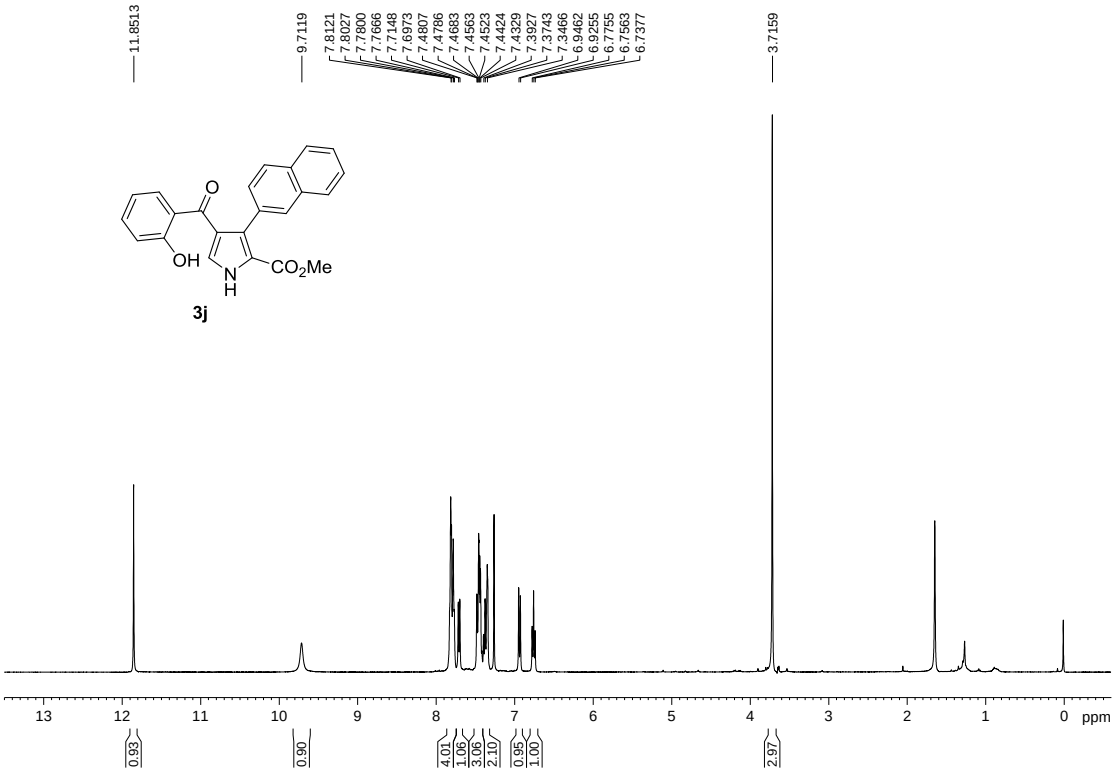
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7.4563
7.4523
7.4424
7.4329
7.3927
7.3743
7.3466
6.9462
6.9255
6.7755
6.7563
6.7377
3.7159
O
OH
N
H
CO2Me
3j
13
12
11
10
9
8
7
6
5
4
3
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ppm
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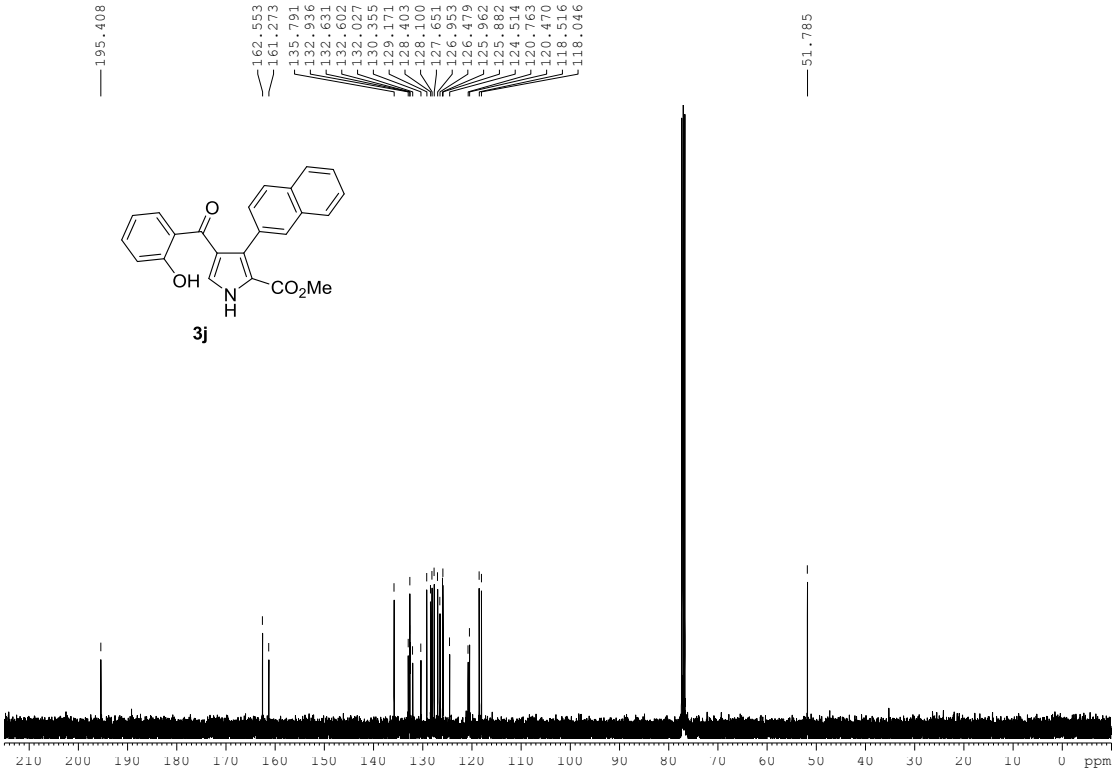
2.97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126.953
126.479
125.962
125.882
124.514
120.763
120.470
118.516
118.046
51.785
O
OH
N
H
CO2Me
3j
210
200
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180
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150
140
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100
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80
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60
50
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30
20
10
0
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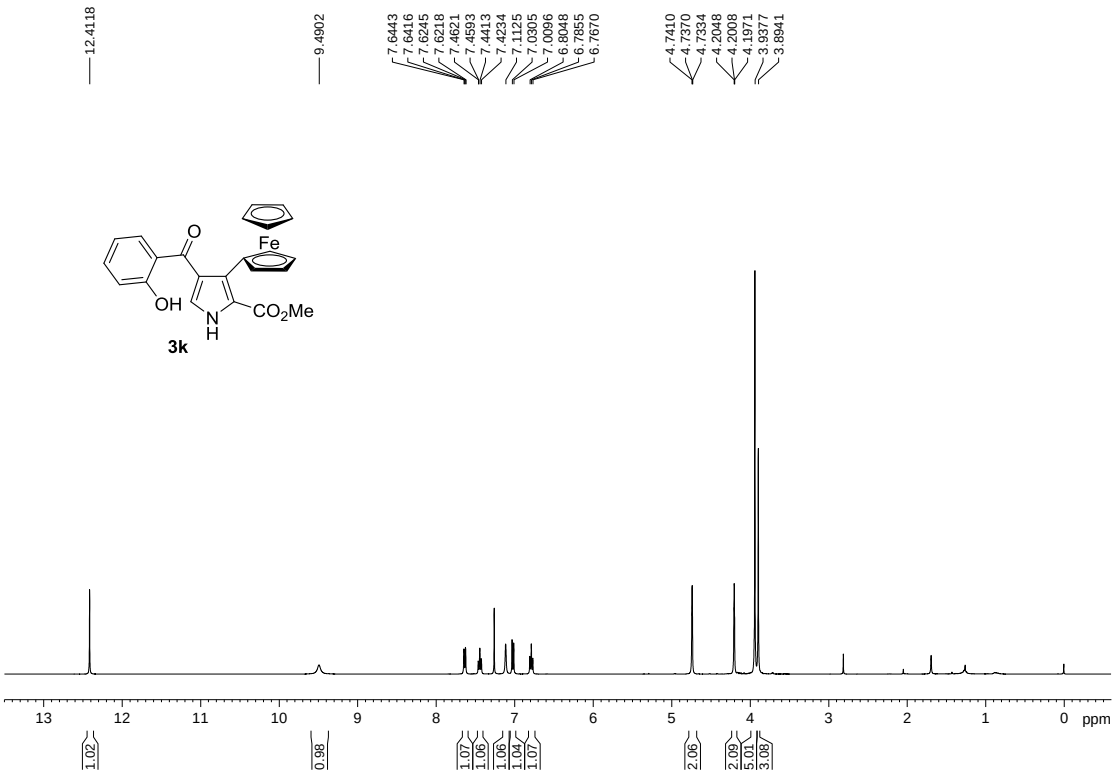
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7.1125
7.0305
7.0096
6.8048
6.7855
6.7670
4.7410
4.7370
4.7334
4.2048
4.2008
4.1971
3.9377
3.8941
O
Fe
OH
N
H
CO2Me
3k
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
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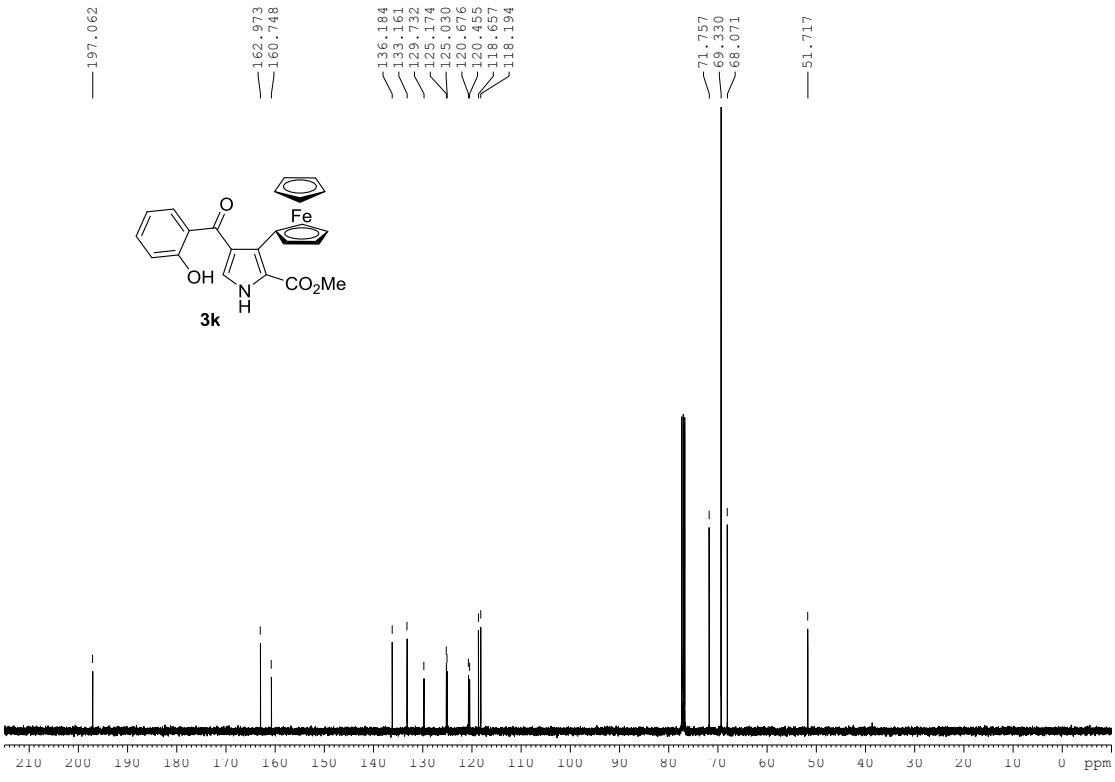
1.06
1.04
1.07
2.06
2.09
5.01
3.08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71.757
69.330
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O
Fe
OH
N
H
CO2Me
3k
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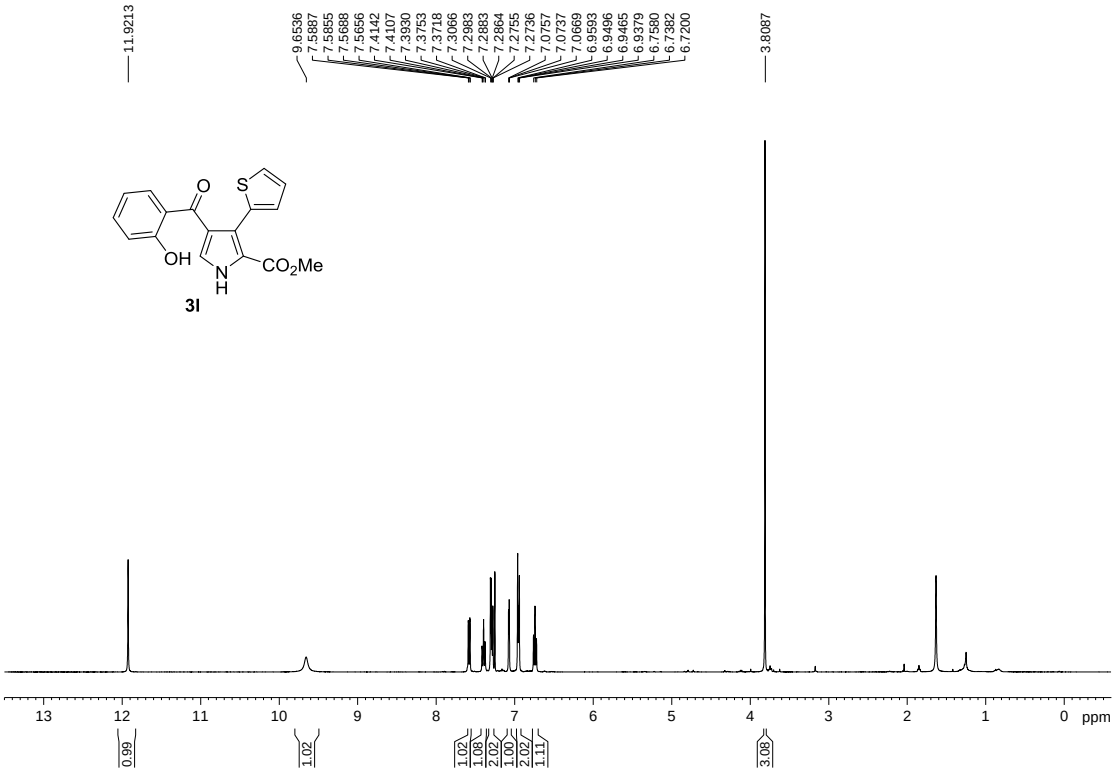
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7.3066
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7.2883
7.2864
7.2755
7.2736
7.0757
7.0737
7.0669
6.9593
6.9496
6.9465
6.9379
6.7580
6.7382
6.7200
3.8087
O
S
OH
N
H
CO2Me
3l
13
12
11
10
9
8
7
6
5
4
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ppm
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2.02
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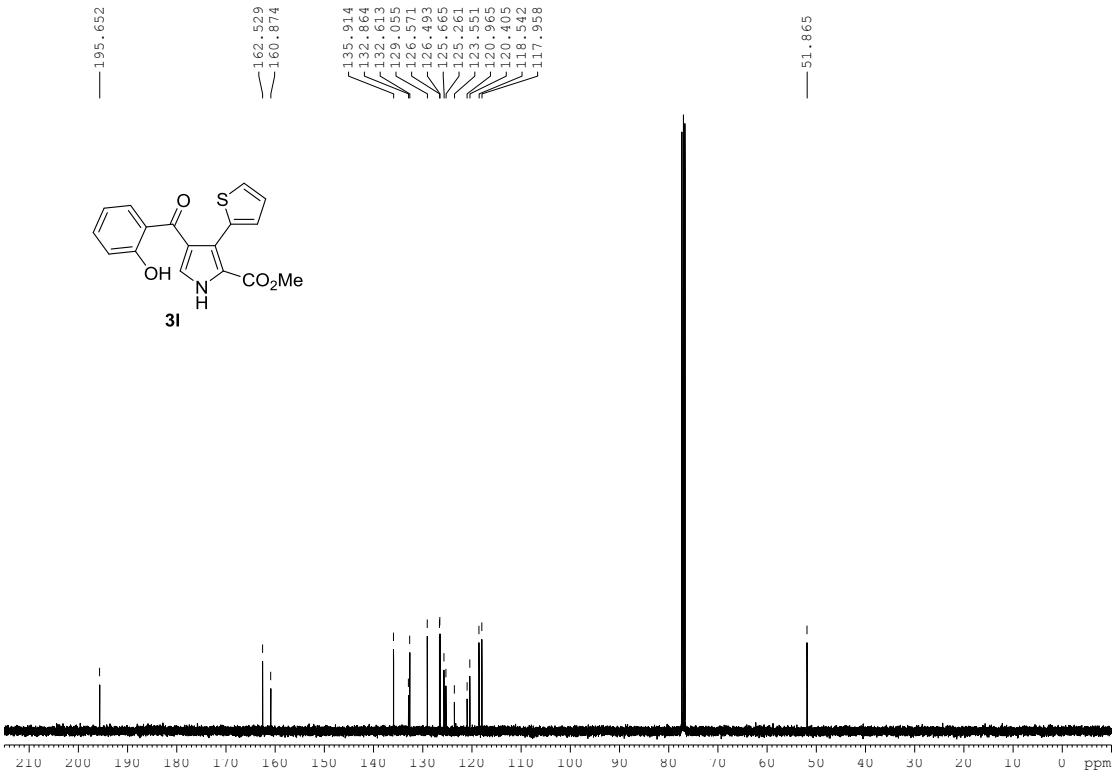
3.08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120.965
120.405
118.542
117.958
51.865
O
S
OH
N
H
CO2Me
3l
210
200
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180
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140
130
120
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100
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80
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60
50
40
30
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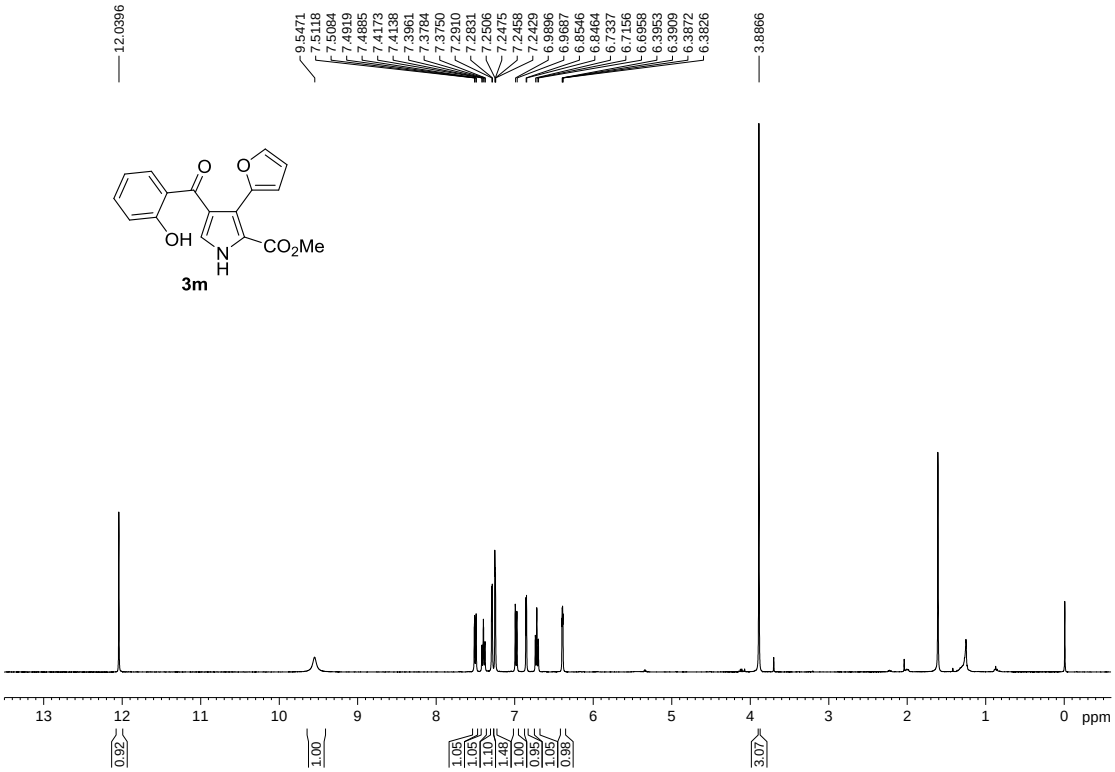
ppm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7.3750
7.2910
7.2831
7.2506
7.2475
7.2458
7.2429
6.9896
6.9687
6.8546
6.8464
6.7337
6.7156
6.6958
6.3953
6.3909
6.3872
6.3826
3.8866
O
O
OH
N
H
CO2Me
3m
13
12
11
10
9
8
7
6
5
4
3
2
1
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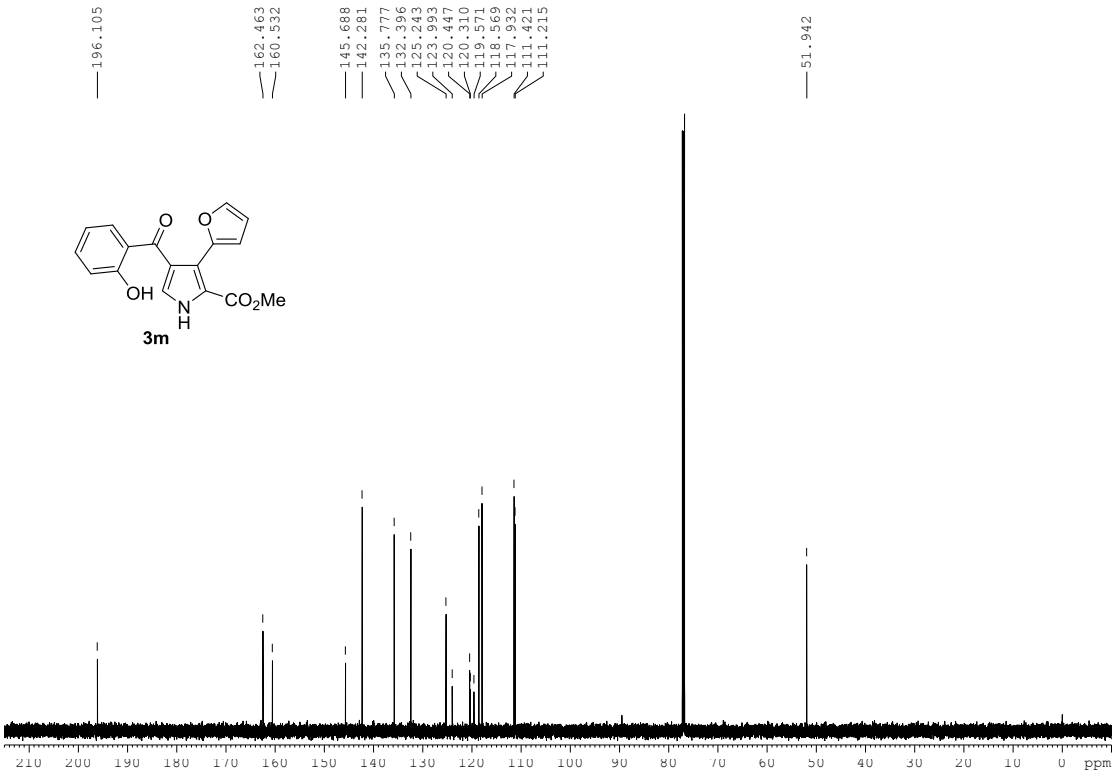
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118.569
117.932
111.421
111.215
51.942
O
O
OH
N
H
CO2Me
3m
210
200
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100
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80
70
60
50
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30
20
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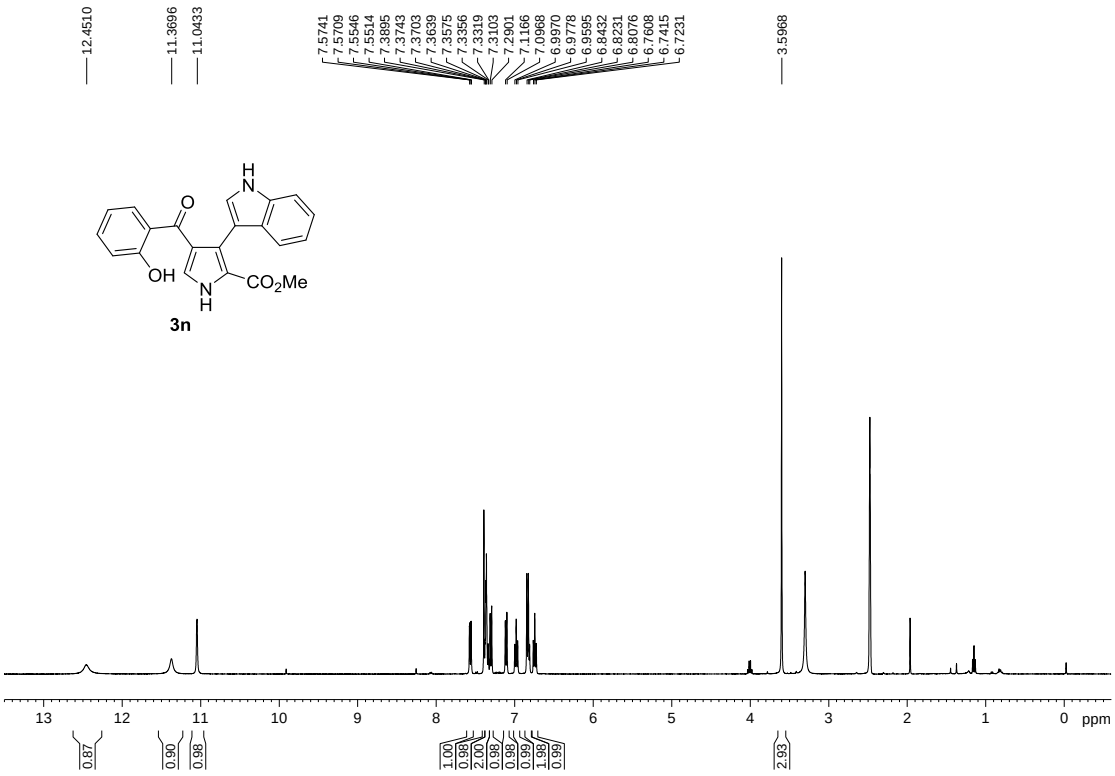
0
ppm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7.3575
7.3356
7.3319
7.3103
7.2901
7.1166
7.0968
6.9970
6.9778
6.9595
6.8432
6.8231
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6.7608
6.7415
6.7231
3.5968
O
H
N
OH
N
H
CO2Me
3n
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
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1.98
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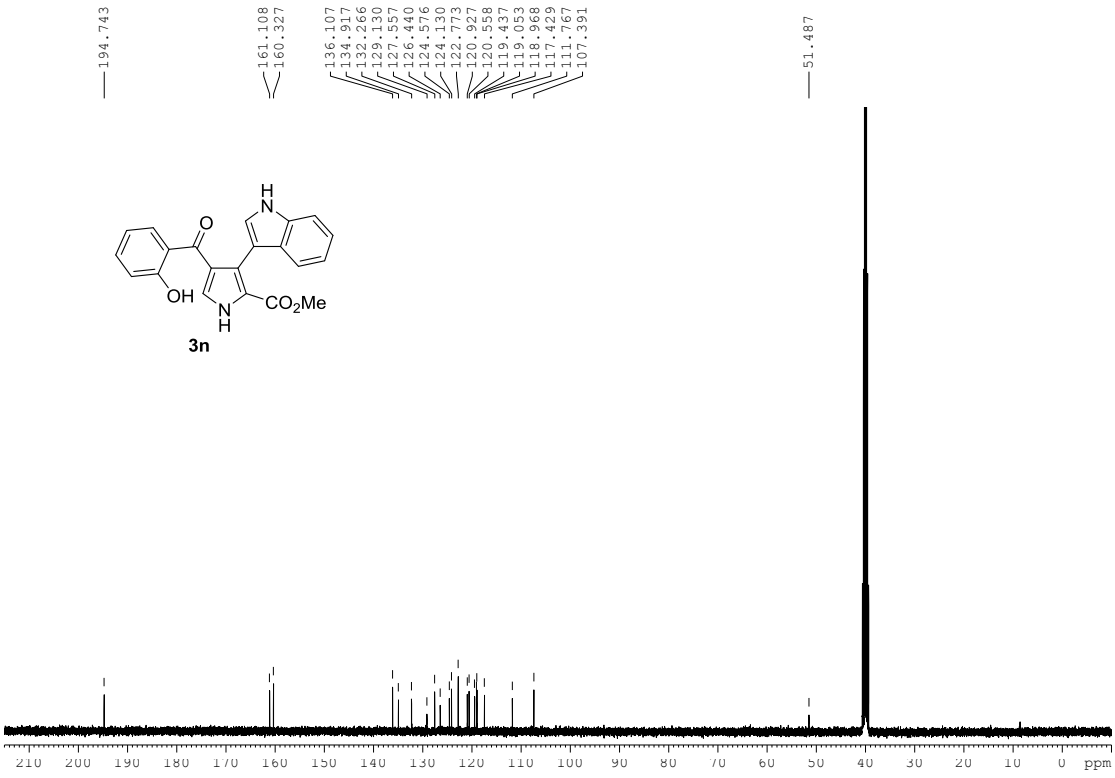
2.93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120.558
119.437
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118.968
117.429
111.767
107.391
51.487
O
H
N
OH
N
H
CO2Me
3n
210
200
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180
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120
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60
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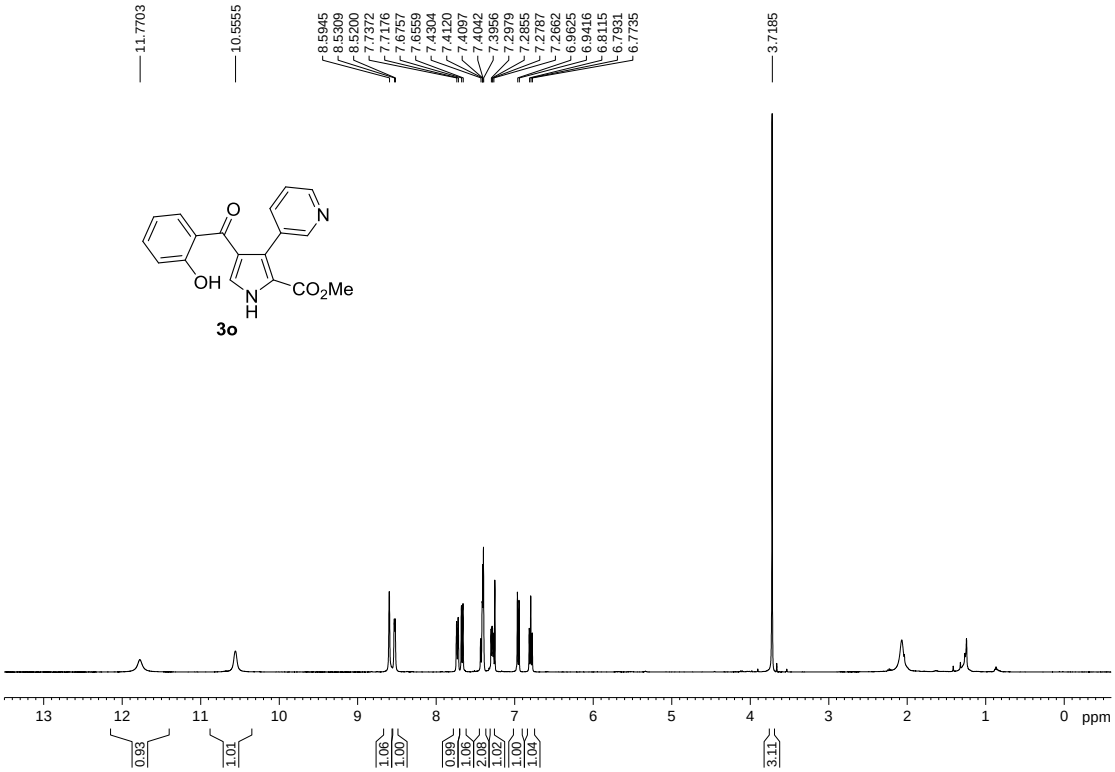
0
ppm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8.5945
8.5309
8.5200
7.7372
7.7176
7.6757
7.6559
7.4304
7.4120
7.4097
7.4042
7.3956
7.2979
7.2855
7.2787
7.2662
6.9625
6.9416
6.8115
6.7931
6.7735
3.7185
O
N
OH
N
H
CO2Me
3o
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
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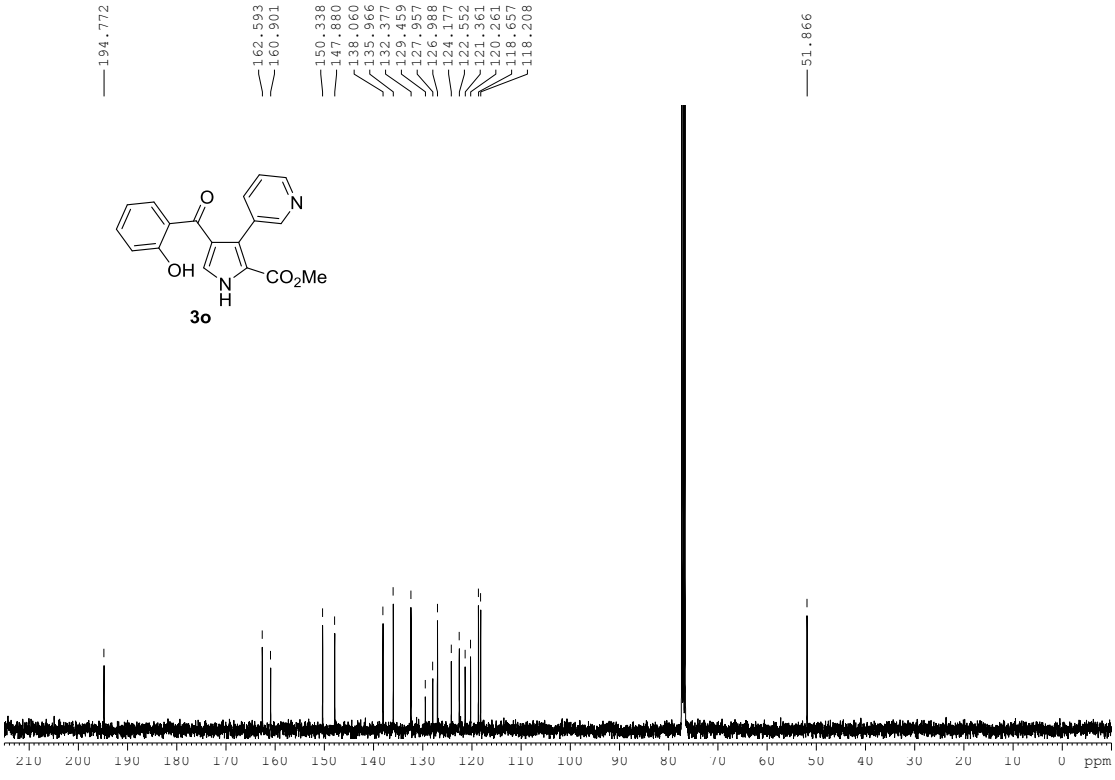
1.01
1.06
1.00
0.99
1.06
2.08
1.02
1.00
1.04
3.11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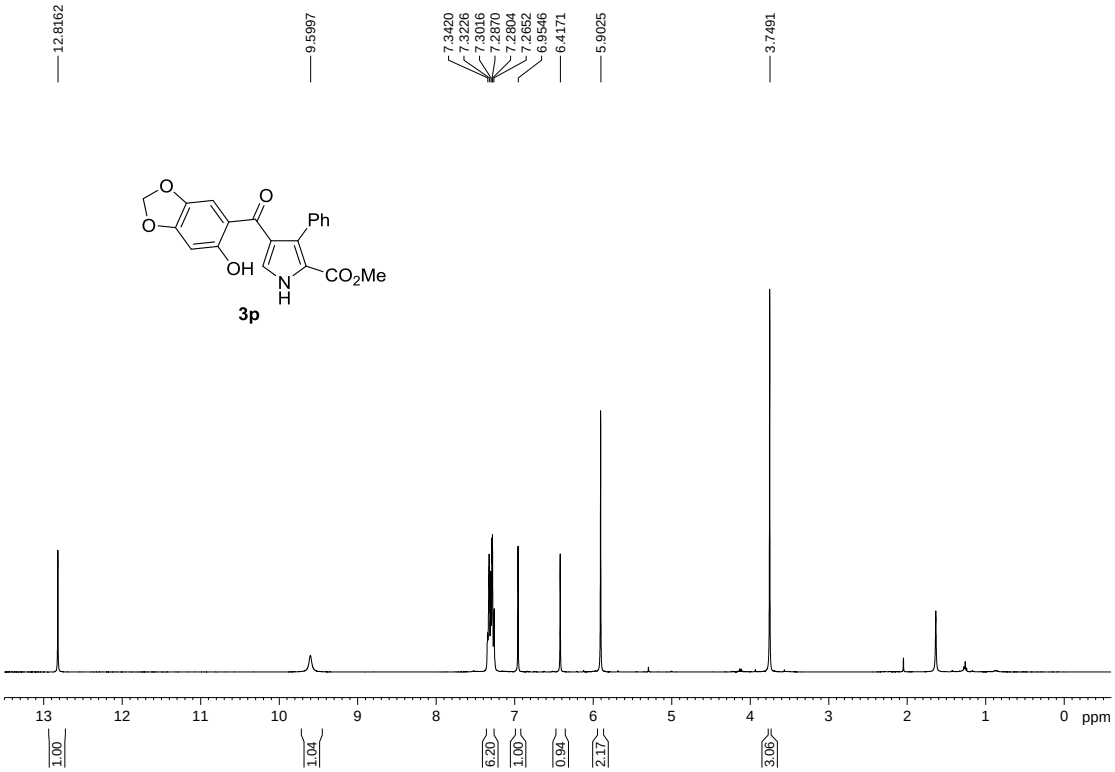
160.901
150.338
147.880
138.060
135.966
132.377
129.459
127.957
126.988
124.177
122.552
121.361
120.261
118.657
118.208
51.866
O
N
OH
N
H
CO2Me
3o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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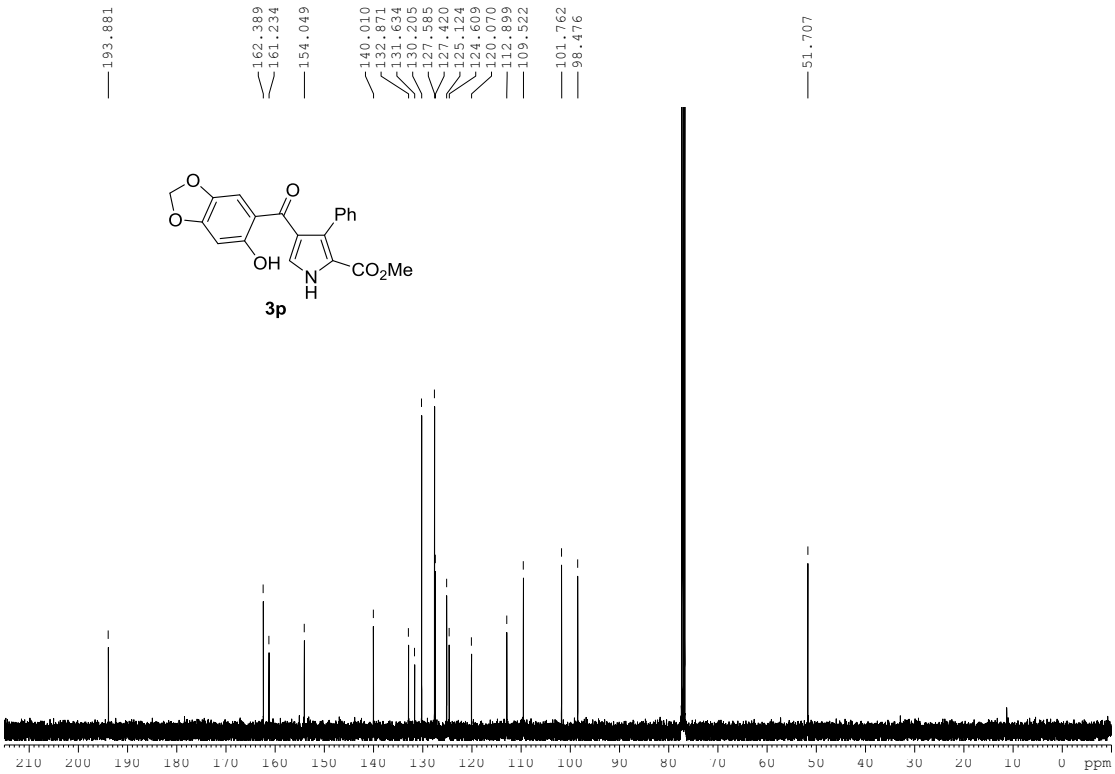
9.5997
7.3420
7.3226
7.3016
7.2870
7.2804
7.2652
6.9546
6.4171
5.9025
3.7491
O
O
O
Ph
OH
N
H
CO2Me
3p
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.04
6.20
1.00
0.94
2.17
3.06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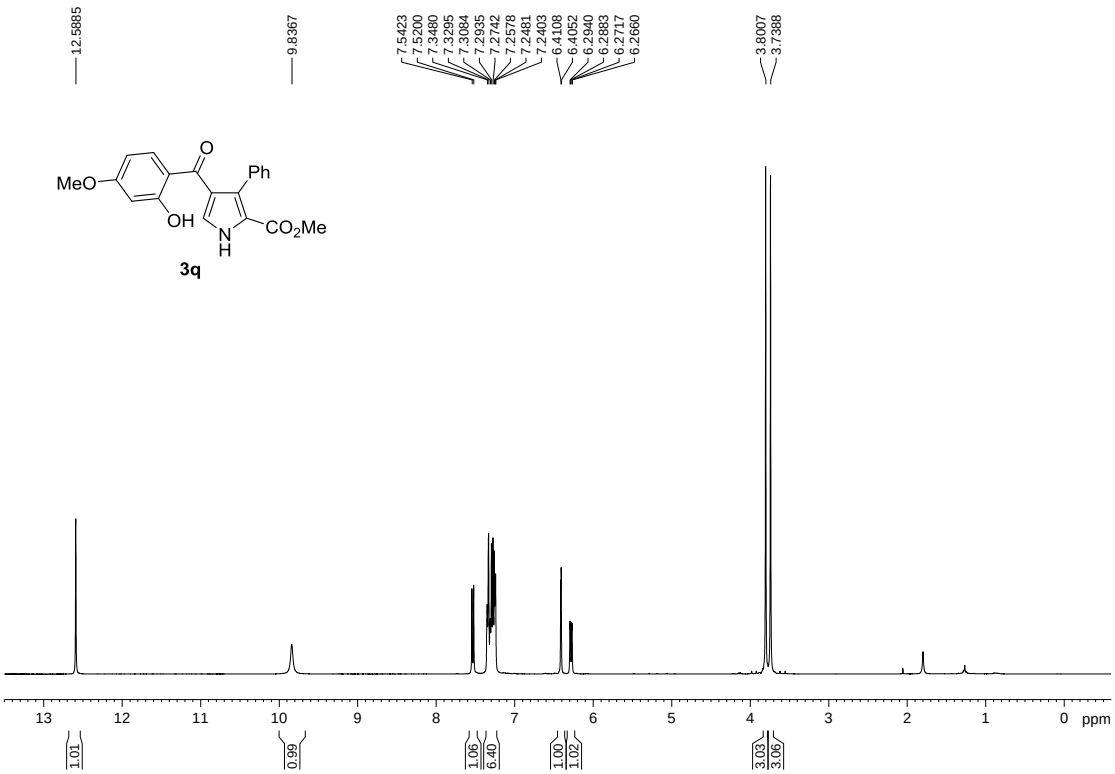
162.389
161.234
154.049
140.010
132.871
131.634
130.205
127.585
127.420
125.124
124.609
120.070
112.899
109.522
101.762
98.476
51.707
O
O
O
Ph
OH
N
H
CO2Me
3p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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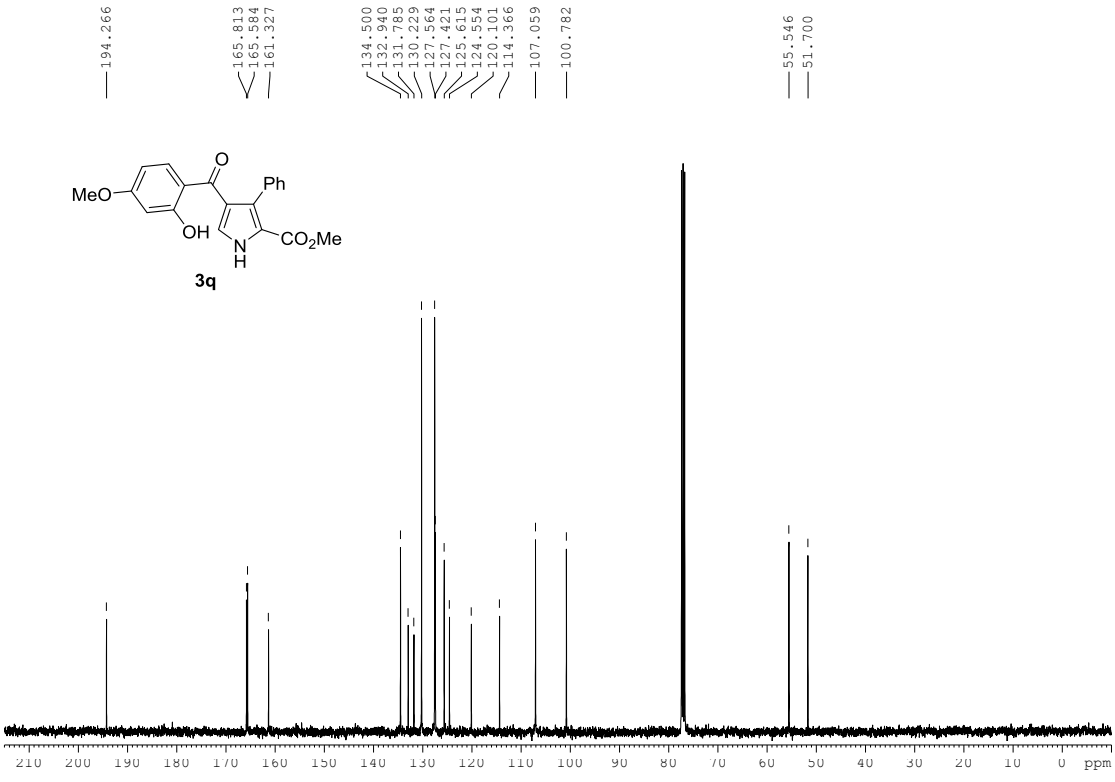
9.8367
7.5423
7.5200
7.3480
7.3295
7.3084
7.2935
7.2742
7.2578
7.2481
7.2403
6.4108
6.4052
6.2940
6.2883
6.2717
6.2660
3.8007
3.7388
MeO
OH
O
Ph
N
H
CO2Me
3q
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.01
0.99
1.06
6.40
1.00
1.02
3.03
3.06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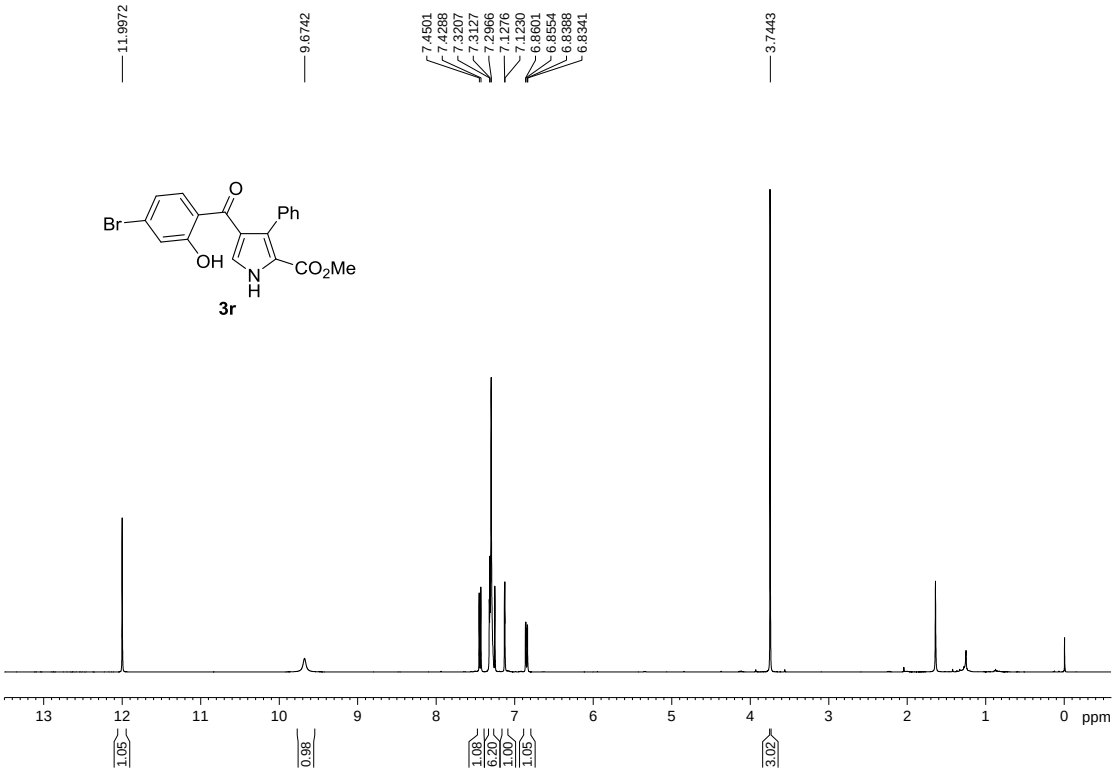
165.813
165.584
161.327
134.500
132.940
131.785
130.229
127.564
127.421
125.615
124.554
120.101
114.366
107.059
100.782
55.546
51.700
MeO
OH
O
Ph
N
H
CO2Me
3q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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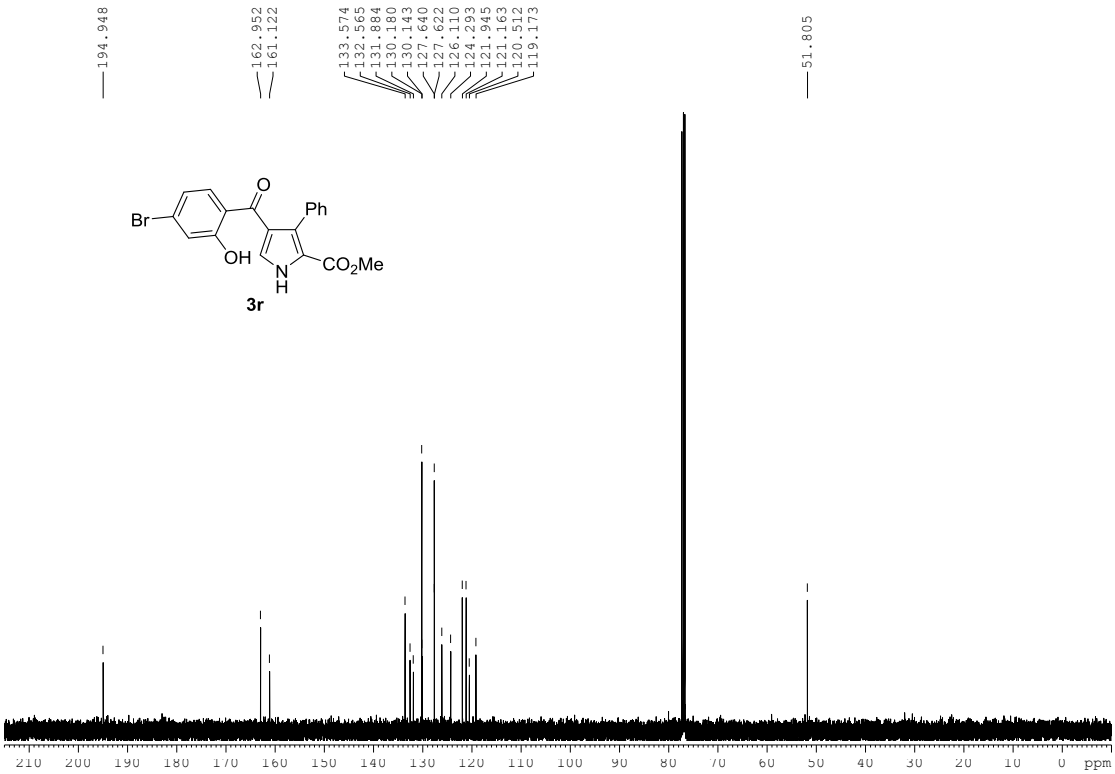
7.4501
7.4288
7.3207
7.3127
7.2966
7.1276
7.1230
6.8601
6.8554
6.8388
6.8341
3.7443
Br
O
Ph
OH
N
H
CO2Me
3r
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.05
0.98
1.08
6.20
1.00
1.05
3.02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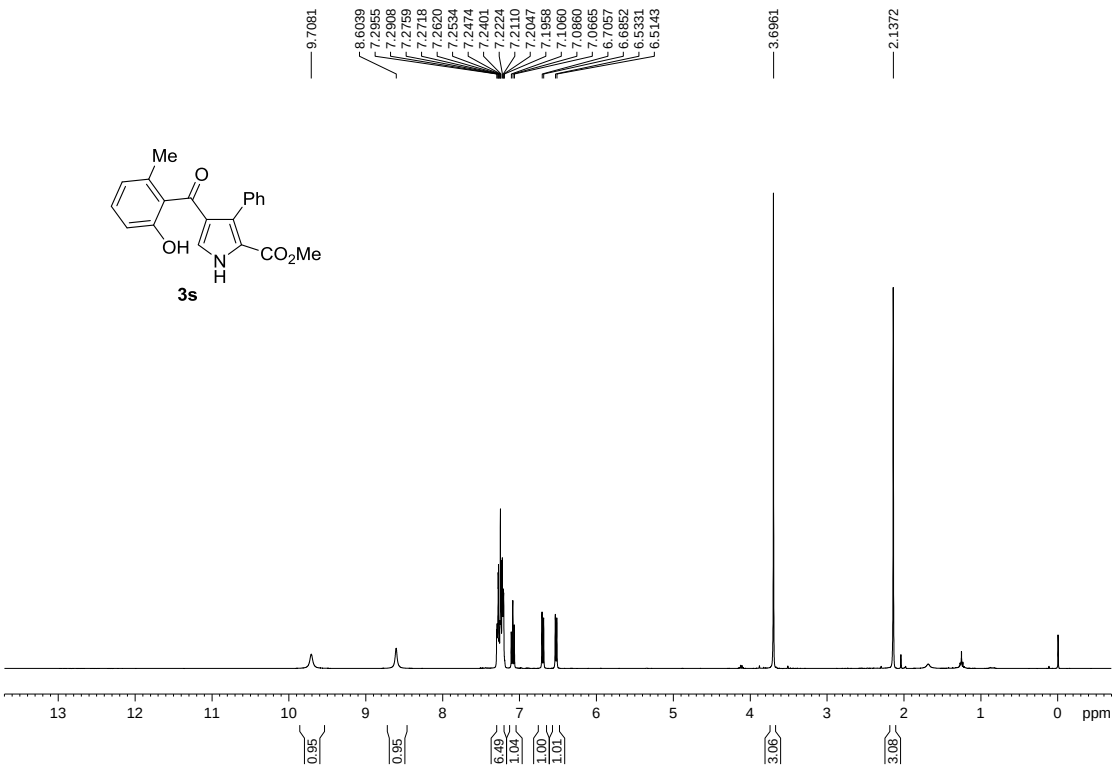
161.122
133.574
132.565
131.884
130.180
130.143
127.640
127.622
126.110
124.293
121.945
121.163
120.512
119.173
51.805
Br
O
Ph
OH
N
H
CO2Me
3r
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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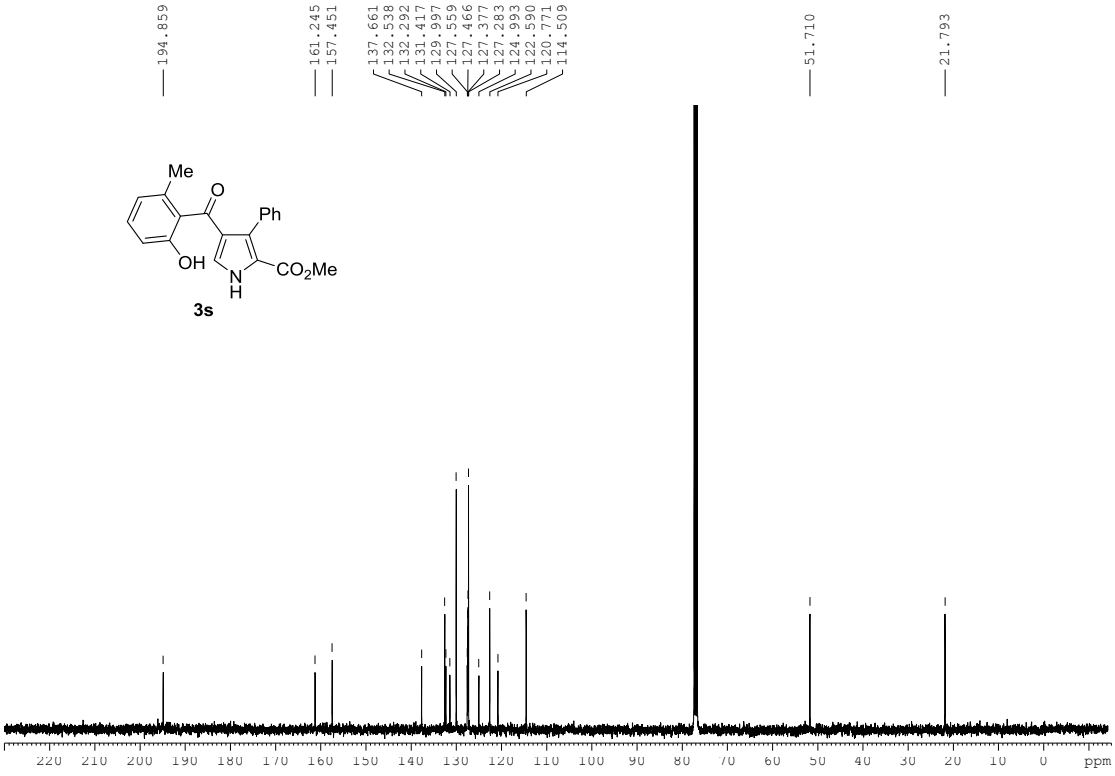
8.6039
7.2955
7.2908
7.2759
7.2718
7.2620
7.2534
7.2474
7.2401
7.2224
7.2110
7.2047
7.1958
7.1060
7.0860
7.0665
7.0057
6.6852
6.5331
6.5143
3.6961
2.1372
Me
O
Ph
OH
N
H
CO2Me
3s
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
0.95
6.49
1.04
1.00
1.01
3.06
3.08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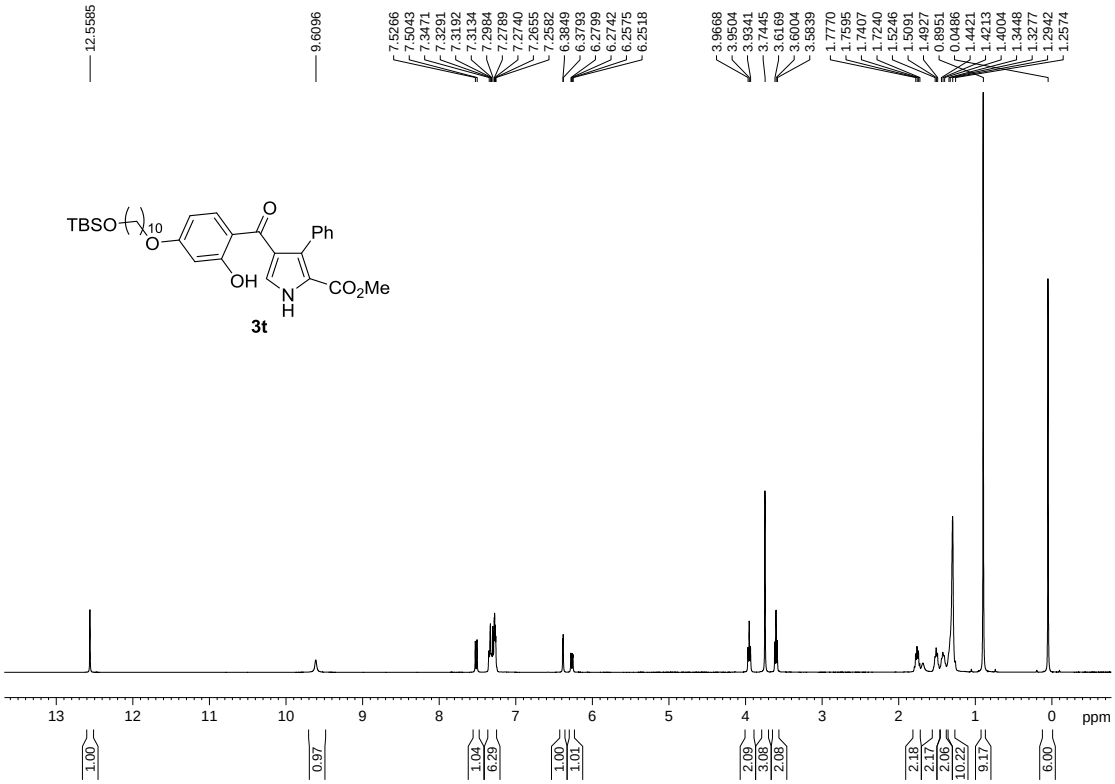
157.451
137.661
132.538
132.292
131.417
129.997
127.559
127.466
127.377
127.283
124.993
122.590
120.771
114.509
51.710
21.793
Me
O
Ph
OH
N
H
CO2Me
3s
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.3192
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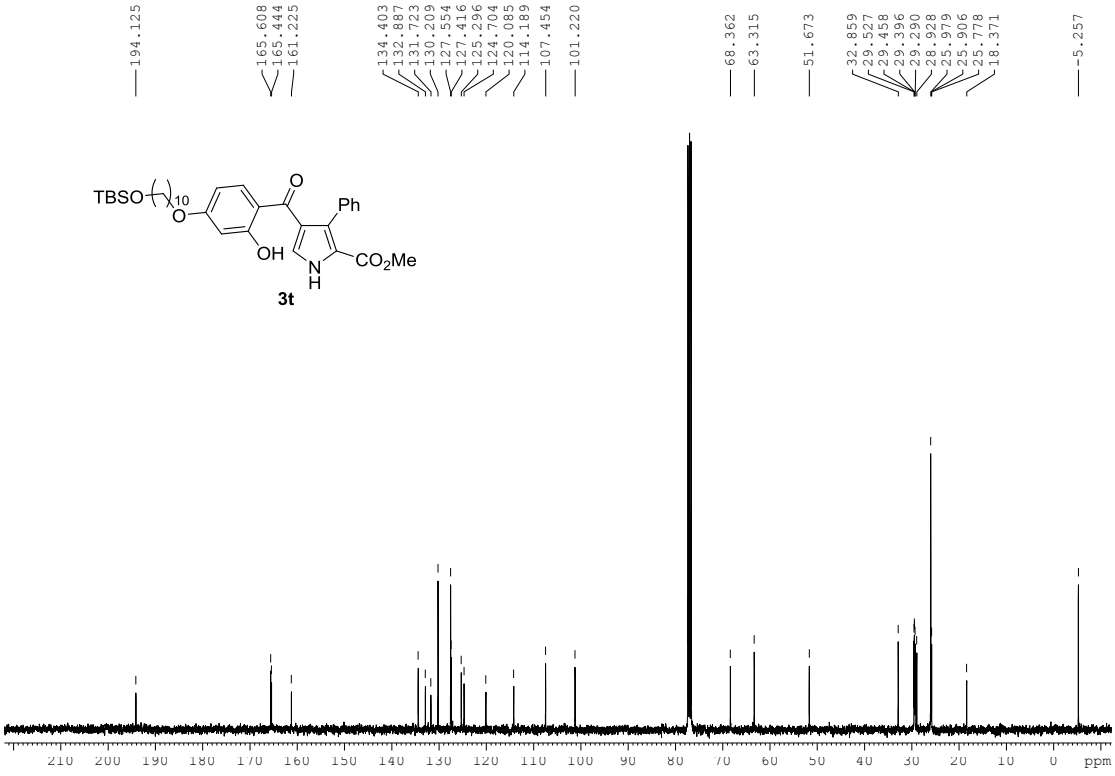
7.2984
7.2789
7.2740
7.2655
7.2582
6.3849
6.3793
6.2799
6.2742
6.2575
6.2518
3.9668
3.9504
3.9341
3.7445
3.6169
3.6004
3.5839
1.7770
1.7595
1.7407
1.7240
1.5246
1.5091
1.4927
0.8951
0.0486
1.4421
1.4213
1.4004
1.3448
1.3277
1.2942
1.2574
TBSO
10
O
Ph
OH
N
H
CO2Me
3t
ppm
1.00
0.97
1.04
6.29
1.00
1.01
2.09
3.08
2.08
2.18
2.17
2.06
10.22
9.17
6.00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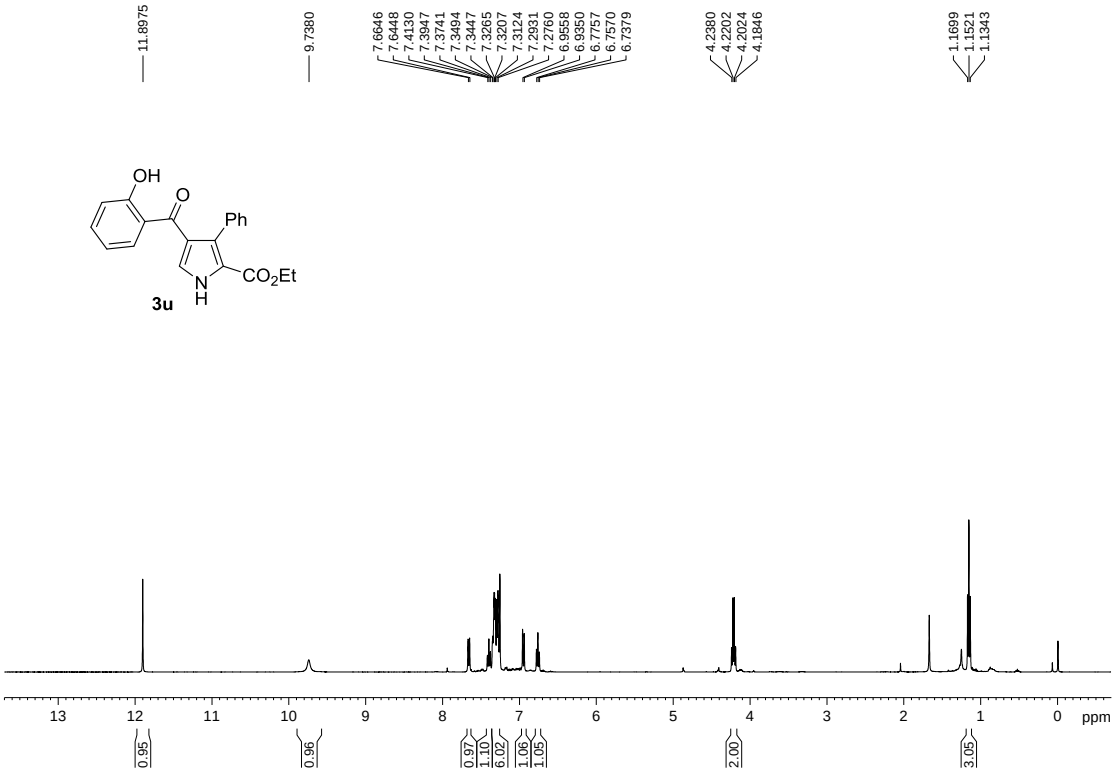
165.608
165.444
161.225
134.403
132.887
131.723
130.209
127.554
127.416
125.296
124.704
120.085
114.189
107.454
101.220
68.362
63.315
51.673
32.859
29.527
29.458
29.396
29.290
28.928
25.979
25.906
25.778
18.371
-5.257
TBSO
10
O
Ph
OH
N
H
CO2Me
3t
ppm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7.6448
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7.3947
7.3741
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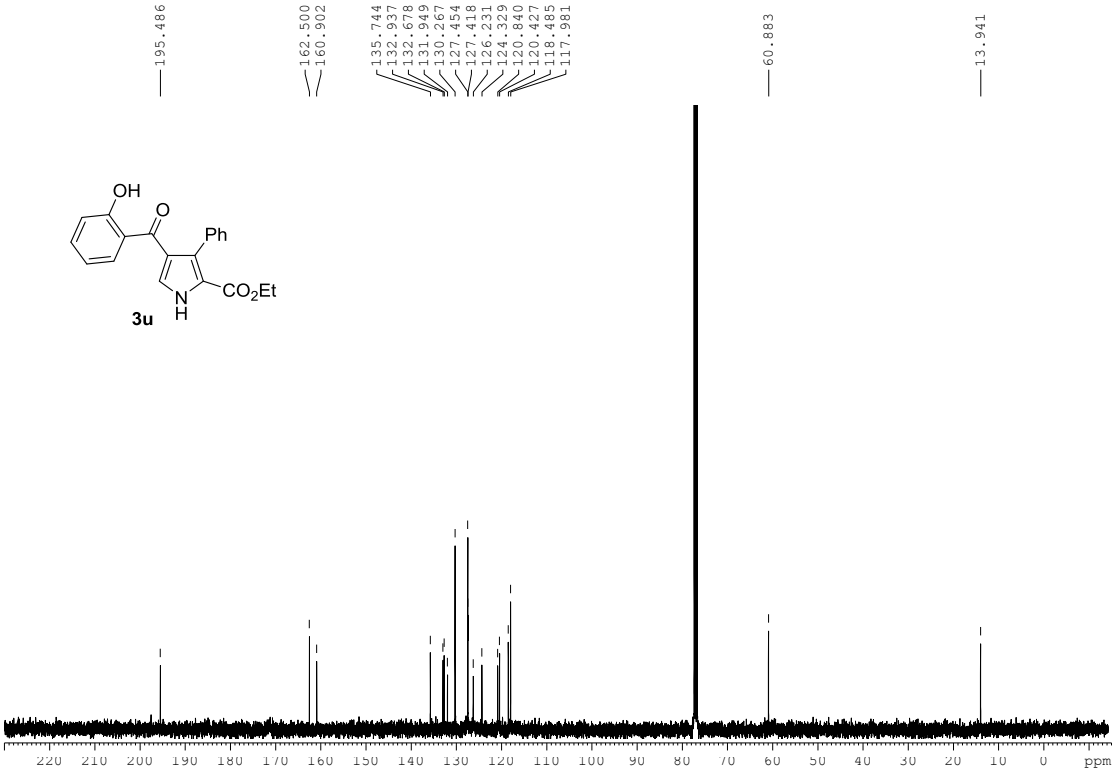
7.3447
7.3265
7.3207
7.3124
7.2931
7.2760
6.9558
6.9350
6.7757
6.7570
6.7379
4.2380
4.2202
4.2024
4.1846
1.1699
1.1521
1.1343
OH
O
Ph
CO2Et
N
H
3u
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
0.96
0.97
1.10
6.02
1.06
1.05
2.00
3.05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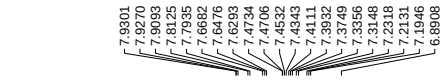
160.902
135.744
132.937
132.678
131.949
130.267
127.454
127.418
126.231
124.329
120.840
120.427
118.485
117.981
60.883
13.941
OH
O
Ph
CO2Et
N
H
3u
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.9301
7.9270
7.9093
7.8125
7.7935
7.6682
7.6476
7.6293
7.4734
7.4706
7.4532
7.4343
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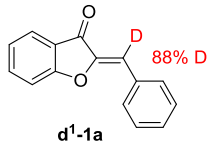
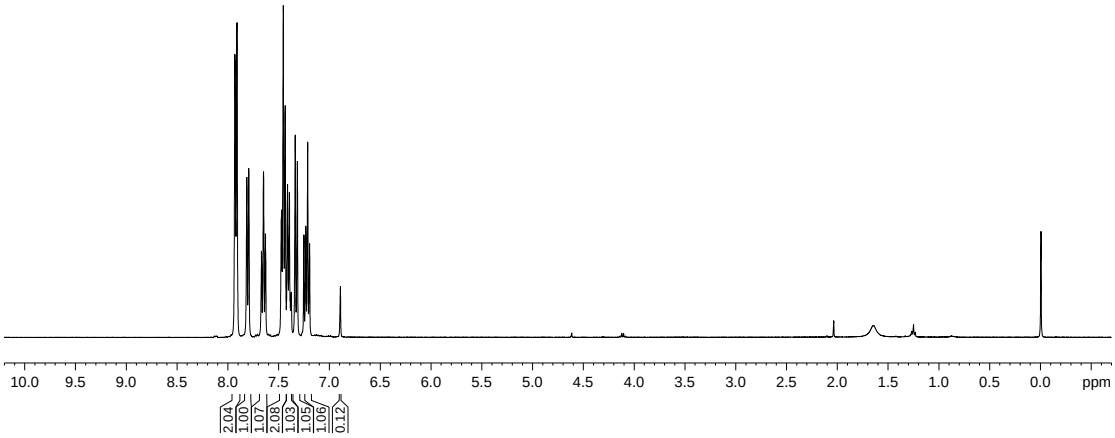
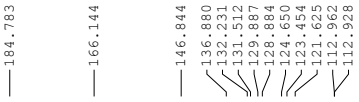
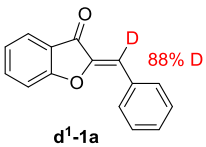
7.3932
7.3749
7.3356
7.3148
7.2318
7.2131
7.1946
6.8908


O
D
88% D
O

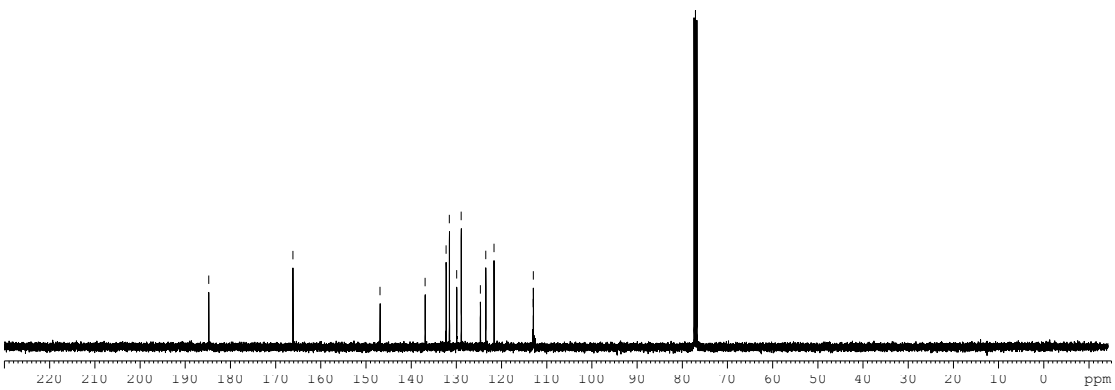
d^1-1a

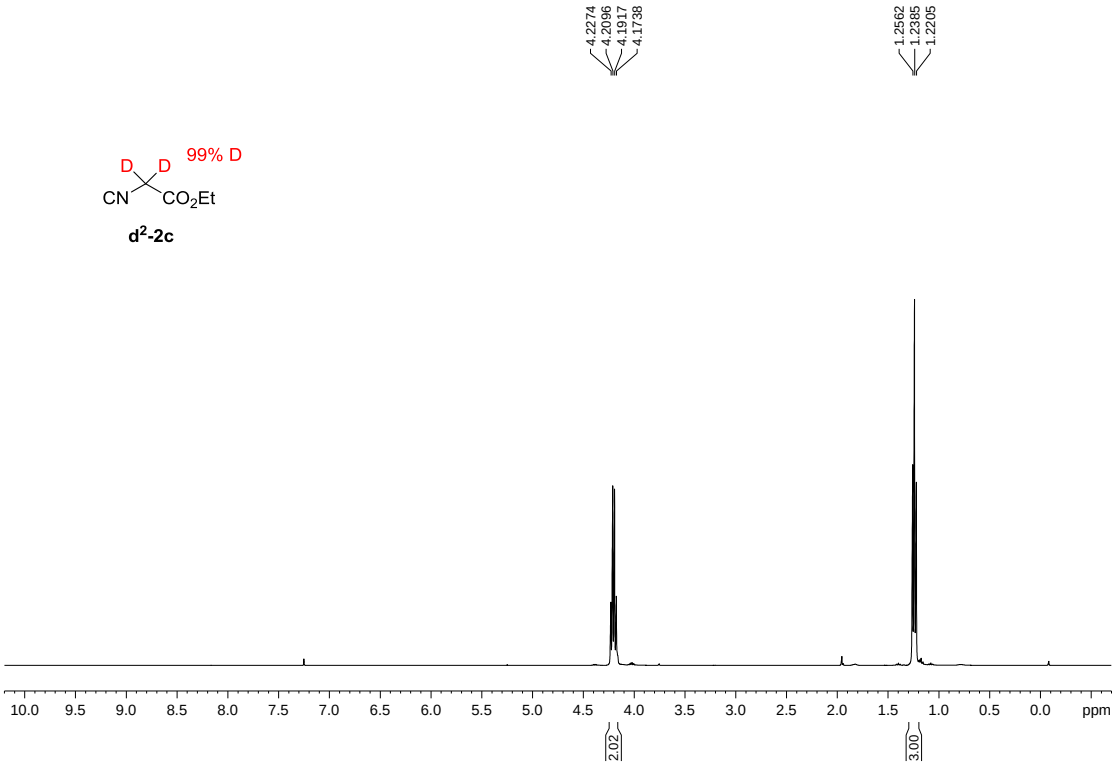

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.04
1.00
1.07
2.08
1.03
1.05
1.06
0.12

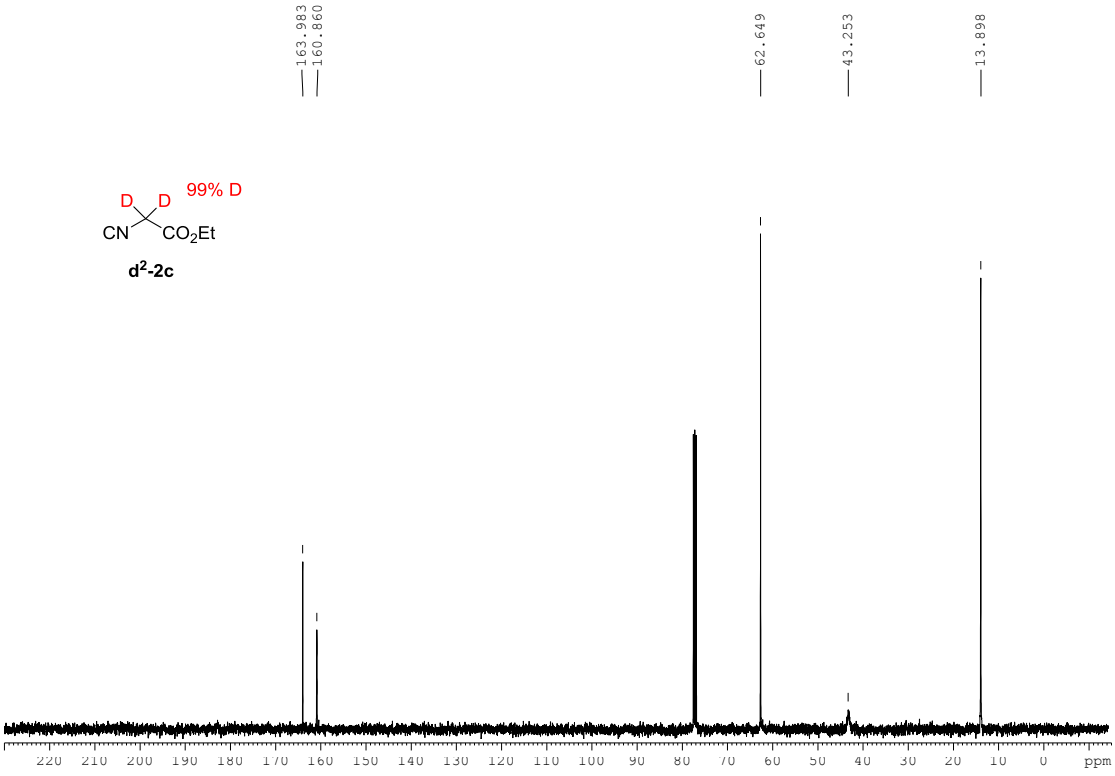

184.783
166.144
146.844
136.880
132.231
131.512
129.887
128.884
124.650
123.454
121.625
112.962
112.928

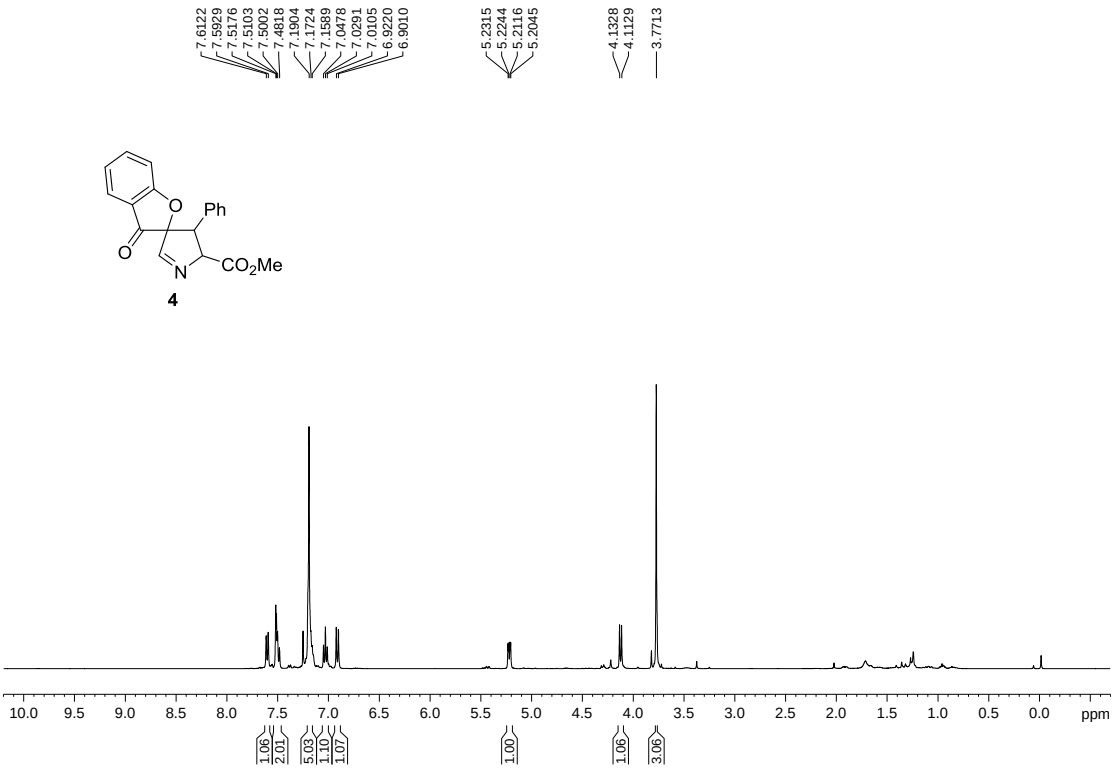

O
D
88% D
O

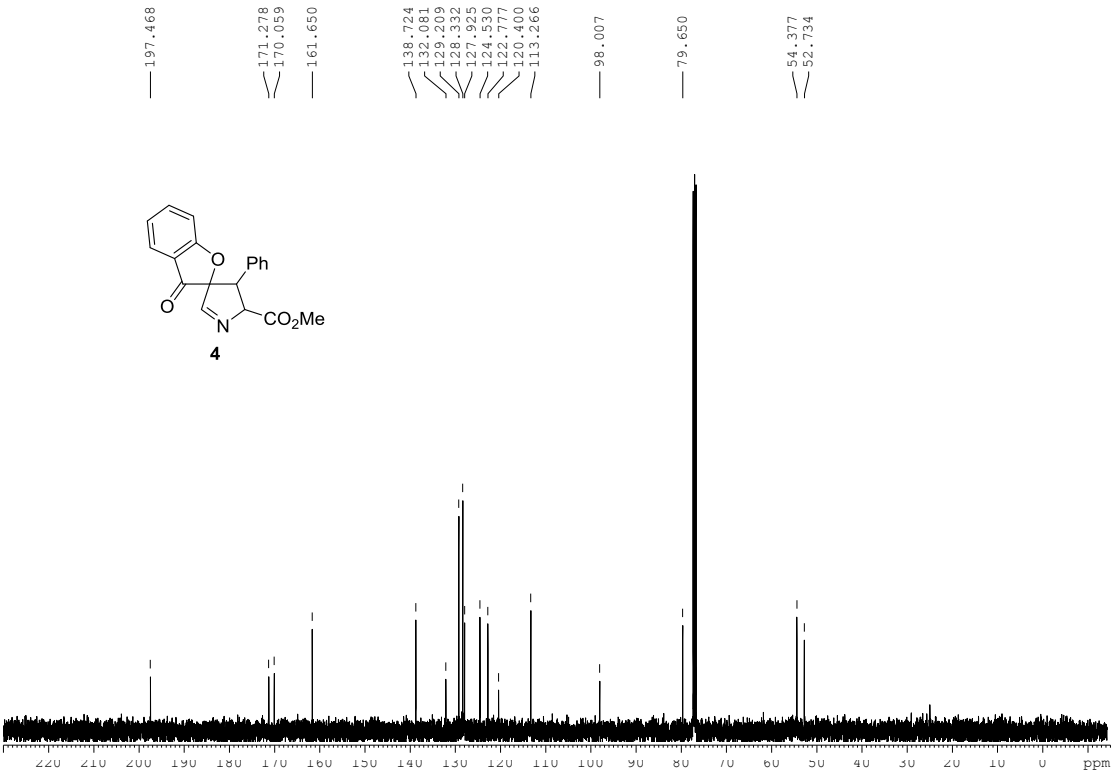
d^1-1a

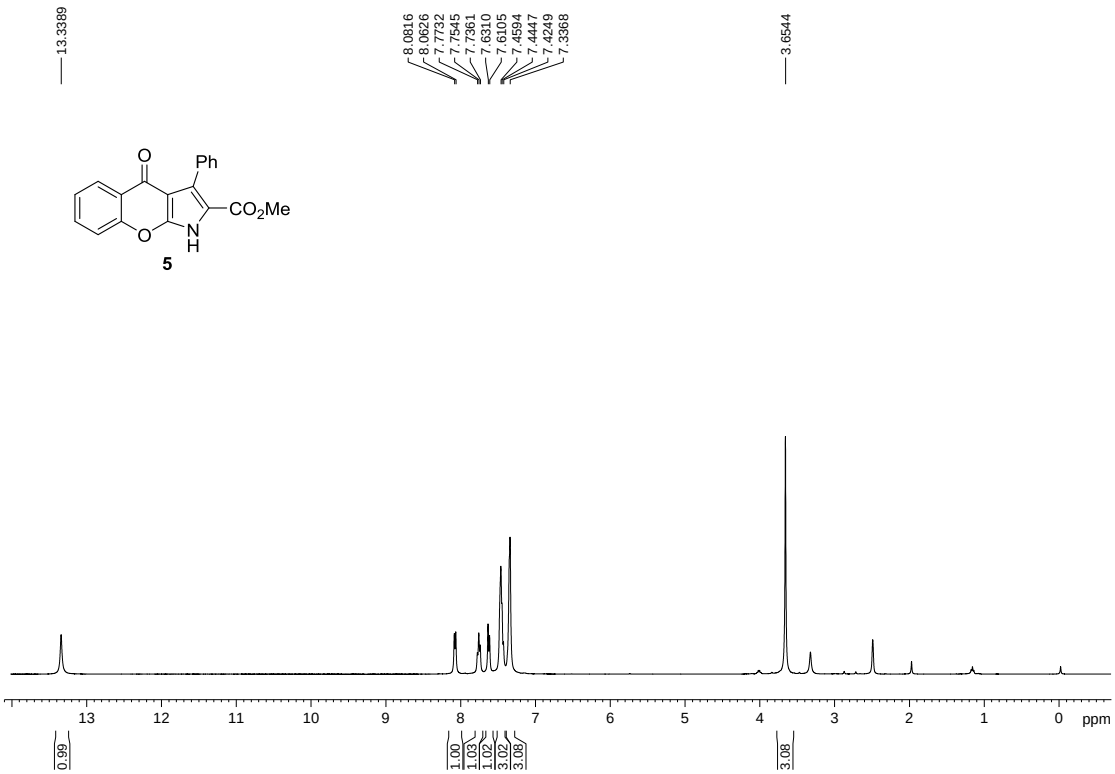

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4.2274
4.2096
4.1917
4.1738
1.2562
1.2385
1.2205
D
D
99% D
CN
CO2Et
d2-2c
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 ppm
2.02
3.00


163.983
160.860
62.649
43.253
13.898
D
D
99% D
CN
CO2Et
d2-2c
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.6122
7.5929
7.5176
7.5103
7.5002
7.4818
7.1904
7.1724
7.1589
7.0478
7.0291
7.0105
6.9220
6.9010
5.2315
5.2244
5.2116
5.2045
4.1328
4.1129
3.7713
Ph
O
N
CO2Me
4
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 ppm
1.06
2.01
5.03
1.10
1.07
1.00
1.06
3.06


197.468
171.278
170.059
161.650
138.724
132.081
129.209
128.332
127.925
124.530
122.777
120.400
113.266
98.007
79.650
54.377
52.734
Ph
O
N
CO2Me
4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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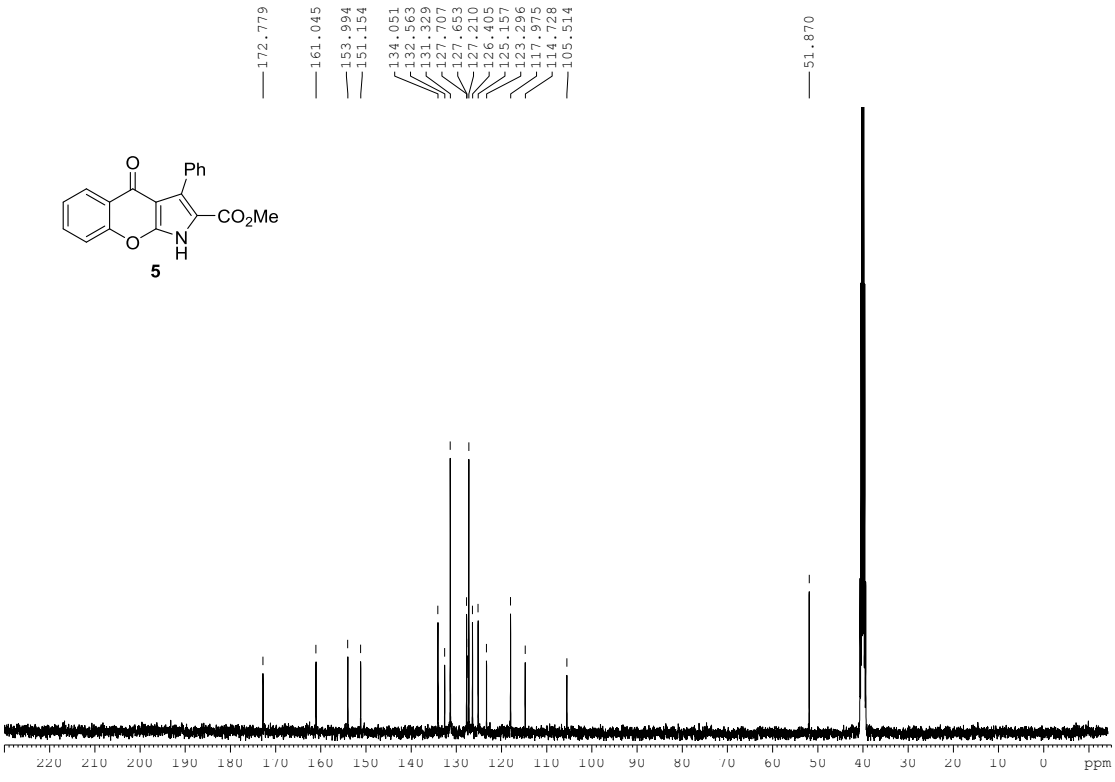
8.0626
7.7732
7.7545
7.7361
7.6310
7.6105
7.4594
7.4447
7.4249
7.3368
3.6544
O
Ph
CO2Me
N
H
O
5
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
1.00
1.03
1.02
3.02
3.08
3.08


172.779
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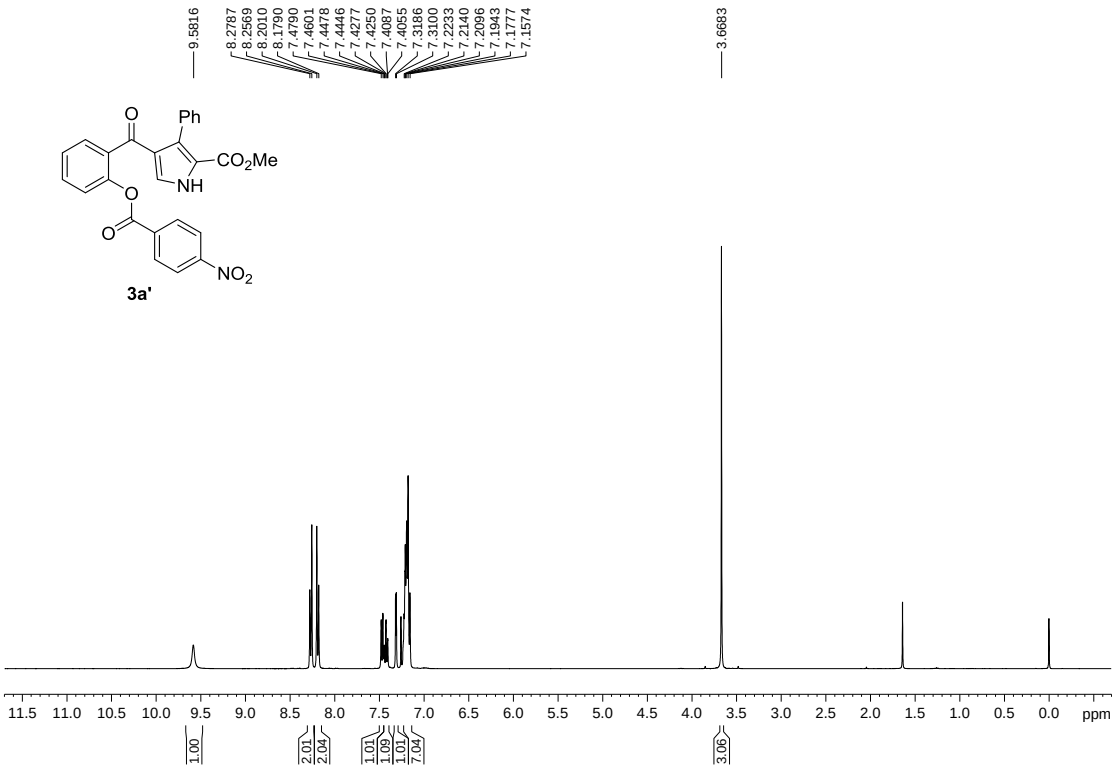
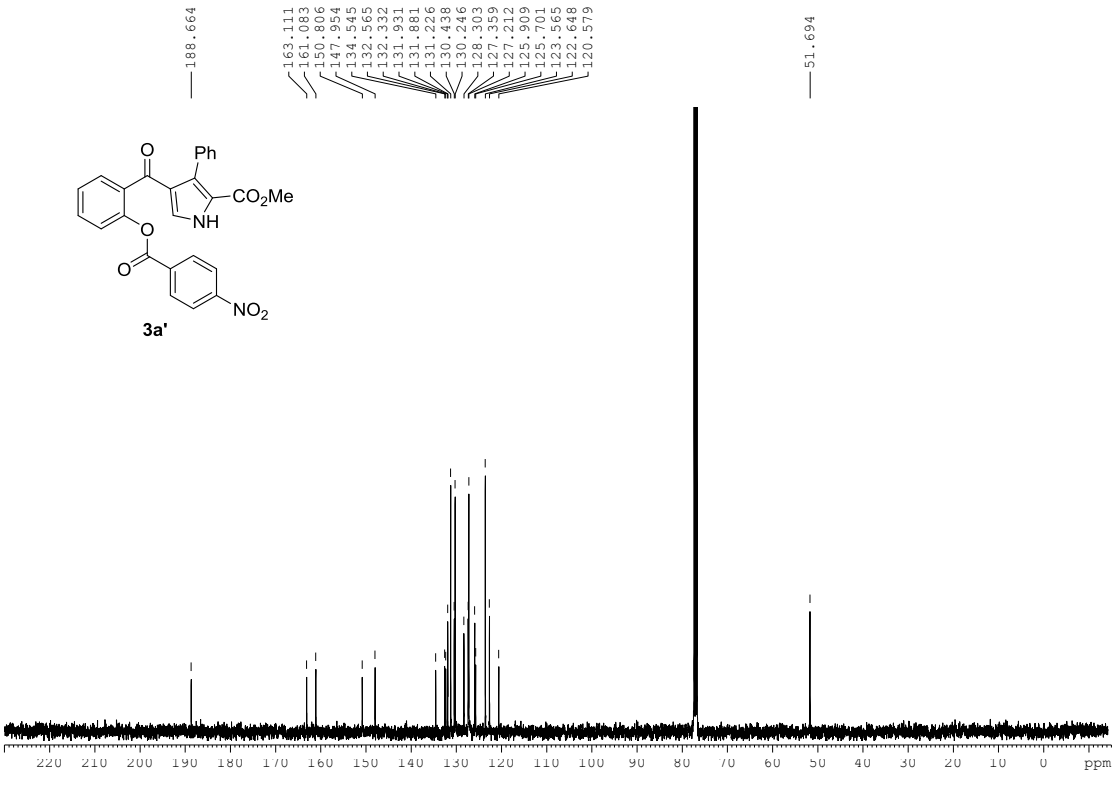
153.994
151.154
134.051
132.563
131.329
127.707
127.653
127.210
126.405
125.157
123.296
117.975
114.728
105.514
51.870
O
Ph
CO2Me
N
H
O
5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


9.5816
8.2787
8.2569
8.2010
8.1790
7.4790
7.4601
7.4478
7.4446
7.4277
7.4250
7.4087
7.4055
7.3186
7.3100
7.2233
7.2140
7.2096
7.1943
7.1777
7.1574
3.6683
Ph
CO2Me
NH
O
O
O
NO2
3a'
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
2.01
2.04
1.01
1.09
1.01
7.04
3.06


188.664
163.111
161.083
150.806
147.954
134.545
132.565
132.332
131.931
131.881
131.226
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130.246
128.303
127.359
127.212
125.909
125.701
123.565
122.648
120.579
51.694
Ph
CO2Me
NH
O
O
O
NO2
3a'
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm