Supporting Information

Copper-catalyzed decarboxylative C3-acylation of free (N–H) indoles with α-oxocarboxylic acids

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1. General Experimental Method

1.1 General Considerations

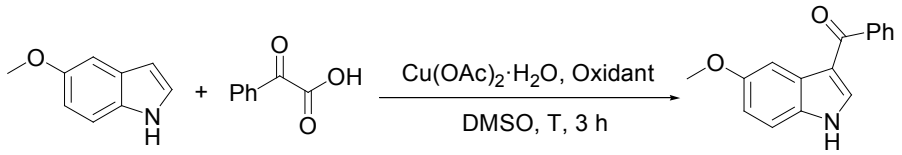
All reactions were carried out in dried glassware. Pd and Cu catalysts, Ag (I) salts, SeO_2, indoles and solvents were purchased from commercial sources and used without further purification. Phenylglyoxylic acid was purchased from Alfa Aesar and other α-oxocarboxylic acids were prepared from oxidation of corresponding methyl ketones with SeO_2 according to the reported procedure[1].

Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 300-400 mesh silica gel in petroleum ether. All melting points are determined on a WRS-2A micro processor melting-point apparatus and uncorrected. IR spectra were recorded on a WQF-200 FTIR spectrometer and only major peaks were recorded in cm^{-1}. ^1H NMR and ^{13}C NMR data were recorded on Bruker Advance NMR spectrometer (500 MHz) in C_2D_6O as solvent. Chemical shifts (δ) were reported in parts per million (ppm) using tetramethylsilane (TMS) as the internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). HRMS (ESI) analysis was obtained from Micromass UPLC/Q-TOF Micro Mass Spectrometer. XRD powder diffraction was carried out on Bruker's D8 ADVANCE X-Ray Diffractometer with Guinier imaging plate detector (Cu-$K_{\alpha 1}$ radiation, λ= 154.056 pm).

1.2 General procedure for Copper-catalyzed decarboxylative C3-acylation of free (N–H) indoles with α-oxocarboxylic acids

A dried two-neck round bottom flask was charged with indole (0.8 mmol), α-oxocarboxylic acid (1.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (39.9 mg, 20 mol%), Ag_2CO_3 (441.2 mg, 1.6 mmol) and DMSO or DMF (4 mL) under air atmosphere. The reaction mixture was heated at 90 ^oC and stirred for 1.5-8 h. After completion of the reaction (monitored by TLC or HPLC), the reaction mixture was cooled to room temperature and diluted with ethyl acetate (5 mL) and water (5 mL), then the filtrate collected by centrifugation and filtration was extracted with ethyl acetate (3×10 mL). The organic layers were combined, washed with saturated $NaHCO_3$, dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5/1, v/v) to afford the desired products. The structures of the products were identified by IR, NMR and HRMS analyses.

2. Optimization of silver oxidants, its loading and the reaction temperature[a] (Table S1)

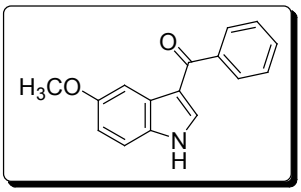


Entry	Catalyst	Oxidant (equiv)	Yield (%)[b]
1	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (2)	71
2	$Cu(OAc)_2 \cdot H_2O$	Ag_2O (2)	63
3	$Cu(OAc)_2 \cdot H_2O$	AgOAc (2)	37
4	$Cu(OAc)_2 \cdot H_2O$	$AgNO_3$ (2)	0
5	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (1)	49
6	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (1.5)	60
7	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (1.7)	64
8	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (2.5)	61
9[c]	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (2)	68
10[d]	$Cu(OAc)_2 \cdot H_2O$	Ag_2CO_3 (2)	58

[a] Conditions: **1a** (0.8 mmol), **2a** (1.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (20 mol%), Oxidant, DMSO (4 mL), 90 °C, 3 h, under air. [b] Isolated yields. [c] The reaction was performed at 80 °C. [d] The reaction was performed at 100 °C.

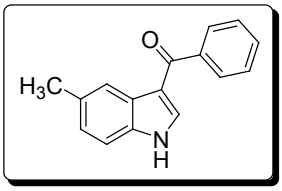
3. Characterization data for products 3a-3u

(5-methoxy-1*H*-indol-3-yl)(phenyl)methanone (3a)[2]



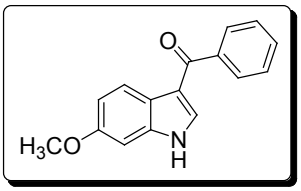
Yield: 71%, pale yellow solid, mp. 223-224 °C. IR (KBr, cm^{-1}): ν_{max} 3143, 1601. ^1H NMR (500 MHz, DMSO-d_6): δ 11.98 (s, 1H), 7.89 (d, *J*=2.5 Hz, 1H), 7.81 (d, *J*=2.0 Hz, 1H), 7.79 (d, *J*=7.5 Hz, 2H), 7.61 (t, *J*=7.0 Hz, 1H), 7.56 (dd, *J*=7.5, 7.0 Hz, 2H), 7.44 (d, *J*=8.5 Hz, 1H), 6.92 (d, *J*=8.5 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.36, 156.06, 141.16, 136.31, 132.05, 131.37, 128.83, 128.73, 127.55, 115.36, 113.48, 113.43, 103.79, 55.80. HRMS (ESI) calcd for $C_{16}H_{13}NO_2Na$ $[M+Na]^+$ 274.0844, found m/z 274.0848.

(5-methyl-1*H*-indol-3-yl)(phenyl)methanone (3b)[3]



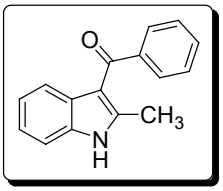
Yield: 77%, yellow solid, mp. 227-228 °C. IR (KBr, cm^{-1}): ν_{max} 3154, 1597. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.97 (s, 1H), 8.08 (s, 1H), 7.87 (d, *J*=3.0 Hz, 1H), 7.77 (d, *J*=7.0 Hz, 2H), 7.61-7.58 (m, 1H), 7.55-7.52 (m, 2H), 7.40 (d, *J*=8.5 Hz, 1H), 7.09 (d, *J*=8.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.38, 141.17, 136.16, 135.52, 131.38, 131.19, 128.81, 128.77, 127.01, 125.06, 121.69, 115.16, 112.33, 21.82. HRMS (ESI) calcd for $C_{16}H_{13}NONa$ $[M+Na]^+$ 258.0895, found m/z 258.0896.

(6-methoxy-1*H*-indol-3-yl)(phenyl)methanone (3c)[4]



Yield: 37%, brown solid, mp. 226-228 °C. IR (KBr, cm^{-1}): ν_{max} 3119, 1596. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.87 (s, 1H), 8.11 (d, *J*=9.0 Hz, 1H), 7.80-7.76 (m, 3H), 7.60 (t, *J*=7.0 Hz, 1H), 7.53 (dd, *J*=7.0, 7.0 Hz, 2H), 7.00 (s, 1H), 6.88 (d, *J*=8.0 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.28, 157.07, 141.03, 138.11, 135.26, 131.42, 128.81, 128.77, 122.59, 120.71, 115.60, 112.13, 95.77, 55.75. HRMS (ESI) calcd for $C_{16}H_{13}NO_2Na$ $[M+Na]^+$ 274.0844, found m/z 274.0848.

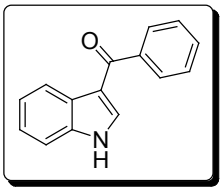
(2-methyl-1*H*-indol-3-yl)(phenyl)methanone (3d)[5]



Yield: 35%, brown solid, mp. 178-180 °C. IR (KBr, cm^{-1}): ν_{max} 3170, 1606. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.96 (s, 1H), 7.61-7.58 (m, 3H), 7.50 (dd, *J*=7.0, 7.5 Hz, 2H), 7.39 (d, *J*=8.0 Hz, 1H), 7.33 (d, *J*=8.0 Hz, 1H), 7.12 (dd, *J*=7.5, 7.5 Hz, 1H), 7.00 (dd, *J*=7.5, 7.5 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.18, 144.87, 142.20, 135.46, 131.46, 128.81, 128.46, 127.78,

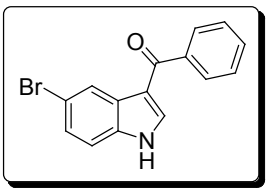
122.27, 121.39, 120.49, 112.98, 111.71, 14.64. HRMS (ESI) calcd for $C_{16}H_{13}NONa$ $[M+Na]^+$ 258.0895, found m/z 258.0896.

(1*H*-indol-3-yl)(phenyl)methanone (3e)[2b, 6]



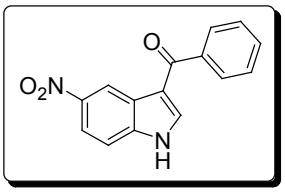
Yield: 55%, pale yellow solid, mp. 244-246 °C. IR (KBr, cm^{-1}): v_{max} 3130, 1593. ^1H NMR (500 MHz, DMSO-d_6): δ 12.08 (s, 1H), 8.26 (d, *J*=7.0 Hz, 1H), 7.94 (d, *J*=3.0 Hz, 1H), 7.79 (d, *J*=7.0 Hz, 2H), 7.63-7.60 (m, 1H), 7.56-7.52 (m, 3H), 7.29-7.23 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.43, 141.05, 137.20, 136.16, 131.48, 128.85, 128.82, 126.74, 123.58, 122.35, 121.94, 115.52, 112.70. HRMS (ESI) calcd for $C_{15}H_{11}NONa$ $[M+Na]^+$ 244.0738, found m/z 244.0742.

(5-bromo-1*H*-indol-3-yl)(phenyl)methanone (3f)[6a]



Yield: 54%, pale yellow solid, mp. 265-266 °C. IR (KBr, cm^{-1}): v_{max} 3136, 1612. ^1H NMR (500 MHz, DMSO-d_6): δ 12.27 (s, 1H), 8.40 (d, *J*=2.0 Hz, 1H), 8.03 (d, *J*=3.0 Hz, 1H), 7.79 (d, *J*=7.0 Hz, 2H), 7.64-7.61 (m, 1H), 7.55 (dd, *J*=7.5, 7.5 Hz, 2H), 7.51 (d, *J*=8.5 Hz, 1H), 7.41 (dd, *J*=8.5, 2.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.28, 140.55, 137.28, 135.95, 131.76, 128.94, 128.86, 128.54, 126.22, 124.10, 115.18, 114.93, 114.83. HRMS (ESI) calcd for $C_{15}H_{10}NOBrNa$ $[M+Na]^+$ 321.9843, found m/z 321.9846.

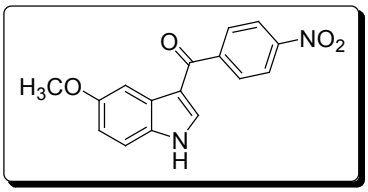
(5-nitro-1*H*-indol-3-yl)(phenyl)methanone (3g)



Yield: 49%, orange yellow solid, mp. 292-294 °C. IR (KBr, cm^{-1}): v_{max} 3118, 1606. ^1H NMR (500 MHz, DMSO-d_6): δ 12.70 (s, 1H), 9.14 (d, *J*=2.5 Hz, 1H), 8.28 (s, 1H), 8.18 (d, *J*=9.0 Hz, 1H),

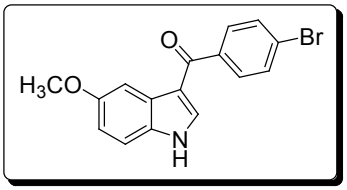
7.85 (d, *J*=7.0 Hz, 2H), 7.73 (d, *J*=9.0 Hz, 1H), 7.66 (m, 1H), 7.58 (dd, *J*=7.5, 7.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.30, 143.36, 140.40, 140.07, 139.40, 132.15, 129.06, 128.98, 126.23, 119.02, 118.41, 116.74, 113.55. HRMS (ESI) calcd for $C_{15}H_{10}N_2O_3Na$ $[M+Na]^+$ 289.0589, found m/z 289.0588.

(5-methoxy-1*H*-indol-3-yl)(4-nitrophenyl)methanone (3h)



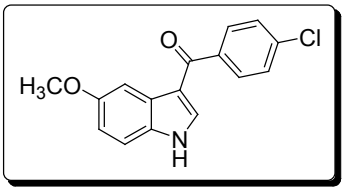
Yield: 90%, yellow solid, mp. 251-253 °C. IR (KBr, cm^{-1}): ν_{max} 3163, 1697. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.16 (s, 1H), 8.37 (d, *J*=8.5 Hz, 2H), 8.00 (d, *J*=8.5 Hz, 2H), 7.93 (d, *J*=2.5 Hz, 1H), 7.80 (d, *J*=2.0 Hz, 1H), 7.45 (d, *J*=9.0 Hz, 1H), 6.94 (d, *J*=9.0 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.53, 156.36, 149.09, 146.58, 137.32, 132.12, 129.92, 127.31, 124.09, 115.17, 113.79, 113.64, 103.75, 55.82. HRMS (ESI) calcd for $C_{16}H_{12}N_2O_4Na$ $[M+Na]^+$ 319.0695, found m/z 319.0706.

(4-bromophenyl)(5-methoxy-1*H*-indol-3-yl)methanone (3i)



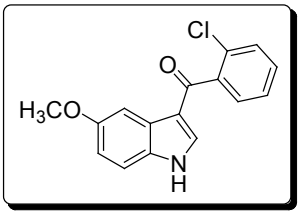
Yield: 86%, yellow solid, mp. 235-236 °C. IR (KBr, cm^{-1}): ν_{max} 3190, 1684. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.01 (s, 1H), 7.89 (s, 1H), 7.77-7.71 (m, 5H), 7.41 (s, 1H), 6.89 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.12, 156.15, 140.11, 136.52, 132.07, 131.86, 130.82, 127.49, 125.04, 115.14, 113.57, 113.48, 103.79, 55.81. HRMS (ESI) calcd for $C_{16}H_{12}NO_2BrNa$ $[M+Na]^+$ 351.9949, found m/z 351.9952.

(4-chlorophenyl)(5-methoxy-1*H*-indol-3-yl)methanone (3j)[7]



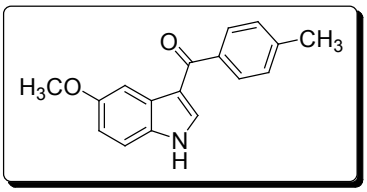
Yield: 89%, yellow solid, mp. 199-201 °C. IR (KBr, cm^{-1}): v_{max} 3176, 1678. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.01 (s, 1H), 7.89 (d, *J*=3.0 Hz, 1H), 7.79-7.77 (m, 3H), 7.58 (d, *J*=8.5 Hz, 2H), 7.40 (d, *J*=8.5 Hz, 1H), 6.89 (dd, *J*=8.5, 2.0 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.01, 156.15, 139.77, 136.49, 136.17, 132.07, 130.63, 128.93, 127.50, 115.16, 113.57, 113.48, 103.78, 55.81. HRMS (ESI) calcd for $C_{16}H_{12}NO_2ClNa$ $[M+Na]^+$ 308.0454, found m/z 308.0448.

(2-chlorophenyl)(5-methoxy-1*H*-indol-3-yl)methanone (3k)



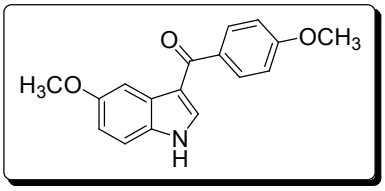
Yield: 44%, yellow solid, mp. 207-209 °C. IR (KBr, cm^{-1}): v_{max} 3177, 1676. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.01 (s, 1H), 7.66 (s, 1H), 7.57-7.46 (m, 5H), 7.41 (d, *J*=7.5 Hz, 1H), 6.90 (d, *J*=5.5 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.54, 156.29, 140.83, 137.29, 132.29, 131.09, 130.20, 130.09, 129.13, 127.51, 126.73, 116.36, 113.73, 113.67, 103.43, 55.79. HRMS (ESI) calcd for $C_{16}H_{12}NO_2ClNa$ $[M+Na]^+$ 308.0454, found m/z 308.0448.

(5-methoxy-1*H*-indol-3-yl)(p-tolyl)methanone (3l)



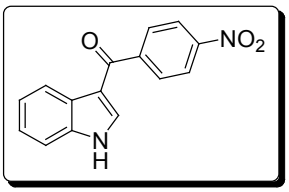
Yield: 36%, brown solid, mp. 235-237 °C. IR (KBr, cm^{-1}): v_{max} 3167, 1678. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.92 (s, 1H), 7.87 (d, *J*=2.5 Hz, 1H), 7.78 (d, *J*=1.5 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 2H), 7.41 (d, *J*=8.5 Hz, 1H), 7.34 (d, *J*=7.5 Hz, 2H), 6.89 (dd, *J*=8.5, 2.5 Hz, 1H), 3.80 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.08, 155.98, 141.34, 138.44, 135.94, 132.01, 129.36, 128.91, 127.61, 115.40, 113.41, 113.36, 103.80, 55.79, 21.49. HRMS (ESI) calcd for $C_{17}H_{15}NO_2Na$ $[M+Na]^+$ 288.1000, found m/z 288.1006.

(5-methoxy-1*H*-indol-3-yl)(4-methoxyphenyl)methanone (3m)[6a]



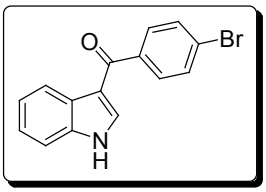
Yield: 38%, brown solid, mp. 210-212 °C. IR (KBr, cm^{-1}): ν_{max} 3169, 1675. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.90 (s, 1H), 7.89 (d, *J*=2.5 Hz, 1H), 7.79 (d, *J*=8.5 Hz, 2H), 7.76 (s, 1H), 7.40 (d, *J*=8.5 Hz, 1H), 7.07 (d, *J*=8.0 Hz, 2H), 6.88 (d, *J*=8.5 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.17, 162.11, 155.88, 135.46, 133.57, 131.98, 130.93, 127.71, 115.37, 114.12, 113.35, 113.31, 103.77, 55.85, 55.78. HRMS (ESI) calcd for $C_{17}H_{15}NO_3Na$ $[M+Na]^+$ 304.0950, found m/z 304.0954.

(1*H*-indol-3-yl)(4-nitrophenyl)methanone (3n)[7, 8]



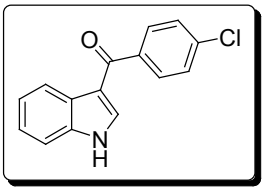
Yield: 88%, orange yellow solid, mp. 194-195 °C. IR (KBr, cm^{-1}): ν_{max} 3151, 1697. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.28 (s, 1H), 8.38 (d, *J*=8.5 Hz, 2H), 8.29 (d, *J*=7.0 Hz, 1H), 8.02 (m, 3H), 7.56 (d, *J*=7.0 Hz, 1H), 7.33-7.28 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.63, 149.15, 146.46, 137.33, 137.26, 130.01, 126.45, 124.08, 123.96, 122.79, 121.91, 115.35, 112.88. HRMS (ESI) calcd for $C_{15}H_{10}N_2O_3Na$ $[M+Na]^+$ 289.0589, found m/z 289.0588.

(4-bromophenyl)(1*H*-indol-3-yl)methanone (3o)



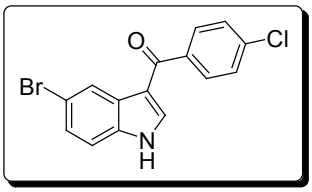
Yield: 72%, yellow solid, mp. 198-200 °C. IR (KBr, cm^{-1}): ν_{max} 3143, 1684. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.13 (s, 1H), 8.23 (d, *J*=7.5 Hz, 1H), 7.96 (s, 1H), 7.72 (s, 4H), 7.51 (d, *J*=7.0 Hz, 1H), 7.27-7.22 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.21, 140.00, 137.23, 136.42, 131.88, 130.91, 126.65, 125.17, 123.70, 122.49, 121.91, 115.30, 112.75. HRMS (ESI) calcd for $C_{15}H_{10}NOBrNa$ $[M+Na]^+$ 321.9843, found m/z 321.9846.

(4-chlorophenyl)(1*H*-indol-3-yl)methanone (3p) [2b, 6a, 7]



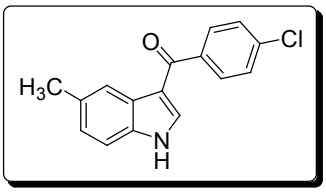
Yield: 67%, yellow solid, mp. 195-197 °C. IR (KBr, cm^{-1}): ν_{max} 3154, 1678. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.12 (s, 1H), 8.24 (d, *J*=7.0 Hz, 1H), 7.96 (d, *J*=2.5 Hz, 1H), 7.79 (d, *J*=8.0 Hz, 2H), 7.58 (d, *J*=8.5 Hz, 2H), 7.51 (d, *J*=7.5 Hz, 1H), 7.27-7.22 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.10, 139.65, 137.23, 136.40, 136.29, 130.73, 128.95, 126.66, 123.70, 122.48, 121.91, 112.75. HRMS (ESI) calcd for $C_{15}H_{10}NOClNa$ $[M+Na]^+$ 278.0349, found m/z 278.0343.

(5-bromo-1*H*-indol-3-yl)(4-chlorophenyl)methanone (3q)



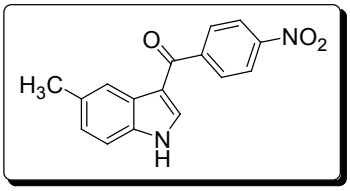
Yield: 62%, yellow solid, mp. 250-251 °C. IR (KBr, cm^{-1}): ν_{max} 3163, 1684. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.30 (s, 1H), 8.38 (s, 1H), 8.04 (s, 1H), 7.80 (d, *J*=8.5 Hz, 2H), 7.58 (d, *J*=8.0 Hz, 2H), 7.49 (d, *J*=8.5 Hz, 1H), 7.39 (d, *J*=8.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.95, 139.17, 137.44, 136.57, 135.99, 130.75, 129.02, 128.47, 126.33, 124.09, 115.30, 114.85, 114.76. HRMS (ESI) calcd for $C_{15}H_9NOBrClNa$ $[M+Na]^+$ 355.9454, found m/z 355.9455.

(4-chlorophenyl)(5-methyl-1*H*-indol-3-yl)methanone (3r)



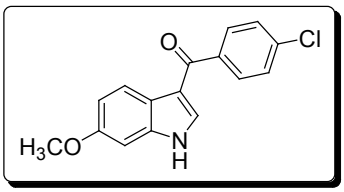
Yield: 84%, yellow solid, mp. 245-247 °C. IR (KBr, cm^{-1}): ν_{max} 3166, 1670. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.03 (s, 1H), 8.08 (s, 1H), 7.91 (d, *J*=3.0 Hz, 1H), 7.80 (d, *J*=8.5 Hz, 2H), 7.60 (d, *J*=8.0 Hz, 2H), 7.41 (d, *J*=8.5 Hz, 1H), 7.10 (d, *J*=8.5 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.02, 139.78, 136.35, 136.18, 135.55, 131.35, 130.67, 128.91, 126.94, 125.17, 121.65, 114.96, 112.36, 21.81. HRMS (ESI) calcd for $C_{16}H_{12}NOClNa$ $[M+Na]^+$ 292.0505, found m/z 292.0508.

(5-methyl-1*H*-indol-3-yl)(4-nitrophenyl)methanone (3s)



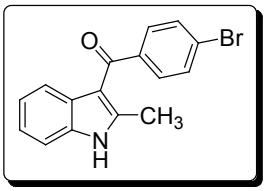
Yield: 87%, yellow solid, mp. 260-262 °C. IR (KBr, cm^{-1}): v_{max} 3170, 1701. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.15 (s, 1H), 8.37 (d, *J*=8.5 Hz, 2H), 8.10 (s, 1H), 8.00 (d, *J*=8.5 Hz, 2H), 7.93 (s, 1H), 7.43 (d, *J*=8.0 Hz, 1H), 7.13 (d, *J*=8.5 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.56, 149.10, 146.58, 137.24, 135.63, 131.74, 129.96, 126.73, 125.43, 124.07, 121.65, 114.98, 112.50, 21.80. HRMS (ESI) calcd for $C_{16}H_{12}N_2O_3Na$ $[M+Na]^+$ 303.0746, found m/z 303.0750.

(4-chlorophenyl)(6-methoxy-1H-indol-3-yl)methanone (3t)



Yield: 53%, yellow solid, mp. 241-243 °C. IR (KBr, cm^{-1}): v_{max} 3122, 1662. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.95 (s, 1H), 8.10 (d, *J*=8.5 Hz, 1H), 7.85 (d, *J*=3.0 Hz, 1H), 7.80 (d, *J*=8.5 Hz, 2H), 7.60 (d, *J*=8.5 Hz, 2H), 7.01 (d, *J*=2.0 Hz, 1H), 6.90 (dd, *J*=8.5, 2.0 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.94, 157.14, 139.63, 138.14, 136.22, 135.51, 130.68, 128.92, 122.56, 120.60, 115.39, 112.26, 95.78, 55.75. HRMS (ESI) calcd for $C_{16}H_{12}NO_2ClNa$ $[M+Na]^+$ 308.0454, found m/z 308.0448.

(4-bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone (3u)



Yield: 75%, yellow solid, mp. 190-191 °C. IR (KBr, cm^{-1}): v_{max} 3201, 1679. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.02 (s, 1H), 7.72 (d, *J*=8.0 Hz, 2H), 7.57 (d, *J*=8.0 Hz, 2H), 7.40 (d, *J*=8.0 Hz, 1H), 7.35 (d, *J*=8.0 Hz, 1H), 7.14 (dd, *J*=7.5, 7.5 Hz, 1H), 7.05 (dd, *J*=7.5, 7.5 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.87, 145.18, 141.10, 135.48, 131.90, 131.74, 130.67, 127.63, 125.13, 122.40, 121.58, 120.41, 112.68, 111.79, 14.72. HRMS (ESI) calcd for $C_{16}H_{12}NOBrNa$

$[M+Na]^+$ 336.0000, found m/z 336.0002.

4. References

(1) K. Wadhwa, C.-X. Yang, P. R. West, K. C. Deming, S. R. Chemburkar and R. E. Reddy, *Synth. Commun.*, 2008, **38**, 4434.

(2) (a) G. Bartoli, G. Palmieri, M. Petrini, M. Bosco and R. Dalpozzo, *Tetrahedron*, 1990, **46**, 1379. (b) Y. Ma, J. You and F. Song, *Chem.-Eur. J.*, 2013, **19**, 1189.

(3) Y. Ito, K. Kobayashi and T. Saegusa, *J. Org. Chem.*, 1979, **44**, 2030.

(4) J.-P. Liou, Y.-L. Chang, F.-M. Kuo, C.-W. Chang, H.-Y. Tseng, C.-C. Wang, Y.-N. Yang, J.-Y. Chang, S.-J. Lee and H.-P. Hsieh, *J. Med. Chem.*, 2004, **47**, 4247.

(5) J. G. Rodríguez and A. Urrutia, *J. Heterocyclic Chem.*, 1999, **36**, 129.

(6) (a) S. K. Guchhait, M. Kashyap and H. Kamble, *J. Org. Chem.*, 2011, **76**, 4753; (b) J. Bergman and L. Venemalm, *Tetrahedron*, 1990, **46**, 6061.

(7) T.-S. Jiang and G.-W. Wang, *Org. Lett.*, 2013, **15**, 788.

(8) A. R. Katritzky, K. Suzuki, S. K. Singh and H.-Y. He, *J. Org. Chem.*, 2003, **68**, 5720.

5. ^{1}H NMR and ^{13}C NMR Spectra of product 3h and its C2-acylated isomer 3h'

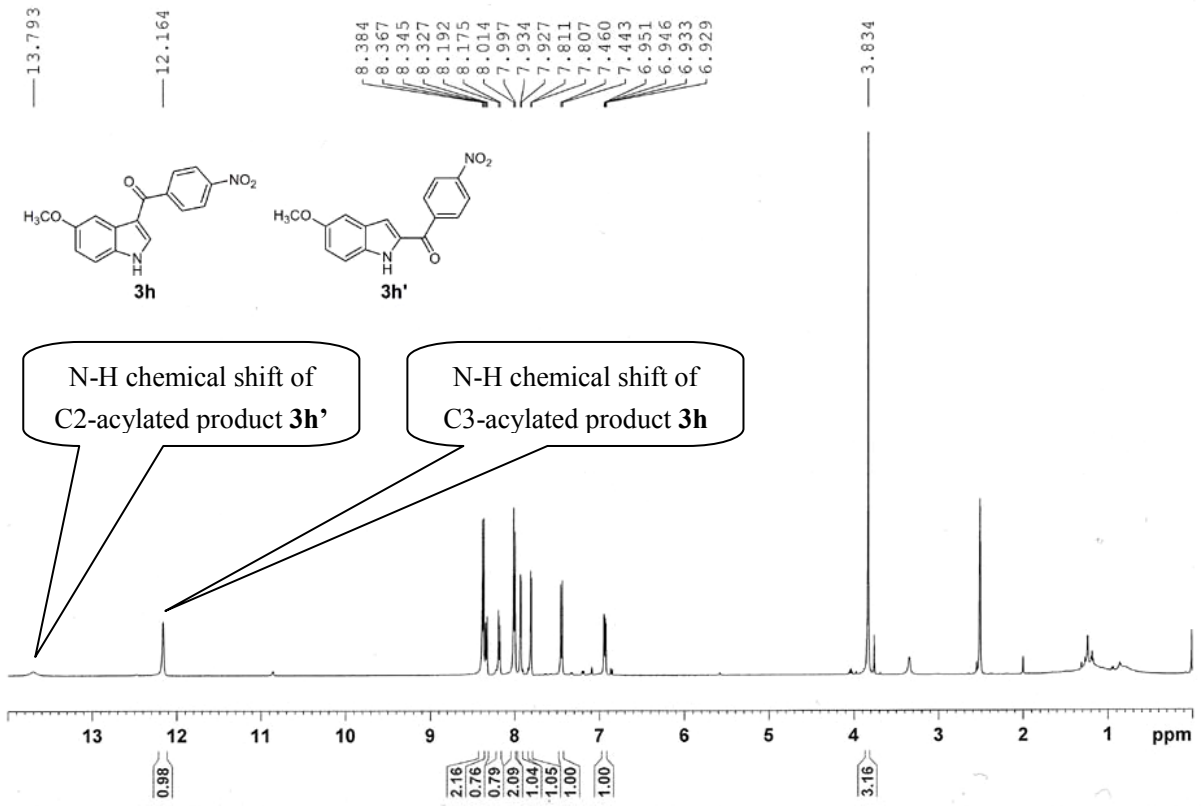


Figure S1. Mixed ^{1}H NMR Spectra of product **3h** and its C2-acylated isomer **3h'**

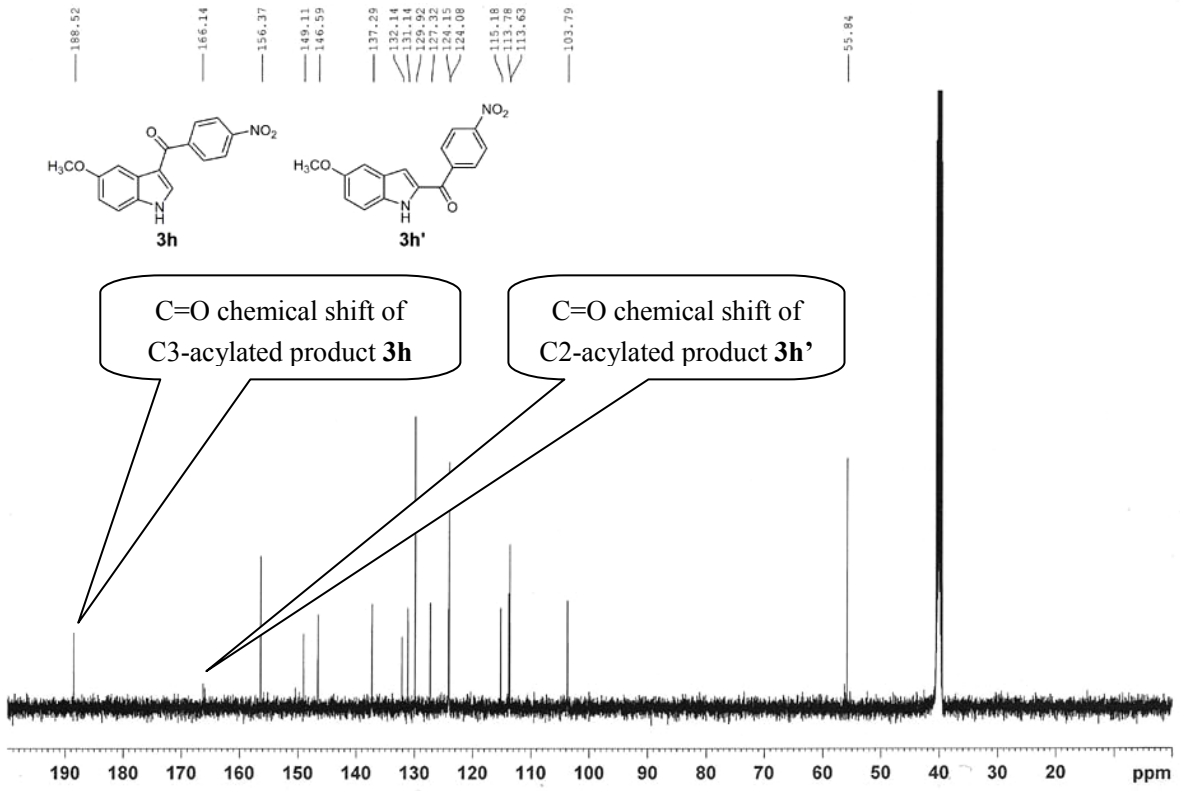
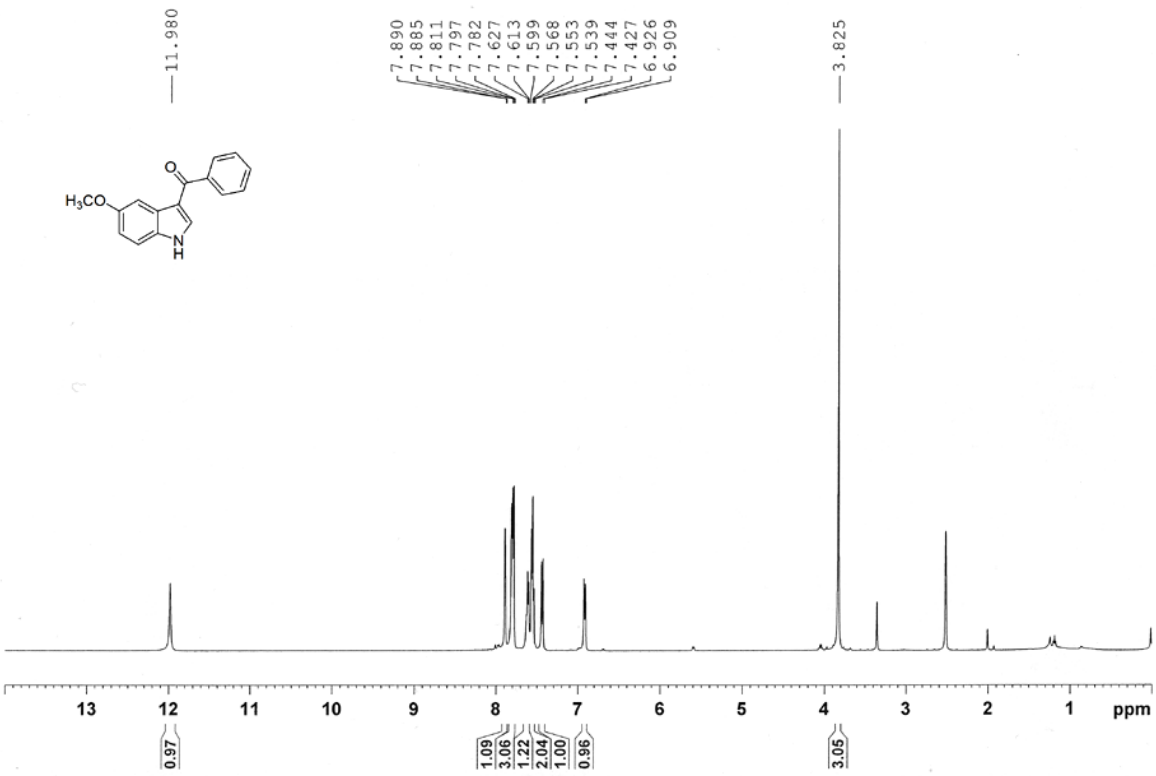
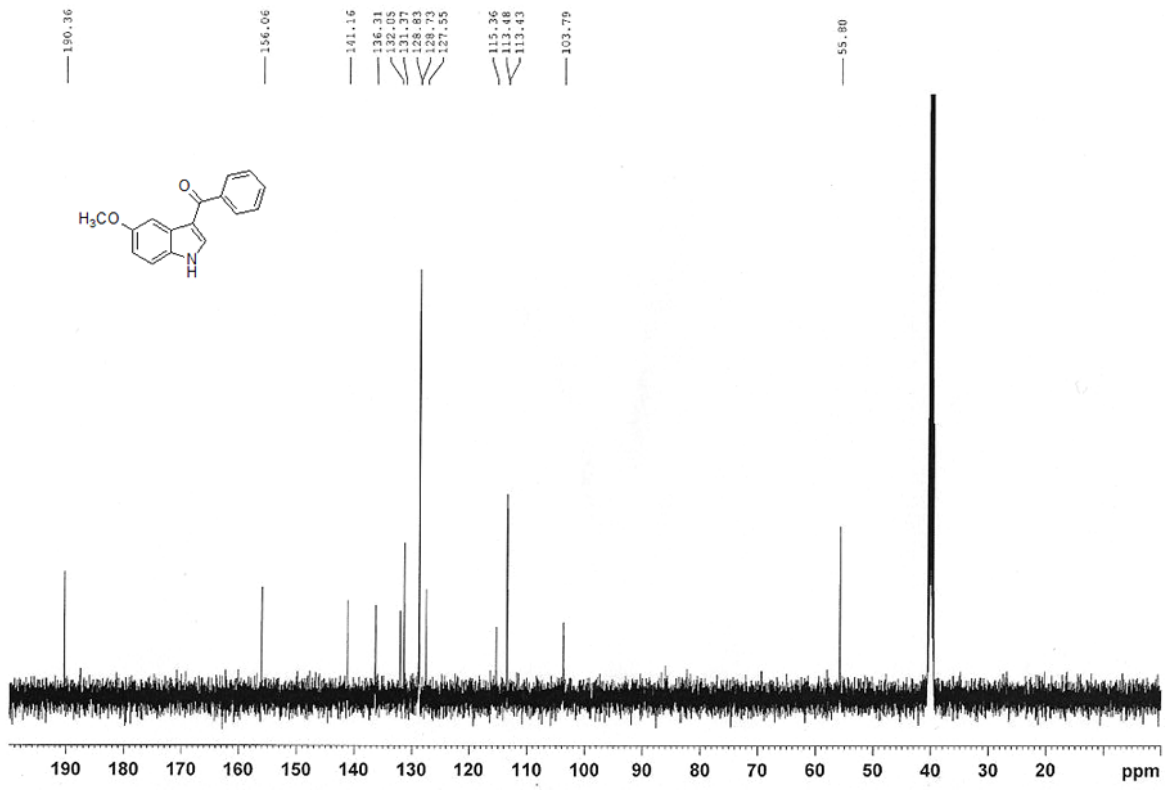
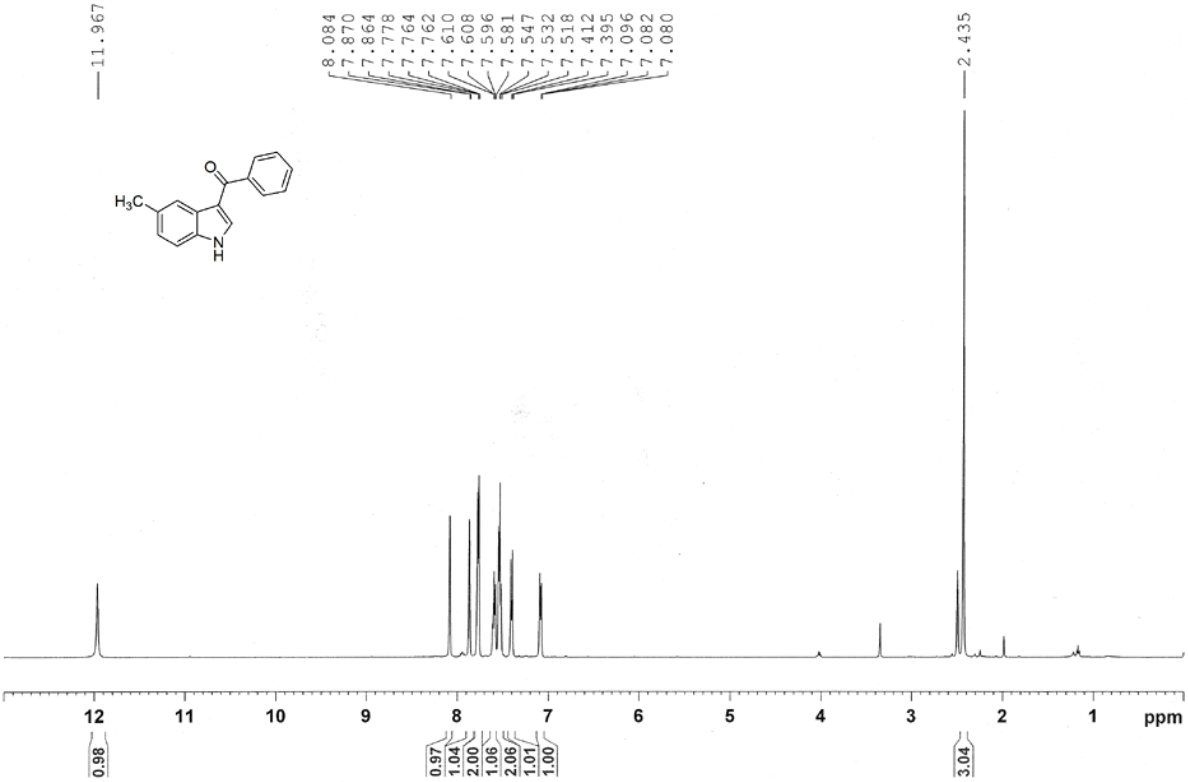


Figure S2. Mixed ^{13}C NMR Spectra of product **3h** and its C2-acylated isomer **3h'**

6. ^{1}H NMR and ^{13}C NMR Spectra of products 3a-3u



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7.870
7.864
7.778
7.764
7.762
7.610
7.608
7.596
7.581
7.547
7.532
7.518
7.412
7.395
7.096
7.082
7.080
2.435
H3C
O
N
H
12
11
10
9
8
7
6
5
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3
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ppm
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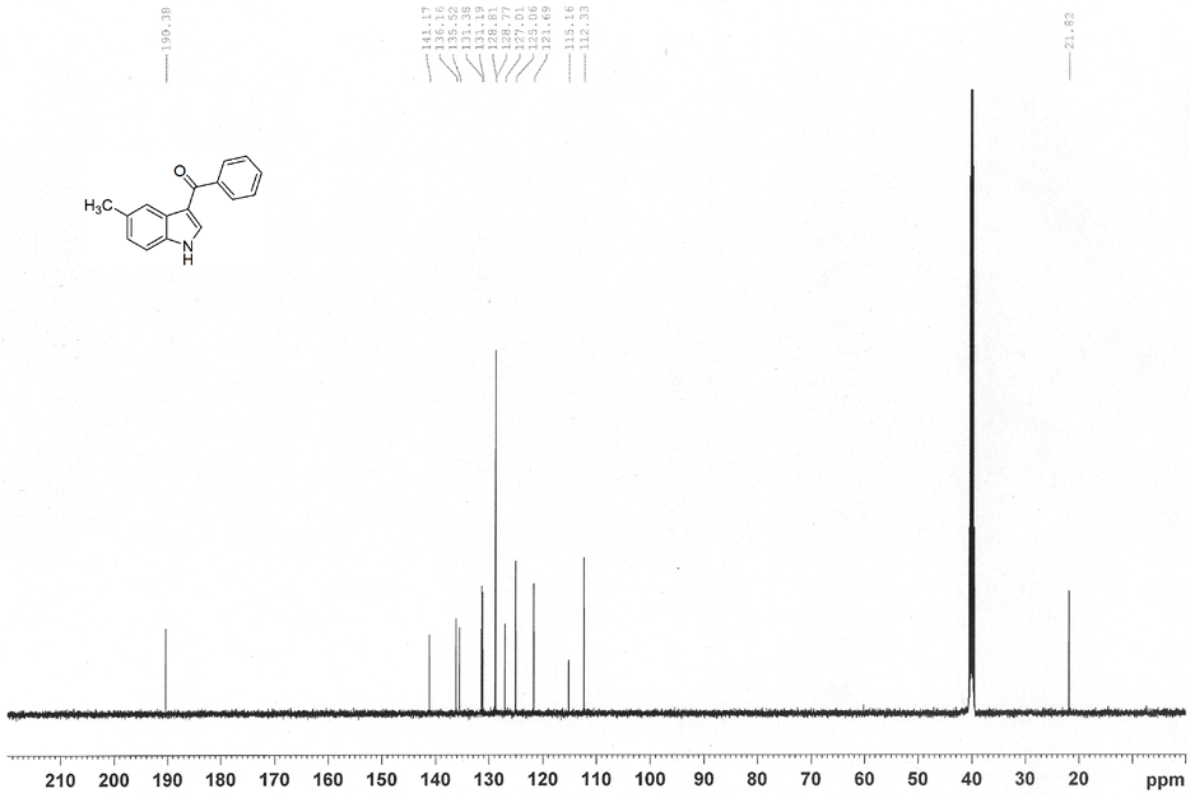
2.00
1.06
2.06
1.01
1.00
3.04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131.19
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128.77
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125.06
121.69
115.16
112.33
21.82
H3C
O
N
H
210
200
190
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160
150
140
130
120
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100
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80
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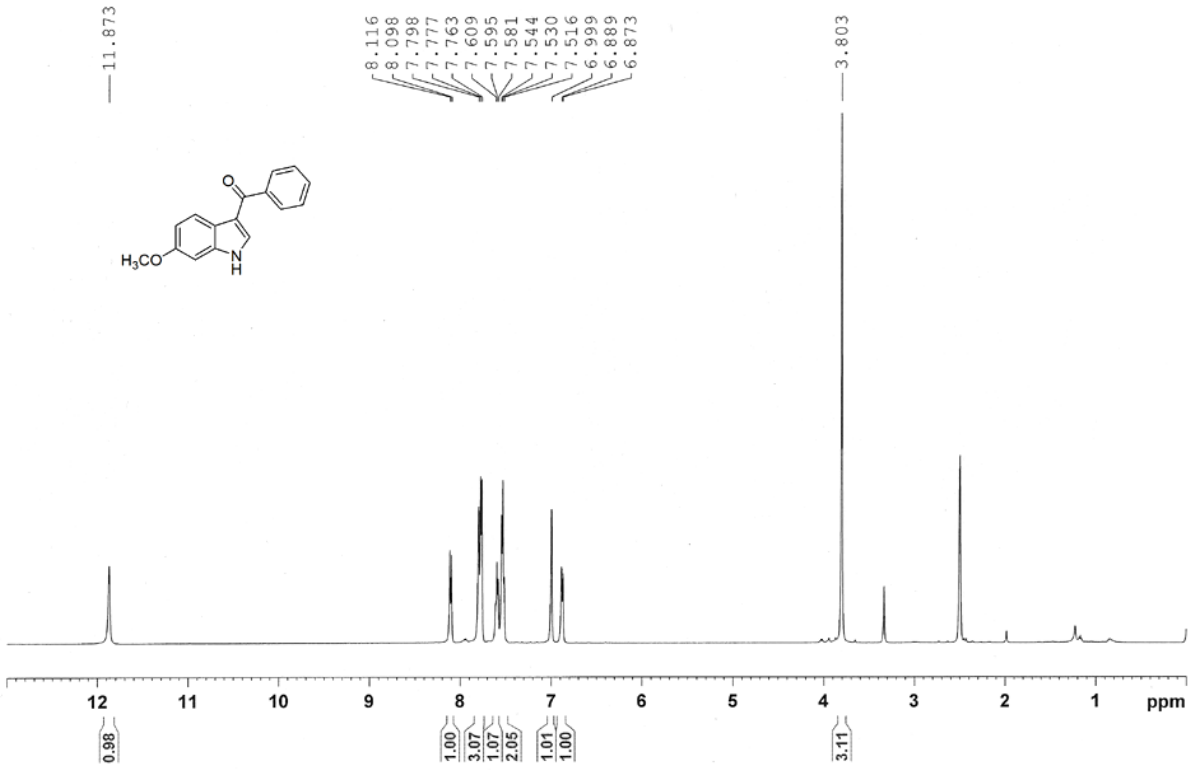
60
50
40
30
20
ppm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7.763
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7.544
7.530
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6.889
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3.803
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N
H
O
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11
10
9
8
7
6
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1.07
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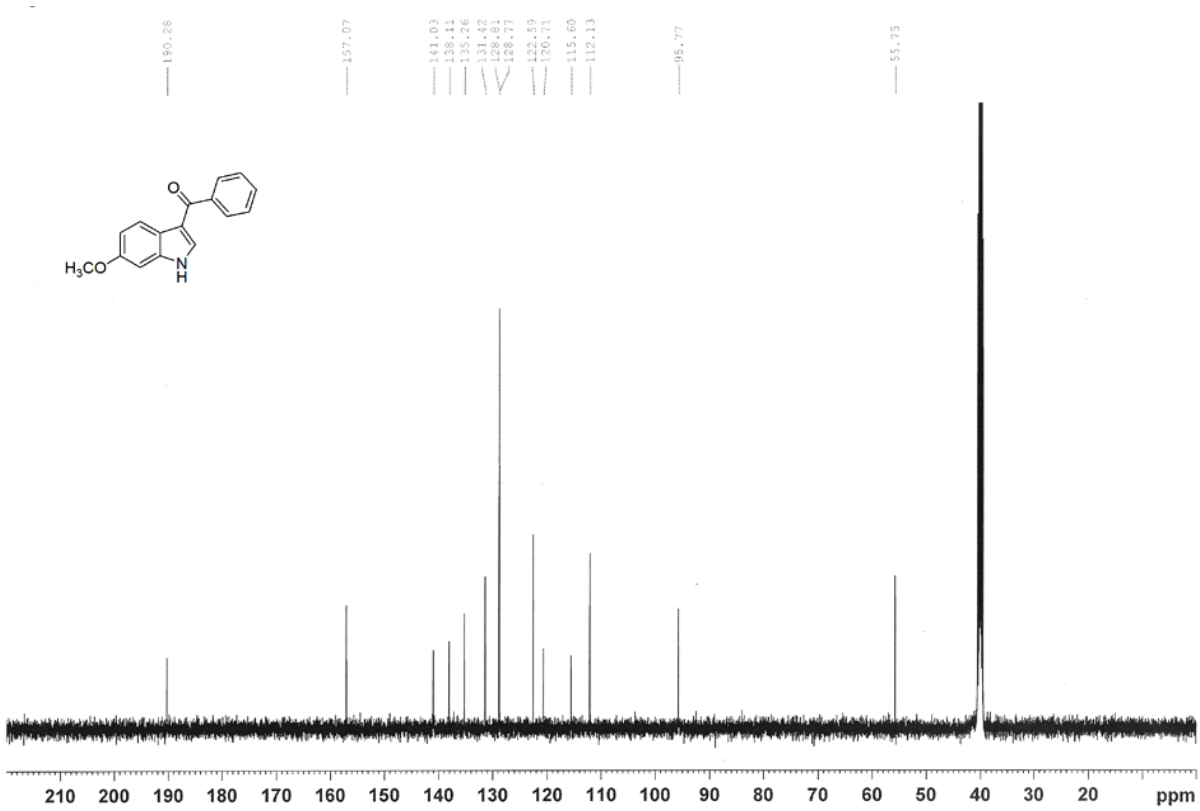
1.00
3.11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128.77
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115.60
112.13
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55.75
H3CO
N
H
O
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200
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120
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80
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40
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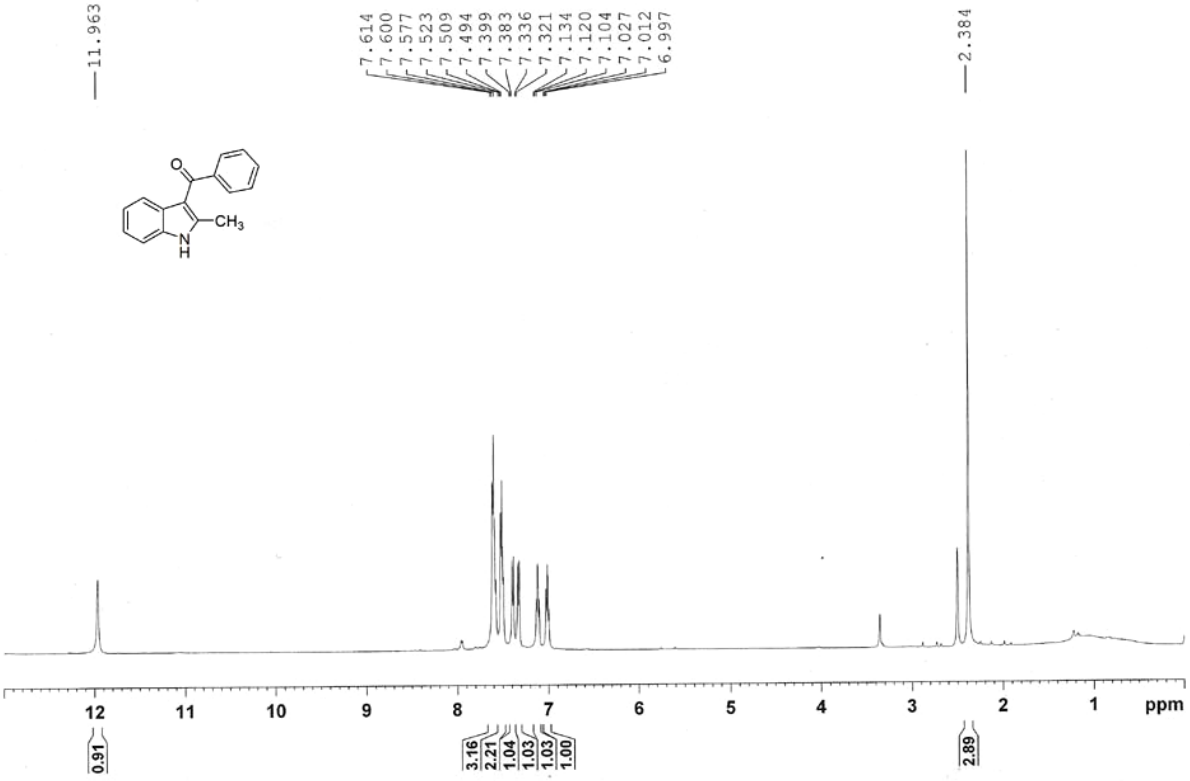
20
ppm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7.104
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7.012
6.997
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CH3
N
H
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11
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9
8
7
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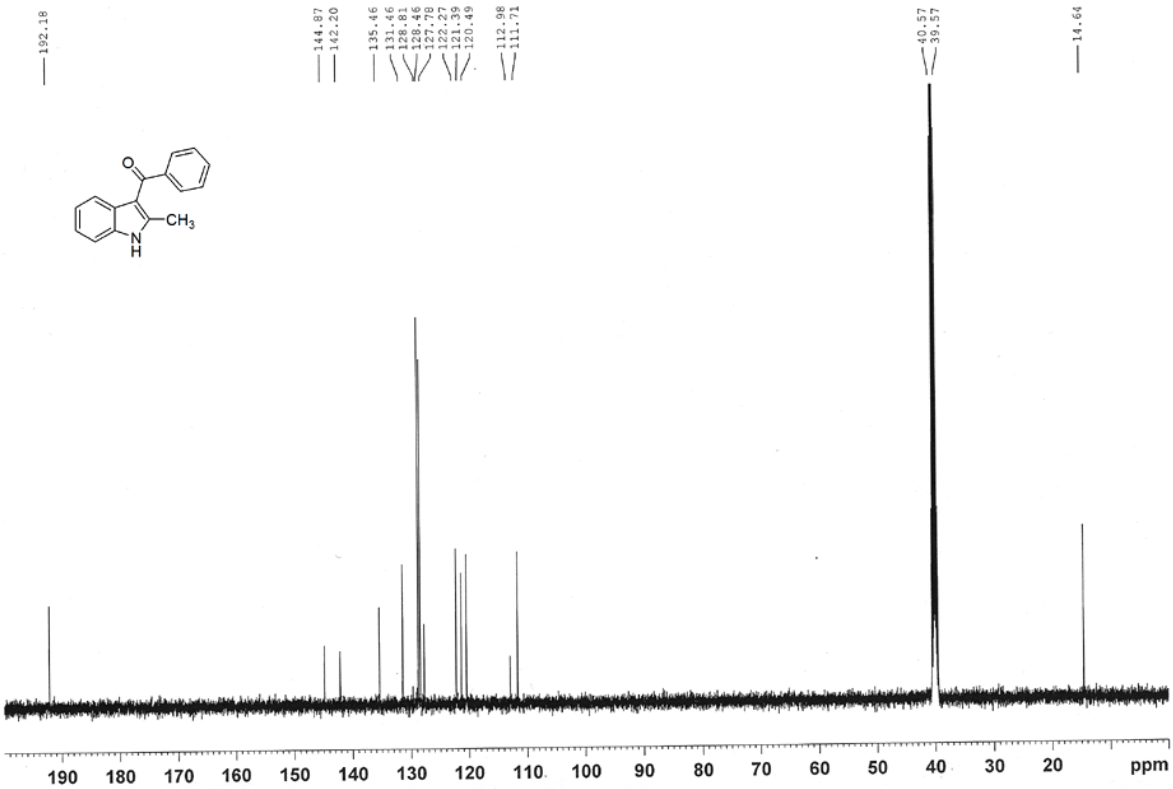
2.89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121.39
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14.64
CH3
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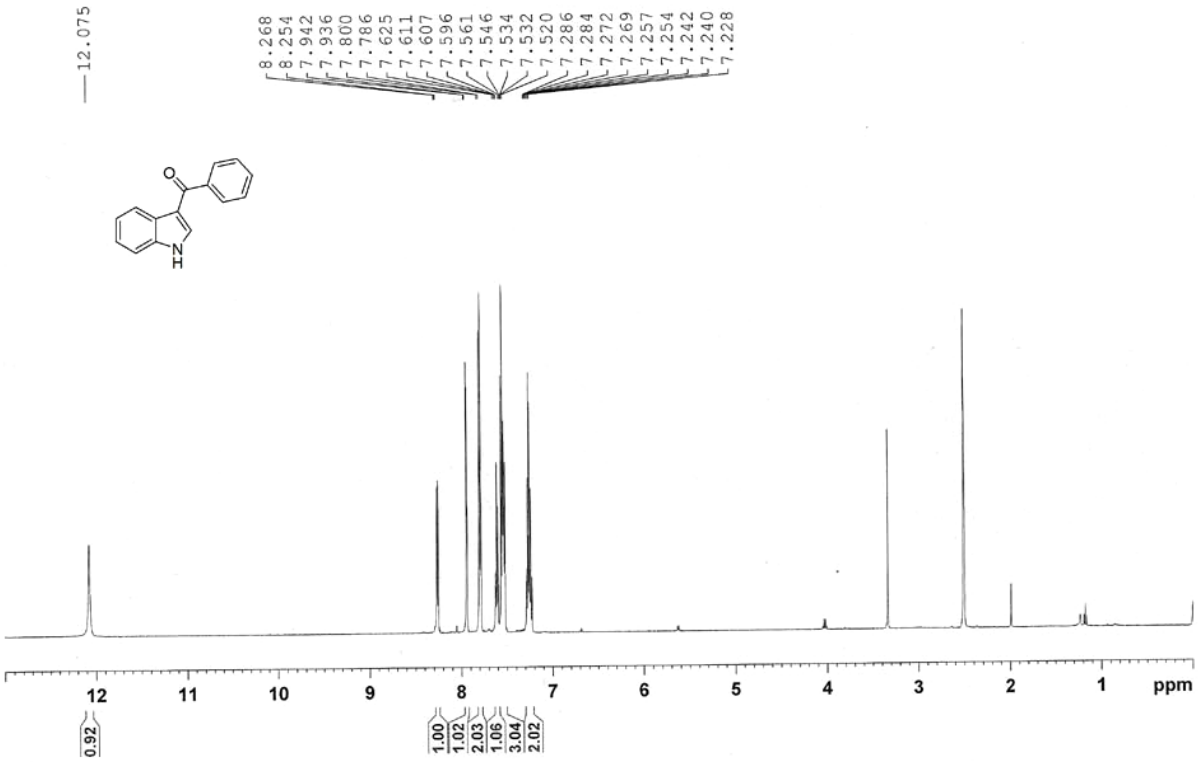
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7.532
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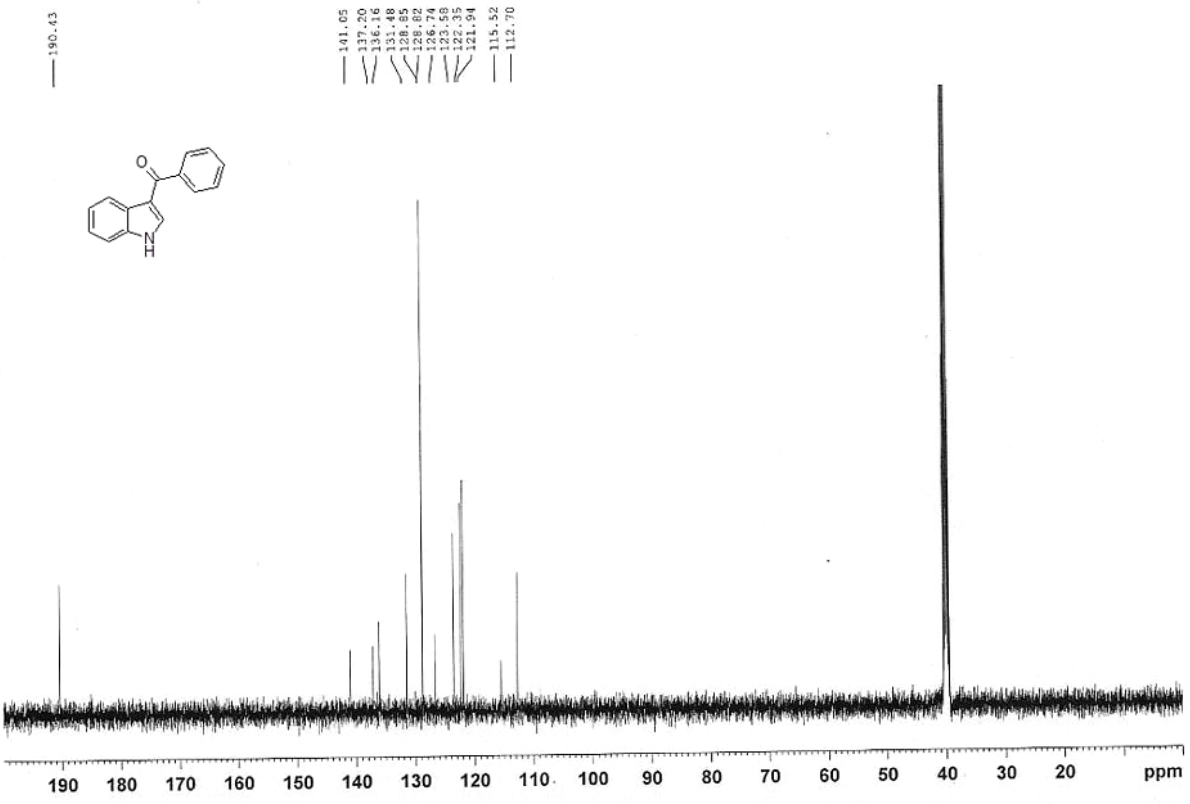
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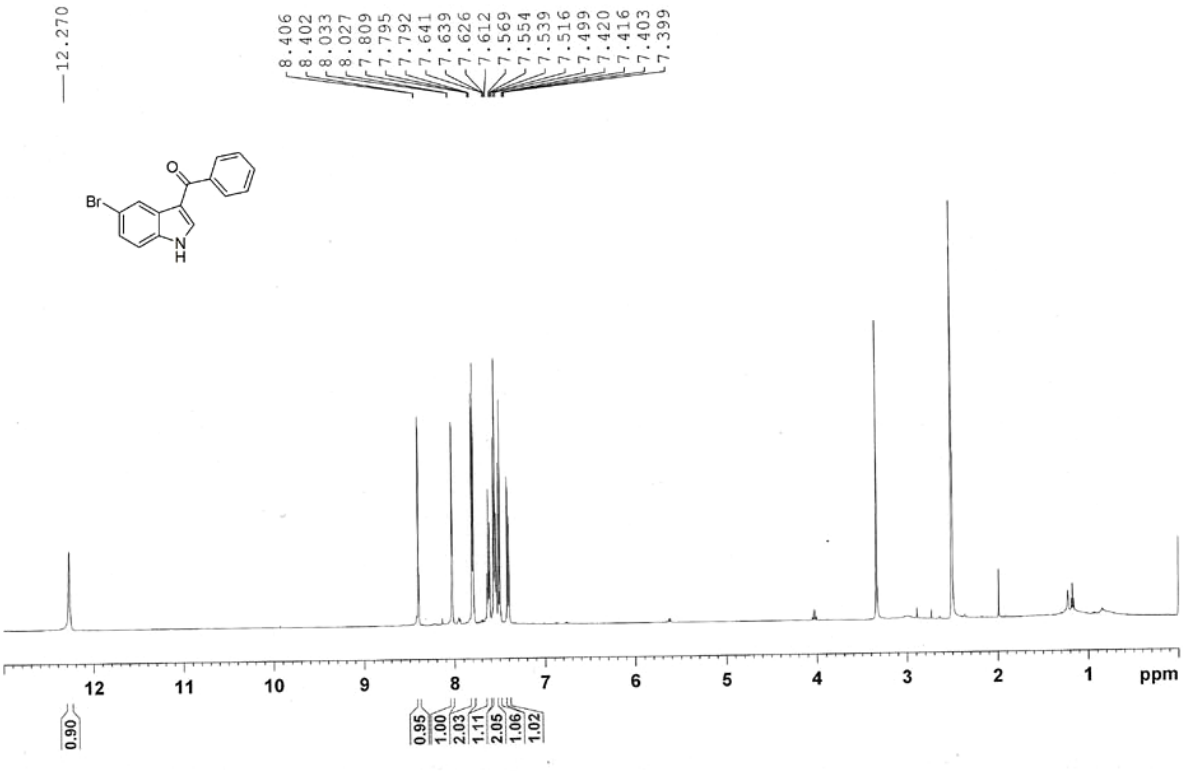
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H
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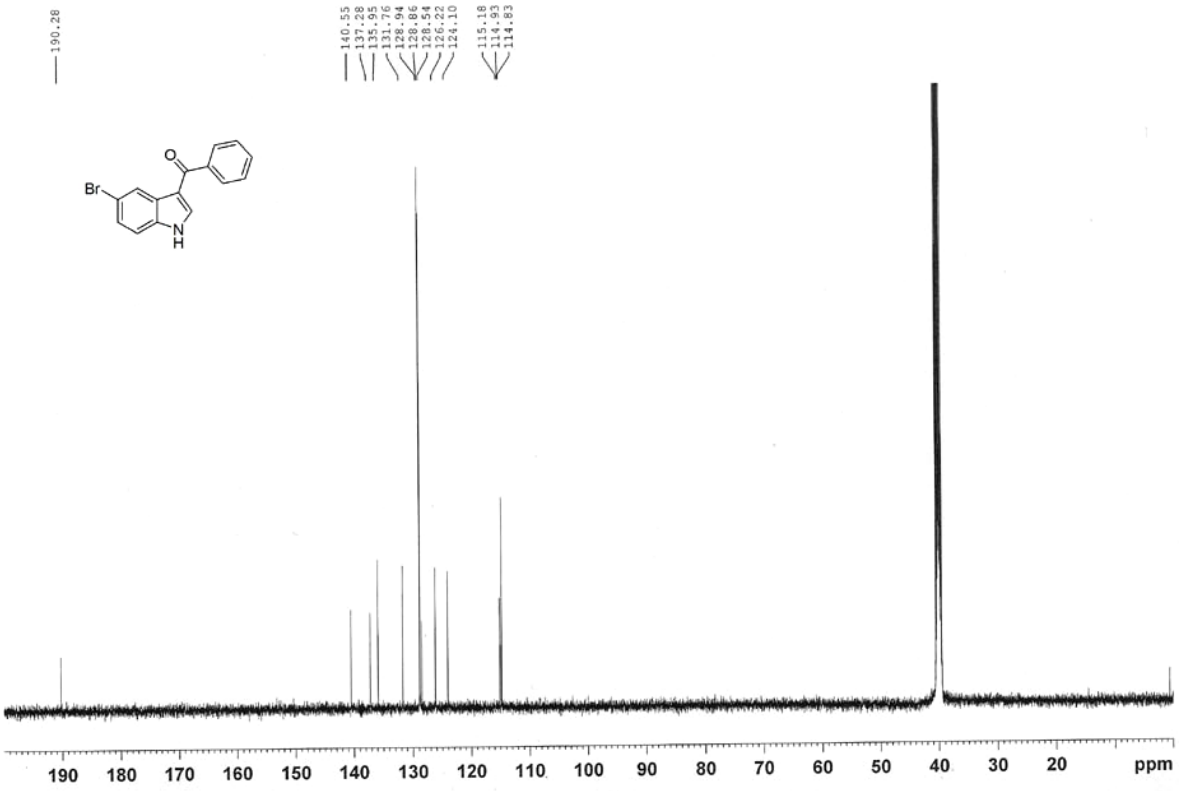
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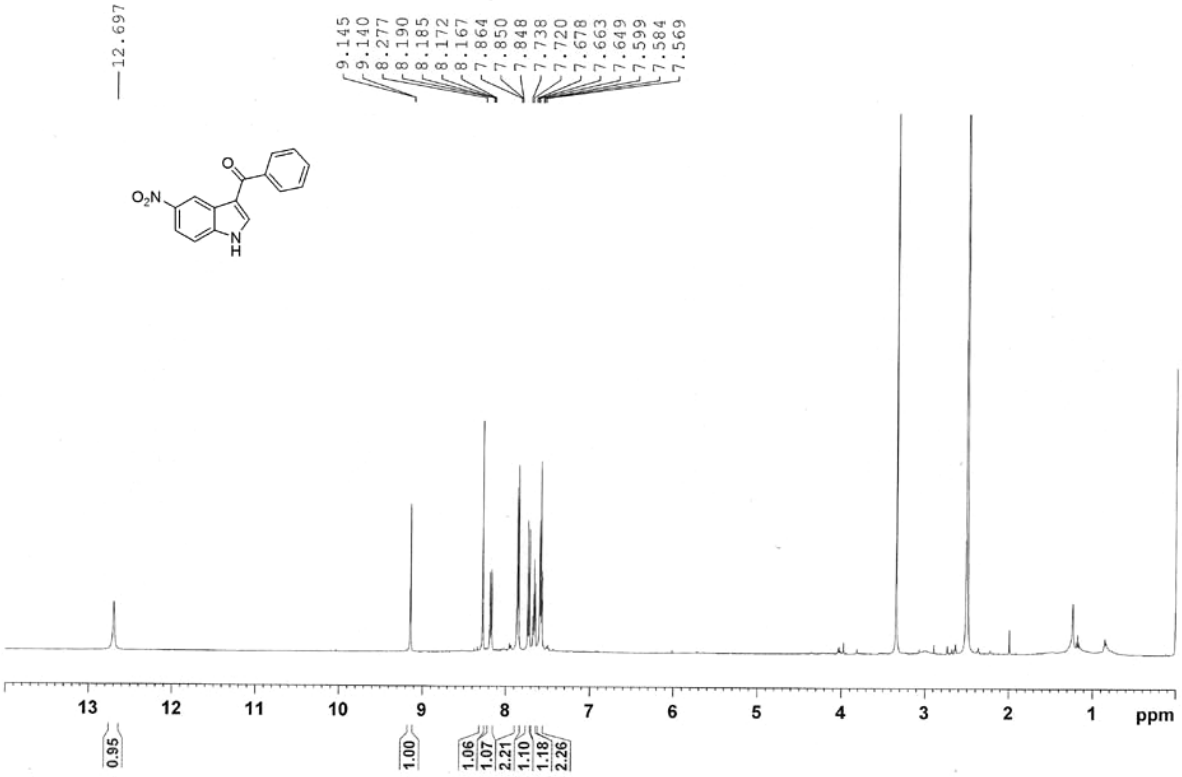
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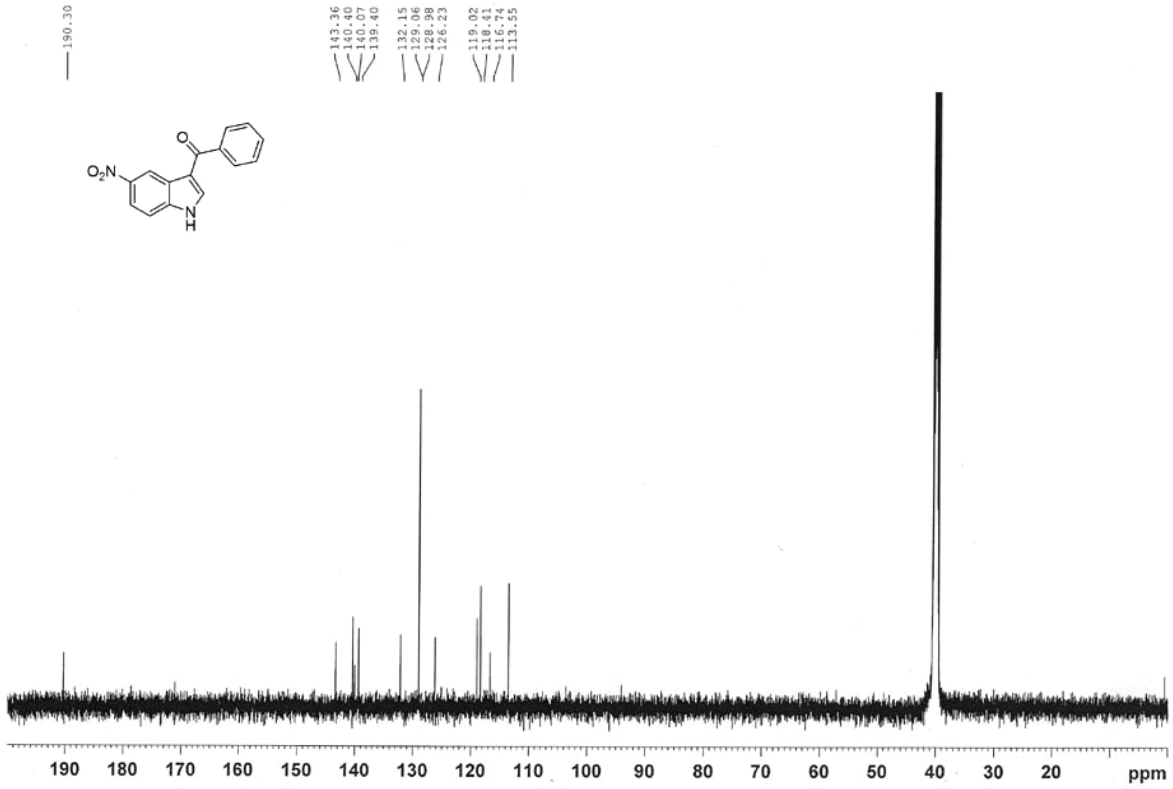
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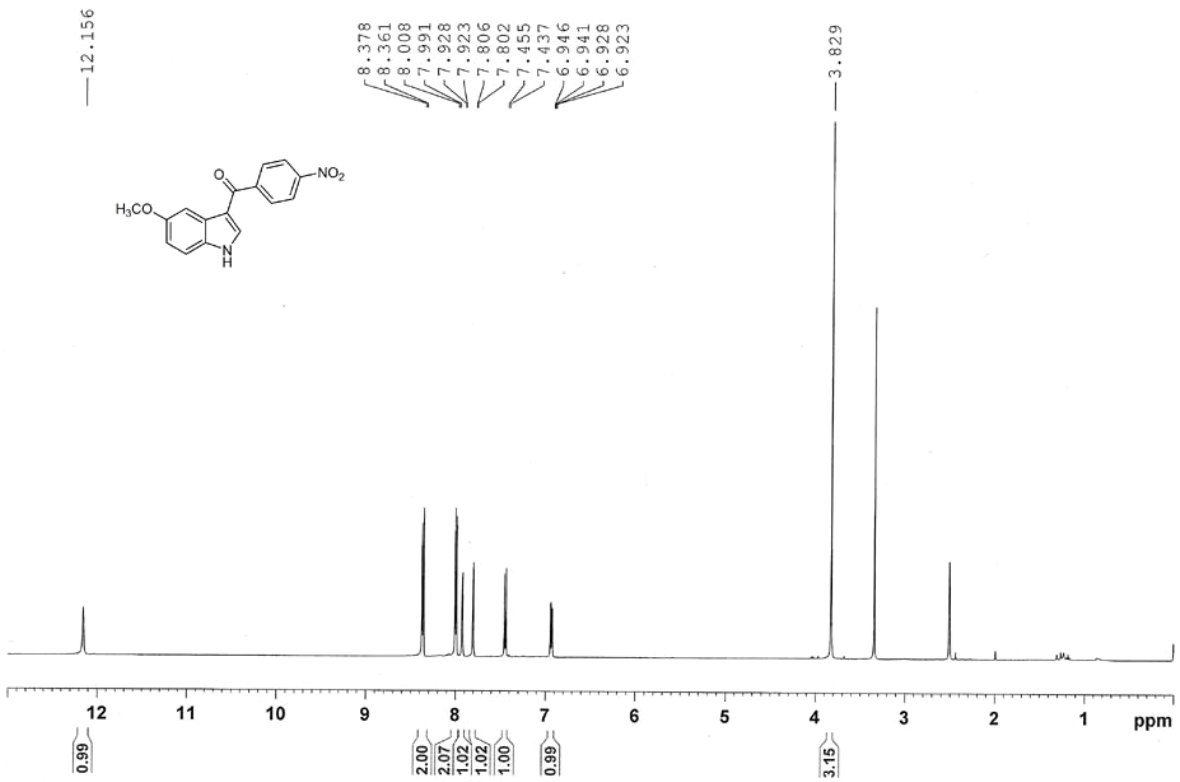
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NO2
H3CO
N
H
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7
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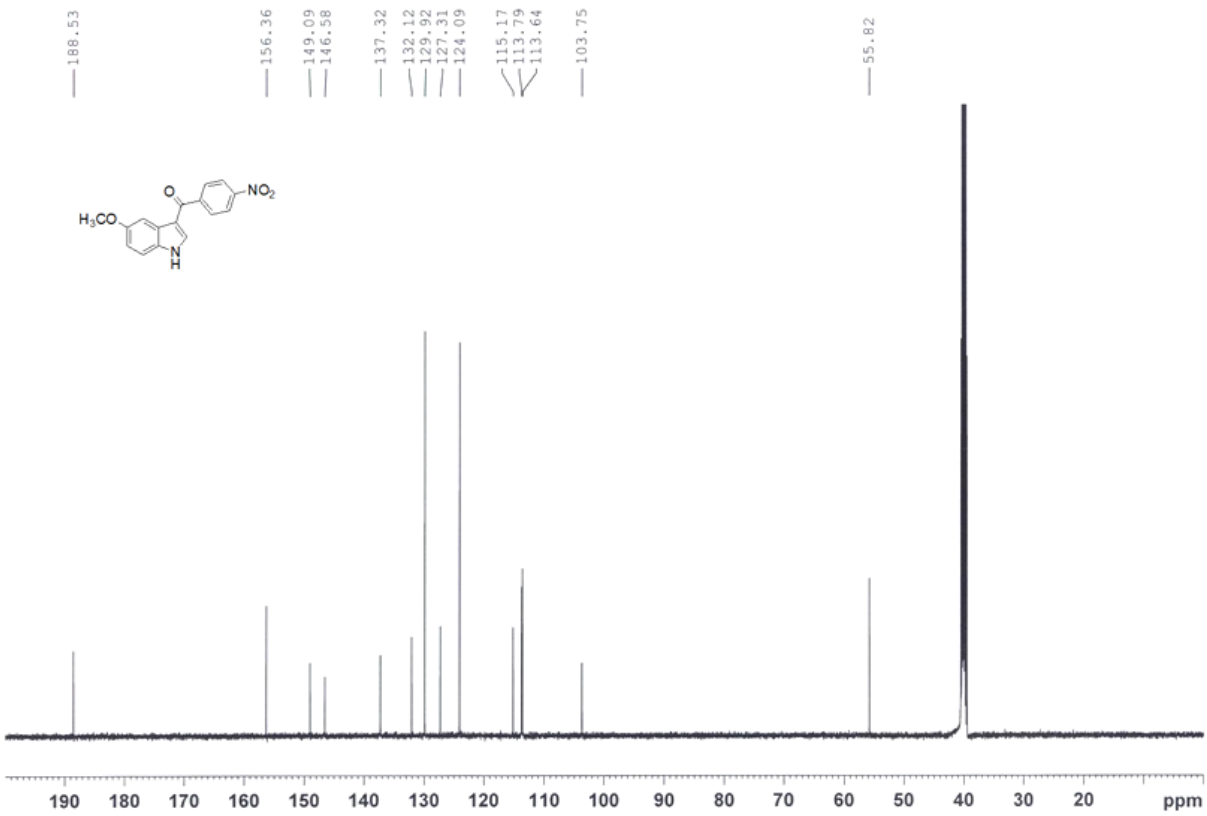
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N
H
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180
170
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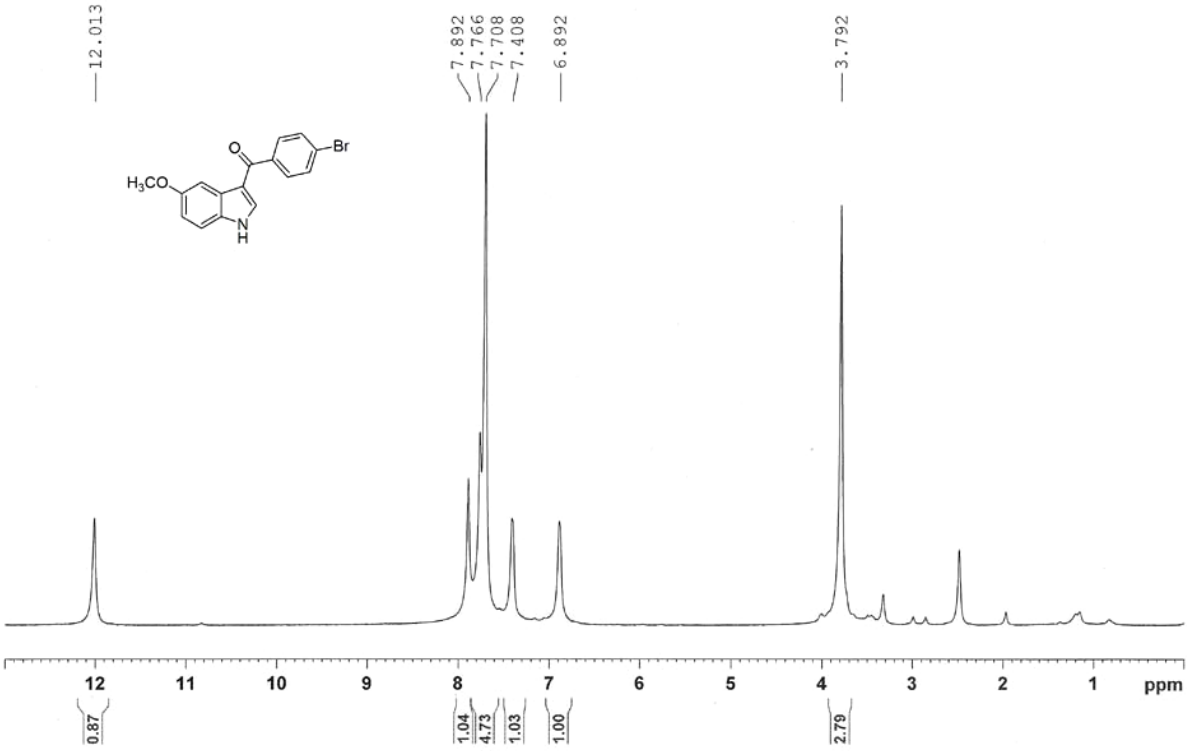
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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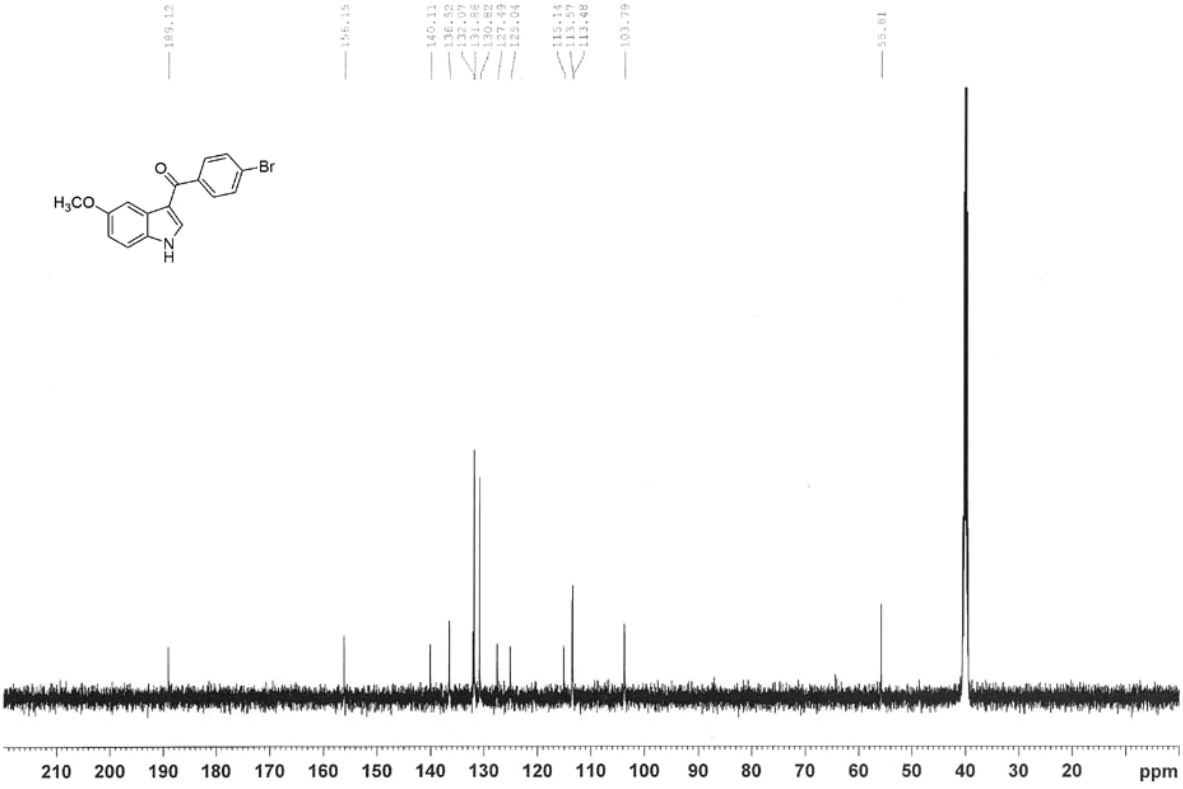
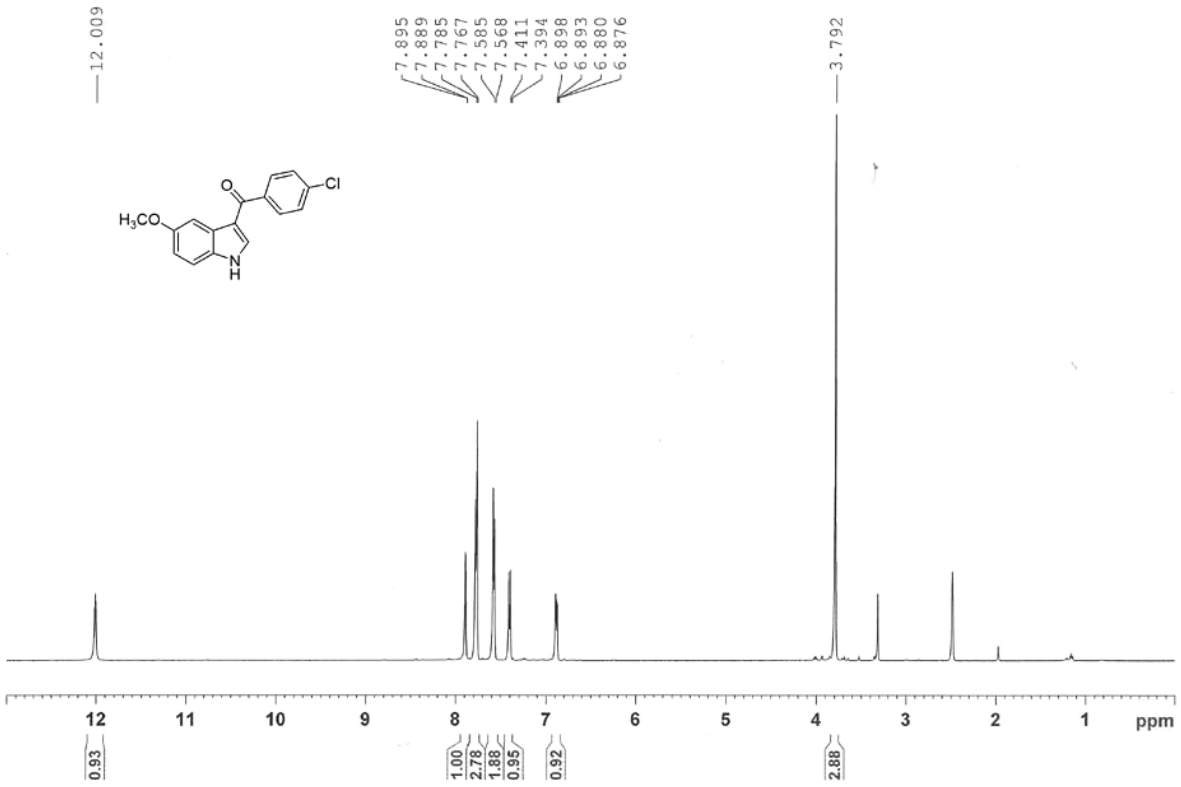
7.892
7.766
7.708
7.408
6.892
3.792
O
Br
H3CO
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.87
1.04
4.73
1.03
1.00
2.79


189.12
156.15
140.11
136.52
132.07
131.86
130.82
127.49
125.04
115.14
113.57
113.48
103.79
55.81
O
Br
H3CO
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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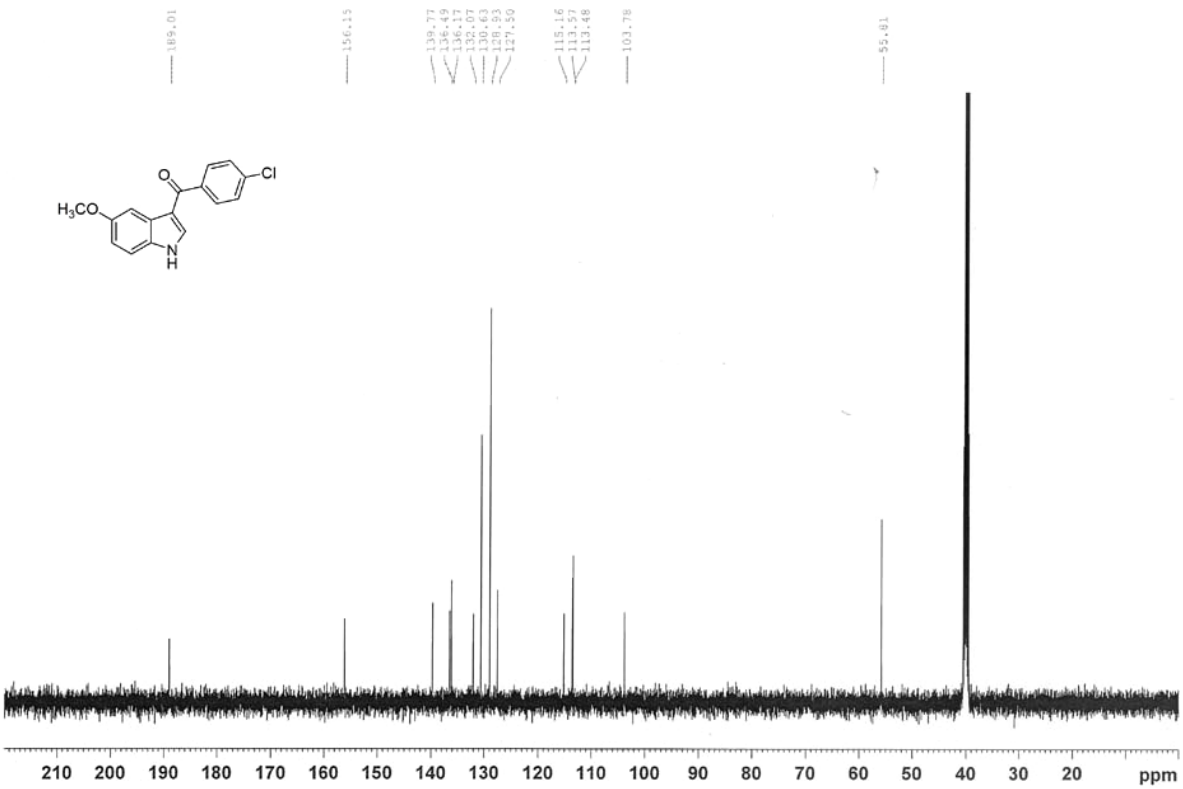
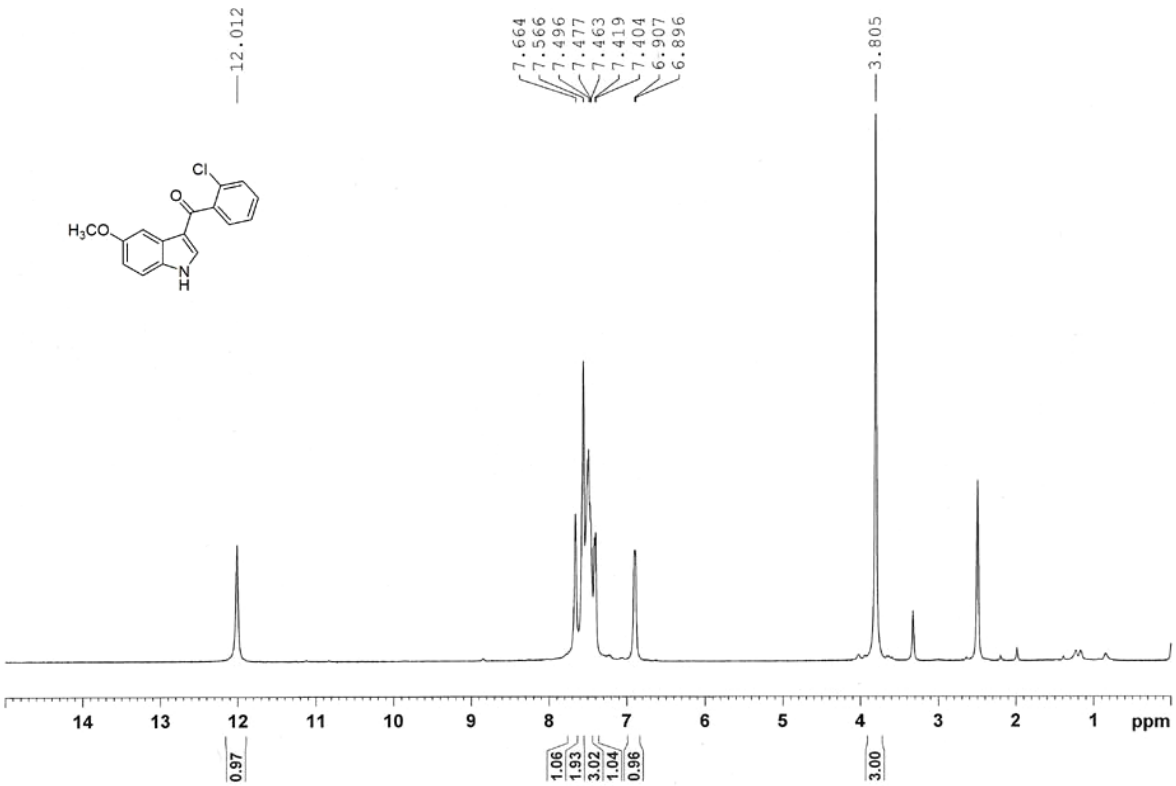
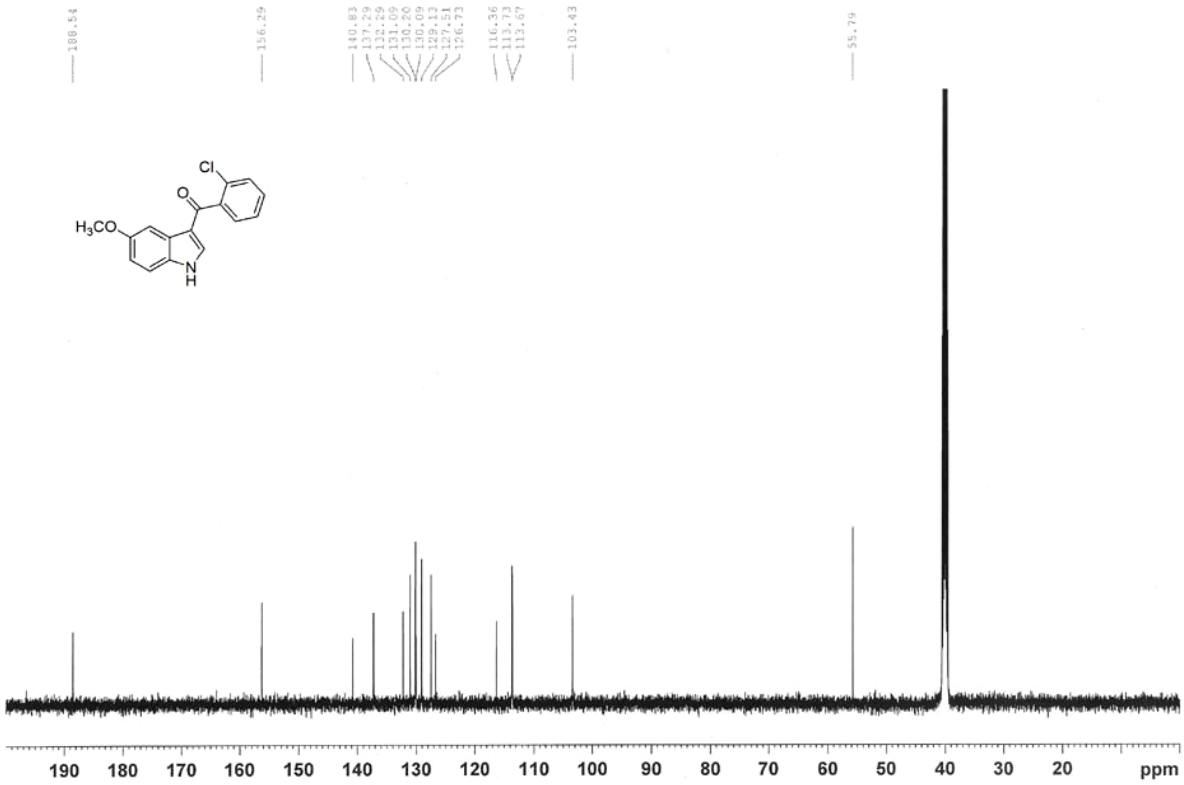
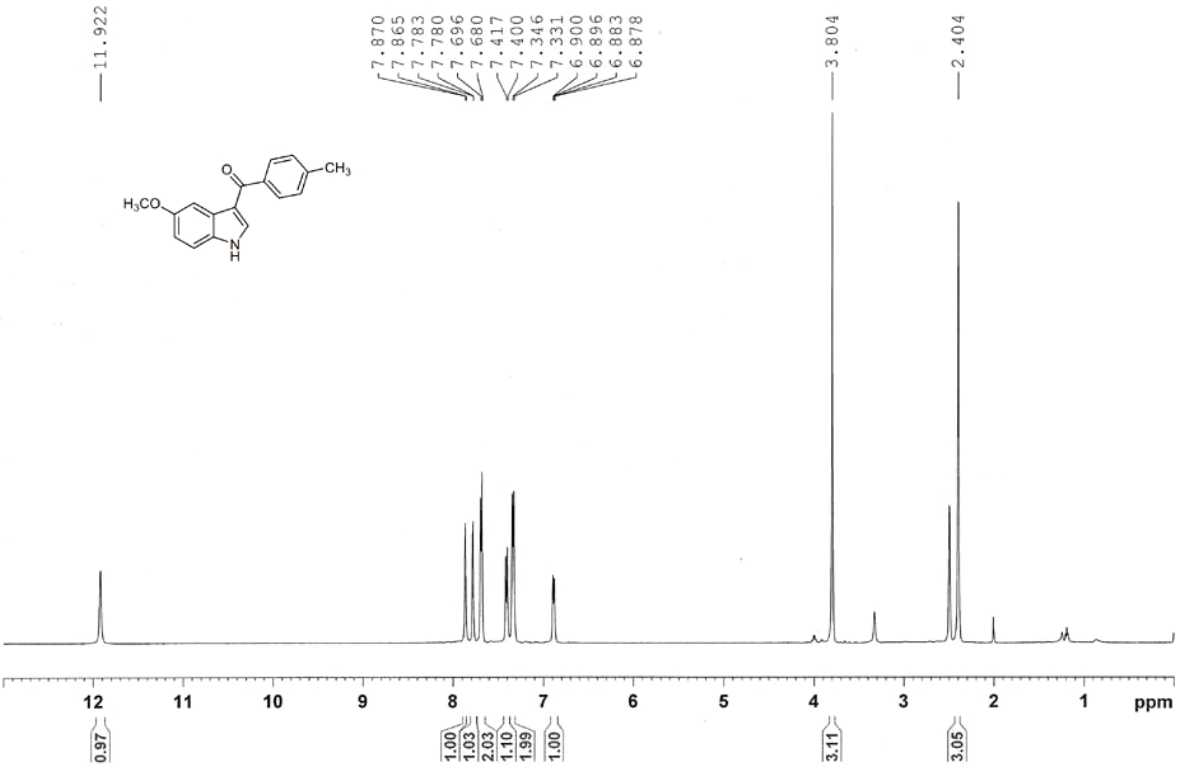
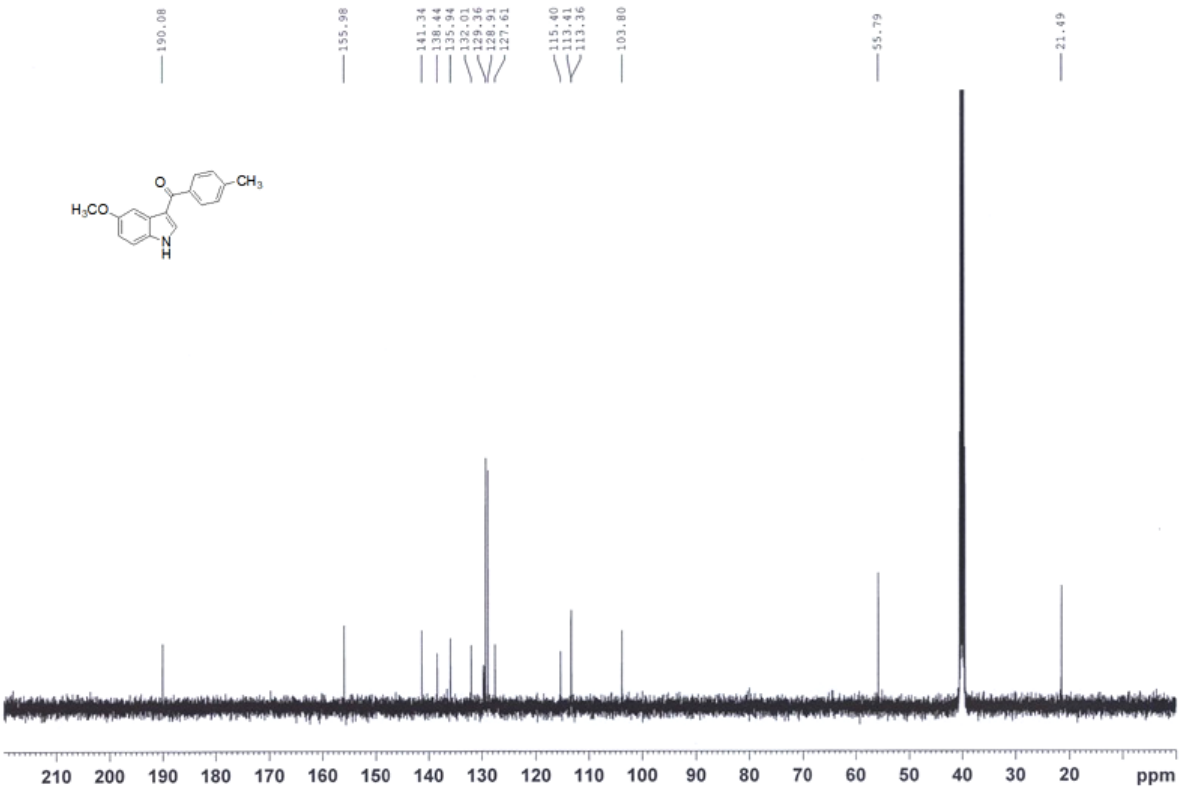
7.895
7.889
7.785
7.767
7.585
7.568
7.411
7.394
6.898
6.893
6.880
6.876
3.792
O
Cl
H3CO
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.93
1.00
2.78
1.88
0.95
0.92
2.88

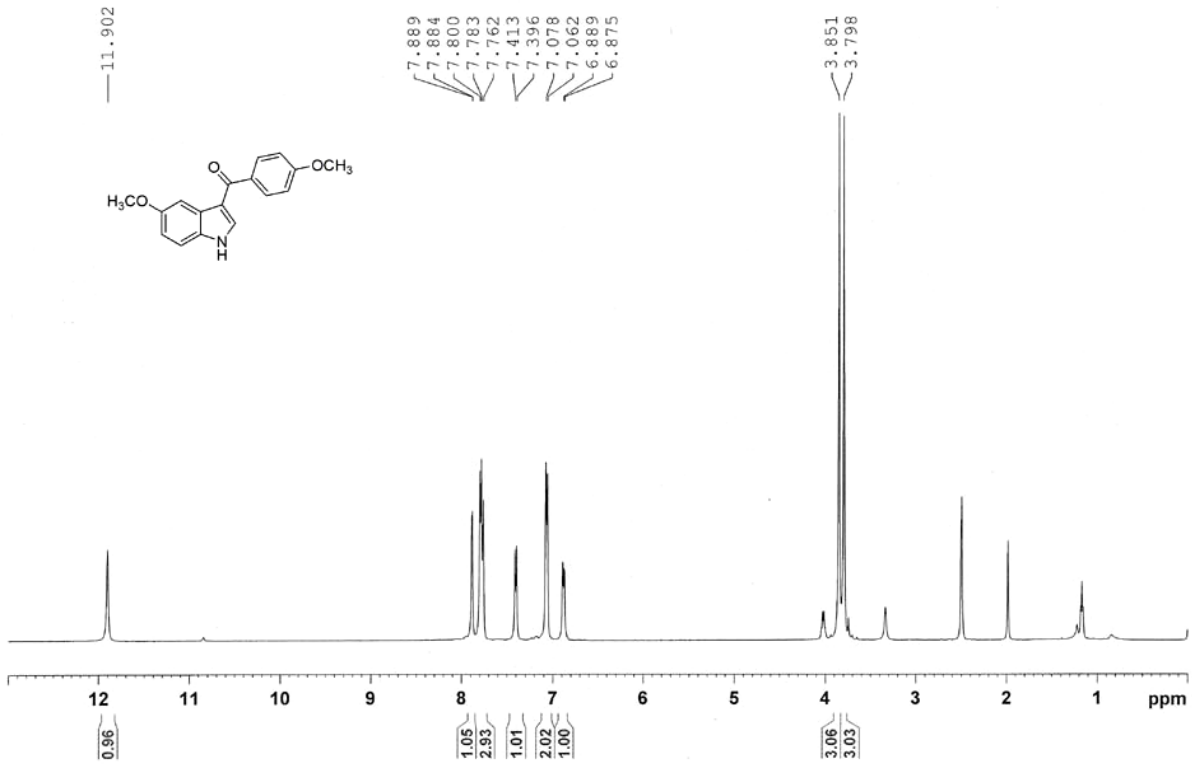

189.01
156.15
139.77
136.49
136.17
132.07
130.63
128.93
127.50
115.16
113.57
113.48
103.78
55.81
O
Cl
H3CO
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

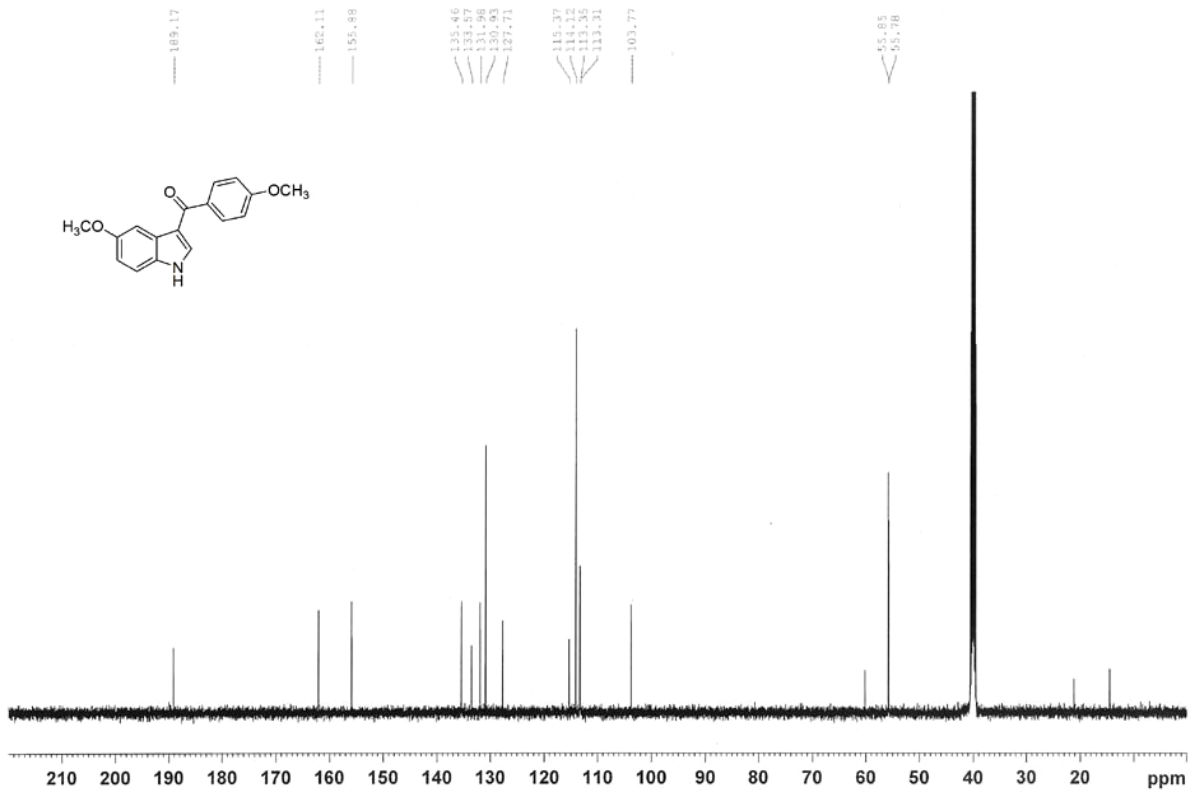

12.012
7.664
7.566
7.496
7.477
7.463
7.419
7.404
6.907
6.896
3.805
Cl
O
H3CO
N
H
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.97
1.06
1.93
3.02
1.04
0.96
3.00

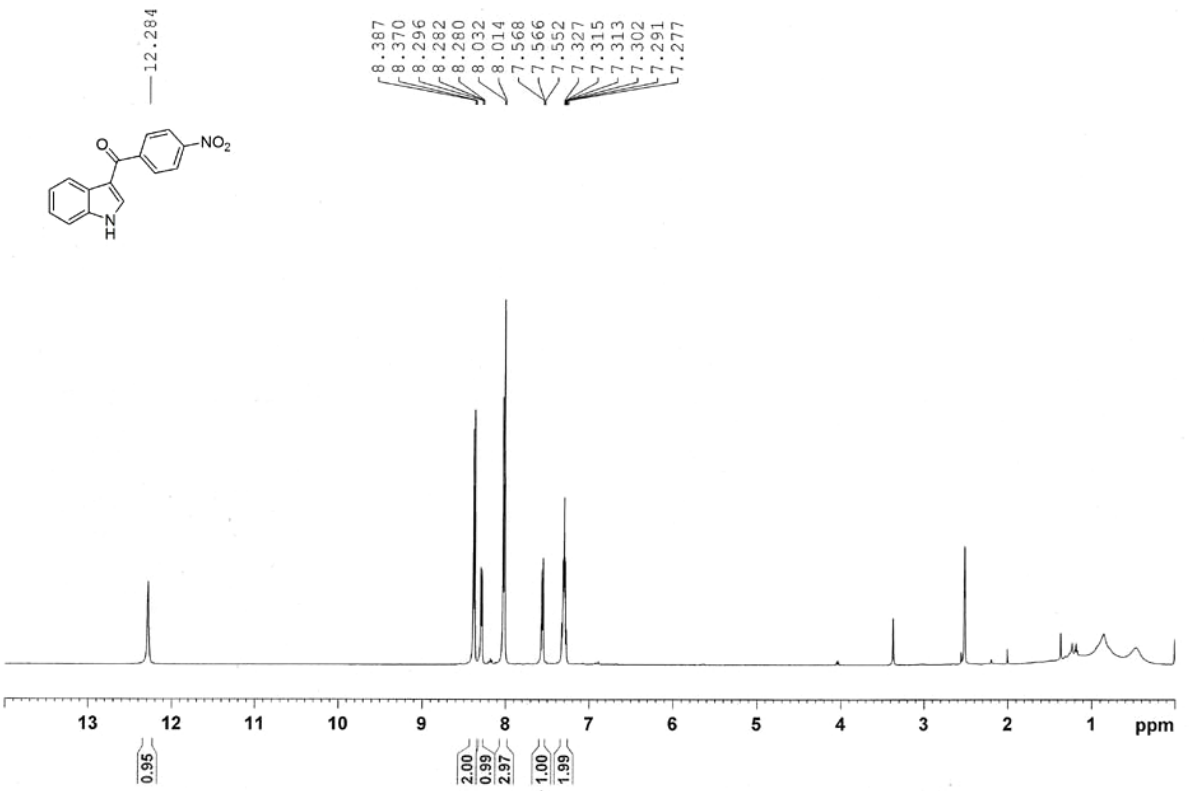

188.54
156.29
140.83
137.29
132.29
131.09
130.20
130.09
129.13
127.51
126.73
116.36
113.73
113.67
103.43
55.79
Cl
O
H3CO
N
H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

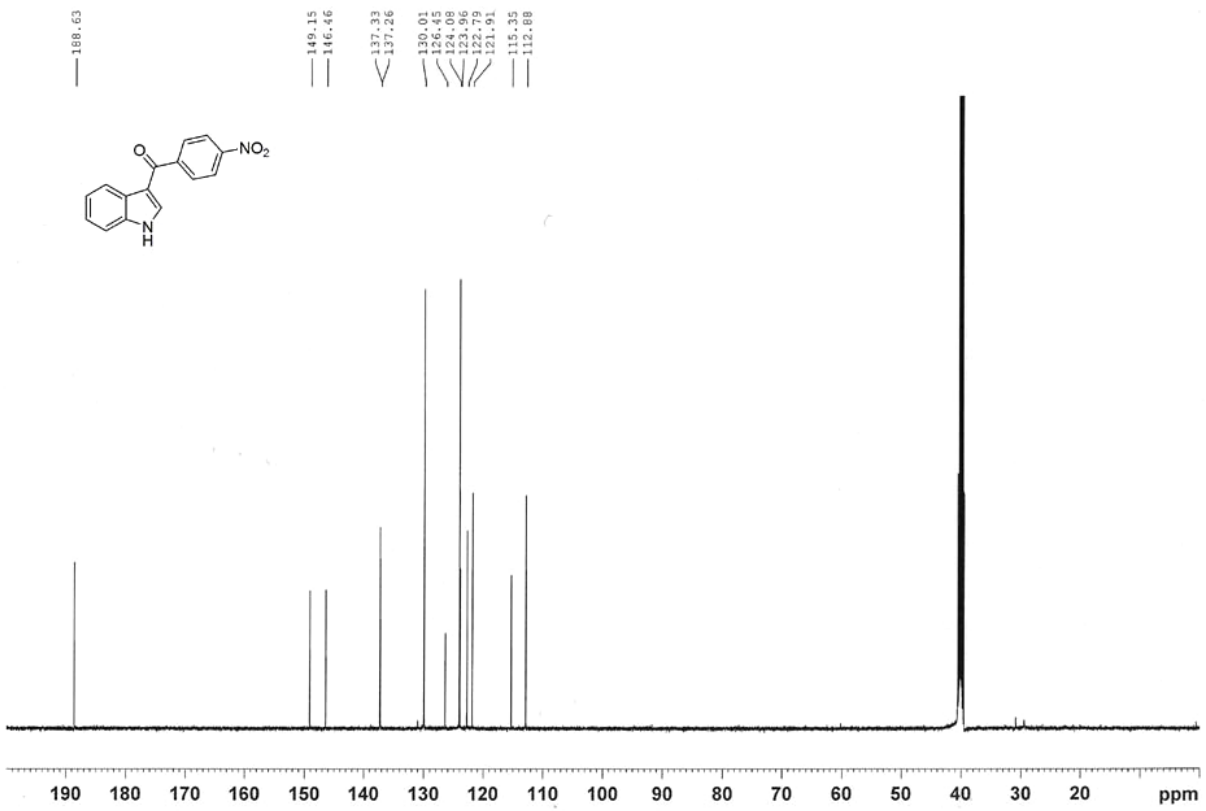

11.922
7.870
7.865
7.783
7.780
7.696
7.680
7.417
7.400
7.346
7.331
6.900
6.896
6.883
6.878
3.804
2.404
O
CH3
H3CO
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.97
1.00
1.03
2.03
1.10
1.99
1.00
3.11
3.05

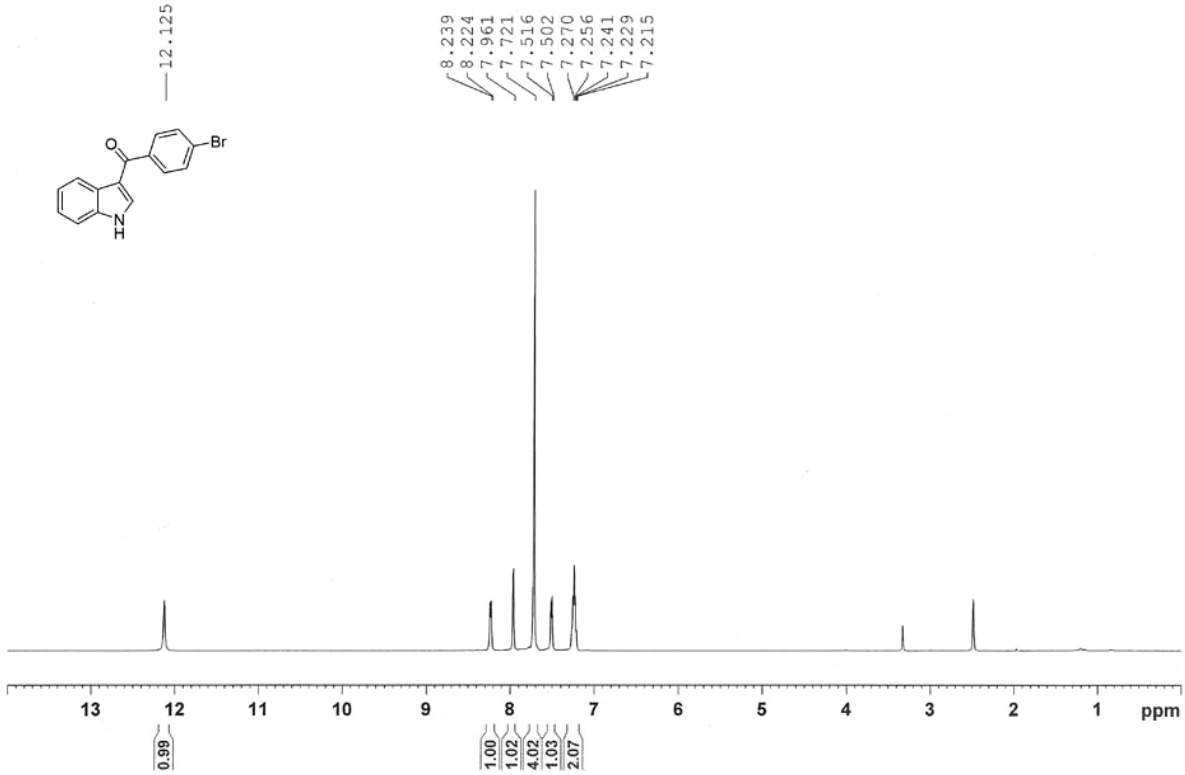

190.08
155.98
141.34
138.44
135.94
132.01
129.36
128.91
127.61
115.40
113.41
113.36
103.80
55.79
21.49
O
CH3
H3CO
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

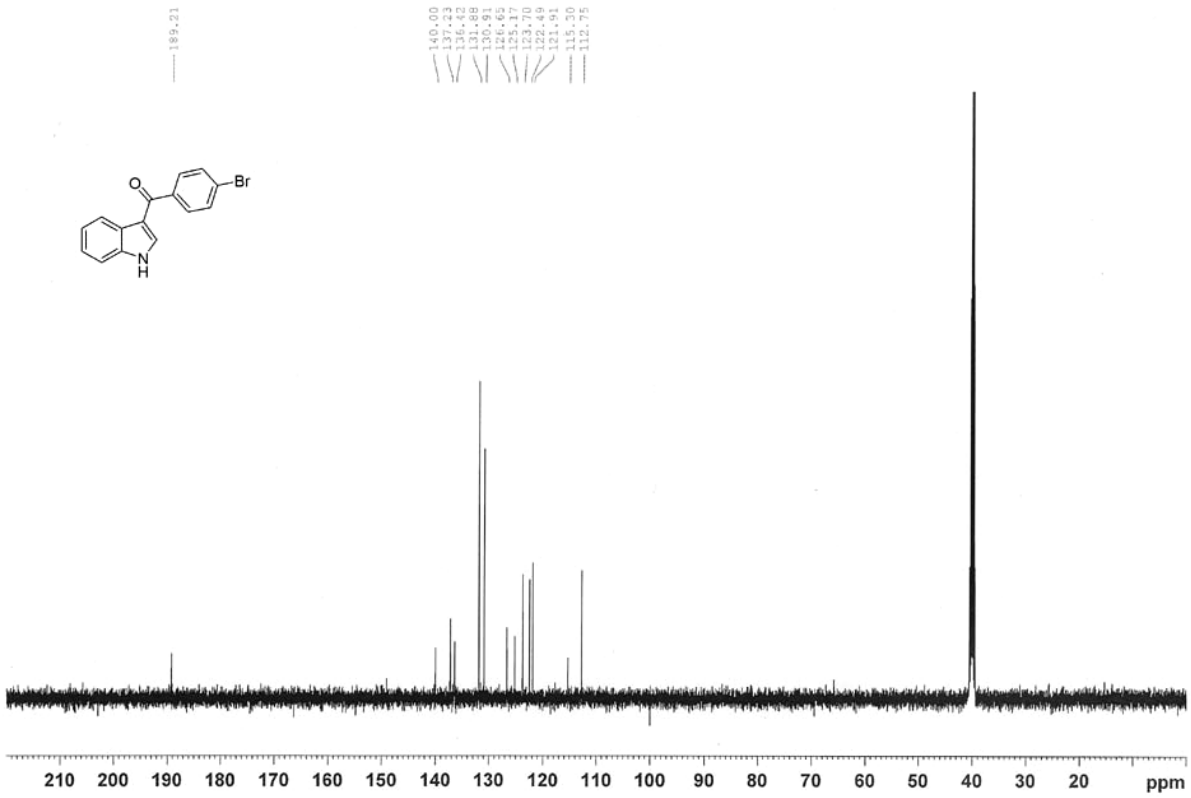

11.902
7.889
7.884
7.800
7.783
7.762
7.413
7.396
7.078
7.062
6.889
6.875
3.851
3.798
OCH3
H3CO
O
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.05
2.93
1.01
2.02
1.00
3.06
3.03

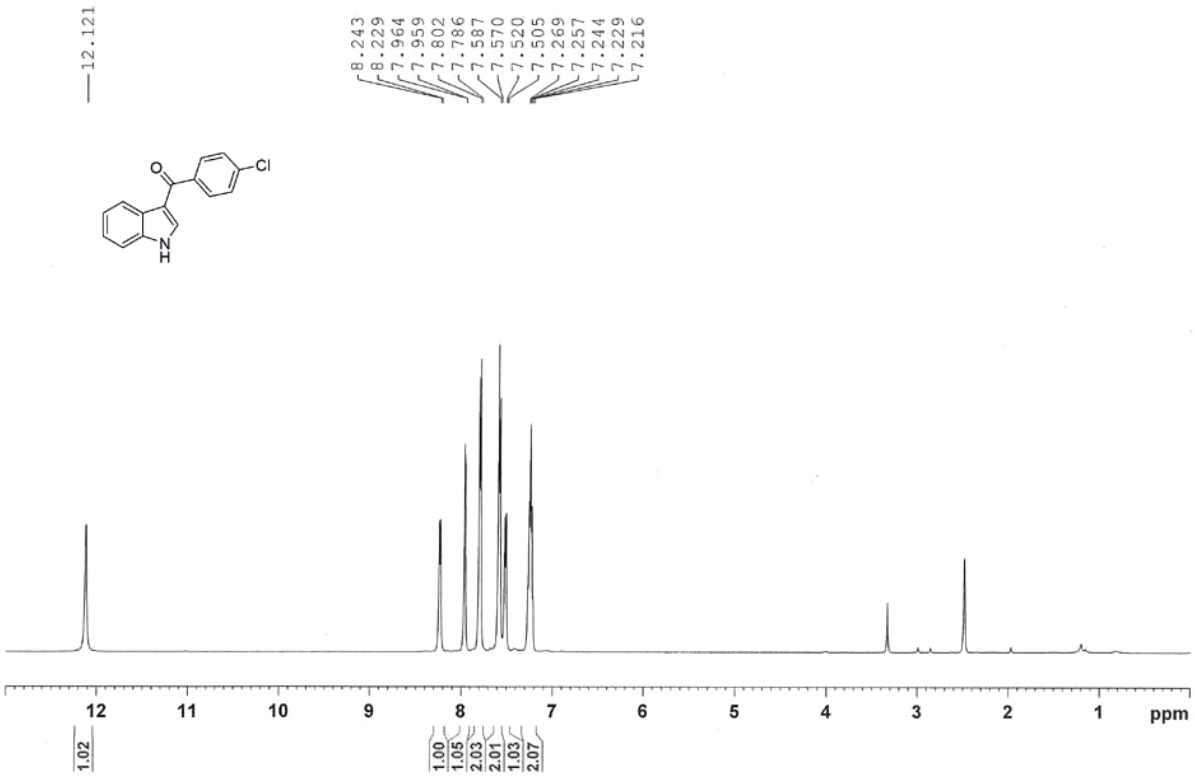

189.17
162.11
155.88
135.46
133.57
131.98
130.93
127.71
115.37
114.12
113.35
113.31
103.77
55.85
55.78
OCH3
H3CO
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

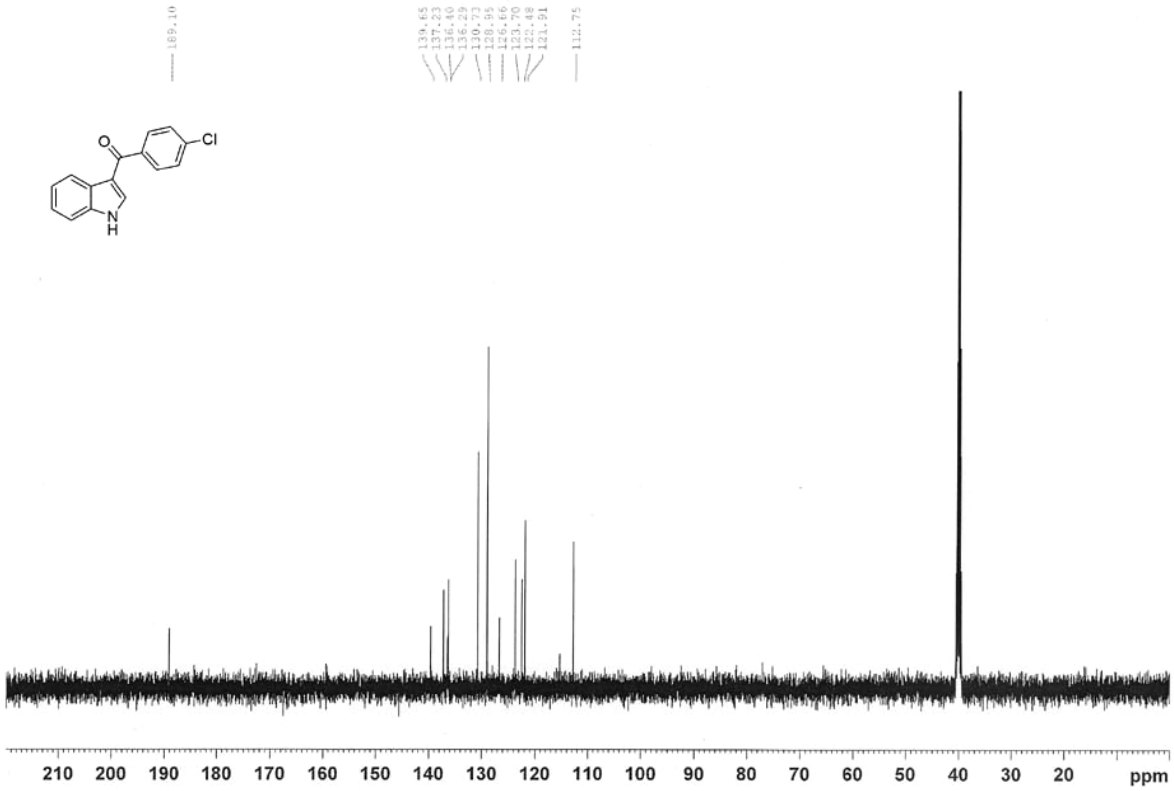

12.284
8.387
8.370
8.296
8.282
8.280
8.032
8.014
7.568
7.566
7.552
7.327
7.315
7.313
7.302
7.291
7.277
NO2
O
N
H
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.95
2.00
0.99
2.97
1.00
1.99

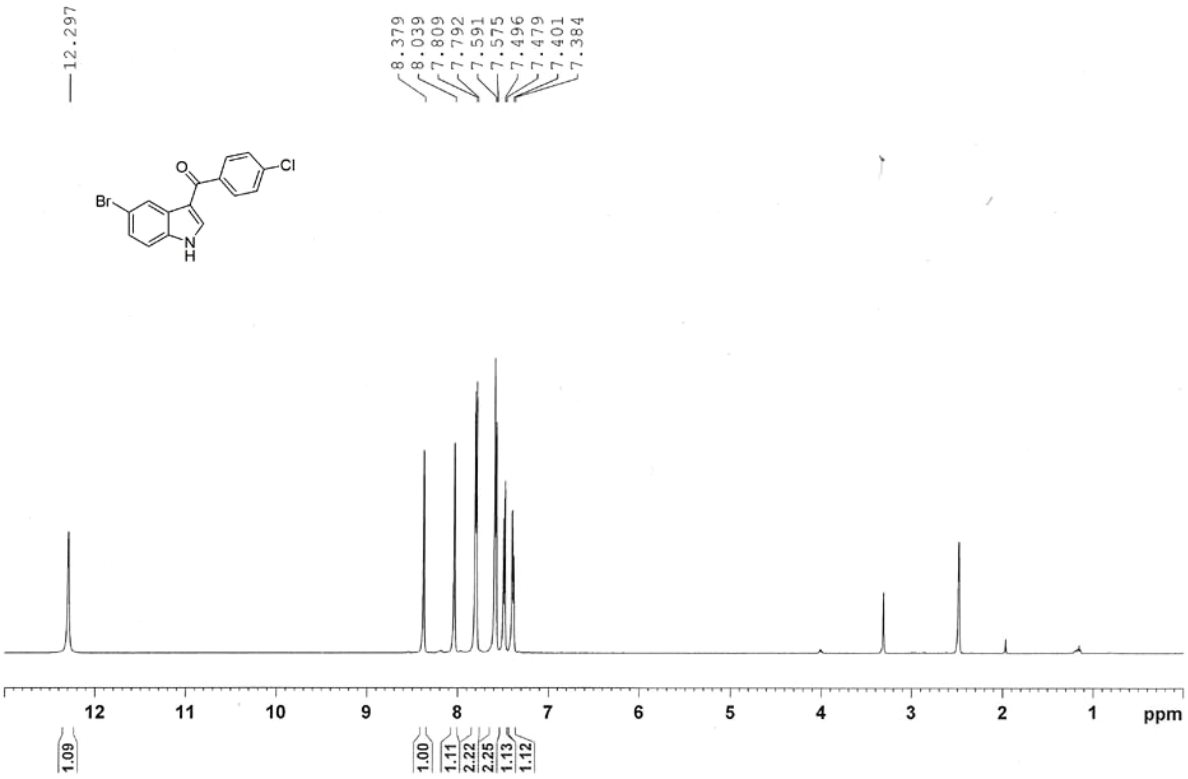

188.63
149.15
146.46
137.33
137.26
130.01
126.45
124.08
123.96
122.79
121.91
115.35
112.88
NO2
O
N
H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

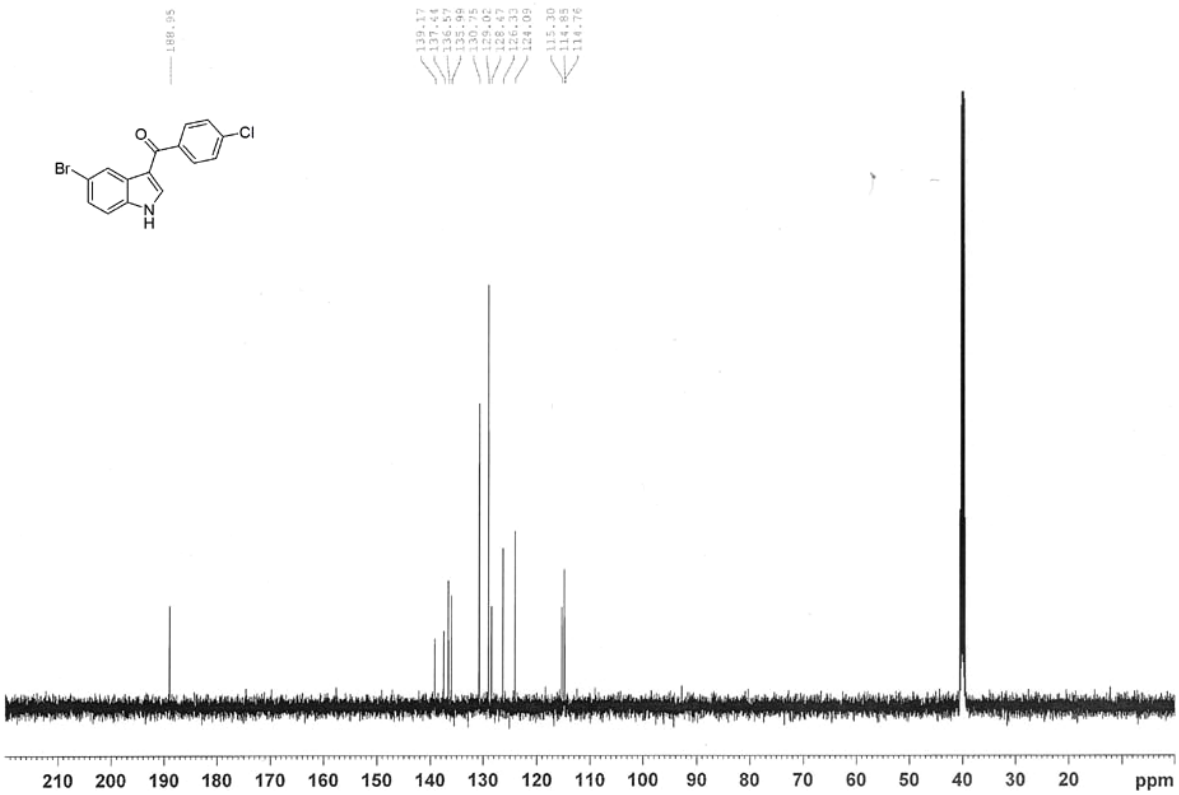

12.125
8.239
8.224
7.961
7.721
7.516
7.502
7.270
7.256
7.241
7.229
7.215
Br
O
N
H
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.00
1.02
4.02
1.03
2.07

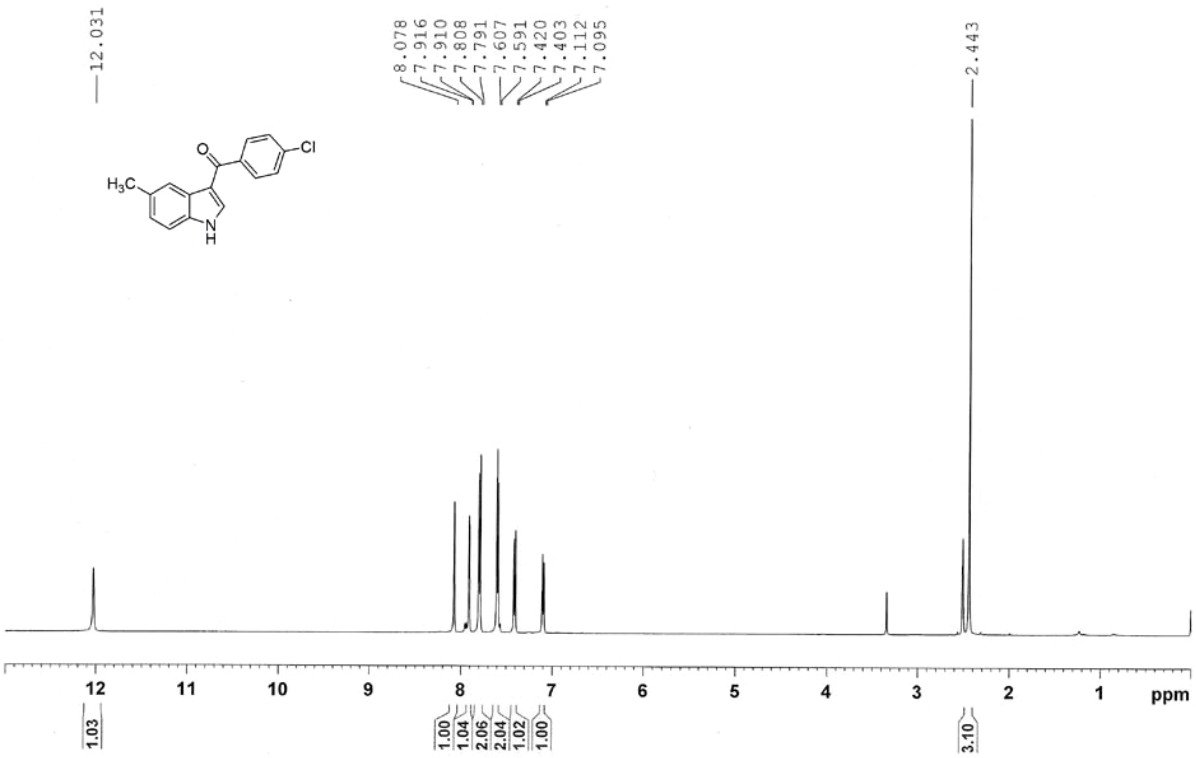

189.21
140.00
137.23
136.42
131.88
130.91
126.65
125.17
123.70
122.49
121.91
115.30
112.75
Br
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

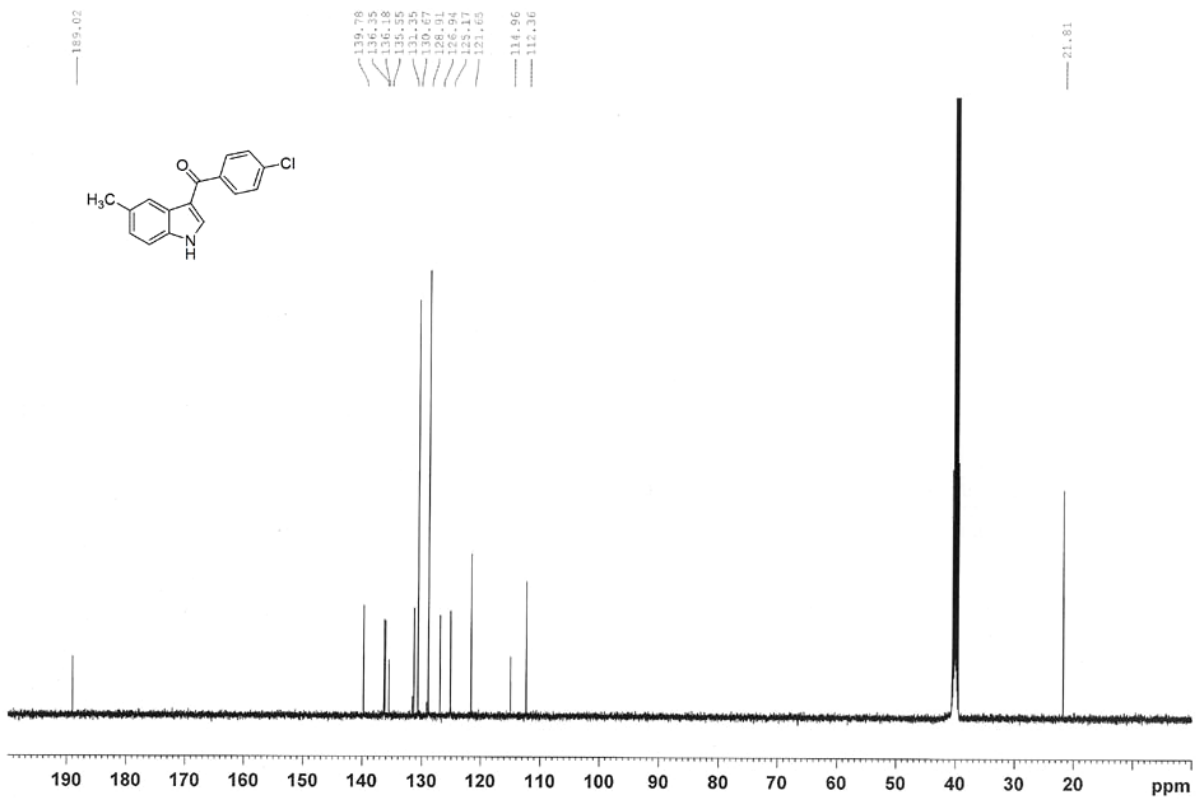

12.121
8.243
8.229
7.964
7.959
7.802
7.786
7.587
7.570
7.520
7.505
7.269
7.257
7.244
7.229
7.216
O
Cl
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.02
1.00
1.05
2.03
2.01
1.03
2.07

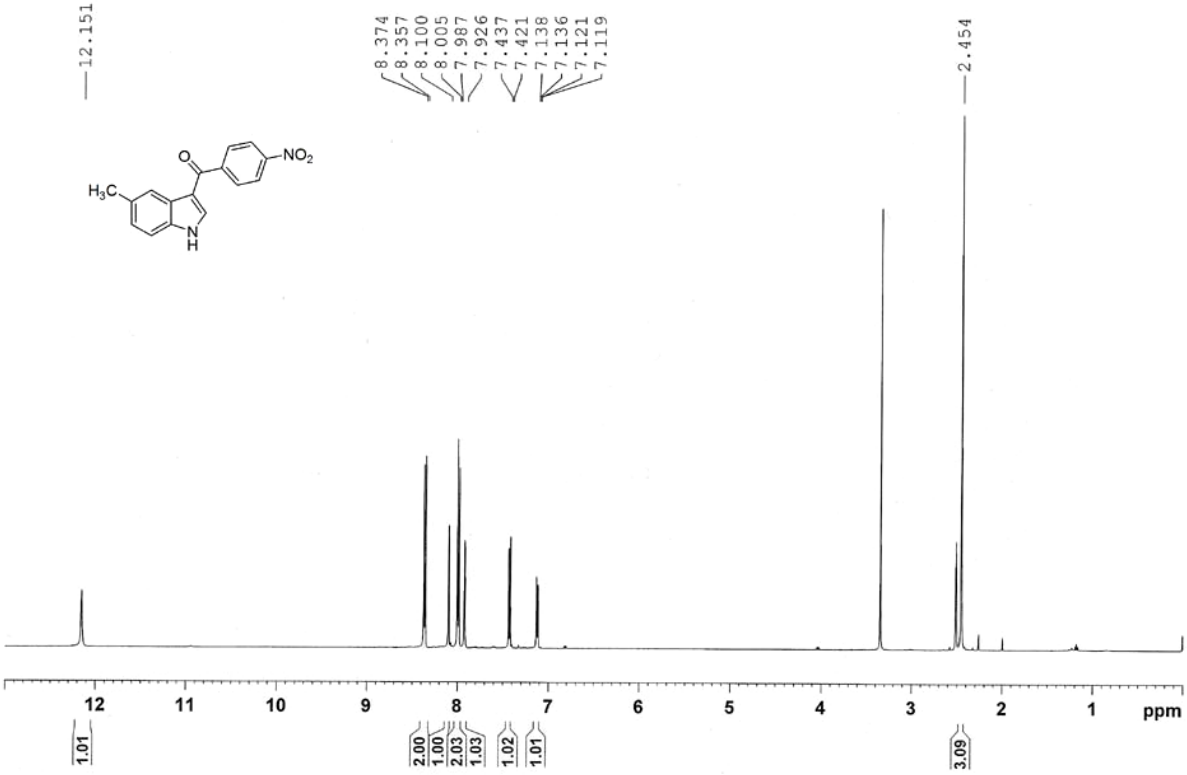

189.10
139.65
137.23
136.40
136.29
130.73
128.95
126.66
123.70
122.48
121.91
112.75
O
Cl
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

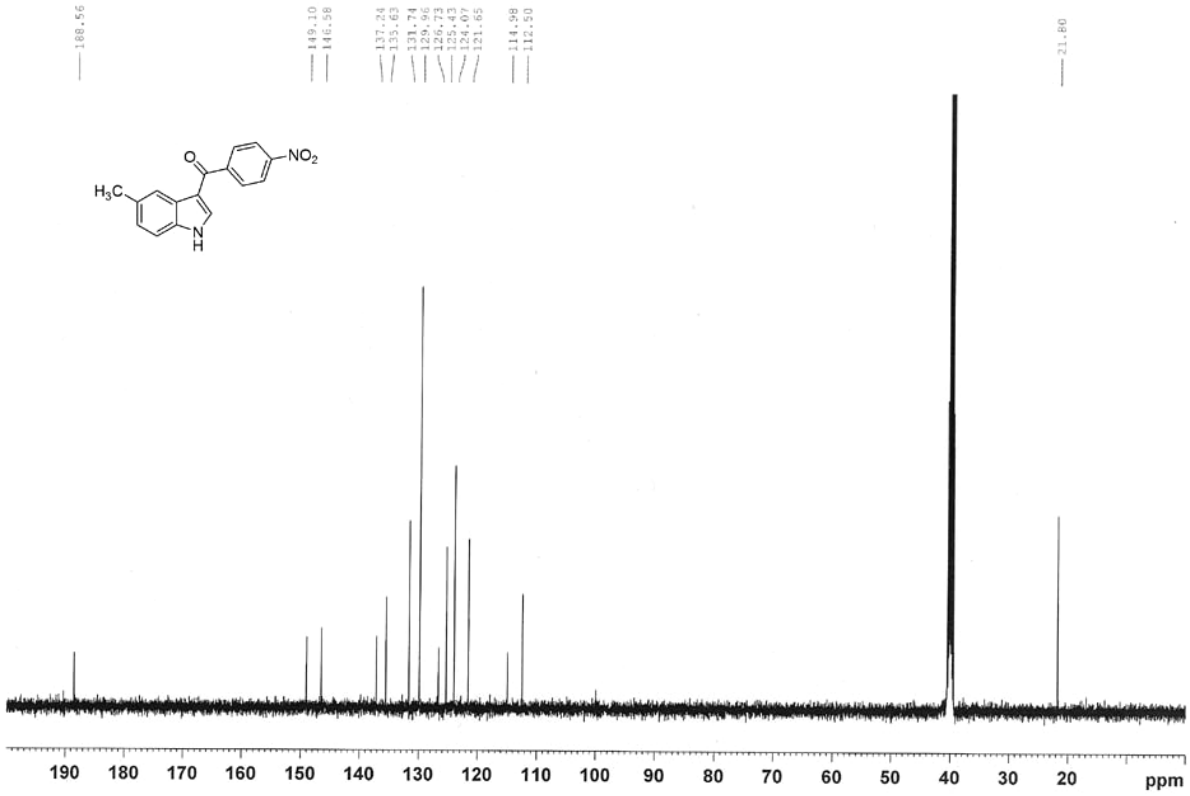

12.297
8.379
8.039
7.809
7.792
7.591
7.575
7.496
7.479
7.401
7.384
Br
O
Cl
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.09
1.00
1.11
2.22
2.25
1.13
1.12

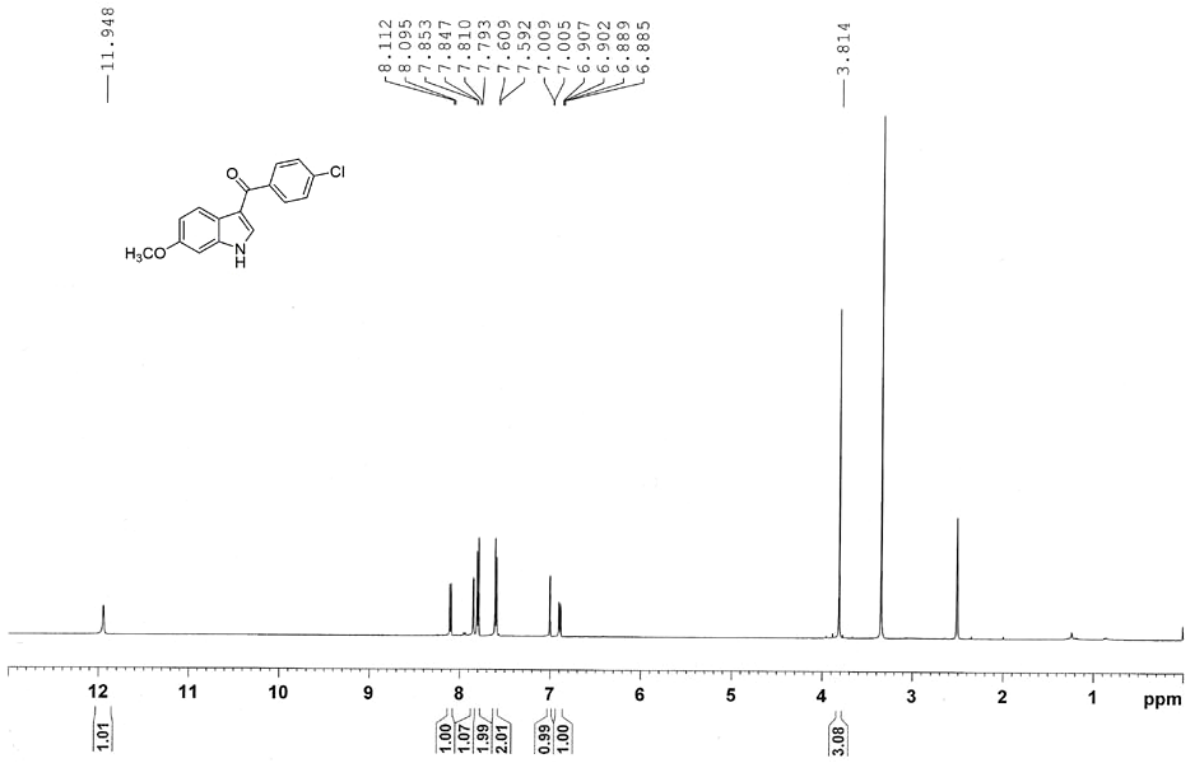

188.95
139.17
137.44
136.57
135.99
130.75
129.02
128.47
126.33
124.09
115.30
114.85
114.76
Br
O
Cl
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

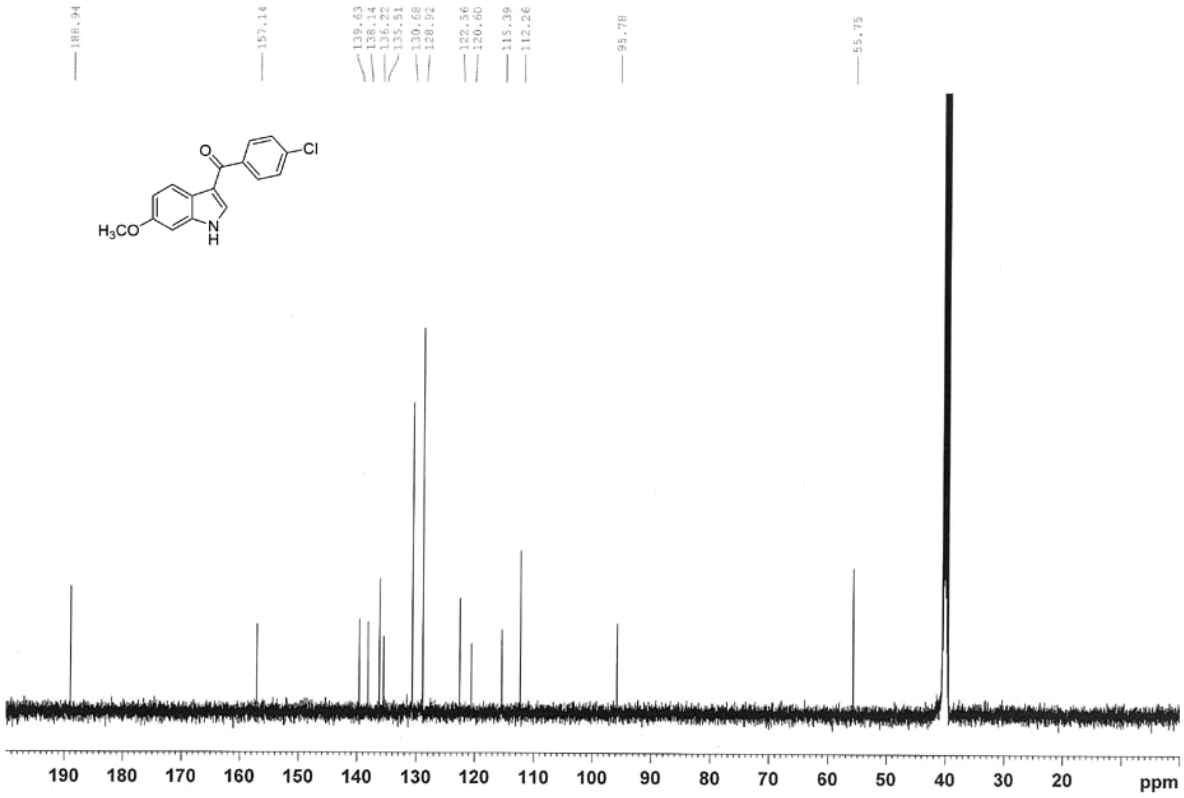

12.031
8.078
7.916
7.910
7.808
7.791
7.607
7.591
7.420
7.403
7.112
7.095
2.443
O
Cl
H3C
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.03
1.00
1.04
2.06
2.04
1.02
1.00
3.10

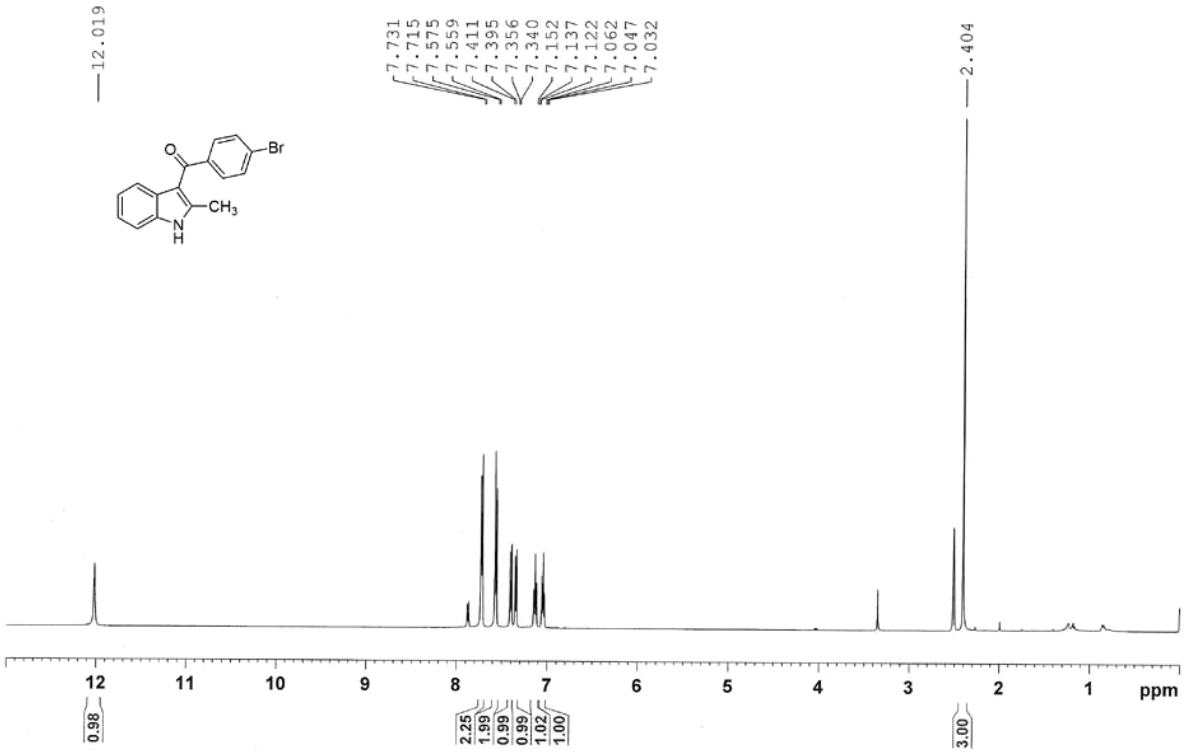

189.02
139.78
136.35
136.18
135.55
131.35
130.67
128.91
126.94
125.17
121.65
114.96
112.36
21.81
O
Cl
H3C
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

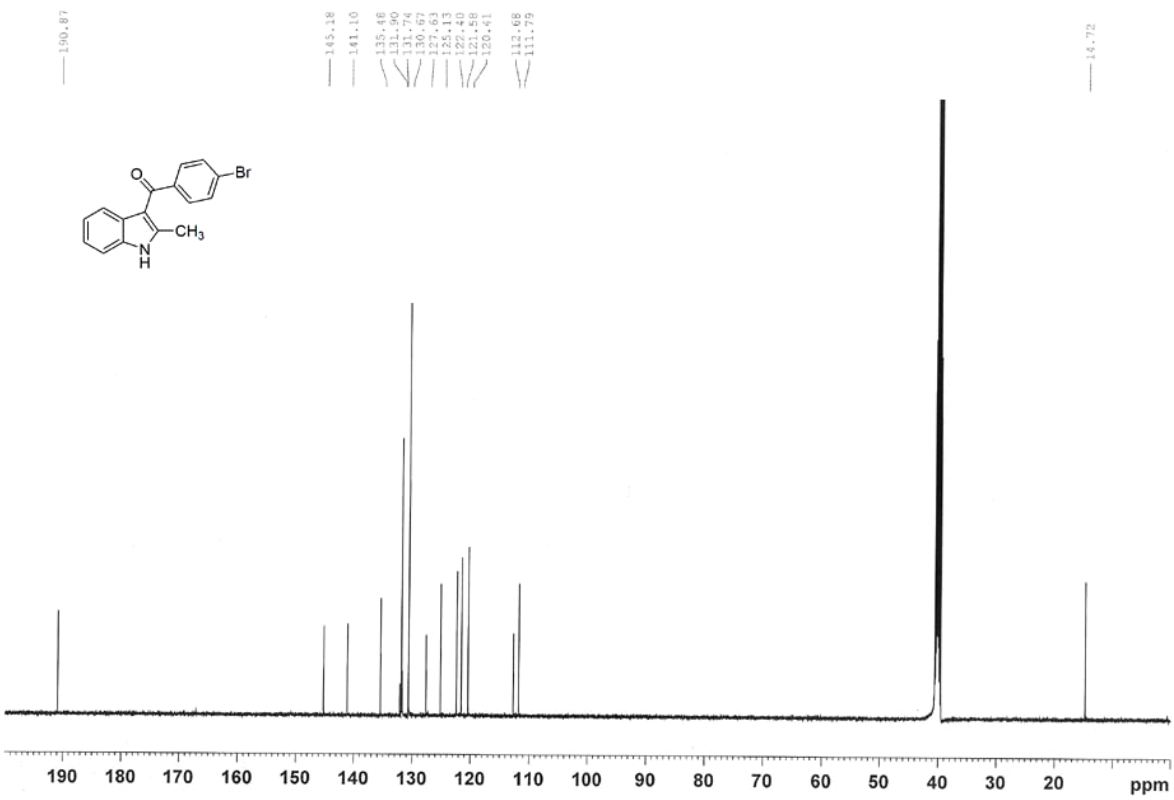

12.151
8.374
8.357
8.100
8.005
7.987
7.926
7.437
7.421
7.138
7.136
7.121
7.119
2.454
O
NO2
H3C
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.01
2.00
1.00
2.03
1.03
1.02
1.01
3.09


188.56
149.10
146.58
137.24
135.63
131.74
129.96
126.73
125.43
124.07
121.65
114.98
112.50
21.80
O
NO2
H3C
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


11.948
8.112
8.095
7.853
7.847
7.810
7.793
7.609
7.592
7.009
7.005
6.907
6.902
6.889
6.885
3.814
Cl
O
H3CO
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.01
1.00
1.07
1.99
2.01
0.99
1.00
3.08


188.94
157.14
139.63
138.14
136.22
135.51
130.68
128.92
122.56
120.60
115.39
112.26
95.78
55.75
Cl
O
H3CO
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


12.019
7.731
7.715
7.575
7.559
7.411
7.395
7.356
7.340
7.152
7.137
7.122
7.062
7.047
7.032
2.404
Br
O
CH3
N
H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.98
2.25
1.99
0.99
0.99
1.02
1.00
3.00


190.87
145.18
141.10
135.48
131.90
131.74
130.67
127.63
125.13
122.40
121.58
120.41
112.68
111.79
14.72
Br
O
CH3
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

7. Powder X-Ray Diffraction Analysis (XRD Analysis)

XRD powder diffraction was carried out on Bruker's D8 ADVANCE X-Ray Diffractometer with Guinier imaging plate detector (Cu-$K_{\alpha 1}$ radiation, λ= 154.056 pm).

A dried two-neck round bottom flask was charged with 5-methoxy-1*H*-indole (117.8 mg, 0.8 mmol), phenylglyoxylic acid (240.2 mg, 1.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (39.9 mg, 20 mol%), Ag_2CO_3 (441.2 mg, 1.6 mmol) and DMSO (4 mL) under air atmosphere. The reaction mixture was heated at 90 ^oC and stirred for 3 h. After completion of the reaction (monitored by TLC or HPLC), the reaction mixture was cooled to room temperature and diluted with EtOAc (5 mL) and water (5 mL), then the precipitate was collected by centrifugation and filtration, washed with EtOAc (2×5 mL) and water (2×5 mL), dried in the vacuum and was analyzed by XRD (Figure S3). Significant peaks labeled were assigned to Ag^0, implying that Ag_2CO_3 additive can be considered as terminal oxidant in the reaction.

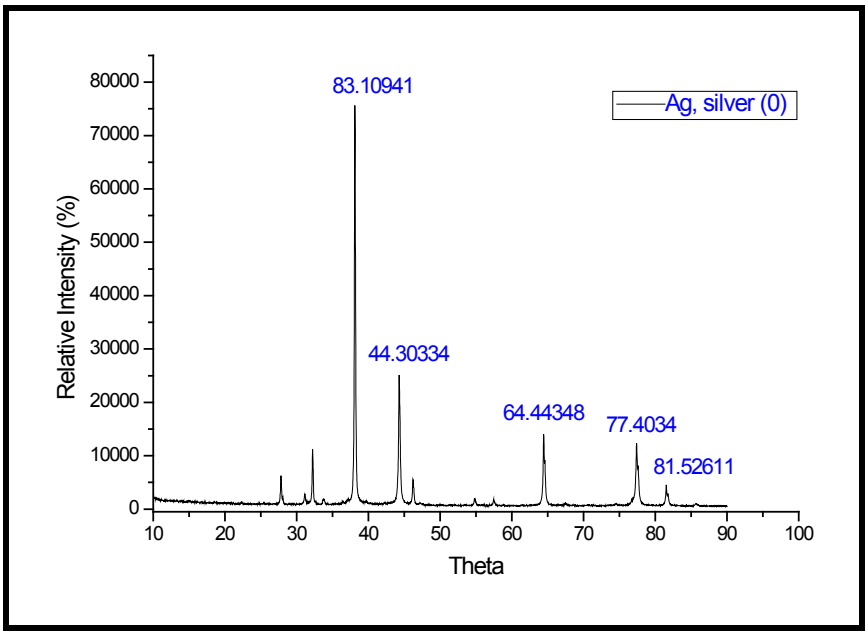


Figure S3. XRD of the precipitate after the reaction