New Journal of Chemistry

ELECTRONIC SUPPORTING INFORMATION (ESI)

Metal free hydrogen transfer reduction of 3-hydroxy-3-indolyloxindoles: a novel method for synthesis 3,3'-biindolin-2-ones

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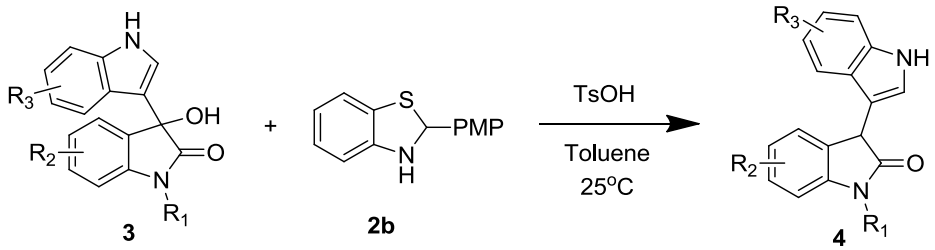
Content

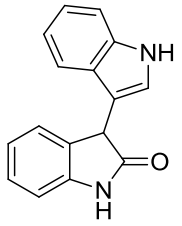
(A) General information

The solvents used were purified by distillation over the drying agents indicated and were transferred under argon: toluene (P_2O_5). All other reagents were used without purification as commercially available. All reactions were monitored by thin layer chromatography. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refer to pure isolated substances. The melting point was recorded on a melting point apparatus (MPA100, Stanford Research Systems, Inc.). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz spectrometers (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Chemical shifts of ^{1}H and ^{13}C signals were given in δ relative to the solvents residual (DMSO, δ_H = 2.5, δ_C = 39.52). The following abbreviations are used: s, singlet, d, doublet, t, triplet, q, quartet, quint, quintuplet, m, multplet, br, broad. High-resolution mass spectral analysis (HRMS) datas were measured on a Bruker ApexII mass spectrometer by means of the ESI technique.

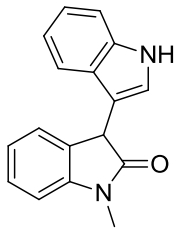
(B) Procedures for the hydrogen transfer reduction of 3-hydroxy-3-indolyloxindoles and the analytic data for the corresponding compounds.



In a 10-mL tube, a mixture of 3-hydroxy-3-indolyloxindole **3** (0.10 mmol), TsOH (2.0 mg, 0.0025 mmol, 5 mol%), in toluene (1 mL) was stirred at 25°C for 5 min. Then benzothiazolines **2b** (0.11 mmol) was added. After the reaction was completed (monitored by TLC), the mixture was purified by silica gel chromatography (PE/EtOAc=20/1) directly to afford the product **4**.

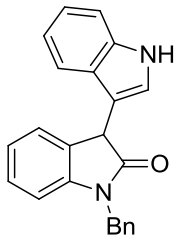

4a

3-indolyl-indolin-2-one **4a**, reaction time: 24 h, white solid, 90% yield, m.p.111 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.02 (s, 1H), 10.54 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 2.3 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.04 (m, 3H), 6.92 (m, 2H), 6.86 (m, 1H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 178.18, 143.02, 136.93, 130.88, 128.23, 126.44, 124.93, 124.89, 121.90, 121.60, 119.02, 118.96, 112.05, 110.42, 109.70, 44.84; **HRMS** (ESI) m/z calcd for $C_{16}H_{12}N_2O$ ([M+H]+): 249.1028, found: 249.1032.


4b

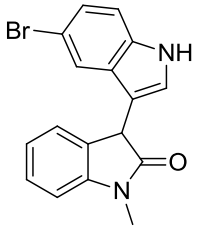
N-methyl-3-indolyl-indolin-2-one **4b**, reaction time: 12 h, white solid, 99% yield, m.p.90 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.04 (s, 1H), 7.38 – 7.27 (m, 3H), 7.13 – 7.02 (m, 3H), 7.02 – 6.92 (m, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 5.00 (s, 1H), 3.24 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.23, 144.46, 136.92, 129.96, 128.35, 126.34, 125.00, 124.56, 122.56, 121.62, 119.02, 118.95,

112.06, 110.19, 108.79, 44.27, 26.60; **HRMS** (ESI) m/z calcd for $C_{17}H_{14}N_2O$ ([M+H]+): 263.1184, found: 263.1175.



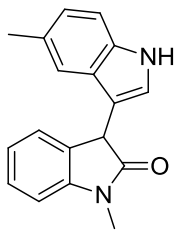
4c

N-benzyl-3-indolyl-indolin-2-one **4c**, reaction time: 18 h, white solid, 92% yield, m.p.128 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.11 (s, 1H), 7.39 (m, 6H), 7.33 – 7.27 (m, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.14 – 7.02 (m, 3H), 7.00 – 6.89 (m, 2H), 6.81 (t, *J* = 7.4 Hz, 1H), 5.16 (s, 1H), 5.01 (q, J = 15.6 Hz, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.54, 143.43, 137.09, 136.99, 130.03, 129.06, 128.26, 128.00, 127.93, 126.34, 125.16, 124.82, 122.71, 121.70, 119.12, 118.95, 112.13, 110.14, 109.45, 44.39, 43.39; **HRMS** (ESI) m/z calcd for $C_{23}H_{18}N_2O$ ([M+H]+): 339.1497, found: 339.1497.



4d

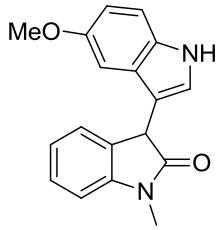
N-methyl-3-(5-bromoindolyl)-indolin-2-one **4d**, reaction time: 24 h, white solid, 95% yield, m.p.109 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.28 (s, 1H), 7.35 (t, *J* = 8.2 Hz, 2H), 7.29 – 7.23 (m, 2H), 7.19 (d, *J* = 8.6 Hz, 1H), 7.12 (d, *J* = 4.9 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 5.06 (s, 1H), 3.23 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.97, 144.47, 135.62, 129.40, 128.54, 128.39, 126.34, 124.64, 124.19, 122.70, 121.38, 114.16, 111.68, 110.08, 108.92, 43.89, 26.62; **HRMS** (ESI) m/z calcd for $C_{17}H_{13}BrN_2O$ ([M+H]+): 341.0290, found: 341.0288.



4e

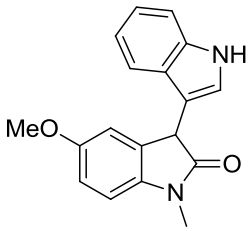
N-methyl-3-(5-methylindolyl)-indolin-2-one **4e**, reaction time: 10 h, white solid, 99% yield, m.p.85 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.92 (s, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* =

8.3 Hz, 1H), 7.19 (d, *J* = 1.7 Hz, 1H), 7.13 – 7.06 (m, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.80 (s, 1H), 4.96 (s, 1H), 3.24 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.28, 144.43, 135.29, 130.02, 128.32, 127.34, 126.69, 124.86, 124.54, 123.26, 122.55, 118.57, 111.80, 109.71, 108.77, 44.21, 26.59, 21.79; **HRMS** (ESI) m/z calcd for $C_{18}H_{16}N_2O$ ([M+H]+): 277.1341, found: 277.1340.



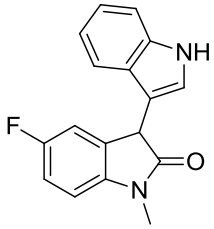
4f

N-methyl-3-(5-methoxylindolyl)-indolin-2-one **4f**, reaction time: 10 h, white solid, 99% yield, m.p.87 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.87 (s, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 2.4 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.46 (d, *J* = 2.3 Hz, 1H), 4.97 (s, 1H), 3.59 (s, 3H), 3.24 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.24, 153.35, 144.52, 132.07, 129.91, 128.35, 126.83, 125.40, 124.66, 122.59, 112.67, 111.32, 109.94, 108.72, 101.16, 55.56, 44.19, 26.55; **HRMS** (ESI) m/z calcd for $C_{18}H_{16}N_2O_2$ ([M+H]+): 293.1290, found: 293.1288.



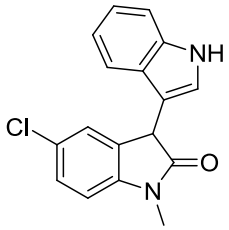
4g

N-methyl-5-methoxyl-3-indolyl-indolin-2-one **4g**, reaction time: 6 h, white solid, 99% yield, m.p.97 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.04 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 7.08 – 7.00 (m, 2H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.92 – 6.82 (m, 2H), 6.70 – 6.66 (m, 1H), 4.96 (s, 1H), 3.65 (s, 3H), 3.21 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.85, 155.82, 137.98, 136.92, 131.29, 126.32, 125.05, 121.62, 119.04, 118.94, 112.70, 112.07, 111.83, 110.20, 109.14, 55.89, 44.72, 26.67; **HRMS** (ESI) m/z calcd for $C_{18}H_{16}N_2O_2$ ([M+H]+): 293.1290, found: 293.1294.



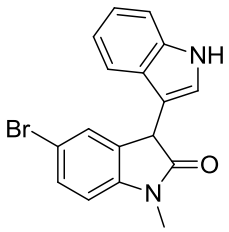
4h

N-methyl-5-fluoro-3-indolyl-indolin-2-one **4h**, reaction time: 10 h, white solid, 99% yield, m.p.98 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.09 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 2.2 Hz, 1H), 7.17 (m, 1H), 7.11 (dd, *J* = 8.5, 4.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.0 Hz, 2H), 6.86 (t, *J* = 7.4 Hz, 1H), 5.05 (s, 1H), 3.24 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.01, 160.09, 157.74, 140.74, 136.91, 131.92, 131.84, 126.19, 125.23, 121.70, 119.15, 118.79, 114.59, 114.36, 112.58, 112.33, 112.14, 109.57, 44.65, 26.78; **HRMS** (ESI) m/z calcd for $C_{17}H_{13}FN_2O$ ([M+H]+): 281.1090, found: 281.1085.



4i

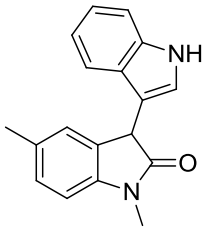
N-methyl-5-chloro-3-indolyl-indolin-2-one **4i**, reaction time: 8 h, white solid, 99% yield, m.p.98 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.10 (s, 1H), 7.38 (dd, *J* = 8.2, 3.6 Hz, 2H), 7.33 (d, *J* = 2.3 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.09 – 7.03 (m, 2H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 7.3 Hz, 1H), 5.06 (s, 1H), 3.24 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.91, 143.40, 136.91, 132.19, 128.16, 126.61, 126.15, 125.29, 124.55, 121.73, 119.21, 118.71, 112.18, 110.29, 109.44, 44.35, 26.78; **HRMS** (ESI) m/z calcd for $C_{17}H_{13}ClN_2O$ ([M+H]+): 297.0795, found: 297.0799.



4j

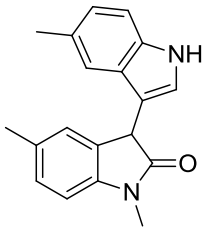
N-methyl-5-bromo-3-indolyl-indolin-2-one **4j**, reaction time: 10 h, white solid, 99% yield, m.p.102 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.11 (s, 1H), 7.51 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 2.3 Hz, 1H), 7.17 (s, 1H), 7.07 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 5.07 (s, 1H), 3.24 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.81,

143.79, 136.91, 132.58, 131.01, 127.21, 126.14, 125.31, 121.74, 119.23, 118.70, 114.33, 112.20, 110.84, 109.44, 44.28, 26.75.; **HRMS** (ESI) m/z calcd for $C_{17}H_{13}BrN_2O$ ([M+H]+): 341.0290, found: 341.0286.



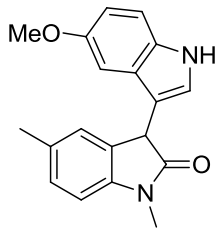
4k

N-methyl-5-methyl-3-indolyl-indolin-2-one **4k**, reaction time: 6 h, white solid, 99% yield, m.p.121 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.93 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 2.2 Hz, 1H), 7.17 (m, 1H), 7.11 (dd, *J* = 8.5, 4.4 Hz, 1H), 6.97 (d, *J* = 9.2 Hz, 1H), 6.73 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 5.02 (s, 1H), 3.61 (s, 3H), 3.23 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.02, 160.11, 157.76, 153.44, 140.80, 132.06, 131.87, 131.79, 126.70, 125.59, 114.58, 114.35, 112.77, 112.66, 112.42, 111.40, 109.53, 109.44, 109.35, 100.95, 55.56, 44.59, 26.71; **HRMS** (ESI) m/z calcd for $C_{18}H_{16}N_2O$ ([M+H]+): 277.1341, found: 277.1345.



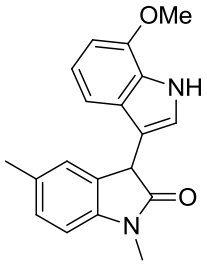
4l

N-methyl-5-methyl-3-(5-methylindolyl)-indolin-2-one **4l**, reaction time: 18 h, white solid, 99% yield, m.p.112 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.89 (s, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 7.20 (d, *J* = 2.2 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 2H), 6.79 (s, 1H), 4.91 (s, 1H), 3.22 (s, 3H), 2.25 (s, 3H), 2.21 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.20, 142.08, 135.30, 131.41, 130.13, 128.44, 127.32, 126.68, 125.23, 124.90, 123.24, 118.54, 111.78, 109.88, 108.47, 44.27, 26.61, 21.80, 21.10; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O$ ([M+H]+): 291.1497, found: 291.1497.



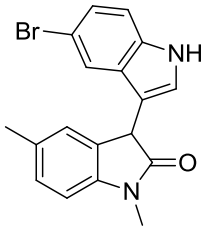
4m

N-methyl-5-methyl-3-(5-methoxylindolyl)-indolin-2-one **4m**, reaction time: 18 h, white solid, 99% yield, m.p.85 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 10.86 (s, 1H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.91 (s, 1H), 6.71 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.44 (d, *J* = 2.3 Hz, 1H), 4.92 (s, 1H), 3.59 (s, 3H), 3.22 (s, 3H), 2.22 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 176.17, 153.32, 142.15, 132.06, 131.48, 130.00, 128.46, 126.82, 125.46, 125.34, 112.66, 111.25, 110.09, 108.44, 101.14, 55.55, 44.24, 26.56, 21.10; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_2$ ([M+H]+): 307.1447, found: 307.1453.



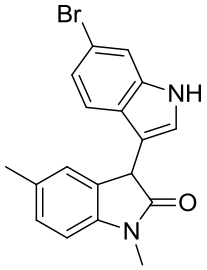
4n

N-methyl-5-methyl-3-(7-methoxylindolyl)-indolin-2-one **4n**, reaction time: 18 h, white solid, 99% yield, m.p.102 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 11.13 (s, 1H), 7.20 (d, *J* = 2.4 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.86 (s, 1H), 6.76 (t, *J* = 7.8 Hz, 1H), 6.61 (d, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 7.9 Hz, 1H), 4.91 (s, 1H), 3.89 (s, 3H), 3.21 (s, 3H), 2.20 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 176.14, 146.69, 142.07, 131.41, 130.12, 128.44, 127.81, 127.01, 125.22, 124.66, 119.65, 111.78, 110.91, 108.46, 102.16, 55.59, 44.37, 26.61, 21.07; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_2$ ([M+H]+): 307.1447, found: 307.1452.



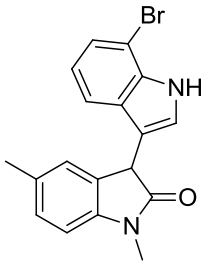
4o

N-methyl-5-methyl-3-(5-bromoindolyl)-indolin-2-one **4o**, reaction time: 24 h, white solid, 97% yield, m.p.122 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 11.27 (s, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.21 (s, 1H), 7.18 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 5.00 (s, 1H), 3.21 (s, 3H), 2.23 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 175.90, 142.09, 135.61, 131.63, 129.52, 128.66, 128.36, 126.40, 125.30, 124.17, 121.31, 114.16, 111.65, 110.23, 108.64, 43.94, 26.64, 21.10; **HRMS** (ESI) m/z calcd for $C_{18}H_{15}BrN_2O$ ([M+H]+): 355.0446, found: 355.0443.



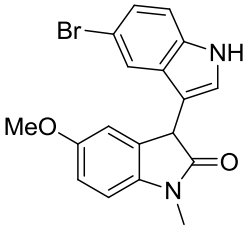
4p

N-methyl-5-methyl-3-(6-bromoindolyl)-indolin-2-one **4p**, reaction time: 24 h, white solid, 97% yield, m.p.207 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.18 (s, 1H), 7.56 (d, *J* = 1.5 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.00 (t, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.89 (s, 1H), 4.97 (s, 1H), 3.21 (s, 3H), 2.21 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.91, 142.07, 137.79, 131.56, 129.69, 128.59, 126.03, 125.45, 125.24, 121.97, 120.73, 114.64, 114.42, 110.77, 108.61, 44.06, 26.65, 21.08; **HRMS** (ESI) m/z calcd for $C_{18}H_{15}BrN_2O$ ([M+H]+): 355.0446, found: 355.0446.



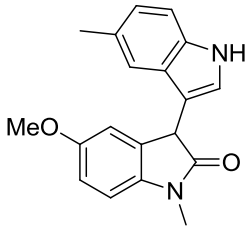
4q

N-methyl-5-methyl-3-(7-bromoindolyl)-indolin-2-one **4q**, reaction time: 24 h, white solid, 92% yield, m.p.196 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.24 (s, 1H), 7.30 (dd, *J* = 16.3, 7.6 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 7.10 (s, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.85 (t, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 3.15 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.76, 141.21, 135.45, 132.82, 131.90, 129.91, 126.99, 125.41, 125.14, 124.18, 120.58, 120.23, 117.30, 108.87, 104.60, 75.04, 26.49, 21.12; **HRMS** (ESI) m/z calcd for $C_{18}H_{15}BrN_2O$ ([M+H]+): 355.0446, found: 355.0440.



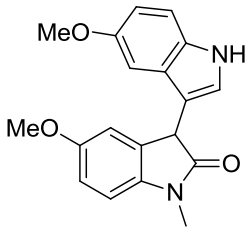
4r

N-methyl-5-methoxyl-3-(5-bromoindolyl)-indolin-2-one **4r**, reaction time: 36 h, white solid, 83% yield, m.p.117 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.27 (s, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 2.4 Hz, 1H), 7.24 (d, *J* = 1.6 Hz, 1H), 7.18 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 6.92 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.73 (d, *J* = 1.4 Hz, 1H), 5.02 (s, 1H), 3.68 (s, 3H), 3.20 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.58, 155.88, 137.97, 135.62, 130.72, 128.35, 126.38, 124.18, 121.36, 114.16, 112.89, 111.91, 111.65, 110.09, 109.30, 55.93, 44.32, 26.69; **HRMS** (ESI) m/z calcd for $C_{18}H_{15}BrN_2O_2$ ([M+H]+): 371.0395, found: 371.0399.



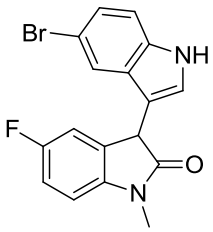
4s

N-methyl-5-methoxyl-3-(5-methylindolyl)-indolin-2-one **4s**, reaction time: 12 h, white solid, 99% yield, m.p.92 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.27 (s, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 2.4 Hz, 1H), 7.24 (d, *J* = 1.6 Hz, 1H), 7.18 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 6.92 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.73 (d, *J* = 1.4 Hz, 1H), 5.02 (s, 1H), 3.68 (s, 3H), 3.20 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.58, 155.88, 137.97, 135.62, 130.72, 128.35, 126.38, 124.18, 121.36, 114.16, 112.89, 111.91, 111.65, 110.09, 109.30, 55.93, 44.32, 26.69; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_2$ ([M+H]+): 307.1447, found: 307.1447.



4t

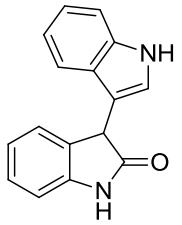
N-methyl-5-methoxyl-3-(5-methoxylindolyl)-indolin-2-one **4t**, reaction time: 12 h, white solid, 99% yield, m.p.74 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.88 (s, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.4 Hz, 2H), 6.46 (d, *J* = 2.3 Hz, 1H), 4.93 (s, 1H), 3.66 (s, 3H), 3.60 (s, 3H), 3.21 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 175.86, 155.83, 153.35, 138.04, 132.07, 131.23, 126.81, 125.46, 112.70, 111.91, 111.29, 109.96, 109.07, 101.16, 55.90, 55.57, 44.63, 26.62; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_3$ ([M+H]+): 323.1396, found: 323.1399.



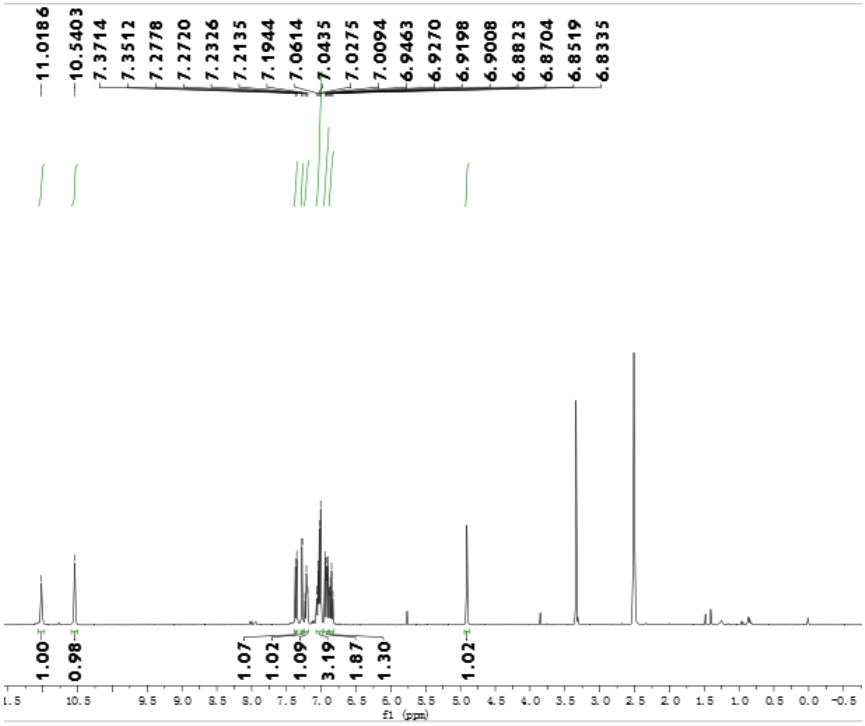
4u

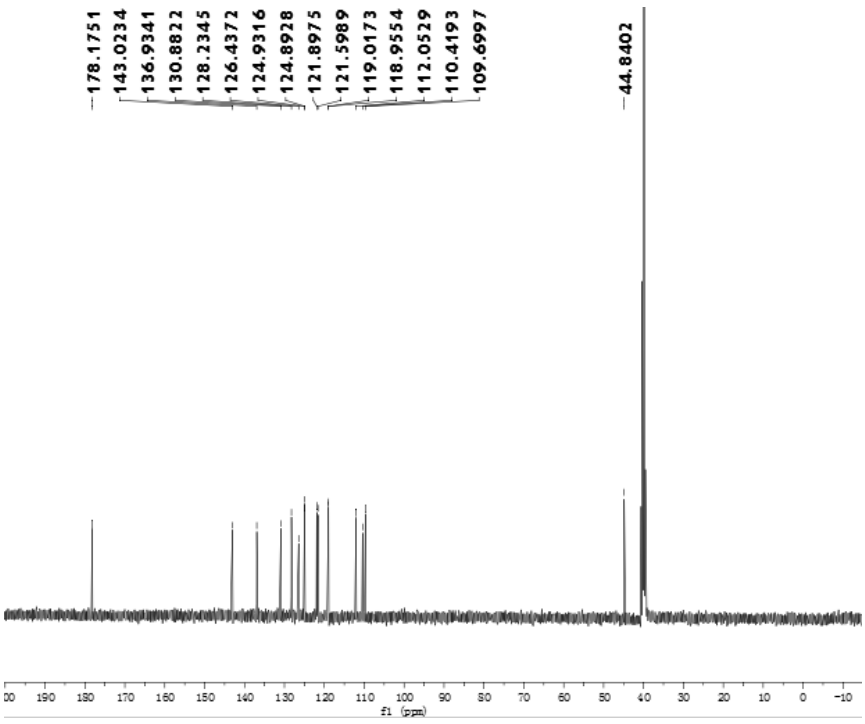
N-methyl-5-fluoro-3-(5-bromoindolyl)-indolin-2-one **4u**, reaction time: 48 h, white solid, 85% yield, m.p.75 ^{o}C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.93 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.23 (s, 1H), 7.17 (t, *J* = 9.0 Hz, 1H), 7.11 (dd, *J* = 8.5, 4.4 Hz, 1H), 6.97 (d, *J* = 9.2 Hz, 1H), 6.73 (d, *J* = 8.8 Hz, 1H), 6.46 (s, 1H), 5.02 (s, 1H), 3.61 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 176.02, 160.11, 157.76, 153.44, 140.80, 132.06, 131.87, 131.79, 126.70, 125.59, 114.58, 114.35, 112.77, 112.66, 112.42, 111.40, 109.53, 109.44, 109.35, 100.95, 55.56, 44.59, 26.71; **HRMS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_3$ ([M+H]+): 359.0195, found: 359.0196.

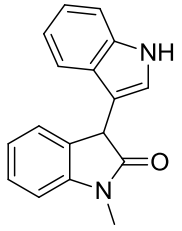
(C)spectra of all products



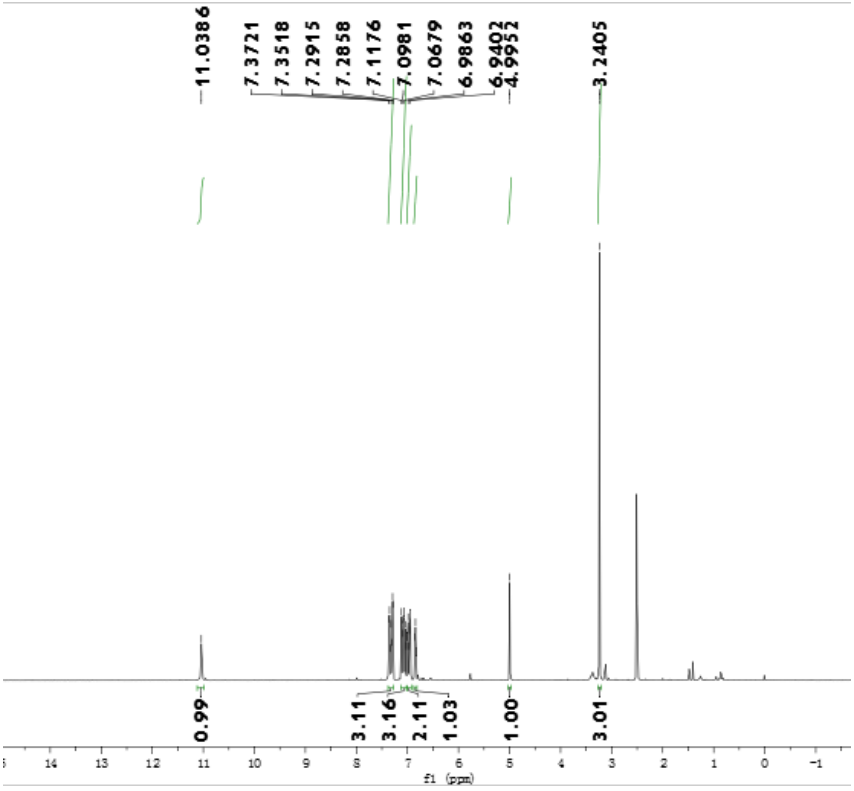
4a






NH
O
N

4b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7.2858
7.1176
7.0981
7.0679
6.9863
6.9402
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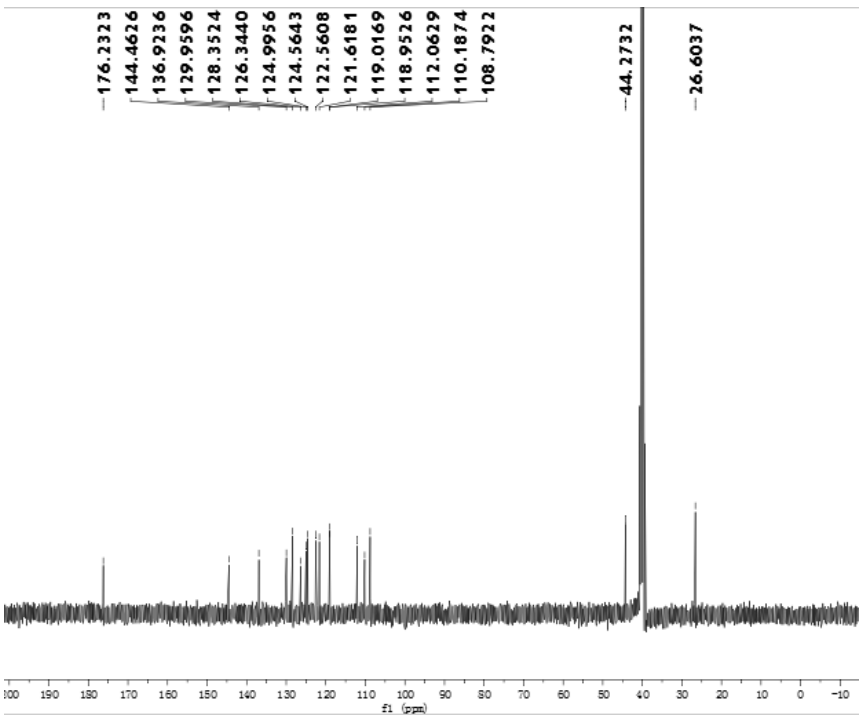
3.2405
0.99
3.11
3.16
2.11
1.03
1.00
3.01
f1 (ppm)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126.3440
124.9956
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118.9526
112.0629
110.1874
108.7922
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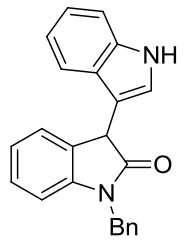
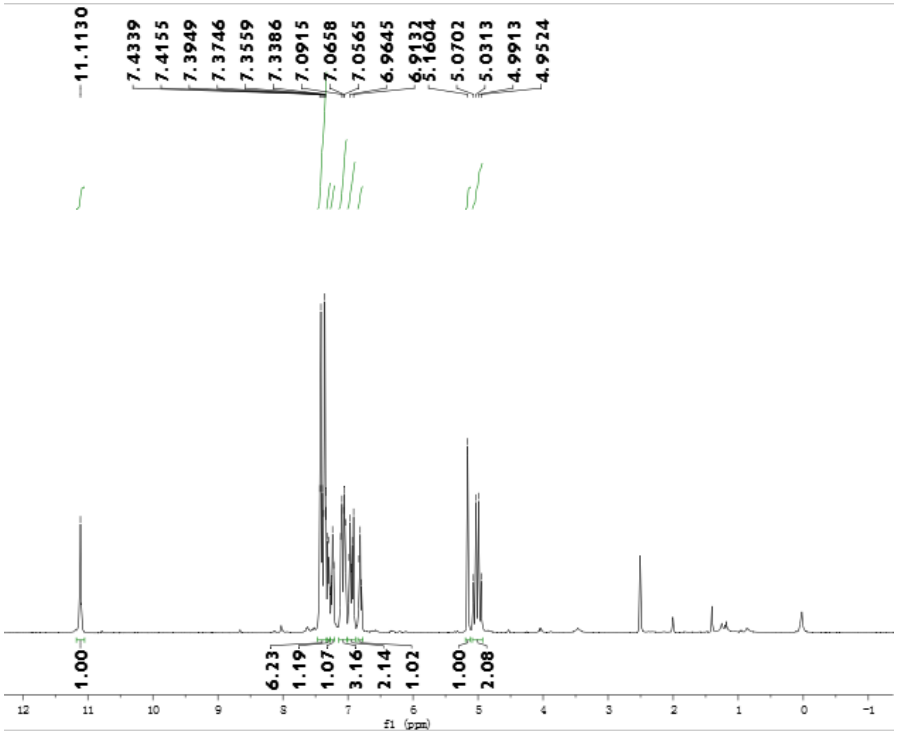
26.6037
f1 (ppm)


NH
O
N
Bn

4c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7.3559
7.3386
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7.0658
7.0565
6.9645
6.9132
5.1604
5.0702
5.0313
4.9913
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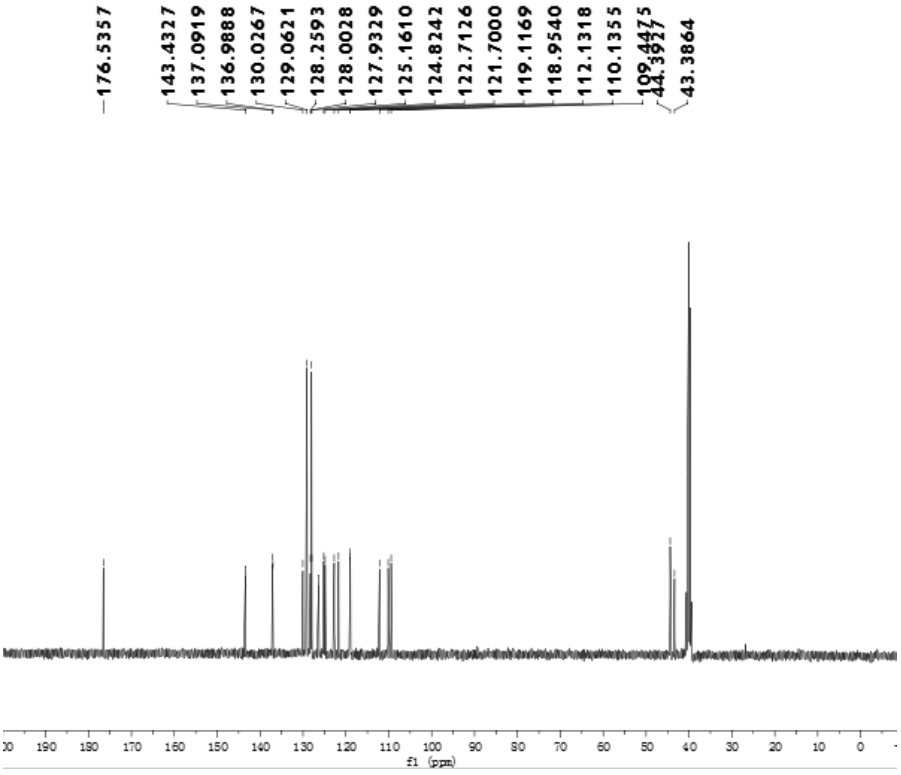
6.23
1.19
1.07
3.16
2.14
1.02
1.00
2.08
f1 (ppm)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129.0621
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127.9329
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124.8242
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112.1318
110.1355
109.4475
44.3927
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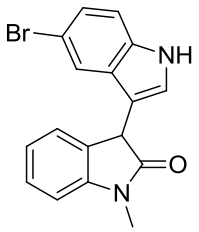
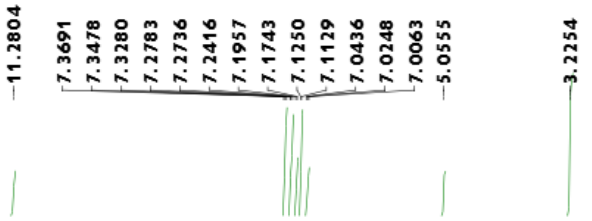
f1 (ppm)


Br
NH
O
N

4d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7.3280
7.2783
7.2736
7.2416
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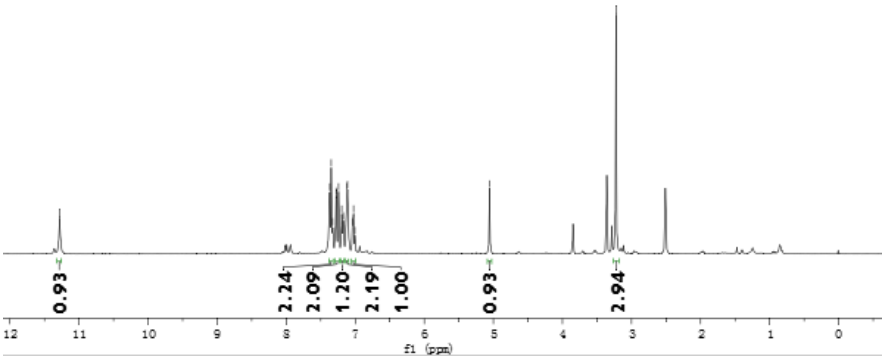
7.1743
7.1250
7.1129
7.0436
7.0248
7.0063
5.0555
3.2254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2.19
1.00
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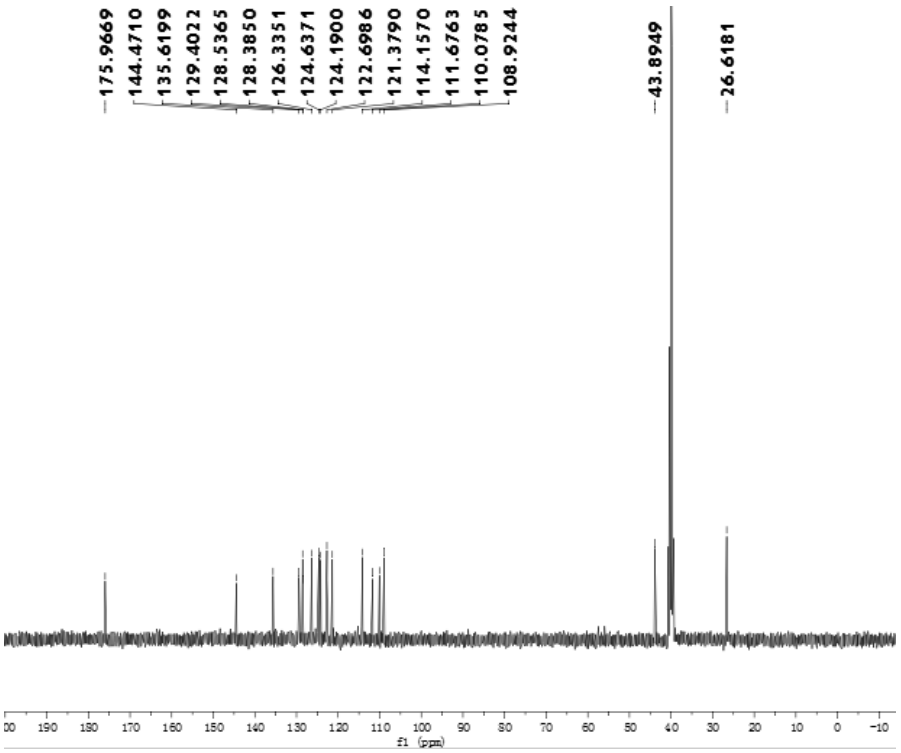
2.94
f1 (ppm)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128.3850
126.3351
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114.1570
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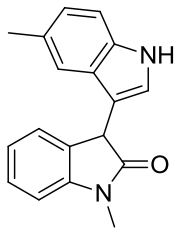
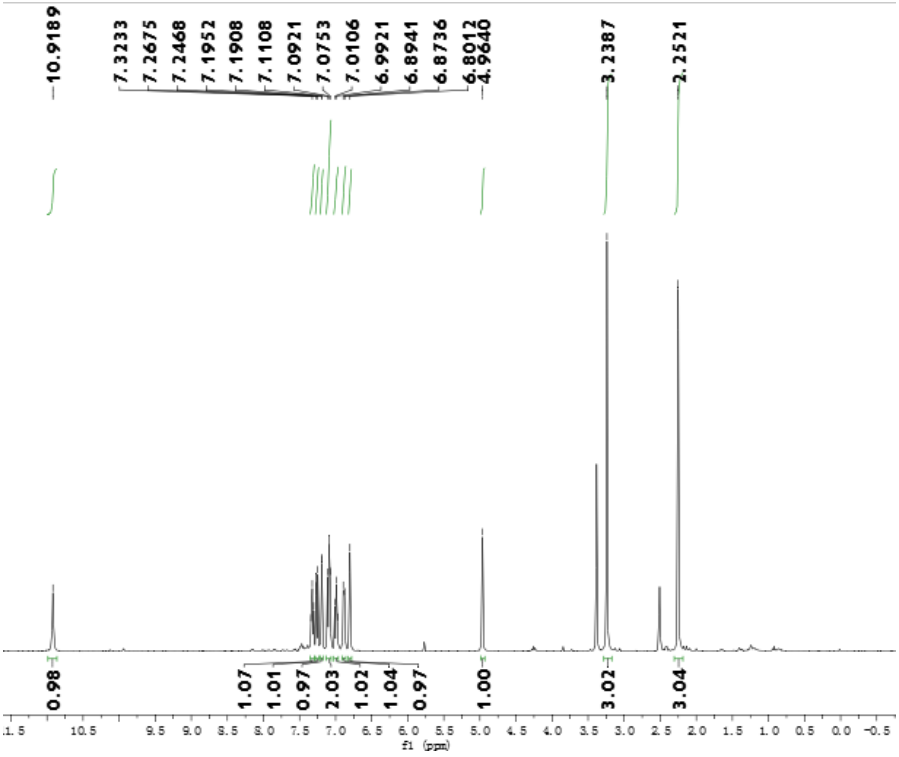
26.6181
f1 (ppm)


NH
O
N

4e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7.1952
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7.0753
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6.9921
6.8941
6.8736
6.8012
4.9640
3.2387
2.2521
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0.97
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1.02
1.04
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1.00
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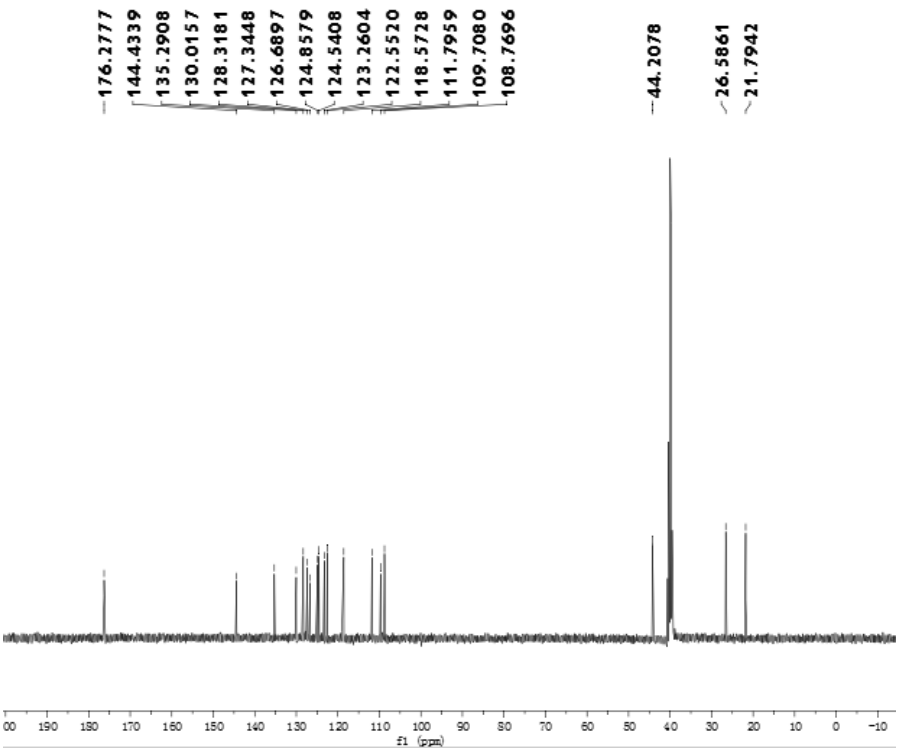
3.04
f1 (ppm)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128.3181
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126.6897
124.8579
124.5408
123.2604
122.5520
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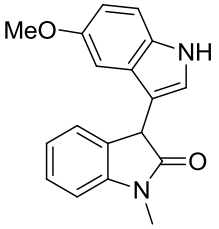
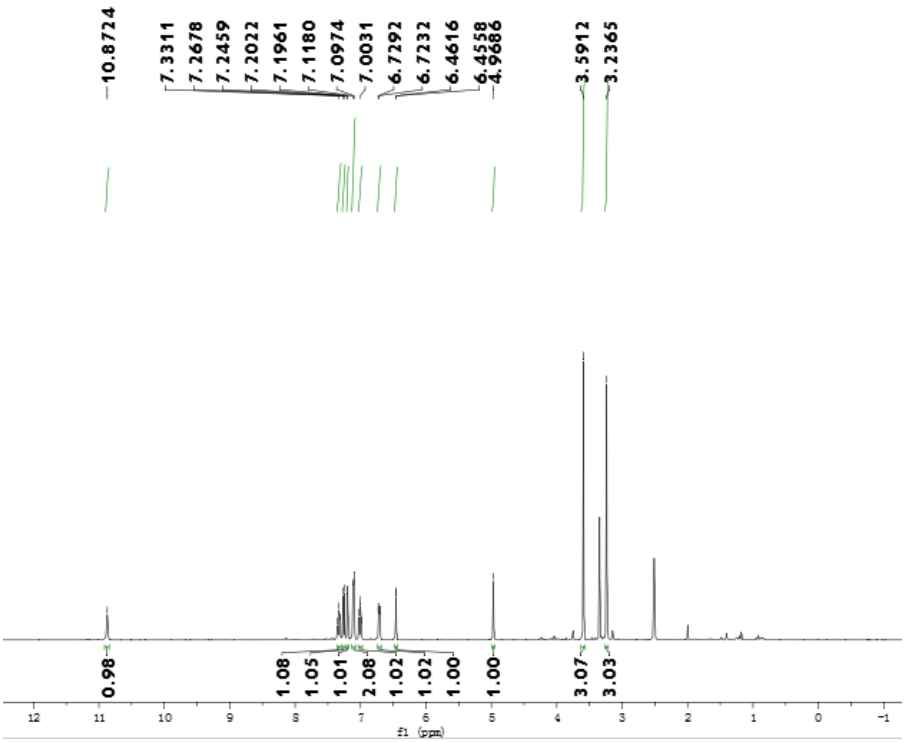
109.7080
108.7696
44.2078
26.5861
21.7942
f1 (ppm)


MeO
NH
O
N

4f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7.2459
7.2022
7.1961
7.1180
7.0974
7.0031
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6.7232
6.4616
6.4558
4.9686
3.5912
3.2365
0.98
1.08
1.05
1.01
2.08
1.02
1.02
1.00
1.00
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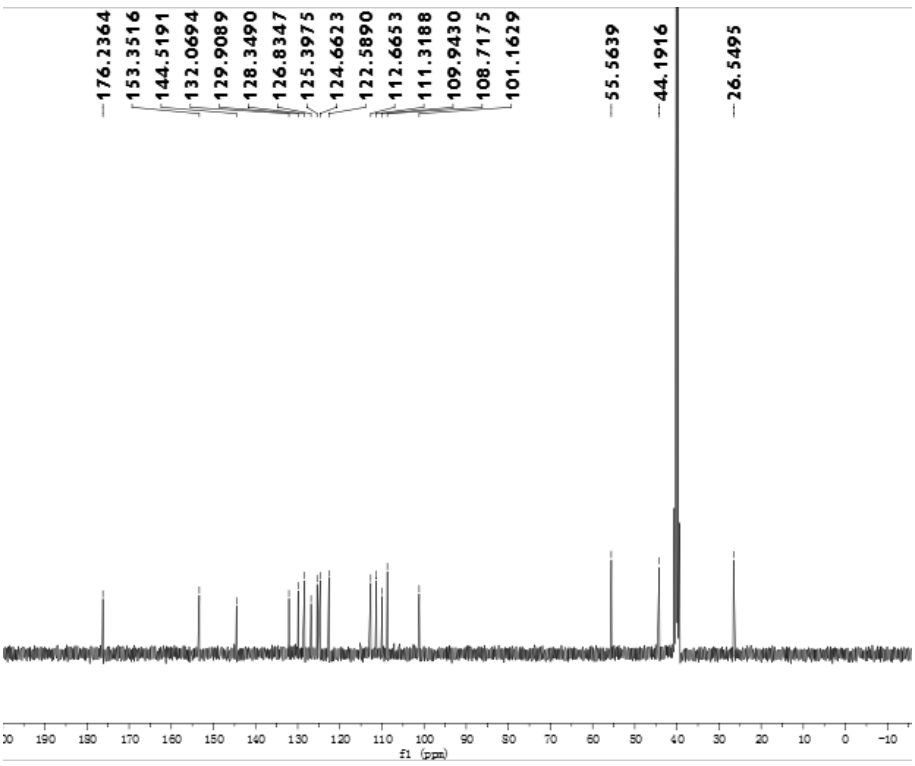
3.03
f1 (ppm)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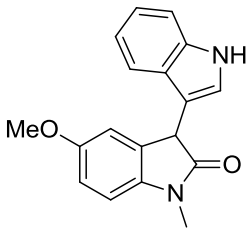
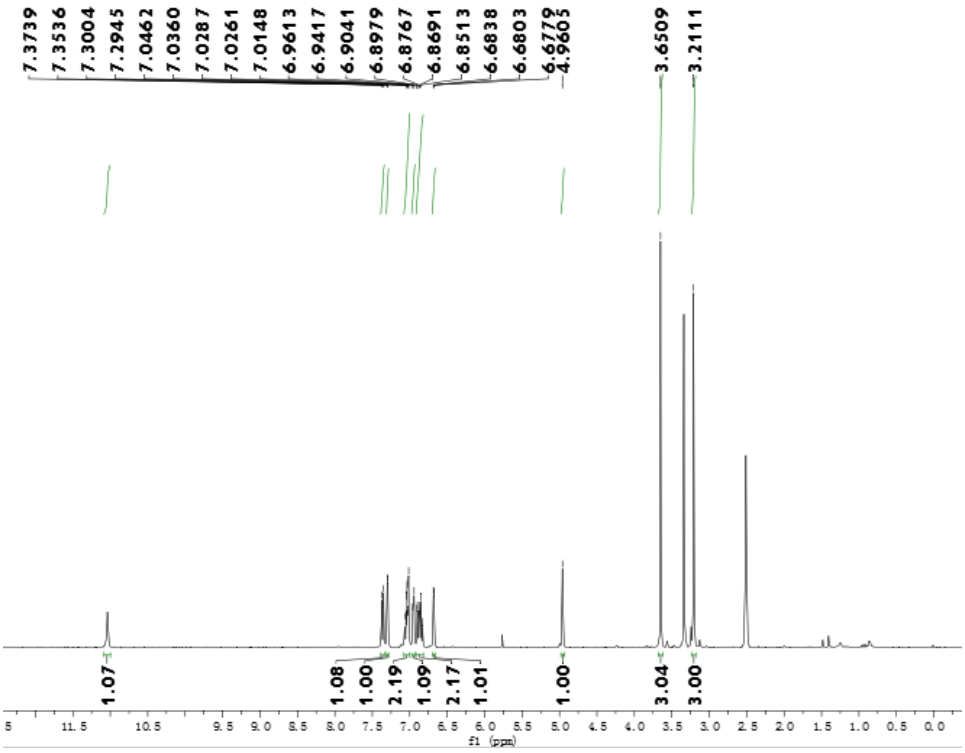
f1 (ppm)


NH
MeO
O
N

4g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6.9041
6.8979
6.8767
6.8691
6.8513
6.6838
6.6803
6.6779
4.9605
3.6509
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1.00
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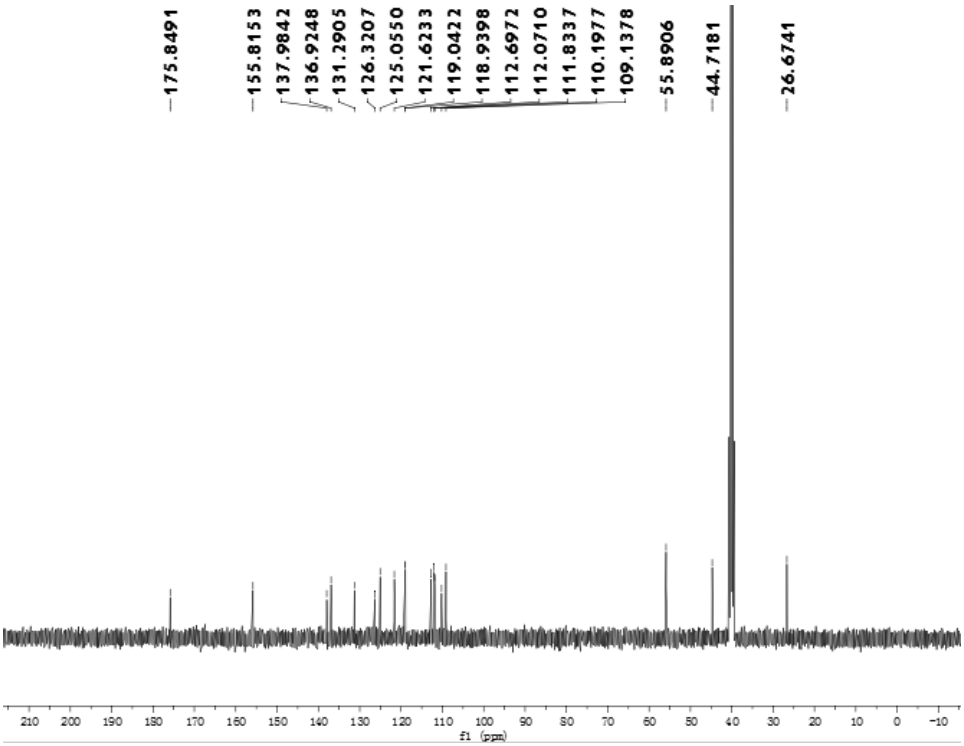
f1 (ppm)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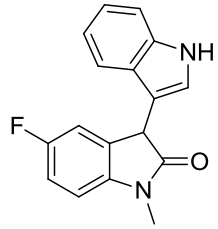
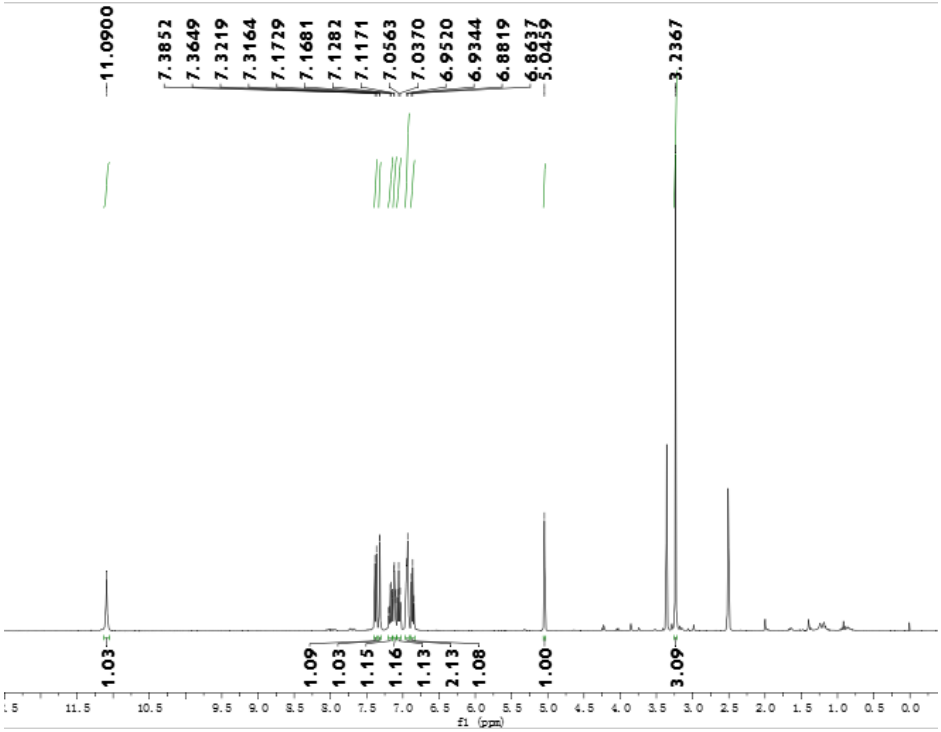
f1 (ppm)


NH
F
O
N

4h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6.8819
6.8637
5.0459
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1.16
1.13
2.13
1.08
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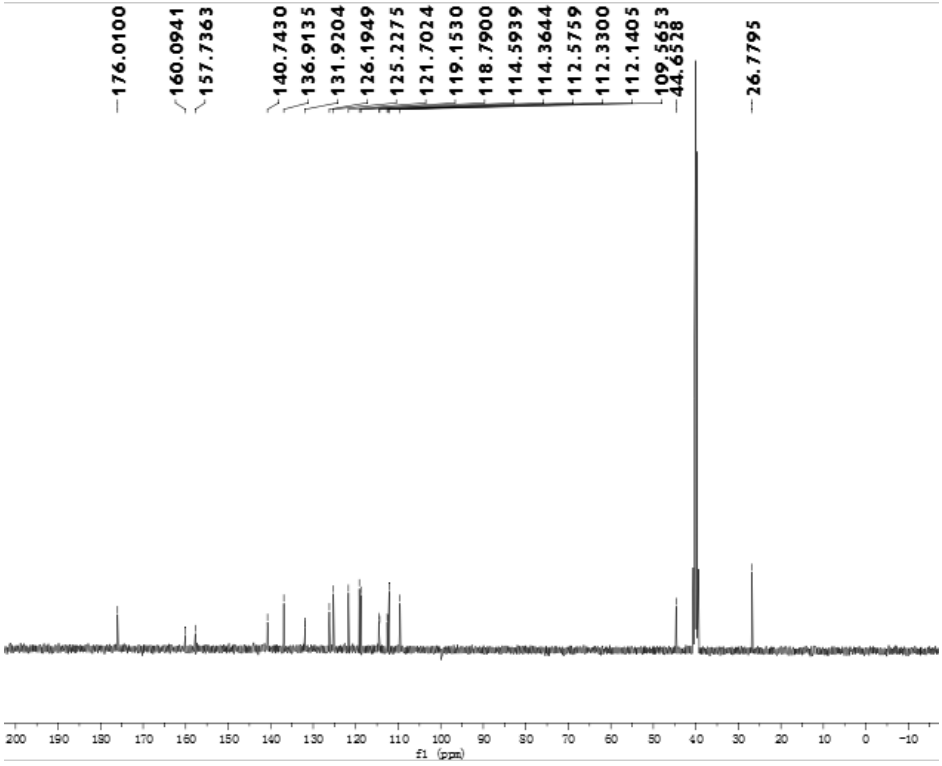
3.09
f1 (ppm)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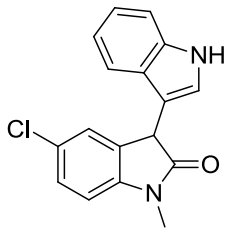
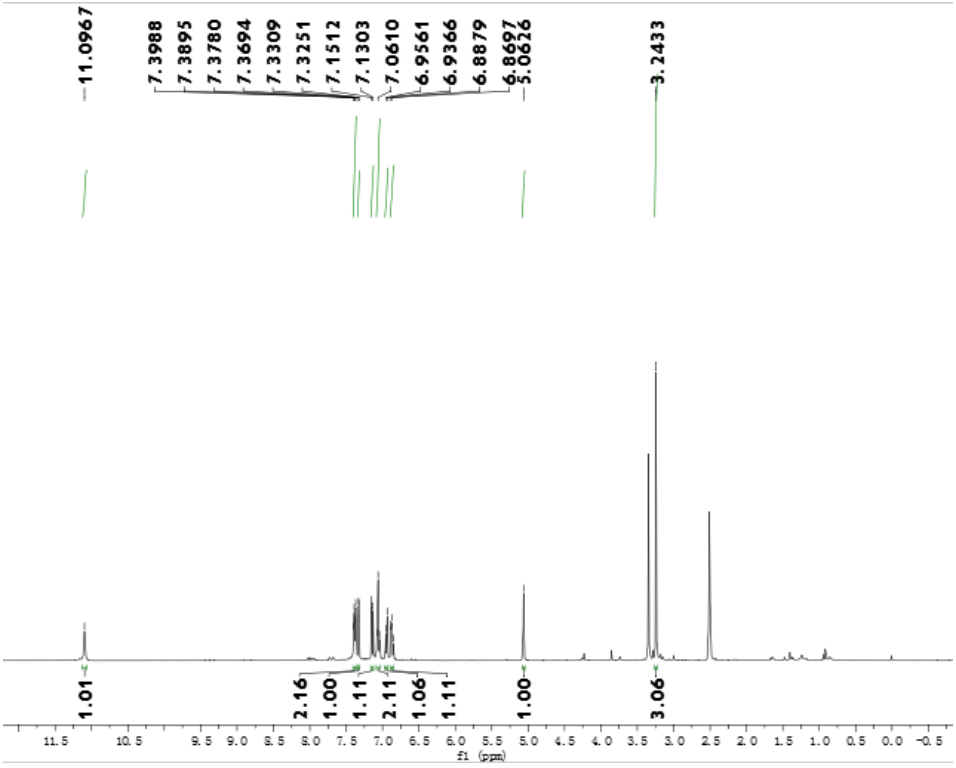
112.3300
112.1405
109.5653
44.6528
26.7795
f1 (ppm)


NH
Cl
O
N

4i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7.3780
7.3694
7.3309
7.3251
7.1512
7.1303
7.0610
6.9561
6.9366
6.8879
6.8697
5.0626
3.2433
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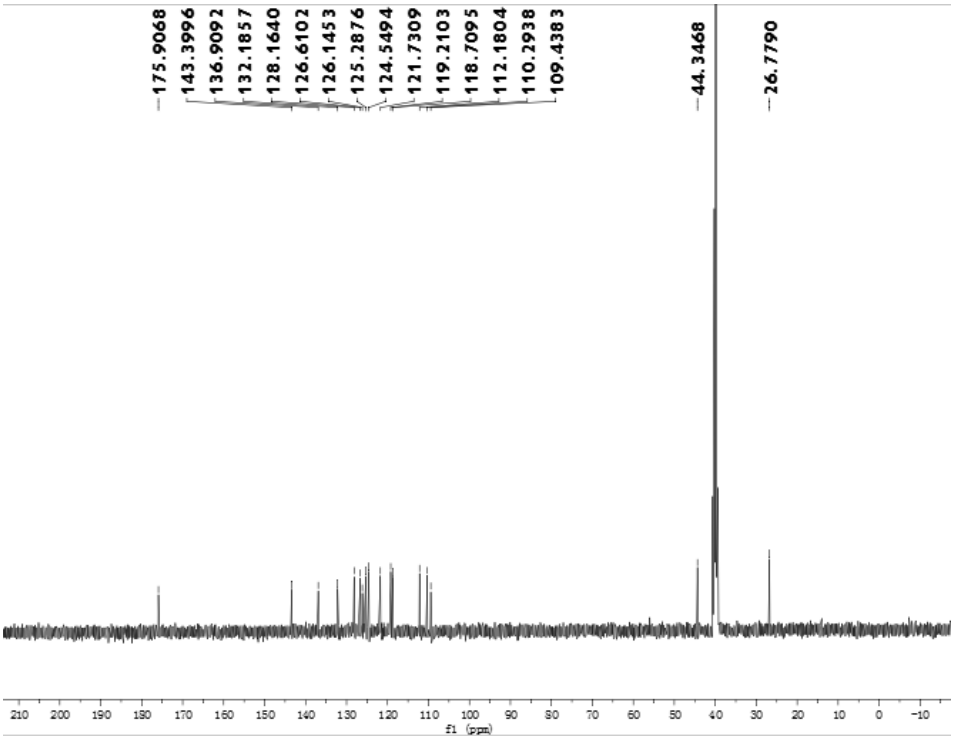
2.16
1.00
1.11
2.11
1.06
1.11
1.00
3.06
f1 (ppm)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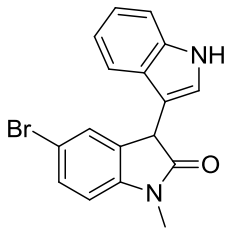
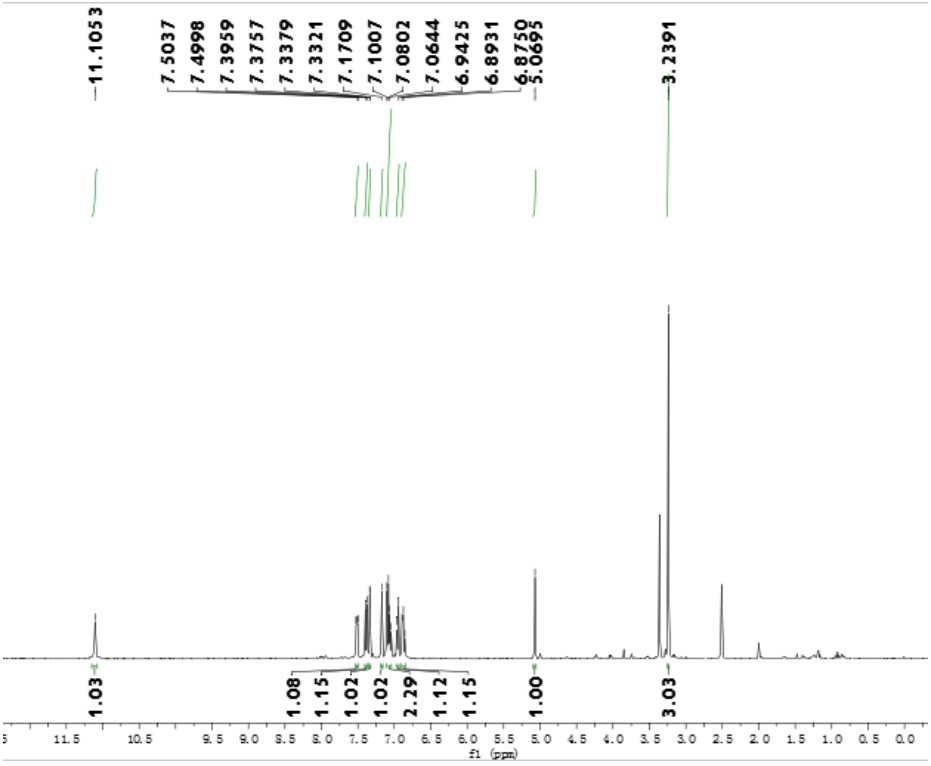
136.9092
132.1857
128.1640
126.6102
126.1453
125.2876
124.5494
121.7309
119.2103
118.7095
112.1804
110.2938
109.4383
44.3468
26.7790
f1 (ppm)


NH
Br
O
N

4j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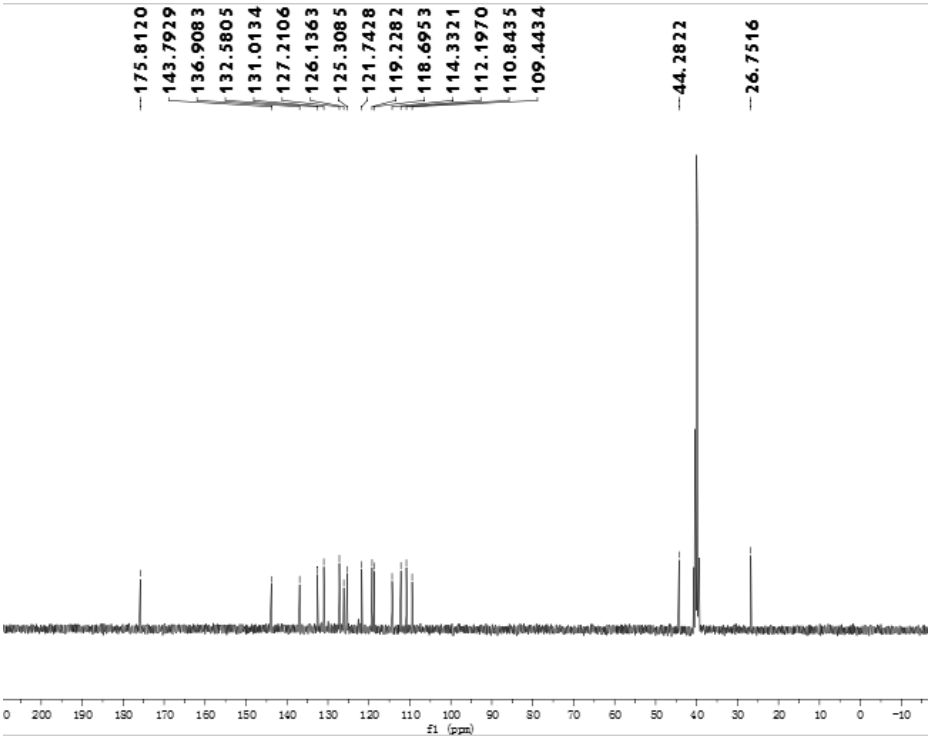
7.3959
7.3757
7.3379
7.3321
7.1709
7.1007
7.0802
7.0644
6.9425
6.8931
6.8750
5.0695
3.2391
1.03
1.08
1.15
1.02
1.02
2.29
1.12
1.15
1.00
3.03
f1 (ppm)


175.8120
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131.0134
127.2106
126.1363
125.3085
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109.4434
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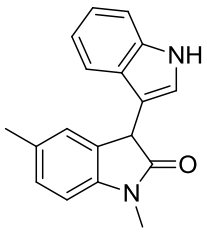
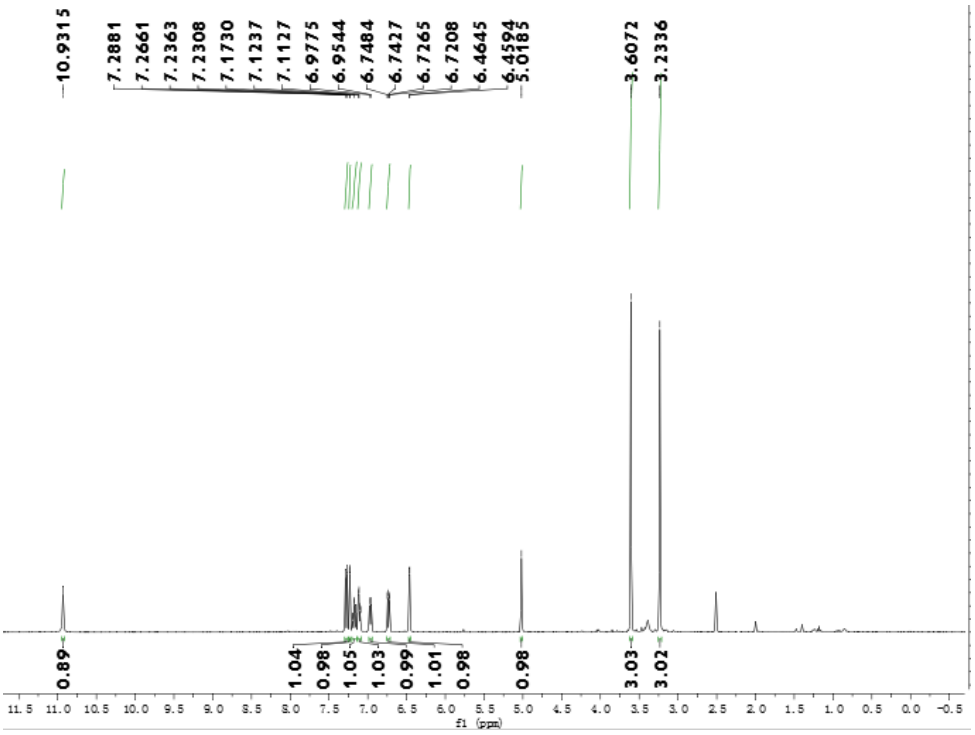
26.7516
f1 (ppm)


NH
O
N

4k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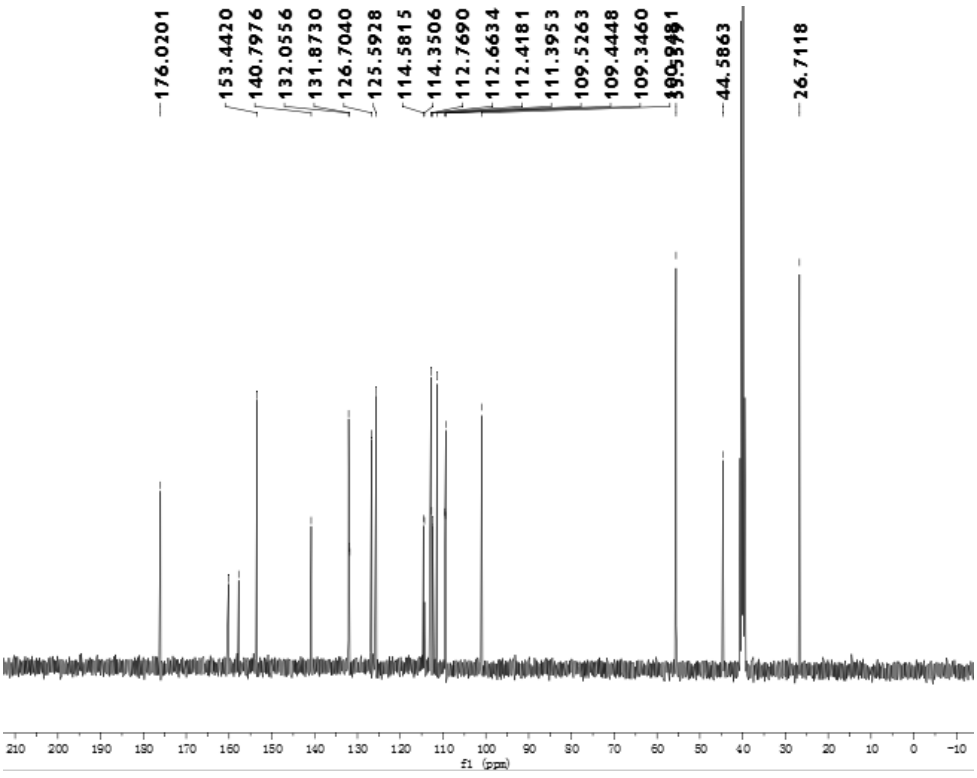
7.2661
7.2363
7.2308
7.1730
7.1237
7.1127
6.9775
6.9544
6.7484
6.7427
6.7265
6.7208
6.4645
6.4594
5.0185
3.6072
3.2336
0.89
1.04
0.98
1.05
1.03
0.99
1.01
0.98
0.98
3.03
3.02
f1 (ppm)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153.4420
140.7976
132.0556
131.8730
126.7040
125.5928
114.5815
114.3506
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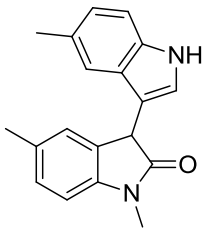
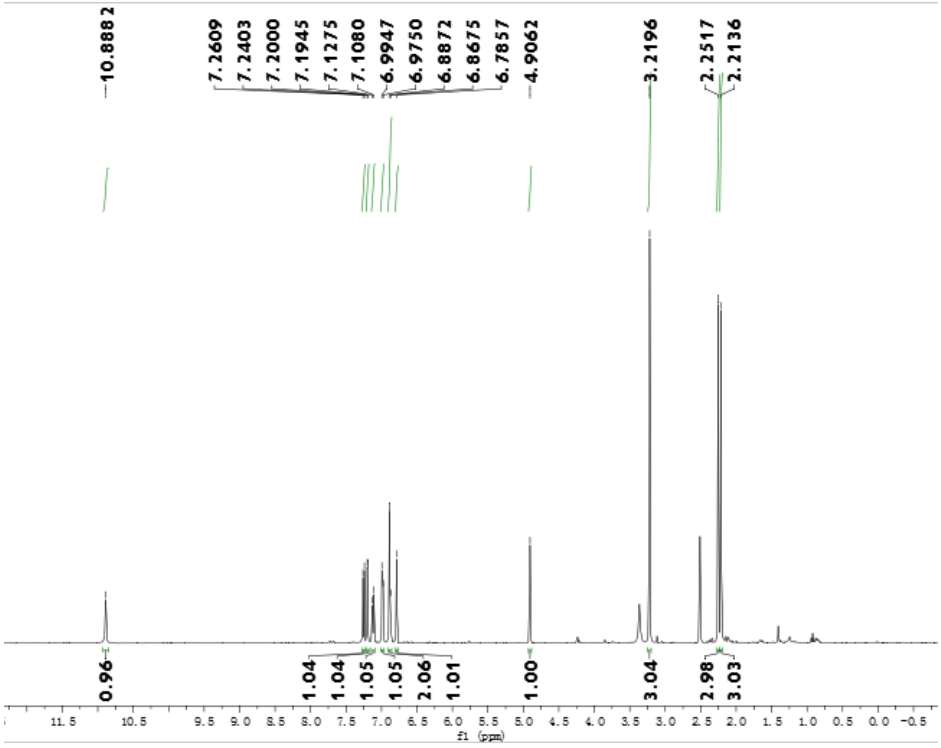
112.6634
112.4181
111.3953
109.5263
109.4448
109.3460
44.5863
26.7118
f1 (ppm)


NH
O
N

4l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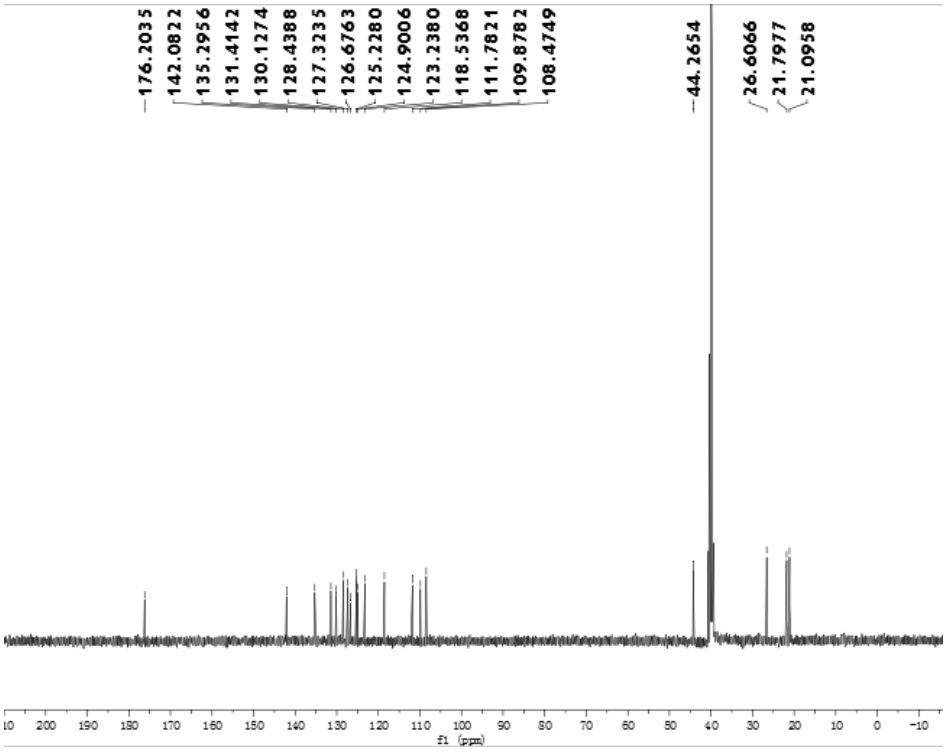
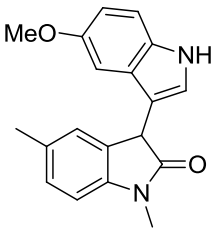
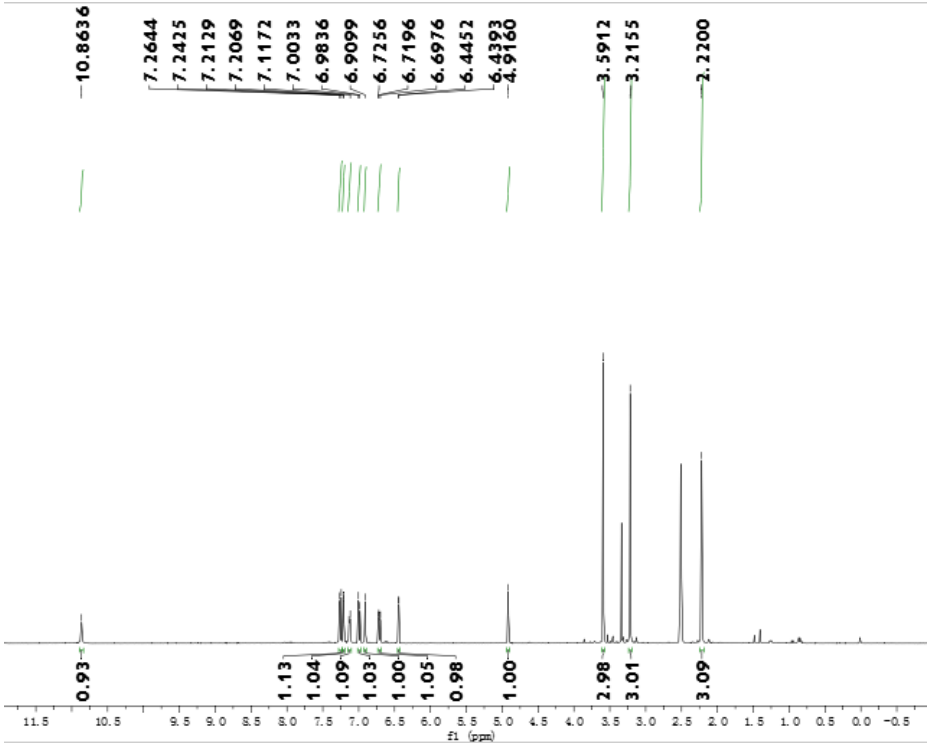
7.2403
7.2000
7.1945
7.1275
7.1080
6.9947
6.9750
6.8872
6.8675
6.7857
4.9062
3.2196
2.2517
2.2136
0.96
1.04
1.04
1.05
1.05
2.06
1.01
1.00
3.04
2.98
3.03
f1 (ppm)


176.2035
142.0822
135.2956
131.4142
130.1274
128.4388
127.3235
126.6763
125.2280
124.9006
123.2380
118.5368
111.7821
109.8782
108.4749
44.2654
26.6066
21.7977
21.0958
f1 (ppm)


MeO
NH
O
N

4m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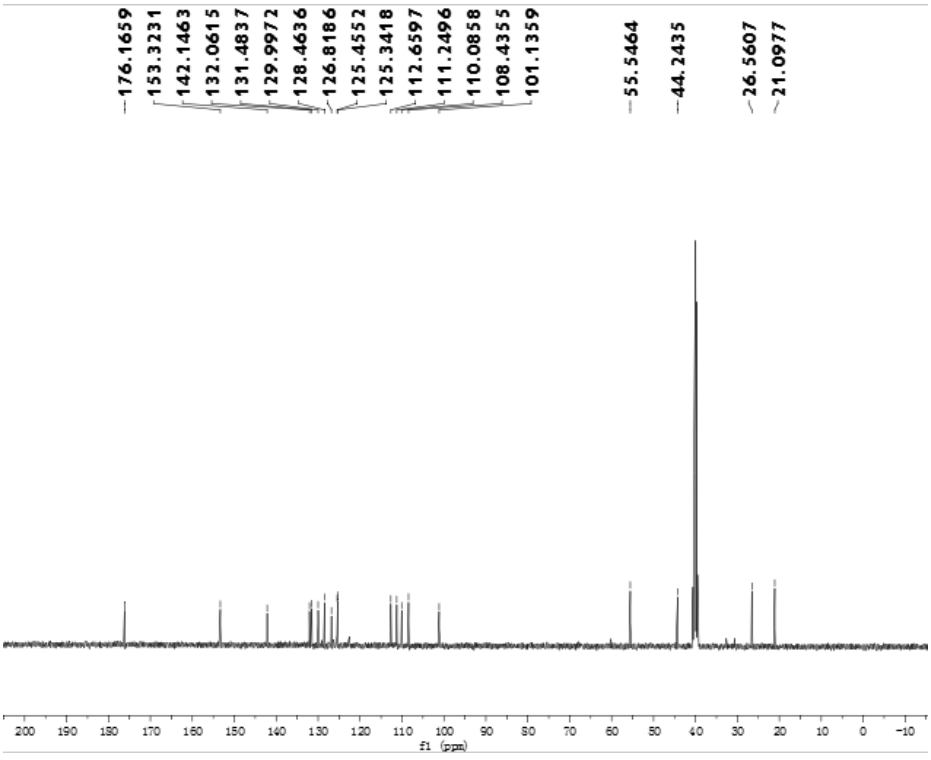
7.2425
7.2129
7.2069
7.1172
7.0033
6.9836
6.9099
6.7256
6.7196
6.6976
6.4452
6.4393
4.9160
3.5912
3.2155
2.2200
0.93
1.13
1.04
1.09
1.03
1.00
1.05
0.98
1.00
2.98
3.01
3.09
f1 (ppm)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142.1463
132.0615
131.4837
129.9972
128.4636
126.8186
125.4552
125.3418
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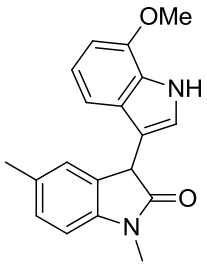
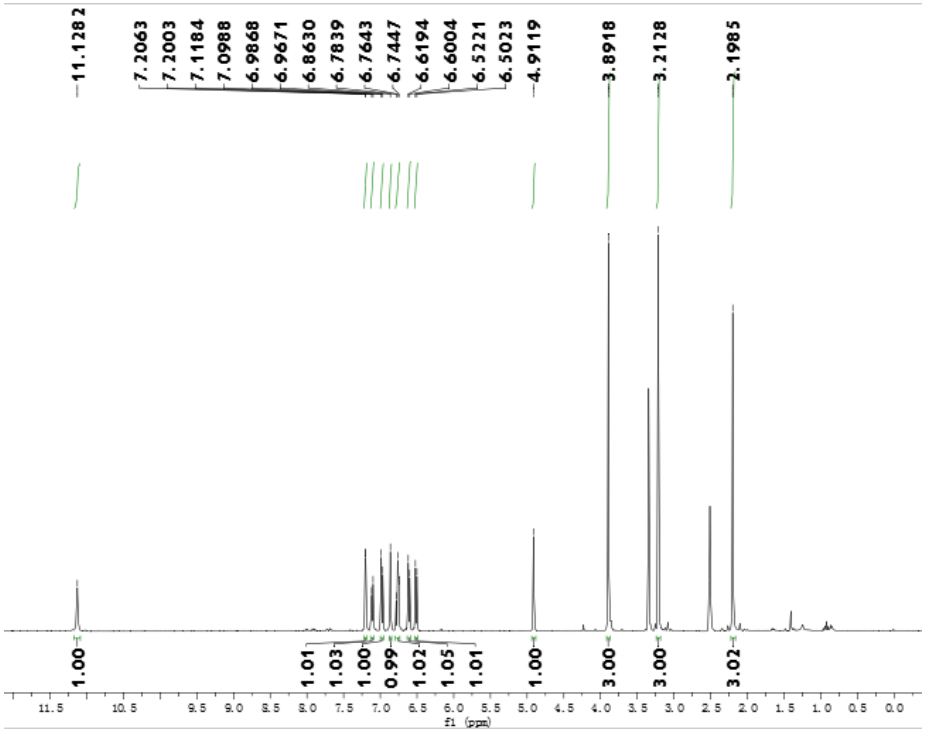
111.2496
110.0858
108.4355
101.1359
55.5464
44.2435
26.5607
21.0977
f1 (ppm)


OMe
NH
O
N

4n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7.2003
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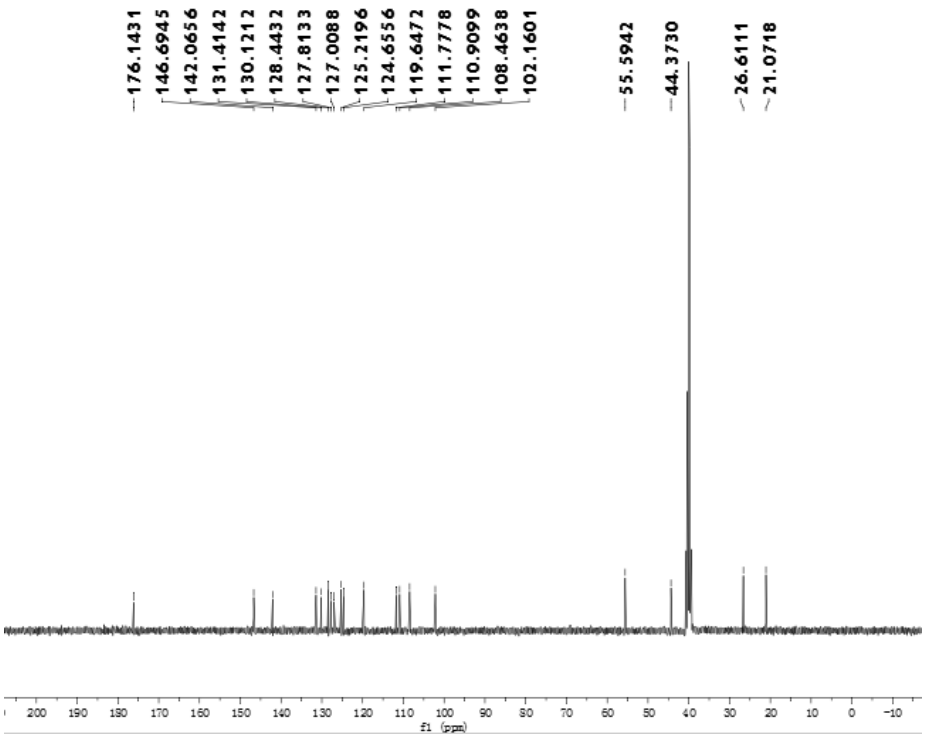
7.0988
6.9868
6.9671
6.8630
6.7839
6.7643
6.7447
6.6194
6.6004
6.5221
6.5023
4.9119
3.8918
3.2128
2.1985
1.00
1.01
1.03
1.00
0.99
1.02
1.05
1.01
1.00
3.00
3.00
3.02
f1 (ppm)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142.0656
131.4142
130.1212
128.4432
127.8133
127.0088
125.2196
124.6556
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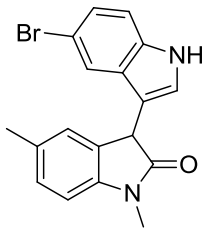
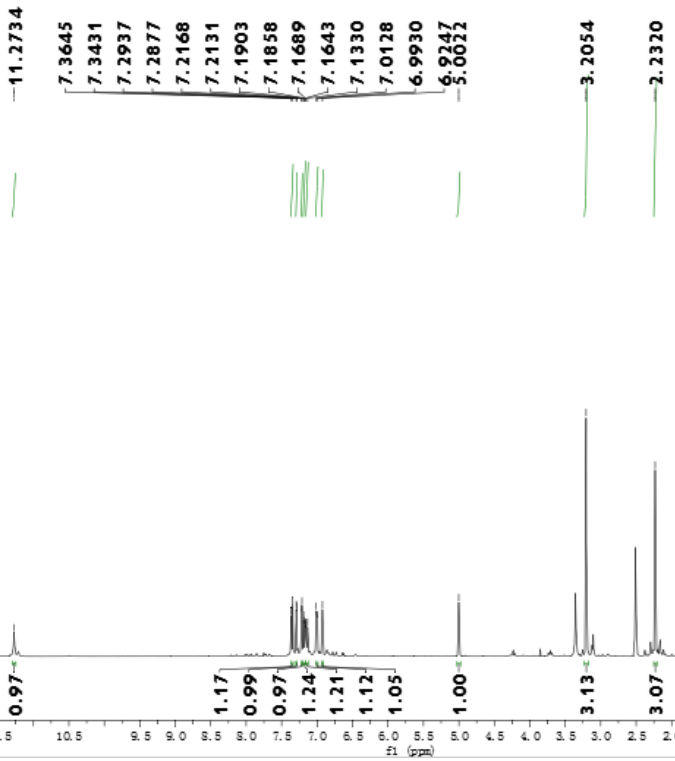
111.7778
110.9099
108.4638
102.1601
55.5942
44.3730
26.6111
21.0718
f1 (ppm)


Br
NH
O
N

4o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7.3431
7.2937
7.2877
7.2168
7.2131
7.1903
7.1858
7.1689
7.1643
7.1330
7.0128
6.9930
6.9247
5.0022
3.2054
2.2320
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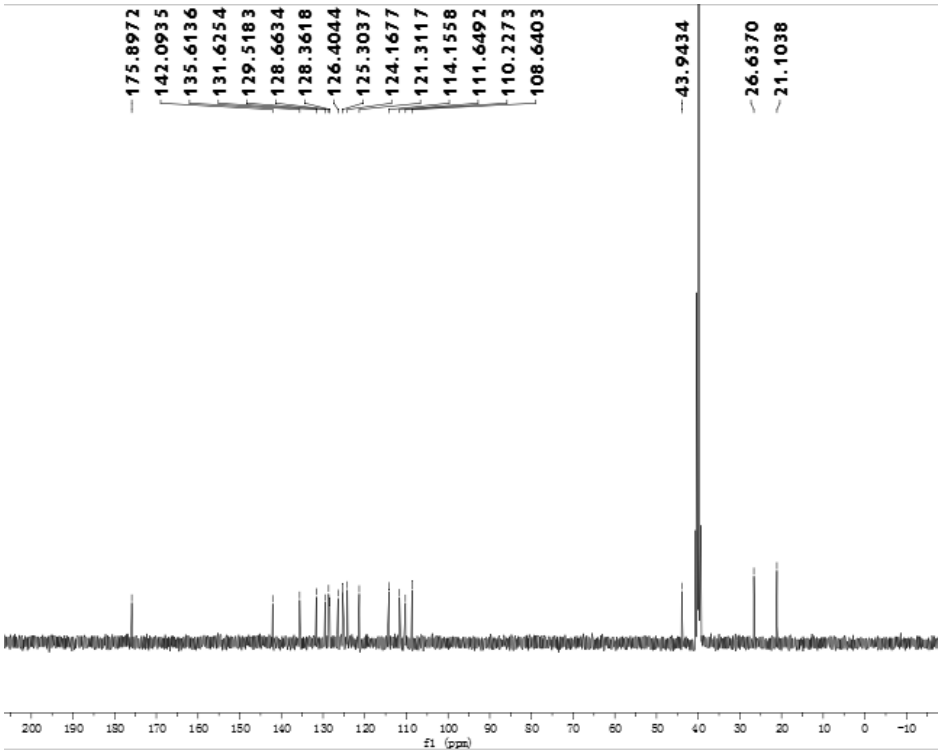
1.17
0.99
0.97
1.24
1.21
1.12
1.05
1.00
3.13
3.07
f1 (ppm)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131.6254
129.5183
128.6634
128.3618
126.4044
125.3037
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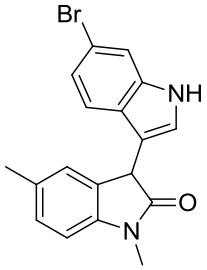
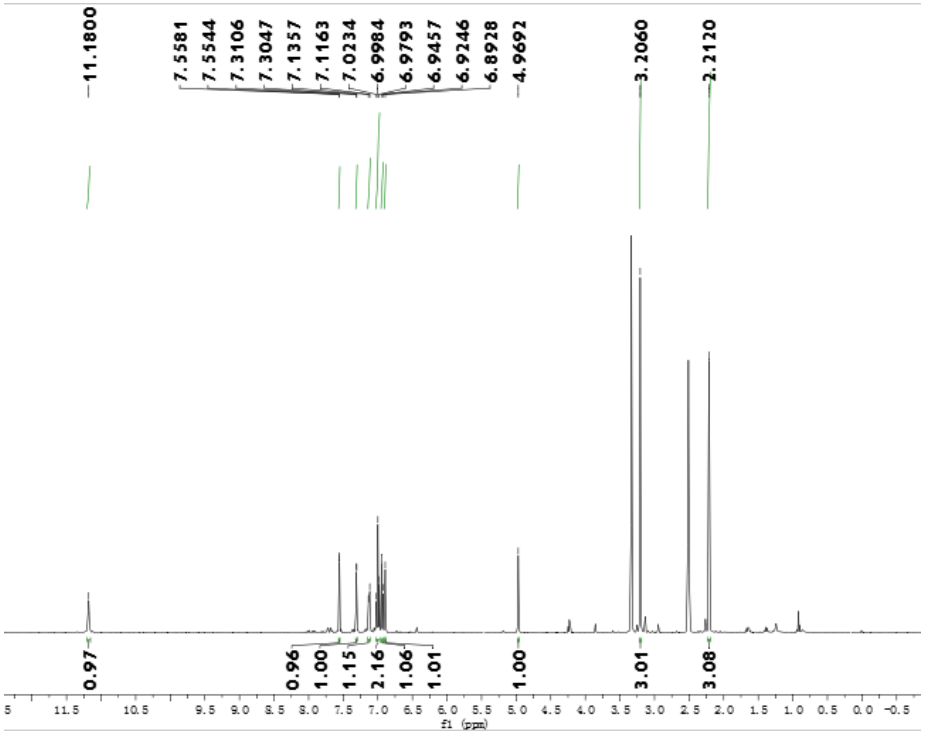
114.1558
111.6492
110.2273
108.6403
43.9434
26.6370
21.1038
f1 (ppm)


Br
NH
O
N

4p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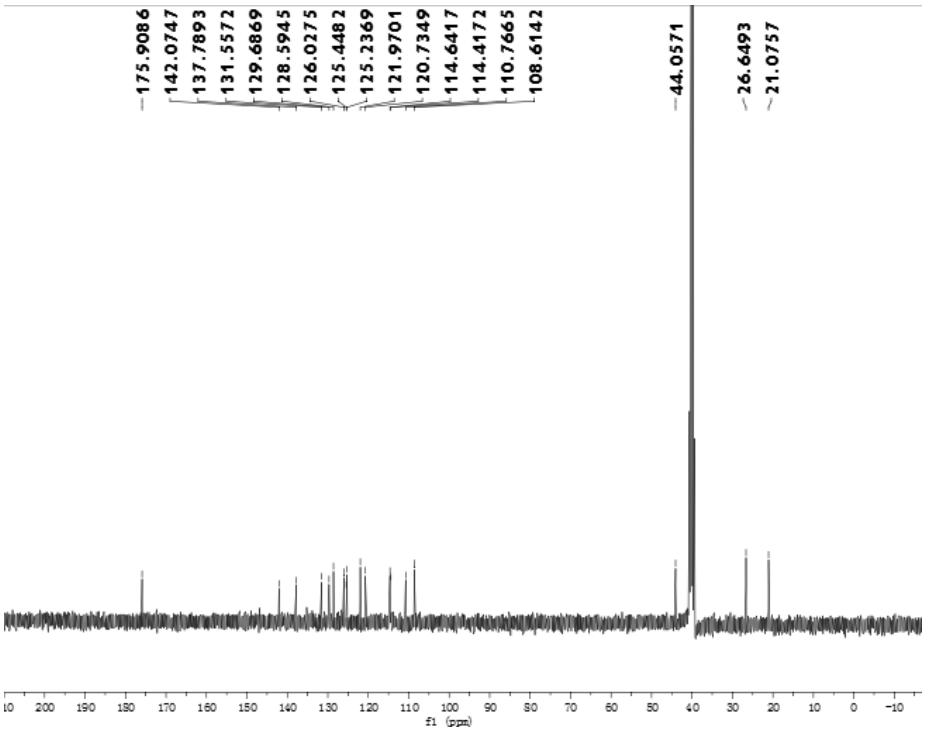
7.1357
7.1163
7.0234
6.9984
6.9793
6.9457
6.9246
6.8928
4.9692
3.2060
2.2120
0.97
0.96
1.00
1.15
2.16
1.06
1.01
1.00
3.01
3.08
f1 (ppm)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126.0275
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125.2369
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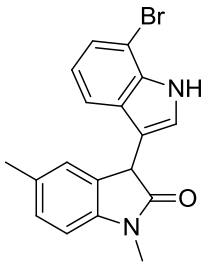
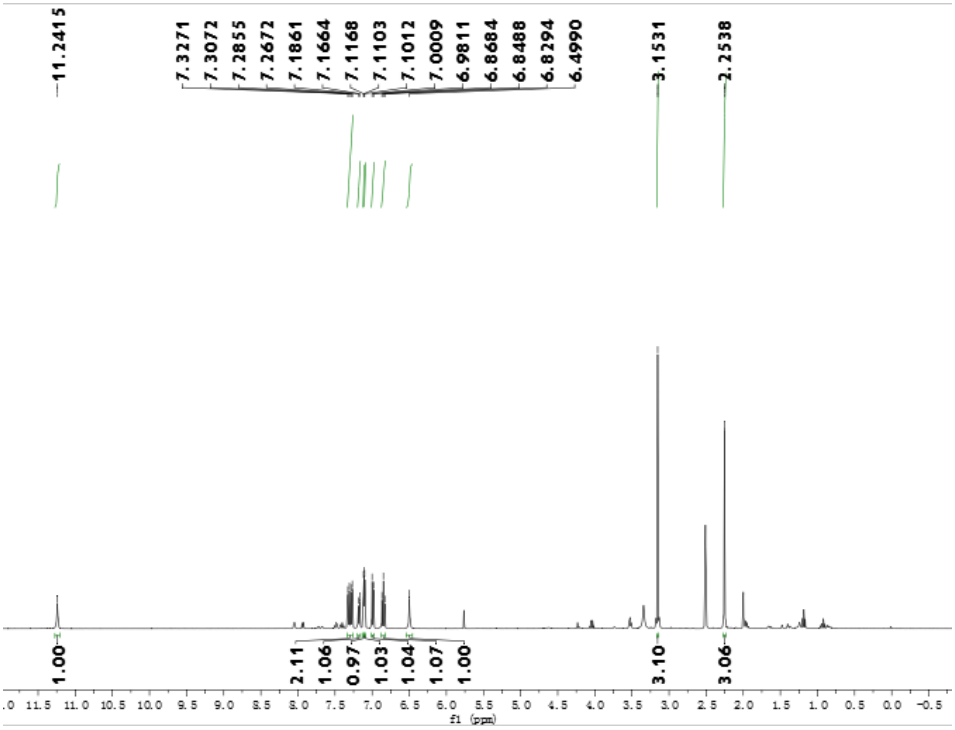
f1 (ppm)


Br
NH
O
N

4q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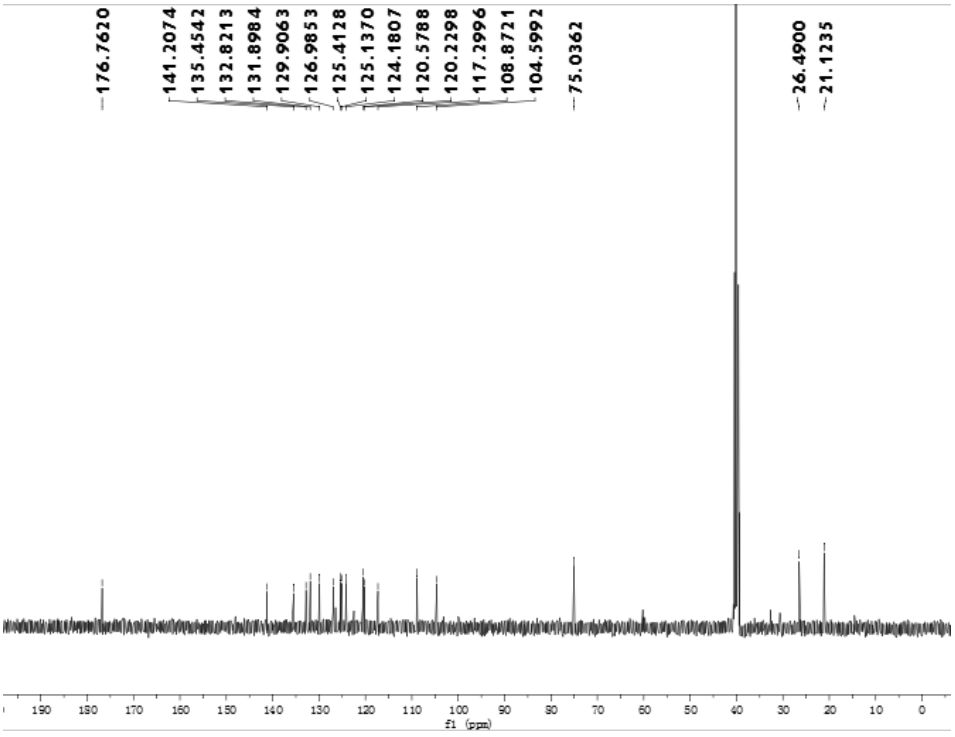
7.2855
7.2672
7.1861
7.1664
7.1168
7.1103
7.1012
7.0009
6.9811
6.8684
6.8488
6.8294
6.4990
3.1531
2.2538
1.00
2.11
1.06
0.97
1.03
1.04
1.07
1.00
3.10
3.06
f1 (ppm)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132.8213
131.8984
129.9063
126.9853
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125.1370
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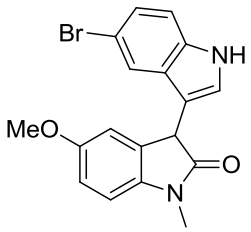
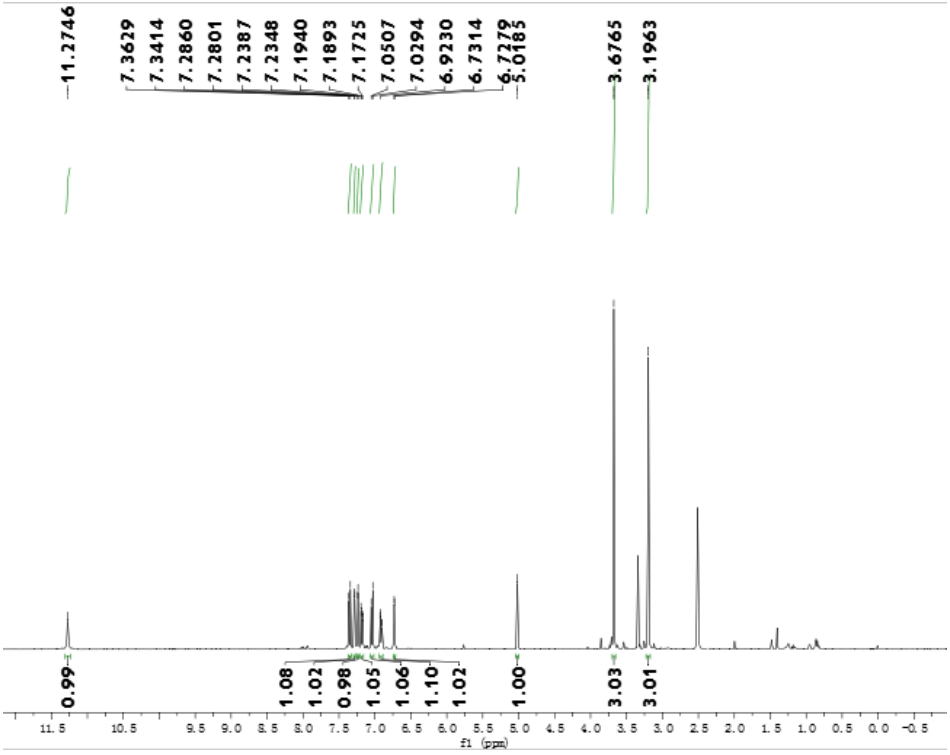
120.2298
117.2996
108.8721
104.5992
75.0362
26.4900
21.1235
f1 (ppm)


Br
NH
MeO
O
N

4r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7.2348
7.1940
7.1893
7.1725
7.0507
7.0294
6.9230
6.7314
6.7279
5.0185
3.6765
3.1963
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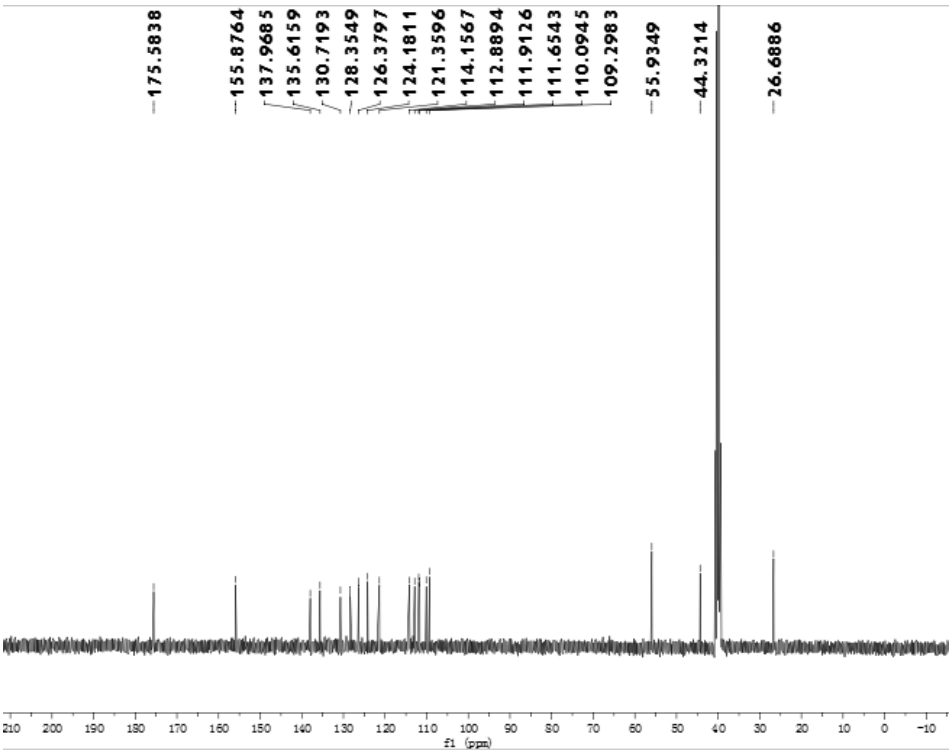
1.08
1.02
0.98
1.05
1.06
1.10
1.02
1.00
3.03
3.01
f1 (ppm)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130.7193
128.3549
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124.1811
121.3596
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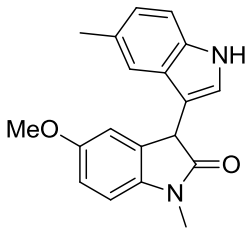
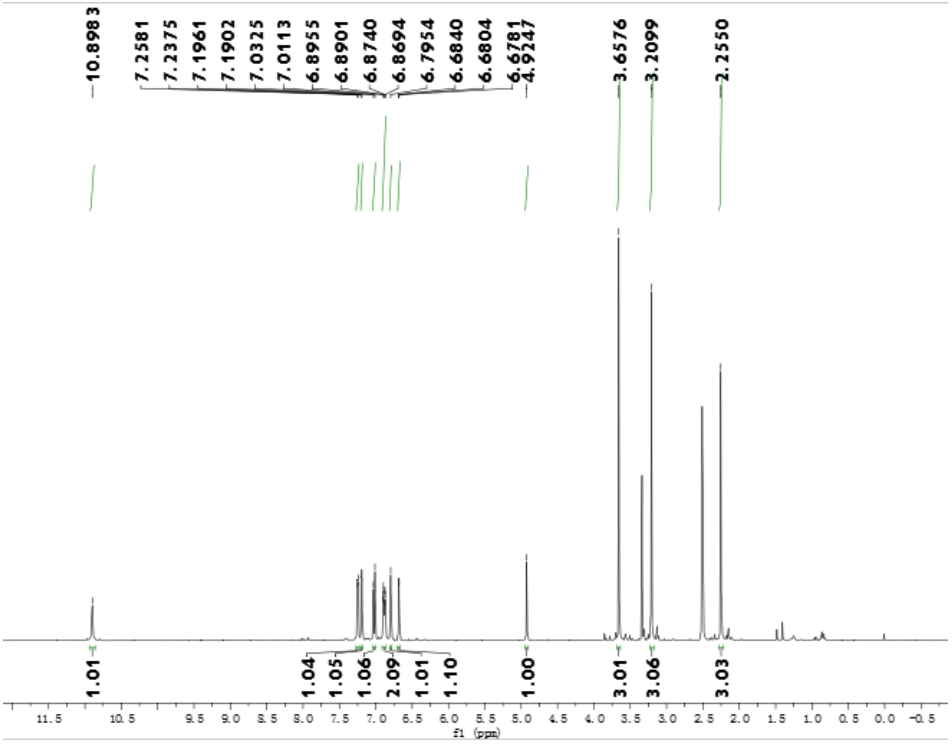
111.9126
111.6543
110.0945
109.2983
55.9349
44.3214
26.6886
f1 (ppm)


NH
MeO
O
N

4s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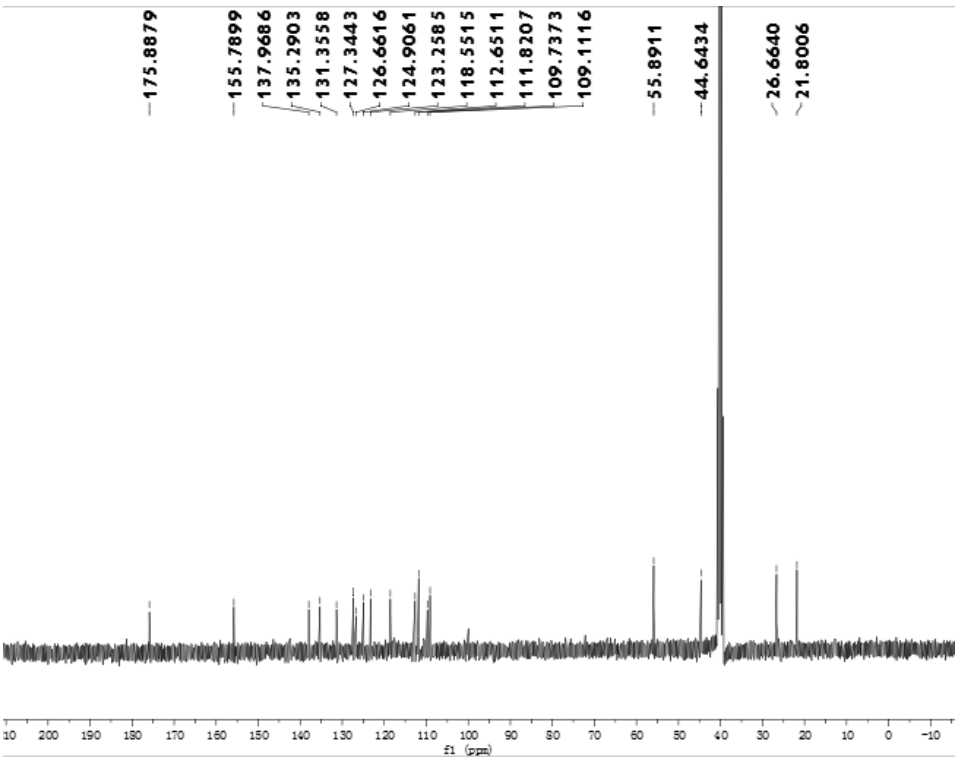
6.8740
6.8694
6.7954
6.6840
6.6804
6.6781
4.9247
3.6576
3.2099
2.2550
1.01
1.04
1.05
1.06
2.09
1.01
1.10
1.00
3.01
3.06
3.03
f1 (ppm)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44.6434
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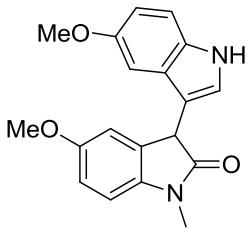
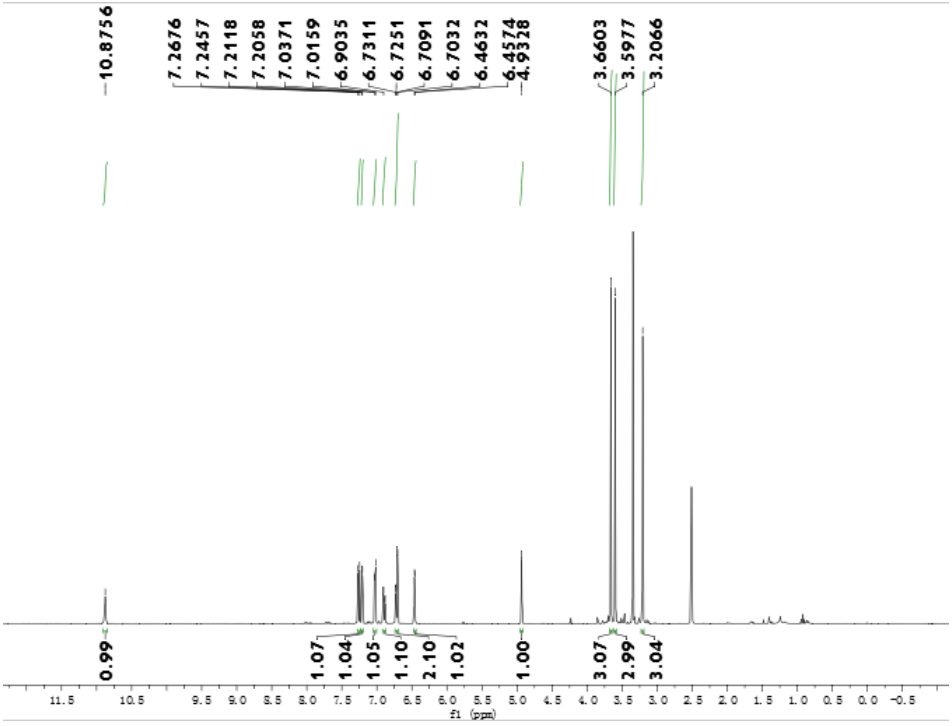
21.8006
f1 (ppm)


MeO
NH
MeO
O
N

4t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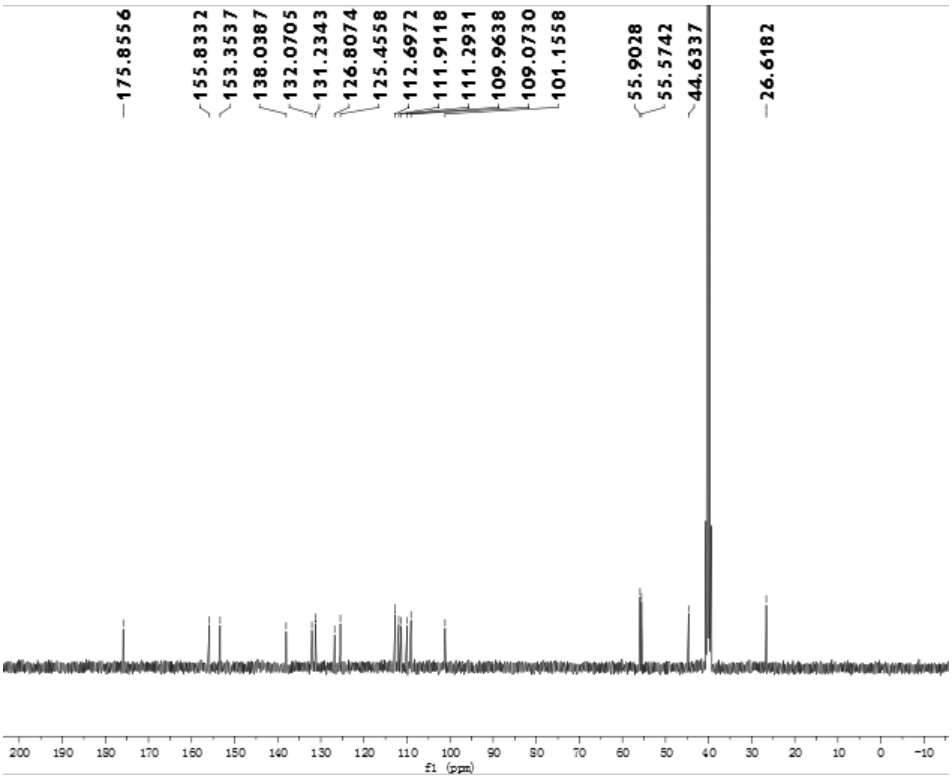
7.2118
7.2058
7.0371
7.0159
6.9035
6.7311
6.7251
6.7091
6.7032
6.4632
6.4574
4.9318
3.6603
3.5977
3.2066
0.99
1.07
1.04
1.05
1.10
2.10
1.02
1.00
3.07
2.99
3.04
f1 (ppm)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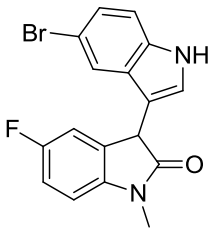
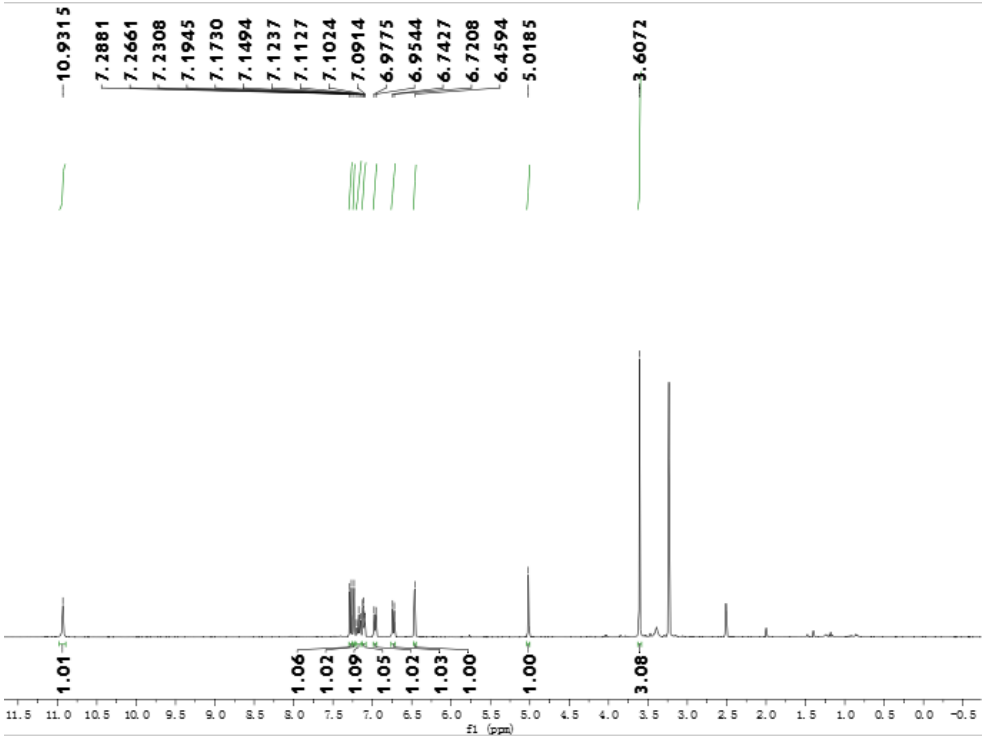
153.3537
138.0387
132.0705
131.2343
126.8074
125.4558
112.6972
111.9118
111.2931
109.9638
109.0730
101.1558
55.9028
55.5742
44.6337
26.6182
f1 (ppm)


Br
NH
F
O
N

4u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7.2308
7.1945
7.1730
7.1494
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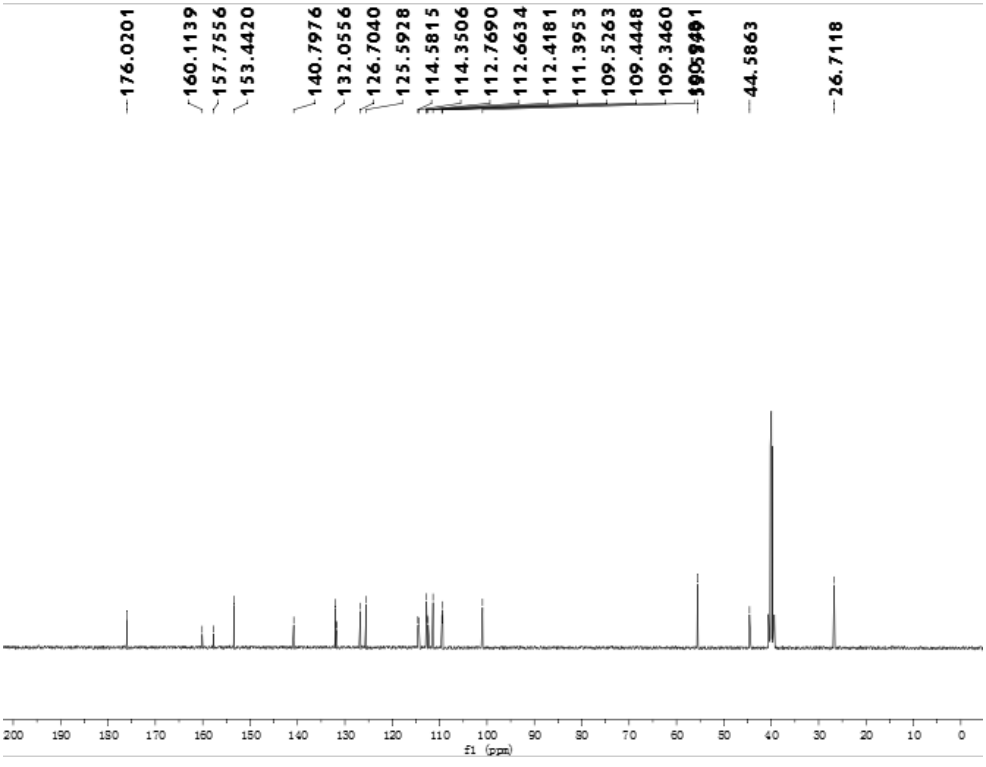
7.1127
7.1024
7.0914
6.9775
6.9544
6.7427
6.7208
6.4594
5.0185
3.6072
1.01
1.06
1.02
1.09
1.05
1.02
1.03
1.00
1.00
3.08
f1 (ppm)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157.7556
153.4420
140.7976
132.0556
126.7040
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114.5815
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112.6634
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111.3953
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109.4448
109.3460
44.5863
26.7118
f1 (ppm)