Supplementary Material (ESI) for RSC Advances
This journal is (c) The Royal Society of Chemistry 2014

Supporting Information:

Microwave Irradiated Synthesis of 2-Bromo(chloro)indoles via Intramolecular Cyclization of 2-(*gem*-Dibromo(chloro)vinyl)anilines in the Presence of TBAF under Metal-free Conditions

Min Wang,[a] Pinhua Li,[a][b] Wei Chen,[a] and Lei Wang*[a][c]

[a] Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, P R China
Tel: + 86-561-3802-069 Fax: + 86-561-3090-518 E-mail: leiwang@chnu.edu.cn
[b] Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P R China
[c] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P R China

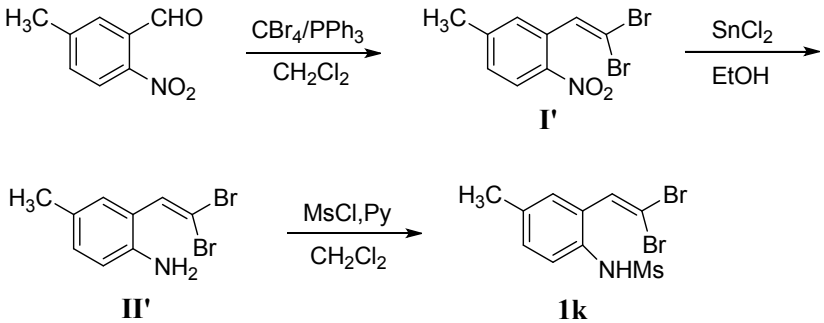
Table of Contents for Supporting Information

1. General considerations

All reagents were purchased from commercial suppliers and used without further purification. 2-(*gem*-Dibromovinyl)-*N*-methylsulfonylanilines were prepared according to the literature.[1] All TBAF (*tetra*-*n*-butylammonium fluoride)-promoted intramolecular cyclization reactions of *gem*-dibromoolefins were carried out under microwave irradiation conditions and air atmosphere. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker Avance NMR spectrometer (400 MHz or 100 MHz, respectively) with $CDCl_3$ as solvent and recorded in ppm relative to internal tetramethylsilane 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). High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument. All MW reactions were carried out in a Discover SP (CEM) microwave reactor.

2. General procedures

(1) Typical procedure for the preparation of 2-(*gem*-dibromovinyl)-*N*-methylsulfonylaniline



At 0 ºC, to a solution of 4-methyl-2-nitrobenzaldehyde (1.65 g, 10 mmol) and CBr_4 (6.65 g, 20 mmol) in DCM (50 mL) was added dropwise a solution of PPh_3 (10.5 g, 40 mmol) in DCM

(50 mL) by an addition funnel. The addition rate was controlled so that the internal temperature was below 5 ºC. After addition (about 1 h), the mixture was stirred for another 2 hrs before warmed to r. t., and stirred for an additional 3 h. The DCM was removed under vacuum, then EtOAc (200 mL) was added and stirred for 0.5 h, the mixture was filtered and washed with EtOAc until no product was found. Solvent was removed under reduced pressure, the residue was purified by flash chromatography using 10% EtOAc in hexanes. The product (**I'**) was obtained as a light yellow solid (2.60 g, 81%).

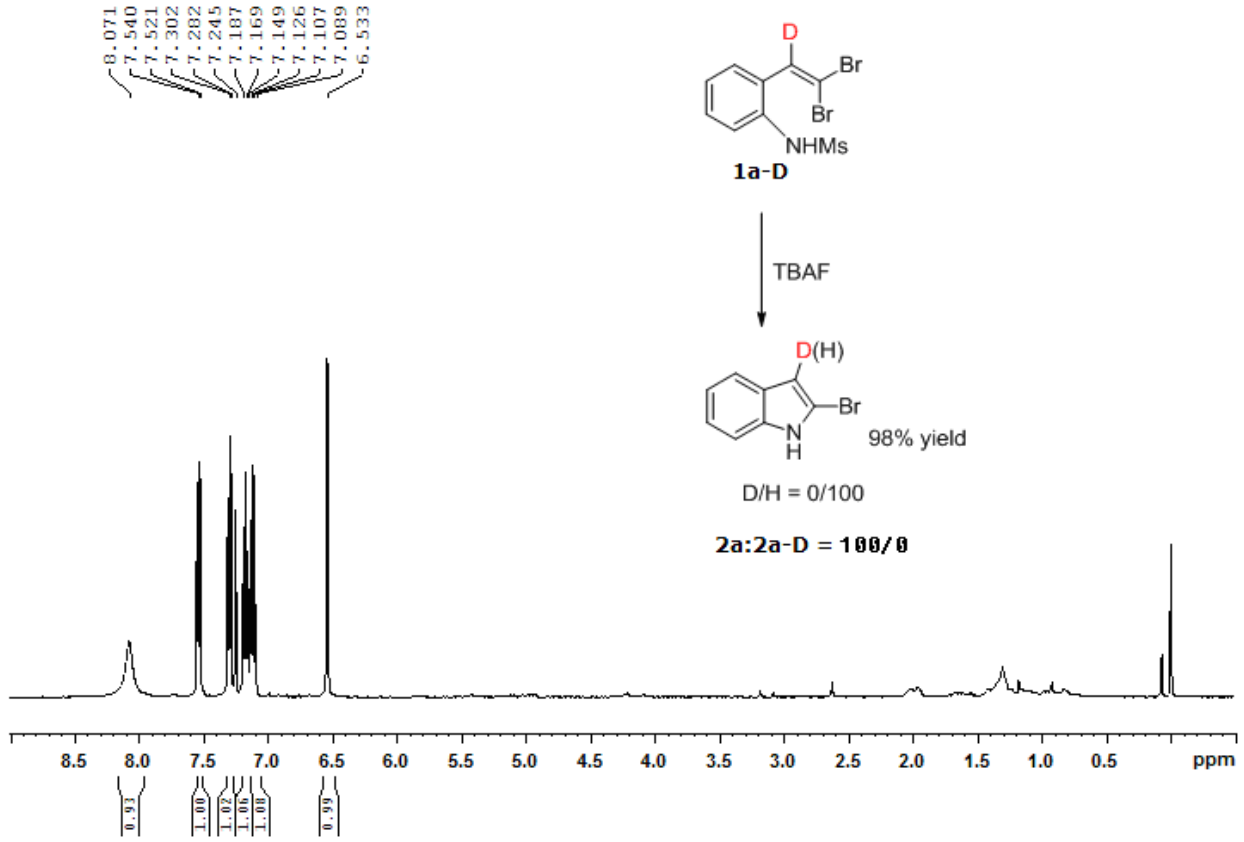
I' (1.61 g, 5.0 mmol) and $SnCl_2 \cdot H_2O$ (67.7 g, 25 mmol) were mixed in EtOH (95%, 50 mL). The mixture was refluxed at 100 ºC for 2 h, and then cooled to r. t. After most of the ethanol was removed under vacuum, H_2O (50 mL) and EtOAc (100 mL) were added. To the resulting mixture, solid $NaHCO_3$ was added carefully until pH >10. The EtOAc layer was separated and the aqueous phase was extracted with EtOAc until it was free of the product. The combined organic solution was washed with brine and dried over Na_2SO_4. Solvent was removed under vacuum. The crude product (**II'**) was resolved in DCM (20 mL), and pyridine (1.0 g, 12.5 mmol) was added. After the mixture was cooled to 0 ºC, methylsulfonyl chloride (0.69 g, 6.0 mmol) was added, the mixture was stirred for 4 h before warmed to r. t., and stirred for an additional 5 h. After the reaction was completed, the mixture was washed with HCl (1.0 mol/L, 15 mL), The DCM layer was separated and the aqueous phase was extracted with DCM until it was free of the product. Solvent was removed and the product was further purified by flash chromatography using 25% EtOAc in hexanes. The product **1k** was obtained as a white solid (1.06 g, 58% yield over 2 steps). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.53 (s, 3H), 3.02 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.22, 133.62, 130.97, 130.58, 130.01, 123.66, 94.95, 39.98, 20.89. HRMS (EI) ($[M]^+$) Calcd. for $C_{10}H_{11}NO_2SBr_2$: 366.8877, Found: 366.8875.

(2) Typical procedure for the synthesis of 2-bromoindole (2a) via TBAF-promoted intramolecular cyclization of 2-(*gem*-dibromovinyl)-*N*-methylsulfonylaniline (1a) under metal-free and microwave irradiation conditions

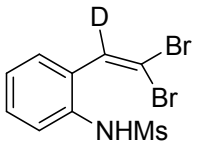
In a 10 mL of sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with 2-(*gem*-dibromovinyl)-*N*-methylsulfonylaniline (**1a**, 0.50

mmol), TBAF (THF solution, 1.0 mol/L, 1.0 mL, 1.0 mmol) and THF (2.0 mL). The reaction vessel was placed in a Discover SP (CEM) microwave reactor, and the reaction mixture was irradiated at 100 W and 100 °C for 5 min. Then it was cooled to room temperature, extracted twice with Et_2O. The organic layers were combined, dried over Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was further purified by flash chromatography on silica gel (eluant: hexane/ethyl acetate) to give the desired product 2-bromoindole (**2a**).

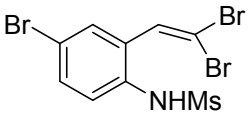
3. The ^{1}H NMR spectra of isotope experiment



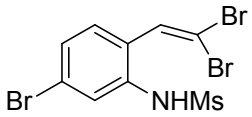
4. Characterization data for starting materials and all the products



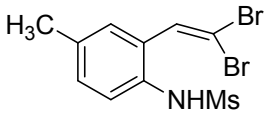
1a-D: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.55–7.53 (m, 1H), 7.45–7.37 (m, 2H), 7.26–7.23 (m, 1H), 6.63 (s, 1H), 3.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 133.76, 130.00, 129.11, 125.79, 122.39, 95.60, 40.15. HRMS (EI) ($[M]^+$) Calcd. for $C_9H_8DBr_2NO_2S$: 353.8784, Found: 353.8788.



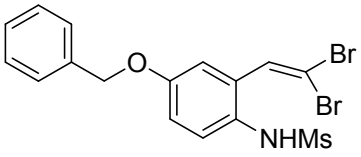
1d: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.57 (d, J = 2.0 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.37–7.31 (m, 2H), 6.66 (s, 1H), 3.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 132.89, 132.88, 132.61, 131.80, 130.68, 123.71, 118.78, 97.16, 40.27. HRMS (EI) ($[M]^+$) Calcd. for $C_9H_8NO_2SBr_3$: 430.7826, Found: 430.7829.



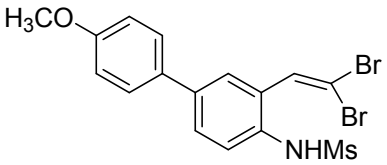
1h: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.73 (s, 1H), 7.36 (d, J = 5.2 Hz, 2H), 7.28 (d, J = 9,2 Hz, 1H), 6.59 (s, 1H), 3.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 135.01, 132.02, 131.16, 128.58, 127.14, 124.18, 123.64, 96.84, 40.45. HRMS (EI) ($[M]^+$) Calcd. for $C_9H_8NO_2SBr_3$: 430.7826, Found: 430.7830.



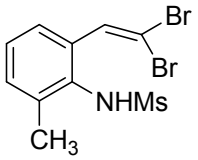
1k: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.50 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.53 (s, 3H), 3.02 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.22, 133.62, 130.97, 130.58, 130.01, 123.66, 94.95, 39.98, 20.89. HRMS (EI) ($[M]^+$) Calcd. for $C_{10}H_{11}NO_2SBr_2$: 366.8877, Found: 366.8875.



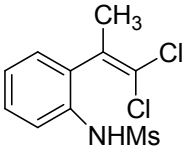
1m: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.53 (s, 1H), 7.44–7.38 (m, 5H), 7.36 (d, *J* = 6.8 Hz, 1H), 7.11 (s, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 5.09 (s, 2H), 3.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 157.32, 136.31, 133.44, 132.88, 128.71, 128.20, 127.44, 127.35, 126.13, 116.49, 115.71, 94.81, 70.41, 39.98. HRMS (EI) ([M]$^+$) Calcd. for $C_{16}H_{15}NO_3SBr_2$: 458.9139, Found: 458.9142.



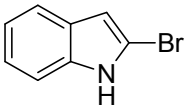
1o: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.62–7.58 (m, 3H), 7.53–7.50 (m, 3H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.42 (s, 1H), 3.87 (s, 3H), 3.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.51, 138.62, 133.19**,** 132.09, 131.93, 129.57, 128.04, 128.02, 122.97, 114.39, 95.96, 55.39, 40.21. HRMS (EI) ([M]$^+$) Calcd. for $C_{16}H_{15}NO_3SBr_2$: 458.9139, Found: 458.9136.



1q: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.58 (s, 1H), 7.33–7.31 (m, 1H), 7.16–7.14 (m, 2H), 6.61 (s, 1H), 2.98 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 138.10, 135.52, 135.23, 131.65, 131.45, 127.87, 127.39, 92.55, 41.64, 18.88. HRMS (EI) ([M]$^+$) Calcd. for $C_{10}H_{11}NO_2SBr_2$: 366.8877, Found: 366.8879.

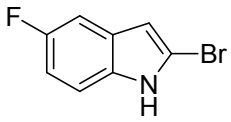


1w: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.63 (d, *J* = 8.4 Hz, 1H), 7.38–7.34 (m, 1H), 7.21–7.18 (m, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.51 (s, 1H), 3.09 (s, 3H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 133.32, 132.25, 131.22, 129.50, 128.74, 125.13, 120.25, 119.85, 40.15, 22.51. HRMS (EI) ([M]$^+$) Calcd. for $C_{10}H_{11}Cl_2NO_2S$: 278.9888, Found: 278.9885.

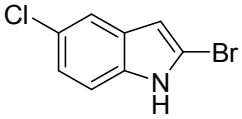


2a:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.10 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz,

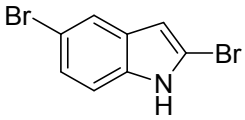
1H), 7.21–7.18 (m, 1H), 7.15–7.12 (m, 1H), 6.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.36, 128.68, 122.22, 120.47, 119.61, 110.30, 108.65, 104.80.



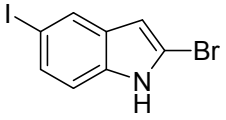
2b: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.11 (s, 1H), 7.18 (m, 2H), 6.94–6.89 (m, 1H), 6.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.16 (J = 234.2 Hz), 132.96, 129.04 (J = 10.4 Hz), 111.02(J = 9.4 Hz), 110.60 (J = 26.2 Hz), 110.25, 105.01 (J = 4.5 Hz), 104.72 (J = 23.8 Hz). HRMS (EI) ([M]$^+$) Calcd. for C_8H_5NFBr: 212.9589, Found: 212.9593.



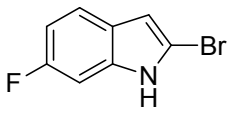
2c: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.18 (s, 1H), 7.51 (d, J = 1.6 Hz, 1H), 7.23–7.21 (m, 1H), 7.15–7.13 (m, 1H), 6.49 (br, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 134.71, 129.65, 126.24, 122.56, 119.05, 111.27, 110.09, 104.56. HRMS (EI) ([M]$^+$) Calcd. for C_8H_5NClBr: 228.9294, Found: 228.9297.



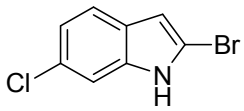
2d:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.24 (s, 1H), 7.67 (d, J = 1.6 Hz, 1H), 7.28–7.26 (m, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.49 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 135.01, 130.30, 125.12, 122.12, 113.77, 111.75, 110.06, 104.43.



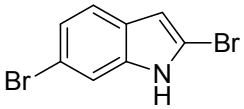
2e:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.36 (s, 1H), 7.87 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 135.46, 131.09, 130.57, 128.33, 112.20, 109.71, 104.07, 84.01.



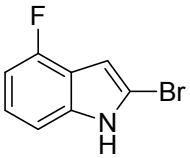
2f:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.14 (s, 1H), 7.43 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.90–6.86 (m, 1H), 6.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.80 (d, *J* = 237.3 Hz), 136.18 (d, *J* = 12.4 Hz), 125.25 (d, *J* = 1.2 Hz), 120.42 (d, *J* = 9.8 Hz), 109.24 (d, *J* = 24.2 Hz), 108.27 (d, *J* = 3.2 Hz), 104.84, 96.97 (d, *J* = 26.4 Hz).



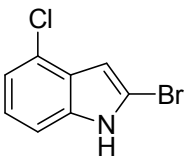
2g: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.18 (s, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.42 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.61, 128.19, 127.26, 121.29, 120.50, 110.34, 109.32, 104.96. HRMS (EI) ($[M]^+$) Calcd. for C_8H_5NClBr: 228.9294, Found: 228.9297.



2h: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (s, 1H), 7.36 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.42 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.02, 127.57, 123.87, 120.82, 115.76, 113.23, 109.31, 105.03. HRMS (EI) ($[M]^+$) Calcd. for $C_8H_5NBr_2$: 272.8789, Found: 272.8792.

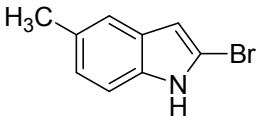


2i: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.19 (s, 1H), 7.09–7.06 (m, 2H), 6.80–6.76 (m, 1H), 6.62 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.80 (d, *J* = 237.3 Hz), 136.18 (d, *J* = 12.4 Hz), 125.25 (d, *J* = 1.2 Hz), 120.42 (d, *J* = 9.9 Hz), 109.24 (d, *J* = 24.2 Hz), 108.27 (d, *J* = 3.2 Hz), 104.84, 96.97 (d, *J* = 26.3 Hz). HRMS (EI) ($[M]^+$) Calcd. for C_8H_5NFBr: 212.9589, Found: 212.9592.

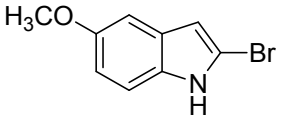


2j: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.31 (s, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.10 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ:

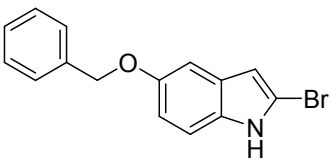
136.92, 127.57, 124.77, 122.79, 120.21, 109.44, 108.90, 103.48. HRMS (EI) ([M]$^+$) Calcd. for C_8H_5NClBr: 228.9294, Found: 228.9296.



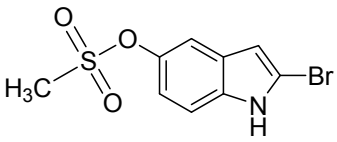
2k: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.91 (s, 1H), 7.30 (s, 1H), 7.14 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.43 (s, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 134.68, 129.73, 128.92, 123.74, 119.27, 109.94, 108.50, 104.35, 21.37. HRMS (EI) ([M]$^+$) Calcd. for C_9H_8NBr: 208.9840, Found: 208.9842.



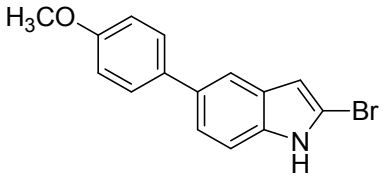
2l:[3] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (s, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.99 (s, 1H), 6.83 (d, J = 8.8 Hz, 1H), 6.45 (s, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.51, 131.55, 129.19, 112.31, 111.11, 108.90, 104.67, 101.56, 55.81.



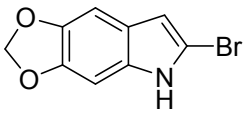
2m: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.86 (s, 1H), 7.37 (d, J = 7.6 Hz, 2H), 7.31–7.27 (m, 2H), 7.23 (d, J = 6.8 Hz, 1H), 7.05 (d, J = 8.8 Hz, 1H), 6.97 (s, 1H), 6.80 (d, J = 8.8 Hz, 1H), 6.34 (s, 1H), 4.98 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 153.73, 137.51, 131.79, 129.20, 128.59, 127.89, 127.60, 113.08, 111.17, 109.02, 104.75, 103.25, 70.88. HRMS (EI) ([M]$^+$) Calcd. for $C_{15}H_{12}NOBr$: 301.0102, Found: 301.0103.



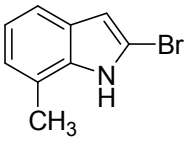
2n: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.41 (s, 1H), 7.45 (s, 1H), 7.30–7.27 (m, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.55 (s, 1H), 3.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 143.46, 134.98, 128.98, 116.49, 112.63, 111.34, 110.84, 105.30, 36.98. HRMS (EI) ([M]$^+$) Calcd. for $C_{16}H_{15}NO_3SBr_2$: 458.9139, Found: 458.9142.



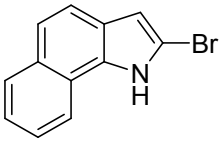
2o: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.09 (s, 1H), 7.68 (s, 1H), 7.54 (d, J = 7.2 Hz, 2H), 7.38–7.31 (m, 2H), 6.98 (d, J = 7.2 Hz, 2H), 6.56 (s, 1H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.64, 135.61, 134.74, 133.77, 129.25, 128.30, 121.86, 117.62, 114.15, 110.46, 109.07, 105.12, 55.36. HRMS (EI) ([M]$^+$) Calcd. for $C_{15}H_{12}NOBr$: 301.0102, Found: 301.0106.



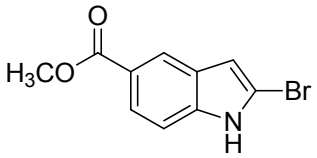
2p: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.99 (s, 1H), 6.93 (s, 1H), 6.78 (s, 1H), 6.40 (d, J = 1.6 Hz, 1H), 5.94 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 144.92, 143.32, 131.19, 122.59, 105.32, 105.00, 100.64, 98.48, 91.59. HRMS (EI) ([M]$^+$) Calcd. for $C_9H_6NO_2Br$: 238.9582, Found: 238.9587.



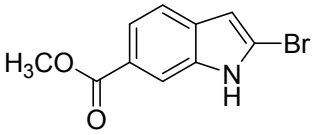
2q: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.99 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.04–7.00 (m, 1H), 6.95 (d, J = 7.2 Hz, 1H), 6.52 (s, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.17, 128.36, 122.89, 120.73, 119.61, 117.41, 108.36, 105.40, 16.55. HRMS (EI) ([M]$^+$) Calcd. for C_9H_8NBr: 208.9840, Found: 208.9841.



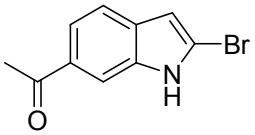
2r: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.86 (s, 1H), 7.90 (dd, J = 4.0, 8.0 Hz, 2H), 7.60 (d, J = 8.4 Hz, 1H), 7.53–7.49 (m, 2H), 7.45–7.41 (m, 1H), 6.65 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 131.14, 130.14, 128.89, 125.79, 124.78, 124.18, 121.31, 120.82, 119.52, 119.17, 106.47, 105.49. HRMS (EI) ([M]$^+$) Calcd. for $C_{12}H_8NBr$: 244.9840, Found: 208.9844.



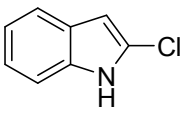
2s:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.60 (s, 1H), 8.30 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.62 (s, 1H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.99, 139.01, 128.28, 123.64, 122.57, 122.43, 110.17, 110.08, 105.99, 51.98.



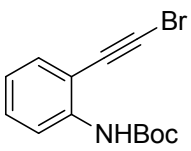
2t:[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.86 (s, 1H), 8.13 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 6.59 (s, 1H), 3.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.14, 135.78, 132.37, 123.70, 121.51, 119.21, 112.69, 105.23, 52.19.



2u: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.09 (s, 1H), 8.03 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 6.58 (s, 1H), 2.66 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 198.53, 136.07, 132.60, 131.40, 120.94, 119.22, 113.31, 111.24, 105.22, 26.79. HRMS (EI) ($[M]^+$) Calcd. for $C_{10}H_8NOBr$: 236.9789, Found: 236.9794.

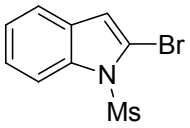


2v:[4] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.91 (s, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.23–7.21 (m, 1H), 7.18–7.14 (m, 1H), 7.13–7.10 (m, 1H), 6.39 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 135.00, 128.16, 123.35, 122.29, 120.63, 119.89, 110.43, 100.79.

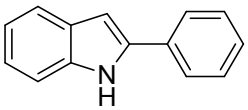


^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.13 (d, J = 8.4 Hz, 1H), 7.39 (dd, J = 1.6, 8.4 Hz, 1H), 7.35–

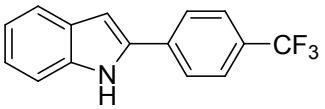
7.30 (m, 1H), 7.13 (s, 1H), 6.98–6.94 (m, 1H), 1.56 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 152.35, 140.27, 132.41, 129.96, 122.09, 117.85, 110.65, 81.01, 75.93, 56.13, 28.29. HRMS (EI) ($[M]^+$) Calcd. for $C_{13}H_{14}NO_2Br$: 295.0208, Found: 295.0206.



3a:[5] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.09 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.34–7.27 (m, 2H), 6.85 (s, 1H), 3.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.24, 129.40, 124.97, 124.07, 120.13, 114.76, 114.62, 109.45, 41.78.

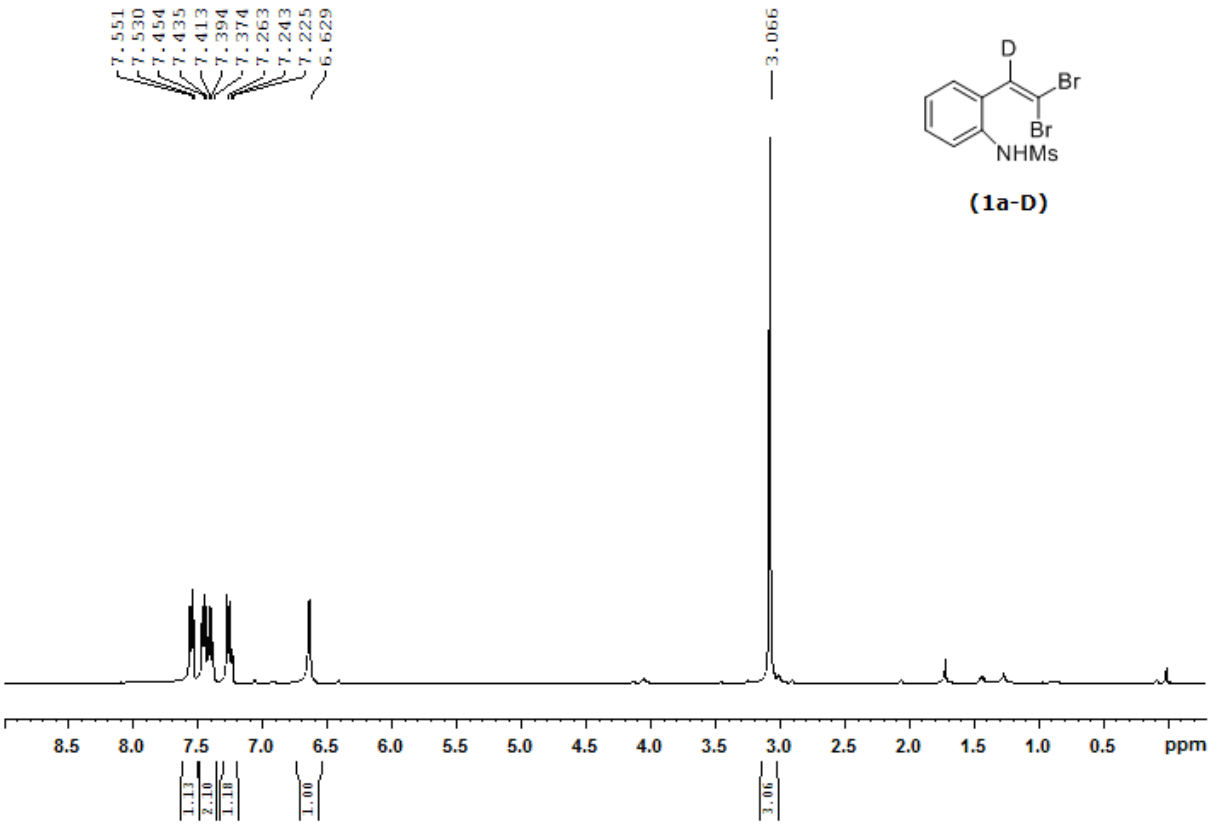


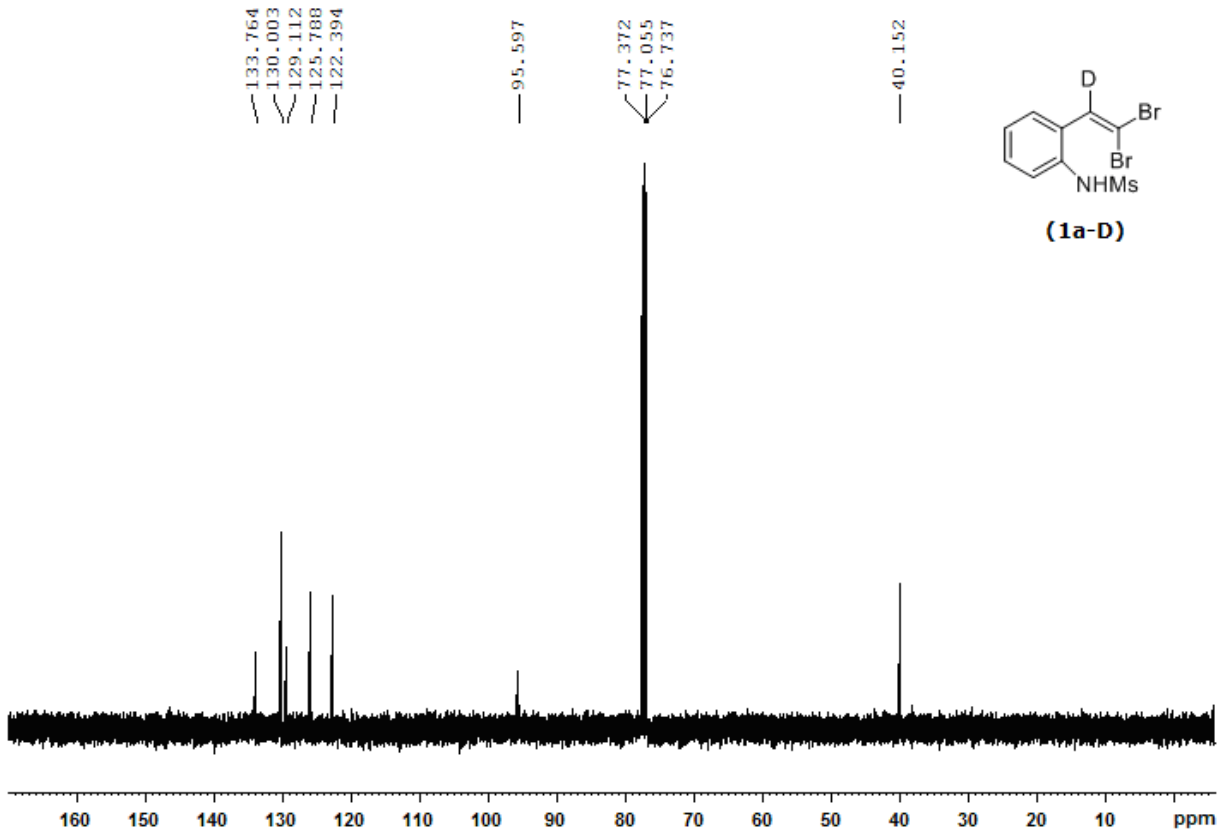
4a:[1] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.33 (s, 1H), 7.49–7.46 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.38–7.34 (m, 1H), 7.27–7.23 (m, 1H), 7.19–7.16 (m, 1H), 6.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.92, 136.86, 132.41, 129.31, 129.04, 127.73, 125.19, 122.38, 120.70, 120.31, 110.94, 100.03.

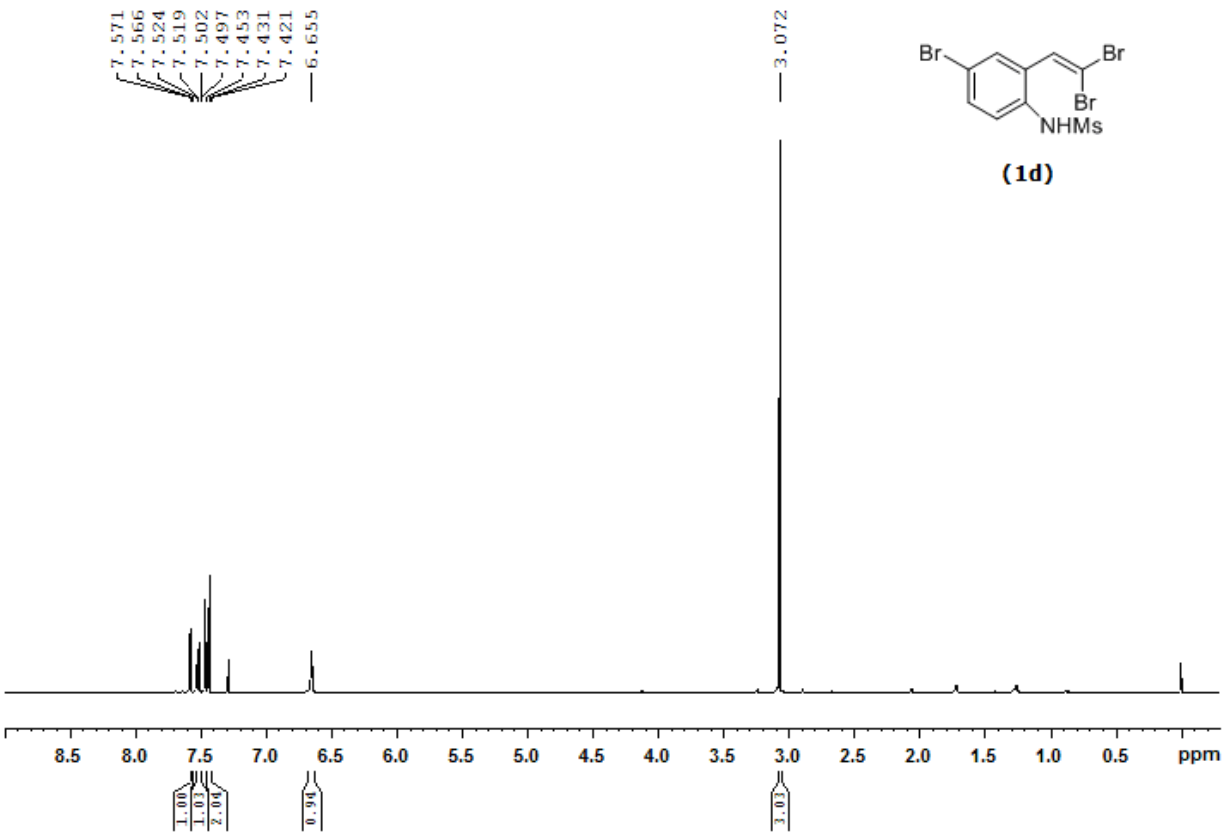


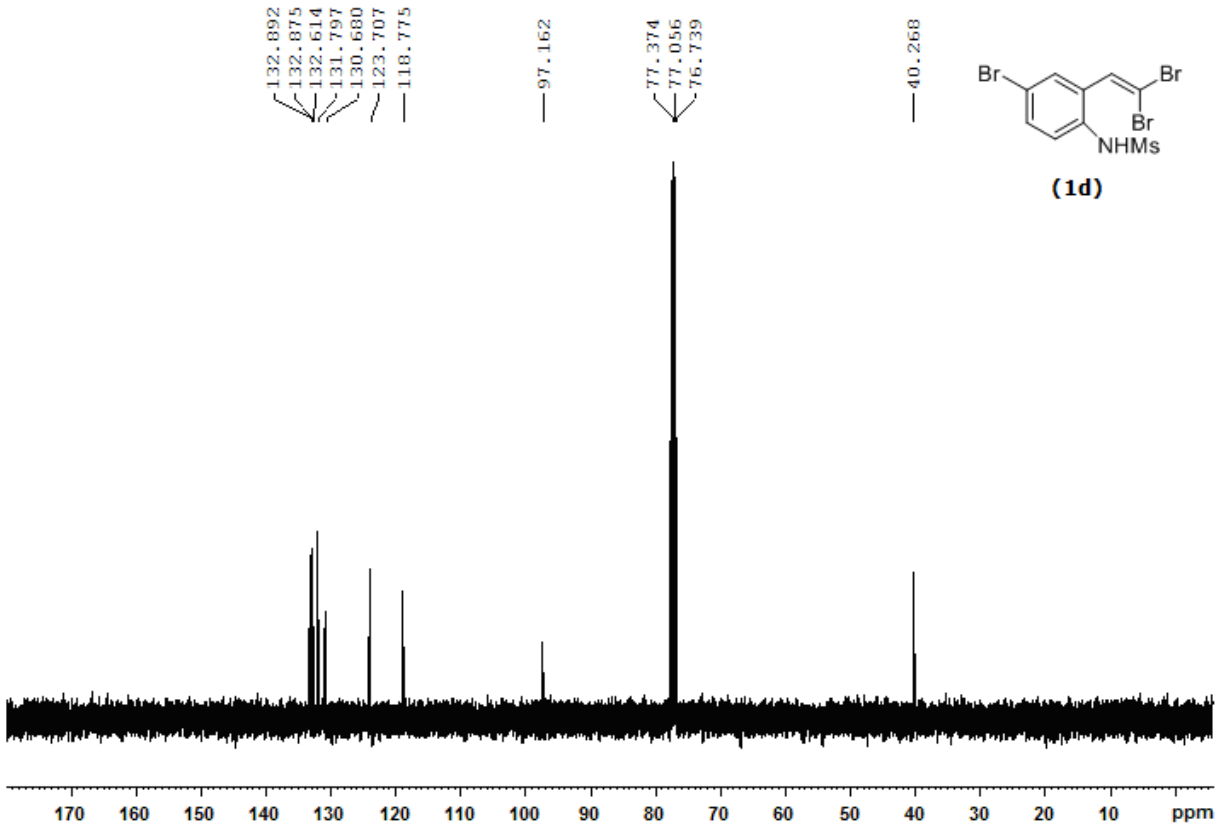
4b:[6] ^{1}H NMR (DMSO, 400 MHz) δ: 11.82 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H),, 7.23–7.19 (m, 1H), 7.13–7.11 (m, 1H), 7.09–7.07 (m, 1H); ^{13}C NMR (DMSO, 100 MHz) δ: 137.82, 136.40, 136.15, 128.72, 126.14 (q, *J* = 284 Hz), 126.01, 125.67, 123.31, 122.79, 120.86, 120.06, 111.90, 101.07.

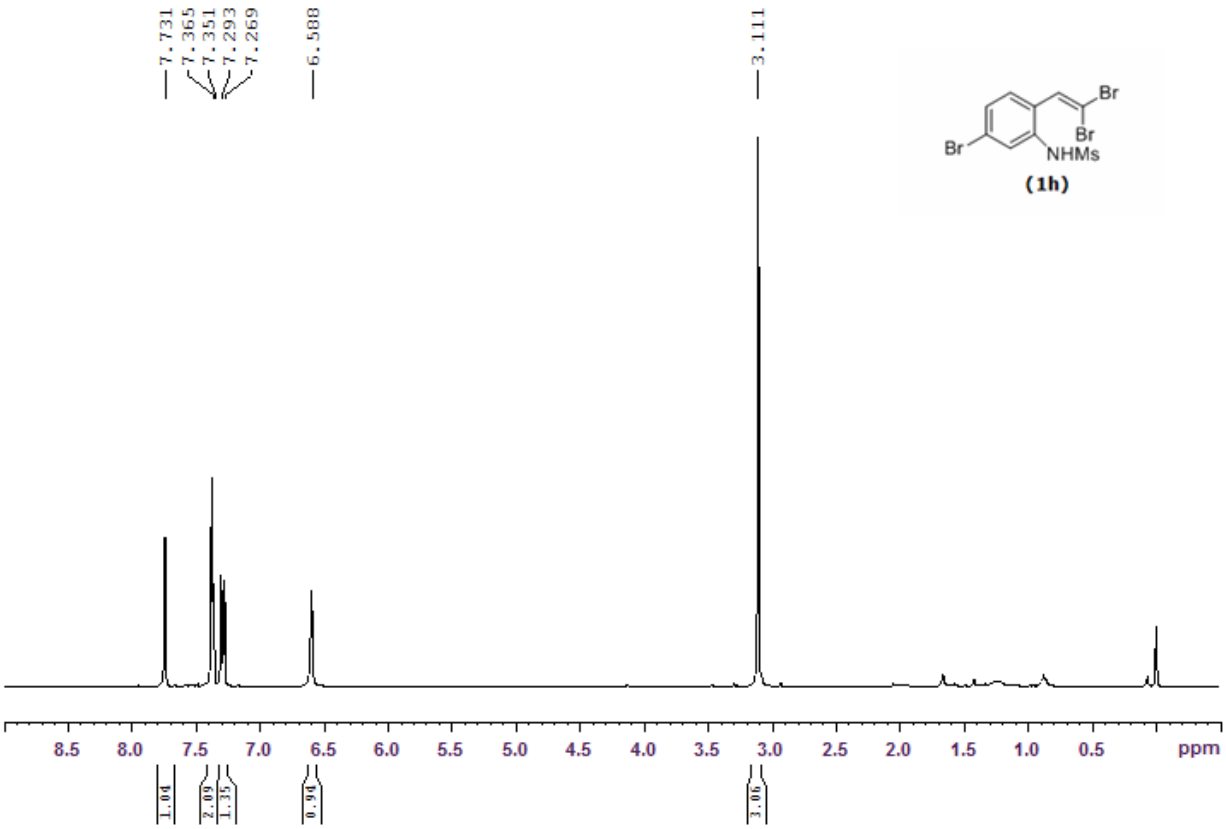
6. ^{1}H and ^{13}C NMR spectra of compounds

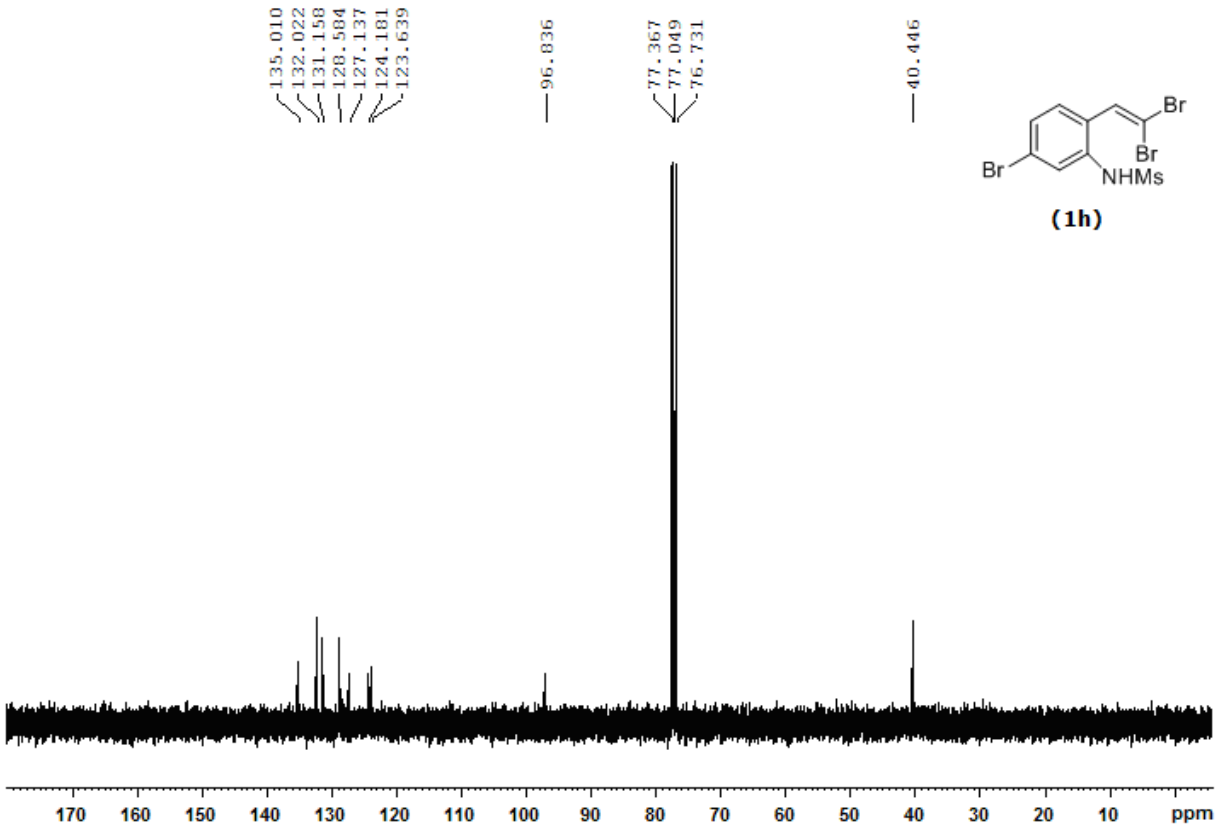

7.551
7.530
7.454
7.435
7.413
7.394
7.374
7.263
7.243
7.225
6.629
3.066
D
Br
Br
NHMs
(1a-D)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.13
2.10
1.18
1.00
3.06

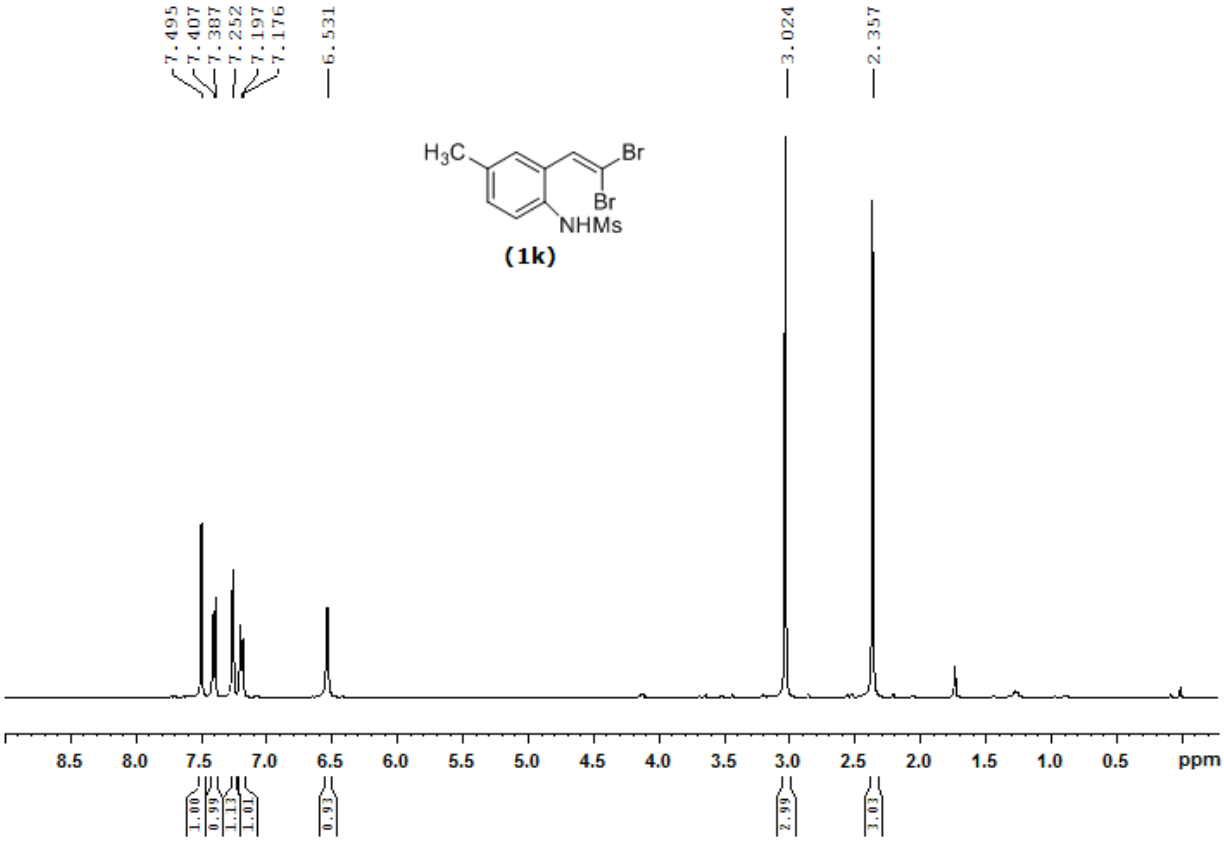

133.764
130.003
129.112
125.788
122.394
95.597
77.372
77.055
76.737
40.152
D
Br
Br
NHMs
(1a-D)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

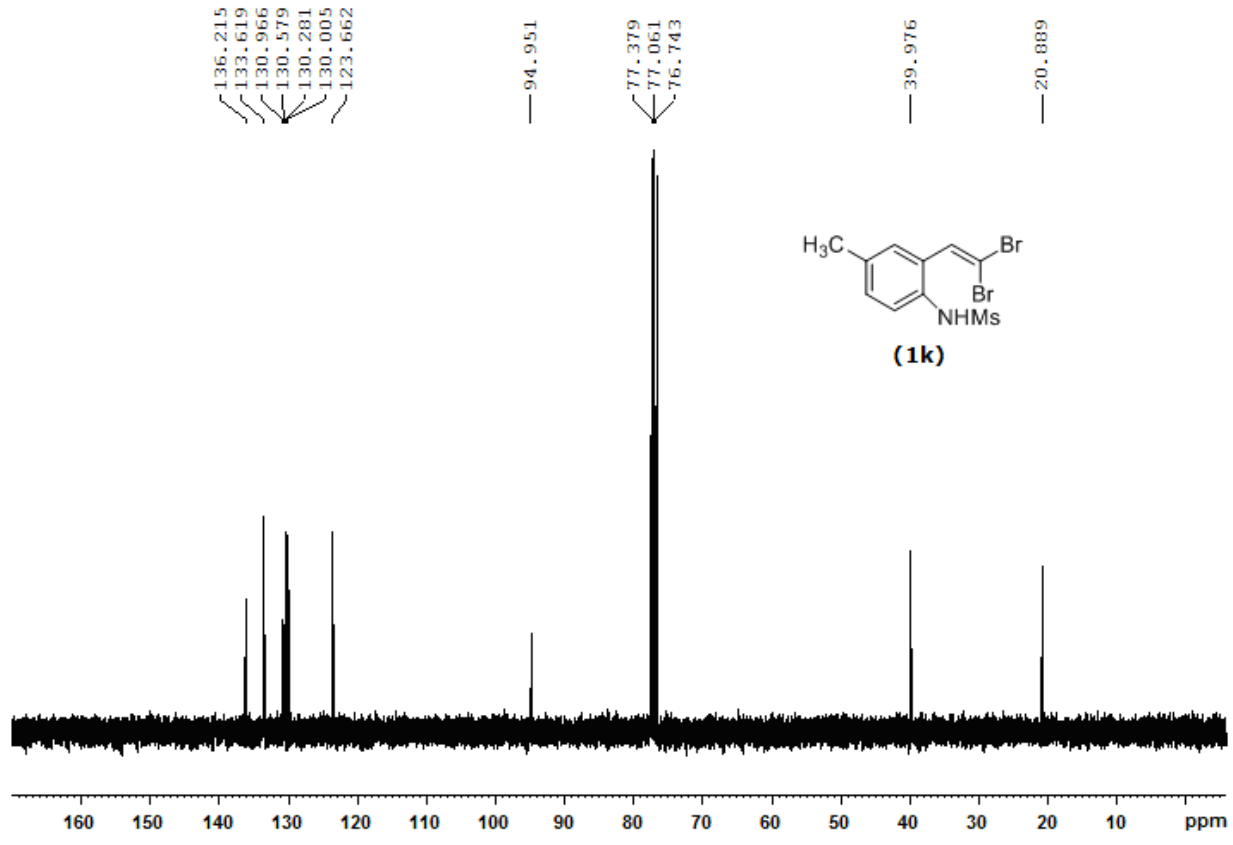

7.571
7.566
7.524
7.519
7.502
7.497
7.453
7.431
7.421
6.655
3.072
Br
Br
Br
NHMs
(1d)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.03
2.04
0.94
3.03

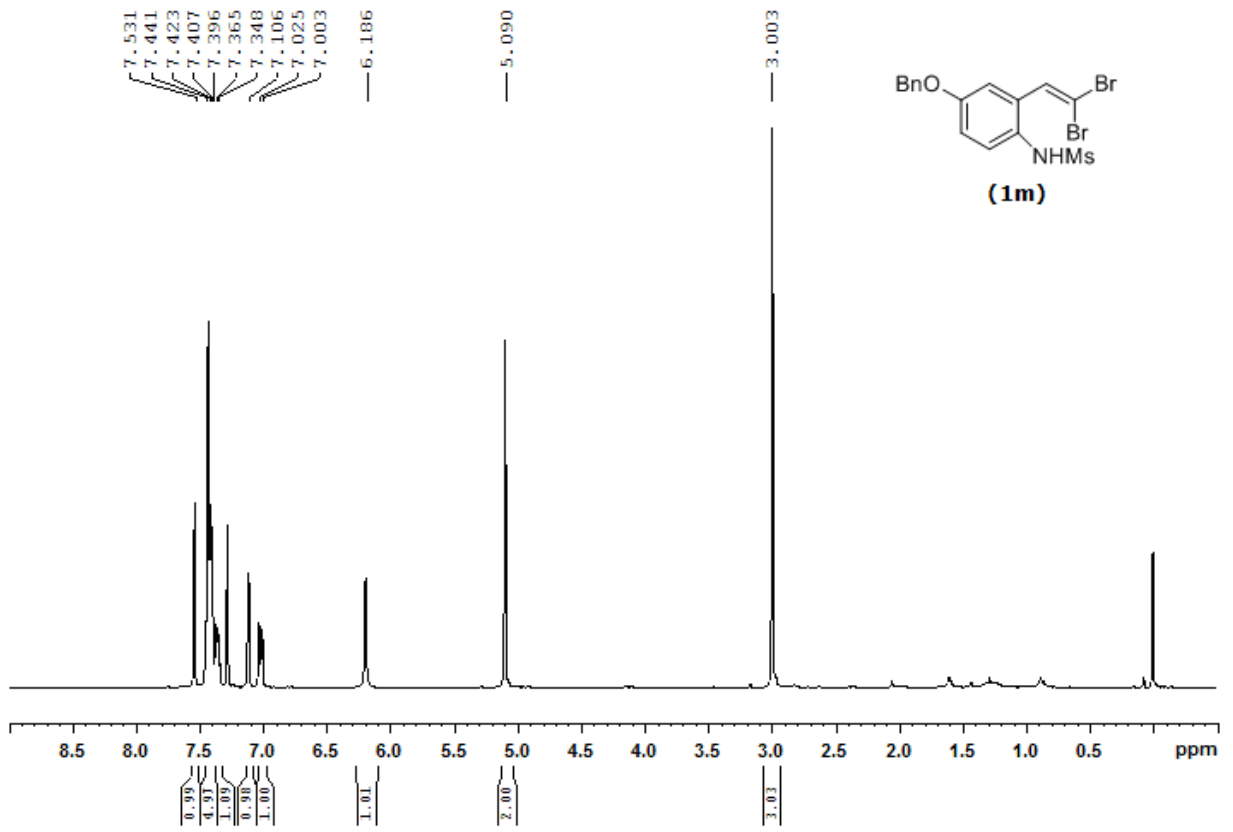

132.892
132.875
132.614
131.797
130.680
123.707
118.775
97.162
77.374
77.056
76.739
40.268
Br
Br
Br
NHMs
(1d)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

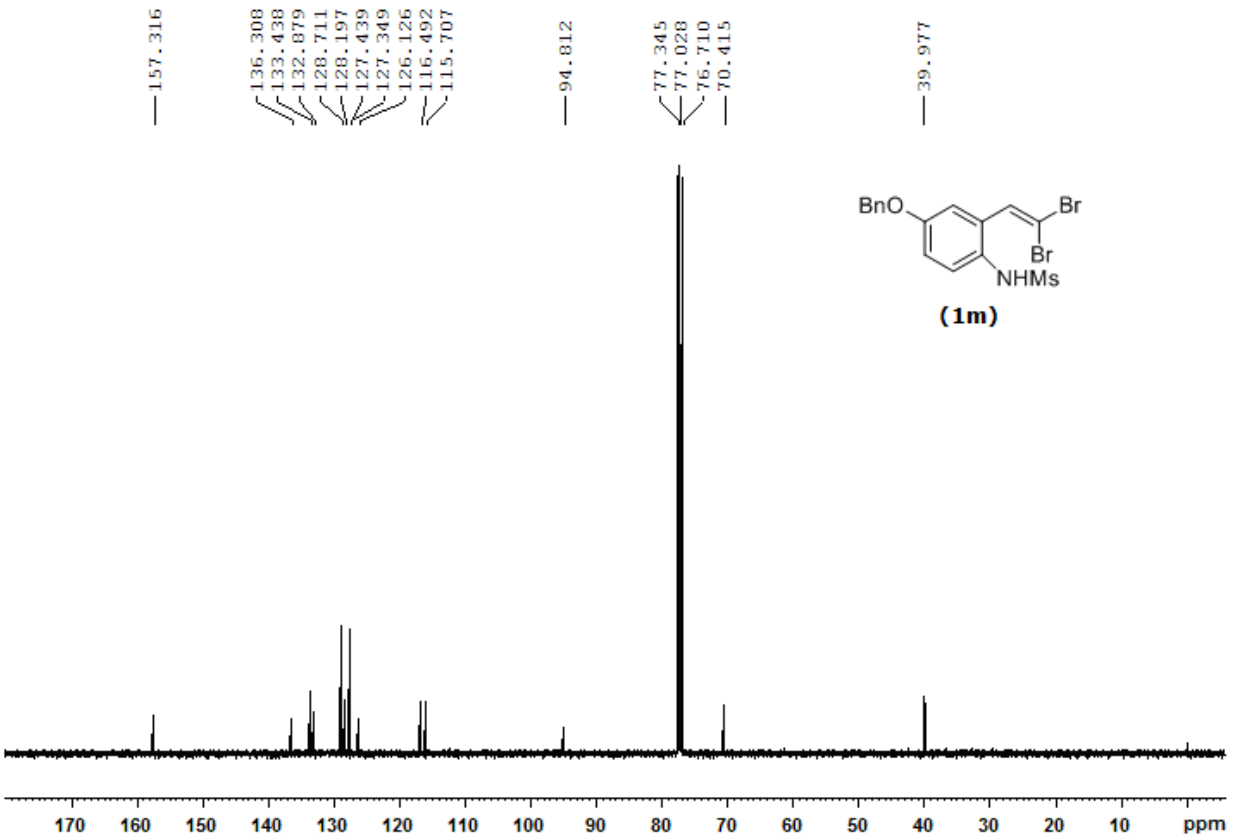

7.731
7.365
7.351
7.293
7.269
6.588
3.111
Br
Br
Br
NHMs
(1h)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.04
2.09
1.35
0.94
3.06

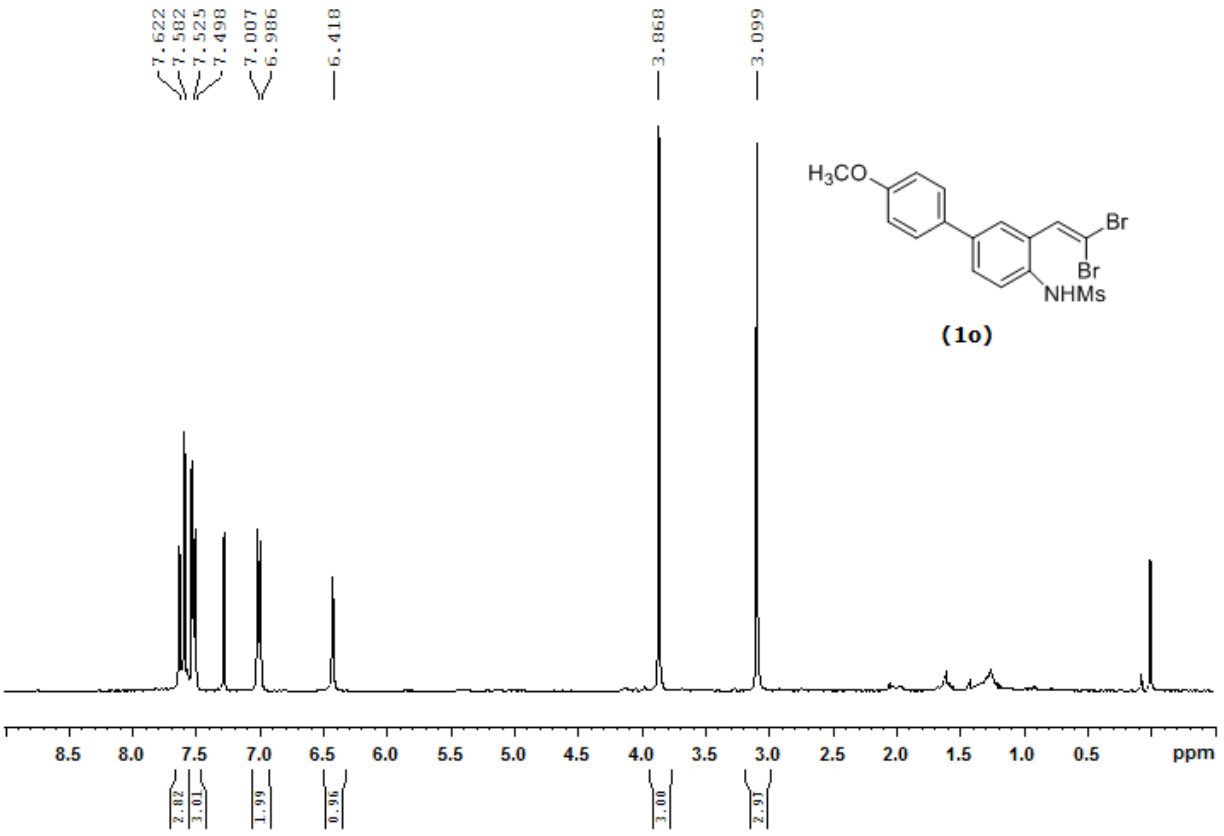

135.010
132.022
131.158
128.584
127.137
124.181
123.639
96.836
77.367
77.049
76.731
40.446
Br
Br
Br
NHMs
(1h)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

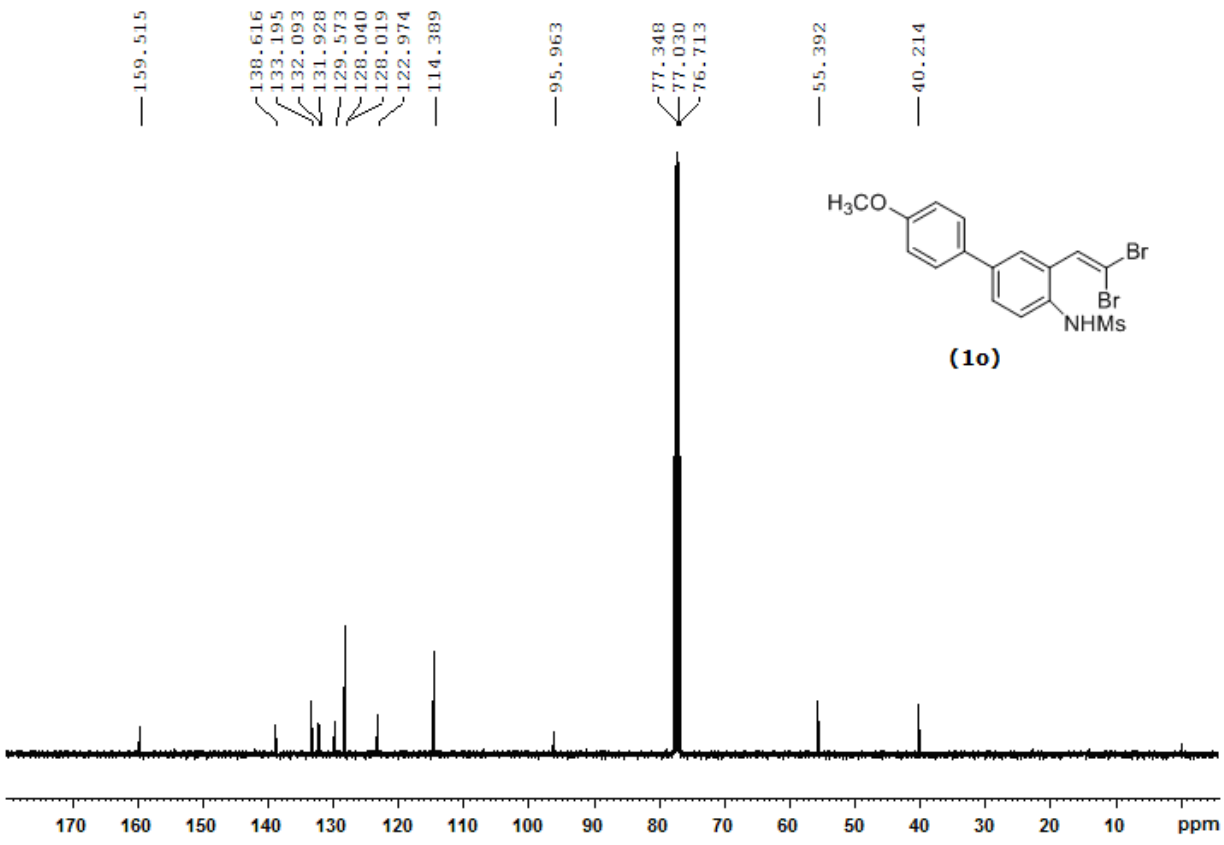

7.495
7.407
7.387
7.252
7.197
7.176
6.531
3.024
2.357
H3C
Br
Br
NHMs
(1k)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.99
1.13
1.01
0.93
2.99
3.03

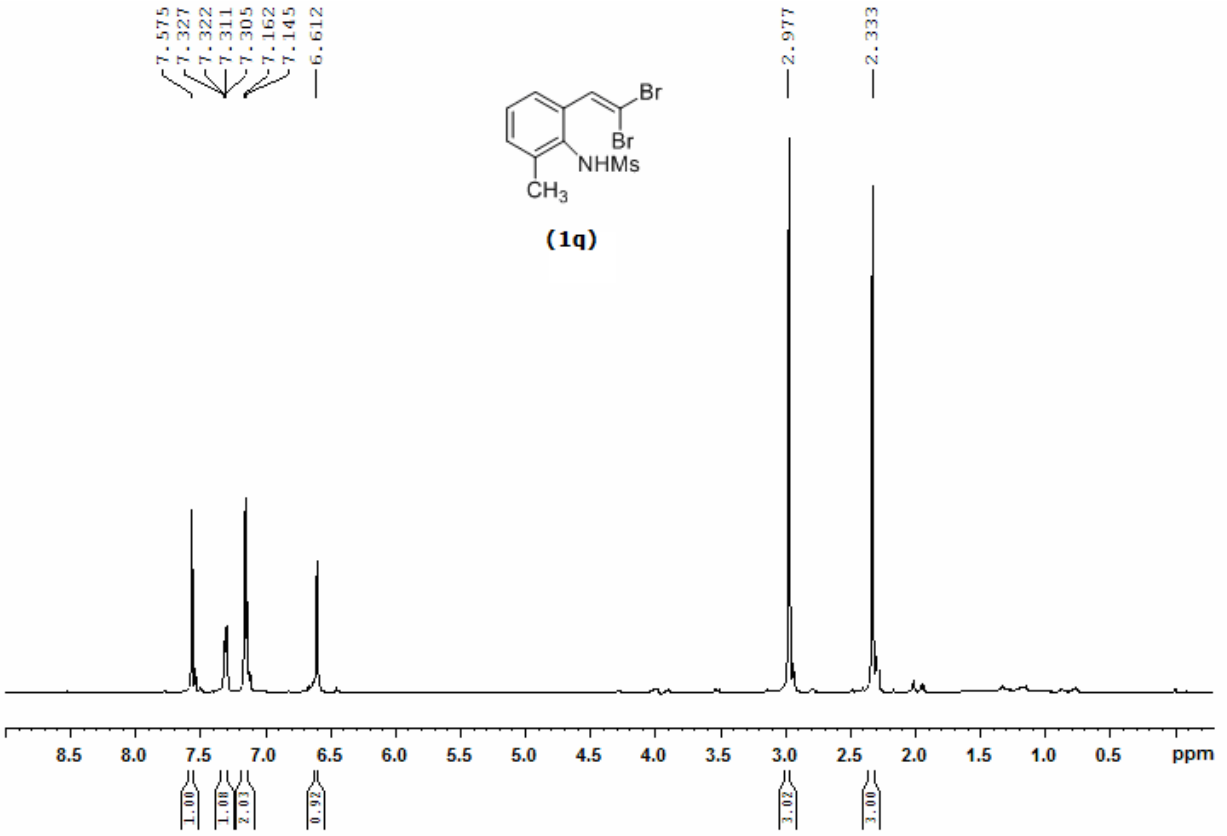

136.215
133.619
130.966
130.579
130.281
130.005
123.662
94.951
77.379
77.061
76.743
39.976
20.889
H3C
Br
Br
NHMs
(1k)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

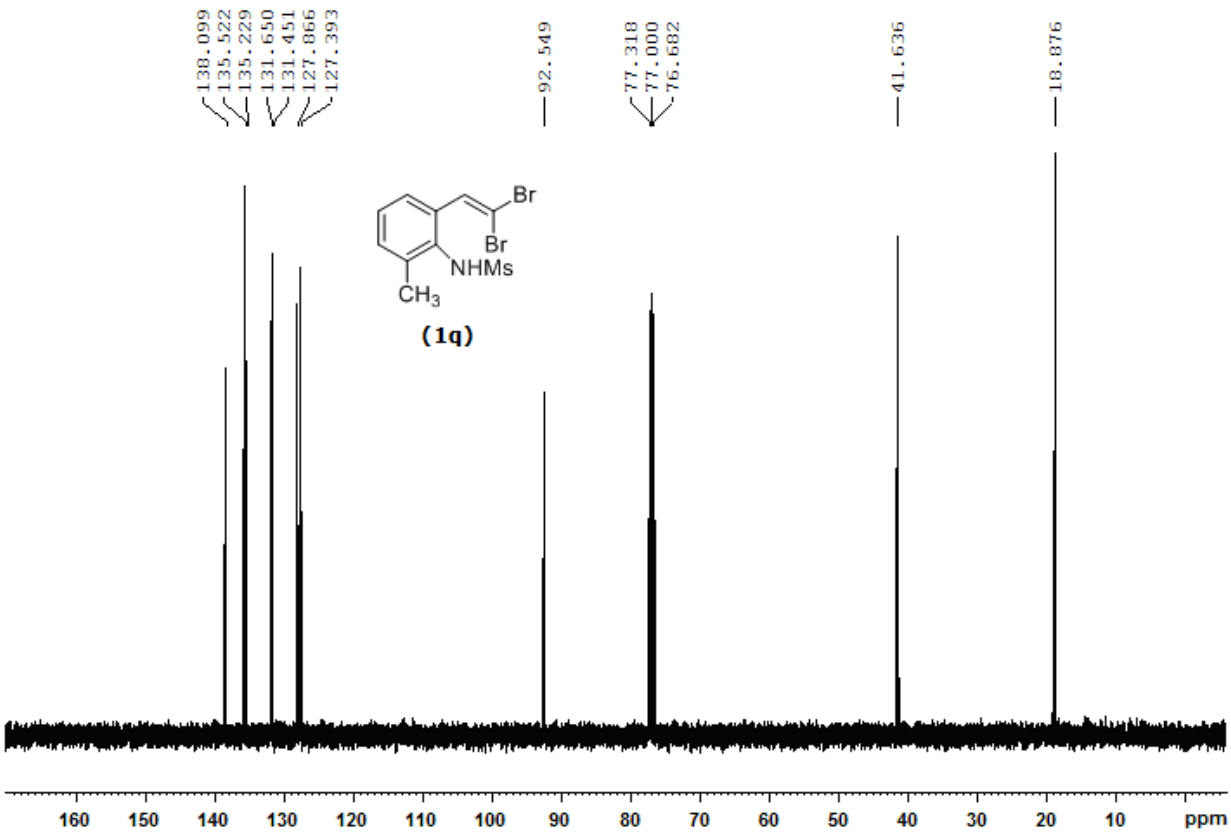

7.531
7.441
7.423
7.407
7.396
7.365
7.348
7.106
7.025
7.003
6.186
5.090
3.003
BnO
Br
Br
NHMs
(1m)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.99
4.91
1.09
0.98
1.00
1.01
2.00
3.03

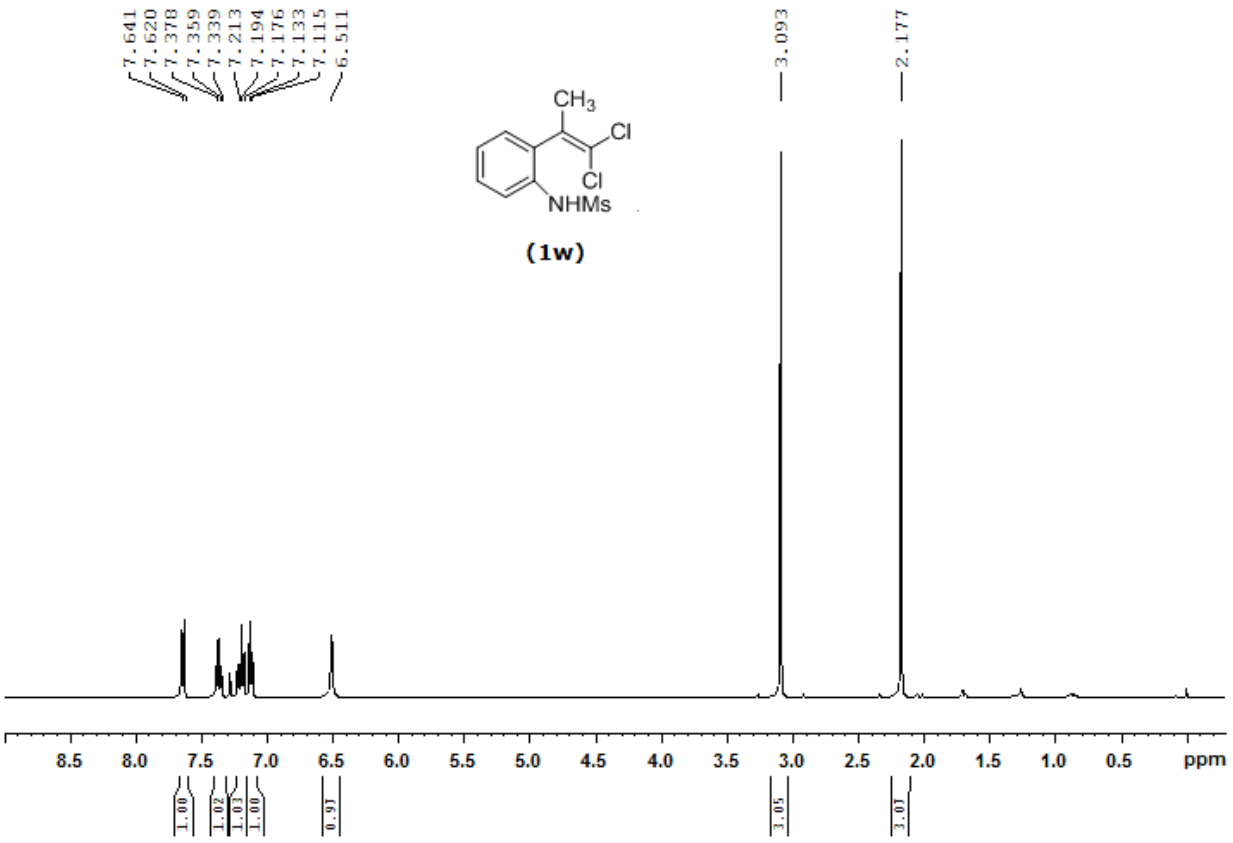

157.316
136.308
133.438
132.879
128.711
128.197
127.439
127.349
126.126
116.492
115.707
94.812
77.345
77.028
76.710
70.415
39.977
BnO
Br
Br
NHMs
(1m)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

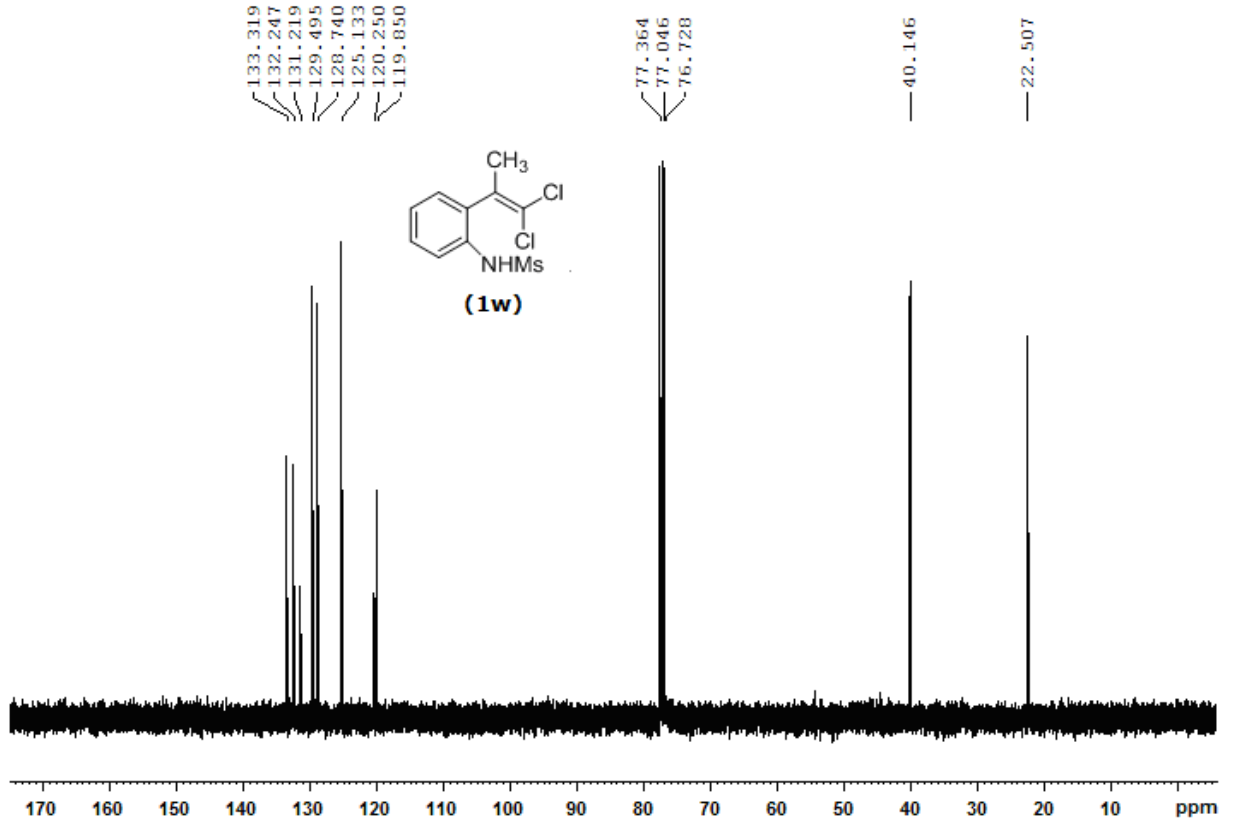

7.622
7.582
7.525
7.498
7.007
6.986
6.418
3.868
3.099
H3CO
Br
Br
NHMs
(1o)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.02
3.01
1.99
0.96
3.00
2.91

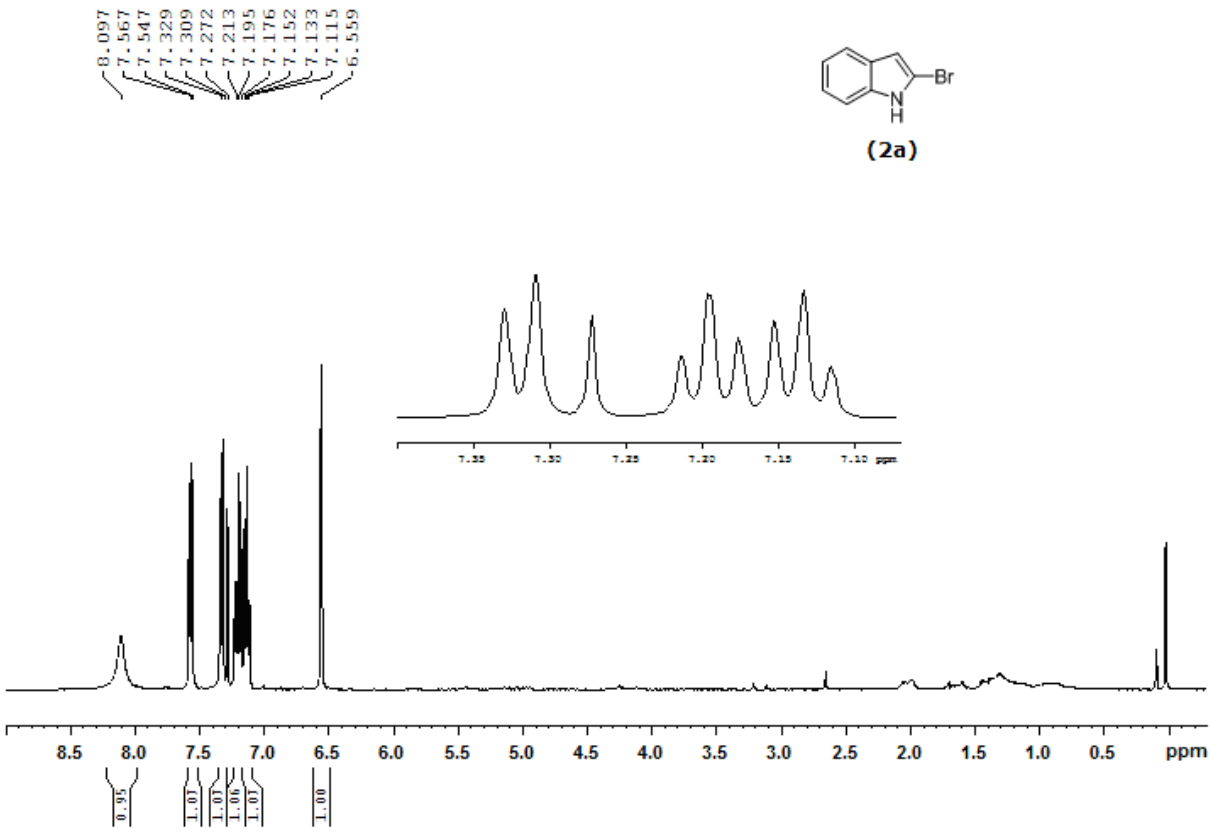

159.515
138.616
133.195
132.093
131.928
129.573
128.040
128.019
122.974
114.389
95.963
77.348
77.030
76.713
55.392
40.214
H3CO
Br
Br
NHMs
(1o)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

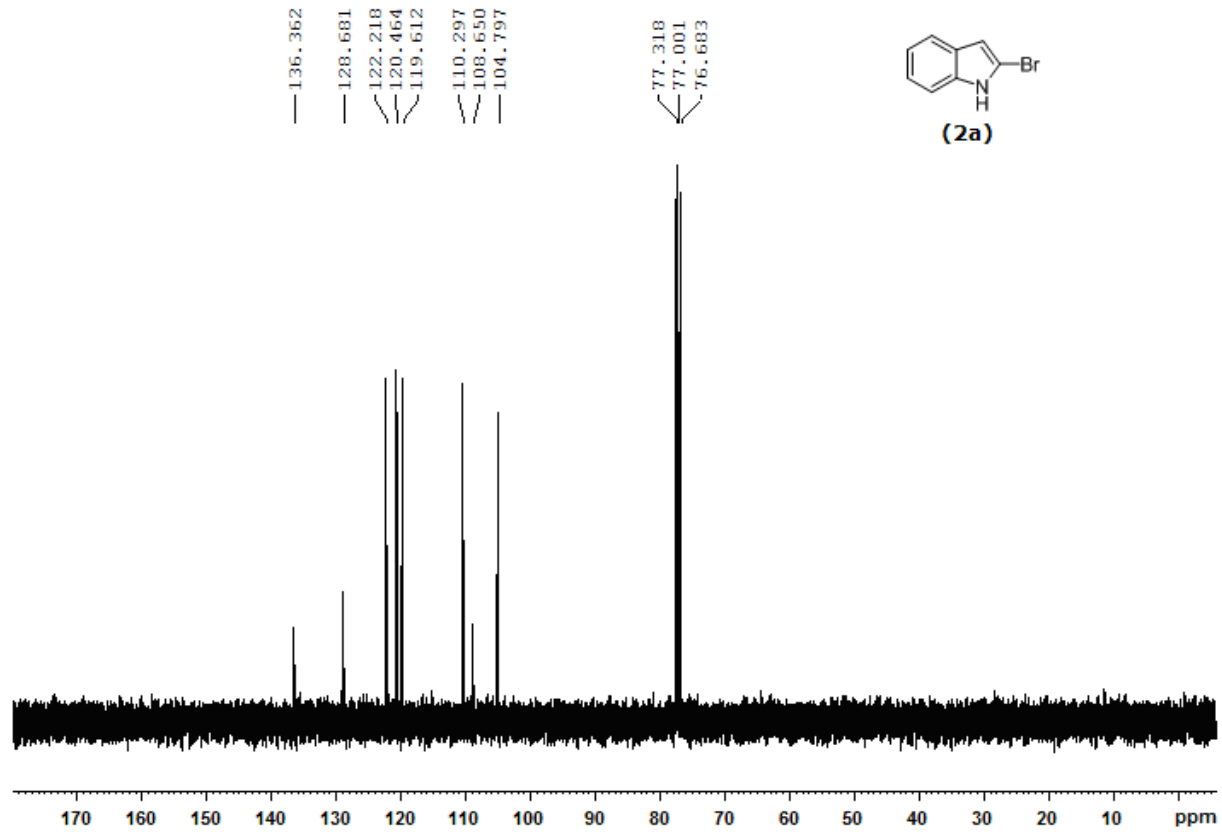

7.575
7.327
7.322
7.311
7.305
7.162
7.145
6.612
2.977
2.333
Br
Br
NHMs
CH3
(1q)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.08
2.07
0.92
3.02
3.00

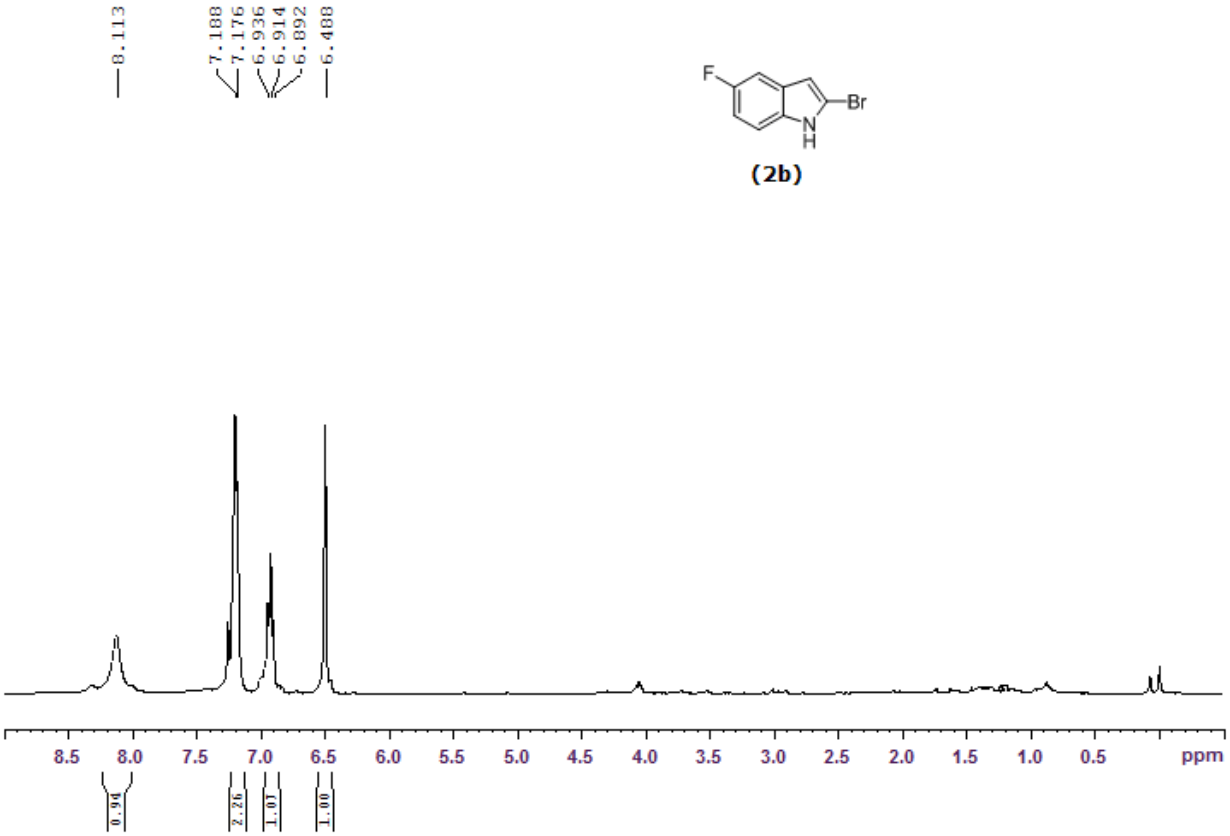

138.099
135.522
135.229
131.650
131.451
127.866
127.393
92.549
77.318
77.000
76.682
41.636
18.876
Br
Br
NHMs
CH3
(1q)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

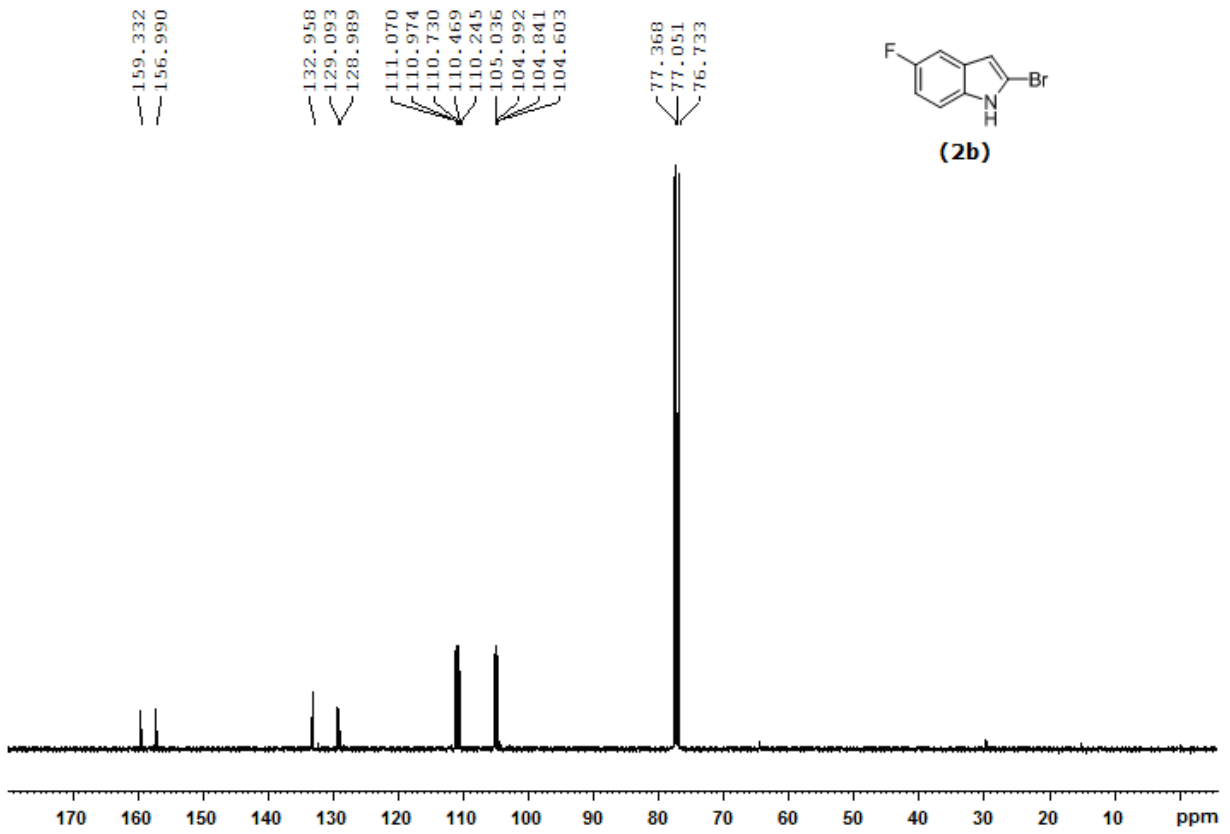

7.641
7.620
7.378
7.359
7.339
7.213
7.194
7.176
7.133
7.115
6.511
3.093
2.177
CH3
Cl
Cl
NHMs
(1w)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.02
1.03
1.00
0.97
3.05
3.07

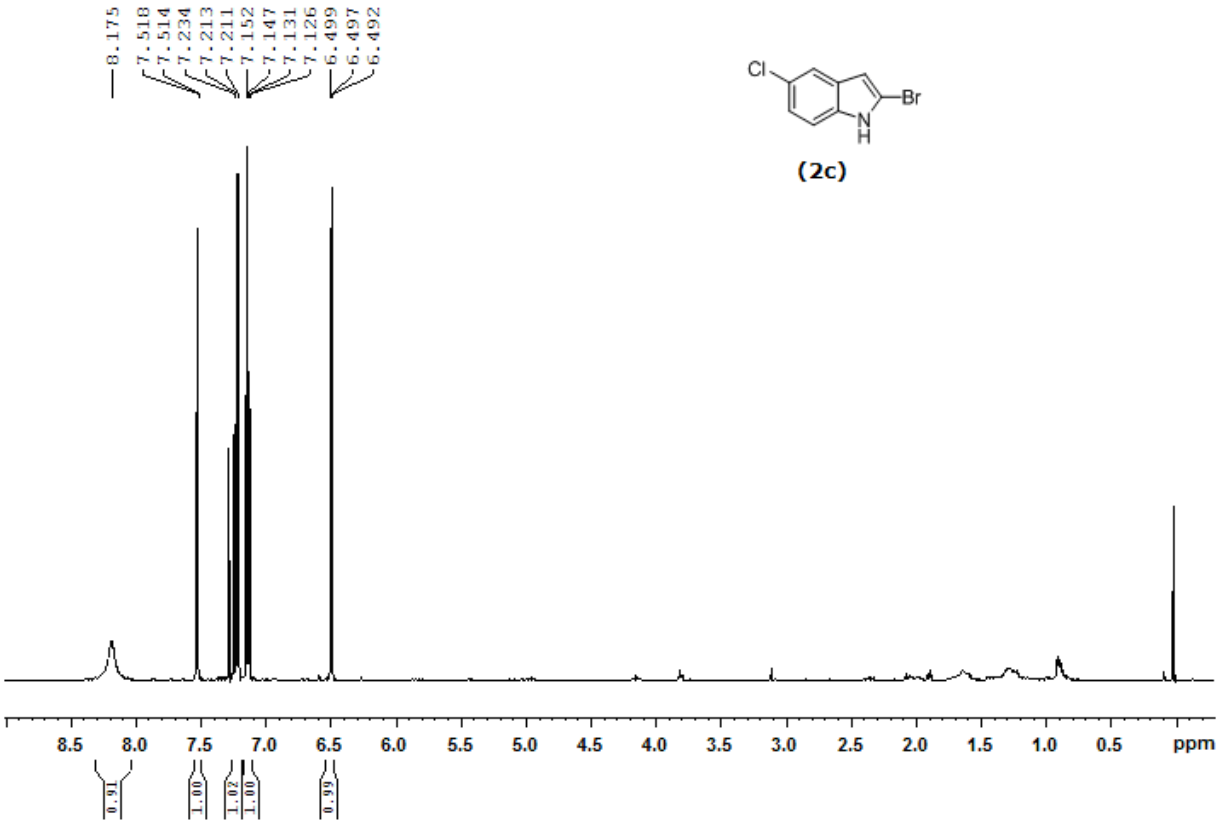

133.319
132.247
131.219
129.495
128.740
125.133
120.250
119.850
77.364
77.046
76.728
40.146
22.507
CH3
Cl
Cl
NHMs
(1w)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

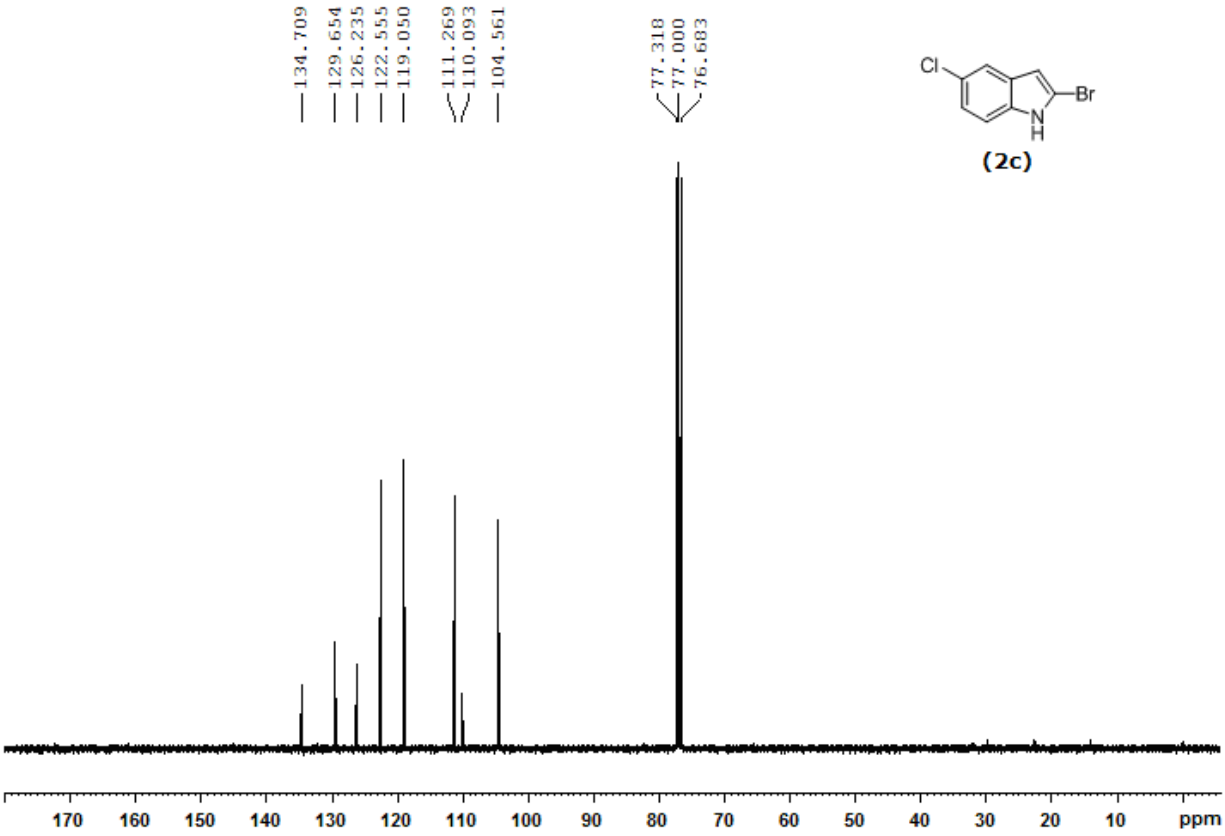

8.097
7.567
7.547
7.329
7.309
7.272
7.213
7.195
7.176
7.152
7.133
7.115
6.559
Br
N
H
(2a)
ppm
0.95
1.07
1.07
1.06
1.07
1.00

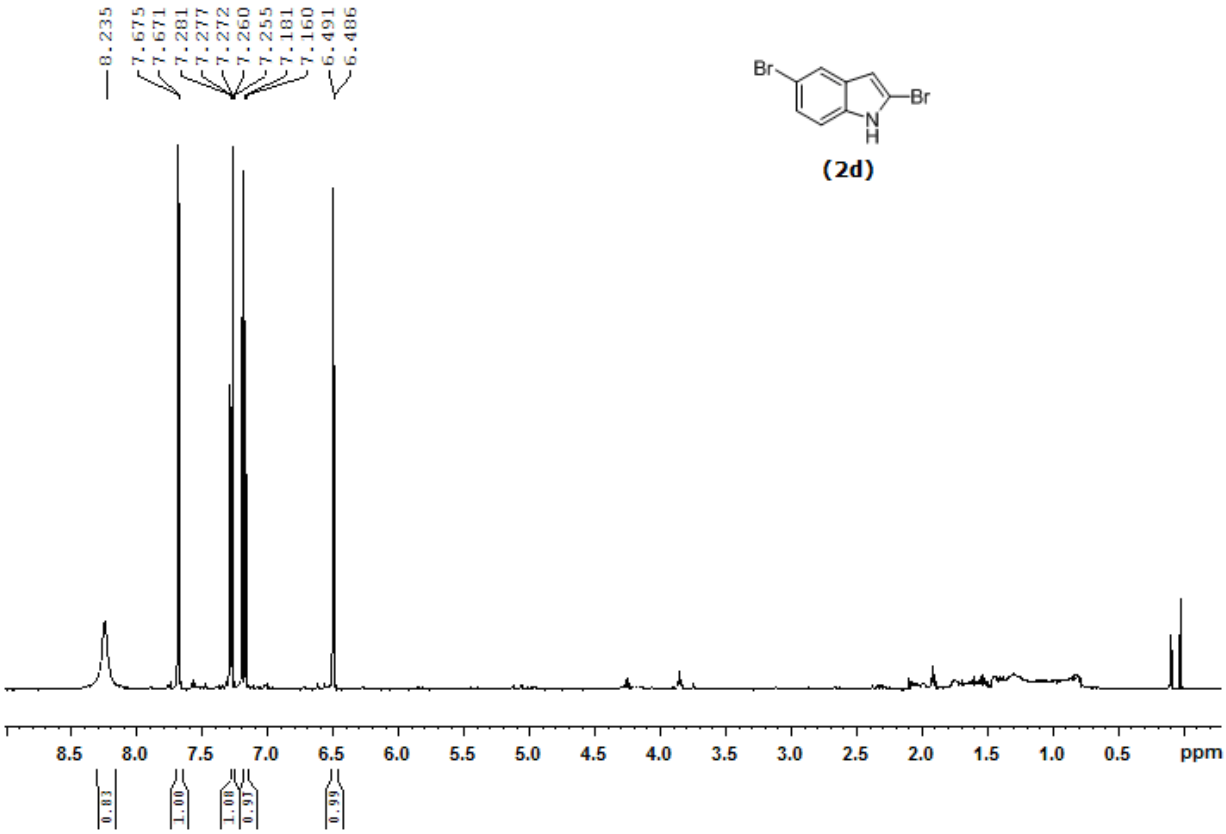

136.362
128.681
122.218
120.464
119.612
110.297
108.650
104.797
77.318
77.001
76.683
Br
N
H
(2a)
ppm

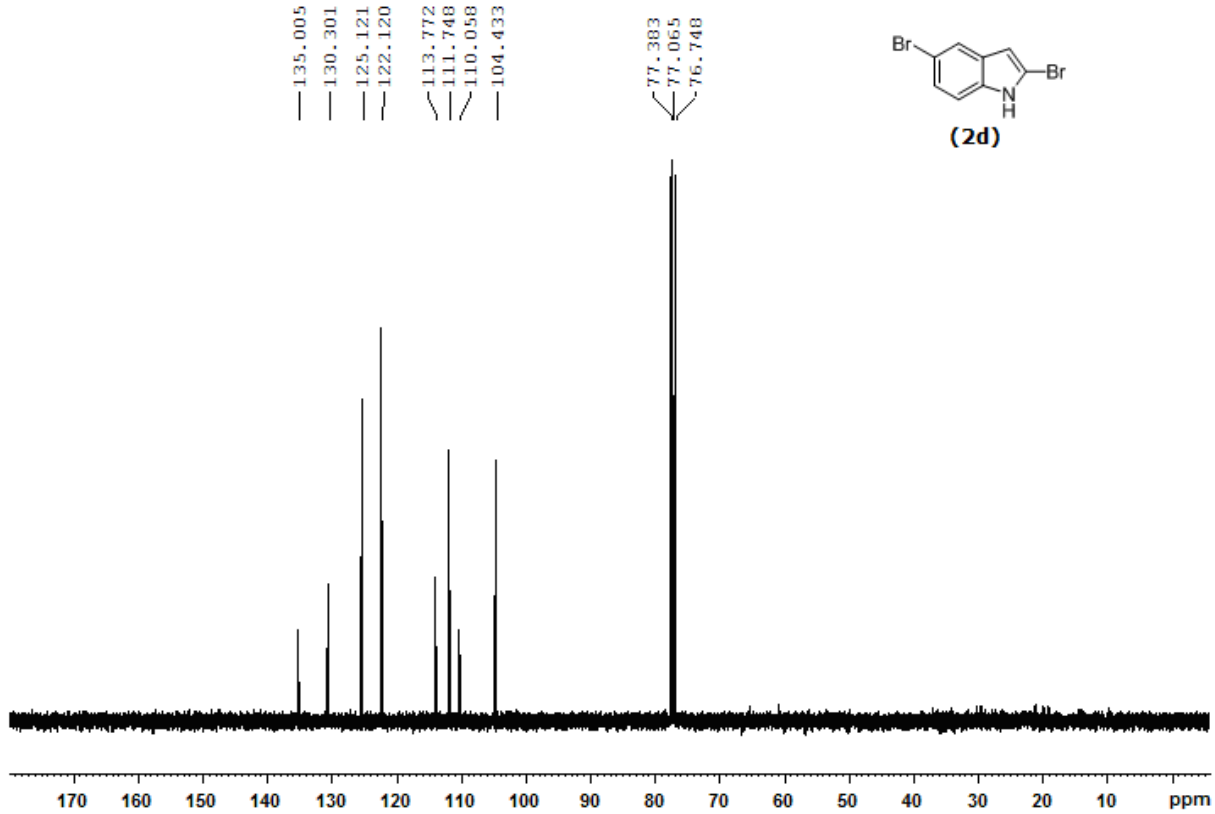

8.113
7.188
7.176
6.936
6.914
6.892
6.488
F
Br
N
H
(2b)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.94
2.26
1.07
1.00

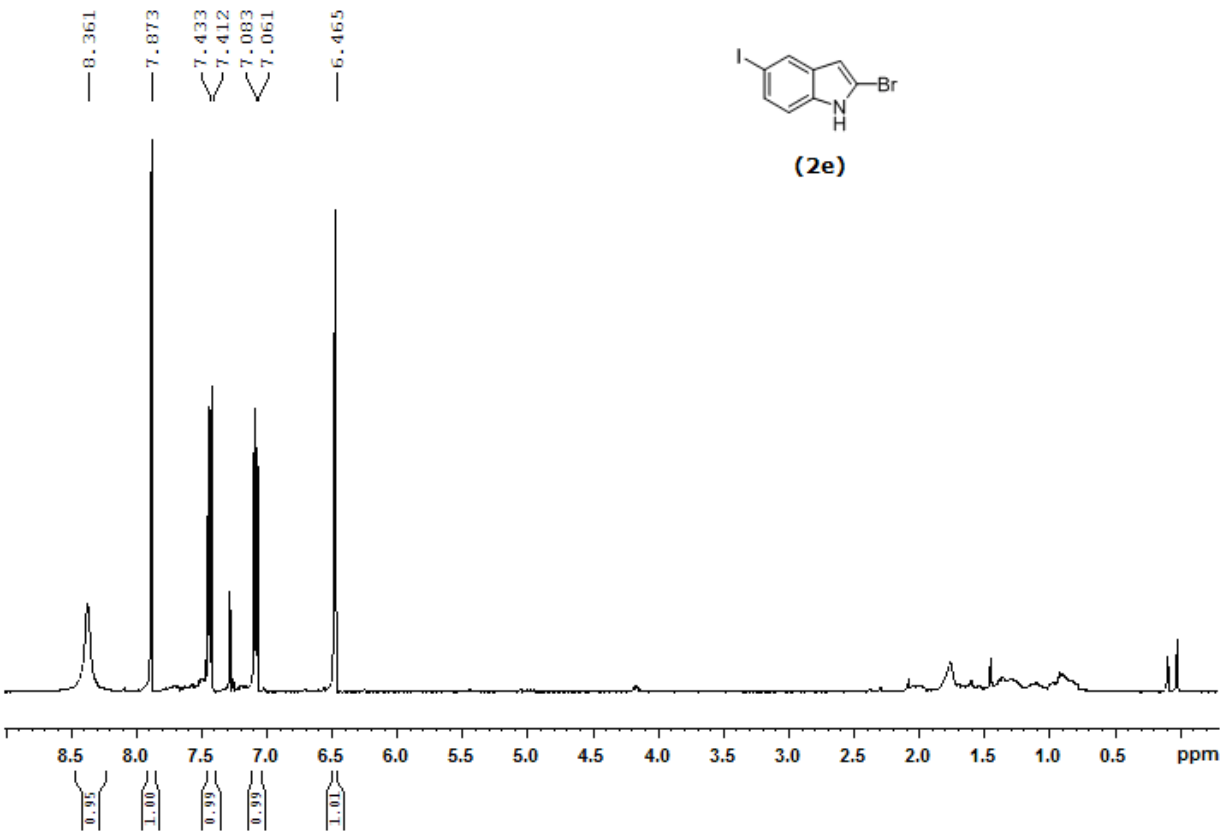

159.332
156.990
132.958
129.093
128.989
111.070
110.974
110.730
110.469
110.245
105.036
104.992
104.841
104.603
77.368
77.051
76.733
F
Br
N
H
(2b)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

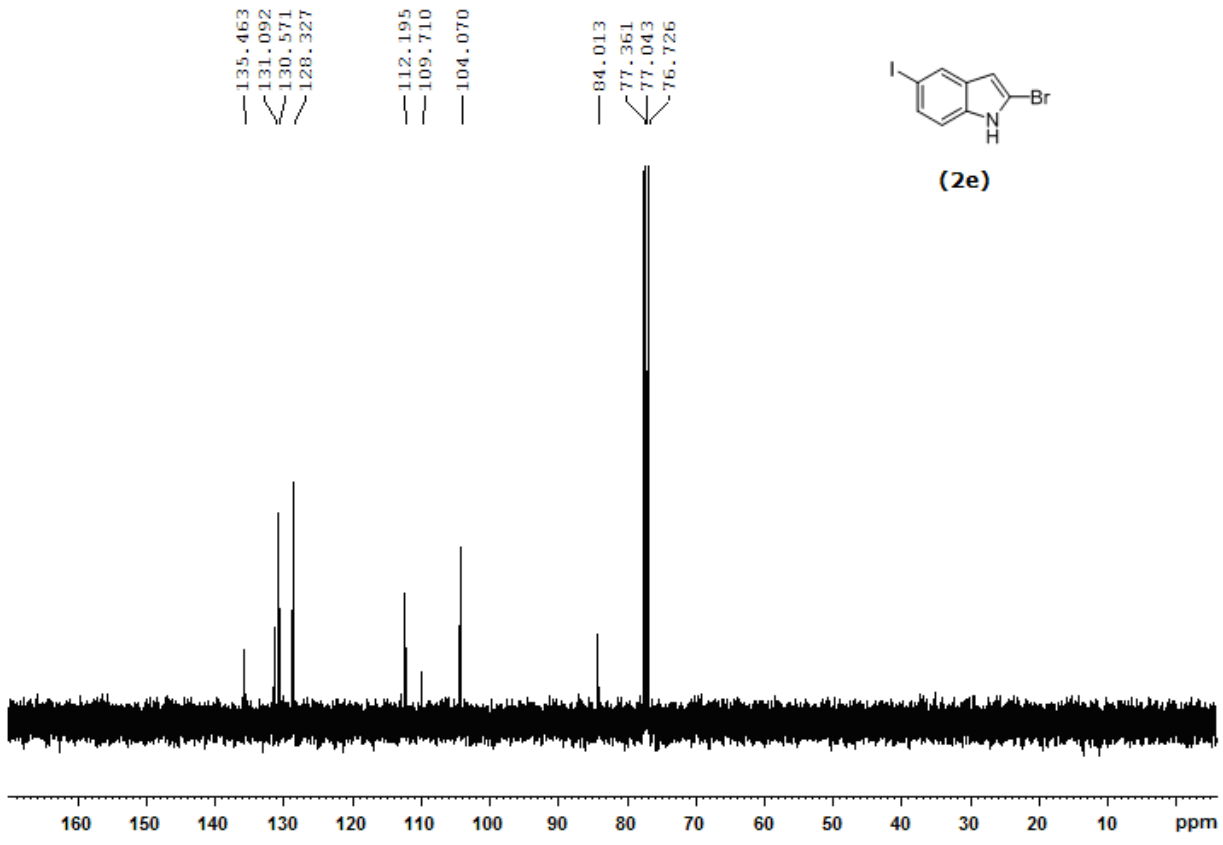

8.175
7.518
7.514
7.234
7.213
7.211
7.152
7.147
7.131
7.126
6.499
6.497
6.492
Cl
Br
N
H
(2c)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.91
1.00
1.02
1.00
0.99

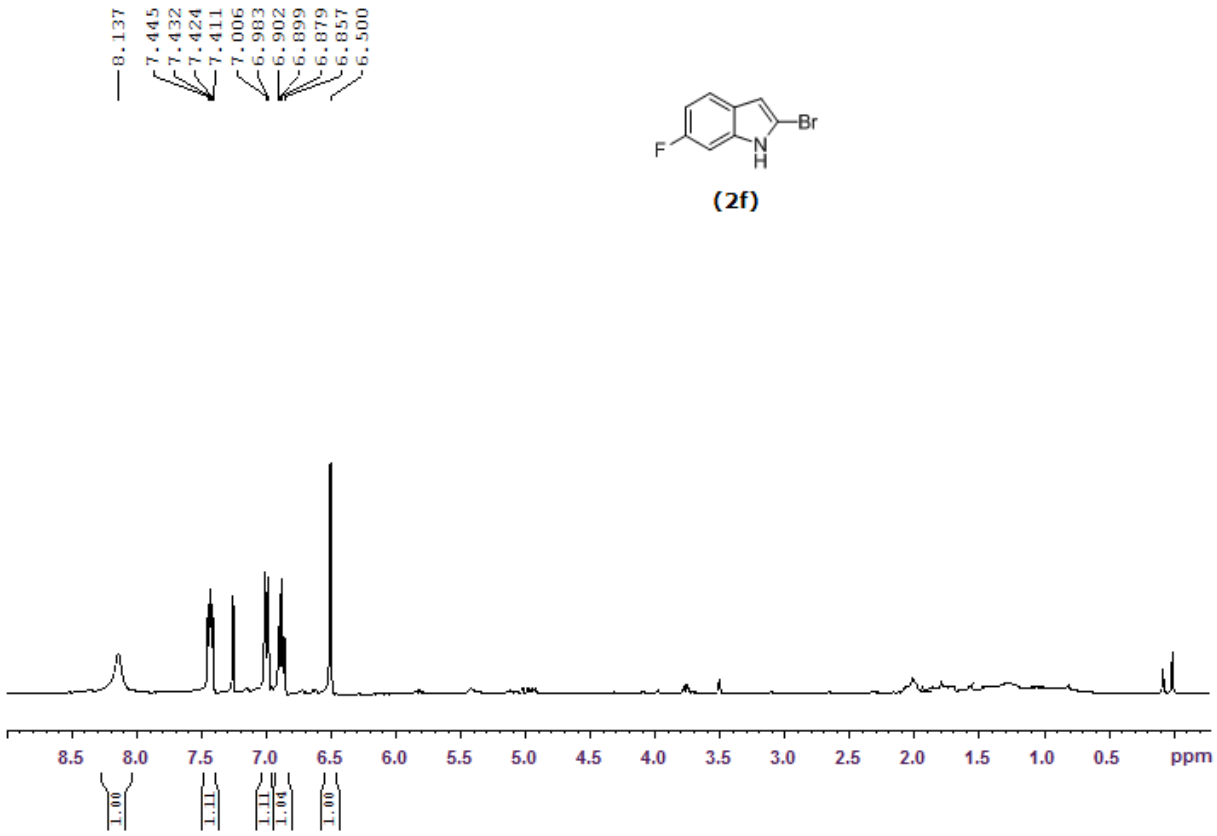

134.709
129.654
126.235
122.555
119.050
111.269
110.093
104.561
77.318
77.000
76.683
Cl
Br
N
H
(2c)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

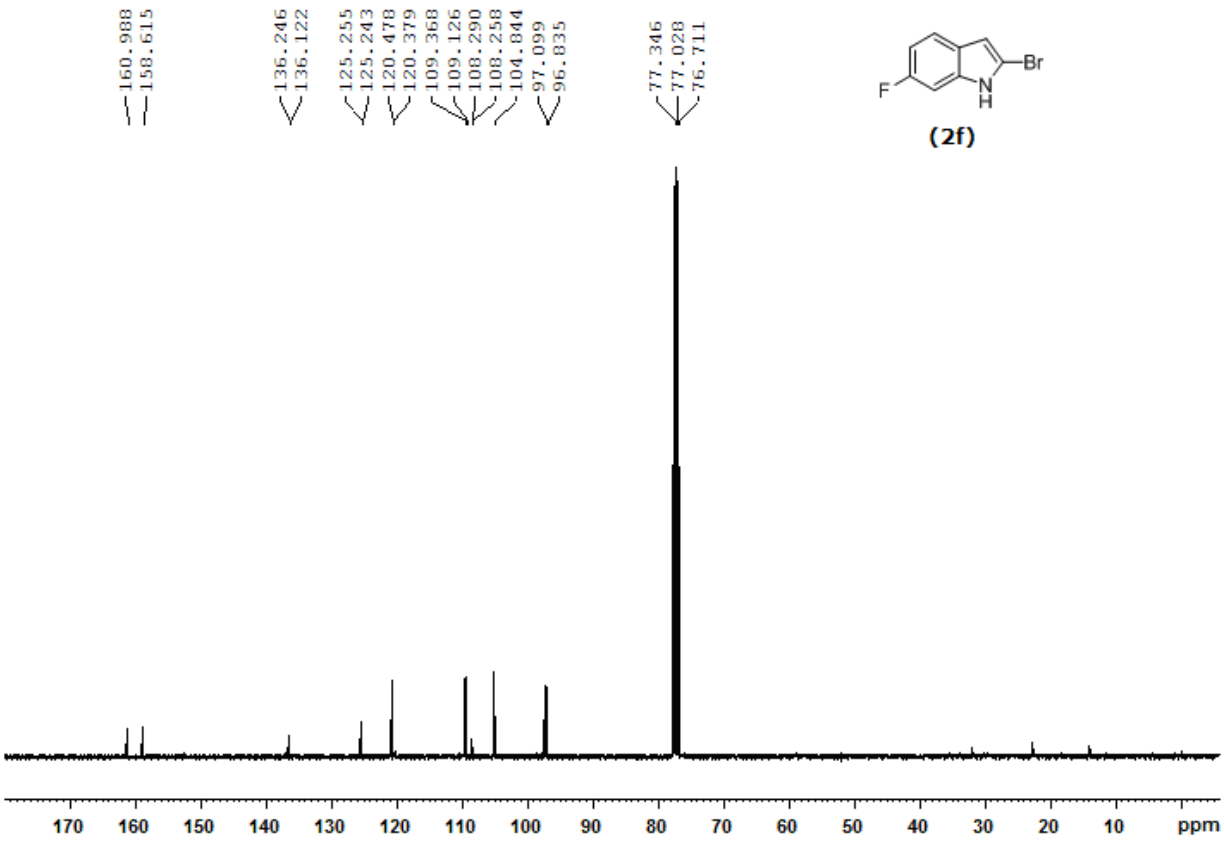

8.235
7.675
7.671
7.281
7.277
7.272
7.260
7.255
7.181
7.160
6.491
6.486
Br
Br
N
H
(2d)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.83
1.00
1.08
0.91
0.99

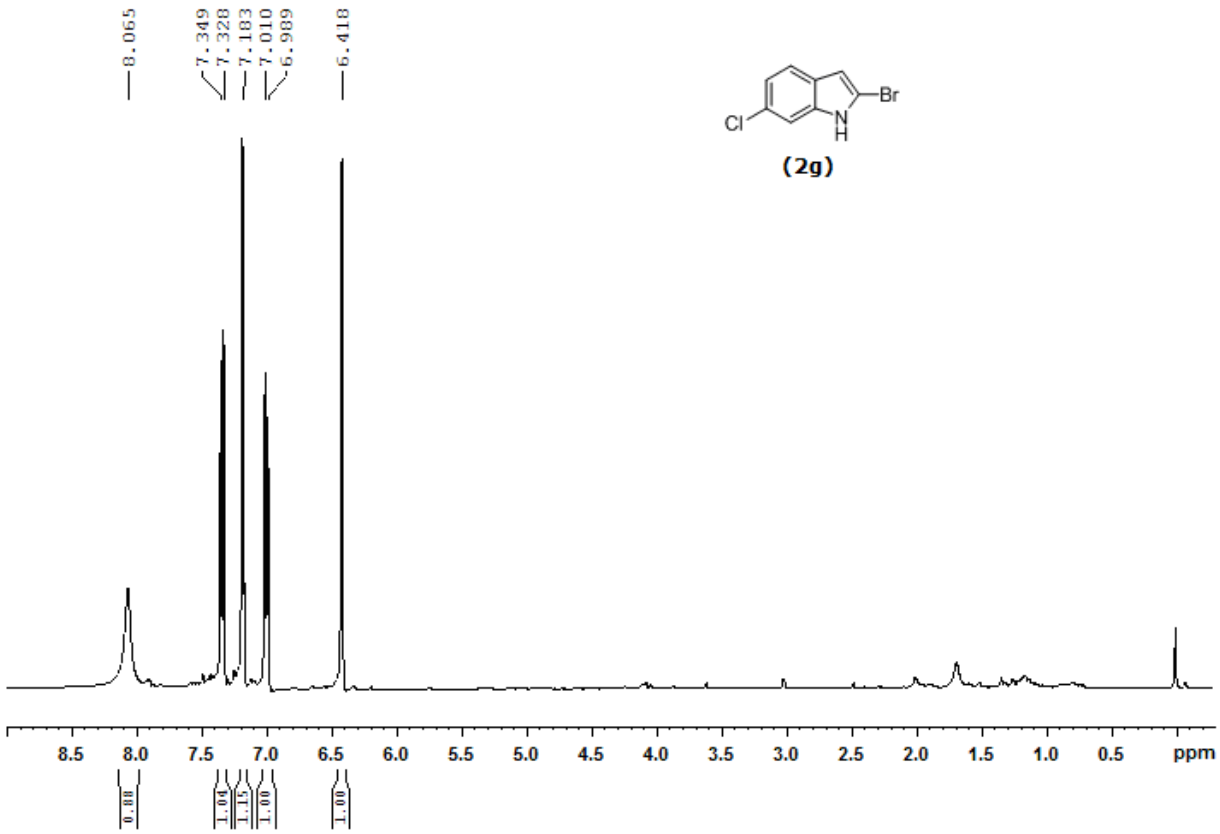

135.005
130.301
125.121
122.120
113.772
111.748
110.058
104.433
77.383
77.065
76.748
Br
Br
N
H
(2d)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

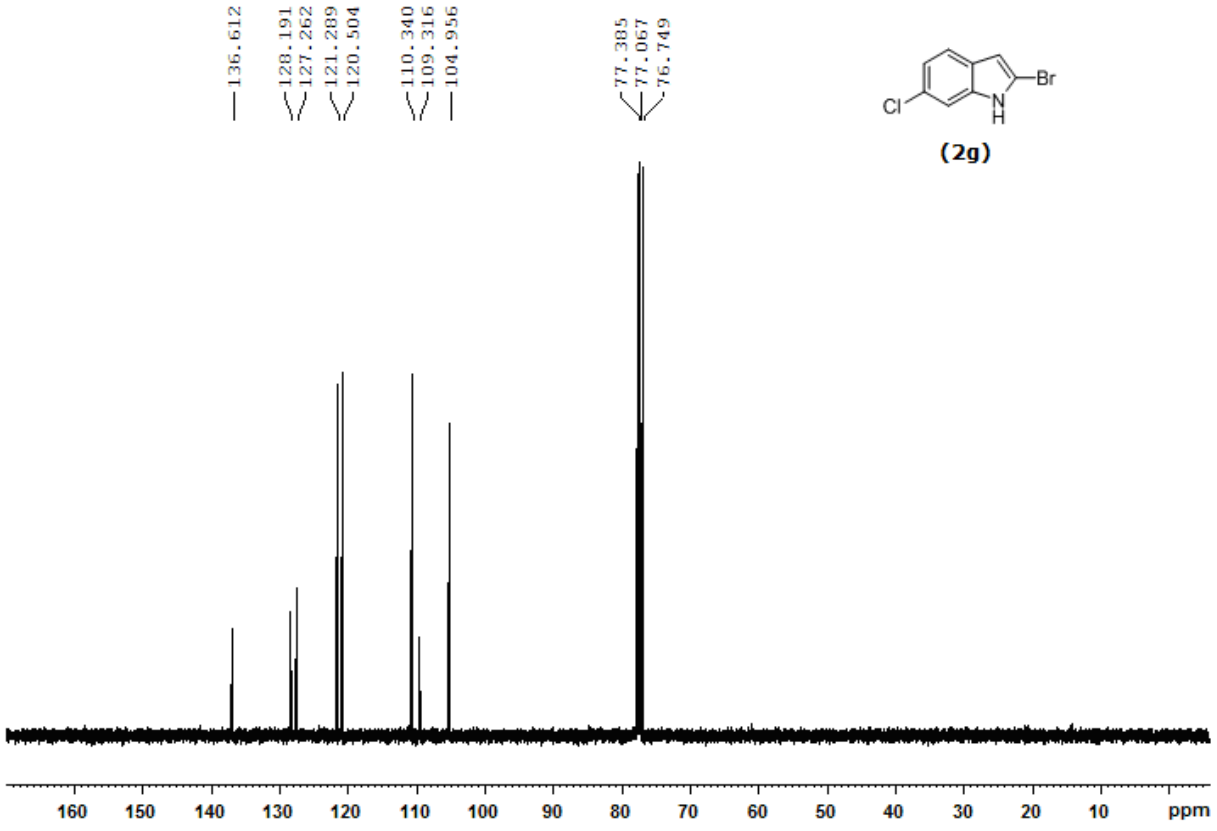

8.361
7.873
7.433
7.412
7.083
7.061
6.465
I
Br
N
H
(2e)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.95
1.00
0.99
0.99
1.01

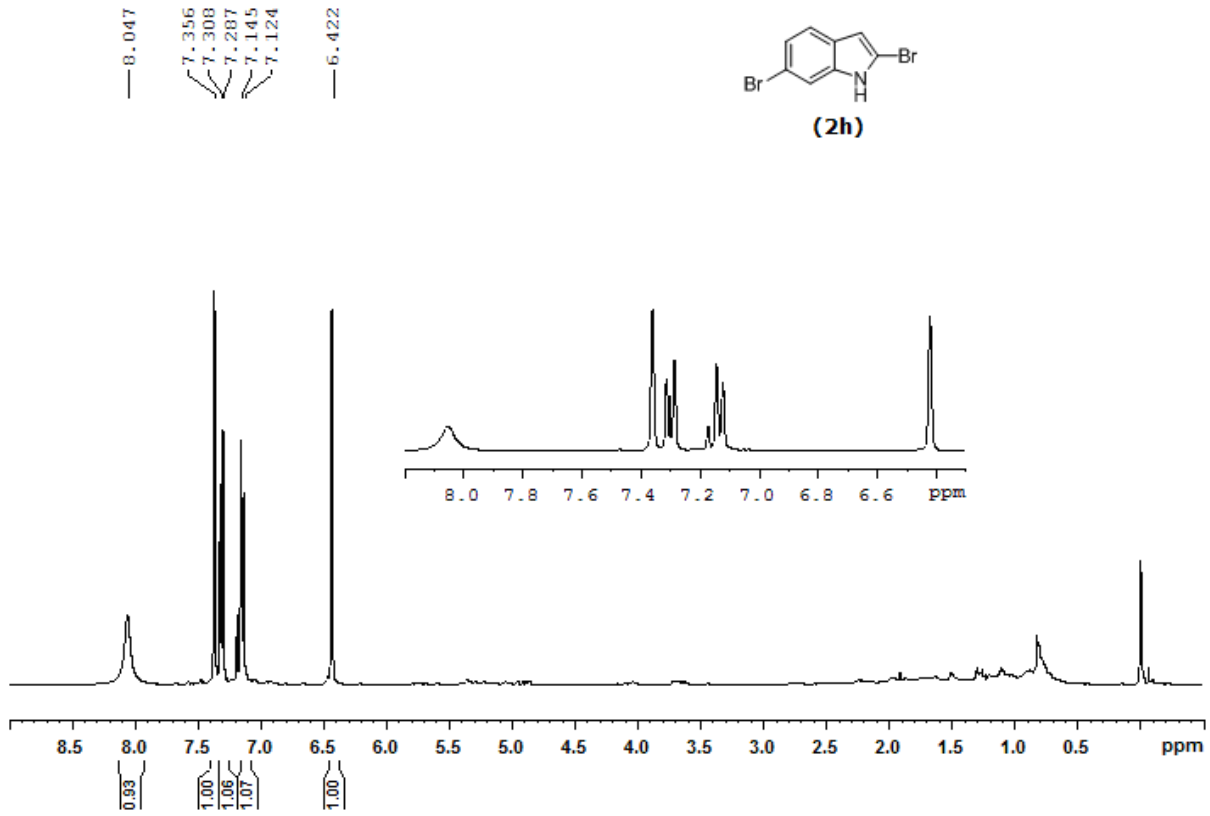

135.463
131.092
130.571
128.327
112.195
109.710
104.070
84.013
77.361
77.043
76.726
I
Br
N
H
(2e)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

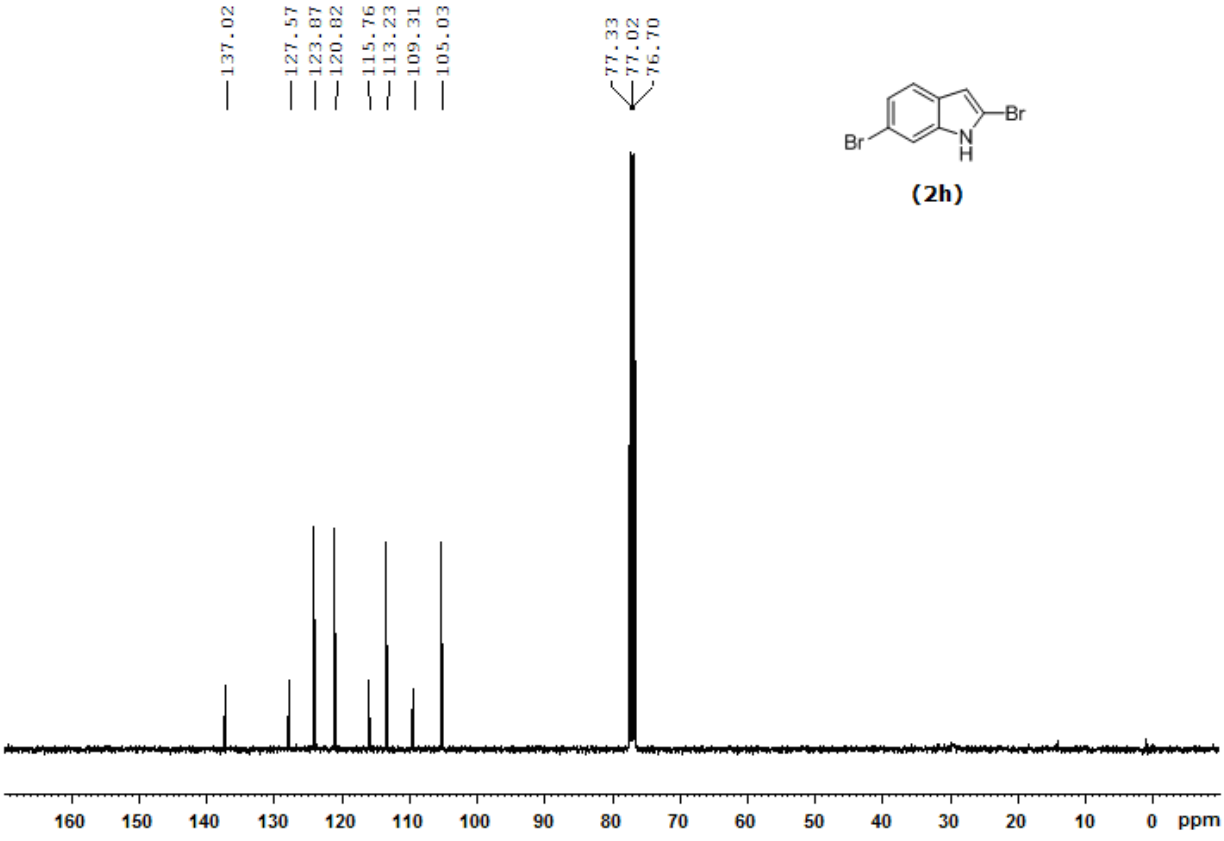

8.137
7.445
7.432
7.424
7.411
7.006
6.983
6.902
6.899
6.879
6.857
6.500
F
Br
N
H
(2f)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.11
1.11
1.04
1.00

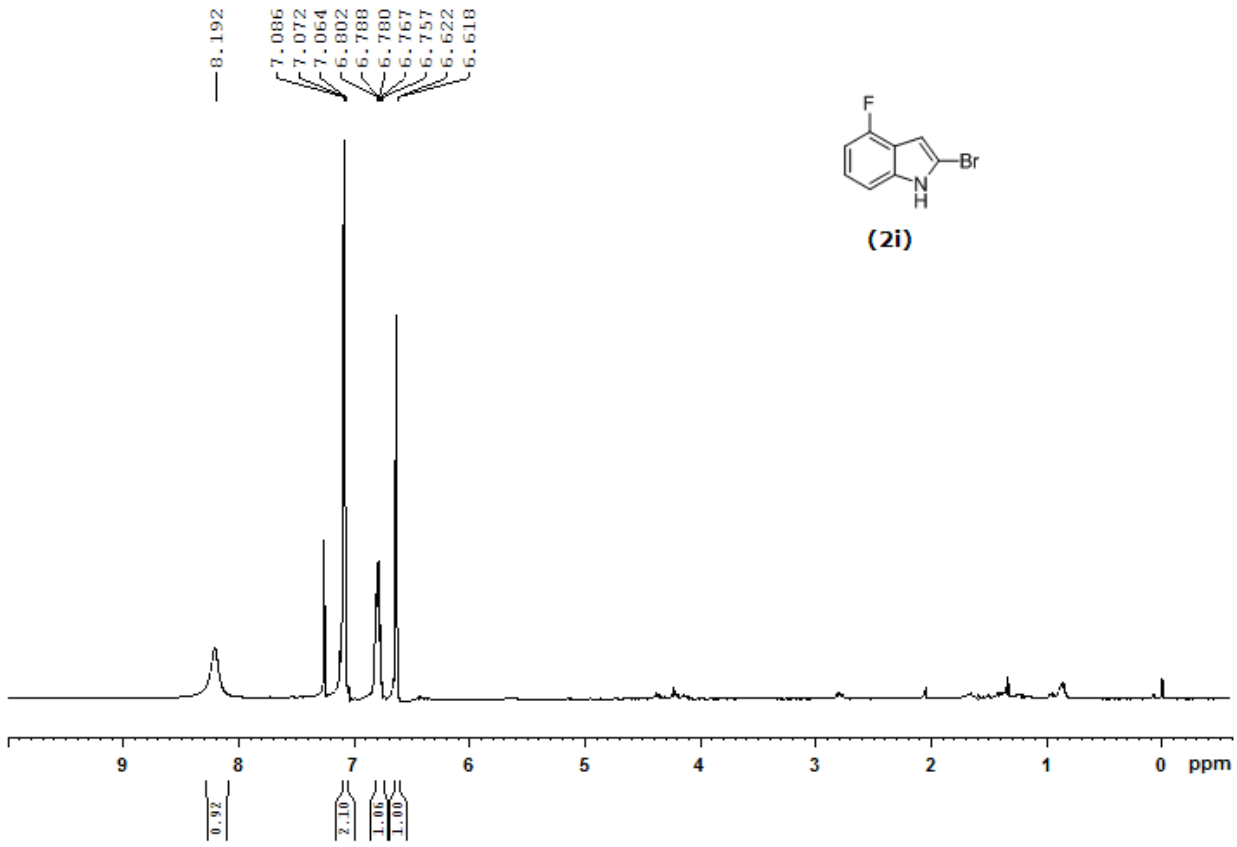

160.988
158.615
136.246
136.122
125.255
125.243
120.478
120.379
109.368
109.126
108.290
108.258
104.844
97.099
96.835
77.346
77.028
76.711
F
Br
N
H
(2f)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

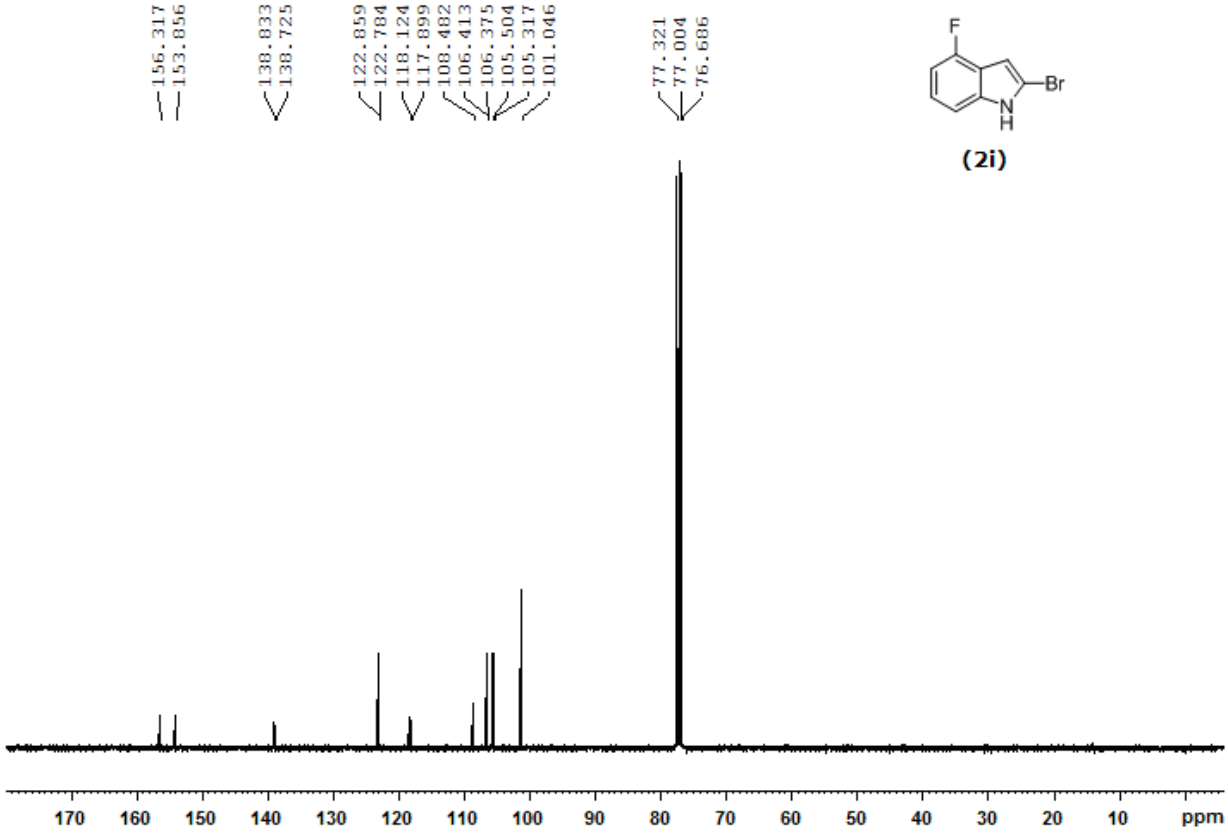

8.065
7.349
7.328
7.183
7.010
6.989
6.418
Cl
Br
N
H
(2g)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.88
1.04
1.15
1.00
1.00

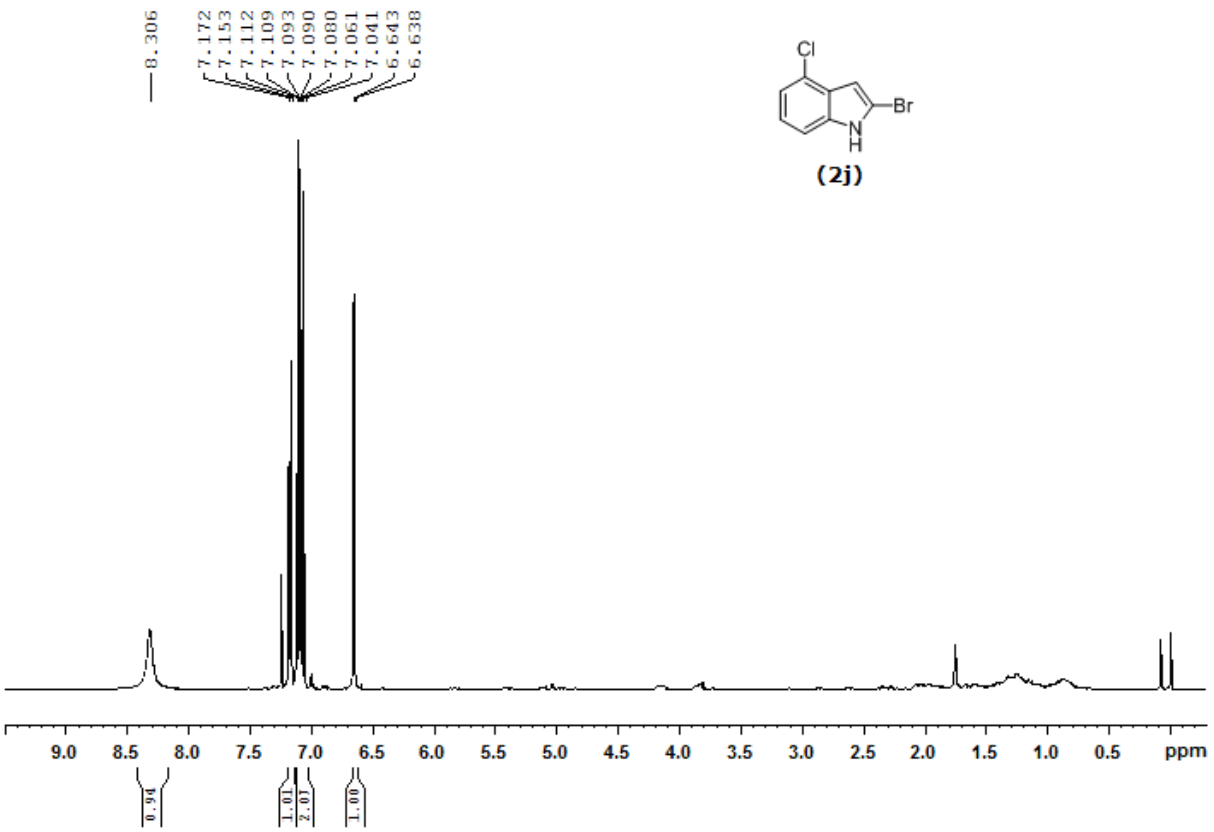

136.612
128.191
127.262
121.289
120.504
110.340
109.316
104.956
77.385
77.067
76.749
Cl
Br
N
H
(2g)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

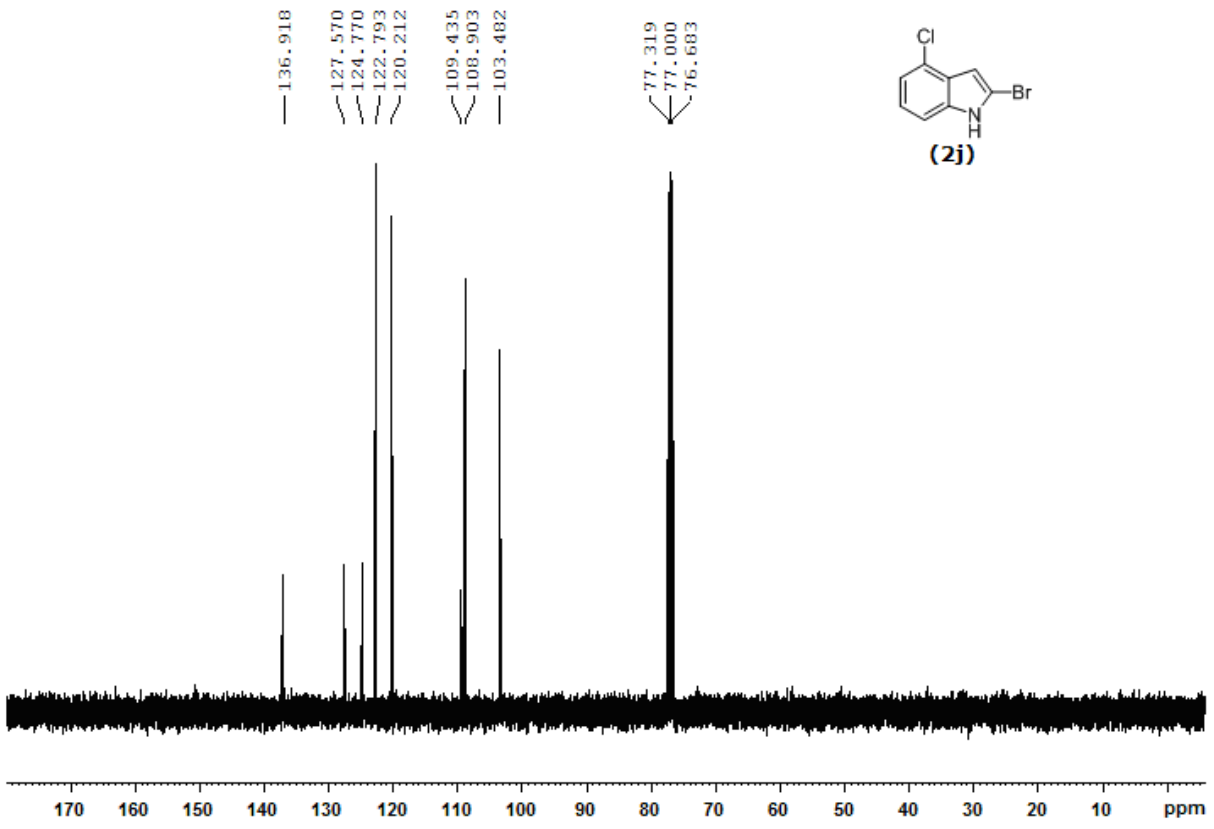

8.047
7.356
7.308
7.287
7.145
7.124
6.422
Br
Br
N
H
(2h)
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.93
1.00
1.06
1.07
1.00

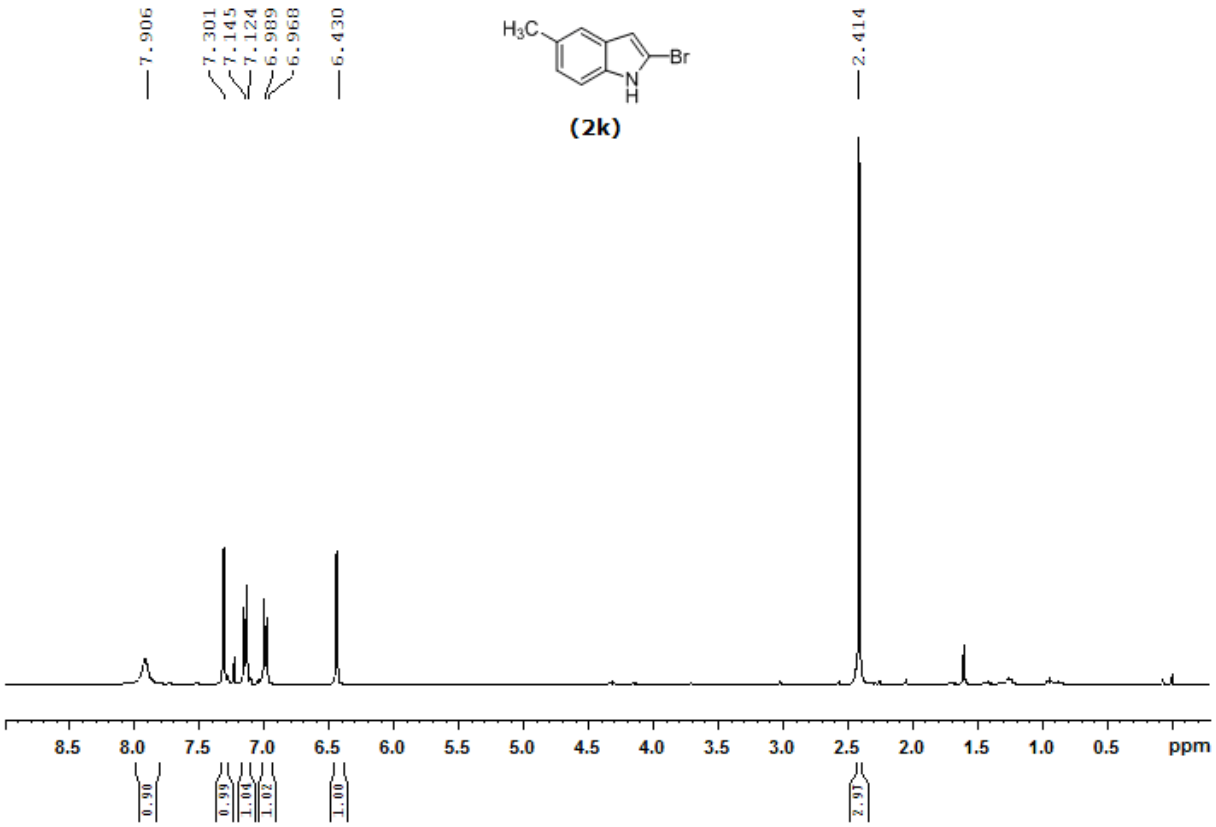

137.02
127.57
123.87
120.82
115.76
113.23
109.31
105.03
77.33
77.02
76.70
Br
Br
N
H
(2h)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

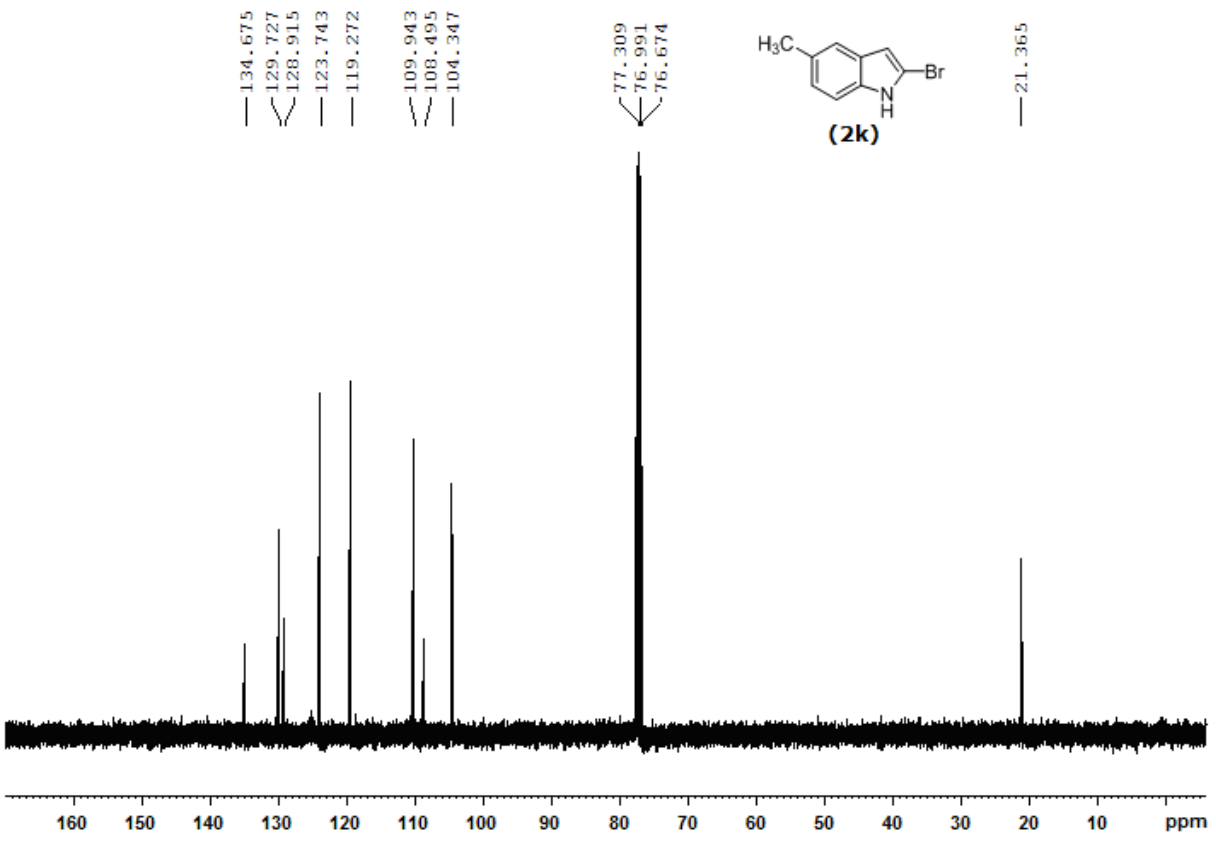

8.192
7.086
7.072
7.064
6.802
6.788
6.780
6.767
6.757
6.622
6.618
F
Br
N
H
(2i)
9
8
7
6
5
4
3
2
1
0
ppm
0.92
2.10
1.06
1.00

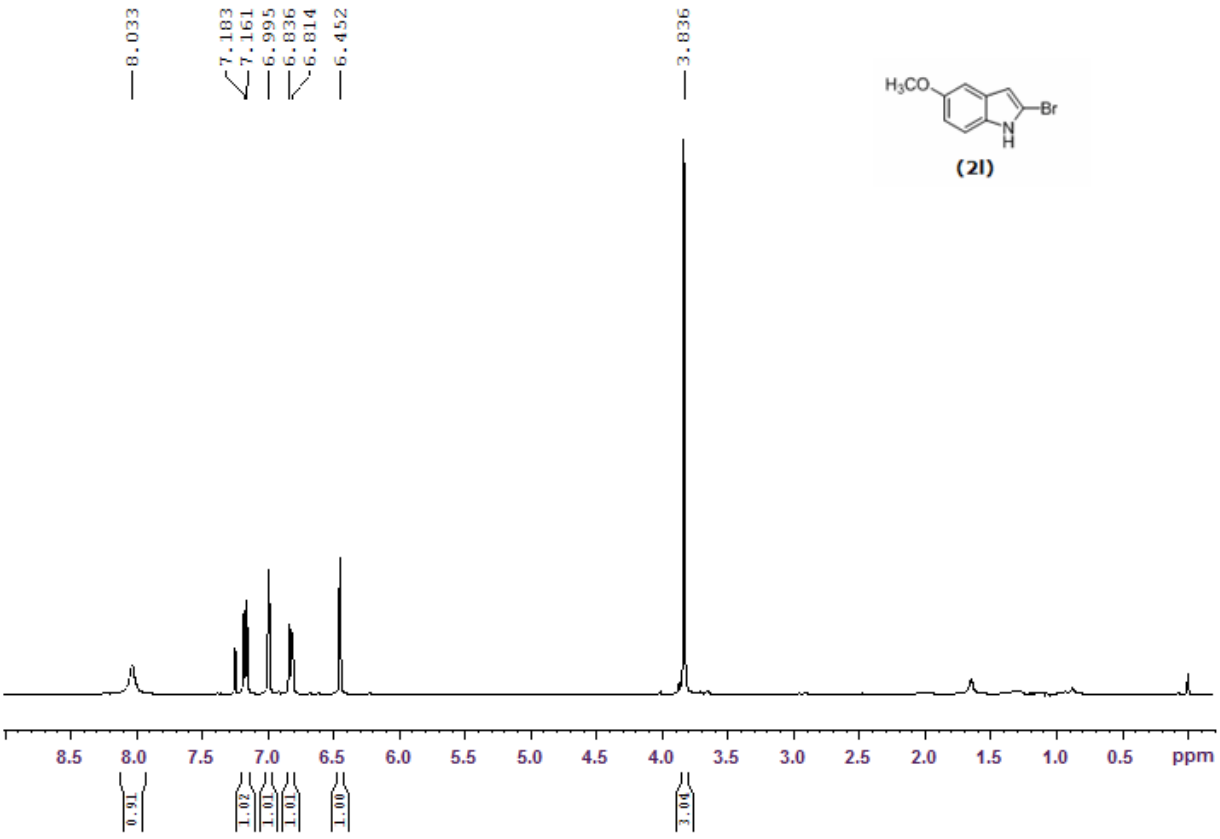

156.317
153.856
138.833
138.725
122.859
122.784
118.124
117.899
108.482
106.413
106.375
105.504
105.317
101.046
77.321
77.004
76.686
F
Br
N
H
(2i)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

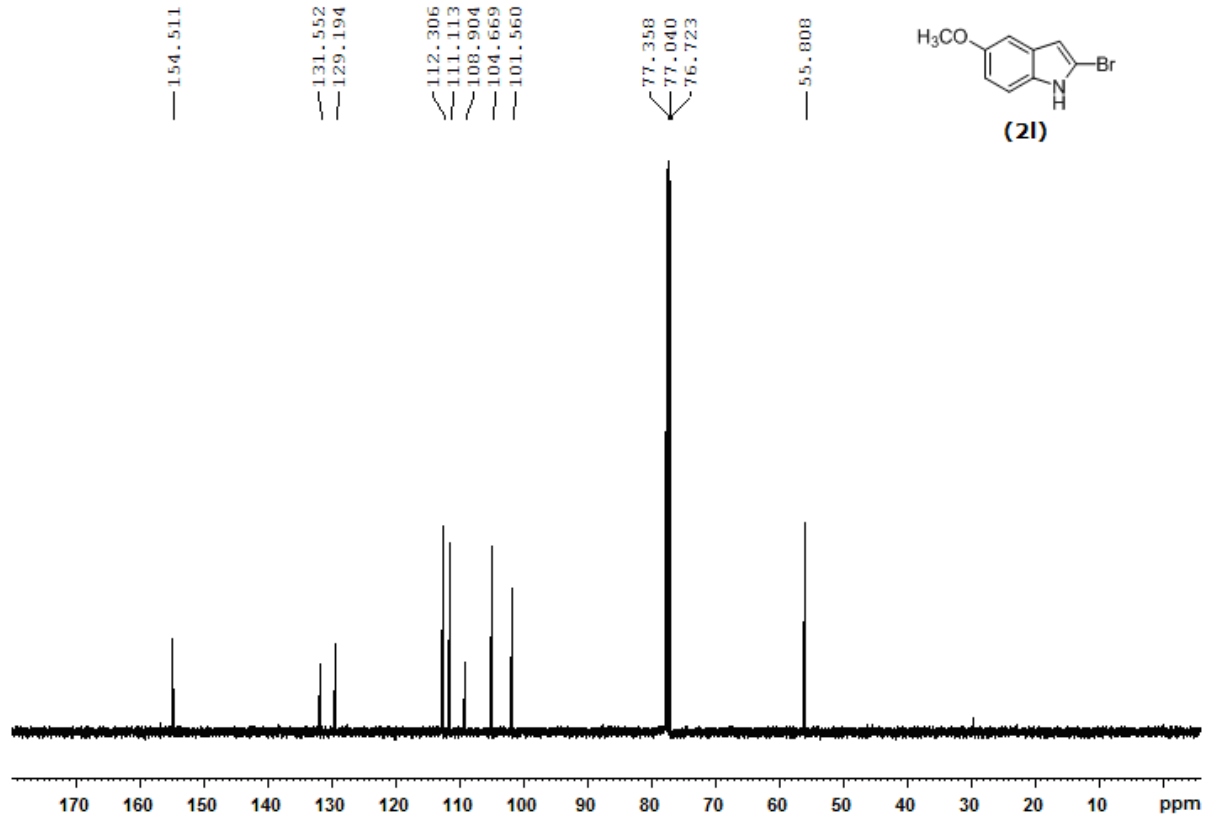

8.306
7.172
7.153
7.112
7.109
7.093
7.090
7.080
7.061
7.041
6.643
6.638
Cl
Br
N
H
(2j)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.94
1.01
2.01
1.00

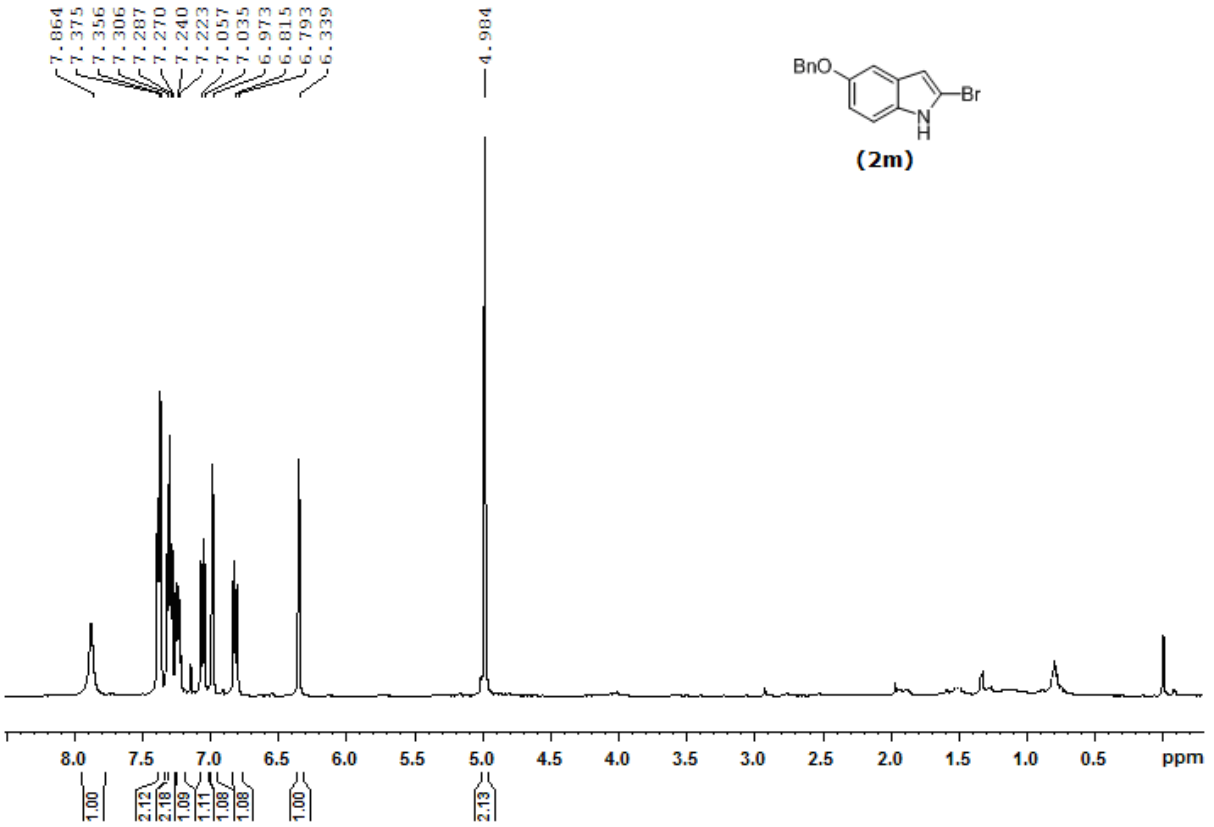

136.918
127.570
124.770
122.793
120.212
109.435
108.903
103.482
77.319
77.000
76.683
Cl
Br
N
H
(2j)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

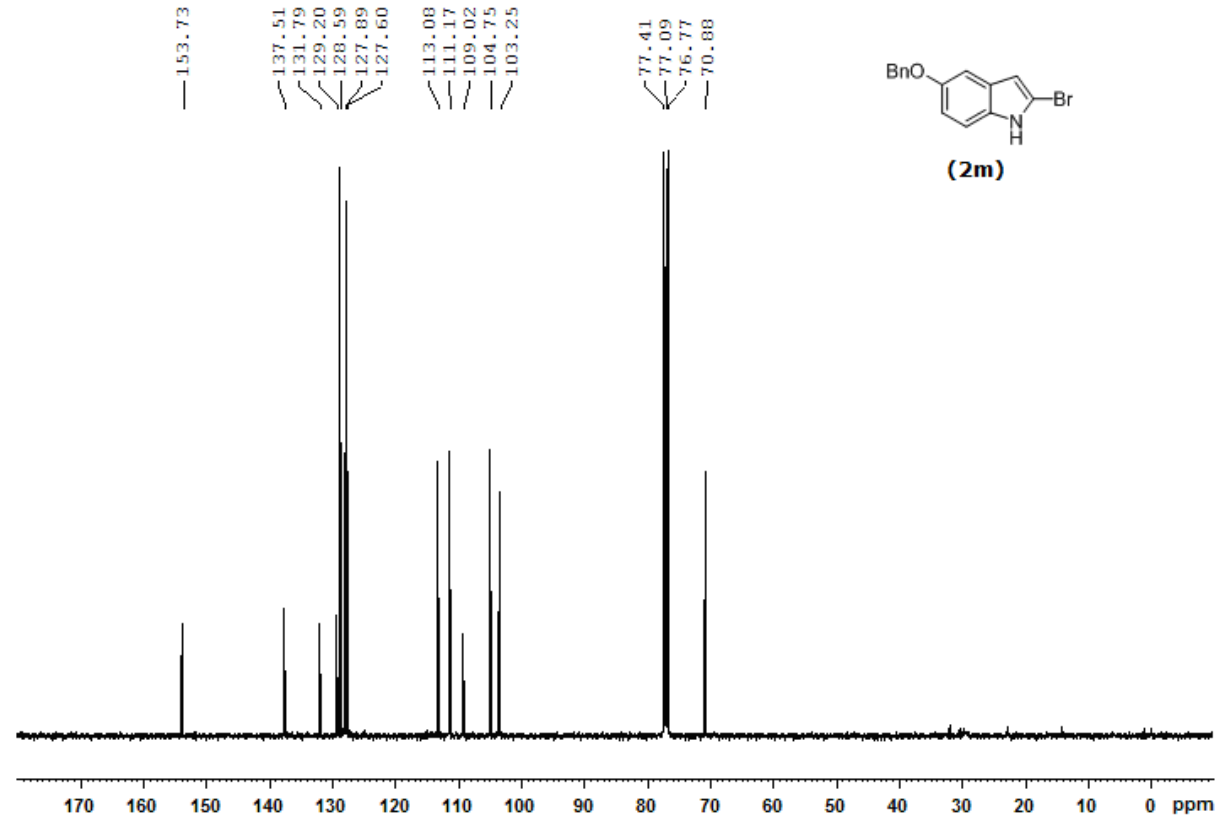

7.906
7.301
7.145
7.124
6.989
6.968
6.430
2.414
H3C
Br
N
H
(2k)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.90
0.99
1.04
1.02
1.00
2.91

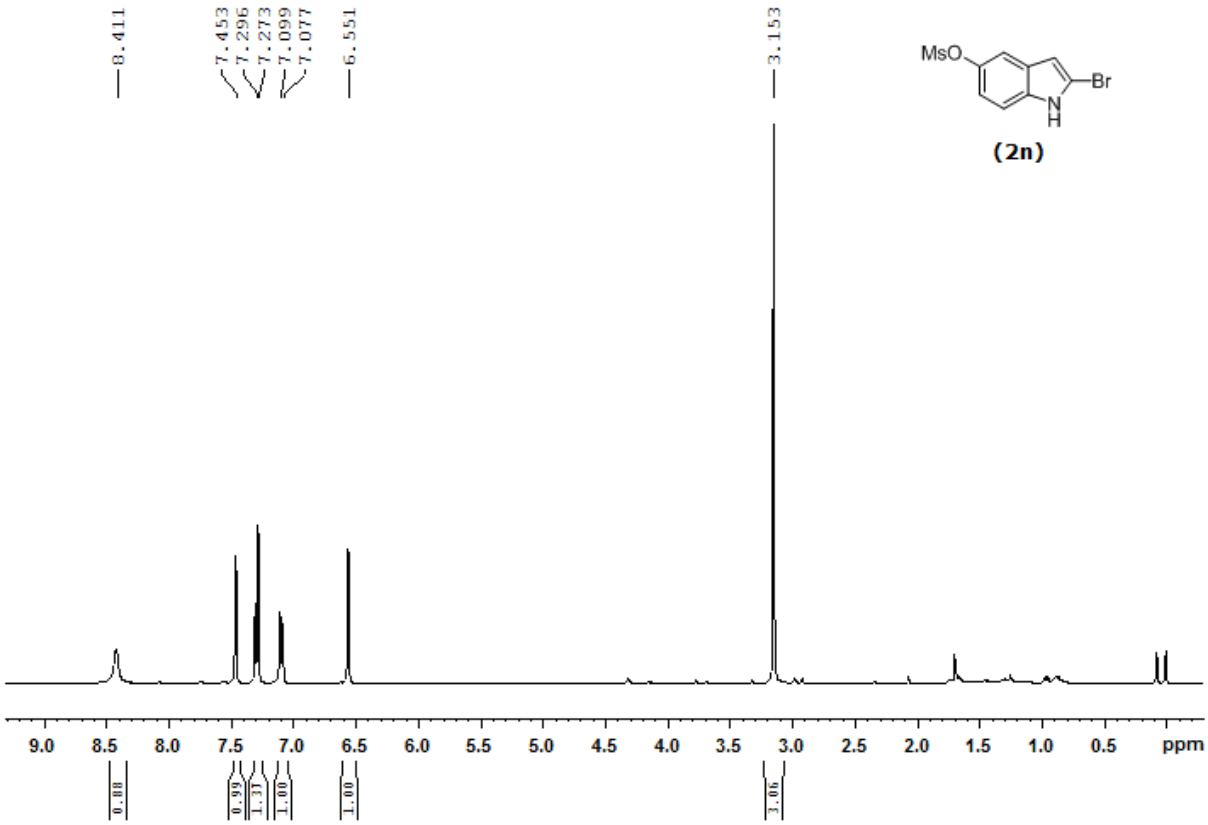

134.675
129.727
128.915
123.743
119.272
109.943
108.495
104.347
77.309
76.991
76.674
21.365
H3C
Br
N
H
(2k)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

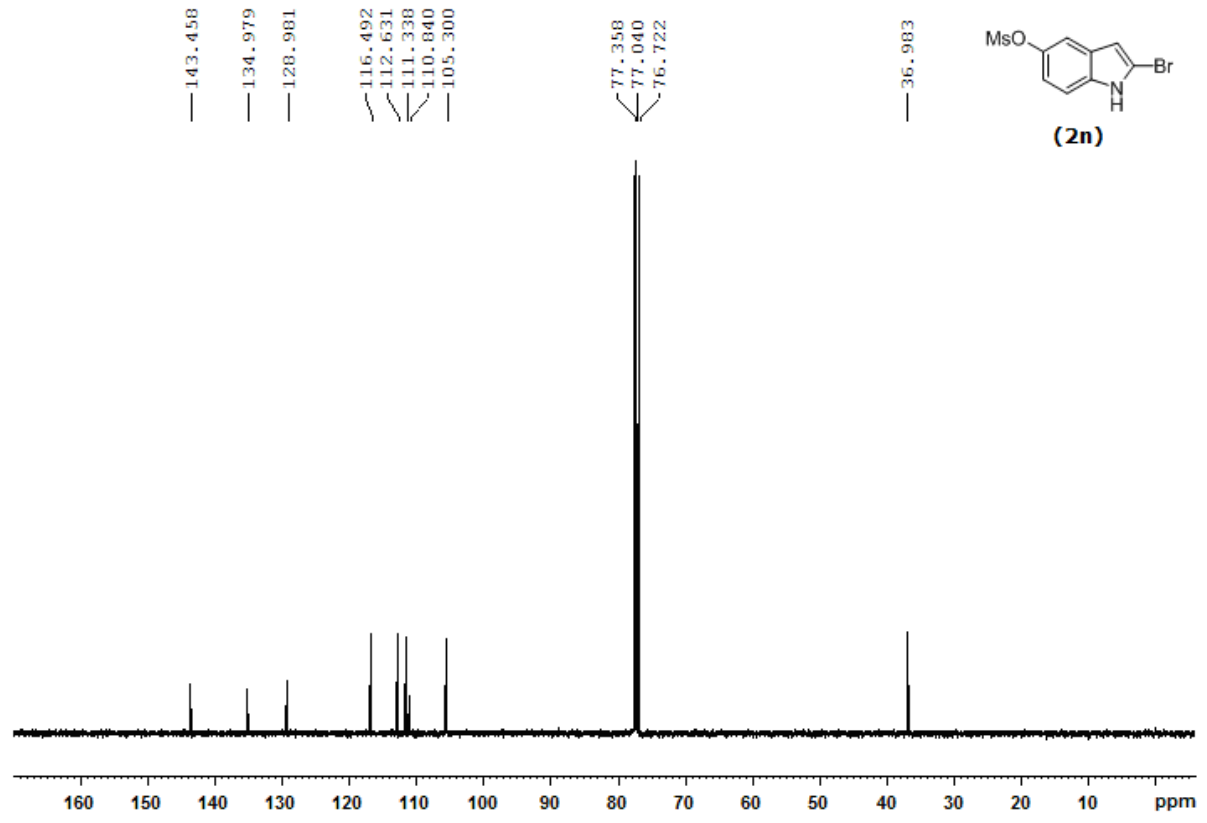

8.033
7.183
7.161
6.995
6.836
6.814
6.452
3.836
H3CO
Br
N
H
(2l)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.91
1.02
1.01
1.01
1.00
3.04

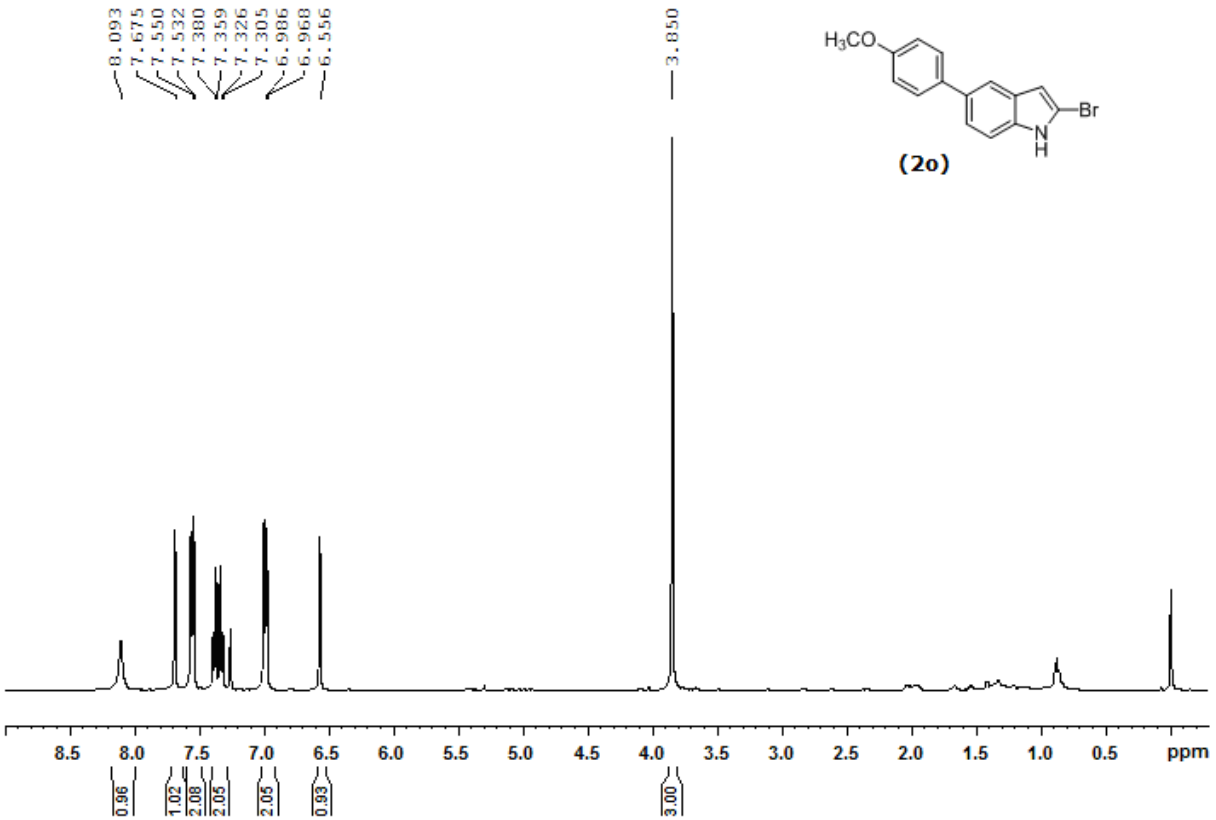

154.511
131.552
129.194
112.306
111.113
108.904
104.669
101.560
77.358
77.040
76.723
55.808
H3CO
Br
N
H
(2l)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

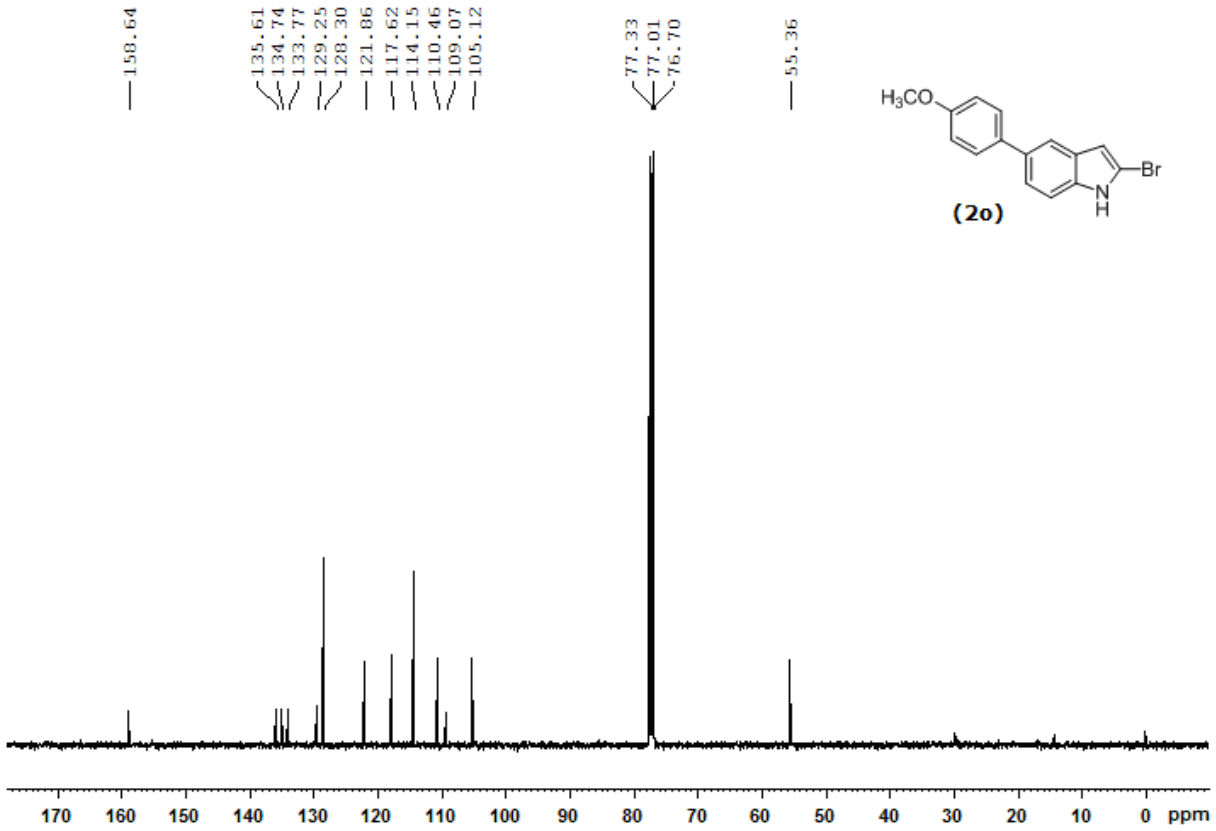

7.864
7.375
7.356
7.306
7.287
7.270
7.240
7.223
7.057
7.035
6.973
6.815
6.793
6.339
4.984
BnO
Br
N
H
(2m)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
2.12
2.18
1.09
1.11
1.08
1.08
1.00
2.13

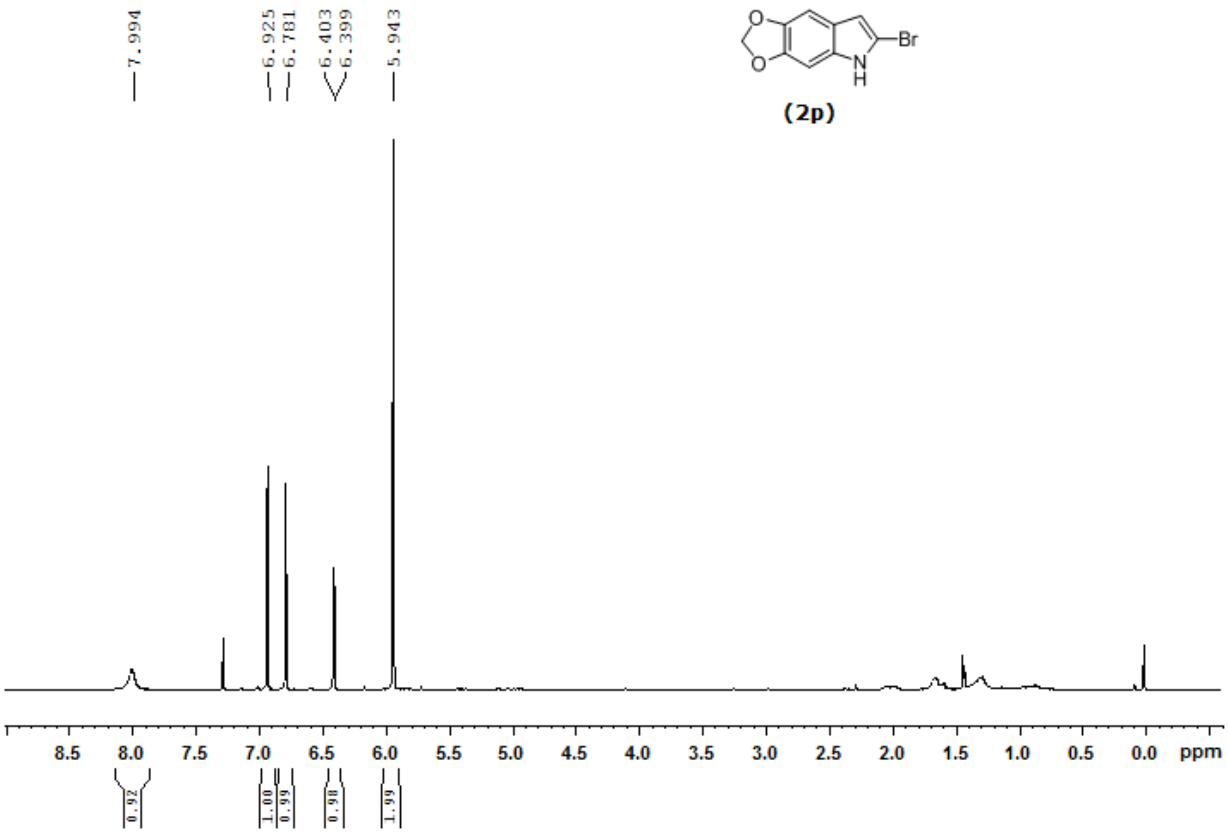

153.73
137.51
131.79
129.20
128.59
127.89
127.60
113.08
111.17
109.02
104.75
103.25
77.41
77.09
76.77
70.88
BnO
Br
N
H
(2m)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

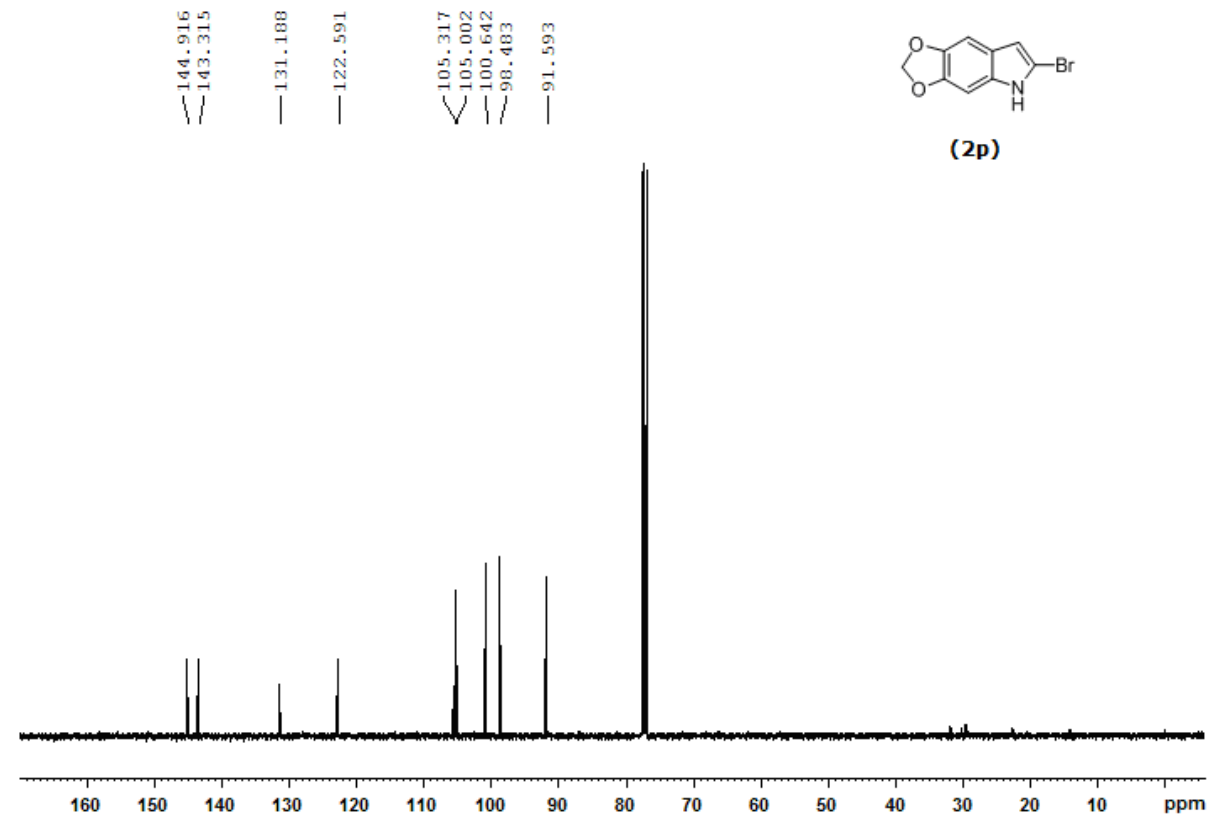

8.411
7.453
7.296
7.273
7.099
7.077
6.551
3.153
MsO
Br
N
H
(2n)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.88
0.99
1.37
1.00
1.00
3.06

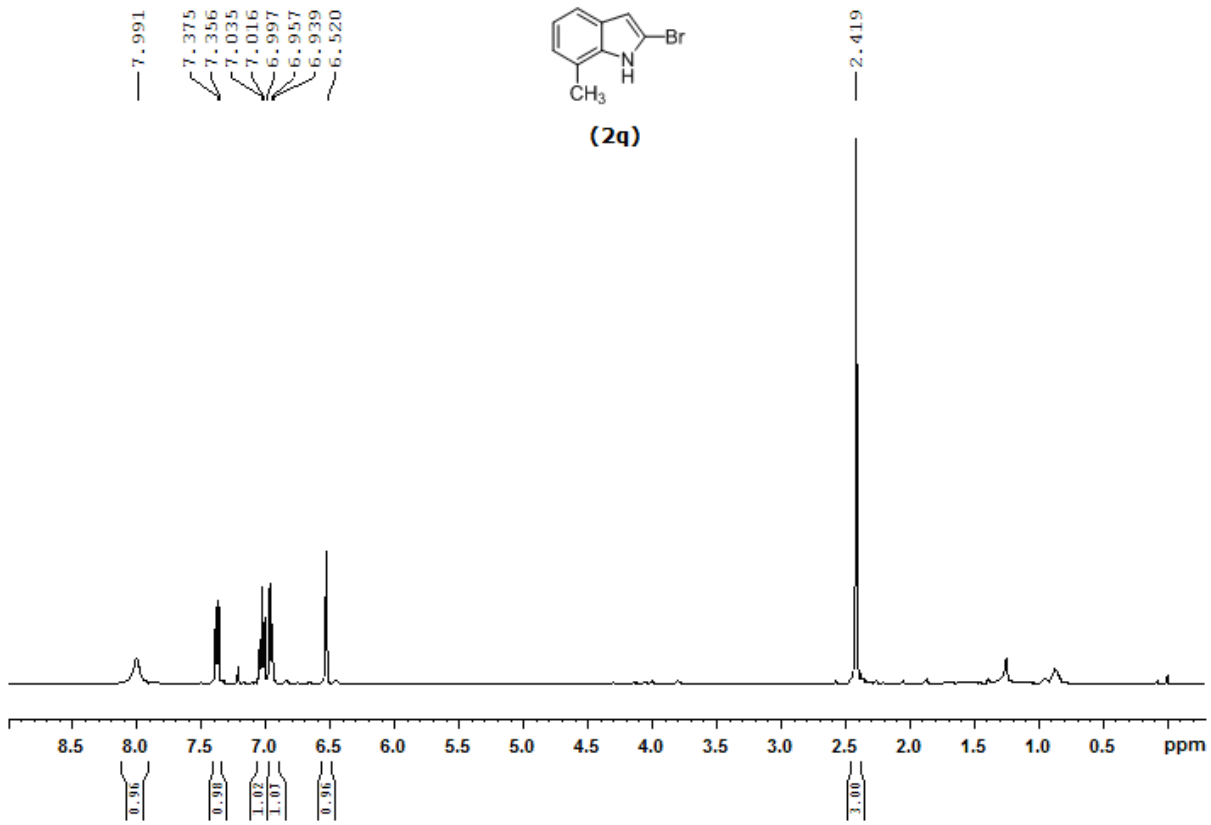

143.458
134.979
128.981
116.492
112.631
111.338
110.840
105.300
77.358
77.040
76.722
36.983
MsO
Br
N
H
(2n)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

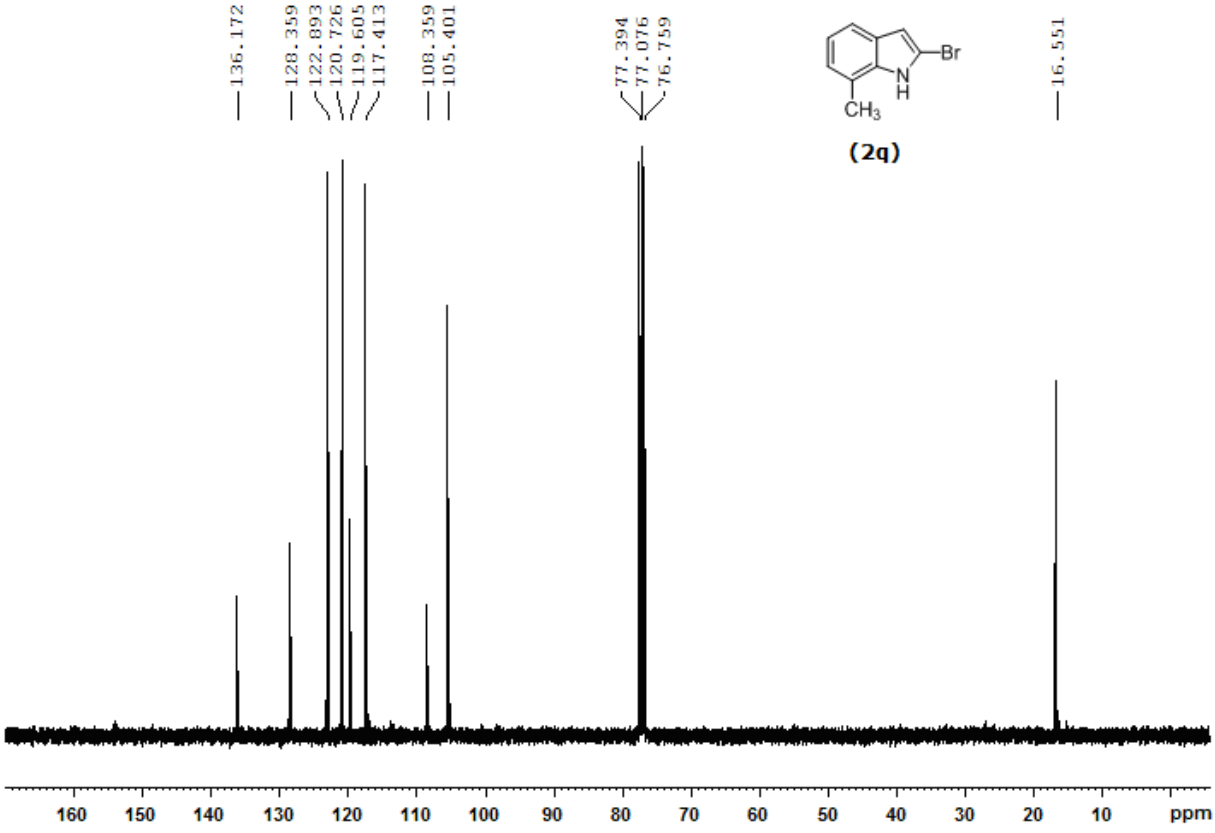

8.093
7.675
7.550
7.532
7.380
7.359
7.326
7.305
6.986
6.968
6.556
3.850
H3CO
Br
N
H
(2o)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.96
1.02
2.08
2.05
2.05
0.93
3.00

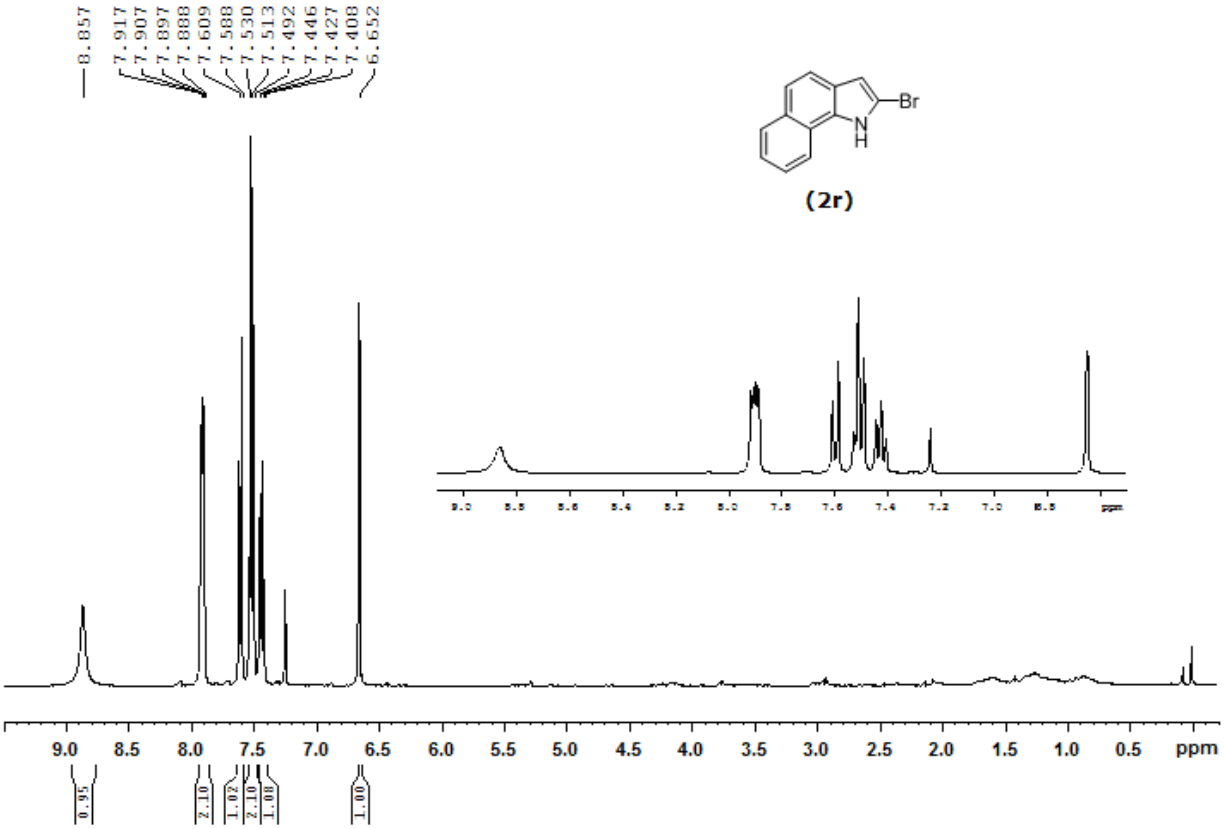

158.64
135.61
134.74
133.77
129.25
128.30
121.86
117.62
114.15
110.46
109.07
105.12
77.33
77.01
76.70
55.36
H3CO
Br
N
H
(2o)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

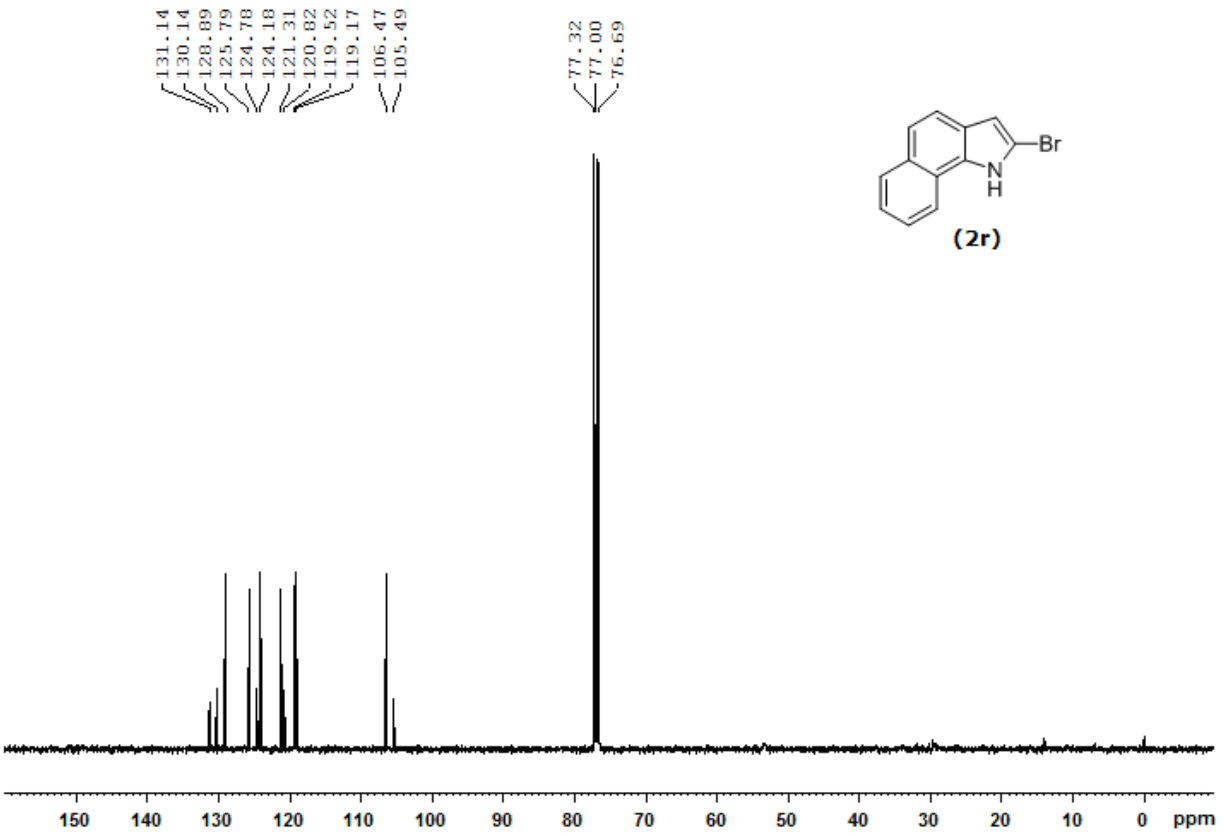

7.994
6.925
6.781
6.403
6.399
5.943
Br
(2p)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.92
1.00
0.99
0.98
1.99

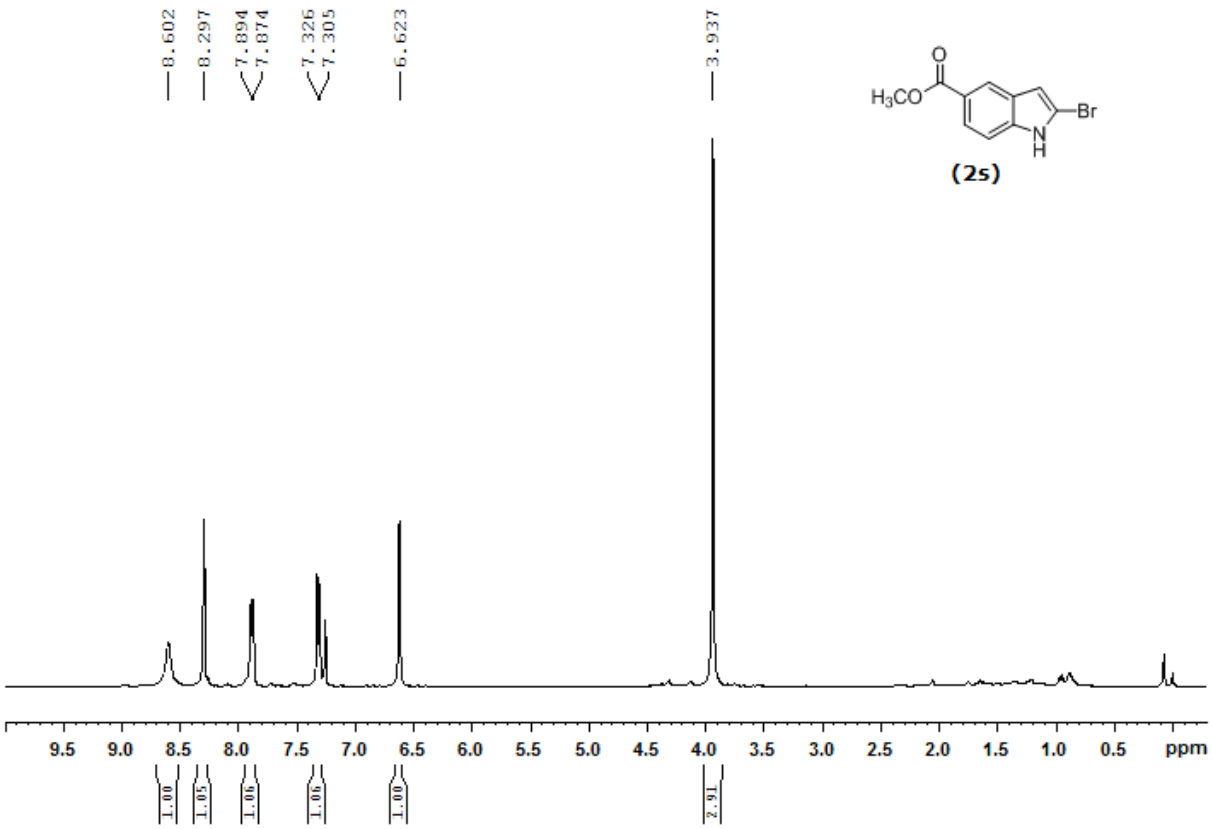

144.916
143.315
131.188
122.591
105.317
105.002
100.642
98.483
91.593
Br
(2p)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

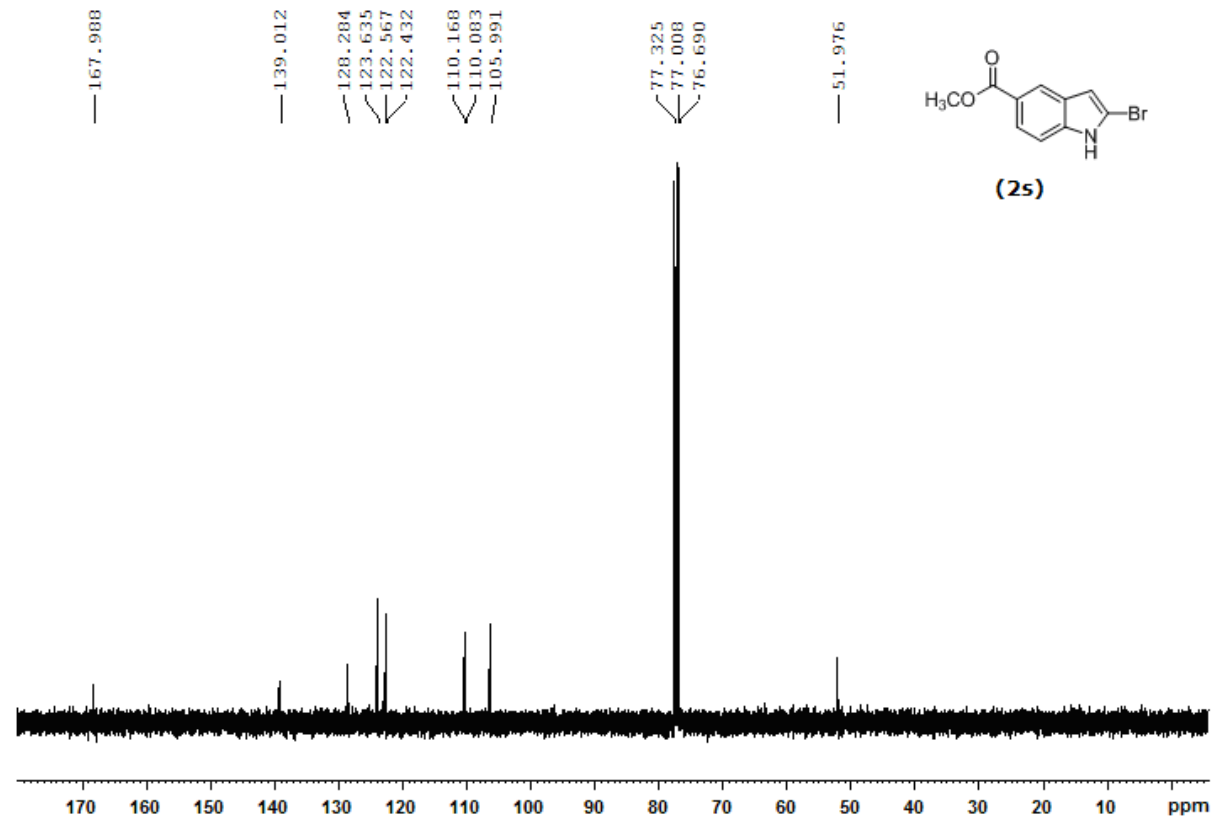

7.991
7.375
7.356
7.035
7.016
6.997
6.957
6.939
6.520
Br
N
H
CH3
(2q)
2.419
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.96
0.98
1.02
1.07
0.96
3.00

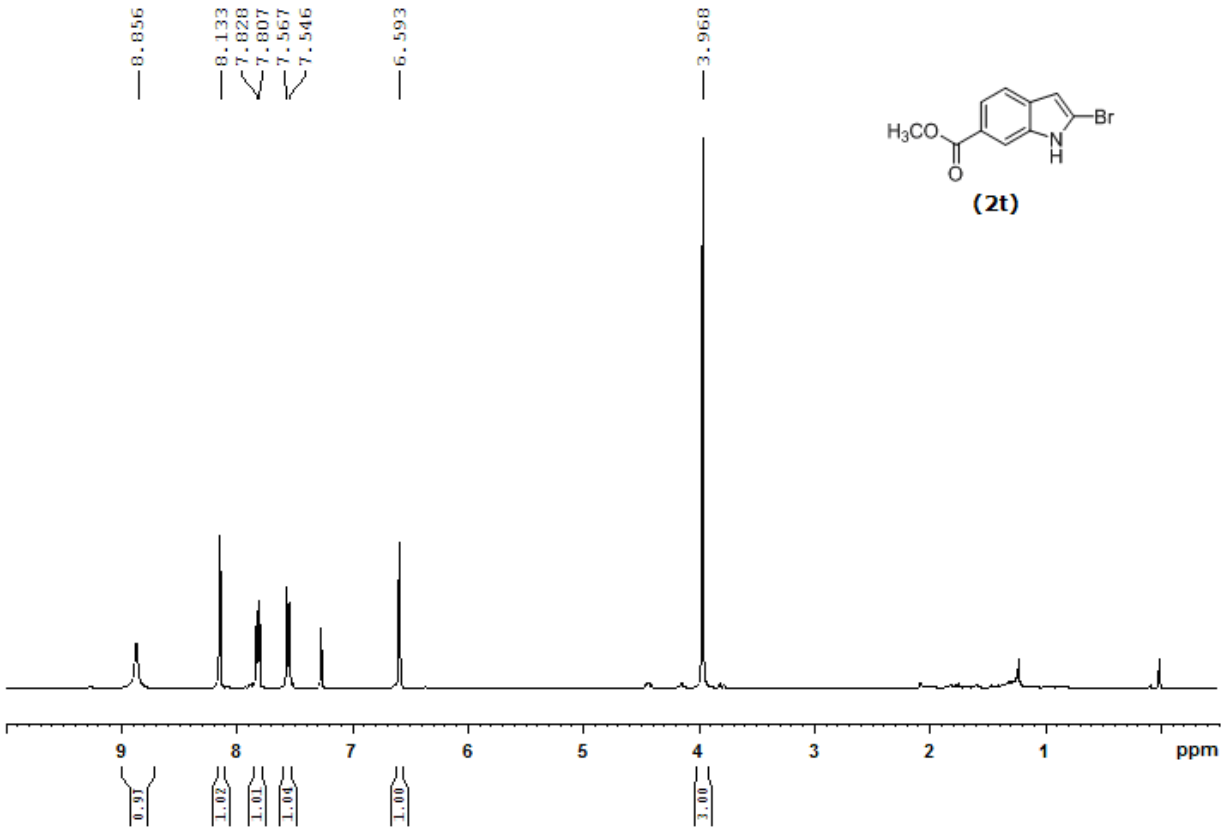

136.172
128.359
122.893
120.726
119.605
117.413
108.359
105.401
77.394
77.076
76.759
Br
N
H
CH3
(2q)
16.551
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

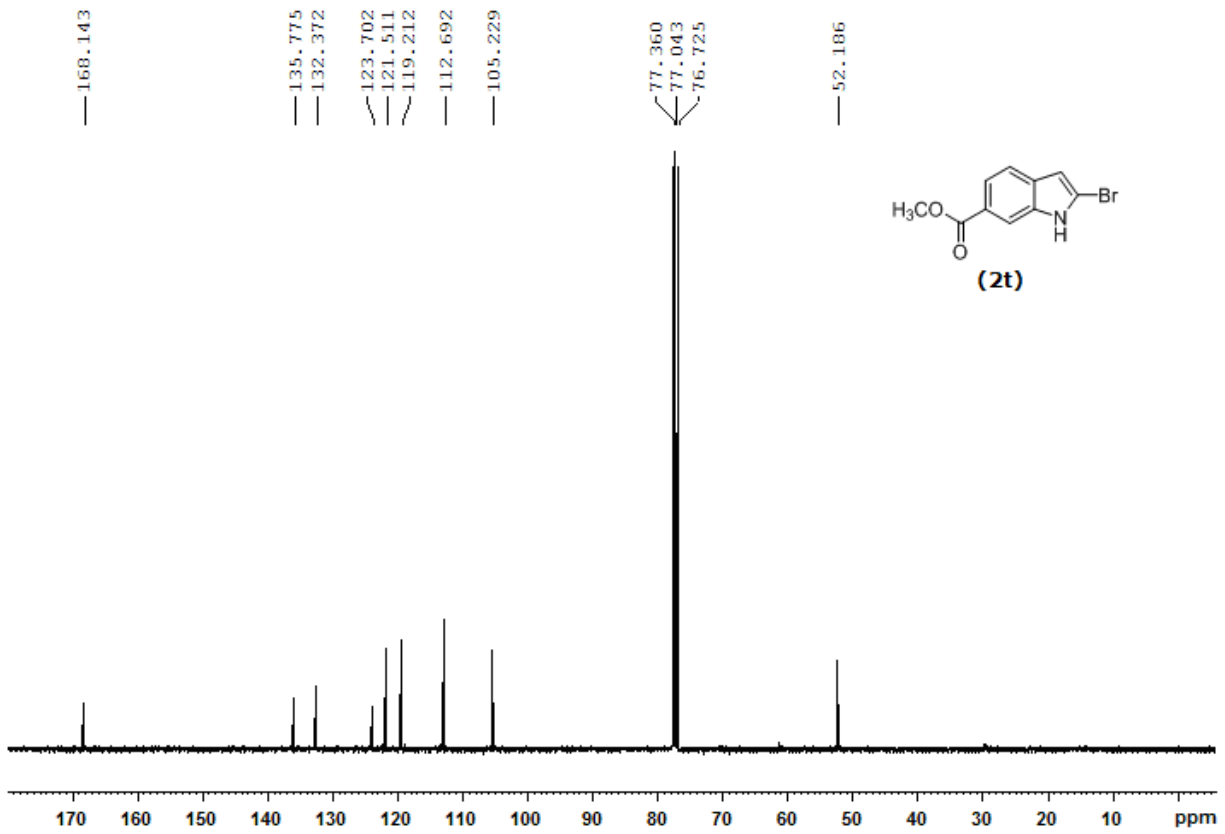

8.857
7.917
7.907
7.897
7.888
7.609
7.588
7.530
7.513
7.492
7.446
7.427
7.408
6.652
Br
N
H
(2r)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.95
2.10
1.02
2.10
1.00
1.00

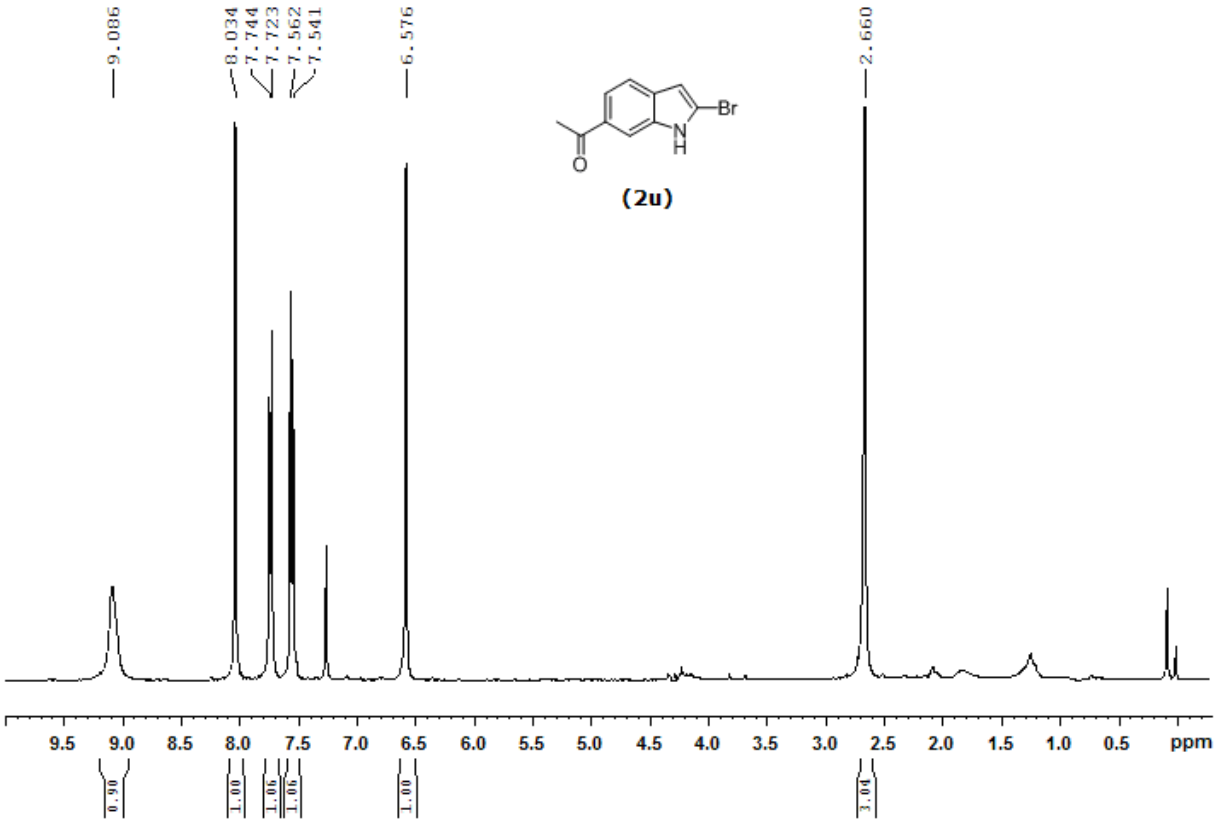

131.14
130.14
128.89
125.79
124.78
124.18
121.31
120.82
119.52
119.17
106.47
105.49
77.32
77.00
76.69
Br
N
H
(2r)
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

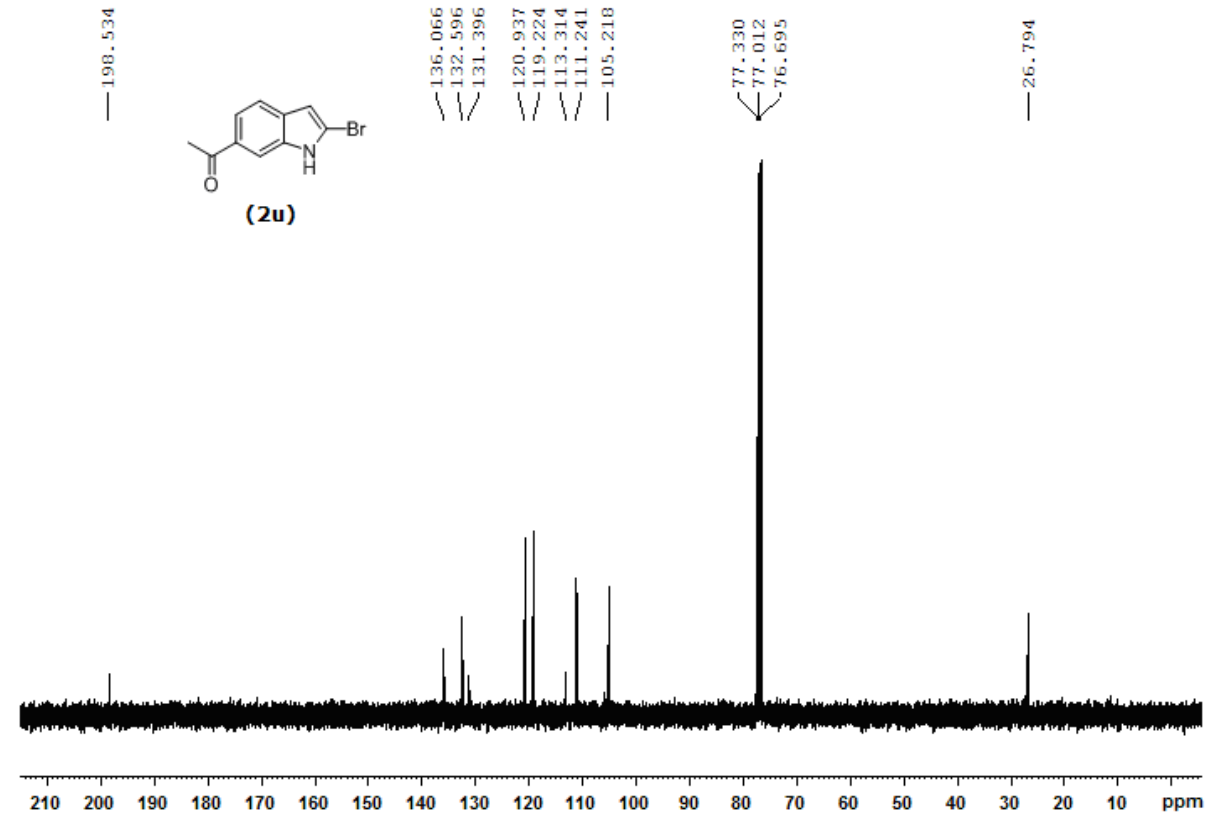

8.602
8.297
7.894
7.874
7.326
7.305
6.623
3.937
O
H3CO
Br
N
H
(2s)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.05
1.06
1.06
1.00
2.91

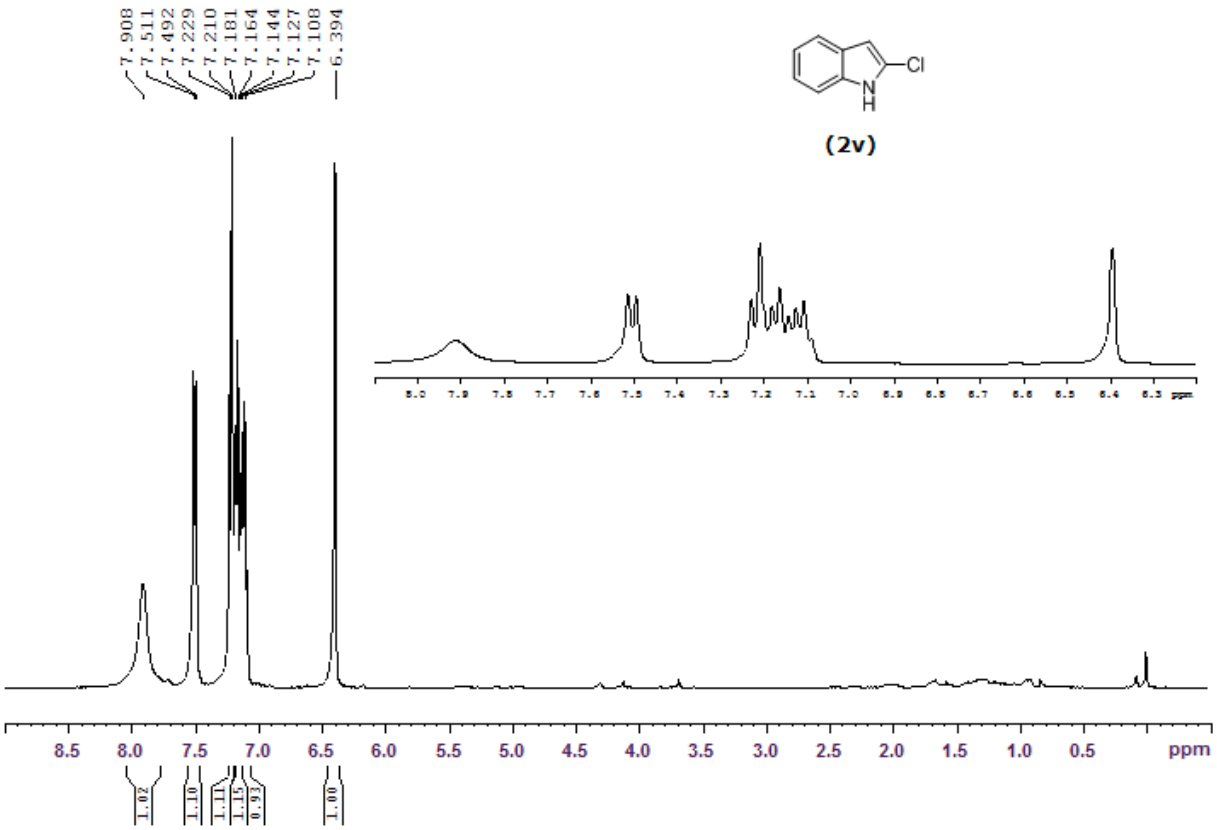

167.988
139.012
128.284
123.635
122.567
122.432
110.168
110.083
105.991
77.325
77.008
76.690
51.976
O
H3CO
Br
N
H
(2s)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

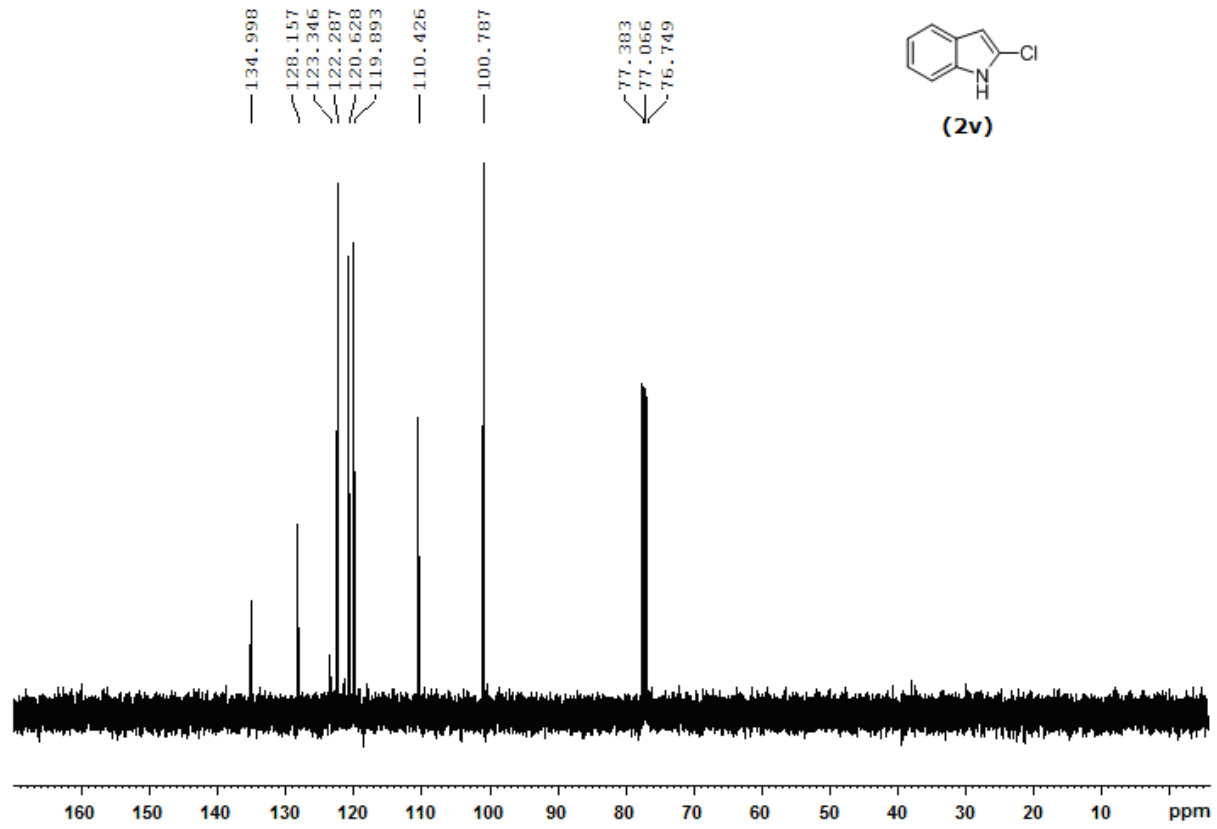

8.856
8.133
7.828
7.807
7.567
7.546
6.593
3.968
H3CO
O
N
H
Br
(2t)
9
8
7
6
5
4
3
2
1
ppm
0.91
1.02
1.01
1.04
1.00
3.00

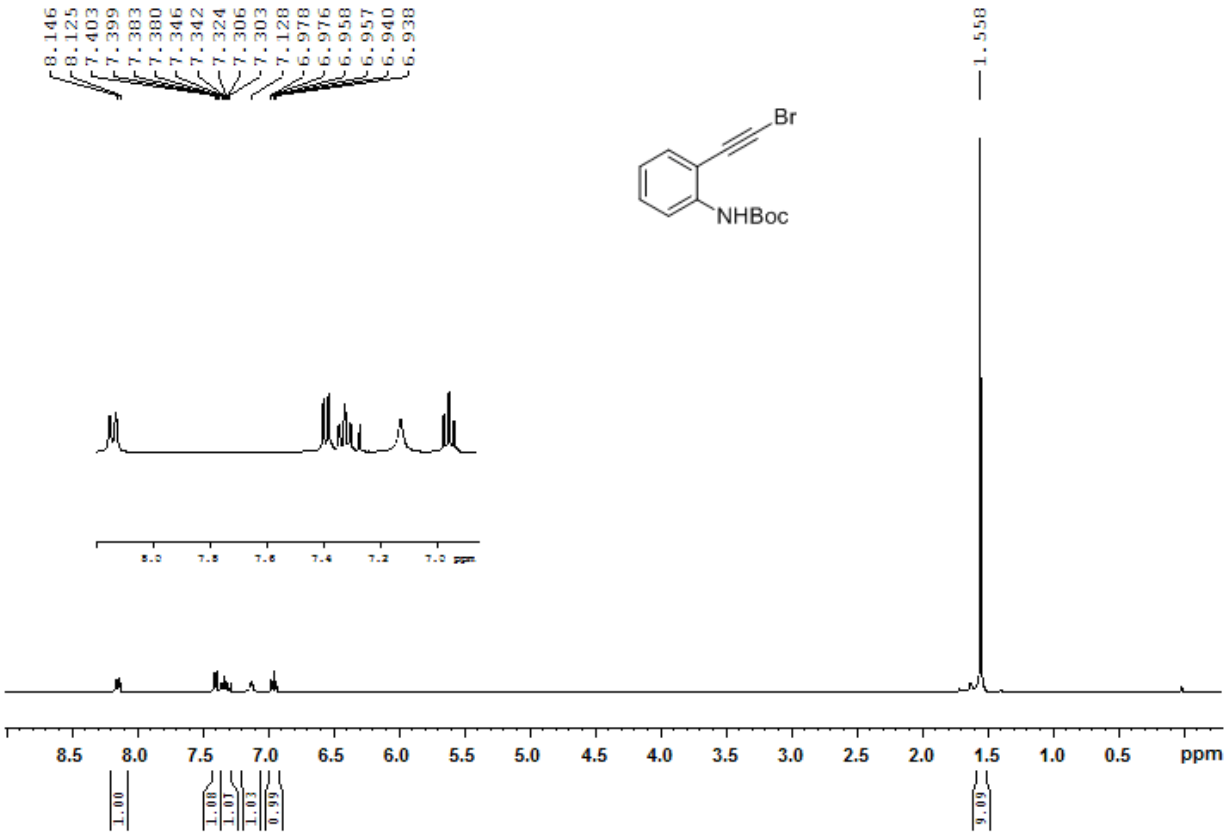

168.143
135.775
132.372
123.702
121.511
119.212
112.692
105.229
77.360
77.043
76.725
52.186
H3CO
O
N
H
Br
(2t)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

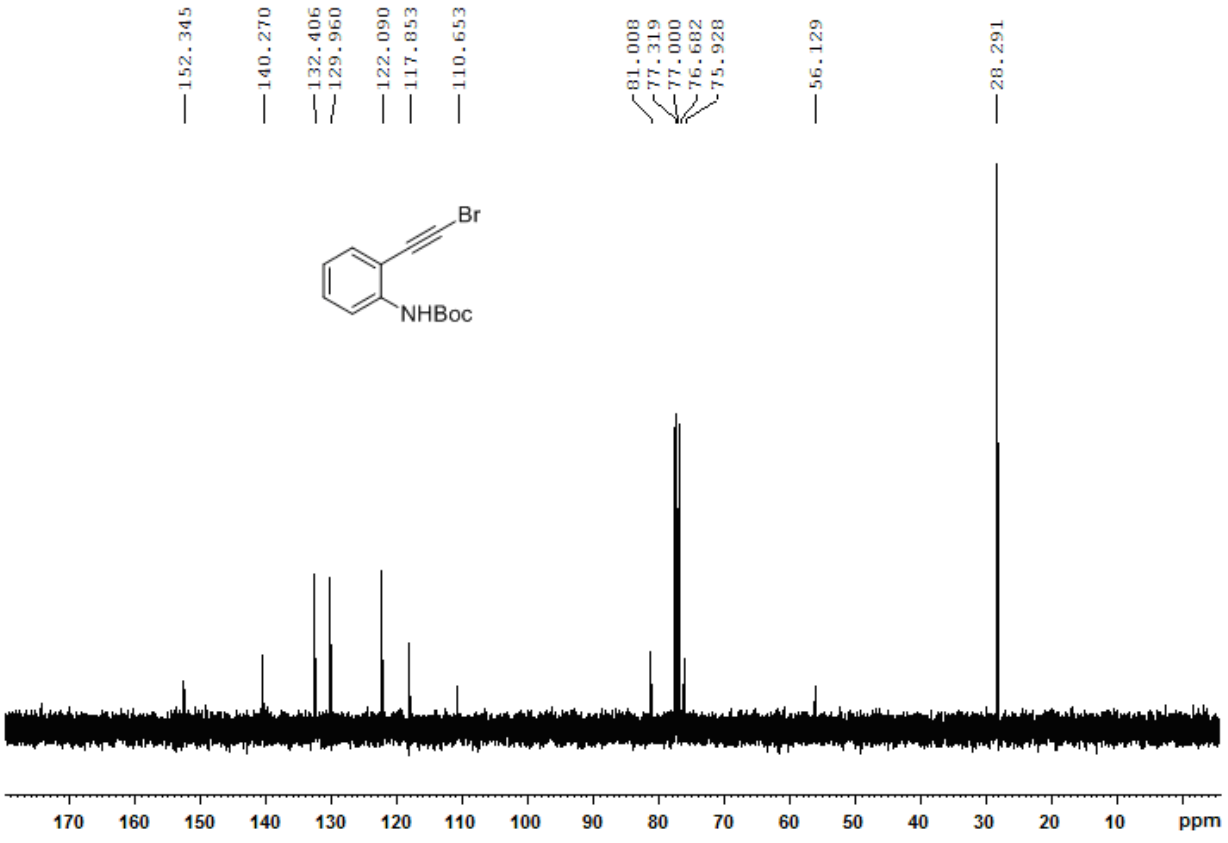

9.086
8.034
7.744
7.723
7.562
7.541
6.576
2.660
Br
N
H
O
(2u)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.90
1.00
1.06
1.06
1.00
3.04

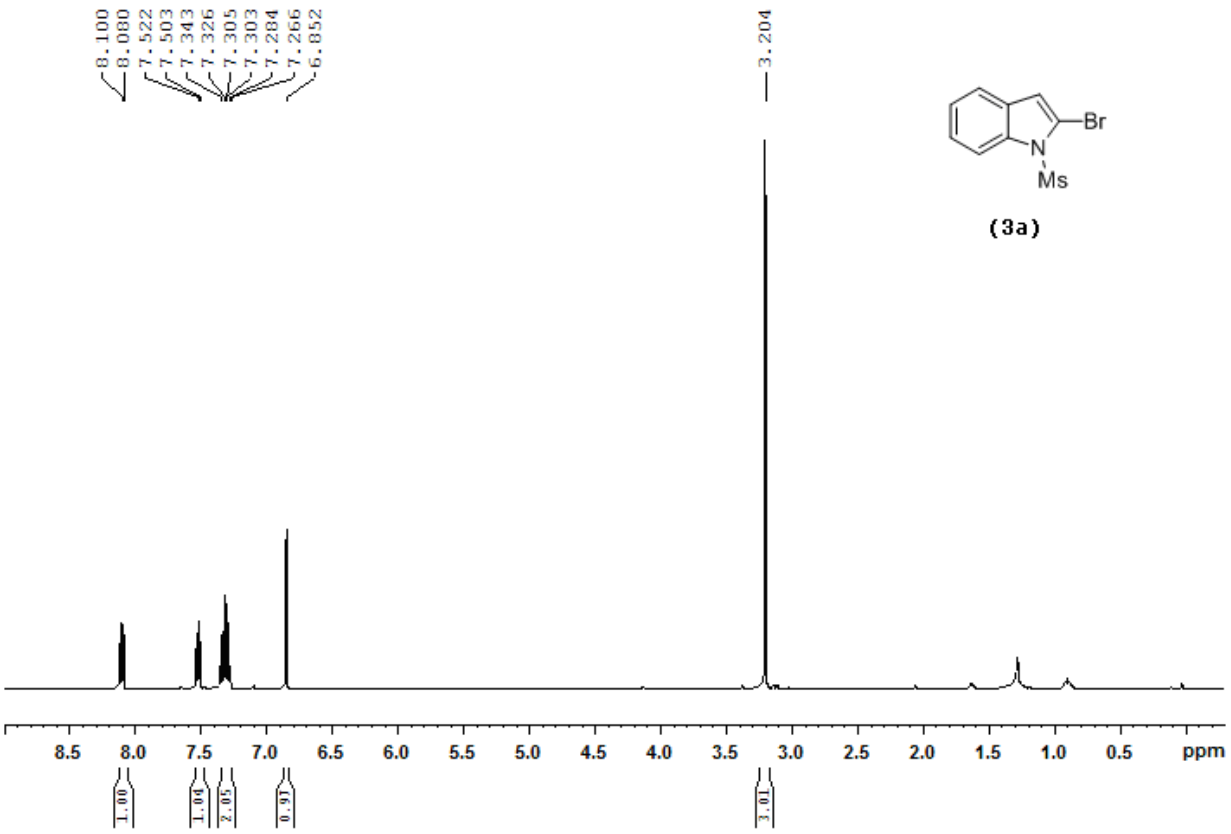

198.534
136.066
132.596
131.396
120.937
119.224
113.314
111.241
105.218
77.330
77.012
76.695
26.794
Br
N
H
O
(2u)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

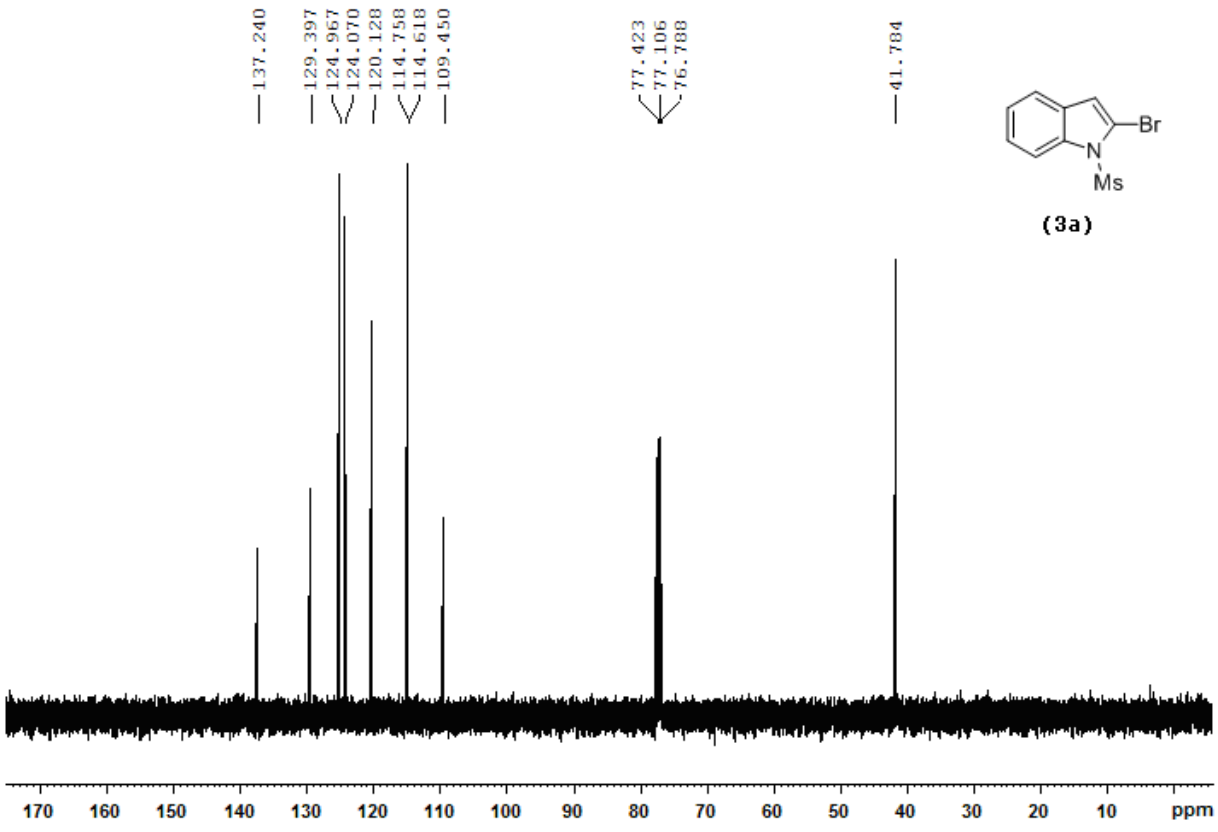

7.908
7.511
7.492
7.229
7.210
7.181
7.164
7.144
7.127
7.108
6.394
Cl
N
H
(2v)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.02
1.10
1.11
1.15
0.93
1.00

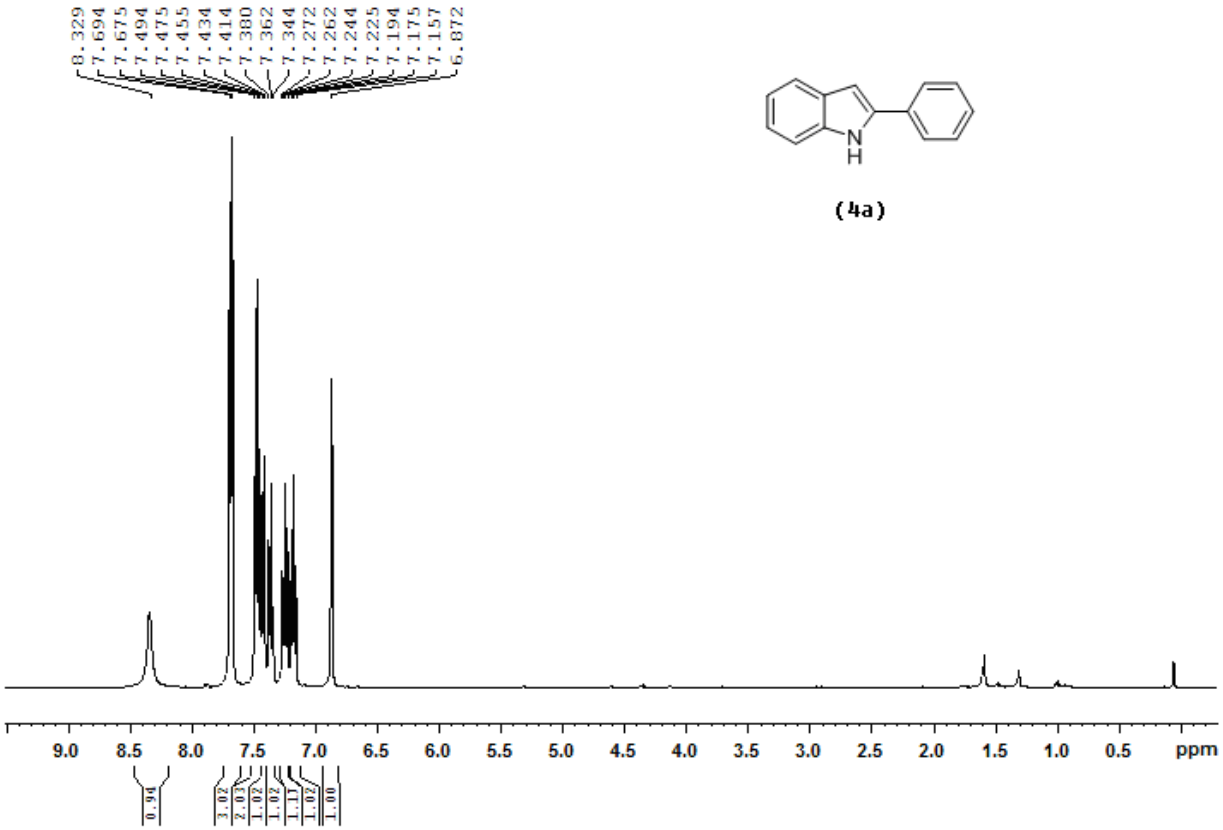

134.998
128.157
123.346
122.287
120.628
119.893
110.426
100.787
77.383
77.066
76.749
Cl
N
H
(2v)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

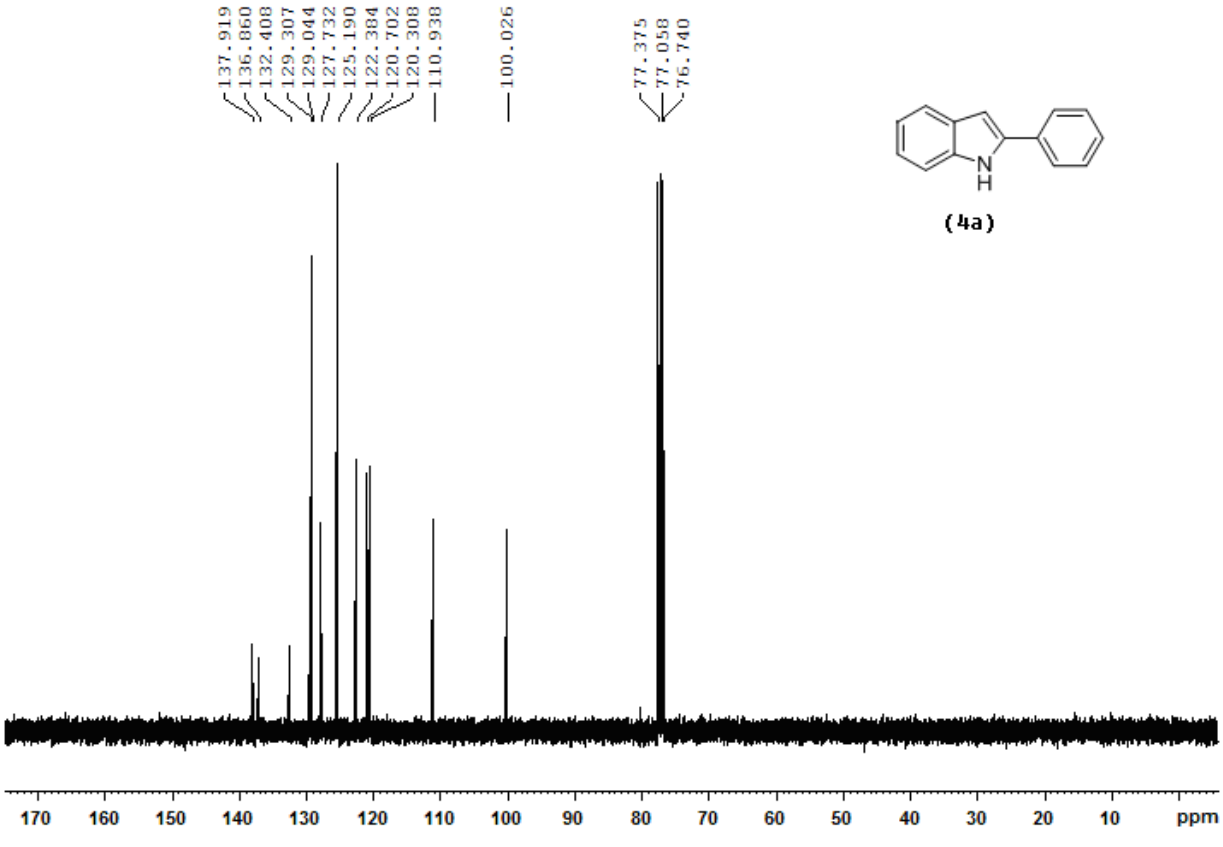

8.146
8.125
7.403
7.399
7.383
7.380
7.346
7.342
7.324
7.306
7.303
7.128
6.978
6.976
6.958
6.957
6.940
6.938
1.558
Br
NHBoc
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.08
1.07
1.03
0.99
9.09

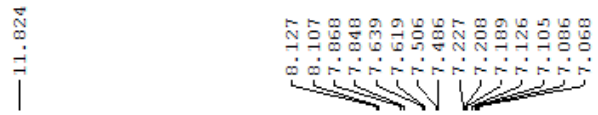

152.345
140.270
132.406
129.960
122.090
117.853
110.653
81.008
77.319
77.000
76.682
75.928
56.129
28.291
Br
NHBoc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

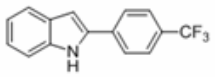

8.100
8.080
7.522
7.503
7.343
7.326
7.305
7.303
7.284
7.266
6.852
3.204
Br
N
Ms
(3a)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.04
2.05
0.97
3.01


137.240
129.397
124.967
124.070
120.128
114.758
114.618
109.450
77.423
77.106
76.788
41.784
Br
N
Ms
(3a)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

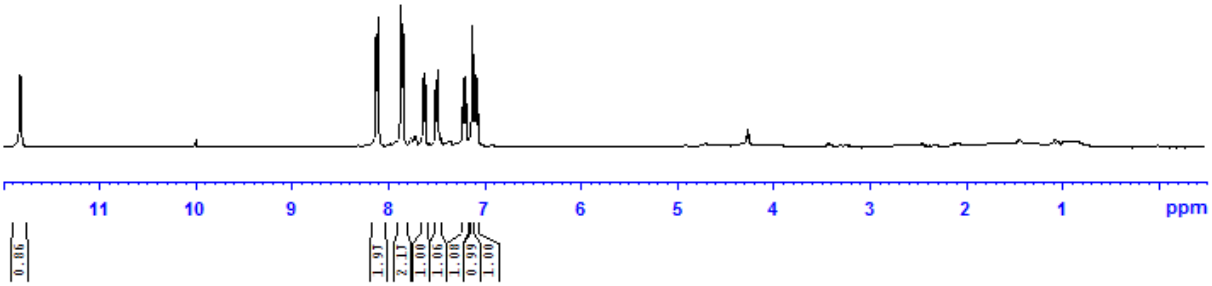

8.329
7.694
7.675
7.494
7.475
7.455
7.434
7.414
7.380
7.362
7.344
7.272
7.262
7.244
7.225
7.194
7.175
7.157
6.872
N
H
(4a)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.94
3.02
2.03
1.02
1.02
1.11
1.02
1.00

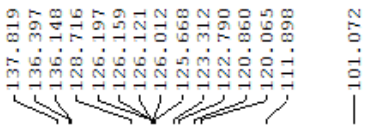

137.919
136.860
132.408
129.307
129.044
127.732
125.190
122.384
120.702
120.308
110.938
100.026
77.375
77.058
76.740
N
H
(4a)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


11.824
8.127
8.107
7.868
7.848
7.639
7.619
7.506
7.486
7.227
7.208
7.189
7.126
7.105
7.086
7.068


CF3
N
H

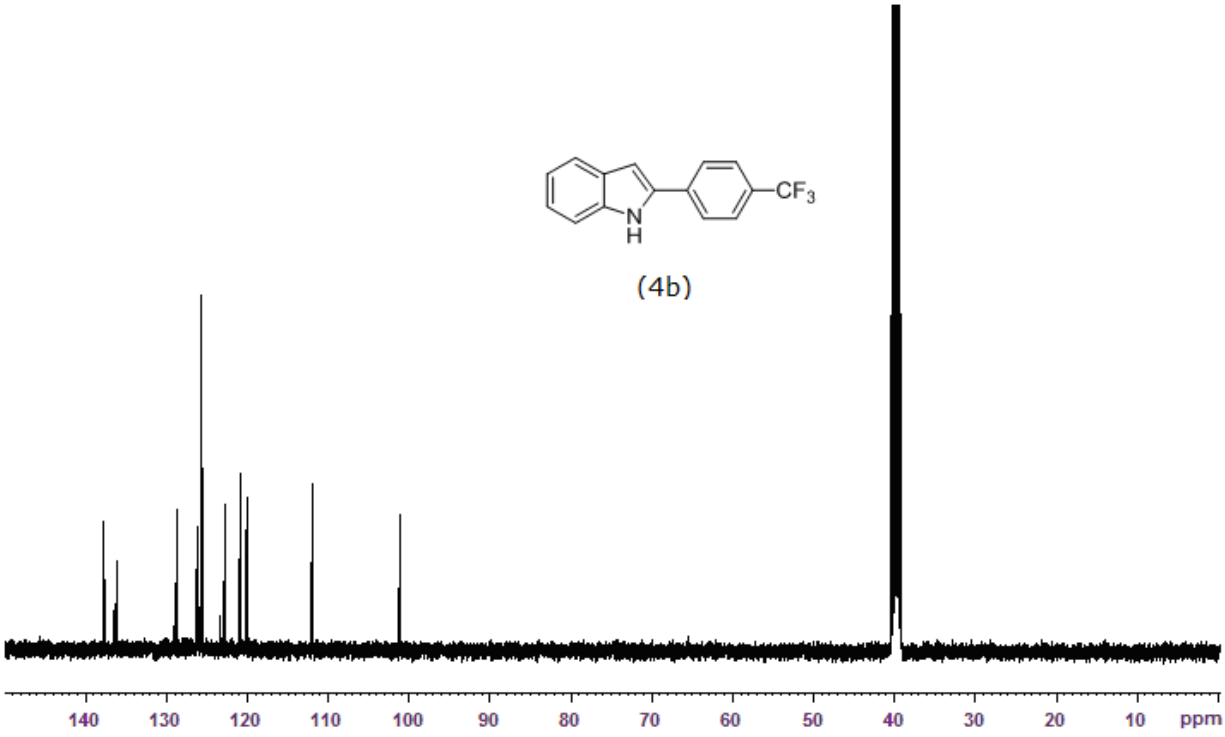
(4b)


11
10
9
8
7
6
5
4
3
2
1
ppm
0.86
1.97
2.17
1.00
1.06
1.08
0.99
1.00


137.819
136.397
136.148
128.716
126.197
126.159
126.121
126.012
125.668
123.312
122.790
120.860
120.065
111.898
101.072

CF3
N
H

(4b)


140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

6. References

[1] Fang, Y.-Q.; Lautens, M. *J. Org. Chem.* **2008**, *73*, 538.

[2] Newman, S. G.; Lautens, M. *J. Am. Chem. Soc.* **2010**, *132*, 11416.

[3] Newman, S. G.; Aureggi, V.; Bryan, C. S.; Lautens, M. *Chem. Commun.* **2009**, 5236.

[4] Bergman, J.; Venemalm, L. *J. Org. Chem.* **1992**, *57*, 2495.

[5] Jiang, B.; Tao, K.; Shen, W.; Zhang, J. *Tetrahedron Lett*. **2010**, *51*, 6342.

[6] Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128*, 8364.