Supporting information

Cu(II)- or Co(II)-Catalyzed C(SP3)-H Oxidation of N,N-Dimethylaminoethanol: Facile Synthesis of Methylene-Bridged Biindoles and 3-Formylindoles Selectively

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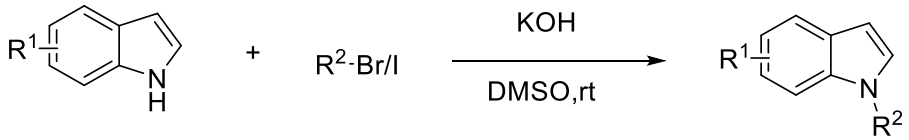
contents

1.General Information

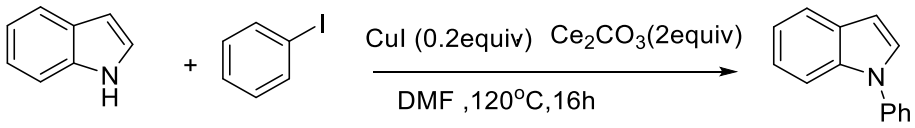
All reagents and solvents were used as supplied without further purification. ^{1}H NMR and ^{13}C NMR were determined in $CDCl_3$ or DMSO-d_6 on a Brucker spectrometer at room temperature, and tetramethylsilane (TMS) served as an internal standard. The chemical shifts are reported in parts per million (ppm), the coupling constants (*J*) are expressed in hertz (HZ). All the reactions were monitored by thin-layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Qingdao Haiyang Chemical Co., Ltd, China).

2. General Procedure for Synthesis of Substrates and products

2.1 General Procedure for Synthesis of N-protected indoles (1a,1b,1d,1f,1h-t) from substituted indoles with alkyl bromides (5.0 mmol scale). A 50ml flask equipped with a stir-bar was charged with substituted indole (5.0mmol,1.0equiv.) and KOH(10mmol,2.0equiv.). 20ml of DMSO was added to the flask and the solution was stirred under room temperature, then alkyl bromides (10mmol,2.0equiv.) was added. The reaction mixture was stirred at room temperature and monitored by TLC. Upon finished the reaction mixture was quenched by water (30ml)and extracted by ethyl acetate(3×30ml). The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo.Purification by silica-gel chromatography with a mixture eluent of petroleumether, ethyl acetate. Products were characterized by ^{1}H- and ^{13}C-NMR.

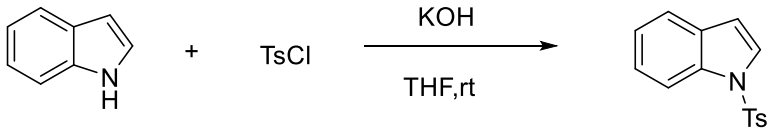


2.2 General Procedure for Synthesis of N-Phenyl-1H- indoles (1e) from unsubstituted indoles with iodobenzene (5.0 mmol scale). A 50ml flask equipped with a stir-bar was charged with unsubstituted indole (7.0mmol, 1.4equiv.), iodobenzene (5mmol, 1.0equiv),cooper(I) iodide (1mmol,20mol%) and cesium carbonate (10mmol,2.0equiv) were stirred for 16 h at 120°C in DMF (10ml). The reaction mixture was monitored by TLC. After cooling down to room temperature, the reaction mixture was quenched by water (30ml) and extracted by ethyl acetate(3×30ml). The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica-gel chromatography with a mixture eluent of petroleumether, ethyl acetate. Products were characterized by ^{1}H- and ^{13}C-NMR.

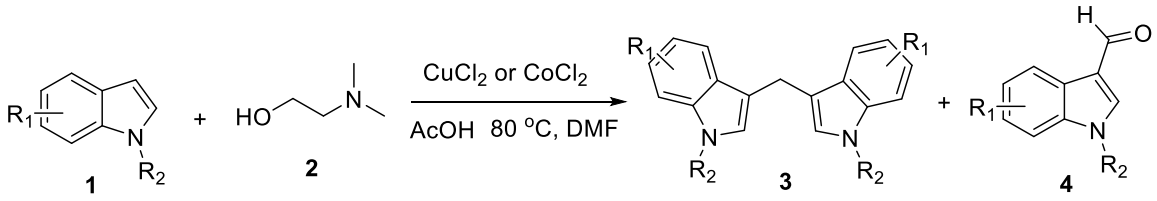


2.3 General Procedure for Synthesis of 1-Tosylindole (1l) from indole with 4-methylbenzene-1-sulfonyl chloride (5 mmol scale) .A 50ml flask equipped with a stir-bar was charged with unsubstituted indole (5.0mmol, 1.0equiv.), 4-methylbenzene-1-sulfonyl chloride (6mmol, 1.2equiv) and KOH(10mmol,2.0equiv) .20ml of THF was added to the flask and the solution was stirred under room temperature. The reaction mixture was monitored by TLC. Upon finished the reaction mixture was quenched by water (30ml) and extracted by ethyl acetate(3×30ml). The combined organic layer was dried over Na_2SO_4, filtered and concentrated in

vacuo. Purification by silica-gel chromatography with a mixture eluent of petroleumether, ethyl acetate. Products were characterized by ^{1}H- and ^{13}C-NMR.

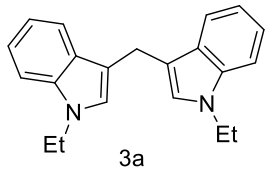


2.4 General procedure for the synthesis of 3,3'-biindoles (3) and 3-formylindoles (4) with N,N-dimethylethanolamine (DMEA). A 25ml flask equipped with a stir-bar was charged with $CuCl_2$ (1.0mmol, 0.5equiv.) or $CoCl_2$ (1.0mmol, 0.5equiv.), substituted indole (2.0mmol, 1.0equiv.) and DMF (5 mL). DMEA (3.0mmol, 1.5equiv.) and AcOH (2.0 mmol, 1.0equiv.) was added to the flask. The reaction mixture was stirred at 80^{o}C and monitored by TLC. Upon finished the reaction mixture was quenched by water (30ml) and extracted by ethyl acetate (3×30ml). The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica-gel chromatography with a mixed eluent of petroleum ether and ethyl acetate. Products were characterized by ^{1}H- and ^{13}C-NMR and MS.



3. Spectrum Data

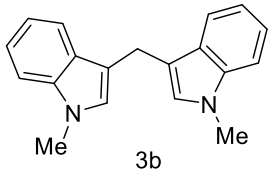
Bis(1-ethyl-1H-indol-3-yl)methane (3a)[1]



3a

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.9 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.23 – 7.17 (m, 2H), 7.12 – 7.04 (m, 2H), 6.86 (s, 2H), 4.23 (s, 2H), 4.10 (q, *J* = 7.3 Hz, 4H), 1.40 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.25, 128.21, 125.38, 121.33, 119.54, 118.60, 114.43, 109.25, 40.82, 21.20, 15.65. ESI-MS: $[M+H]^+$ 303.

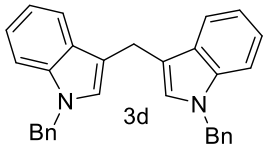
Bis(1-methyl-1H-indol-3-yl)methane (3b)[1]



3b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 2H), 6.86 (s, 2H), 4.29 (s, 2H), 3.77 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.19, 127.96, 126.99, 121.43, 119.32, 118.59, 114.37, 109.10, 32.60, 20.95. ESI-MS: $[M+H]^+$ 275.

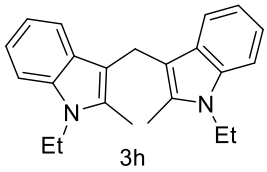
Bis(1-benzyl-1H-indol-3-yl)methane (3d)[1]



3d

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.9 Hz, 2H), 7.27 – 7.22 (m, 8H), 7.15 (t, *J* = 8.1 Hz, 2H), 7.07 (m, 6H), 6.91 (s, 2H), 5.25 (s,4H), 4.26 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.85, 135.81, 127.62, 127.21, 126.38, 125.63, 125.45, 120.57, 118.44, 117.80, 113.80, 108.56, 48.83, 20.22. ESI-MS: $[M+H]^+$ 427.

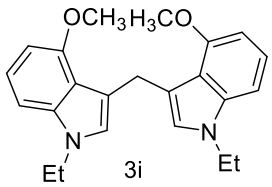
Bis(1-ethyl-2-methyl-1H-indol-3-yl)methane (3h)[1]



3h

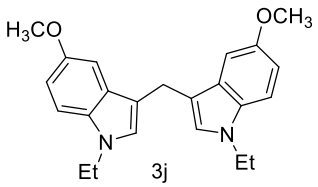
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 2H), 6.95 (t, *J* = 7.5 Hz, 2H), 4.15 (s, 2H), 4.10 (q, *J* = 7.2 Hz, 4H), 2.35 (s, 6H), 1.29 (t, *J* = 7.2 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 135.44, 131.89, 128.35, 120.15, 118.54, 118.44, 110.50, 108.38, 37.64, 19.95, 15.39, 10.24. ESI-MS: $[M+H]^+$ 331.

Bis(1-ethyl-4-methoxy-1H-indol-3-yl)methane (3i)



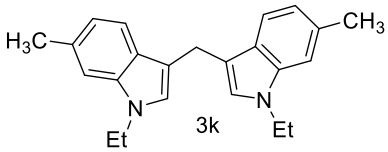
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.08 (t, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 6.69 (s, 2H), 6.47 (d, *J* = 7.7 Hz, 2H), 4.55 (s, 2H), 4.02 (q, *J* = 7.3 Hz, 4H), 3.88 (s, 6H), 1.36 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.34, 137.66, 124.24, 121.64, 117.98, 116.55, 102.56, 98.86, 55.20, 40.86, 23.75, 15.49. HRMS (ESI) Calcd for $C_{23}H_{27}N_2O_2$ $[M+H]^+$:363.2067, found 363.2079.

Bis(1-ethyl-5-methoxy-1H-indol-3-yl)methane (3j)[1]



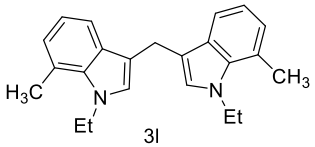
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 2.4 Hz, 2H), 6.87 (m, *J* = 8.8, 2.4 Hz, 2H), 6.83 (s, 2H), 4.15 (s, 2H), 4.05 (q, *J* = 7.3 Hz, 4H), 3.81 (s, 6H), 1.38 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 153.52, 131.55, 128.32, 125.92, 113.67, 111.54, 109.94, 101.25, 56.01, 40.90, 21.23, 15.63. ESI-MS: $[M+H]^+$ 363.

Bis(1-ethyl-6-methyl-1H-indol-3-yl)methane (3k)



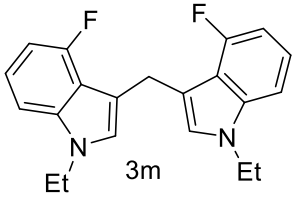
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.10 (s, 2H), 6.90 (d, *J* = 8.0Hz, 2H), 6.77 (s, 2H), 4.17 (s, 2H), 4.04 (q, *J* = 7.3 Hz, 4H), 2.49 (s, 6H), 1.38 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (151 MHz, DMSO) δ 131.83, 126.22, 121.35, 120.00, 115.52, 114.44, 109.55, 104.44, 35.90, 17.25, 16.50, 10.86. HRMS (ESI) Calcd for $C_{23}H_{27}N_2$ $[M+H]^+$:331.2169, found 331.2160.

Bis(1-ethyl-7-methyl-1H-indol-3-yl)methane (3l)[1]



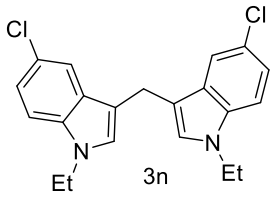
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 2H), 6.91 (d, *J* = 7.0 Hz, 2H), 6.76 (s, 2H), 4.29 (q, *J* = 7.2 Hz, 4H), 4.16 (s, 2H), 2.71 (s, 6H), 1.36 (t, *J* = 7.2 Hz, 6H).^{13}C NMR (151 MHz, $CDCl_3$) δ 134.90, 129.23, 127.05, 124.28, 120.59, 118.77, 117.47, 114.52, 43.15, 21.04, 19.86, 17.93. ESI-MS: $[M+H]^+$ 331.

Bis(1-ethyl-4-fluoro-1H-indol-3-yl)methane (3m)



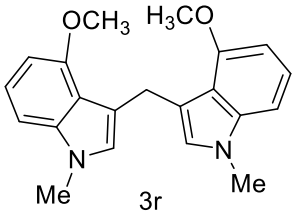
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 – 7.02 (m, 4H), 6.88 (s, 2H), 6.71 (m, 2H), 4.41 (s, 2H), 4.05 (q, *J* = 7.3 Hz, 4H), 1.39 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.53 (d, $J_{C\text{-}F}$ = 247 Hz), 138.94 (d, $J_{C\text{-}F}$ = 12 Hz), 125.33, 121.53 (d, $J_{C\text{-}F}$ = 8 Hz), 116.53 (d, $J_{C\text{-}F}$ = 20 Hz), 113.98 (d, $J_{C\text{-}F}$ = 4 Hz), 105.29 (d, $J_{C\text{-}F}$ = 3 Hz), 103.78 (d, $J_{C\text{-}F}$ = 19 Hz), 41.08, 23.09, 15.38. HRMS (ESI) Calcd for $C_{21}H_{21}F_2N_2$ $[M+H]^+$:339.1667, found 339.1672.

Bis(5-chloro-1-ethyl-1H-indol-3-yl)methane (3n)[1]



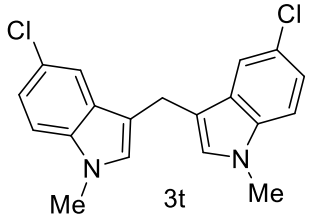
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.8 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.14 (dd, *J* = 8.7, 1.9 Hz, 2H), 6.87 (s, 2H), 4.11 (s, 2H), 4.07 (q, *J* = 7.3 Hz, 4H), 1.40 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.62, 128.95, 126.55, 124.43, 121.61, 118.79, 113.58, 110.26, 41.00, 20.98, 15.51. ESI-MS: $[M+H]^+$ 371.

Bis(4-methoxy-1-methyl-1H-indol-3-yl)methane (3r)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.69 (s, 2H), 6.55 (d, *J* = 7.7 Hz, 2H), 4.61 (s, 2H), 3.95 (s, 6H), 3.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.67, 130.88, 128.80, 125.87, 121.82, 117.76, 116.54, 102.46, 55.22, 32.75, 29.70. HRMS (ESI) Calcd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$:335.1754 , found 335.1750.

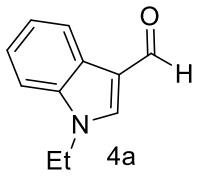
Bis(5-chloro-1-methyl-1H-indol-3-yl)methane (3t)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.85 (s, 2H), 4.15 (s, 2H), 3.75 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 135.64, 128.78, 128.25, 124.59, 121.80,

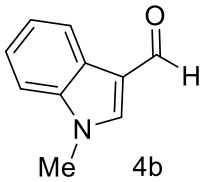
118.65, 113.61, 110.24, 32.82, 20.80. HRMS (ESI) Calcd for $C_{19}H_{17}Cl_2N_2$ $[M+H]^+$:343.0763, found 343.0752.

1-ethyl-1H-indole-3-carbaldehyde (4a)[1]



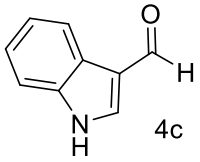
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.31 (d, *J* = 8.2 Hz, 1H), 7.75 (s, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.36 – 7.33 (m, 1H), 7.31 (d, *J* = 7.1 Hz, 1H), 4.24 (q, *J* = 7.3 Hz, 2H), 1.56 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.47, 137.55, 137.02, 125.50, 122.89, 122.13, 118.14, 109.98, 41.89, 15.05. ESI-MS: $[M+H]^+$ 174.

1-methyl-1H-indole-3-carbaldehyde (4b)[1]



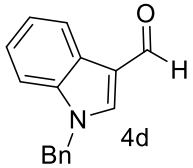
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.35 (d, *J* = 6.6 Hz, 1H), 7.69 (s, 1H), 7.50 – 7.33 (m, 3H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.43, 137.90, 125.29, 124.04, 122.94, 122.04, 118.09, 109.87, 33.69. ESI-MS: $[M+H]^+$ 160.

1H-indole-3-carbaldehyde (4c)[1]



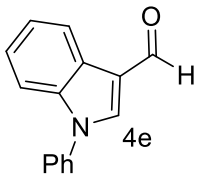
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 8.79 (s, 1H), 8.40 – 8.27 (m, 1H), 7.86 (d, *J* = 2.8 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.39 – 7.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.34, 136.79, 135.75, 124.39, 123.04, 121.88, 120.55, 118.38, 111.70. ESI-MS: $[M+H]^+$ 146.

1-benzyl-1H-indole-3-carbaldehyde (4d)[1]



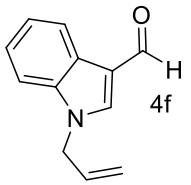
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.38 – 8.28 (m, 1H), 7.72 (s, 1H), 7.39 – 7.30 (m, 6H), 7.22 – 7.16 (m, 2H), 5.37 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.62, 138.43, 137.48, 135.30, 129.14, 128.41, 127.23, 125.53, 124.17, 123.09, 122.19, 118.53, 110.35, 50.95. ESI-MS: $[M+H]^+$ 236.

1-phenyl-1H-indole-3-carbaldehyde (4e)[2]



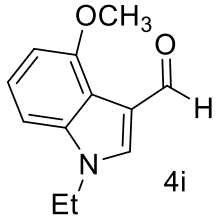
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.44 (d, *J* = 7.2 Hz, 1H), 7.94 (s, 1H), 7.65 – 7.59 (m, 2H), 7.57 – 7.51 (m, 4H), 7.39 (pd, *J* = 7.1, 1.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.99, 138.22, 137.51, 130.02, 128.32, 125.59, 124.87, 124.64, 123.49, 122.27, 119.73, 111.12. ESI-MS: $[M+H]^+$ 222.

1-allyl-1H-indole-3-carbaldehyde (4f)[3]



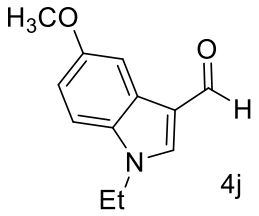
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.32 (d, *J* = 6.3 Hz, 1H), 7.74 (s, 1H), 7.39 – 7.32 (m, 3H), 6.07 – 5.99 (m, 1H), 5.36 – 5.31 (m, 1H), 5.23 – 5.17 (m, 1H), 4.80 (d, *J* = 5.6 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 184.58, 138.28, 137.32, 131.75, 125.46, 124.06, 123.01, 122.16, 119.07, 118.42, 110.28, 49.54. ESI-MS: $[M+H]^+$ 186.

1-ethyl-4-methoxy-1H-indole-3-carbaldehyde (4i)



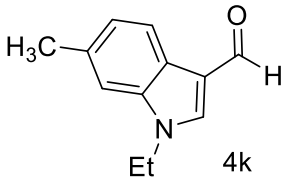
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.87 (s, 1H), 7.23 (t, *J* = 8.1 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 4.00 (s, 3H), 1.52 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.96, 154.72, 137.91, 130.36, 123.69, 118.23, 117.01, 103.53, 102.38, 55.38, 42.07, 15.05. HRMS (ESI) Calcd for $C_{12}H_{14}NO_2[M+H]^+$:204.1019, found 204.1025.

1-ethyl-5-methoxy-1H-indole-3-carbaldehyde (4j)[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, *J* = 2.4 Hz, 1H), 7.73 (s, 1H), 7.32 – 7.29 (m, 1H), 7.01 (dd, *J* = 8.9, 2.5 Hz, 1H), 4.23 (q, *J* = 7.3 Hz, 2H), 3.94 (s, 3H), 1.58 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 184.41, 156.66, 137.54, 131.93, 126.26, 117.94, 114.42, 110.80, 103.42, 55.85, 42.05, 15.08. ESI-MS: $[M+H]^+$ 204.

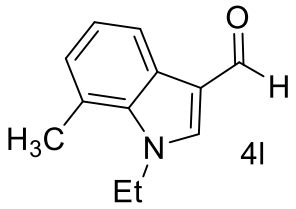
1-ethyl-6-methyl-1H-indole-3-carbaldehyde (4k)



4k

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.68 (s, 1H), 7.18 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 2.51 (s, 3H), 1.54 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 184.40, 137.43, 137.18, 133.97, 124.56, 123.25, 121.77, 118.17, 109.91, 41.78, 21.95, 15.09. HRMS (ESI) Calcd for $C_{12}H_{14}NO$ $[M+H]^+$:188.1070, found 188.1075.

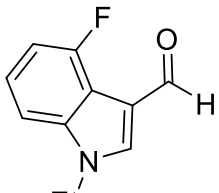
1-ethyl-7-methyl-1H-indole-3-carbaldehyde (4l)[1]



4l

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.66 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 2.72 (s, 3H), 1.52 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 184.43, 139.03, 135.82, 127.02, 126.59, 123.00, 121.33, 120.04, 118.00, 44.51, 19.63, 17.34. ESI-MS: $[M+H]^+$ 188.

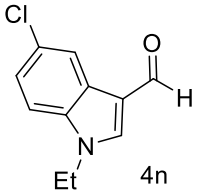
1-ethyl-4-fluoro-1H-indole-3-carbaldehyde (4m)



4m

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.89 (s, 1H), 7.29 – 7.16 (m, 2H), 7.06 – 6.94 (m, 1H), 4.23 (q, *J* = 7.3 Hz, 2H), 1.54 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 185.20 (d, $J_{C\text{-}F}$ = 3 Hz), 157.02 (d, $J_{C\text{-}F}$ = 250 Hz), 139.12 (d, $J_{C\text{-}F}$ = 12 Hz), 132.91, 123.74 (d, $J_{C\text{-}F}$ = 7 Hz), 116.62 (d, $J_{C\text{-}F}$ = 5 Hz), 115.3 (d, $J_{C\text{-}F}$ = 22 Hz), 107.89 (d, $J_{C\text{-}F}$ = 20 Hz), 106.55 (d, $J_{C\text{-}F}$ = 3 Hz), 42.29, 14.94. HRMS (ESI) Calcd for $C_{11}H_{11}FNO$ $[M+H]^+$:192.0819, found 192.0825.

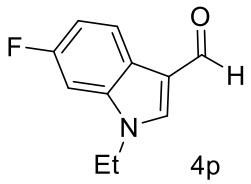
5-chloro-1-ethyl-1H-indole-3-carbaldehyde (4n)[1]



4n

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.31 (s, 1H), 7.75 (s, 1H), 7.29 (d, J = 1.2 Hz, 2H), 4.22 (q, J = 7.3 Hz, 2H), 1.55 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.17, 138.00, 135.36, 128.93, 126.44, 124.33, 121.77, 117.65, 110.95, 42.11, 15.02. ESI-MS: $[M+H]^+$ 208.

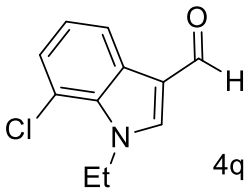
1-ethyl-6-fluoro-1H-indole-3-carbaldehyde (4p)



4p

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.29 – 8.19 (m, 1H), 7.74 (s, 1H), 7.07 (s, 1H), 7.05 (s, 1H), 4.18 (q, J = 7.3 Hz, 2H), 1.55 (t, J = 7.3 Hz, 3H). δ 184.33, 160.62 (d, J_{C-F} = 241 Hz), 137.93, 137.25 (d, J_{C-F} = 12 Hz), 123.31 (d, J_{C-F} = 10 Hz), 121.75 (d, J_{C-F} = 1 Hz), 118.25, 111.45 (d, J_{C-F} = 24Hz), 96.70 (d, J_{C-F} = 26 Hz), 42.05, 14.92. HRMS (ESI) Calcd for $C_{11}H_{11}FNO$ $[M+H]^+$:192.0819, found 192.0820.

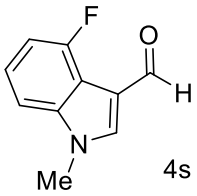
7-chloro-1-ethyl-1H-indole-3-carbaldehyde (4q)



4q

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.25 (d, J = 8.9 Hz, 1H), 7.71 (s, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 4.63 (q, J = 7.2 Hz, 2H), 1.56 (t, J = 7.2 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 184.22, 139.88, 132.46, 130.87, 125.76, 123.65, 120.83, 117.97, 117.05, 44.91, 17.38. HRMS (ESI) Calcd for $C_{11}H_{11}ClNO$ $[M+H]^+$:208.0524, found 208.0529.

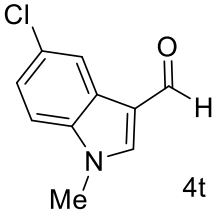
4-fluoro-1-methyl-1H-indole-3-carbaldehyde (4s)[4]



4s

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.87 (s, 1H), 7.35 – 7.26 (m, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.06 (dd, J = 10.5, 7.9 Hz, 1H), 3.93 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) 185.18 (d, J_{C-F} = 8 Hz), 156.95 (d, J_{C-F} = 250 Hz), 139.98 (d, J_{C-F} = 11 Hz), 134.64, 123.90 (d, J_{C-F} = 7 Hz), 116.60 (d, J_{C-F} = 6 Hz), 115.14 (d, J_{C-F} = 23 Hz), 108.01 (d, J_{C-F} = 19 Hz), 106.45 (d, J_{C-F} = 3 Hz), 34.11. ESI-MS: $[M+H]^+$ 178.

5-chloro-1-methyl-1H-indole-3-carbaldehyde (4t)[2]



4t

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.32 (s, 1H), 7.71 (s, 1H), 7.31 (d, *J* = 5.8 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.14, 139.80, 136.23, 129.03, 126.20, 124.44, 121.66, 117.56, 110.90, 33.91. ESI-MS: $[M+H]^+$ 194.

4.References

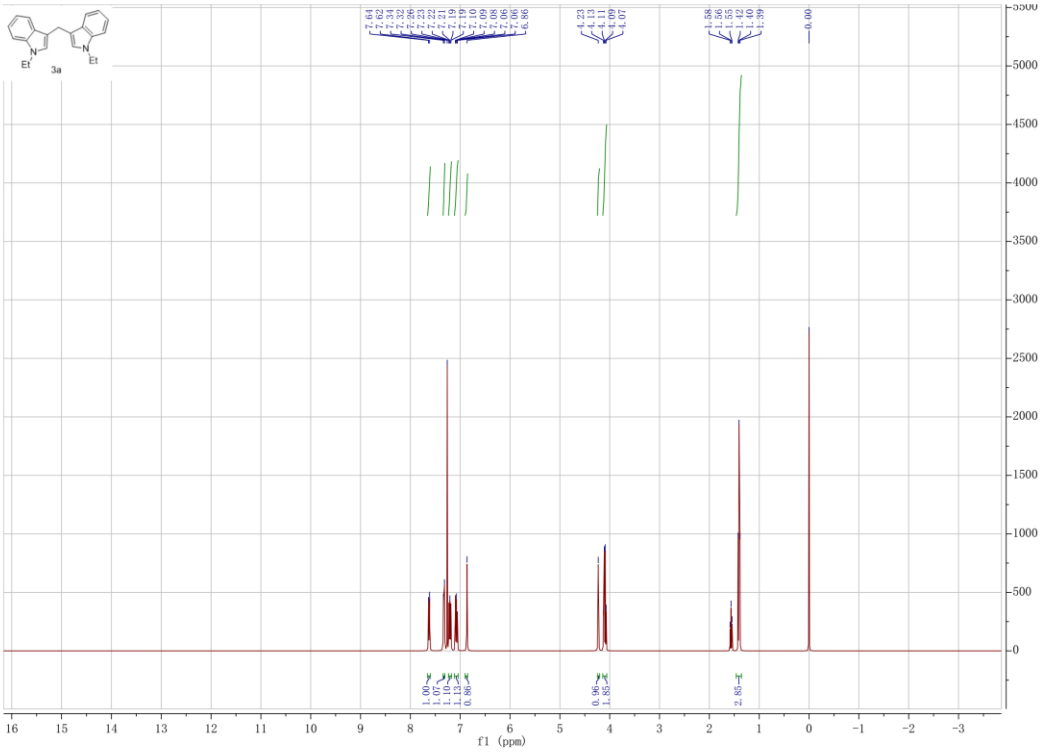
1 L. Zhang, C. Peng, D. Zhao, Y. Wang, H.-J. Fu, Q. Shen and J.-X. Li, *Chem. Commun.*, 2012, **48**, 5928.

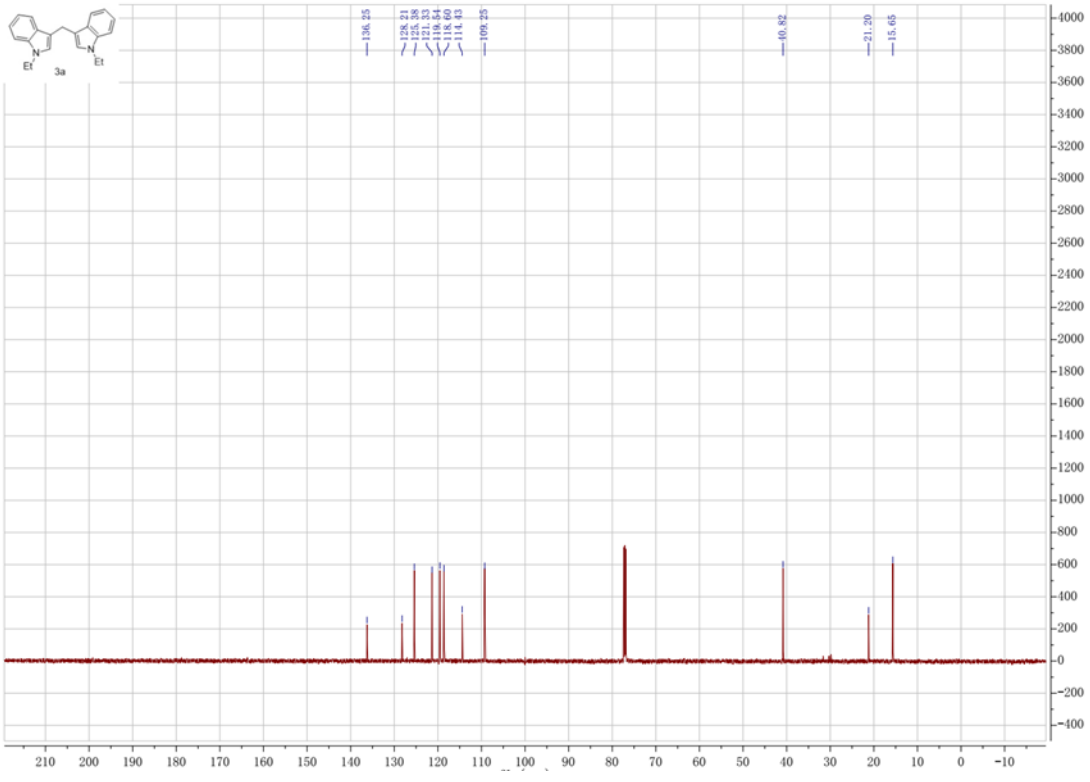
2 H.Y. Fei, J.T. Yu, Y. Jiang, H. Guo, J. Cheng, *Org. Biomol. Chem.*, 2013, **11**, 7092.

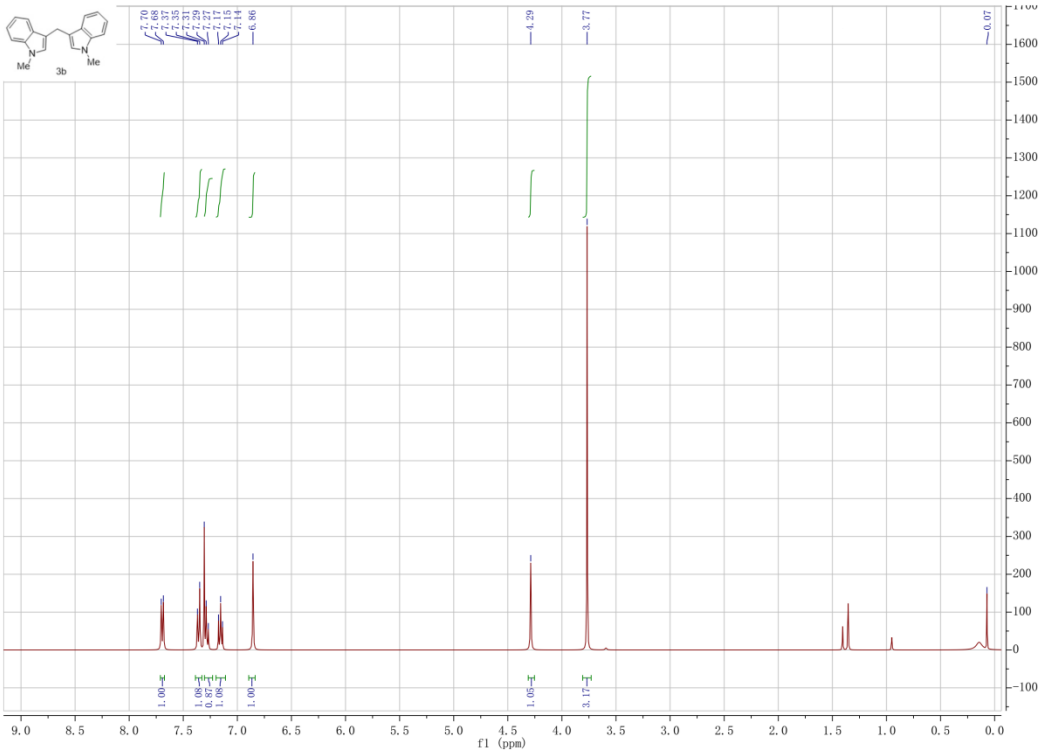
3 S. Olguin-Uribe, M.V. Mijangos, Y.A. Sanchez, M.A. Sanchez-Carmona, L.D. Miranda. *Eur. J. Org. Chem.*, 2017,**11**,2481.

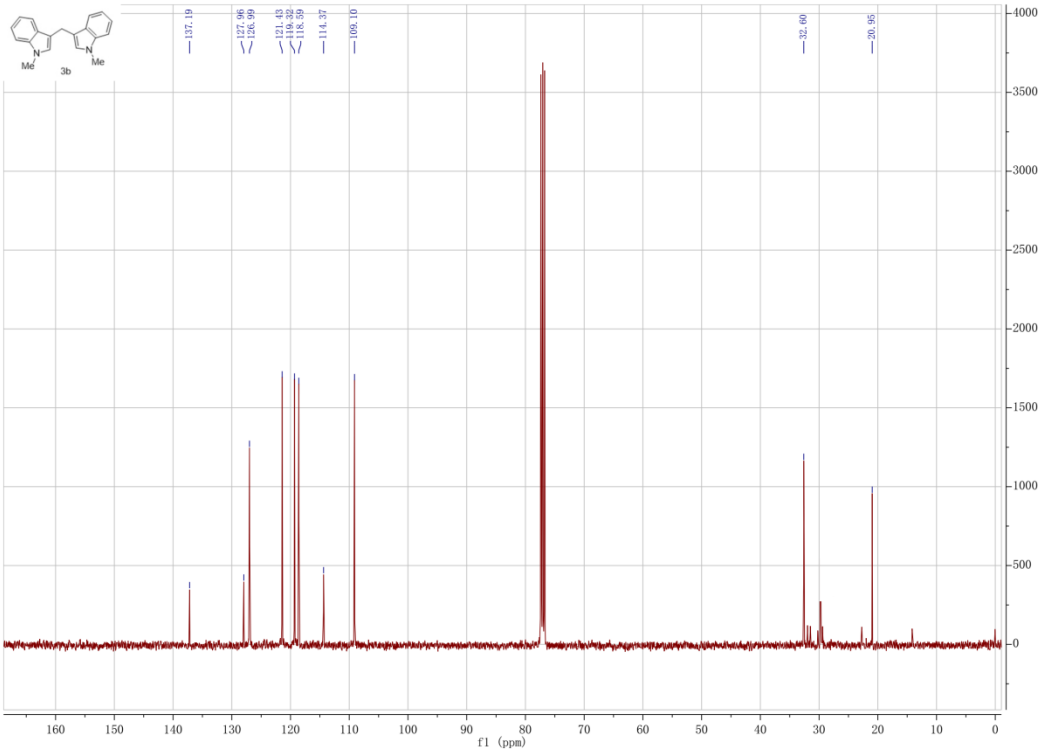
4 J.M. Berman, M.B. Schmid, J.D. Mendlein, N. Kaplan. *U.S. Patent* 2012, US2012/0010127

5. Copies of NMR Spectra






3b
Me
Me
7.70
7.68
7.37
7.35
7.31
7.29
7.27
7.17
7.15
7.14
6.86
4.29
3.77
0.07
1.00
1.08
0.87
1.08
1.00
1.05
3.17
f1 (ppm)


3b
Me
Me
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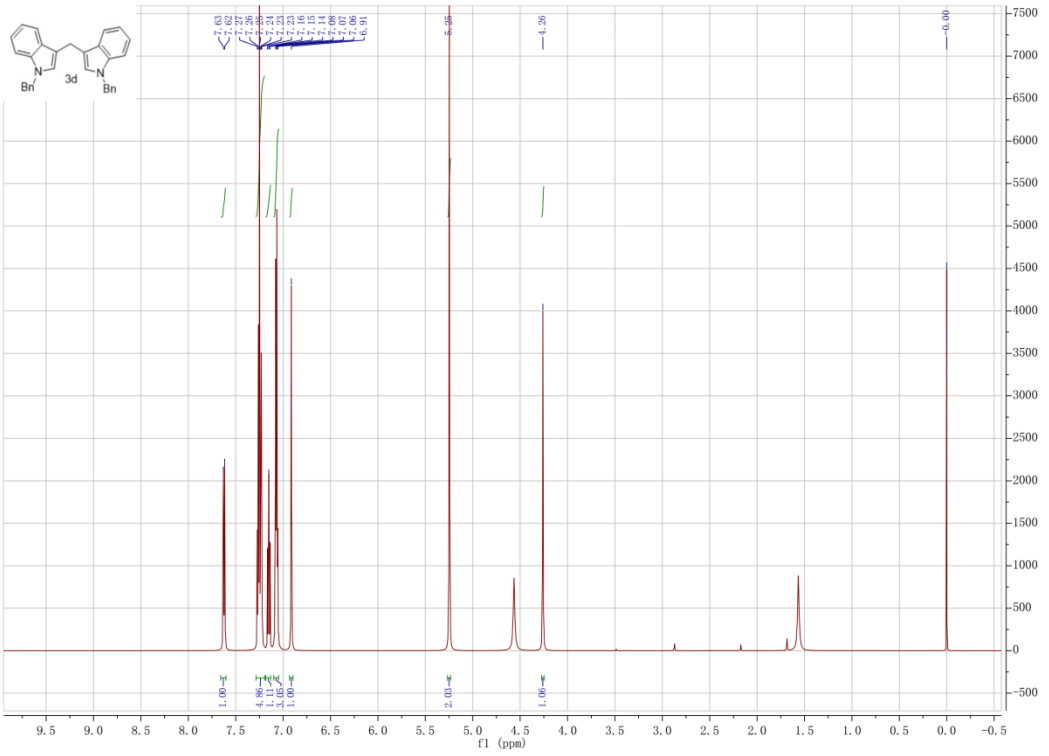
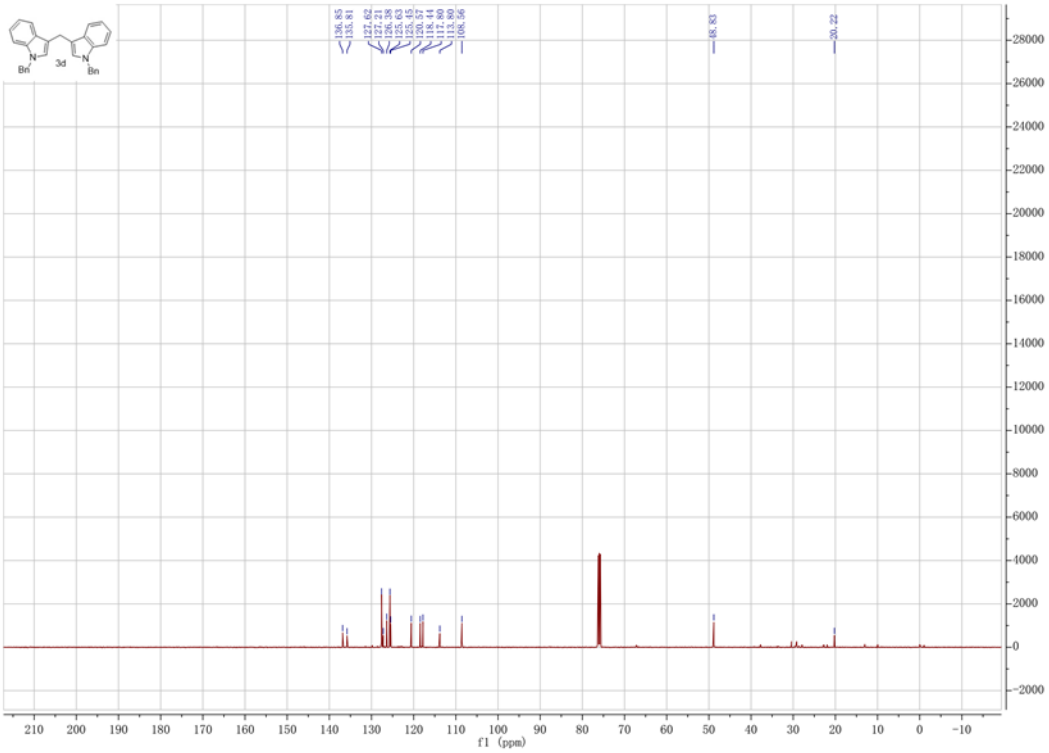
127.96
126.99
121.43
119.32
118.59
114.37
109.10
32.60
20.95
f1 (ppm)


3d
Bn
Bn
7.63
7.62
7.27
7.25
7.24
7.23
7.16
7.15
7.14
7.08
7.07
7.06
6.91
6.26
4.26
0.00
1.00
4.86
1.11
3.05
1.00
2.03
1.06
f1 (ppm)


3d
Bn
Bn
136.85
133.81
127.62
127.21
125.38
125.63
125.45
120.57
118.44
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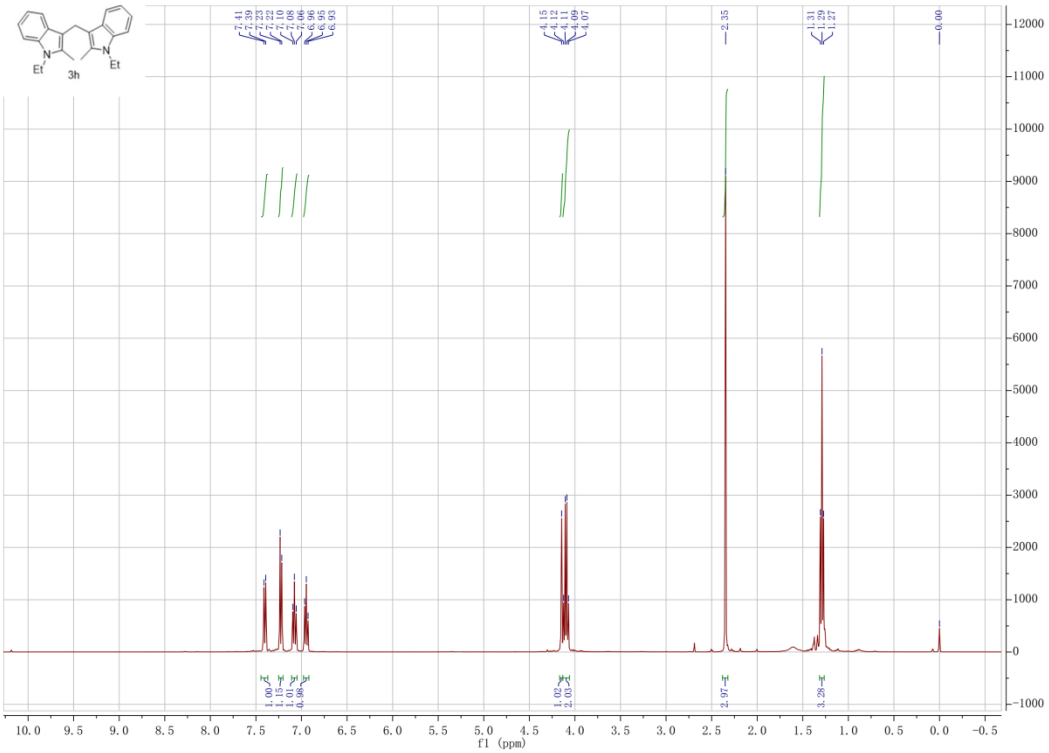
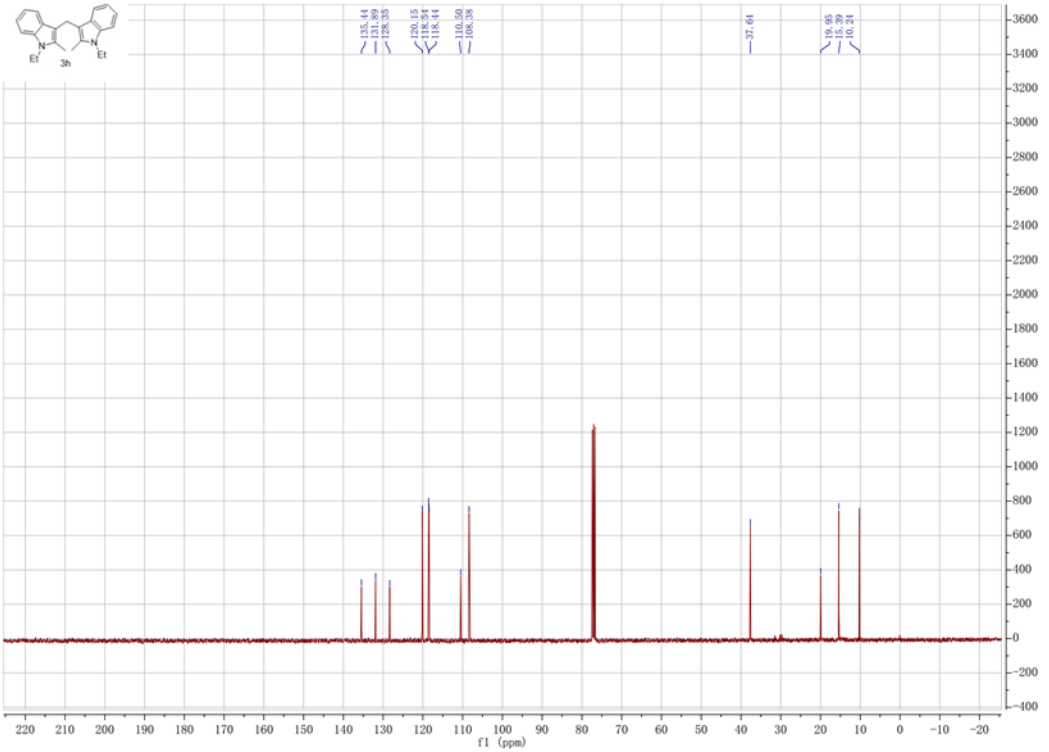
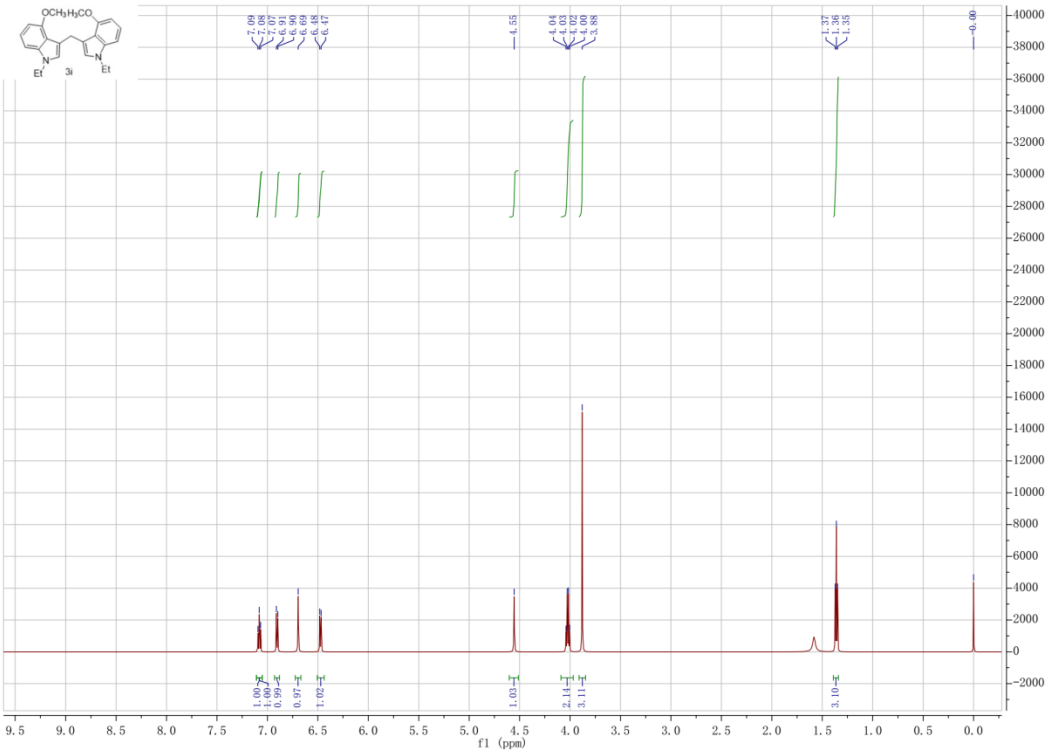
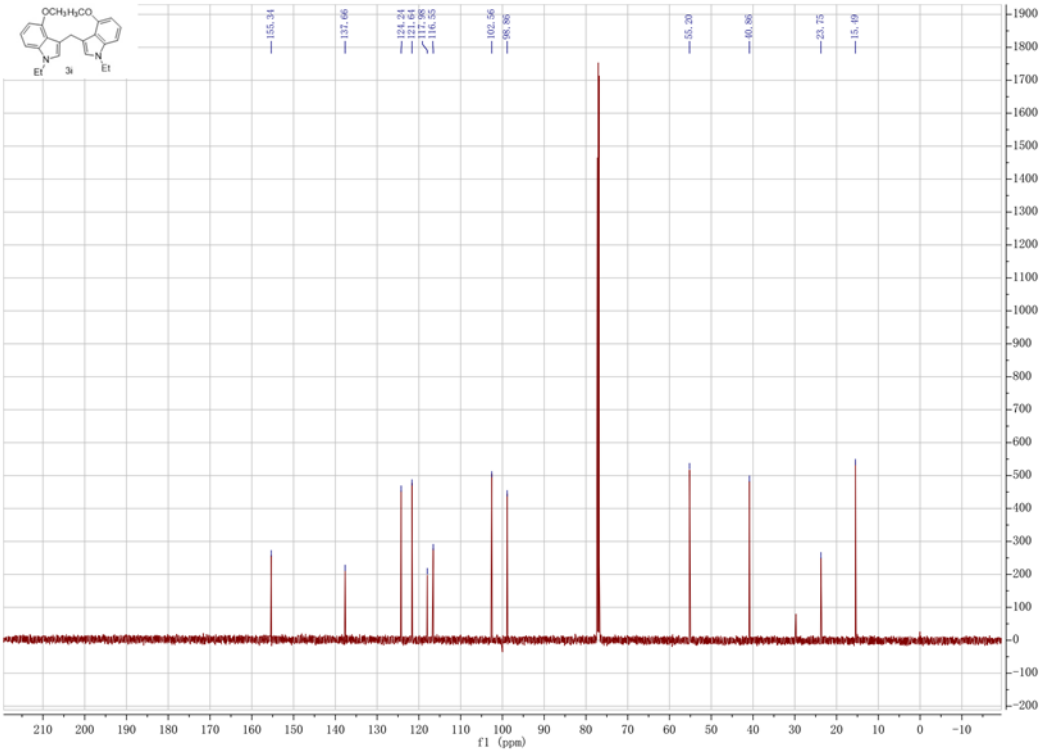
113.80
108.56
68.83
20.22
f1 (ppm)


3h
7.41
7.39
7.23
7.22
7.10
7.08
7.06
6.96
6.95
6.93
4.15
4.12
4.11
4.09
4.07
2.35
1.31
1.29
1.27
0.00
1.00
1.15
1.01
0.98
1.02
2.03
2.97
3.28
f1 (ppm)


3h
135.44
131.99
128.35
120.15
118.54
118.44
110.50
108.38
37.64
19.95
15.39
10.24
f1 (ppm)


OCH3H3CO
Et
3i
N
Et
7.09
7.08
7.07
6.91
6.90
6.48
6.47
4.55
4.04
4.03
4.02
4.00
3.88
1.37
1.36
1.35
0.00
1.00
1.00
0.99
0.97
1.02
1.03
2.14
3.11
3.10
f1 (ppm)


OCH3H3CO
Et
3i
N
Et
155.34
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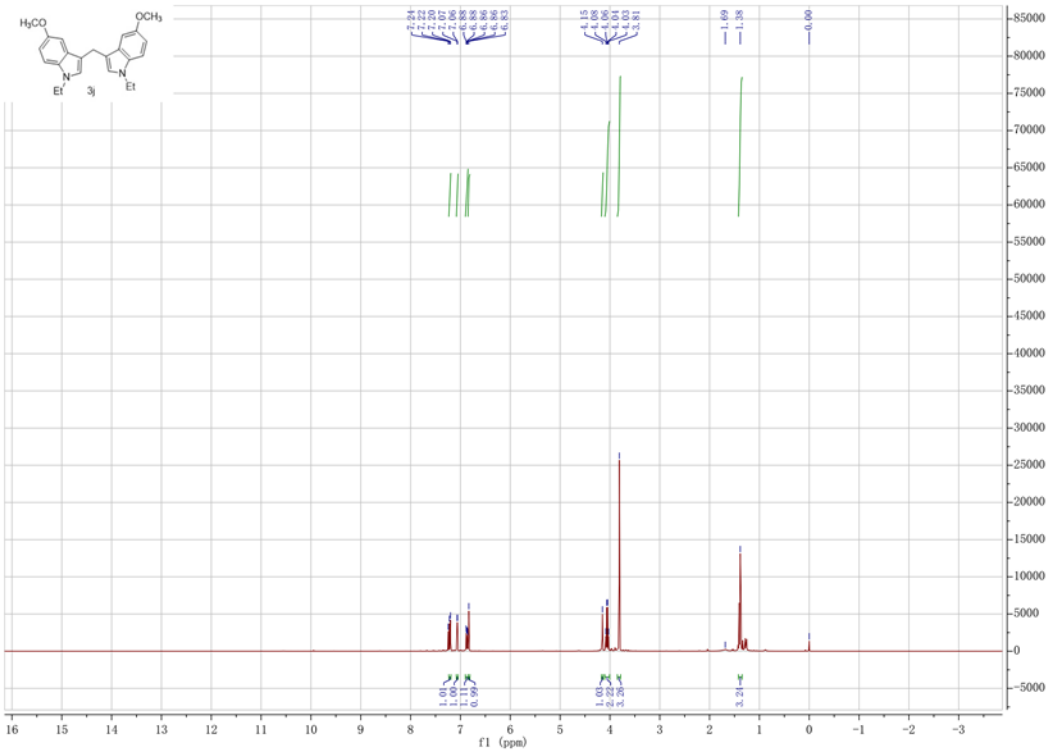
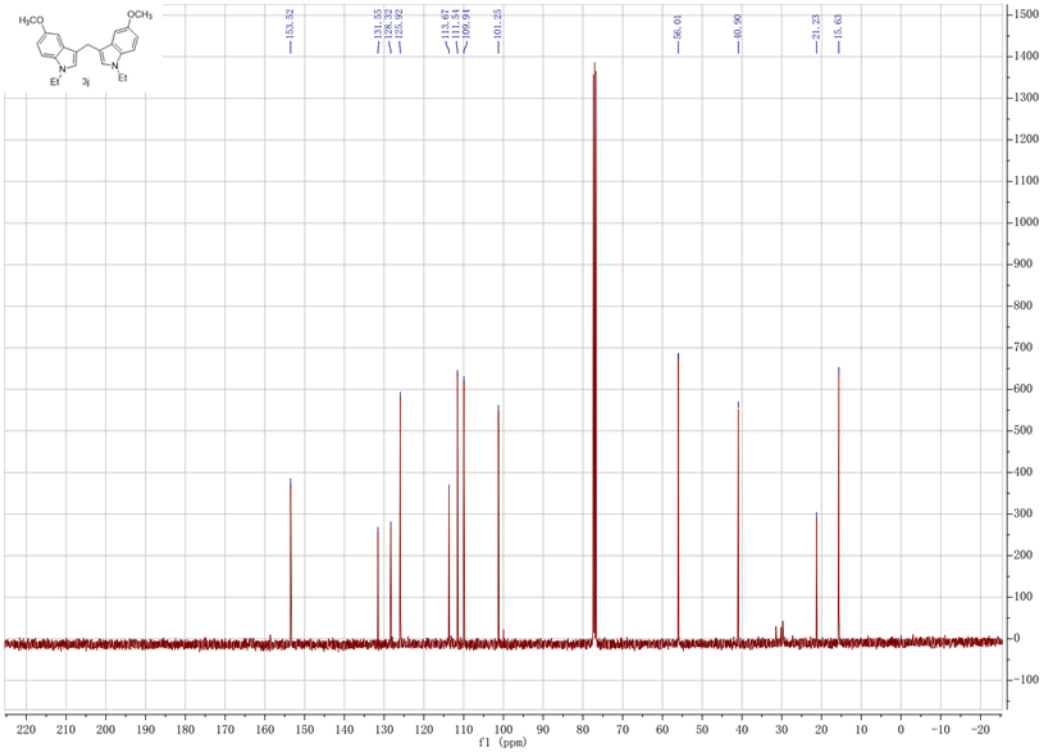
40.86
23.75
15.49
f1 (ppm)


H3CO
OCH3
N
Et
3j
Et
f1 (ppm)


H3CO
OCH3
N
Et
3j
Et
153.52
131.55
128.32
125.92
113.67
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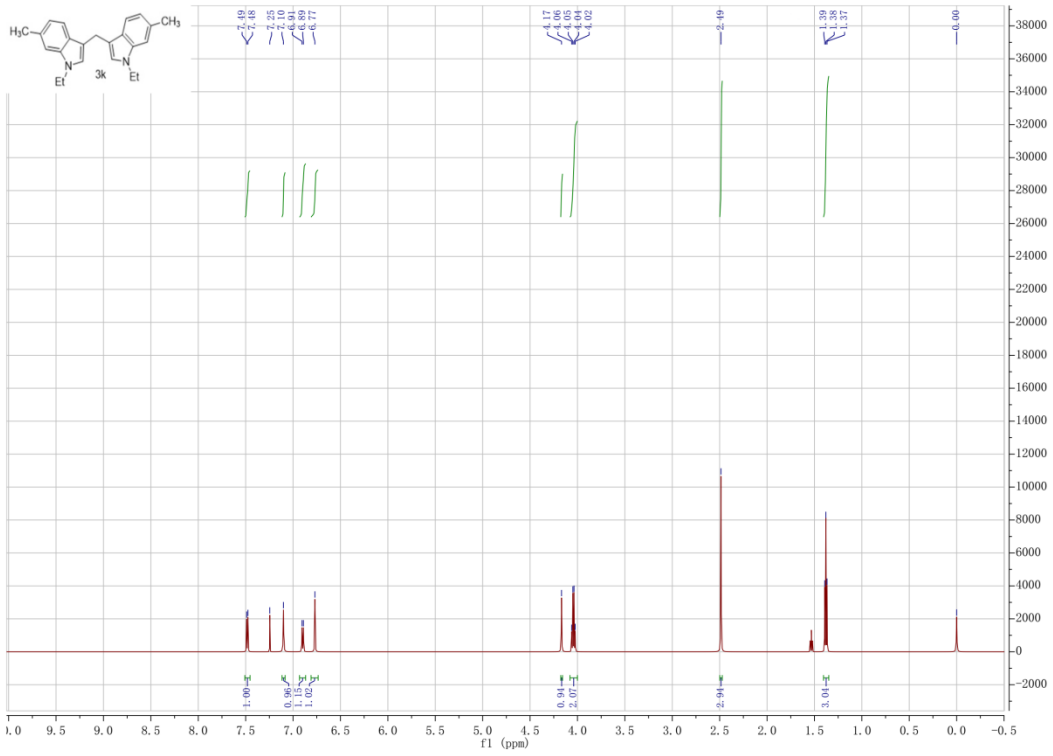
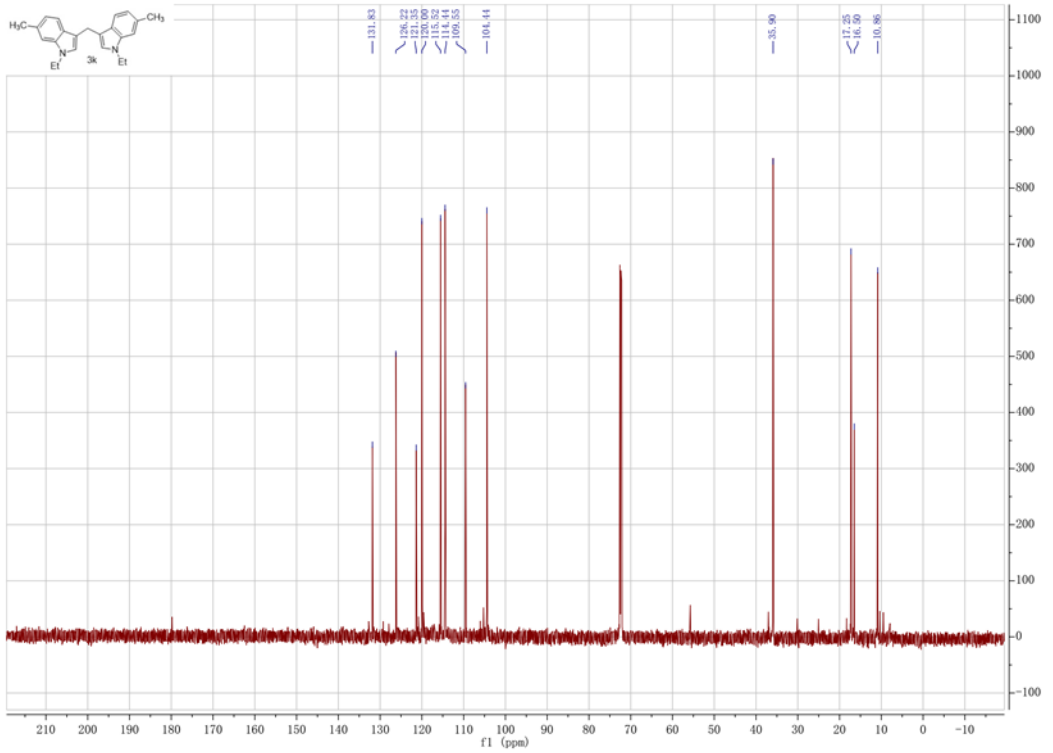
109.91
101.25
56.01
40.90
21.23
15.63
f1 (ppm)


3k
7.49
7.48
7.25
7.10
6.91
6.89
6.77
4.17
4.06
4.05
4.04
4.02
2.49
1.39
1.38
1.37
0.00
1.00
0.96
1.15
1.02
0.94
2.07
2.94
3.04
f1 (ppm)


3k
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55.90
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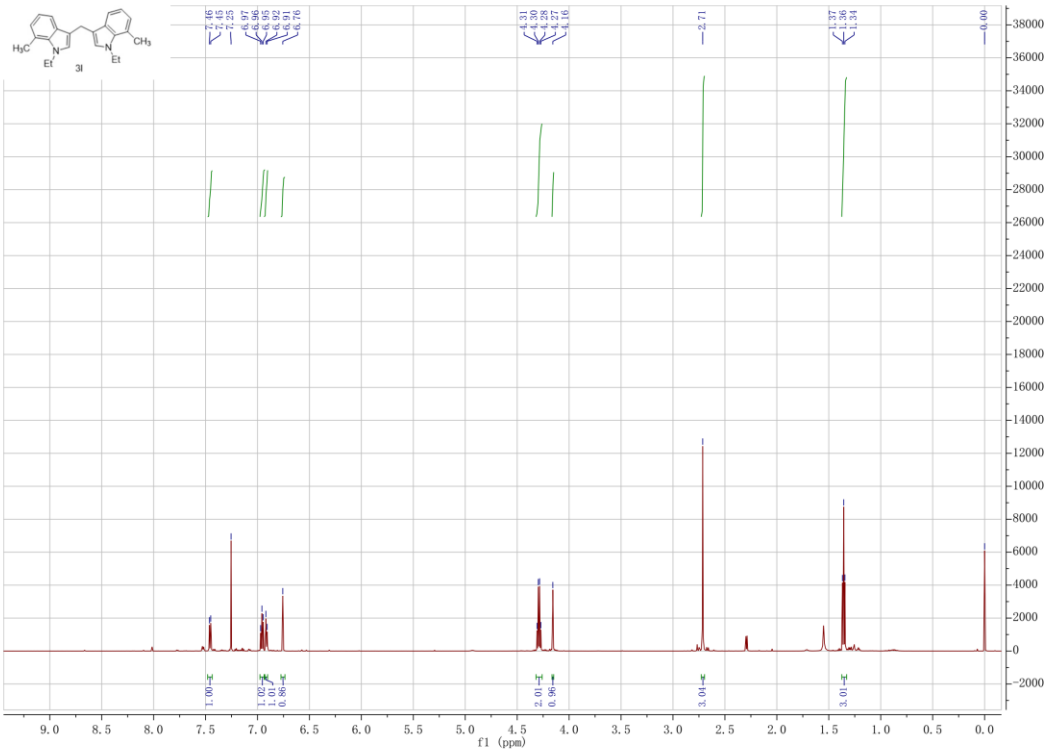
16.50
10.86
f1 (ppm)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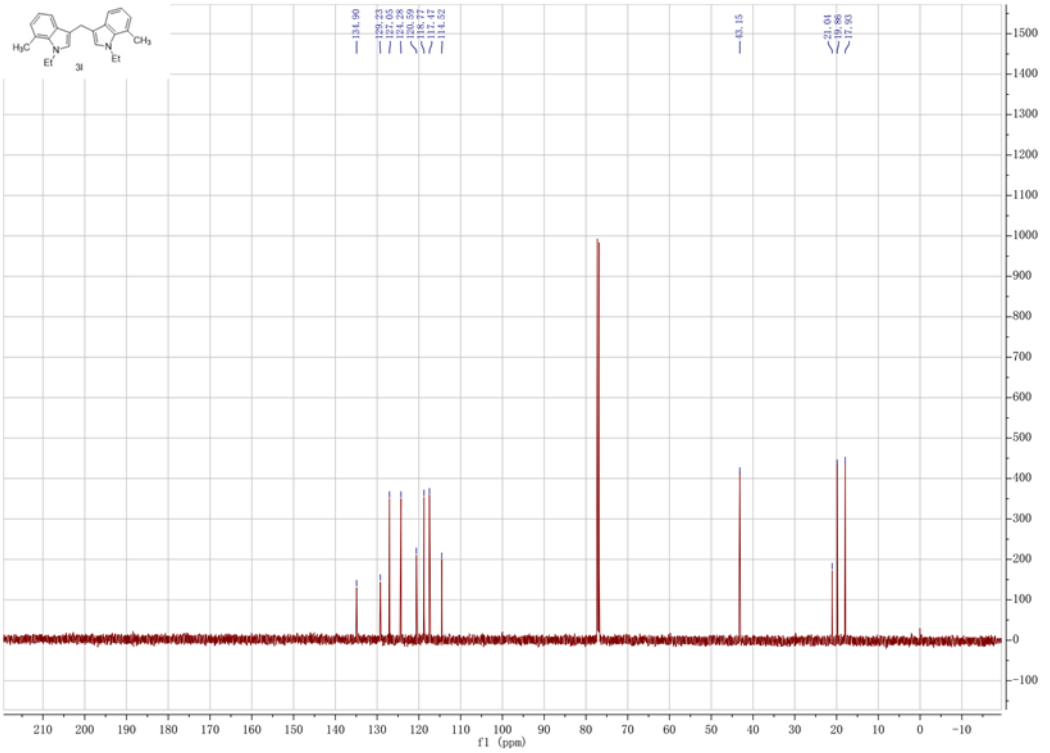
6.96
6.95
6.92
6.91
6.76
4.31
4.30
4.28
4.27
4.16
2.71
1.37
1.36
1.34
0.00
1.00
1.02
1.01
0.86
2.01
0.96
3.04
3.01
f1 (ppm)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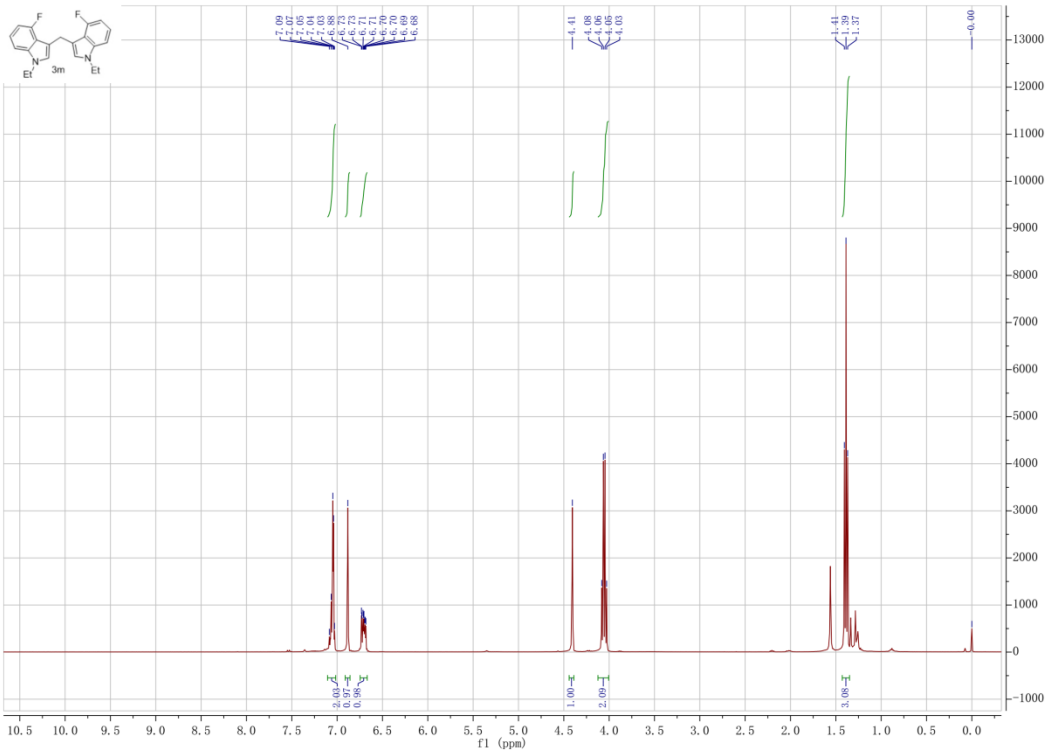
17.50
f1 (ppm)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7.03
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6.73
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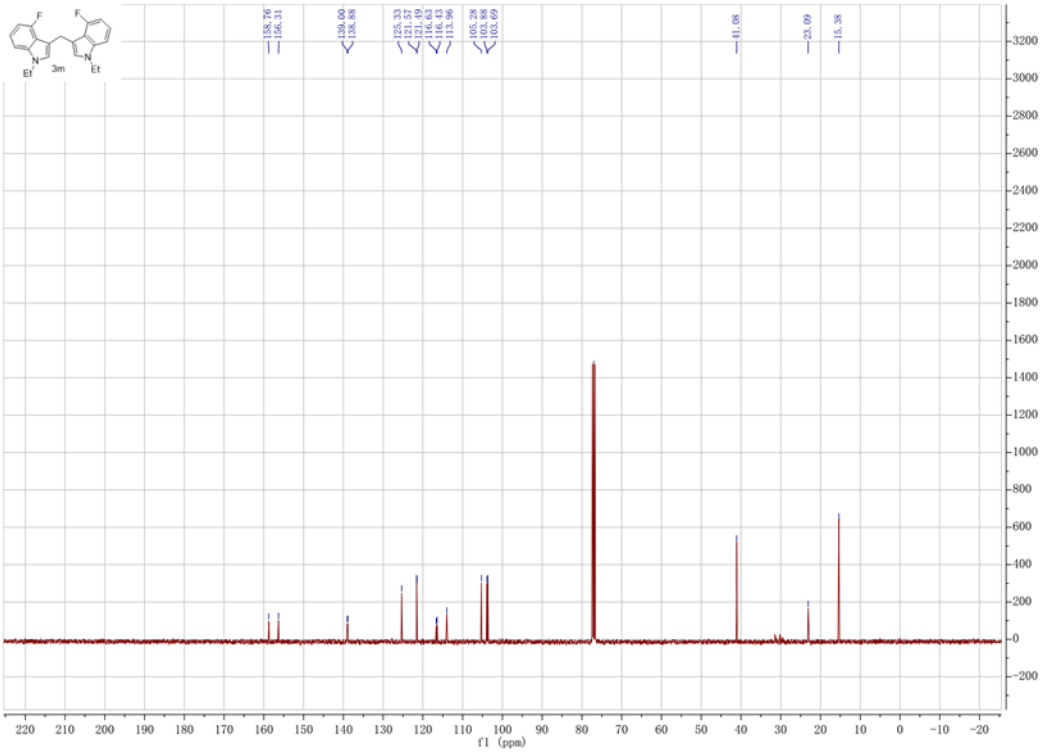
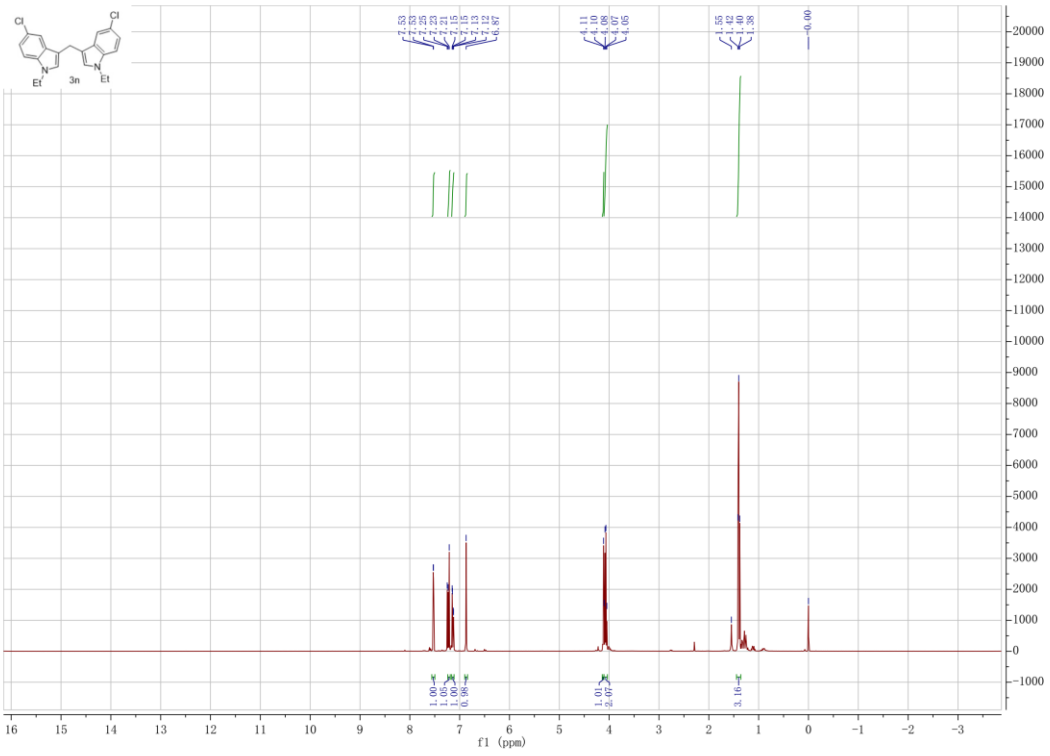
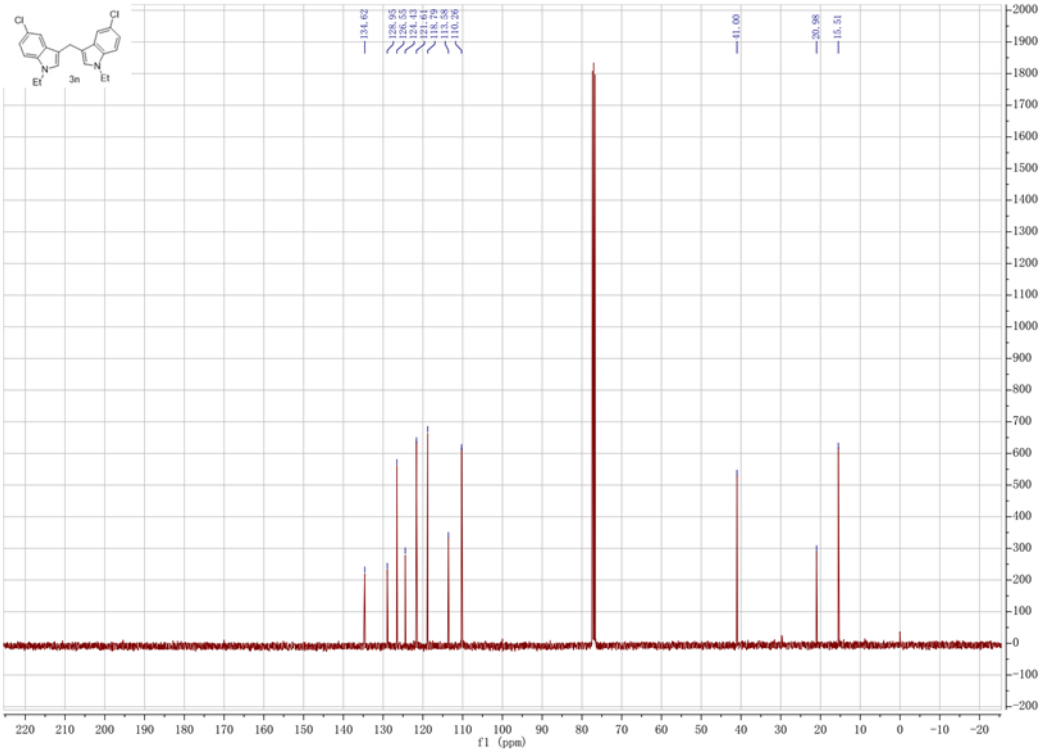
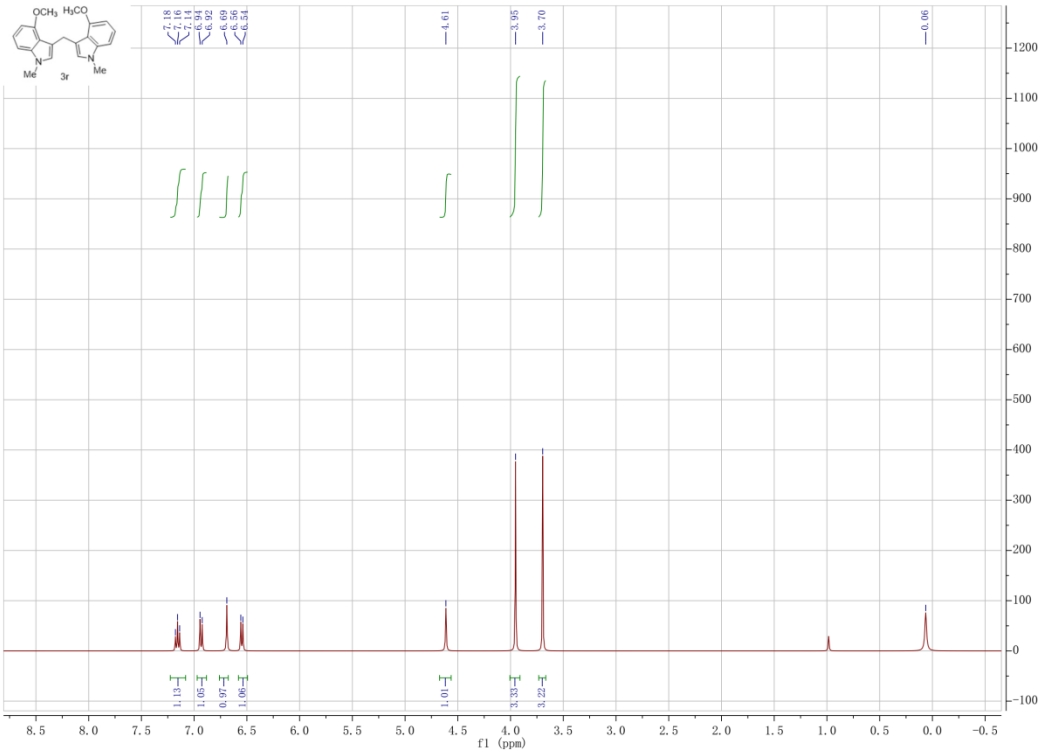
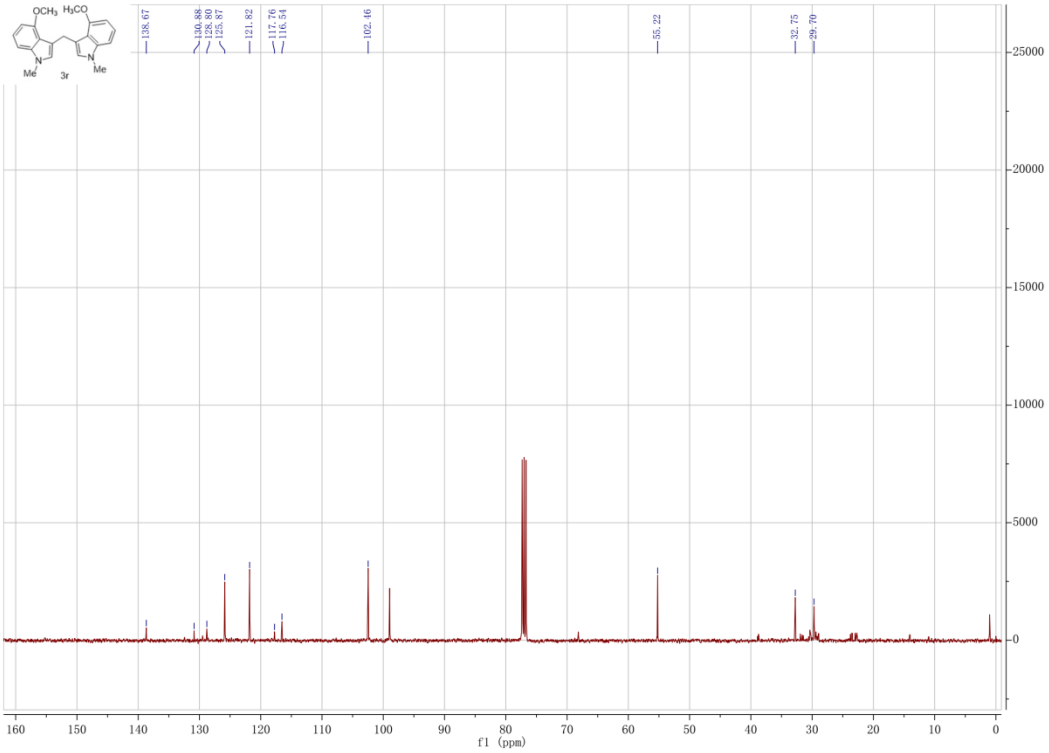
6.71
6.70
6.69
6.68
4.41
4.08
4.06
4.05
4.03
1.41
1.39
1.37
0.00
2.09
0.97
0.98
1.00
2.09
3.08
f1 (ppm)

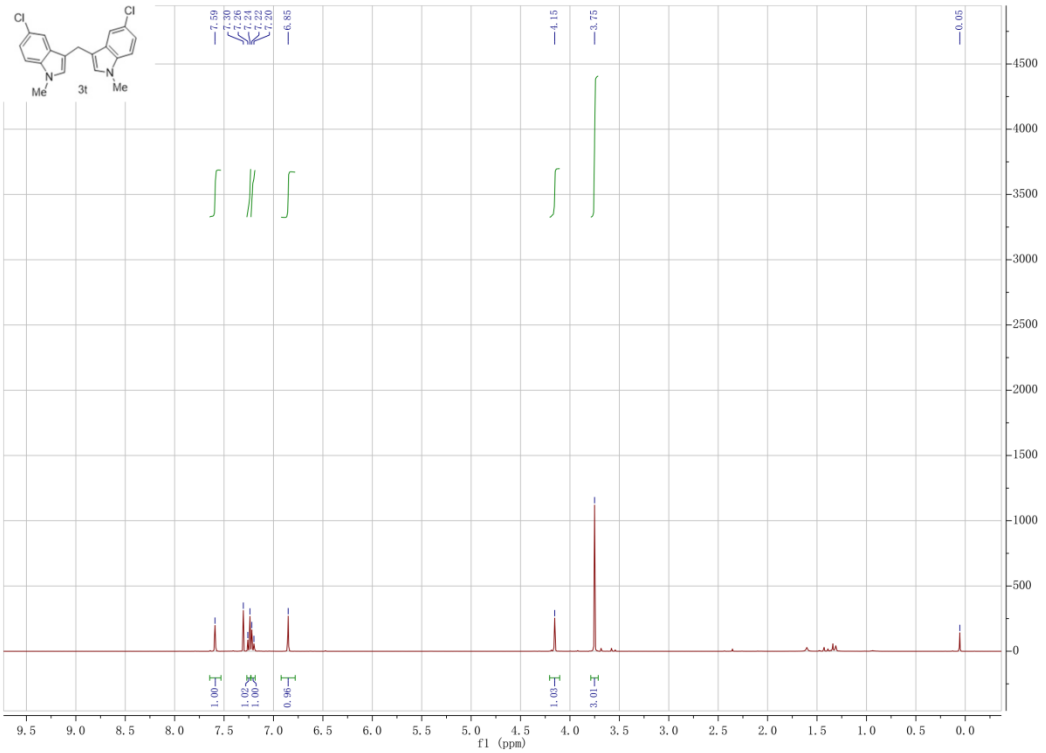

3m
158.76
156.31
139.00
138.88
125.33
121.57
121.49
116.63
116.43
113.96
105.28
103.88
103.69
41.08
23.69
15.38
f1 (ppm)

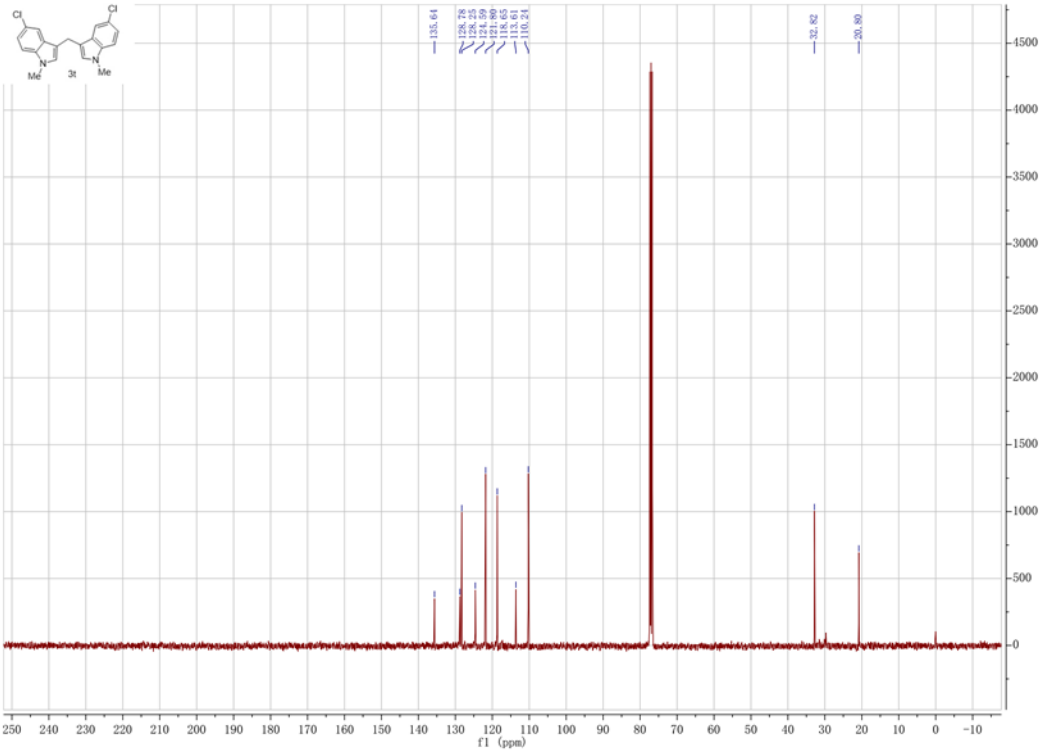

Cl
Et
3n
Et
Cl
7.53
7.53
7.25
7.23
7.21
7.15
7.15
7.13
7.12
6.87
4.11
4.10
4.08
4.07
4.05
1.55
1.42
1.40
1.38
0.00
1.00
1.05
1.00
0.98
1.01
2.07
3.16
f1 (ppm)

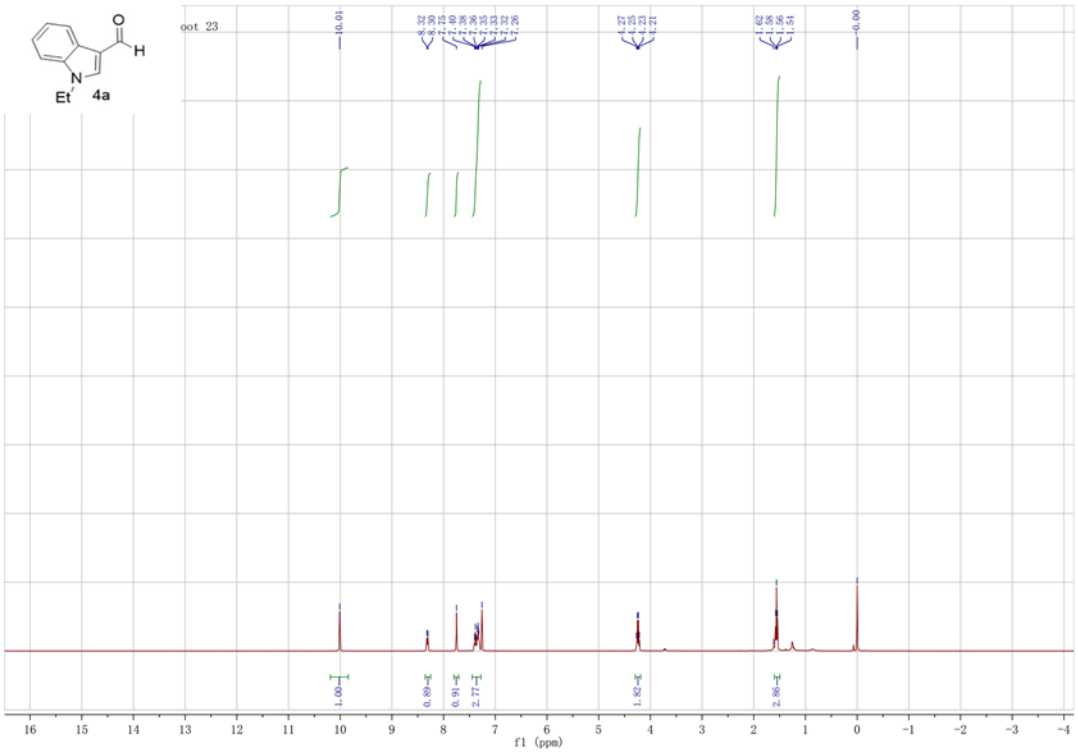

Cl
Et
3n
Et
Cl
134.62
128.95
126.55
124.43
121.61
118.79
111.58
110.26
41.00
20.98
15.51
f1 (ppm)

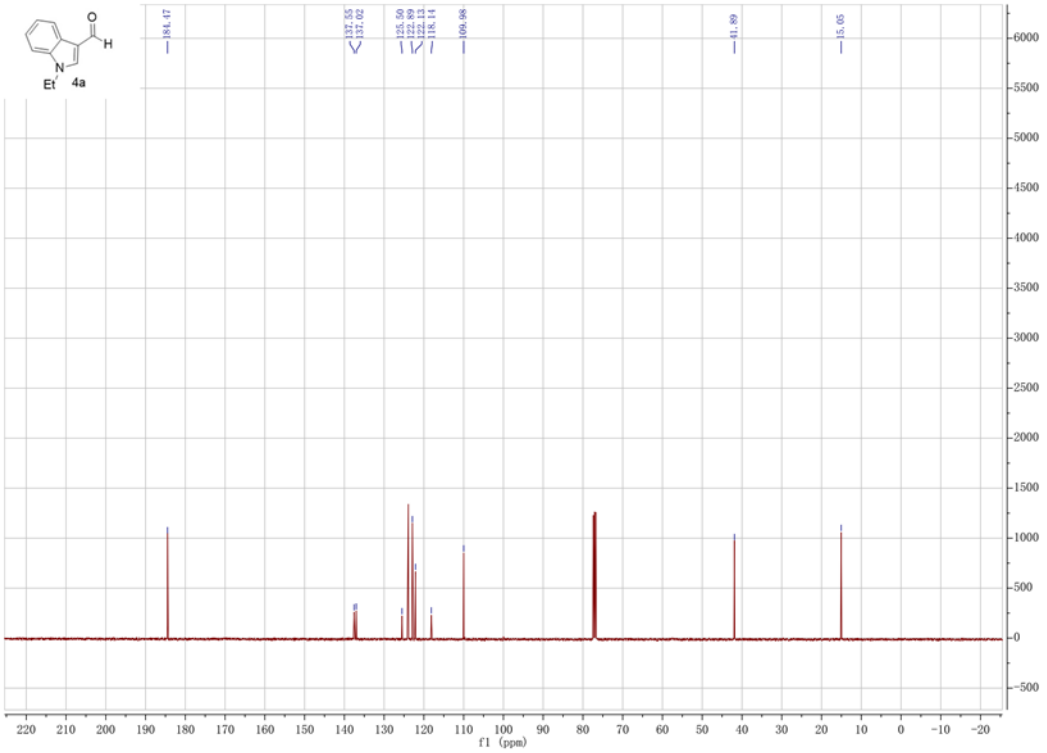

OCH3 H3CO
Me
3r
N
Me
7.18
7.16
7.14
6.94
6.92
6.69
6.56
6.54
4.61
3.95
3.70
0.06
1.13
1.05
0.97
1.06
1.01
3.33
3.22
f1 (ppm)

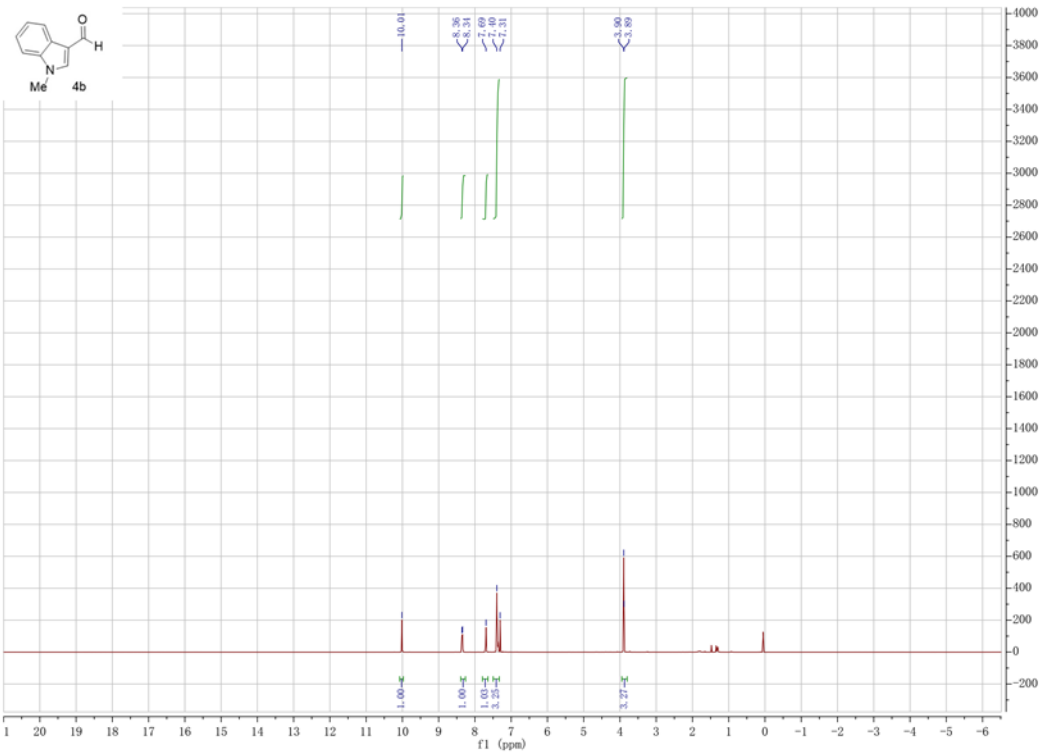

OCH3 H3CO
Me
3r
N
Me
138.67
130.88
128.80
125.87
121.82
117.76
116.54
102.46
55.22
32.75
29.70
f1 (ppm)

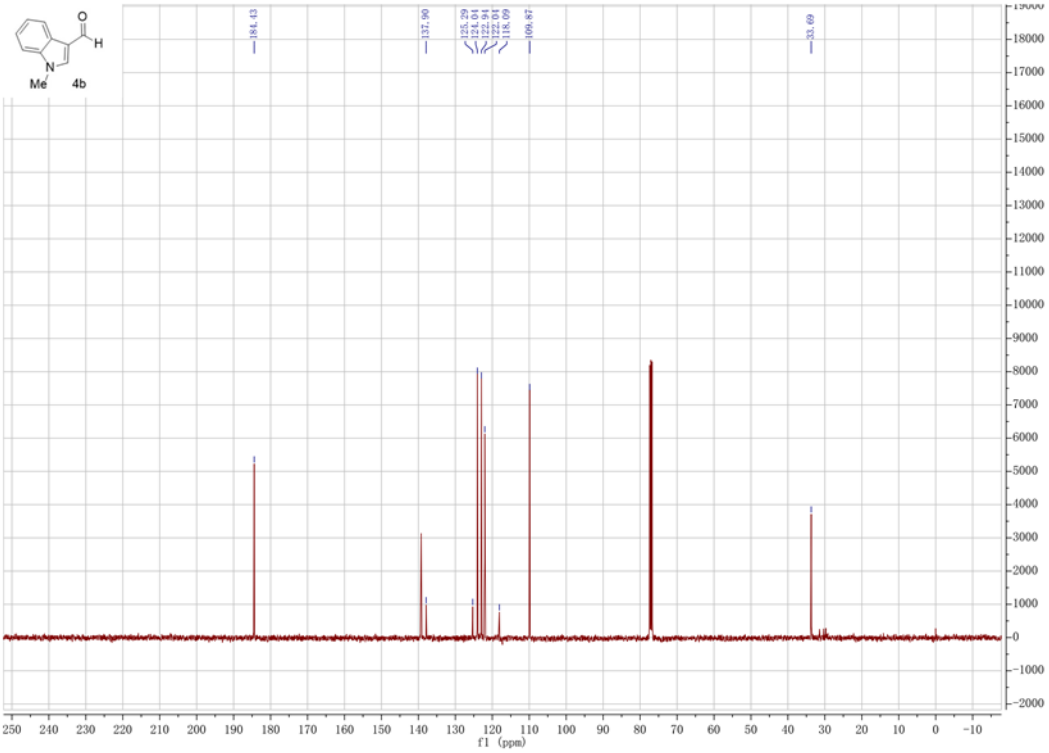

Cl
Cl
N
Me
3t
N
Me
7.59
7.30
7.26
7.24
7.22
7.20
6.85
4.15
3.75
0.05
1.00
1.02
1.00
0.96
1.03
3.01
f1 (ppm)

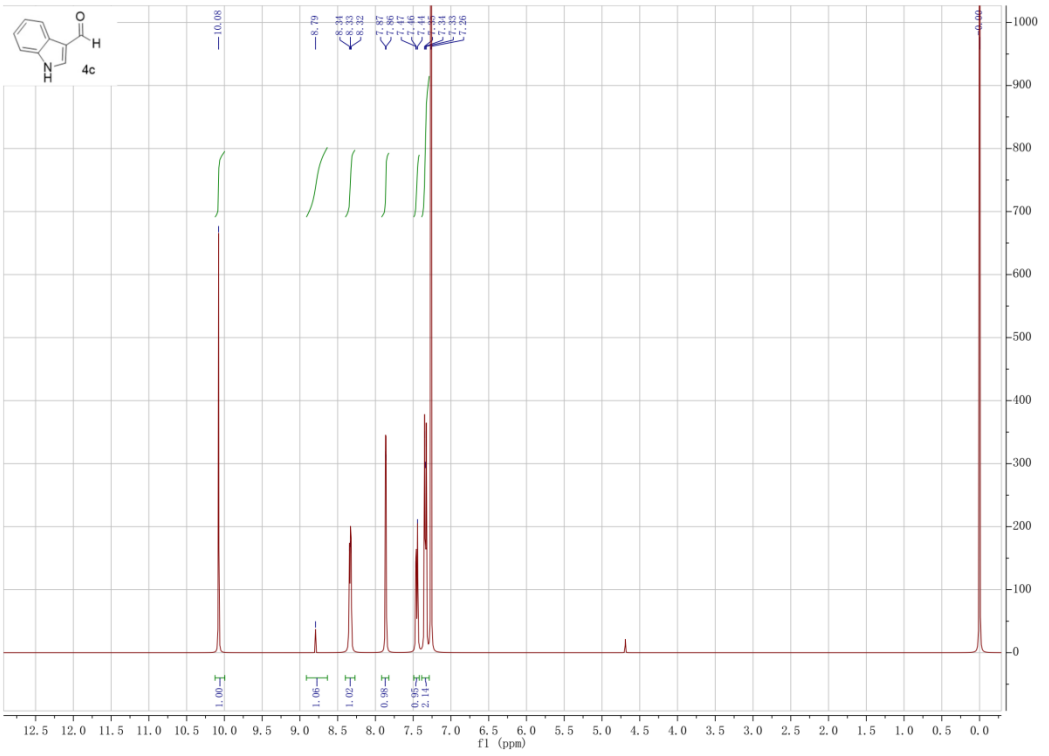

Cl
Cl
N
Me
3t
N
Me
135.64
128.78
128.35
124.59
121.89
118.65
113.61
110.24
32.82
20.80
f1 (ppm)

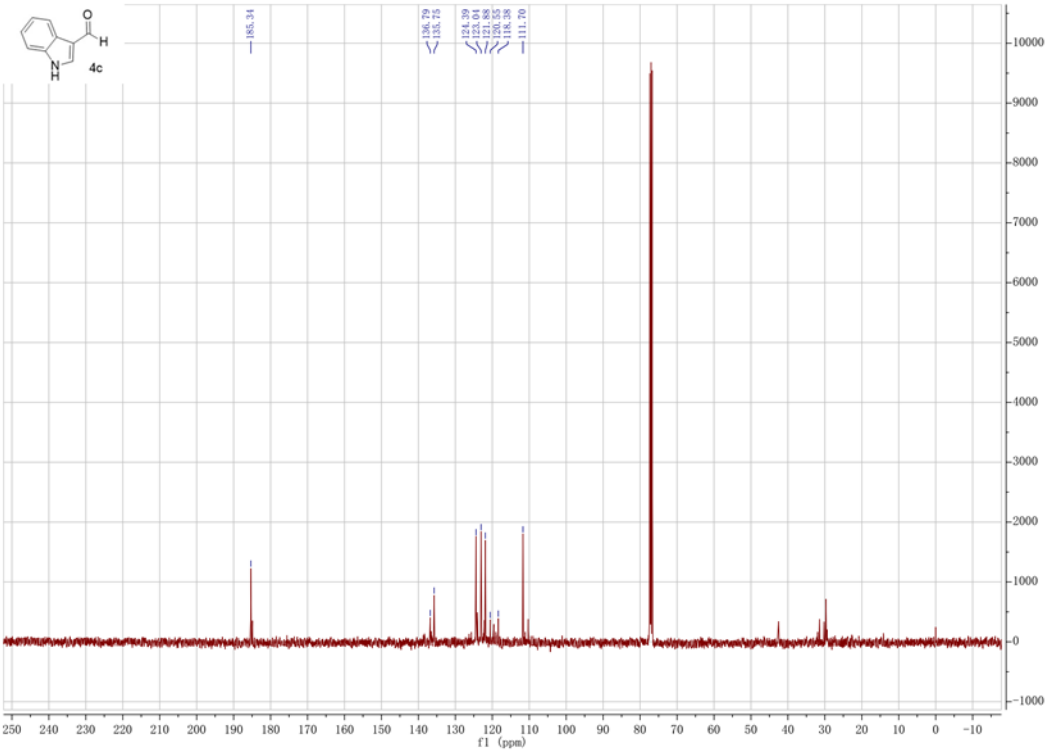

oot 23
10.01
8.32
8.30
7.75
7.40
7.38
7.36
7.35
7.33
7.32
7.26
4.27
4.25
4.23
4.21
1.62
1.58
1.56
1.54
0.00
1.00
0.89
0.91
2.77
1.82
2.86
f1 (ppm)
4a

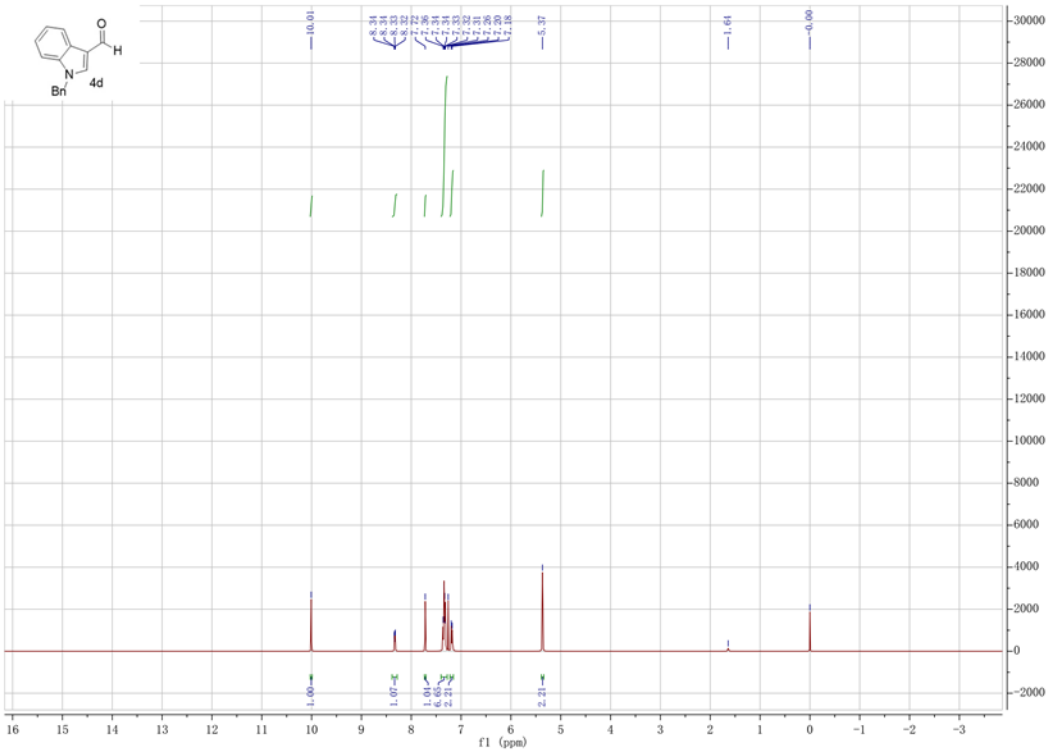

184.47
137.55
137.02
125.50
122.89
122.13
118.14
109.98
41.89
15.05
f1 (ppm)
4a

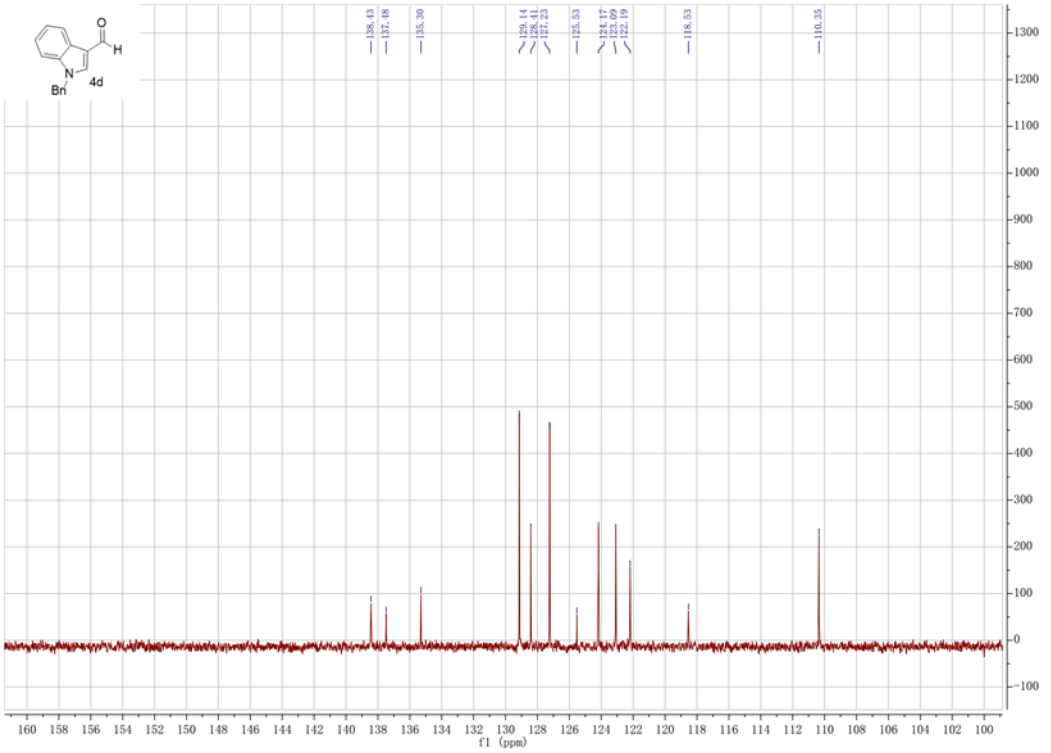

O
H
N
Me
4b
10.01
8.36
8.34
7.69
7.40
7.31
3.90
3.89
1.00
1.00
1.03
3.25
3.27
f1 (ppm)

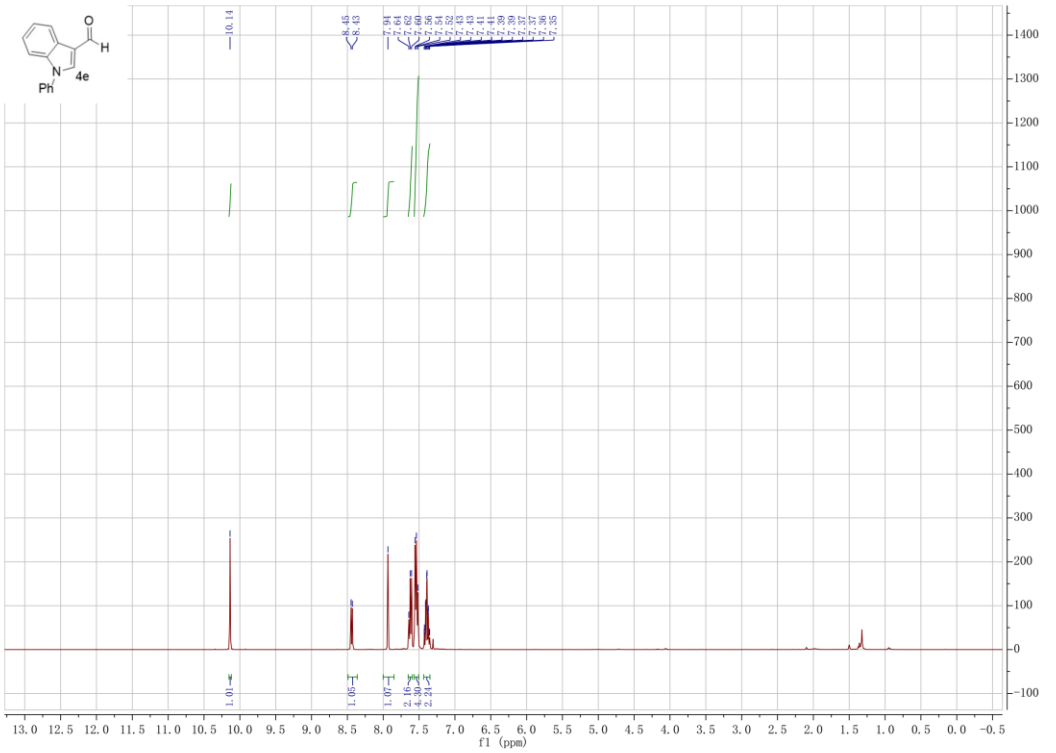

O
H
N
Me
4b
184.43
137.90
125.29
124.04
122.34
122.01
118.09
109.87
33.69
f1 (ppm)

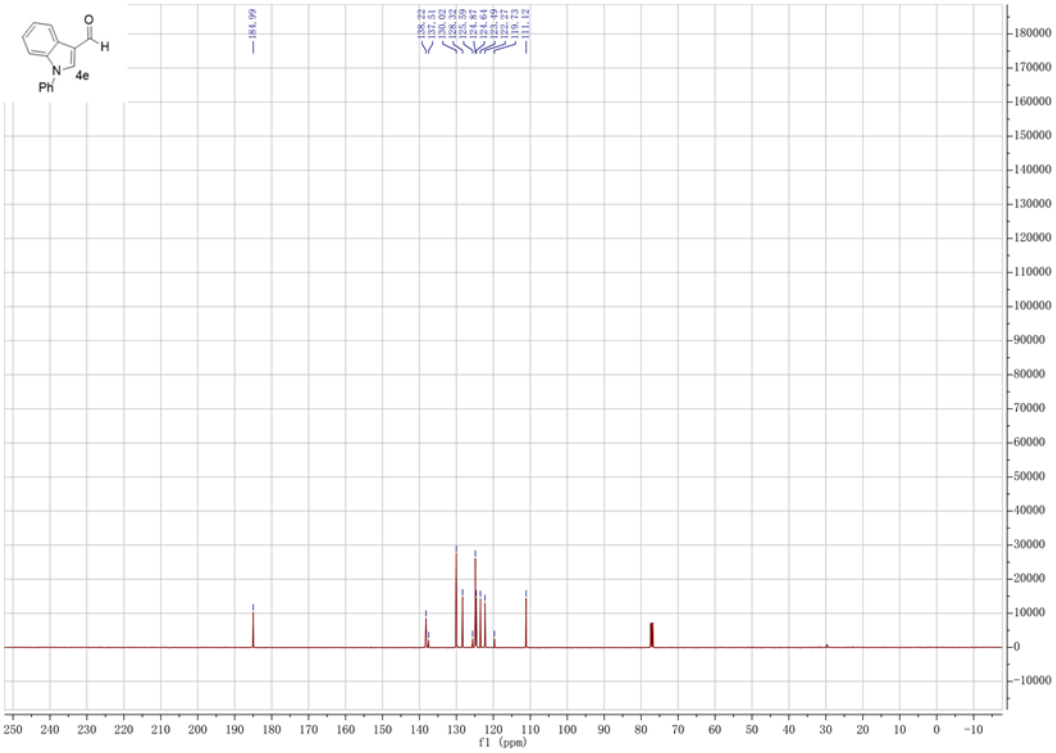

4c
10.08
8.79
8.34
8.33
8.32
7.87
7.86
7.17
7.46
7.44
7.34
7.33
7.26
0.00
1.00
1.06
1.02
0.98
0.95
2.14
f1 (ppm)

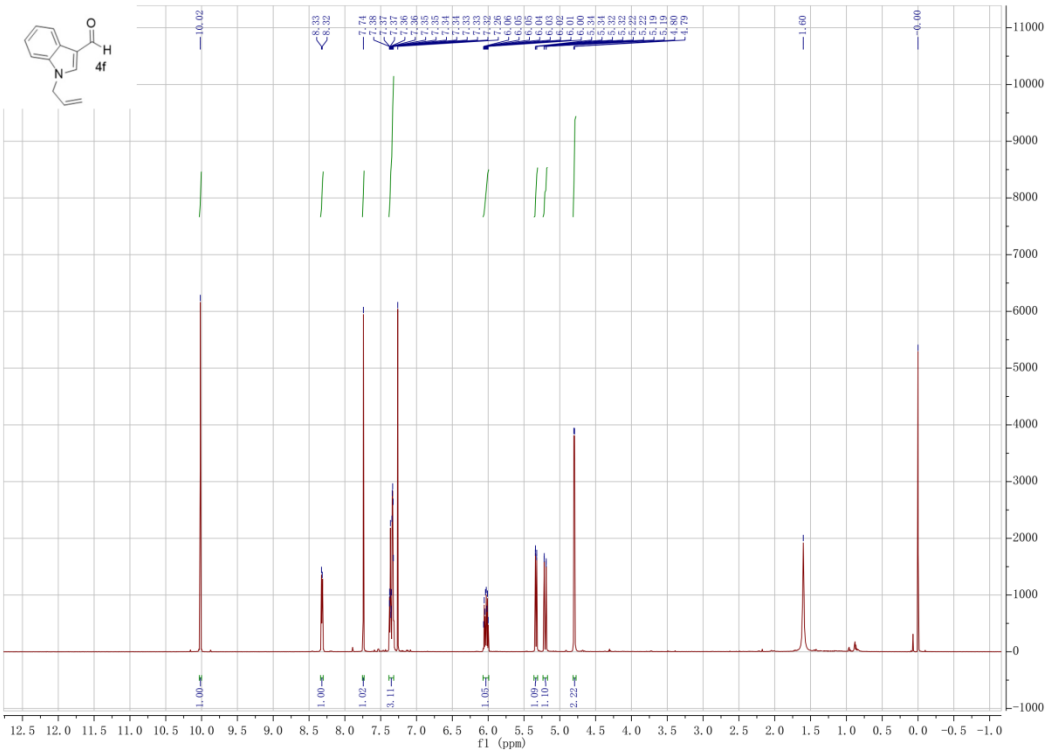

4c
185.34
136.79
135.75
124.39
123.04
121.98
120.55
118.38
111.70
f1 (ppm)

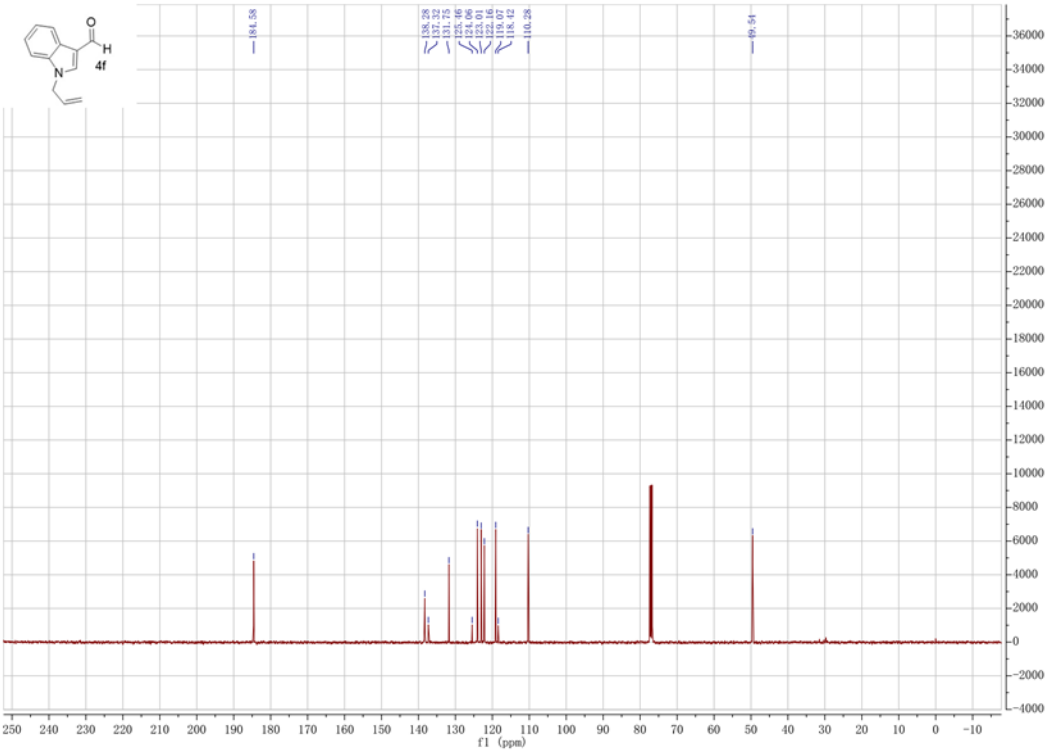

4d
10.01
8.34
8.34
8.33
8.32
7.36
7.34
7.34
7.33
7.32
7.31
7.26
7.20
7.18
5.37
1.64
0.00
1.00
1.07
1.04
6.65
2.21
2.21
f1 (ppm)

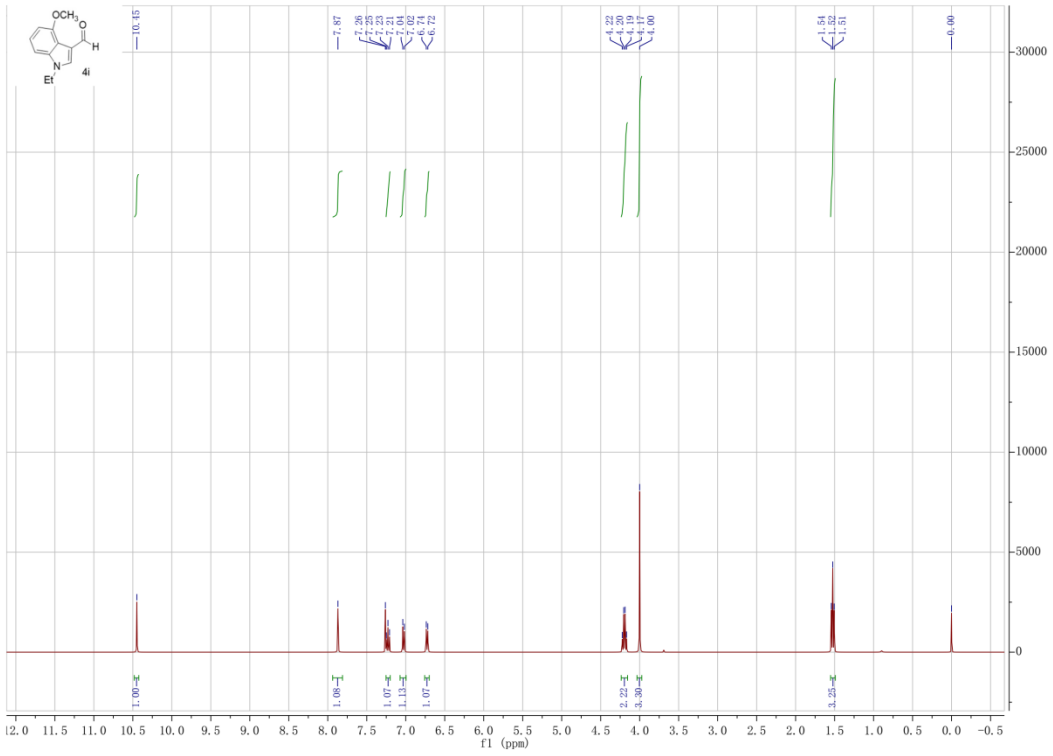

4d
138.43
137.48
135.30
129.14
128.41
127.23
125.53
124.17
123.09
122.19
118.53
110.35
f1 (ppm)

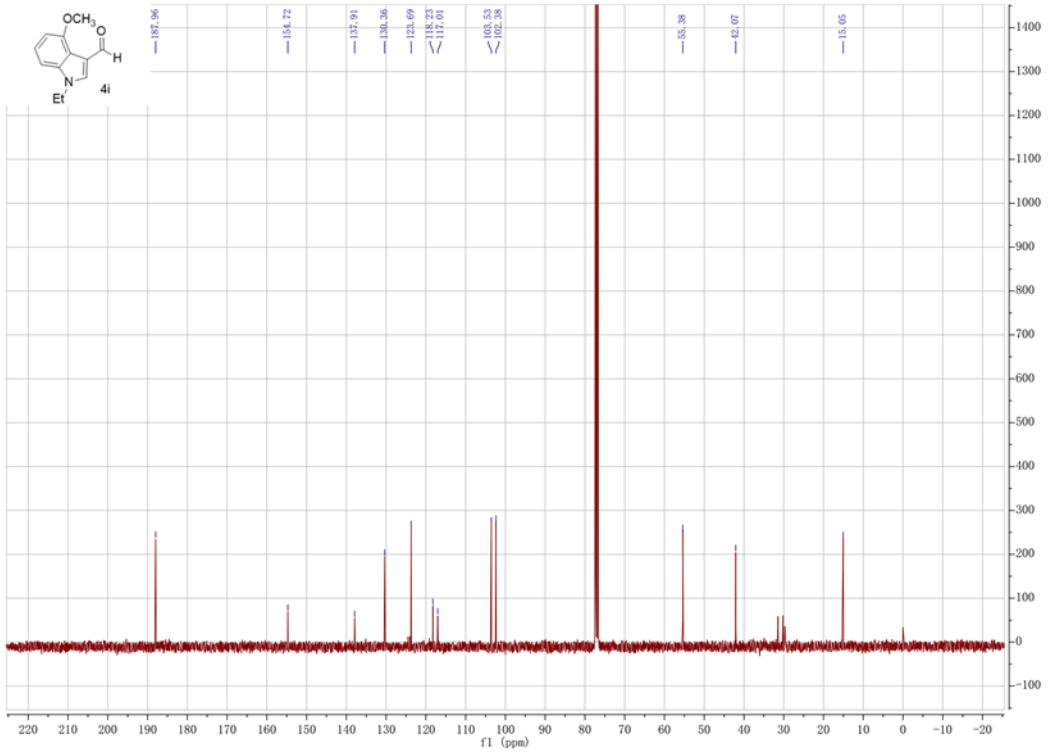

4e
Ph
10.14
8.45
8.43
7.94
7.64
7.62
7.60
7.56
7.54
7.52
7.43
7.41
7.39
7.37
7.36
7.35
1.01
1.05
1.07
2.16
6.00
2.24
f1 (ppm)

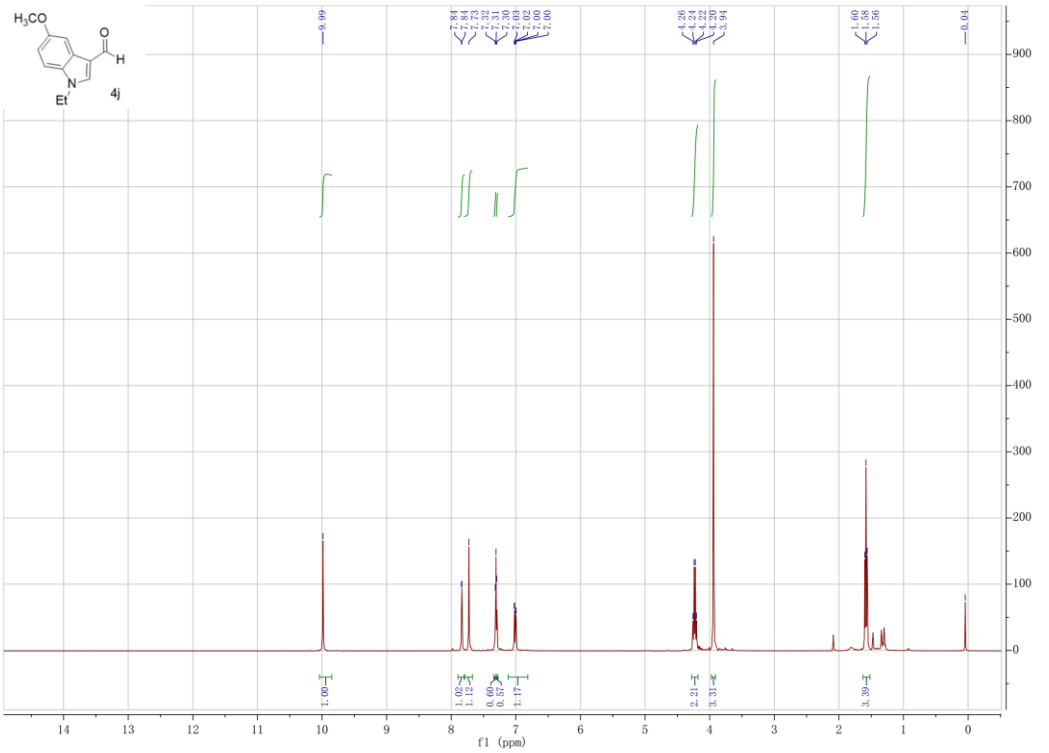

4e
Ph
184.99
138.22
137.81
130.02
128.32
125.59
124.87
124.64
123.49
122.27
120.73
111.12
f1 (ppm)

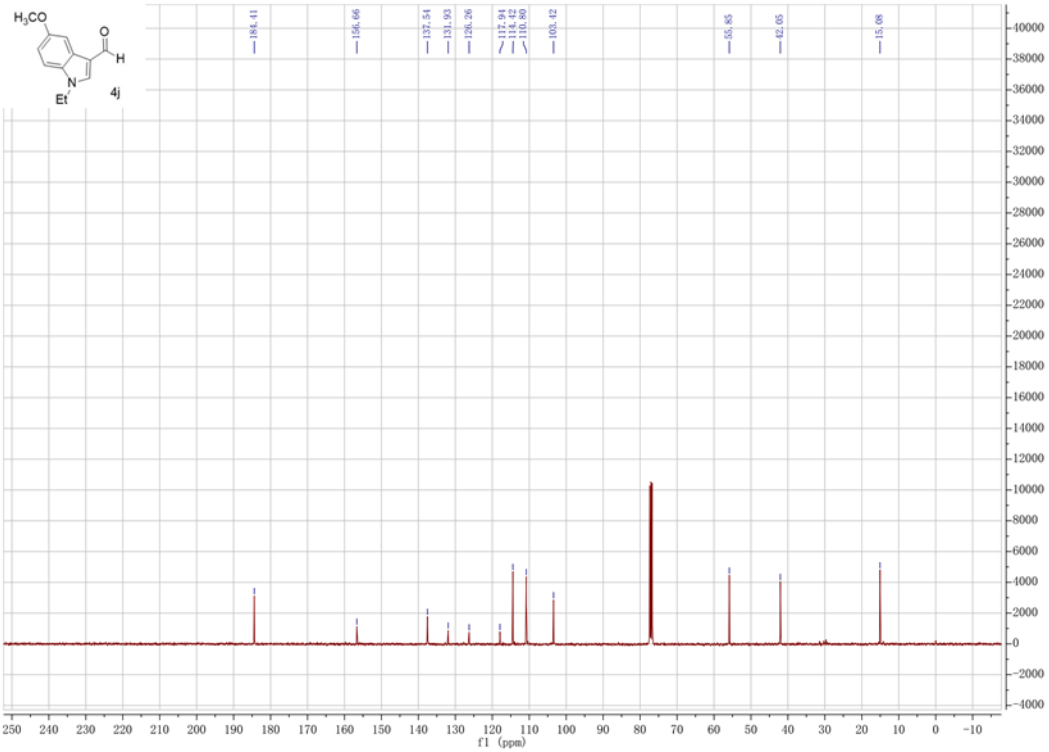

4f
10.02
8.33
8.32
7.74
7.38
7.37
7.36
7.35
7.34
7.33
7.32
7.26
6.06
6.05
6.04
6.03
6.02
6.01
6.00
5.34
5.32
5.22
5.22
5.19
5.19
4.80
4.79
1.60
0.00
1.00
1.00
1.02
3.11
1.05
1.09
1.10
2.22
f1 (ppm)

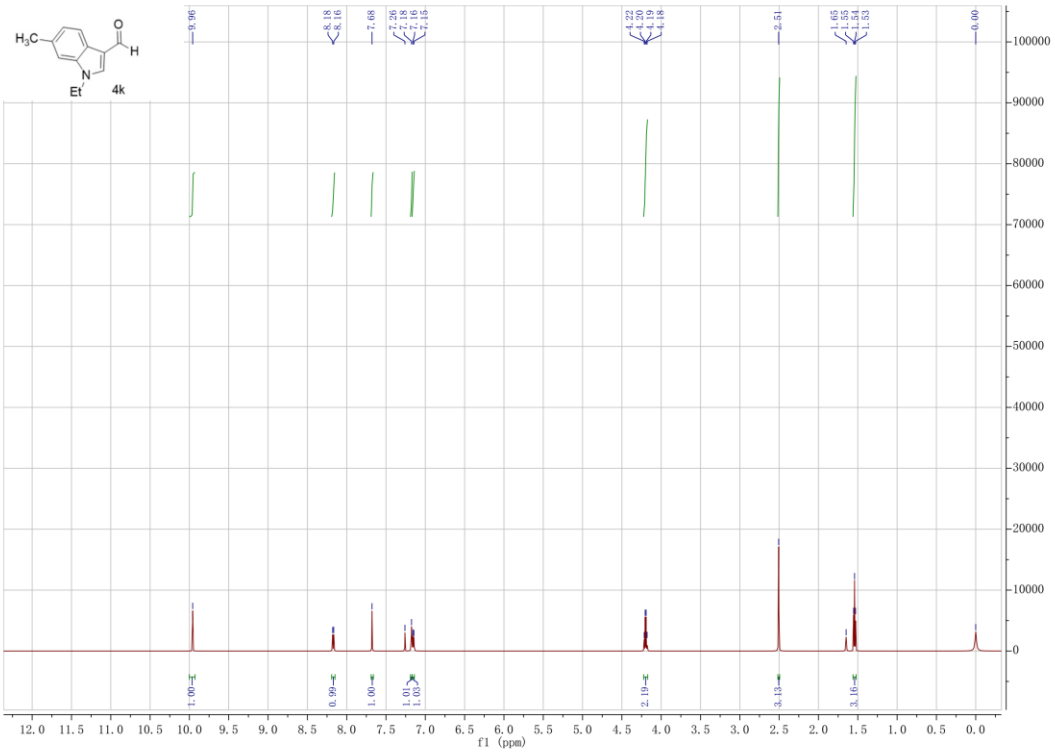

4f
184.58
138.28
137.32
131.75
125.46
124.06
123.01
122.16
119.07
118.42
110.28
69.54
f1 (ppm)

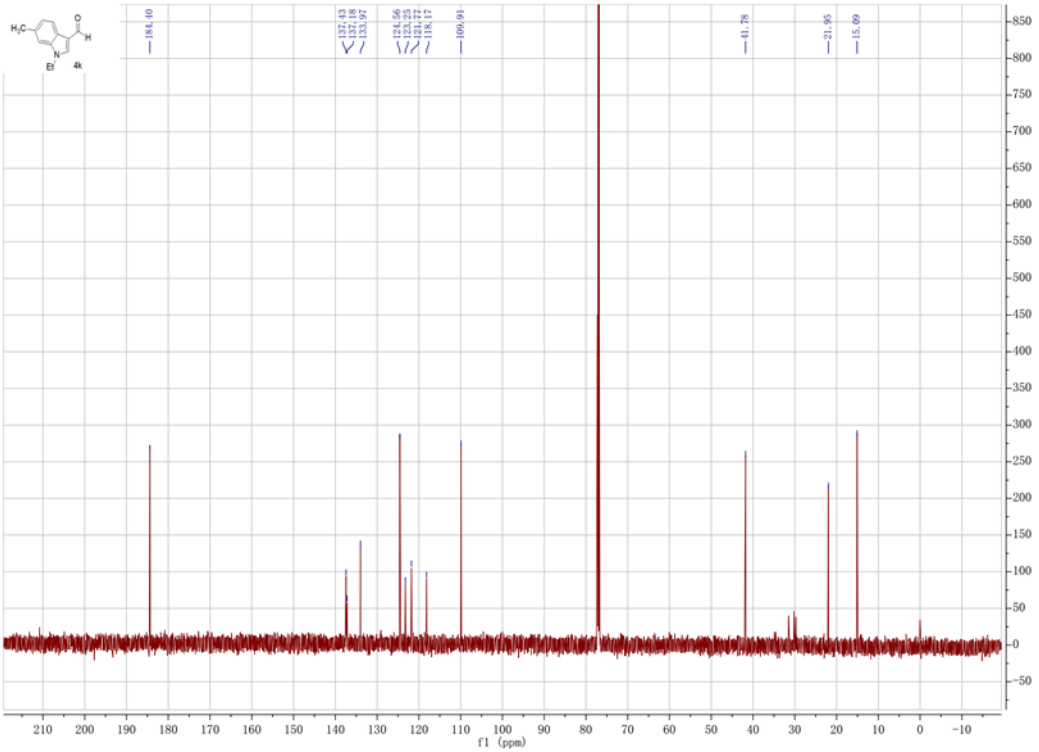

OCH3
O
H
N
Et
4i
10.45
7.87
7.26
7.25
7.23
7.21
7.04
7.02
6.74
6.72
4.22
4.20
4.19
4.17
4.00
1.54
1.52
1.51
0.00
1.00
1.08
1.07
1.13
1.07
2.22
3.30
3.25
f1 (ppm)

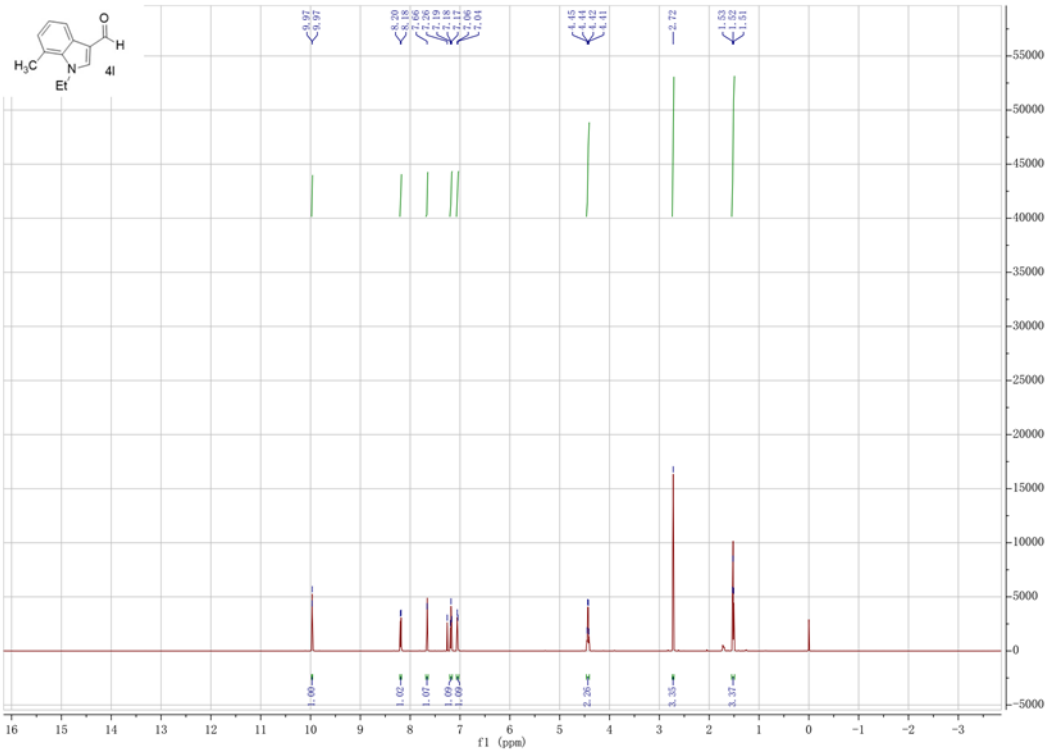

OCH3
O
H
N
Et
4i
187.96
154.72
137.91
130.36
123.69
118.23
117.01
103.53
102.38
55.38
42.07
15.05
f1 (ppm)

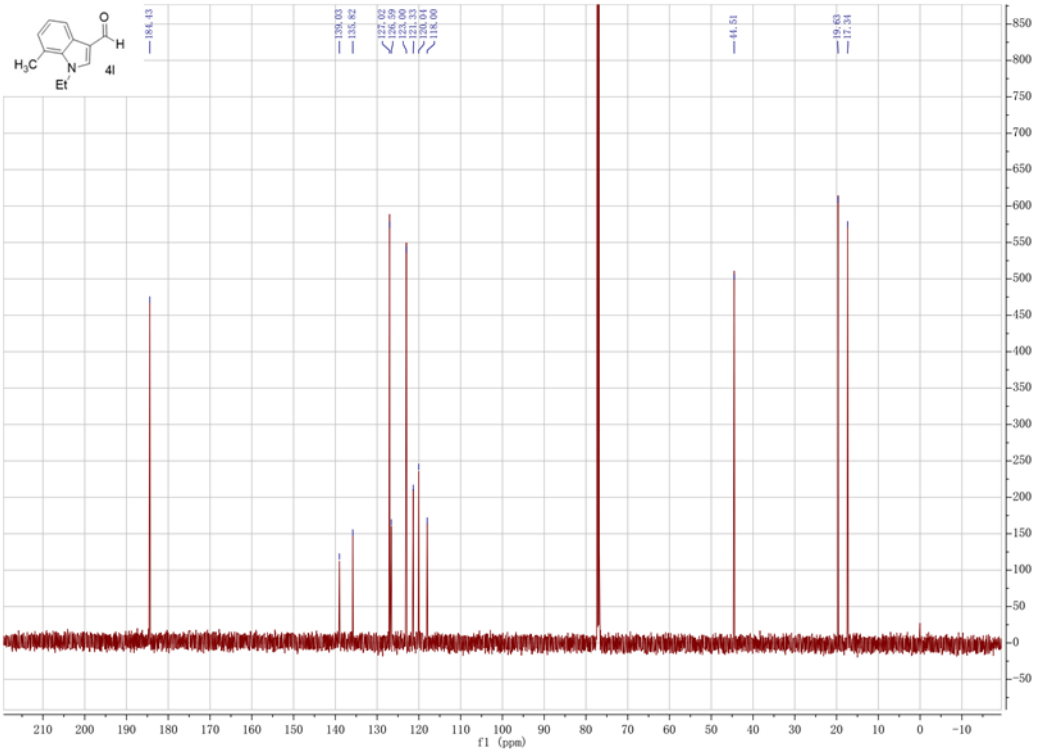

4j
9.99
7.84
7.84
7.73
7.32
7.31
7.30
7.03
7.02
7.00
7.00
4.26
4.24
4.22
4.20
3.94
1.60
1.58
1.56
0.04
1.00
1.02
1.12
0.60
0.57
1.17
2.21
3.31
3.39
f1 (ppm)

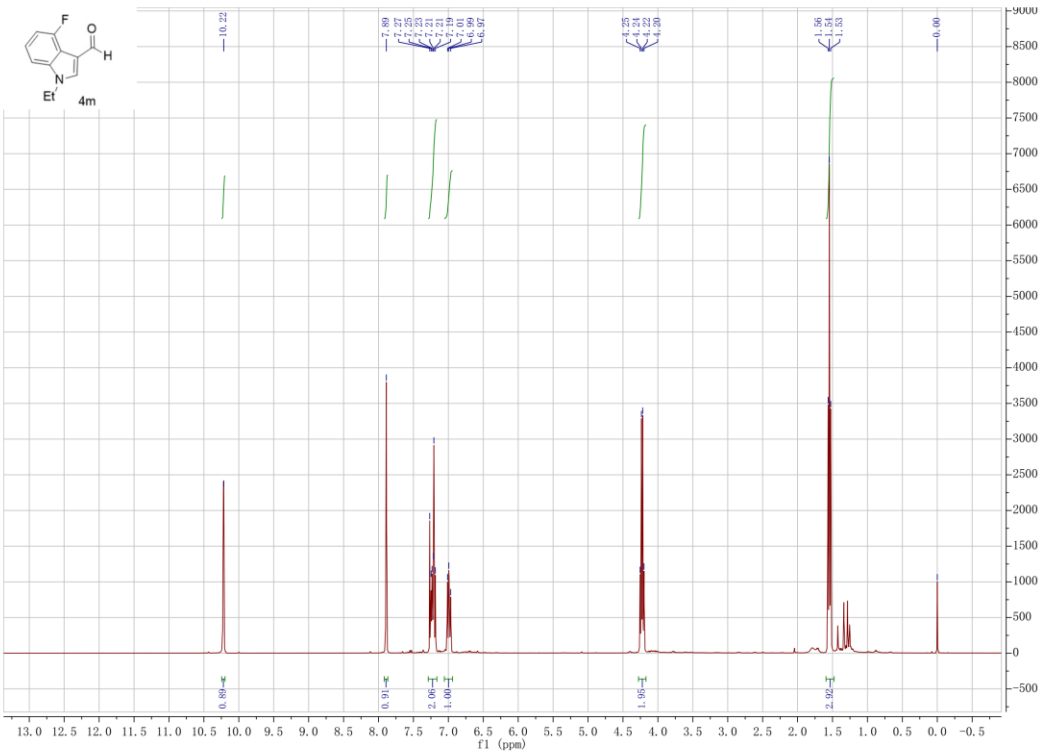

4j
184.41
156.66
137.54
131.93
126.26
117.94
114.42
110.89
103.42
65.85
42.65
15.08
f1 (ppm)

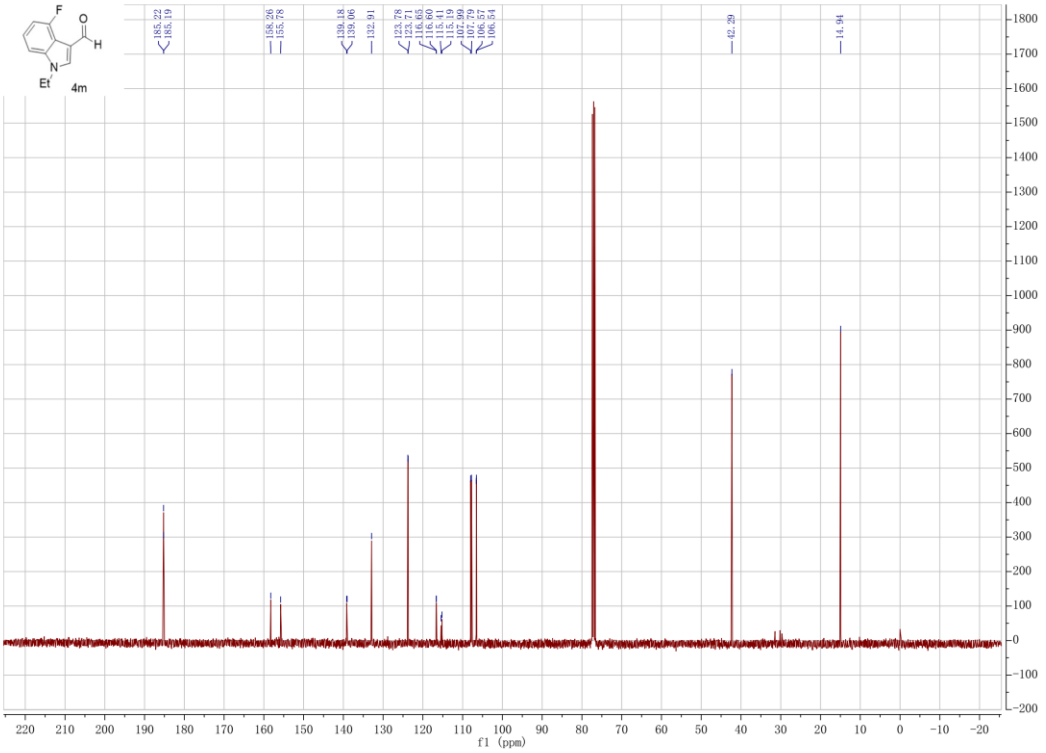

4k
9.96
8.18
8.16
7.68
7.26
7.18
7.16
7.15
4.22
4.20
4.19
4.18
2.51
1.65
1.55
1.54
1.53
0.00
1.00
0.99
1.00
1.01
1.03
2.19
3.13
3.16
f1 (ppm)

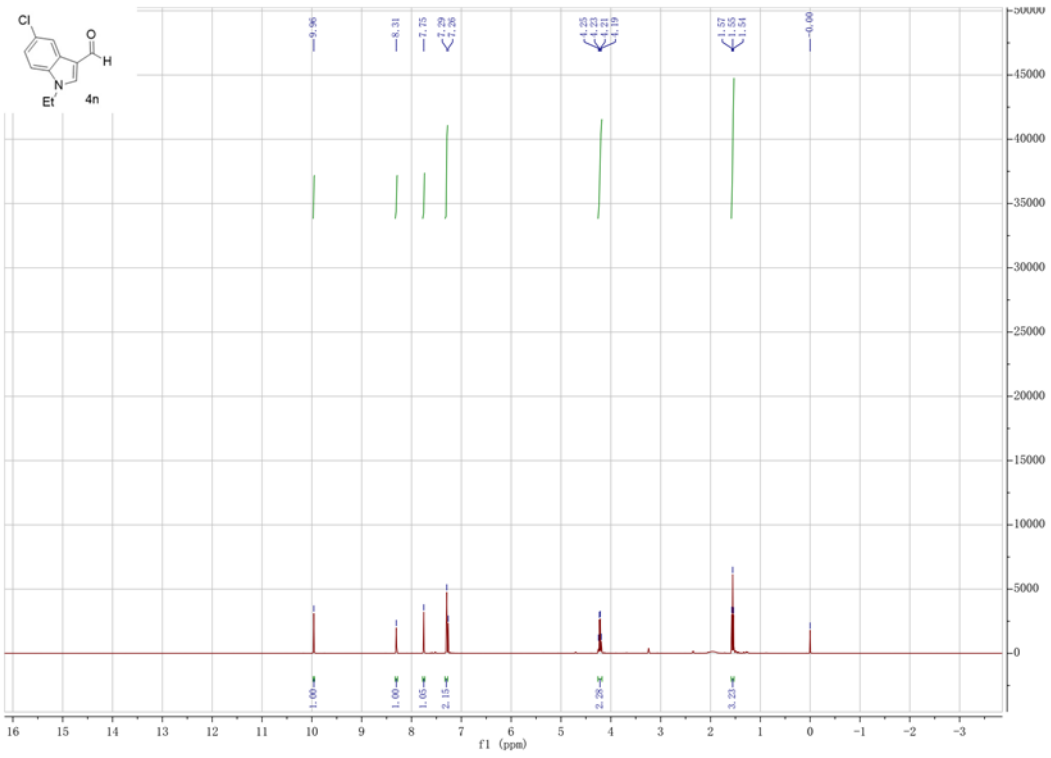

4k
184.40
137.43
137.18
133.97
124.56
123.25
121.77
118.17
109.91
41.78
21.95
15.09
f1 (ppm)

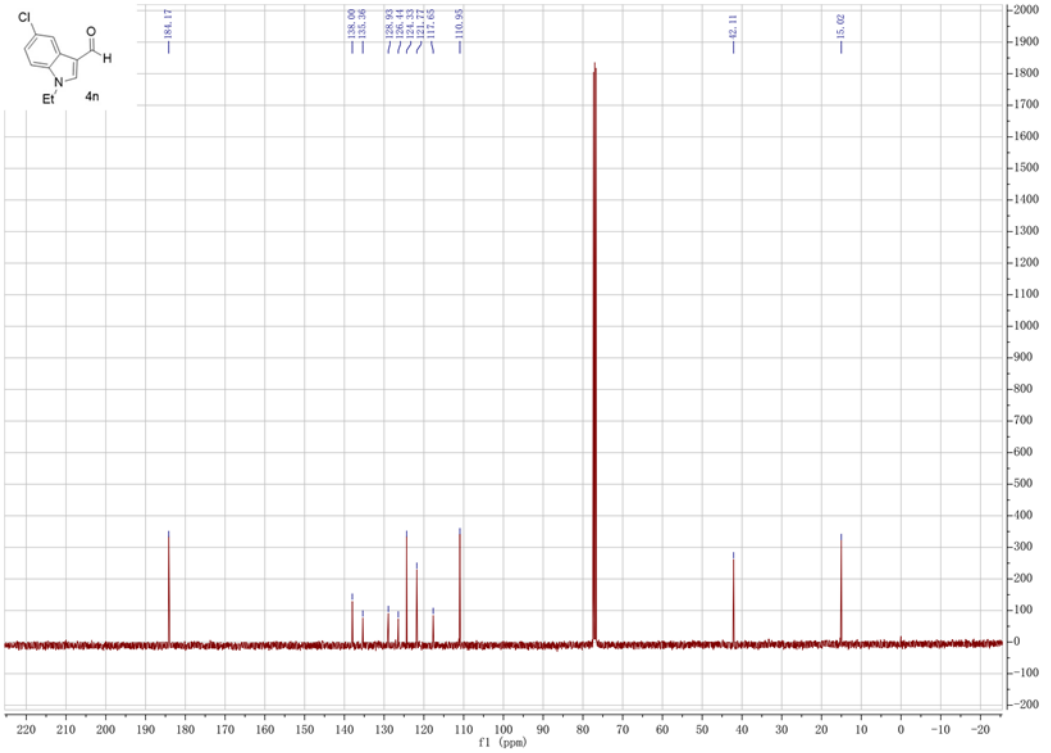

4l
9.97
9.97
8.20
8.18
7.66
7.26
7.19
7.18
7.17
7.06
7.04
4.45
4.44
4.42
4.41
2.72
1.53
1.52
1.51
1.00
1.02
1.07
1.09
1.00
2.26
3.33
3.37
f1 (ppm)

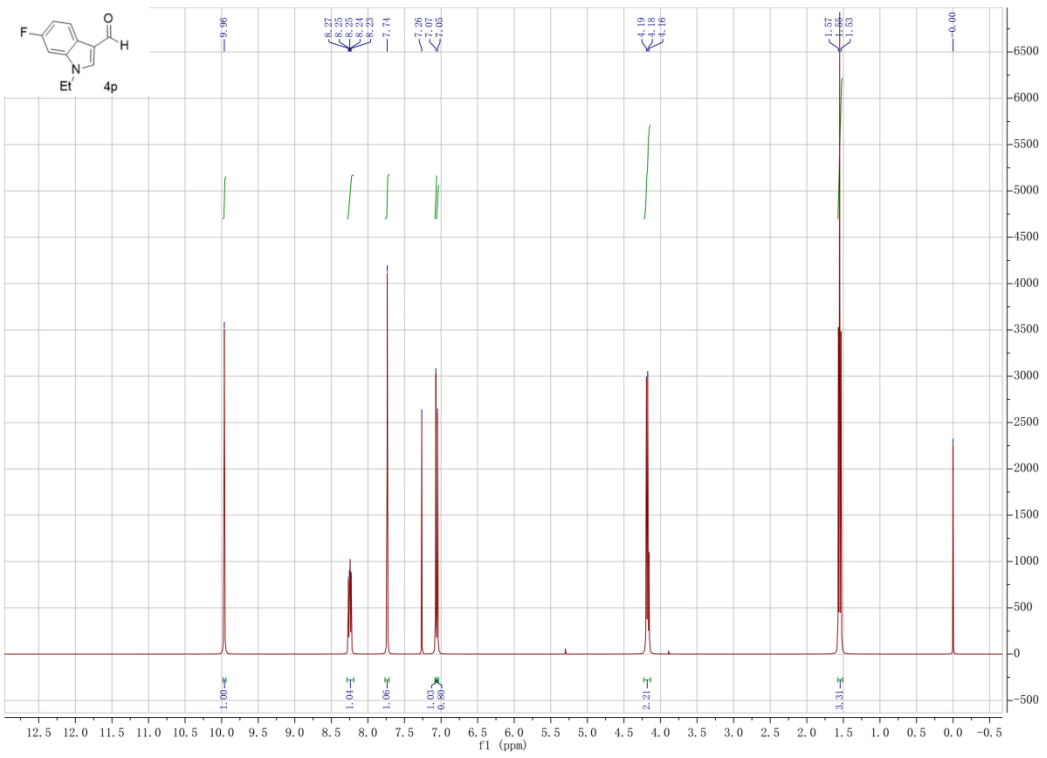

4l
184.43
139.03
135.82
127.02
126.59
123.09
121.33
120.04
118.00
64.51
19.63
17.34
f1 (ppm)

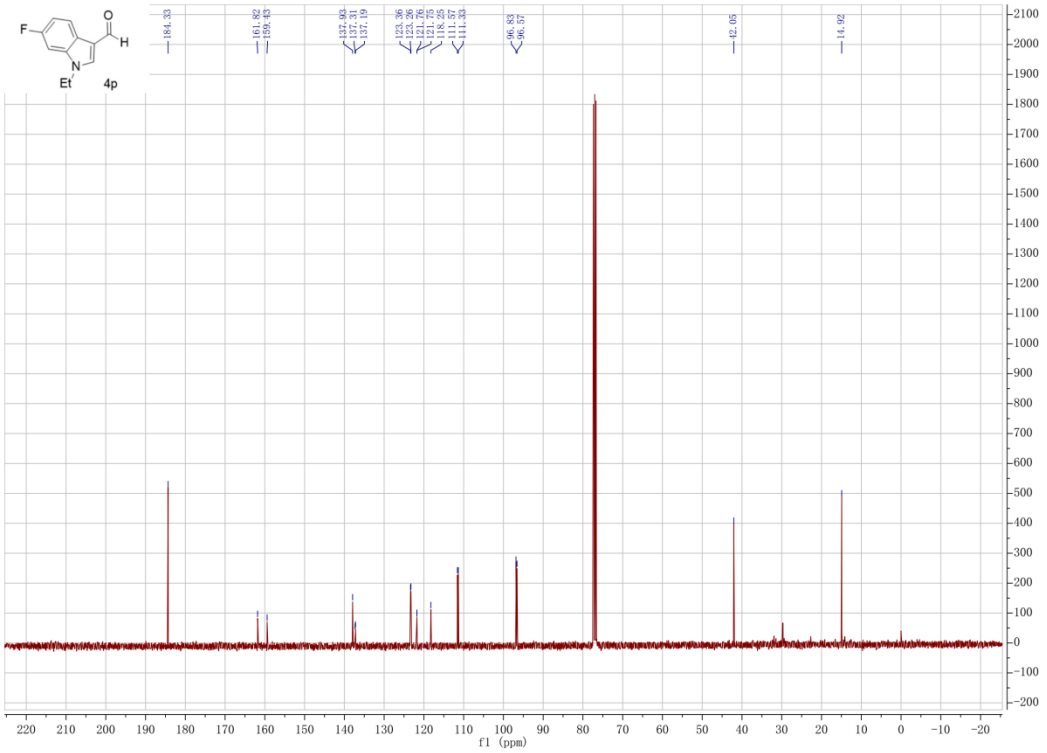

F
O
H
N
Et
4m
10.22
7.89
7.27
7.25
7.23
7.21
7.19
7.01
6.99
6.97
4.25
4.24
4.22
4.20
1.56
1.54
1.53
0.00
0.89
0.91
2.06
4.00
1.95
2.92
f1 (ppm)

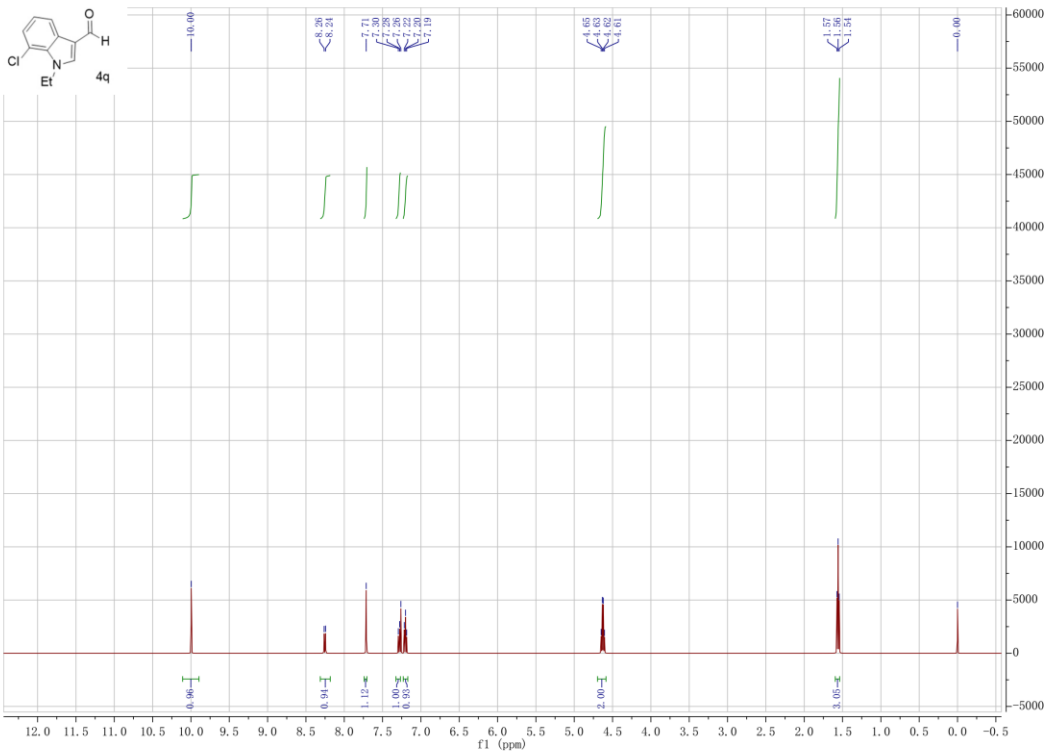

F
O
H
N
Et
4m
185.22
185.19
158.26
155.78
139.18
139.06
132.91
123.78
123.71
116.65
116.60
115.41
115.19
107.99
107.79
106.57
106.54
42.29
14.94
f1 (ppm)

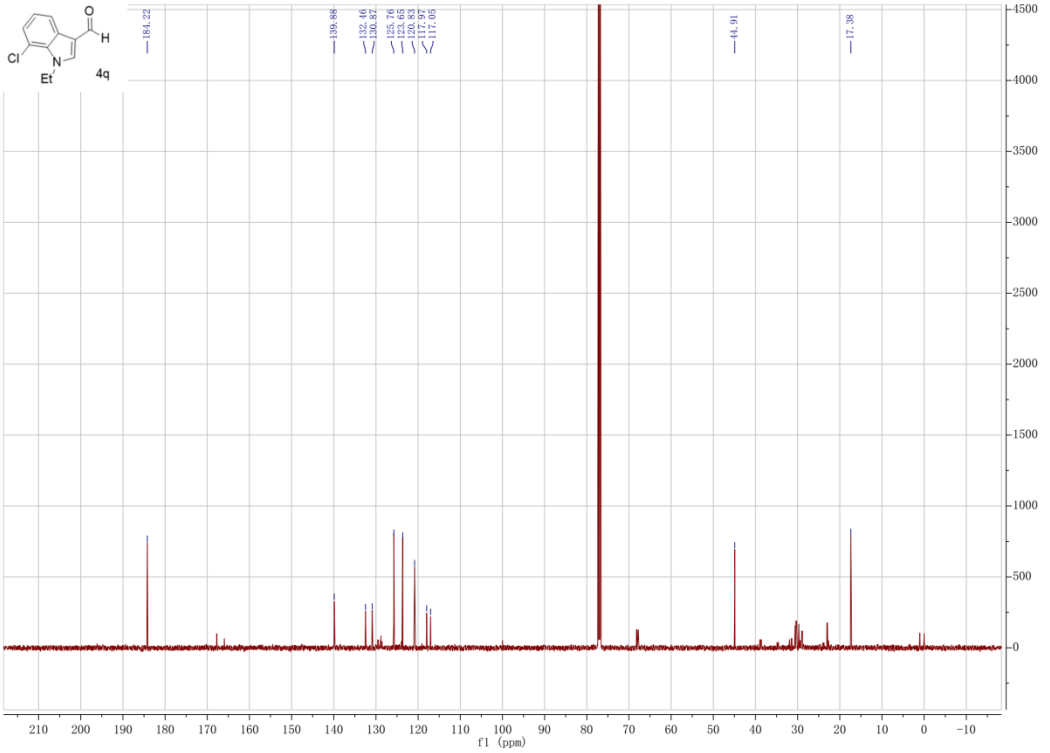

Cl
O
H
N
Et
4n
9.96
8.31
7.75
7.29
7.26
4.25
4.23
4.21
4.19
1.57
1.55
1.54
0.00
1.00
1.00
1.05
2.15
2.28
3.23
f1 (ppm)

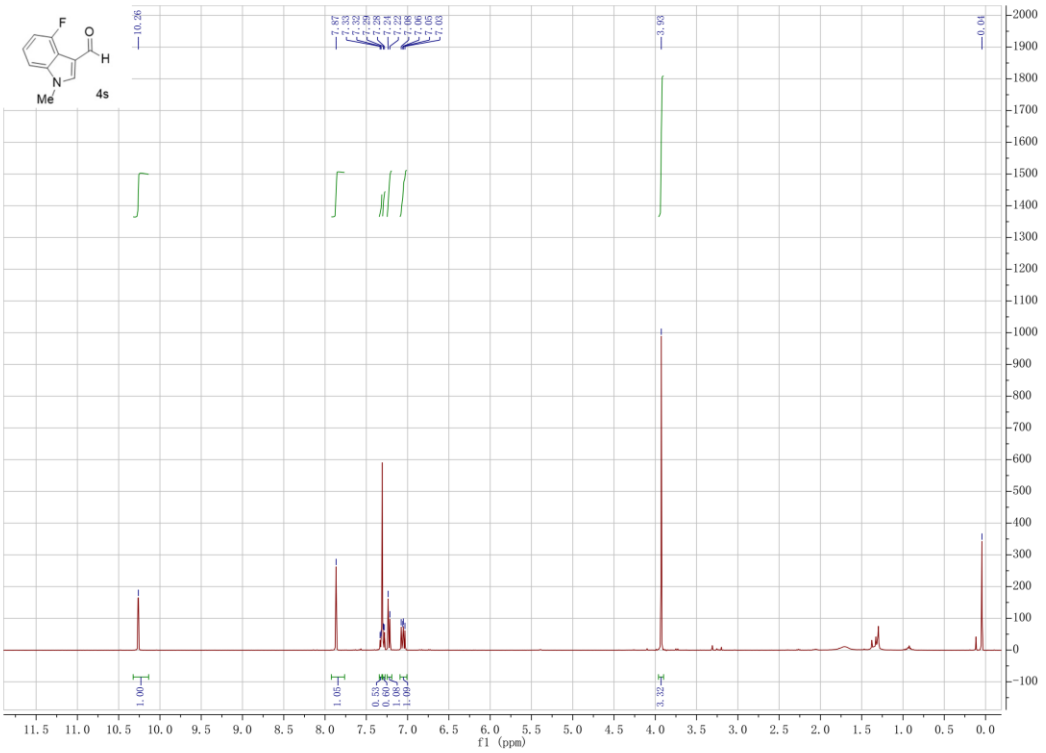

Cl
O
H
N
Et
4n
184.17
138.09
135.36
128.93
126.44
124.33
121.27
117.68
110.95
62.11
15.02
f1 (ppm)

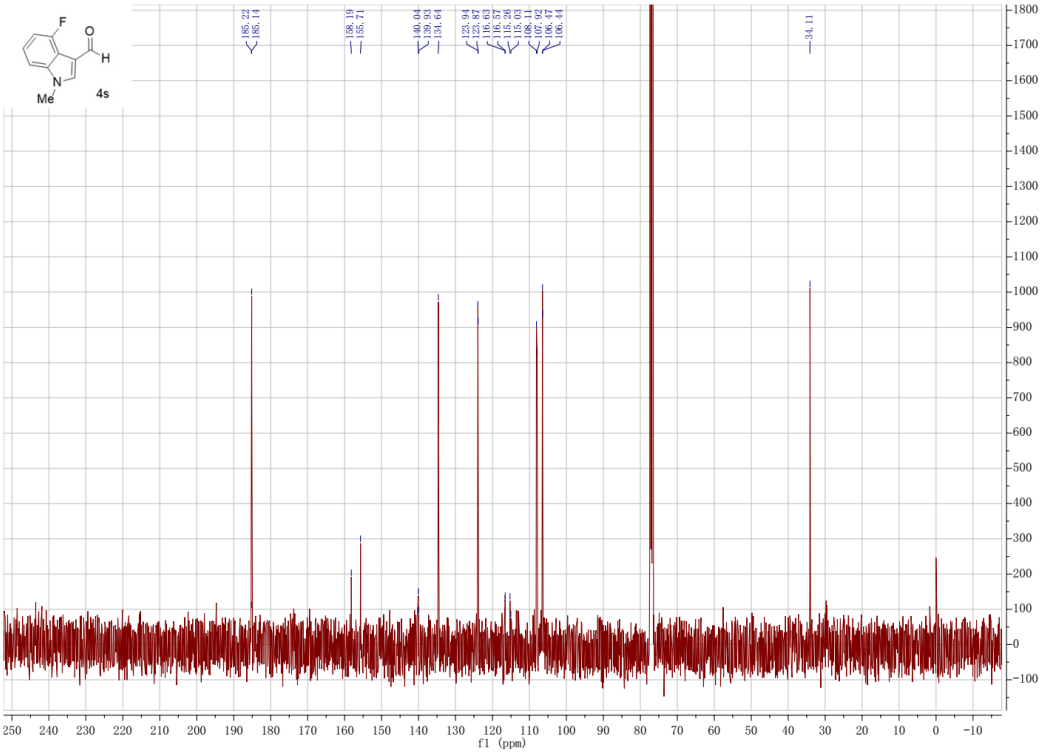

F
O
H
N
Et
4p
9.96
8.27
8.25
8.25
8.24
8.23
7.74
7.26
7.07
7.05
4.19
4.18
4.16
1.57
1.55
1.53
0.00
1.00
1.04
1.06
1.03
0.80
2.21
3.31
f1 (ppm)

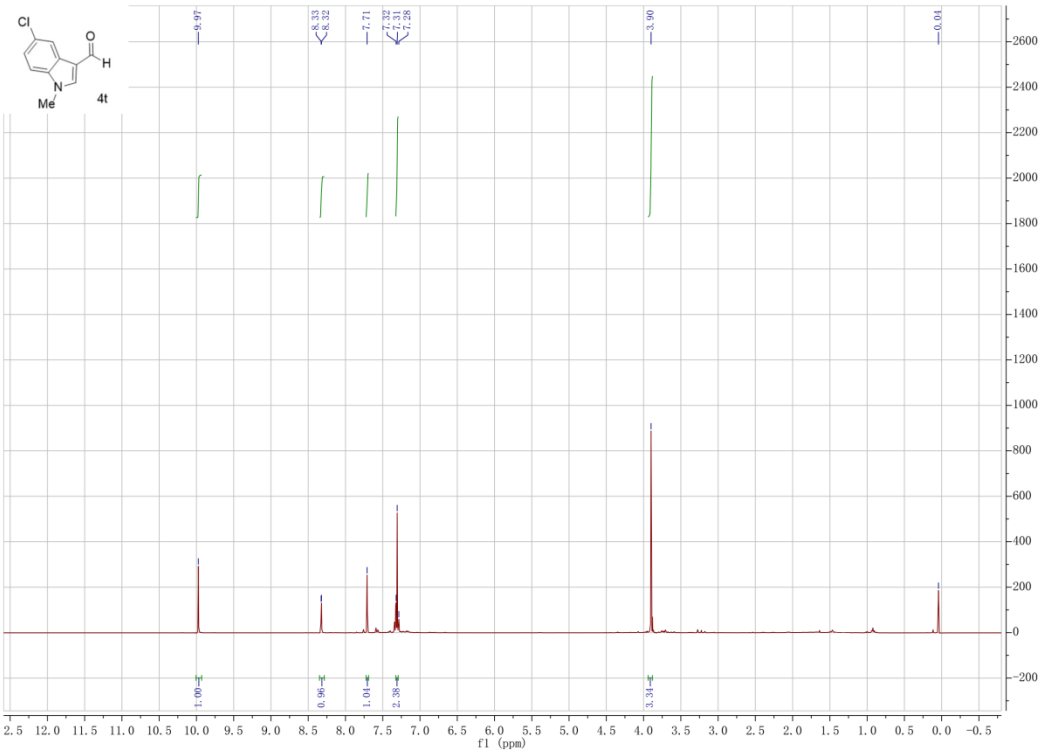

F
O
H
N
Et
4p
184.33
161.82
159.43
137.93
137.31
137.19
123.36
123.26
121.76
121.75
118.25
111.57
111.33
96.83
96.57
42.05
14.92
f1 (ppm)

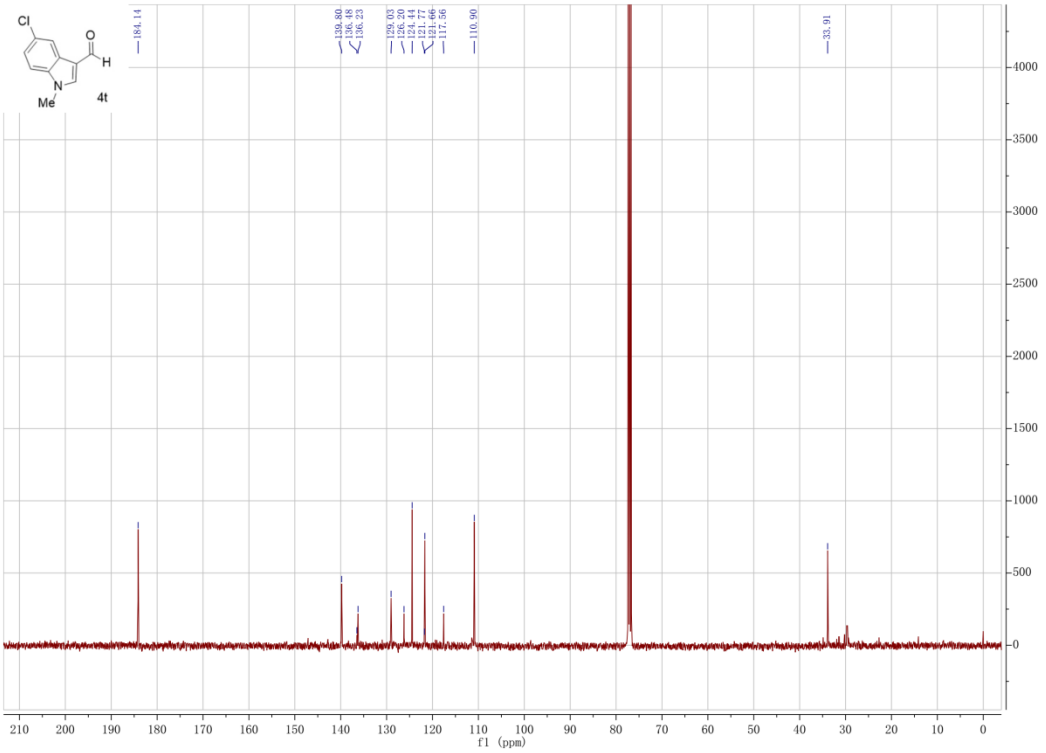

4q
10.00
8.26
8.24
7.71
7.39
7.26
7.22
7.20
7.19
4.65
4.63
4.62
4.61
1.57
1.56
1.54
0.00
0.96
0.94
1.12
1.00
0.93
2.00
3.05
f1 (ppm)


4q
184.22
139.88
132.46
130.82
125.76
123.65
120.83
117.97
117.05
44.91
17.38
f1 (ppm)


F
O
H
N
Me
4s
10.26
7.87
7.33
7.32
7.29
7.28
7.24
7.22
7.08
7.06
7.05
7.03
3.93
0.94
1.00
1.05
0.53
0.60
1.08
1.09
3.32
f1 (ppm)


F
O
H
N
Me
4s
185.22
185.14
158.19
155.71
140.04
139.93
131.64
123.94
123.87
116.62
116.57
115.26
115.03
108.11
107.92
106.47
106.44
34.11
f1 (ppm)


Cl
O
H
N
Me
4t
9.97
8.33
8.32
7.71
7.32
7.31
7.28
3.90
0.04
1.00
0.96
1.04
2.38
3.34
f1 (ppm)


Cl
O
H
N
Me
4t
184.14
139.80
136.48
126.23
129.03
129.00
124.44
121.77
111.66
111.08
110.90
33.91
f1 (ppm)