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Supporting Information

Imine Induced Metal-Free C−H Arylation of Indoles

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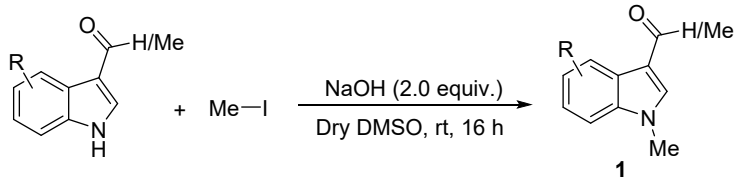
1. General Information

Unless otherwise noted, all reagents and solvents were purchased from commercial sources (Adamas-beta, Alfa Aesar) and used without further purification. Reactions were monitored using Thin Layer Chromatography (TLC) carried out on Merck silica gel plates ($60F_{254}$) using UV light as the visualizing agent. Column chromatography was performed using silica gel 60 (300-400 mesh). HRMS data were recorded on Thermo Fisher Scientific Q-Exactive. All ^{1}H NMR, ^{13}C NMR, ^{19}F NMR spectra were recorded on 600 MHz NMR spectrometers (Bruker AVANCE NEO 600) or 400 MHz NMR spectrometers (Varian Inova-400). Chemical shifts were given in parts per million (ppm, δ), referenced to the solvent peak of $CDCl_3$ or DMSO-d_6, defined at δ = 7.26 or 2.50 (^{1}H NMR), defined at δ = 77.0 or 39.70 (^{13}C NMR). Coupling constants were quoted in Hz (J). ^{1}H NMR Spectroscopy splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m). EPR spectra were recorded on a Bruker EMX plus spectrometer. MS data were recorded on Agilent 6125C. Melting point (M.P.) was recorded on BÜCHI (M-560). IR spectra were recorded on a Mettler Toledo React IR I5.

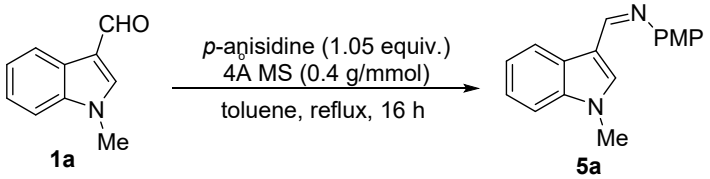
2. Synthesis of Indoles[1]

2.1 Synthesis of 1-methylindole-3-carbaldehyde derivative



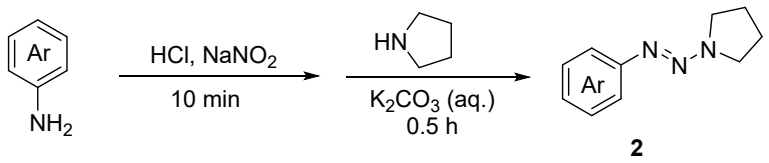
A mixture of 1*H*-indole-3-carbaldehyde derivative or 1-(1*H*-indol-3-yl)ethan-1-one (2 mmol, 1.0 equiv.), NaOH (4 mmol, 2.0 equiv.) and dry DMSO (5 mL, 0.4 M) was added to a dried round bottom flask. Then, MeI (4 mmol, 2.0 equiv.) was added dropwise to the reaction mixture and the resulting mixture was stirred at room temperature for 16 h. When the reaction completed, 5 mL of water was added to the mixture, the aqueous mixture was extracted with ethyl acetate (3×5 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure, the residue was purified by flash column chromatography (petroleum ether / ethyl acetate 30:1-10:1) to afford the desired product.

2.2 Synthesis of (*E*)-*N*-(4-methoxyphenyl)-1-(1-methyl-1*H*-indol-3-yl)methanimine



In a dried round bottom flask under nitrogen, were added 1-methylindole-3-carbaldehyde (2.0 mmol, 159.2 mg), *p*-anisidine (2.1 mmol, 1.05 equiv.) and 4Å molecular sieves (0.4 g/mmol) and dry toluene (5 mL) was added and the reaction mixture was refluxed for 16 h. After completion of the reaction, the reaction mixture was cooled to room temperature, filtered through a pad of Celite (eluted with ethyl acetate) and concentrated in vacuo to give the crude product. The purified product **5a** was obtained from petroleum ether.

3. Synthesis of Aryltriazenes[2]

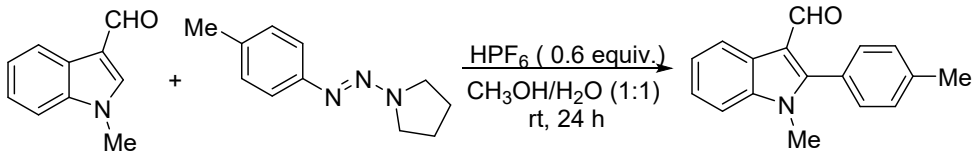


2

A solution of arylamine (20 mmol) in concentrated HCl (4 mL) was cooled in an ice bath while a solution of $NaNO_2$ (20 mmol) in water (10 mL) was added dropwise. The resulting solution of the diazonium salt was stirred in an ice bath for 10 min and then added all at once to a chilled solution of amine (22 mmol) and 1.2 M K_2CO_3 aqueous (20 mL) to the above solution, and the resulting mixture was stirred for 0.5 h. The resulting precipitate was recrystallized in EtOH or separated by column chromatography to obtain the desired purified aryltriazenes products.

4. Experimental Procedures

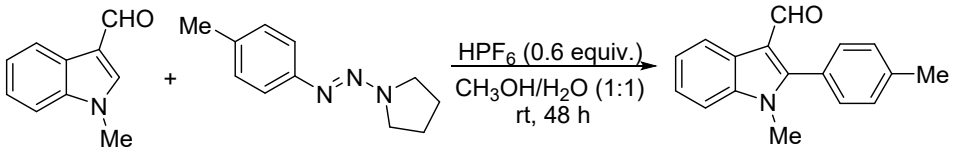
4.1 General procedure for the synthesis of products (taking **3a** as an example)



1a **2a** **3a**

A mixture of 1-methylindole-3-carbaldehyde **1a** (0.1 mmol, 15.9 mg), *p*-methylphenyltriazene **2a** (0.3 mmol, 56.7 mg), CH_3OH (0.5 mL) and H_2O (0.5 mL) was added to a dried tube. Then, a solution of HPF_6 (0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added dropwise to the above stirred solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 24 h. When the reaction was finished, 5 mL of water was added to the mixture and the aqueous mixture was extracted with ethyl acetate (3×5 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure, the residue was purified by flash column chromatography (eluent: petroleum ether/EtOAc = 30:1 to 10:1, v/v) to afford the desired product **3a** as a yellow semisolid (19.6 mg, 79% yield).

4.2 Gram-scale reaction



1a 10 mmol 1.59 g

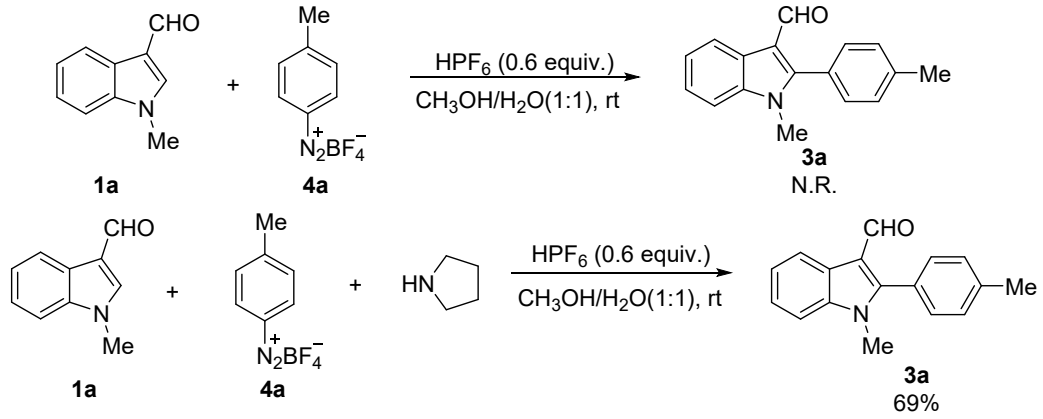
2a 30 mmol 5.67 g

3a 55 % 1.37 g

A mixture of 1-methylindole-3-carbaldehyde **1a** (10.0 mmol, 1.59 g), *p*-methylphenyltriazene **2a** (30.0 mmol, 5.67 g), CH_3OH (50.0 mL) and H_2O (50.0 mL) was added to a dried round bottom flask. Then, a solution of HPF_6 (6 mmol, 0.88 mL) in CH_3OH (50.0 mL) and H_2O (50.0 mL) was added dropwise to the above stirred solution over 30 minutes. The reaction mixture was stirred at ambient temperature for 48 h. When the reaction was finished, 50 mL of water was added to the mixture and the aqueous mixture was extracted with ethyl acetate (3×50 mL). The combined organic phase was dried over anhydrous MgSO4, filtered and concentrated under reduced pressure, the residue was purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 30:1 to 10:1, v/v) to afford the desired product **3a** as a yellow semisolid (1.37 g, 55% yield).

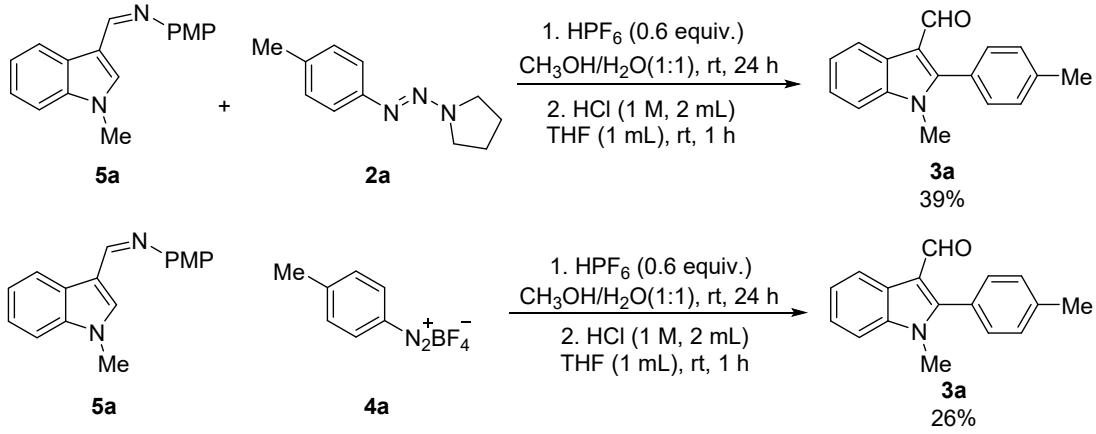
4.3 Control experiments

4.3.1 Synthesis of 2-(4-tolyl)-1-methylindole-3-carbaldehyde by aryldiazonium salt



A mixture of 1-methylindole-3-carbaldehyde **1a** (0.1 mmol, 15.9 mg), *p*-methylbenzendiazonium tetrafluoroborate **4a** (0.3 mmol, 61.8 mg), CH_3OH (0.5 mL) and H_2O (0.5 mL) was added and stirred at ambient temperature. Then, a solution of HPF_6 (60 wt.% solution in water, 0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added dropwise to the above stirred solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 24 h. When the reaction was finished, product **3a** was not detected by TLC. However, tetrahydropyrrole (0.3 mmol, 25 μL) was added to the above system, obtained the corresponding product **3a**. When the reaction was finished, 5 mL of water was added to the mixture, the aqueous mixture was extracted with ethyl acetate (3×5 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure, the residue was purified by flash column chromatography (eluent: petroleum ether/EtOAc = 30:1 to 10:1, v/v) to afford the desired product **3a** as yellow semisolid (17.2 mg, 69% yield).

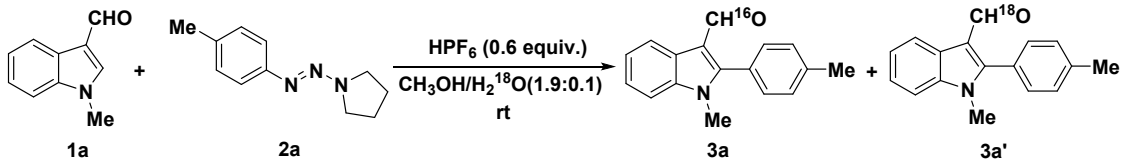
4.3.2 Imine-directed arylation of indole C-2



A mixture of (*E*)-*N*-(4-methoxyphenyl)-1-(1-methyl-1*H*-indol-3-yl)methanimine **5a** (0.1 mmol, 26.4 mg), *p*-methylphenyltriazene **2a** (0.3 mmol, 56.7 mg), CH_3OH (0.5 mL) and H_2O (0.5 mL) was added and stirred at ambient temperature. Then, a solution of HPF_6 (60 wt.% solution in water, 0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added dropwise to the above stirred solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 24 h. When the reaction was finished, the reaction mixture was quenched by addition of HCl (1M, 2 mL) and THF (1 mL), stirred at room temperature for 1 h. When the reaction was finished, 5 mL of water was added to the mixture, the aqueous mixture was extracted with ethyl acetate (3×5 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure, the residue was purified by flash column chromatography (eluent: petroleum ether/EtOAc = 30:1 to 10:1, v/v) to afford the desired product **3a** as yellow semisolid (9.7 mg, 39% yield). Similarly, (*E*)-*N*-(4-methoxyphenyl)-1-(1-

methyl-1*H*-indol-3-yl)methanimine **5a** (0.1 mmol, 26.4 mg), and *p*-methylbenzendiazonium tetrafluoroborate **4a** (0.3 mmol, 56.7 mg), the corresponding product **3a** (6.5 mg, 26% yield) was also obtained after the above operation.

4.3.3 Labeling experiment with $H_2{}^{18}O$



A mixture of 1-methylindole-3-carbaldehyde **1a** (0.1 mmol, 15.9 mg), *p*-methylphenyltriazene **2a** (0.3 mmol, 56.7 mg), dry CH_3OH (0.9 mL) and $H_2{}^{18}O$ (0.1 mL) was added and stirred at ambient temperature. Then, a solution of HPF_6 (60 wt.% solution in water, 0.06 mmol, 8.8 μL) in dry CH_3OH (1.0 mL) was added dropwise to the above solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 24 h. When the reaction was finished, a mixture of **3a** and **3a'** was obtained from the mass spectrum of the mixed sample, **3a**: MS (ESI) *m/z* found 250.10; **3a'**: MS (ESI) *m/z* found 252.10 with a ratio close to 3:2.

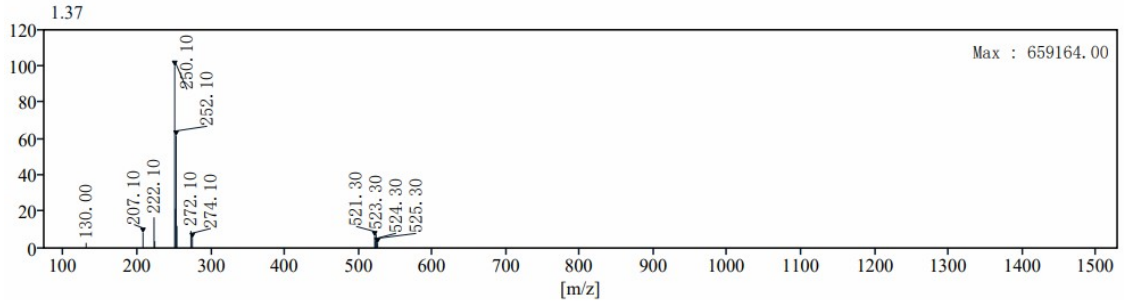
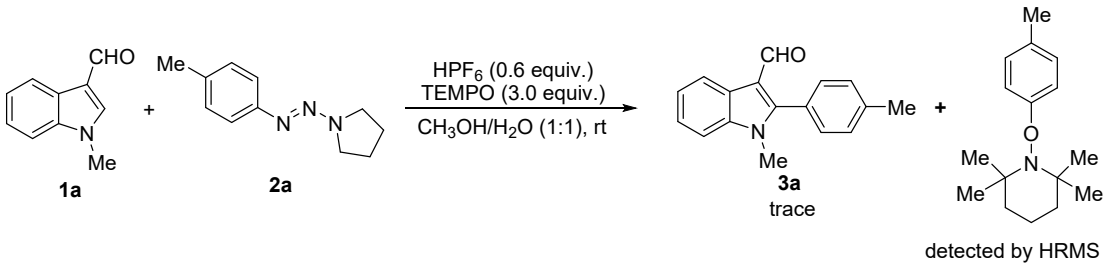


Figure S1 Mass spectrometry data of ^{18}O labeling experiment

4.3.4 Free radical capture experiment



A mixture of 1-methylindole-3-carbaldehyde **1a** (0.1 mmol, 15.9 mg), *p*-methylphenyltriazene **2a** (0.3 mmol, 56.7 mg), 2,2,6,6-tetramethyl-1-piperidinyloxy (0.3 mmol, 46.9 mg), CH_3OH (0.5 mL) and H_2O (0.5 mL) was added and stirred at ambient temperature. Then, a solution of HPF_6 (60 wt.% solution in water, 0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added dropwise to the above solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 24 h. When the reaction was finished, TLC showed that only trace **3a** was formed and the aryl radical-TEMPO adduct was detected by HRMS. HRMS (ESI^+): m/z calcd. for $C_{23}H_{24}N_3$ $[M+H]^+$: 248.2009, found: 248.2002.

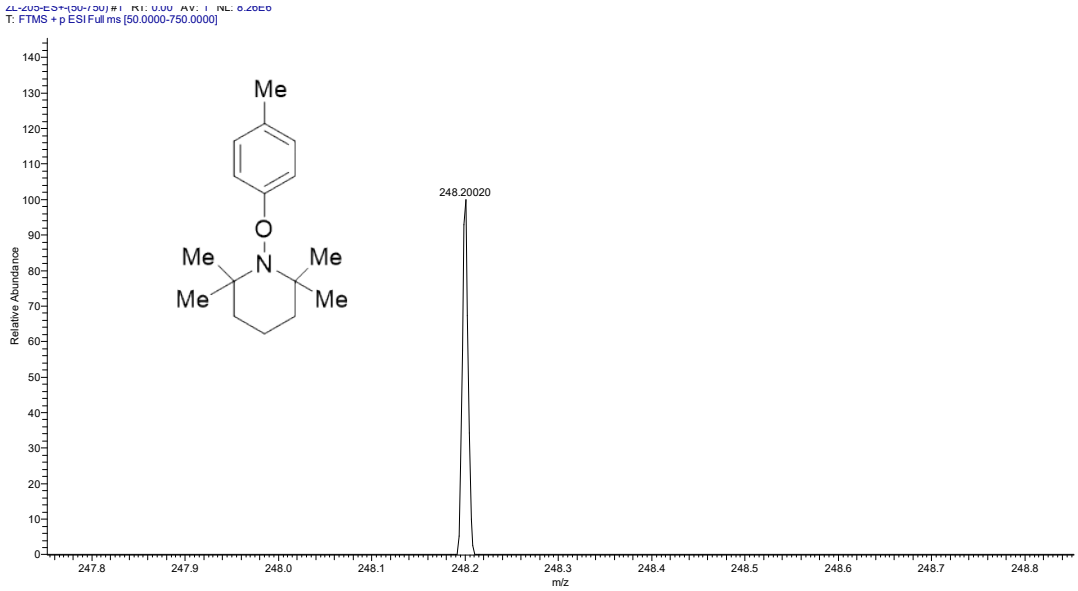


Figure S2 High resolution mass spectrometry for free radical capture experiment

4.3.5 Electron paramagnetic resonance (EPR) experiments

A mixture of 1-methylindole-3-carbaldehyde **1a** (0.1 mmol, 15.9 mg), *p*-methylphenyltriazene **2a** (0.3 mmol, 56.7 mg), 5,5-dimethyl-1-pyrroline *N*-oxide (20 μL), CH_3OH (0.5 mL) and H_2O (0.5 mL) was added and stirred at ambient temperature. Then, a solution of HPF_6 (60 wt.% solution in water, 0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added by dropwise to the above solution in 30 minutes. The reaction mixture was stirred at ambient temperature for 30 minutes, transferred to a capillary, and the EPR spectra were recorded. An obvious free radical signal was observed, which indicates that there are aryl radicals should be involved in the present reaction system. In another dried tube, were added 5,5-dimethyl-1-pyrroline *N*-oxide (20 μL), CH_3OH (0.5 mL) and H_2O (0.5 mL) stirred at room temperature. Then, a solution of HPF_6 (0.06 mmol, 8.8 μL) in CH_3OH (0.5 mL) and H_2O (0.5 mL) was added by dropwise to the above solution in 30 minutes as blank reaction. The reaction mixture was stirred at ambient temperature for 30 minutes, transferred to a capillary, and the EPR spectra were recorded, no free radical signal is generated.

Measurement conditions: frequency: 9.6 GHz; power: 0.9187 mW; modulation amplitude: 5 G; time constant: 20.48 ms; Sweep time: 20 s; Number of scans: 3.

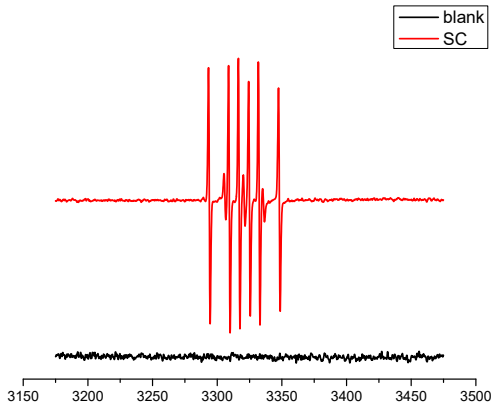


Figure S3 Electron spin resonance (ESR) spectrum.

4.4 In-situ IR experiment

In a dried round bottom flask, were added MeOH (4 mL), 1-methylindole-3-carbaldehyde **1a** (0.2 mmol, 31.8 mg), *p*-methylphenyltriazene **2a** (0.6 mmol, 113.4 mg), HPF_6 (0.12 mmol, 17.6 μL). The mixture was allowed to stir at ambient temperature for 1 h and then recorded by in-situ IR.

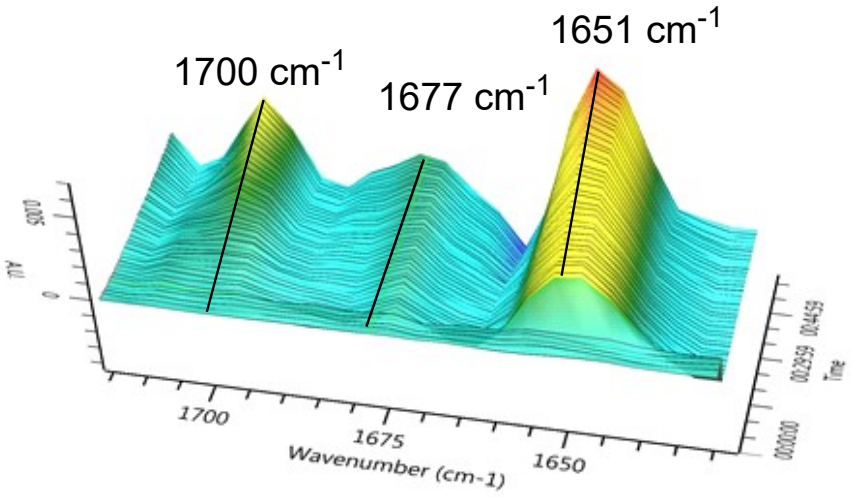
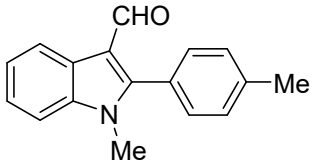
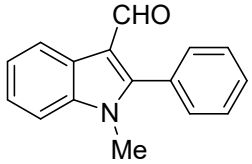


Figure S3b 3D-surface plot of the observed vibrations at 1677 cm^{-1}

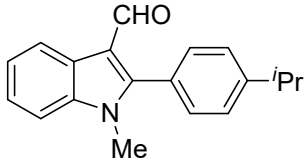
5. NMR Spectra



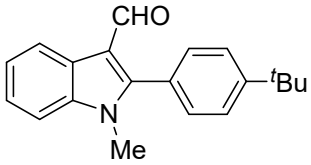
1-Methyl-2-(*p*-tolyl)-1*H*-indole-3-carbaldehyde (3a): Yellow semisolid, 19.6 mg, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.45-8.42 (m, 1H), 7.39-7.32 (m, 7H), 3.67 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.69, 151.72, 140.05, 130.79, 129.35, 125.59, 125.22, 123.91, 123.23, 122.15, 115.33, 109.69, 30.96, 21.42; Konwn compound.[3]



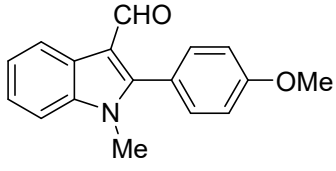
1-Methyl-2-phenyl-1*H*-indole-3-carbaldehyde (3b): Yellow semisolid, 15.8 mg, 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73(s, 1H), 8.48-8.44 (m, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.58-7.55 (m, 2H), 7.51-7.49 (m, 2H), 7.42-7.40 (m, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.79, 151.71, 137.37, 130.87, 129.90, 128.67, 128.53, 124.92, 124.09, 123.40, 122.18, 115.90, 109.79, 31.01; Konwn compound.[3]



2-(4-*iso*−Propylphenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3c): Yellow solid, 15.2 mg, 55% yield, mp: 99.0-100.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.45-8.42 (m, 1H), 7.42-7.41 (br, 4H), 7.40-7.39 (m, 1H), 7.38-7.35 (m, 2H) 3.69 (s, 3H), 3.03 (sept, *J* = 7.0 Hz, 1H), 1.34 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.76, 151.77, 150.81, 137.33, 130.89, 126.72, 125.87, 125.21, 123.87, 122.74, 121.50, 115.62, 109.70, 34.04, 31.00, 23.83; HRMS (ESI$^+$): *m/z* calcd. for $C_{19}H_{20}NO$ $[M+H]^+$: 278.1539, found: 278.1541.

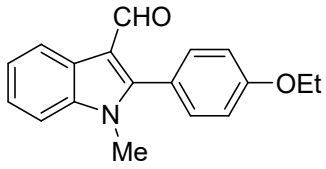


2-(4-(*tert*-Butyl)phenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3d): Yellow solid, 12.2 mg, 42% yield, mp: 81.3-83.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 8.29-8.27 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.24-7.15 (m, 3H), 7.08 (d, *J* = 8.1 Hz, 1H), 6.65 (d, *J* = 8.6 Hz, 1H) 3.52 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.03, 153.16, 137.38, 130.62, 126.27, 125.61, 125.41, 125.20, 123.95, 123.30, 122.13, 115.59, 114.81, 34.89, 31.52, 31.21; HRMS (ESI$^+$): *m/z* calcd. for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1696, found: 292.1696.

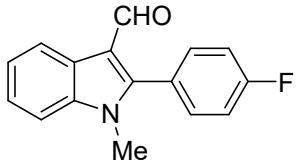


2-(4-Methoxyphenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3e): Yellow solid, 19.2 mg, 72% yield, mp: 135.5-136.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.44-8.40 (m, 1H), 7.43-7.33 (m, 5H), 7.07 (d, *J* = 8.2 Hz,

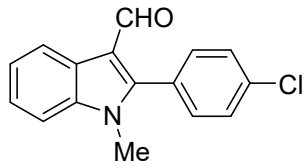
2H), 3.91 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.66, 160.81, 151.56, 137.31, 132.25, 125.22, 123.86, 123.20, 122.46, 120.59, 115.61, 114.15, 109.68, 55.44, 30.93; Konwn compound.[4]



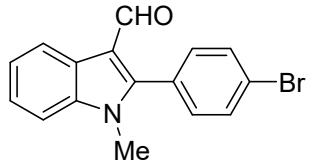
2-(4-Ethoxyphenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3f): Yellow semisolid, 14.2 mg, 51% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.42 (d, *J* = 8.8 Hz, 1H), 7.40 (s, 1H), 7.39 (d, *J* = 5.4 Hz, 2H), 7.37-7.33 (m, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 3.67 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.70, 160.21, 151.70, 137.31, 132.22, 125.22, 123.83, 123.17, 122.04, 120.34, 115.56, 114.59, 109.67, 63.70, 30.92, 14.74; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO_2$ $[M+H]^+$: 280.1332, found: 280.1329.



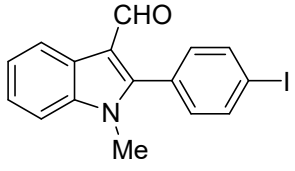
2-(4-Fluorophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3g): Yellow semisolid, 14.2 mg, 56% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.60 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.74 (td, *J* = 5.6, 2.2 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.46 (t, *J* = 6.6 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.33, 163.23 (d, *J* = 249.5 Hz), 150.32, 137.28, 133.59 (d, *J* = 9.1 Hz), 124.70, 123.60 (d, *J* = 83.8 Hz), 121.04, 115.99 (d, *J* = 21.2 Hz), 114.79, 111.21, 31.21. Known products.[4]



2-(4-Chlorophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3h): Yellow semisolid, 19.4 mg, 72% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 8.23 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.73-7.65 (m, 5H), 7.39 (td, *J* = 7.2 Hz, 1.3, 1H), 7.32 (td, *J* = 7.9, 1.1, 1H), 3.69 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.30, 149.90, 137.36, 135.17, 133.03, 128.96, 127.19, 125.10, 124.10, 123.22, 121.09, 115.32, 111.25, 31.27. Known products.[5]

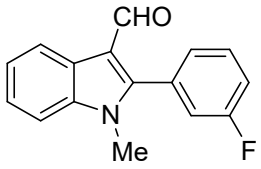


2-(4-Bromophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3i): Yellow semisolid, 26.7 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.43 (d, *J* = 7.3 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.42-7.33 (m, 5H), 3.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.61, 137.38, 132.34, 132.00, 127.53, 125.10, 124.62, 124.28, 123.48, 122.22, 117.29, 115.88, 109.79, 31.01; HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{13}BrNO$ $[M+H]^+$: 314.0175, found: 314.0174.

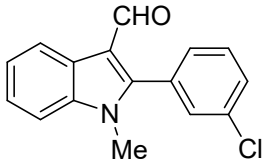


2-(4-Iodophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3j): Yellow solid, 8.3 mg, 23% yield, mp: 146.6-147.7 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 8.34 (d, *J* = 6.1 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.35-7.25 (m, 3H), 7.13 (d, *J* = 7.9 Hz, 2H), 3.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.92, 149.96, 137.89, 132.37, 127.99,

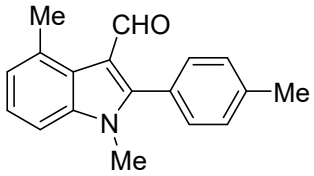
125.05, 124.25, 123.45, 122.14, 118.01, 115.72, 109.80, 96.46, 31.01; HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{13}INO$ $[M+H]^+$: 362.0036, found: 362.0039.



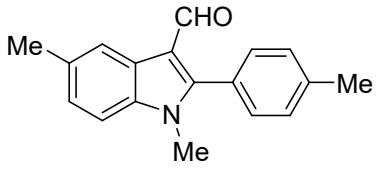
2-(3-Fluorophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3k): Yellow solid, 16.0 mg, 63% yield, mp: 180.5 - 181.5 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.43 (d, *J* = 8.8 Hz, 1H), 7.57-7.53 (m, 1H), 7.41 (d, *J* = 4.6 Hz, 2H), 7.38 (td, *J* = 7.6, 2.6 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.22 (dt, *J* = 9.1, 2.1 Hz, 1H), 3.69 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.22, 162.43(d, *J* = 249.2 Hz), 149.55, 137.35, 130.63 (d, *J* = 9.1 Hz), 130.45 (d, *J* = 9.1 Hz), 126.82, 125.02, 124.33, 123.51, 122.26, 117.94 (d, *J* = 22.7 Hz), 117.04 (d, *J* = 21.1 Hz), 115.91, 109.83, 31.04; ^{19}F NMR (565 MHz, $CDCl_3$) δ -111.33; HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{13}FNO$ $[M+H]^+$: 254.0976, found: 254.0973.



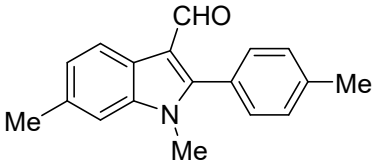
2-(3-Chlorophenyl)-1-methyl-1*H*-indole-3-carbaldehyde (3l): Yellow semisolid, 15.3 mg, 57% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.43 (d, *J* = 7.1 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.50 (s, 1H), 7.42-7.41 (m, 2H), 7.40-7.38 (m, 2H), 3.69 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.89, 137.38, 134.82, 130.71, 130.30, 130.16, 130.00, 129.09, 124.98, 124.44, 123.64, 118.64, 117.13, 115.93, 109.89, 31.09; HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{12}ClNONa^+$ $[M+H]^+$: 294.0470, found: 294.0461.



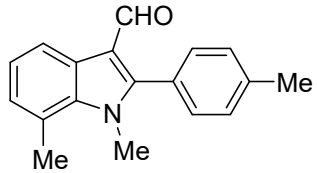
1,4-Dimethyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3m): Yellow brown solid, 13.2 mg, 50% yield, mp: 107.9-109.3 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.34-7.27 (m, 4H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 7.1 Hz, 1H), 3.54 (s, 3H), 2.95 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.82, 152.68, 139.73, 137.98, 133.19, 130.72, 129.11, 126.16, 124.78, 124.16, 123.89, 116.83, 107.20, 30.84, 23.00, 21.31; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO$ $[M+H]^+$: 264.1383, found: 264.1382.



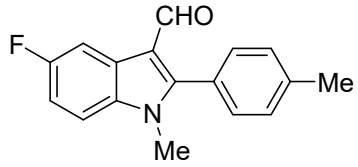
1,5-Dimethyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3n): Yellow semisolid, 9.3 mg, 35% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 8.24 (s, 1H), 7.38-7.30 (m, 4H), 7.27 (d, *J* = 11.7 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.63 (s, 3H), 2.51 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.69, 151.71, 139.94, 135.72, 132.97, 130.76, 129.30, 125.69, 125.40, 125.32, 121.86, 115.29, 109.34, 30.96, 21.46, 21.40; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO$ $[M+H]^+$: 264.1383, found: 264.1383.



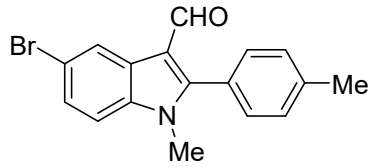
1,6-Dimethyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3o): Yellow solid, 12.6 mg, 48% yield, mp: 138.1-139.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 8.22 (s, 1H), 7.36-7.30 (m, 4H), 7.24 (d, *J* = 3.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 3.61 (s, 3H), 2.49 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.69, 151.71, 139.94, 135.72, 132.97, 130.76, 129.30, 125.69, 125.40, 125.32, 121.86, 115.29, 109.34, 30.96, 21.46, 21.40; HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{18}NO$ $[M+H]^+$: 264.1383, found: 264.1382.



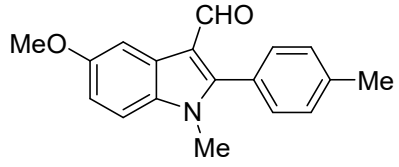
1,7-Dimethyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3p): Yellow solid, 8.2 mg, 31% yield, mp: 152.8-153.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 7.40-7.29 (m, 4H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 3.86 (s, 3H), 2.80 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.73, 152.68, 139.92, 135.48, 130.87, 129.25, 126.96, 126.05, 125.73, 123.18, 121.41, 120.01, 115.56, 34.41, 21.36, 20.15; HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{18}NO$ $[M+H]^+$: 264.1383, found: 264.1384.



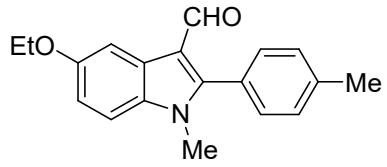
5-Fluoro-1-methyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3q): Yellow solid, 12.1 mg, 45% yield, mp: 199.0-200.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 8.10 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.37 (br, 4H), 7.31 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.09 (td, *J* = 9.0, 2.6 Hz, 1H), 3.66 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.39, 160.23 (d, *J* = 278.8), 151.98, 140.27, 133.83, 130.69, 129.44, 125.88 (d, *J* = 12.1), 124.80, 115.56, 112.06 (d, *J* = 26.3), 110.51 (d, *J* = 9.1 Hz), 107.59 (d, *J* = 24.2), 30.59, 21.88; ^{19}F NMR (565 MHz, $CDCl_3$) δ -120.07; HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{15}FNO$ $[M+H]^+$: 268.1132, found: 268.1133.



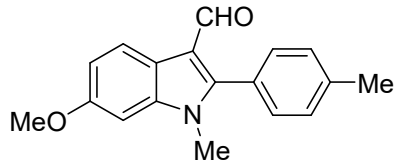
5-Bromo-1-methyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3r):Yellow solid, 14.4 mg, 44% yield, mp: 160.1-161.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.51 (d, *J* = 1.9 Hz, 1H), 7.37 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.29 (br, 4H), 7.17 (d, *J* = 9.2 Hz, 1H), 3.58 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.38, 152.18, 140.37, 136.04, 130.71, 129.47, 126.82, 126.73, 125.10, 124.70, 116.75, 115.01, 111.13, 31.10, 21.43; HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{15}BrNO$ $[M+H]^+$: 328.0331, found: 328.0336.



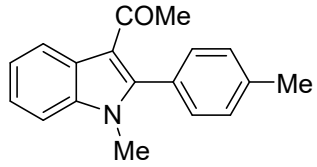
5-Methoxy-1-methyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3s): Yellow solid, 15.7 mg, 56% yield, mp: 123.5-125.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.89 (d, *J* = 2.5 Hz, 1H), 7.34-7.28 (m, 4H), 7.22 (dd, *J* = 8.2, 3.0 Hz, 2H), 6.95 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.88 (s, 3H), 3.59 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.64, 156.88, 151.60, 139.94, 132.22, 130.74, 129.31, 125.96, 125.65, 115.47, 114.17, 110.55, 103.34, 55.85, 31.04, 21.39; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO_2$ $[M+H]^+$: 280.1332, found: 280.1333.



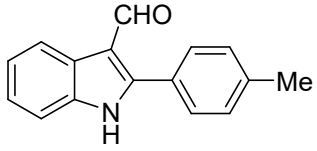
5-Ethoxy-1-methyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3t): Yellow brown solid, 14.7 mg, 50% yield, mp: 114.6-116.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.88 (s, 1H), 7.30 (br, 4H), 7.21 (d, *J* = 6.4 Hz, 1H), 6.94 (dd, *J* = 8.9, 2.2 Hz, 1H), 4.11 (q, *J* = 6.9 Hz, 2H), 3.58 (s, 3H), 2.42 (s, 3H), 1.41 (t, *J* = 5.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.58, 156.72, 151.57, 139.89, 132.18, 130.72, 129.28, 125.94, 125.65, 115.42, 114.56, 110.50, 104.29, 64.03, 31.00, 21.36, 14.89; HRMS (ESI$^+$): *m/z* calcd. for $C_{19}H_{20}NO_2$ $[M+H]^+$: 294.1489, found:294.1487.



6-Methoxy-1-methyl-2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3u): Yellow solid, 15.3 mg, 55% yield, mp: 130.7-132.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 7.37-7.29 (m, 4H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.83 (s, 1H), 3.91 (s, 3H), 3.61 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.57, 157.55, 151.13, 139.84, 138.32, 130.76, 129.27, 125.62, 122.76, 119.15, 115.55, 111.94, 93.83, 55.69, 30.92, 21.36; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO_2$ $[M+H]^+$: 280.1332, found: 280.1333.



1-**(1-Methyl-2-(4-tolyl)-1*H*-indol-3-yl)ethan-1-one (3v):** Yellow semisolid, 14.5 mg, 55% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (dt, *J* = 8.5, 0.8 Hz, 1H), 7.56 (dt, *J* = 8.2, 0.8 Hz, 1H), 7.42 (br, 4H), 7.30 (td, *J* = 7.1, 1.4 Hz, 1H), 7.25 (td, *J* = 7.1, 1.3 Hz, 1H), 3.49 (s, 3H), 2.44 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.76, 146.71, 139.72, 136.63, 130.11, 129.53, 129.08, 126.71, 123.25, 122.73, 115.89, 109.38, 30.77, 30.16, 21.45; HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{18}NO$ $[M+Na]^+$: 286.1202, found: 286.1199.



2-(4-tolyl)-1*H*-indole-3-carbaldehyde (3w): Yellow solid, 14.5 mg, 55% yield, mp: 211.0-212.3 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.08 (s, 1H), 8.78 (s, 1H), 8.44-8.41 (m, 1H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.44-7.42 (m, 1H), 7.35 (d, *J* = 7.8 Hz, 2H), 7.32 (dd, *J* = 6.0, 3.1 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.85, 149.28, 140.46, 135.40, 129.92, 127.10, 126.25, 124.29, 123.19, 122.31, 114.79, 110.98, 21.42; HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{13}NO$ $[M+H]^+$: 208.1121, found: 208.1117. Konwn compound.[6]

6. References

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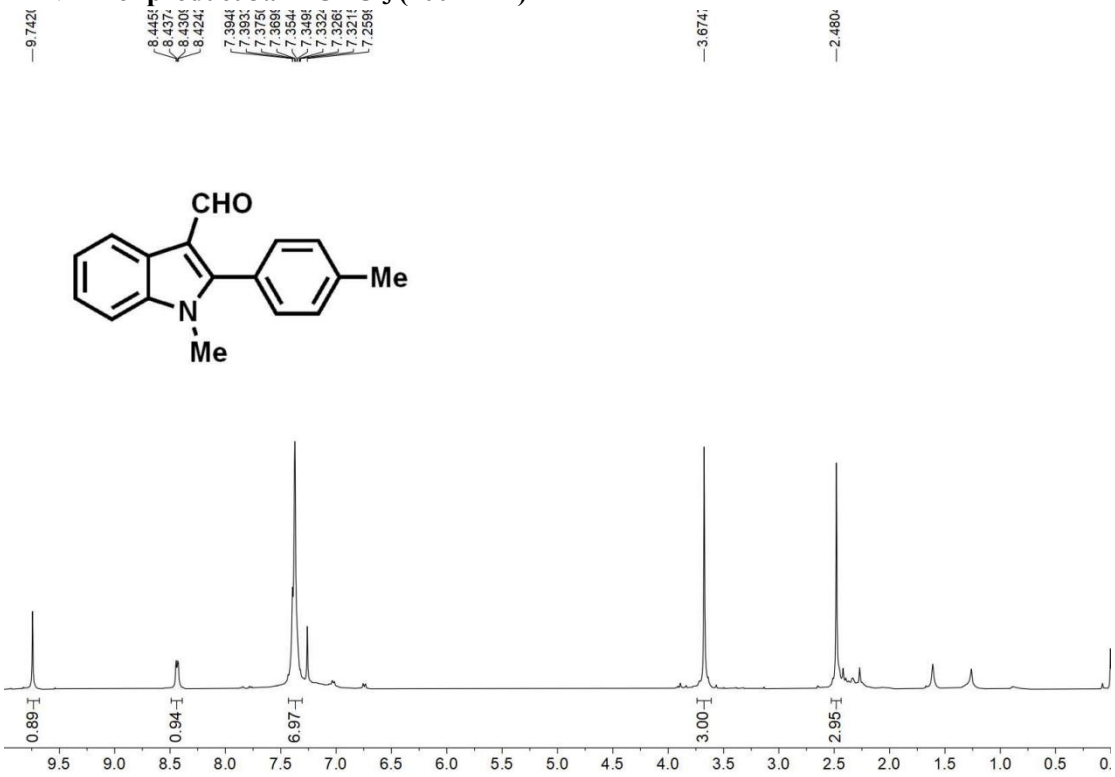
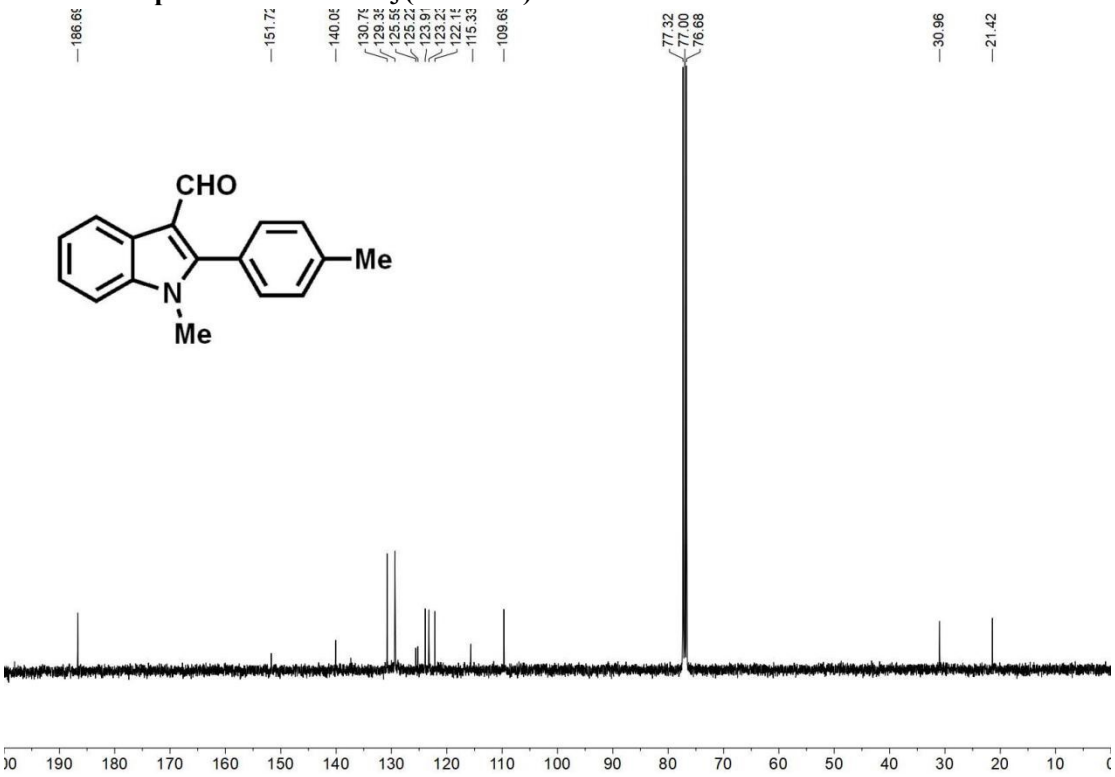
7. Copies of 1H NMR and 13C NMR for the Products

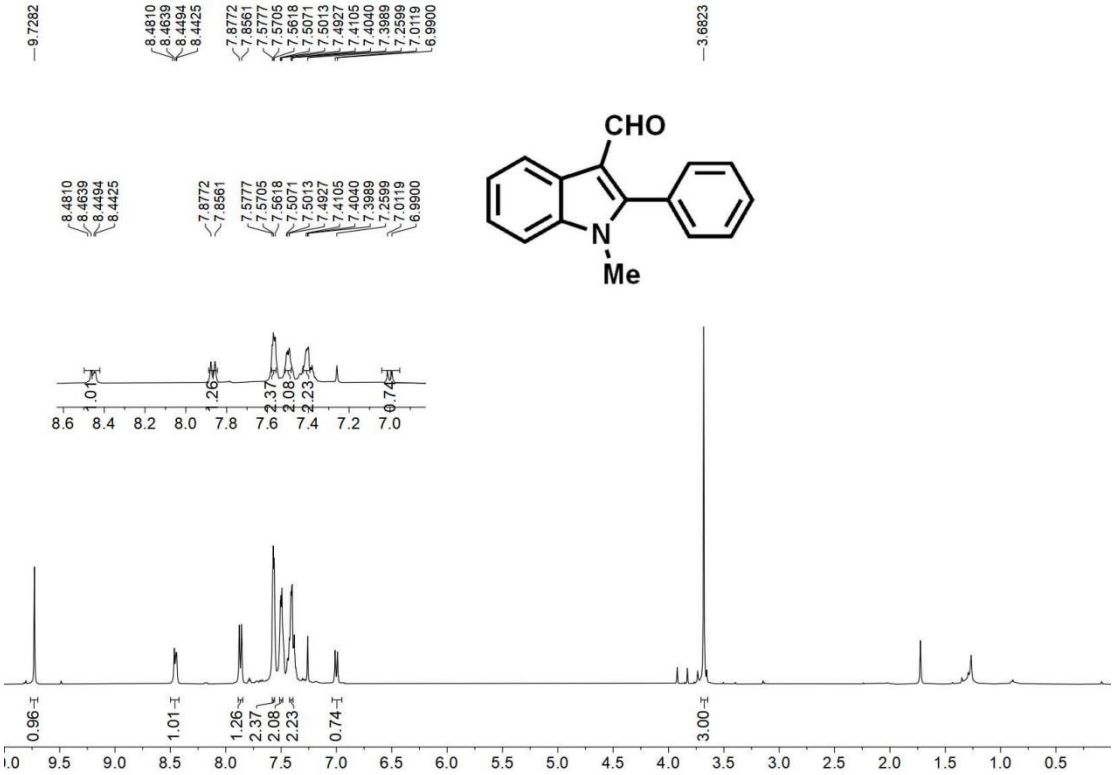
^{1}H NMR of product 3a in $CDCl_3$ (400 MHz)



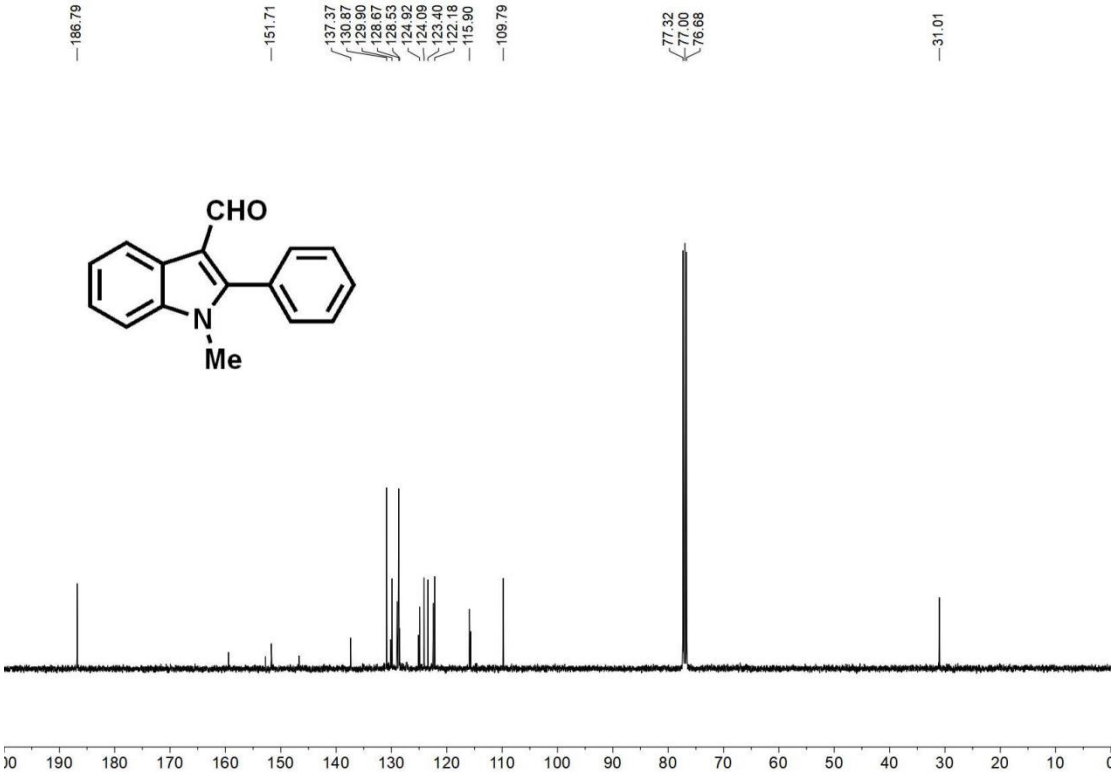
^{13}C NMR of product 3a in $CDCl_3$ (101 MHz)



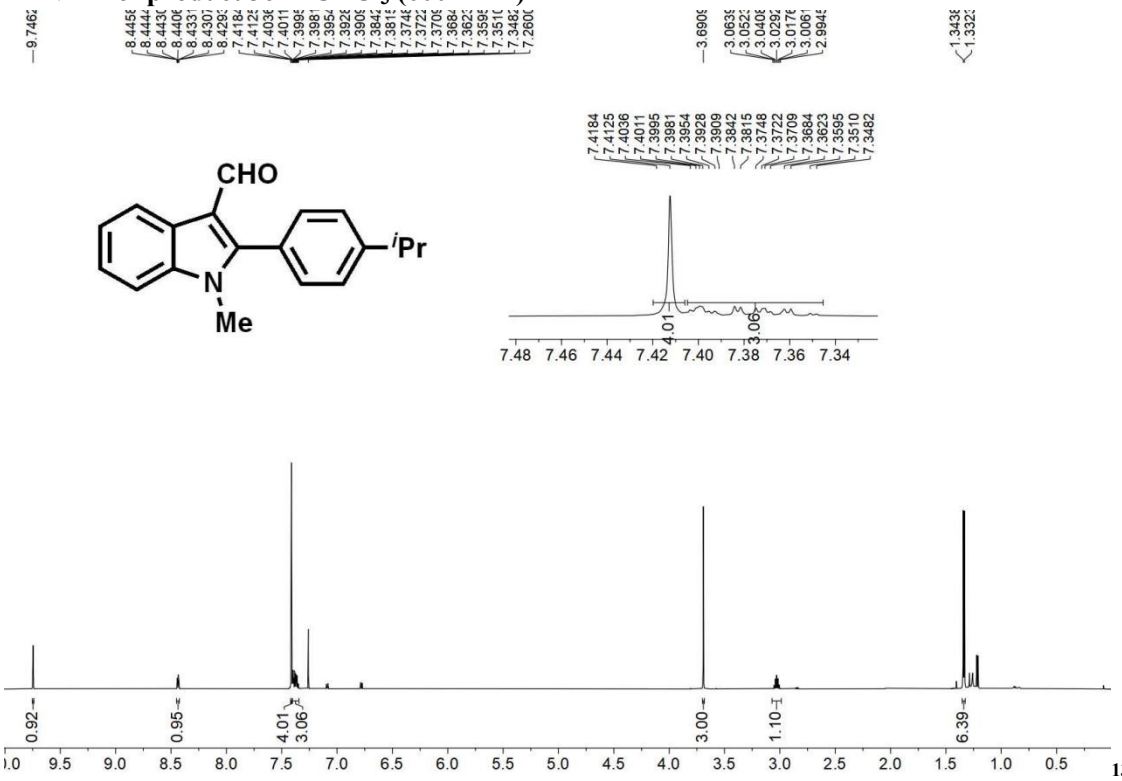
^{1}H NMR of product 3b in $CDCl_3$ (400 MHz)



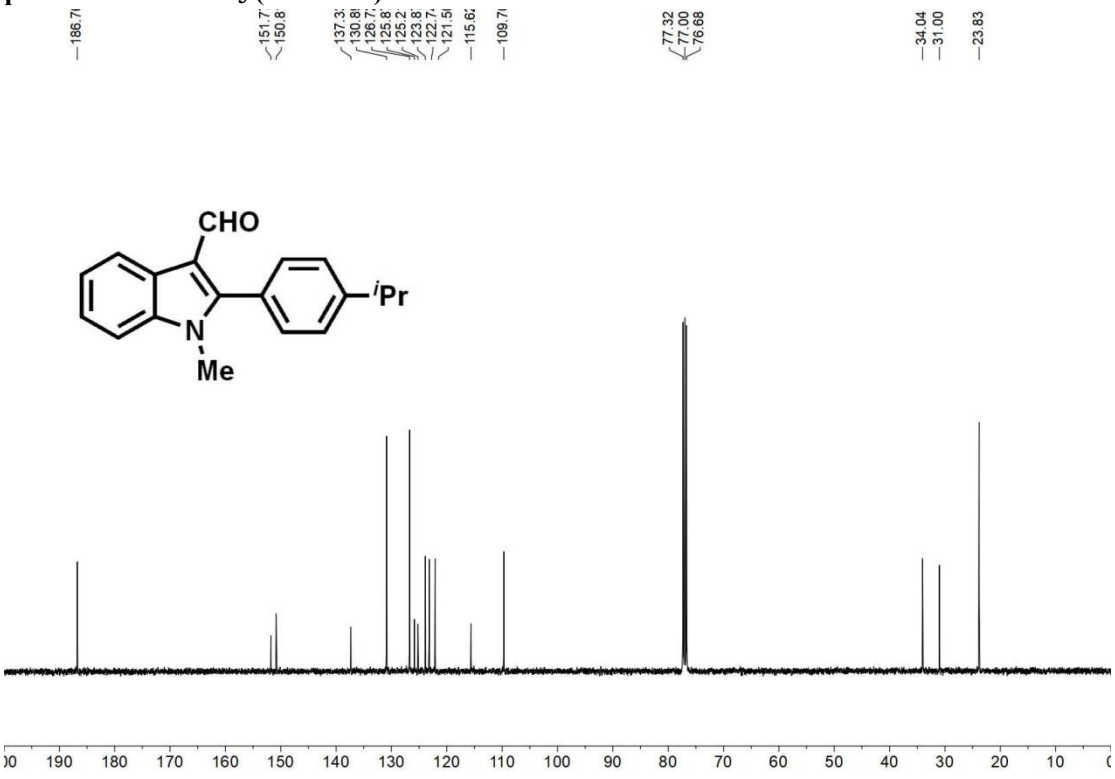
^{13}C NMR of product 3b in $CDCl_3$ (101 MHz)



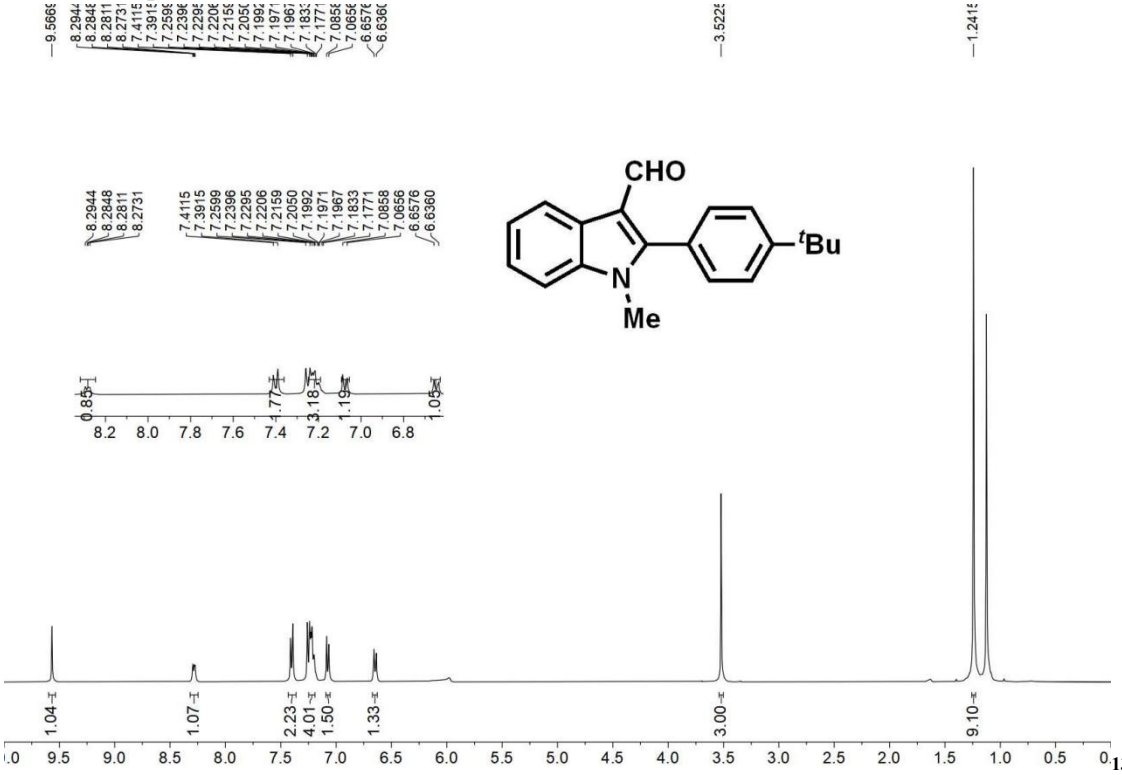
^{1}H NMR of product 3c in $CDCl_3$ (600 MHz)



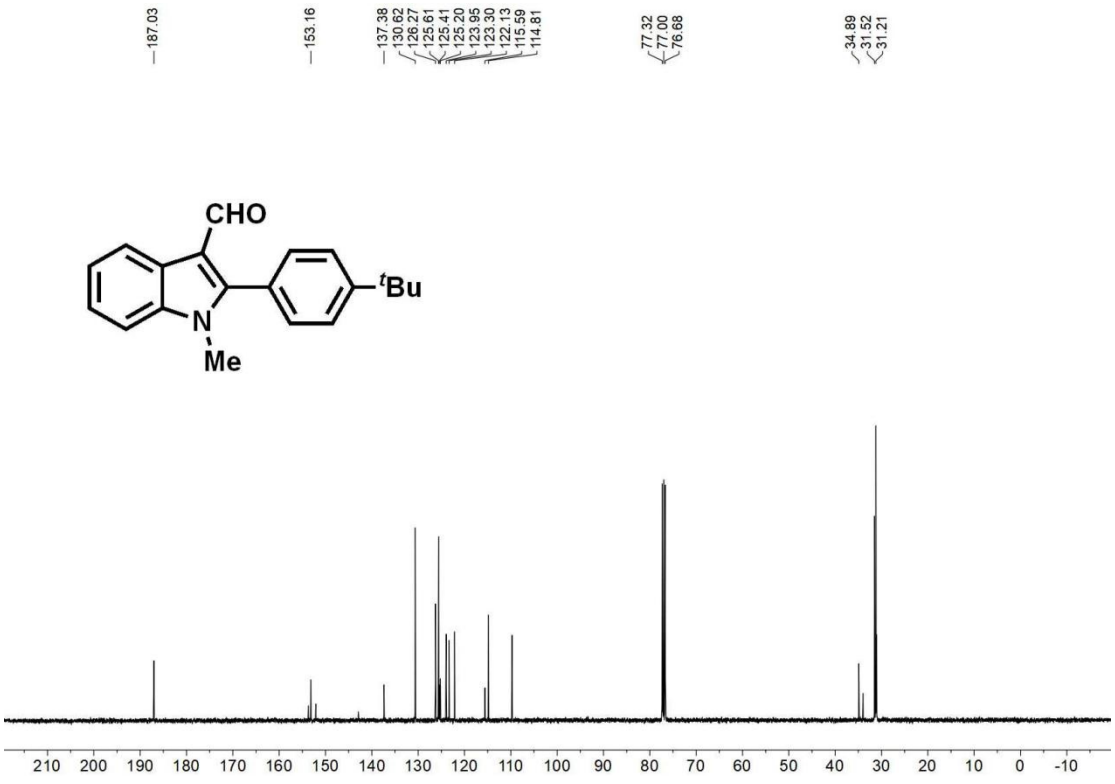
^{13}C NMR of product 3c in $CDCl_3$ (101 MHz)



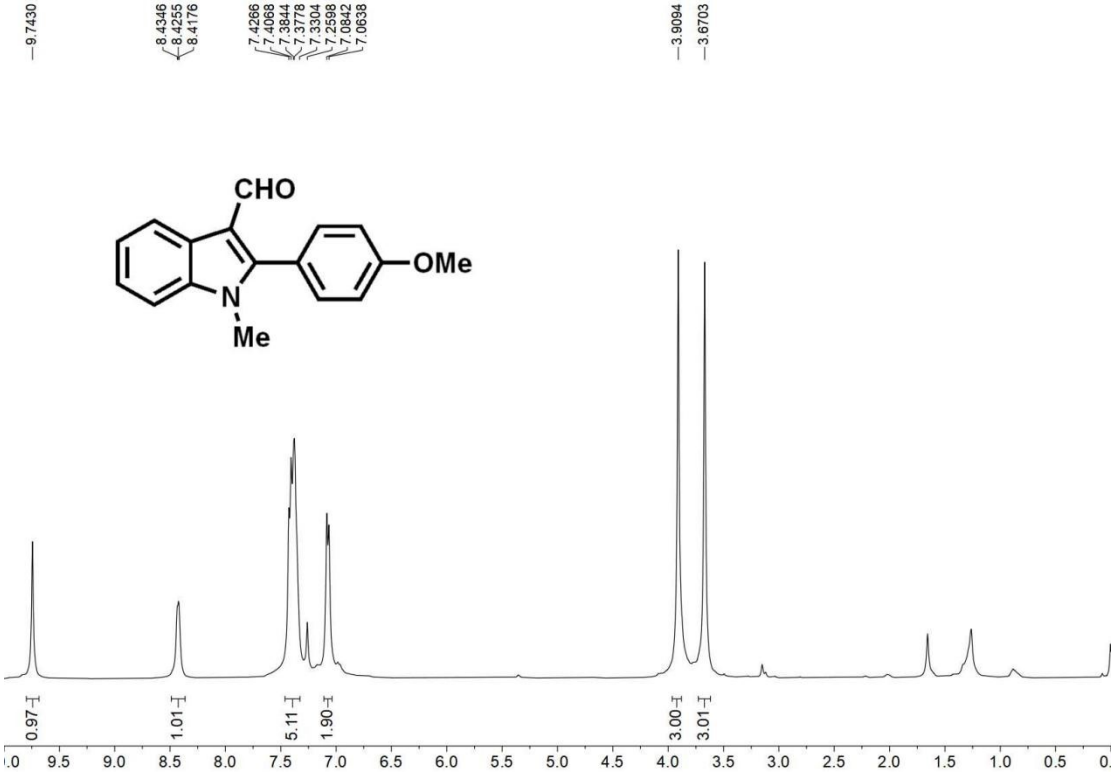
^{1}H NMR of product 3d in $CDCl_3$ (400 MHz)



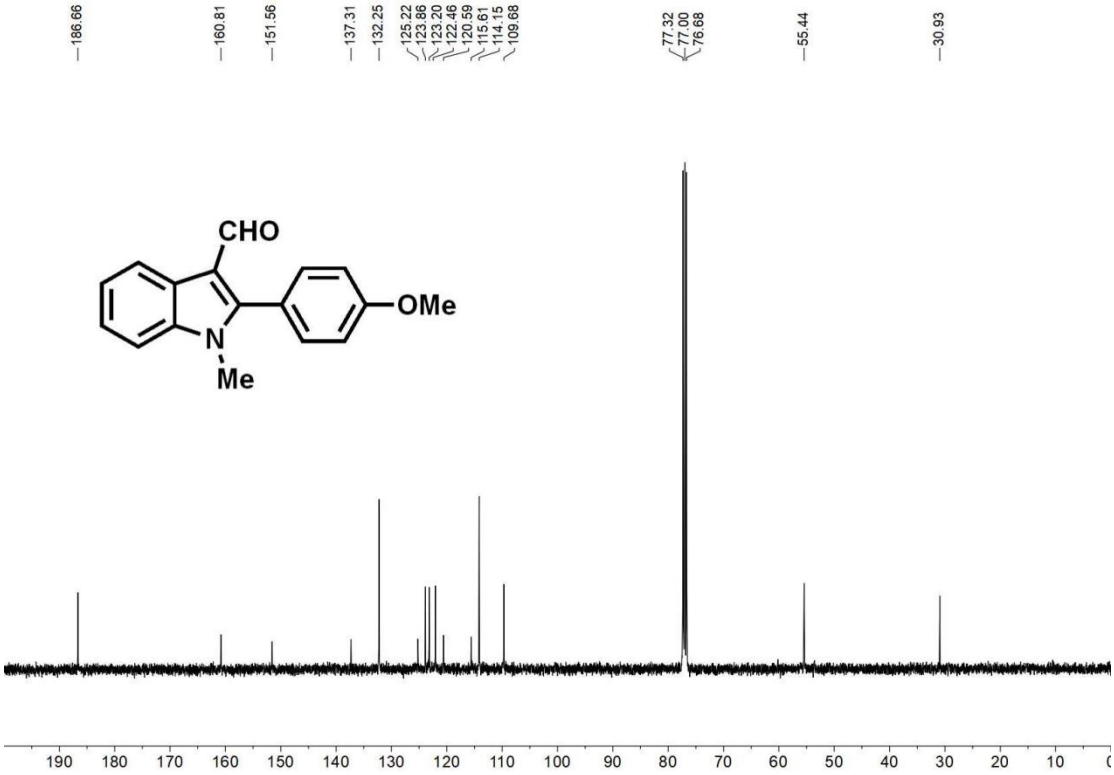
^{13}C NMR of product 3d in $CDCl_3$ (101 MHz)



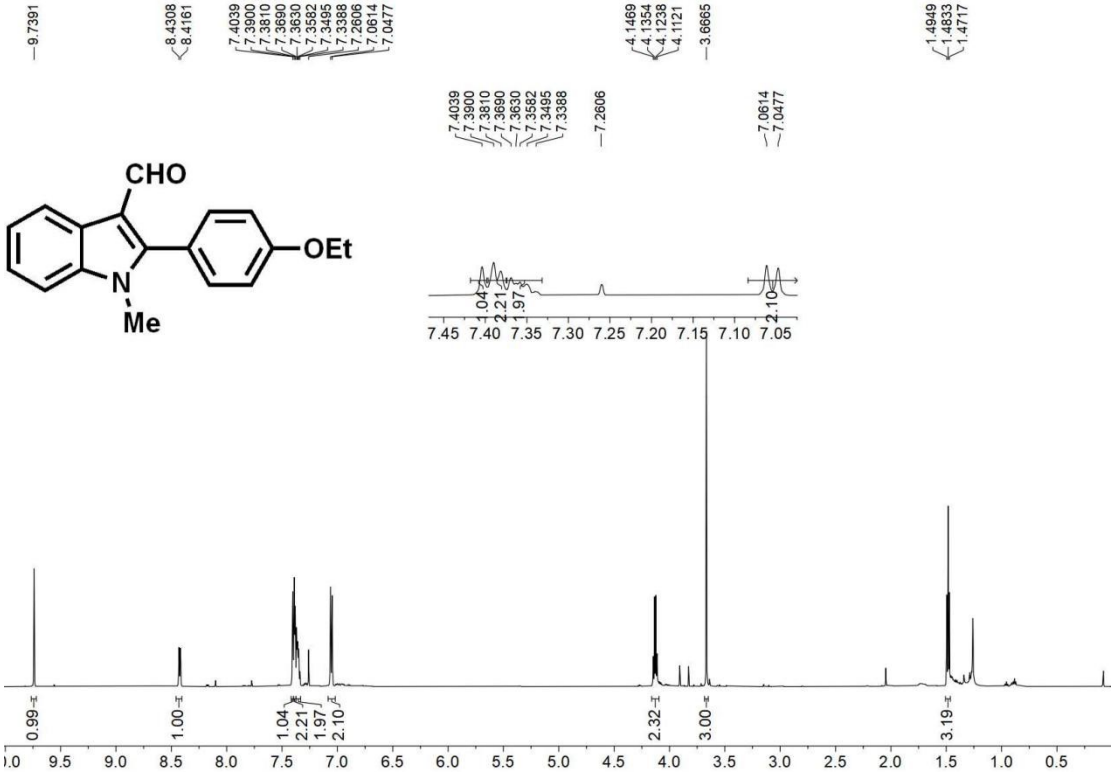
^{1}H NMR of product 3e in $CDCl_3$ (400 MHz)



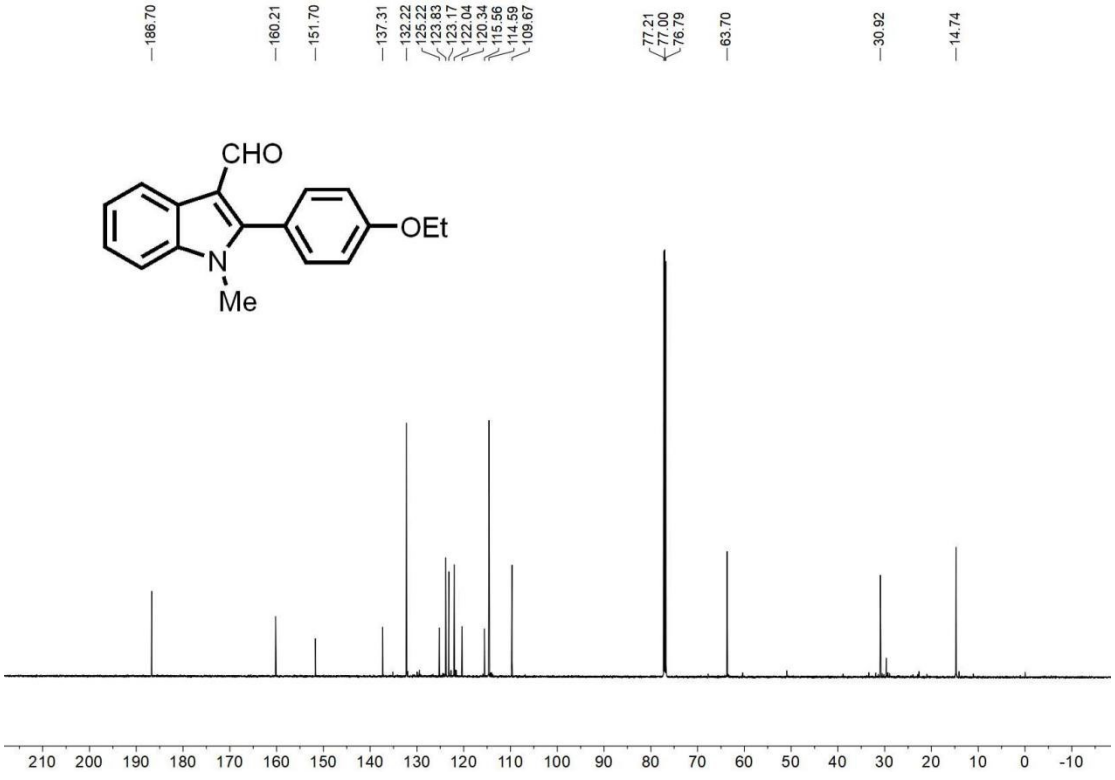
^{13}C NMR of product 3e in $CDCl_3$ (101 MHz)



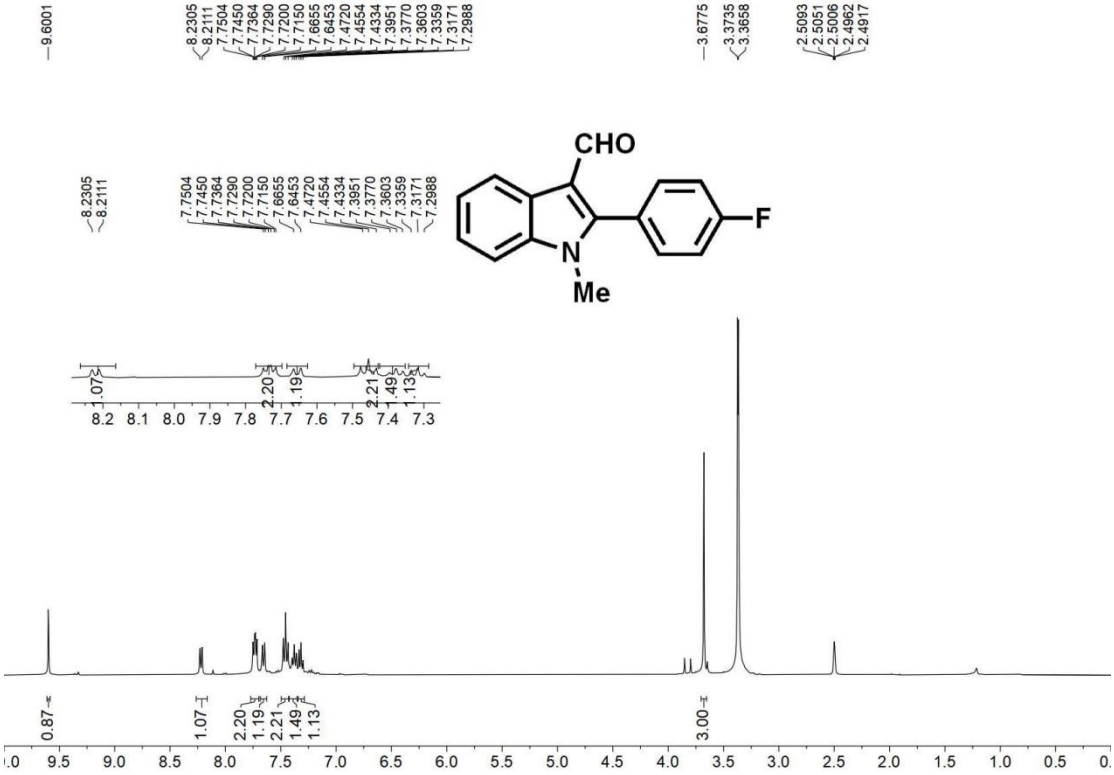
^{1}H NMR of product 3f in $CDCl_3$ (600 MHz)



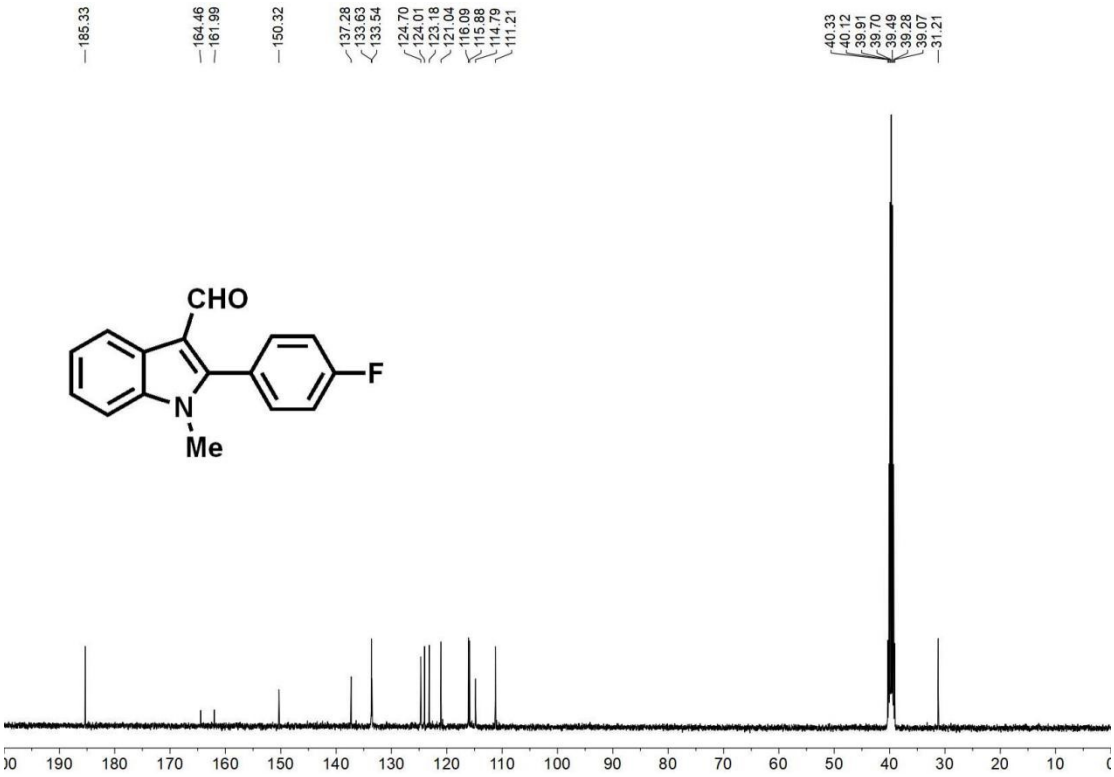
^{13}C NMR of product 3f in $CDCl_3$ (151 MHz)



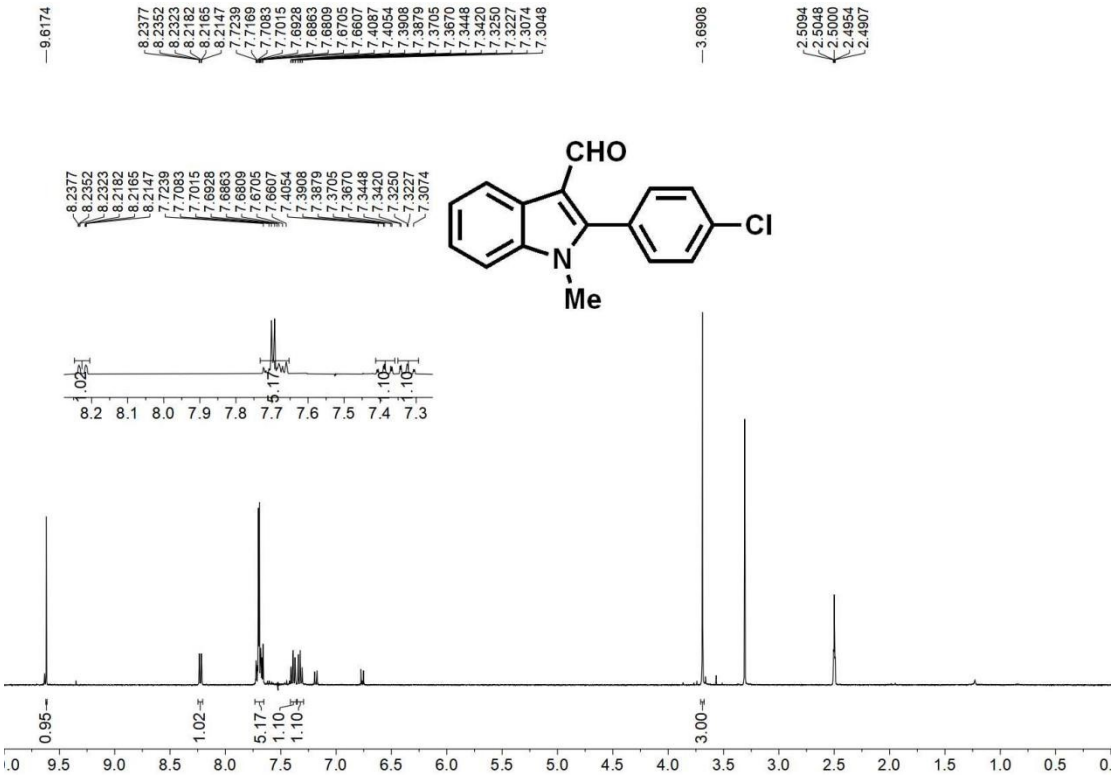
^{1}H NMR of product 3g in DMSO (400 MHz)



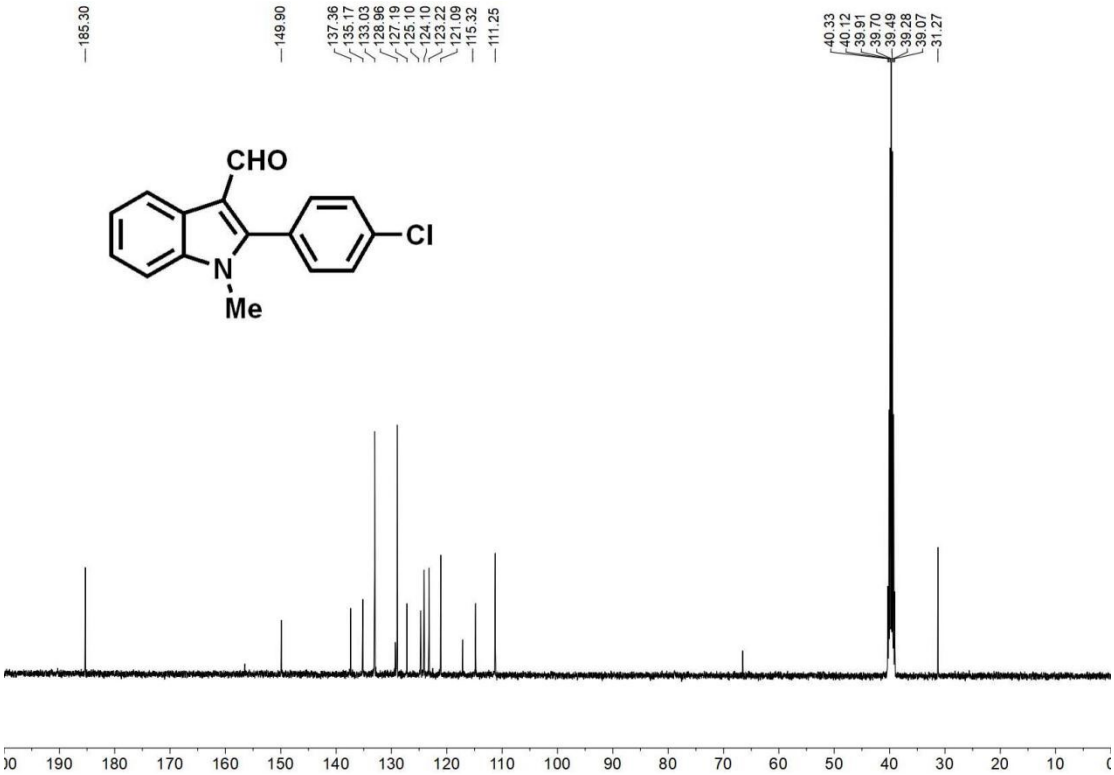
^{13}C NMR of product 3g in DMSO (101 MHz)



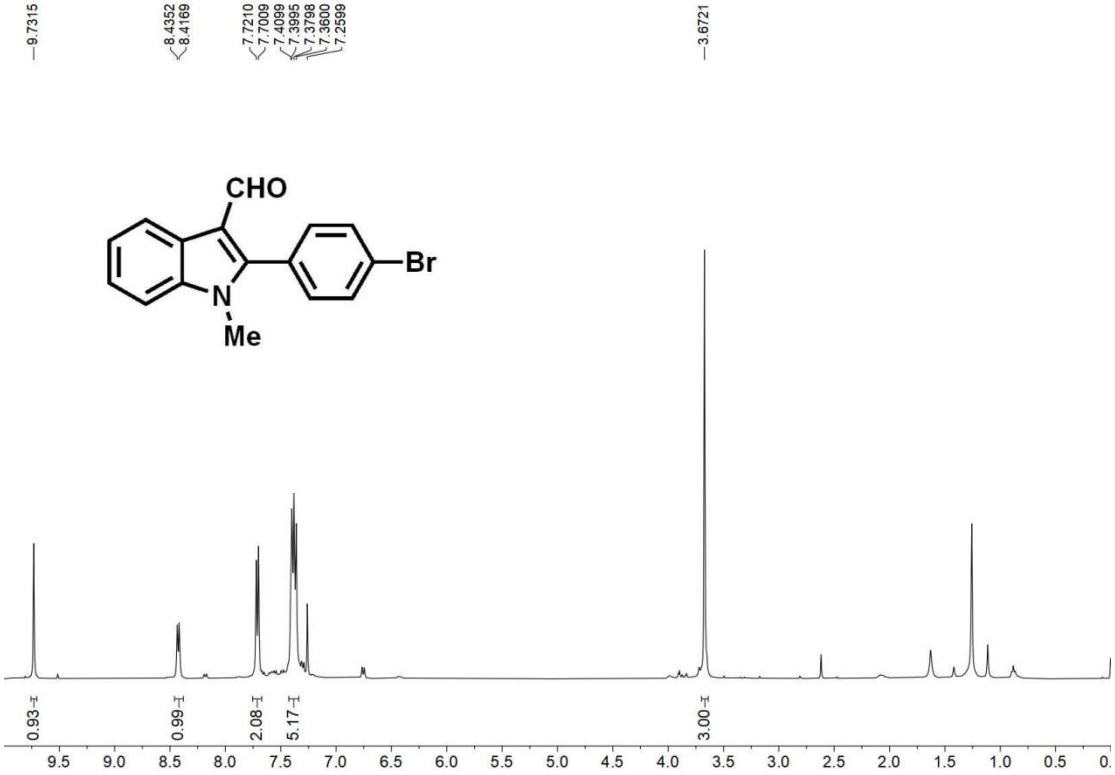
^{1}H NMR of product 3h in DMSO (400 MHz)



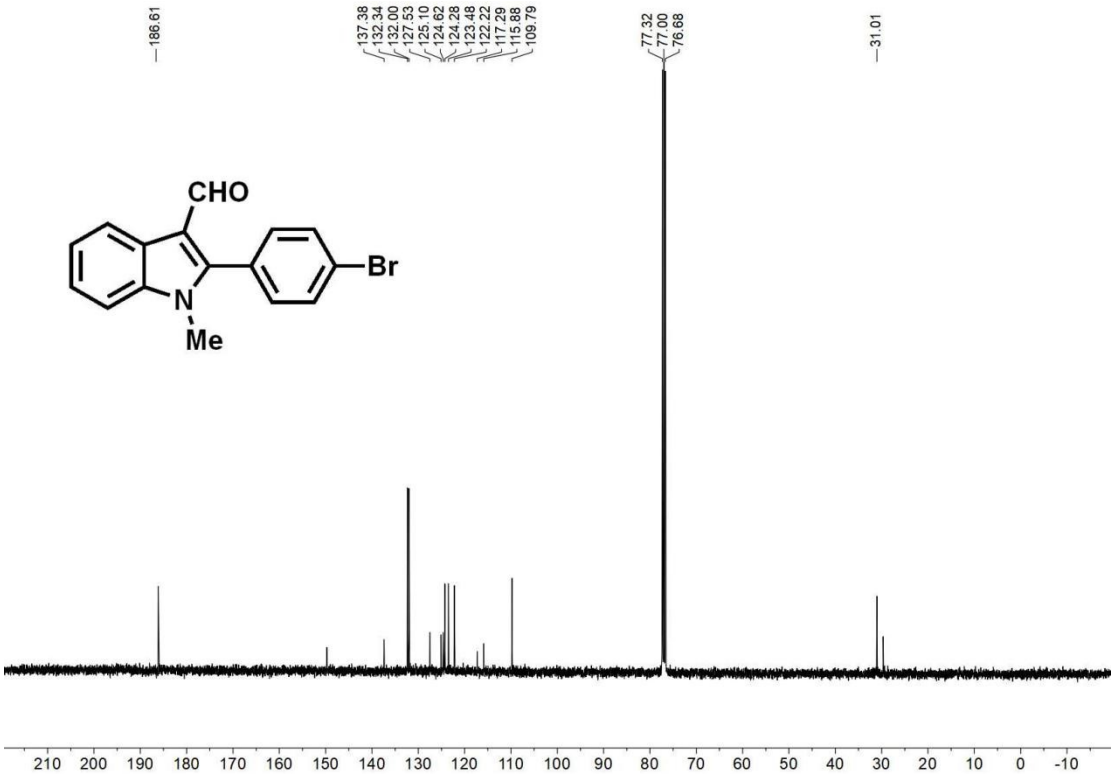
^{13}C NMR of product 3h in DMSO (101 MHz)



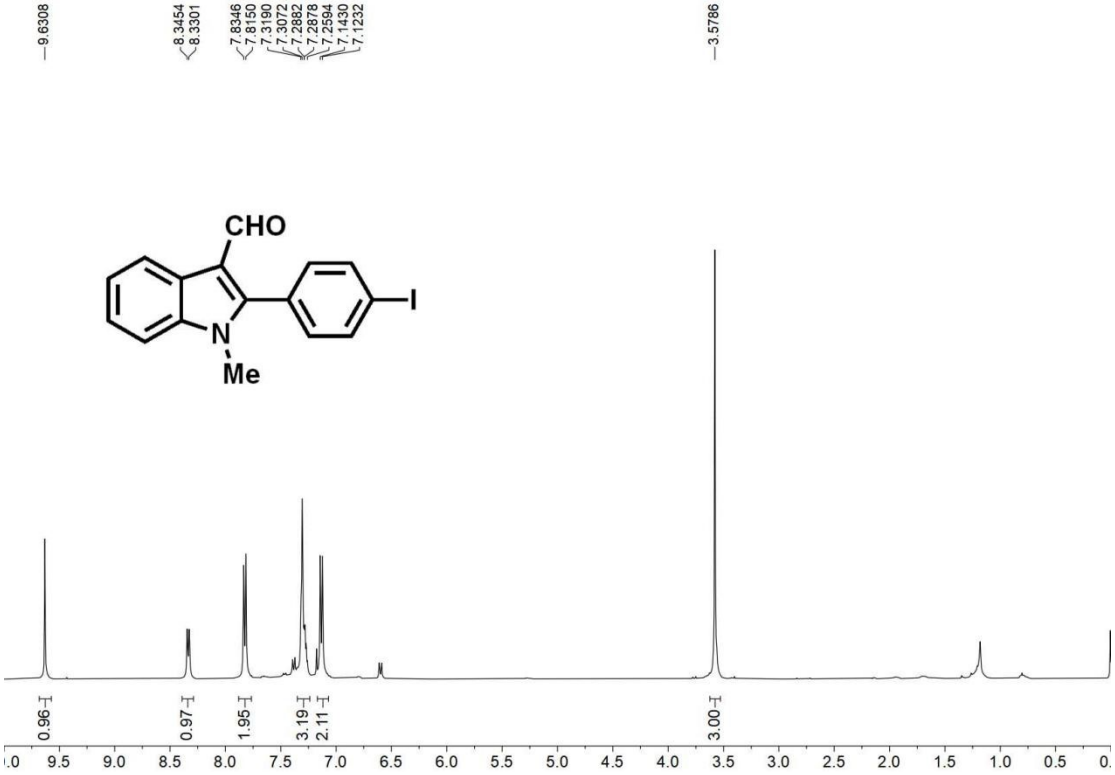
^{1}H NMR of product 3i in $CDCl_3$ (400 MHz)



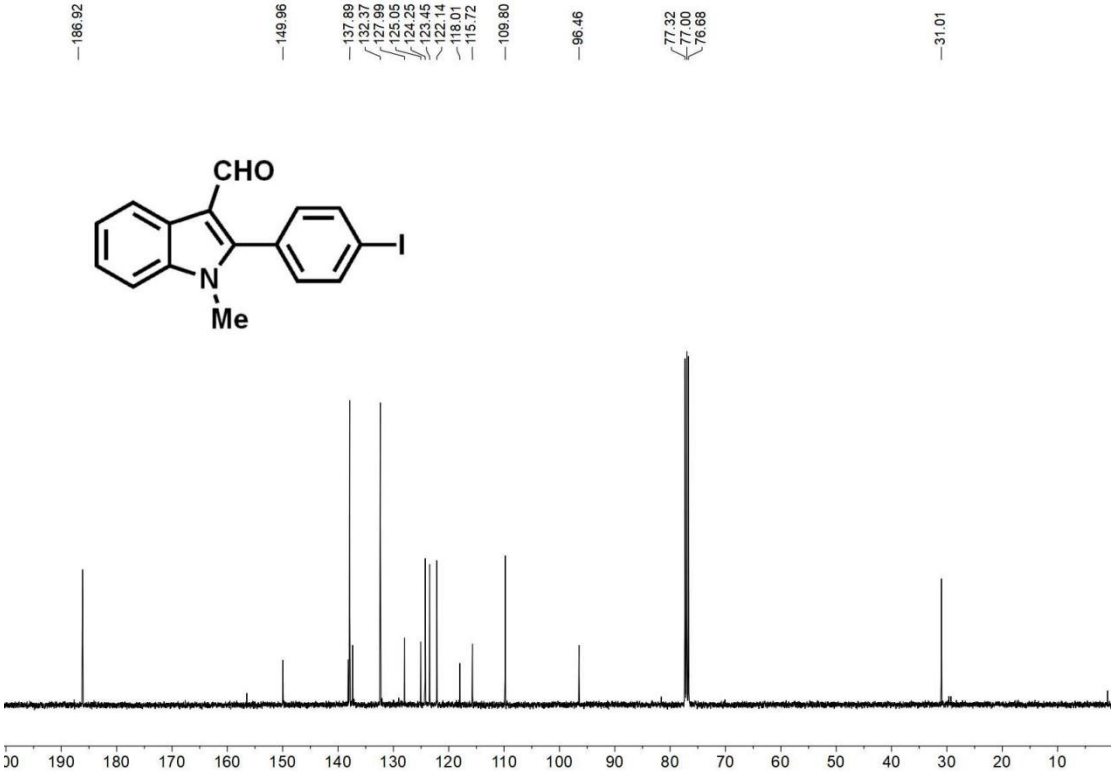
^{13}C NMR of product 3i in $CDCl_3$ (101 MHz)



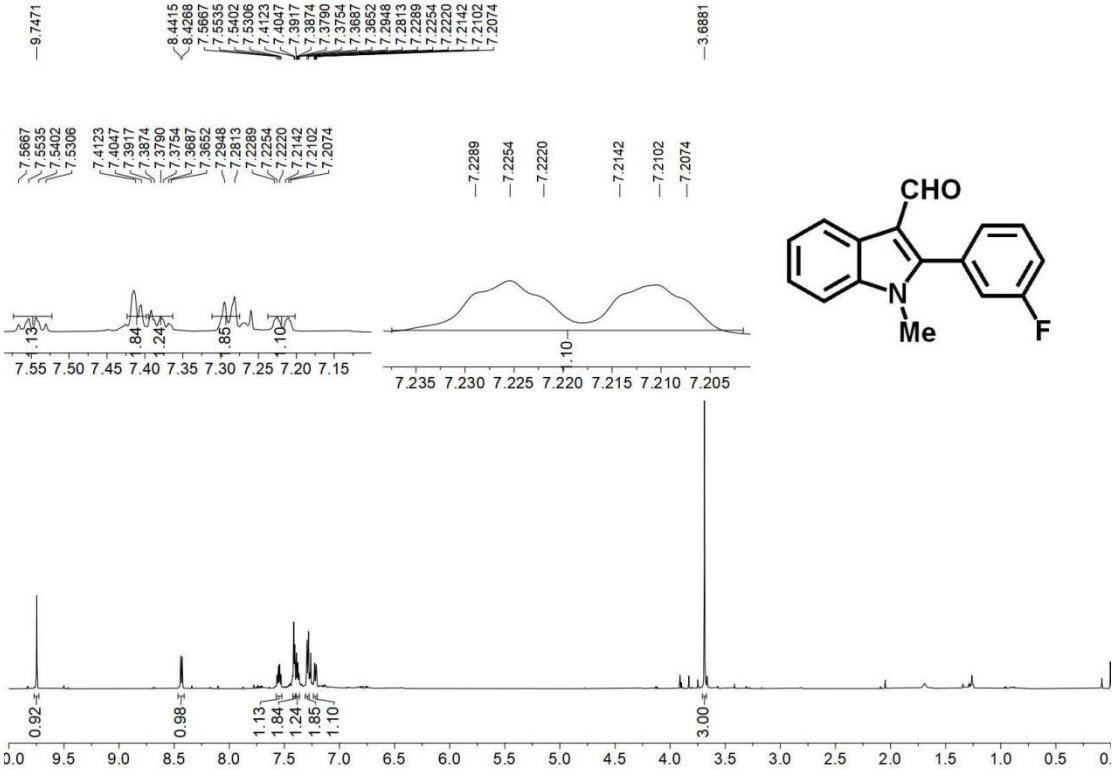
^{1}H NMR of product 3j in $CDCl_3$ (400 MHz)



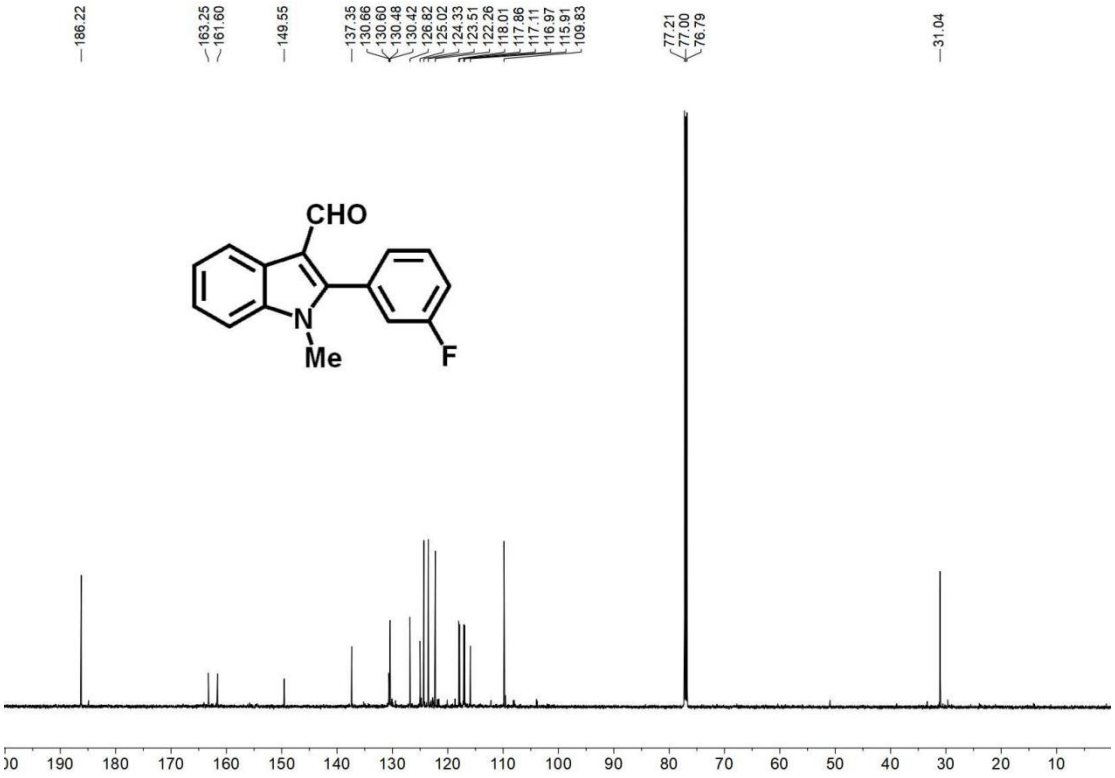
^{13}C NMR of product 3j in $CDCl_3$ (101 MHz)



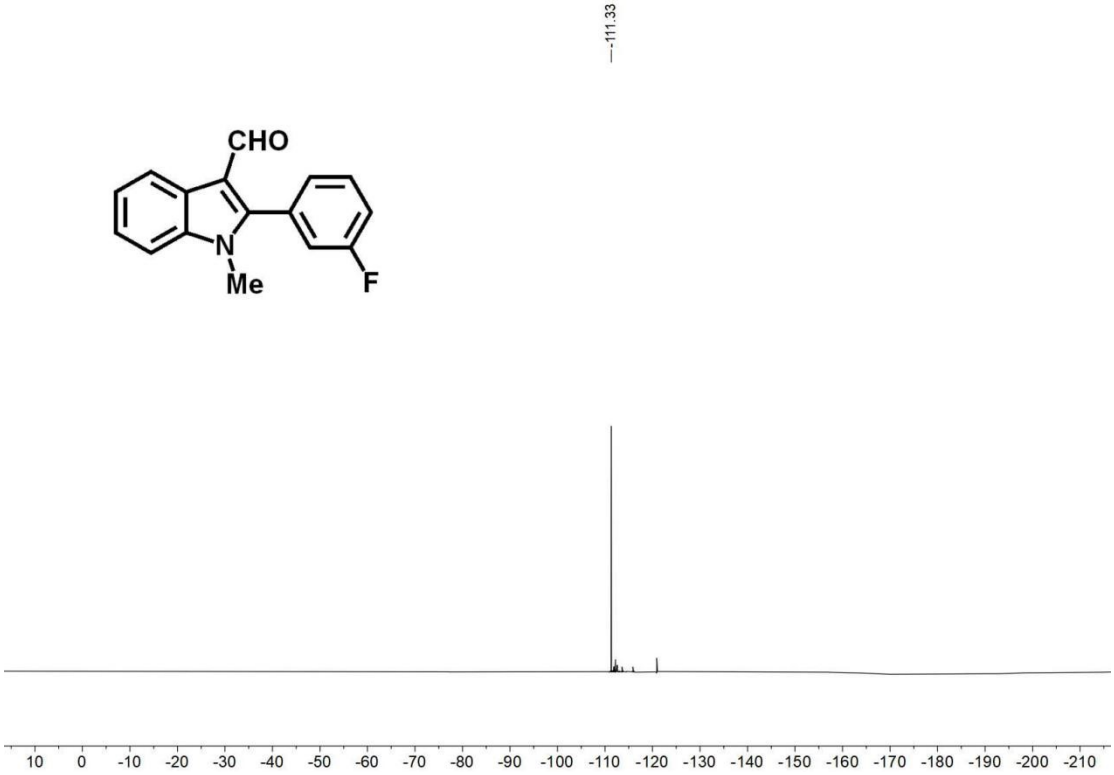
^{1}H NMR of product 3k in $CDCl_3$ (600 MHz)



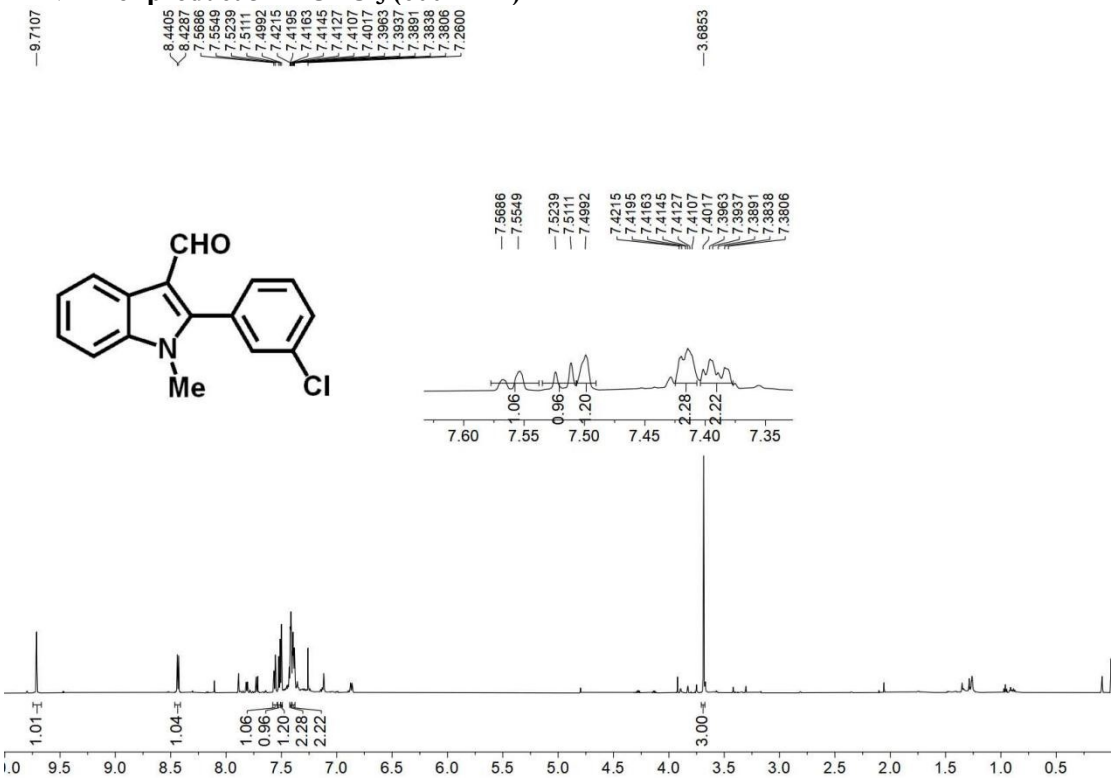
^{13}C NMR of product 3k in $CDCl_3$ (151 MHz)



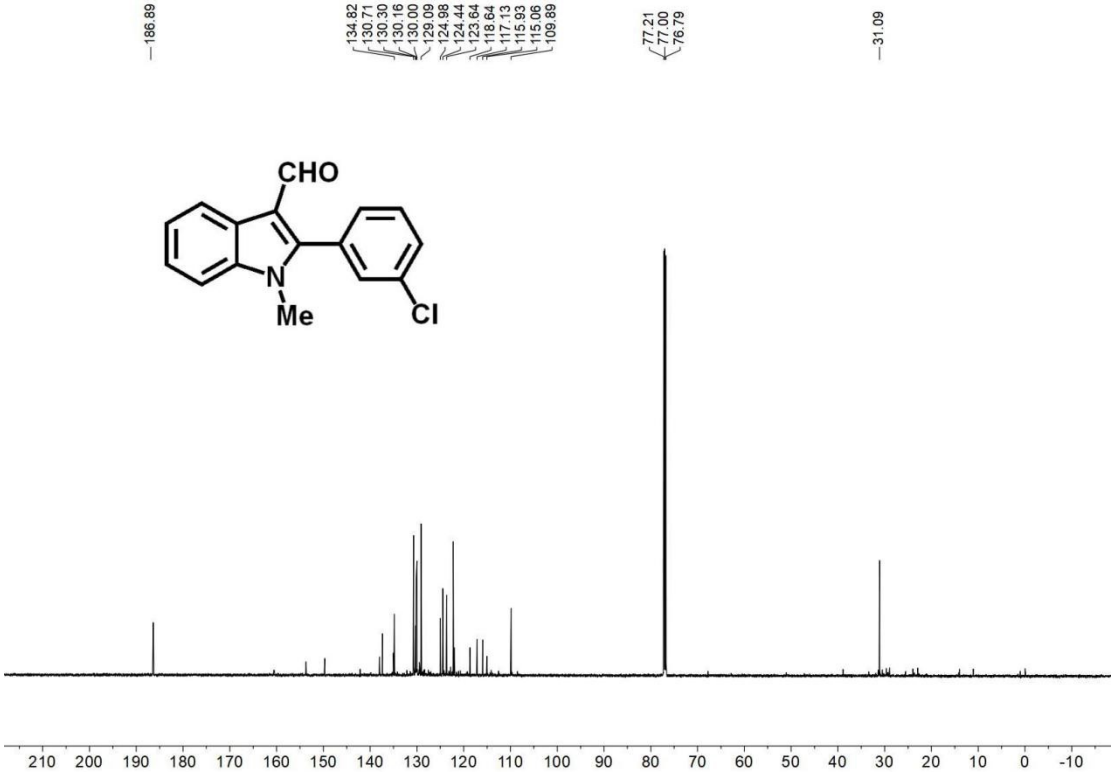
^{19}F NMR of product 3k in $CDCl_3$ (565 MHz)



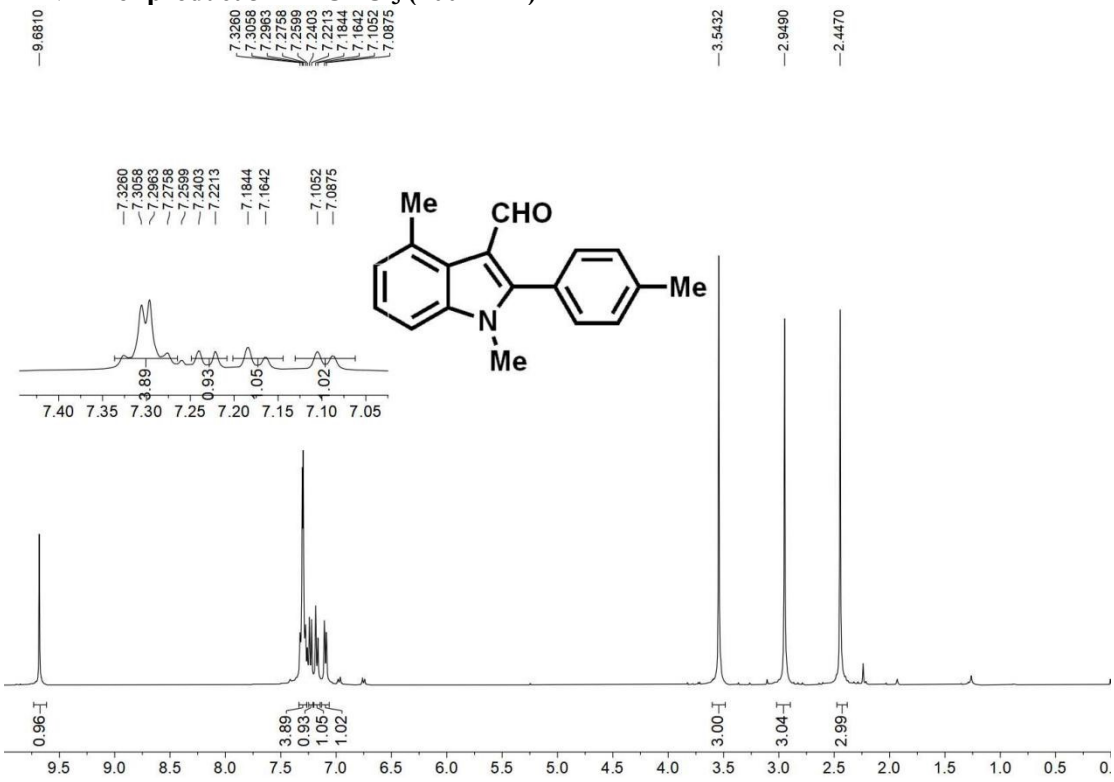
^{1}H NMR of product 3l in $CDCl_3$ (600 MHz)



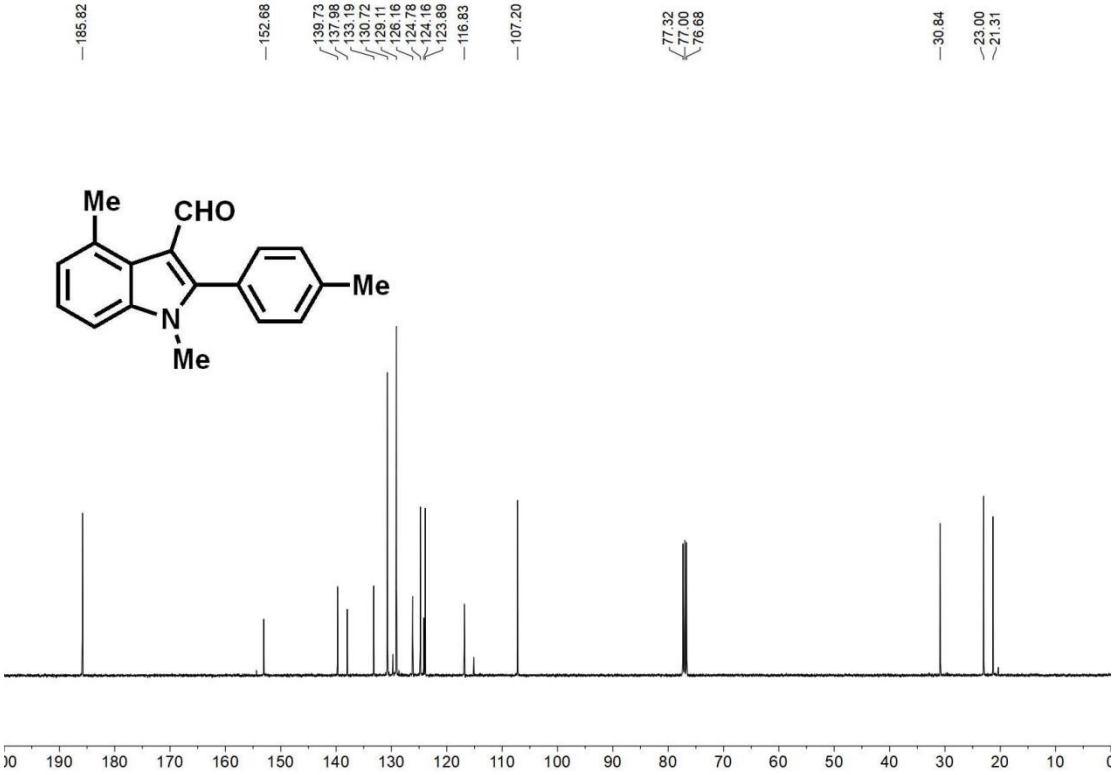
^{13}C NMR of product 3l in CDCl3 (151 MHz)



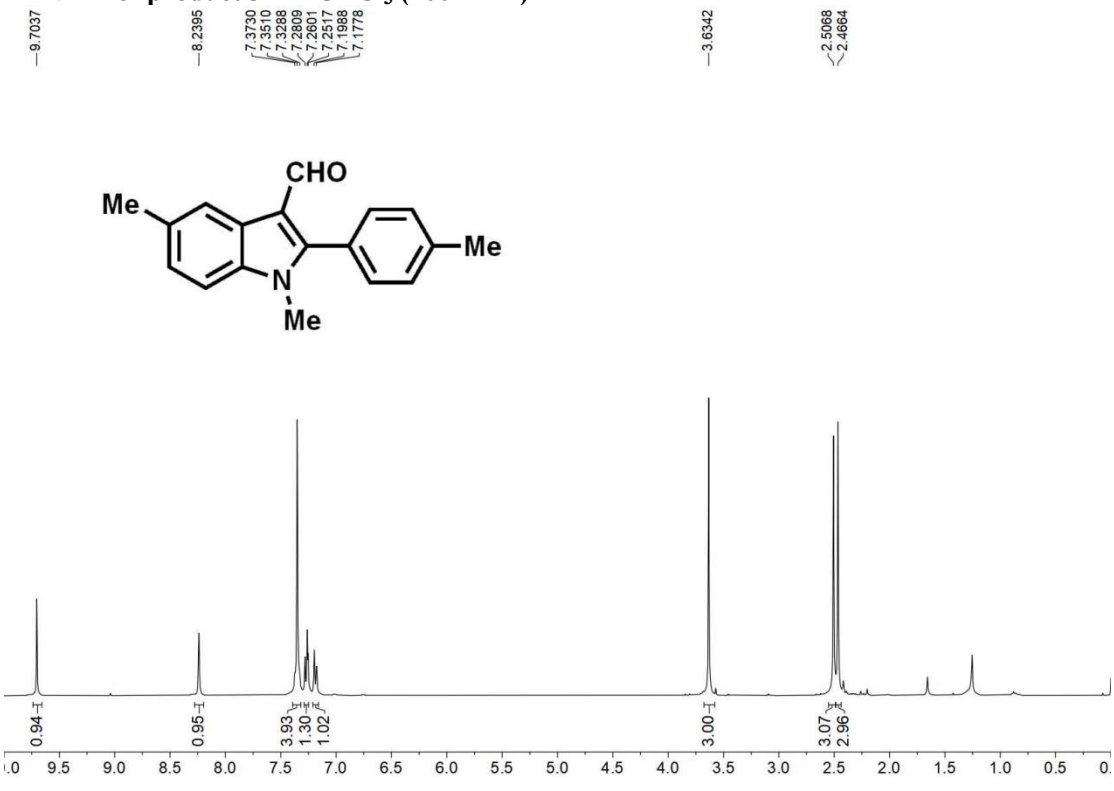
^{1}H NMR of product 3m in $CDCl_3$ (400 MHz)



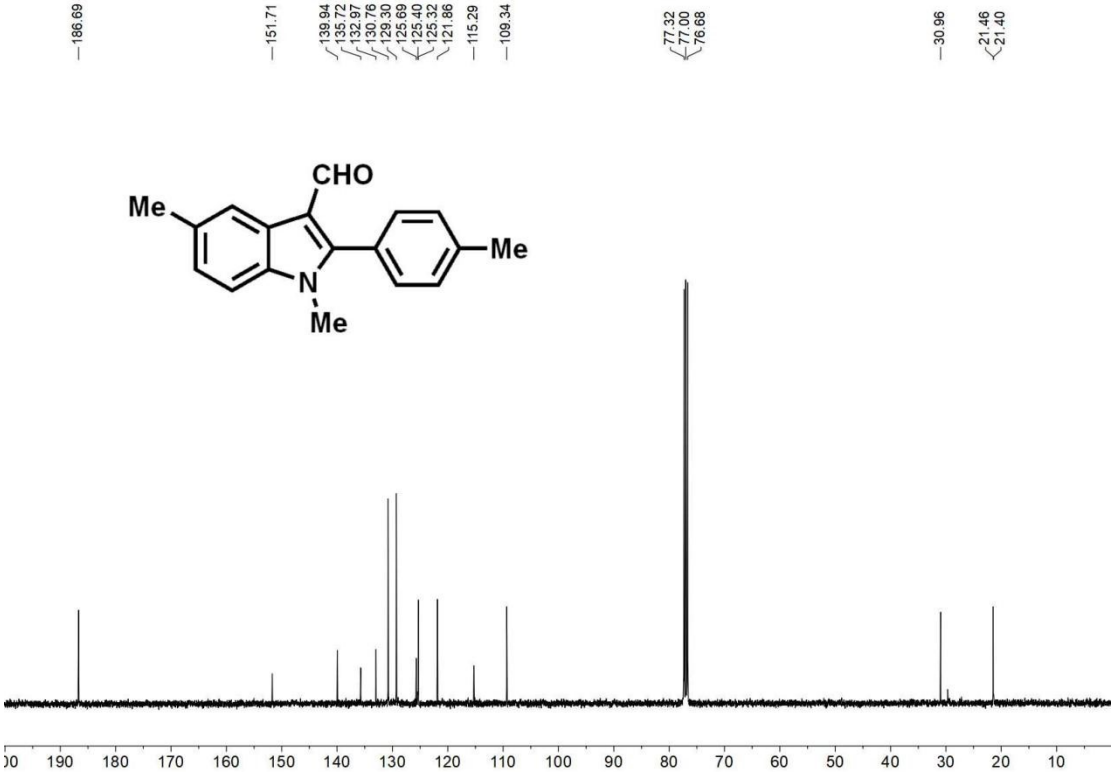
^{13}C NMR of product 3m in $CDCl_3$ (101 MHz)



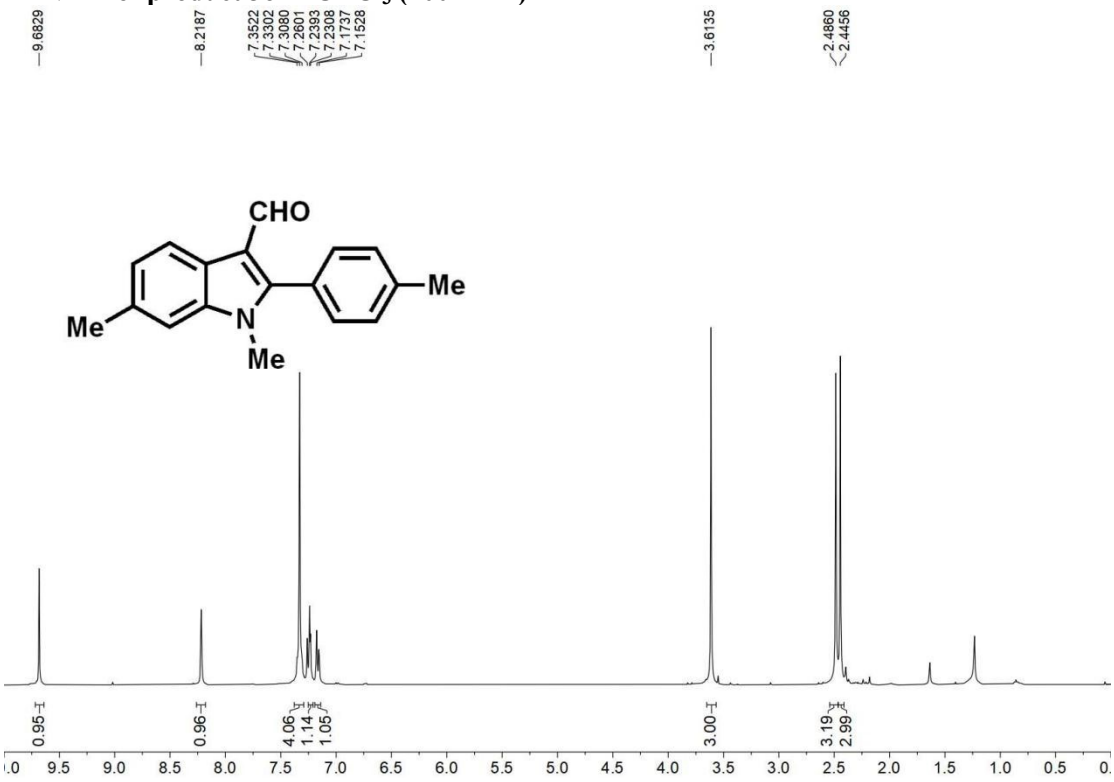
^{1}H NMR of product 3n in $CDCl_3$ (400 MHz)



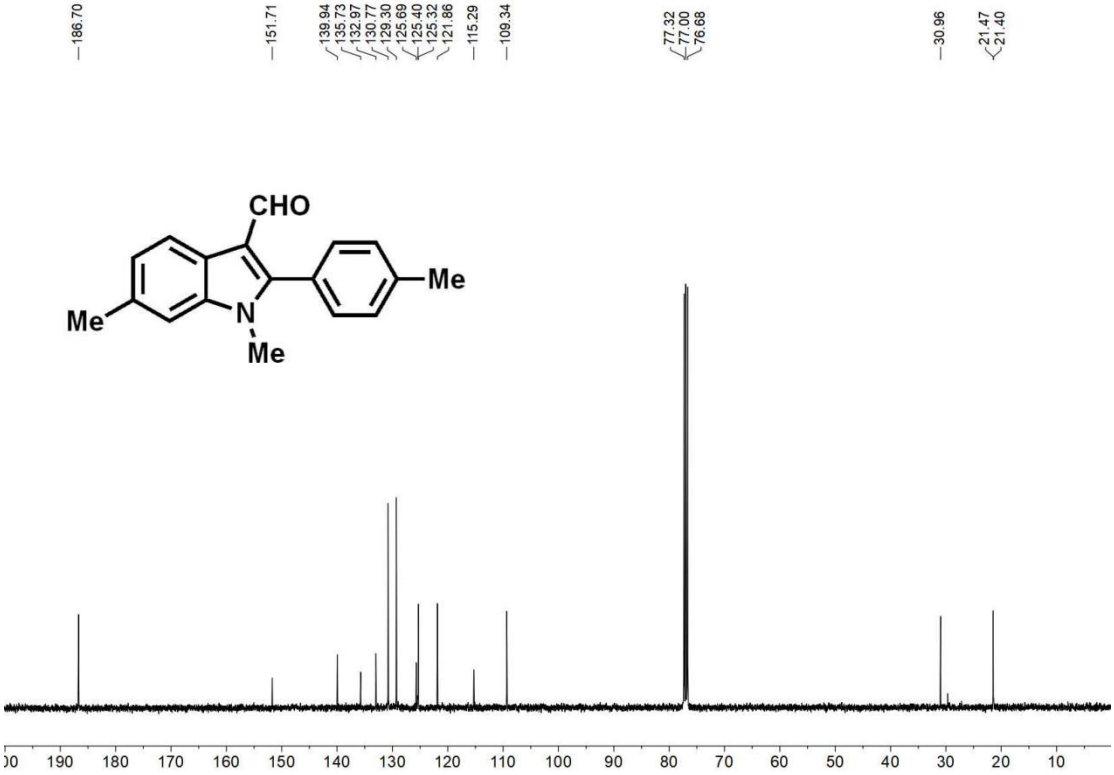
^{13}C NMR of product 3n in $CDCl_3$ (101 MHz)



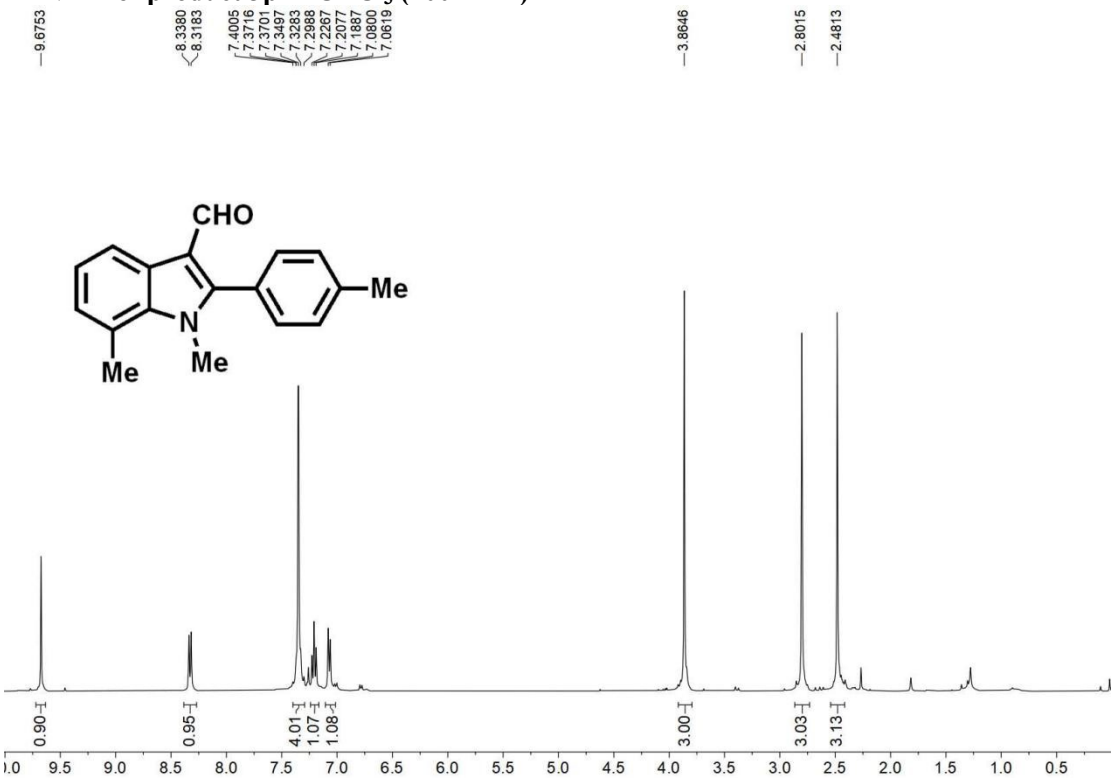
^{1}H NMR of product 3o in $CDCl_3$ (400 MHz)



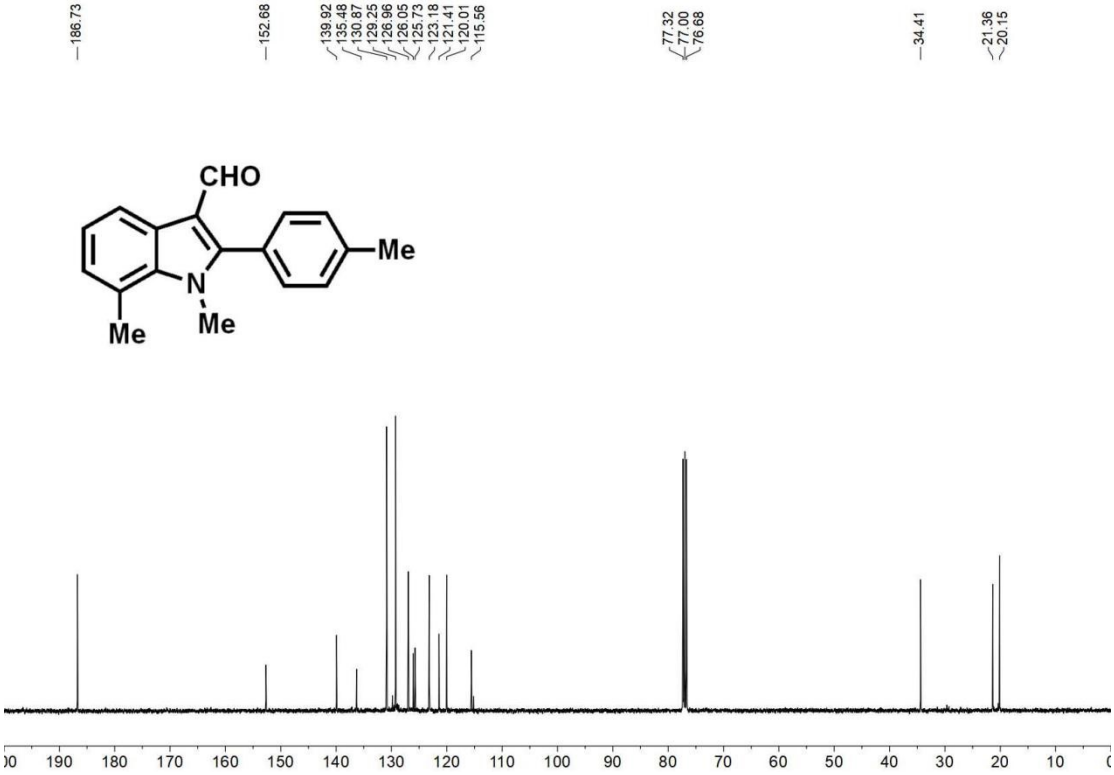
^{13}C NMR of product 3o in $CDCl_3$ (101 MHz)



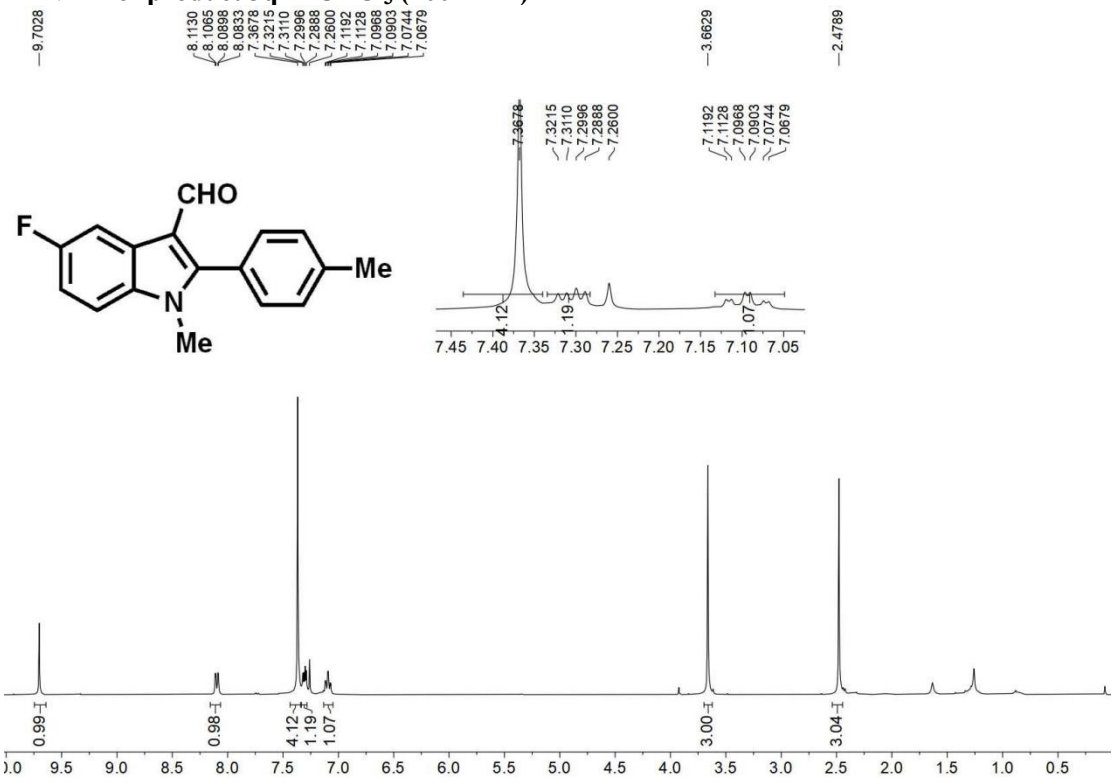
^{1}H NMR of product 3p in $CDCl_3$ (400 MHz)



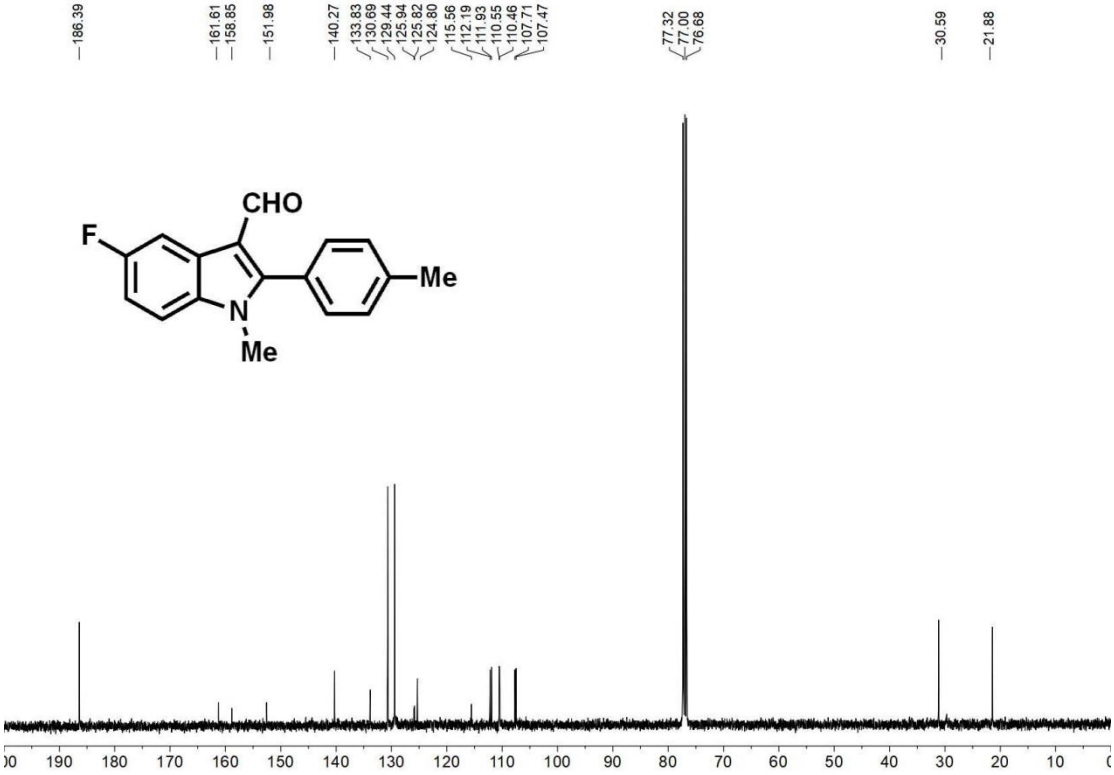
^{13}C NMR of product 3p in $CDCl_3$ (101 MHz)



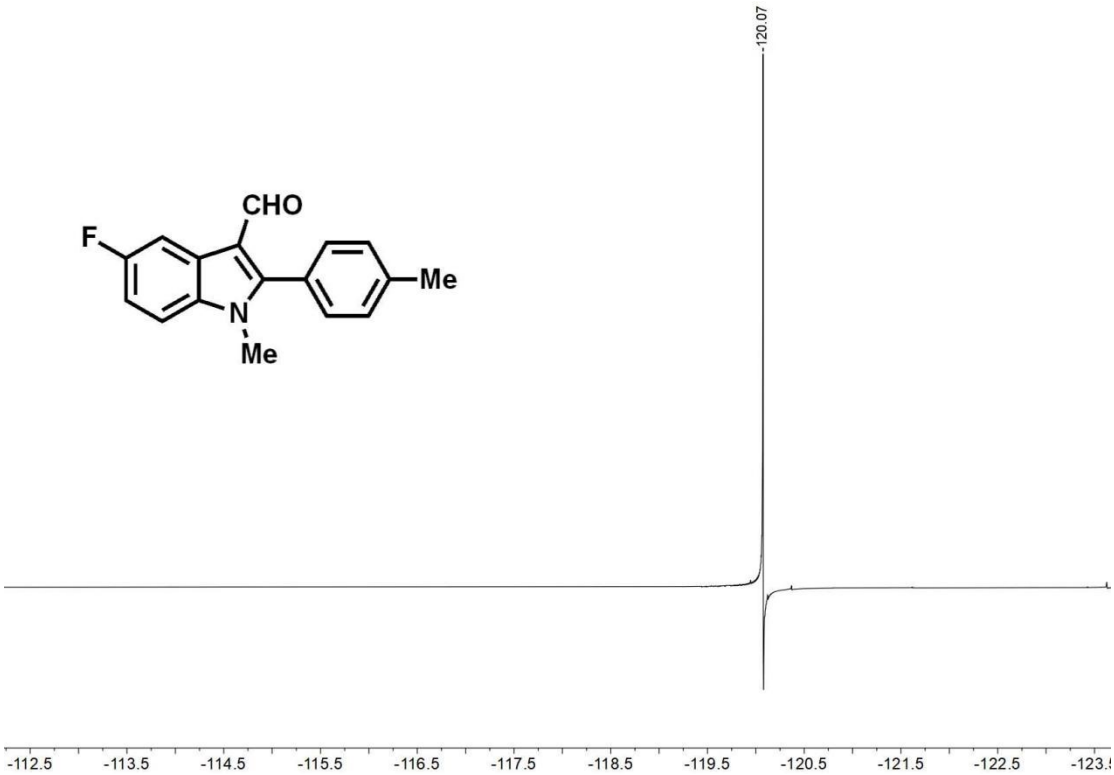
^{1}H NMR of product 3q in $CDCl_3$ (400 MHz)



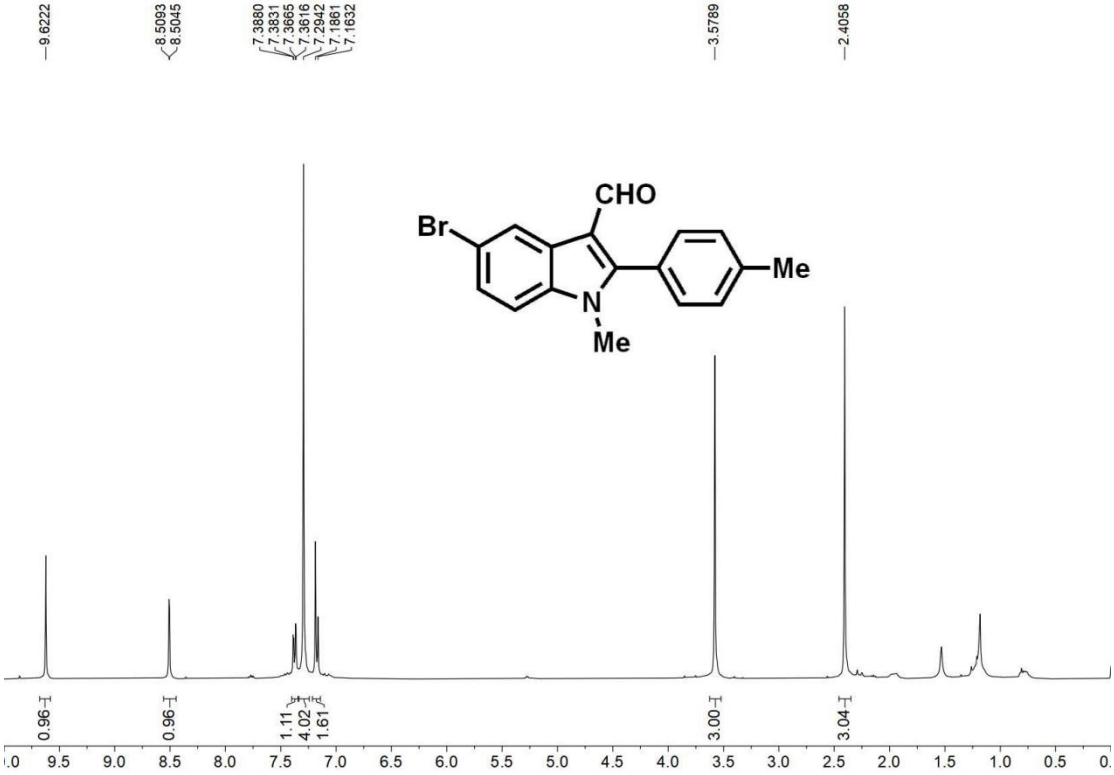
^{13}C NMR of product 3q in $CDCl_3$ (101 MHz)



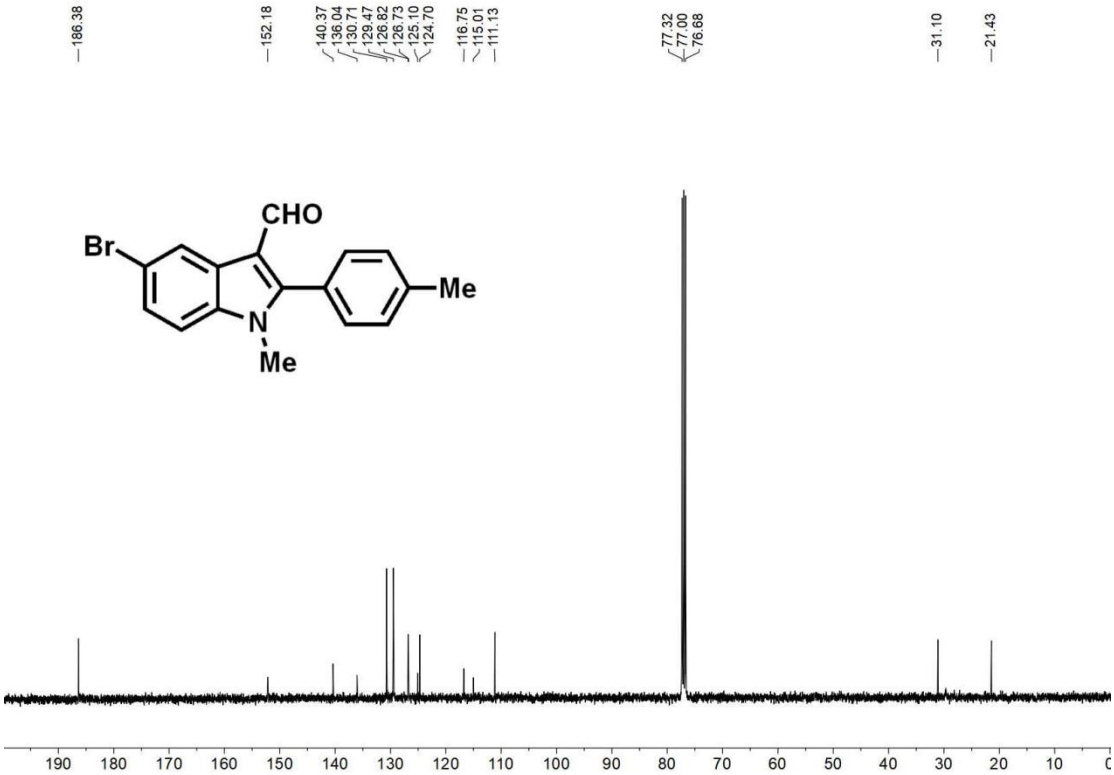
^{19}F NMR of product 3q in $CDCl_3$ (565 MHz)



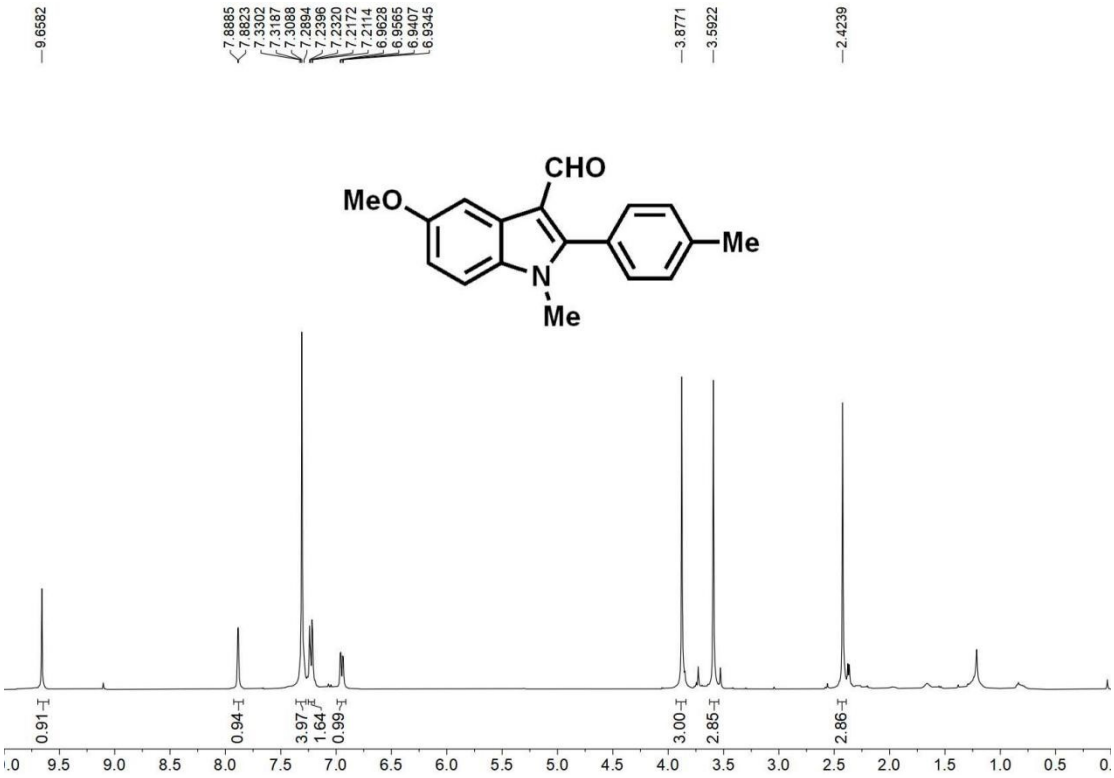
^{1}H NMR of product 3r in $CDCl_3$ (400 MHz)



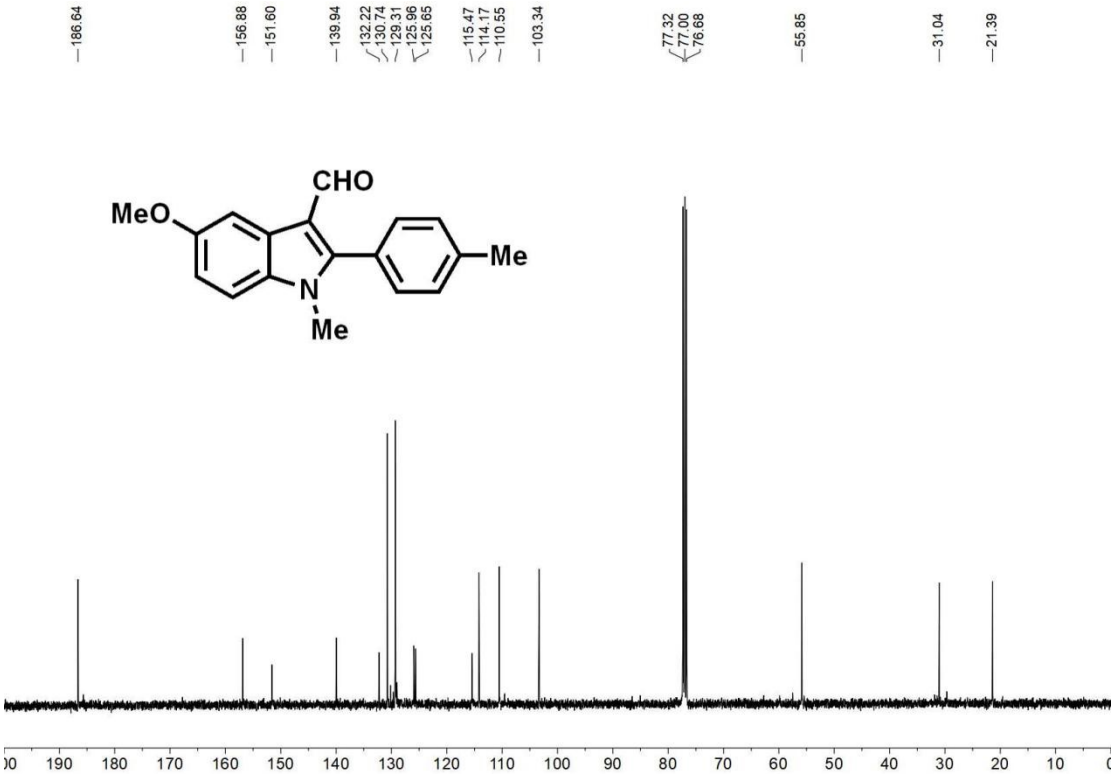
^{13}C NMR of product 3r in $CDCl_3$ (101 MHz)



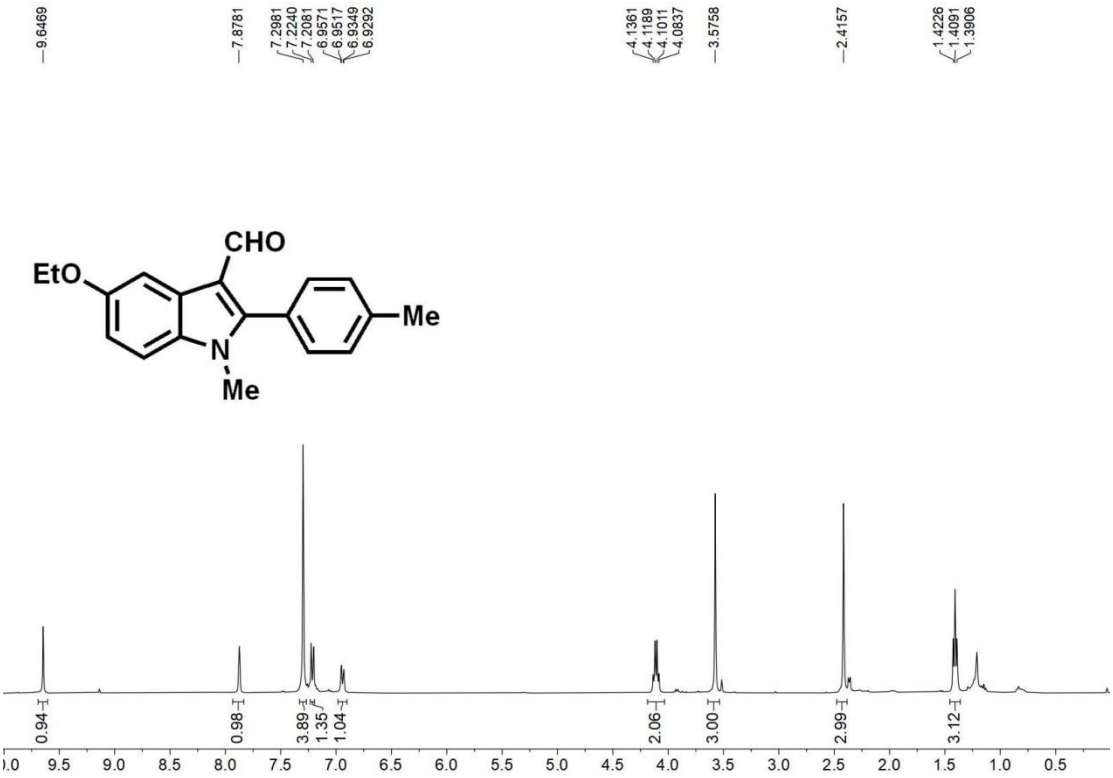
^{1}H NMR of product 3s in $CDCl_3$ (400 MHz)



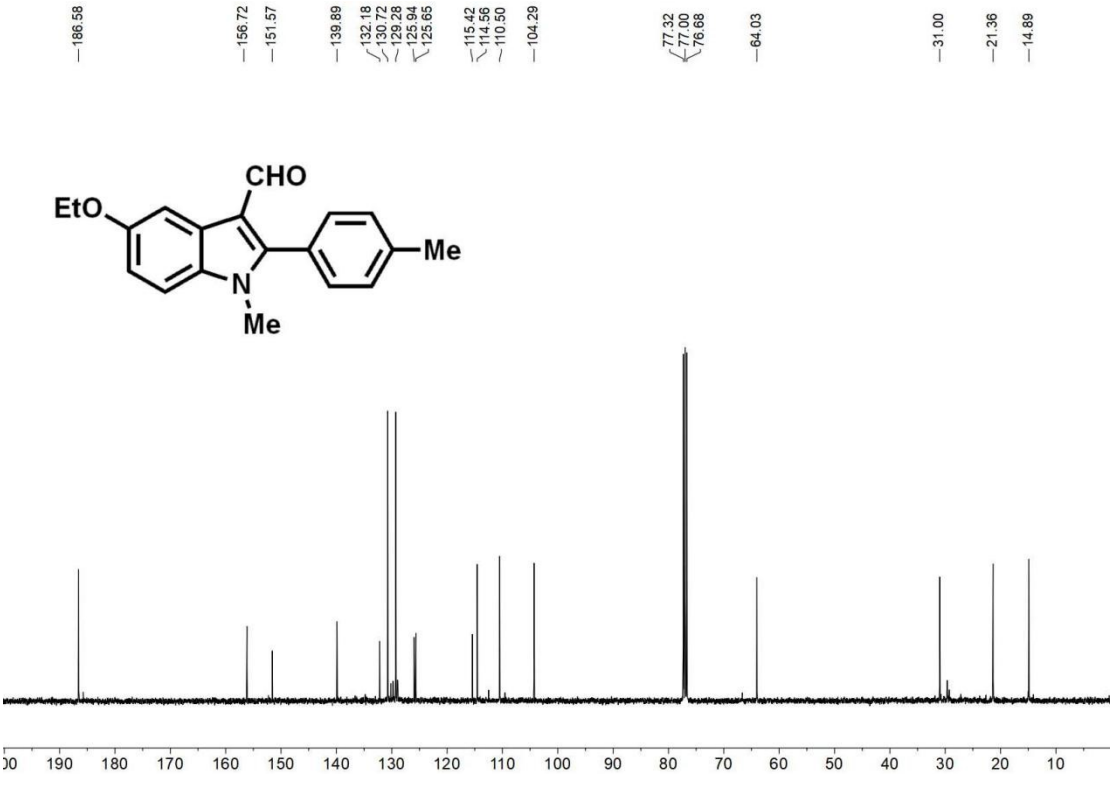
^{13}C NMR of product 3s in $CDCl_3$ (101 MHz)



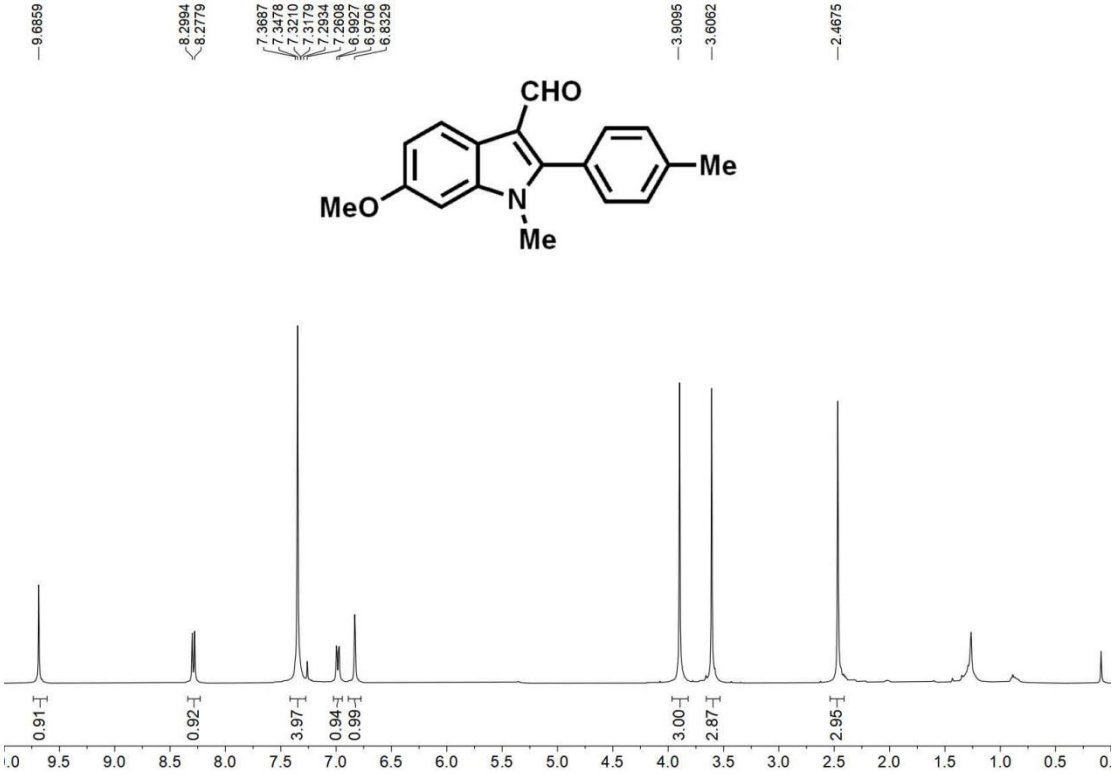
^{1}H NMR of product 3t in $CDCl_3$ (400 MHz)



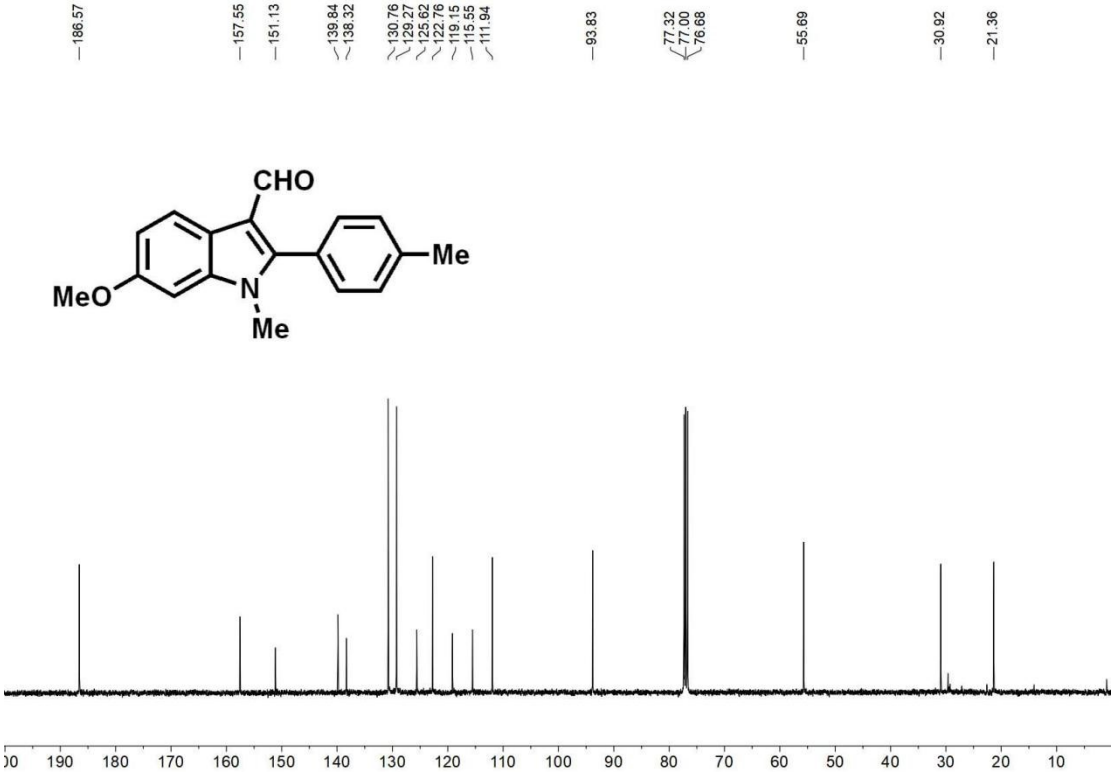
^{13}C NMR of product 3t in $CDCl_3$ (101 MHz)



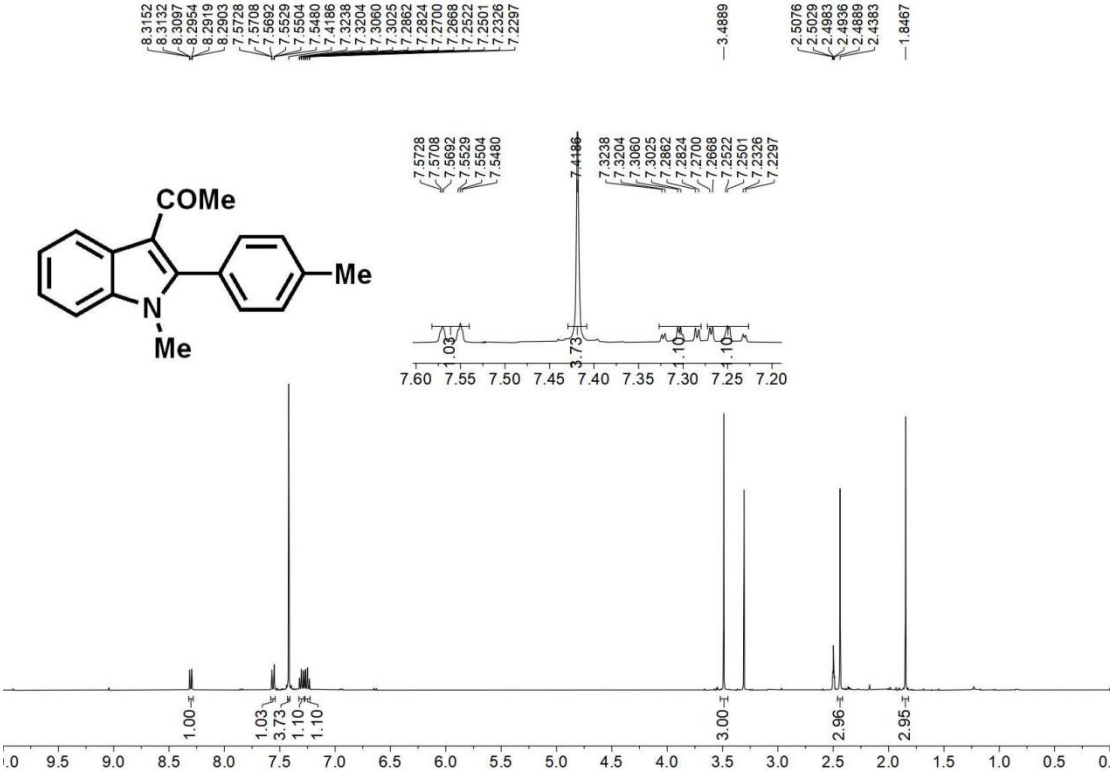
^{1}H NMR of product 3u in $CDCl_3$ (400 MHz)



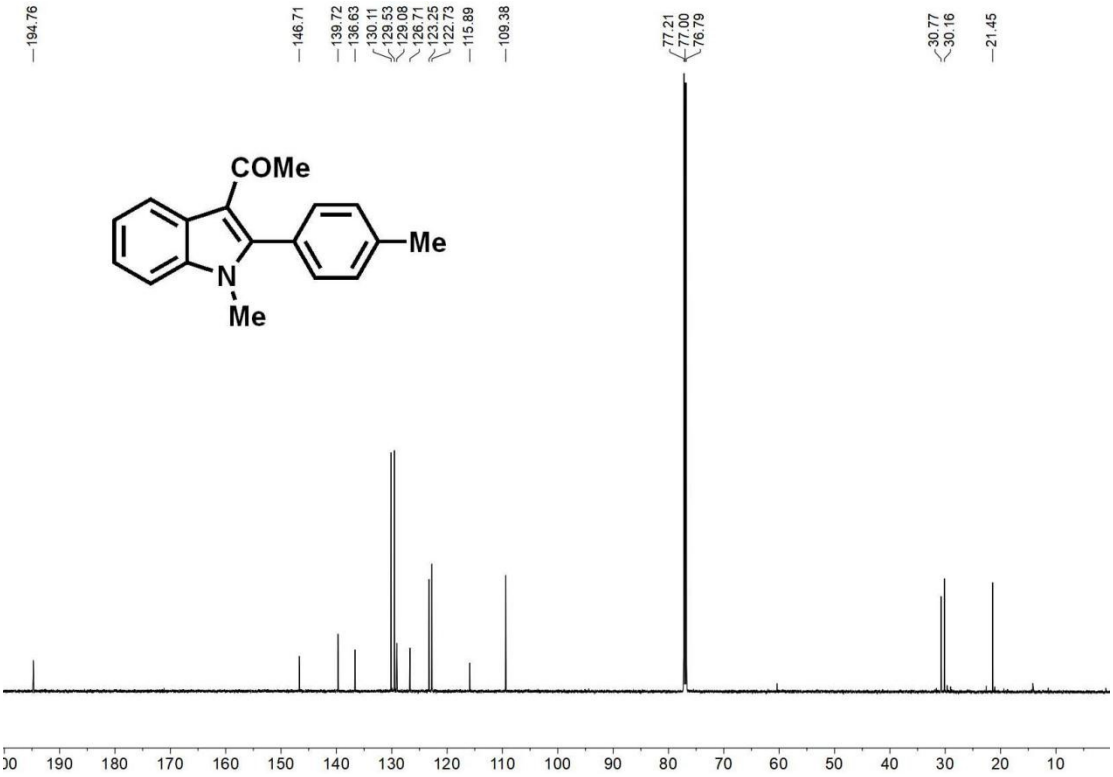
^{13}C NMR of product 3u in $CDCl_3$ (101 MHz)



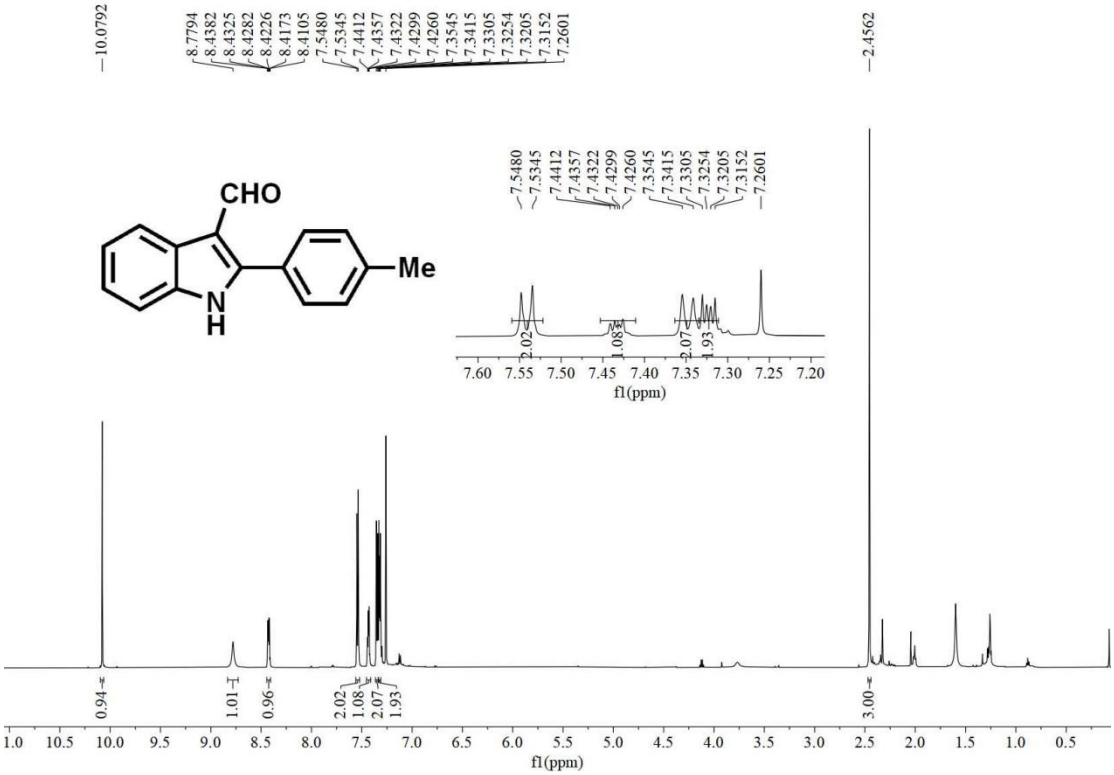
^{1}H NMR of product 3v in DMSO-d_6 (400 MHz)



^{13}C NMR of product 3v in $CDCl_3$ (151 MHz)



^{1}H NMR of product 3w in $CDCl_3$ (600 MHz)



^{13}C NMR of product 3w in $CDCl_3$ (151 MHz)