Supporting Information for Efficient Construction of Diverse 3-cyanoindoles Under Novel Tandem Catalysis

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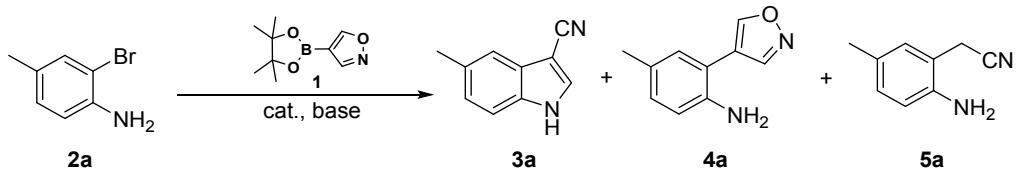
Contents

1. General information

Unless otherwise noted, all experiments were carried out under an atmosphere of nitrogen using standard Schlenk techniques or in a nitrogen-filled glovebox. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Model Avance DMX 300 Spectrometer (^{1}H 400 MHz and ^{13}C 100 MHz, respectively), Bruker Model Avance DMX 400 Spectrometer (^{1}H 500 MHz and ^{13}C 125 MHz, respectively). Chemical shifts (δ) were given in ppm and were referenced to residual solvent or TMS peaks. High resolution mass spectra (P-ESI HRMS) were obtained on P-SIMS-Gly of Bruker Daltonics Inc. All organic solvents were dried using standard, published methods and were distilled before use. All other chemicals were used as received from Aldrich or Acros without further purification.

2. Optimization of reaction conditions in the tandem reaction

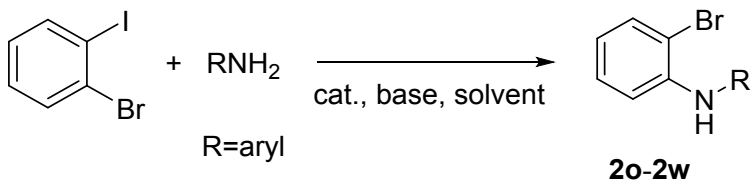
Table S1: Optimization of Reaction Conditions in the Tandem Catalysis[a]



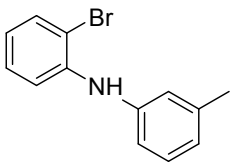
Entry[a]	Catalyst	Solvent	Conv. (%)[b]	Yield (%)[c]	
				3a	4a
1	$PdCl_2dppf$	DMF	75	73	--[d]
2	$PdCl_2dppf$	DMSO	92	91	--[d]
3	$PdCl_2dppf$	DMAc	78	78	--[d]
4	$PdCl_2dppf$	Toluene	25	25	--[d]
5	$PdCl_2dppf$	Acetone	36	34	--[d]
6	$PdCl_2dppf$	1,4dioxane	65	60	--[d]
7	$PdCl_2dppf$	IPA	48	45	--[d]

[a] Reaction conditions: **2a** (0.15 mmol, 1.0 equiv.), **1** (1.2 equiv.), KF (3 equiv., 1 M in water), Pd-cat. (10 mol %), 0.1 M solution in solvent, 130℃, 16 h. **5a** was not detected for all reactions. [b] Determined by ^{1}H NMR analysis of the crude product with 1,3,5-trimethoxybenzene as an internal standard. [c] Isolated yields. [d] Compound 3a, 4a or 5a was not observed.

3. General procedure for the synthesis of substrates

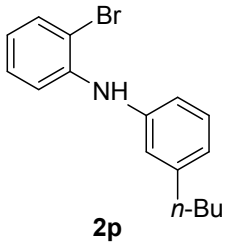


Using **2o** as an example.1-bromo-2-iodobenzene (1.12 g, 3.96 mmol) was added to a mixture of *m*-toluidine (518 mg, 4.83 mmol), palladium(II) acetate (44.9 mg, 200 μmol), 1,1'- bis (diphenylphosphino) ferrocene (222 mg, 400 μmol), and sodium tert-butoxide (538 mg, 5.60 mmol) in toluene (5.0 mL) at 25 °C under N_2. The reaction was stirred at 110 °C for 5 h before being cooled to 25 °C, and 1 N aqueous HCl (10 mL) was added to the reaction mixture at 25 °C. The organics were extracted from the aqueous layer with ethyl acetate and the combined organic extracts were concentrated under reduced pressure. The crude product was purified by column chromatography to afford the compound **2o**.[1]



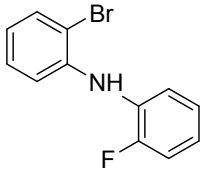
2o

2o: (new compound). Whtie oil; isolated yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51 (d, *J* = 8.0 Hz, 1H), 7.25-7.13 (m, 3H), 6.97-6.95 (m, 2H), 6.86 (d, *J* = 4.0 Hz, 1H), 6.72 (t, *J* = 8.0 Hz, 1H), 6.04 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 141.9, 139.5, 133.1, 129.4, 128.2, 123.7, 121.2, 120.9, 117.5, 116.1, 112.3, 21.6. HRMS (ESI) m/z calcd. for $C_{13}H_{13}BrN^+$ $(M+H)^+$ 262.0226, found 262.0219.



2p

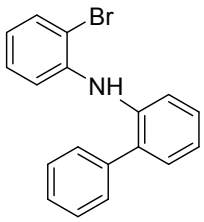
2p: (new compound). Whtie oil; isolated yield 95%;. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.52(d, *J* = 8.0 Hz, 1H), 7.20-7.09 (m, 6H), 6.71 (t, *J* = 8.0 Hz, 1H), 6.05 (s, 1H), 2.61(t, *J* = 8.0 Hz, 2H), 1.66-1.57 (m, 2H), 1.44-1.34 (m, 2H), 0.96 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 142., 139.2, 138.0, 133.0, 129.5, 128.2, 121.4, 120.4, 115.3, 111.7, 35.2, 33.9, 22.5, 14.1. HRMS (ESI) m/z calcd. for $C_{16}H_{19}BrN^+$ $(M+H)^+$ 304.0695, found 304.0683.



2r

2r: (new compound). White oil; isolated yield 90%; ^{1}H NMR (400

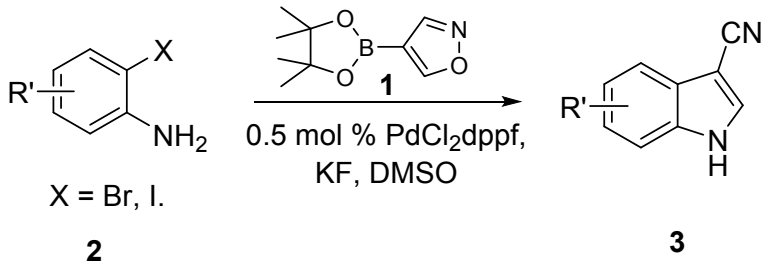
MHz, $CDCl_3$): δ (ppm) 7.60 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 2H), 7.18 (s, 1H), 7.05-7.02 (m, 2H), 6.86 (t, *J* = 8.0 Hz, 1H), 6.12(s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 143.4, 140.5, 135.2, 133.3, 130.5, 128.3, 122.3, 122.2, 119.2, 117.4, 117.3, 113.4. HRMS (ESI) m/z calcd. for $C_{12}H_{10}BrNF^+$ $(M+H)^+$ 265.9975, found 265.9980.



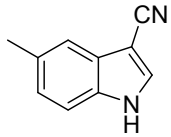
2w

2w: (new compound). Whtie oil; isolated yield 92%;. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.49-7.47(m, 2H), 7.45-7.43(m, 1H), 7.35-7.20 (m, 6H), 7.18-7.14 (m, 1H), 7.10-7.02 (m, 2H), 6.65 (t, *J* = 8.0 Hz, 1H), 6.06 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 142.9, 142.3, 141.6, 141.0, 133.2, 130.0, 128.9, 128.3, 127.6, 127.3, 121.7, 121.3, 119.1, 116.3, 112.6. HRMS (ESI) m/z calcd. for $C_{18}H_{15}BrN^+$ $(M+H)^+$ 324.0382, found 324.0392.

4. General procedure for the synthesis of 3-cyanoindoles

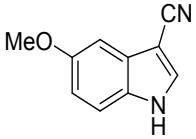


Using **3a** as an example. An oven dried schlenk tube was charged with a magnetic stir bar, **2a** (26.1 mg, 0.15 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) isoxazole (35.2 mg, 0.18 mmol), $PdCl_2dppf$ (0.5 mol %, 0.05M solution in the solvent), KF (26.2 mg, 0.45 mmol, 1 M in water). The schlenk tube was capped, and then evacuated and backfilled with nitrogen. Under a positive pressure of nitrogen, DMSO (1.5 mL) was added via a syringe and the schlenk tube was sealed and allowed to stir at 130℃ for 16 h. The organics were extracted from the aqueous layer with ethyl acetate and the combined organic extracts were concentrated under reduced pressure. The crude product was purified by column chromatography to afford the compound **3a**.[2]



3a

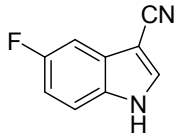
3a: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). Yellow solid; isolated yield 91%; mp 161-162℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.79 (s, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.56 (s, 1H), 7.36 (d, J = 12.0 Hz, 1H), 7.16 (d, J = 12.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 133.4, 132.3, 131.8, 127.5, 126.2, 119.4, 116.1, 111.8, 87.2, 21.5. HRMS (ESI) m/z calcd. for $C_{10}H_9N_2^+$ $(M+H)^+$ 157.0760 , found 157.0764.



3b

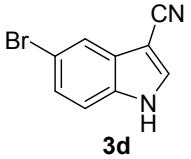
3b: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). White oil; isolated yield 90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 12.06 (s, 1H), 8.16 (s, 1H), 7.44 (d, J = 10.0 Hz, 1H), 7.08 (s, 1H), 6.91 (d, J = 10.0 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 155.3, 134.3, 130.0, 127.5, 116.5, 113.7, 99.8, 84.0, 55.4. HRMS (ESI) m/z calcd. for $C_{10}H_9N_2O^+$ $(M+H)^+$ 173.0709,

found 173.0712.



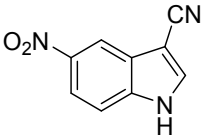
3c

3c: (known compound, see: S. Paget, D. Smith, W. Takasugi, T. James, A. Anthony, H. Ren, X. Zhang, J. Zhu, Indole Derivatives And Methods For Antiviral Treatment. WO2010/117932-A1, 2010). Yellow oil; isolated yield 80%; mp 147-148℃. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 12.30 (s, 1H), 8.31 (d, *J* = 4.0 Hz, 1H), 7.57 (dd, *J1* = *J2* = 4.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.14(t, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 159.3, 157.4, 136.2, 131.9, 127.3, 116.0, 114.3, 112.0, 111.8, 103.7, 103.5, 84.6. HRMS (ESI) m/z calcd. for $C_9H_6FN_2^+$ $(M+H)^+$ 161.0510, found 161.0515.



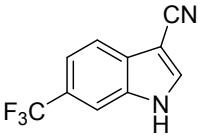
3d

3d: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). White solid; isolated yield 82%; mp 165-166℃. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 12.13 (s, 1H), 8.29 (s, 1H), 7.78 (s, 1H), 7.51 (d, *J* = 8 Hz, 1H), 7.39 (d, *J* = 8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 135.9, 134.1, 128.4, 126.1, 120.7, 115.7, 115.0, 114.4, 84.0. HRMS (ESI) m/z calcd. for $C_{10}H_6N_3^+$ $(M+H)^+$ 220.9709, found 220.9711.



3e

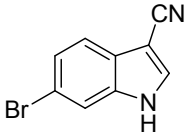
3e: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). White solid; isolated yield 84%; mp 194-195℃. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 12.81 (s, 1H), 8.52 (s, 1H), 8.46 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.72(d, *J* = 12.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 142.5, 138.5, 138.3, 126.0, 118.6, 115.1, 114.9, 113.8, 86.8. HRMS (ESI) m/z calcd. for $C_9H_6N_3O_2^+$ $(M+H)^+$ 188.0455, found 188.0460.



3f

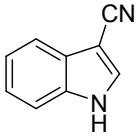
3f: (known compound, see: S. Paget, D. Smith, W. Takasugi, T. James, A. Anthony, H. Ren, X. Zhang, J. Zhu, Indole Derivatives And Methods For Antiviral Treatment. WO2010/117932-A1, 2010). White solid; isolated yield 85%; mp 138-139℃. ^{1}H NMR (500 MHz, DMSO): δ (ppm) 12.62 (s, 1H), 8.49 (s, 1H), 7.90 (s, 1H), 7.86(d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 137.6, 134.3, 129.4, 123.7, 119.5, 117.9, 115.5, 110.5, 84.9. HRMS (ESI) m/z calcd. for $C_{10}H_6F_3N_2^+$ $(M+H)^+$ 211.0478, found

211.0466.



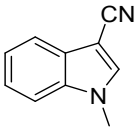
3g

3g: (known compound, see: S. Paget, D. Smith, W. Takasugi, T. James, A. Anthony, H. Ren, X. Zhang, J. Zhu, Indole Derivatives And Methods For Antiviral Treatment. WO2010/117932-A1, 2010). White solid; isolated yield 89%; mp 185-186℃. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 12.69 (s, 1H), 8.46 (d, *J* = 3.0 Hz, 1H), 8.18 (s, 1H), 7.67 (q, *J* =13.2 Hz, 2H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 137.2, 137.0, 126.2, 124.0, 119.5, 115.1, 114.3, 104.2, 85.5. HRMS (ESI) m/z calcd. for $C_9H_6BrN_2^+$ $(M+H)^+$ 220.9709, found 220.9700.



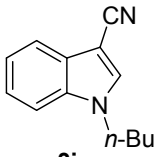
3h

3h: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). Yellow solid; isolated yield 80%; mp179-180℃. ^{1}H NMR (500 MHz, DMSO): δ (ppm) 12.21 (s, 1H), 8.23 (s, 1H), 7.60 (dd, *J1* = 10.0 Hz, *J2* = 30.0 Hz 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 135.2, 134.3, 126.7, 123.3, 121.6, 118.4, 116.3, 112.9, 84.3. HRMS (ESI) m/z calcd. for $C_9H_6BrN_2^+$ $(M+H)^+$ 143.0604, found 143.0610.



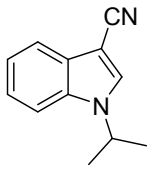
3i

3i: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). White oil; isolated yield 90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.74 (d, *J* = 10.0 Hz, 1H), 7.53 (s, 1H), 7.40-7.27 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 136.1, 135.6, 127.8, 123.9, 122.2, 119.8, 116.0, 110.4, 85.4, 33.6. HRMS (ESI) m/z calcd. for $C_{10}H_9N_2^+$ $(M+H)^+$ 157.0760, found 157.0749.



3j

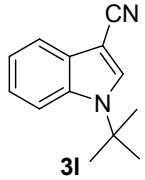
3j: (known compound, see: J. Xiao, Q. Li, T. Chen, L. B. Han, *Tetrahedron Lett*. 2015, 56, 5937). White oil; isolated yield 94%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.77 (d, *J* = 5.0 Hz, 1H), 7.60 (s, 1H), 7.41 (d, *J* = 10.0 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 5.0 Hz, 1H), 4.16 (t, *J* = 7.5 Hz, 2H), 1.88-1.82 (m, 2H), 1.36-1.32 (m, 1H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 135.6, 134.7, 128.2, 123.9, 122.2, 120.2, 116.1, 110.6, 85.8, 47.1, 32.1, 20.2, 13.7. HRMS (ESI) m/z calcd. for $C_{13}H_{15}N_2^+$ $(M+H)^+$ 199.1230, found 199.1241.



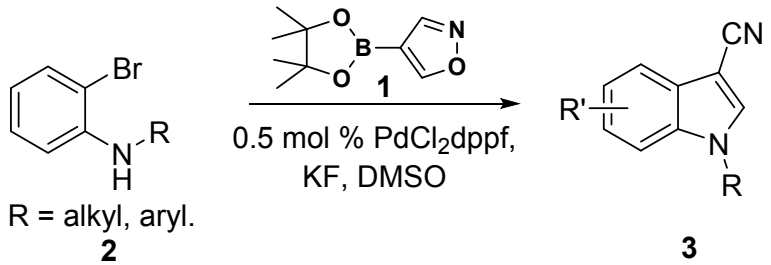
3k

3k: (known compound, see: J. Xiao, Q. Li, T. Chen, L. B. Han,

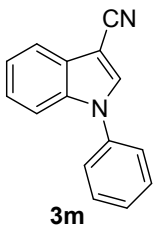
Tetrahedron Lett. 2015, 56, 5937). White oil; isolated yield 89%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.76 (d, *J* = 10.0 Hz, 1H), 7.72 (s, 1H), 7.46 (d, *J* = 10.0 Hz, 1H), 7.36-7.27 (m, 2H), 4.75-4.68 (m, 1H), 1.57(d, *J* = 10.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm)135.1, 131.2, 128.2, 123.7, 122.2, 120.1, 116.3, 110.7, 85.8, 48.4, 22.8. HRMS (ESI) m/z calcd. for $C_{12}H_{13}N_2^+$ $(M+H)^+$ 185.1073, found 185.1061.



3l: (known compound, see: J. Xiao, Q. Li, T. Chen, L. B. Han, *Tetrahedron Lett*. 2015, 56, 5937). White oil; isolated yield 89%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.81 (t, *J* = 5.0 Hz, 2H), 7.74 (d, *J* = 10.0 Hz, 1H), 7.31-7.29 (m, 2H), 1.80 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 134.6, 132.7, 129.6, 123.2, 121.8, 120.3, 116.3, 114.5, 84.9, 57.7, 29.7. HRMS (ESI) m/z calcd. for $C_{13}H_{14}N_2^+$ $(M+H)^+$ 199.1230, found 199.1234.

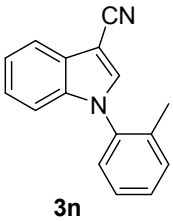


Using **3m** as an example. An oven dried Schlenk tube was charged with a magnetic stir bar, **2m** (37.1 mg, 0.15 mmol), **1** (35.2 mg, 0.18 mmol), $PdCl_2$dppf (0.5 mol %, 0.05M solution in the solvent), KF (26.2 mg, 0.45 mmol, 1 M in water). The Schlenk tube was capped, and then evacuated and backfilled with nitrogen. Under a positive pressure of nitrogen, DMSO (1.5 mL) was added via a syringe and the Schlenk tube was sealed and allowed to stir at 130℃ for 16 h. The organics were extracted from the aqueous layer with ethyl acetate and the combined organic extracts were concentrated under reduced pressure. The crude product was purified by column chromatography to afford the compound **3m**. [2]



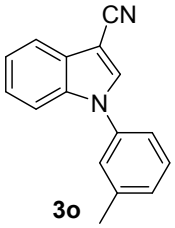
3m: (known compound, see: J. Xiao, Q. Li, T. Chen, L. B. Han, *Tetrahedron Lett*. 2015, 56, 5937). White oil; isolated yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.85-7.82 (m, 1H), 7.81 (s, 1H), 7.60-7.56 (m, 2H), 7.53-7.47 (m, 4H), 7.36-7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 138.0, 135.8, 134.7, 130.2, 128.5, 128.1, 125.0,

124.7, 122.9, 120.2, 115.6, 111.7, 88.4. HRMS (ESI) m/z calcd. for $C_{15}H_{11}N_2^+$ $(M+Na)^+$ 241.0736, found 241.0759.



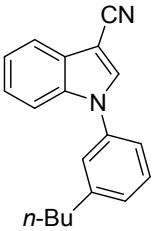
3n

3n: (new compound). White oil; isolated yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.0 Hz, 1H), 7.66 (s, 1H), 7.47-7.42 (m, 2H), 7.39-7.26 (m, 4H), 7.07 (d, J = 8.0 Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 136.6, 136.5, 135.8, 135.4, 131.7, 129.7, 128.0, 127.4, 124.5, 122.7, 120.0, 115.8, 87.6, 17.5. HRMS (ESI) m/z calcd. for $C_{16}H_{13}N_2^+$ $(M+H)^+$ 233.1073, found 233.1059.



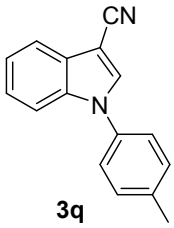
3o

3o: (new compound). White oil; isolated yield 84%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84-7.82 (m, 1H), 7.79 (s, 1H), 7.52-7.50 (m, 1H), 7.47-7.43 (m, 1H), 7.37-7.33 (m, 3H), 7.29(t, J = 4.0 Hz, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 140.4, 138.0, 135.8, 134.8, 129.9, 129.3, 128.1, 125.7, 124.6, 122.9, 122.1, 120.2, 115.7, 111.8, 88.1, 21.5. HRMS (ESI) m/z calcd. for $C_{16}H_{13}N_2^+$ $(M+H)^+$ 233.1073, found 233.1060.



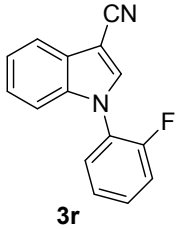
3p

3p: (new compound). White solid; isolated yield 94%; mp 170-171℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.83-7.81 (m, 1H), 7.78 (s, 1H), 7.51-7.49 (m, 1H), 7.37-7.33 (m, 6H), 2.71 (t, J = 6.0 Hz, 2H), 1.71-1.63(m, 2H), 1.46-1.37 (m, 2H), 0.97 (t, J = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 143.7, 136.0, 135.6, 134.9, 130.0, 128.1, 124.9, 124.5, 122.8, 120.2, 115.7, 111.8, 88.0, 35.4, 33.6, 22.5, 14.1. HRMS (ESI) m/z calcd. for $C_{19}H_{19}N_2^+$ $(M+H)^+$ 188.0455, found 188.0448.



3q

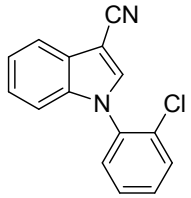
3q: (new compound). White solid; isolated yield 85%; mp 152-153℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84-7.82 (m, 1H), 7.77 (s, 2H), 7.49-7.46 (m, 1H), 7.36-7.32 (m, 6H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 139.4, 136.6, 136.1, 135.6, 131.4, 128.8, 125.5, 125.3, 123.6, 120.7, 116.5, 112.5, 88.6, 22.0. HRMS (ESI) m/z calcd. for $C_{16}H_{13}N_2^+$ $(M+H)^+$ 233.1073, found 233.1066.



3r

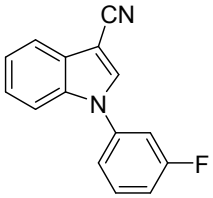
3r: (new compound). White solid; isolated yield 90%; mp 130-131℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)7.86-7.82 (m, 1H), 7.77

(s, 1H), 7.54-7.48 (m, 2H), 7.38-7.31 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 157.9, 155.9, 136.2, 135.5, 130.5, 128.1, 127.6, 125.3, 124.9, 123.1, 120.1, 117.5, 115.3, 111.6, 89.0. HRMS (ESI) m/z calcd. for $C_{15}H_{10}FN_2^+$ $(M+H)^+$ 237.0823, found 237.0838.



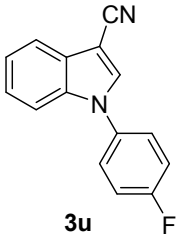
3s

3s: (new compound). White solid; isolated yield 89%; mp 146-147℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.0 Hz, 1H), 7.74 (s, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.53-7.46 (m, 3H), 7.38-7.31 (m, 2H), 7.15 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 136.3, 135.5, 135.0, 131.9, 131.2, 130.6, 129.3, 128.1, 127.3, 124.6, 122.9, 120.0, 115.3, 111.6, 88.4. HRMS (ESI) m/z calcd. for $C_{15}H_{10}ClN_2^+$ $(M+H)^+$ 253.0527, found 253.0508.



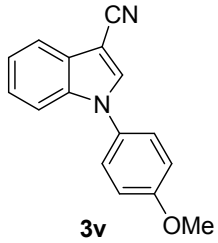
3t

3t: (new compound). White solid; isolated yield 79%; mp 128-129℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.92-7.85 (m, 2H), 7.66-7.54 (m, 2H), 7.46-7.44 (m, 2H), 7.39-7.37 (m, 1H), 7.34-7.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 164.3, 162.3, 137.6, 135.4, 134.4, 131.6, 128.1, 125.0, 123.2, 120.6, 120.3, 115.6, 112.6, 111.5, 89.0. HRMS (ESI) m/z calcd. for $C_{15}H_{10}FN_2^+$ $(M+H)^+$ 237.0823, found 237.0826.



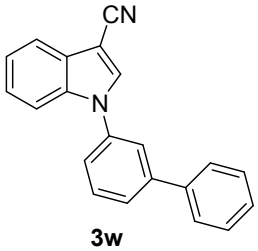
3u

3u: (new compound). White solid; isolated yield 81%; mp 135-136℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84-7.83 (m, 1H), 7.76 (s, 1H), 7.78-7.43 (m, 3H), 7.37-7.35 (m, 2H), 7.30-7.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 136.0, 134.8, 127.9, 127.1, 127.0, 124.8, 123.1, 120.3, 117.3, 117.1, 111.4, 88.4. HRMS (ESI) m/z calcd. for $C_{15}H_{10}FN_2^+$ $(M+H)^+$ 237.0823, found 237.0831.



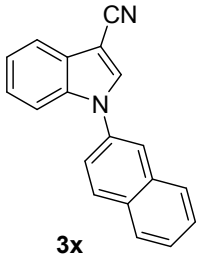
3v

3v: (known compound, see: L. Zhang, P. Lu, Y. Wang, *Org. Biomol. Chem.* 2015, 13, 8322). White solid; isolated yield 92%; mp 144-145℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.83-7.81 (m, 1H), 7.74 (s, 1H), 7.44-7.32 (m, 5H), 7.07 (d, J = 5.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 159.7, 136.3, 135.1, 130.8, 127.9, 126.6, 124.5, 122.8, 120.1, 115.3, 111.6, 87.7, 55.8, 53.5. HRMS (ESI) m/z calcd. for $C_{16}H_{13}N_2O^+$ $(M+H)^+$ 249.1022, found 249.1048.



3w

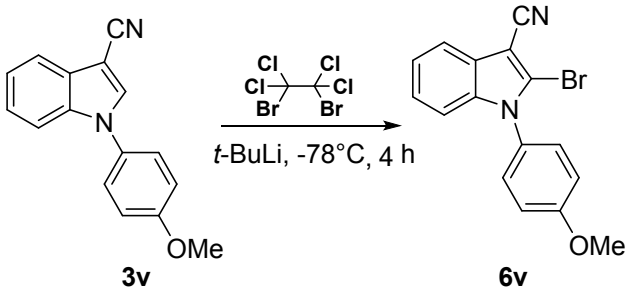
3w: (new compound). White solid; isolated yield 80%; mp 176-177℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.86-7.84 (m, 2H), 7.72-7.70 (m, 2H), 7.66-7.62 (m, 3H), 7.58-7.56 (m, 1H), 7.51-7.36 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 143.7, 139.7, 138.5, 135.9, 134.8, 130.6, 129.2, 128.4, 128.2, 127.3, 127.2, 124.8, 123.7, 123.0, 120.3, 115.6, 111.7, 88.5. HRMS (ESI) m/z calcd. for $C_{21}H_{15}N_2^+$ $(M+H)^+$ 295.1230, found 295.1226.



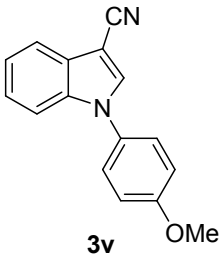
3x

3x: (new compound). White solid; isolated yield 91%; mp 180-182℃.^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.05 (d, J = 8.0 Hz, 1H), 7.98-7.86 (m, 5H), 7.63-7.58 (m, 4H), 7.38-7.36 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 136.0, 135.4, 135.0, 133.7, 132.8, 130.3, 128.2, 128.1, 128.1, 127.6, 127.2, 124.8, 123.4, 123.0, 123.0, 120.3, 115.6, 111.7, 88.5. HRMS (ESI) m/z calcd. for $C_{19}H_{13}N_2^+$ $(M+H)^+$ 269.1073, found 269.1069.

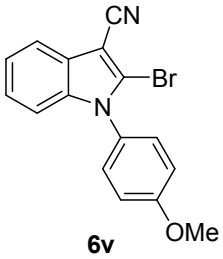
5. Synthetic transformations of 3-cyanoindoles



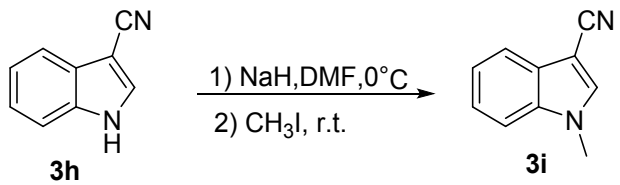
3v (50 mg, 0.2 mmol) was dissolved in dry THF and cooled to -78℃, then *t*-BuLi (14.1 mg, 0.22 mmol) was added drop wise and mixture stirred for one hour. A solution of 1,2-dibromotetrachloroethane (84.7 mg, 0.26 mmol) was added and the mixture stirred for 4 hours while slowly wanning up to r.t. and quenched with the addition of H_2O. The reaction mixture was diluted with DCM, phases separated and the organic phase evaporated in vacuo. The crude product was purified on silica column using *n*-heptane:DCM=1:1 as mobile phase to give the product **6v**. [3]



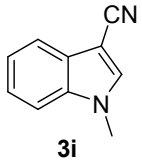
3v: (known compound, see: L. Zhang, P. Lu, Y. Wang, *Org. Biomol. Chem.* 2015, 13, 8322). White solid; isolated yield 92%; mp 144-145℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.83-7.81 (m, 1H), 7.74 (s, 1H), 7.44-7.32 (m, 5H), 7.07 (d, *J* = 5.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 159.7, 136.3, 135.1, 130.8, 127.9, 126.6, 124.5, 122.8, 120.1, 115.3, 111.6, 87.7, 55.8, 53.5. HRMS (ESI) m/z calcd. for $C_{16}H_{13}N_2O^+$ $(M+H)^+$ 249.1022, found 249.1048.



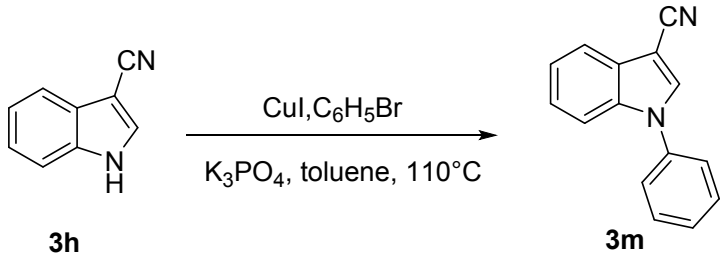
6v: (known compound, see: L. Zhang, P. Lu, Y. Wang, *Org. Biomol. Chem.* 2015, 13, 8322). White solid; isolated yield 44%; mp 172-173℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.76 (d, *J* = 10.0 Hz, 1H), 7.32-7.26 (m, 4H), 7.12 (d, *J* = 10.0 Hz, 3H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 160.5, 137.9, 129.5, 128.3, 127.2, 124.5, 123.1, 122.7, 119.0, 115.1, 111.7, 90.8, 55.8. HRMS (ESI) m/z calcd. for $C_{16}H_{12}BrN_2O^+$ $(M+H)^+$ 327.0128, found 327.0125.



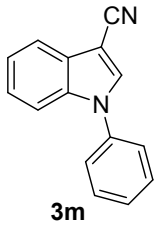
3h (2.0 g, 14.1 mmol) was treated with NaH (0.40 g, 16.8 mmol) in DMF (30 mL) at 0 °C for 10 min, and then iodomethane (2.4 g, 16.8 mmol) was added to the resulting mixture at r.t. After being stirred at rt for 1 h, the reaction was quenched with H_2O and extracted with ethyl acetate. Combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give **3i** as a white oil. [4]



3i: (known compound, see: B. Liu, J. Wang, B. Zhang, Y. Sun, L. Wang, J. Chen, J. Cheng, *Chem. Commun.* 2014, 50, 2315). White oil; isolated yield 90%; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.74 (d, J = 10.0 Hz, 1H), 7.53 (s, 1H), 7.40-7.27 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm). HRMS (ESI) m/z calcd. for $C_{10}H_9N_2^+$ $(M+H)^+$ 157.0760, found 157.0749.

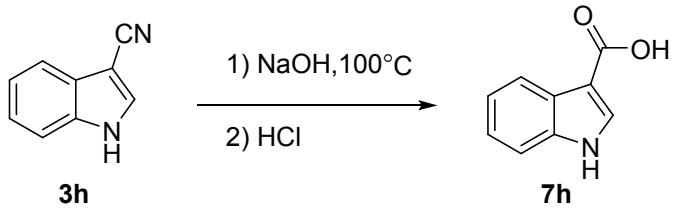


CuI (19.1 mg, 0.1 mmol), **3h** (142.1 mg, 1.0 mmol), K_3PO_4 (445.8 mg, 2.1 mmol) and a stir bar were added to a resealable Schlenk tube. The vessel was evacuated and back-filled with nitrogen. Bromobenzene (188.4 mg, 1.2 mmol), N,N'-dimethylethylenediamine (17.7 mg, 0.2 mmol) and toluene (2 mL) were then added successively under a stream of nitrogen. The reaction tube was sealed and the contents were stirred with heating at 110 °C for 24 h. The reaction mixture was cooled to ambient temperature, diluted with ethyl acetate, filtered through a plug of silica gel, eluting with additional ethyl acetate. The filtrate was concentrated and the resulting residue was purified by column chromatography to give **3m**. [5]

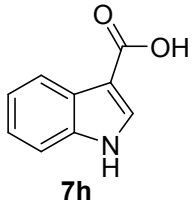


3m: (known compound, see: J. Xiao, Q. Li, T. Chen, L. B. Han,

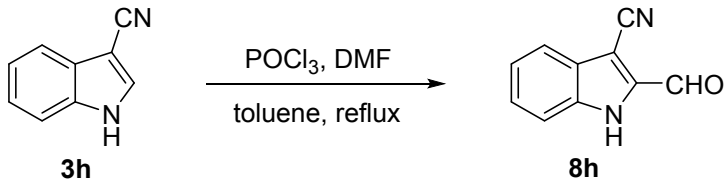
Tetrahedron Lett. 2015, 56, 5937). White oil; isolated yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.85-7.82 (m, 1H), 7.81 (s, 1H), 7.60-7.56 (m, 2H), 7.53-7.47 (m, 4H), 7.36-7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 138.0, 135.8, 134.7, 130.2, 128.5, 128.1, 125.0, 124.7, 122.9, 120.2, 115.6, 111.7, 88.4. HRMS (ESI) m/z calcd. for $C_{15}H_{11}N_2^+$ $(M+Na)^+$ 241.0736, found 241.0759.



3h (710 mg, 5 mmol) was treated with NaOH (400mg, 10 mmol) in H_2O (10 mL) at 100 °C for 20 h. Then the mixture was acidified with dilute HCl/H_2O to pH =5. The organic layer was washed with brine and dried by Na_2SO_4, and volatiles were evaporated to give **7h** (490 mg, 70%) as a white solid.

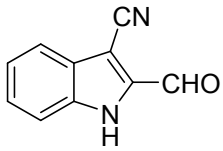


7h: (known compound, see: K. Nemoto, S. Tanaka, M. Konno, S. Onozawa, M. Chiba, Y. Tanaka, Y. Sasaki, R. Okubo, T. Hattori, *Tetrahedron.* 2016, 72, 734). White solid; isolated yield 90%; mp 204-205℃. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 11.93 (s, 1H), 11.80 (s, 1H), 8.02 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.19-7.13 (m, 2H); ^{13}C NMR (125 MHz, DMSO): δ (ppm) 166.0, 136.5, 132.3, 126.1, 121.2, 121.0, 120.6, 112.2, 107.4. HRMS (ESI) m/z calcd. for $C_9H_8NO_2^+$ $(M+H)^+$ 162.0550, found 162.0555.



DMF (17.6 mg, 0.24 mmol) was added to $POCl_3$ (60.8 mg, 0.4 mmol) at 0℃ under an atmosphere of N_2. The resulting salt was treated with a solution of **3h** (24.5mg, 0.2mmol) in toluene (1mL). The resulting reaction mixture was heated at reflux for 42 hours under N_2 atmosphere. The reaction mixture was then cooled to r.t., quenched with water. The excess $POCl_3$ was neutralized with Na_2CO_3 solution. The crude

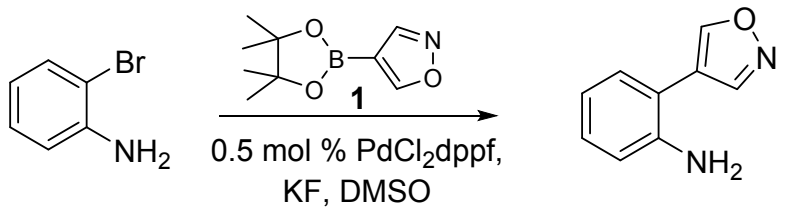
product was extracted with DCM, the combined organic extracts dried over Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by column chromatography to afford product **8h**. [6]



8h

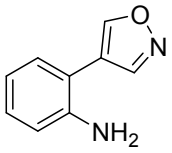
8h: (known compound, see: A. Toro, F. J. Martin, M. D. Surman, D. Manning, Therapeutic Agents, And Methods Of Marking And Using The Same. Canada Pat. CA2568914-A1, 2005). White oil; isolated yield 94%. ^{1}H NMR (400 MHz, DMSO): δ (ppm) 12.19 (s, 1H), 8.24 (s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.30-7.21 (m, 2H); ^{13}C NMR (125 MHz, DMSO): δ (ppm)135.2, 134.6, 126.7, 123.4, 121.7, 118.4, 116.4, 112.9, 84.2. HRMS (ESI) m/z calcd. for $C_{10}H_7N_2O^+$ $(M+H)^+$ 171.0553, found 171.0550.

6. Control experiments for the catalysis tandem reaction



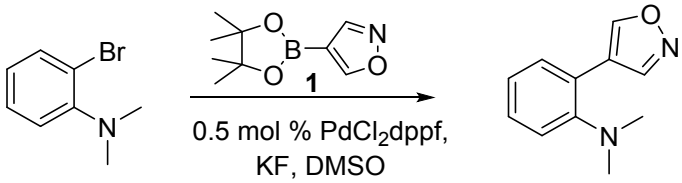
4h

An oven dried Schlenk tube was charged with a magnetic stir bar, 2-Bromoaniline (25.8 mg, 0.15 mmol), **1** (35.2 mg, 0.18 mmol), $PdCl_2dppf$ (0.5 mol %, 0.05M solution in the solvent), KF (26.2 mg, 0.45 mmol, 1 M in water). The Schlenk tube was capped, and then evacuated and backfilled with nitrogen. Under a positive pressure of nitrogen, DMSO (1.5 mL) was added via a syringe and the Schlenk tube was sealed and allowed to stir at 50℃ for 3h. The crude product was purified by flash chromatography on silica gel to provide **4h**.



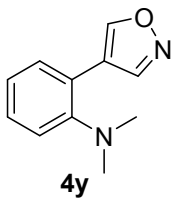
4h

4h: (new compound). White oil; isolated yield 94%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.66 (s, 1H), 8.52 (s, 1H), 7.20-7.17 (m, 2H), 6.85-6.79 (m, 2H), 3.73(s,2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm)154.9, 149.7, 144.3, 130.0, 129.6, 119.3, 118.0, 116.4, 114.4. HRMS (ESI) m/z calcd. for $C_9H_9N_2O^+$ $(M+H)^+$ 161.0709, found 161.0701.

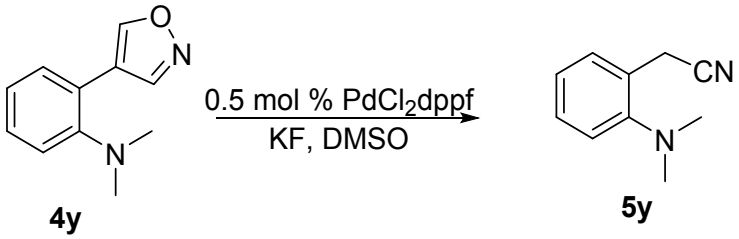


4y

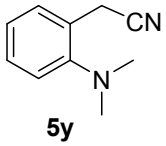
An oven dried Schlenk tube was charged with a magnetic stir bar, 2-bromo-N,N-dimethyl (30.1mg, 0.15 mmol), **1** (35.2 mg, 0.18 mmol.), $PdCl_2dppf$ (0.5 mol %, 0.05M solution in the solvent), KF (26.2 mg, 0.45 mmol, 1 M in water). The Schlenk tube was capped, and then evacuated and backfilled with nitrogen. Under a positive pressure of nitrogen, DMSO (1.5 mL) was added via a syringe and the Schlenk tube was sealed and allowed to stir at 50℃ for 3 h. The crude product was purified by flash chromatography on silica gel to provide **4y**.



4y: (new compound). White oil; isolated yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.87 (s, 1H), 8.75 (s, 1H), 7.37 (d, J = 8.0 Hz, 1H) , 7.29-7.26 (m, 1H), 7.16 (d, J = 8.0 Hz, 1H) , 7.07 (t, J = 8.0 Hz, 1H), 2.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm)154.9, 152.1, 129.4, 128.9, 123.3, 119.7, 44.1. HRMS (ESI) m/z calcd. for $C_{11}H_{13}N_2O^+$ $(M+H)^+$ 189.1022, found 189.1023.



An oven dried Schlenk tube was charged with a magnetic stir bar, 2-Bromo-N,N-dimethyl (30.1mg, 0.15 mmol), **1** (35.2 mg, 0.18 mmol), $PdCl_2$dppf (0.5 mol %, 0.05M solution in the solvent), KF (26.2 mg, 0.45 mmol, 1 M in water). The Schlenk tube was capped, and then evacuated and backfilled with nitrogen. Under a positive pressure of nitrogen, DMSO (1.5 mL) was added via a syringe and the Schlenk tube was sealed and allowed to stir at 130℃ for 16 h. The crude product was purified by flash chromatography on silica gel to provide **5y**.



5y: (known compound). White oil; isolated yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (d, J = 8.0 Hz, 1H) , 7.31 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H) , 7.11 (t, J = 8.0 Hz, 1H), 3.84 (s, 2H) , 2.66 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 152.6, 129.5, 129.1, 125.9, 124.3, 120.5, 119.0, 45.0, 19.6. HRMS (ESI) m/z calcd. for $C_{10}H_{13}N_2^+$ $(M+H)^+$ 161.1073, found 161.1077.

7. References

[1] Y. Aoki, H. M. O'Brien, H. Kawasaki, H. Takaya, M. Nakamura, *Org. Lett.* 2019, **21**, 461.

[2] J. Velcicky, A. Soicke, R. Steiner, H. G. Schmalz, *J. Am. Chem. Soc.* 2011, **133**, 6948.

[3] L. Zhang, P. Lu, Y. Wang, *Org. Biomol. Chem.* 2015, **13**, 8322.

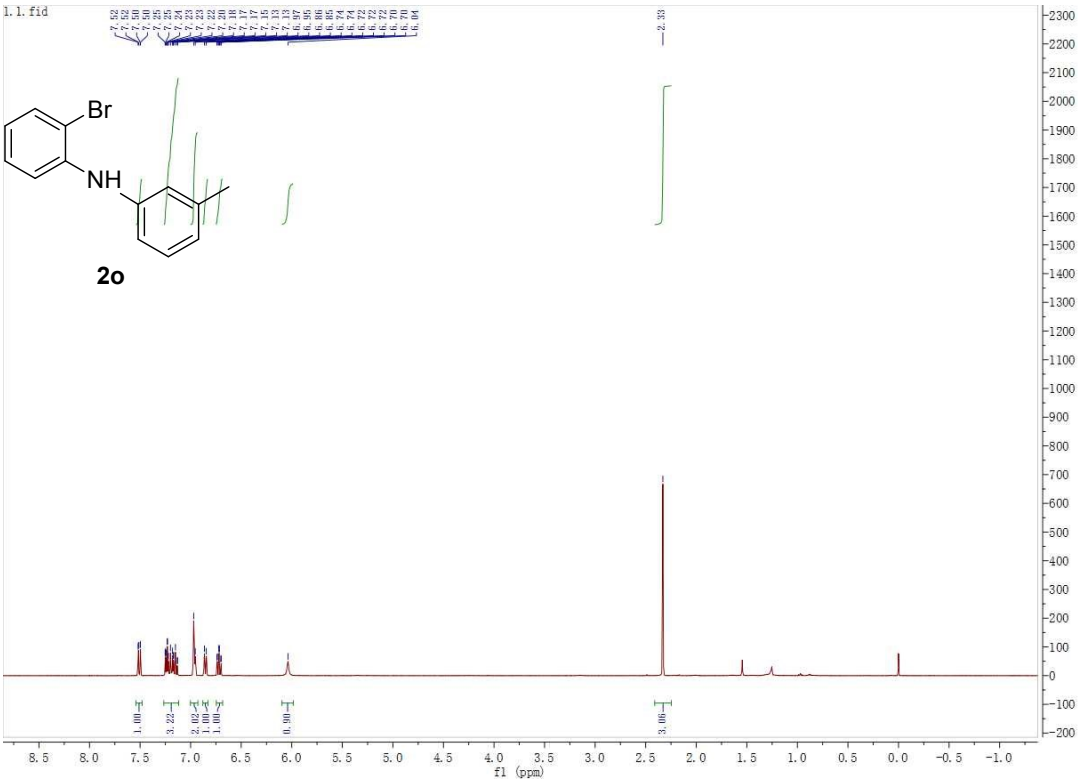
[4] N. Yoshiaki, S. K. Kyalo, O. Shinichi, H. Tamejiro, *J. Am. Chem. Soc.* 2006, **128**, 8146.

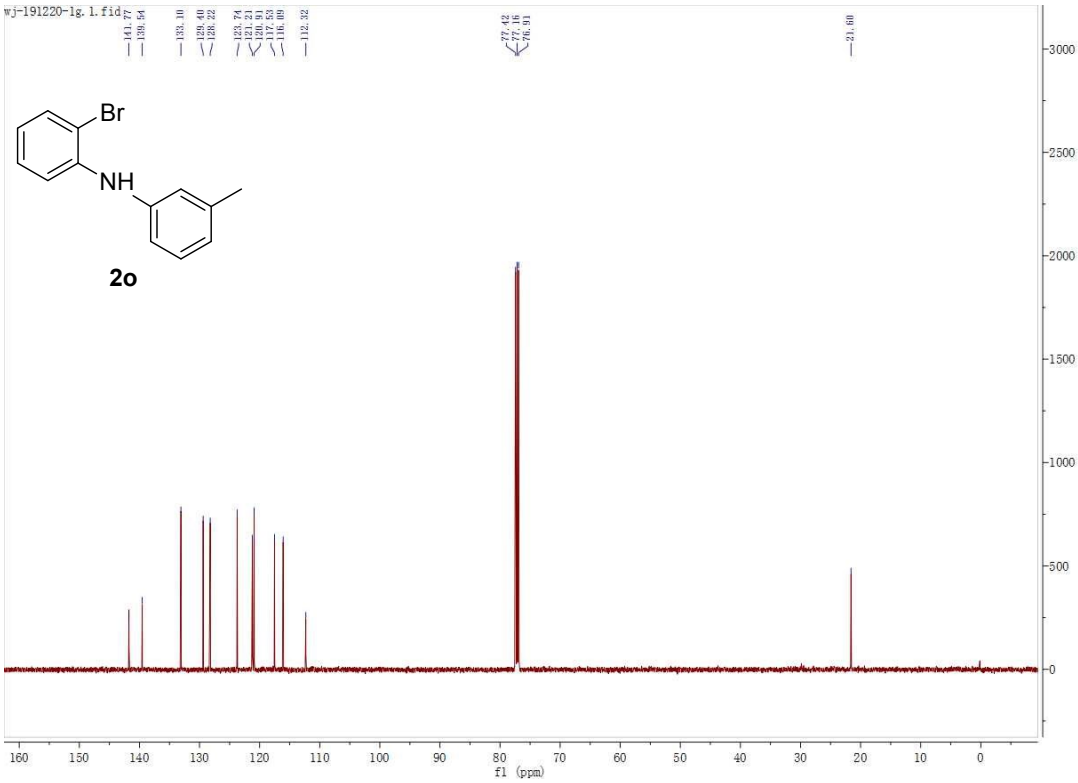
[5] C. A. Jon, K. Artis, L. B. Stephen, *J. Am. Chem. Soc.* 2002, **124**, 11684.

[6] H. Yuan, L. Guo, F. Liu, Z. Miao, L. Feng, H. Gao, *ACS. Catalysis.* 2019, **9** , 3906.

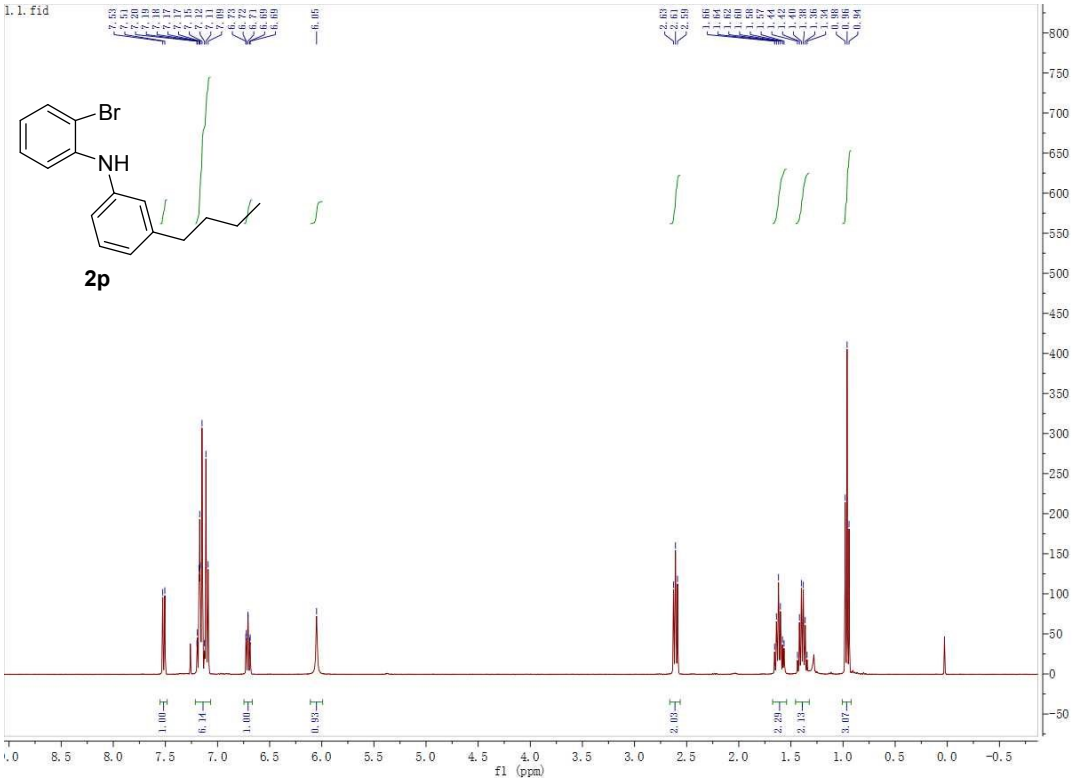
8. Copy of NMR spectra

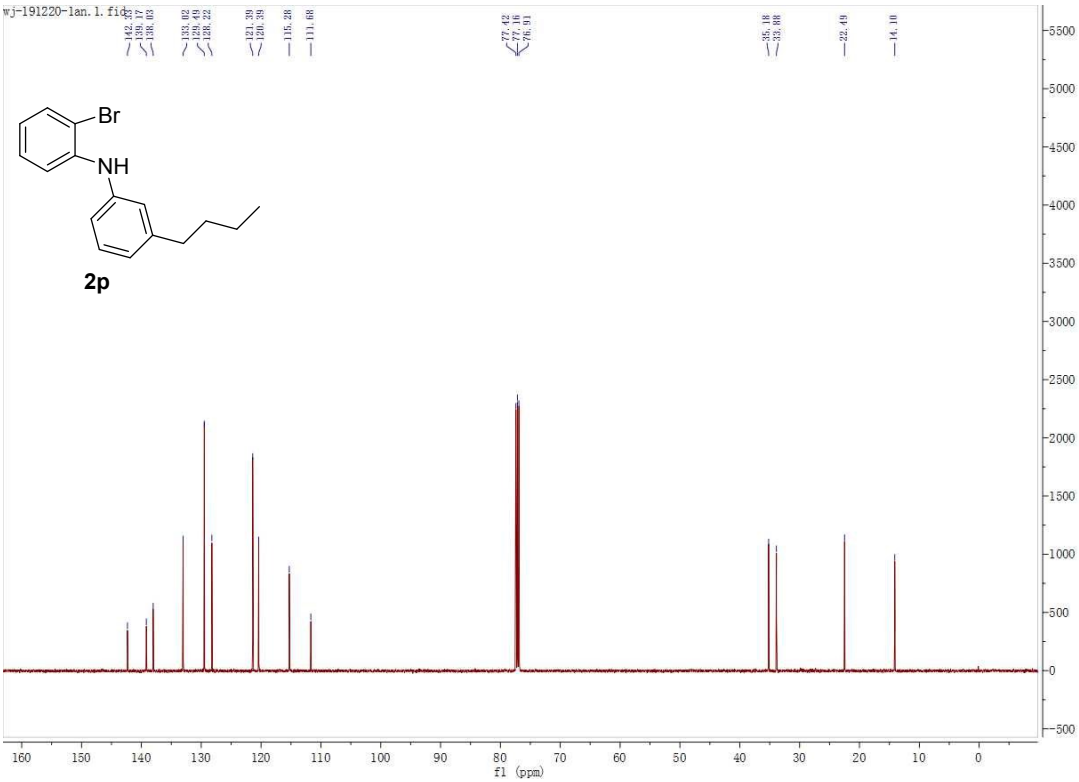
compound **2o**



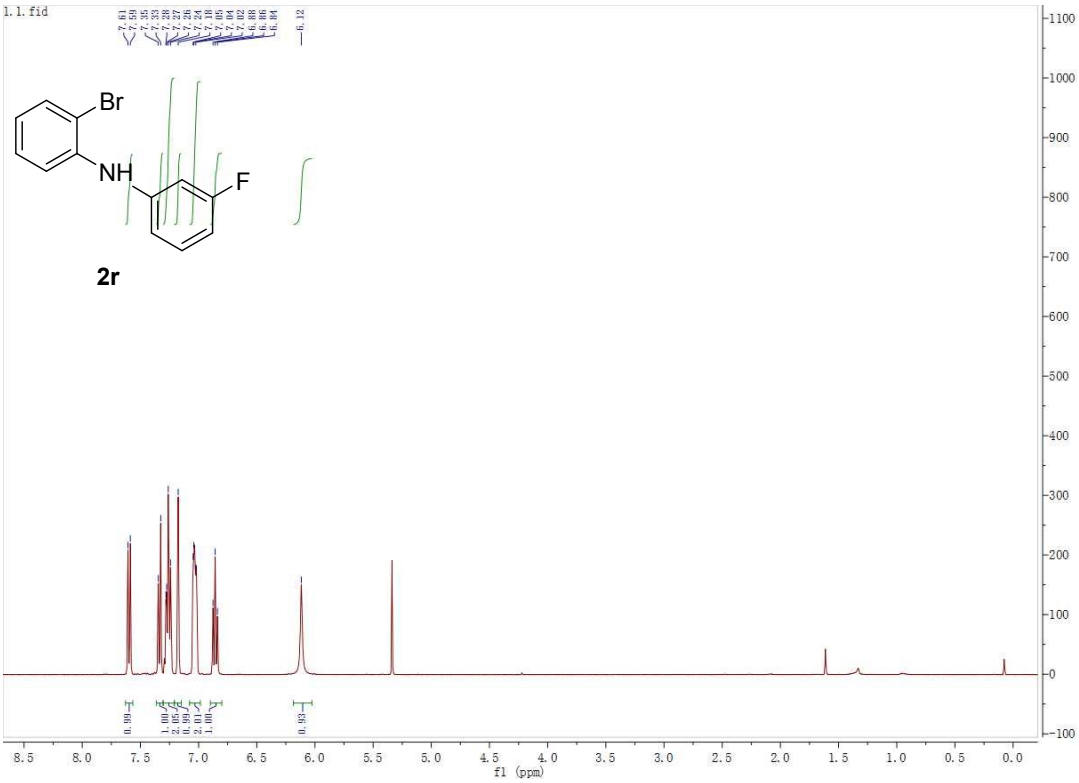


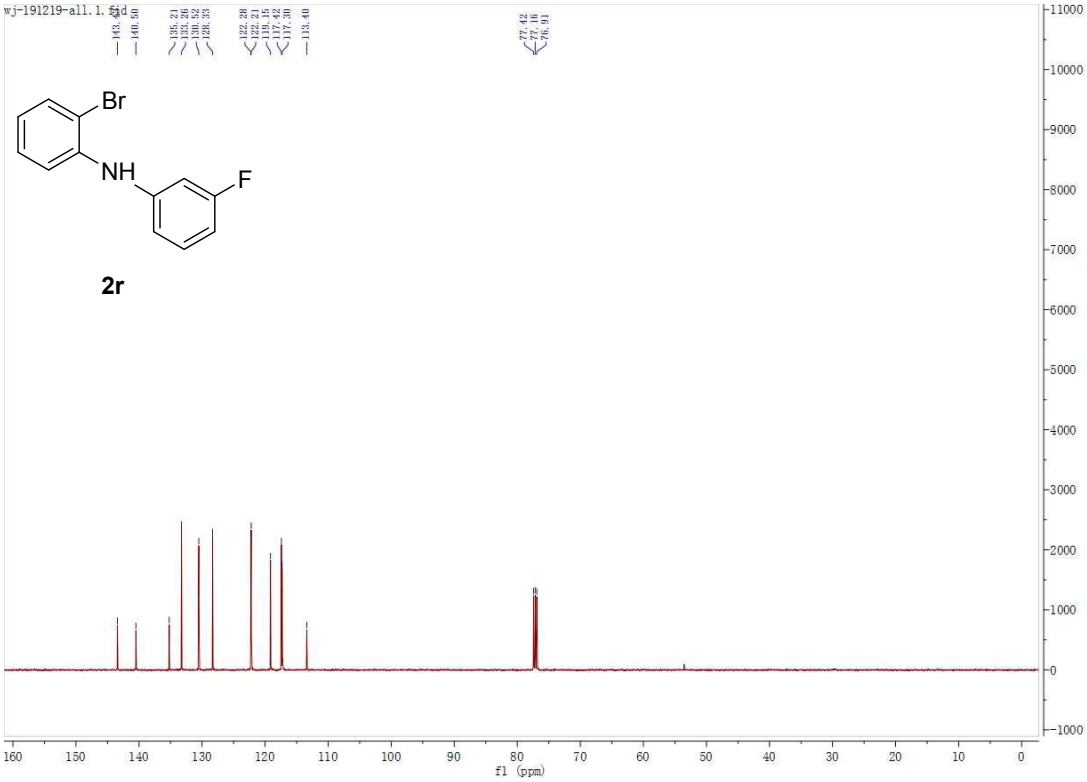
compound **2p**



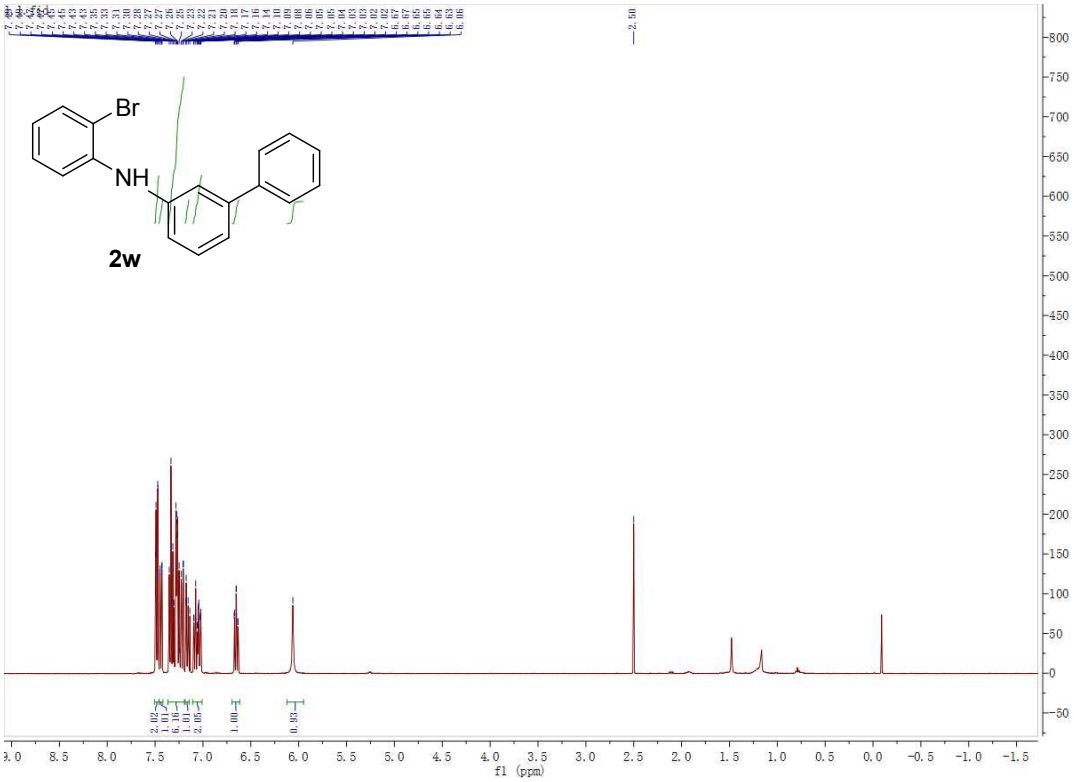


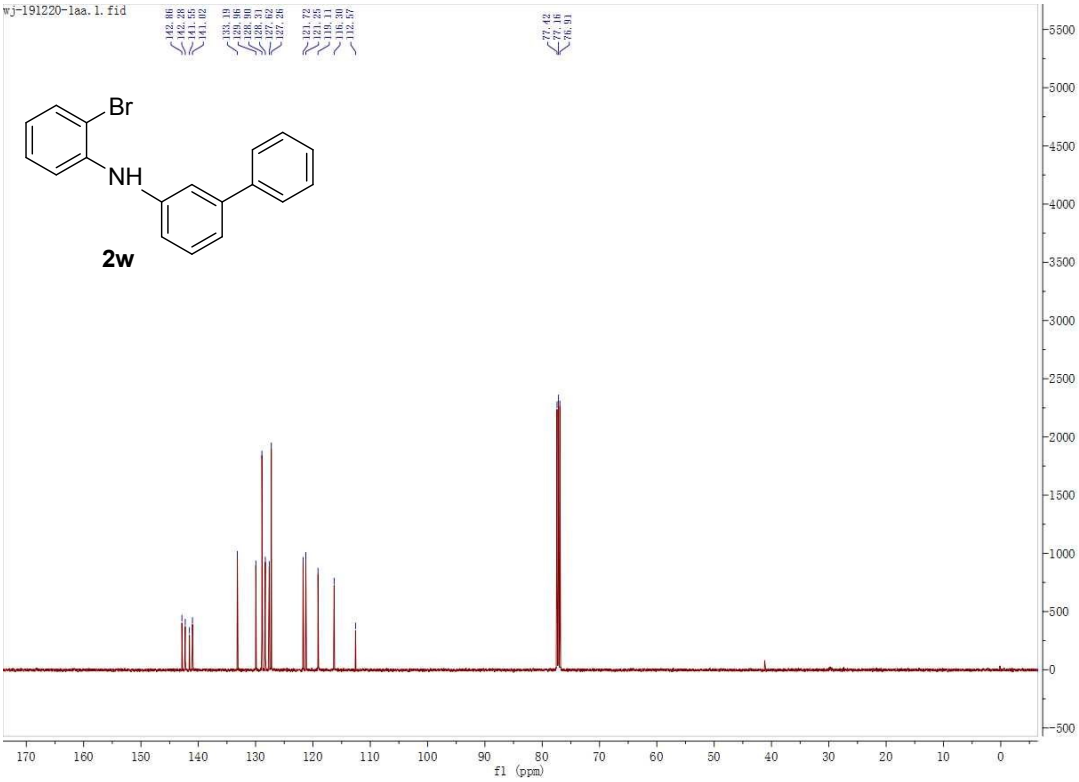
compound **2r**



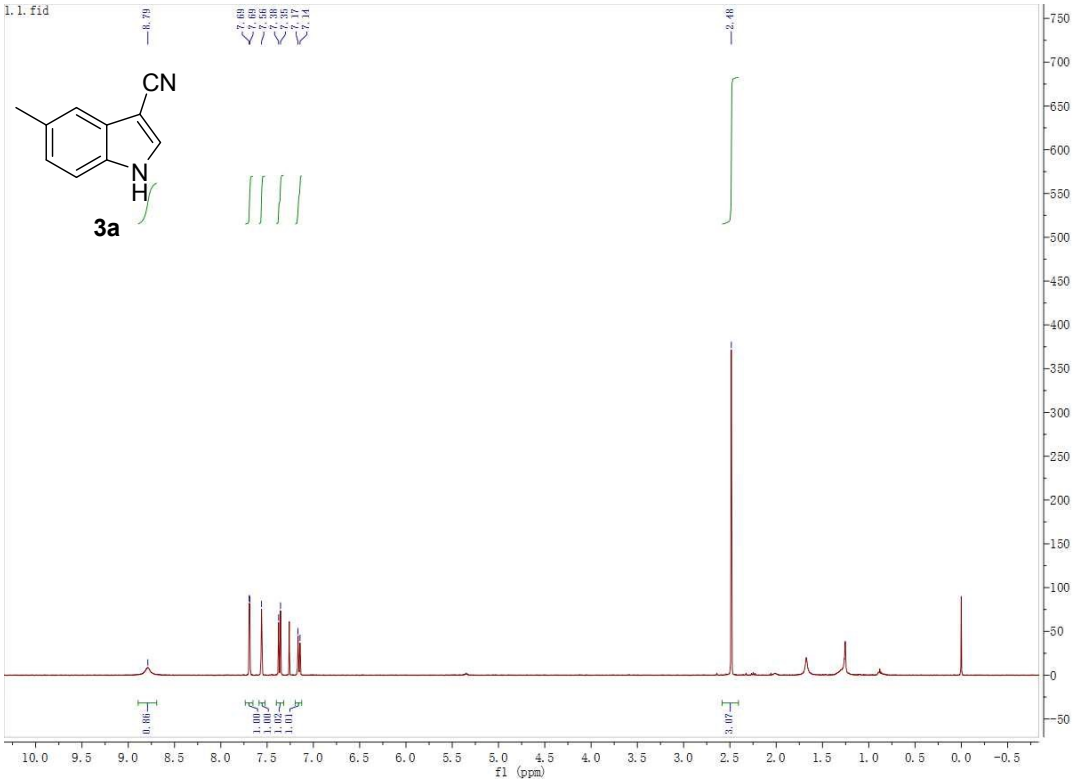


compound **2w**





compound **3a**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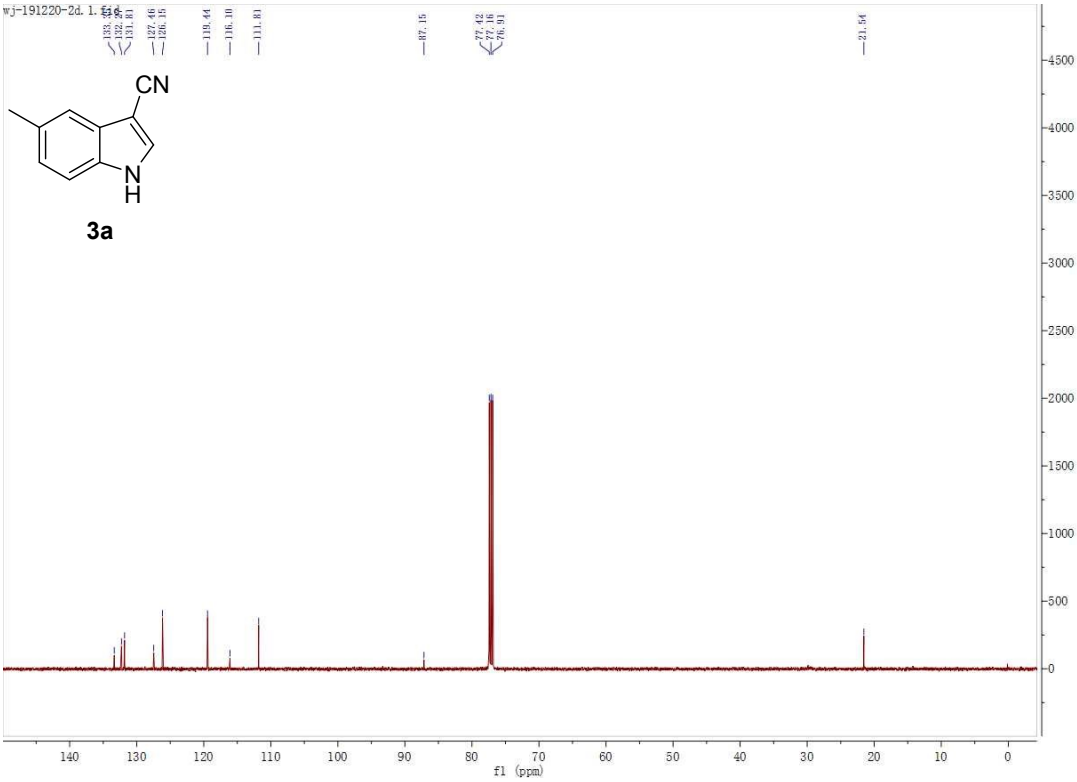
7.68
7.56
7.38
7.35
7.17
7.14
2.48
CN
N
H
3a
0.86
1.00
1.00
1.02
1.01
3.07
f1 (ppm)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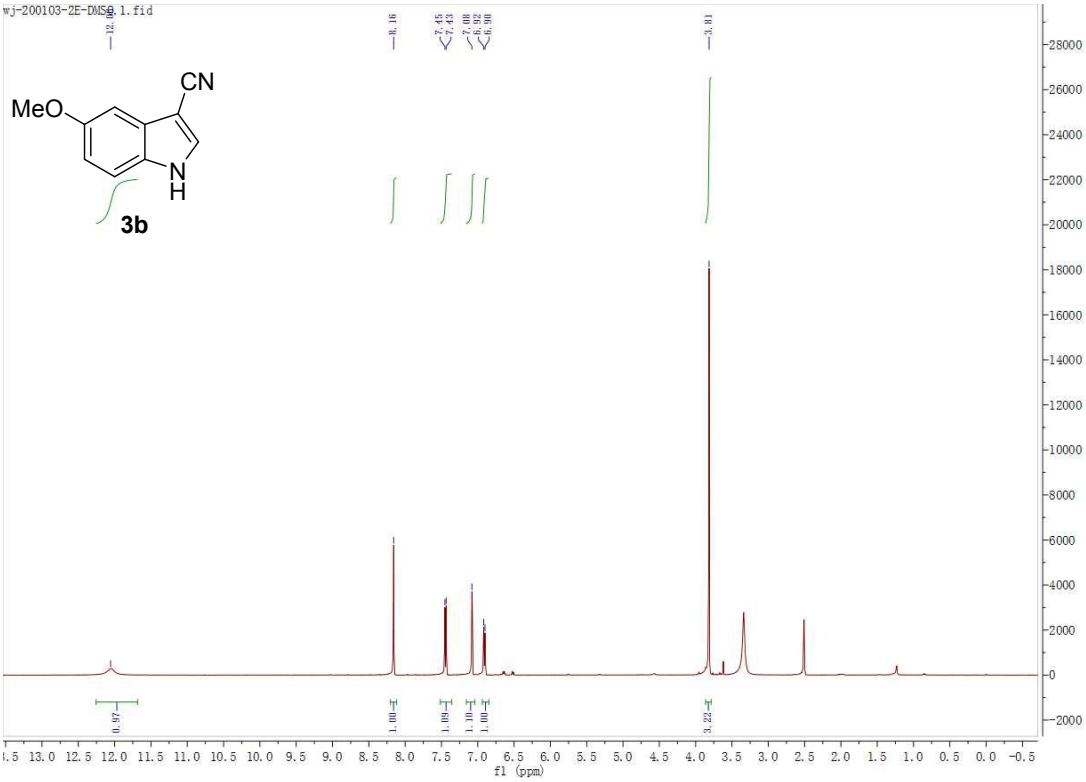
132.29
131.83
127.46
126.15
119.44
116.10
111.83
87.15
77.42
77.16
76.91
21.54
CN
N
H
3a
f1 (ppm)

compound **3b**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MeO
N
H
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8.16
7.45
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6.90
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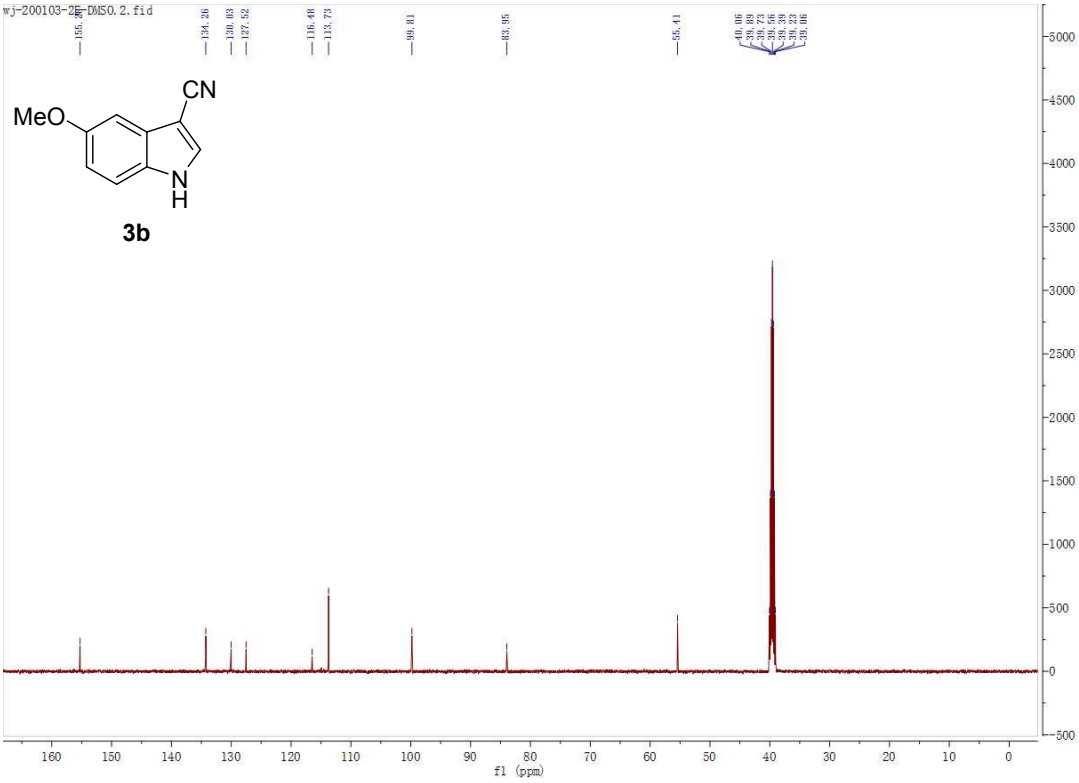
0.97
1.00
1.09
1.10
1.00
3.22
f1 (ppm)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134.26
130.03
127.52
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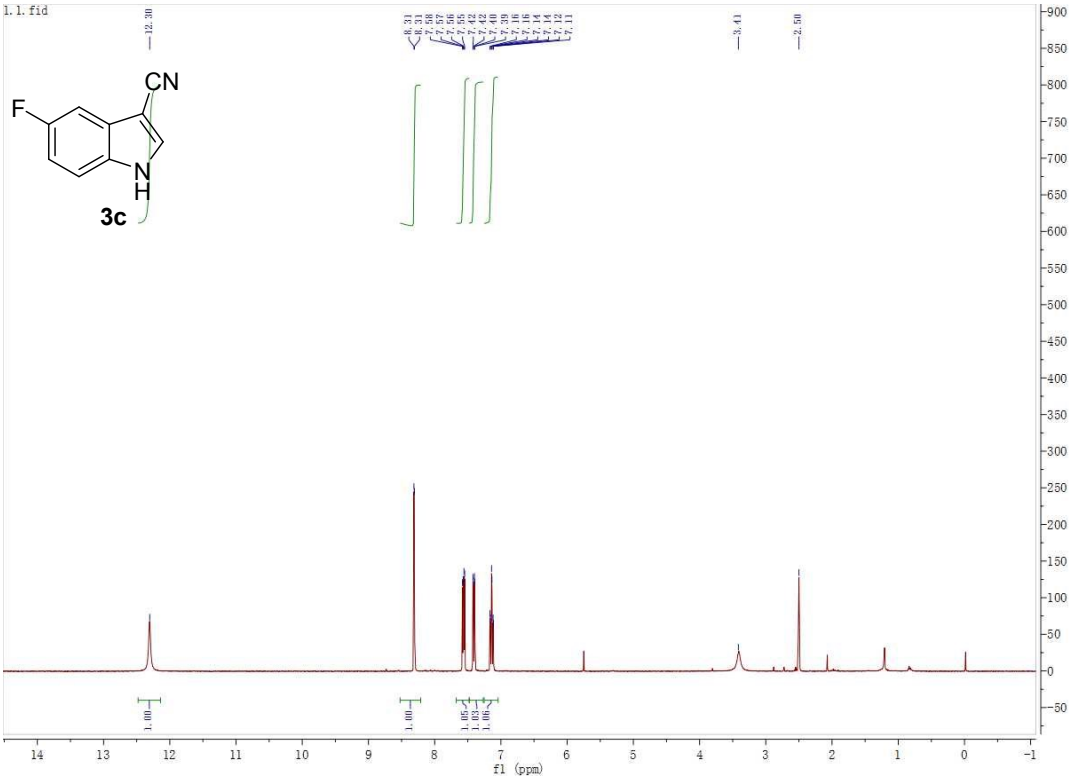
113.73
99.81
83.95
55.41
40.06
39.89
39.72
39.55
39.39
39.23
39.06
CN
MeO
N
H
3b
f1 (ppm)

compound **3c**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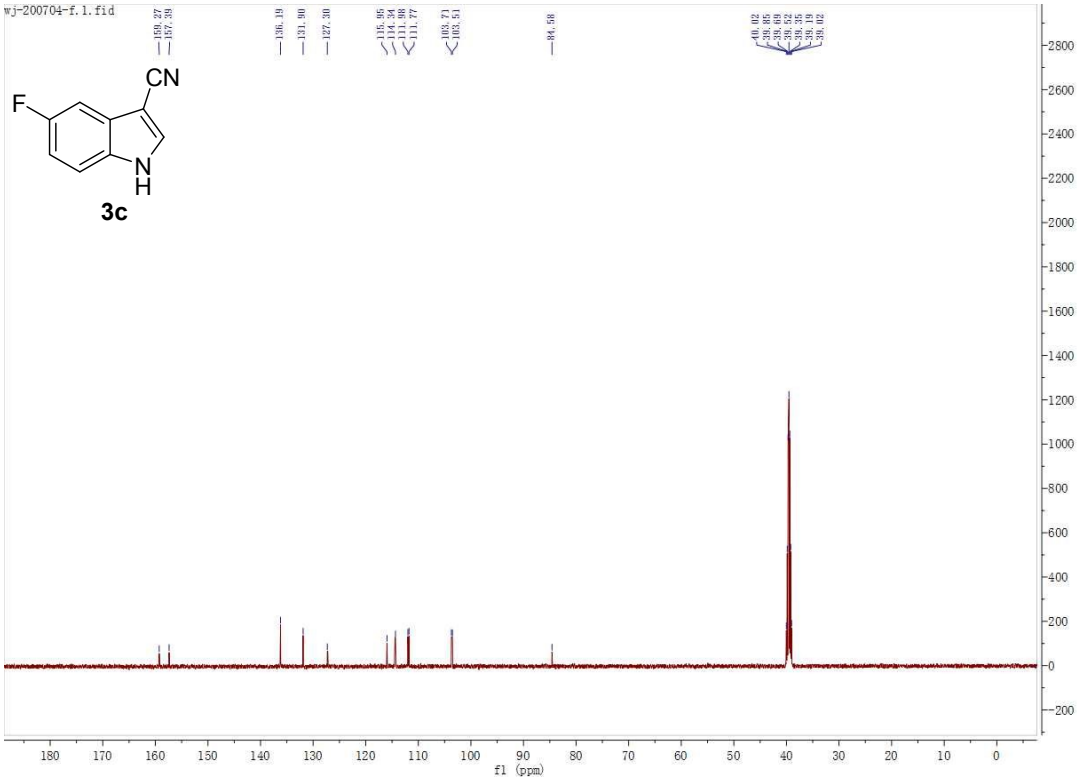
7.56
7.55
7.42
7.42
7.40
7.39
7.16
7.16
7.14
7.14
7.12
7.12
7.11
3.41
2.50
CN
F
N
H
3c
1.00
1.00
1.05
1.02
1.06
f1 (ppm)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114.34
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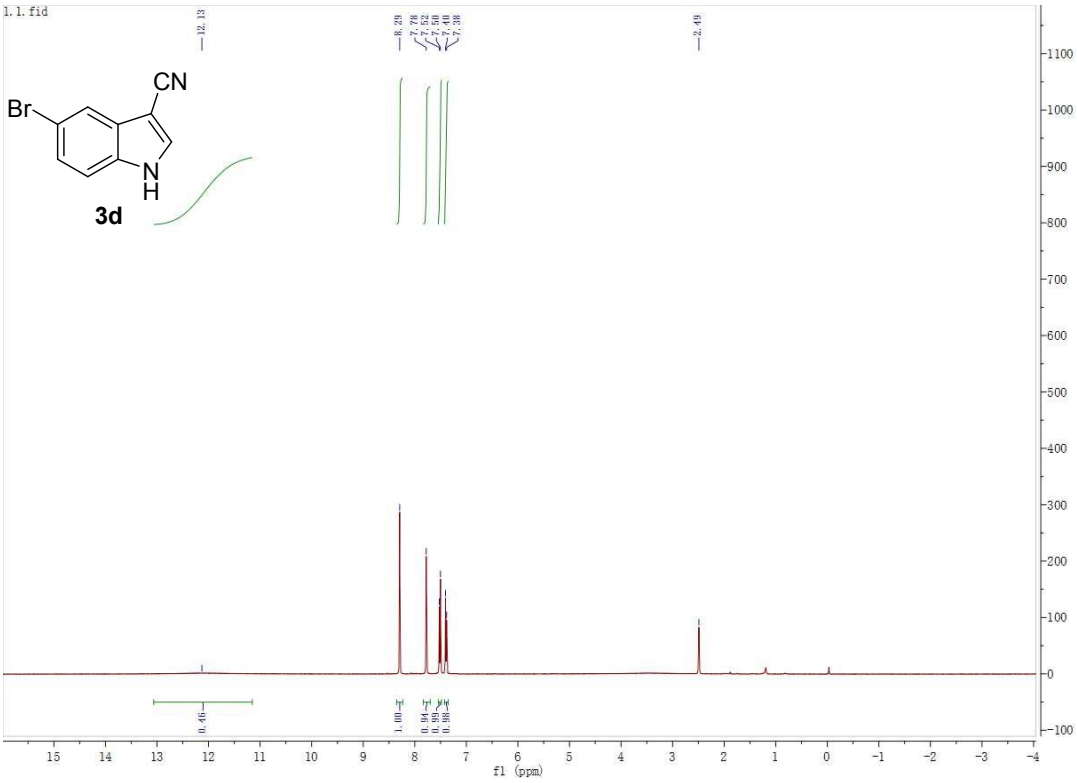
103.71
103.51
84.58
40.02
39.85
39.69
39.52
39.35
39.19
39.02
CN
F
N
H
3c
f1 (ppm)

compound **3d**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CN
Br
N
H
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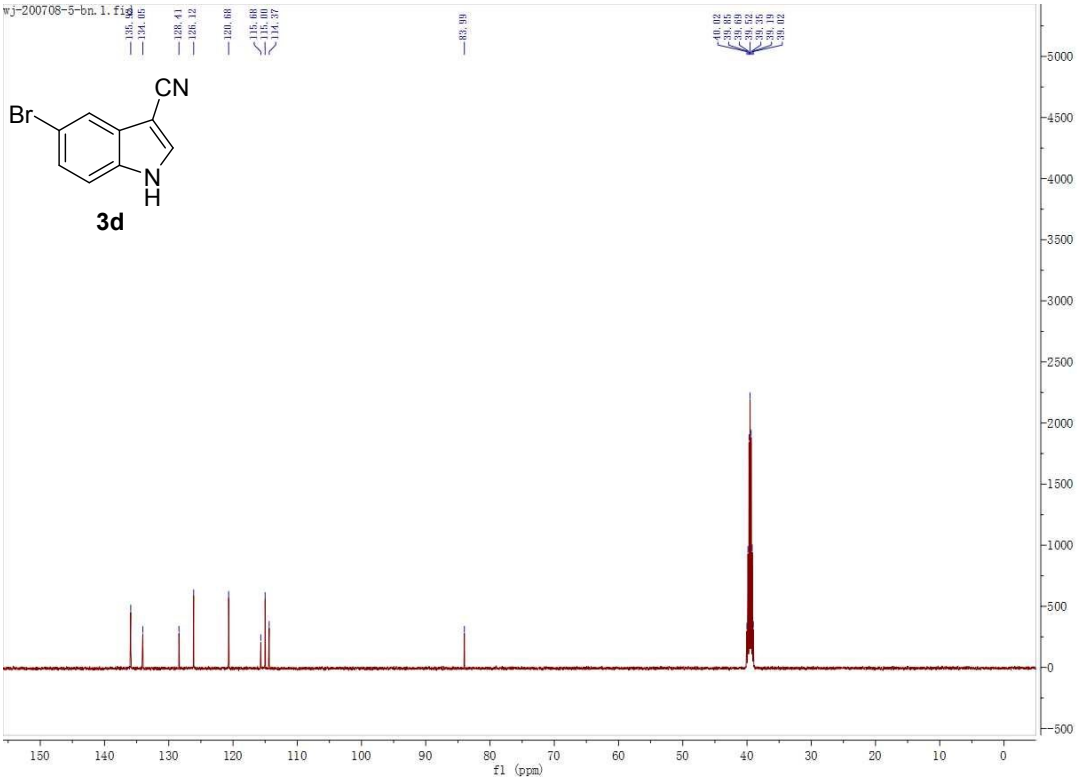
0.88
f1 (ppm)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83.99
40.02
39.85
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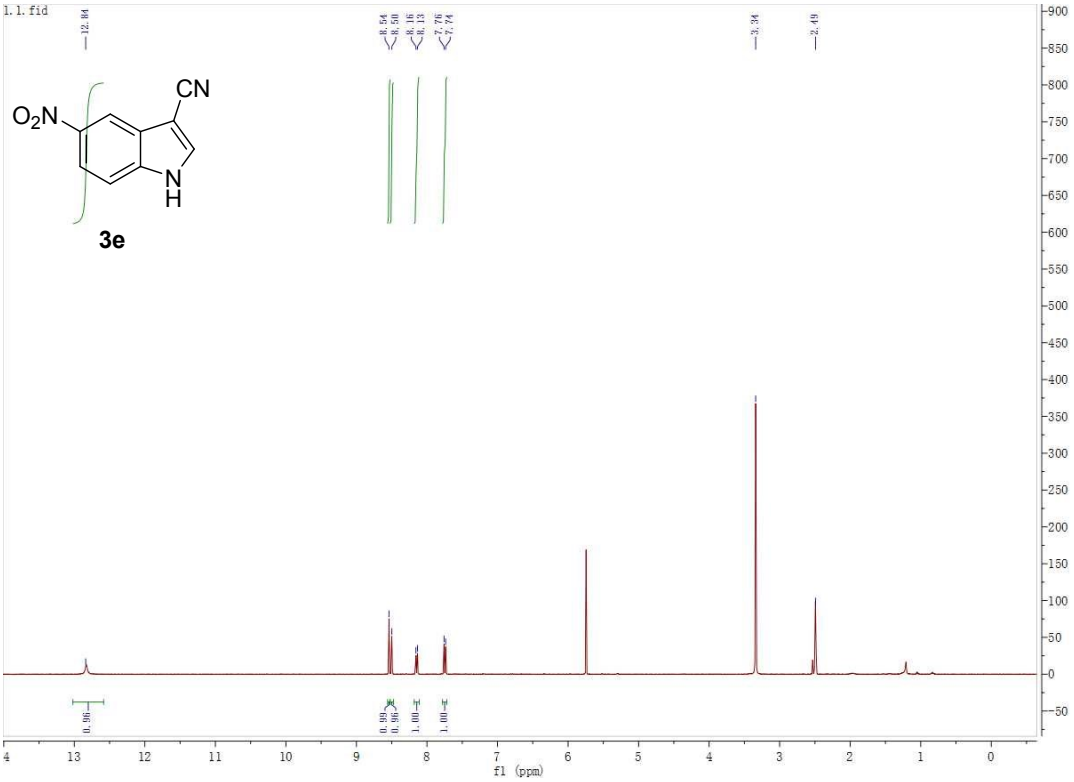
39.52
39.35
39.19
39.02
CN
Br
N
H
3d
f1 (ppm)

compound **3e**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O2N
N
H
3e
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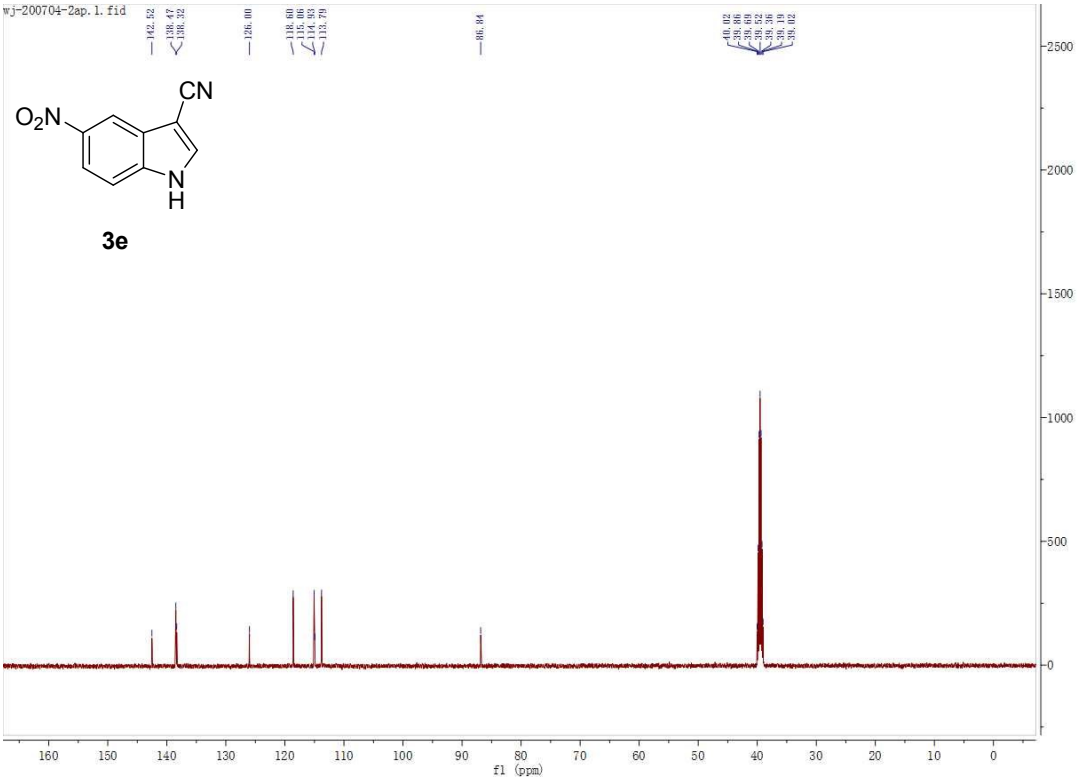
0.98
0.98
1.00
1.00
f1 (ppm)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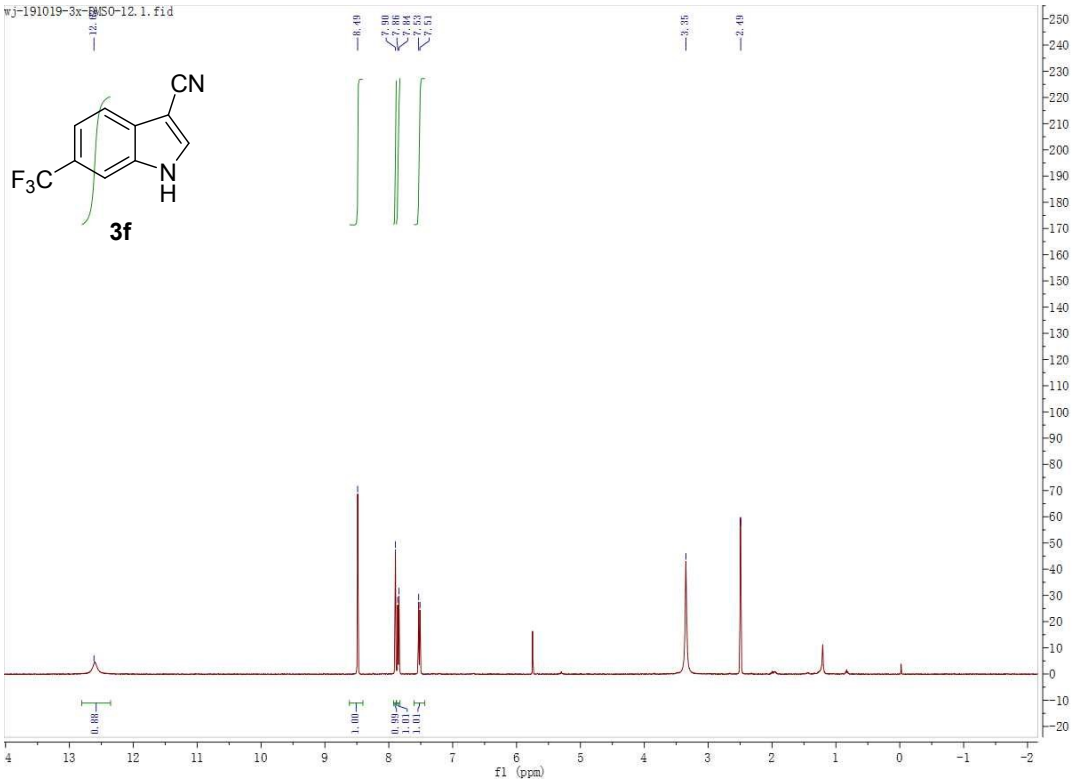
39.19
39.02
CN
O2N
N
H
3e
f1 (ppm)

compound **3f**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H
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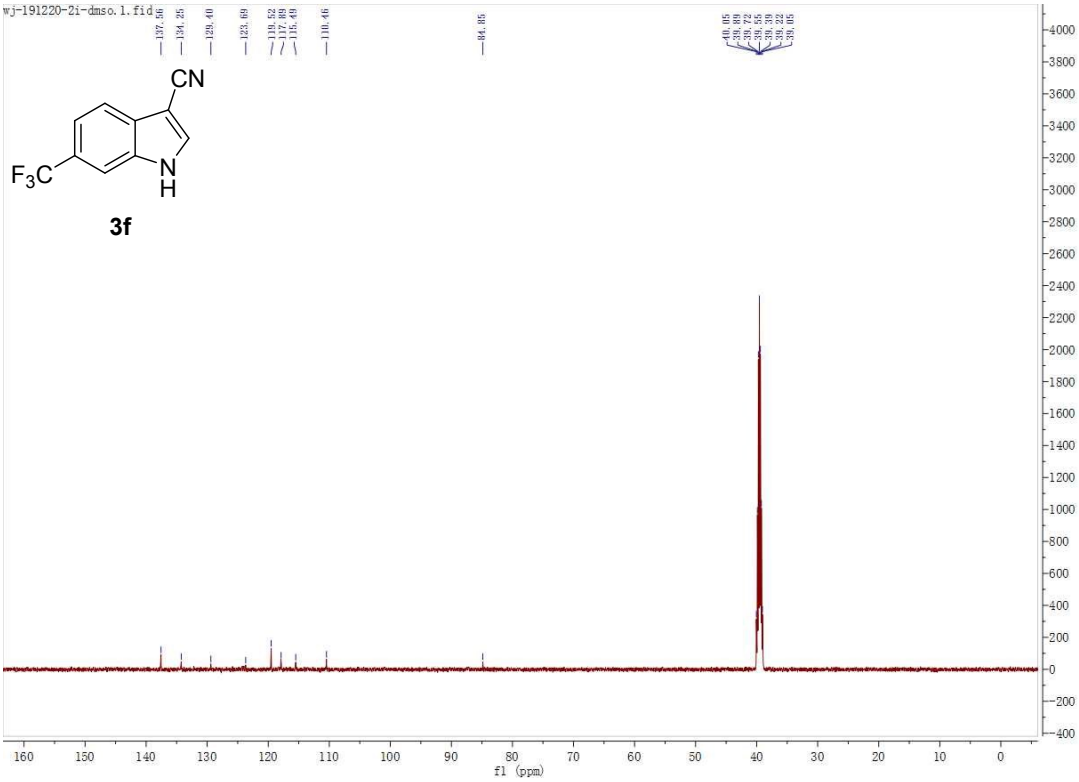
f1 (ppm)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40.05
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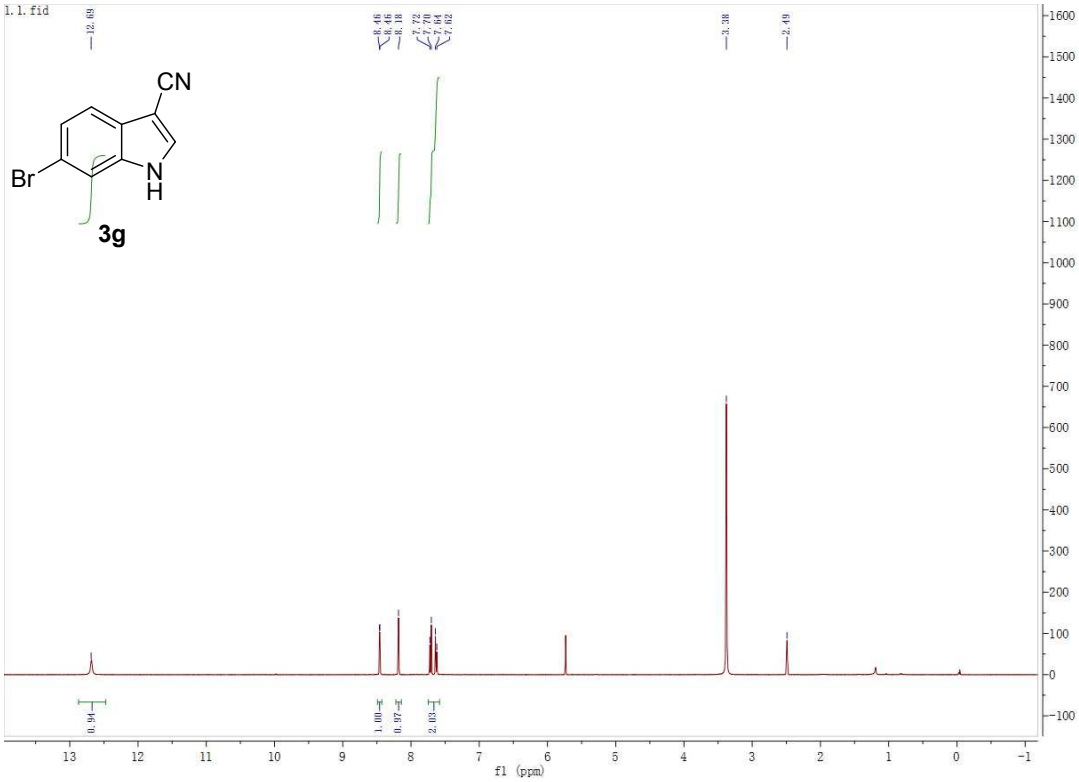
39.39
39.22
39.05
CN
F3C
N
H
3f
f1 (ppm)

compound **3g**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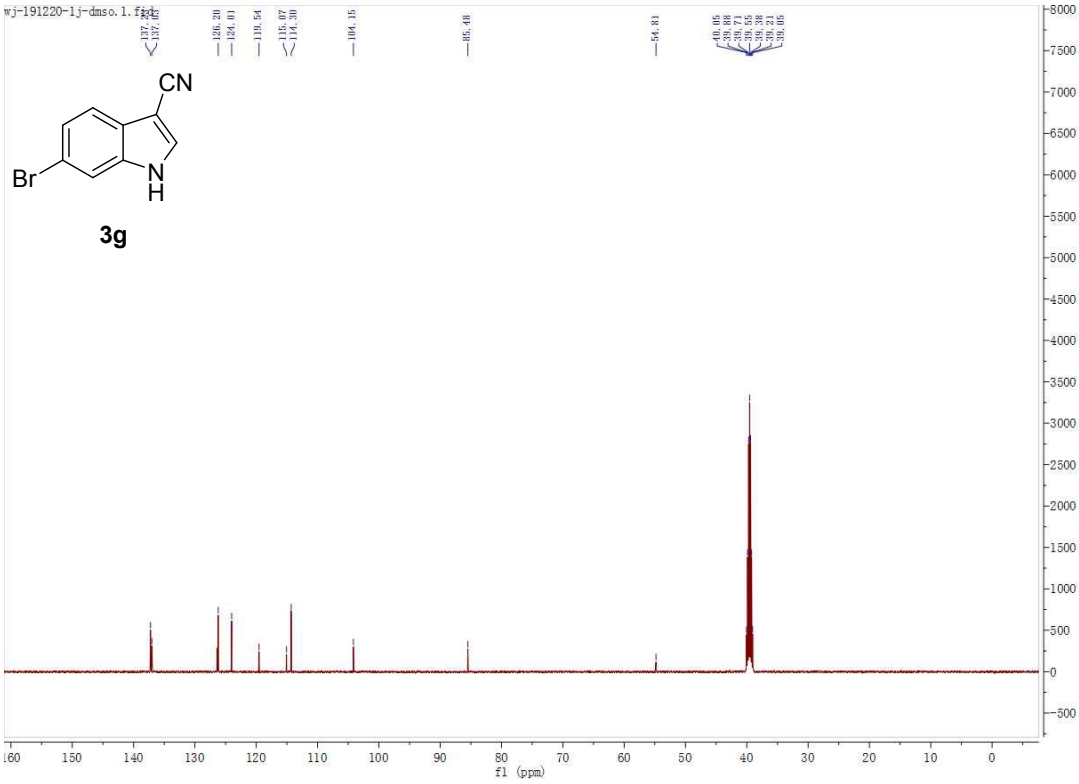
f1 (ppm)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40.05
39.88
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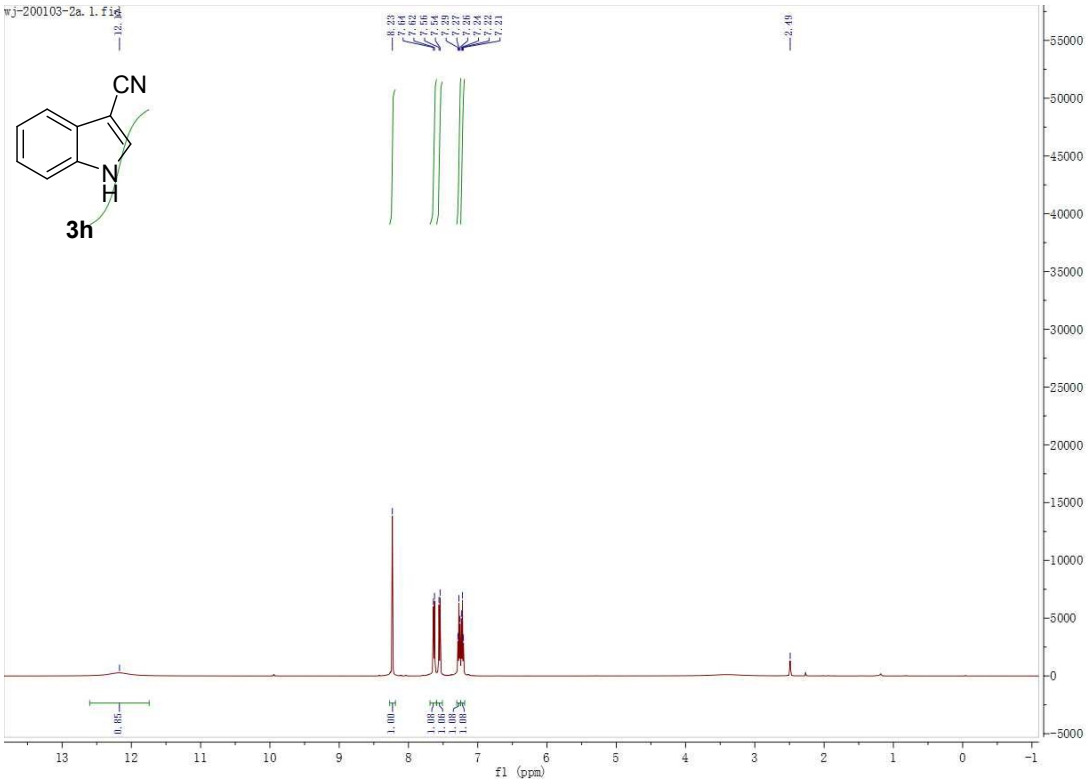
39.38
39.21
39.05
CN
Br
N
H
3g
f1 (ppm)

compound **3h**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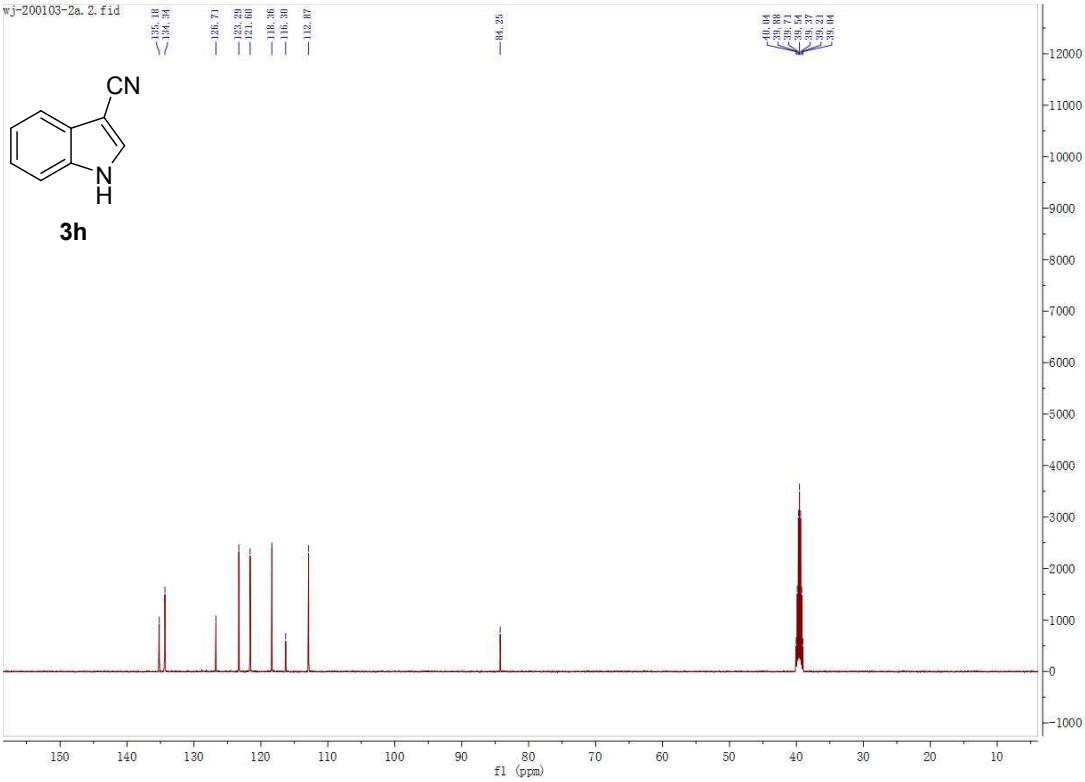
CN
N
H
3h
f1 (ppm)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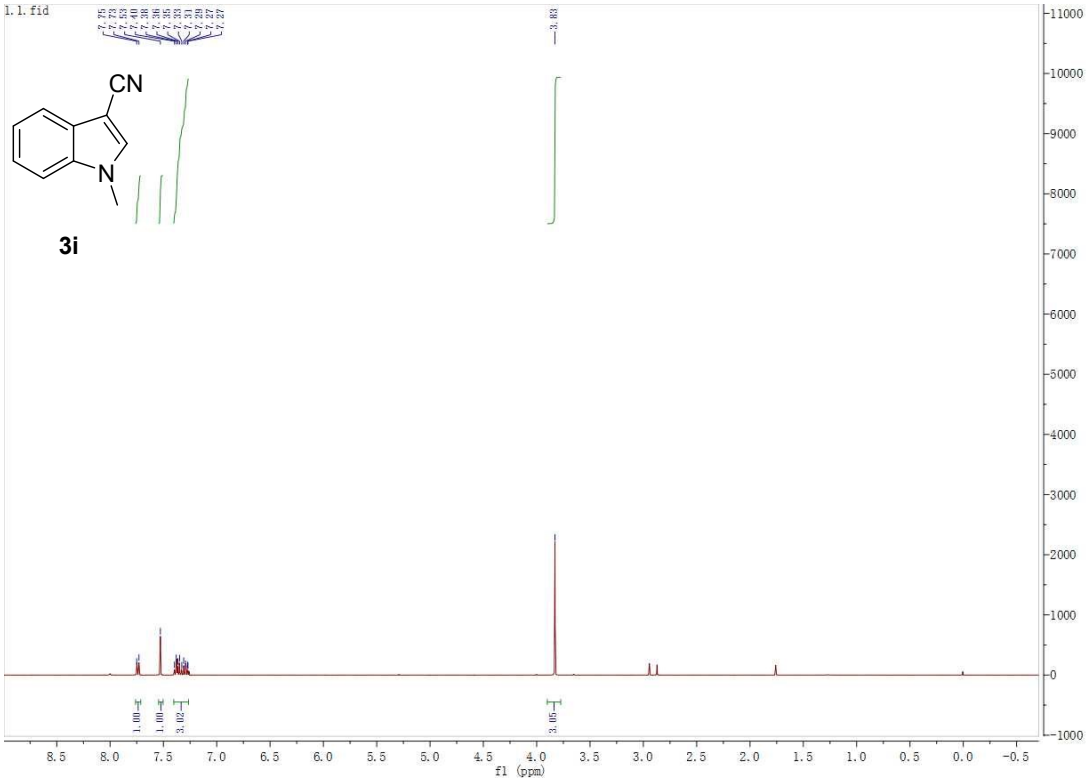
CN
N
H
3h
f1 (ppm)

compound **3i**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7.40
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7.35
7.33
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7.27
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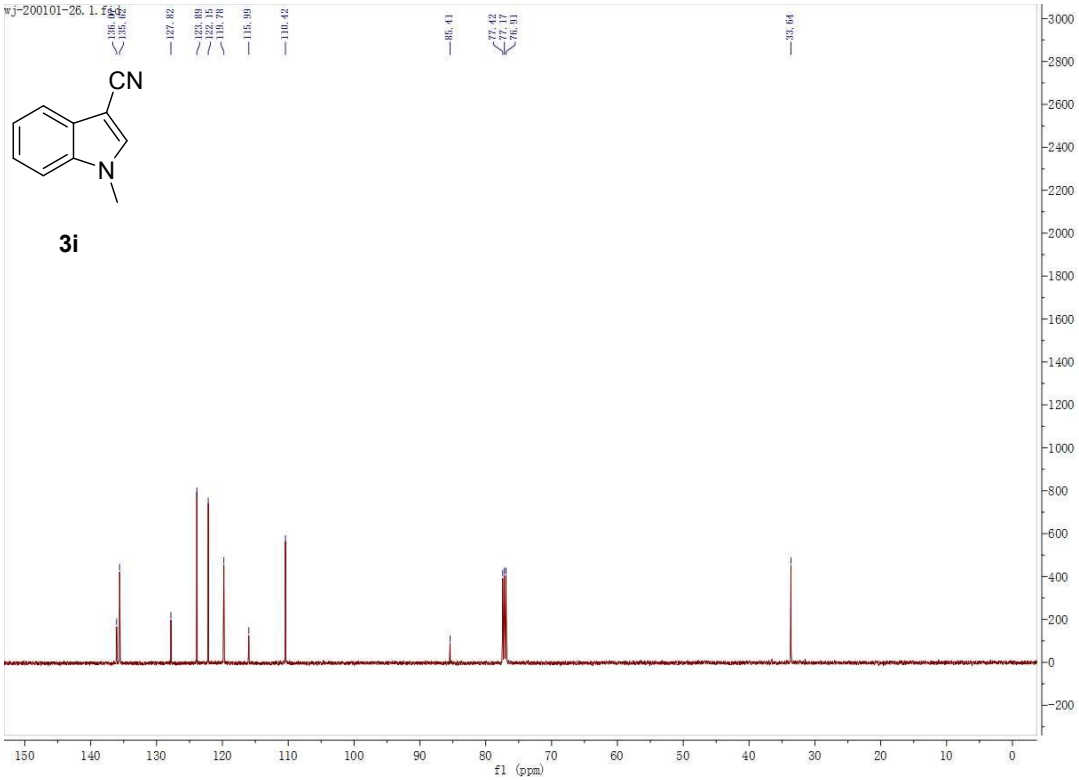
CN
N
3i
1.00
1.00
3.02
3.05
f1 (ppm)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110.42
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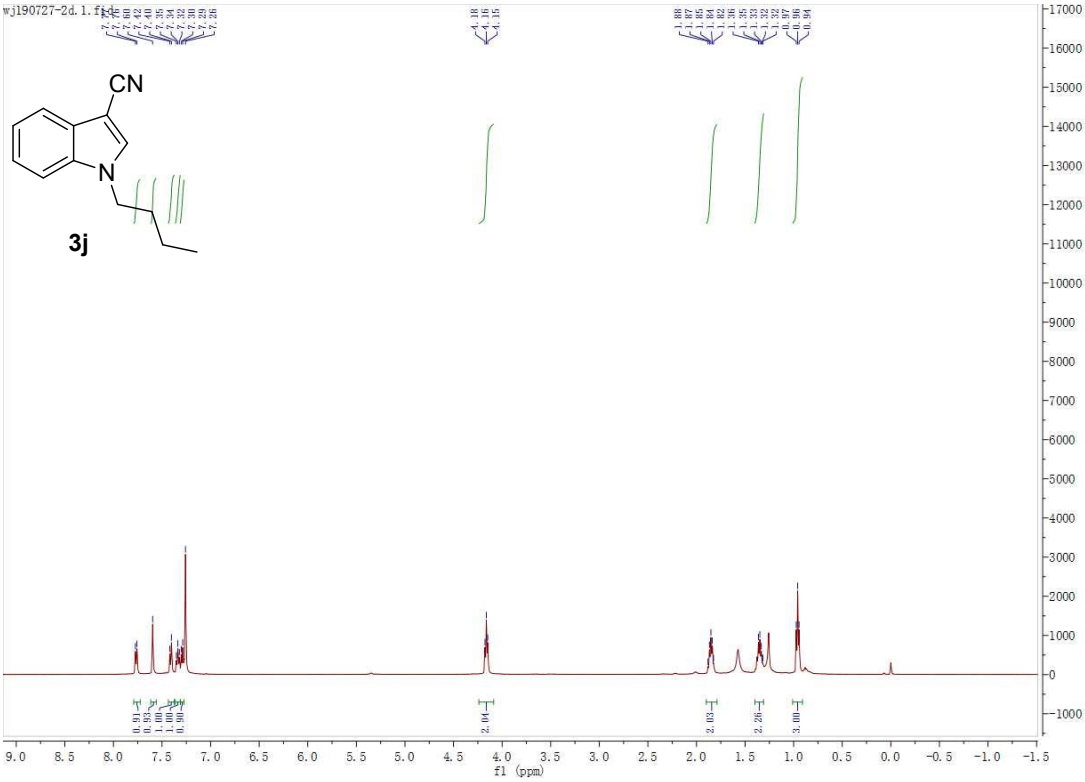
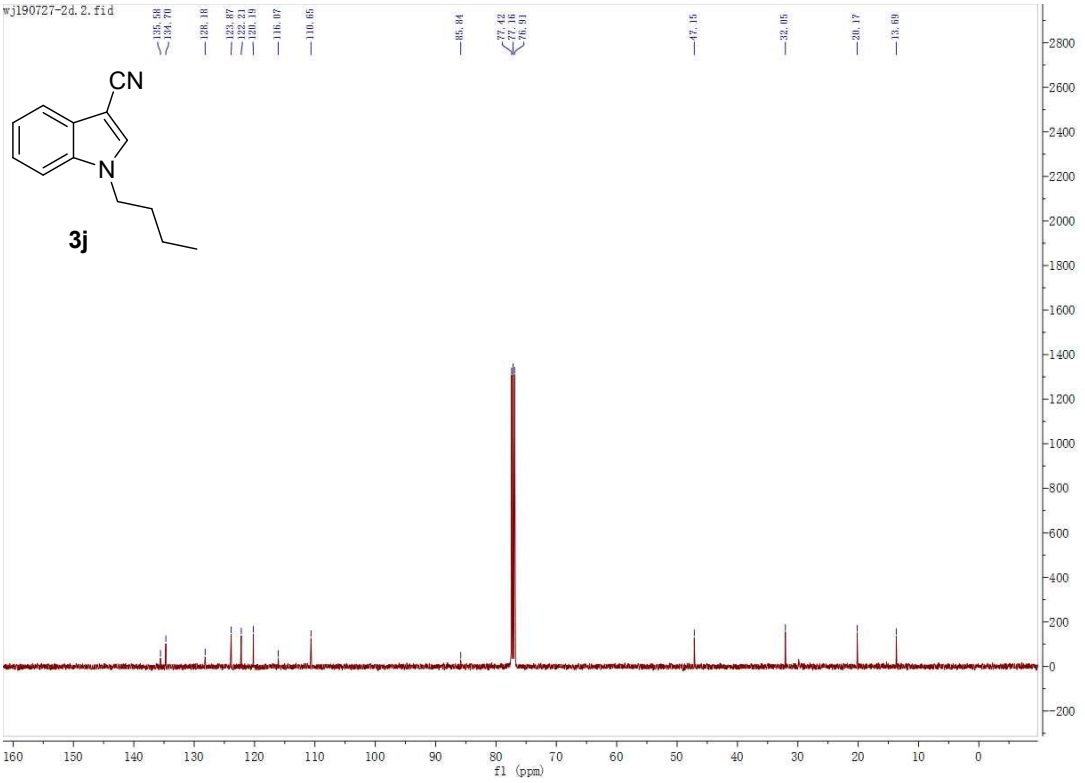
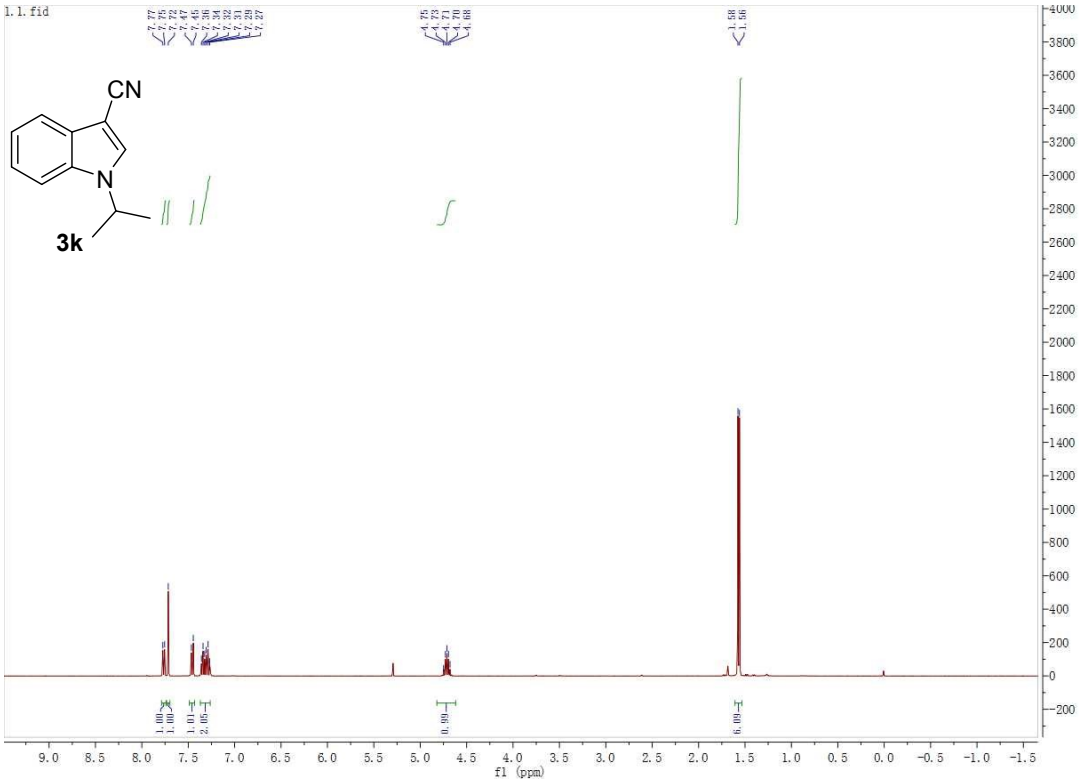
77.42
77.17
76.91
33.64
CN
N
3i
f1 (ppm)

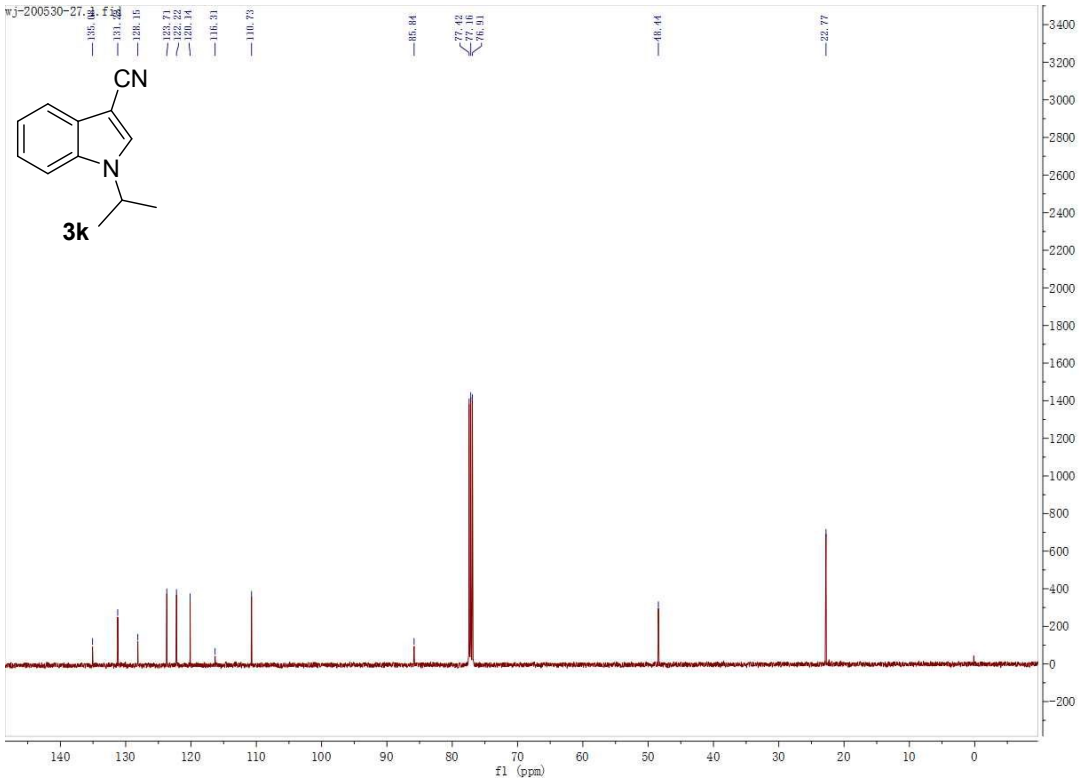
compound **3j**



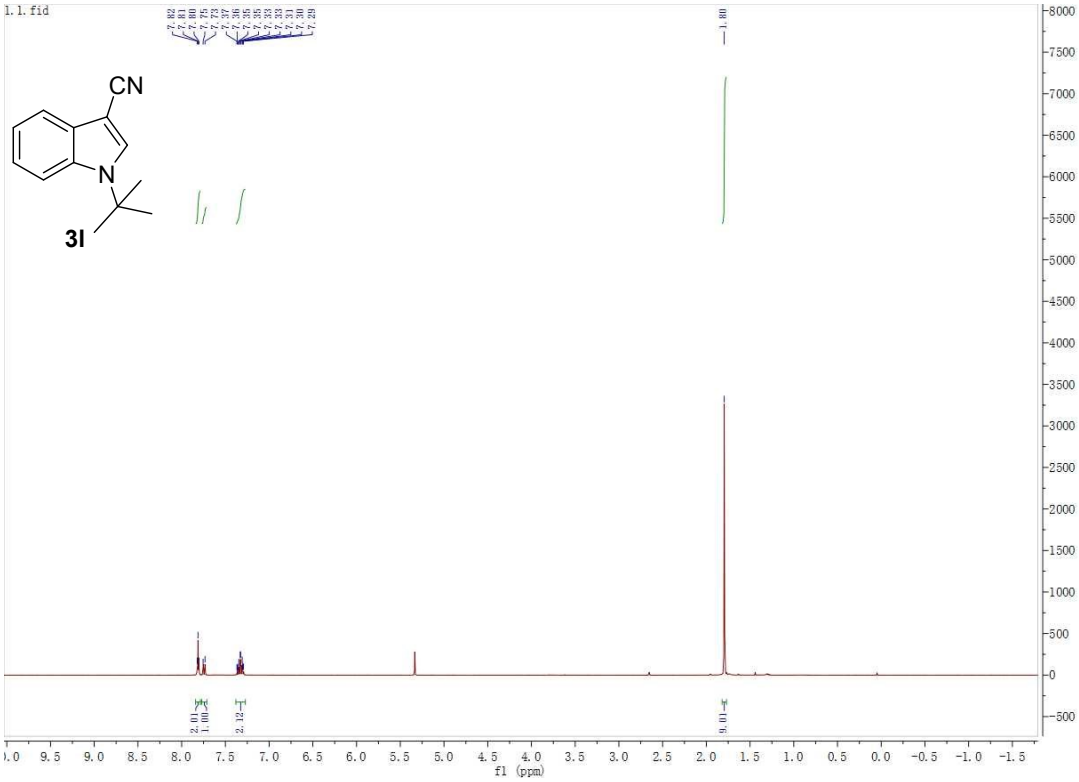


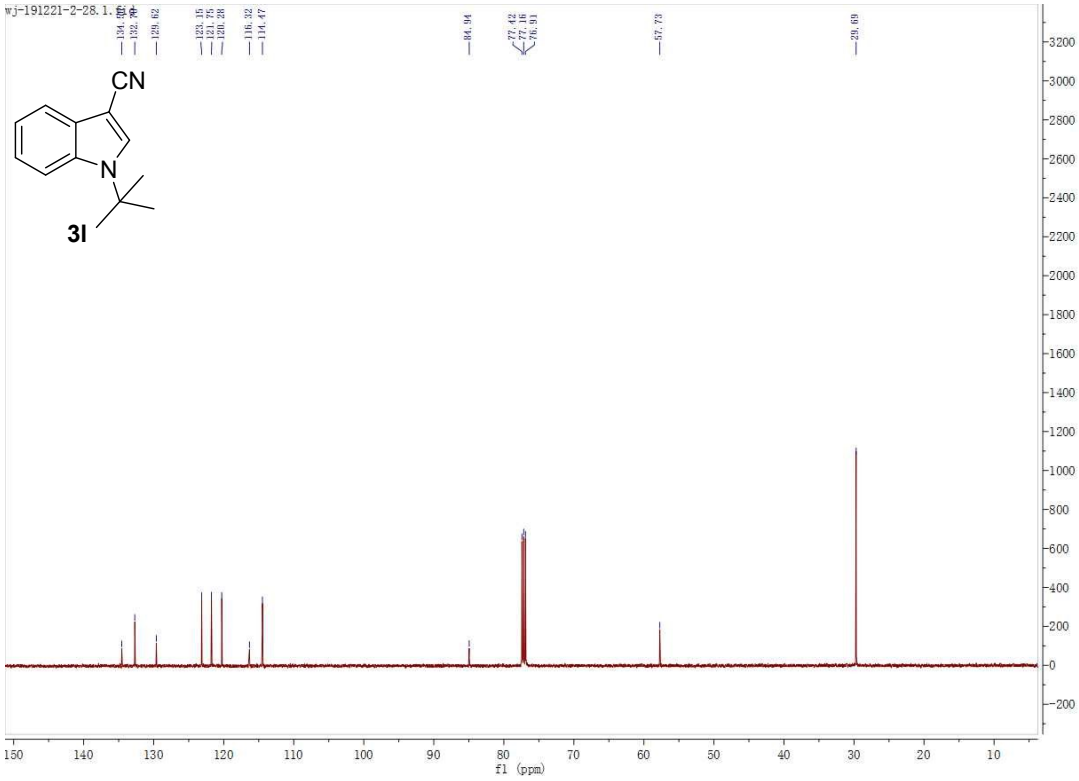
compound **3k**



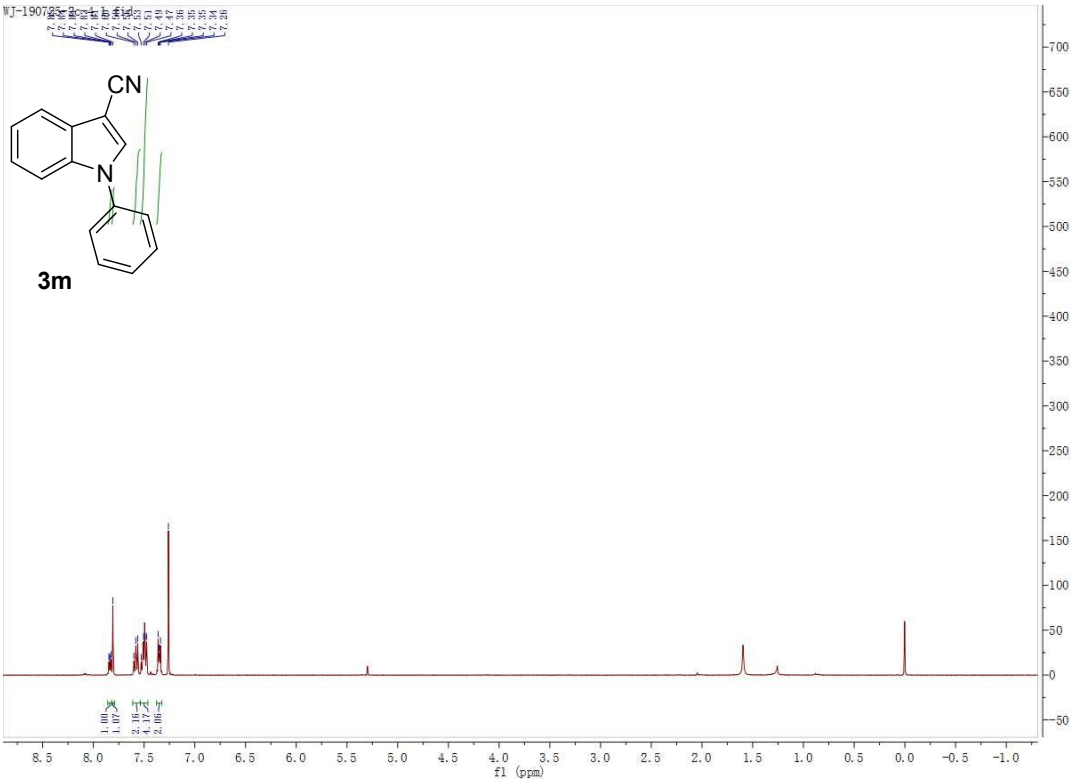


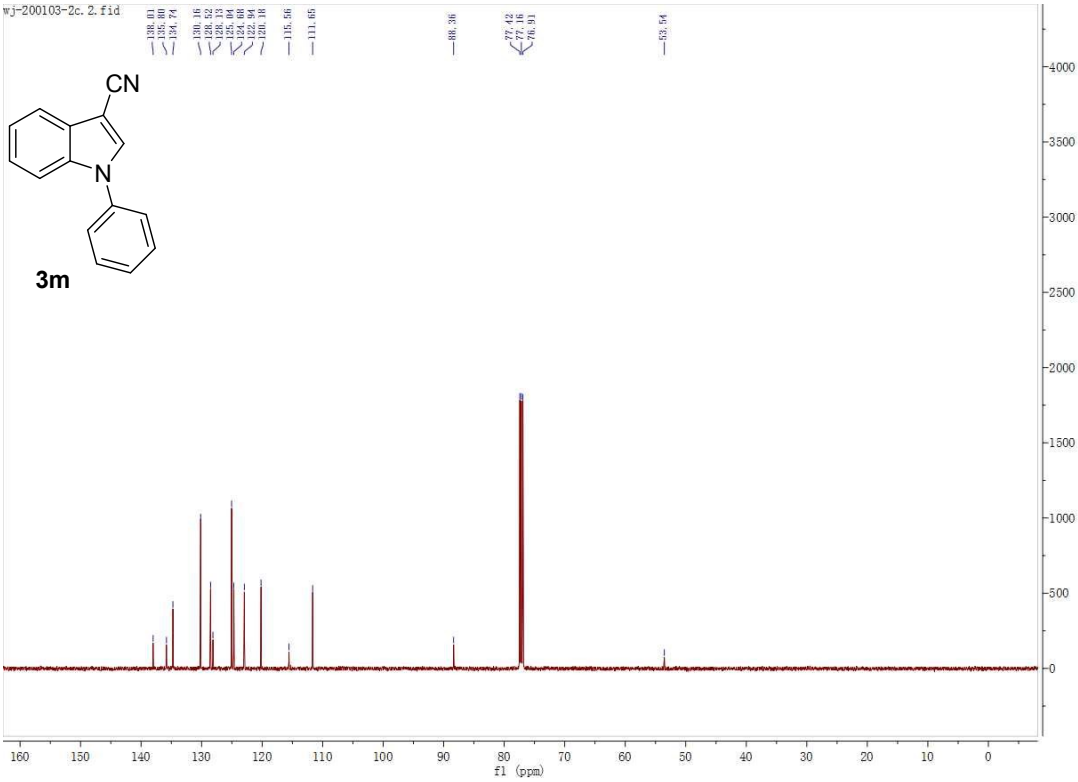
compound **3l**


1.1.fid
CN
N
3l
7.82
7.81
7.80
7.75
7.73
7.37
7.36
7.35
7.33
7.31
7.30
7.29
1.80
2.01
1.00
2.12
9.01
f1 (ppm)

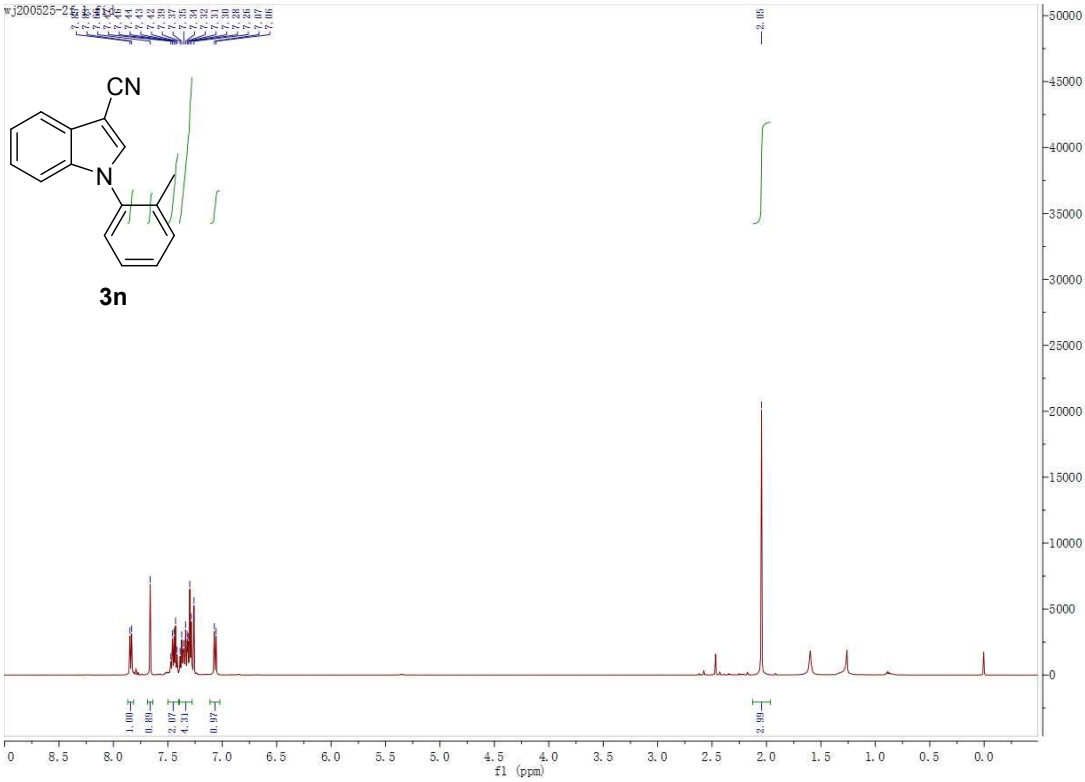

wj-191221-2-28.1.1
CN
N
3l
134.06
132.20
129.62
123.15
121.35
120.28
116.32
114.47
84.94
77.42
77.16
76.91
57.73
29.69
f1 (ppm)

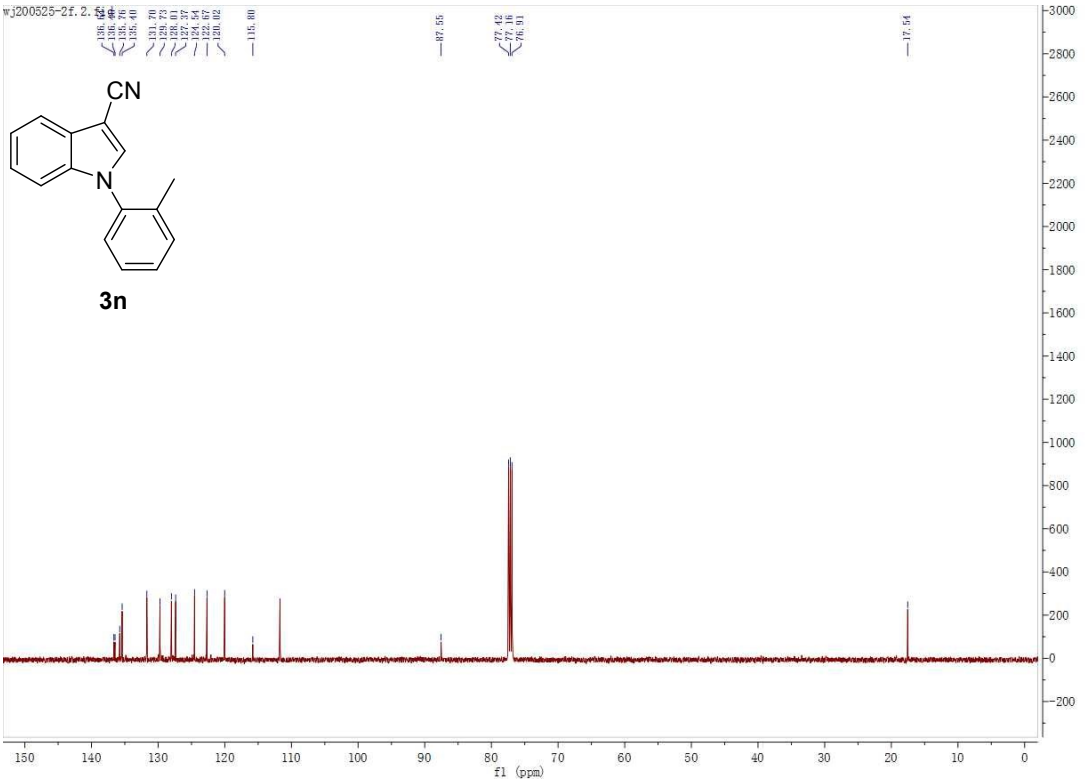
compound **3m**



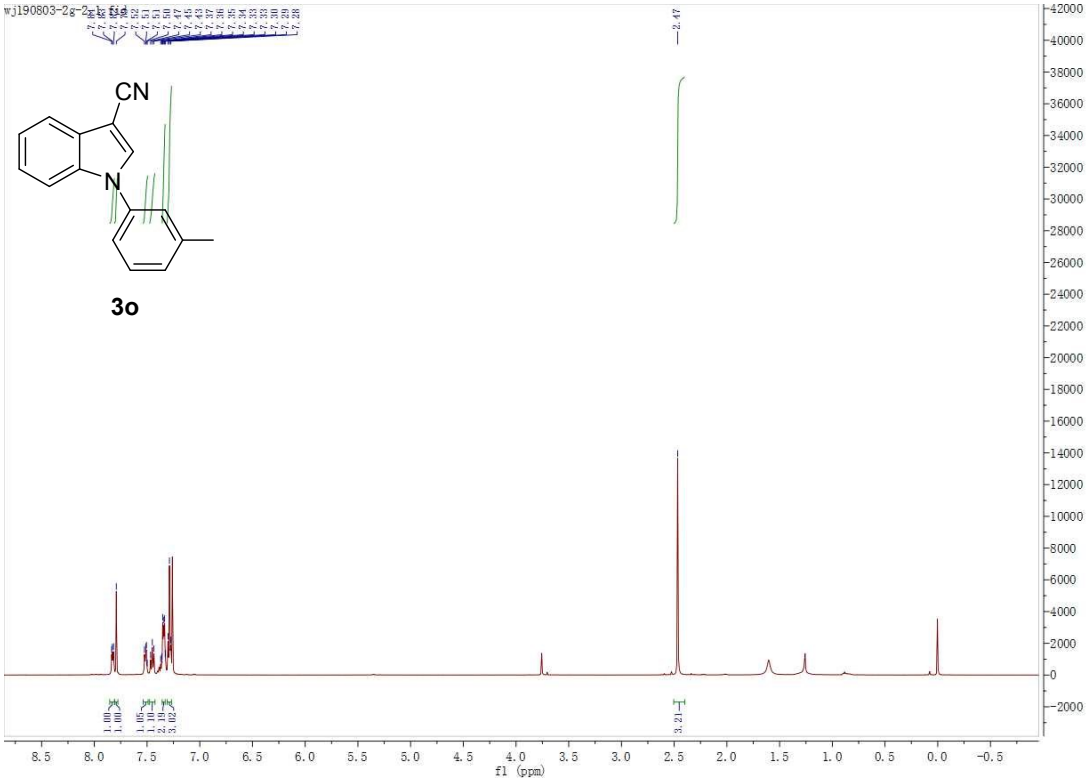


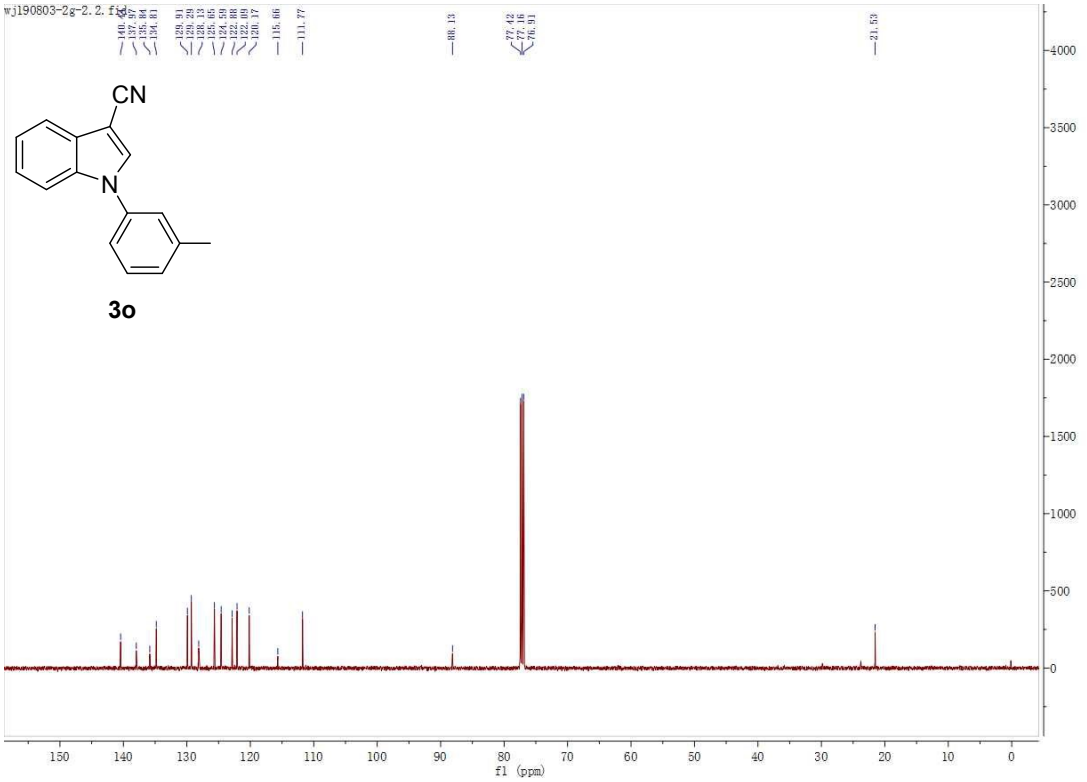
compound **3n**


CN
N
3n
2.05
1.00
0.89
2.07
4.31
0.97
2.99
f1 (ppm)

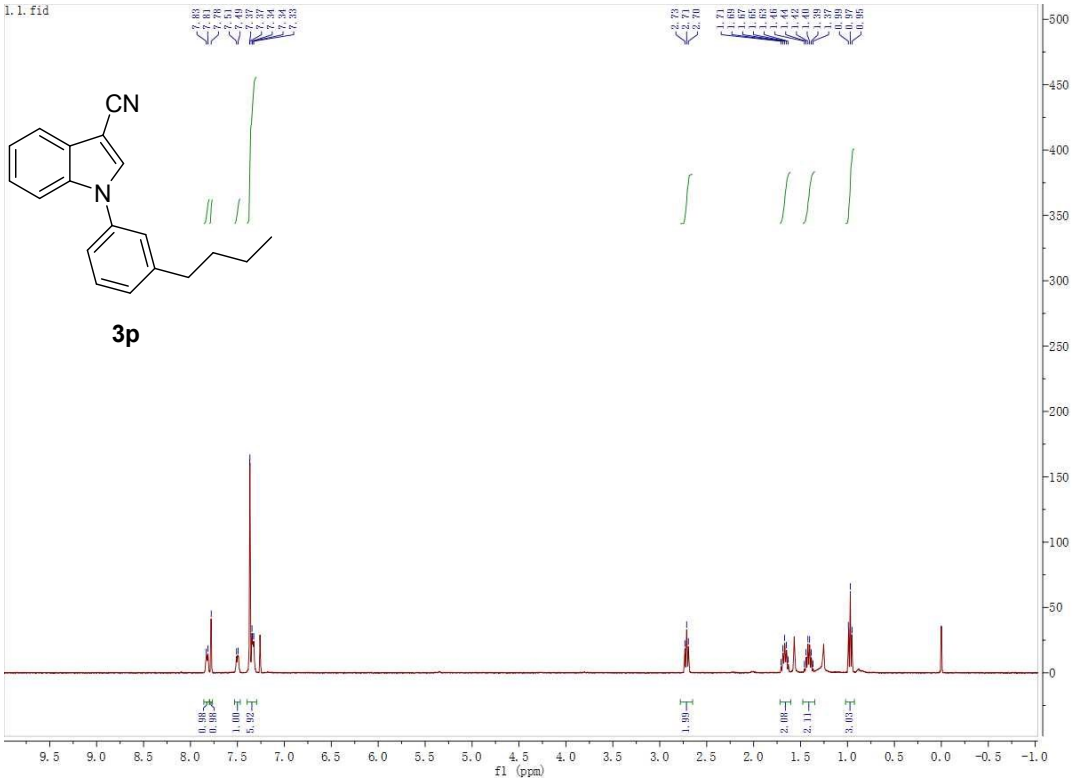

CN
N
3n
136.42
136.06
135.76
135.40
131.70
129.73
128.01
127.27
124.54
122.67
120.02
115.80
87.55
77.42
77.16
76.91
17.54
f1 (ppm)

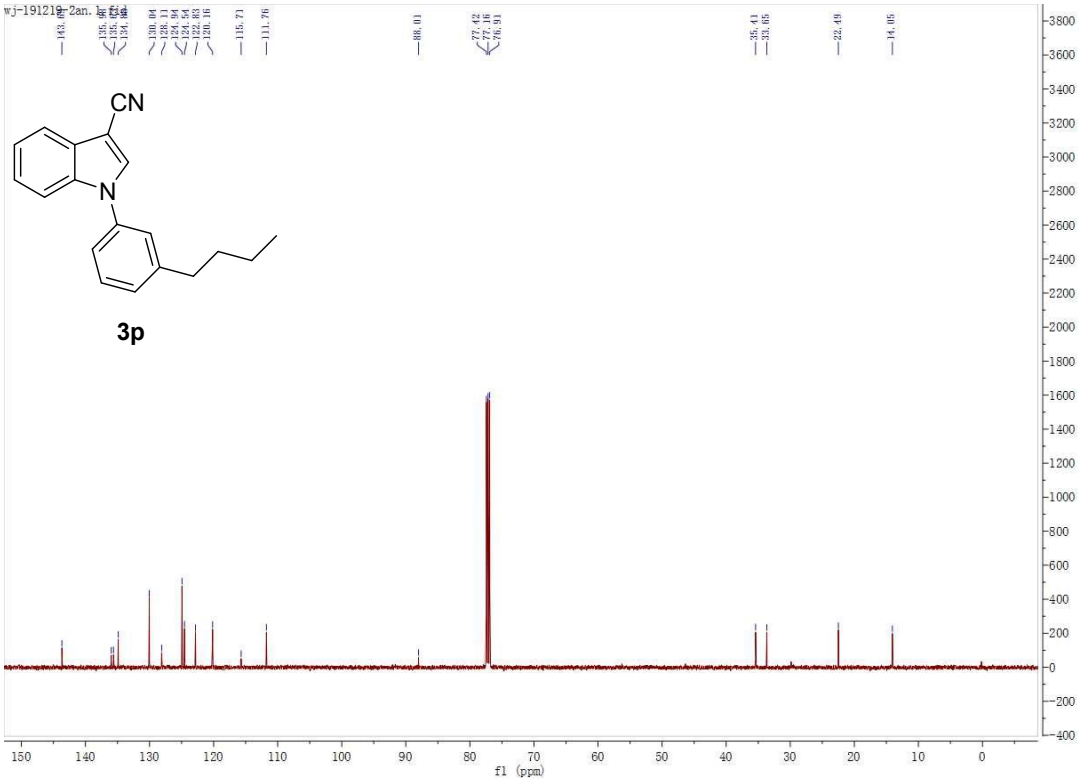
compound **3o**


CN
N
3o
2.47
3.21
f1 (ppm)

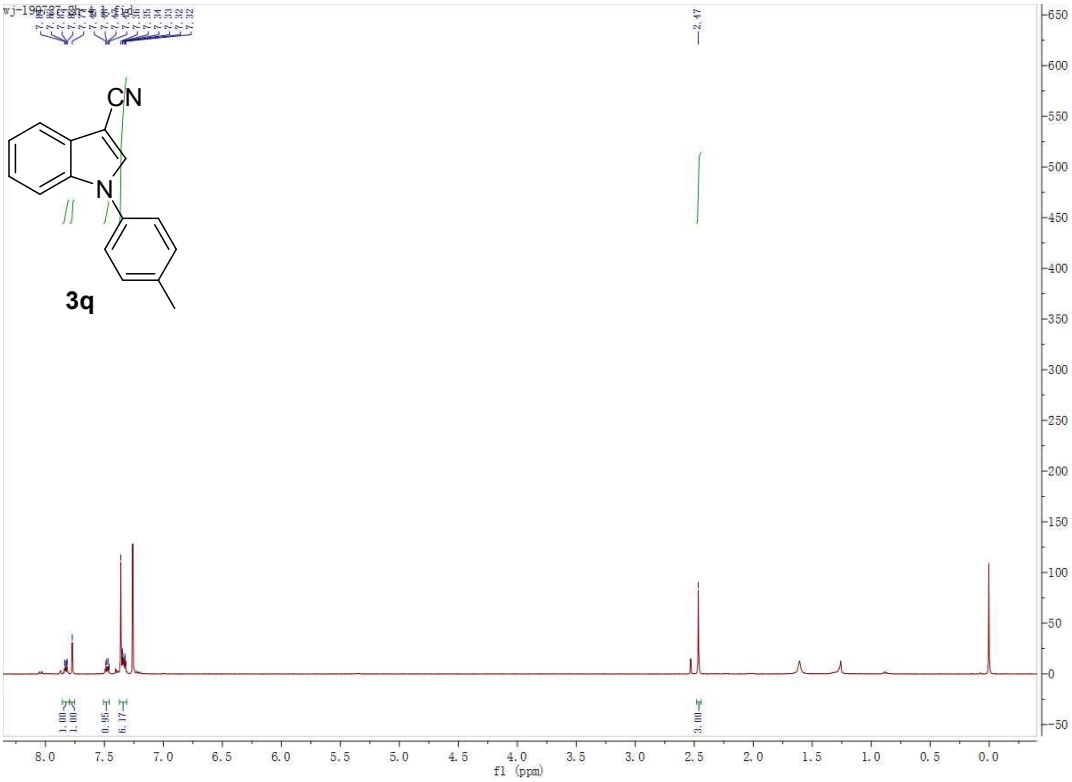

CN
N
3o
88.13
77.42
77.16
76.91
21.53
111.77
f1 (ppm)

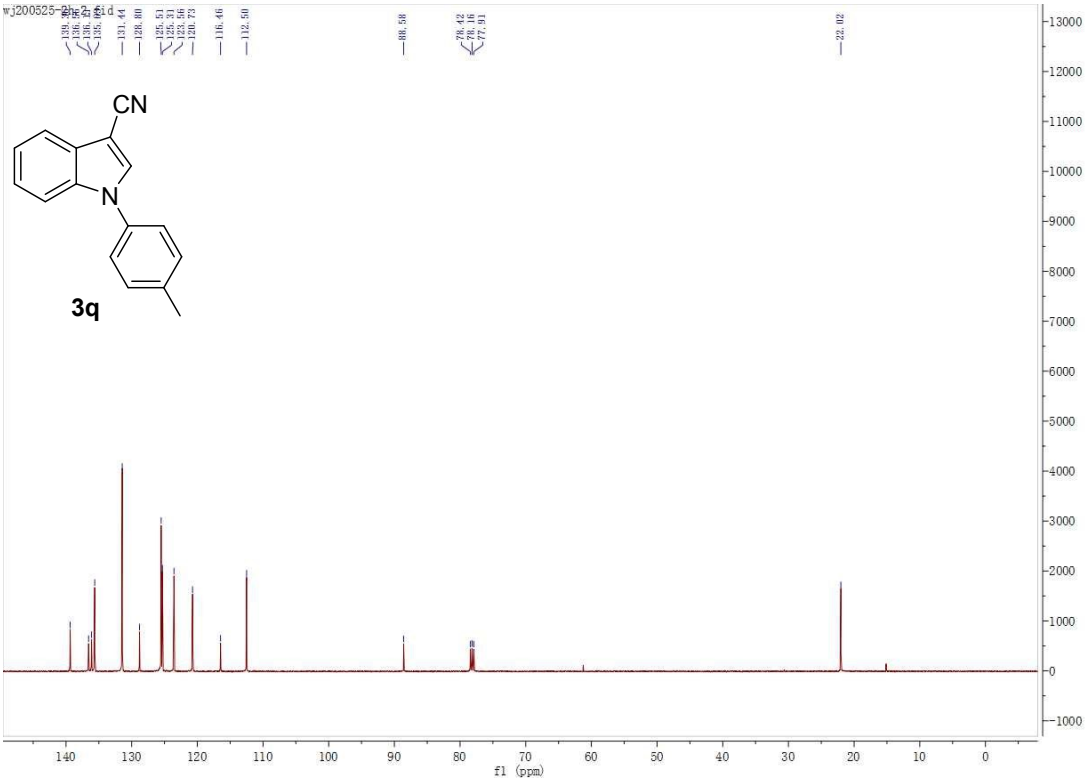
compound **3p**



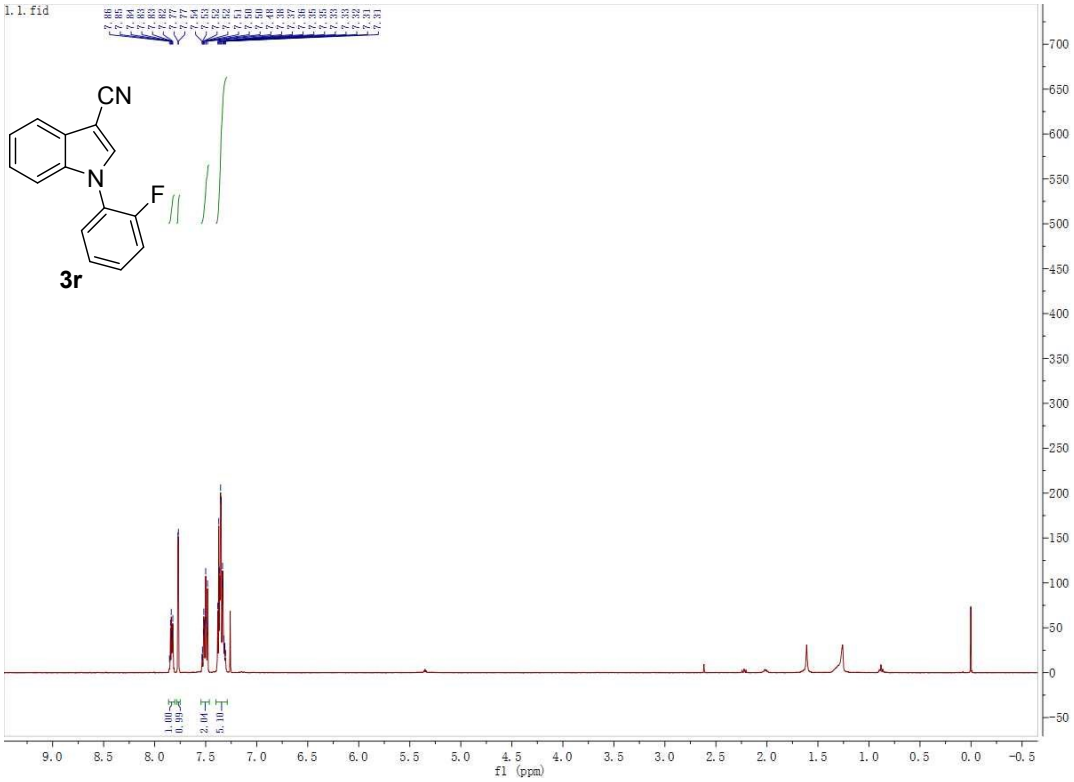


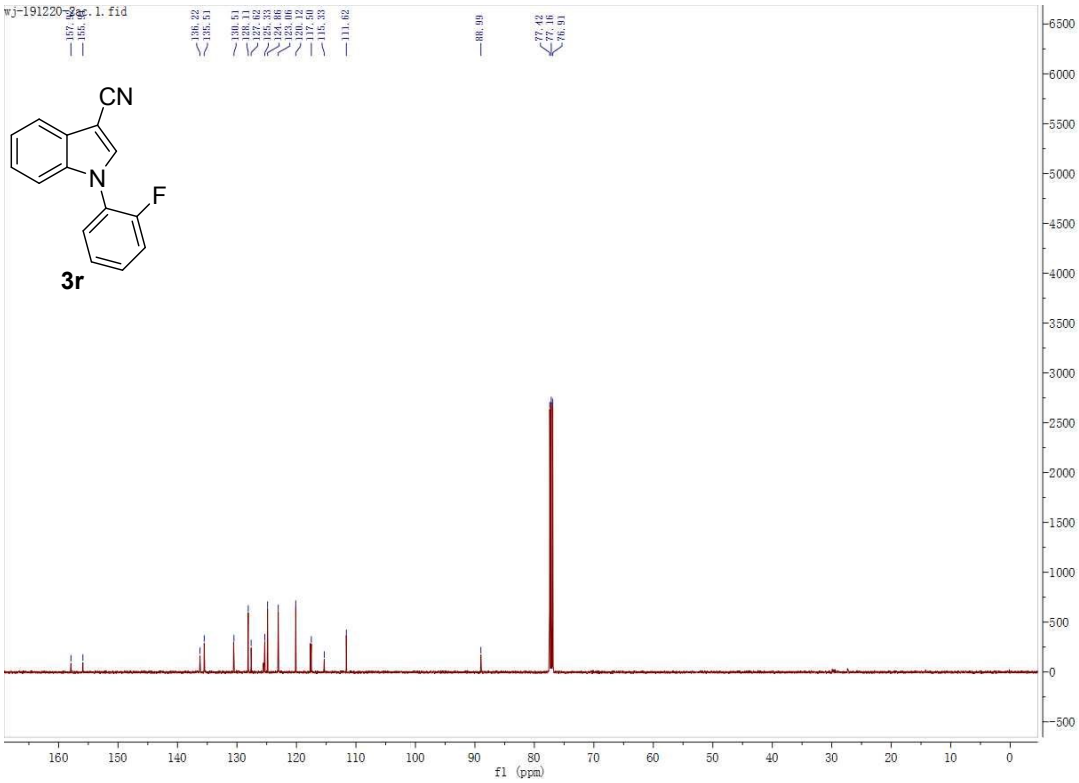
compound **3q**



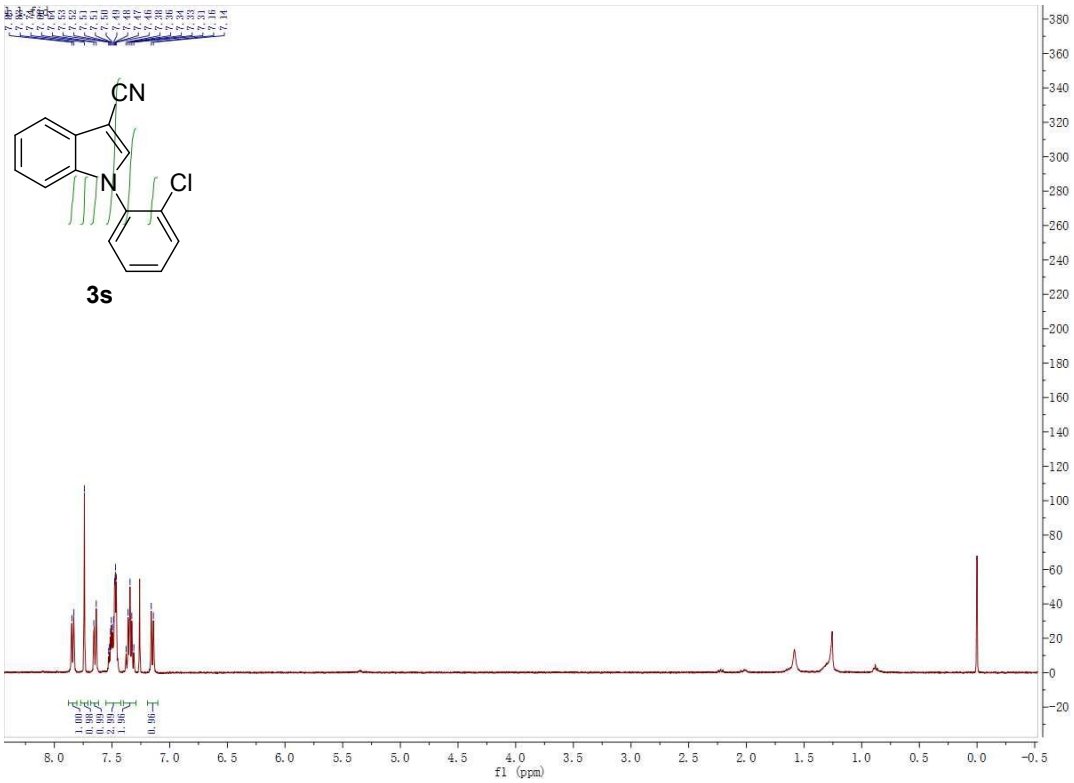


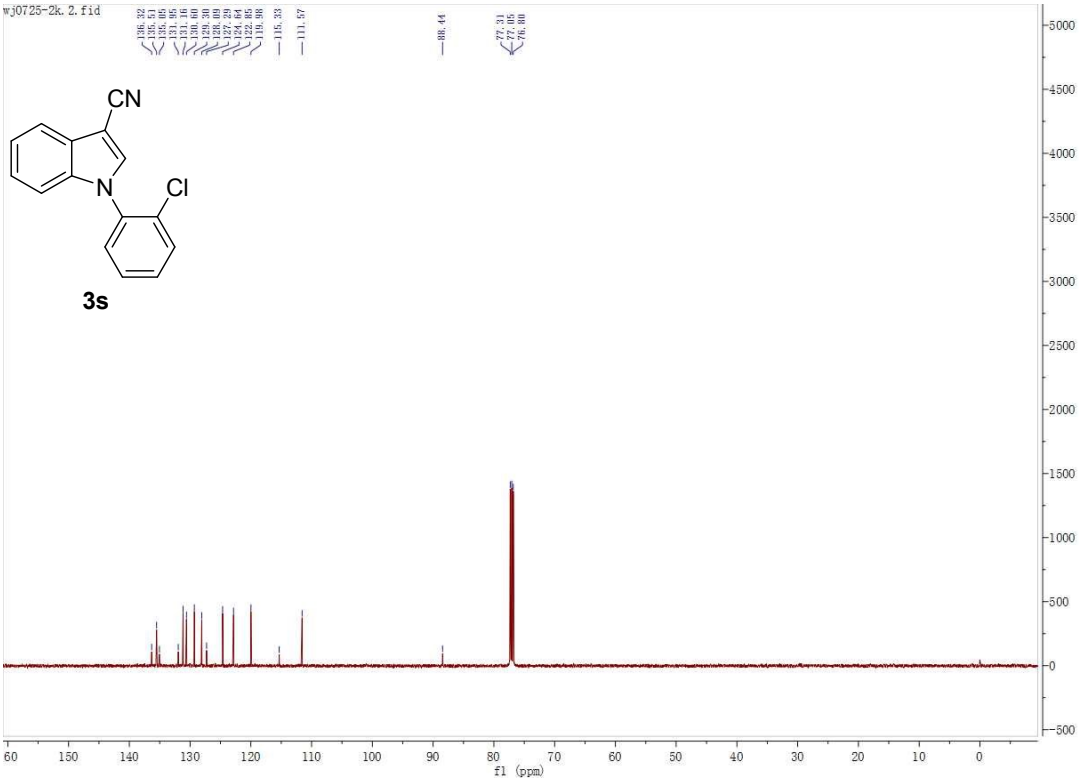
compound **3r**



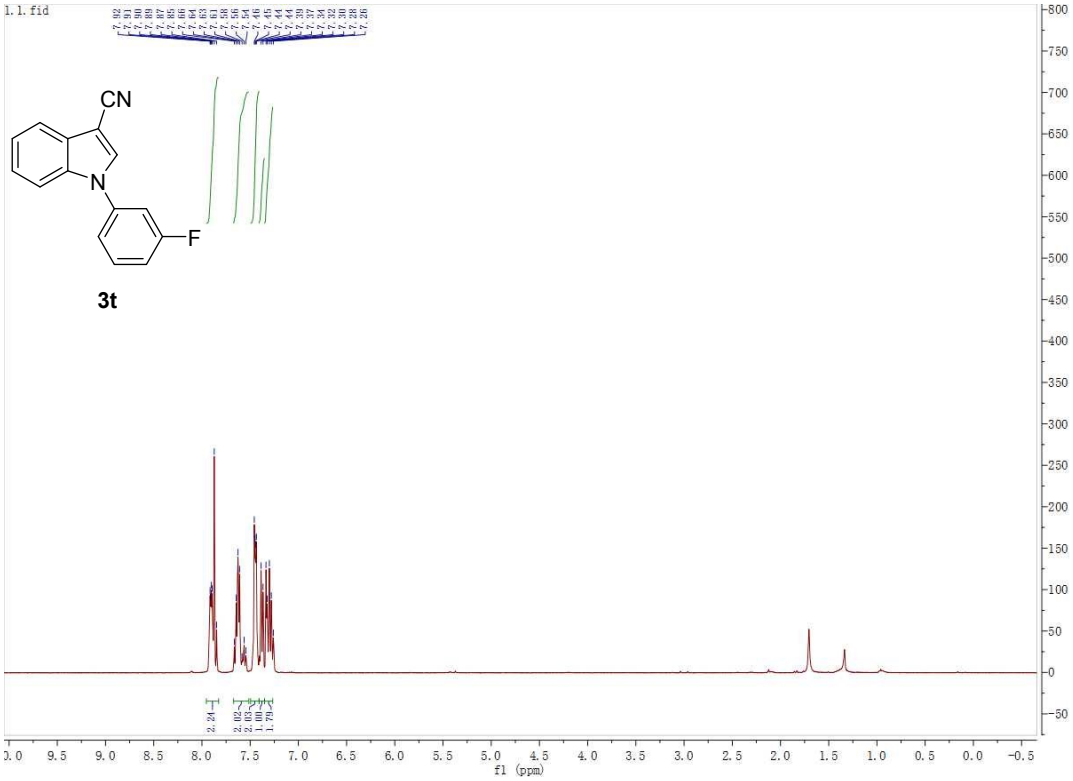


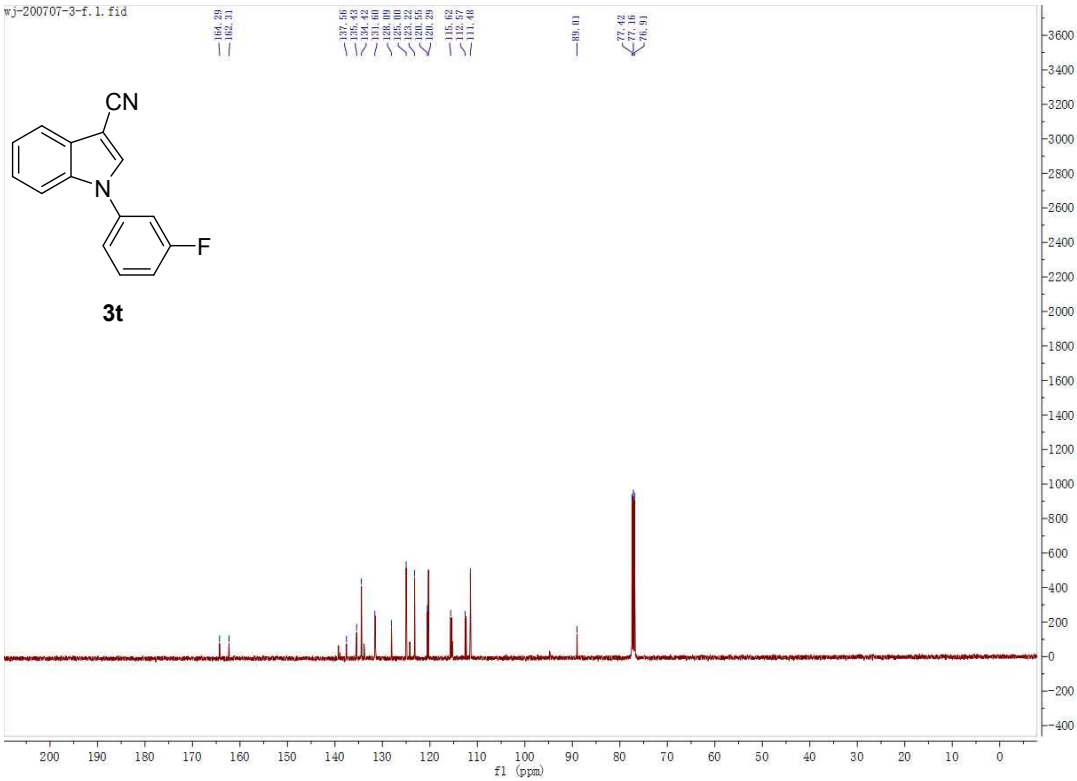
compound **3s**



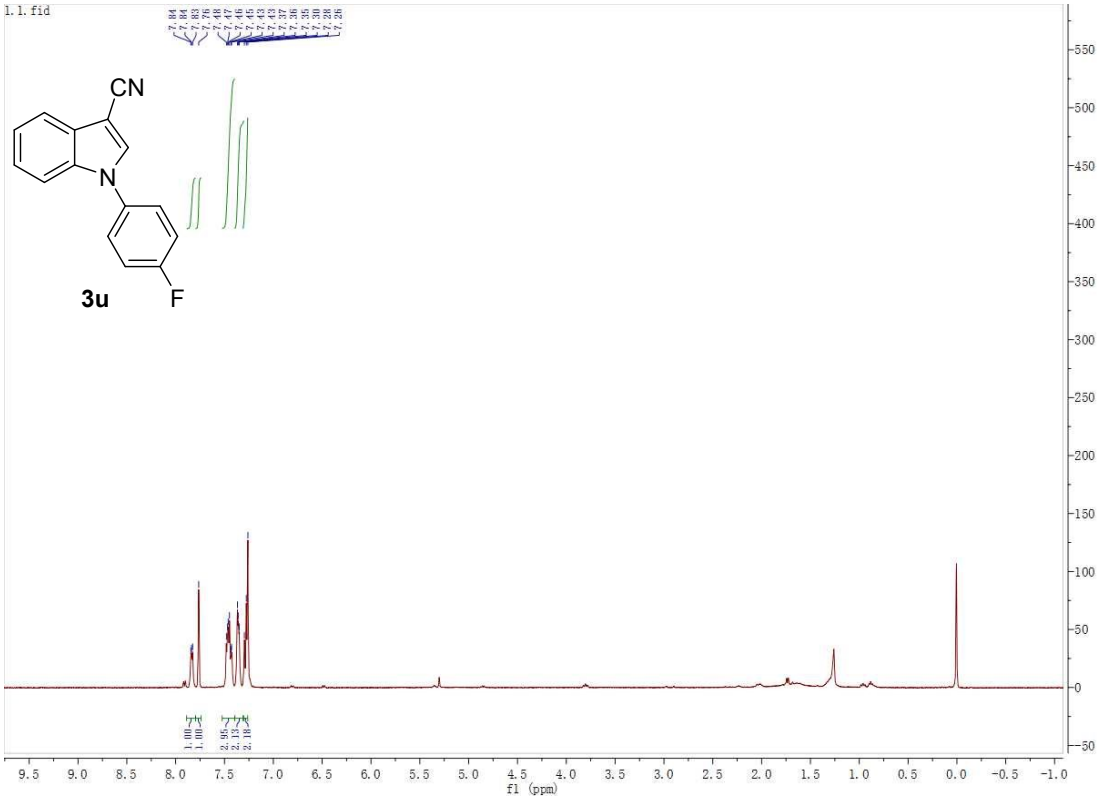


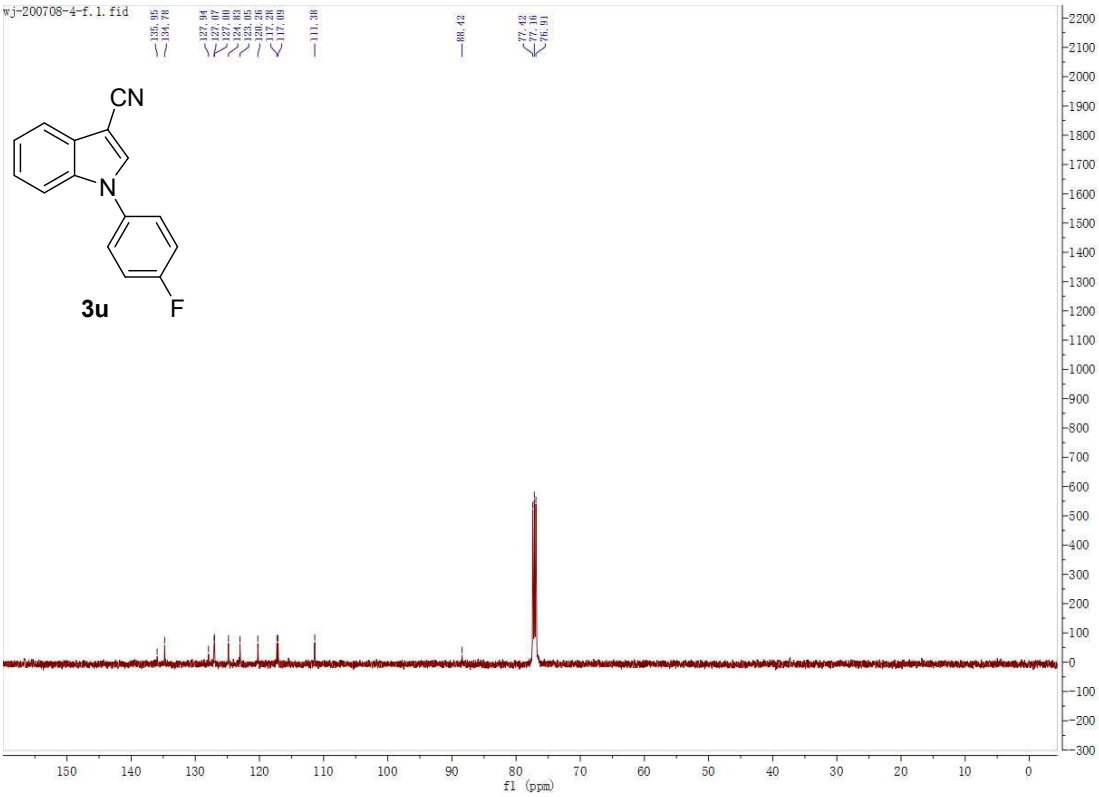
compound **3t**



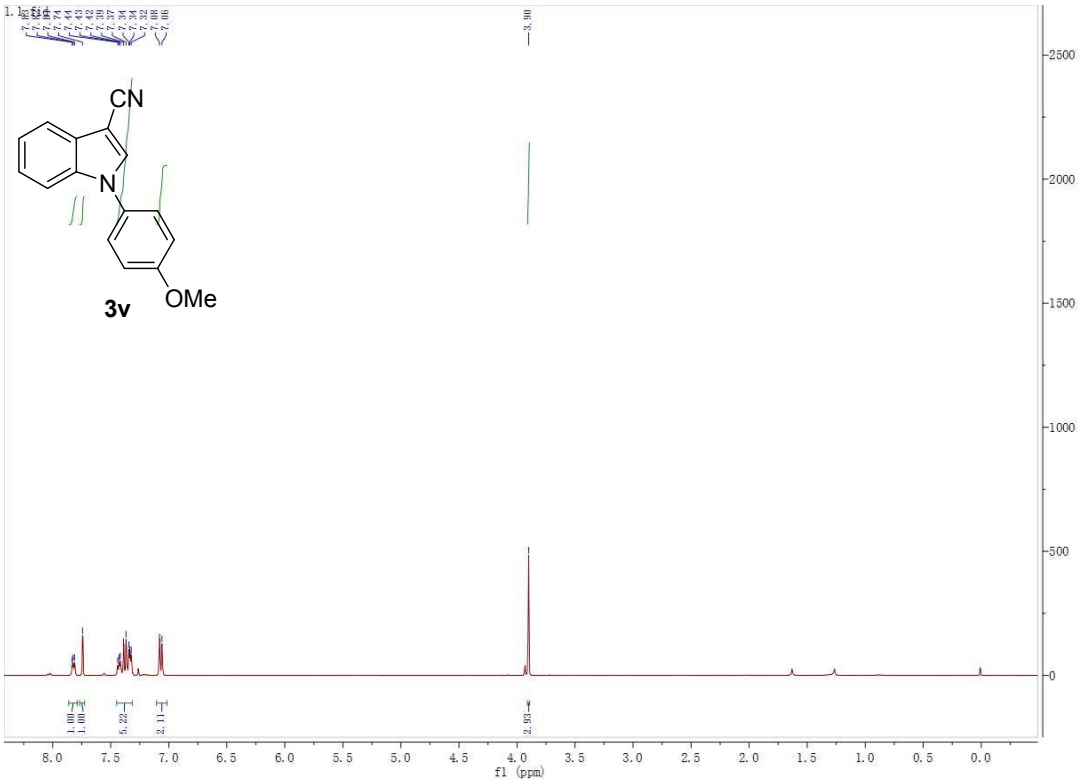


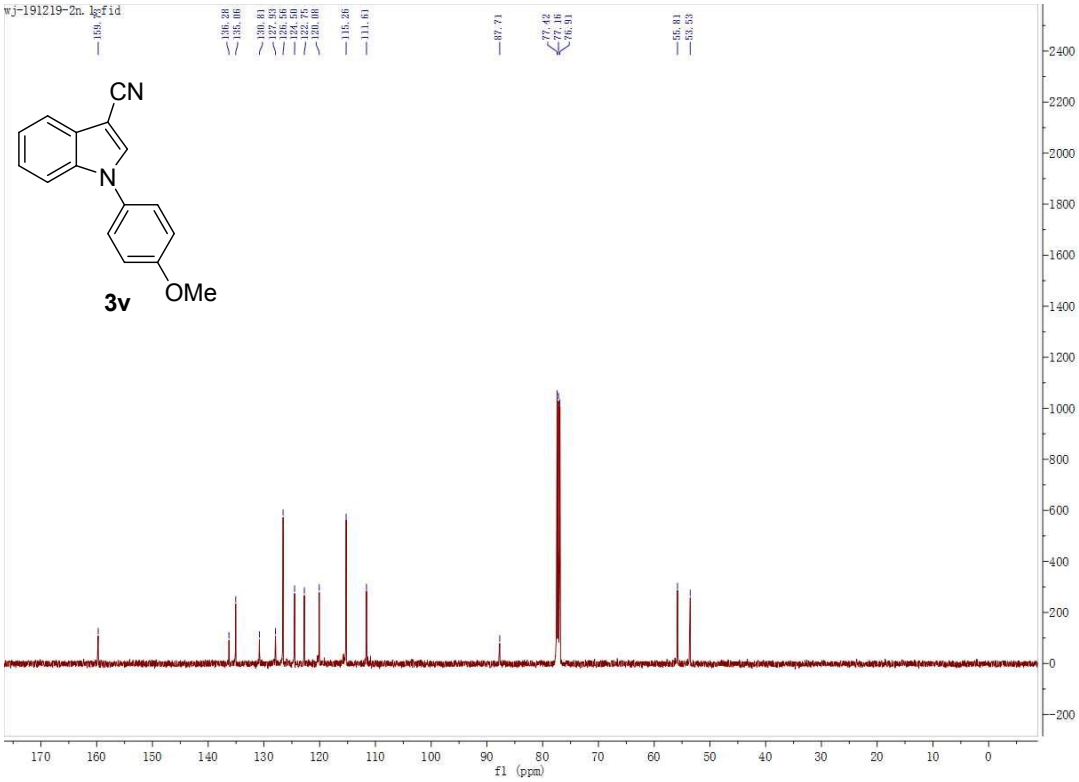
compound **3u**



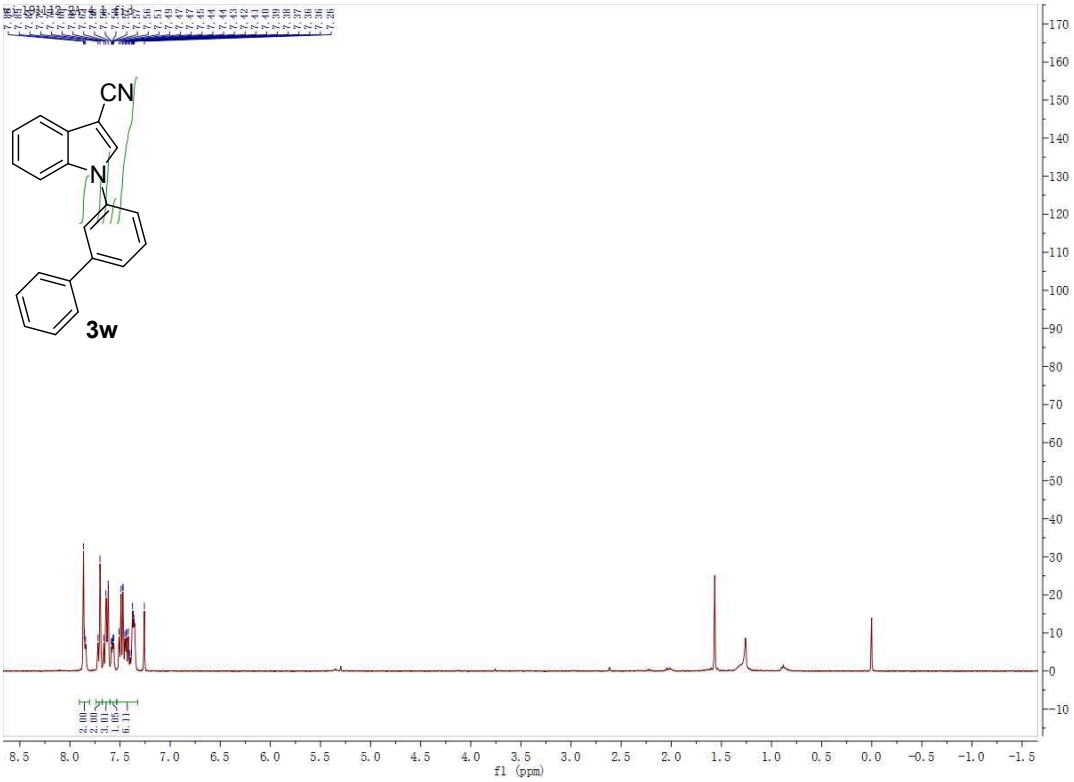


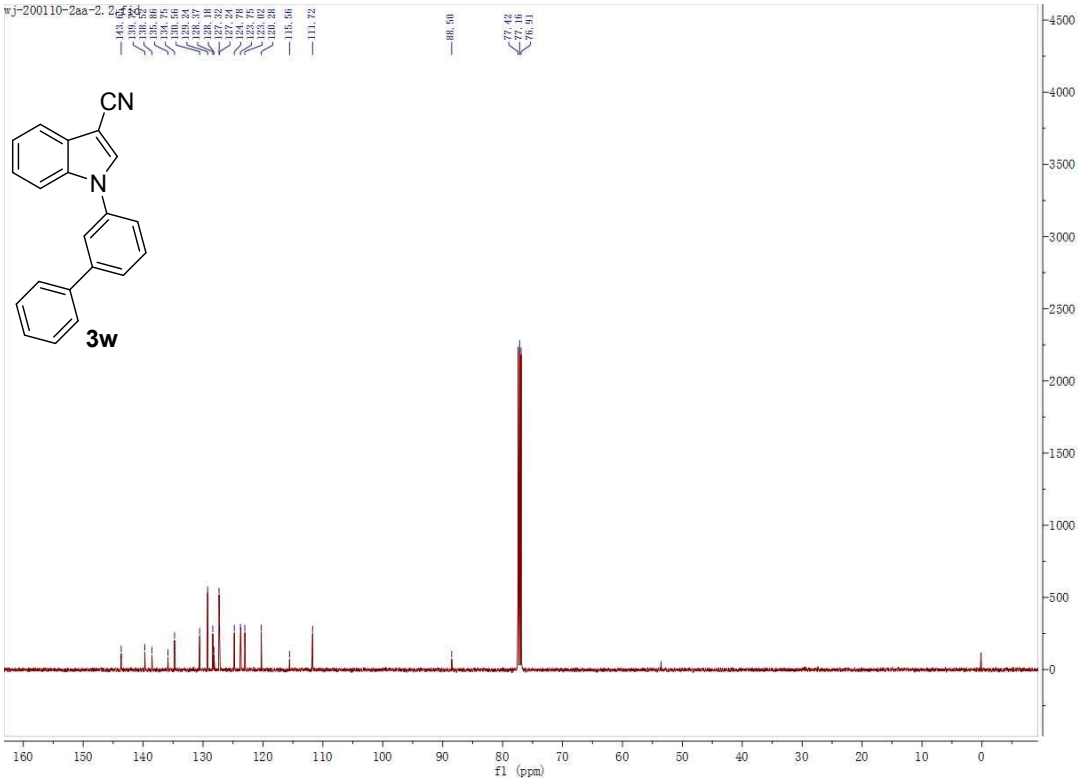
compound **3v**


CN
N
OMe
3v
3.90
1.00
1.00
5.22
2.11
2.93
f1 (ppm)

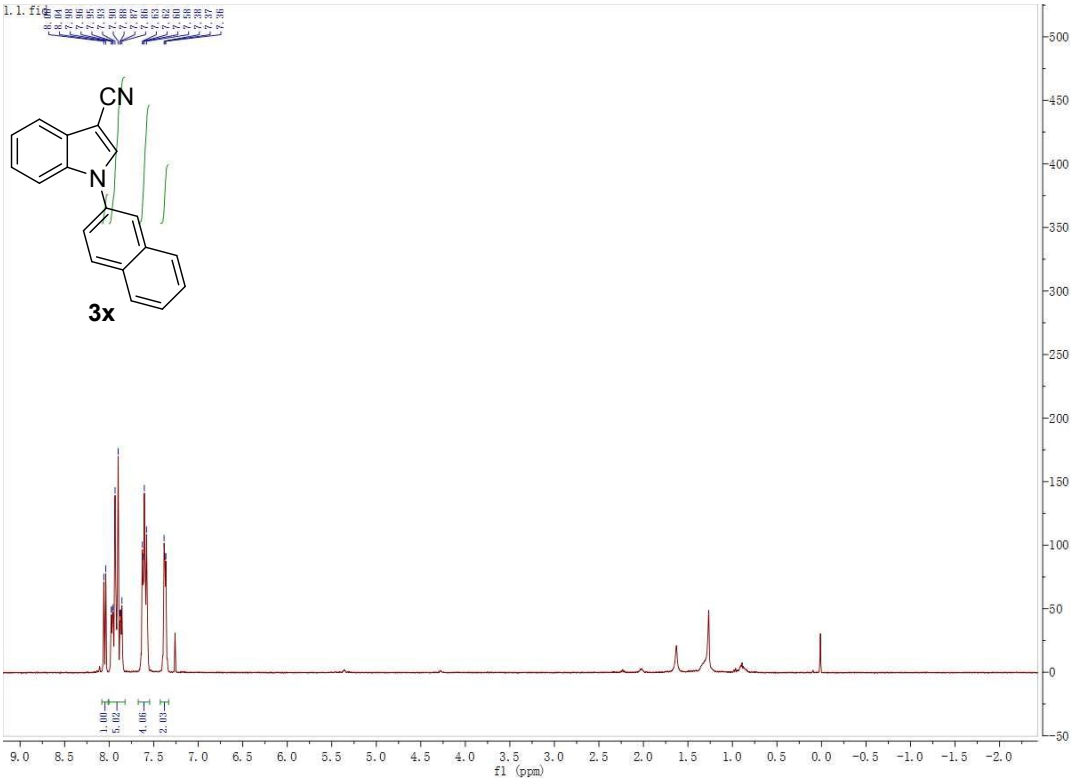

wj-191219-2n.1.fid
159.
136.28
135.06
130.81
127.93
126.56
124.51
122.75
120.08
115.26
111.63
87.71
77.42
77.16
76.91
55.81
55.53
CN
N
OMe
3v
f1 (ppm)

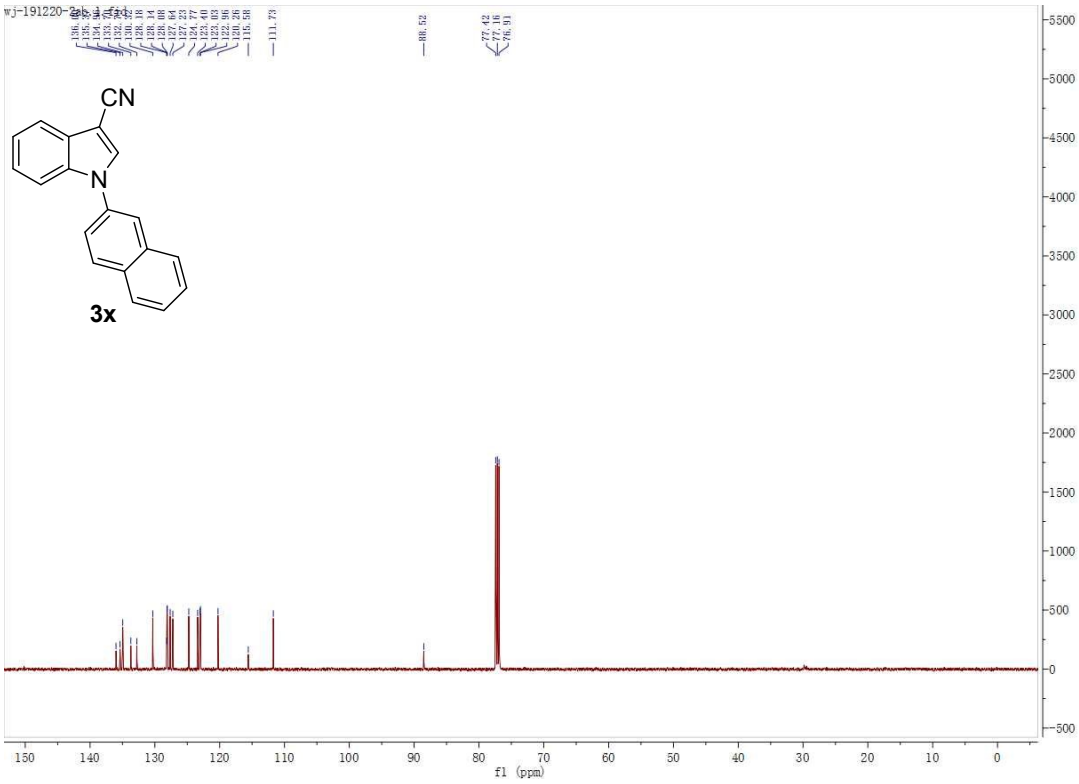
compound **3w**



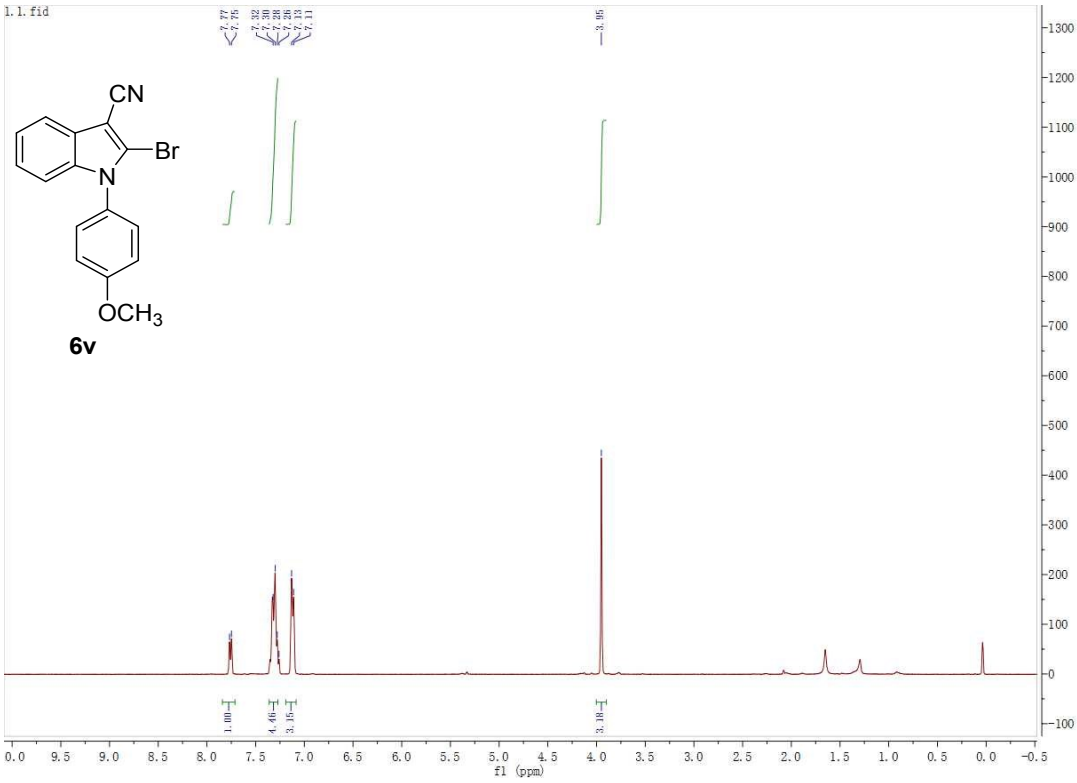


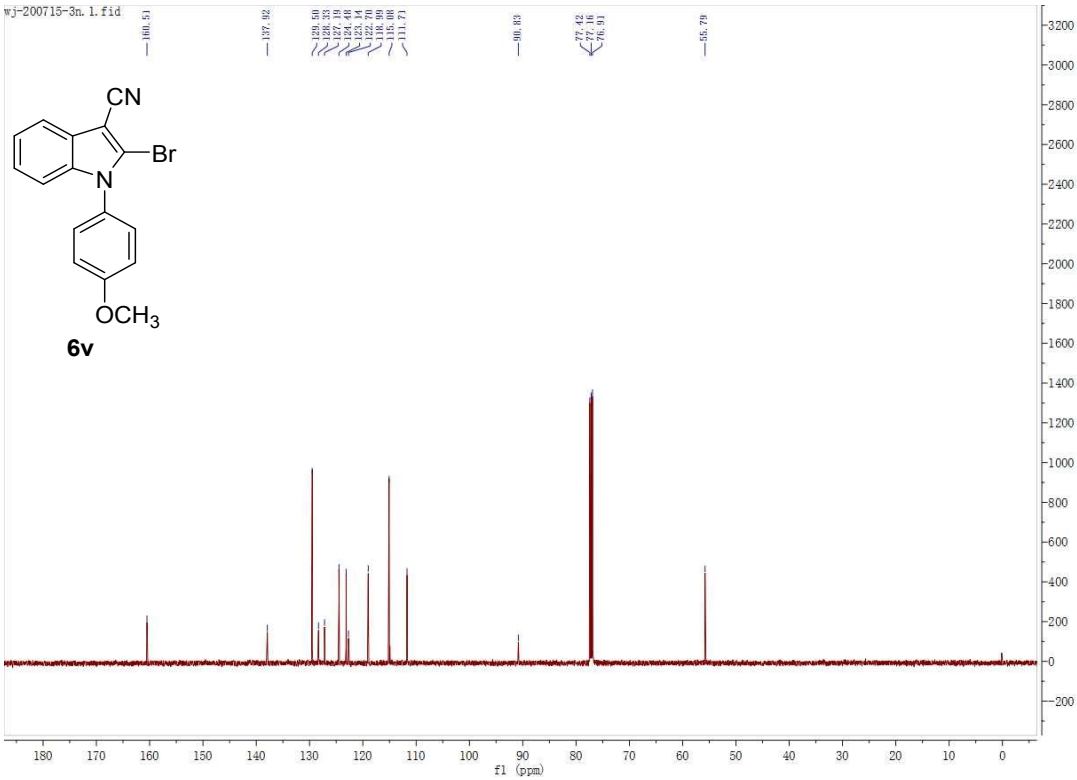
compound **3x**



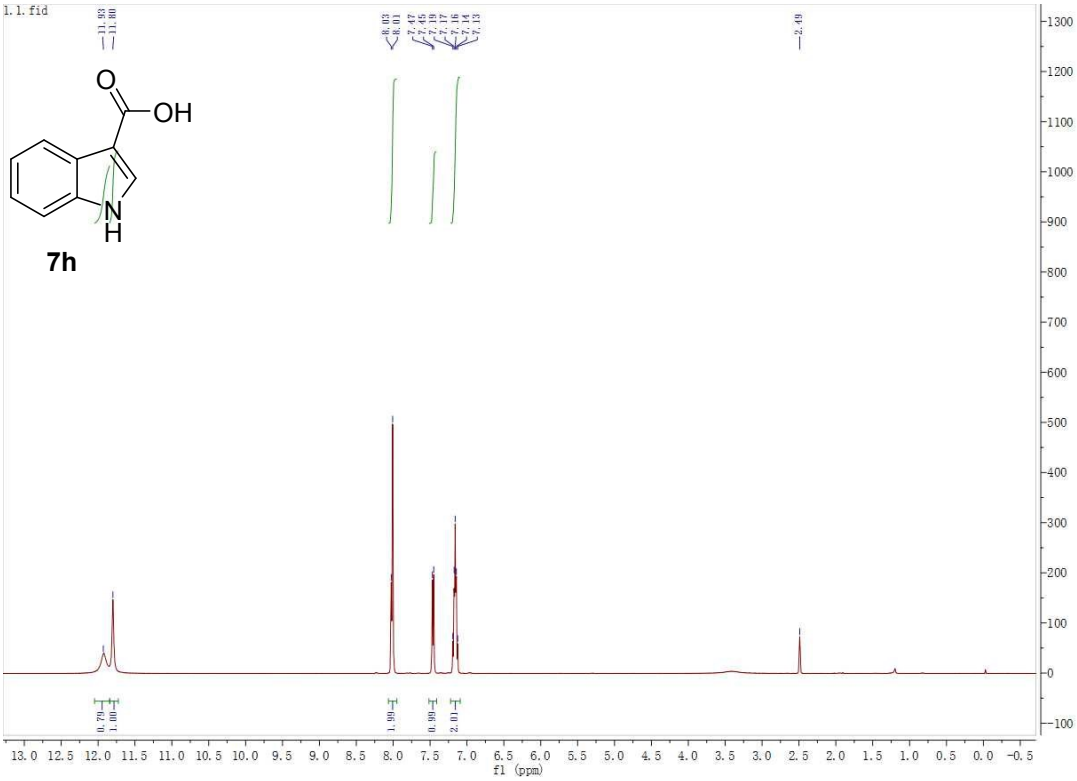


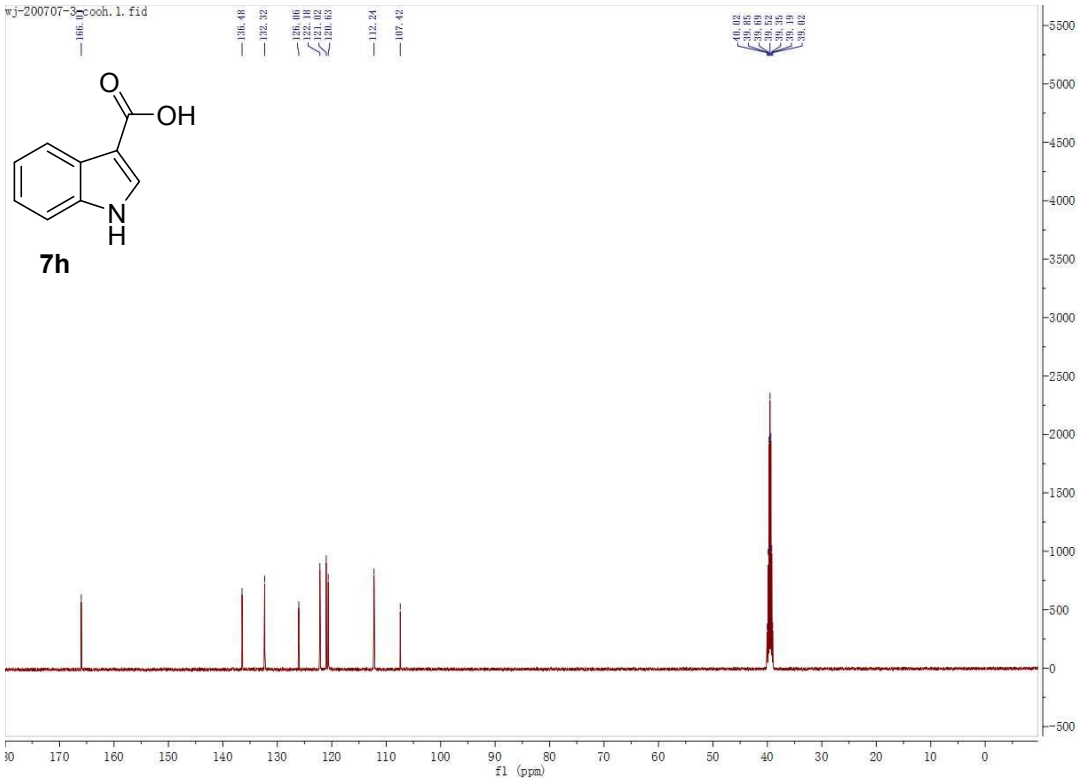
compound **6v**


1.1.fid
7.77
7.75
7.32
7.30
7.28
7.26
7.13
7.11
3.95
CN
Br
N
OCH3
6v
1.00
4.40
3.15
3.18
f1 (ppm)

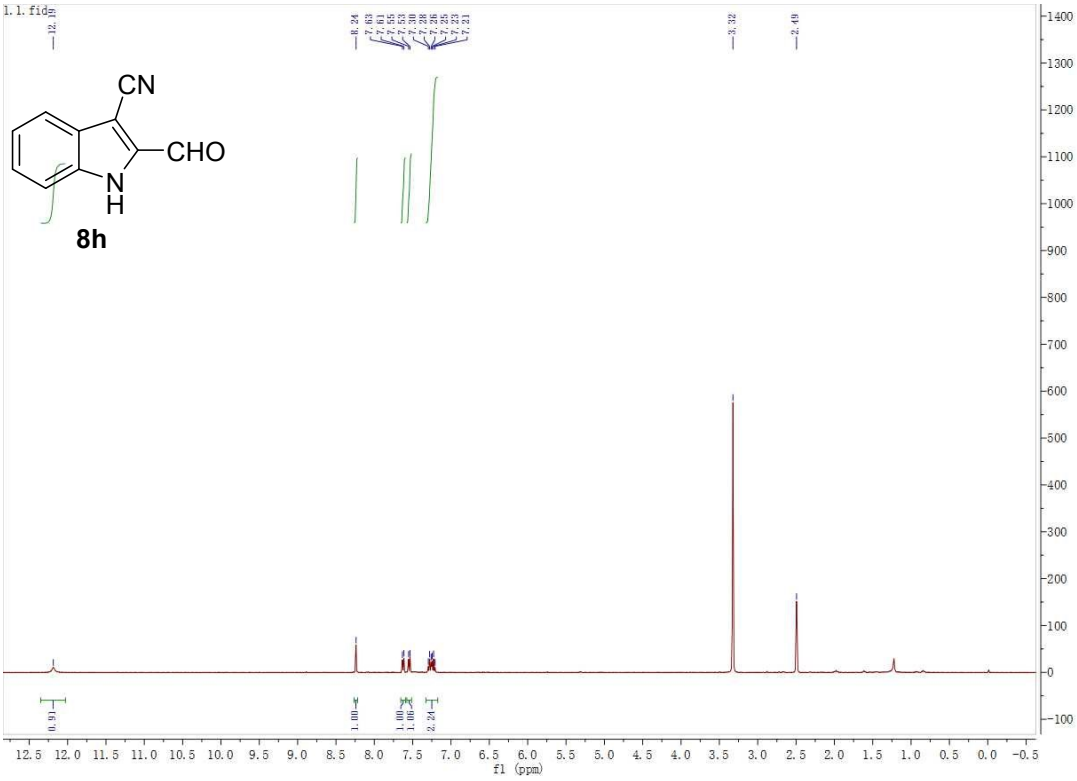

wj-200715-3n.1.fid
160.51
137.92
129.50
126.33
122.19
122.19
124.48
123.14
122.70
118.89
118.89
115.08
111.71
90.83
77.42
77.15
76.91
55.79
CN
Br
N
OCH3
6v
f1 (ppm)

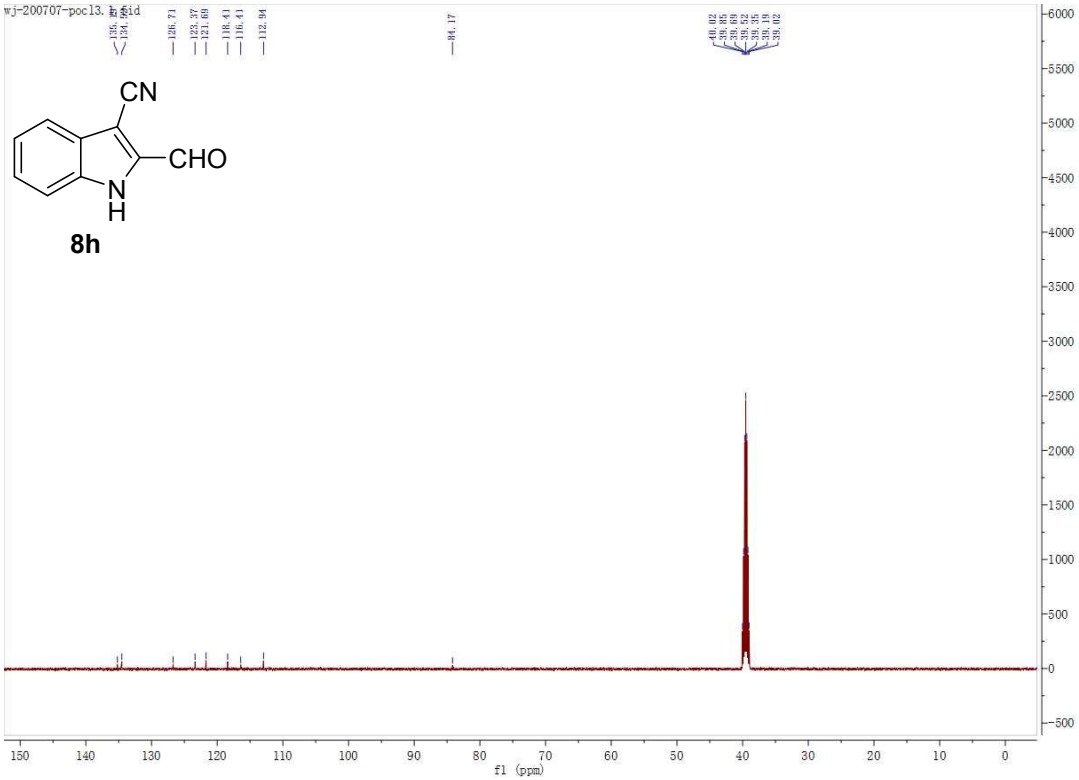
compound **7h**


1.1.fid
11.93
11.80
8.03
8.01
7.47
7.45
7.19
7.17
7.16
7.14
7.13
2.49
O
OH
N
H
7h
0.79
1.00
1.99
0.99
2.01
f1 (ppm)

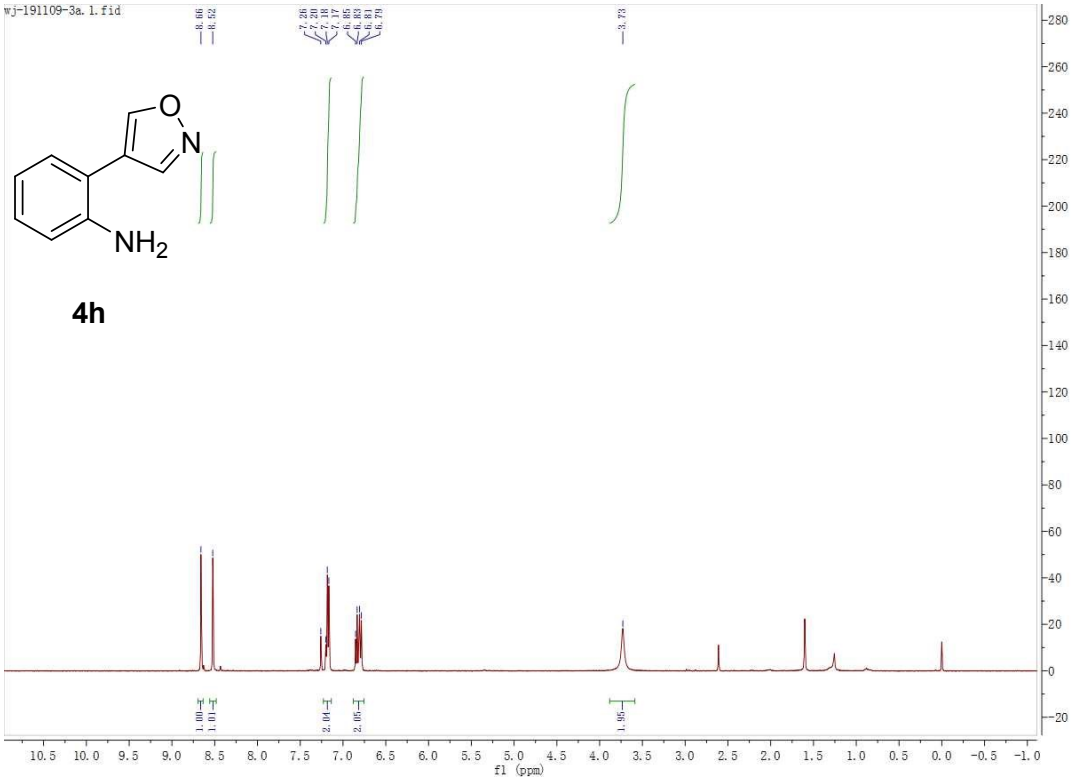

wj-200707-3-cooh.1.fid
166.0
136.48
132.32
126.86
122.38
121.02
120.63
112.24
107.42
40.02
39.85
39.69
39.52
39.35
39.19
39.02
O
OH
N
H
7h
f1 (ppm)

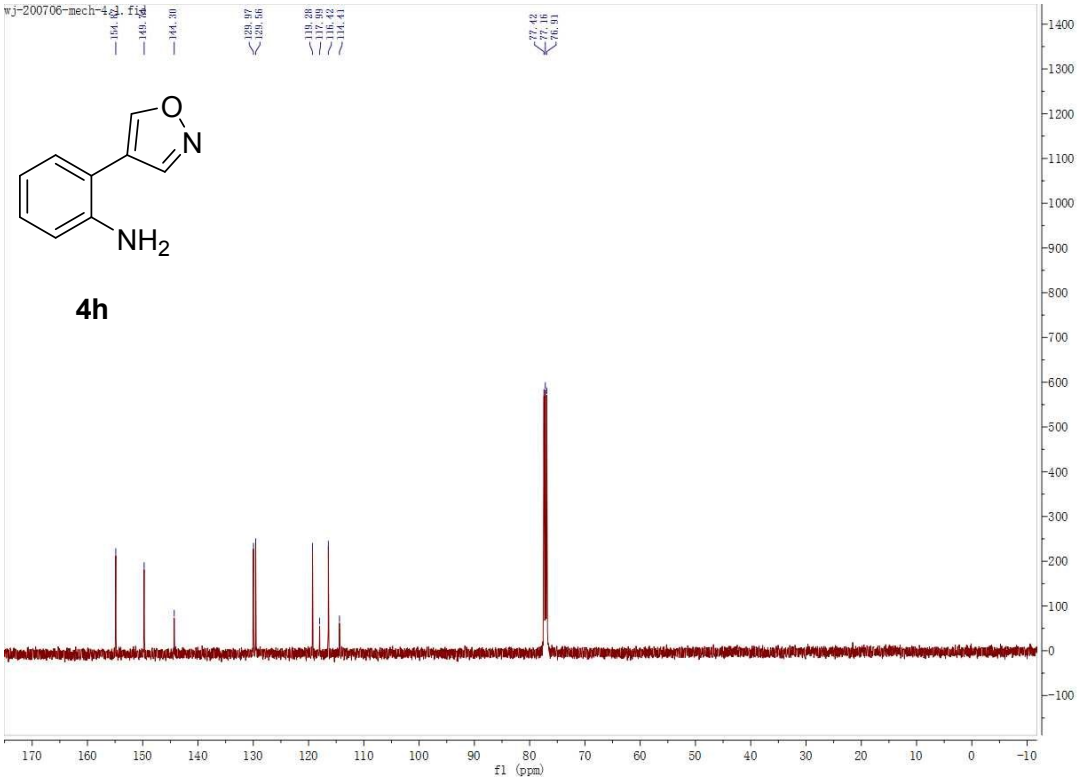
compound **8h**


CN
CHO
N
H
8h
12.91
8.24
7.63
7.61
7.55
7.55
7.53
7.30
7.28
7.26
7.25
7.23
7.21
3.32
2.49
0.91
1.00
1.00
1.06
2.24
f1 (ppm)

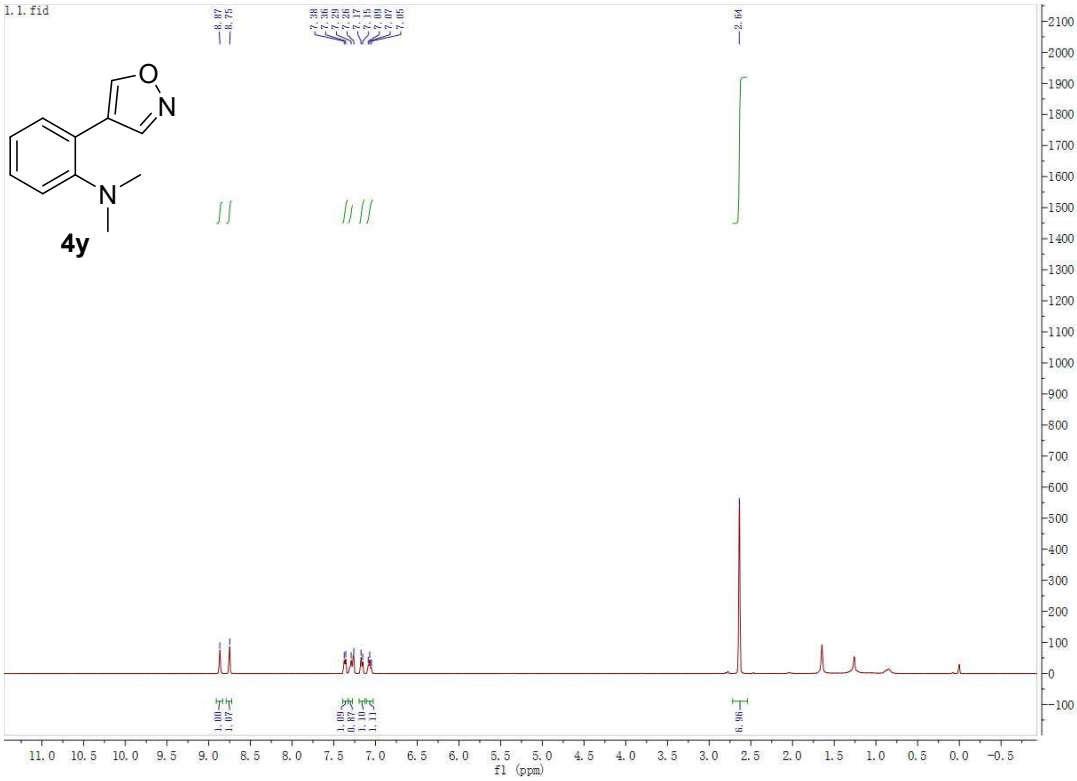

wj-200707-pocl3.1.fid
135.47
134.92
126.71
123.37
121.69
118.41
116.41
112.94
84.17
40.02
39.85
39.69
39.52
39.35
39.19
39.02
CN
CHO
N
H
8h
f1 (ppm)

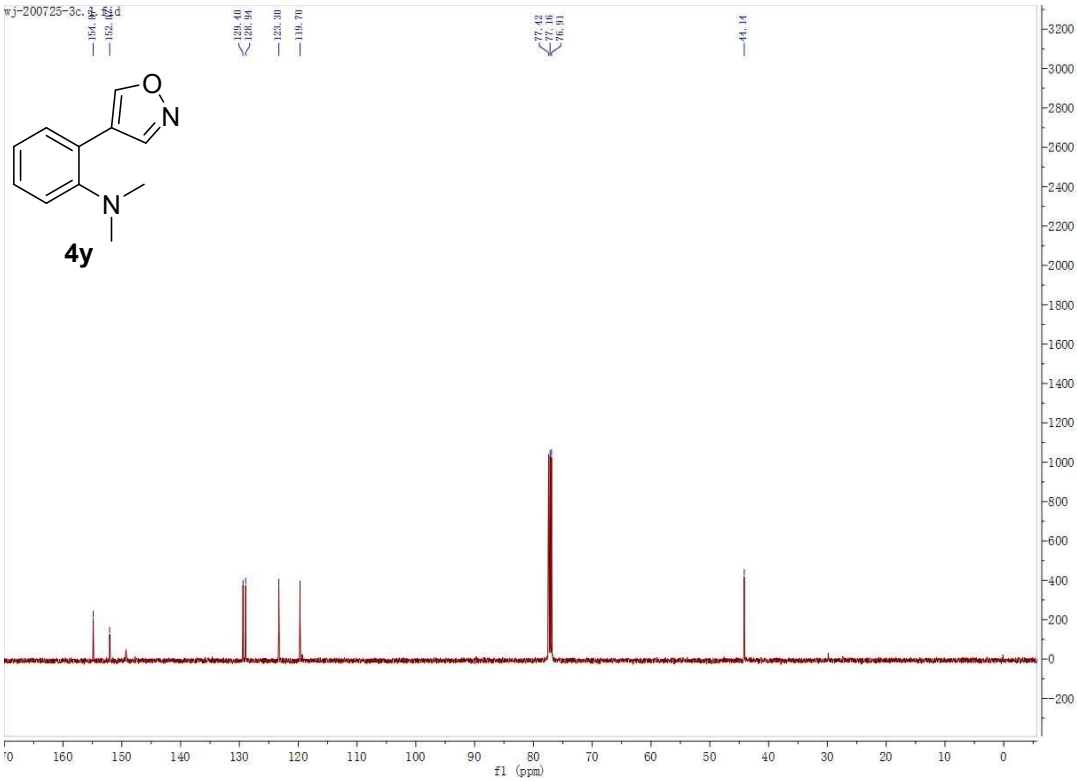
compound **4h**


wj-191109-3a.1.fid
8.66
8.52
7.26
7.20
7.18
7.17
6.85
6.83
6.81
6.79
3.73
O
N
NH2
4h
1.00
1.01
2.04
2.05
1.95
f1 (ppm)

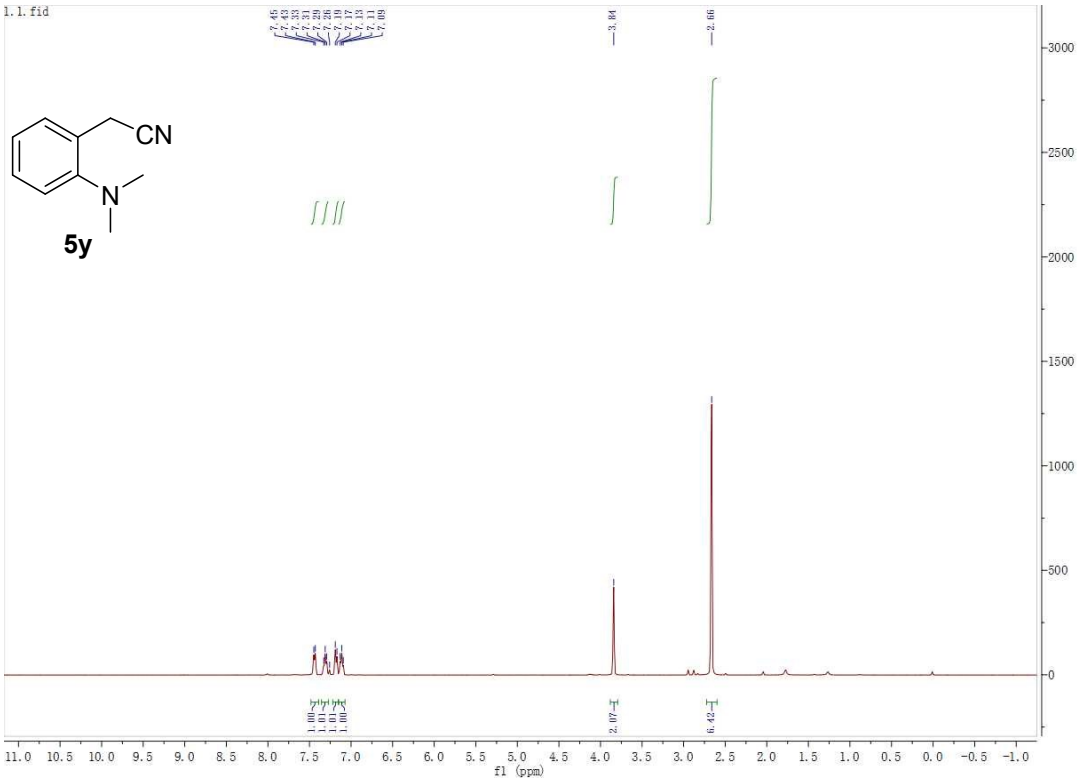

wj-200706-mech-4z.fid
154.62
149.76
144.30
129.97
129.56
119.28
117.89
116.42
114.41
77.42
77.16
76.91
O
N
NH2
4h
f1 (ppm)

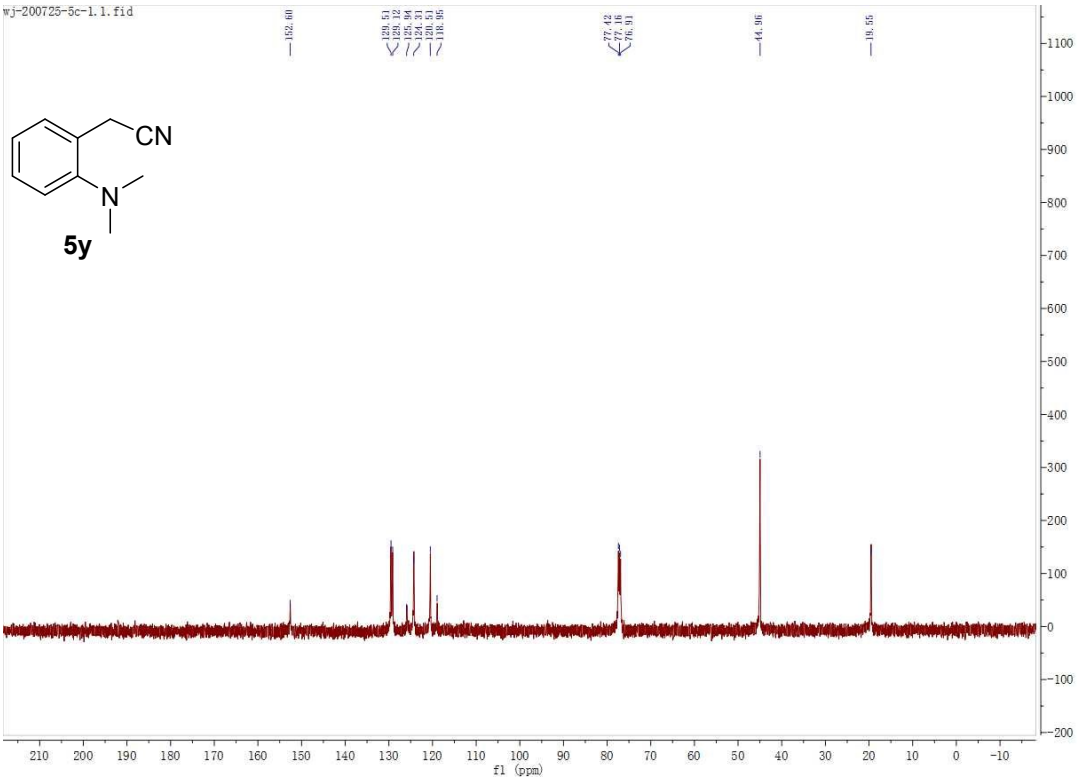
compound **4y**





compound **5y**


1.1.fid
CN
N
5y
7.45
7.43
7.35
7.33
7.29
7.26
7.19
7.17
7.13
7.11
7.09
3.84
2.66
1.00
1.00
1.01
1.01
1.00
2.07
6.42
f1 (ppm)


wj-200725-5c-1.1.fid
CN
N
5y
152.60
129.51
129.12
125.94
124.31
120.51
118.95
77.42
77.16
76.91
44.96
19.56
f1 (ppm)