Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Three-Component Redox-Neutral 1,2-Alkylarylation of Vinylarenes involving C–H Functionalization enabled by Copper Catalysis

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General Methods and Materials:

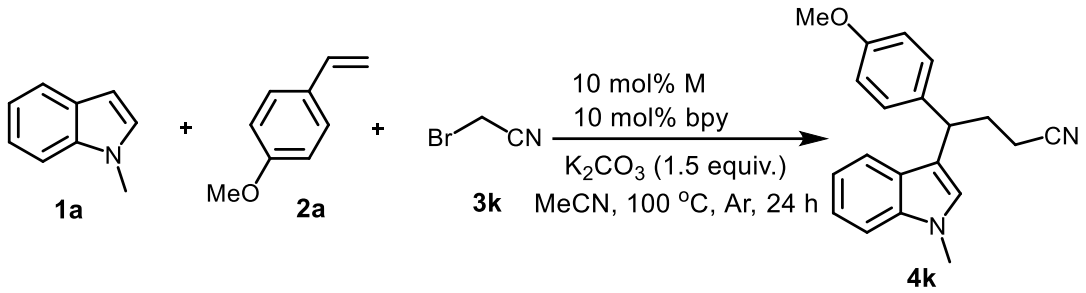
Unless specified, all reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions. For reactions that require heating, the heat source is SCILOGEX (type: MS-H-Pro+) magnetic stirrer with metal heating module. Styrene derivatives, halides, and indole materials were purchased from *Bidepharm, Leyan,* and directly used without further purification. All other reagents were purchased and used without further purification unless specified otherwise. Solvents for chromatography were technical grade and distilled prior to use.

Flash chromatography was performed using 200-300 mesh silica gel with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance (254 nm).

^{1}H NMR and ^{13}C NMR data were recorded on Bruker 300/400 M nuclear resonance spectrometers unless otherwise specified, respectively. Chemical shifts (δ) in ppm are reported as quoted relative to the residual signals of TMS or chloroform (^{1}H 0.00 ppm or ^{13}C 77.16 ppm). Multiplicities are described as: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet); and coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded with total proton decoupling. High resolution mass spectrometry (HRMS) analysis was performed using electrospray ionization (ESI) with a quadrupole-time of flight (QTOF) mass analyzer. HRMS (ESI) analysis was performed by The Analytical Instrumentation Center at College of Chemistry and Materials Science, Jinan University, and (HRMS) data were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

Conditions Screening

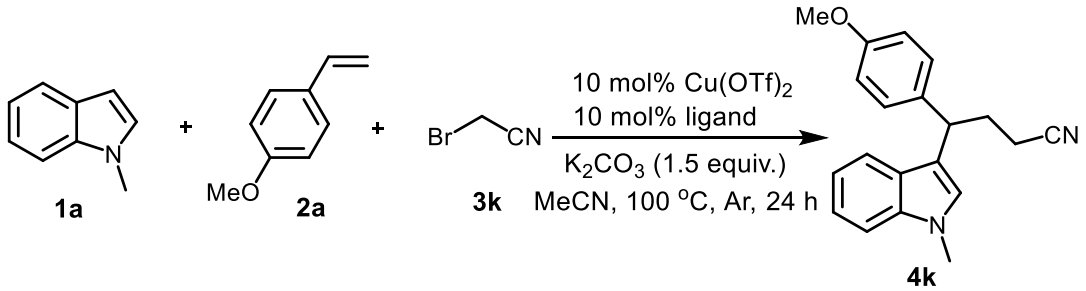
Table 1 Catalyst optimization



Entry	Catalyst	Yield of **4k**[a]
1	**$Cu(OTf)_2$**	**76%**
2	$Cu(OAc)_2$	27%
3	$CuCl_2$	Trace
4	CuCl	73%
5	$FeCl_2$	Trace
6	$Pd(OAc)_2$	N.D.
7	$NiBr_2$·glyme	N.D.
8	$CoCl_2$	Trace
9	$Fe(acac)_3$	N.D.
10	$In(OTf)_3$	N.D.
11	$ZnCl_2$	N.D.
12	CuOTf	29%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), M (10 mol%), bpy (10 mol%), K_2CO_3 (1.5 equiv.), MeCN (1.0 mL), 100 ℃, under Ar, 24 h, and ^{1}H NMR yield.

Table 2 Ligand optimization

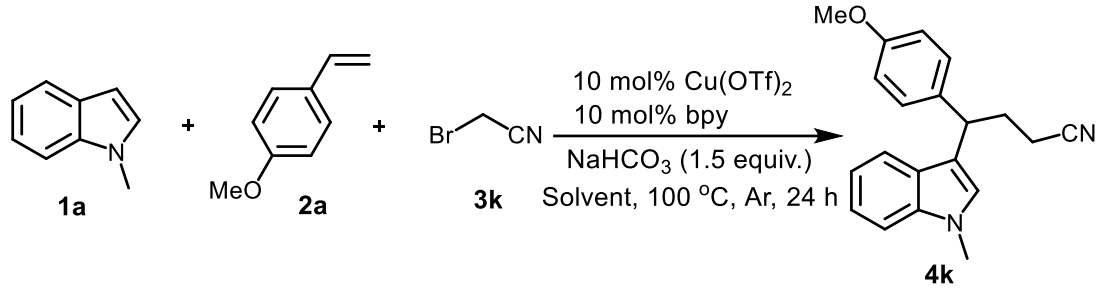


Entry	Ligand	Yield of **4k**[a]
1	**bpy**	**76%**
2	1,10-phen	73%

3	2,2'-biquinoline	15%
4	4,7-diphenyl-1,10-phenanthroline	68%
5	4,4'-dimethoxybpy	65%
6	bathocuproine	13%
7	5,5'-dimethylbpy	17%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), K_2CO_3 (1.5 equiv.), MeCN (1.0 mL), 100 ℃, under Ar, 24 h, and ^1H NMR yield.

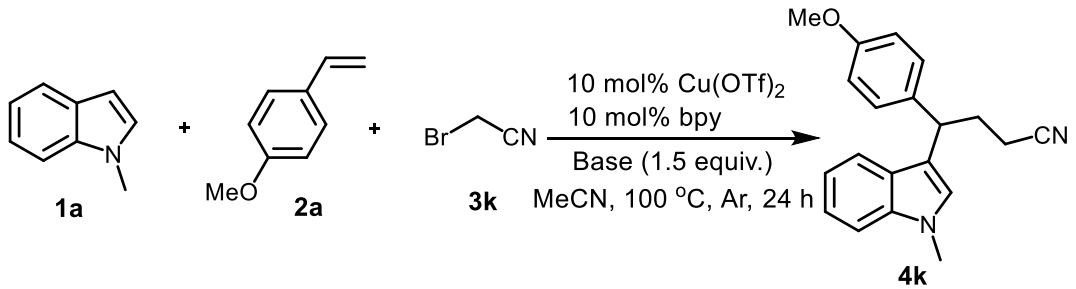
Table 3 Solvent optimization



Entry	Solvent	Yield of **4k**[a]
1	1,4-dioxane	72%
2	**MeCN**	**92%**
3	DMF	90%
4	DCE	32%
5	PhMe	73%
6	MTBE	73%
7	DCM	64%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (1.5 equiv.), solvent (1.0 mL), 100 ℃, under Ar, 24 h, and ^1H NMR yield.

Table 4 Base optimization

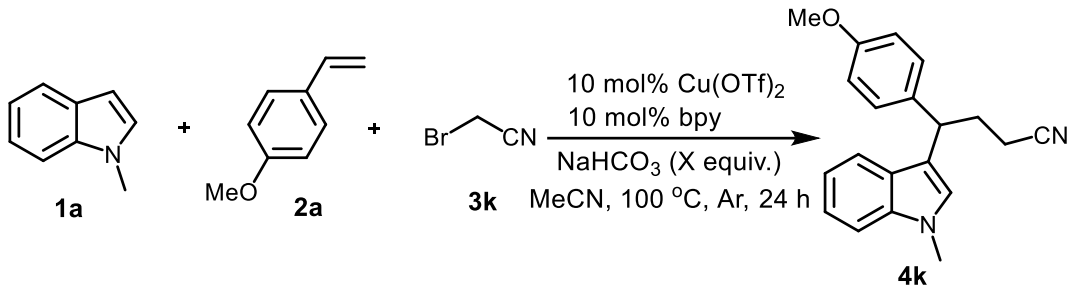


Entry	Base	Yield of **4k**[a]

1	K_3PO_4	65%
2	Li_2CO_3	27%
3	Na_2CO_3	77%
4	K_2CO_3	76%
5	**$NaHCO_3$**	**92%**
6	$KHCO_3$	90%
7	CsF	59%
8	DMAP	Trace
9	Et_3N	Trace
10	DIPEA	76%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), base (1.5 equiv.), MeCN (1.0 mL), 100 ℃, under Ar, 24 h, and ^1H NMR yield.

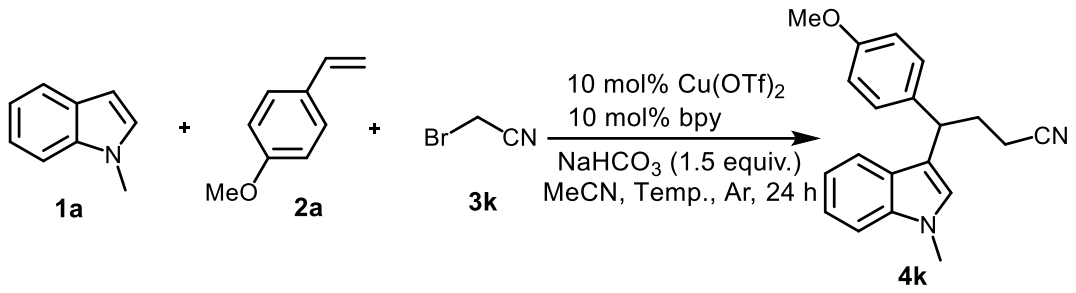
Table 5 Amounts of base



Entry	$NaHCO_3$ (equiv.)	Yield of **4k**[a]
1	0.2	29%
2	0.5	38%
3	0.8	62%
4	1.0	68%
5	1.2	77%
6	**1.5**	**92%**
7	2.0	81%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (X equiv.), MeCN (1.0 mL), 100 ℃, under Ar, 24 h, and ^1H NMR yield.

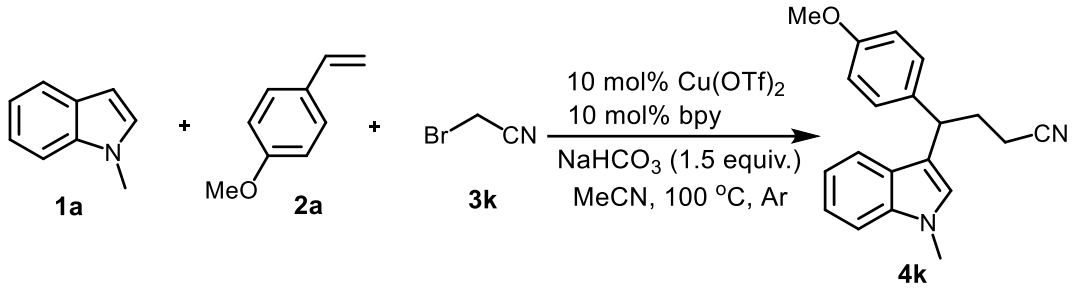
Table 6 Temperature optimization



Entry	Temperature (℃)	Yield of **4k**[a]
1	60	Trace
2	80	66%
3	**100**	**92%**
4	110	77%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (1.5 equiv.), MeCN (1.0 mL), under Ar, 24 h, and ^1H NMR yield.

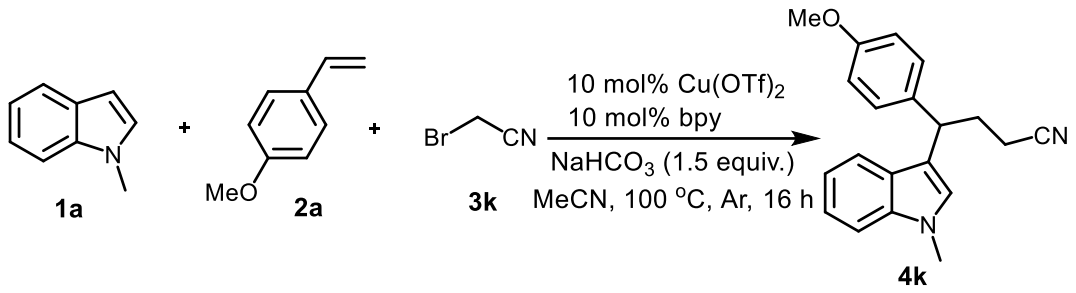
Table 7 Reaction time optimization



Entry	Time (h)	Yield of **4k**[a]
1	4	78%
2	8	84%
3	**16**	**94%**
4	24	92%

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (1.5 equiv.), MeCN (1.0 mL), 100 ℃, under Ar, and ^1H NMR yield.

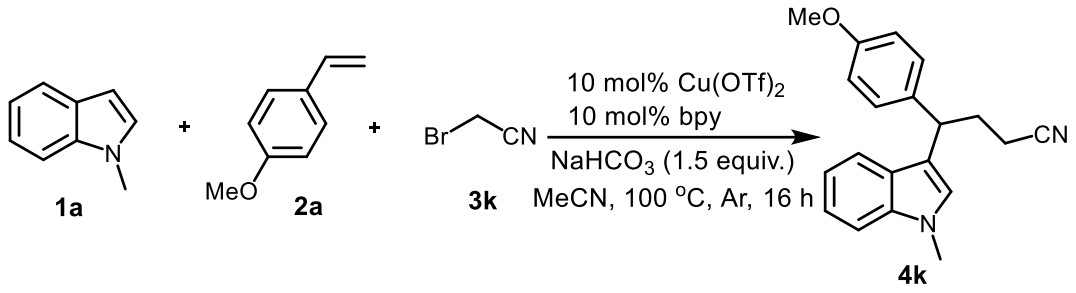
Table 8 Ratio of **1a**/**2a**/**3k** optimization



Entry	**1a**	**2a**	**3k**	Yield of **4k**[a]
1	1.0	1.0	1.0	59%
2	1.0	1.0	2.0	78%
3	**1.0**	**1.5**	**2.0**	**94%**
4	1.0	2.0	2.0	93%
5	1.5	1.0	2.0	77%

[a] 0.2 mmol scale, using **1a** (X equiv.), **2a** (Y equiv.), **3k** (Z equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (1.5 equiv.), MeCN (1.0 mL), 100 ℃, under Ar, 16 h, and ^1H NMR yield.

Table 9 Control experiments



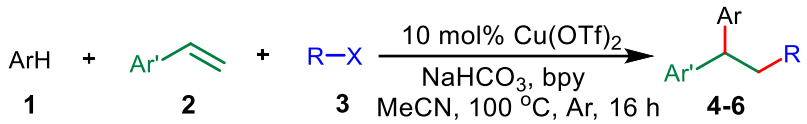
Entry	Variation from standard conditions	Yield of **4k**[a]
1	Without $Cu(OTf)_2$	N.D.
2	Without $NaHCO_3$	N.D.
3	Without bpy	<5%
4	**None**	**94%**

[a] 0.2 mmol scale, using **1a** (1.0 equiv.), **2a** (1.5 equiv.), **3k** (2.0 equiv.), $Cu(OTf)_2$ (10 mol%), bpy (10 mol%), $NaHCO_3$ (1.5 equiv.), MeCN (1.0 mL), 100 ℃, 16 h, under Ar, and ^1H NMR yield.

Note:

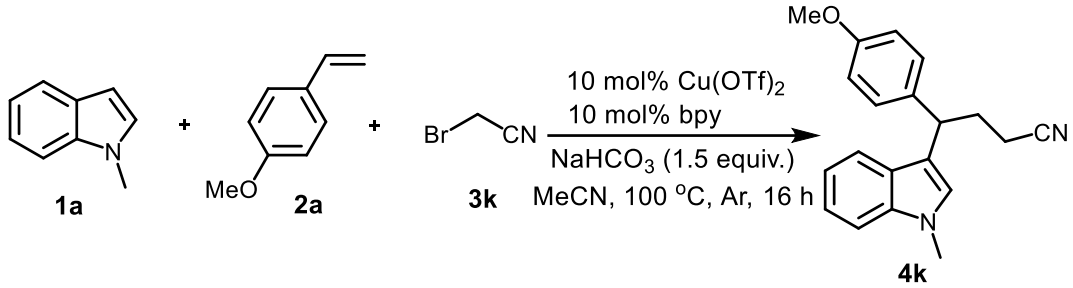
bpy = 2,2-bispyridine; DCE = 1,2-dichloroethane; MTBE = methyl *tert*-butyl ether; DMAP = 4-dimethylaminopyridine; DIPEA = N,N-diisopropylethylamine; N.D. = Not detected.

General Procedure for Three-Component 1,2-Alkylarylation



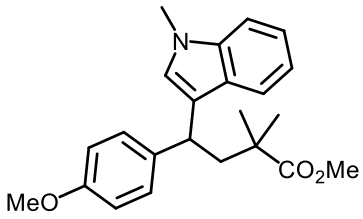
Arene **1** (0.2 mmol, 1.0 equiv.), $Cu(OTf)_2$ (0.02 mmol, 10 mol%), bpy (0.02 mmol, 10 mol%), and $NaHCO_3$ (0.3 mmol, 1.5 equiv.) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then alkene **2** (0.3 mmol, 1.5 equiv.) and halide **3** (0.4 mmol, 2.0 equiv.) in MeCN (1.0 mL) were added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (10 mL × 3). The organic layer was washed with saturated brine (10 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 20:1) to afford the desired products **4**-**6**.

Scale-up Reaction

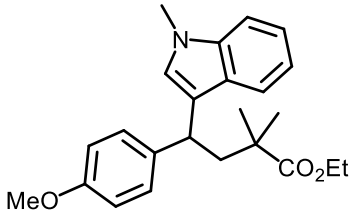


N-methyl indole **1a** (5.0 mmol, 624 μL), $Cu(OTf)_2$ (0.5 mmol, 180.8 mg), bpy (0.5 mmol, 78.1 mg), and $NaHCO_3$ (7.5 mmol, 630.1 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then alkene **2a** (7.5 mmol, 997 μL) and bromoacetonitrile **3k** (10.0 mmol, 697 μL) in MeCN (25 mL) were added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (50 mL) was added to the above solution, and the mixture was extracted with EtOAc (50 mL × 3). The organic layer was washed with saturated brine (50 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 20:1) to afford the desired product **4k**, 1.1 g, 72% yield.

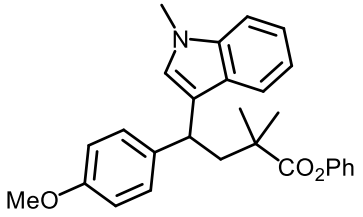
Characterization of Products



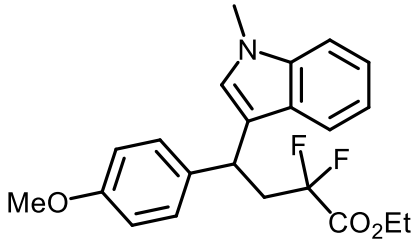
methyl 4-(4-methoxyphenyl)-2,2-dimethyl-4-(1-methyl-1H-indol-3-yl)butanoate (4a). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 68.0 mg, yield: 93%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.52 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 2H), 6.75 (s, 1H), 4.25 (t, *J* = 6.8 Hz, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 3.15 (s, 3H), 2.42 (d, *J* = 7.0 Hz, 2H), 1.25 (s, 3H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.9, 157.9, 137.3, 136.8, 129.2, 127.0, 126.2, 121.6, 119.5, 119.5, 118.8, 113.6, 109.2, 55.3, 51.3, 46.8, 42.0, 38.8, 32.7, 26.8, 25.6. IR (ATR): 2948, 2836, 1727, 1472, 1302, 1325, 1245, 1035, 1014, 794 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{27}NO_3Na$ 388.1883; Found 388.1898.



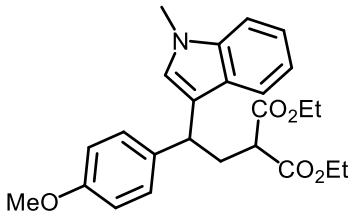
ethyl 4-(4-methoxyphenyl)-2,2-dimethyl-4-(1-methyl-1H-indol-3-yl)butanoate (4b).[1] Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 70.6 mg, yield: 93%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 7.18 (d, *J* = 5.5 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 6.9 Hz, 1H), 6.78 (d, *J* = 8.3 Hz, 2H), 6.74 (s, 1H), 4.26 (t, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.65 (s, 3H), 3.61-3.56 (m, 2H), 2.47-2.35 (m, 2H), 1.23 (s, 3H), 1.15 (s, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.5, 157.8, 137.2, 137.0, 129.2, 127.0, 126.2, 121.5, 119.6, 119.5, 118.7, 113.5, 109.2, 60.1, 55.2, 46.7, 42.0, 38.8, 32.6, 26.6, 25.8, 14.0.



phenyl 4-(4-methoxyphenyl)-2,2-dimethyl-4-(1-methyl-1H-indol-3-yl)butanoate (4c). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 30.8 mg, yield: 36%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.30-7.22 (m, 5H), 7.20-7.13 (m, 2H), 7.03 (t, *J* = 6.9 Hz, 1H), 6.80-6.77 (m, 3H), 6.67 (d, *J* = 7.9 Hz, 2H), 4.39 (t, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 3.65 (s, 3H), 2.66 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.52 (dd, *J* = 14.1, 8.1 Hz, 1H), 1.36 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.1, 158.1, 151.0, 137.3, 129.2, 129.1, 127.1, 126.4, 125.4, 121.7, 121.5, 119.6, 119.4, 118.9, 113.9, 109.3, 55.3, 46.6, 42.8, 39.0, 32.8, 26.5, 26.3. IR (ATR): 2931, 1593, 1510, 1372, 1325, 832, 740. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{29}NO_3Na$ 450.2040; Found 450.2051.

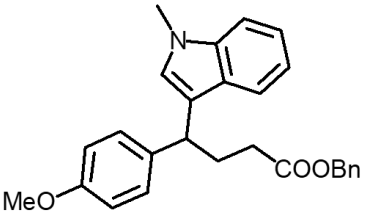


ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate (4d).[2] Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 51.1 mg, yield: 66%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.47 (d, *J* = 7.9 Hz, 1H), 7.27-7.18 (m, 4H), 7.04 (t, *J* = 7.0 Hz, 1H), 6.83-6.78 (m, 3H), 4.49 (t, *J* = 7.3 Hz, 1H), 3.76-3.67 (m, 8H), 3.05-2.83 (m, 2H), 1.06 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 137.4, 134.9, 129.1, 126.7, 126.5, 121.9, 119.5, 119.2, 117.2, 113.9, 112.7, 109.4, 62.7, 55.4, 40.9 (t, *J* = 23.3 Hz), 36.0, 32.8, 13.7; ^{19}F NMR (282 MHz, $CDCl_3$): δ -102.5 (d, *J* = 259.4 Hz), -104.3 (d, *J* = 259.4 Hz).

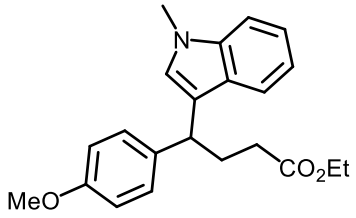


diethyl 2-(2-(4-methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)malonate (4e). Following the *General Procedure*, using **1a** (1.0 equiv.), **2a** (2.0 equiv.), **3e** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 34.7 mg, yield: 41%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.47 (d, *J* = 7.9 Hz, 1H), 7.25-7.16 (m, 4H), 7.02 (t, *J* = 7.1 Hz, 1H), 6.87-6.82 (m, 3H), 4.23-4.14 (m, 4H), 3.79-3.73 (m, 7H), 3.35 (dd, *J* = 8.2, 6.5 Hz, 1H), 2.85-2.75 (m, 1H), 2.61-2.46 (m, 1H), 1.28-1.23 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.7, 158.2, 137.4, 135.8, 129.0, 127.3, 126.1, 121.8, 119.7, 118.9, 117.8, 114.0,

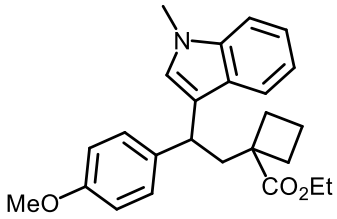
109.2, 61.5, 55.3, 50.6, 39.9, 35.2, 32.8, 14.2. IR (ATR): 2981, 1729, 1611, 1328, 1302, 1095, 830, 742 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{29}NO_5Na$ 446.1938; Found 446.1953.



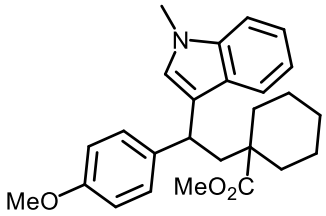
benzyl 4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate (4f). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 40.5 mg, yield: 49%, brown oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.41 (d, *J* = 7.9 Hz, 1H), 7.35-7.28 (m, 5H), 7.24-7.16 (m, 4H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.82-6.77 (m, 3H), 5.07 (s, 2H), 4.12 (t, *J* = 7.3 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 2.57-2.46 (m, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.32-2.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.6, 158.0, 137.3, 136.6, 136.1, 128.9, 128.6, 128.3, 128.3, 127.3, 125.9, 121.7, 119.7, 118.8, 113.9, 109.2, 66.2, 55.3, 41.4, 32.9, 32.7, 31.3. IR (ATR): 3032, 2852, 1732, 1610, 1483, 1328, 1176, 1151, 1013, 825 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{27}NO_3Na$ 436.1883; Found 436.1891.



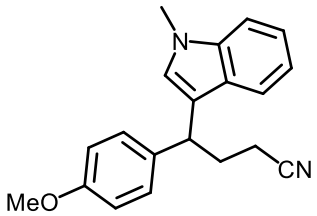
ethyl 4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate (4g). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 47.8 mg, yield: 68%, yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.44 (d, *J* = 7.9 Hz, 1H), 7.26-7.16 (m, 4H), 7.00 (t, *J* = 7.1 Hz, 1H), 6.85-6.79 (m, 3H), 4.16-4.05 (m, 3H), 3.74 (s, 3H), 3.71 (s, 3H), 2.54-2.44 (m, 1H), 2.35-2.23 (m, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.8, 158.0, 137.3, 136.6, 128.9, 127.3, 125.9, 121.6, 119.6, 118.8, 113.8, 109.2, 60.3, 55.2, 41.4, 33.0, 32.7, 31.3, 14.3. IR (ATR): 2920, 1730, 1633, 1511, 1247, 1038, 807 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{25}NO_3Na$ 374.1727; Found 374.1741.



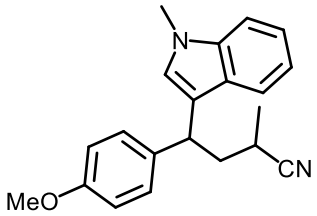
ethyl 1-(2-(4-methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)cyclobutane-1-carboxylate (4h). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 40:1 to 30:1), 61.9 mg, yield: 79%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46 (d, *J* = 7.9 Hz, 1H), 7.23-7.12 (m, 4H), 7.02-6.97 (m, 1H), 6.79-6.76 (m, 3H), 4.12 (t, *J* = 6.9 Hz, 1H), 3.72-3.67 (m, 8H), 2.76-2.70 (m, 1H), 2.59-2.51 (m, 1H), 2.43-2.33 (m, 1H), 2.25-2.17 (m, 1H), 2.03-1.94 (m, 1H), 1.86-1.73 (m, 3H), 1.06 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.0, 157.9, 137.3, 136.6, 129.3, 127.1, 126.1, 121.5, 119.7, 119.1, 118.7, 113.5,109.2, 60.2, 55.2, 47.9, 44.3, 39.2, 32.7, 31.1, 30.9, 16.2, 14.0. IR (ATR): 2921, 2851, 1721, 1611, 1471, 1371, 1325, 1246, 1097, 1035, 826 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{29}NNaO_3$ 414.2040; Found 414.2036.



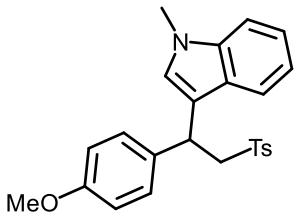
methyl 1-(2-(4-methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)ethyl)cyclohexane-1-carboxylate (4i). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 72.2 mg, yield: 89%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.24-7.16 (m, 4H), 7.04 (t, *J* = 7.0 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 2H), 6.67 (s, 1H), 4.28 (t, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.65 (s, 3H), 3.11 (s, 3H), 2.43-2.23 (m, 3H), 2.08-2.04 (m, 1H), 1.60-1.52 (m, 3H), 1.33-1.20 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.6, 157.8, 137.3, 137.1, 129.1, 126.9, 126.3, 121.6, 119.8, 119.4, 118.8, 113.6, 109.2, 55.3, 51.0, 47.1, 46.7, 37.6, 35.6, 34.8, 32.7, 26.0, 23.4, 23.3. IR (ATR): 2935, 2856, 1728, 1611, 1453, 1326, 1208, 1177, 1037, 740 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{31}NO_3Na$ 428.2196; Found 428.2211.



4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanenitrile (4k).[1] Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 49.9 mg, yield: 82%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.27-7.15 (m, 7H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.84-6.80 (m, 3H), 4.23 (t, *J* = 7.1 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.54-2.44 (m, 1H), 2.30-2.22 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 137.4, 135.2, 128.7, 127.0, 126.0, 121.9, 119.9, 119.5, 119.1, 116.9, 114.1, 109.4, 55.3, 41.0, 32.8, 31.7, 15.9.

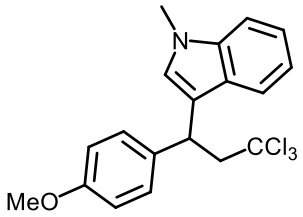


4-(4-methoxyphenyl)-2-methyl-4-(1-methyl-1H-indol-3-yl)butanenitrile (4l). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 55.4 mg, yield: 87%, d.r. = 1:1, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.49-7.44 (m, 1H), 7.27-7.18 (m, 4H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.91-6.79 (m, 3H), 4.41-4.35 (m, 1H), 3.75 (s, 1.5H), 3.73 (s, 1.5H), 3.71 (s, 1.5H), 3.70 (s, 1.5H), 2.49-2.45 (m, 1.5H), 2.34 (t, *J* = 7.8 Hz, 1H), 2.13-2.07 (m, 0.5H), 1.32-1.28 (m, 3H); ^{13}C NMR (CDCl3, 75 MHz): δ 158.4, 158.2, 137.5, 137.3, 135.9, 135.1, 128.9, 128.5, 127.0, 126.9, 126.5, 125.6, 123.2, 123.0, 121.9, 121.9, 119.6, 119.4, 119.1, 119.0, 117.8, 116.4, 114.2, 114.0, 109.5, 109.3, 55.3, 40.7, 40.4, 40.1, 39.7, 32.8, 24.1, 24.0, 18.4, 18.0. IR (ATR): 2238, 1611, 1511, 1247, 1178, 1035, 829 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{22}N_2ONa$ 341.1624; Found 341.1640.

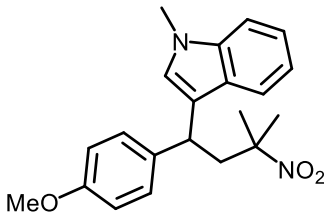


3-(1-(4-methoxyphenyl)-2-tosylethyl)-1-methyl-1H-indole (4m). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 76.3 mg, yield: 91%, reddish brown solid, mp 145-

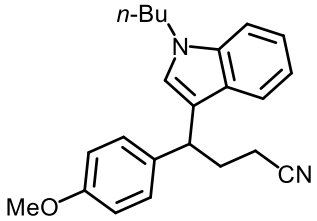
146 ℃. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.47 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.17-7.10 (m, 4H), 7.06-7.00 (m, 3H), 6.71 (d, *J* = 8.7 Hz, 2H), 6.58 (s, 1H), 4.79 (t, *J* = 7.0 Hz, 1H), 3.98 (dd, *J* = 14.6, 6.5 Hz, 1H), 3.81 (dd, *J* = 14.6, 7.6 Hz, 1H), 3.72 (s, 3H), 3.59 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 143.9, 137.3, 136.7, 133.7, 129.2, 128.8, 128.0, 126.9, 126.4, 121.9, 119.3, 119.2, 115.5, 114.0, 109.4, 62.0, 55.3, 37.4, 32.7, 21.6. IR (ATR): 2923, 1611, 1511, 1295, 1180, 1086, 1035, 813, 741 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{26}NO_3S$ 420.1628; Found 420.1641.



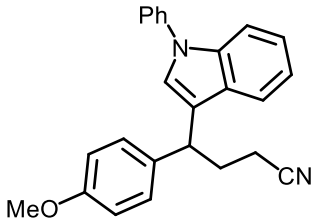
1-methyl-3-(3,3,3-trichloro-1-(4-methoxyphenyl)propyl)-1H-indole (4n). Following the *General Procedure*, using **1a** (1.0 equiv.), **2a** (2.0 equiv.), **3n** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 32.1 mg, yield: 42%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.26-7.19 (m, 2H), 7.08 (t, *J* = 6.7 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.74 (s, 1H), 4.77 (dd, *J* = 7.6, 4.1 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.62 (dd, *J* = 15.0, 4.1 Hz, 1H), 3.50 (dd, *J* = 15.0, 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 137.5, 135.5, 129.3, 126.7, 122.0, 119.4, 119.2, 117.9, 114.0, 109.5, 99.4, 60.2, 55.4, 40.6, 32.9. IR (ATR): 2924, 1611, 1249, 1178, 1036, 824 cm^{-1}. HRMS (ESI) m/z: $[M+K]^+$ Calcd for $C_{19}H_{19}Cl_3NO$ 382.0527; Found 382.0539.



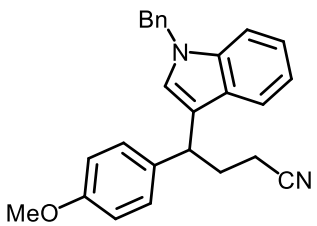
3-(1-(4-methoxyphenyl)-3-methyl-3-nitrobutyl)-1-methyl-1H-indole (4o). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 38.8 mg, yield: 55%, white solid, mp 132-133 ℃. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.26-7.19 (m, 4H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.72 (s, 1H), 4.21 (dd, *J* = 8.3, 5.3 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 2.87 (dd, *J* = 14.6, 5.3 Hz, 1H), 2.70 (dd, J = 14.6, 8.6 Hz, 1H), 1.50 (s, 3H), 1.47 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 137.4, 136.0, 128.9, 126.7, 126.2, 121.9, 119.3, 119.1, 118.6, 114.0, 109.4, 88.7, 55.3, 46.5, 38.5, 32.8, 27.0, 26.6. IR (ATR): 2989, 2919, 1584, 1510, 1373, 1347, 1247, 1066, 742 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{24}N_2O_3Na$ 375.1679; Found 375.1695.



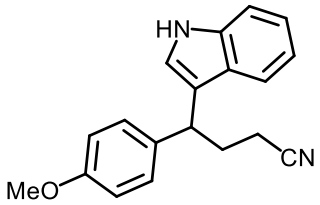
4-(1-butyl-1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5a). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 58.2 mg, yield: 84%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.16-7.13 (m, 1H), 7.02-6.97 (m, 1H), 6.91 (s, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.24 (t, *J* = 7.3 Hz, 1H), 4.05 (t, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 2.58-2.42 (m, 1H), 2.33-2.23 (m, 2H), 1.79 (p, *J* = 7.3 Hz, 2H), 1.31 (dt, *J* = 14.7, 7.4 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 136.7, 135.2, 128.8, 127.0, 125.0, 121.7, 119.9, 119.6, 119.0, 116.8, 114.1, 109.6, 55.3, 46.2, 41.1, 32.4, 31.7, 20.3, 15.9, 13.8. IR (ATR): 2932, 2837,2245, 1609, 1510, 1481, 1367, 1155, 1034, 741 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{26}N_2ONa$ 369.1937; Found 369.1948.



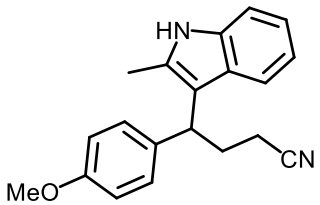
4-(4-methoxyphenyl)-4-(1-phenyl-1H-indol-3-yl)butanenitrile (5b). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 30:1 to 20:1), 47.6 mg, yield: 65%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.53-7.47 (m, 6H), 7.34-7.30 (m, 1H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.20-7.16 (m, 2H), 7.07 (t, *J* = 7.1 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.31 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 2.60-2.51 (m, 1H), 2.37-2.27 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.5, 139.7, 136.5, 134.5, 129.7, 128.8, 128.0, 126.5, 124.9, 124.3, 122.8, 120.2, 119.8, 119.7, 114.2, 110.7, 55.3, 41.0, 31.5, 15.9. IR (ATR): 2922, 2249, 1732, 1609, 1422, 1303, 1179, 1031, 775 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{22}N_2NaO$ 389.1624; Found 389.1645.



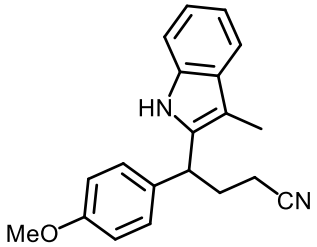
4-(1-benzyl-1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5c). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 68.5 mg, yield: 90%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.31-7.18 (m, 6H), 7.12-6.98 (m, 4H), 6.94 (s, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.24 (s, 2H), 4.25 (t, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 2.54-2.44 (m, 1H), 2.30-2.21 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 137.6, 137.1, 135.0, 128.9, 128.8, 127.7, 127.2, 126.7, 125.3, 122.2, 119.8, 119.7, 119.4, 117.7, 114.2, 109.9, 55.3, 50.0, 41.1, 31.6, 15.8. IR (ATR): 3030, 2836, 2245, 1883, 1610, 1510, 1356, 1302, 1245, 1155, 967, 821 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}N_2O$ 381.1961; Found 381.1974.



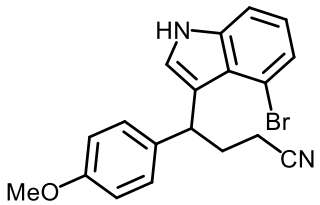
4-(1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5d). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 47.6 mg, yield: 82%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.09 (s, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.20-7.11 (m, 3H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 2.5 Hz, 1H), 6.81 (d, J = 8.3 Hz, 2H), 4.22 (t, *J* = 7.1 Hz, 1H), 3.73 (s, 3H), 2.52-2.43 (m, 1H), 2.27-2.21 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 136.7, 135.0, 128.8, 126.5, 122.3, 121.2, 119.9, 119.6, 119.4, 118.3, 114.1, 111.4, 55.3, 41.0, 31.5, 15.8. IR (ATR): 2935, 2247, 1676, 1600, 1458, 1363, 1247, 1030, 975, 815 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{18}N_2ONa$ 313.1311; Found 313.1323.



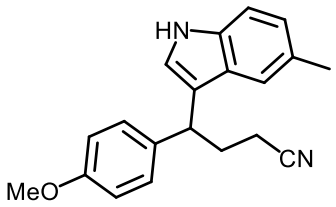
4-(4-methoxyphenyl)-4-(2-methyl-1H-indol-3-yl)butanenitrile (5e). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 45.1 mg, yield: 74%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.95 (s, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.25-7.21 (m, 3H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.1 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.28 (t, *J* = 8.3 Hz, 1H), 3.73 (s, 3H), 2.57-2.49 (m, 2H), 2.37 (s, 3H), 2.31-2.24 (m, 1H), 2.19-2.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.0, 135.7, 135.6, 132.6, 128.4, 127.1, 121.1, 120.0, 119.4, 119.1, 113.9, 111.4, 110.7, 55.3, 39.8, 30.0, 16.0, 12.2. IR (ATR): 2925, 2260, 1611, 1511, 1247, 1033, 745 cm^{-1}. HRMS (ESI) m/z: $[M+K]^+$ Calcd for $C_{20}H_{20}N_2ONa$ 327.1468; Found 327.1482.



4-(4-methoxyphenyl)-4-(3-methyl-1H-indol-2-yl)butanenitrile (5f). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 36.5 mg, yield: 60%, colorless oil. ^{1}H NMR (d_6-DMSO, 300 MHz): δ 10.80 (s, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.29-7.26 (m, 3H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.28 (t, *J* = 5.6 Hz, 1H), 3.69 (s, 3H), 2.43-2.29 (m, 4H), 2.22 (s, 3H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 158.0, 135.8 (2C), 134.5, 128.6, 128.5, 120.7, 120.3, 118.3, 117.9, 114.1, 110.8, 106.2, 55.1, 40.3, 29.4, 15.2, 8.5. IR (ATR): 2955, 2853, 2226, 1458, 1378, 1249, 1066 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2ONa$ 327.1468; Found 327.1477.

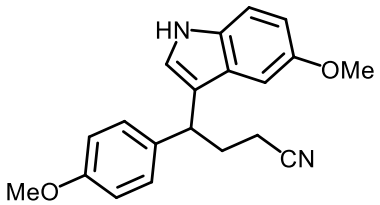


4-(4-bromo-1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5g). Following the *General Procedure*, using **1h** (1.0 equiv.), **2a** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 30:1 to 20:1), 27.3 mg, yield: 37%, yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12 (s, 1H), 7.21-7.16 (m, 4H), 6.92 (t, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.94 (dd, *J* = 9.3, 6.1 Hz, 1H), 3.72 (s, 3H), 2.54-2.45 (m, 1H), 2.29 (t, *J* = 7.1 Hz, 2H), 2.22-2.13 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 137.9, 134.8, 129.3, 124.7, 124.6, 123.3, 120.2, 119.8, 114.2 (2C), 110.8, 55.4, 40.2, 33.4, 16.0. IR (ATR): 2920, 2247, 1729, 1510, 1335, 1247, 1143, 1036, 812 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{17}BrN_2ONa$ 391.0416; Found 391.0410.

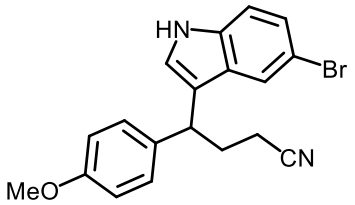


4-(4-methoxyphenyl)-4-(5-methyl-1H-indol-3-yl)butanenitrile (5h). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 39.0 mg, yield: 64%, brown oil. ^{1}H NMR ($CDCl_3$, 300

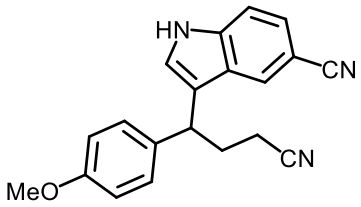
MHz): δ 7.96 (s, 1H), 7.21-7.17 (m, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.90 (d, *J* = 1.5 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 2H), 4.20 (t, *J* = 7.4 Hz, 1H), 3.74 (s, 3H), 2.50-2.42 (m, 1H), 2.37 (s, 3H), 2.29-2.21 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3, 135.1, 135.0, 128.8, 128.7, 126.8, 124.0, 121.4, 120.0, 118.9, 117.8, 114.1, 111.0, 55.3, 41.0, 31.6, 21.6, 15.9. IR (ATR): 2927, 2246, 1610, 1421, 1303, 1108, 1034, 798 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2ONa$ 327.1468; Found 327.1481.



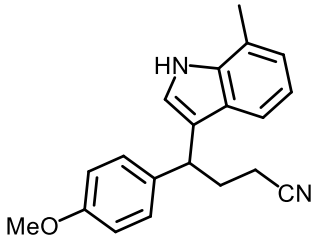
4-(5-methoxy-1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5i). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 37.2 mg, yield: 58%, reddish brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.01 (s, 1H), 7.24-7.19 (m, 3H), 6.97 (d, *J* = 2.2 Hz, 1H), 6.84-6.80 (m, 4H), 4.20 (t, *J* = 8.0 Hz, 1H), 3.76 (s, 6H), 2.53-2.44 (m, 1H), 2.32-2.23 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 153.9, 135.0, 131.8, 128.8, 127.0, 121.9, 119.9, 118.1, 114.2, 112.3, 112.0, 101.4, 55.9, 55.4, 41.0, 31.5, 15.9. IR (ATR): 2935, 2245, 1611, 1510, 1421, 1302, 1211, 1109, 801 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{21}N_2O_2$ 321.1598; Found 321.1611.



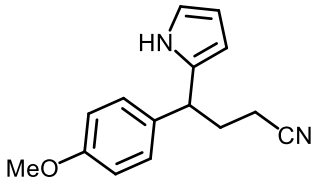
4-(5-bromo-1H-indol-3-yl)-4-(4-methoxyphenyl)butanenitrile (5j). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 58.3 mg, yield: 79%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.22 (s, 1H), 7.51 (s, 1H), 7.20-7.15 (m, 4H), 7.00 (s, 1H), 6.83 (d, J = 8.4 Hz, 2H), 4.16 (t, *J* = 8.0 Hz, 2H), 3.76 (s, 3H), 2.48-2.41 (m, 1H), 2.29-2.23 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.5, 135.3, 134.4, 128.7, 128.3, 125.2, 122.4, 121.8, 119.8, 118.1, 114.3, 112.9, 112.8, 55.3, 40.9, 31.4, 15.8 . IR (ATR): 2836, 2247, 1731, 1510, 1420, 1303, 1109, 885 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{17}BrN_2ONa$ 391.0416; Found 391.0434.



3-(3-cyano-1-(4-methoxyphenyl)propyl)-1H-indole-5-carbonitrile (5k). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 37.8 mg, yield: 60%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.94 (s, 1H), 7.70 (s, 1H), 7.42-7.32 (m, 2H), 7.20-7.16 (m, 3H), 6.85 (d, *J* = 8.3 Hz, 2H), 4.22 (t, *J* = 8.1 Hz, 1H), 3.77 (s, 3H), 2.50-2.45 (m, 1H), 2.31-2.30 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.6, 138.4, 134.0, 128.7, 126.4, 125.1, 125.0, 123.3, 120.9, 119.6, 119.3, 114.4, 112.4, 102.2, 55.3, 40.7, 31.3, 15.7. IR (ATR): 3350, 2220, 1701, 1511, 1365, 1178, 1034, 810 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{17}N_3ONa$ 338.1264; Found 338.1262.

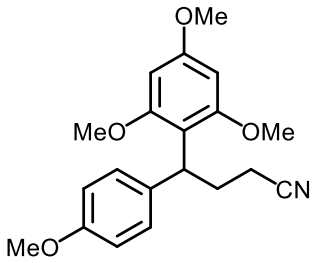


4-(4-methoxyphenyl)-4-(7-methyl-1H-indol-3-yl)butanenitrile (5l). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 51.1 mg, yield: 84%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99 (s, 1H), 7.29-7.26 (m, 1H), 7.23-7.19 (m, 2H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.97-6.95 (m, 2H), 6.85-6.81 (m, 2H), 4.25 (t, *J* = 7.4 Hz, 1H), 3.76 (s, 1H), 2.56-2.50 (m, 1H), 2.46 (s, 3H), 2.34-2.27 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 136.3, 135.1, 128.8, 126.1, 123.0, 120.9, 120.5, 119.9, 119.0, 117.2, 114.2, 55.4, 41.2, 31.6, 16.7, 15.9. IR (ATR): 3385, 2230, 1610, 1447, 1177, 1034, 812 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2ONa$ 327.1468; Found 327.1470.

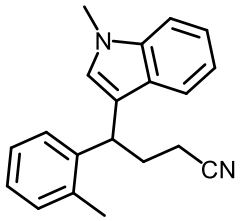


4-(4-methoxyphenyl)-4-(1H-pyrrol-2-yl)butanenitrile (5m). Following the *General Procedure*, using **1n** (1.0 equiv.), **2a** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 14.4 mg, yield: 30%,

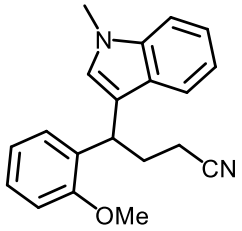
colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.75 (s, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.66 (dd, *J* = 4.1, 2.6 Hz, 1H), 6.17 (dd, *J* = 6.0, 2.9 Hz, 1H), 6.09 (dd, *J* = 2.7, 1.2 Hz, 1H), 4.02 (t, *J* = 8.5 Hz, 1H), 3.79 (s, 3H), 2.42-2.18 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.0, 133.4, 133.3, 129.0, 119.6, 117.5, 114.5, 108.4, 105.1, 55.5, 42.7, 31.2, 15.6. IR (ATR): 3356, 2246, 1729, 1610, 1443, 1303, 1112, 732 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{17}N_2O$ 241.1335; Found 241.1334.



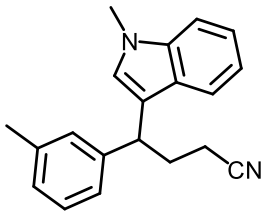
4-(4-methoxyphenyl)-4-(2,4,6-trimethoxyphenyl)butanenitrile (5n). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 46.4 mg, yield: 68%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.95 (d, *J* = 8.3 Hz, 2H), 5.51 (d, *J* = 8.2 Hz, 2H), 4.85 (s, 2H), 3.35 (t, *J* = 7.4 Hz, 1H), 2.51 (s, 3H), 2.48 (s, 9H), 1.40-1.28 (m, 1H), 1.23-1.11 (m, 1H), 0.94 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.1, 159.3, 157.6, 136.1, 128.7, 120.4, 113.4, 111.2, 91.2, 55.7, 55.3, 55.2, 38.1, 28.4, 16.0. IR (ATR): 2838, 2244, 1493, 1225, 1065, 780 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{24}NO_4$ 342.1700; Found 342.1713.



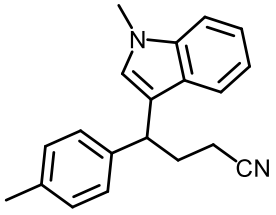
4-(1-methyl-1H-indol-3-yl)-4-(o-tolyl)butanenitrile (6a). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 40:1 to 20:1), 37.5 mg, yield: 65%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.22-7.16 (m, 2H), 7.12-7.00 (m, 4H), 6.88 (s, 1H), 4.29-4.24 (m, 1H), 3.75 (s, 3H), 2.56-2.47 (m, 1H), 2.40-2.31 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.1, 138.4, 137.4, 128.7, 128.6, 127.6, 127.1, 126.1, 124.8, 122.0, 119.5, 119.2, 116.8, 109.4, 41.8, 32.9, 31.7, 21.7, 16.1. IR (ATR): 2925, 2245, 1606, 1484, 1329, 1246, 1013, 784 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2Na$ 311.1519; Found 311.1517.



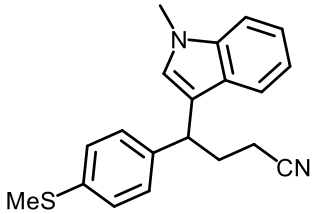
4-(2-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanenitrile (6b). Following the *General Procedure*, using **1a** (1.0 equiv.), **2c** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 34.7 mg, yield: 57%, white solid, mp 140-141 ℃. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.48 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.21-7.14 (m, 3H), 7.02 (td, *J* = 8.0, 1.0 Hz, 1H), 6.91 (s, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.83 (t, *J* = 7.5 Hz, 1H), 4.82-4.77 (m, 1H), 3.88 (s, 3H), 3.74 (s, 3H), 2.48-2.40 (m, 1H), 2.38-2.27 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.0, 137.3, 131.7, 128.2, 127.7, 127.5, 126.4, 121.8, 120.8, 120.2, 119.6, 119.0, 116.3, 110.7, 109.3, 55.6, 34.3, 32.9, 31.2, 16.0. IR (ATR): 2927, 2245, 1586, 1489, 1328, 1240, 1155, 1028, 910, 799 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2ONa$ 327.1468; Found 327.1469.



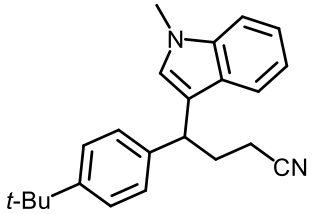
4-(1-methyl-1H-indol-3-yl)-4-(m-tolyl)butanenitrile (6c). Following the *General Procedure*, using **1a** (1.0 equiv.), **2d** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 20.8 mg, yield: 36%, brownish oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.53 (d, *J* = 7.9 Hz, 1H), 7.32-7.26 (m, 2H), 7.22-7.13 (m, 4H), 7.11-7.07 (m, 1H), 6.70 (s, 1H), 4.58-4.53 (m, 1H), 3.71 (s, 3H), 2.56-2.48 (m, 1H), 2.38 (s, 3H), 2.37-2.32 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.1, 137.3, 136.4, 131.0, 127.3, 126.8, 126.6, 126.4, 126.2, 122.0, 120.0, 119.3, 119.1, 116.5, 109.5, 37.1, 32.9, 31.7, 19.9, 16.0. IR (ATR): 2925, 2244, 1614, 1423, 1242, 1133, 1155, 1013, 739 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{21}N_2$ 289.1699; Found 289.1690.



4-(1-methyl-1H-indol-3-yl)-4-(p-tolyl)butanenitrile (6d). Following the *General Procedure*, using **1a** (1.0 equiv.), **2e** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 34.0 mg, yield: 59%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.22-7.19 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.06-7.01 (m, 1H), 6.87 (s, 1H), 4.27 (t, *J* = 7.2 Hz, 1H), 3.75 (s, 3H), 2.58-2.49 (m, 1H), 2.33-2.27 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.1, 137.4, 136.4, 129.5, 127.7, 127.0, 126.1, 122.0, 119.9, 119.5, 119.1, 116.9, 109.4, 41.5, 32.9, 31.7, 21.2, 16.0. IR (ATR): 2923, 2245, 1614, 1471, 1374, 1213, 1078, 809 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2Na$ 311.1519; Found 311.1526.

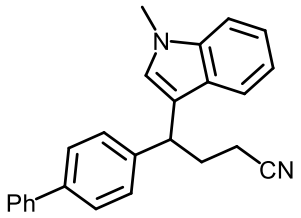


4-(1-methyl-1H-indol-3-yl)-4-(4-(methylthio)phenyl)butanenitrile (6e). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 43.6 mg, yield: 68%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.25-7.15 (m, 6H), 7.02 (td, *J* = 7.9, 1.1 Hz, 1H), 6.86 (s, 1H), 4.25 (t, *J* = 7.4 Hz, 1H), 3.72 (s, 3H), 2.54-2.46 (m, 1H), 2.42 (s, 3H), 2.31-2.23 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.1, 137.4, 136.6, 128.3, 127.1, 126.9, 126.1, 122.0, 119.7, 119.4, 119.2, 116.4, 109.4, 41.3, 32.8, 31.4, 16.0. IR (ATR): 2925, 2245, 1597, 1492, 1210, 1014, 730 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{20}N_2SNa$ 343.1239; Found 343.1238.

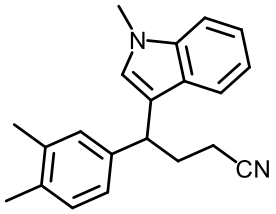


4-(4-(*tert*-butyl)phenyl)-4-(1-methyl-1H-indol-3-yl)butanenitrile (6f). Following the *General Procedure*, using **1a** (1.0 equiv.), **2g** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 33.7 mg, yield: 51%, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.35-7.26 (m, 4H), 7.22-7.18 (m, 2H), 7.07-7.02 (m, 1H), 6.89 (s, 1H), 4.30-4.25 (m, 1H), 3.75 (s, 3H), 2.56-2.47 (m, 1H), 2.36-2.28 (m, 3H), 1.28 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.6, 148.2, 140.1, 137.4, 127.4, 126.2, 125.7, 122.0, 119.6, 119.1, 116.8, 109.5, 103.4, 41.4, 34.5, 32.9, 31.7, 31.5, 16.1. IR

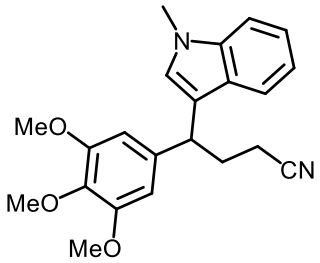
(ATR): 2959, 2246, 1615, 1472, 1374, 1242, 1122, 910 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{26}N_2Na$ 353.1988; Found 353.1983.



4-([1,1'-biphenyl]-4-yl)-4-(1-methyl-1H-indol-3-yl)butanenitrile (6g). Following the *General Procedure*, using **1a** (1.0 equiv.), **2h** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 30.1 mg, yield: 43%, yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.59-7.51 (m, 5H), 7.47-7.37 (m, 5H), 7.31-7.29 (m, 1H), 7.21-7.18 (m, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.92 (s, 2H), 4.38-4.33 (m, 1H), 3.76 (s, 3H), 2.63-2.53 (m, 1H), 2.42-2.31 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.3, 140.9, 139.7, 137.4, 128.9, 128.2, 127.5, 127.3, 127.1, 127.0, 126.2, 122.1, 119.8, 119.5, 119.2, 116.5, 109.5, 41.6, 32.9, 31.6, 16.1. IR (ATR): 2922, 2245, 1614, 1485, 1133, 1008, 843 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{22}N_2Na$ 373.1675; Found 373.1673.



4-(3,4-dimethylphenyl)-4-(1-methyl-1H-indol-3-yl)butanenitrile (6h). Following the *General Procedure*, using **1a** (1.0 equiv.), **2i** (2.0 equiv.), **3k** (3.0 equiv.), $Cu(OTf)_2$ (20 mol%), bpy (20 mol%), $NaHCO_3$ (2.0 equiv.), 120 ℃, Ar, 24 h. The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 19.4 mg, yield: 32%, brown oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.48 (d, *J* = 7.9 Hz, 1H), 7.28-7.26 (m, 1H), 7.22-7.19 (m, 1H), 7.06-7.04 (m, 4H), 6.86 (s, 1H), 4.23 (t, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 2.36-2.25 (m, 4H), 2.21 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.5, 137.4, 136.9, 135.0, 130.0, 129.1, 127.1, 126.0, 125.1, 121.9, 120.0, 119.5, 119.1, 117.0, 109.4, 41.5, 32.9, 31.7, 20.0, 19.5, 16.0. IR (ATR): 2925, 2245, 1614, 1503, 1328, 1155, 1014, 817 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{22}N_2Na$ 325.1675; Found 325.1674.

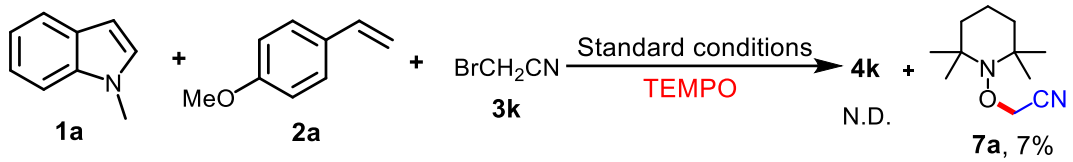


4-(1-methyl-1H-indol-3-yl)-4-(3,4,5-trimethoxyphenyl)butanenitrile (6i). Following the *General Procedure*, the product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 50.3 mg, yield: 69%, brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.88 (s, 1H), 6.54 (s, 2H), 4.23 (t, *J* = 7.7 Hz, 1H), 3.80 (s, 9H), 3.74 (s, 3H), 2.55-2.46 (m, 1H), 2.32-2.25 (m, 3H) ; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.4, 138.9, 137.4, 136.7, 126.9, 126.0, 122.0, 119.8, 119.4, 119.1, 116.4, 109.5, 104.8, 60.9, 56.2, 42.2, 32.8, 31.6, 15.9. IR (ATR): 2929, 2247, 1590, 1505, 1184, 1006, 824 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{25}N_2O_3$ 365.1860; Found 365.1852.

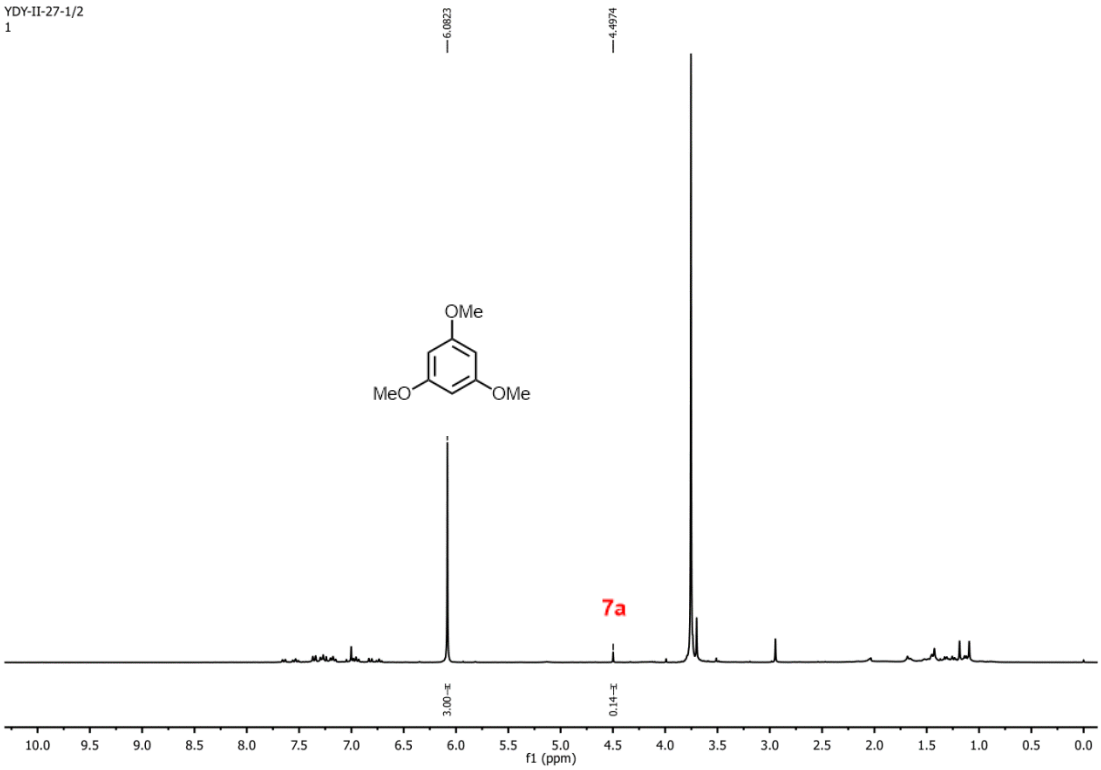
Mechanistic Study

(1) Reactions with radical inhibitors

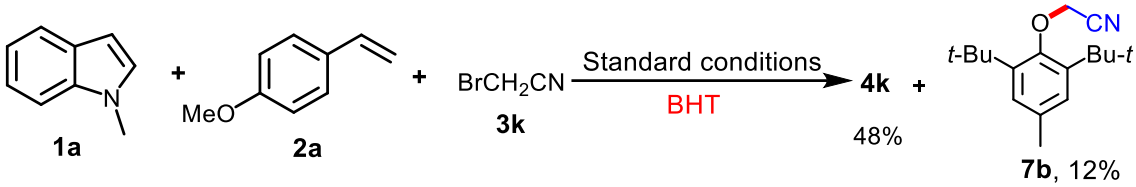
(a) TEMPO



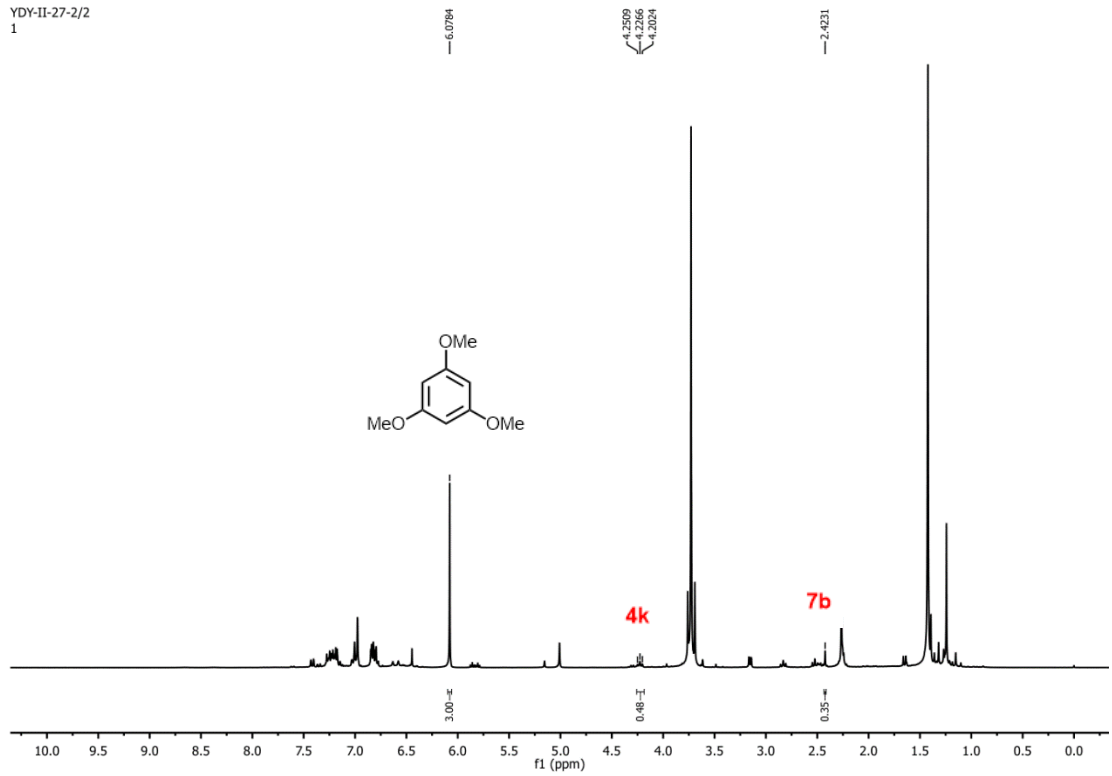
N-methyl indole **1a** (0.2 mmol, 25 μL), TEMPO (0.4 mmol, 62.5 mg), $Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then 4-methoxystyrene **2a** (7.5 mmol, 40 μL) and bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) were added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was submitted to ^{1}HNMR (1,3,5-trimethoxybenzene was added as an internal standard), no product of **4k** was detected; yield of TEMPO-adduct **7a** was 7%.



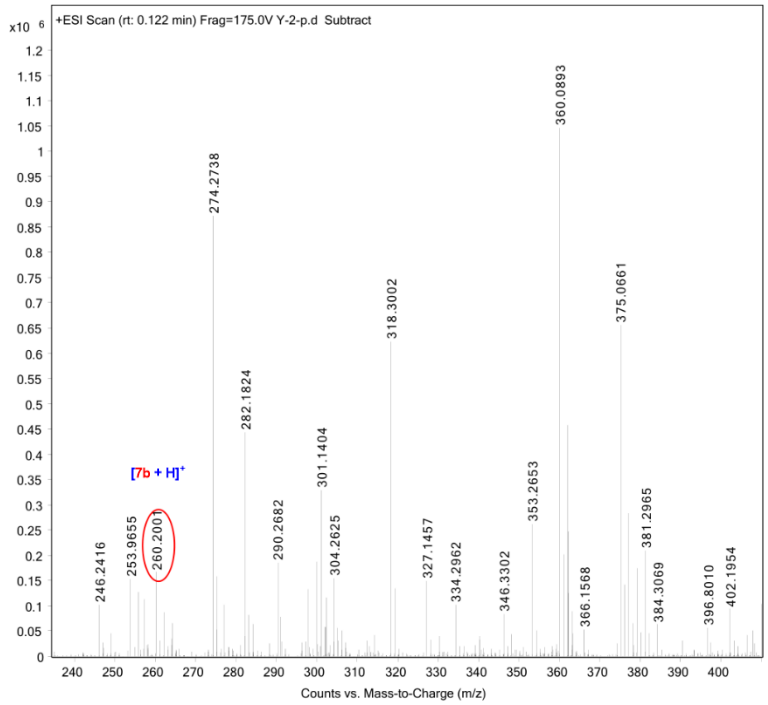
(b) BHT



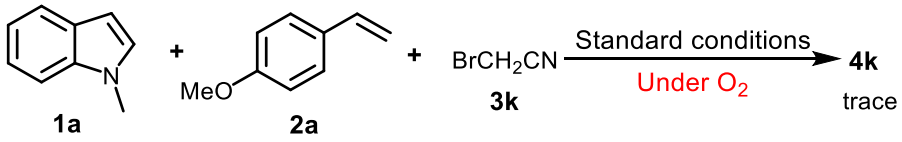
N-methyl indole **1a** (0.2 mmol, 25 μL), BHT (0.4 mmol, 88.1 mg), $Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then 4-methoxystyrene **2a** (7.5 mmol, 40 μL) and bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) were added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was submitted to ^{1}HNMR (1,3,5-trimethoxybenzene was added as an internal standard), the yield of **4k** was 48%; yield of BHT-adduct **7b** was 12%.



Sample Name	Y-2-p	**Position**	P2C2	**Instrument Name**	Instrument 1
User Name		**Inj Vol**	1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	Y-2-p.d
ACQ Method	5-95-30min-msms-lyq.m	**Comment**		**Acquired Time**	7/15/2022 11:05:45 AM (UTC+08:00)



(c) Under O_2

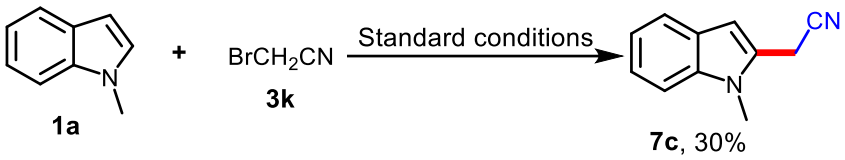


1a **2a** **3k**

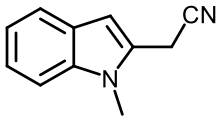
N-methyl indole **1a** (0.2 mmol, 25 μL), $Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/oxygen-flush cycles. Then 4-methoxystyrene **2a** (0.3 mmol, 40 μL) and bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) were added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was submitted to ^{1}HNMR (1,3,5-trimethoxybenzene was added as an internal standard), only trace amounts of **4k** was detected.

(2) Control experiments

(a)

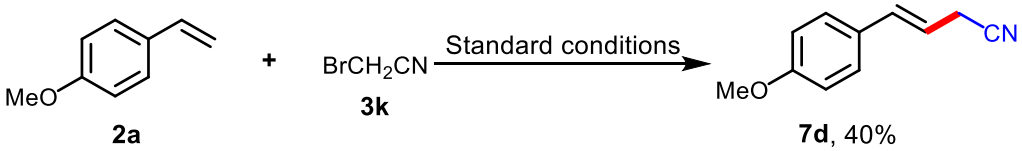


N-Methyl indole **1a** (0.2 mmol, 25 μL), $Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (30:1 to 20:1) to afford compound **7c**.



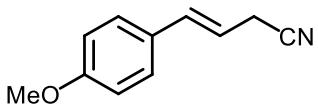
2-(1-methyl-1H-indol-2-yl)acetonitrile (7c).[3] The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 30:1 to 20:1), 10.2 mg, yield: 30%, colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 6.0 Hz, 1H), 7.24 (d, *J* = 9.0 Hz, 1H), 7.13 (td, *J* = 7.9, 1.1 Hz, 1H), 6.52 (s, 1H), 3.86 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 127.7, 127.2, 122.5, 120.8, 120.3, 116.1, 109.3, 102.4, 30.0, 16.9.

(b)



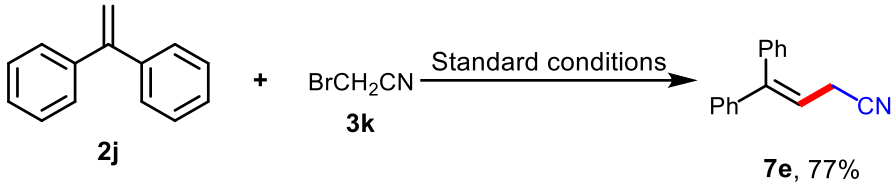
$Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then 4-methoxystyrene **2a** (0.3 mmol, 40 μL) and bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 30:1)

to afford compound **7d**.



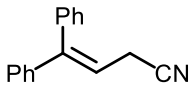
(*E*)-4-(4-methoxyphenyl)but-3-enenitrile (7d).[4] The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 20.8 mg, yield: 40%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.66 (d, *J* = 15.8 Hz, 1H), 5.90 (dt, *J* = 15.8, 5.7 Hz, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 5.7, 1.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 133.8, 128.5, 127.7, 117.6, 114.7, 114.1, 55.3, 20.7.

(c)



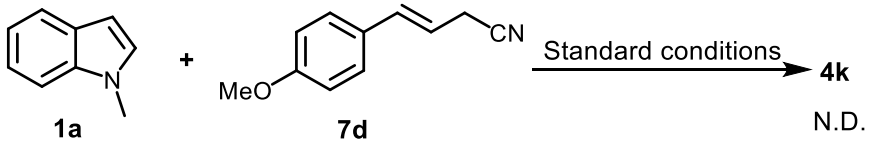
2j + **3k** → **7e**, 77%

$Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then 1,1-diphenylethylene **2j** (0.3 mmol, 53 μL) and bromoacetonitrile **3k** (0.4 mmol, 28 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 30:1) to afford compound **7e**.



(*E*)-4-(4-methoxyphenyl)but-3-enenitrile (7e).[5] The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 50.7 mg, yield: 77%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.36 (m, 3H), 7.31-7.26 (m, 3H), 7.23-7.20 (m, 2H), 7.18-7.15 (m, 2H), 6.02 (t, *J* = 7.4 Hz, 1H), 3.13 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 140.7, 138.0, 129.4, 128.8, 128.4, 128.2, 128.2, 127.5, 118.2, 115.5, 18.4.

(d)



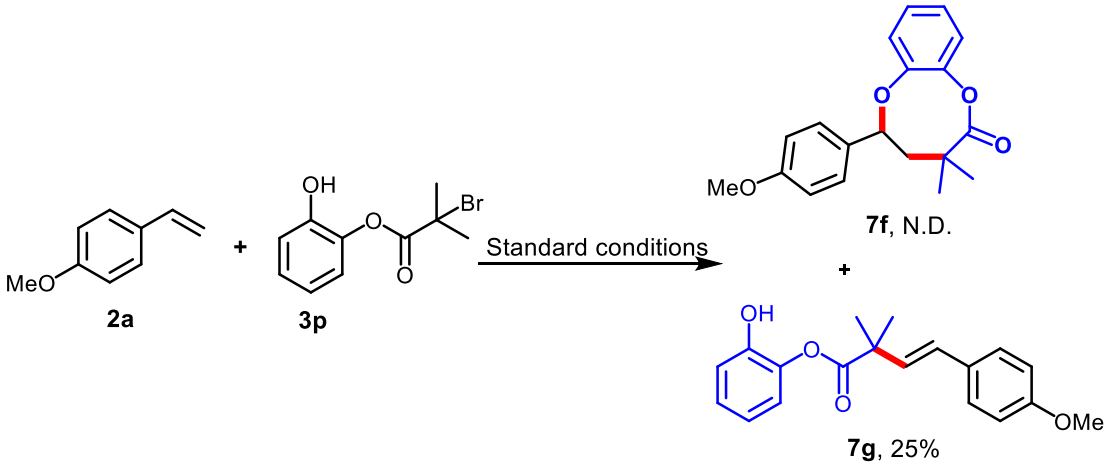
1a + **7d** → **4k**

N.D.

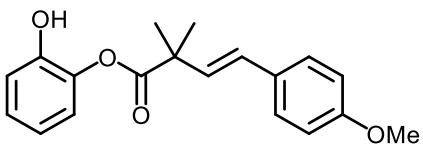
N-methyl indole **1a** (0.2 mmol, 25 μL), $Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then alkene **7d** (0.3 mmol, 50 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was submitted to ^{1}HNMR (1,3,5-trimethoxybenzene was added as an internal standard), no desired product **4k** was detected.

(3) Benzylic cation trapping by other nucleophiles

(a)

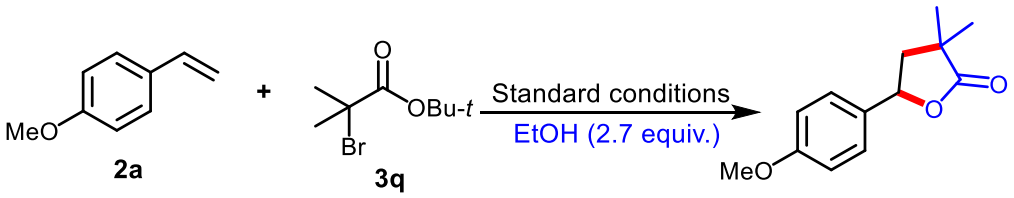


$Cu(OTf)_2$ (0.02 mmol, 7.2 mg), bpy (0.02 mmol, 3.1 mg), and $NaHCO_3$ (0.3 mmol, 25.2 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then alkene **2a** (0.3 mmol, 40 μL) and ester **3p** (0.4 mmol, 69 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 30:1) to afford compound **7g**, no product **7f** was detected.



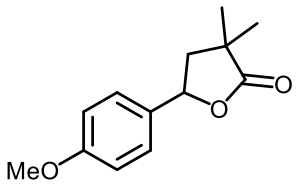
2-hydroxyphenyl (*E*)-4-(4-methoxyphenyl)-2,2-dimethylbut-3-enoate (7g). The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 30:1), 23.4 mg, yield: 25%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.7 Hz, 2H), 7.12-7.04 (m, 2H), 6.97-6.83 (m, 4H), 6.56 (d, *J* = 16.2 Hz, 1H), 6.37 (d, *J* = 16.2 Hz, 1H), 5.53 (brs, 1H), 3.80 (s, 3H), 1.57 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 159.5, 147.3, 138.9, 131.3, 129.5, 129.0, 127.7, 127.1, 122.5, 121.0, 117.8, 114.2, 55.5, 45.0, 25.3. IR (ATR): 2932, 1608, 1461, 1288, 1107, 1034, 749 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}O_4$ 313.1434; Found 313.1452.

(b)



7h, 78%

$Cu(OTf)_2$ (0.03 mmol, 10.8 mg), bpy (0.03 mmol, 4.8 mg), and $NaHCO_3$ (0.45 mmol, 37.8 mg) were weighed into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/argon-flush cycles. Then alkene **2a** (0.3 mmol, 40 μL) and α-bromo ester **3q** (0.4 mmol, 72 μL), EtOH (1.2 mmol, 72 μL) in MeCN (1.0 mL) was added through the side-arm by syringe. The reaction was stirred under argon at 100 °C for 16 h. After the reaction, the mixture was cooled to room temperature. Water (10 mL) was added to the above solution, and the mixture was extracted with EtOAc (5 mL × 3). The organic layer was washed with saturated brine (5 mL) and dried over Na_2SO_4. Volatile solvent and reagents were removed by rotary evaporation and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (50:1 to 20:1) to afford compound **7h**.



5-(4-methoxyphenyl)-3,3-dimethyldihydrofuran-2(3H)-one (7h).[6] The product was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 50:1 to 20:1), 51.1 mg, yield: 78%, colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.40 (dd, *J* = 10.1, 6.1 Hz, 1H), 3.81 (s, 3H), 2.43 (dd, *J* = 12.9, 6.1 Hz, 1H), 2.07 (dd, *J* = 12.8, 10.1 Hz, 1H), 1.36 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.8, 159.8, 131.3, 127.1, 114.1, 77.8, 55.4, 46.0, 41.0, 25.0, 24.2.

References

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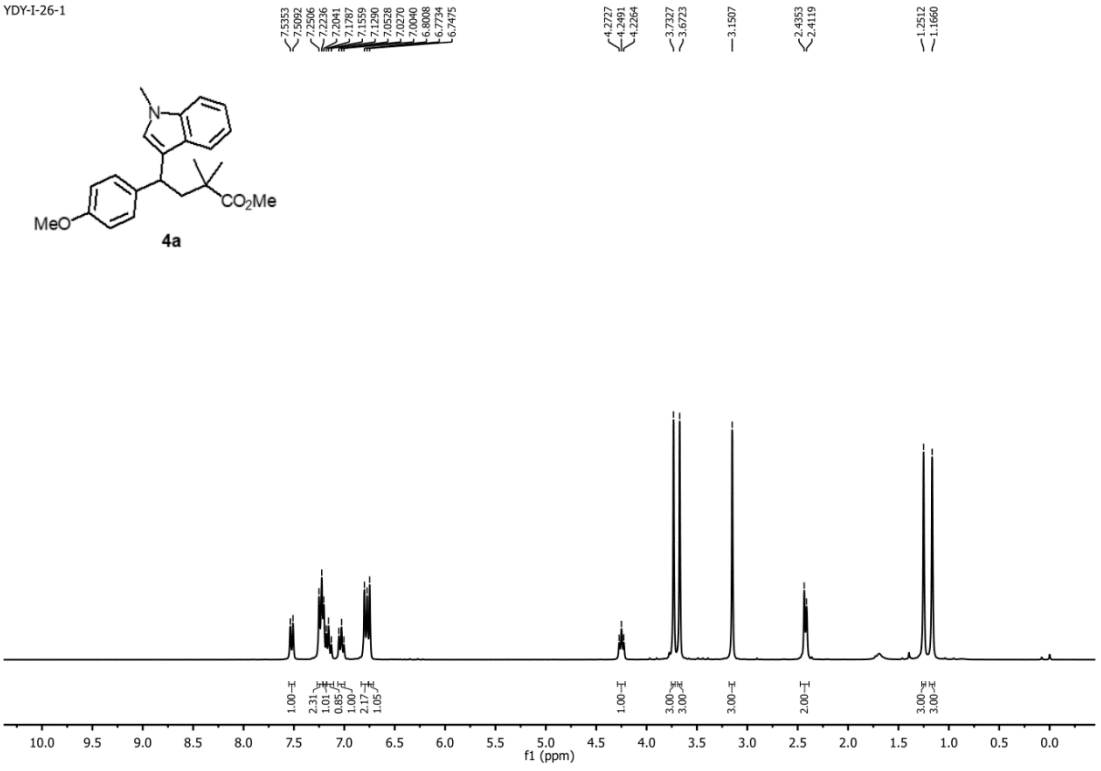
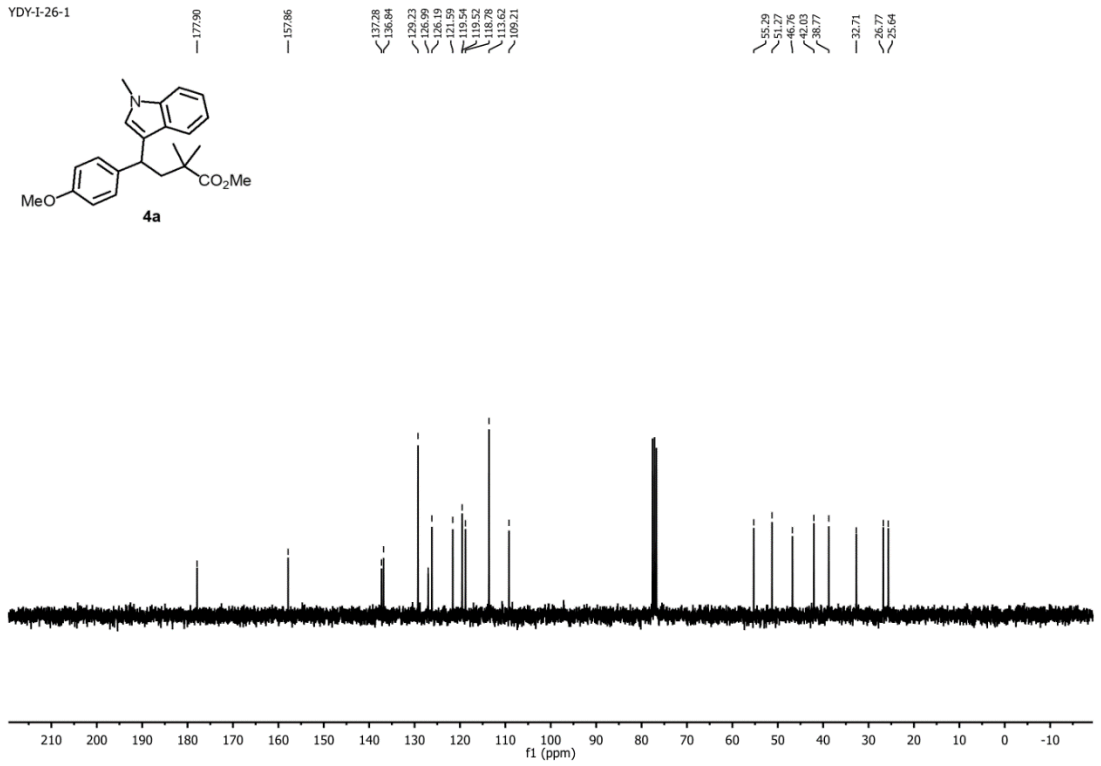
2. Duan, Y.; Li, W.; Xu, P.; Zhang, M.; Cheng, Y.; Zhu, C. *Org. Chem. Front.* **2016**, *3*, 1443–1446.
3. O'Brien, C. J.; Droege, D. G.; Jiu, A. Y.; Gandhi, S. S.; Paras, N. A.; Olson, S. H.; Conrad, J. *J. Org. Chem.* **2018**, *83*, 8926–8935.
4. Pan, C.; Yang, C.; Li, K.; Zhang, K.; Zhu, Y.; Wu, S.; Zhou, Y.; Fan, B. *Org. Lett.* **2021**, 23, 7188–7193.
5. Zhang, J.-Q.; Liu, J.; Hu, D.; Song, J.; Zhu, G.; Ren, H. *Org. Lett.* **2022**, *24*, 786–790.
6. Pan, G.-H.; Song, R.-J.; Li, J.-H. *Org. Chem. Front.* **2018**, *5*, 179–183.

NMR Spectra Images of Products

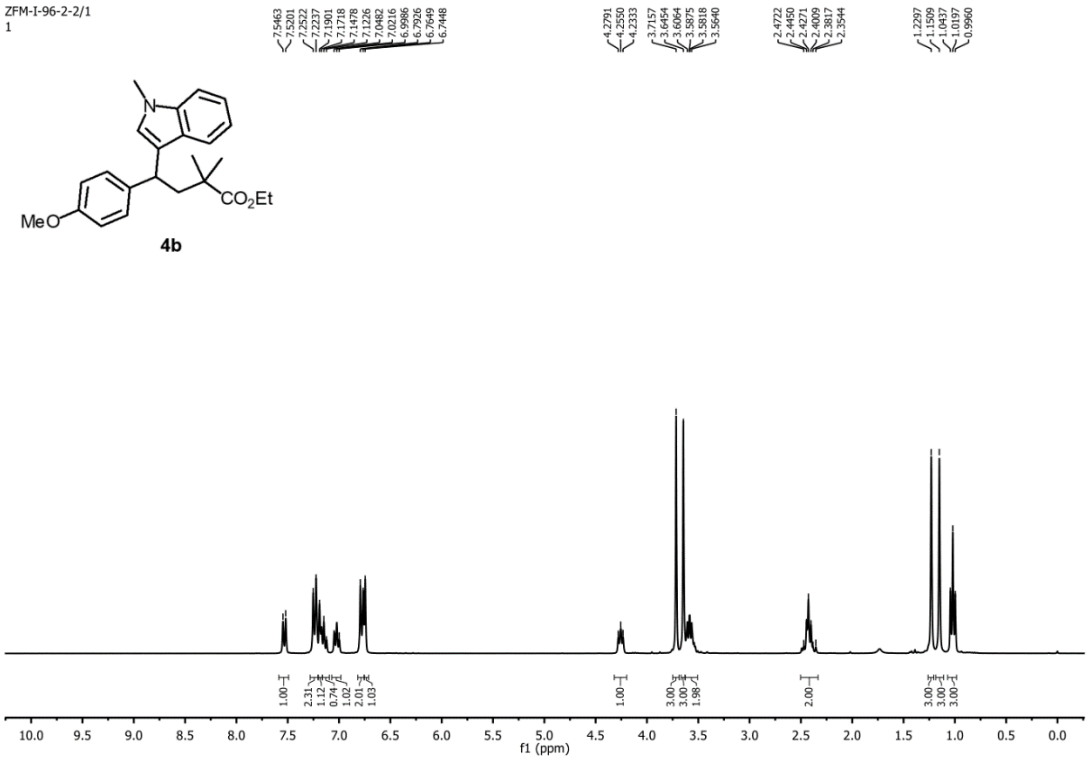
^{1}H NMR of compound **4a** (300 MHz in $CDCl_3$)



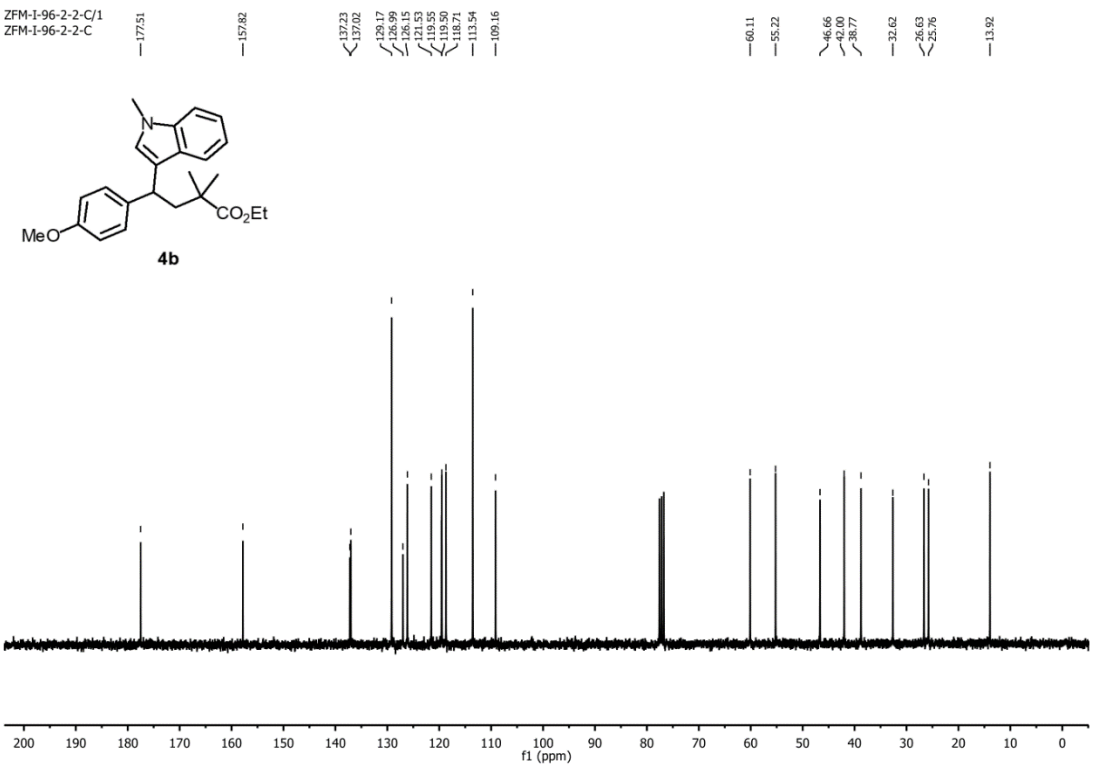
^{13}C NMR of compound **4a** (75 MHz in $CDCl_3$)



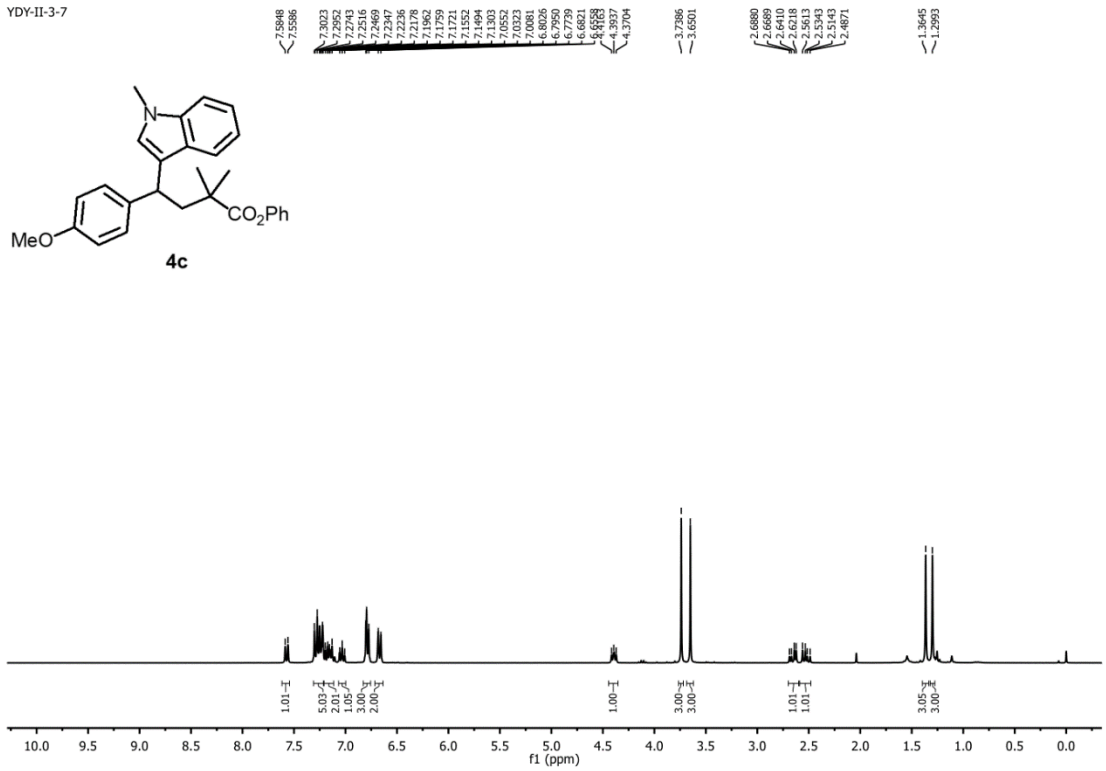
^{1}H NMR of compound **4b** (300 MHz in $CDCl_3$)



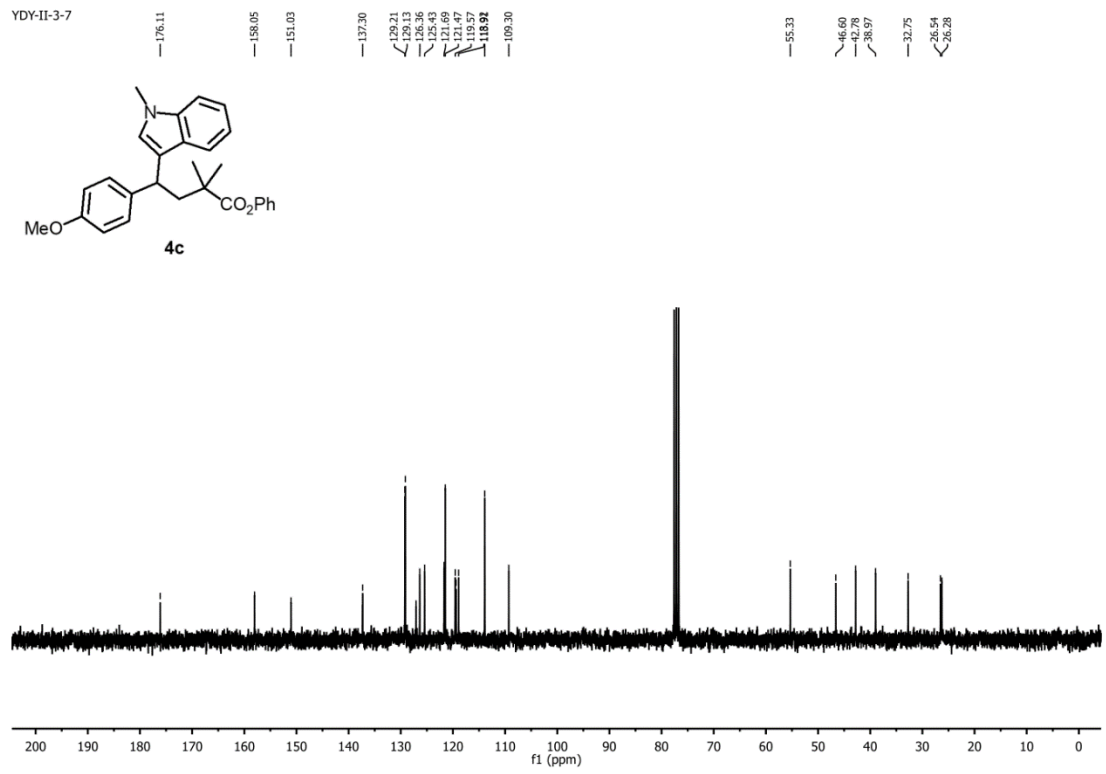
^{13}C NMR of compound **4b** (75 MHz in $CDCl_3$)



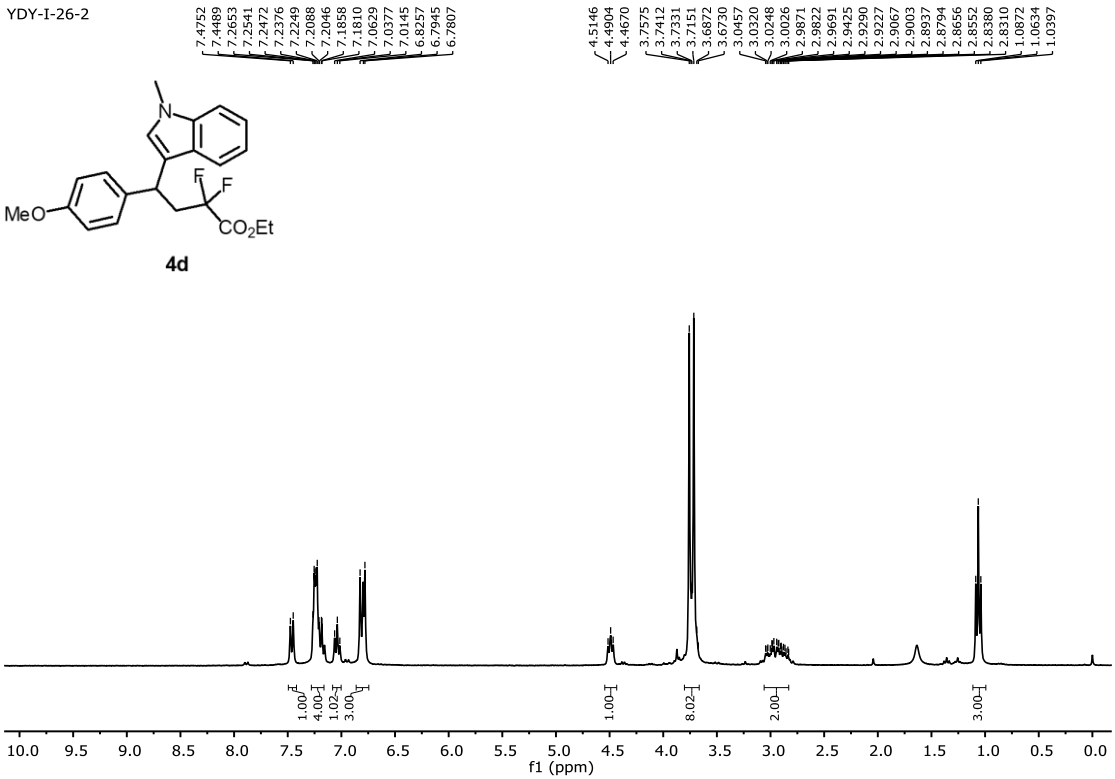
^{1}H NMR of compound **4c** (300 MHz in $CDCl_3$)



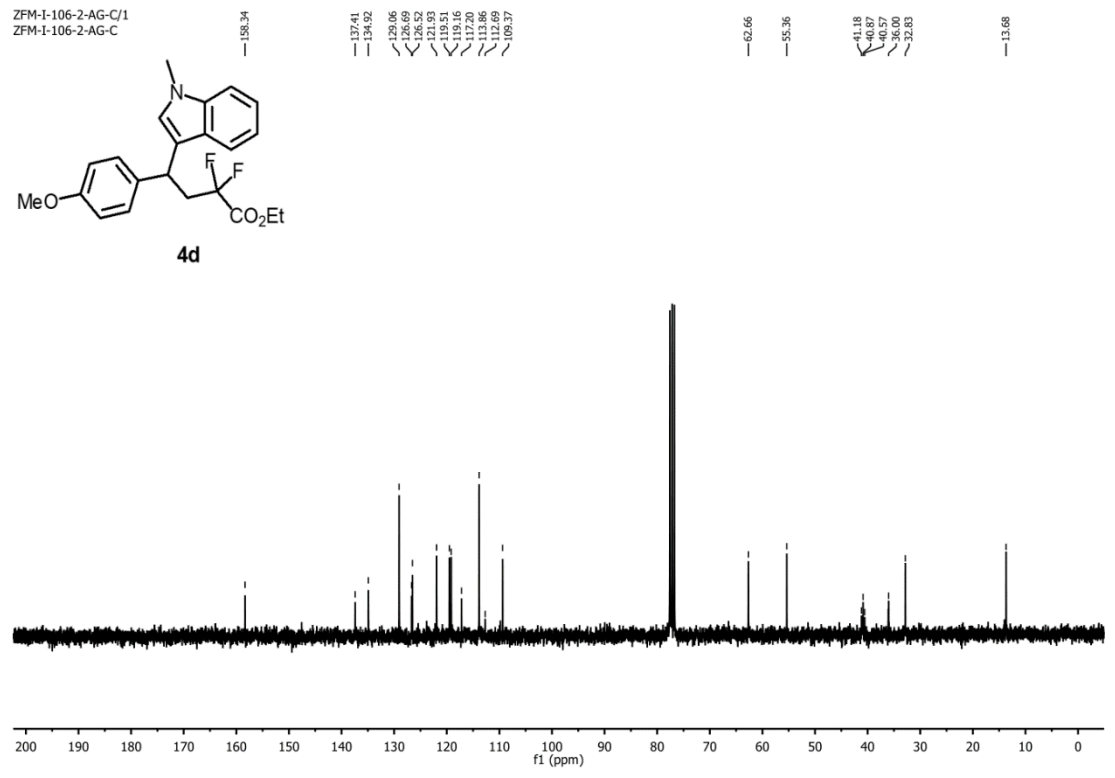
^{13}C NMR of compound **4c** (75 MHz in $CDCl_3$)



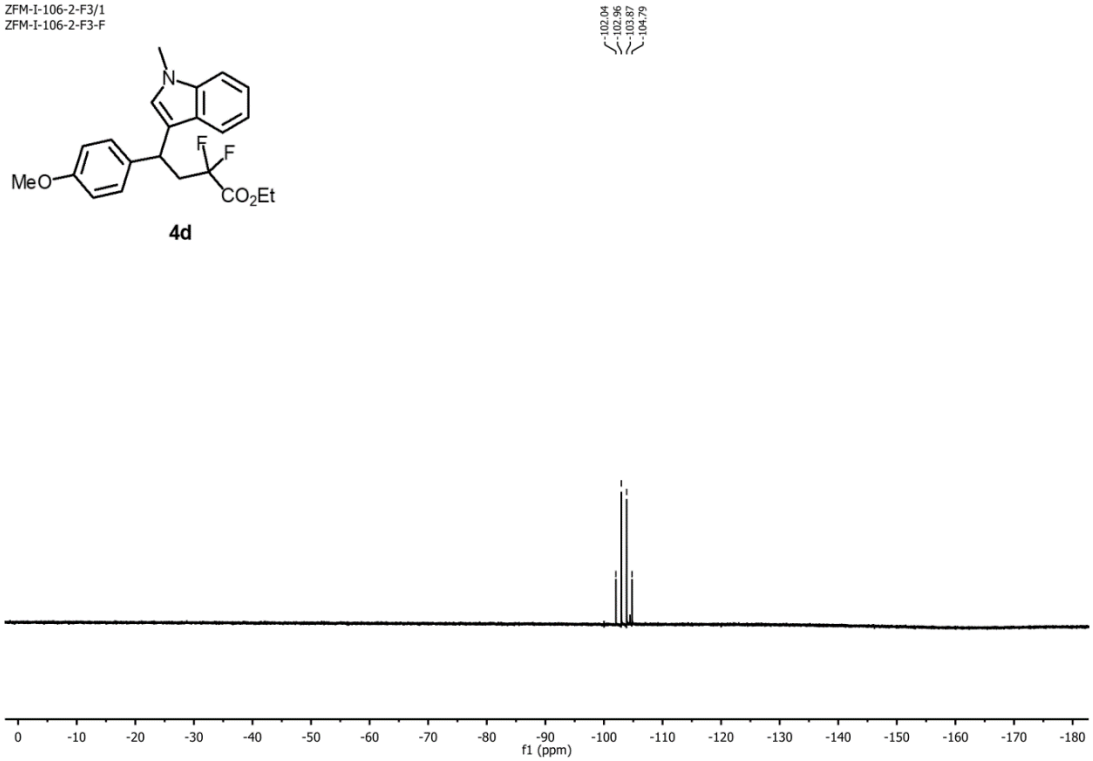
^{1}H NMR of compound **4d** (300 MHz in $CDCl_3$)



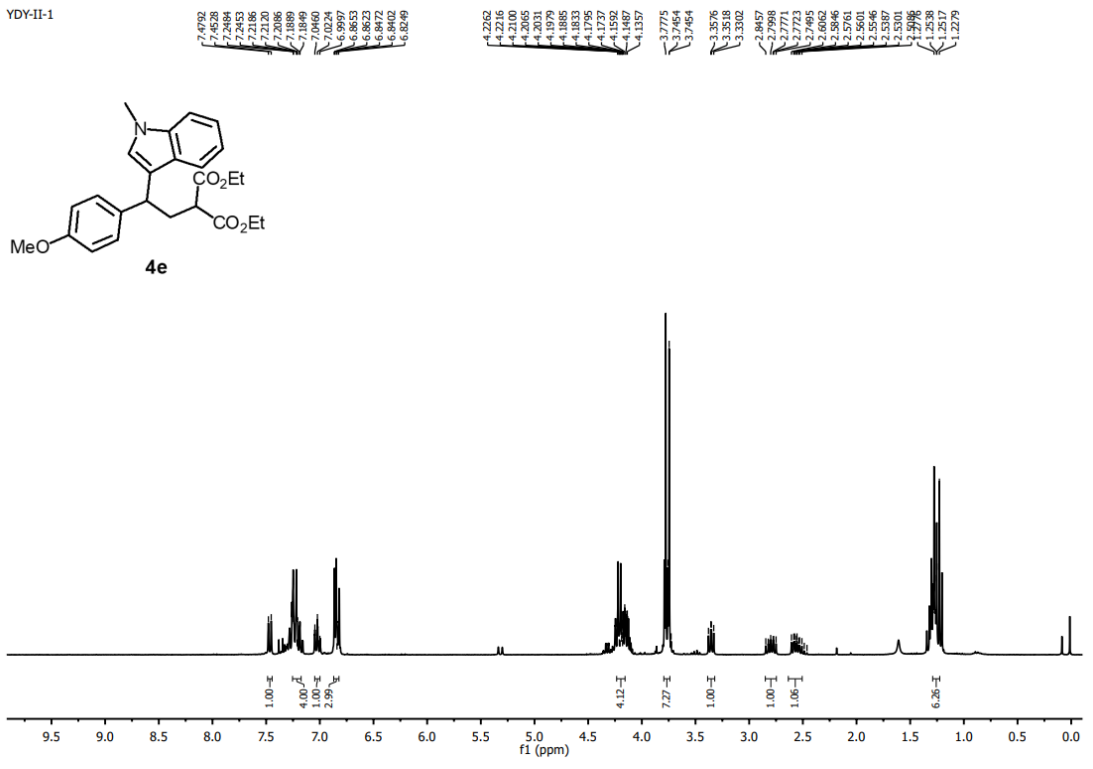
^{13}C NMR of compound **4d** (75 MHz in $CDCl_3$)



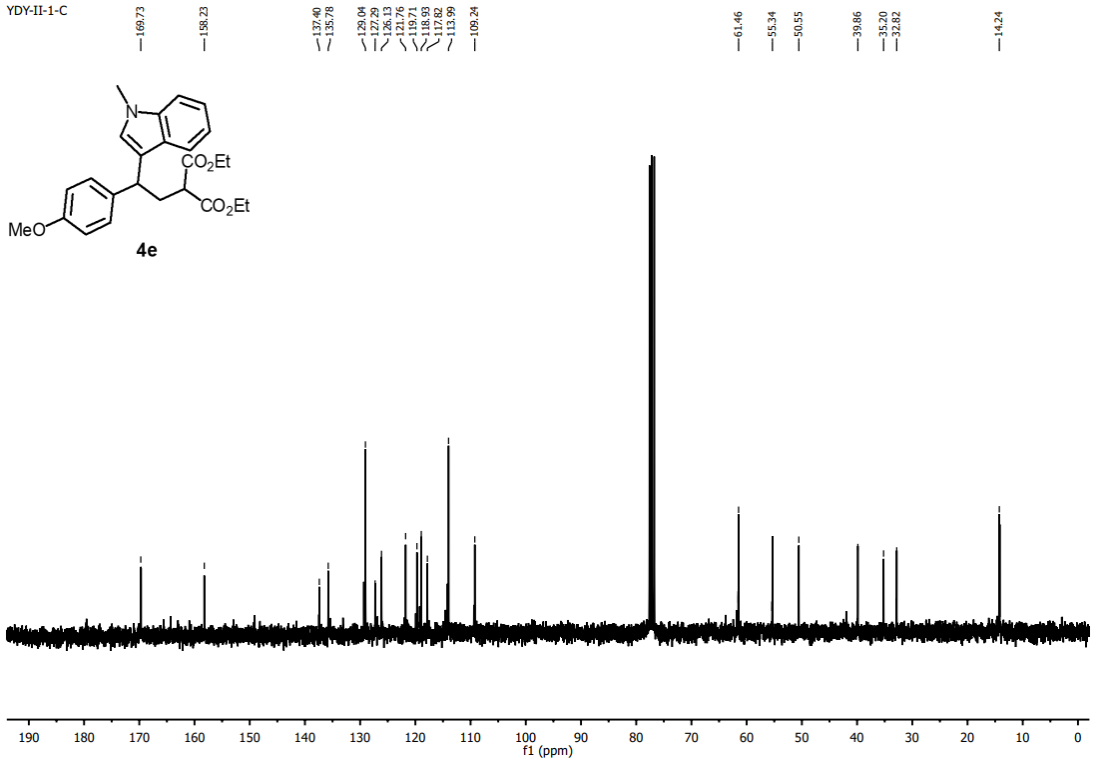
^{19}F NMR of compound **4d** (282 MHz in $CDCl_3$)



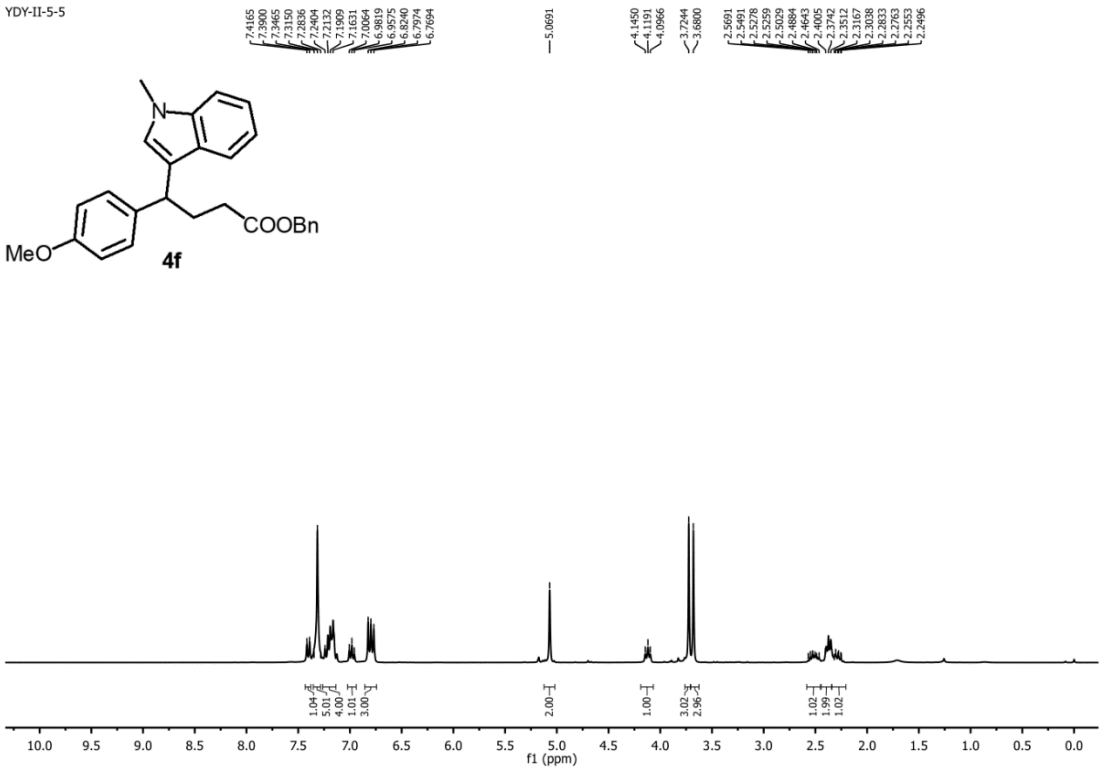
^{1}H NMR of compound **4e** (300 MHz in $CDCl_3$)



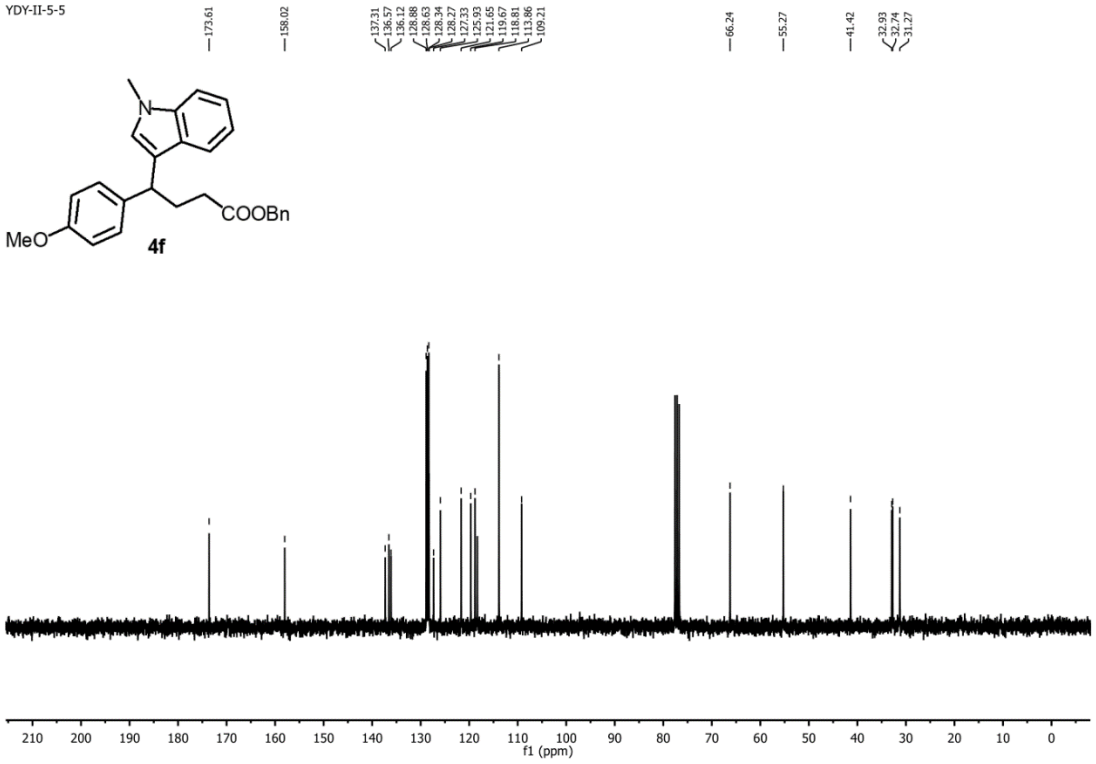
^{13}C NMR of compound **4e** (75 MHz in $CDCl_3$)



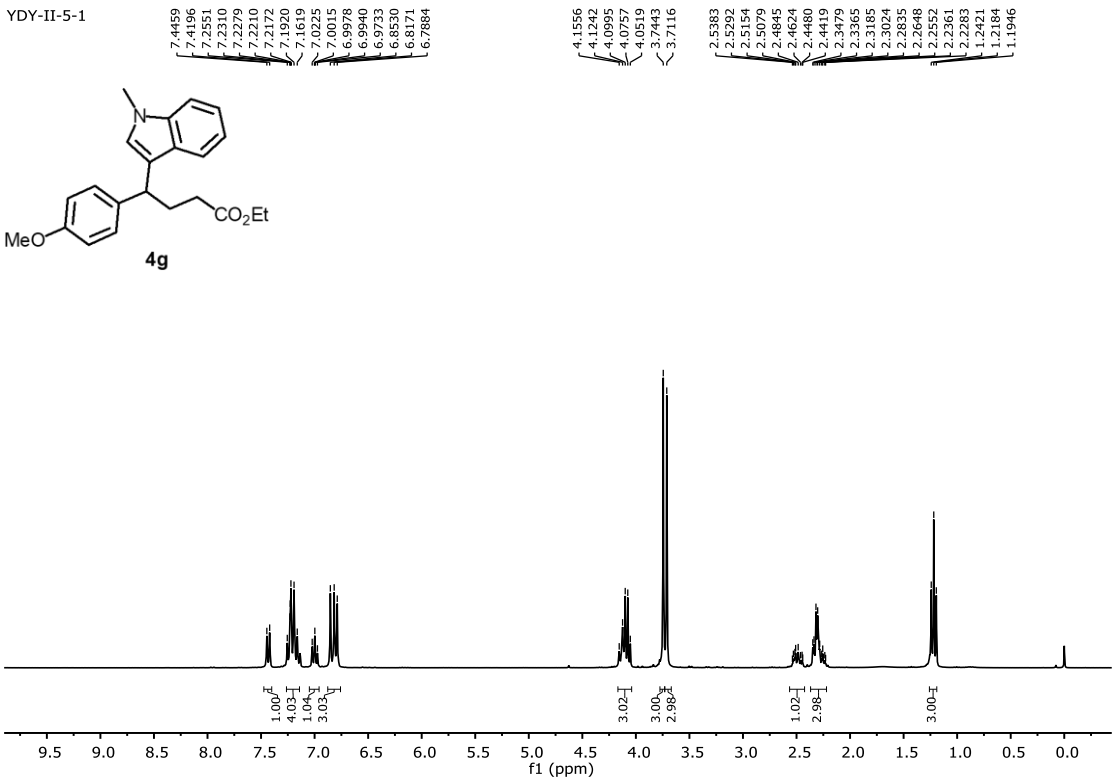
^{1}H NMR of compound **4f** (300 MHz in $CDCl_3$)



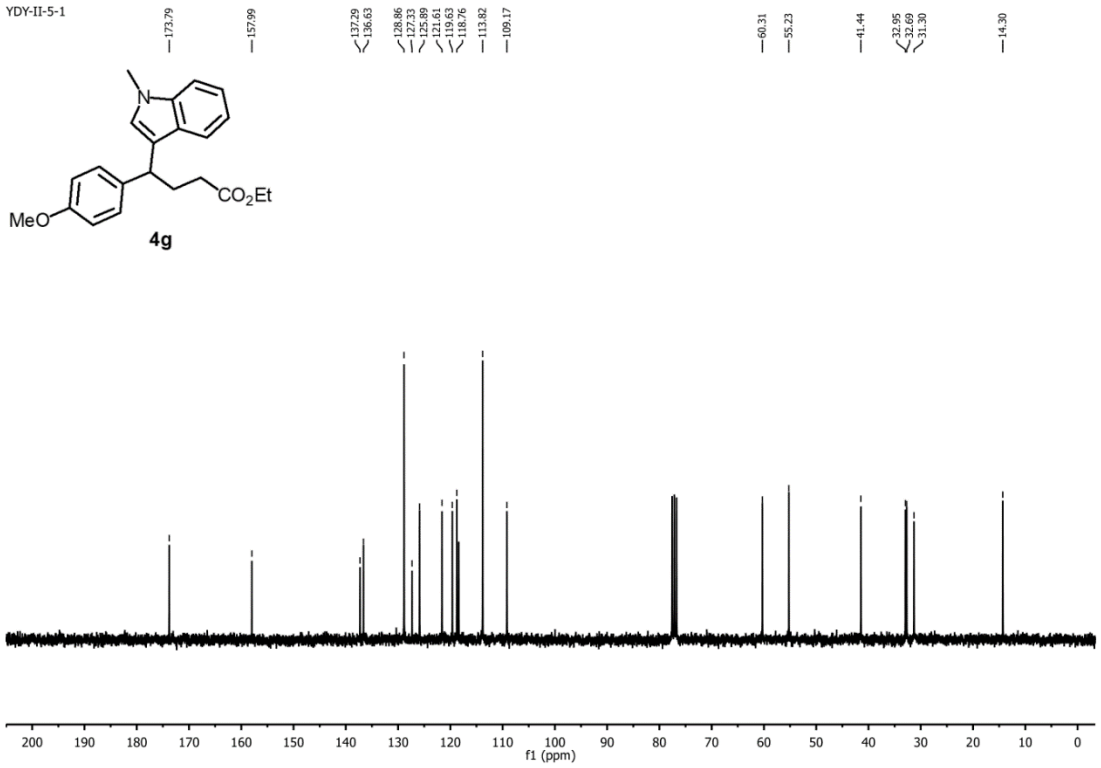
^{13}C NMR of compound **4f** (75 MHz in $CDCl_3$)



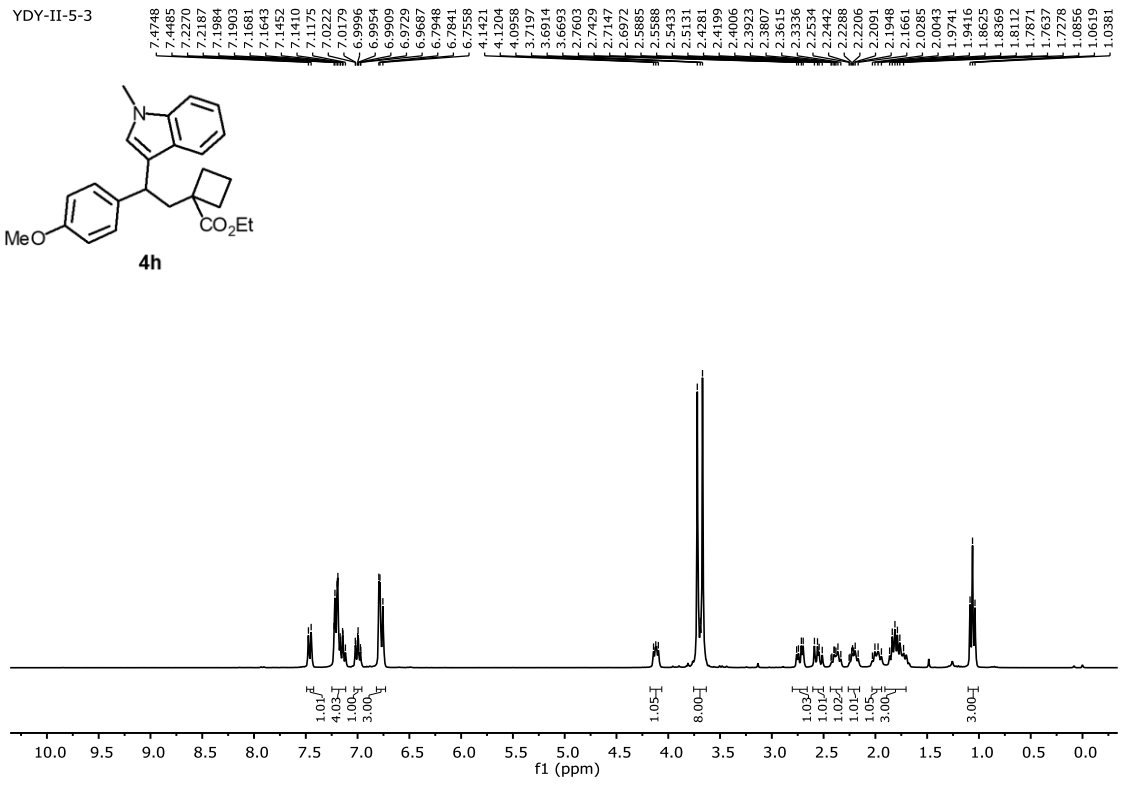
^{1}H NMR of compound **4g** (300 MHz in $CDCl_3$)



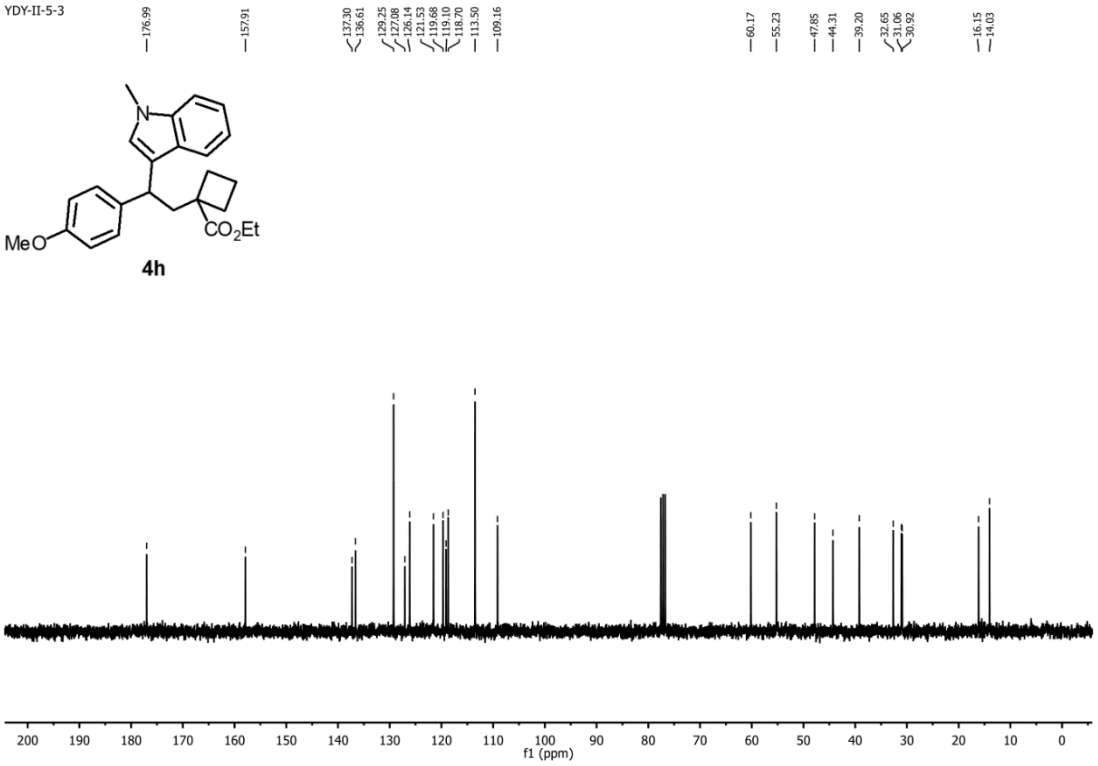
^{13}C NMR of compound **4g** (75 MHz in $CDCl_3$)



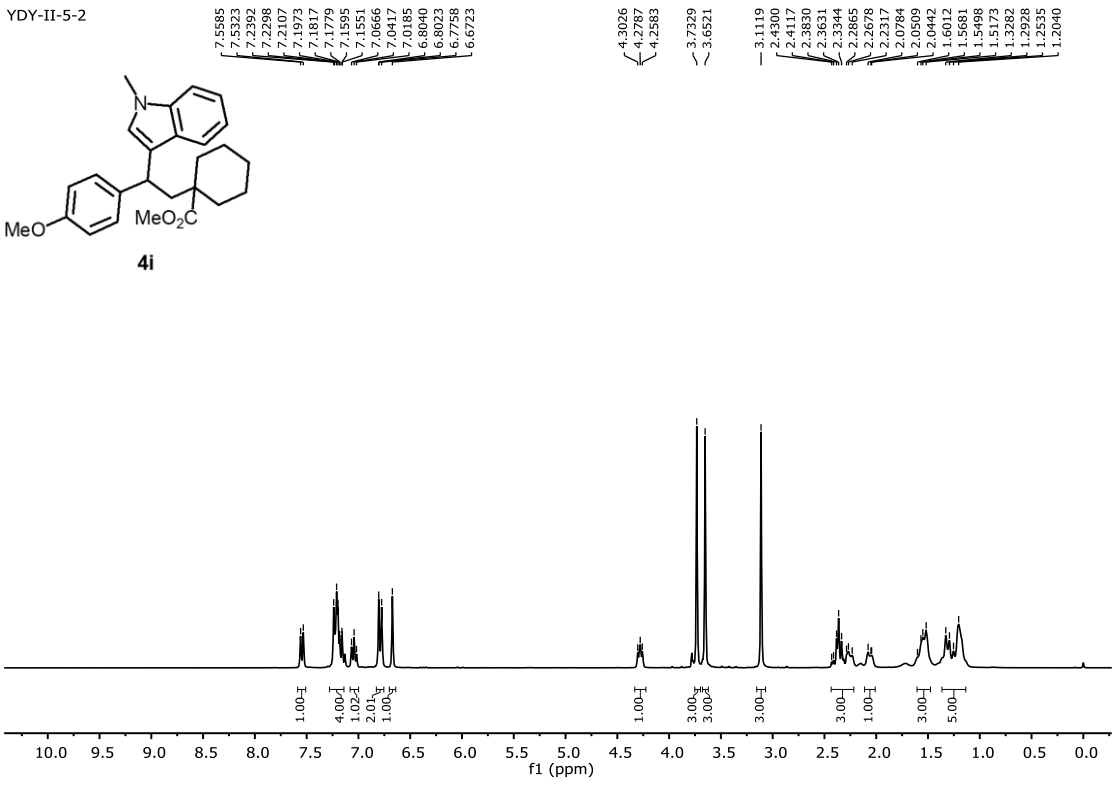
^{1}H NMR of compound **4h** (300 MHz in $CDCl_3$)



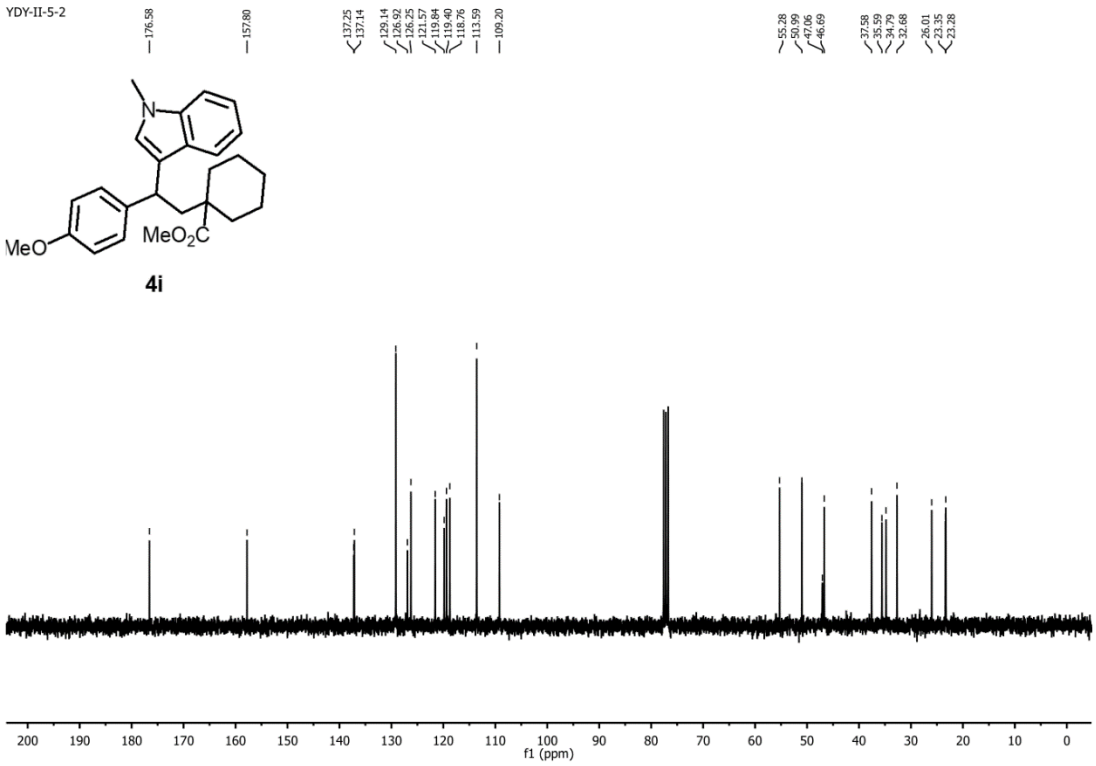
^{13}C NMR of compound **4h** (75 MHz in $CDCl_3$)



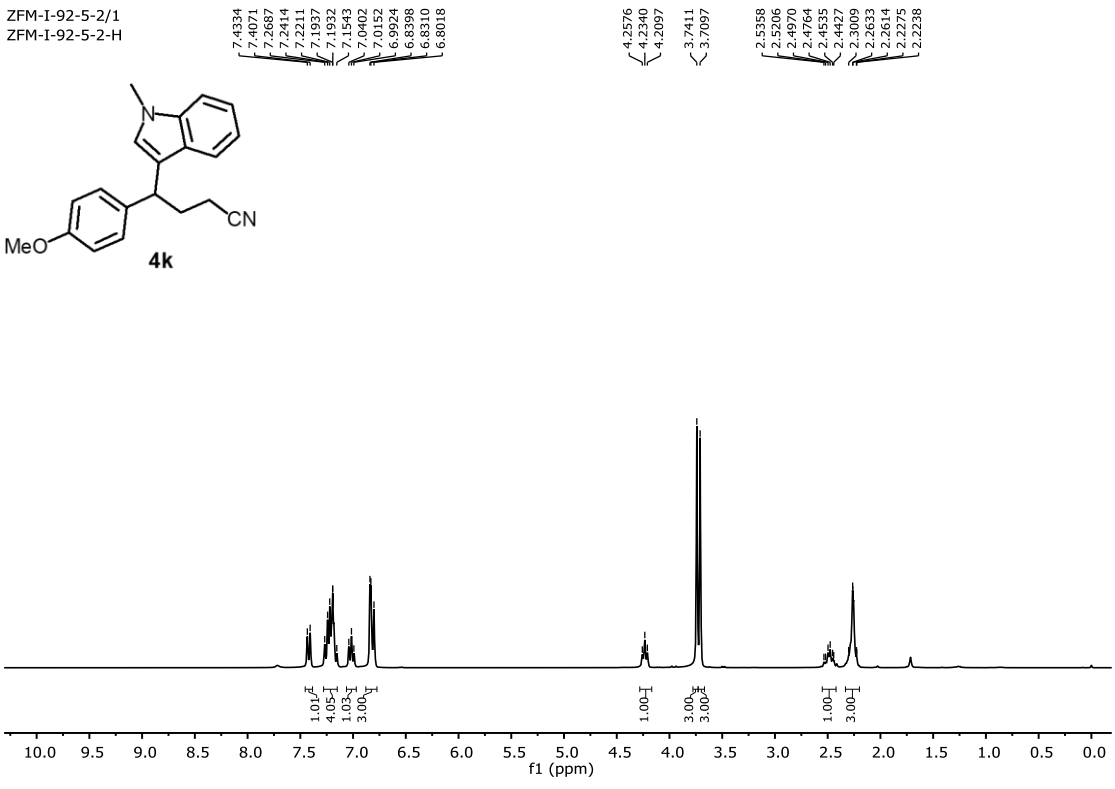
^{1}H NMR of compound **4i** (300 MHz in $CDCl_3$)



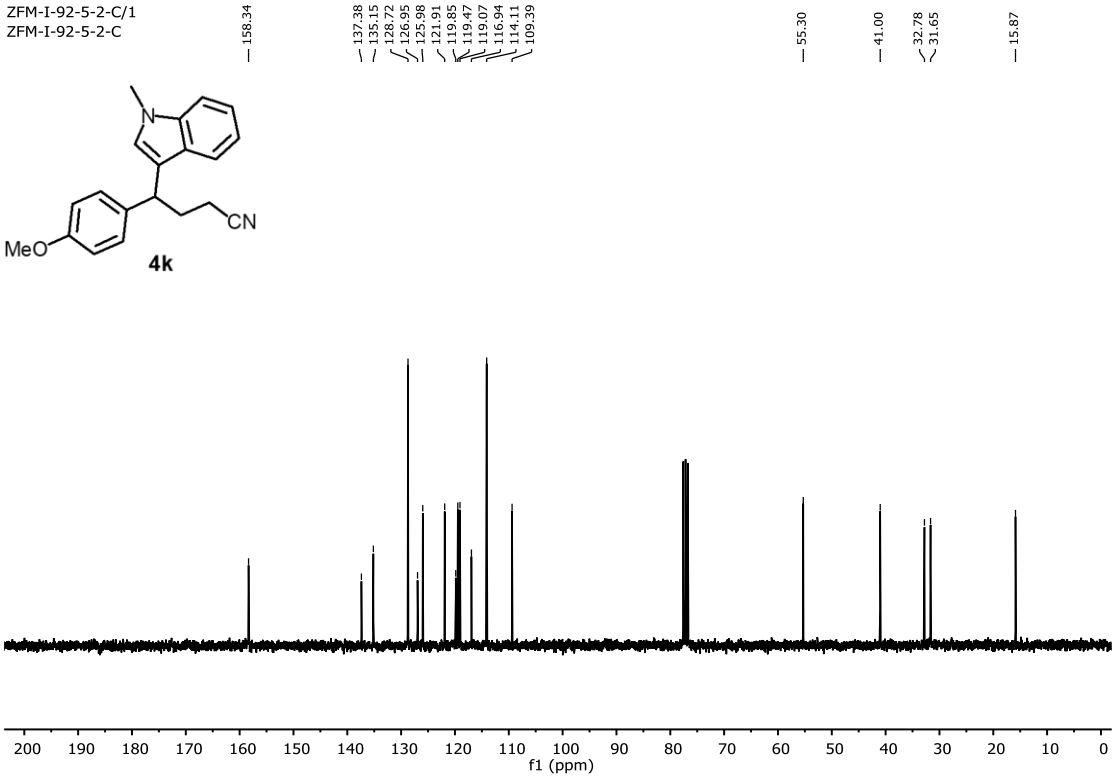
^{13}C NMR of compound **4i** (75 MHz in $CDCl_3$)



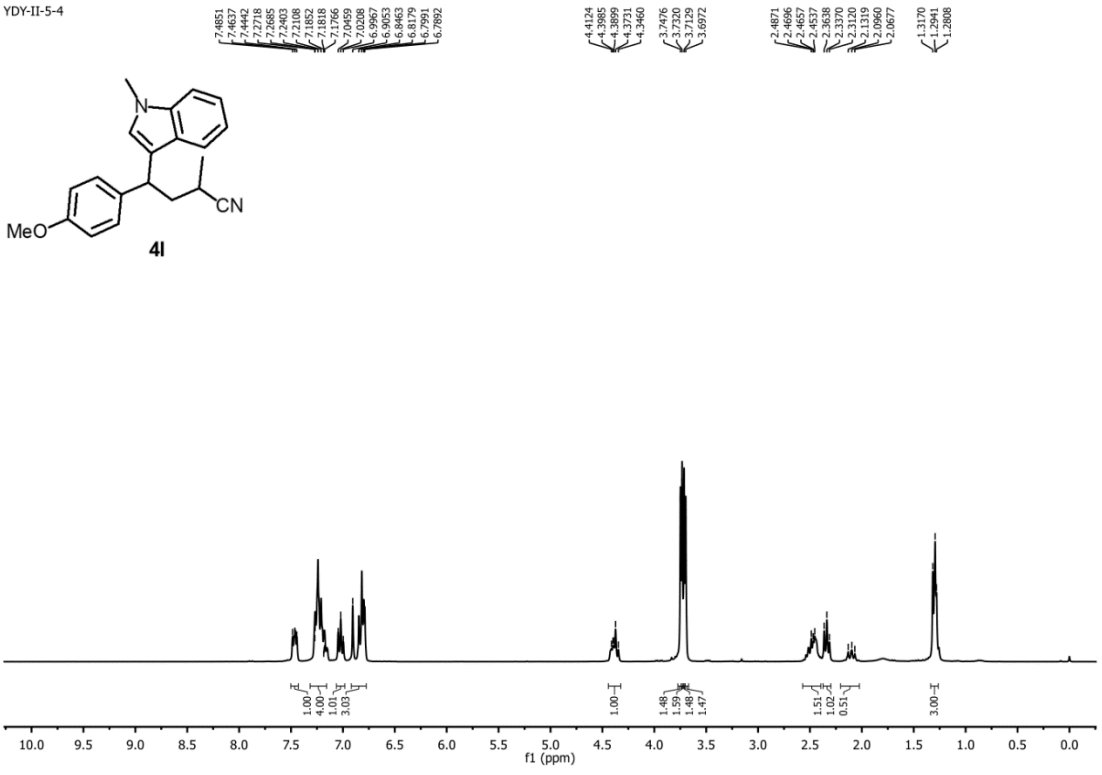
^{1}H NMR of compound **4k** (300 MHz in $CDCl_3$)



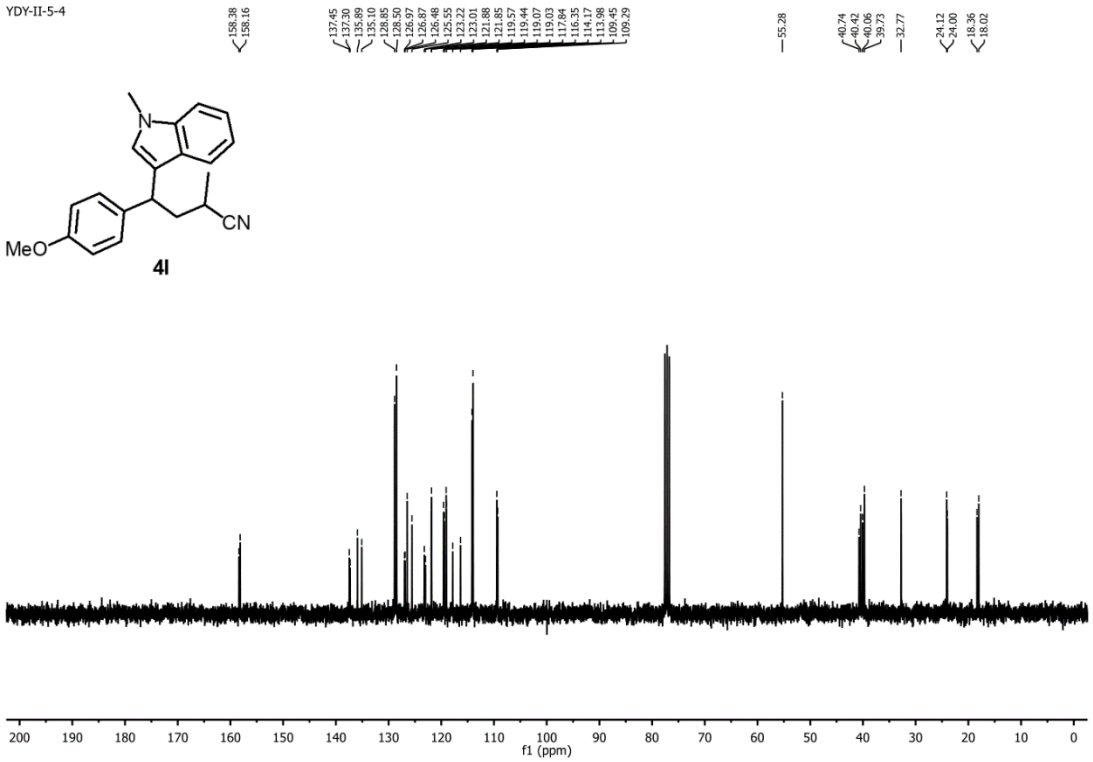
^{13}C NMR of compound **4k** (75 MHz in $CDCl_3$)



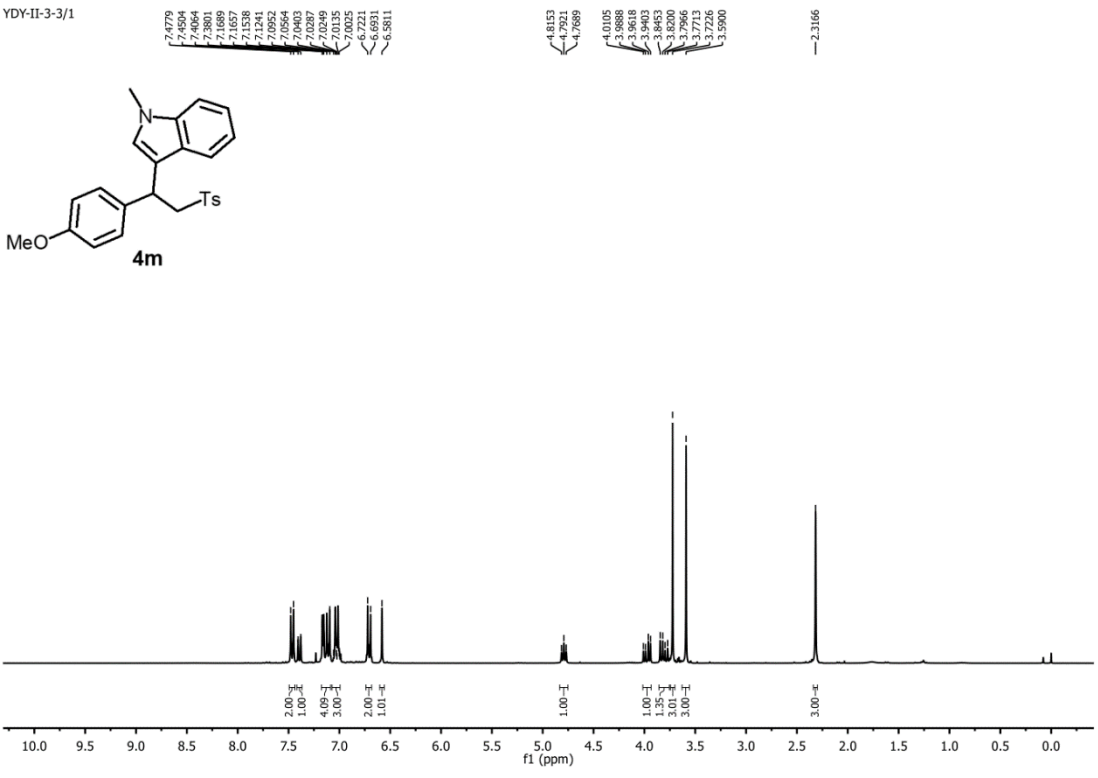
^{1}H NMR of compound **4l** (300 MHz in $CDCl_3$)



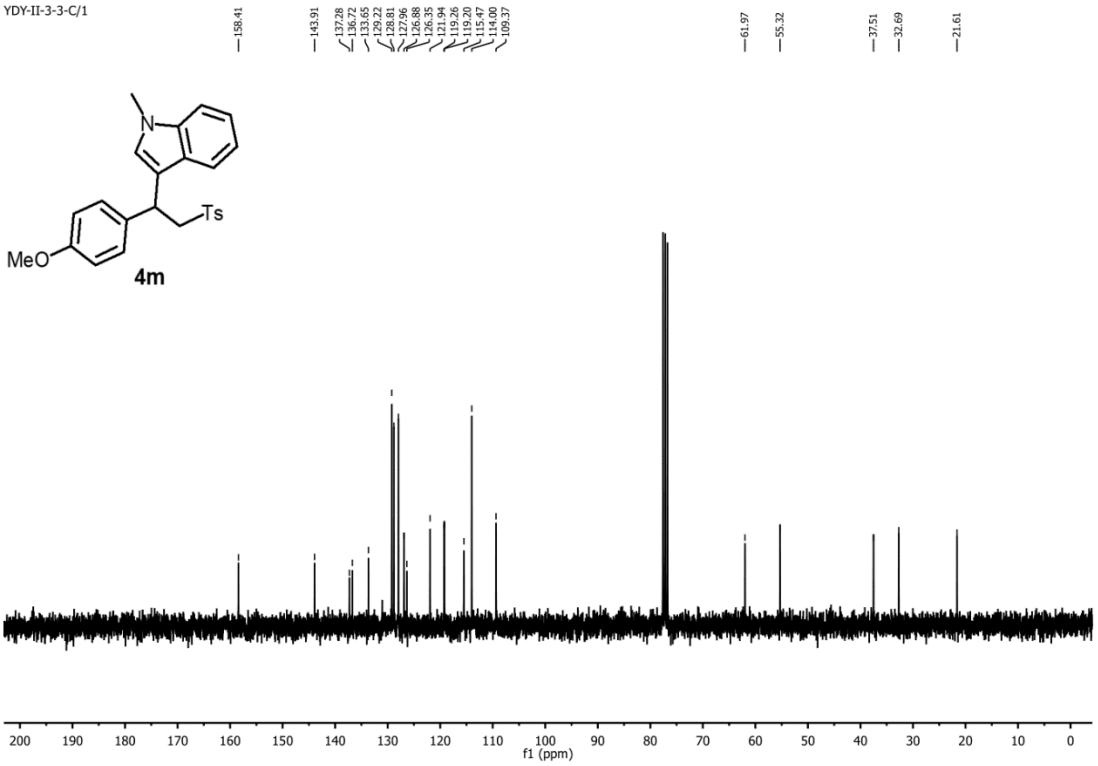
^{13}C NMR of compound **4l** (75 MHz in $CDCl_3$)



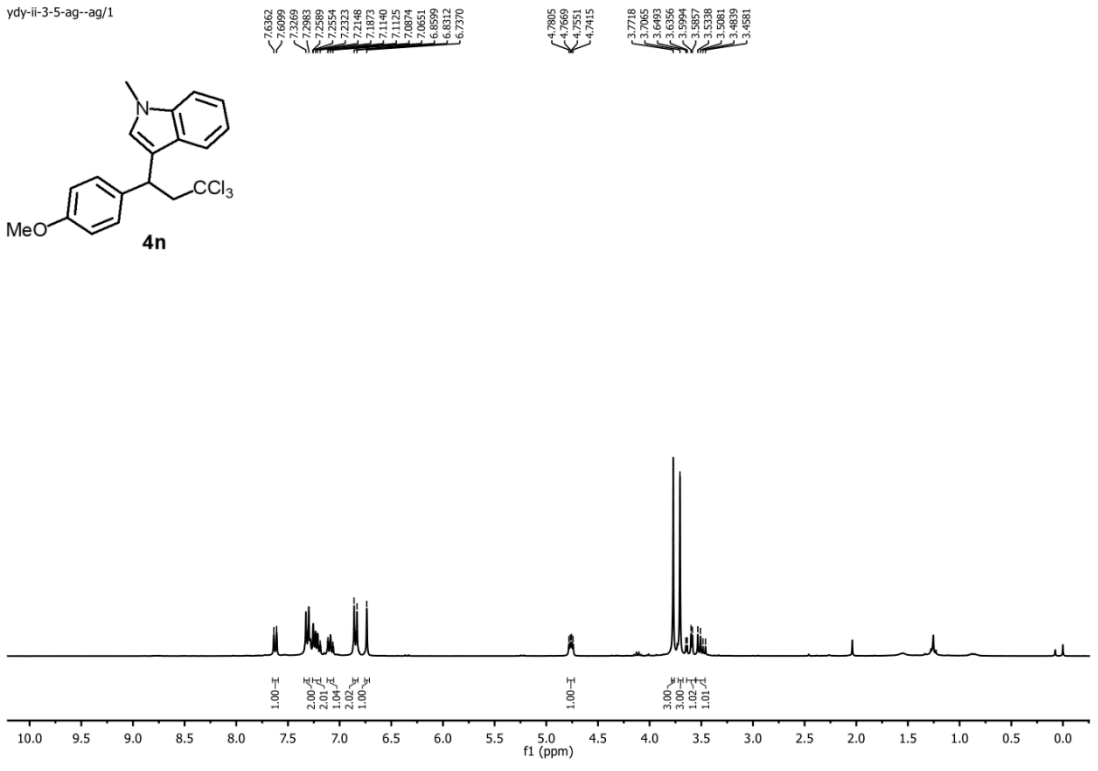
^{1}H NMR of compound **4m** (300 MHz in $CDCl_3$)



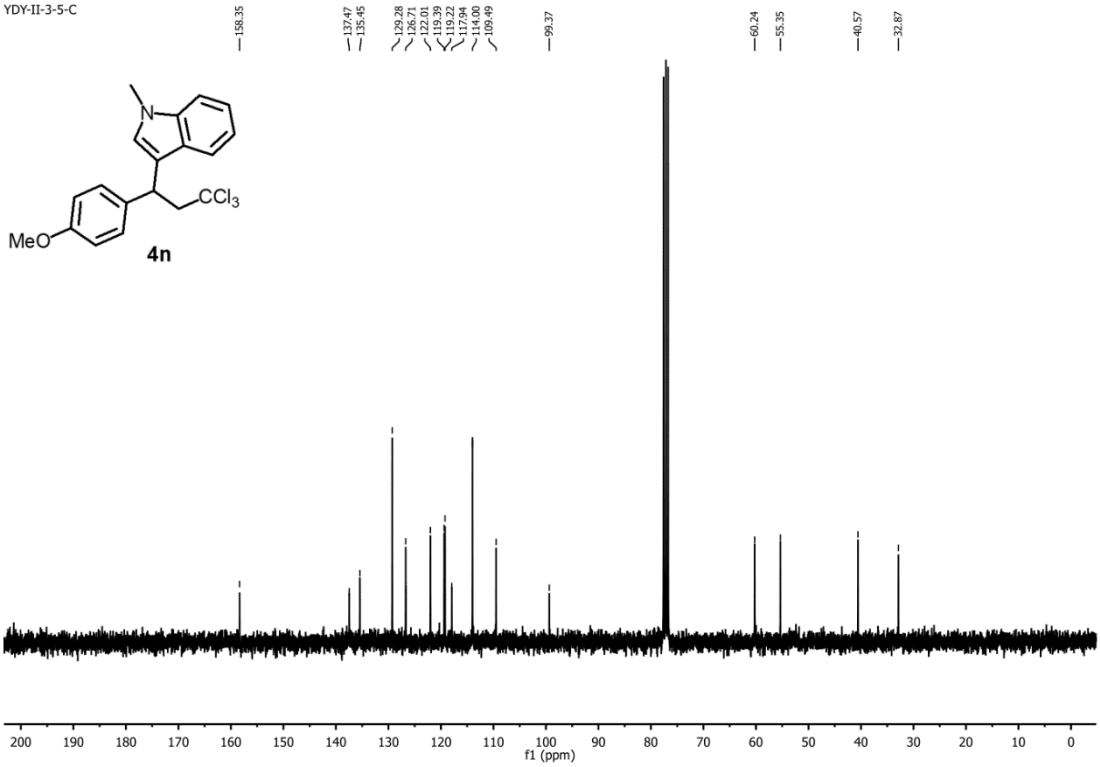
^{13}C NMR of compound **4m** (75 MHz in $CDCl_3$)



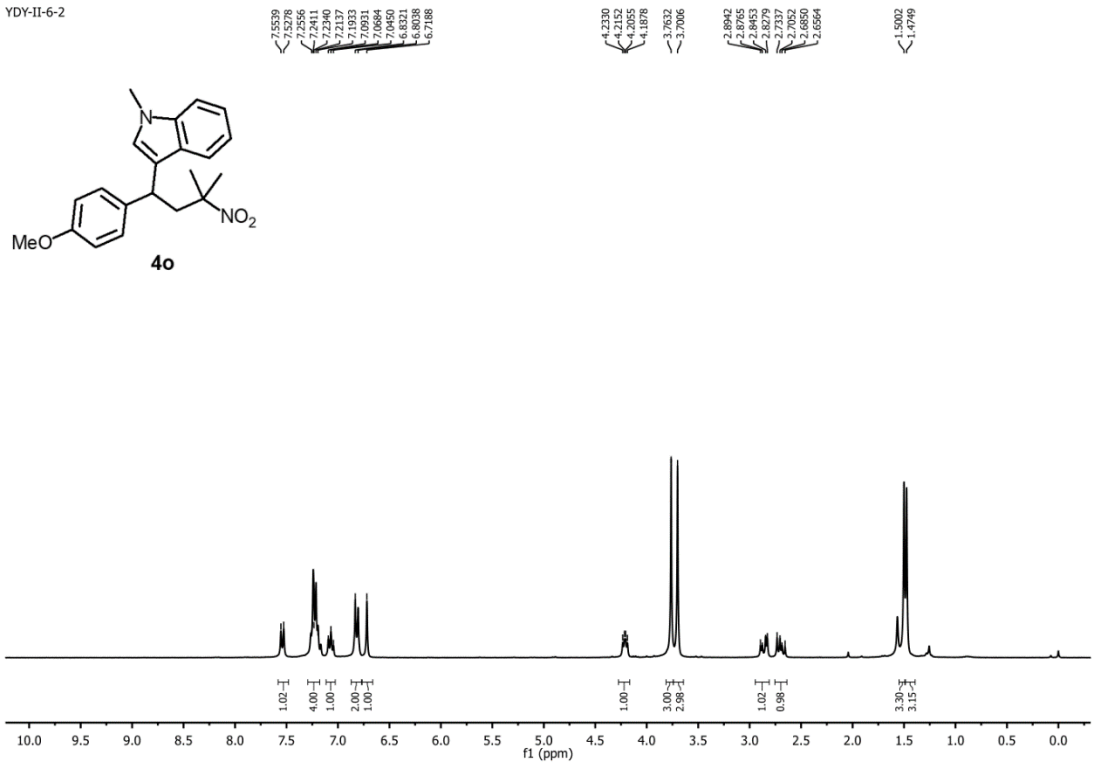
^{1}H NMR of compound **4n** (300 MHz in $CDCl_3$)



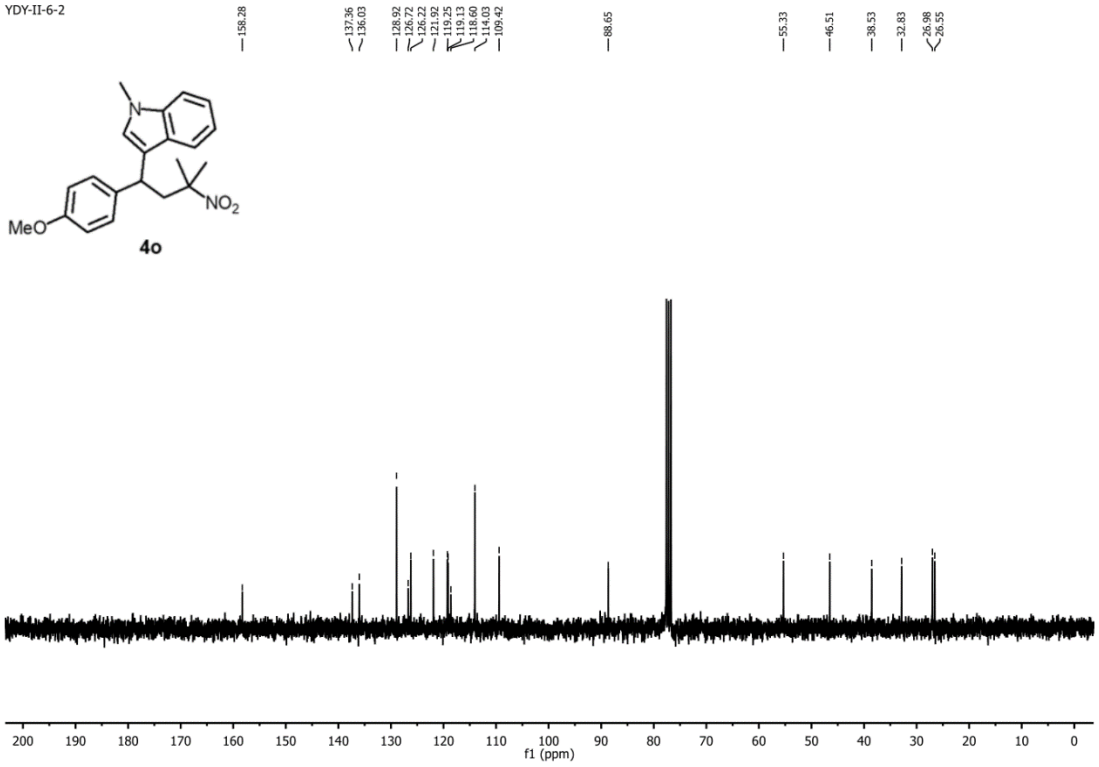
^{13}C NMR of compound **4n** (75 MHz in $CDCl_3$)



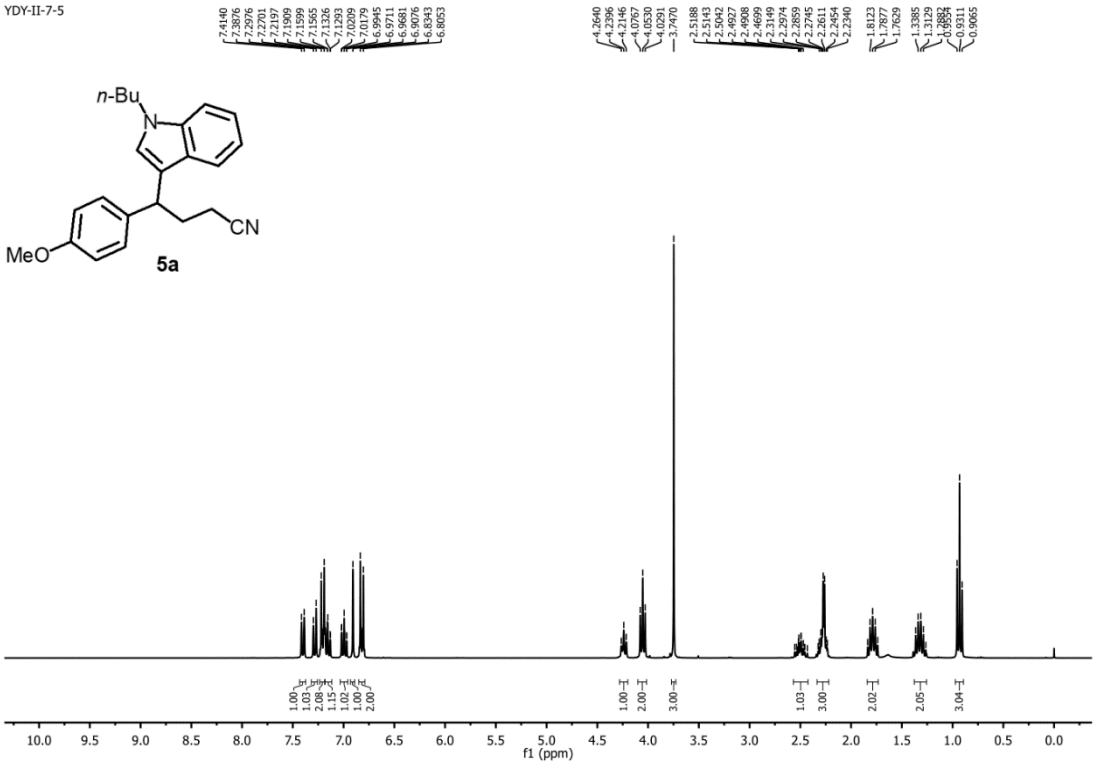
^{1}H NMR of compound **4o** (300 MHz in $CDCl_3$)



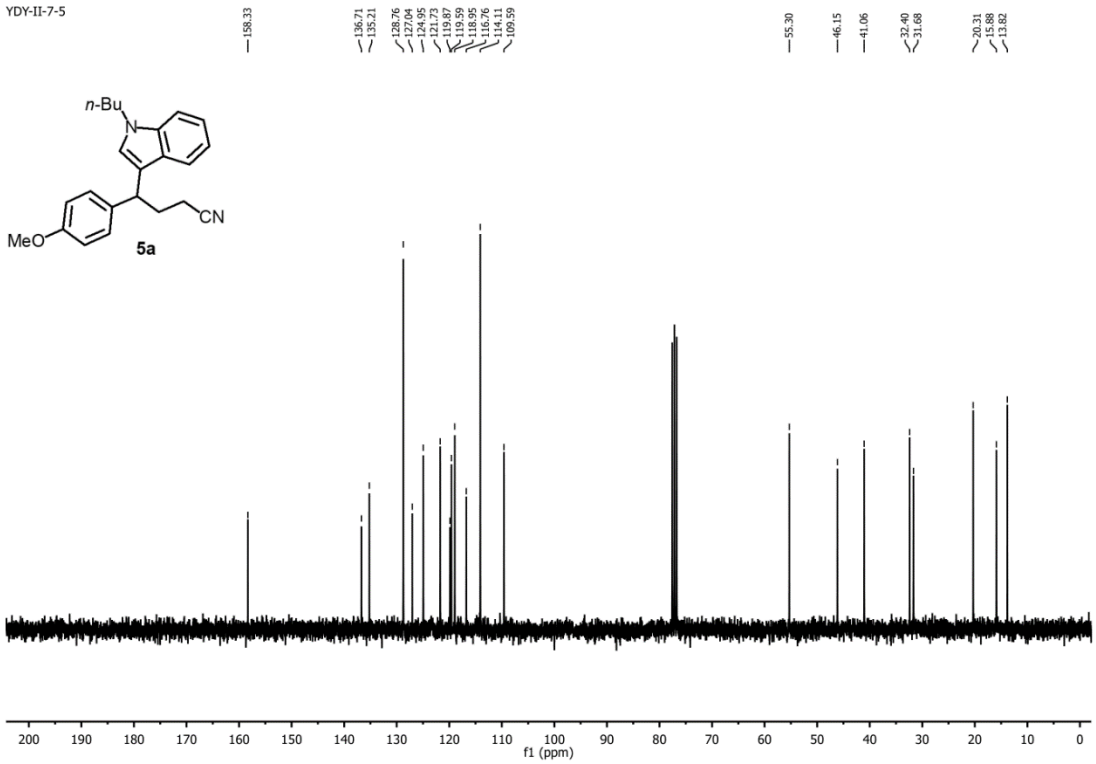
^{13}C NMR of compound **4o** (75 MHz in $CDCl_3$)



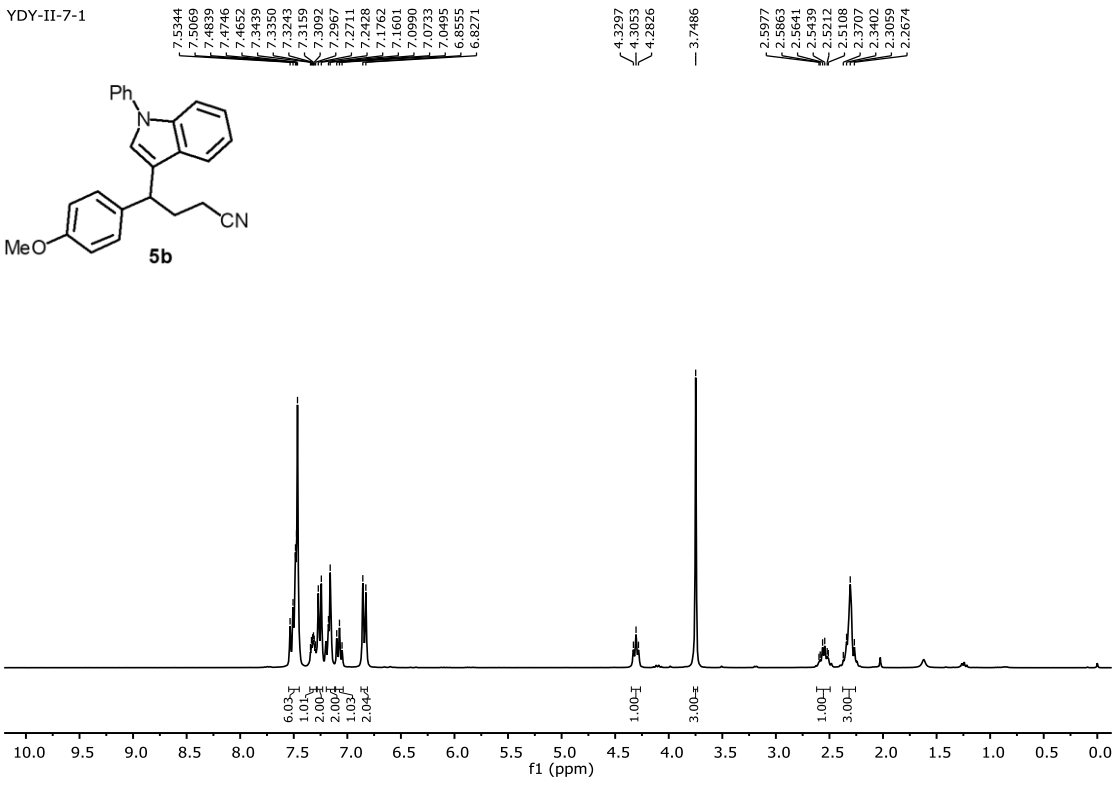
^{1}H NMR of compound **5a** (300 MHz in $CDCl_3$)



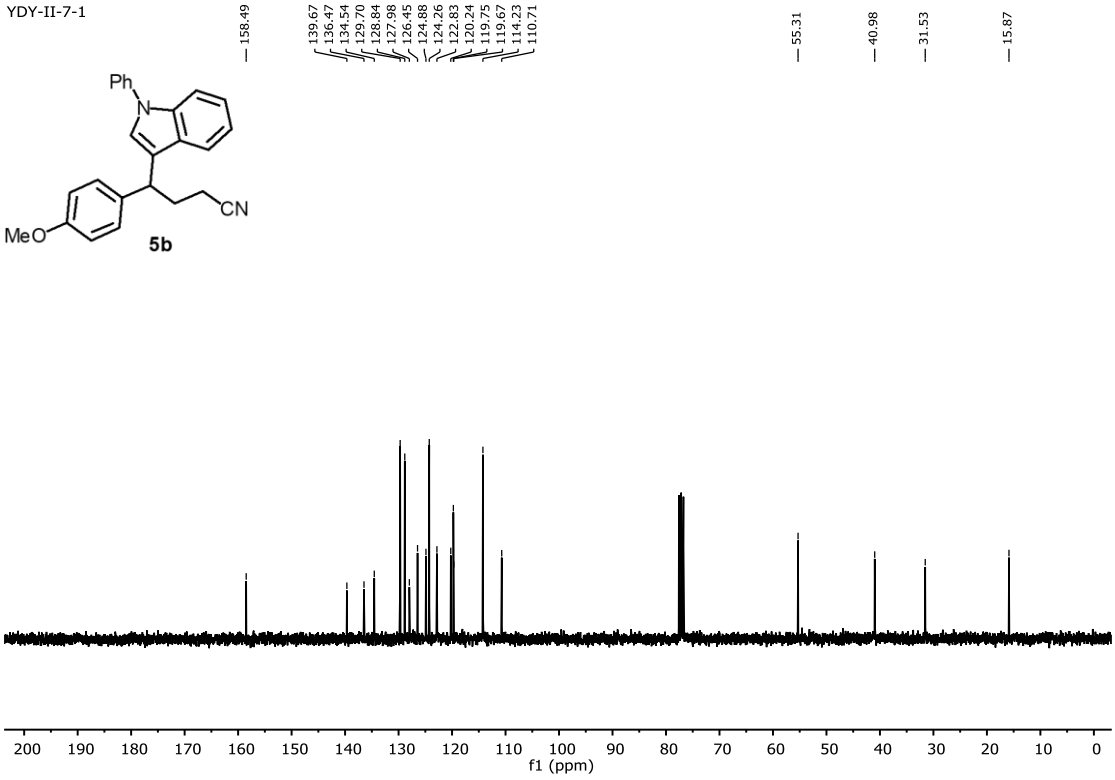
^{13}C NMR of compound **5a** (75 MHz in $CDCl_3$)



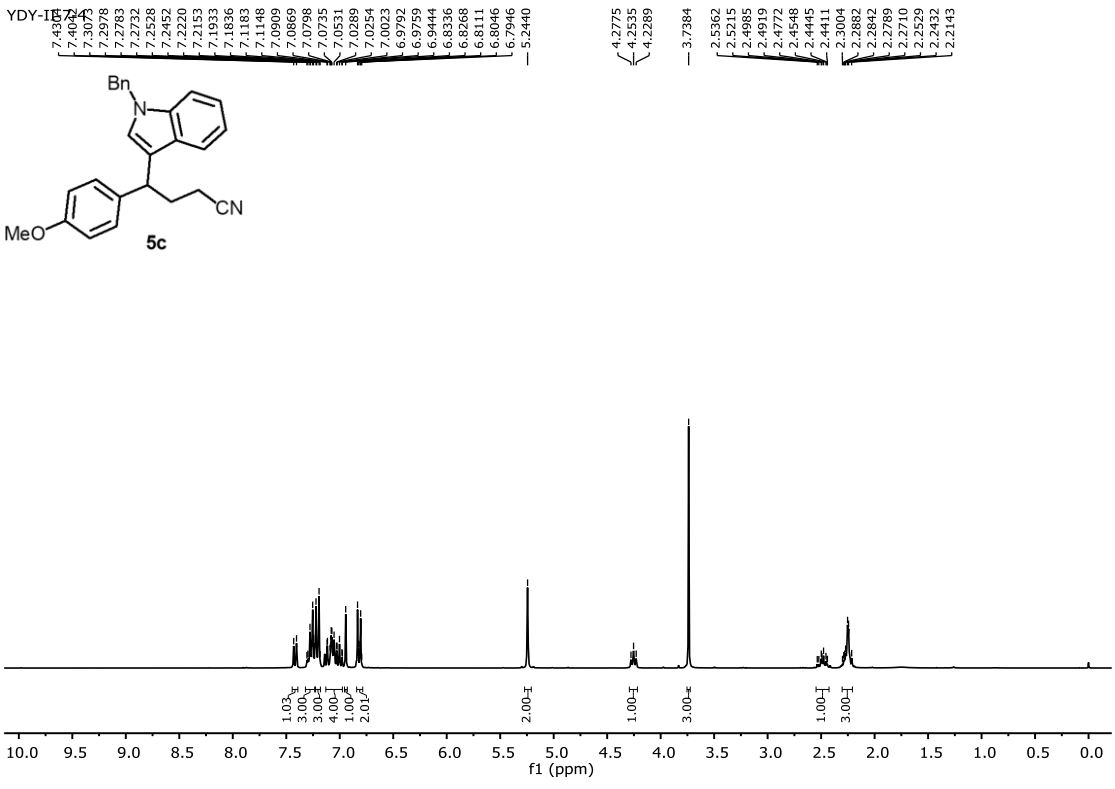
^{1}H NMR of compound **5b** (300 MHz in $CDCl_3$)



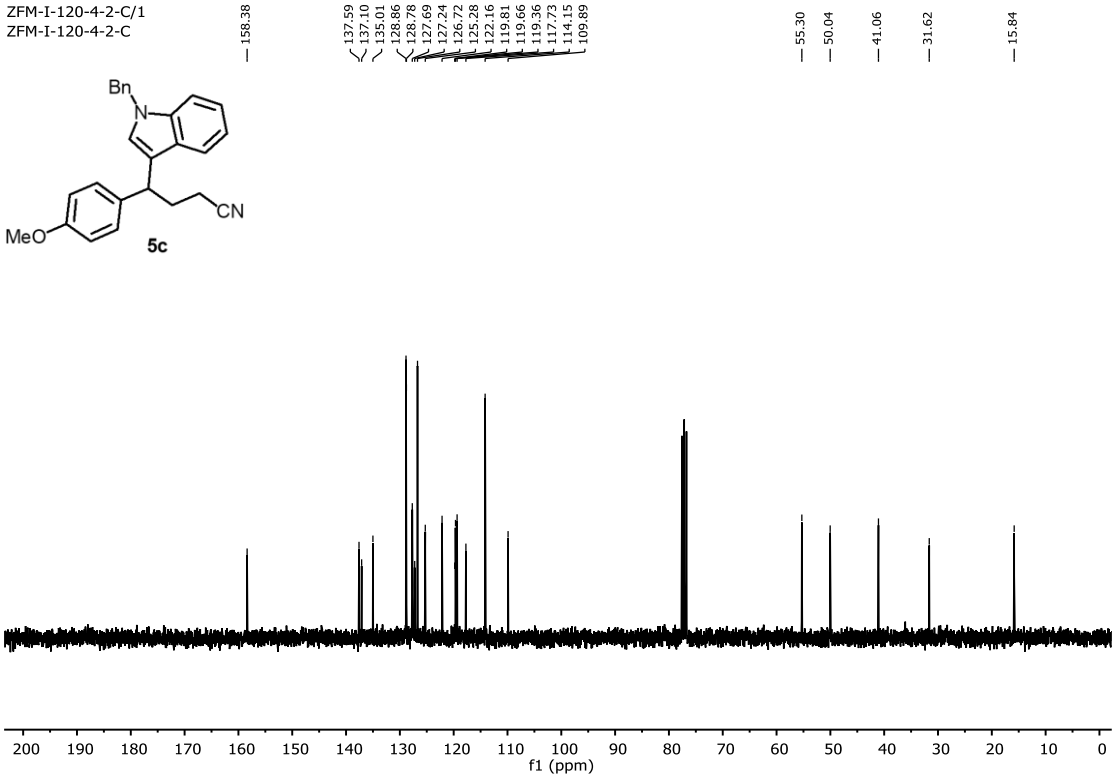
^{13}C NMR of compound **5b** (75 MHz in $CDCl_3$)



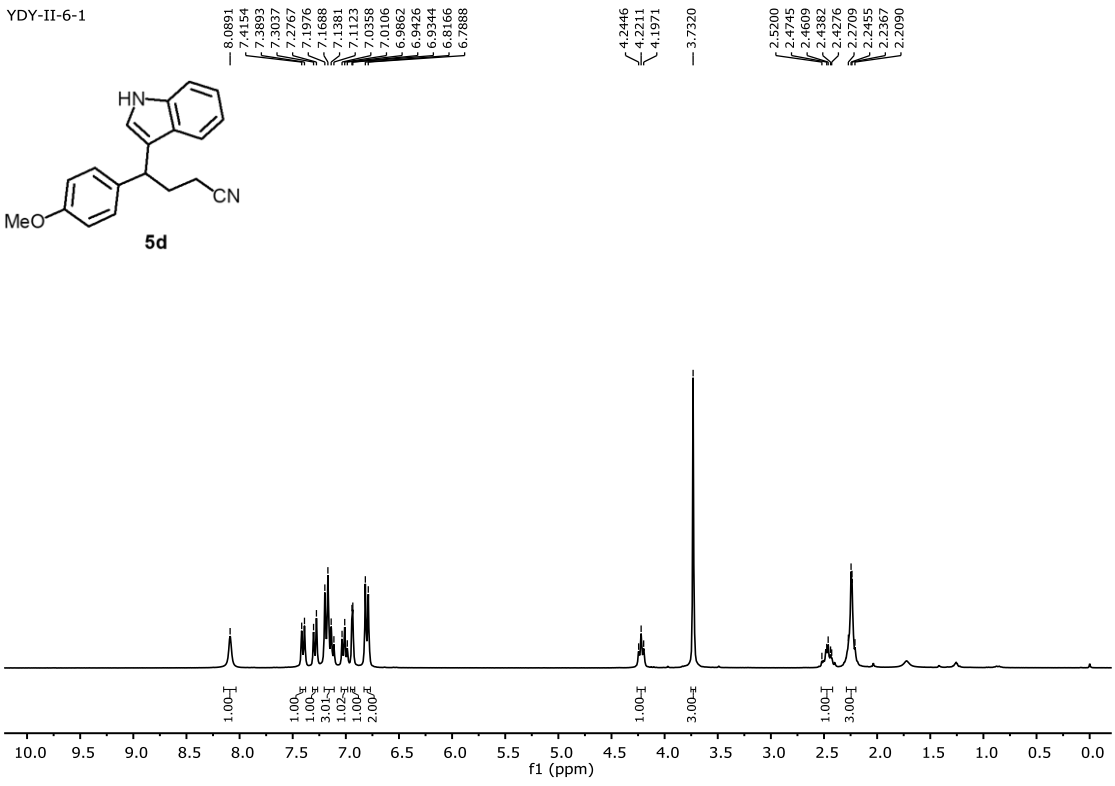
^{1}H NMR of compound **5c** (300 MHz in $CDCl_3$)



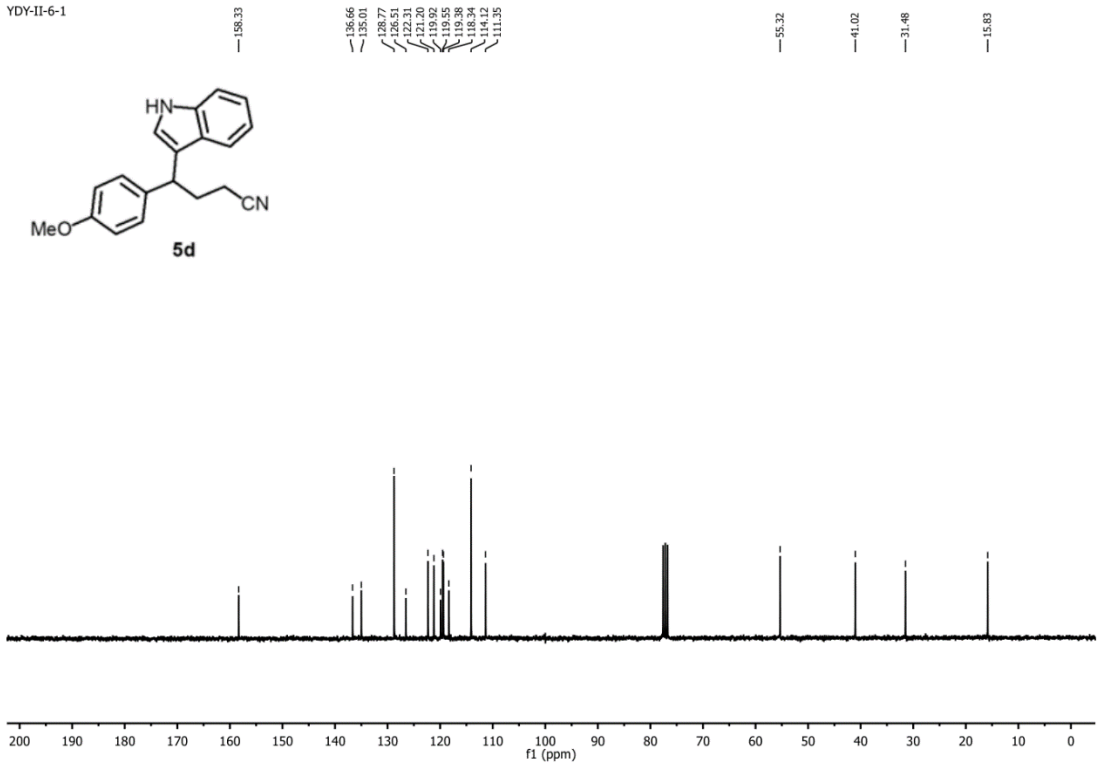
^{13}C NMR of compound **5c** (75 MHz in $CDCl_3$)



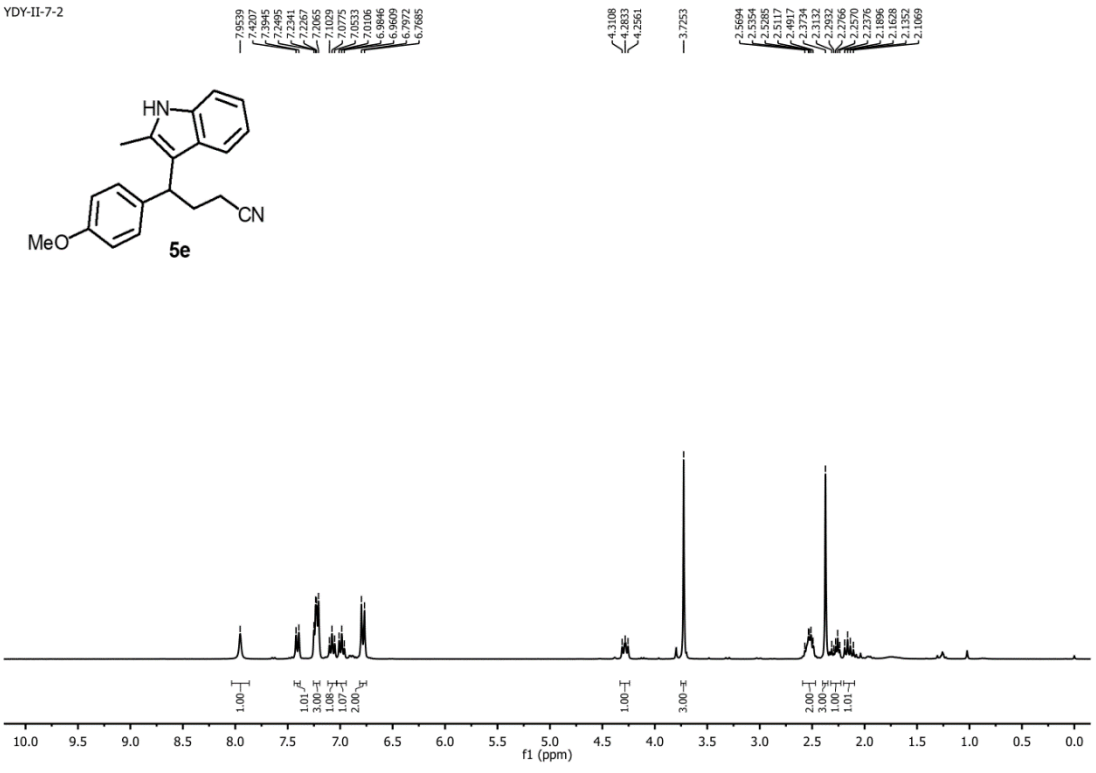
^{1}H NMR of compound **5d** (300 MHz in $CDCl_3$)



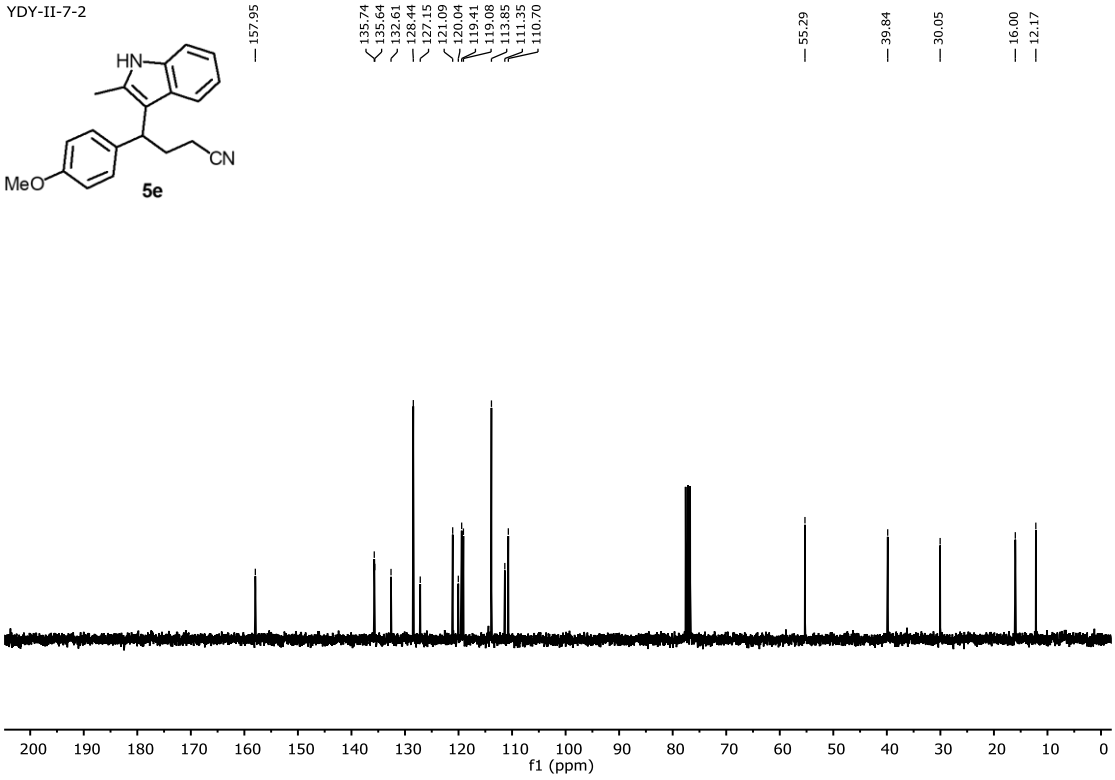
^{13}C NMR of compound **5d** (75 MHz in $CDCl_3$)



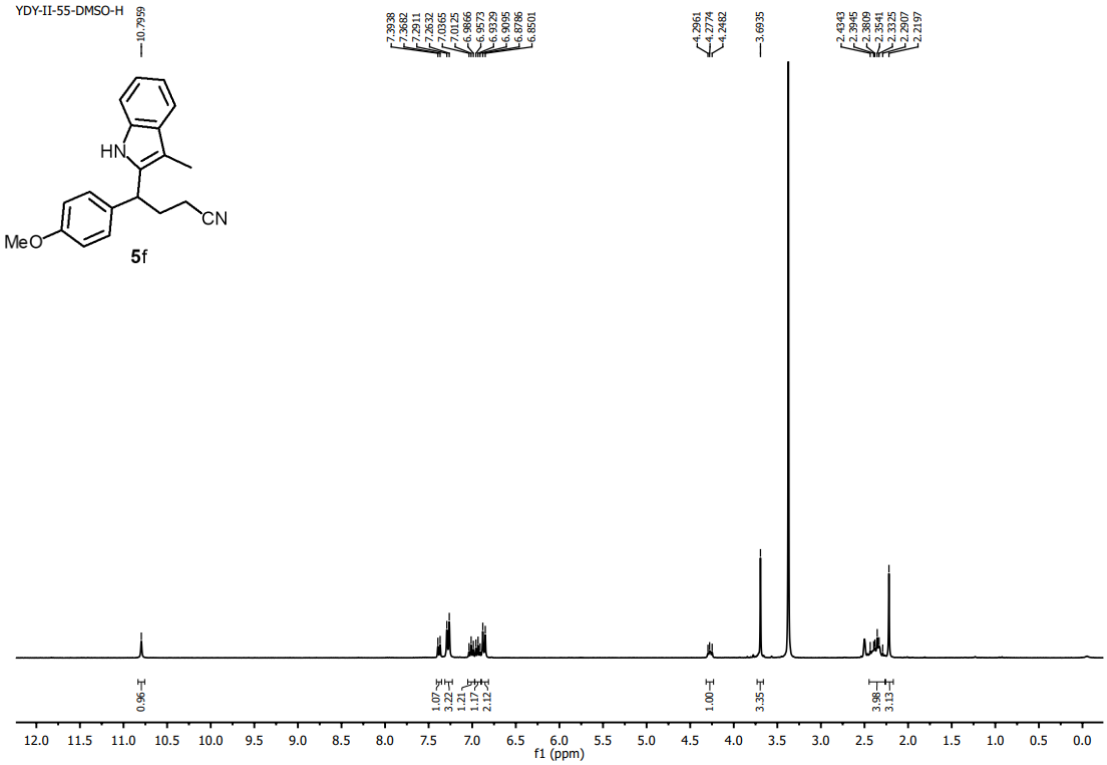
^{1}H NMR of compound **5e** (300 MHz in $CDCl_3$)



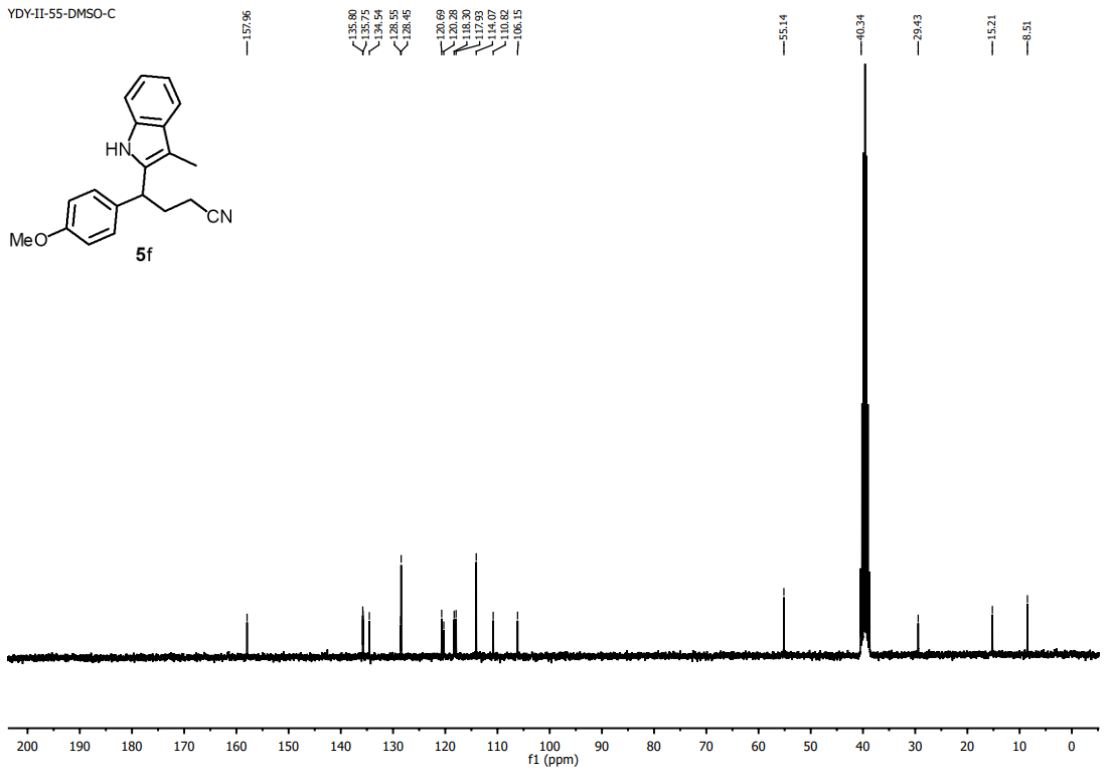
^{13}C NMR of compound **5e** (75 MHz in $CDCl_3$)



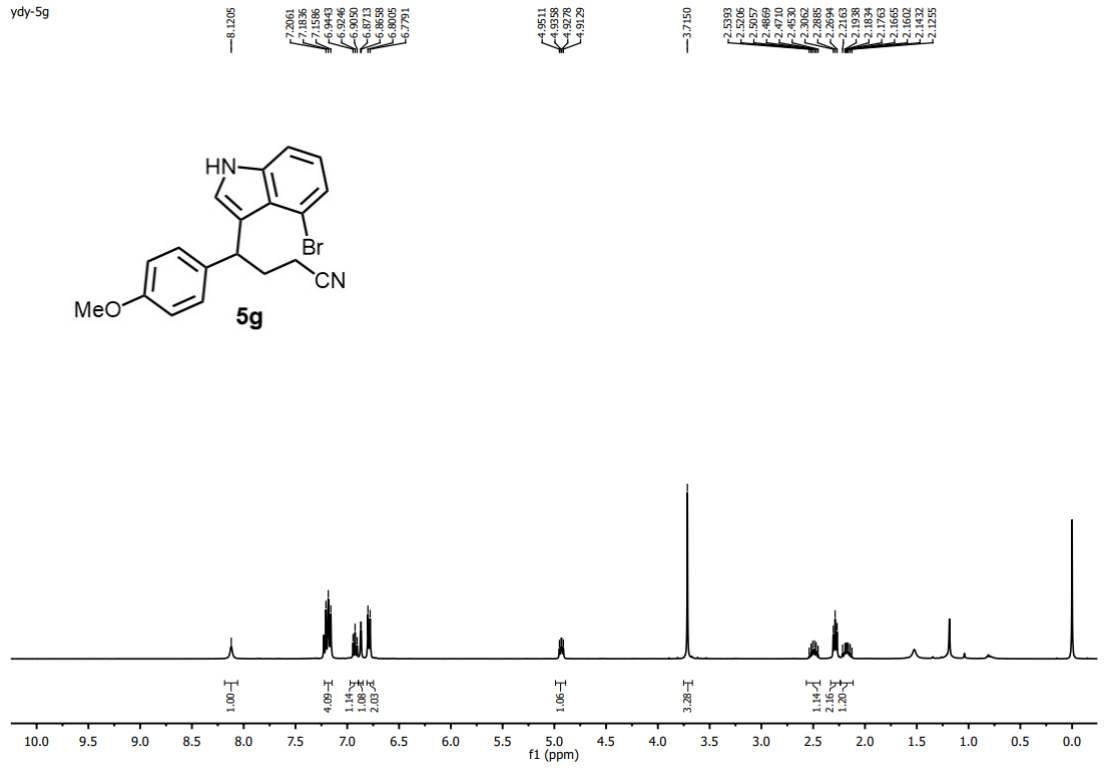
^{1}H NMR of compound **5f** (300 MHz in d_6-DMSO)



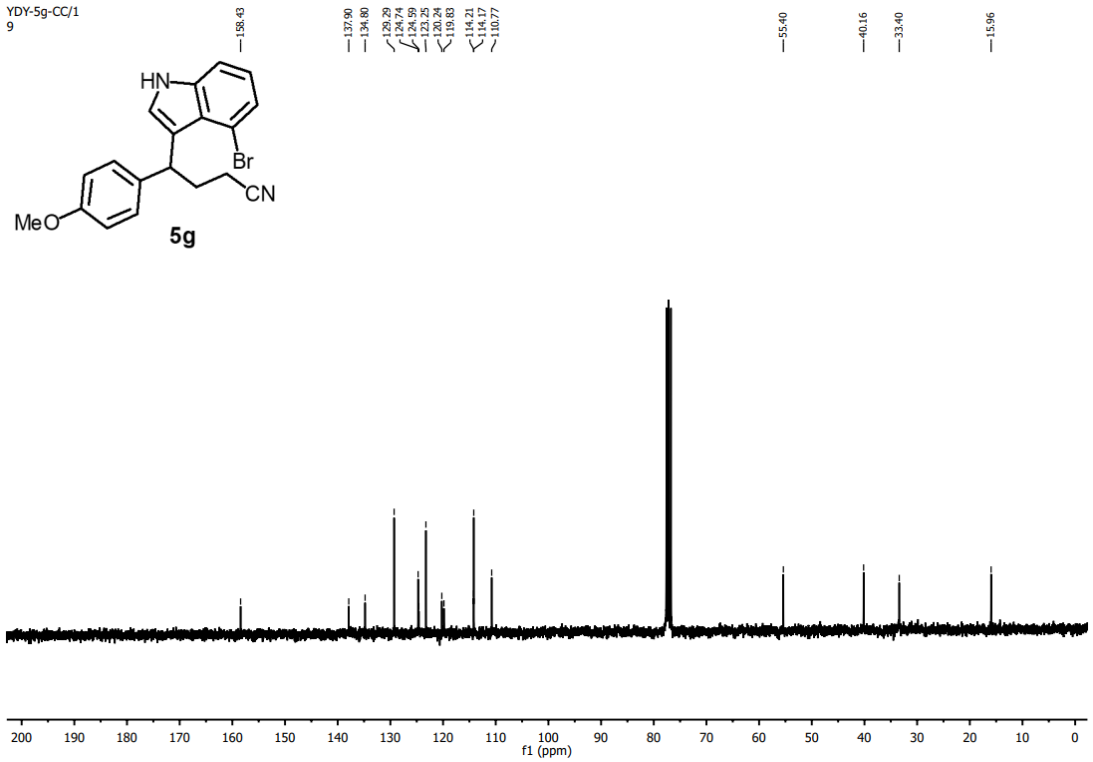
^{13}C NMR of compound **5f** (75 MHz in d_6-DMSO)



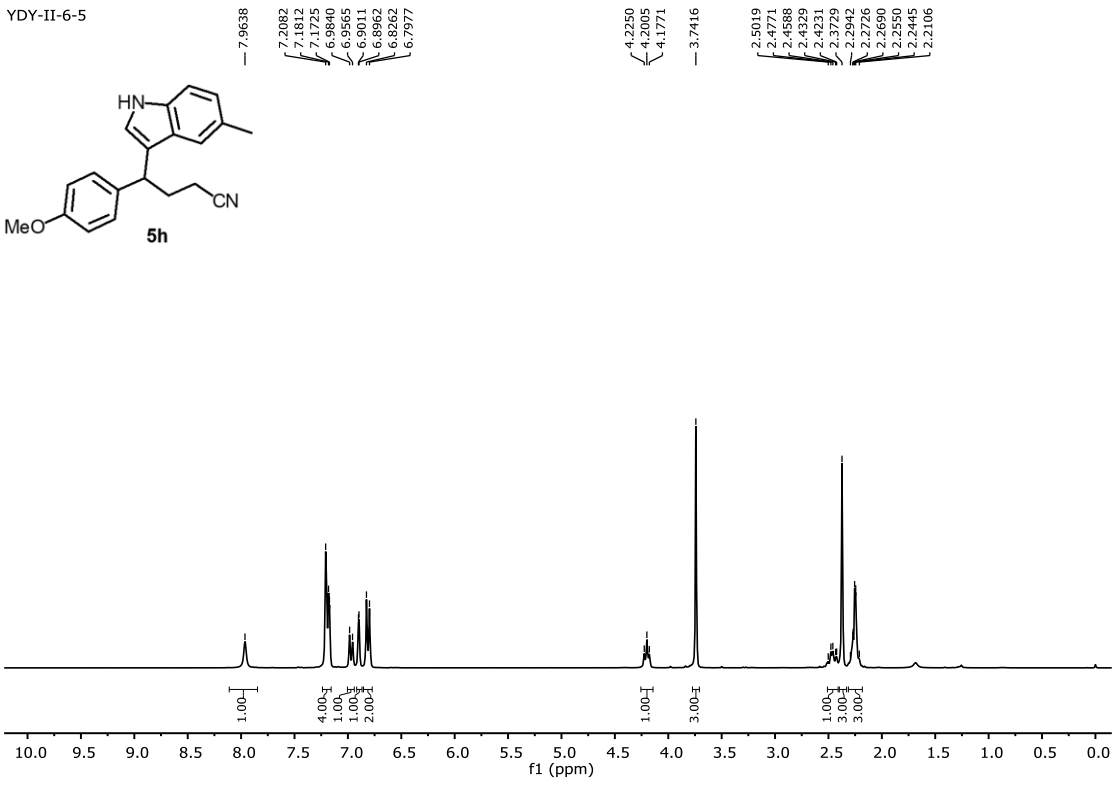
^{1}H NMR of compound **5g** (400 MHz in $CDCl_3$)



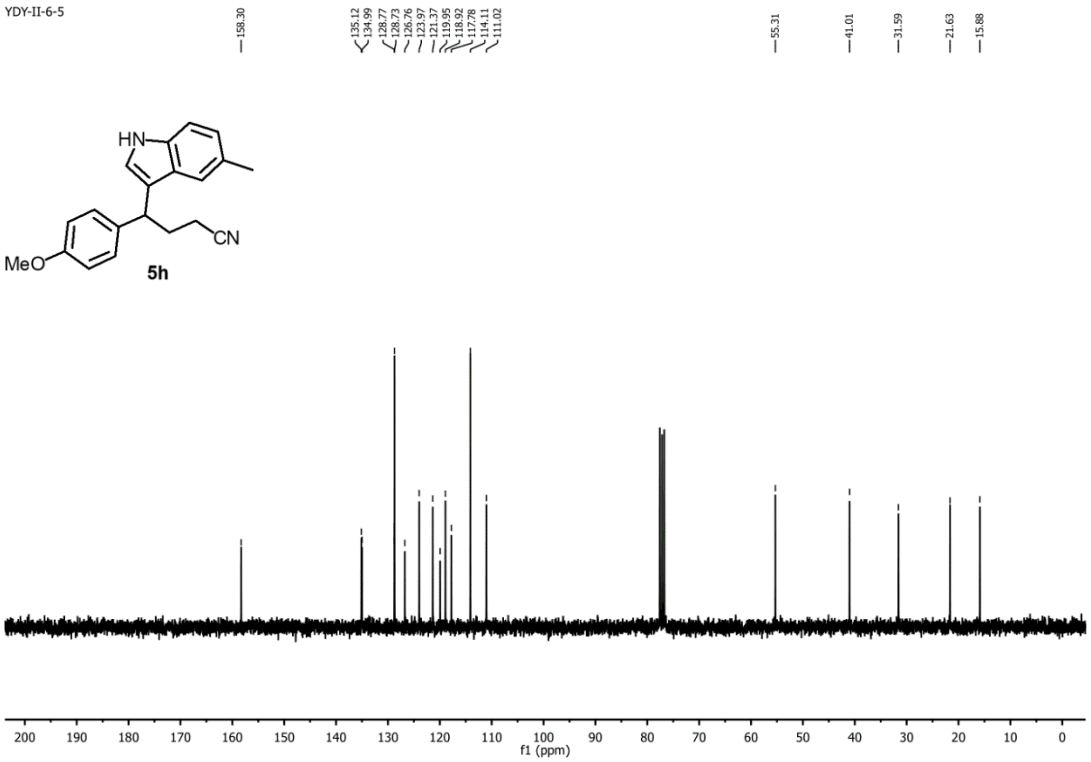
^{13}C NMR of compound **5g** (75 MHz in $CDCl_3$)



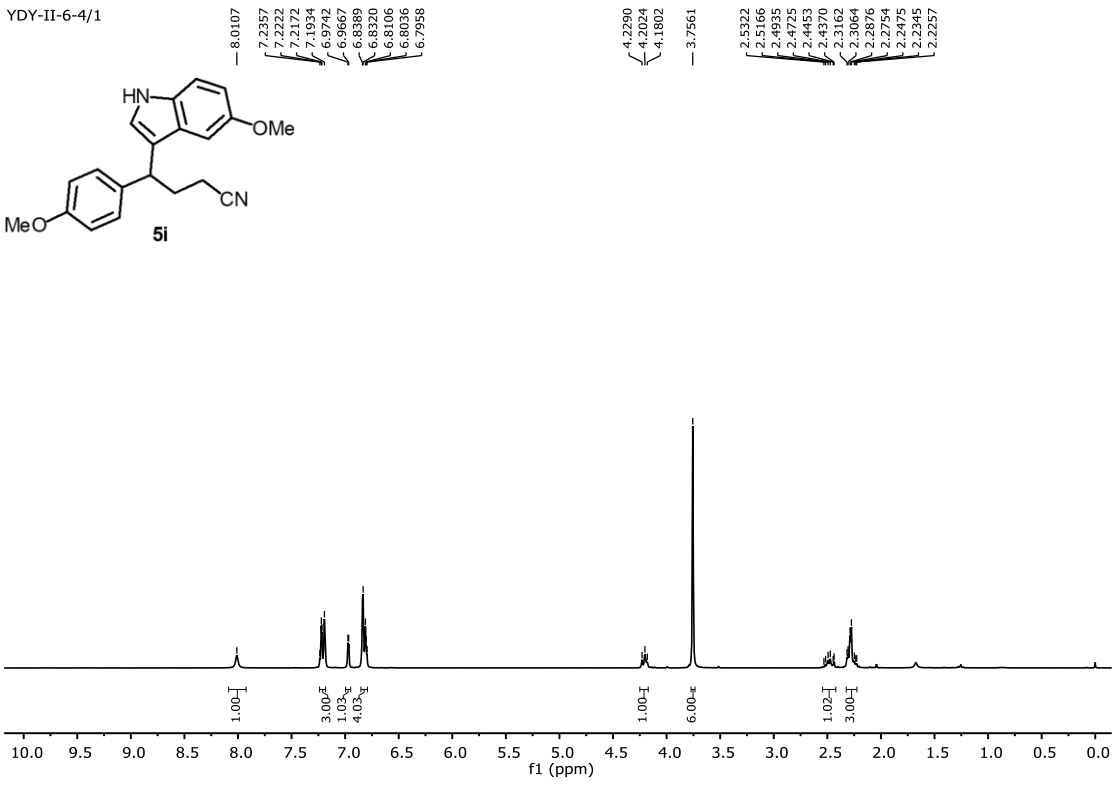
^{1}H NMR of compound **5h** (300 MHz in $CDCl_3$)



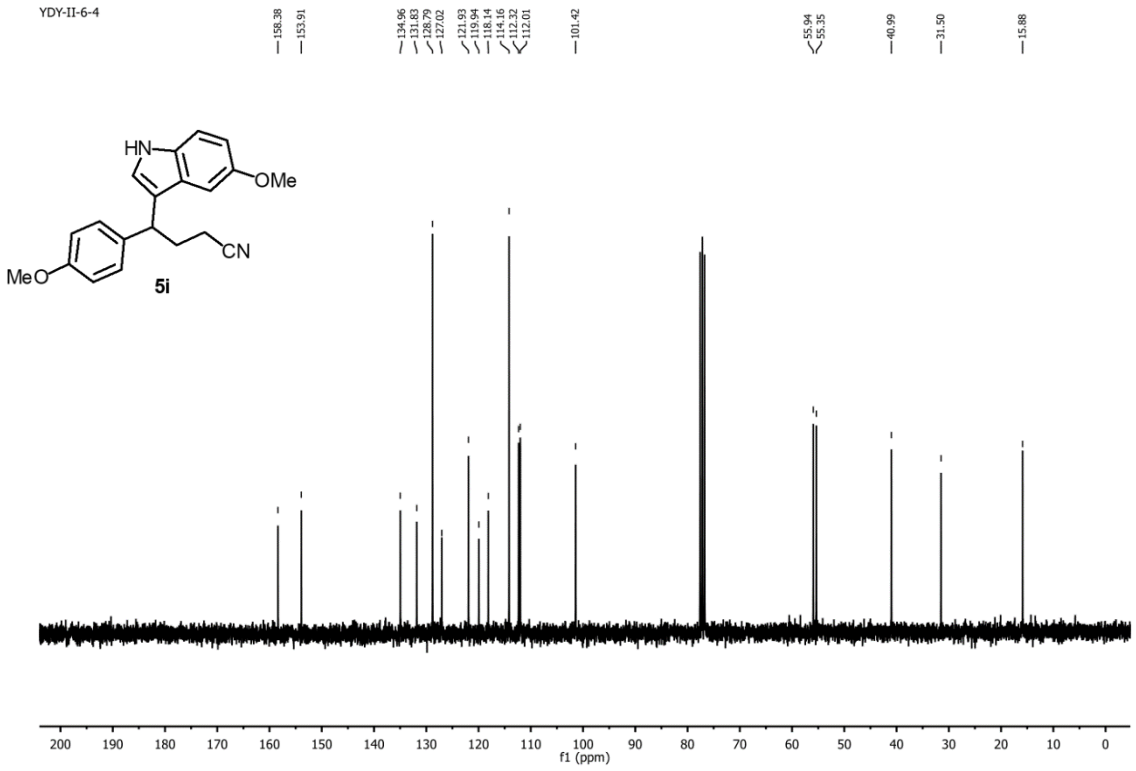
^{13}C NMR of compound **5h** (75 MHz in $CDCl_3$)



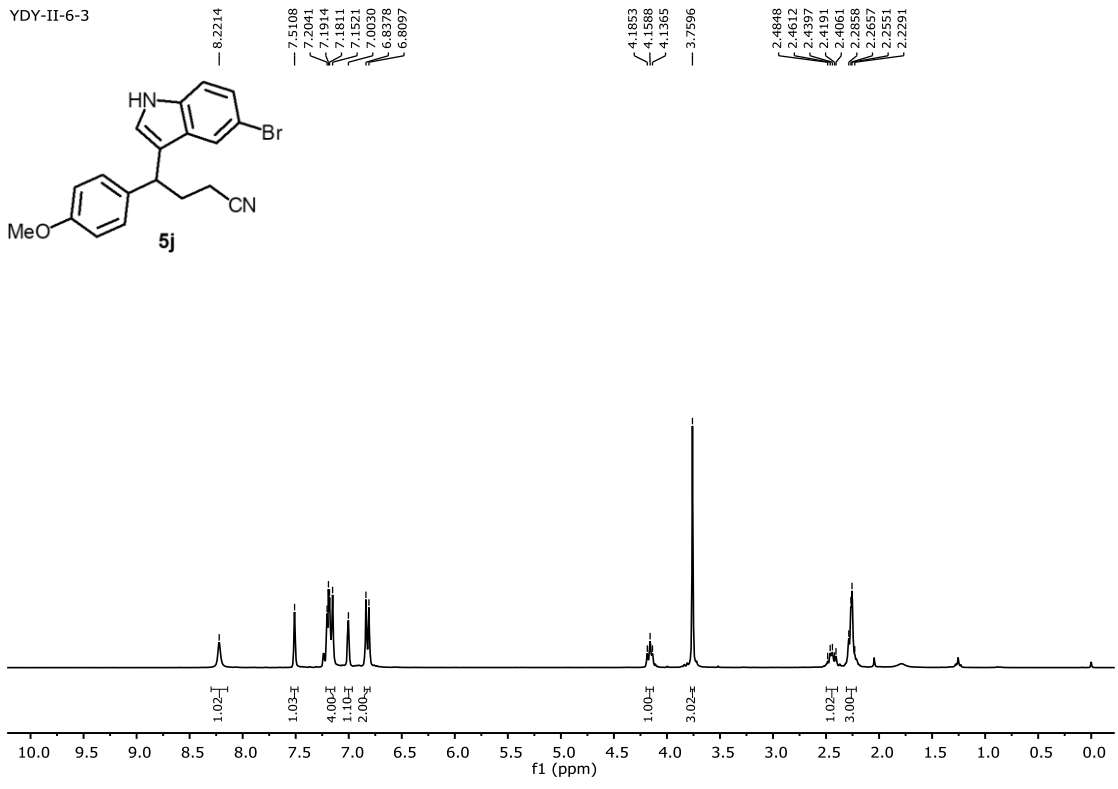
^{1}H NMR of compound **5i** (300 MHz in $CDCl_3$)



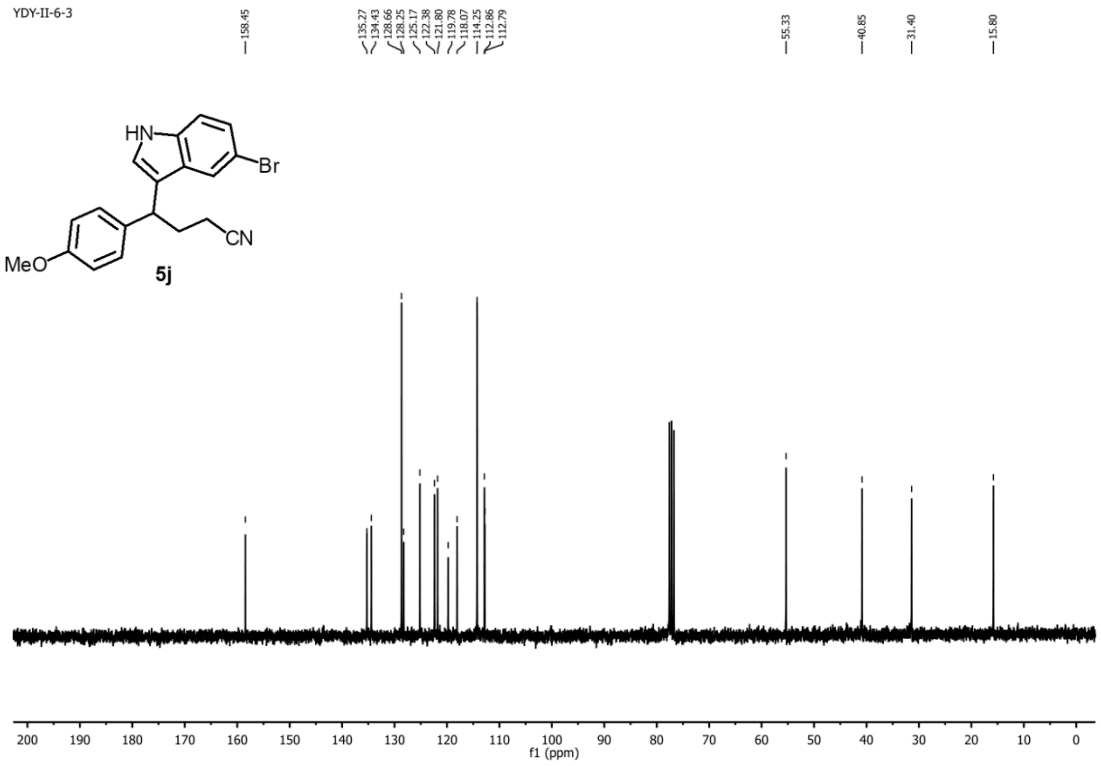
^{13}C NMR of compound **5i** (75 MHz in $CDCl_3$)



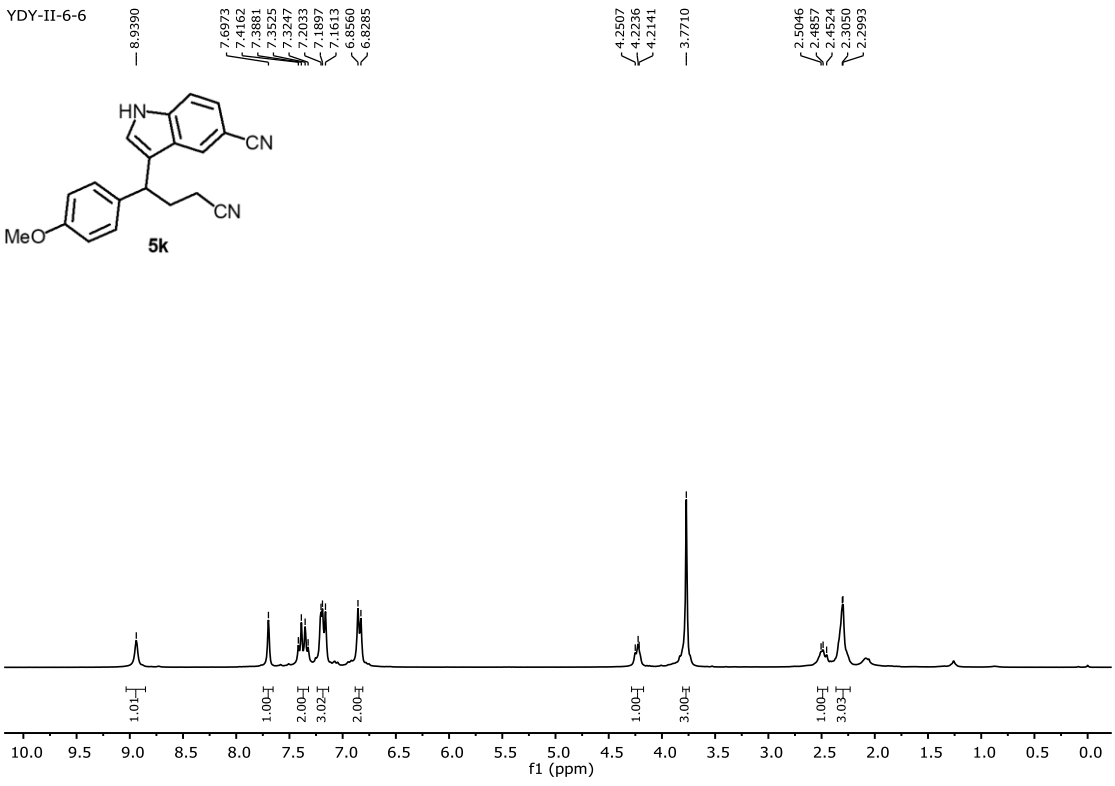
^{1}H NMR of compound **5j** (300 MHz in $CDCl_3$)



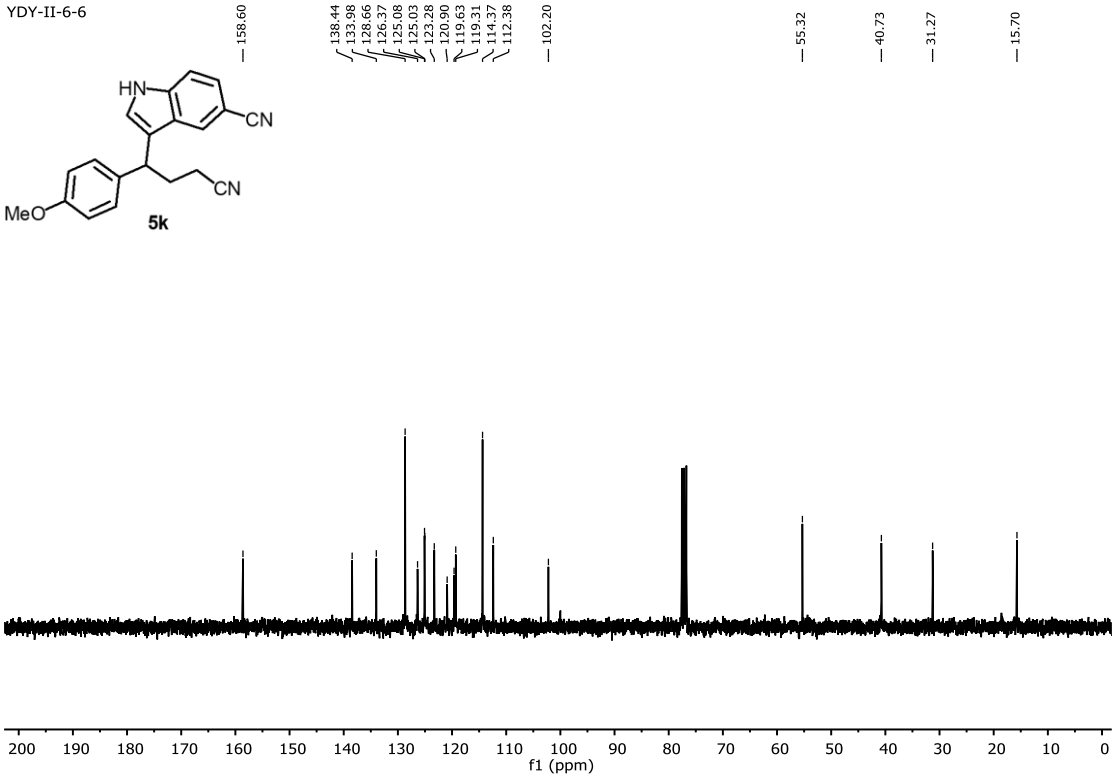
^{13}C NMR of compound **5j** (75 MHz in $CDCl_3$)



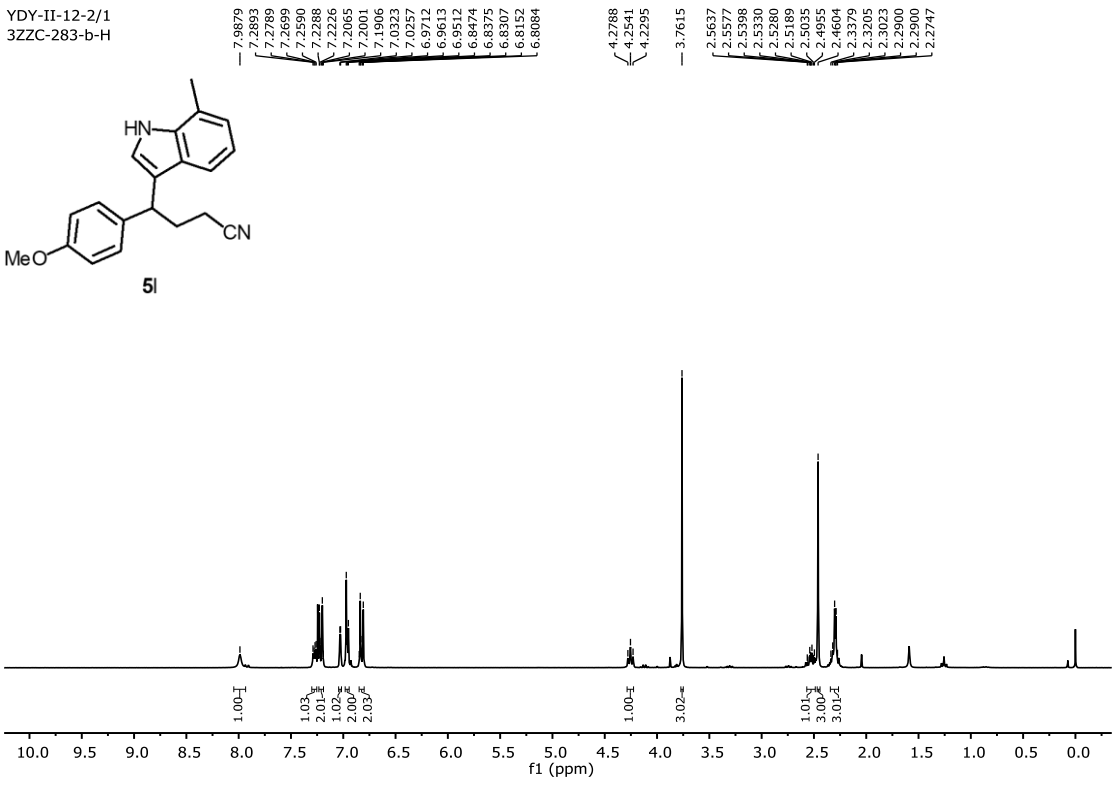
^{1}H NMR of compound **5k** (300 MHz in $CDCl_3$)



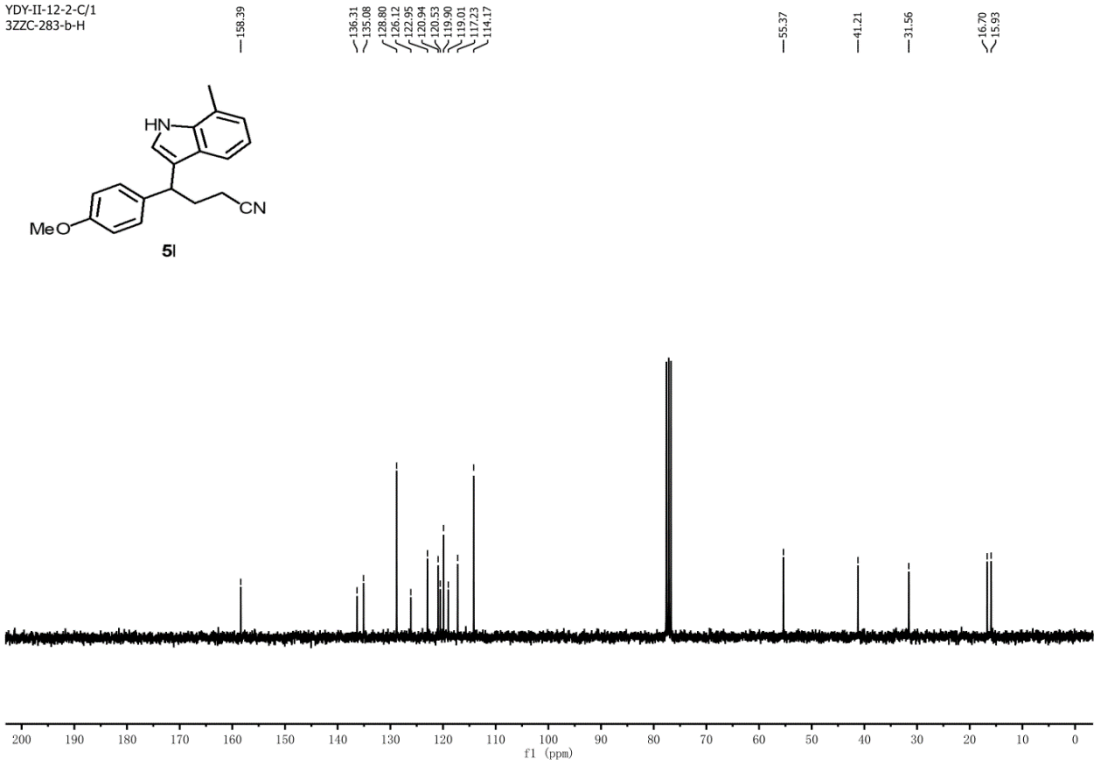
^{13}C NMR of compound **5k** (75 MHz in $CDCl_3$)



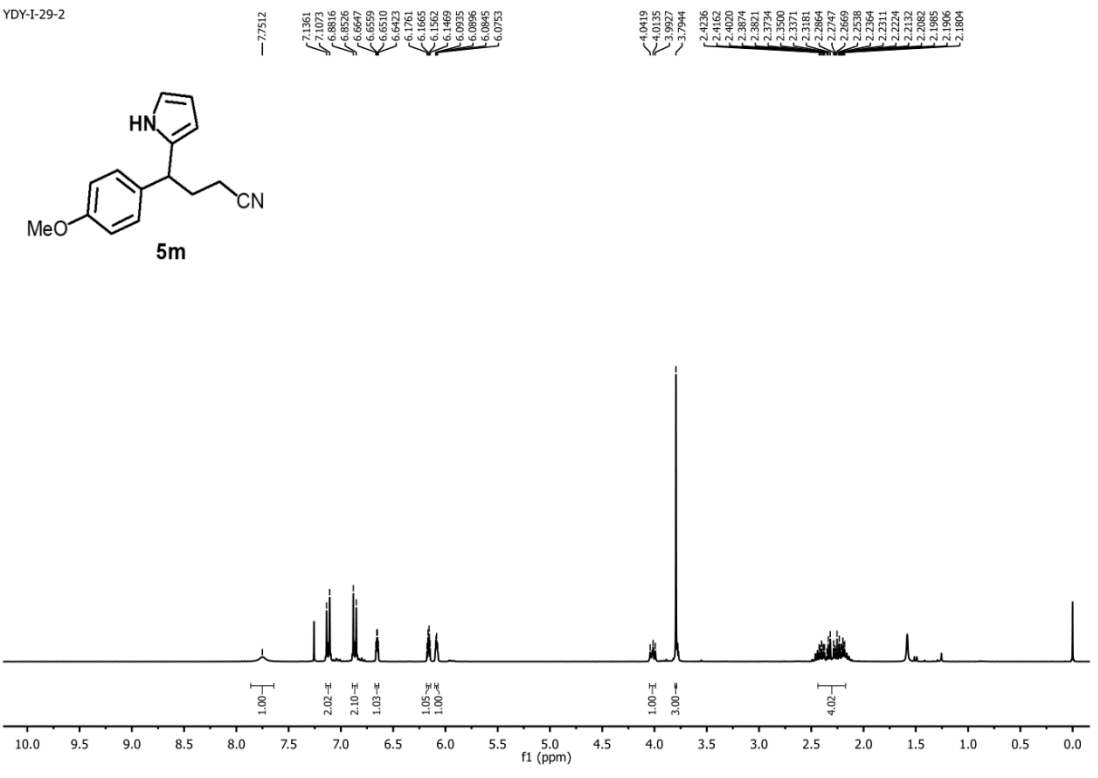
^{1}H NMR of compound **5l** (300 MHz in $CDCl_3$)



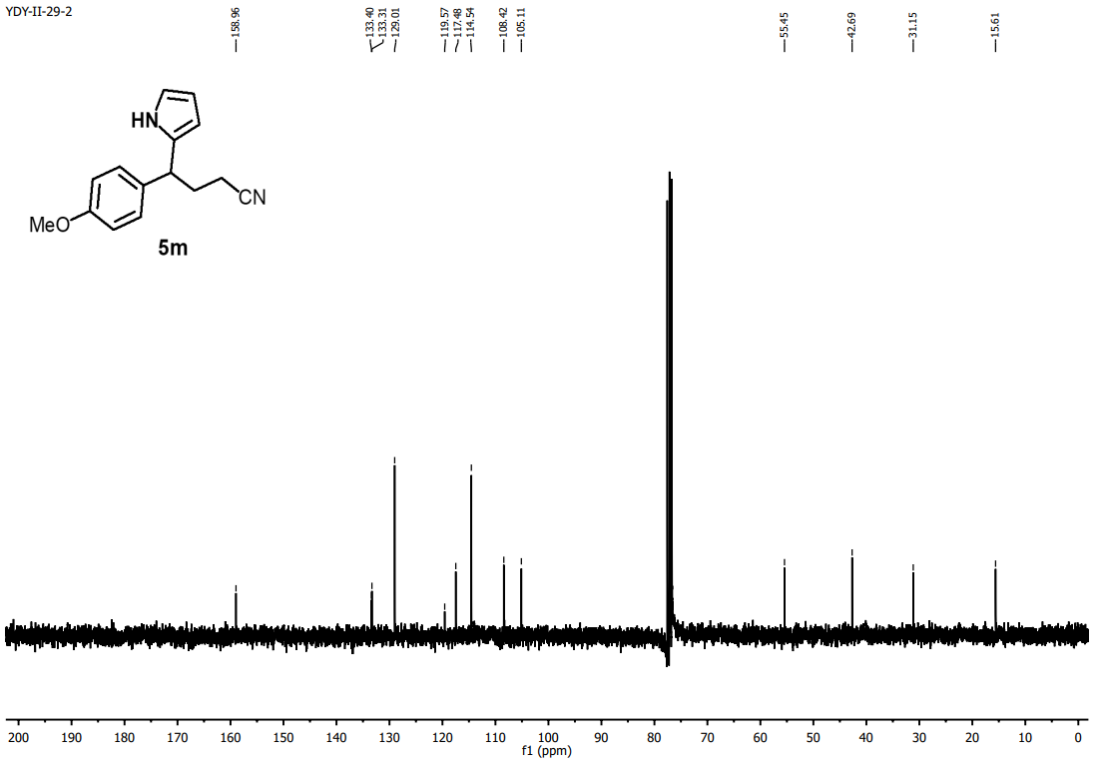
^{13}C NMR of compound **5l** (75 MHz in $CDCl_3$)



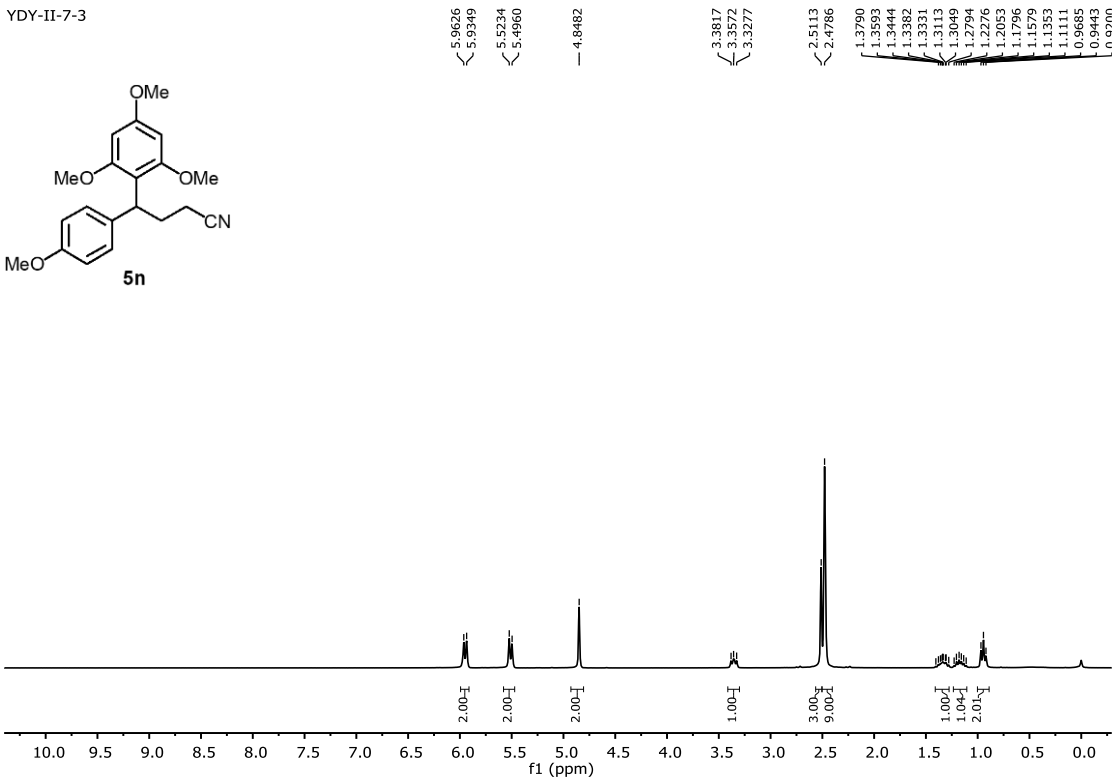
^{1}H NMR of compound **5m** (300 MHz in $CDCl_3$)



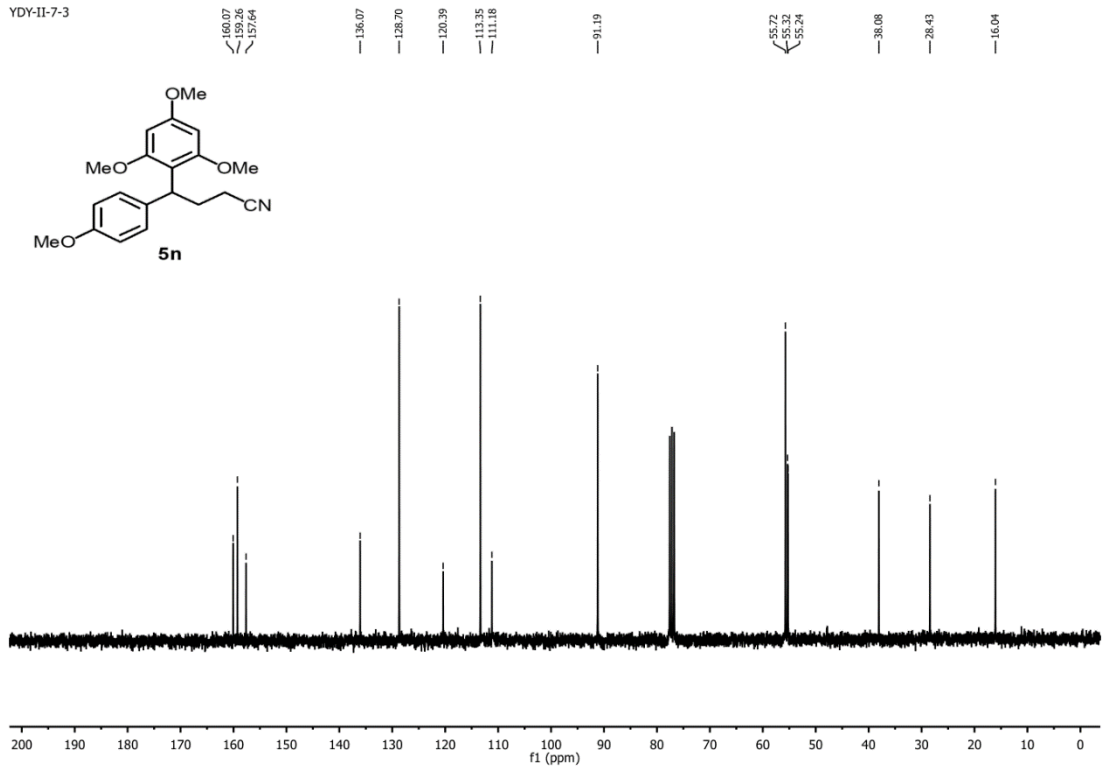
^{13}C NMR of compound **5m** (75 MHz in $CDCl_3$)



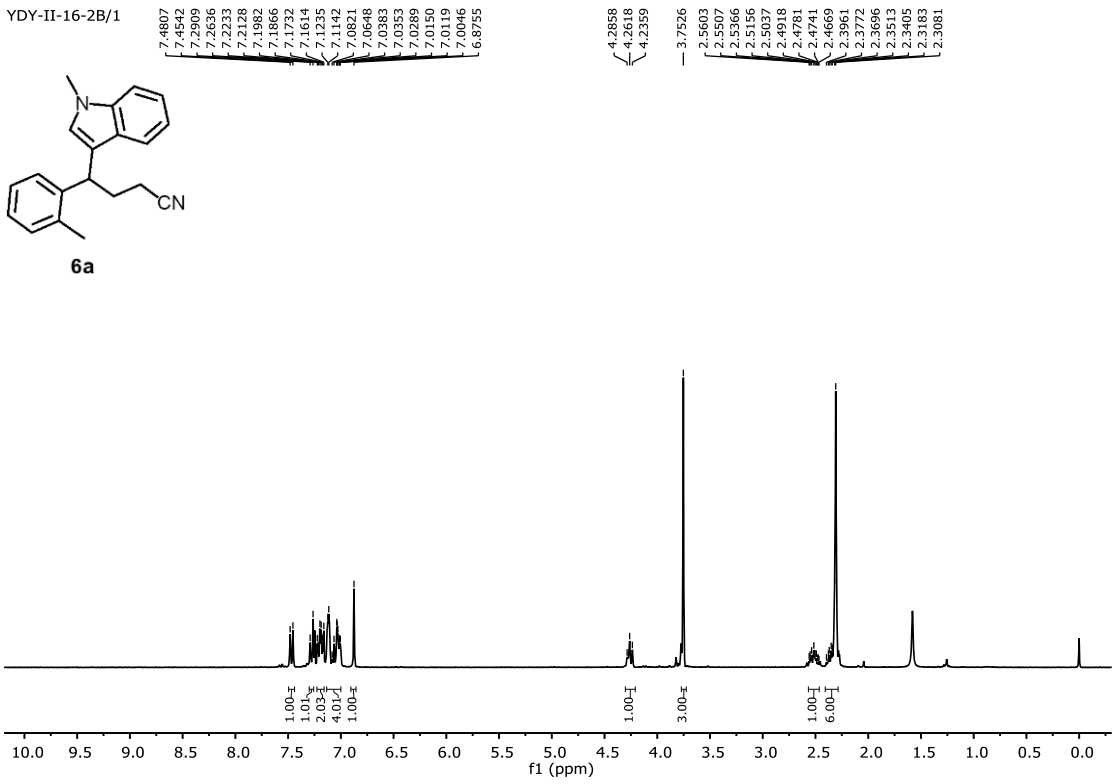
^{1}H NMR of compound **5n** (300 MHz in $CDCl_3$)



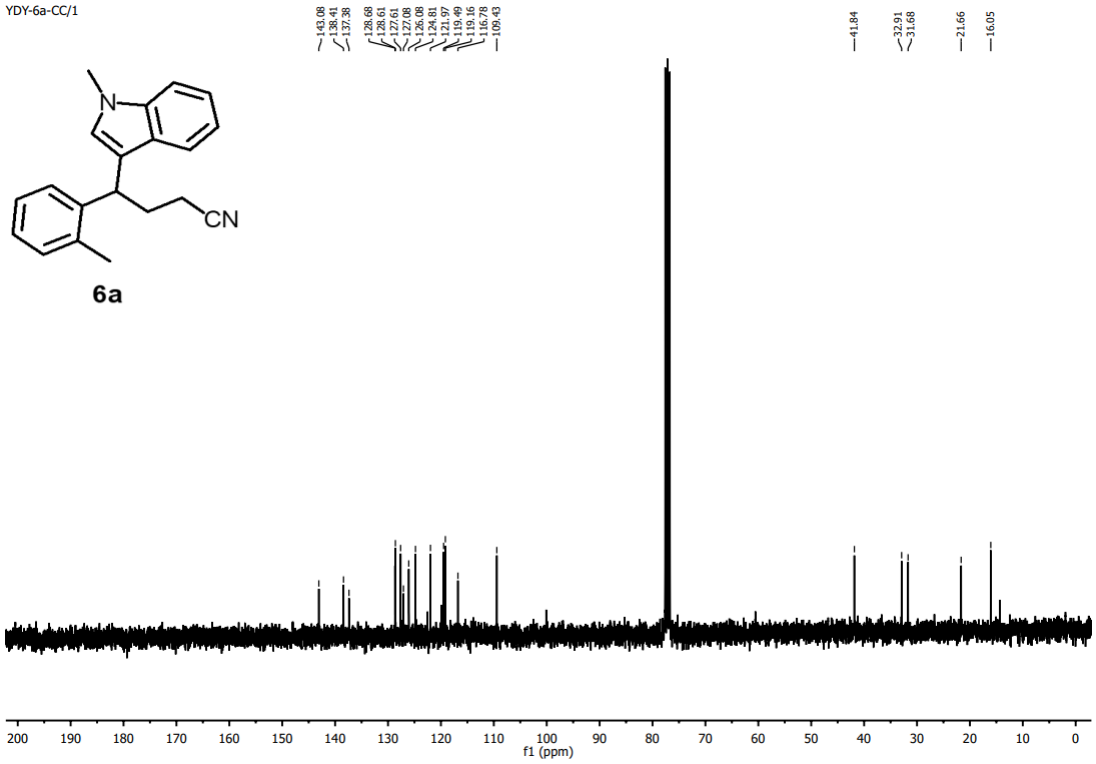
^{13}C NMR of compound **5n** (75 MHz in $CDCl_3$)



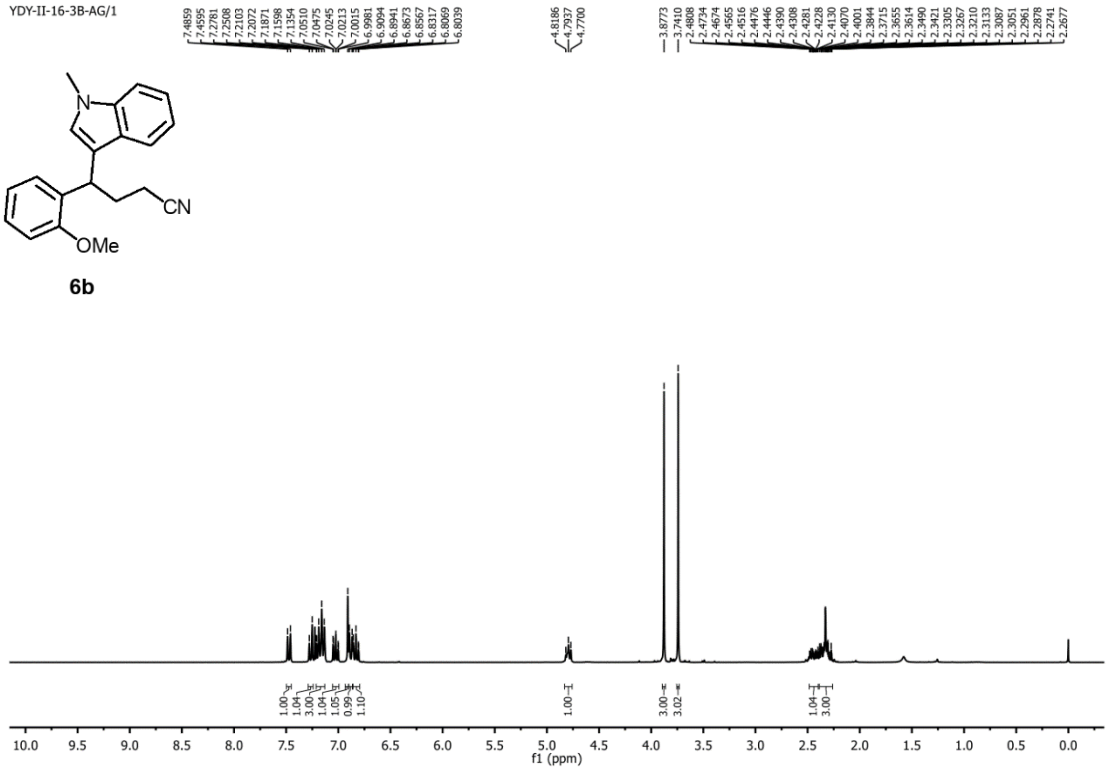
^{1}H NMR of compound **6a** (300 MHz in $CDCl_3$)



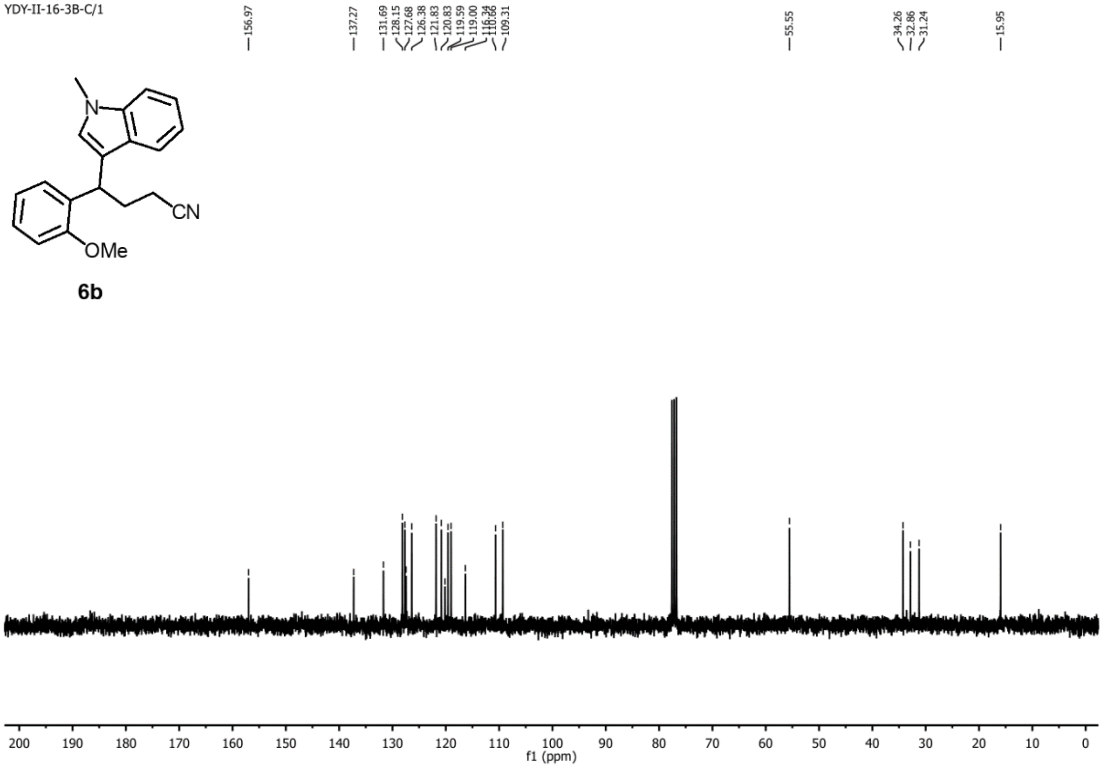
^{13}C NMR of compound **6a** (75 MHz in $CDCl_3$)



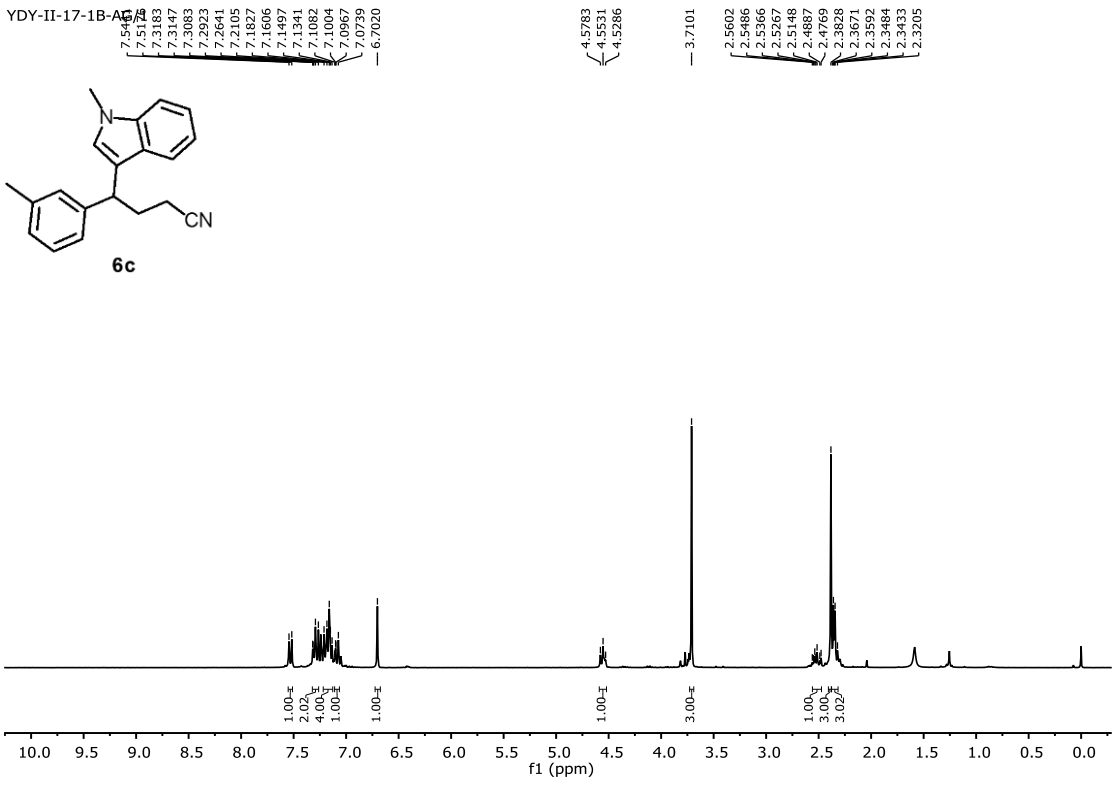
^{1}H NMR of compound **6b** (300 MHz in $CDCl_3$)



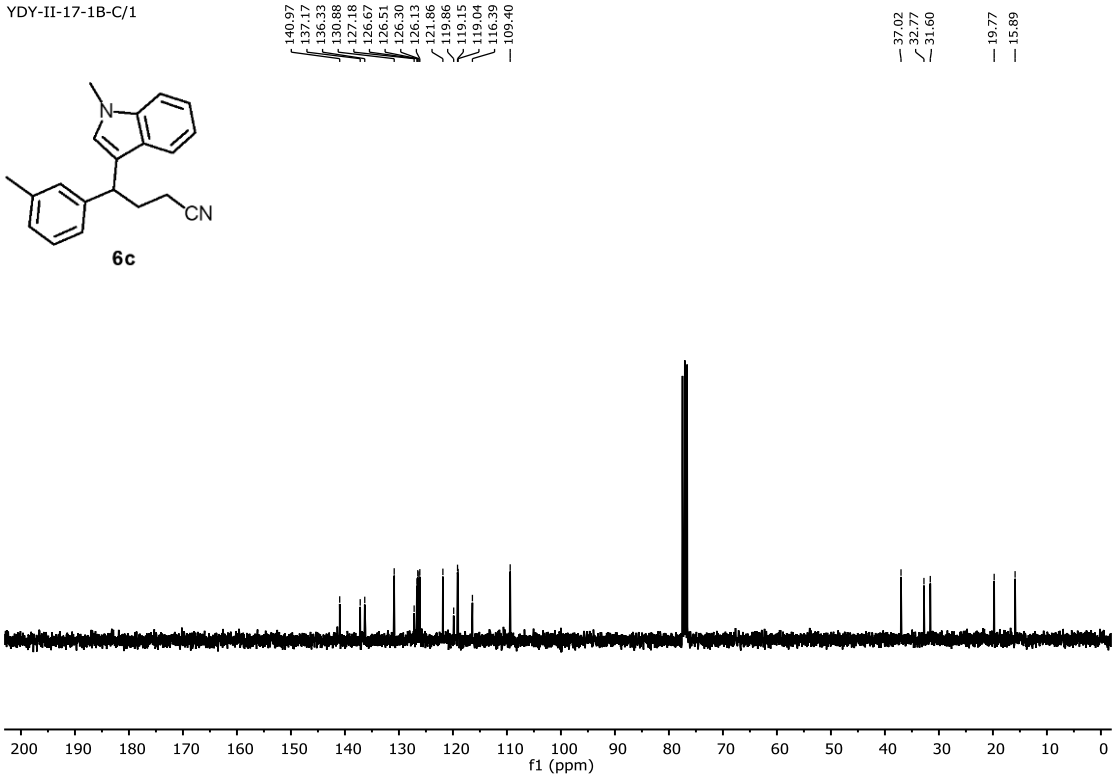
^{13}C NMR of compound **6b** (75 MHz in $CDCl_3$)



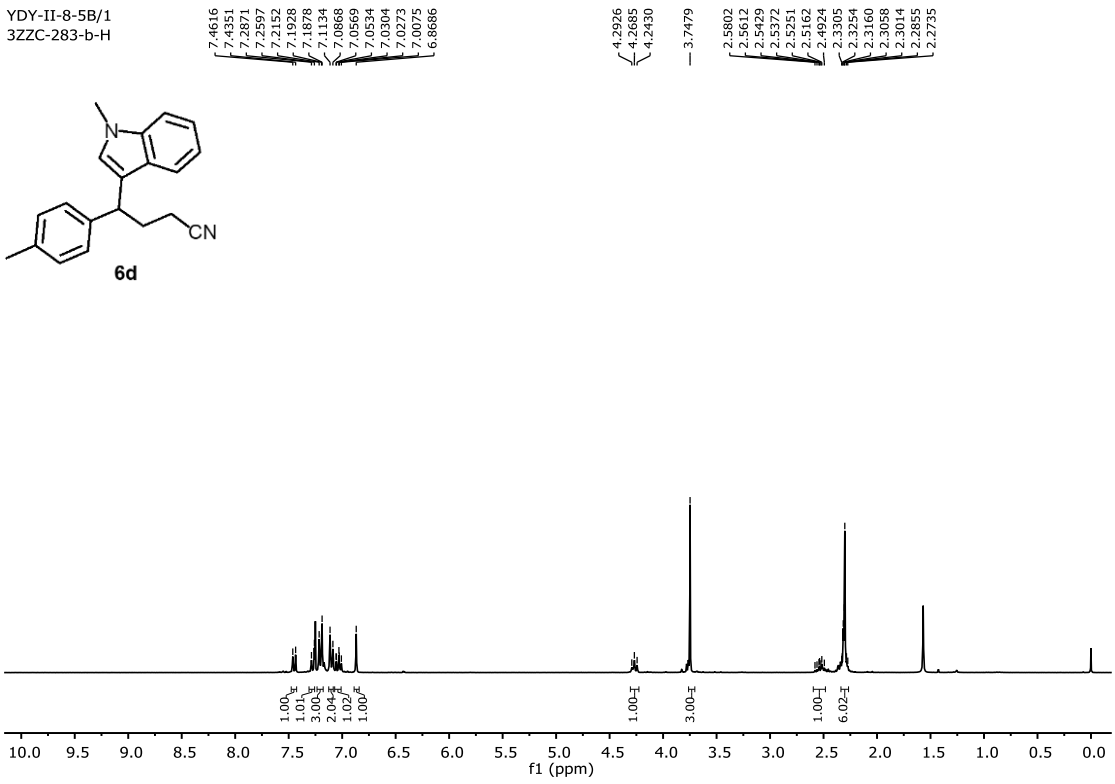
^{1}H NMR of compound **6c** (300 MHz in $CDCl_3$)



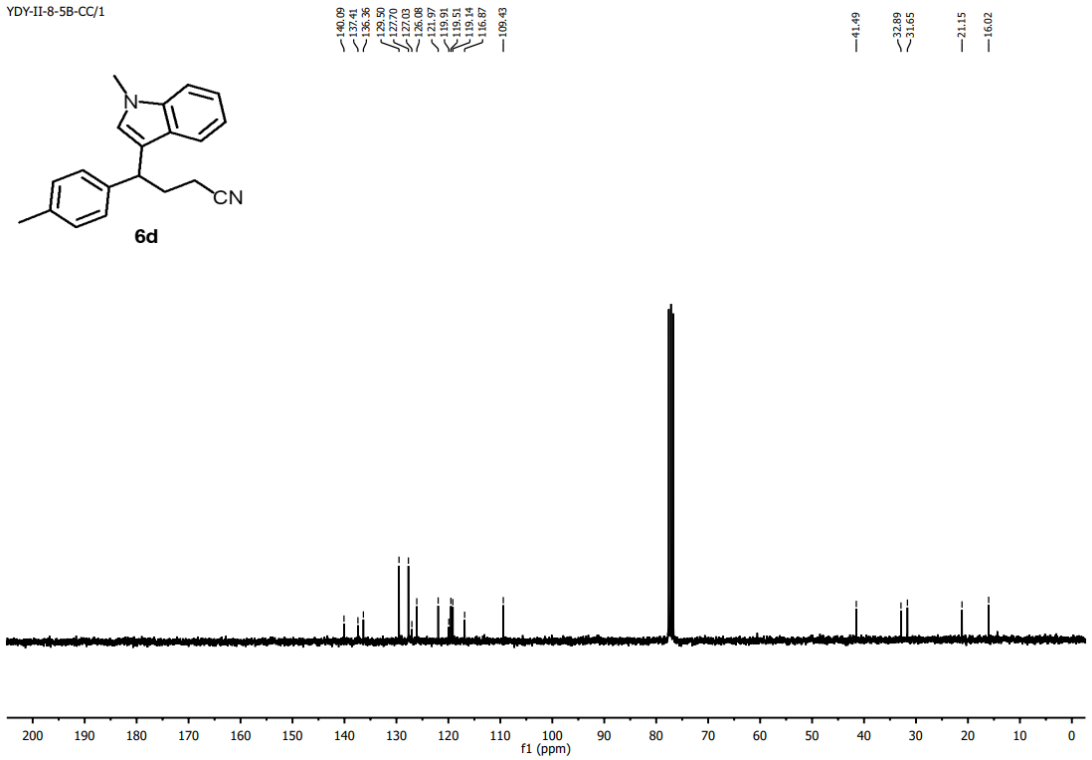
^{13}C NMR of compound **6c** (75 MHz in $CDCl_3$)



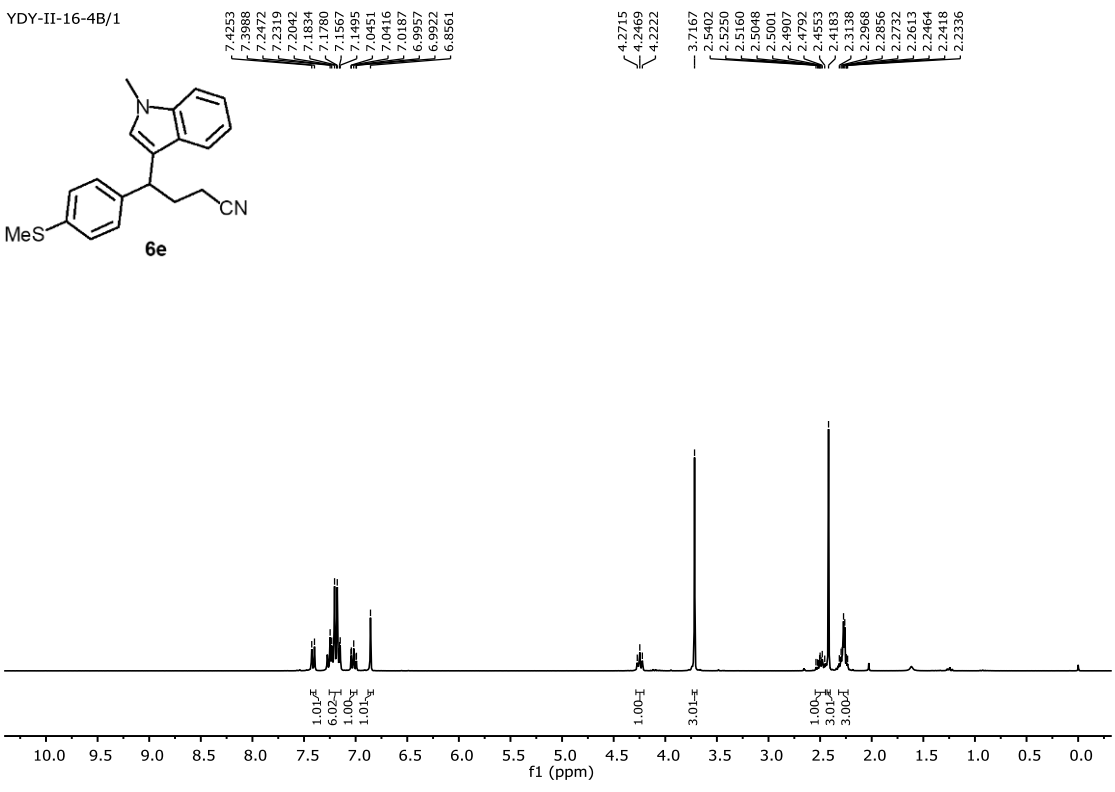
^{1}H NMR of compound **6d** (300 MHz in $CDCl_3$)



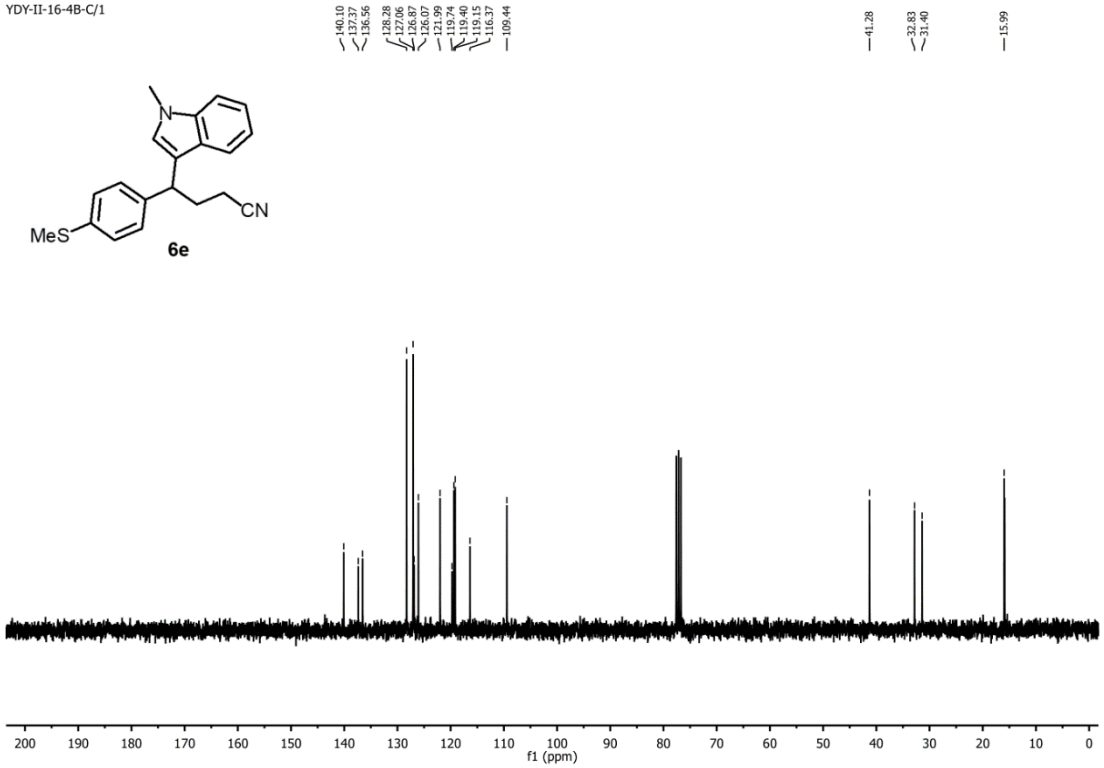
^{13}C NMR of compound **6d** (75 MHz in $CDCl_3$)



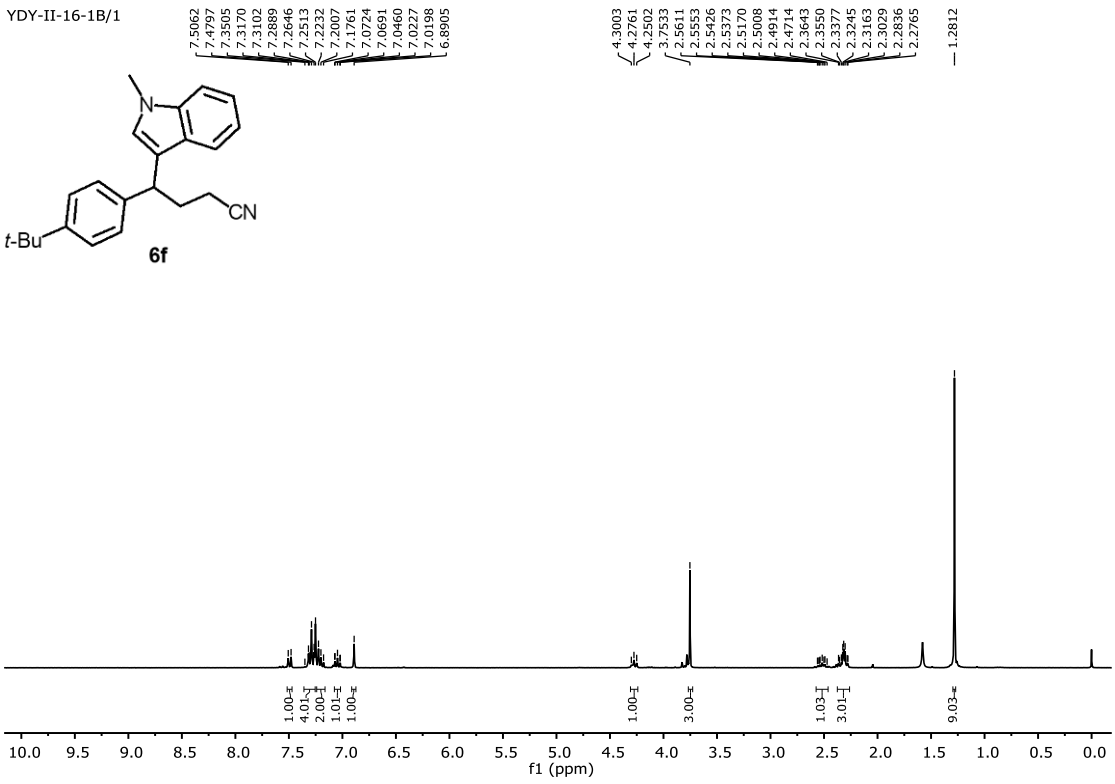
^{1}H NMR of compound **6e** (300 MHz in $CDCl_3$)



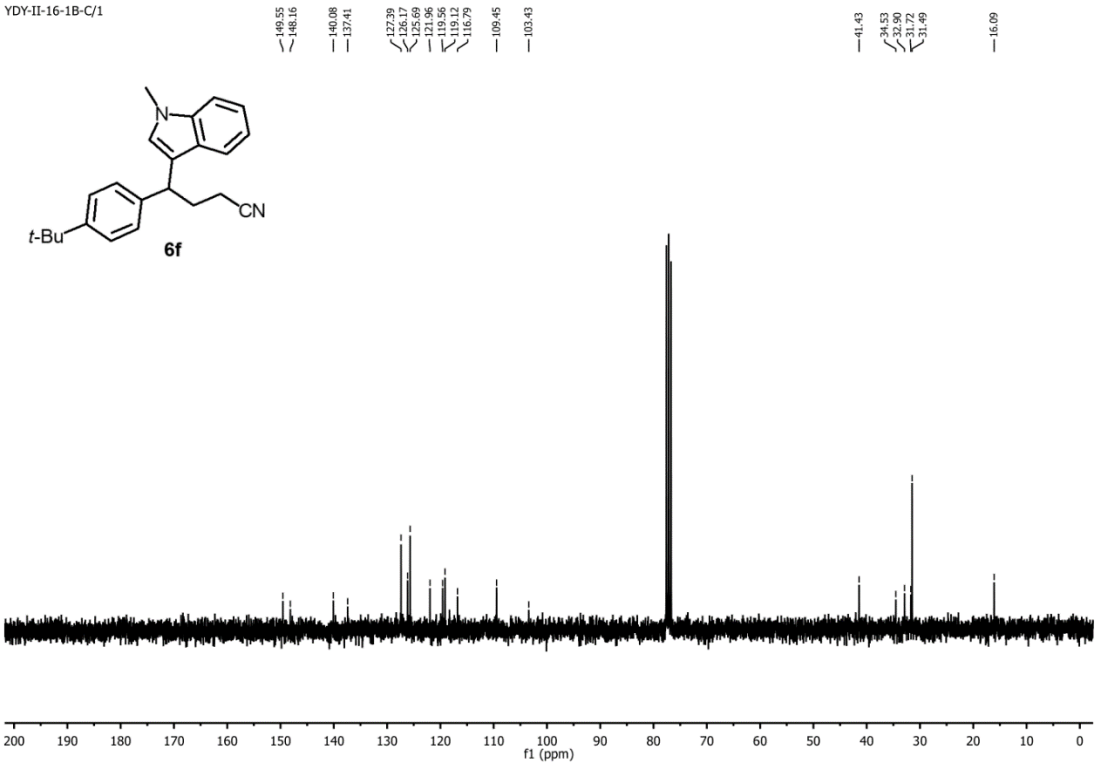
^{13}C NMR of compound **6e** (75 MHz in $CDCl_3$)



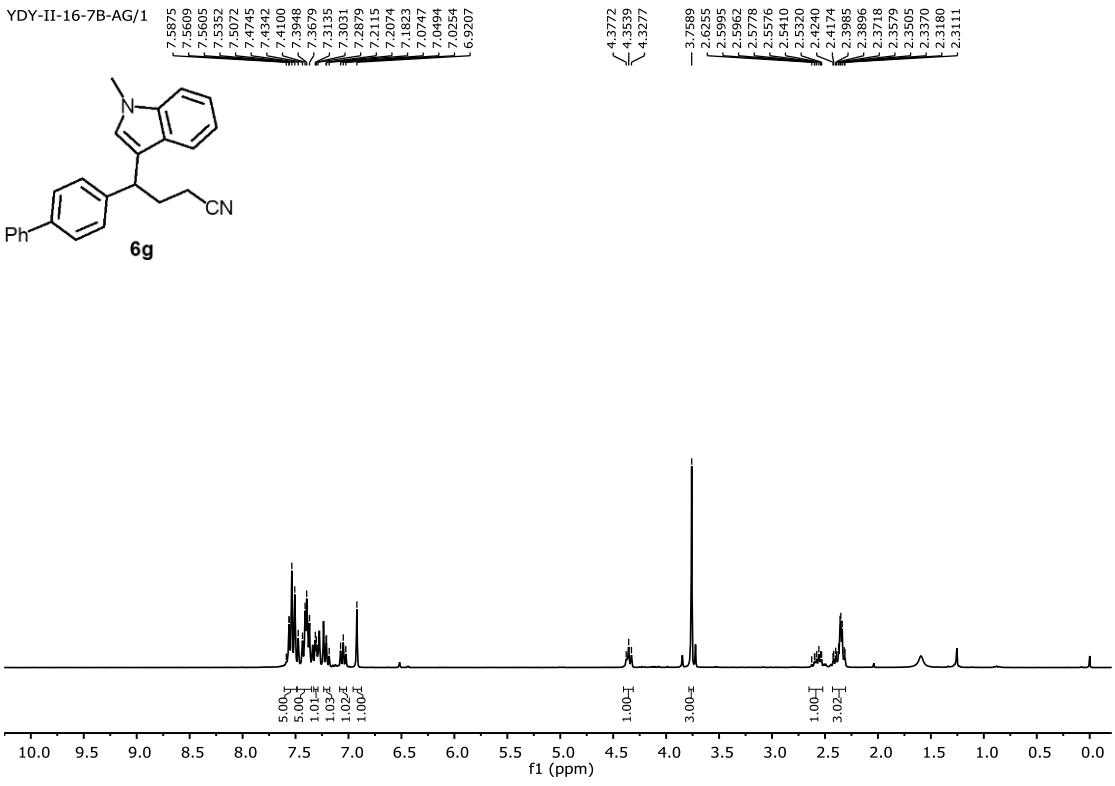
^{1}H NMR of compound **6f** (300 MHz in $CDCl_3$)



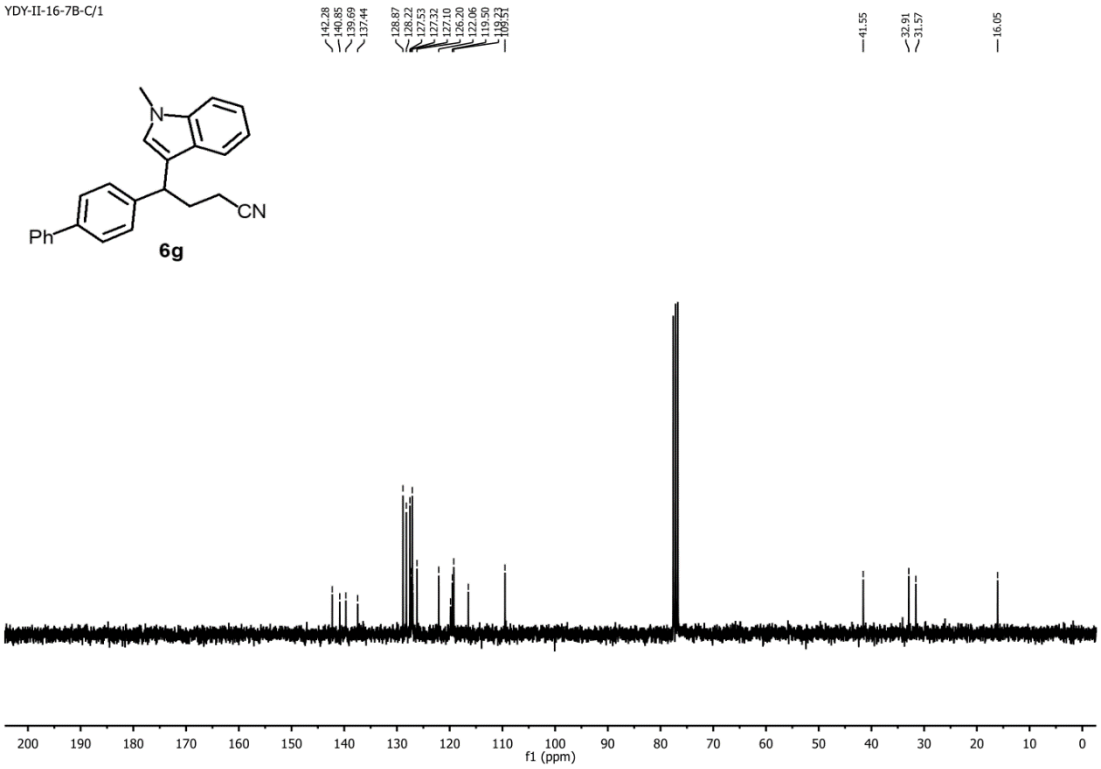
^{13}C NMR of compound **6f** (75 MHz in $CDCl_3$)



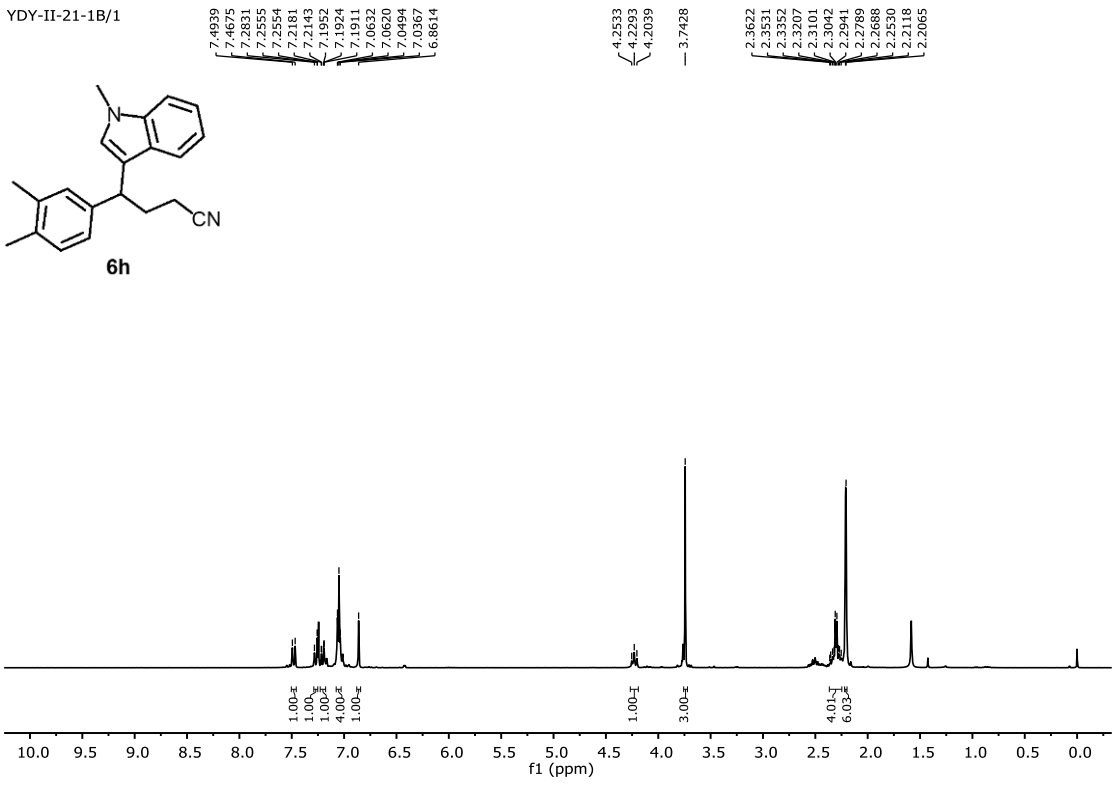
^{1}H NMR of compound **6g** (300 MHz in $CDCl_3$)



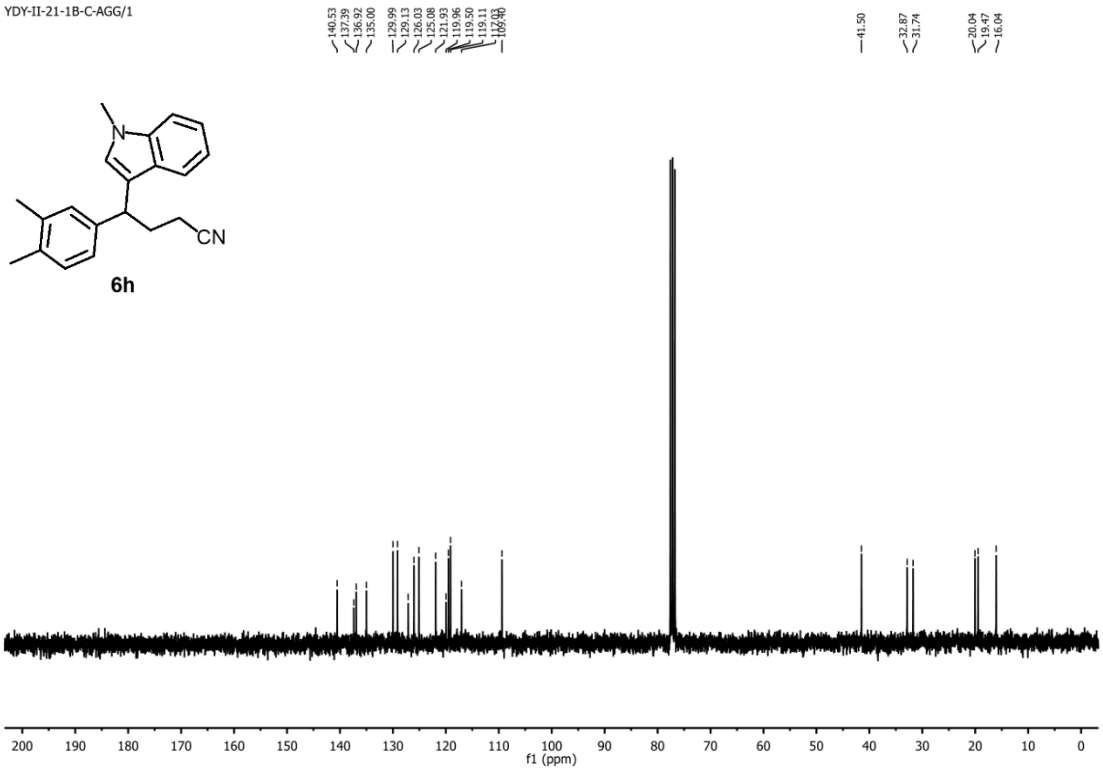
^{13}C NMR of compound **6g** (75 MHz in $CDCl_3$)



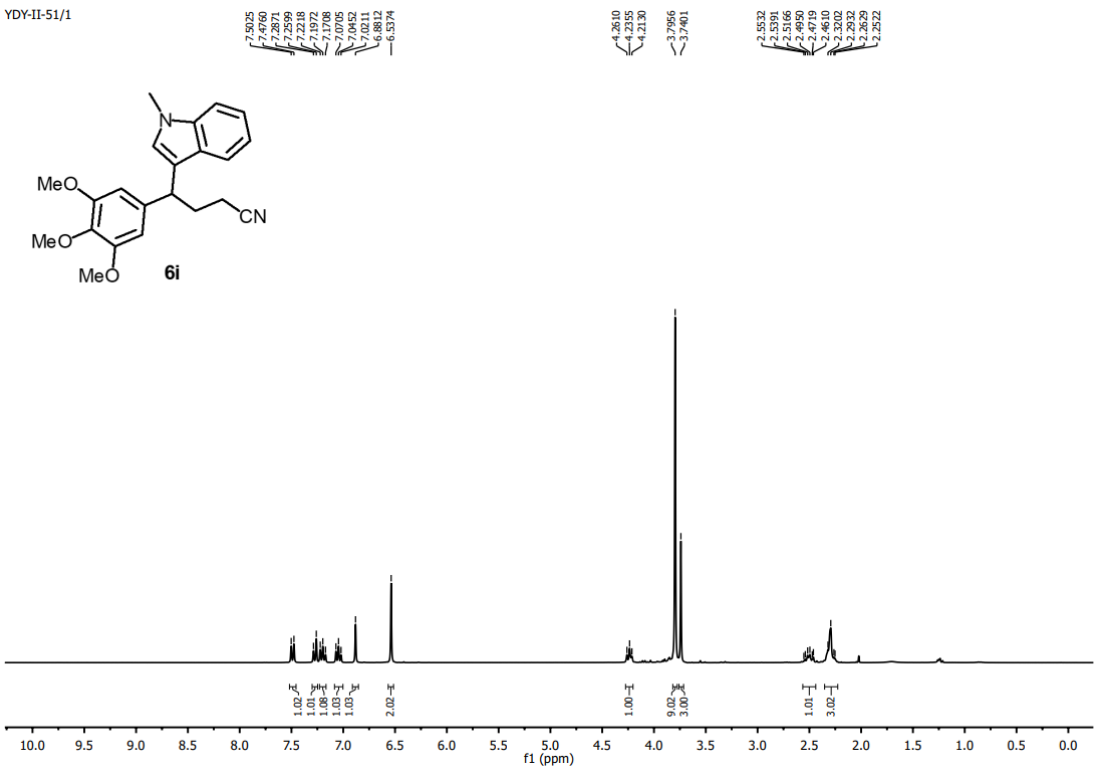
^{1}H NMR of compound **6h** (300 MHz in $CDCl_3$)



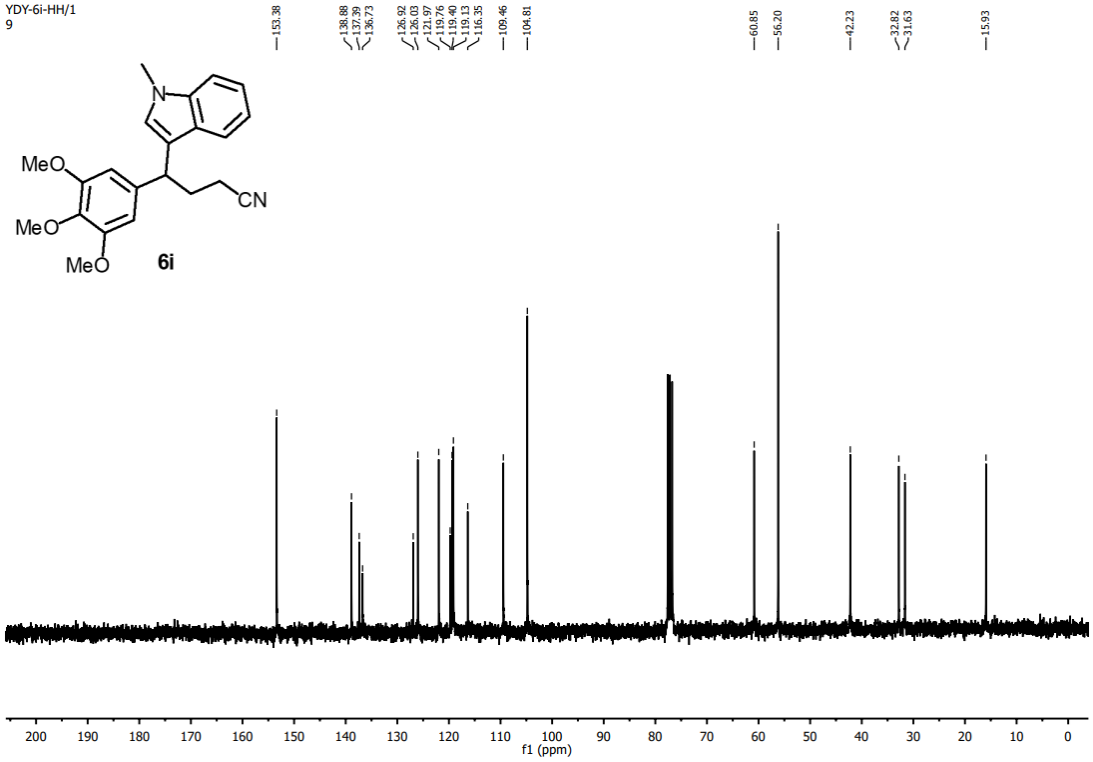
^{13}C NMR of compound **6h** (75 MHz in $CDCl_3$)



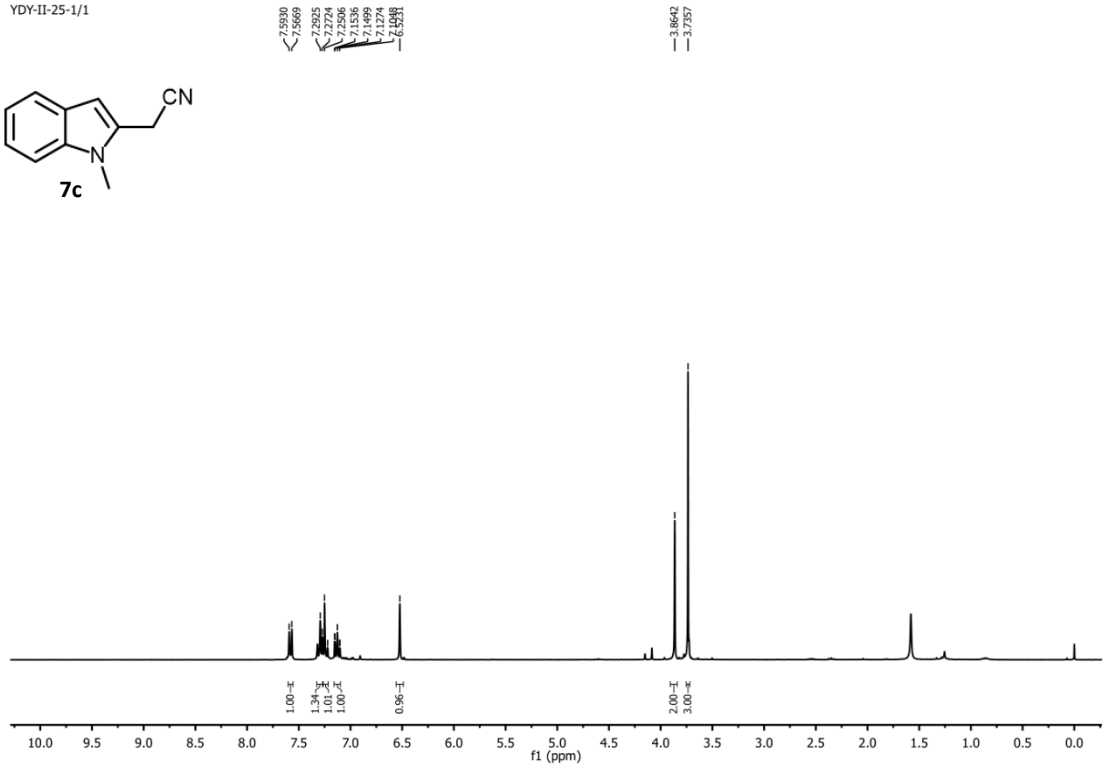
^{1}H NMR of compound **6i** (300 MHz in $CDCl_3$)



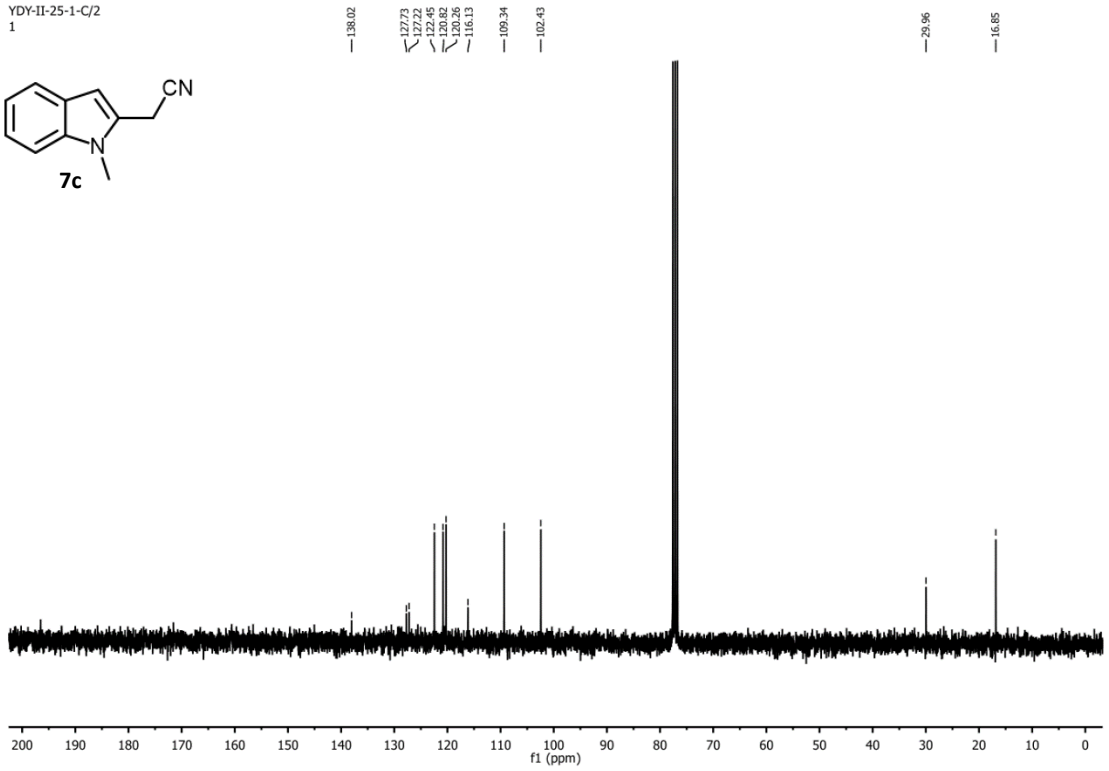
^{13}C NMR of compound **6i** (75 MHz in $CDCl_3$)



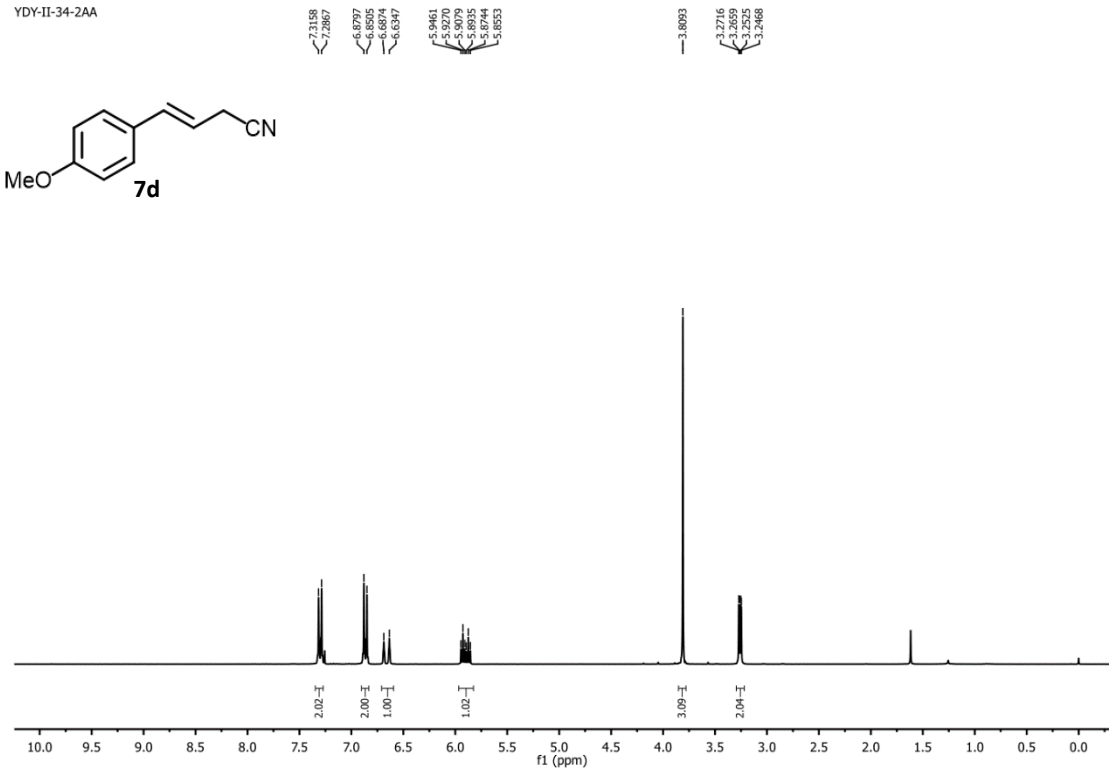
^{1}H NMR of compound **7c** (300 MHz in $CDCl_3$)



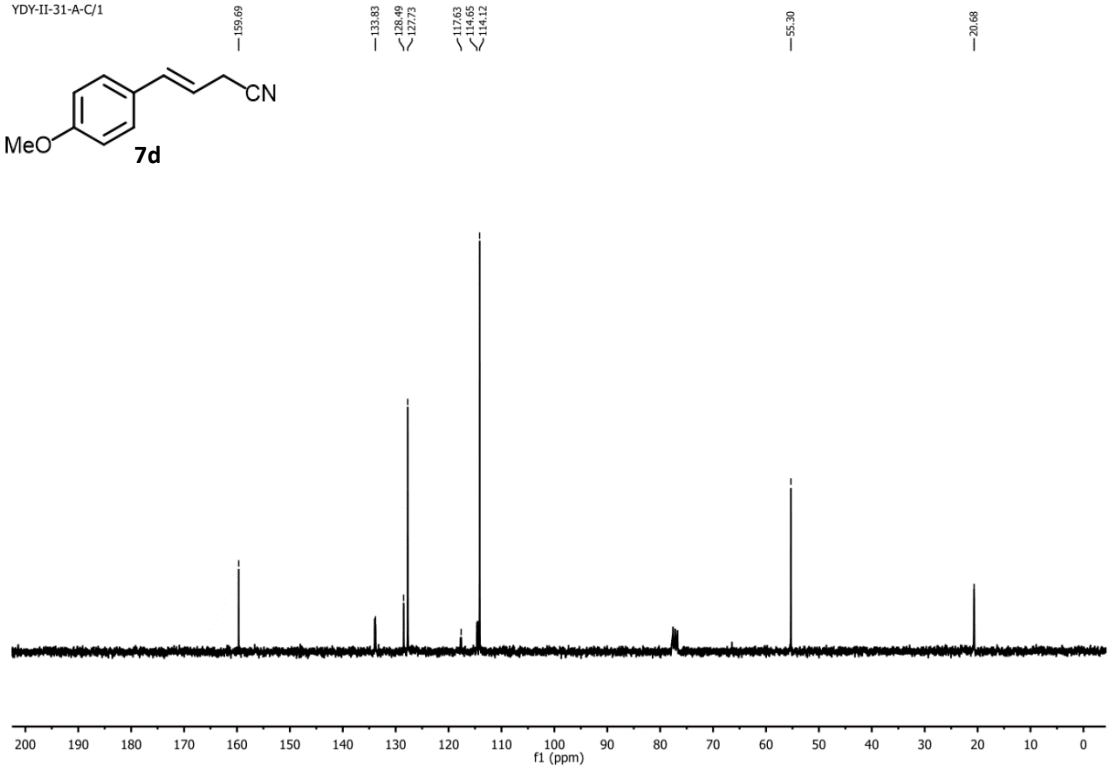
^{13}C NMR of compound **7c** (75 MHz in $CDCl_3$)



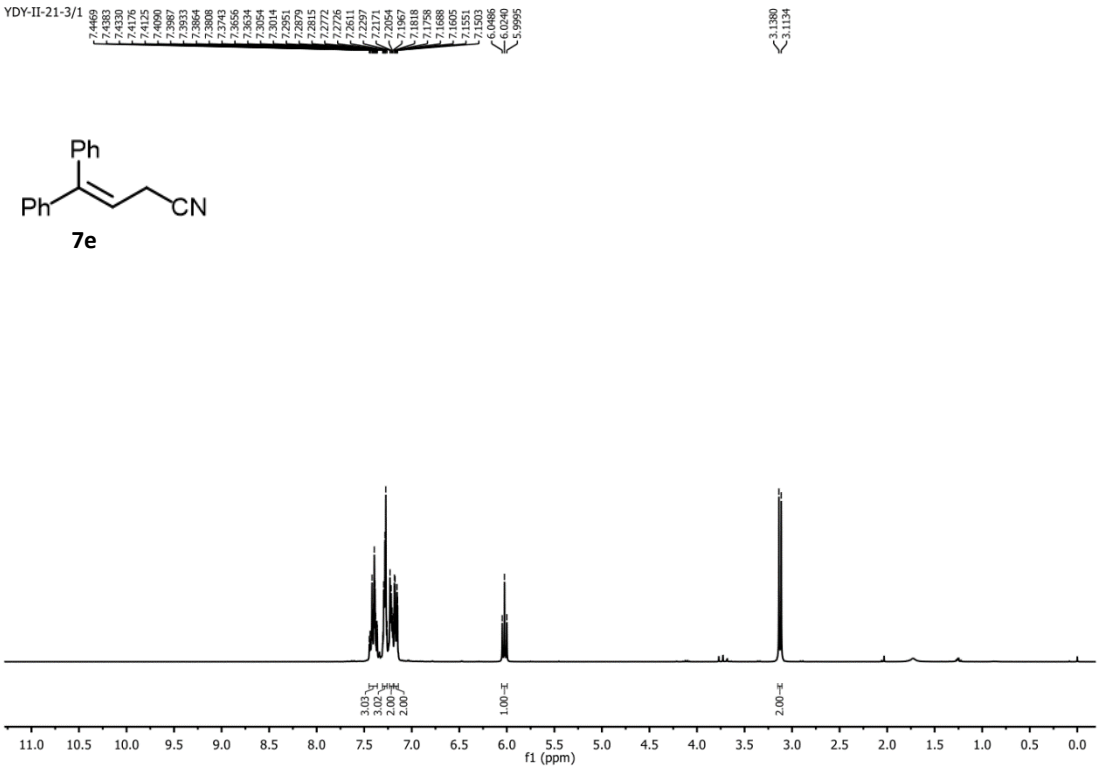
^{1}H NMR of compound **7d** (300 MHz in $CDCl_3$)



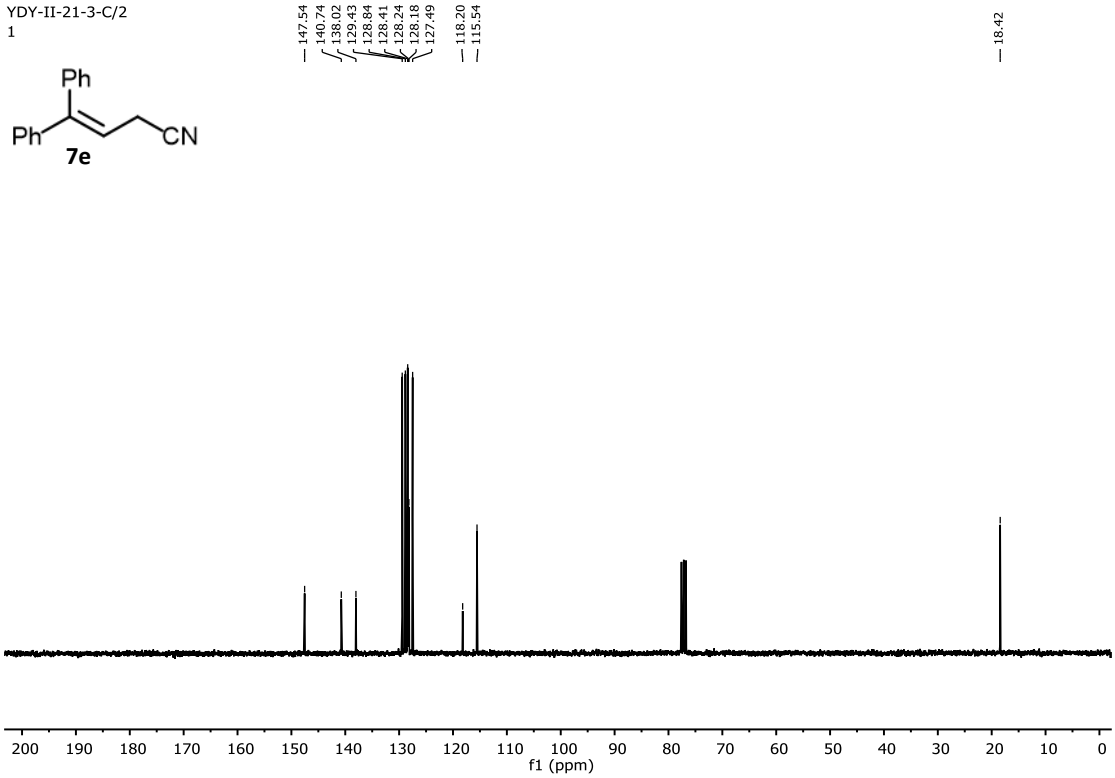
^{13}C NMR of compound **7d** (75 MHz in $CDCl_3$)



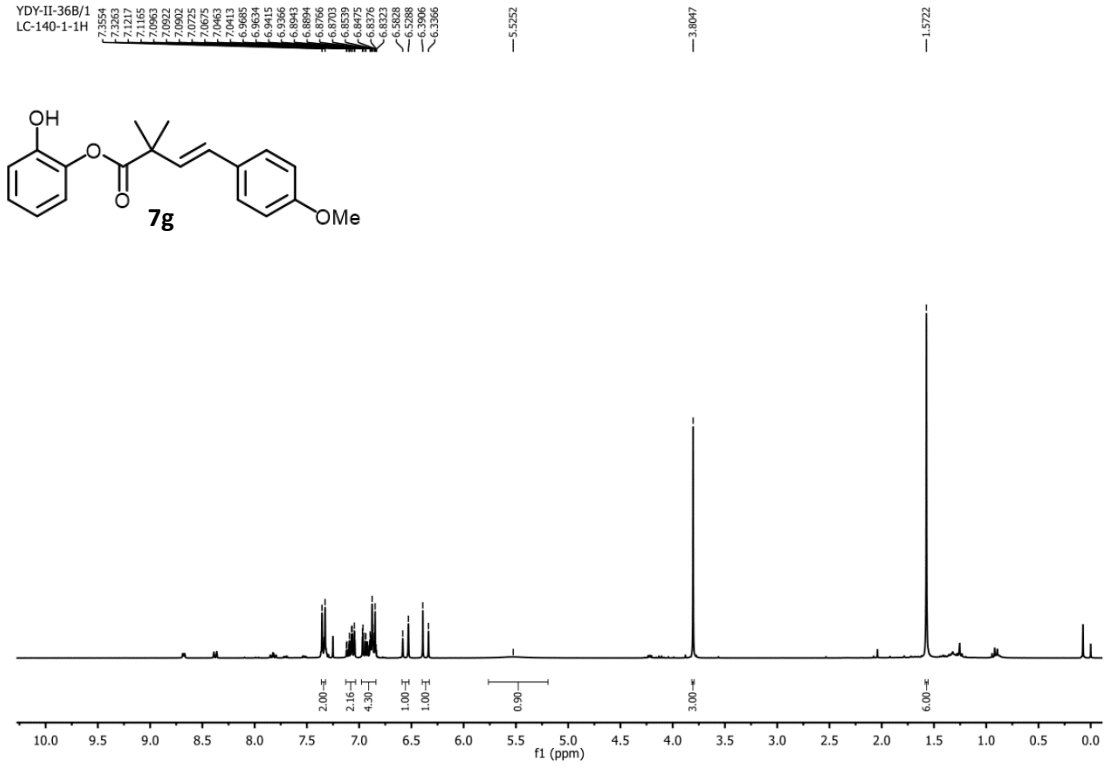
^{1}H NMR of compound **7e** (300 MHz in $CDCl_3$)



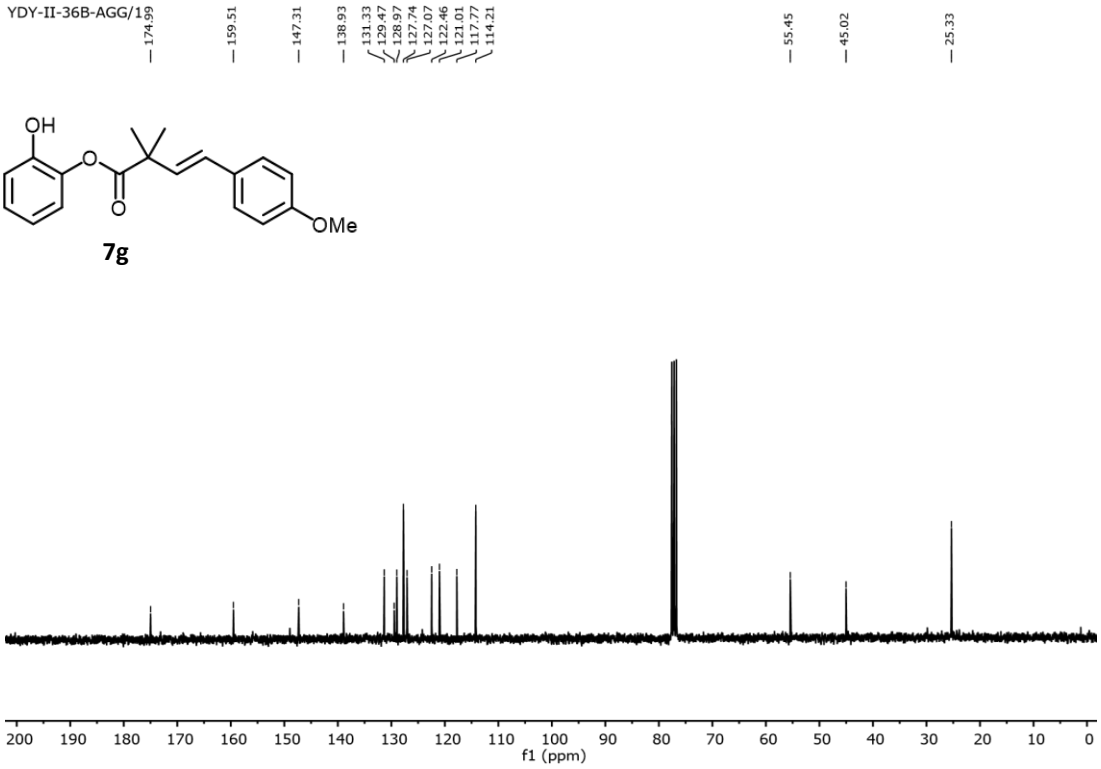
^{13}C NMR of compound **7e** (75 MHz in $CDCl_3$)



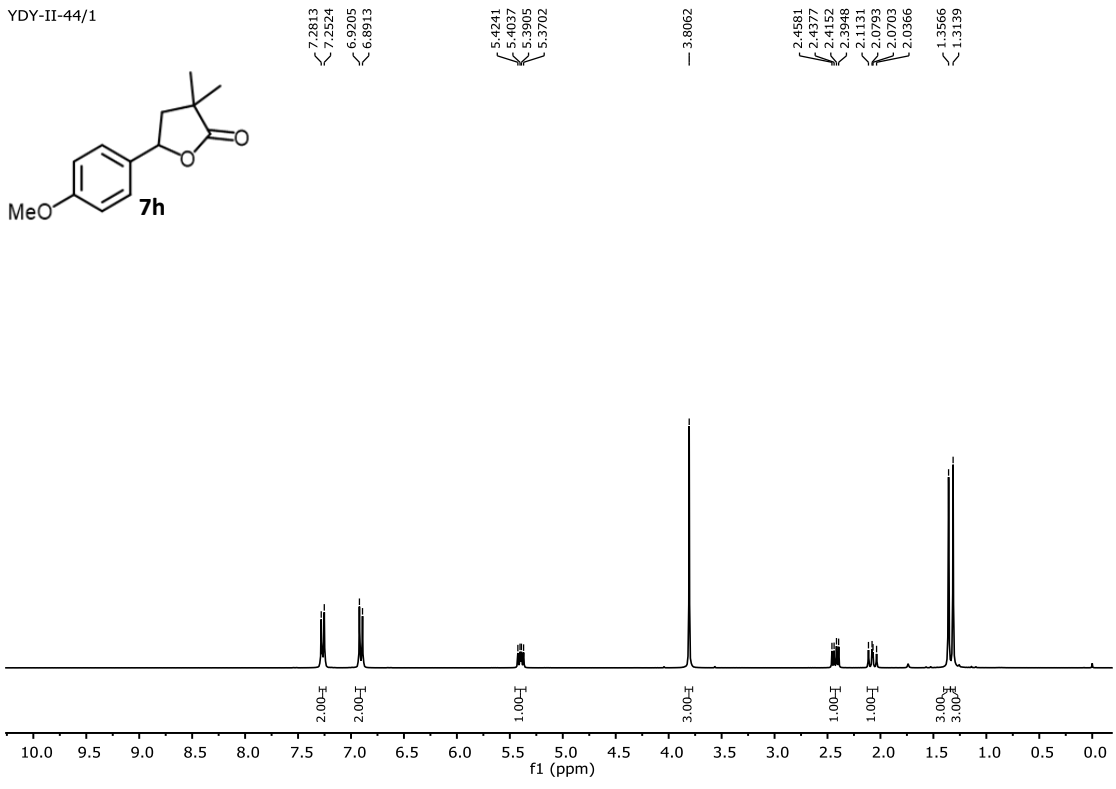
^{1}H NMR of compound **7g** (300 MHz in $CDCl_3$)



^{13}C NMR of compound **7g** (75 MHz in $CDCl_3$)



^{1}H NMR of compound **7h** (300 MHz in $CDCl_3$)



^{13}C NMR of compound **7h** (75 MHz in $CDCl_3$)