Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Organophotoredox-Enabled Cascade Cyclization Reactions for the Construction of Cyanoalkyl Indole[2,1-*a*]isoquinolinones

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Supporting Information

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1. General Information

^{1}H NMR spectra were recorded on Bruker 400 MHz spectrometer and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak pamerns are indicated as follows: s, singlet. d, doublet. dd, doublet of doublet. t, triplet. m, multiplet. q, quartet. The coupling constants, J, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained at Bruker 100 MHz and referenced to the internal solvent signals (central peak is 77.160 ppm in $CDCl_3$). $CDCl_3$ and DMSO-d6 was used as the NMR solvent. High-resolution mass spectra (HRMS) were acquired on Thermo Q-Exactive instrument (quadrupole mass analyzer) using electrospray ionization mode (ESI). Flash column chromatography was performed over silica gel 200-300. All reagents were weighed and handled in air at room temperature. All chemical reagents were purchased from Energy Chemical and aladdin and used without further purification. Cyclobutanone oxime esters **1** and 2-aryl-*N*-methacryloyl indoles **2** were prepared according to the previous reported protocols.[1-3]

2. Optimization of the Reaction Conditions

Photocatalysts:

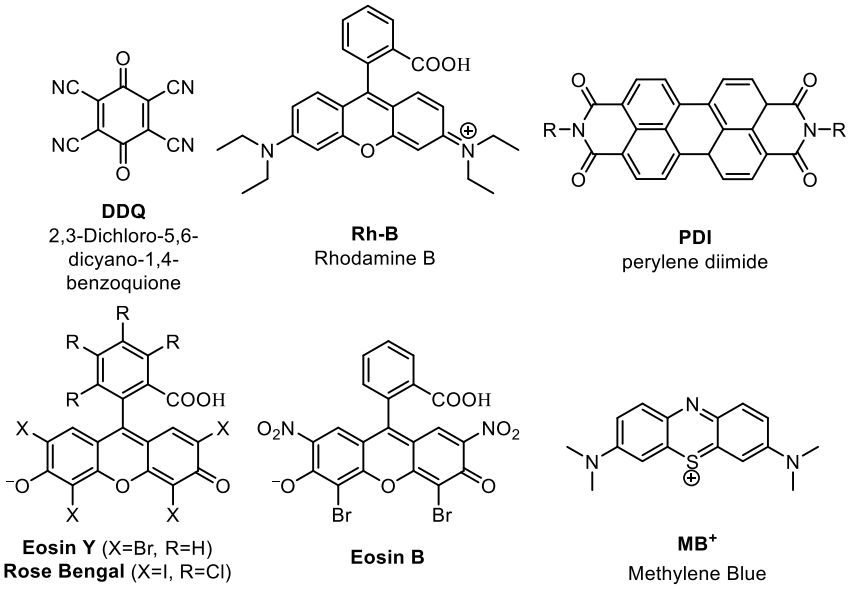
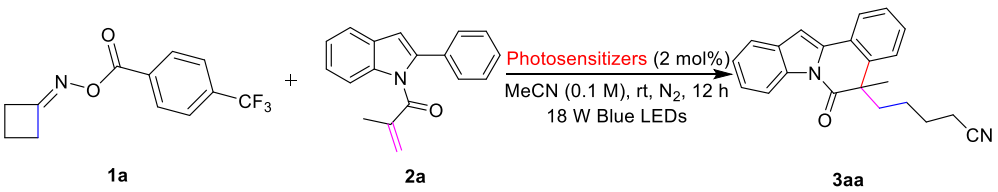


Figure S1

Table S1. Screen of photosensitizers[a]

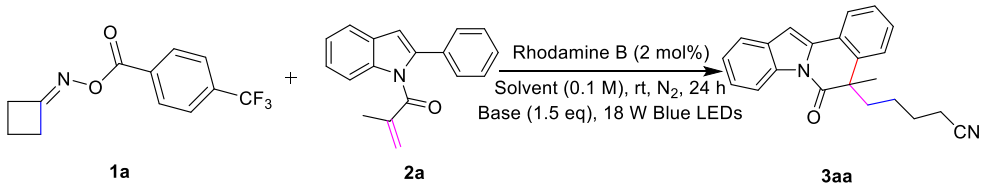


Entry	Photosensitizers	Yield (%)[b]
1	Rhodamine B	47
2	Eosin B	45

3	Eosin Y	trace
4	Rose Bengal	trace
5	Methylene blue	trace
6	PDI	trace
7	1,4-Anthraquinone	trace
8	Benzoquinone	trace
9[c]	none	NR
10[d]	Rhodamine B	NR
11[e]	Rhodamine B	trace

[a] Unless otherwise noted, reactions were carried out with **1a** (0.4 mmol), **2a** (0.2 mmol) and photosensitizers (2 mol%) in MeCN (0.1 M) at room temperature under 18 W blue LEDs for 12 h. [b] isolated yields based on **2a**. [c] Without photocatalyst. [d] Without blue LED light. [e] Under air.

Table S2. Screening of solvents and additives[a]

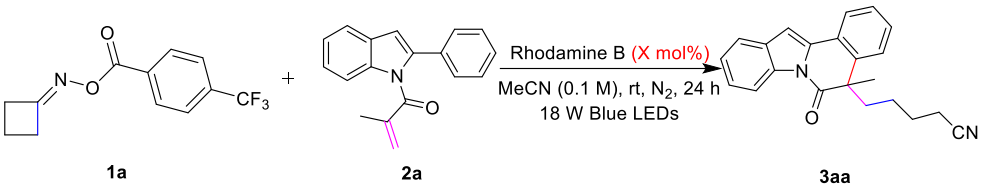


1a **2a** **3aa**

Entry	Solvent	Yield (%)[b]
1	MeCN	58
2	DMF	NR
3	DMA	NR
4	DMSO	55
5	THF	21
6	DCM	10
7	DCE	50
8	EtOH	trace
9[c]	MeCN	trace
10[d]	MeCN	56
11[e]	MeCN	54

[a] Unless otherwise noted, reactions were carried out with **1a** (0.4 mmol), **2a** (0.2 mmol) and Rhodamine B (2 mol%) in solvent (0.1 M) at room temperature under 18 W blue LEDs for 24 h. [b] isolated yields based on **2a**. [c] Cs_2CO_3, Na_2CO_3, Na_2HPO_4, 2,6-Lutidine and 2,4,6-trimethylpyridine were added as bases. [d] NH_4Cl was added as acid additive. [e] CH_3COOH was added as acid.

Table S3. Screen of photocatalyst loading[a]

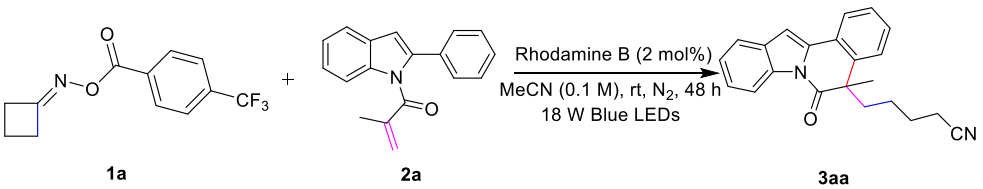


1a **2a** **3aa**

Entry	Rhodamine B (x mol%)	Yield (%)[b]
1	1.0	19
2	1.5	45
3	2.0	58
4	3.0	57
5	5.0	55
6[c]	2.0	65

[a] Unless otherwise noted, reactions were carried out with, **1a** (0.4 mmol), **2a** (0.2 mmol) and Rhodamine B (x mol%) in MeCN (0.1 M) at room temperature under 18 W blue LEDs for 24 h. [b] isolated yields. [c] 48 h.

Table S4. Screen of mole ratios[a]

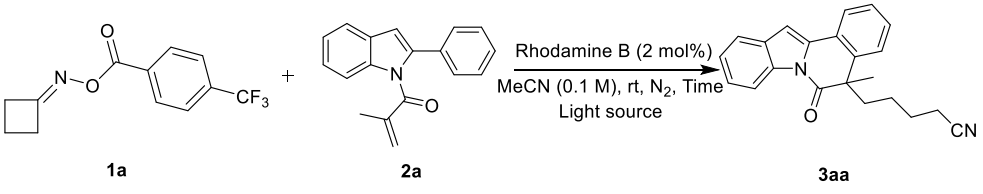


1a **2a** **3aa**

Entry	Mole ratio (**1a** : **2a**)	Yield (%)[b]
1	2.0 : 1.0	65
2	1.5 : 1.0	83
3	1.0 : 1.0	80
4	1.0 : 1.5	87
5	1.0 : 2.0	78
6[c]	1.0 : 1.5	82
7[d]	1.0 : 1.5	73

[a] Unless otherwise noted, reactions were carried out with, **1a**, **2a** and Rhodamine B (2 mol%) in MeCN (0.1 M) at room temperature under 18 W blue LEDs for 48 h. [b] isolated yields. [c] $Ir(ppy)_3$, [d] $Ru(bpy)_3Cl_2 \cdot 6H_2O$.

Table S5. Screen of reaction time and light source[a]

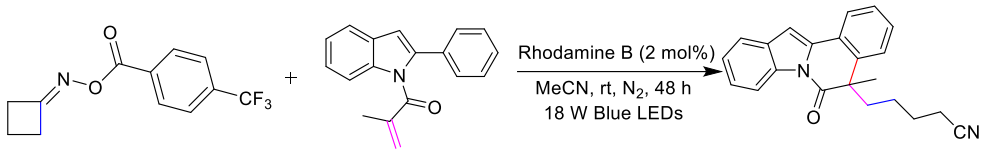


1a **2a** **3aa**

Entry	Time	Light source	Yield (%)[b]
1	24	18 W Blue Light	69
2	36	18 W Blue Light	81
3	48	18 W Blue Light	87
4	48	12 W Blue Light	86
5	48	30 W Blue Light	85
6	48	36 W Blue Light	83
7	48	395 nm Light	51
8	48	455 nm Light	84
9	48	Green Light (520-525 nm)	62
10	48	White Light	76

[a] Unless otherwise noted, reactions were carried out with, **1a** (0.3 mol), **2a** (0.2 mol) and Rhodamine B (2 mol%) in MeCN (0.1 M) at room temperature. [b] isolated yields.

3. General Procedure

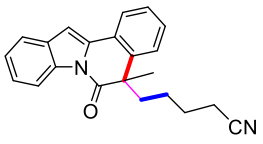


1a **2a** **3aa**

To a Schlenk tube equipped with a magnetic stir bar was charged with Cyclobutanone Oximes **1a** (0.2 mmol), *N*-methylpropenyl-2-phenylindole **2a** (0.3 mmol) and Rhodamine B (2 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 2.0 mL acetonitrile (MeCN) was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under 18 W blue LEDs for 48 h. The residue was purified directly by thin layer chromatography, eluting with ethyl acetate/ cyclohexane (1:5 v/v), to afford compound **3aa**.

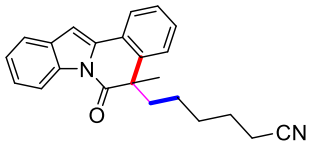
4. Characterization Data

5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3aa)[4]



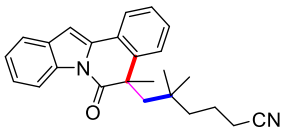
Colorless oil. 57.1 mg, 87% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.58 (d, *J* = 8.0 Hz, 1H), 7.89-7.83 (m, 1H), 7.61 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.42-7.31 (m, 5H), 7.04 (s, 1H), 2.43 (ddd, *J* = 13.3, 11.4, 5.1 Hz, 1H), 2.26-2.04 (m, 2H), 1.97 (ddd, *J* = 13.3, 11.5, 5.1 Hz, 1H), 1.69 (s, 3H), 1.53 (dddd, *J* = 30.2, 13.4, 9.0, 6.8 Hz, 2H), 1.05 (mdd, *J* = 13.5, 11.0, 8.7, 5.2 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.03, 137.90, 135.47, 135.28, 130.77, 129.27, 127.54, 126.16, 125.39, 124.85, 124.80, 123.94, 120.62, 119.48, 116.84, 103.20, 77.16, 48.70, 41.65, 29.35, 25.53, 24.62, 16.88. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

6-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)hexanenitrile (4aa)



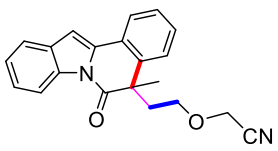
Colorless oil. 7.5 mg, 11% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.6-8.55 (m, 1H), 7.91-7.83 (m, 1H), 7.65-7.58 (m, 1H), 7.39 (m, *J* = 4.5, 3.4, 1.4 Hz, 3H), 7.37 (dd, *J* = 5.5, 1.6 Hz, 1H), 7.33 (m, *J* = 7.4, 1.1 Hz, 1H), 7.03 (s, 1H), 2.41 (td, *J* = 12.8, 4.6 Hz, 1H), 2.17 (t, *J* = 7.1 Hz, 2H), 1.92 (td, *J* = 12.9, 4.4 Hz, 1H), 1.69 (s, 3H), 1.51-1.40 (m, 2H), 1.36-1.25 (m, 2H), 0.98 (dp, *J* = 15.5, 5.2, 3.7 Hz, 1H), 0.88 (tdd, *J* = 12.4, 8.1, 5.8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.26, 138.33, 135.61, 135.29, 130.78, 129.21, 127.42, 126.25, 125.36, 124.90, 124.76, 123.85, 120.59, 119.73, 116.88, 103.04, 77.16, 48.82, 42.50, 29.23, 28.70, 25.03, 24.48, 17.09. HRMS (ESI) calcd for $C_{23}H_{22}N_2O$ $(M+H)^+$ 343.1805, found 343.1802. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5,5-Dimethyl-6-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)hexanenitrile (3ba)



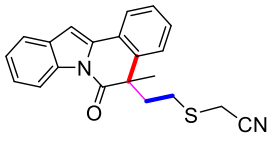
Colorless oil. 56.2 mg, 76% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.59 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 6.4, 3.1 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.42 (dt, *J* = 8.0, 3.9 Hz, 1H), 7.40-7.31 (m, 4H), 7.07 (s, 1H), 2.58 (d, *J* = 14.3 Hz, 1H), 2.10-2.01 (m, 2H), 1.95 (dt, *J* = 16.7, 7.2 Hz, 1H), 1.72-1.66 (m, 3H), 1.49 (dm, *J* = 38.4, 12.7, 5.9 Hz, 2H), 0.93 (pd, *J* = 13.2, 4.9 Hz, 2H), 0.49 (d, *J* = 17.4 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.34, 138.53, 135.39, 135.33, 130.74, 128.46, 127.61, 127.39, 125.39, 124.80, 124.31, 123.84, 120.61, 119.78, 116.87, 103.22, 77.16, 53.05, 46.85, 42.67, 34.39, 32.96, 28.37, 27.73, 20.36, 17.65. HRMS (ESI) calcd for $C_{25}H_{26}N_2O$ $(M+H)^+$ 371.2118, found 371.2115. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

2-(2-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethoxy)acetonitrile (3ca)



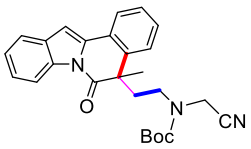
Colorless oil. 55.4 mg, 84% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.57 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.91-7.87 (m, 1H), 7.65-7.57 (m, 1H), 7.44-7.36 (m, 4H), 7.36-7.30 (m, 1H), 7.05 (s, 1H), 3.77 (dd, *J* = 16.2, 1.4 Hz, 1H), 3.65 (dd, *J* = 16.3, 1.2 Hz, 1H), 3.43 (ddd, *J* = 9.6, 5.9, 3.6 Hz, 1H), 3.13 (td, *J* = 9.7, 5.0 Hz, 1H), 2.93 (ddd, *J* = 14.1, 9.8, 6.0 Hz, 1H), 2.16 (ddd, *J* = 14.3, 5.0, 3.5 Hz, 1H), 1.74 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.94, 136.97, 135.42, 135.32, 130.64, 129.17, 127.73, 126.36, 125.41, 124.98, 124.68, 124.09, 120.61, 116.78, 115.33, 103.14, 77.16, 68.19, 55.90, 46.51, 41.33, 29.48. HRMS (ESI) calcd for $C_{21}H_{18}N_2O_2$ $(M+H)^+$ 331.1441, found 331.1439. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

2-((2-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl)thio)acetonitrile (3da)



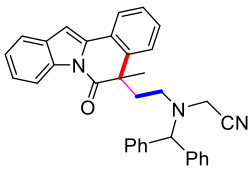
Colorless oil. 50.5 mg, 73% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.4 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.40 (dq, *J* = 14.8, 7.8, 6.5 Hz, 4H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.05 (s, 1H), 3.27 (d, *J* = 17.2 Hz, 1H), 3.06 (d, *J* = 17.1 Hz, 1H), 2.86 (m, *J* = 11.8, 5.7 Hz, 1H), 2.48 (q, *J* = 9.8, 9.4 Hz, 1H), 2.41-2.28 (m, 2H), 1.70 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.55, 136.64, 135.40, 135.26, 130.73, 129.39, 127.81, 126.21, 125.47, 125.04, 124.83, 124.19, 120.68, 116.82, 116.40, 103.44, 77.16, 48.32, 39.56, 30.34, 28.51, 16.70. HRMS (ESI) calcd for $C_{21}H_{18}N_2OS$ $(M+H)^+$ 347.1213, found 347.1209. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

Tert-butyl (cyanomethyl)(2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl) carbamate (3ea)



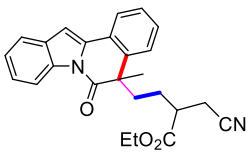
Colorless oil. 70.3 mg, 82% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.55 (dd, *J* = 8.1, 2.5 Hz, 1H), 7.93-7.82 (m, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.48-7.31 (m, 5H), 7.03 (s, 1H), 4.18-3.74 (m, 2H), 3.23-2.92 (m, 2H), 2.80 (d, *J* = 13.9 Hz, 1H), 2.29 (t, *J* = 10.3 Hz, 1H), 1.75-1.63 (m, 3H), 1.28 (d, *J* = 51.5 Hz, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.70, 172.16, 154.40, 153.60, 136.96, 135.28, 130.71, 129.39, 127.79, 126.09, 125.55, 124.86, 124.76, 124.13, 120.65, 116.76, 116.18, 103.49, 103.30, 81.82, 77.16, 47.11, 44.69, 44.18, 38.86, 37.74, 35.59, 35.22, 31.15, 30.46, 28.16, 27.97 (3). HRMS (ESI) calcd for $C_{34}H_{29}N_3O$ $(M+H)^+$ 430.2125, found 430.2121. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

2-(Benzhydryl(2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl)amino)aceto -nitrile (3fa)



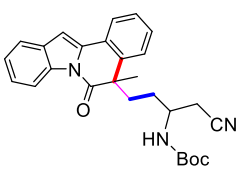
White solid. 40.5 mg, 41% yield. m.p. 138-141 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.66-8.58 (m, 1H), 7.90 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.77-7.67 (m, 1H), 7.48-7.39 (m, 2H), 7.35-7.29 (m, 1H), 7.21-7.15 (m, 2H), 7.12 (d, *J* = 7.9 Hz, 1H), 6.98-6.87 (m, 4H), 6.85-6.79 (m, 2H), 6.73 (d, *J* = 6.3 Hz, 4H), 4.29 (s, 1H), 3.96 (d, *J* = 17.8 Hz, 1H), 3.35 (d, *J* = 17.8 Hz, 1H), 2.89 (ddd, *J* = 15.4, 9.5, 6.5 Hz, 1H), 2.32-2.20 (m, 2H), 2.13 (dt, *J* = 14.8, 4.4 Hz, 1H), 1.63 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.99, 141.20, 140.26, 137.22, 135.74, 135.61, 130.84, 129.16, 128.67 (2), 128.50 (2), 127.69 (2), 127.44, 127.33, 127.11 (2), 127.08, 126.16, 125.57, 124.93, 124.85, 124.14, 120.77, 117.17, 114.99, 103.08, 77.16, 73.43, 47.64, 46.98, 39.61, 37.46, 32.04. HRMS (ESI) calcd for $C_{34}H_{29}N_3O$ $(M+H)^+$ 496.2383, found 496.2381. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

Ethyl 2-(cyanomethyl)-4-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)butanoate (3ga)



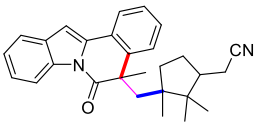
Colorless oil. 71.2 mg, 89% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.57 (dd, *J* = 8.2, 3.1 Hz, 1H), 7.87 (dd, *J* = 7.0, 1.8 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.44-7.30 (m, 5H), 7.04 (s, 1H), 4.23-4.07 (m, 2H), 2.66-2.34 (m, 4H), 2.00 (dtd, *J* = 42.5, 12.9, 4.6 Hz, 1H), 1.67 (d, *J* = 7.0 Hz, 3H), 1.48-1.28 (m, 2H), 1.23 (dt, *J* = 18.4, 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.61, 172.46, 172.11, 172.01, 137.40, 137.30, 135.36, 135.33, 135.29, 130.74, 130.71, 129.36, 129.36, 129.31, 127.68, 126.07, 126.03, 125.45, 125.43, 124.94, 124.85, 124.82, 124.04, 124.04, 120.64, 120.62, 117.64, 117.51, 116.85, 116.80, 103.32, 103.31, 77.16, 61.61, 61.59, 48.64, 48.56, 41.47, 41.45, 38.34, 38.17, 29.93, 29.60, 27.24, 27.02, 19.30, 18.99, 14.22, 14.18. HRMS (ESI) calcd for $C_{25}H_{24}N_2O_3$ $(M+H)^+$ 401.1860, found 401.1857. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

Tert-butyl (1-cyano-4-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)butan-2-yl) carbamate (3ha)



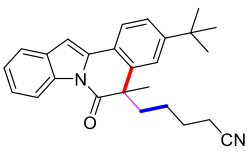
Colorless oil. 77.9 mg, 88% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (dd, *J* = 8.1, 4.1 Hz, 1H), 7.92-7.82 (m, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.46-7.30 (m, 5H), 7.04 (s, 1H), 4.66 (d, *J* = 8.1 Hz, 0.5H), 4.49 (d, *J* = 8.4 Hz, 0.5H), 3.82-3.53 (m, 1H), 2.68-2.51 (m, 1.5H), 2.52-2.33 (m, 1.5H), 2.05 (dddd, *J* = 19.5, 17.1, 13.8, 7.7 Hz, 1H), 1.67 (d, *J* = 7.1 Hz, 3H), 1.43 (s, 9H), 1.31-1.16 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.87, 172.74, 155.23, 155.08, 137.44, 137.36, 135.33, 135.31, 130.79, 130.77, 129.50, 129.41, 127.77, 126.04, 126.00, 125.52, 124.95, 124.92, 124.91, 124.88, 124.14, 124.11, 120.70, 120.69, 117.12, 117.05, 116.88, 116.85, 103.48, 80.37, 77.16, 48.70, 48.58, 47.61, 47.43, 38.02, 37.72, 30.30, 29.72, 29.53, 29.43, 28.41(3), 23.95, 23.74. HRMS (ESI) calcd for $C_{34}H_{29}N_3O$ $(M+H)^+$ 444.2282, found 444.2296. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

2-(2,2,3-Trimethyl-3-((5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)methyl)cyclo p-entyl)acetonitrile (3ia)



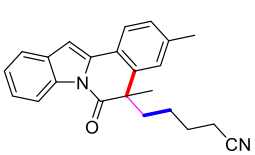
Colorless oil. 27.8 mg, 34% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.65-8.59 (m, 2H), 7.87 (ddd, *J* = 9.3, 6.2, 3.7 Hz, 2H), 7.66-7.59 (m, 2H), 7.43 (m, *J* = 6.5, 2.9 Hz, 2H), 7.40-7.31 (m, 8H), 7.06 (d, *J* = 1.8 Hz, 2H), 2.69 (d, *J* = 6.4 Hz, 1H), 2.66 (d, *J* = 6.6 Hz, 1H), 2.34-2.20 (m, 4H), 2.17-2.09 (m, 1H), 2.08-1.99 (m, 4H), 1.97-1.88 (m, 1H), 1.69 (d, *J* = 5.0 Hz, 8H), 1.29 (dd, *J* = 8.7, 4.3 Hz, 2H), 1.08-1.00 (m, 2H), 0.98 (s, 6H), 0.69 (s, 3H), 0.60 (s, 3H), 0.44 (s, 3H), 0.23 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.74, 173.11, 138.89, 138.30, 135.38, 130.70, 128.43, 128.35, 127.81, 127.63, 127.45, 127.24, 125.42, 125.30, 124.75, 124.71, 124.27, 124.21, 123.89, 123.86, 120.53, 120.02, 119.93, 117.01, 103.12, 103.09, 77.16, 48.03, 47.70, 47.60, 47.46, 47.03, 46.98, 46.90, 46.78, 44.59, 43.75, 35.05, 34.04, 33.73, 33.57, 28.82, 28.37, 25.56, 23.39, 22.35, 20.71, 20.40, 19.68, 18.96, 18.93. HRMS (ESI) calcd for $C_{34}H_{29}N_3O$ $(M+H)^+$ 411.2431, found 411.2427. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(3-(Tert-butyl)-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ab)



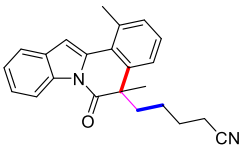
Colorless oil. 50.7 mg, 66% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.59 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.42 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.40-7.30 (m, 3H), 6.98 (s, 1H), 2.43 (ddd, *J* = 13.5, 11.4, 5.1 Hz, 1H), 2.26-2.08 (m, 2H), 1.98 (ddd, *J* = 13.4, 11.6, 5.0 Hz, 1H), 1.69 (s, 3H), 1.65-1.42 (m, 2H), 1.38 (d, *J* = 0.8 Hz, 9H), 1.08 (dddd, *J* = 26.0, 15.7, 7.3, 5.2 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.28, 152.59, 137.52, 135.65, 135.21, 130.95, 125.13, 124.96, 124.74, 123.74, 122.59, 122.19, 120.49, 119.48, 116.79, 102.49, 77.16, 48.93, 41.63, 35.13, 31.37 (3), 29.39, 25.55, 24.59, 16.86. HRMS (ESI) calcd for $C_{26}H_{28}N_2O$ $(M+H)^+$ 385.2274, found 385.2269. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(3,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ac)



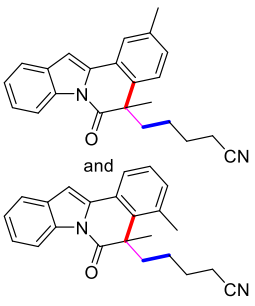
Colorless oil. 49.3 mg, 72% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.57 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.41-7.29 (m, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.97 (s, 1H), 2.44 (s, 3H), 2.43-2.37 (m, 1H), 2.25-2.06 (m, 2H), 1.96 (ddd, *J* = 13.3, 10.8, 5.9 Hz, 1H), 1.68 (s, 3H), 1.54 (dm, *J* = 15.1, 7.9, 4.2 Hz, 2H), 1.14-0.98 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.16, 139.36, 137.89, 135.71, 135.17, 130.91, 128.62, 126.47, 125.10, 124.73, 123.90, 122.16, 120.44, 119.51, 116.77, 102.39, 77.16, 48.63, 41.72, 29.33, 25.52, 24.60, 21.85, 16.86. HRMS (ESI) calcd for $C_{23}H_{22}N_2O$ $(M+H)^+$ 343.1805, found 343.1795. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(1,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ad)



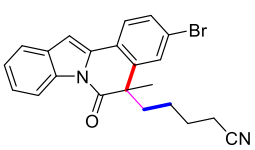
Colorless oil. 62.2 mg, 91% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.66-8.58 (m, 1H), 7.64 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.40 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.34 (td, *J* = 7.5, 1.1 Hz, 1H), 7.32-7.29 (m, 2H), 7.26-7.24 (m, 2H), 7.14 (s, 1H), 2.75 (s, 3H), 2.44-2.34 (m, 1H), 2.25-2.06 (m, 2H), 2.00-1.90 (m, 1H), 1.68 (s, 3H), 1.62-1.43 (m, 2H), 1.15-1.02 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.25, 139.10, 135.65, 134.69, 134.47, 131.04, 130.78, 128.33, 125.77, 124.65, 124.27 (2), 120.73, 119.53, 116.83, 109.43, 77.16, 48.64, 41.86, 29.40, 25.55, 25.08, 24.56, 16.89. HRMS (ESI) calcd for $C_{23}H_{22}N_2O$ $(M+H)^+$ 343.1805, found 343.1802. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(2,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ae)
5-(4,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ae')



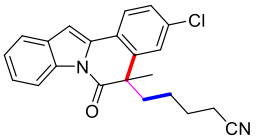
Colorless oil. 63.6 mg, 93% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.55 (d, *J* = 8.0 Hz, 1H), 7.65 (s, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.39-7.28 (m, 2H), 7.24 (d, *J* = 1.4 Hz, 1H), 7.19 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.00 (s, 1H), 2.41 (s, 3H), 2.41-2.35 (m, 2H), 2.22-2.04 (m, 2H), 1.92 (ddd, *J* = 13.4, 10.6, 6.0 Hz, 1H), 1.64 (s, 3H), 1.51 (dtq, *J* = 21.4, 14.5, 7.2 Hz, 2H), 1.03 (dqd, *J* = 19.0, 10.2, 8.7, 5.2 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.28, 137.19, 135.68, 135.31, 135.10, 130.83, 130.44, 126.09, 125.30, 124.75, 124.64, 124.19, 120.57, 119.54, 116.85, 102.96, 77.16, 48.45, 41.65, 29.46, 25.58, 24.66, 21.26, 16.91. HRMS (ESI) calcd for $C_{23}H_{22}N_2O$ $(M+H)^+$ 343.1805, found 343.1800. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(3-Bromo-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3af)



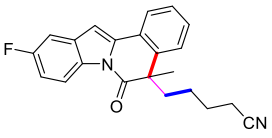
Colorless oil. 49.6 mg, 61% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.64-7.57 (m, 1H), 7.54-7.47 (m, 2H), 7.39 (td, *J* = 7.7, 1.3 Hz, 1H), 7.34 (td, *J* = 7.5, 1.2 Hz, 1H), 7.03 (s, 1H), 2.42 (ddd, *J* = 13.4, 11.2, 5.4 Hz, 1H), 2.26-2.09 (m, 2H), 1.91 (ddd, *J* = 13.4, 11.3, 5.5 Hz, 1H), 1.68 (s, 3H), 1.54 (dp, *J* = 14.1, 6.9, 6.4 Hz, 2H), 1.14-0.97 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.18, 139.95, 135.31, 134.45, 130.94, 130.59, 129.29, 125.78, 125.49, 125.00, 123.96, 123.09, 120.78, 119.39, 116.87, 103.84, 77.16, 48.73, 41.84, 29.16, 25.48, 24.59, 16.93. HRMS (ESI) calcd for $C_{22}H_{19}BrN_2O$ $(M+H)^+$ 407.0754, found 407,0750. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(3-Chloro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ag)



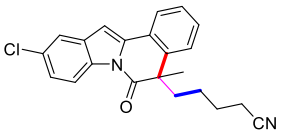
Colorless oil. 25.3 mg, 35% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.37 (h, *J* = 7.8 Hz, 4H), 7.01 (s, 1H), 2.49-2.38 (m, 1H), 2.18 (tq, *J* = 16.9, 9.3, 8.4 Hz, 2H), 1.97-1.87 (m, 1H), 1.68 (s, 3H), 1.55 (tp, *J* = 14.5, 6.8 Hz, 2H), 1.15-0.98 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.21, 139.71, 135.26, 134.95, 134.42, 130.59, 128.09, 126.31, 125.71, 125.34, 124.97, 123.53, 120.74, 119.38, 116.85, 103.72, 77.16, 48.75, 41.80, 29.15, 25.46, 24.57, 16.91. HRMS (ESI) calcd for $C_{22}H_{19}ClN_2O$ $(M+H)^+$ 363.1259, found 363.1256. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(10-Fluoro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ah)



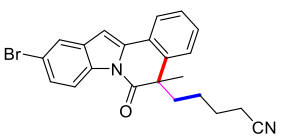
Colorless oil. 60.9 mg, 88% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.52 (dd, *J* = 9.0, 4.7 Hz, 1H), 7.89-7.82 (m, 1H), 7.46-7.34 (m, 3H), 7.25 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.08 (tdd, *J* = 9.0, 2.6, 0.9 Hz, 1H), 6.99 (s, 1H), 2.42 (ddd, *J* = 13.3, 11.4, 5.1 Hz, 1H), 2.26-2.07 (m, 2H), 1.97 (ddd, *J* = 13.4, 11.5, 5.1 Hz, 1H), 1.68 (s, 3H), 1.53 (dddd, *J* = 31.8, 13.6, 8.9, 6.6 Hz, 2H), 1.04 (dddd, *J* = 17.2, 11.1, 9.1, 5.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.83, 161.36, 159.44, 138.11, 137.00, 131.98, 131.90, 131.59, 129.62, 127.62, 126.20, 124.46, 124.06, 119.45, 117.90, 117.83, 112.96, 112.76, 106.34, 106.15, 102.72, 102.69, 77.16, 48.63, 41.63, 29.38, 25.47, 24.58, 16.88. HRMS (ESI) calcd for $C_{22}H_{19}FN_2O$ $(M+H)^+$ 347.1554, found 347.1551. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(10-Chloro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ai)



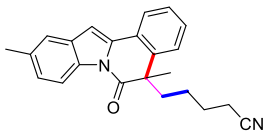
Colorless oil. 61.5mg, 85% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.48 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.46-7.35 (m, 3H), 7.32 (dd, *J* = 8.7, 2.1 Hz, 1H), 6.96 (s, 1H), 2.42 (ddd, *J* = 13.3, 11.2, 5.4 Hz, 1H), 2.16 (qt, *J* = 16.9, 7.3 Hz, 2H), 1.97 (ddd, *J* = 13.4, 11.3, 5.4 Hz, 1H), 1.68 (s, 3H), 1.61-1.45 (m, 2H), 1.04 (dm, *J* = 10.6, 8.6, 5.3 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.97, 138.09, 136.78, 133.57, 132.09, 130.34, 129.71, 127.67, 126.21, 125.40, 124.40, 124.13, 120.18, 119.44, 117.79, 102.25, 77.16, 48.72, 41.68, 29.35, 25.48, 24.59, 16.90. HRMS (ESI) calcd for $C_{22}H_{19}ClN_2O$ $(M+H)^+$ 363.1259, found 363.1263. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(10-Bromo-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3aj)



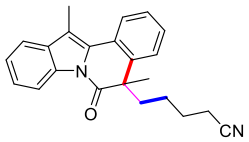
Colorless oil. 64.9 mg, 80% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.43 (d, *J* = 8.7 Hz, 1H), 7.87-7.82 (m, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.47-7.35 (m, 4H), 6.95 (s, 1H), 2.41 (ddd, *J* = 13.4, 11.1, 5.4 Hz, 1H), 2.15 (qt, *J* = 16.9, 7.3 Hz, 2H), 1.96 (ddd, *J* = 13.5, 11.2, 5.4 Hz, 1H), 1.68 (d, *J* = 2.3 Hz, 3H), 1.53 (dddd, *J* = 30.0, 13.4, 8.6, 6.5 Hz, 2H), 1.04 (dddd, *J* = 14.1, 10.8, 8.8, 6.3 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.98, 138.09, 136.64, 133.90, 132.56, 129.72, 128.08, 127.66, 126.20, 124.34, 124.14, 123.21, 119.41, 118.14, 118.12, 102.10, 77.16, 48.74, 41.67, 29.29, 25.46, 24.56, 16.87. HRMS (ESI) calcd for $C_{22}H_{19}BrN_2O$ $(M+H)^+$ 407.0754, found 407.0761. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(5,10-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ak)



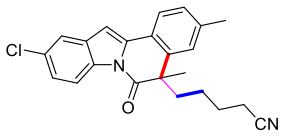
Colorless oil. 25.3 mg, 37% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.43 (d, *J* = 8.3 Hz, 1H), 7.84 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.46-7.31 (m, 4H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.96 (s, 1H), 2.47 (s, 3H), 2.42 (ddd, *J* = 13.3, 11.4, 5.2 Hz, 1H), 2.26-2.04 (m, 2H), 1.95 (ddd, *J* = 13.4, 11.4, 5.2 Hz, 1H), 1.68 (s, 3H), 1.52 (dddd, *J* = 30.4, 13.5, 8.8, 6.8 Hz, 2H), 1.15-0.91 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.80, 137.91, 135.51, 134.47, 133.44, 131.01, 129.14, 127.49, 126.68, 126.16, 124.97, 123.87, 120.60, 119.50, 116.45, 103.01, 77.16, 48.59, 41.74, 29.30, 25.54, 24.62, 21.62, 16.89. HRMS (ESI) calcd for $C_{23}H_{22}N_2O$ $(M+H)^+$ 343.1805, found 343.1803. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5-(5,12-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3al)[5]



White solid. 50.6 mg, 74% yield. m.p. 146-148 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.60 (d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.40 (m, *J* = 16.2, 7.7 Hz, 5H), 2.66 (s, 3H), 2.39 (ddd, *J* = 13.1, 10.3, 6.1 Hz, 1H), 2.17 (dtd, *J* = 24.3, 16.7, 8.3 Hz, 2H), 2.01-1.88 (m, 1H), 1.68 (s, 3H), 1.54 (ddp, *J* = 21.4, 14.1, 7.1 Hz, 2H), 1.18-1.01 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.82, 138.23, 134.15, 132.55, 129.74, 128.20, 127.31, 126.64, 126.32, 125.85, 125.21, 124.39, 119.52, 118.50, 116.74, 114.47, 77.16, 48.45, 41.56, 29.06, 25.55, 24.57, 16.89, 11.59. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

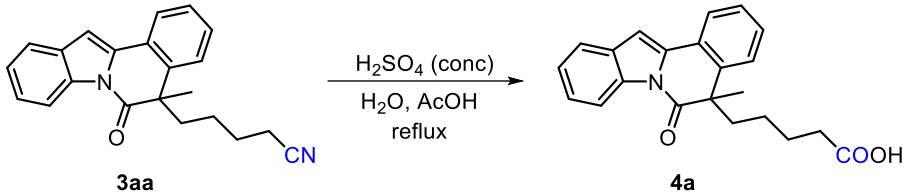
5-(10-Chloro-3,5-dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3am)



Colorless oil. 57.9 mg, 77% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.47 (d, *J* = 8.7 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.29 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.22-7.15 (m, 2H), 6.89 (s, 1H), 2.43 (s, 3H), 2.42-2.35 (m, 1H), 2.25-2.08 (m, 2H), 2.00-1.91 (m, 1H), 1.67 (s, 3H), 1.53 (ddp, *J* = 21.1, 13.9, 6.8 Hz, 2H), 1.04 (ddt, *J* = 15.0, 10.3, 5.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.12, 139.91, 138.09, 137.04, 133.47, 132.25, 130.27, 128.75, 126.53, 125.09, 124.09, 121.72, 120.01, 119.47, 117.72, 101.47, 77.16, 48.66, 41.76, 29.34, 25.48, 24.58, 21.90, 16.90. HRMS (ESI) calcd for $C_{23}H_{21}ClN_2O$ $(M+H)^+$ 377.1415, found 377.1406. Purification by flash chromatography (cyclohexane/ethyl acetate = 5/1).

5. Transformation of Cyanoalkylated Product

(a) Hydrolysis of *β*-cyanoalkylated indolo[2,1-*α*]isoquinoline (3aa)



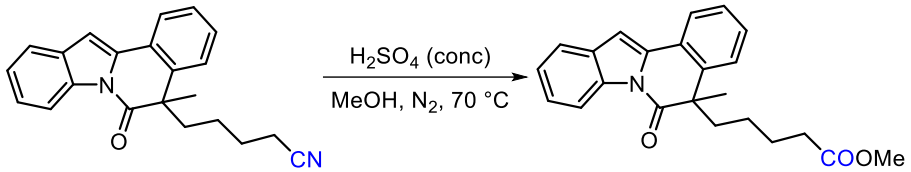
3aa **4a**

3aa (164.5 mg, 0.5 mmol) was added into 10 mL RBF. H_2SO_4 (0.3 mL), CH3COOH (0.5 mL) and H_2O (0.5 mL) were then added sequentially via syringe. The resulting mixture was heated to reflux. Upon completion of the reaction as monitored by TLC, the solvent was removed under

vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1 : 2 *v/v*) to give product **4a**.

5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanoic acid. Colorless oil. 156.1 mg, 90% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.59 (d, *J* = 8.1 Hz, 1H), 7.89-7.80 (m, 1H), 7.60 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.38 (dd, *J* = 5.3, 1.7 Hz, 3H), 7.37-7.35 (m, 1H), 7.35-7.32 (m, 1H), 7.02 (s, 1H), 2.46-2.36 (m, 1H), 2.22-2.06 (m, 2H), 1.93 (td, *J* = 12.9, 4.4 Hz, 1H), 1.68 (s, 3H), 1.60-1.37 (m, 2H), 1.08-0.84 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.47, 173.26, 138.32, 135.61, 135.29, 130.76, 129.14, 127.34, 126.25, 125.31, 124.87, 124.70, 123.82, 120.55, 116.87, 103.00, 77.16, 48.80, 42.37, 33.64, 29.20, 24.72, 24.64. HRMS (ESI) calcd for $C_{22}H_{21}NO_3$ $(M+H)^+$ 348.1594, found 348.1587.

(b) Esterification of *β*-cyanoalkylated indolo[2,1-*α*]isoquinoline (3aa)

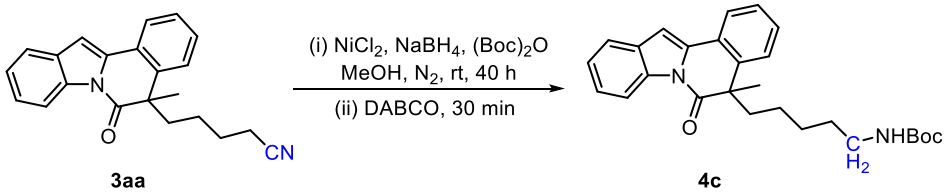


3aa **4b**

To a solution of **3aa** (0.2 mmol, 65.6 mg) in methanol (3.0 mL) at 0 °C was added concentrated sulphuric acid (1.0 mL), the reaction was heated to 70 °C in a sealed tube and stirred overnight under nitrogen atmosphere. The reaction was quenched with cold water and extracted with EtOAc. The combined organic phase were dried over Na_2SO_4, filtered and concentrated under vacuum. Purification by column chromatography on silica gel, get product **4b**.

Methyl 5-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanoate. Colorless oil. 54.2 mg, 75% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.59 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.85 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.60 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.40-7.31 (m, 5H), 7.02 (s, 1H), 3.54 (s, 3H), 2.41 (ddd, *J* = 13.5, 12.3, 4.6 Hz, 1H), 2.19-2.04 (m, 2H), 1.93 (td, *J* = 12.9, 4.3 Hz, 1H), 1.68 (s, 3H), 1.58-1.39 (m, 2H), 1.05-0.94 (m, 1H), 0.88 (qdd, *J* = 13.1, 6.0, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.95, 173.25, 138.40, 135.63, 135.28, 130.75, 129.12, 127.32, 126.27, 125.29, 124.88, 124.68, 123.80, 120.53, 116.86, 102.94, 77.16, 51.52, 48.80, 42.50, 33.72, 29.13, 24.98, 24.77. HRMS (ESI) calcd for $C_{23}H_{23}NO_3$ $(M+H)^+$ 362.1751, found 362.1755.

(c) Reduction of *β*-cyanoalkylated indolo[2,1-*α*]isoquinoline (3aa)



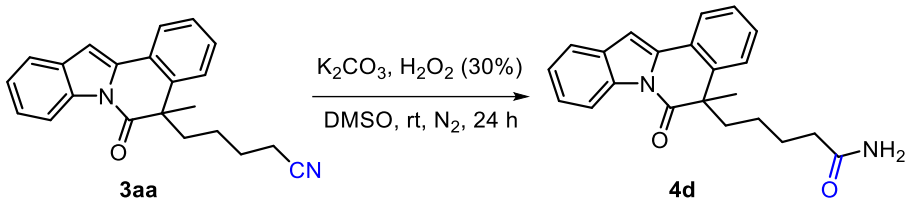
3aa **4c**

3aa (0.3 mmol, 98.4 mg), $NaBH_4$ (2.1 mmol, 79.4 mg) and $NiCl_2$ (0.12 mmol, 15.6 mg) were added into a Schlenk tube. The reaction vessel was capped and subjected to three vacuum-purge/nitrogen-flush cycles. Then MeOH (2.3 mL) and Boc_2O (0.6 mmol, 131.0 mg) were added through the side-arm by syringe at 0 °C. The mixture was stirred at rt for 40 h. After reaction, the mixture was added diethylenetriamine (0.3 mmol, 31.0 mg) and stirred at rt for 30 min. Water (10 mL) was added and it was extracted with EtOAc (10 mL × 3), washed with saturated brine (10 mL),

then dried over anhydrous Na_2SO4. After filtration, the filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash chromatography using petroleum ether/EtOAc (5 : 1) to afford the desired product **4c**.

Tert-butyl (5-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentyl)carbamate. Colorless oil. 53.1 mg, 41% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.59 (d, *J* = 8.1 Hz, 1H), 7.88-7.82 (m, 1H), 7.65-7.55 (m, 1H), 7.38 (t, *J* = 4.2 Hz, 3H), 7.37-7.30 (m, 2 H), 7.02 (s, 1H), 4.39 (s, 1H), 2.93 (d, *J* = 5.8 Hz, 2H), 2.38 (td, *J* = 12.8, 4.6 Hz, 1H), 1.91 (td, *J* = 12.8, 4.4 Hz, 1H), 1.68 (s, 3H), 1.40 (s, 9H), 1.31-1.22 (m, 2H), 1.22-1.06 (m, 2H), 0.96 (dtd, *J* = 16.2, 9.1, 8.0, 5.0 Hz, 1H), 0.86 (ddd, *J* = 18.7, 9.9, 5.4 Hz, 1 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.40, 155.99, 138.55, 135.69, 135.29, 130.77, 129. 11, 127.29, 126.30, 125.27, 124.87, 124.66, 123.78, 120.53, 116.88, 102.90, 79.11, 77.16, 48.85, 42.99, 40.55, 29.81, 29.09, 28.51 (3), 26.96, 25.00. HRMS (ESI) calcd for $C_{27}H_{32}N_2O_3$ $(M+H)^+$ 433.2486, found 433.2471.

(d) Amidation of *β*-cyanoalkylated indolo[2,1-*α*]isoquinoline (3aa)



3aa (0.3 mmol, 98.4 mg) and K_2CO_3 (0.3 mmol, 41.5 mg) were weighed into a Schlenk tube, then 30% H_2O_2 (0.3 mL) and DMSO (1.2 mL) was added through the side-arm by syringe. The mixture was stirred at rt for 24 h. After reaction, water (10 mL) was added, and the reaction mixture was extracted with EtOAc (5 mL×3), washed with saturated brine (10 mL), then dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash chromatography using EtOAc/CH_2Cl_2 (5 : 1) to afford the desired product **4d**.

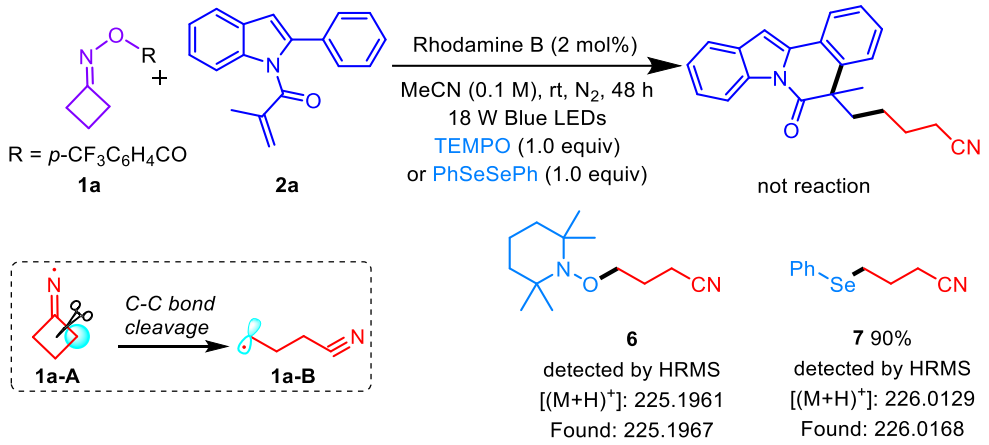
5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanamide. Colorless oil. 98.6 mg, 95% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.84 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.59 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.42-7.28 (m, 5H), 7.01 (s, 1H), 5.46 (d, *J* = 42.6 Hz, 2H), 2.41 (ddd, *J* = 13.4, 11.4, 5.2 Hz, 1H), 2.07-1.98 (m, 2H), 1.98-1.89 (m, 1H), 1.67 (s, 3H), 1.48 (p, *J* = 7.6 Hz, 2H), 0.94 (tddd, *J* = 17.6, 13.1, 9.4, 4.1 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.37, 173.41, 138.30, 135.64, 135.25, 130.77, 129.19, 127.36, 126.28, 125.29, 124.79, 124.73, 123.81, 120.59, 116.78, 102.98, 77.16, 48.84, 42.22, 35.39, 29.29, 25.42, 24.80. HRMS (ESI) calcd for $C_{22}H_{22}N_2O_2$ $(M+H)^+$ 347.1754, found 347.1740.

6. Preliminary Mechanistic Studies

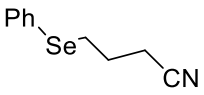
(a) Radical-Trapping Experiment

To a Schlenk tube equipped with a magnetic stir bar was charged with Cyclobutanone Oximes **1a** (0.3 mmol), *N*-methylpropenyl-2-phenylindole **2a** (0.2 mmol) and Rhodamine B (2 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 2.0 mL acetonitrile (MeCN) was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under 18 W blue LEDs. It was observed that the transformation was completely inhibited by TEMPO or PhSeSePh, along with the interception of the cyanoalkyl radical species as

detected by high-resolution mass spectrometry (HRMS) (Figure S2).



4-(Phenylselanyl)butanenitrile (7)



Colorless oil. 40.5 mg, 90% yield. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.51 (qd, *J* = 3.9, 1.7 Hz, 2H), 7.29 (dt, *J* = 9.5, 2.8 Hz, 3H), 2.99 (t, *J* = 7.0 Hz, 2H), 2.50 (td, *J* = 7.0, 2.9 Hz, 2H), 1.99 (p, *J* = 7.1 Hz, 2H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 133.36, 129.43, 127.64, 119.17, 77.16, 26.16, 25.79, 17.13. HRMS (ESI) calcd for $C_{27}H_{32}N_2O_3$ $(M+H)^+$ 226.0129, found 226.0168.

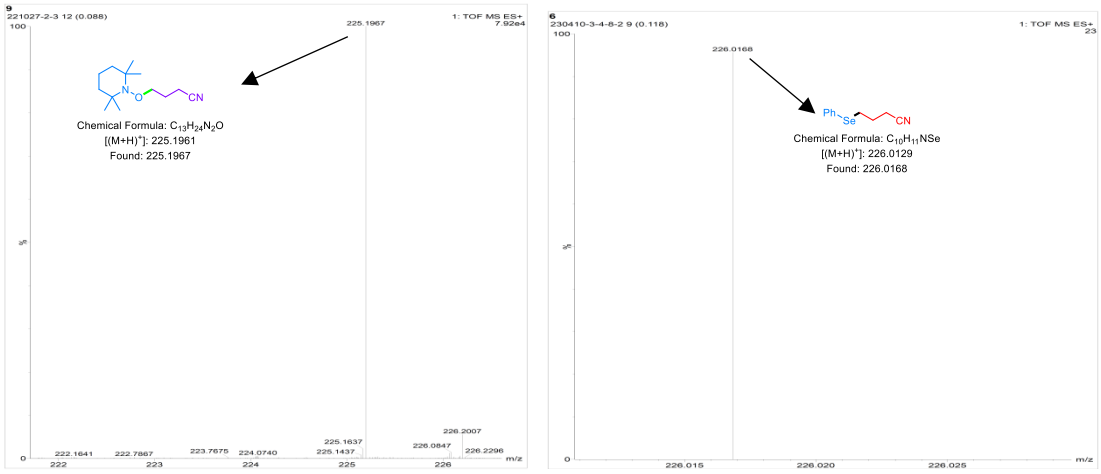


Figure S2 TEMPO or $(PhSe)_2$ trapping cyanoalkyl Free Radicals (HRMS)

(b) Cyclic Voltammetry Experiment

Cyclic voltammetry (CV) was taken using a CHI6043E potentiostation. CV measurement of **1a** was carried out in 0.1 M of ^{n}Bu$_4$NBF$_4$/MeCN at a scan rate of 100 mV/s with the protection of N_2. The working electrode is a glassy carbon, the counter electrode is a Pt wire, and the reference electrode is Ag/AgCl. Hence, E_{1a} = -1.205 versus SCE. E_{2a} = -1.456 versus SCE. E_{ox} (Rhodamine B$^+$/ Rhodamine B*) = -1.31 versus SCE. E_{red} (Rhodamine B*/Rhodamine B$^-$) = +1.26 versus SCE. These results suggested that **1a** was suitable for SET reduction in the excited state of the Rhodamine B* and **2a** was completely unsuitable for SET reduction in the excited state of the Rhodamine B*.

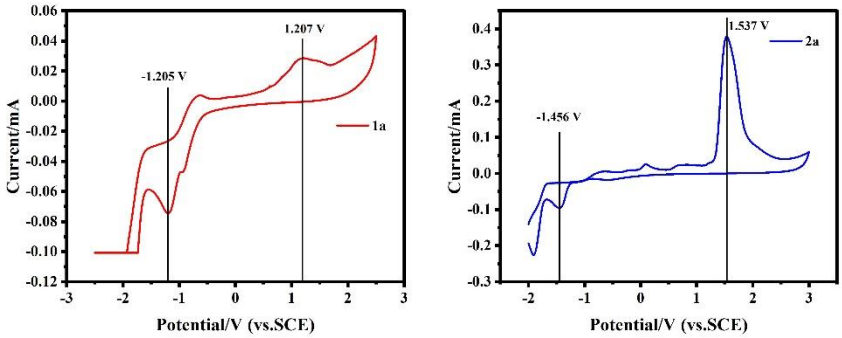


Figure S3 Cyclic Voltammograms of Reaction Substrates

(b) Stern-Volmer Fluorescence Quenching Experiments[6]

The fluorescence quenching experiment was taken using a Hitachi f-7000 fluorescence spectrophotometer (Japan). To a solution of Rhodamine B in anhydrous, N_2-saturated DMF (5×10^{-4} mol/L) in a quartz cuvette, different amounts of cyclobutanone oxime ester (**1a**) and *N*-methylpropenyl-2-phenylindole (**2a**) were added, respectively, and the resulting changes in fluorescence intensity (concentration of **1a** and **2a**: 0.025 mol/L, 0.050 mol/L, 0.100 mol/L, 0.150 mol/L, 0.200 mol/L were collected. The results are shown in Figure S4.

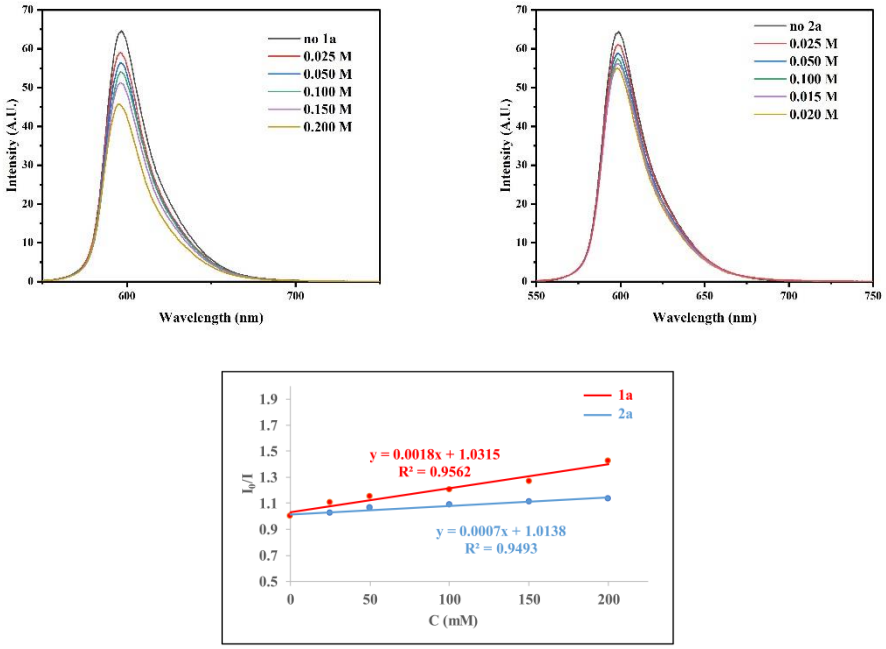


Figure S4 The fluorescence emission spectra of Rhodamine B with different concentration of **1a** or **2a** added. I_0 is the inherent fluorescence intensity of Rhodamine B. I is the fluorescence intensity of Rhodamine B in the presence of **1a** or **2a**.

To a solution of Rhodamine B in anhydrous, N_2-saturated DMF (5 × 10-4 mol/L) in a quartz cuvette, different additives were added, respectively, and the resulting changes in fluorescence intensity (concentration of additive: 0.1 mol/L were collected. The results are shown in Figure S5.

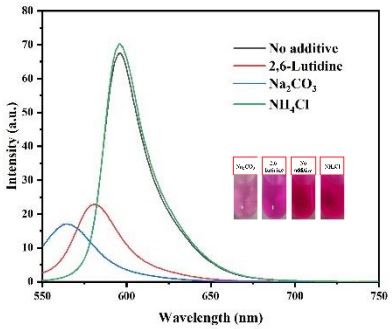


Figure S5 The fluorescence emission spectra of Rhodamine B with different concentration of additives added

7. References

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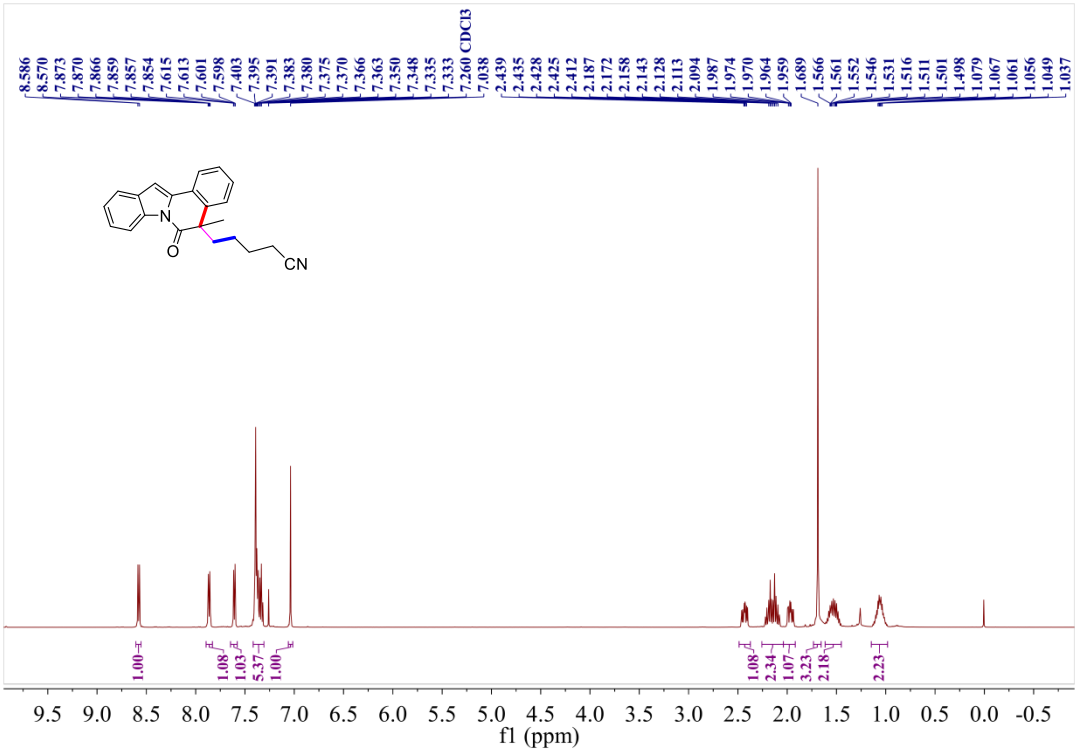
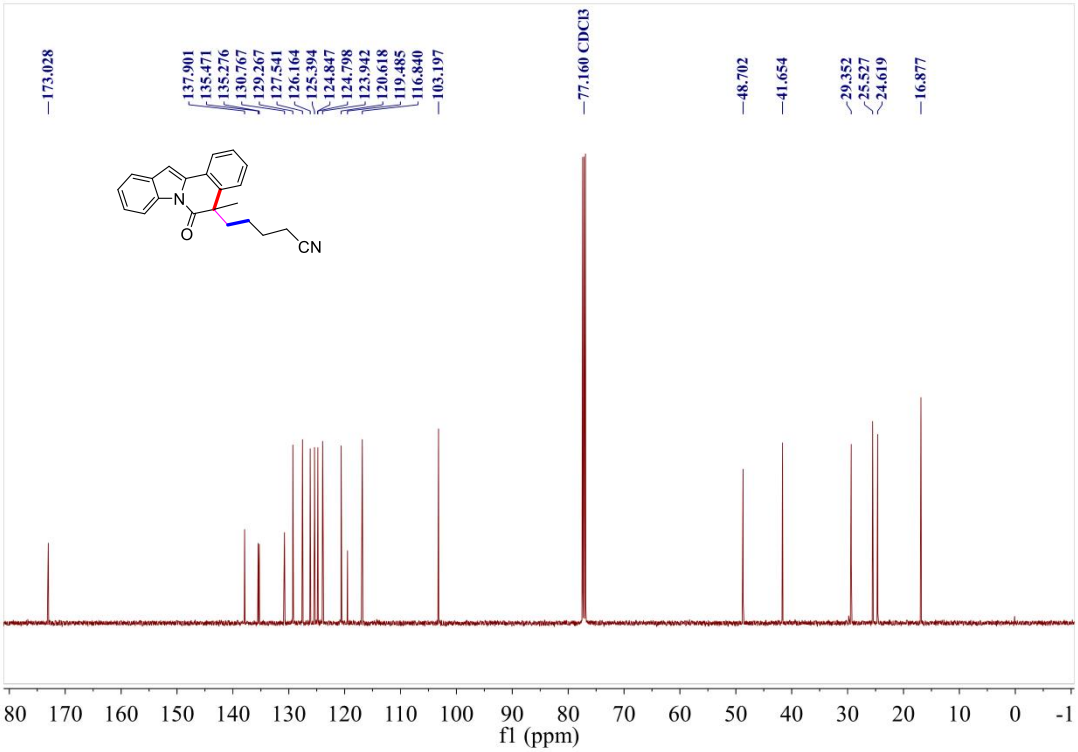
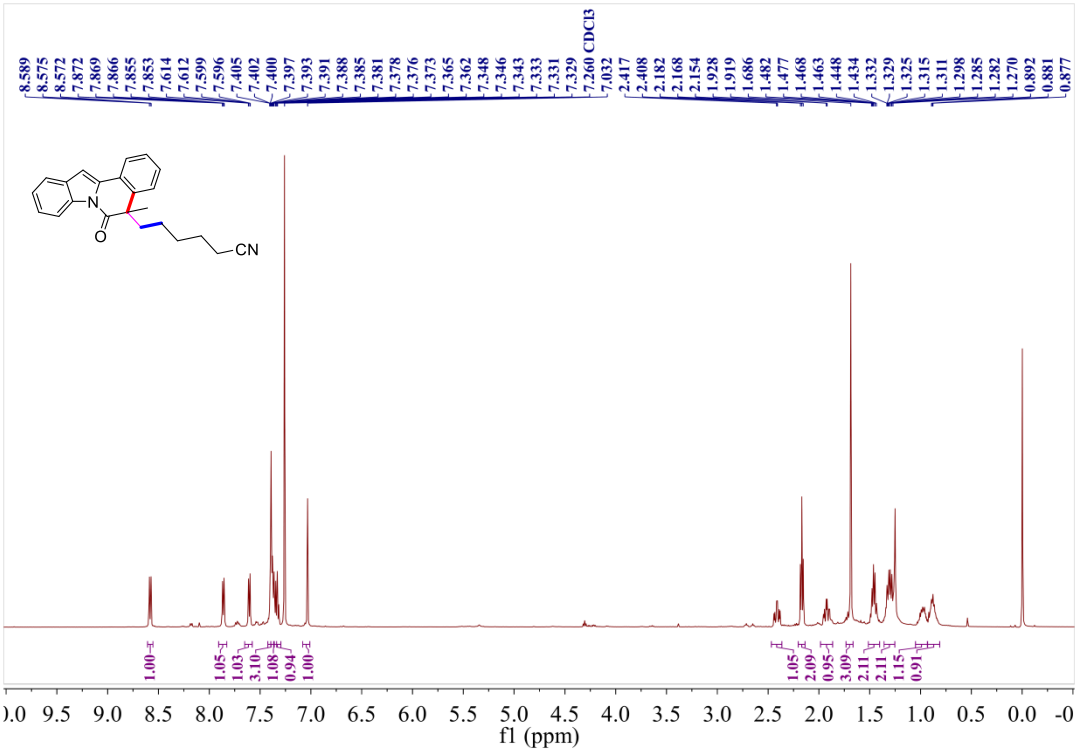
8. NMR Spectra of Products

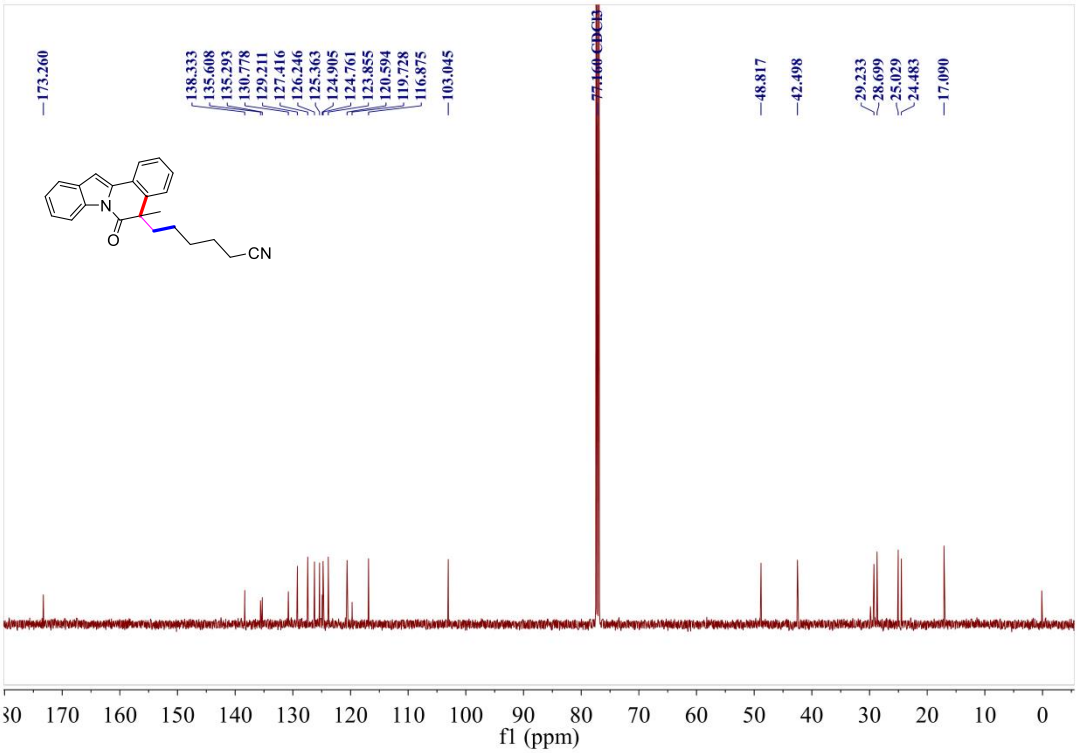
5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3aa)



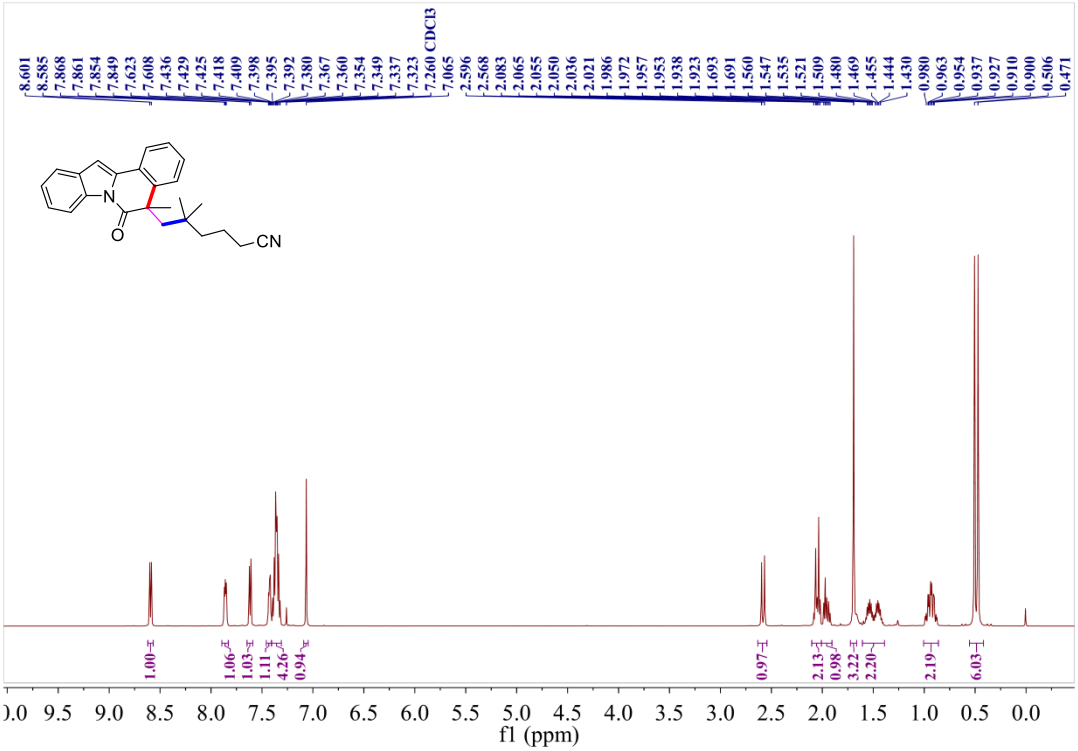


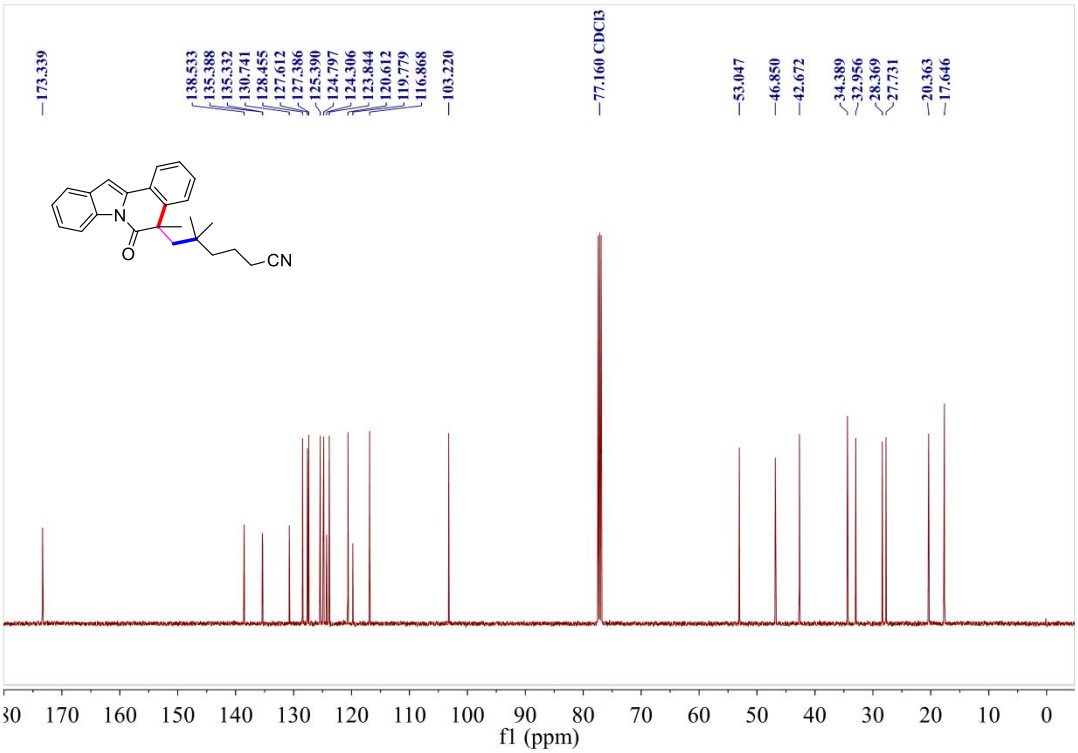
6-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)hexanenitrile (4aa)



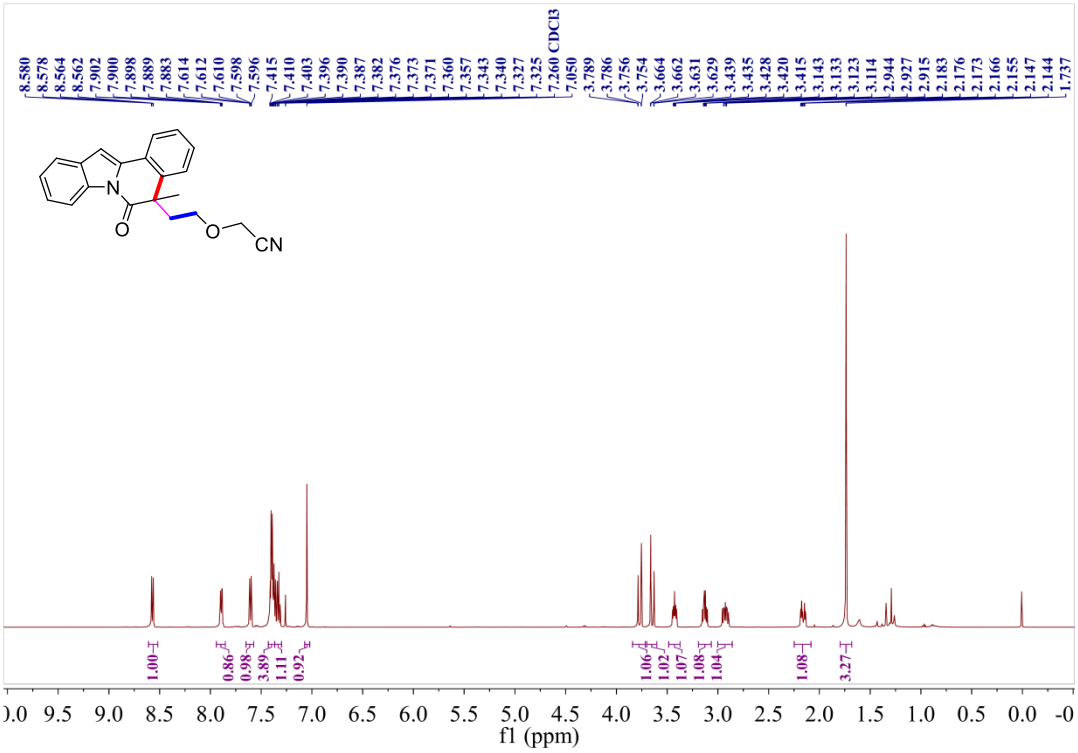


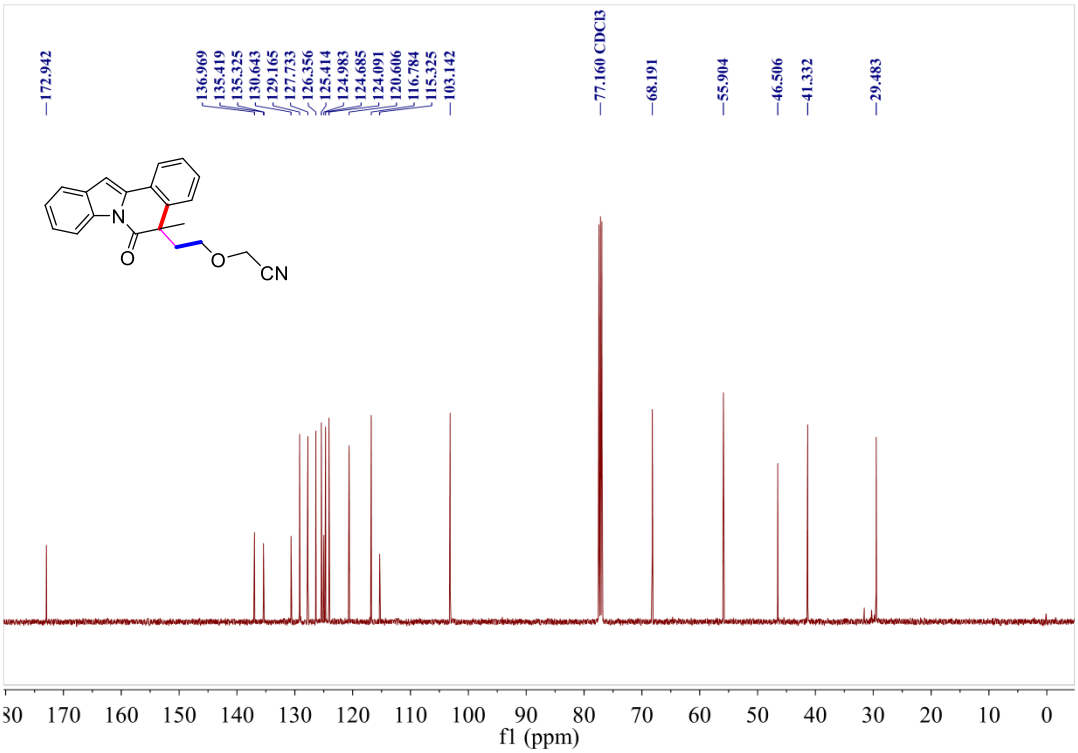
5,5-Dimethyl-6-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)hexanenitrile (3ba)



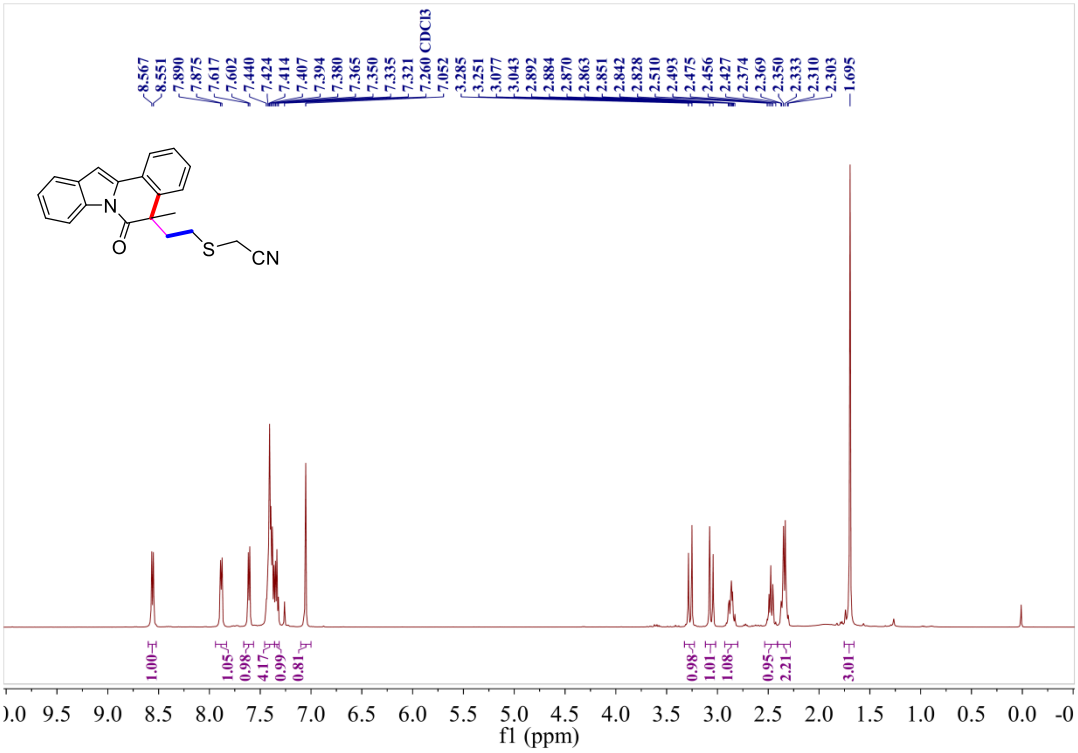


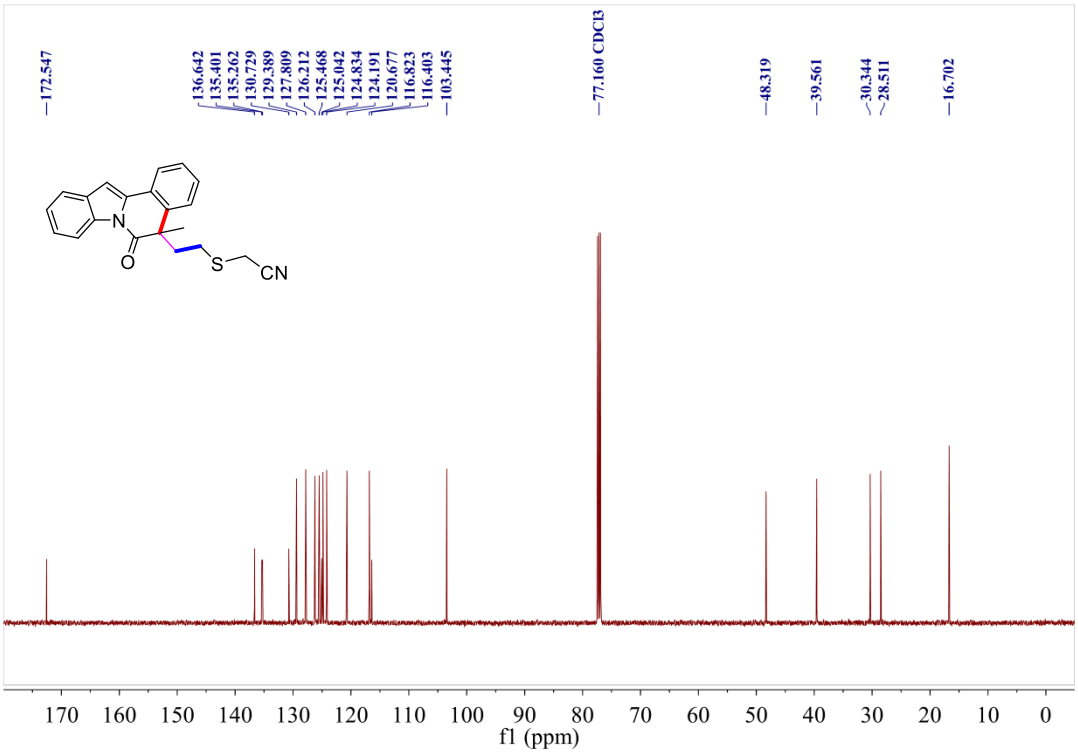
2-(2-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethoxy)acetonitrile (3ca)



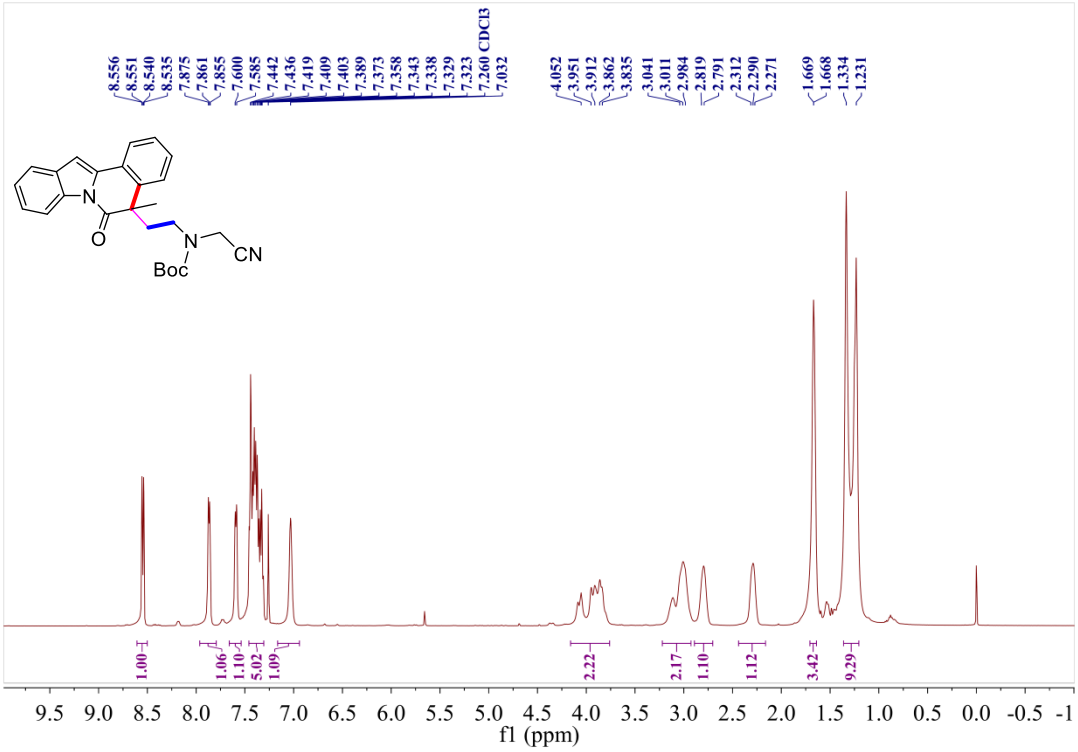


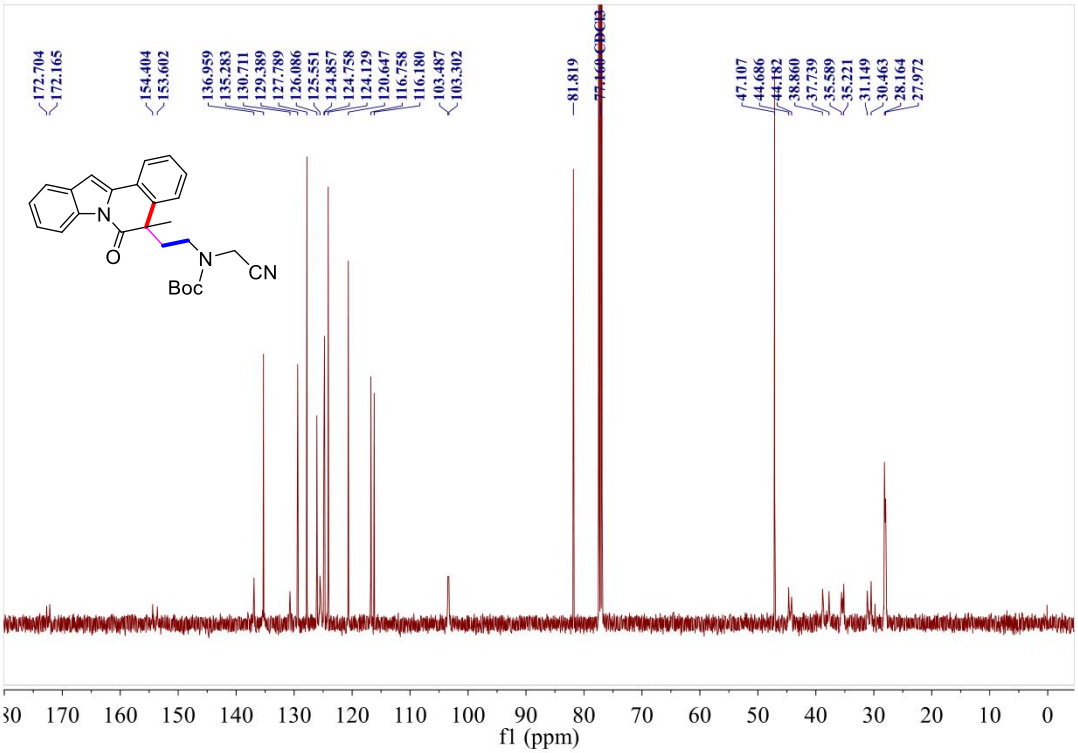
2-((2-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl)thio)acetonitrile (3da)



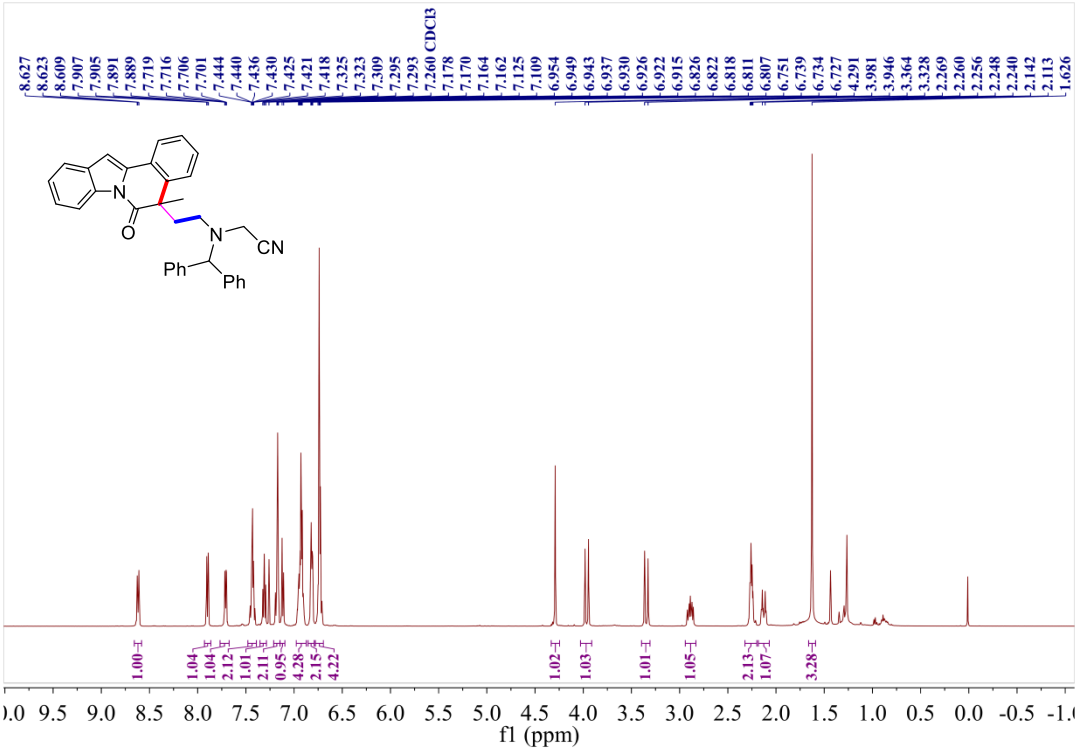


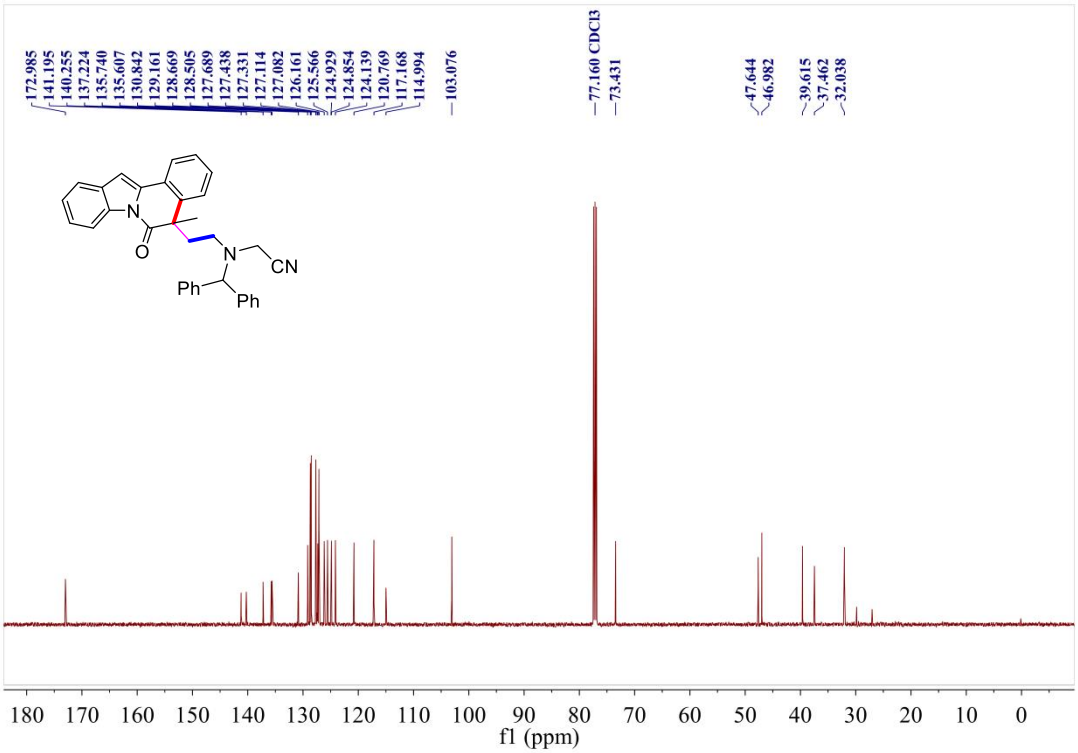
Tert-butyl (cyanomethyl)(2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl) carbamate (3ea)



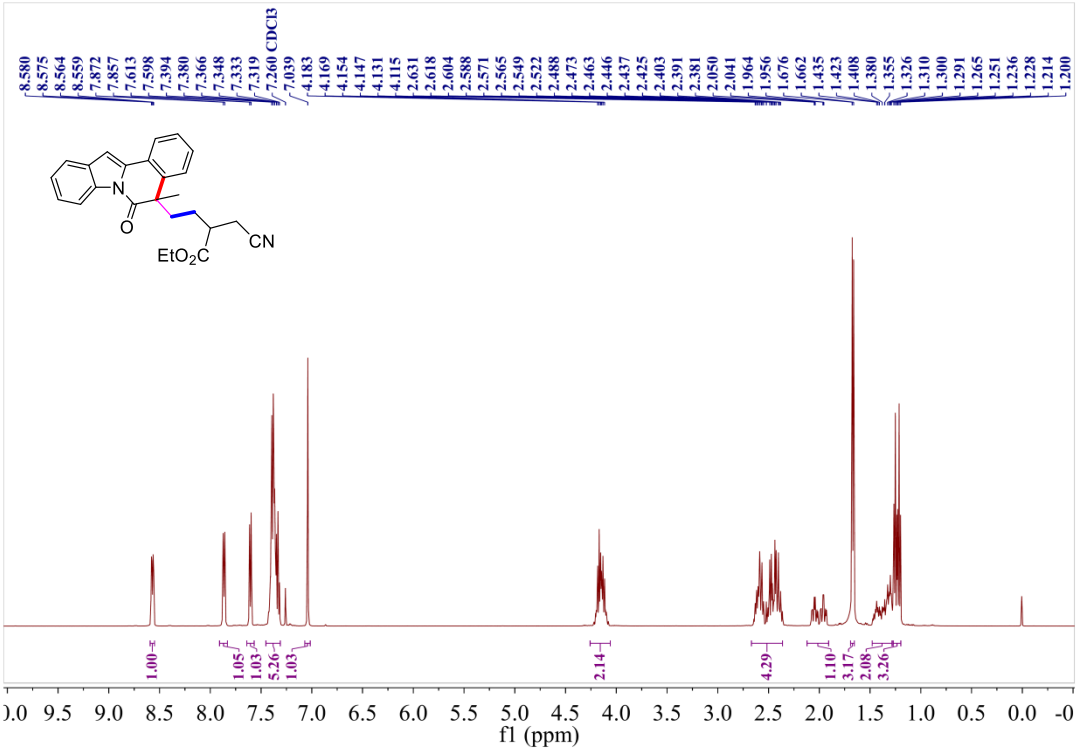


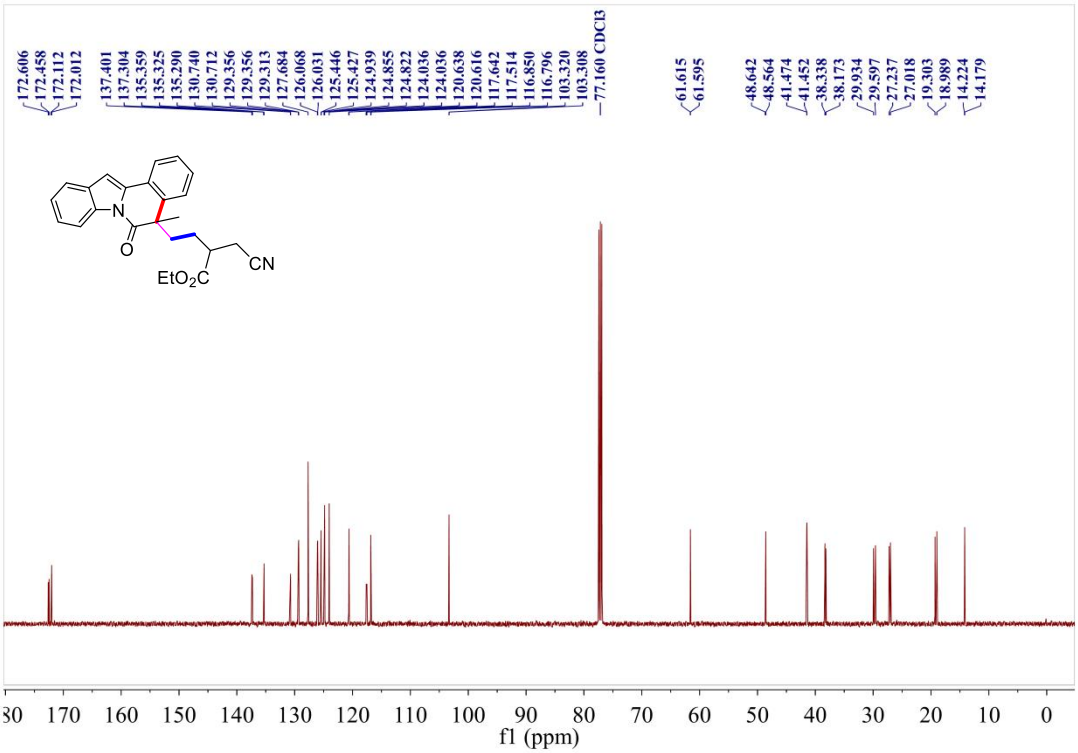
2-(Benzhydryl(2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)ethyl)amino)aceto-nitrile (3fa)



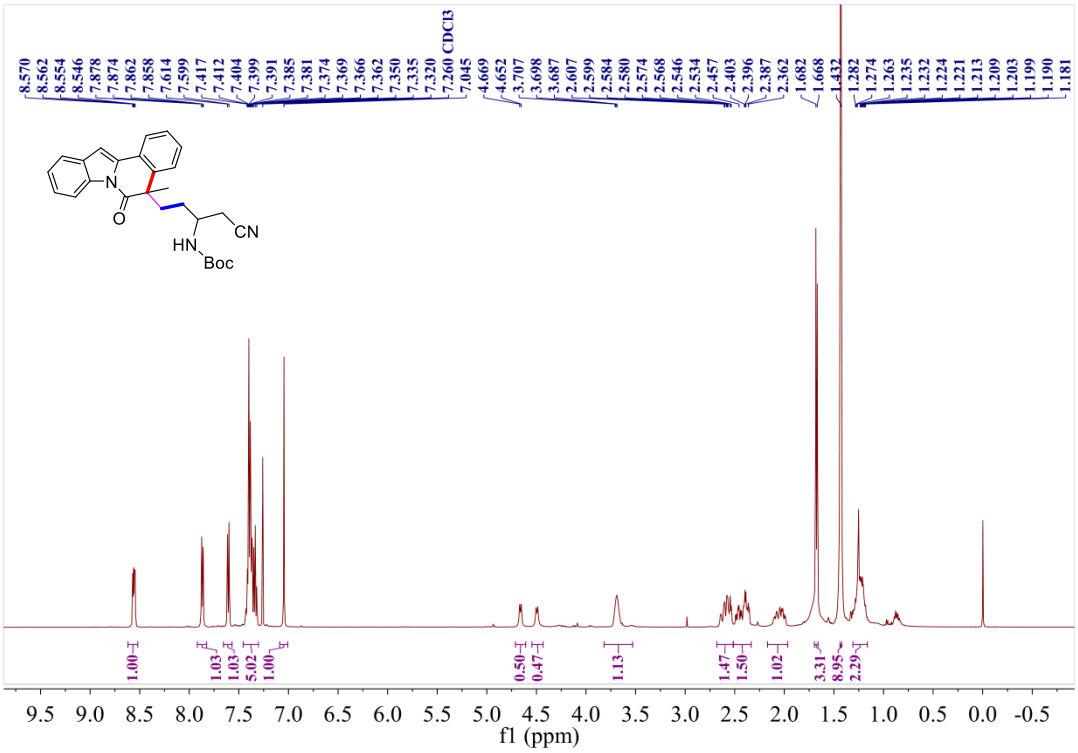


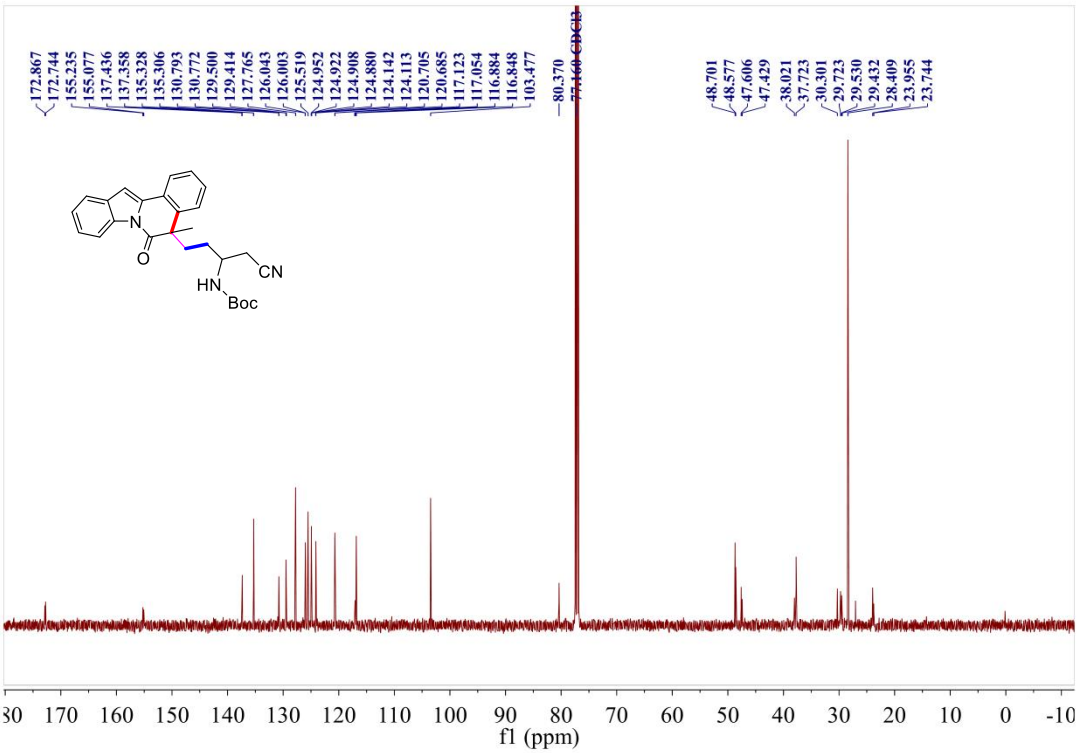
Ethyl 2-(cyanomethyl)-4-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)butanoate (3ga)



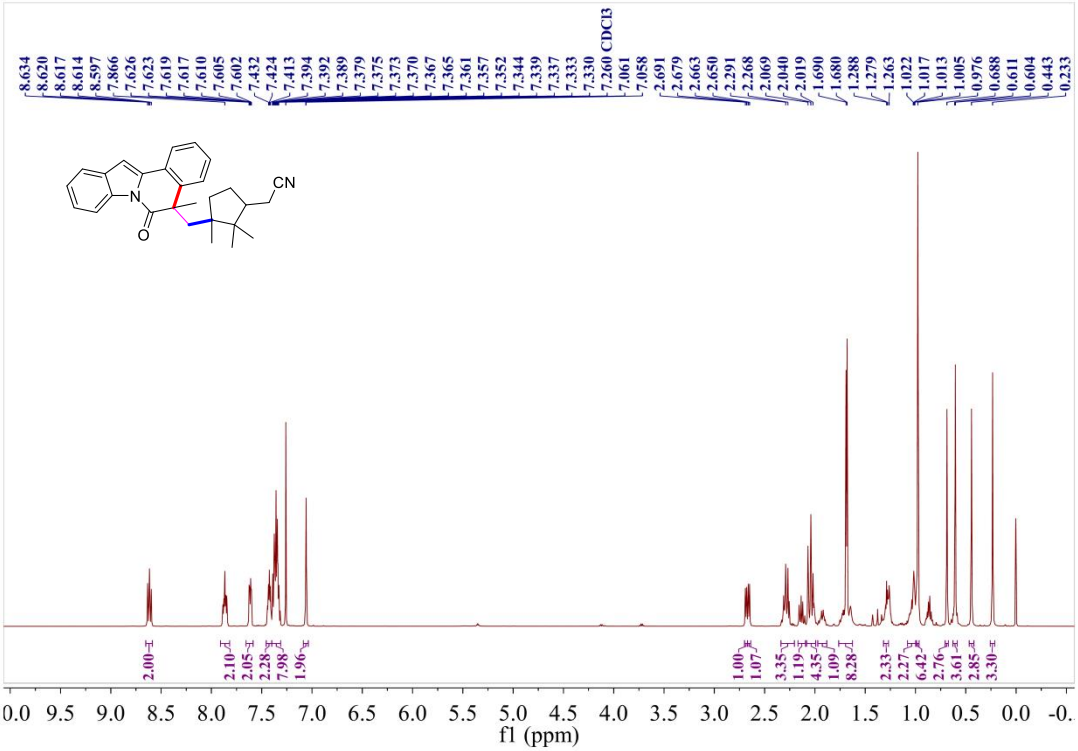


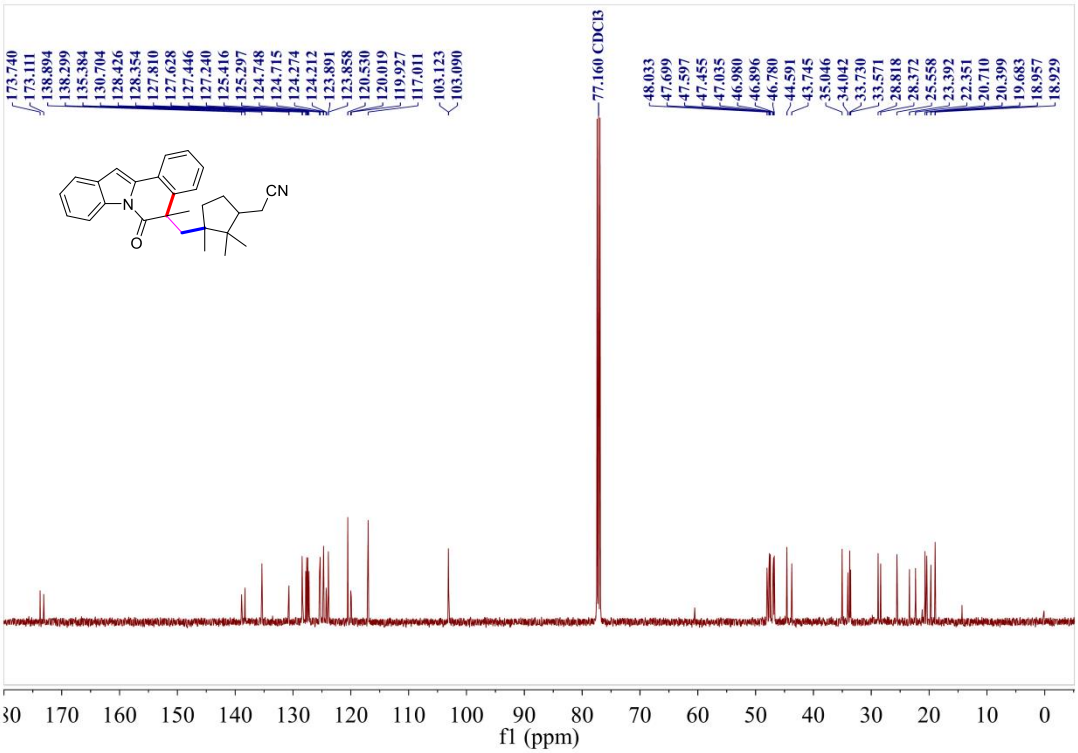
Tert-butyl (1-cyano-4-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)butan-2-yl) carbamate (3ha)



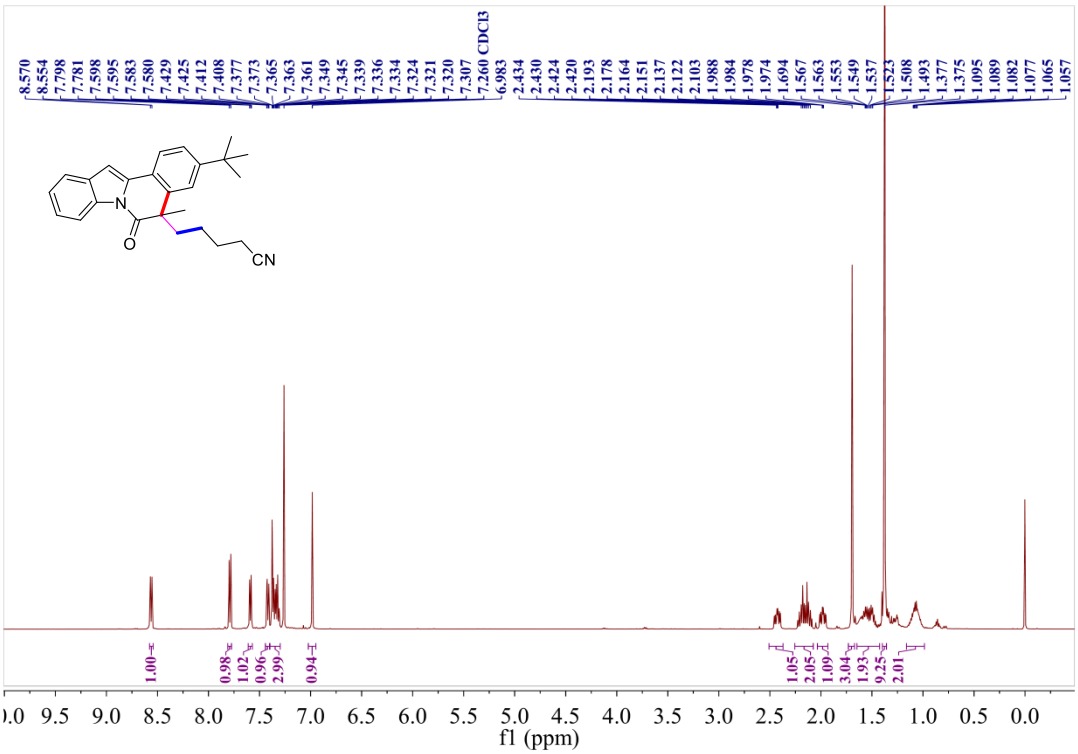


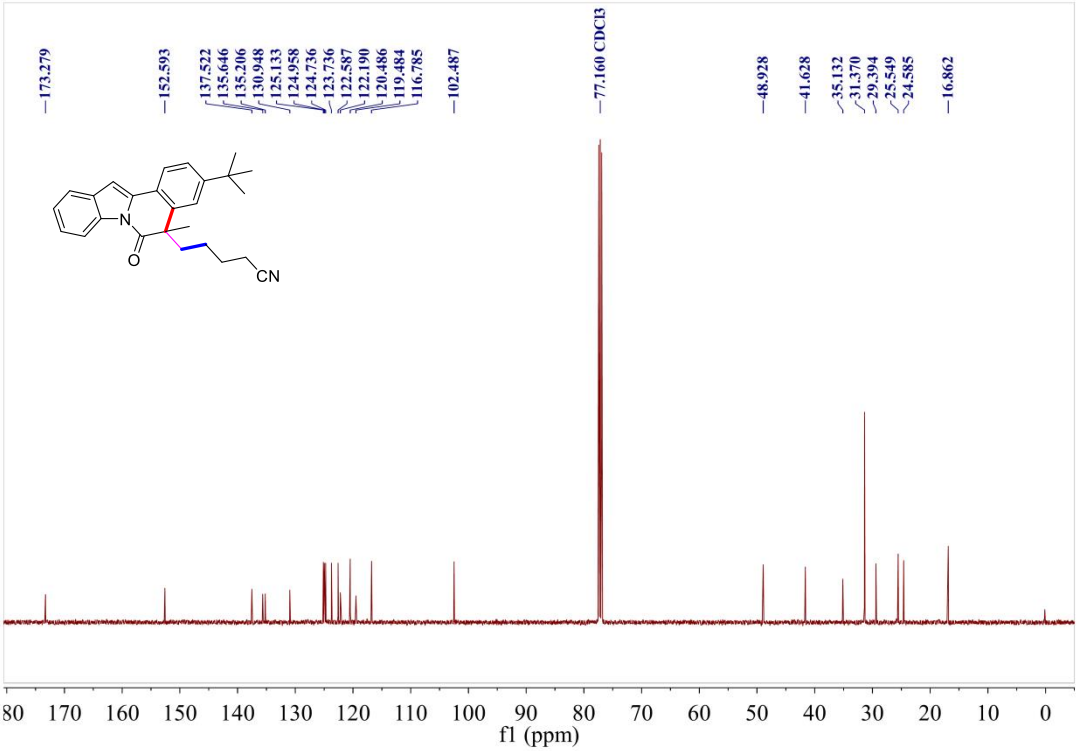
2-(2,2,3-Trimethyl-3-((5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)methyl)cyclop-entyl)acetonitrile (3ia)



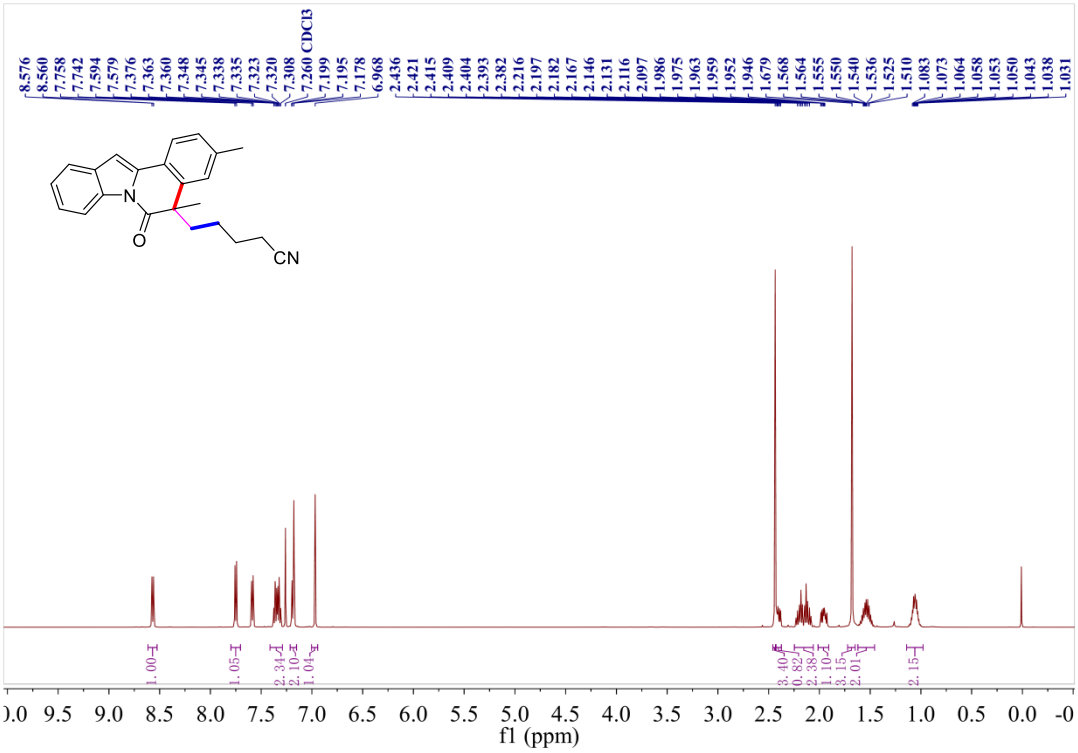


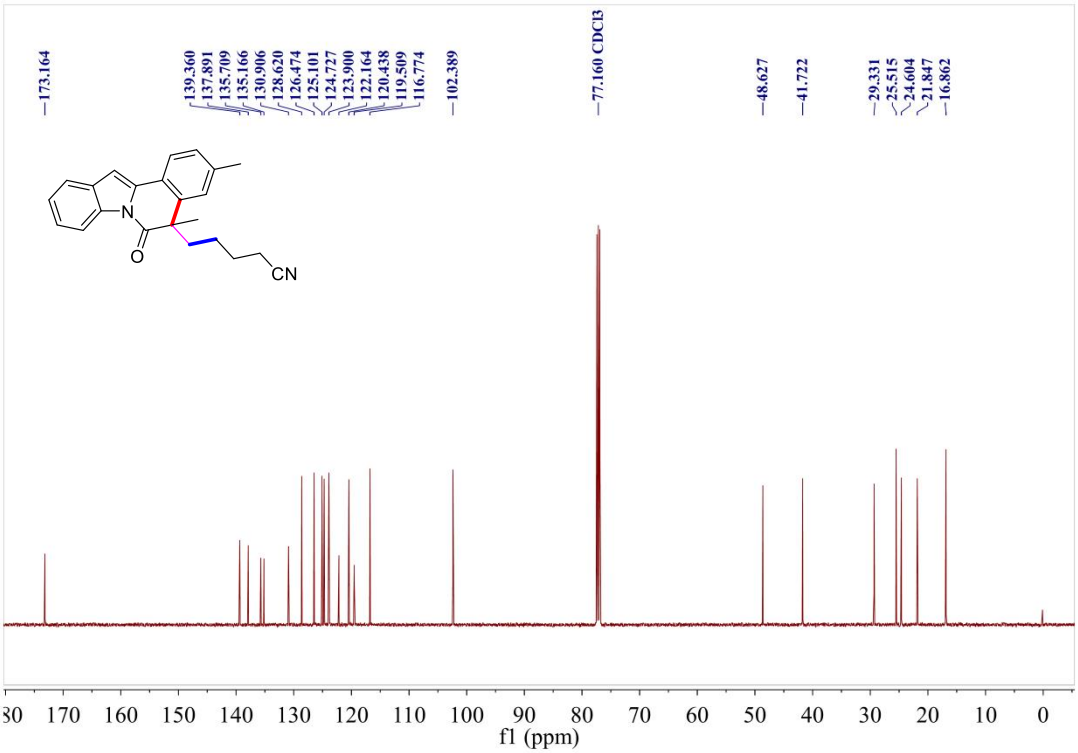
5-(3-(Tert-butyl)-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ab)



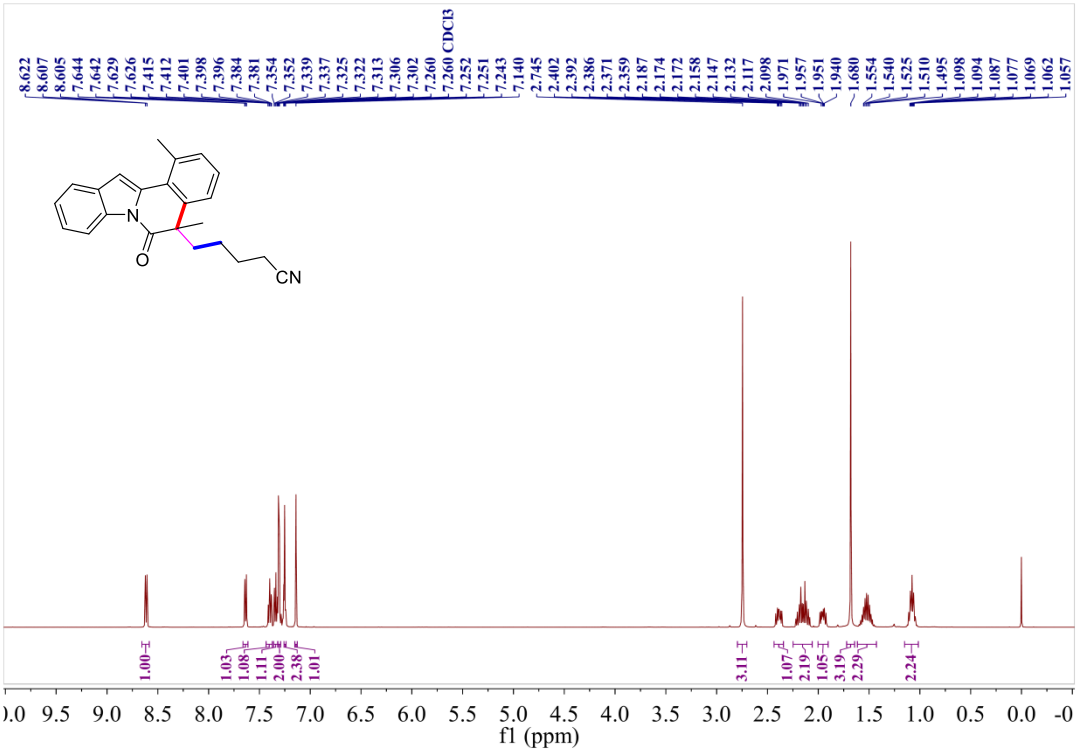


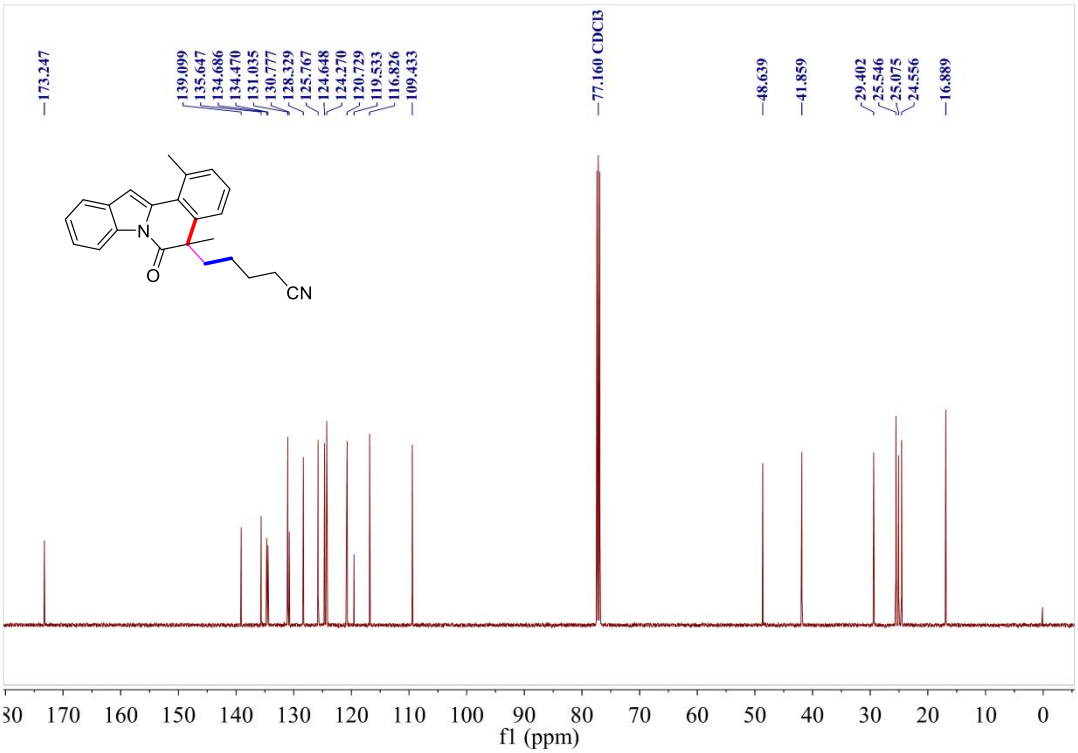
5-(3,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ac)



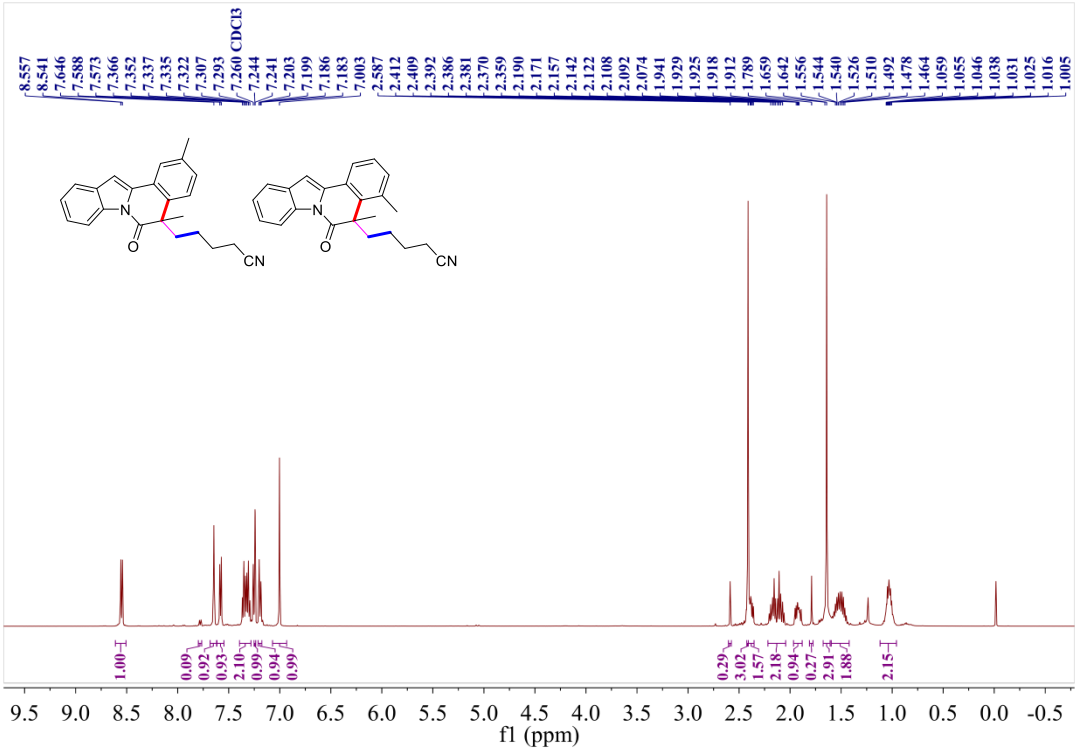


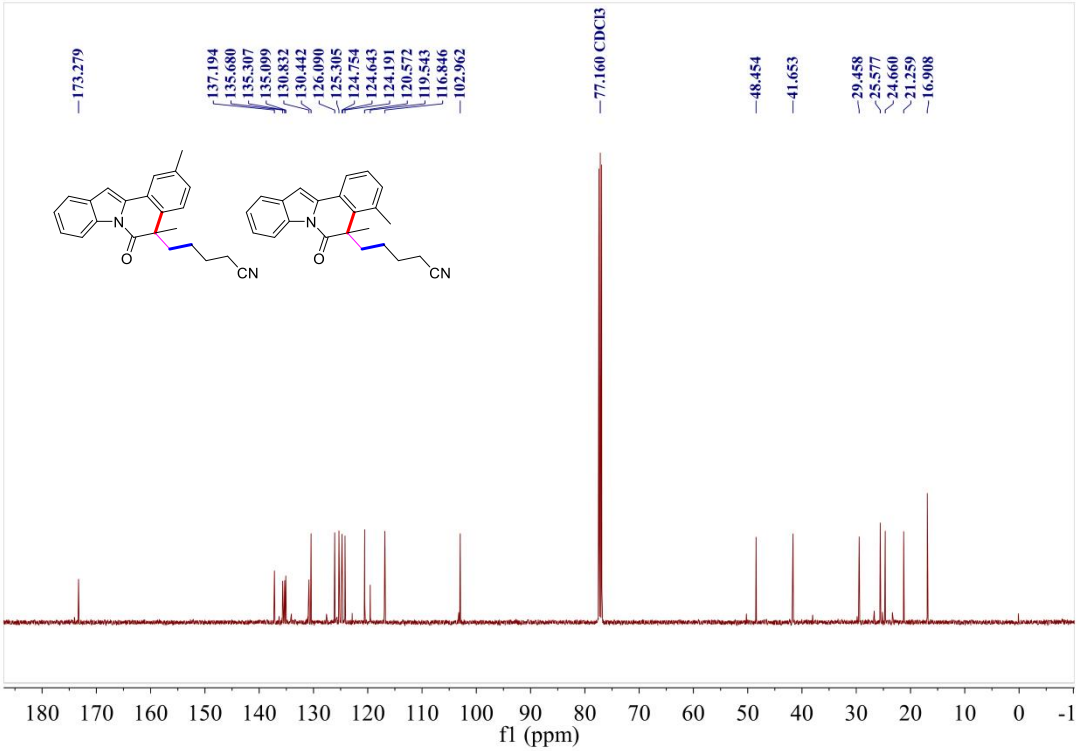
5-(1,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ad)



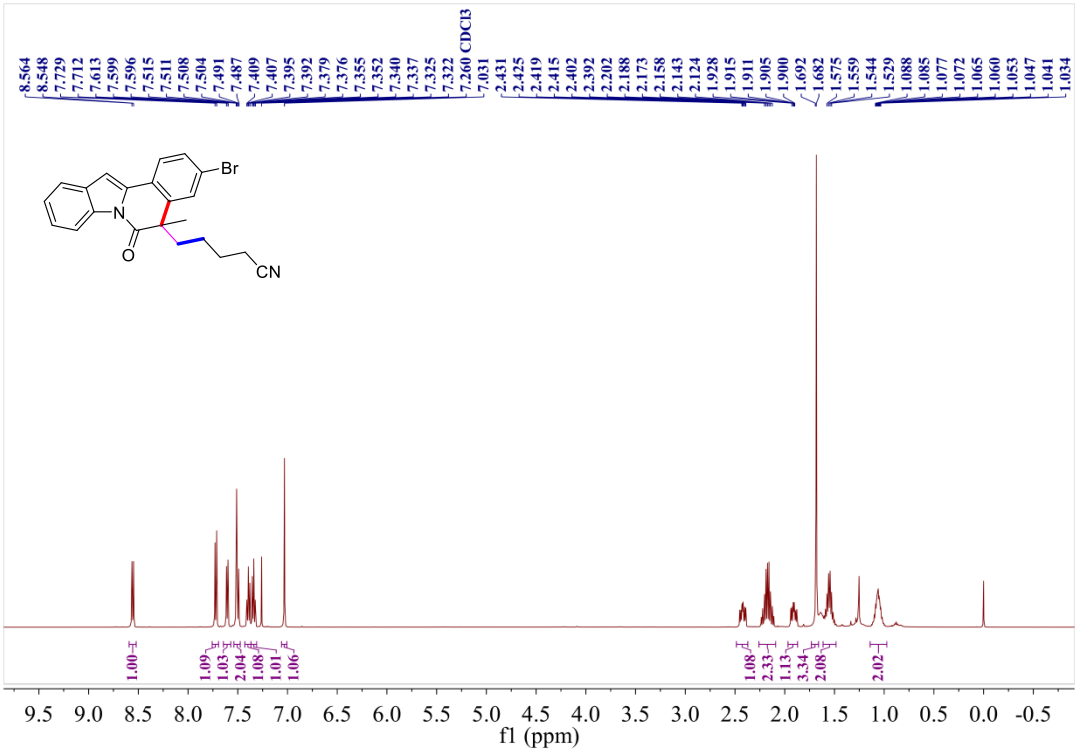


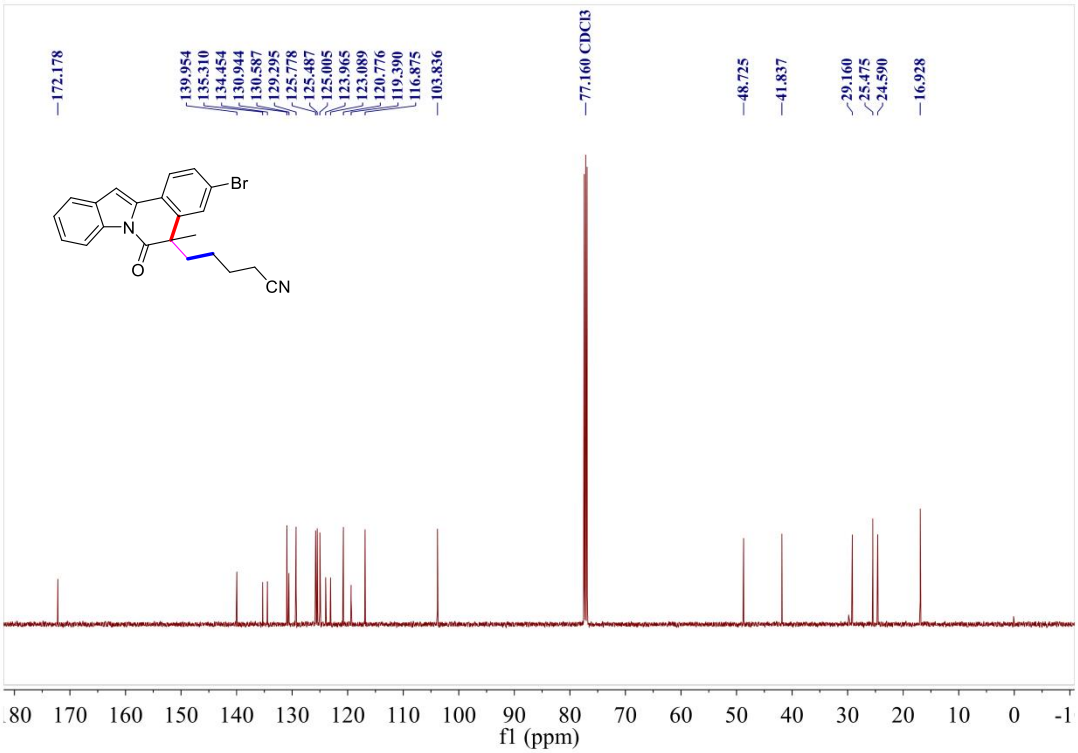
5-(2,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ae)
5-(4,5-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ae')



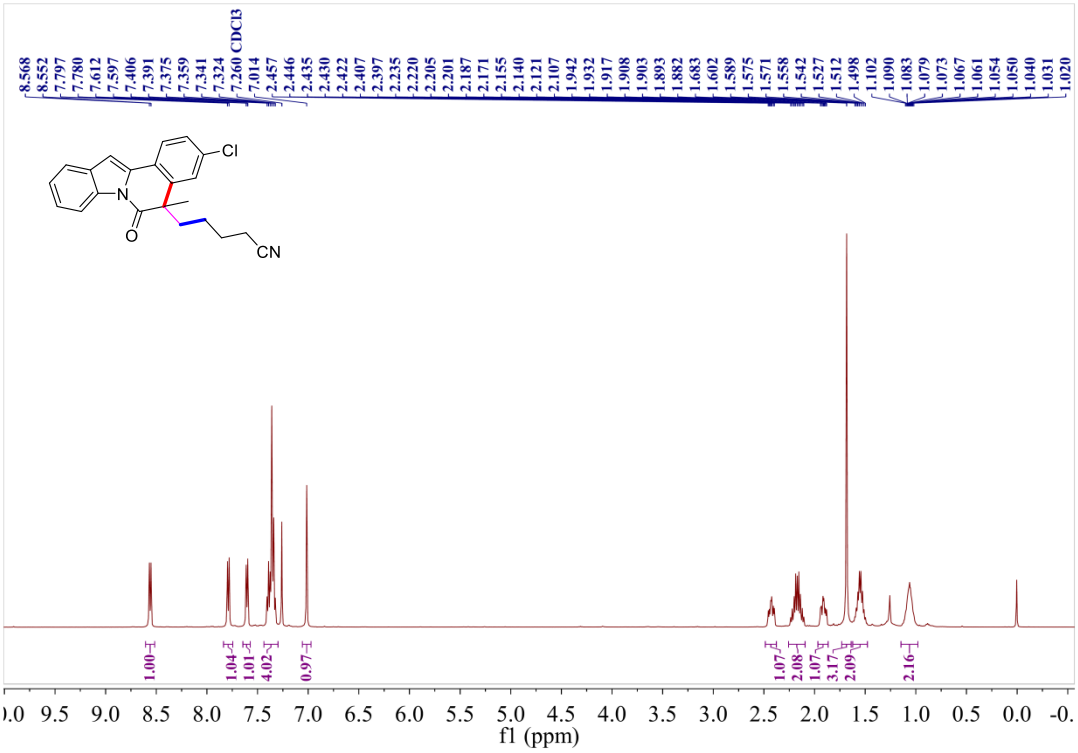


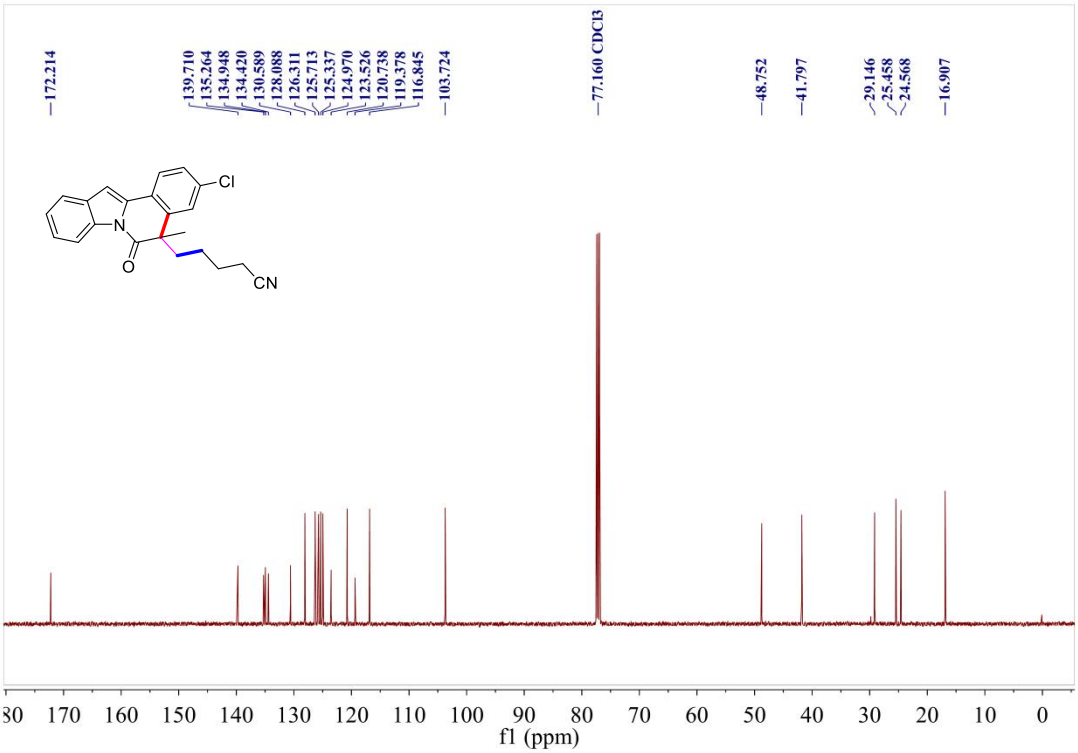
5-(3-Bromo-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3af)



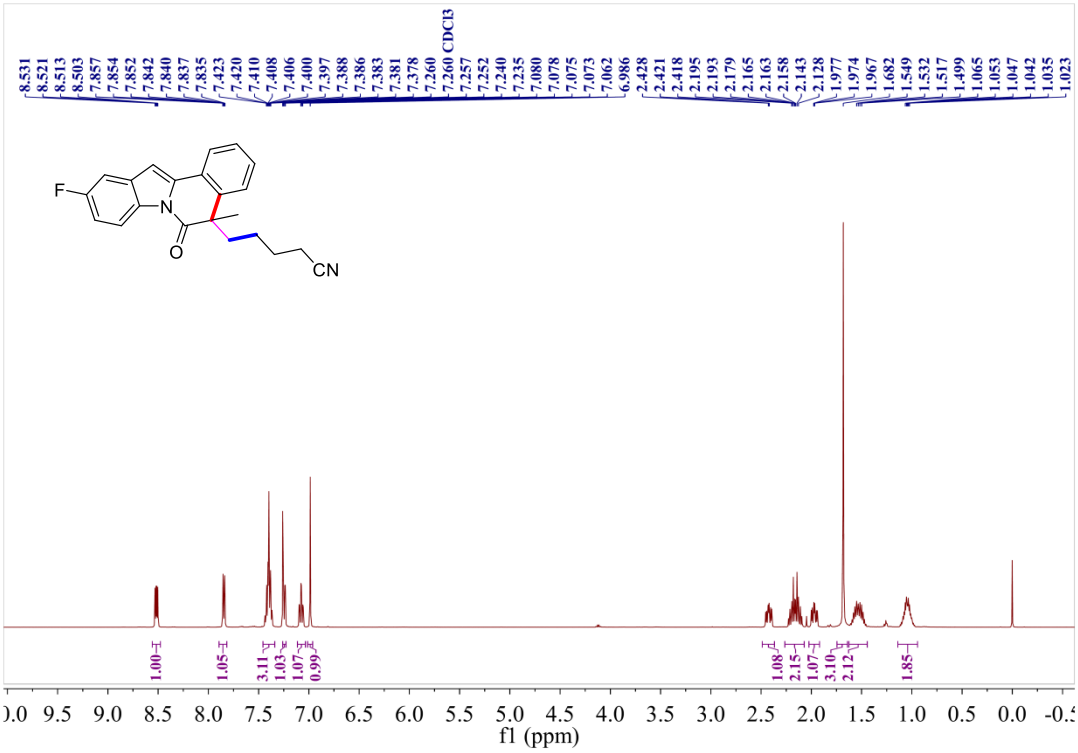


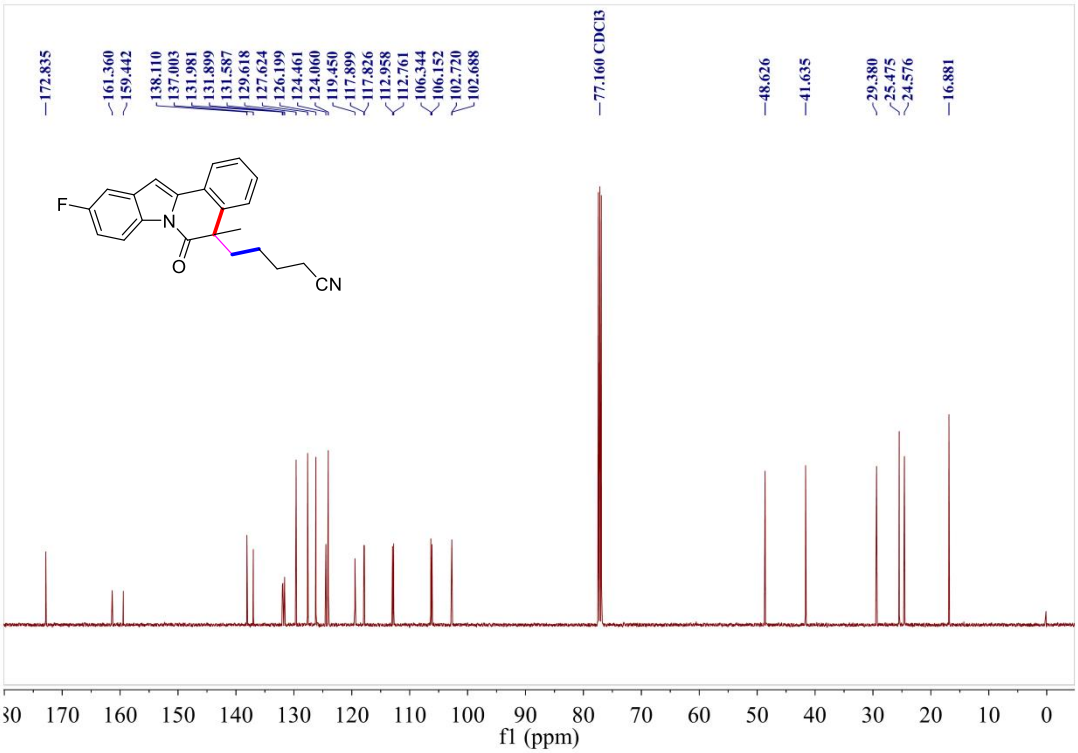
5-(3-Chloro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ag)



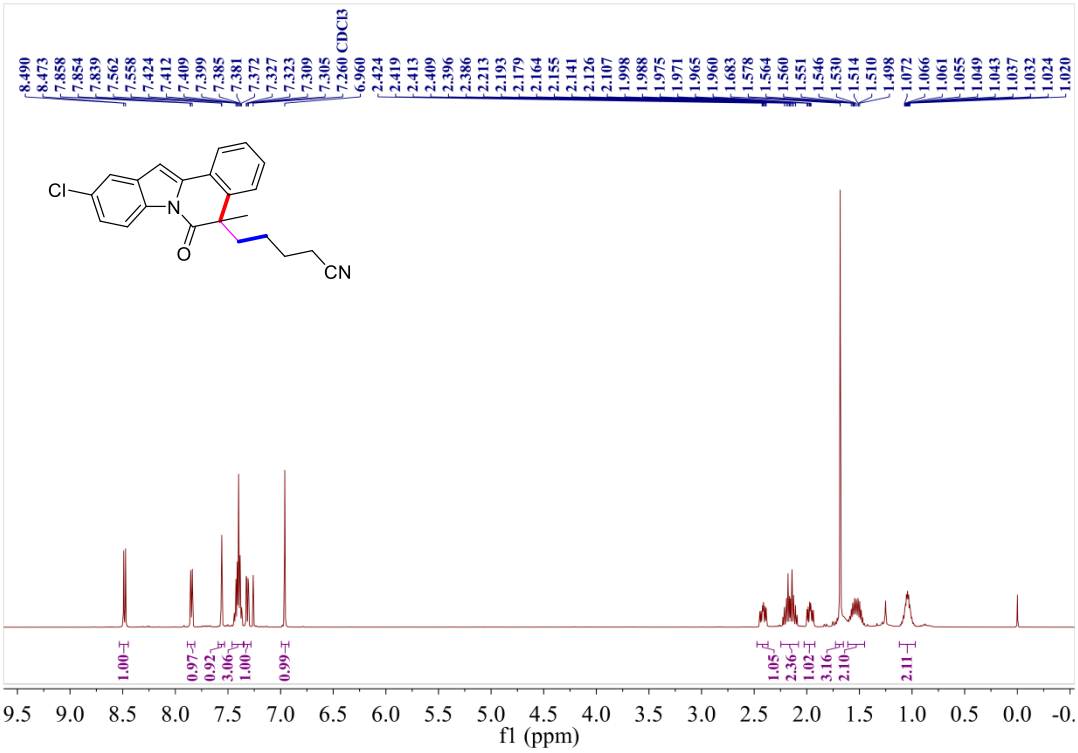


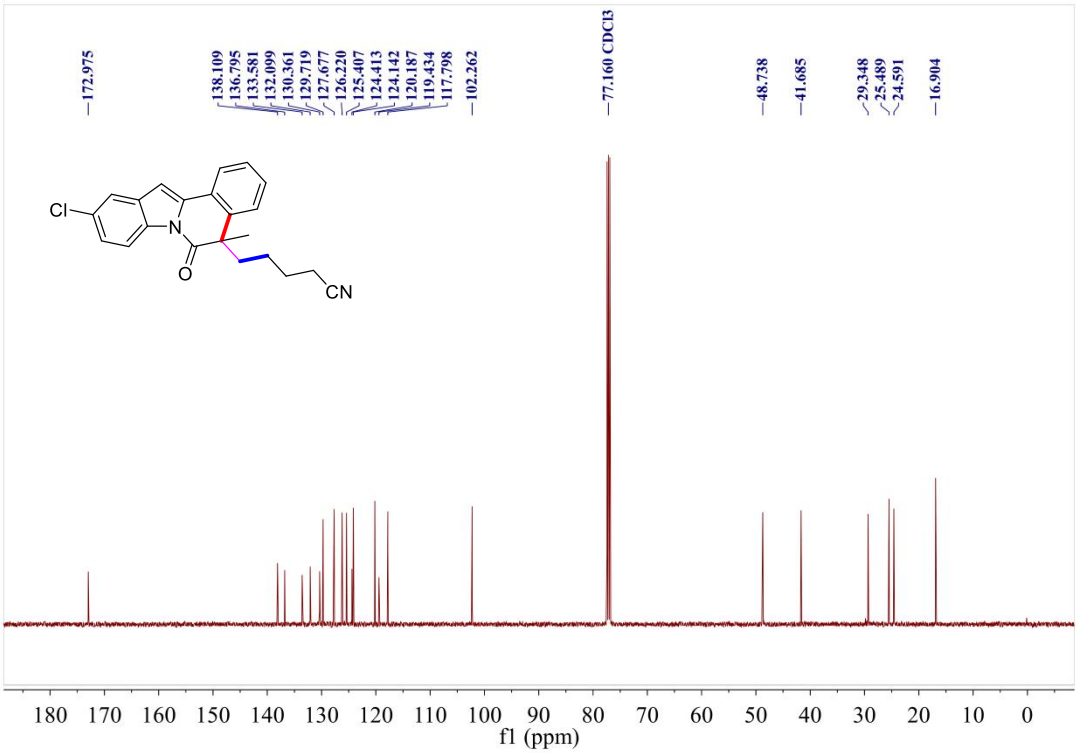
5-(10-Fluoro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ah)



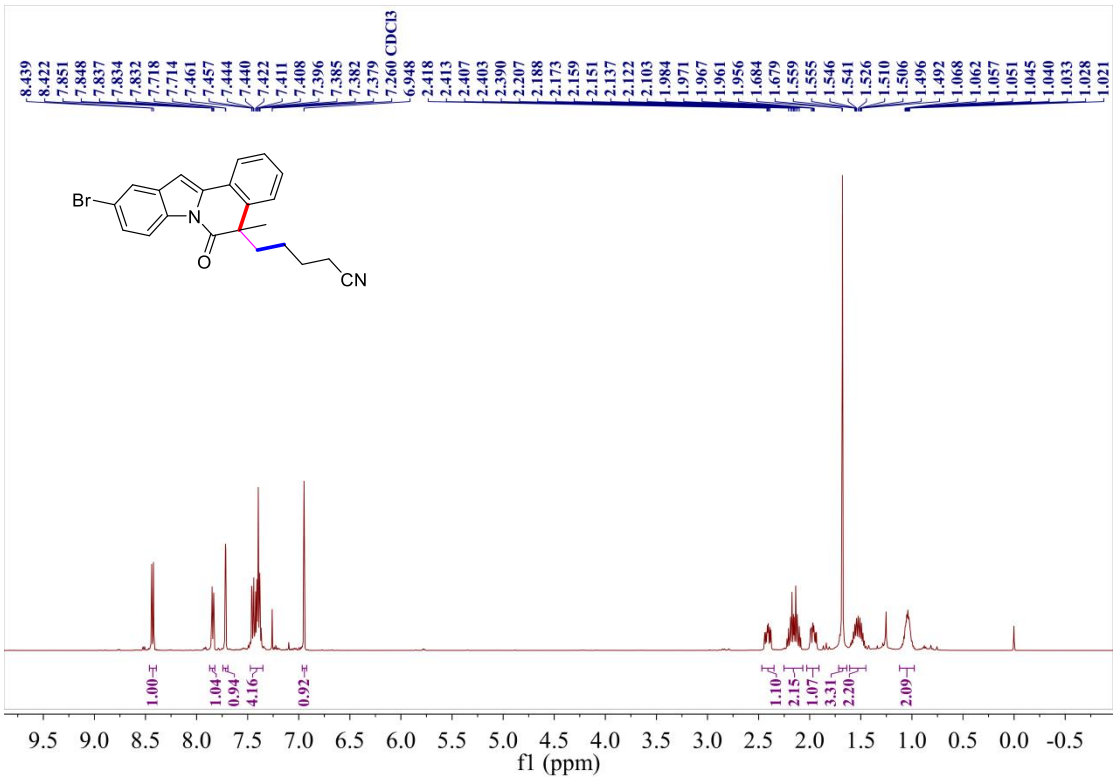


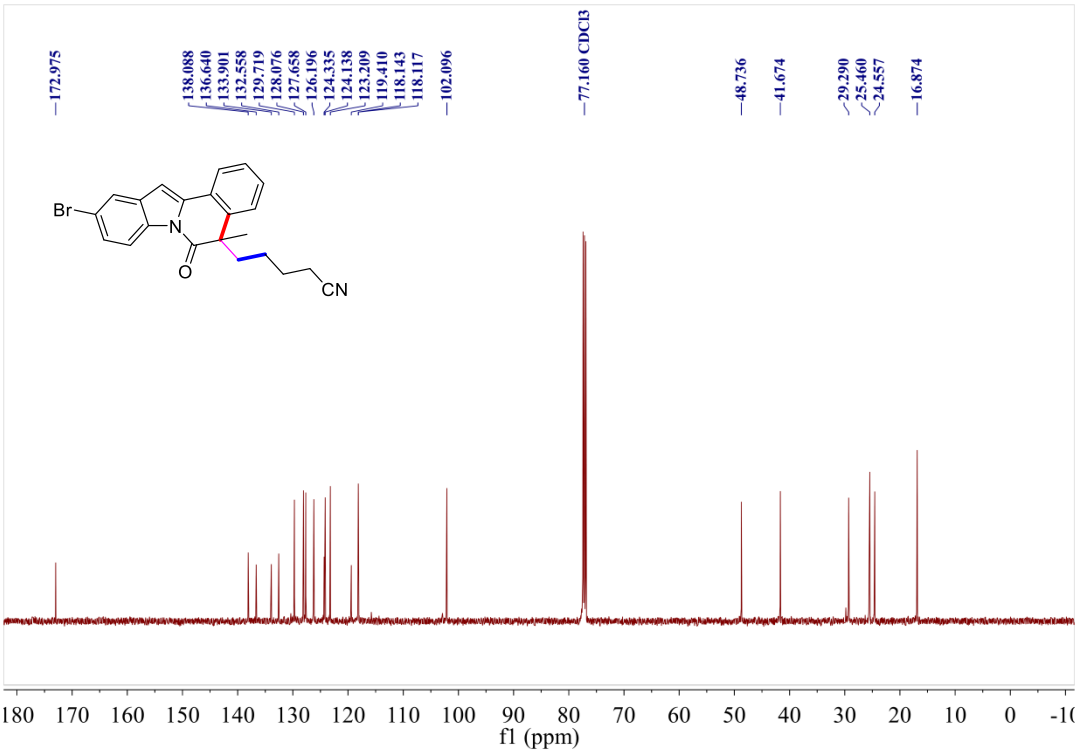
5-(10-Chloro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ai)



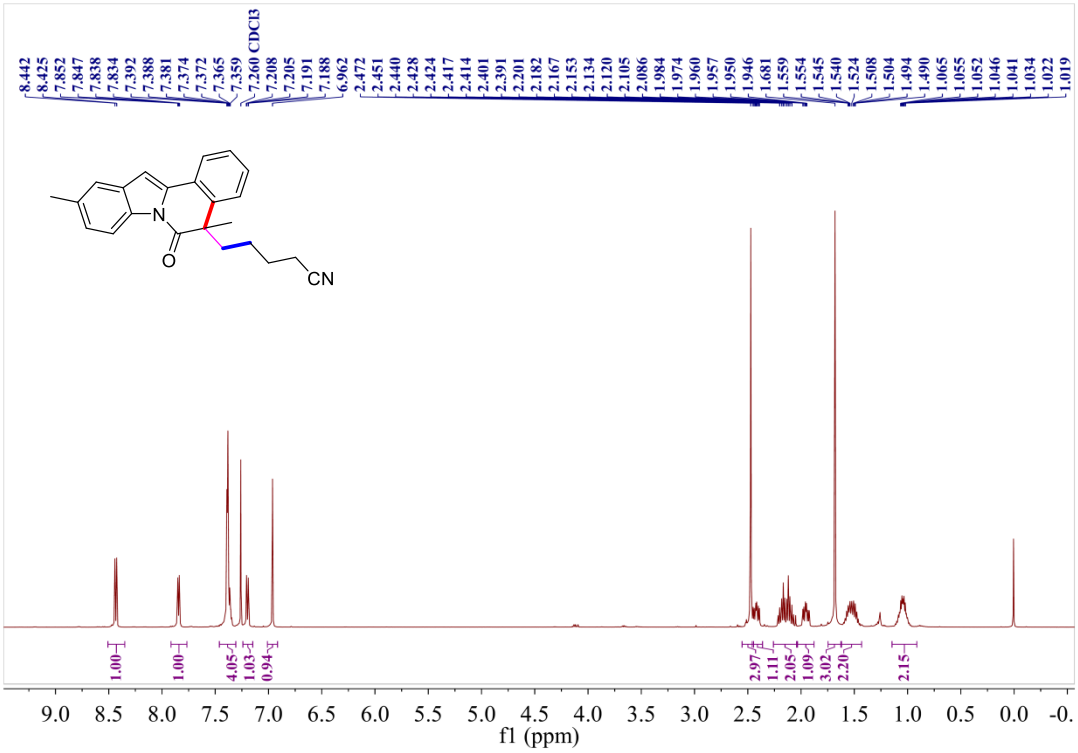


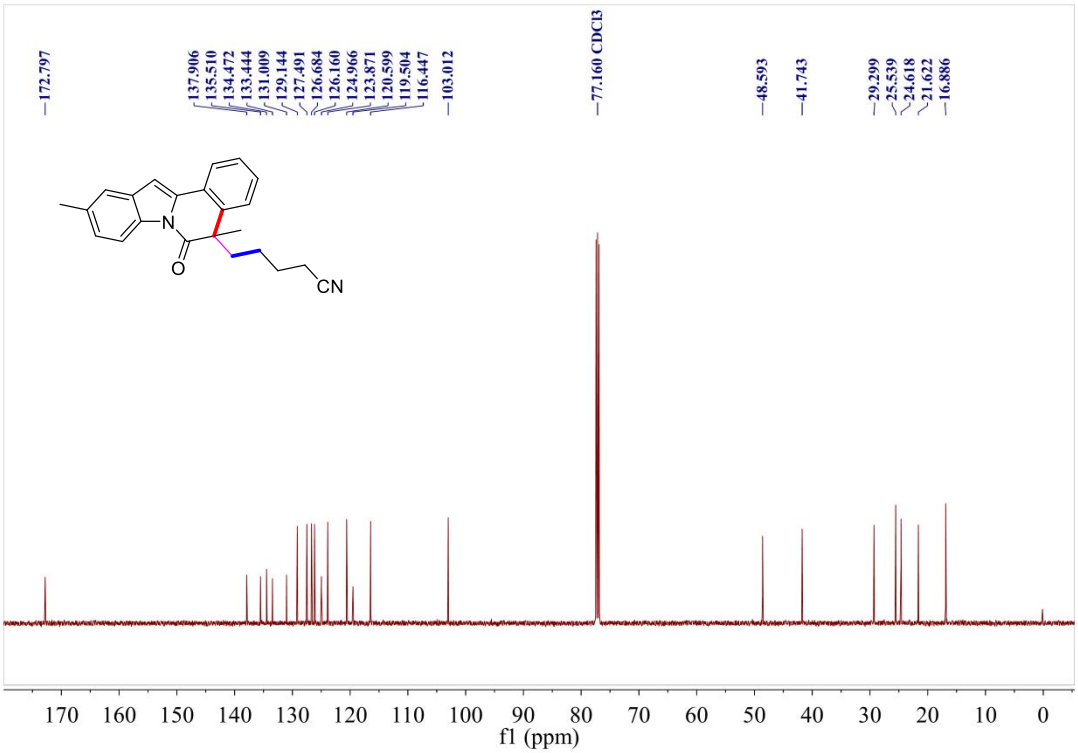
5-(10-Bromo-5-methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3aj)



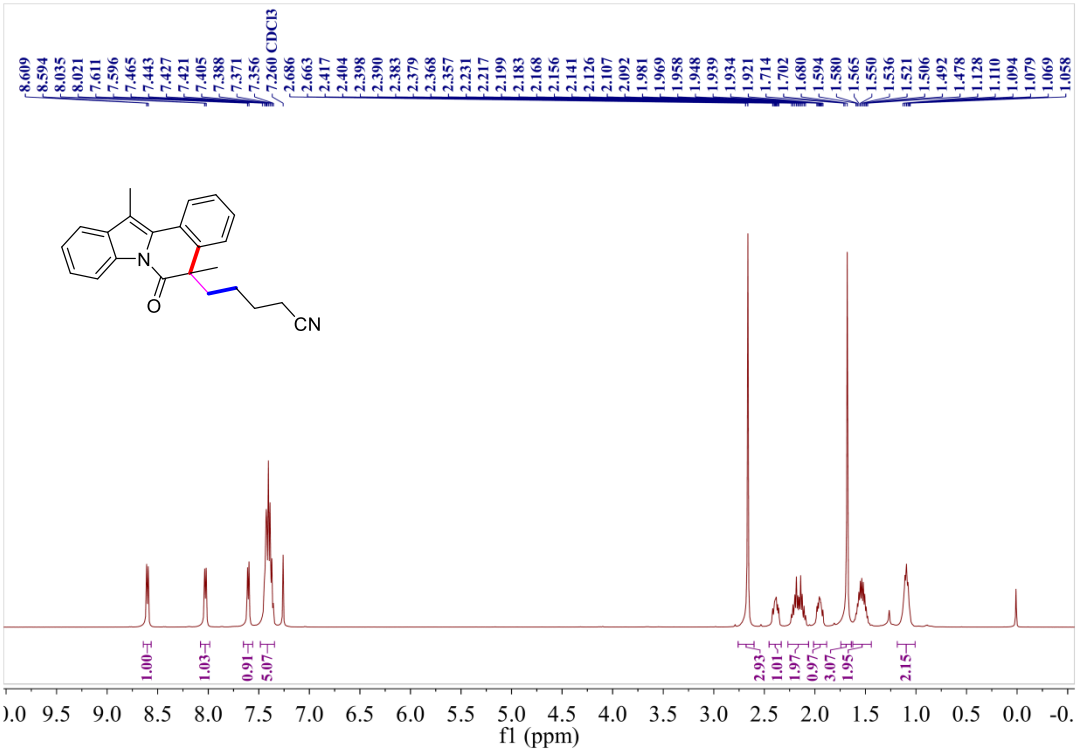


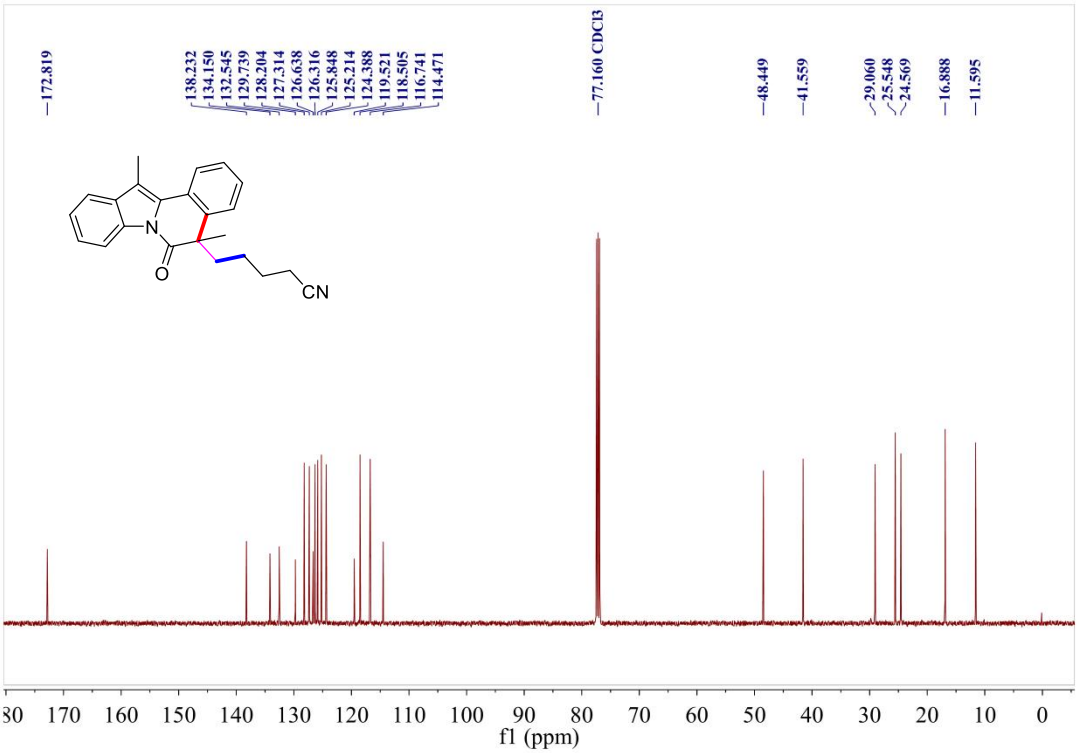
5-(5,10-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3ak)



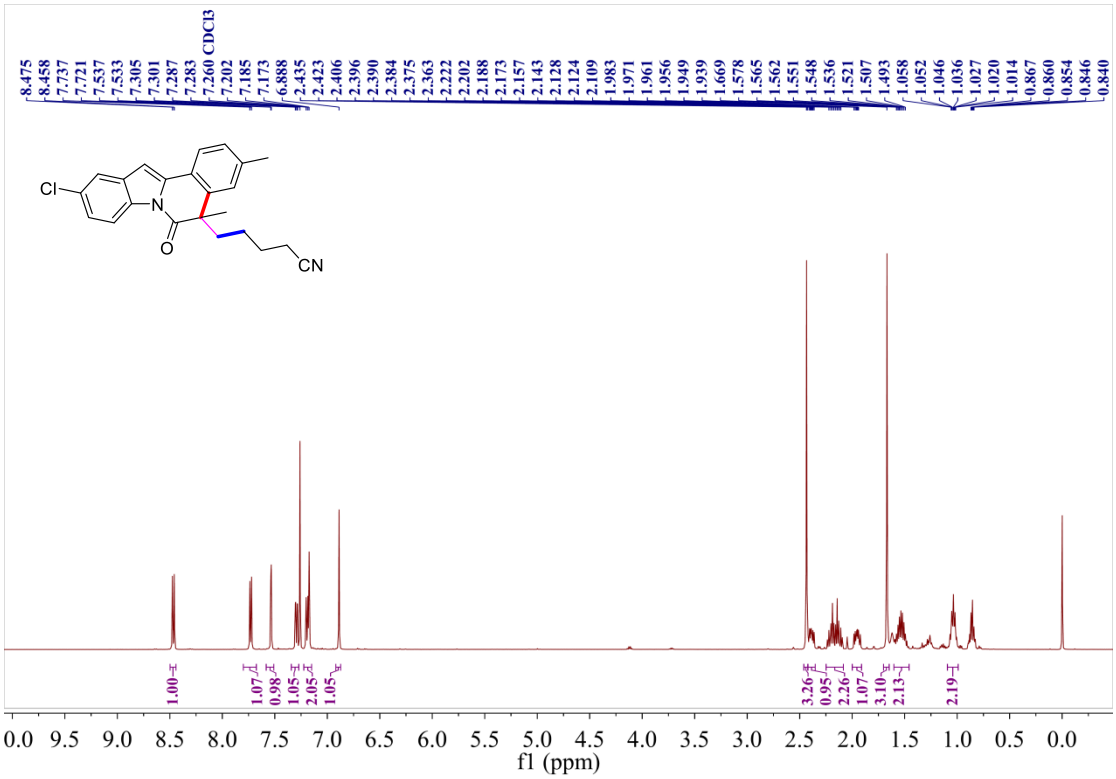


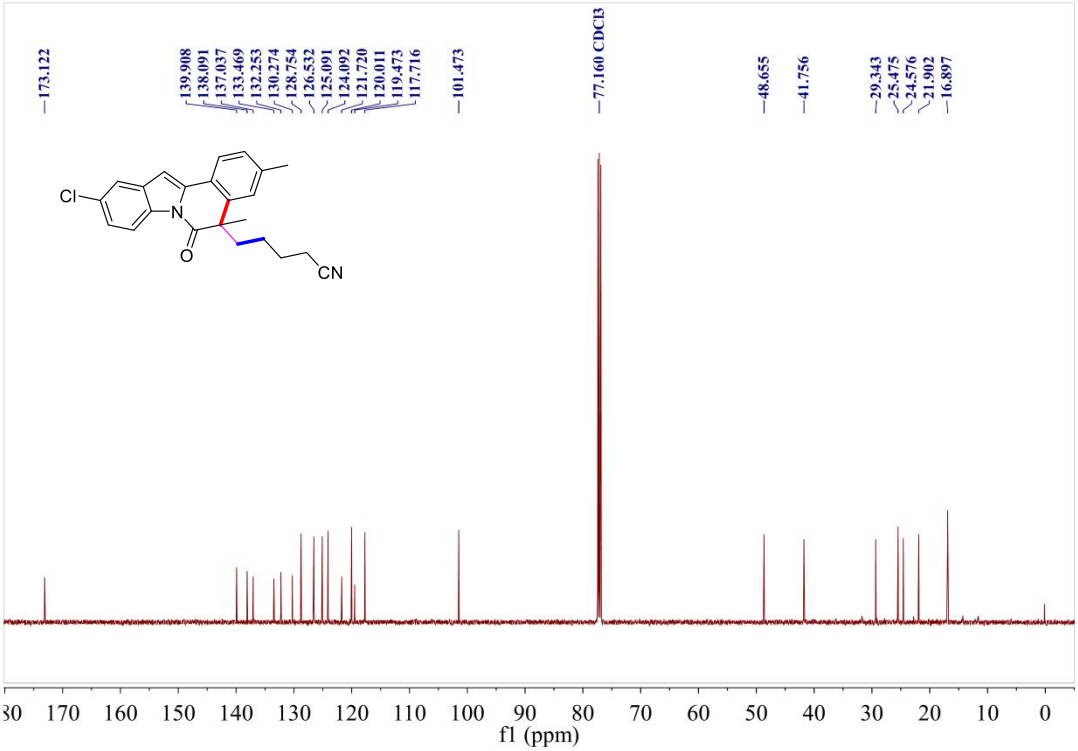
5-(5,12-Dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3al)



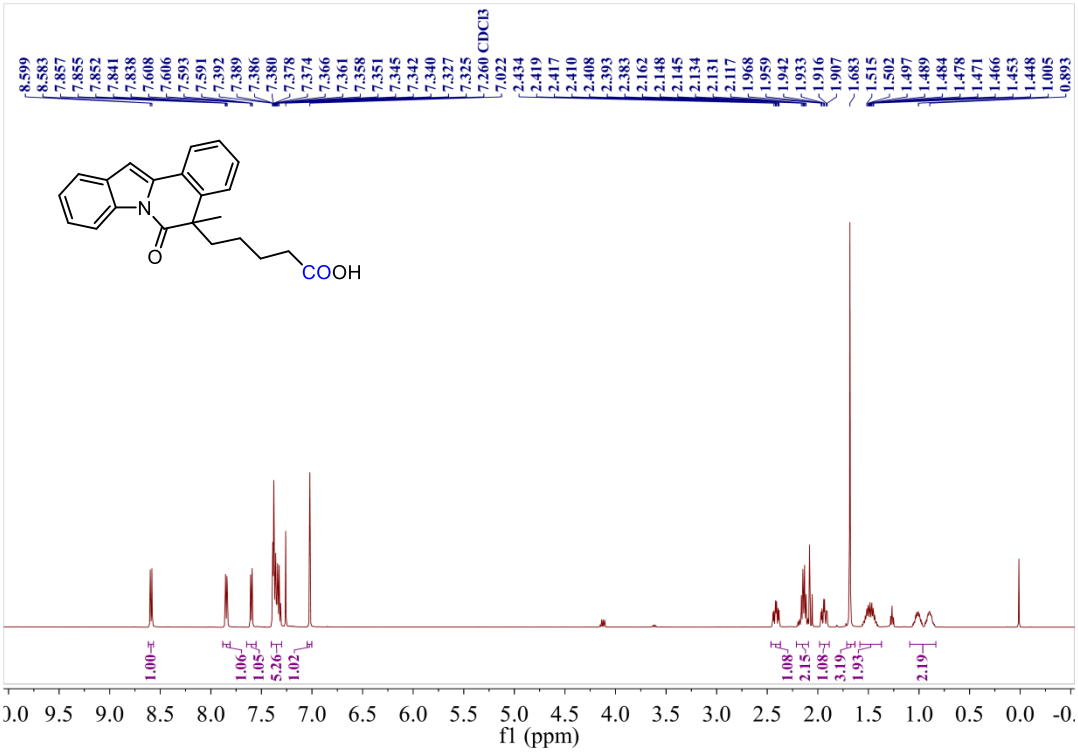


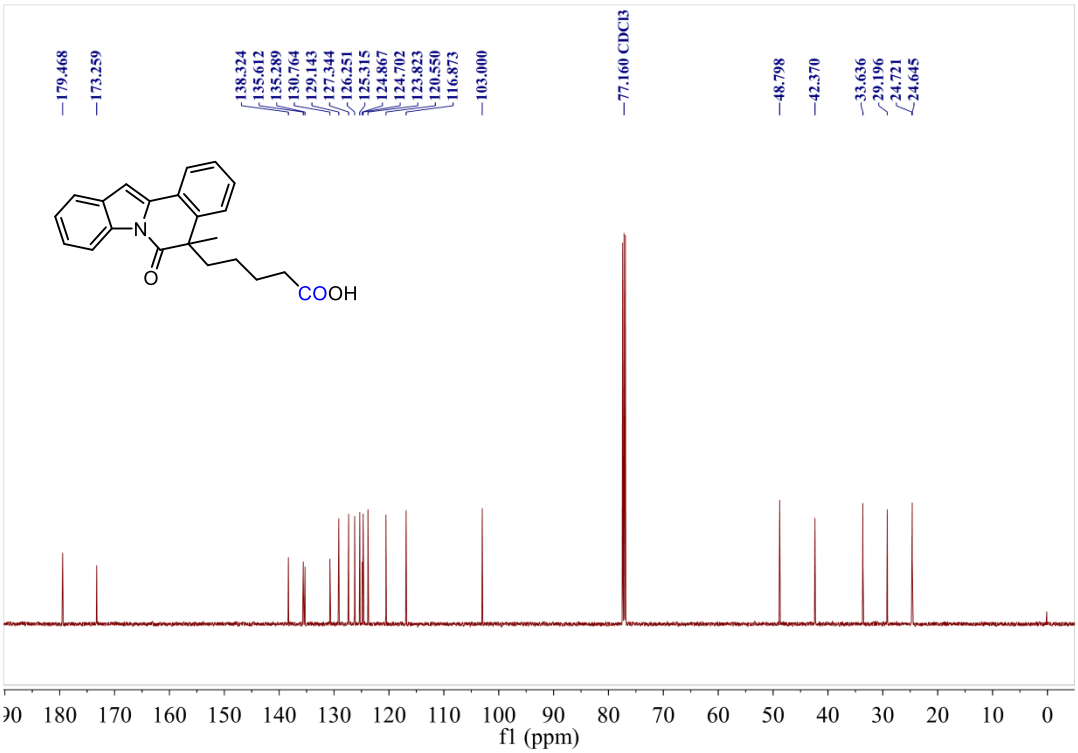
5-(10-Chloro-3,5-dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanenitrile (3am)



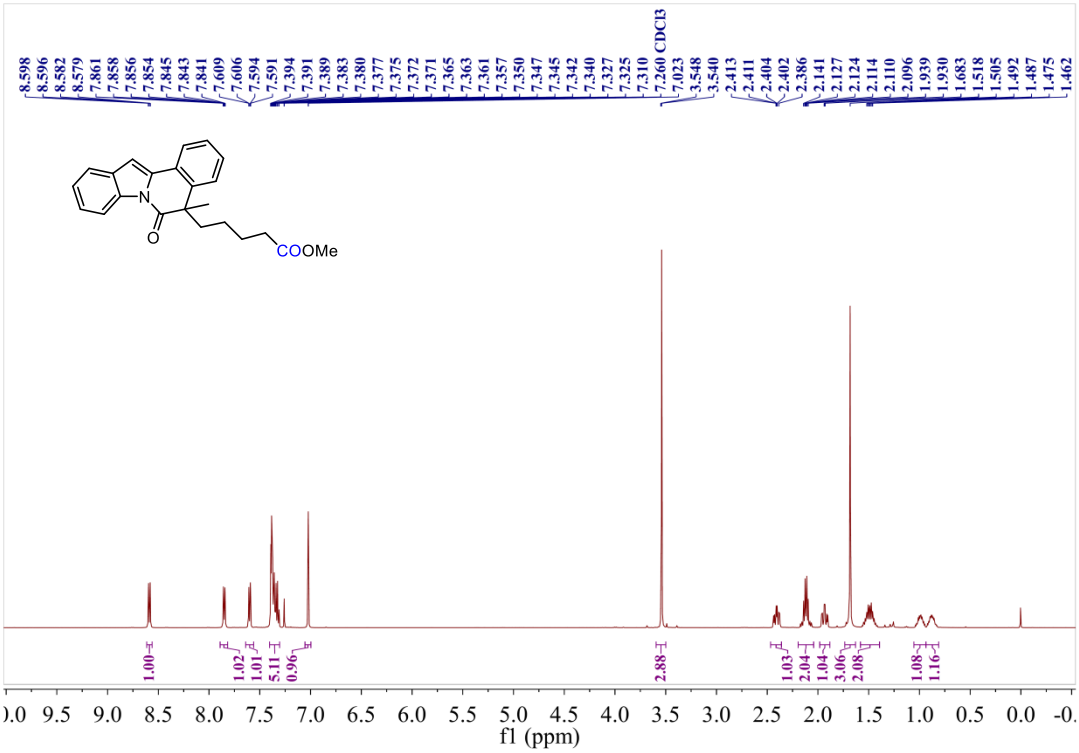


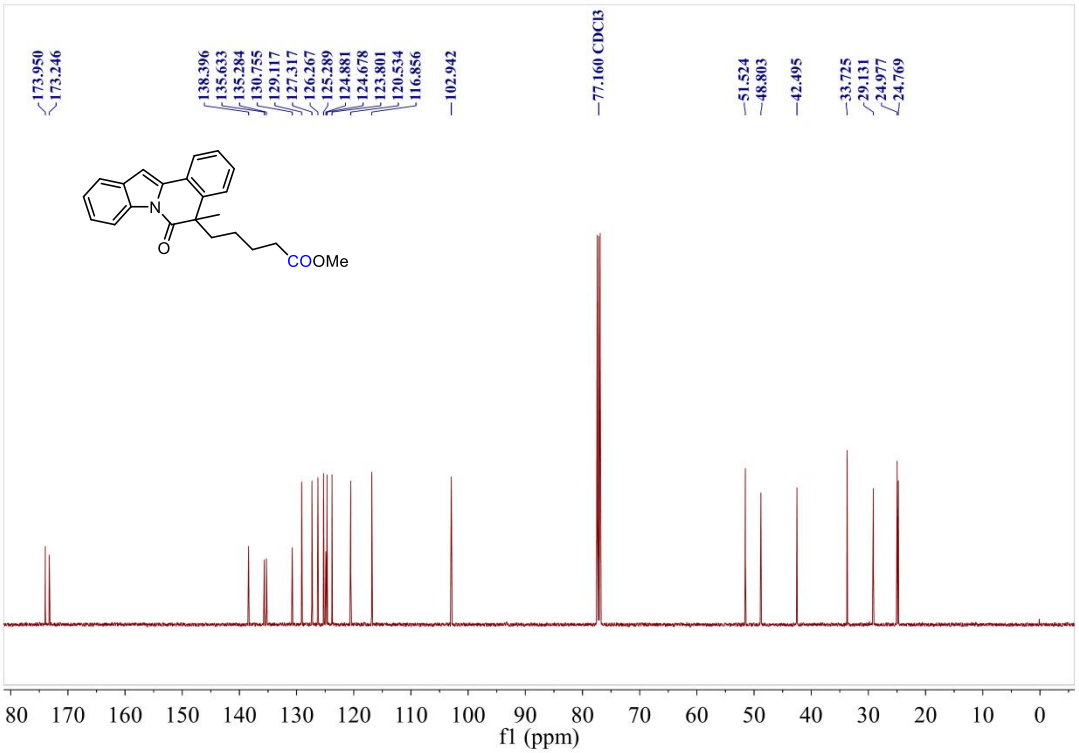
5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanoic acid (4a)



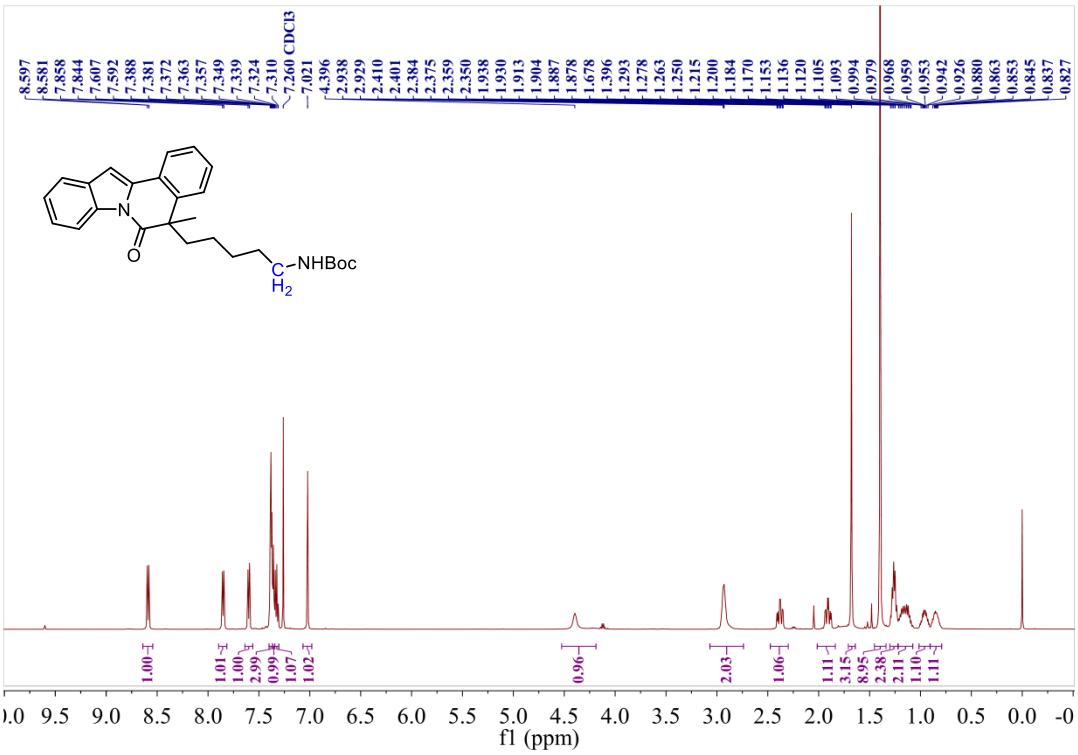


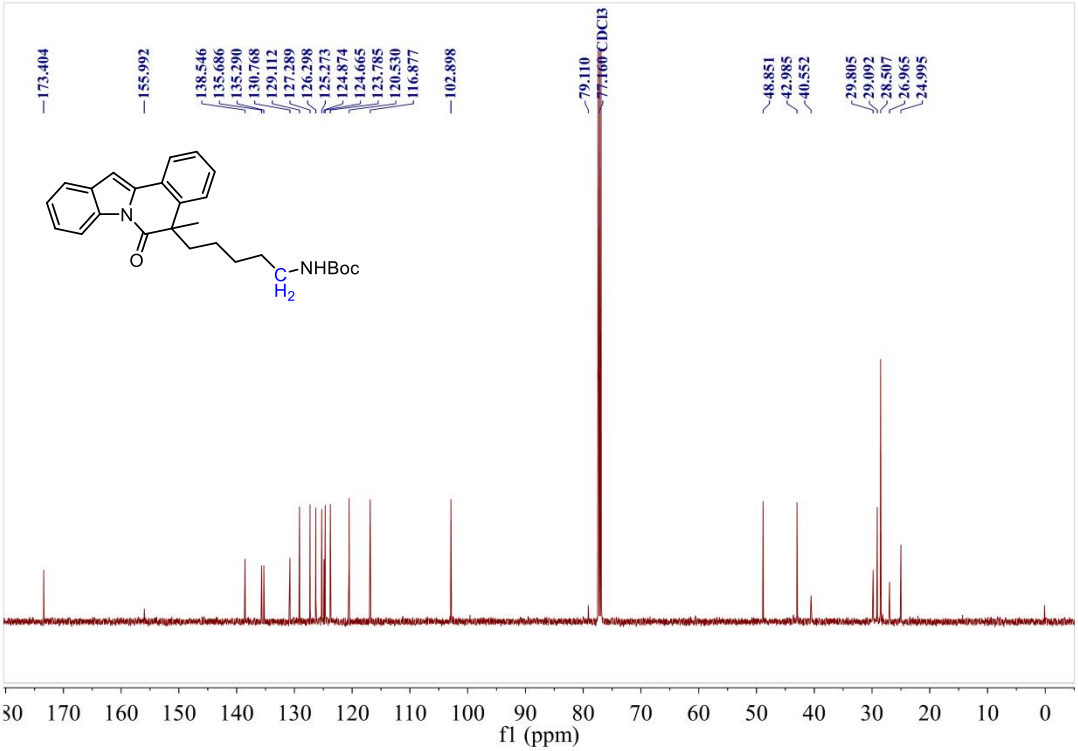
Methyl 5-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)pentanoate (4b)



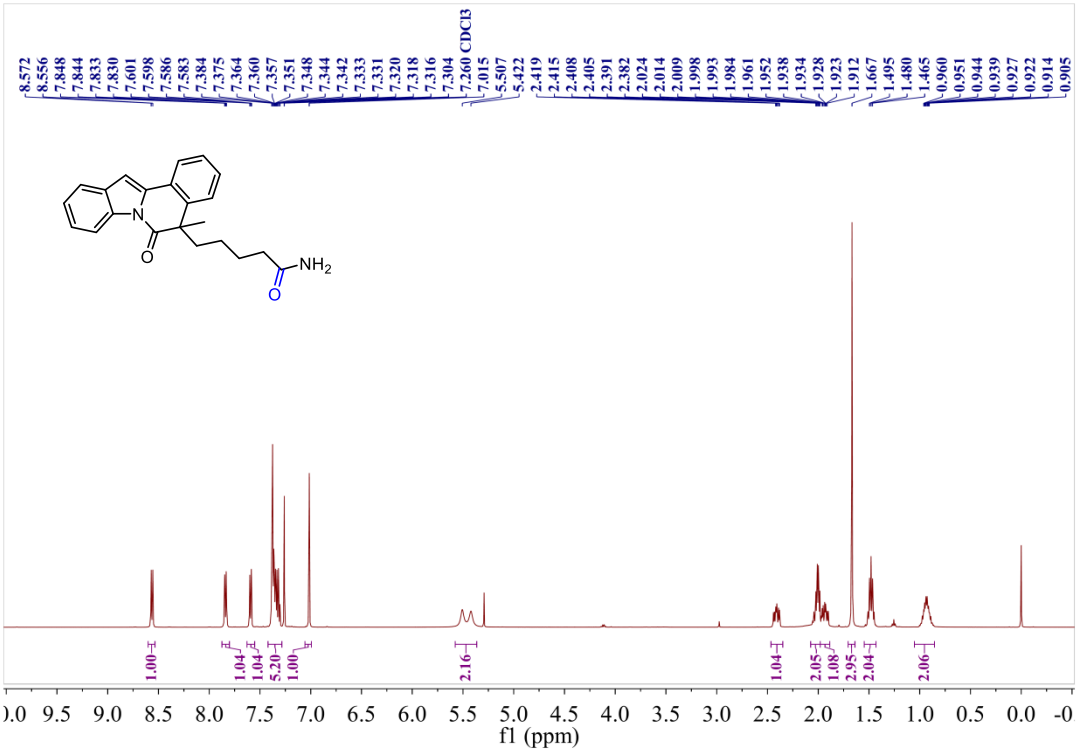


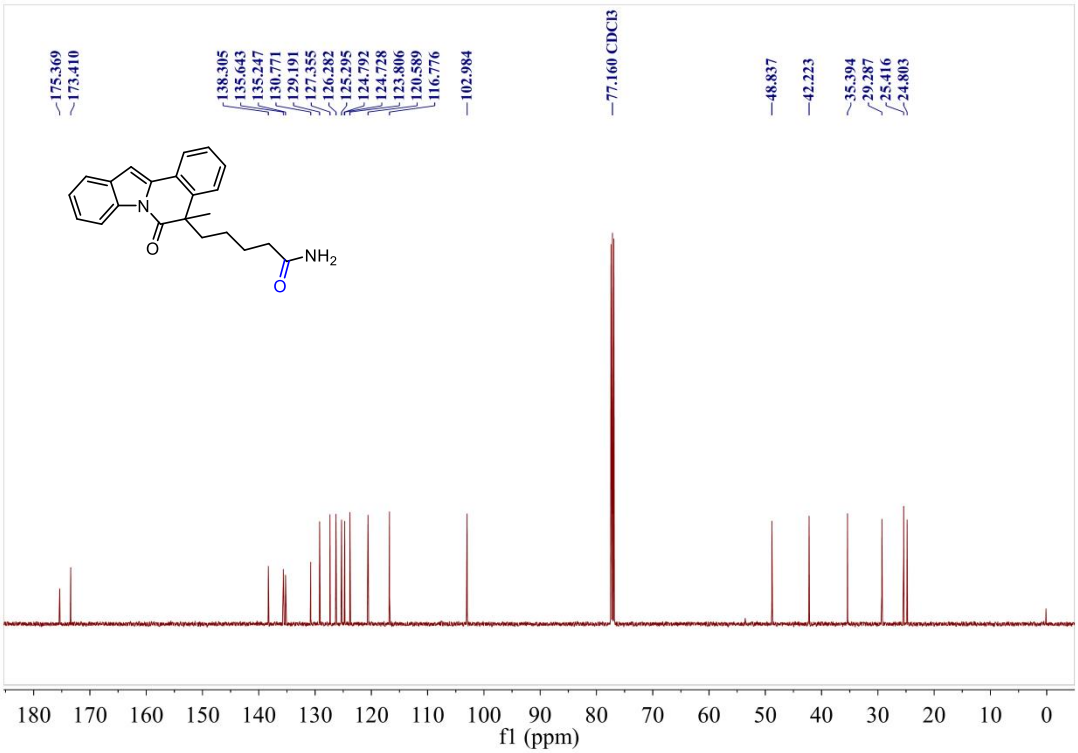
Tert-butyl (5-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)pentyl)carbamate (4c)





5-(5-Methyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)pentanamide (4d)





4-(Phenylselanyl)butanenitrile (7)