Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Synthesis of Indolo[2,1-a]isoquinoline Derivatives *via* Visible-light-induced Radical Cascade Cyclization Reactions

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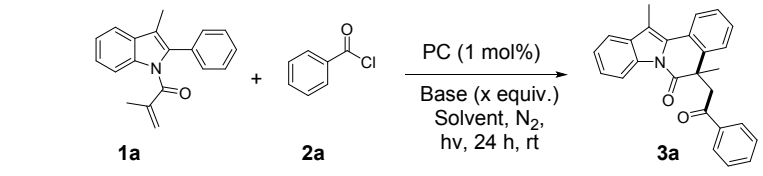
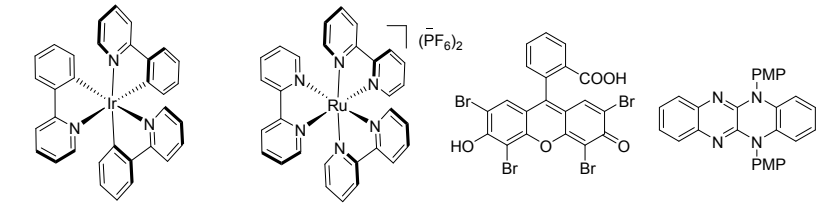
1. General information

All glassware was thoroughly oven-dried. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. Thin-layer chromatography plates were visualized by exposure to ultraviolet light and/or staining with phosphomolybdic acid followed by heating on a hot plate. Flash chromatography was carried out using silica gel (200−300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 (400 MHz). The spectra were recorded in deuterochloroform ($CDCl_3$) as solvent at room temperature, ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to the residual solvent peak. The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.0 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet, br = broad), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported as chemical shift. IR spectra were recorded using Bruker Vertex 70v IR instrument and are reported in wave numbers (cm^{-1}). Ultraviolet-visible spectroscopy was performed on a Perkin Elmer Lambda 950 spectrophotometer using CH_3CN as the solvent. HRMS were performed on a Bruker Apex II mass instrument (ESI). All luminescence spectra were surveyed on a PE-LS55 fluorescence spectrophotometer and equipped with a 1 cm quartz cell.

2. Optimization of the reaction conditions

Table S1 : Optimization of the reaction conditions[a]



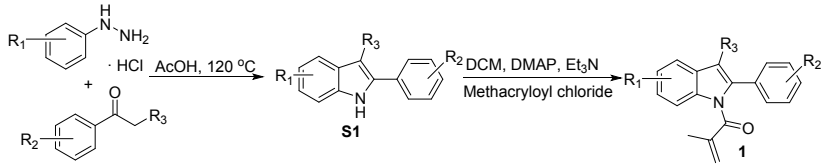


Entry	PC	Solvent	Base (x equiv.)	Yield (%)[b]
1	*fac*-Ir(ppy)$_3$	CH_3CN	2,6-lutidine (1.0)	67
2[c]	Cat-1	CH_3CN	2,6-lutidine (1.0)	28
3	$Ru(bpy)_3(PF_6)_2$	CH_3CN	2,6-lutidine (1.0)	-
4	Eosin Y	CH_3CN	2,6-lutidine (1.0)	-
5	*fac*-Ir(ppy)$_3$	CH_3CN	K_2HPO_4 (1.0)	40
6	*fac*-Ir(ppy)$_3$	CH_3CN	Et_3N (1.0)	38
7	*fac*-Ir(ppy)$_3$	CH_3CN	Pyridine (1.0)	35
8	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.0)	70
9	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.25)	80
10	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.5)	56
11	*fac*-Ir(ppy)$_3$	DCM	2,4,6-collidine (1.25)	78
12	*fac*-Ir(ppy)$_3$	Acetone	2,4,6-collidine (1.25)	79
13	*fac*-Ir(ppy)$_3$	THF	2,4,6-collidine (1.25)	77
14	*fac*-Ir(ppy)$_3$	Toluene	2,4,6-collidine (1.25)	65
15	*fac*-Ir(ppy)$_3$	DMF	2,4,6-collidine (1.25)	58
16[d]	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.25)	87
17[e]	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.25)	91
18	-	CH_3CN	2,4,6-collidine (1.25)	-
19[f]	*fac*-Ir(ppy)$_3$	CH_3CN	2,4,6-collidine (1.25)	-

[a]Unless otherwise noted, reaction conditions are as follows: **1a** (0.2 mmol), **2a** (0.4 mmol), photocatalyst (0.002 mmol), base (0.2 mmol), solvent (4 mL), blue LEDs, 25 °C and under a N_2 atmosphere. [b]Isolated yield.[c]Using our own photocatalyst, see *ref 1*. [d]2 mol% PC was used; [e]3 mol% PC was used; [f]In the dark.

3. Preparation of substrates

3.1 General procedure for the synthesis of substrates 1a-1g and 1i-1q.[2-3]

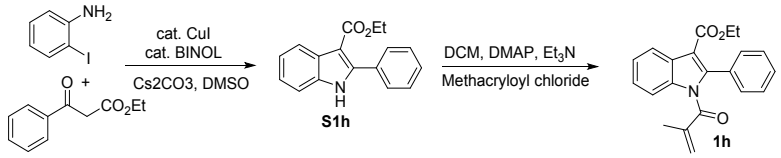


Fischer indole synthesis and the following acylation reaction.

According to a modified literature procedure[2], a mixture of phenylhydrazine or substituted phenylhydrazine hydrochloride (11 mmol, 1.1 equiv), ketone (10 mmol, 1.0 equiv) and acetic acid (10 mL, 1.0 M) was heated to 120 ºC for 12-24 h in a 100 mL round-bottomed flask under N_2 atmosphere. The reaction mixture was cooled to rt., AcOH was removed by rotory evaporation and the residue was portioned between water (50 mL) and EtOAc (20 mL). The organic and aqueous layers were separated. The aqueous layer was extracted with EtOAc (20 mL x 2 times), and the combined organic phase was washed with a saturated solution of sodium bicarbonate (20 mL) and brine (20 mL), dried with Na_2SO_4 and the solvent was evaporated. The crude product was purified by column chromatography to afford the desired product indole **S1.**

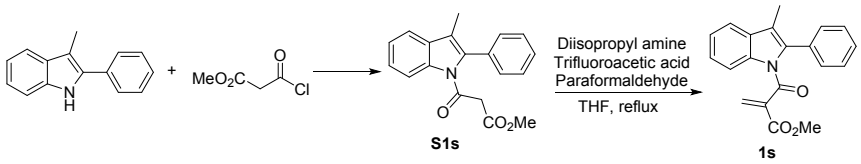
According to a modified literature procedure[3], to the solution of indole **S1** (5 mmol, 1.0 equiv) and DMAP (1.0 mmol, 0.2 equiv) in DCM (0.5 M) was added Et_3N (10 mmol, 2.0 equiv.) and methacryloyl chloride (10 mmol, 2.0 equiv.) at 0 °C. The solution was warmed up to room temperature and stirred for 2-3 days. The mixture was diluted with DCM (20 mL) and saturated NH_4Cl solution (20 mL). The organic and aqueous layers were separated. The aqueous layer was extracted with DCM (20 mL x 2 times). The combined organic layer was washed with brine, dried over $NaSO_4$, filtered and concentrated in vacuo to give a residue, which was purified by flash chromatography and then recrystallized from *n*-hexane/ EtOAc to afford the product.

3.2 Synthesis of substrate 1h[4]



According to a literature procedure.[4] 2-Iodoaniline (9.1 mmol), ethyl benzoylacetate (10 mmol), CuI (173 mg, 0.91mmol), (*rac*)-binol (521 mg, 1.8mmol), and Cs_2CO_3 (3.0 g, 9.1 mmol) were placed in a two-neck flask under nitrogen. DMSO (20 mL) was added to the mixture, and the solution was stirred at 50 ºC for 2 days. Saturated NH_4Cl solution was added to the mixture and the resulting mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with PE/EtOAc (8:1) to give **S1h** as a yellow solid. The following acylation procedure will deliver substrate **1h**.

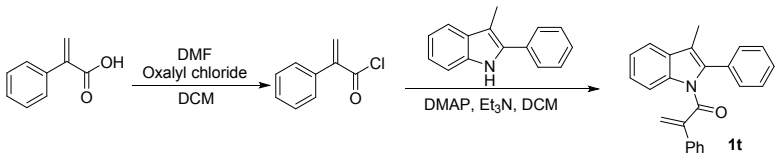
3.3 Synthesis of substrate 1s[5,6]



According to a literature procedure.[5] To a dry flask charged with a stir bar was added a 1.0 M solution of indole (5.0 mmol) in DCE. Methyl malonyl chloride (7.5 mmol) was syringed into the mixture and the reaction was heated to reflux until complete conversion of starting material (monitored by TLC) was observed (6 h). Once the reaction was complete, the solvent and excess methyl malonyl chloride was removed under reduced pressure. The residue was purified by silica gel flash chromatography to give **S1s** as a white solid.

According to a modified procedure literature procedure.[6] A flame-dried 50 mL round-bottom flask was charged with 10 mL dry THF, diisopropyl amine (0.42 mL, 3.0 mmol), trifluoroacetic acid (0.25 mL, 3.3 mmol), **S1s** (920 mg, 3 mmol) and paraformaldehyde (180 mg, 6 mmol). A condenser was added and the reaction mixture was stirred at reflux for two hours. Paraformaldehyde (180 mg, 6 mmol) was added and the reaction mixture was refluxed for another six hours. The reaction mixture was cooled to room temperature and THF was removed under reduced pressure. The crude product was purified by silica gel chromatography (PE/EA = 6:1) to afford the desired substrate **1s**.

3.4 Synthesis of substrate 1t[7]



According to a literature procedure.[7] To a solution of the Atropic acid (1.48 g, 10 mmol) dissolved in DCM (0.4 M) cooled to 0 °C, a catalytic amount of DMF (1 drop per mmol of acid) was added. To this solution, $(COCl)_2$ (1.69 Ml, 20 mmol) was added dropwise. The solution was gradually warmed to room temperature to stir 1 h. The resulting acyl chloride is concentrated to yield a crude residue that is subsequently re-dissolved in DCM (10 mL) to use in next acylation procedure. The following acylation procedure (similar to **1a**) will deliver substrate **1t**.

4. General procedure for the visible-light-induced radical cascade cyclization reactions

4.1 General procedure for the synthesis of compounds 3

Acyl chloride **2** (0.4 mmol) and 2,4,6-collidine (0.25 mmol) were added to a solution of substrate **1** (0.2 mmol) and photocatalyst *fac*-Ir(ppy)$_3$ (3 mol%) in dry CH_3CN (4

mL) at room temperature. The mixture was degassed by three cycles of freeze-pump-thaw and then placed in the irradiation apparatus equipped with a 25 W blue light-emitting diode (LED) strip. The resulting mixture was stirred at 25 °C for 24 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resulting crude mixture was purified by flash column chromatography on silica gel (PE/EA=20:1-10:1) to afford the desired product.

4.2 Procedure for scale-up preparation of 3aa

Acyl chloride **2** (2 mmol) and 2,4,6-collidine (1.25 mmol) were added to a solution of substrate **1a** (1 mmol) and photocatalyst *fac*-Ir(ppy)$_3$ (3 mol%) in dry CH_3CN (20 mL) at room temperature. The mixture was degassed by three cycles of freeze-pump-thaw and then placed in the irradiation apparatus equipped with a 25 W blue light-emitting diode (LED) strip. The resulting mixture was stirred at 25 °C for 24 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resulting crude mixture was purified by flash column chromatography on silica gel (PE/EA=20:1-10:1) to afford the desired product.

4.3 General procedure for the synthesis of polycyclic compounds 5aa-5ad

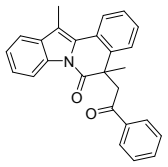
The corresponding alkyl bromides **4** (0.4 mmol) and 2,4,6-collidine (0.25 mmol) were added to a solution of substrate **1a** (0.2 mmol) and photocatalyst *fac*-Ir(ppy)$_3$ (3 mol%) in dry CH_3CN (4 mL) at room temperature. The mixture was degassed by three cycles of freeze-pump-thaw and then placed in the irradiation apparatus equipped with a 25 W blue light-emitting diode (LED) strip. The resulting mixture was stirred at 25 °C for 24 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resulting crude mixture was purified by flash column chromatography on silica gel (PE/EA=20:1-10:1) to afford the desired product.

4.4 Procedure for the synthesis of polycyclic compounds 5ae

The corresponding oxime ester **4e** (0.2 mmol) and DABCO (0.2 mmol) were added to a solution of substrate **1a** (0.1 mmol) and photocatalyst *fac*-Ir(ppy)$_3$ (1 mol%) in dry CH_3CN (2 mL) at room temperature. The mixture was degassed by three cycles of freeze-pump-thaw and then placed in the irradiation apparatus equipped with a 25 W blue light-emitting diode (LED) strip. The resulting mixture was stirred at 25 °C for 36 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resulting crude mixture was purified by flash column chromatography on silica gel (PE/EA=20:1-10:1) to afford the desired product **5ae**.

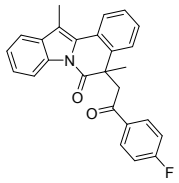
5. Characterization of products

5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3aa)



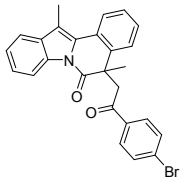
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3aa**. White solid; 68.8 mg, 91% yield; m.p. 184-186 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.61 (s, 3H), 2.65 (s, 3H), 4.03 (d, *J* = 18.2 Hz, 1H), 4.29 (d, *J* = 18.2 Hz, 1H),7.16-7.20 (m, 1H), 7.22−7.25 (m, 1H), 7.27-7.37 (m, 5H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.57-7.60 (m, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 8.03 (d, *J* = 7.9 Hz, 2H), 8.58-8.61 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 45.6, 48.4, 114.1, 116.5, 118.2, 123.8, 124.5, 125.3, 125.3, 126.3, 126.7, 127.6, 127.9, 128.4, 129.9 132.4, 133.2, 134.3, 136.1, 139.0, 172.9, 196.3; IR (KBr, cm^{-1}): 3062, 2975, 2926, 1685, 1599, 1451, 1374, 1340, 1243, 1120, 1048, 752, 690; HRMS (ESI) for $C_{26}H_{22}NO_2^+$ $[M+H]^+$ calcd. 380.1645, found 380.1651.

5-(2-(4-fluorophenyl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ab)



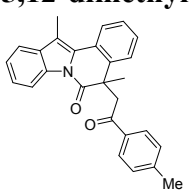
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ab**. White solid; 70.0 mg, 88% yield; m.p. 167-168 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.63 (s, 3H), 2.68 (s, 3H), 3.99 (d, *J* = 18.1 Hz, 1H), 4.27 (d, *J* = 18.1 Hz, 1H), 7.04 (t, *J* = 8.5 Hz, 2H), 7.20−7.26 (m, 2H), 7.31-7.38 (m, 3H), 7.59-7.61 (m, 1H), 7.87-7.90 (m, 2H), 8.06 (d, *J* = 8.0 Hz,1H), 8.56-8.58 (m,1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 45.6, 48.4, 114.3, 115.6 (d, J_F = 21.7 Hz), 116.6, 118.3, 123.9, 124.5, 125.4, 125.4, 126.4, 126.8, 127.7, 129.9, 130.7 (d, J_F = 9.2Hz), 132.4, 132.6 (d, J_F = 2.9 Hz), 134.3, 139.0, 165.8 (d, J_F = 253.4 Hz), 172.8, 194.8; IR (KBr, cm^{-1}): 3069, 2976, 1735, 1686, 1598, 1452, 1375, 1340; 1231, 1157, 1099, 1046; 846; 754, 552; HRMS (ESI) for $C_{26}H_{21}FNO_2^+$ $[M+H]^+$ calcd. 398.1551, found 398.1555.

5-(2-(4-bromophenyl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ac)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ab**. White solid; 86.3 mg, 94% yield; m.p. 197-198 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.61 (s, 3H), 2.67 (s, 3H), 3.96 (d, *J* = 18.1 Hz, 1H), 4.24 (d, *J* = 18.1 Hz, 1H), 7.18-7.23 (m, 2H), 7.30-7.36 (m, 3H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.58-7.61 (m, 1H), 7.70 (d, *J* = 8.6 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.56-8.58 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 45.6, 48.4, 114.3, 116.5, 118.3, 124.0, 124.4, 125.4, 125.5, 126.4, 126.9, 127.7, 128.4, 129.5, 129.8, 131.8, 132.4, 134.3, 134.8, 172.7, 195.5; IR (KBr, cm^{-1}): 3063, 2972, 2924, 2869, 1685, 1585, 1452, 1397, 1340, 1215, 1177, 1069, 1005, 755, 550; HRMS (ESI) for $C_{26}H_{21}BrNO_2^+$ $[M+H]^+$ calcd. 458.0750, found 458.0756.

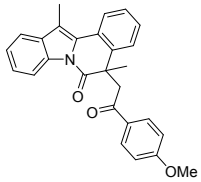
5,12-dimethyl-5-(2-oxo-2-(p-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ad)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ad**. White solid; 73.0mg, 93% yield; m.p. 163-164 °C; **^{1}H NMR (400**

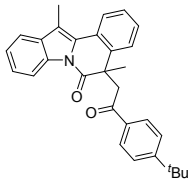
MHz, $CDCl_3$) δ (ppm) = 1.63 (s, 3H), 2.35 (s, 3H), 2.68 (s, 3H), 4.03 (d, *J* = 18.1 Hz, 1H), 4.27 (d, *J* = 18.1 Hz, 1H), 7.17 (d, *J* =8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 6.7 Hz, 1H), 7.30-7.38 (m, 3H), 7.59-7.61 (m, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.57-8.59 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 21.5, 30.5, 45.6, 48.4, 114.1, 116.6, 118.2, 123.8, 124.5, 125.4, 126.4, 126.7, 127.6, 128.1, 129.1, 130.0, 132.4, 133.8, 134.4, 139.2, 144.0, 172.9, 195.9; IR (KBr, cm^{-1}): 3034, 2973, 2924, 2869, 1735, 1683, 1606, 1452, 1375, 1340, 1239, 1179, 1046, 753, 550; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1806.

5-(2-(4-methoxyphenyl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ae)



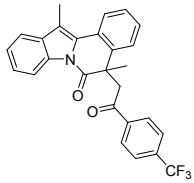
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ae**. White solid; 72.0 mg, 88% yield; m.p. 229-232 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.69 (s, 3H), 3.82 (s, 3H), 4.01 (d, *J* = 18.0 Hz, 1H), 4.26 (d, *J* = 18.0 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 2H), 7.21-7.28 (m, 2H), 7.31-7.38 (m, 3H), 7.60-7.62 (m, 1H), 7.86 (d, *J* = 8.9 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.56-8.58 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.7, 48.3, 55.4, 113.6, 114.1, 116.7, 118.2, 123.9, 124.6, 125.4, 126.4, 126.7, 127.6, 129.5, 130.0, 130.3, 132.5, 134.4, 139.3, 163.6, 173.0, 194.8; IR (KBr, cm^{-1}): 2991, 2923, 2852, 1761, 1659, 1635, 1588, 1243, 695, 543; HRMS (ESI) for $C_{27}H_{24}NO_3^+$ $[M+H]^+$ calcd. 410.1751, found 410.1755.

5-(2-(4-(tert-butyl)phenyl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3af)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3af**. White solid; 75.6 mg, 87% yield; m.p. 86-89 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.29 (s, 9H), 1.63 (s, 3H), 2.67 (s, 3H), 4.04 (d, *J* = 18.1 Hz, 1H), 4.28 (d, *J* = 18.1 Hz, 1H), 7.17-7.22 (m, 1H), 7.25 (d, *J* = 6.8 Hz, 1H), 7.29-7.36 (m, 3H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.59-7.61 (m, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.57-8.59 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 31.0, 35.0, 45.6, 48.5, 114.1, 116.6, 118.2, 123.8, 124.5, 125.4, 125.4, 126.4, 126.7, 127.6, 128.0, 130.0, 132.4, 133.7, 134.4, 139.2, 157.0, 172.9, 196.0; IR (KBr, cm^{-1}): 3063, 2964, 2869, 1736, 1683, 1604, 1452, 1374, 1340, 1238, 1006, 944, 754, 550; HRMS (ESI) for $C_{30}H_{30}NO_2^+$ $[M+H]^+$ calcd. 436.2271, found 436.2274.

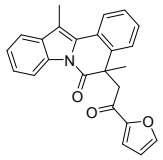
5,12-dimethyl-5-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ag)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ag**. White solid; 69.5 mg, 78% yield; m.p. 187-188 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.68 (s, 3H), 4.00 (d, *J* = 18.2 Hz, 1H), 4.31 (d, *J* = 18.2 Hz, 1H), 7.19-7.25 (m, 2H), 7.32-7.38 (m, 3H), 7.59-7.64 (m, 3H), 7.94 (d, *J* = 8.1 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.55-8.57 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 45.7,

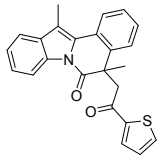
48.7, 114.5, 116.5, 118.4, 123.5 (q, J_F = 271.1 Hz), 124.0, 124.4, 125.4, 125.5 (q, J_F = 3.6 Hz), 126.4, 127.0, 127.8, 128.3, 129.8, 132.4, 134.3, 134.5 (q, J_F = 32.2 Hz), 138.7, 138.8, 172.7, 195.6; IR (KBr, cm^{-1}): 3069, 2976, 2927, 2871, 1735, 1689, 1506, 1452, 1375, 1341, 12321, 1157, 1046, 846, 754; HRMS (ESI) for $C_{27}H_{21}F_3NO_2^+$ $[M+H]^+$ calcd. 448.1519, found 448.1525.

5-(2-(furan-2-yl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ah)



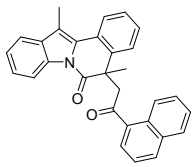
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ah**. White solid; 48.7 mg, 66% yield; m.p. 194-195 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.66 (s, 3H), 3.92 (d, *J* = 18.2 Hz, 1H), 4.12 (d, *J* = 18.2 Hz, 1H), 6.43 (dd, *J* =1.7, 3.5 Hz, 1H), 7.04 (d, *J* = 3.6 Hz, 1H), 7.23 (t, *J* = 8.3 Hz, 1H), 7.29-7.38 (m, 4H), 7.49 (t, *J* = 0.9 Hz, 1H),7.58-7.60 (m, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 8.55-8.60 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.3, 45.3, 48.3, 112.3, 114.2, 116.6, 116.8, 118.2, 123.9, 124.8, 125.3, 125.4, 126.4, 126.9, 127.7, 129.9, 132.4, 134.4, 138.7, 146.1, 152.4, 172.7, 185.8; IR (KBr, cm^{-1}): 2975, 2926, 2869, 1677, 1569, 1452, 1371, 1338, 1246, 1043, 912, 754; HRMS (ESI) for $C_{24}H_{20}NO_3^+$ $[M+H]^+$ calcd. 370.1438, found 370.1441.

5,12-dimethyl-5-(2-oxo-2-(thiophen-2-yl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ai)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ah**. White solid; 68.2 mg, 89% yield; m.p. 182-184 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.61 (s, 3H), 2.65 (s, 3H), 3.93 (d, *J* = 17.8 Hz, 1H), 4.23 (d, *J* = 17.8 Hz, 1H), 7.02 (t, *J* = 4.8 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.28-7.38 (m, 4H), 7.50 (d, *J* = 4.9 Hz, 1H), 7.57-7.59 (m, 1H), 7.70 (d, *J* = 3.8 Hz, 1H), 8.02 (d, *J* = 7.9Hz, 1H), 8.57-8.59 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 45.6, 49.0, 114.2, 116.6, 118.2, 123.9, 124.6, 125.3, 125.4, 126.3, 126.9, 127.7, 127.9, 129.9, 131.9, 132.4, 133.6, 134.3, 138.7, 143.2, 172.6, 189.2; IR (KBr, cm^{-1}): 2972, 2924, 2854, 1689, 1660, 1516, 1452, 1413, 1375, 1239, 1055, 752; HRMS (ESI) for $C_{24}H_{20}NO_2S^+$ $[M+H]^+$ calcd. 386.1209, found 386.1215.

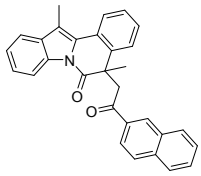
5,12-dimethyl-5-(2-(naphthalen-1-yl)-2-oxoethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3aj)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3af**. White solid; 63.1 mg, 74% yield; m.p. 192-193 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.62 (s, 3H), 4.00 (d, *J* = 17.8 Hz, 1H), 4.45 (d, *J* = 17.8 Hz, 1H), 7.20-7.25 (m, 1H), 7.31-7.42 (m, 7H), 7.57-7.59 (m, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 8.60-8.62 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 46.2, 51.9, 114.2, 116.6, 118.2, 123.9, 124.1, 124.7, 125.4, 125.7, 126.3, 126.5, 126.9, 127.4, 127.7,

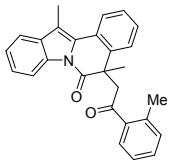
127.7, 128.1, 129.8, 129.9, 132.4, 132.6, 133.7, 134.4, 135.1, 138.9, 172.8, 200.6; IR (KBr, cm^{-1}): 2972, 2924, 2853, 1760, 1687, 1598, 1452, 1374, 1337, 1241, 1170, 1048, 938, 755; HRMS (ESI) for $C_{30}H_{24}NO_2^+$ $[M+H]^+$ calcd. 430.1802, found 430.1806.

5,12-dimethyl-5-(2-(naphthalen-2-yl)-2-oxoethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ak)



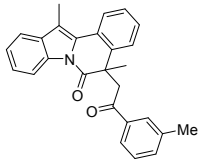
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3af**. White solid; 53.2 mg, 62% yield; m.p. 216-217 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.69 (s, 3H), 2.69 (s, 3H), 4.20 (d, *J* = 18.0 Hz, 1H), 4.44 (d, *J* = 18.0 Hz, 1H), 7.19-7.23 (m, 1H), 7.30-7.38 (m, 4H), 7.49-7.62 (m, 3H), 7.77-7.92 (m, 4H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.46 (s, 1H), 8.58-8.60 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.8, 48.7, 114.2, 116.6, 118.3, 123.7, 123.9, 124.6, 125.4, 126.5, 126.7, 126.8, 127.7, 127.7, 128.3, 128.5, 129.5, 129.8, 130.0, 132.4, 132.5, 133.6, 134.4, 135.6, 139.1, 173.0, 196.4; IR (KBr, cm^{-1}): 2990, 2922, 2852, 1761, 1684, 1549, 1453, 1376, 1244, 1127, 1054, 750, 664; $C_{30}H_{24}NO_2^+$ $[M+H]^+$ calcd. 430.1802, found 430.1806.

5,12-dimethyl-5-(2-oxo-2-(o-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3al)



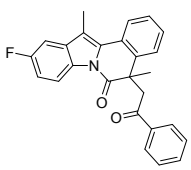
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3al**. White solid; 67.6 mg, 86% yield; m.p. 150-151 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.59 (s, 3H), 2.12 (s, 3H), 2.65 (s, 3H), 3.89 (d, *J* = 17.9 Hz, 1H), 4.29 (d, *J* = 17.9 Hz, 1H), 7.10 (d *J* = 7.5 Hz, 1H), 7.19-7.38 (m, 7H), 7.57-7.59 (m, 1H), 7.67-7.69 (m, 1H), 8.03 (d, *J* =7.0 Hz, 1H), 8.58-8.60 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 20.8, 30.5, 46.0, 51.1, 114.1, 116.6, 118.2, 123.8, 124.5, 125.4, 125.4, 125.5, 126.5, 126.8, 127.6, 128.2, 129.9, 131.3, 131.7, 132.4, 134.4, 137.2, 138.1, 139.1, 172.8, 200.4; IR (KBr, cm^{-1}): 2975, 2924, 2867, 1760, 1684, 1452, 1375, 1339, 1246, 1164, 1048, 752, 690; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1807.

5,12-dimethyl-5-(2-oxo-2-(m-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3am)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3am**. White solid; 70.7 mg, 90% yield; m.p. 173-174 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.63 (s, 3H), 2.31 (s, 3H), 2.67 (s, 3H), 4.04 (d, *J* = 18.1 Hz, 1H), 4.29 (d, *J* = 18.1 Hz, 1H), 7.18-7.37 (m, 7H), 7.58-7.61 (m, 1H), 7.68 (d, *J* = 7.1 Hz, 2H), 8.05 (d, *J* =7.9 Hz, 1H), 8.56-8.60 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 21.2, 30.5, 45.6, 48.6, 114.1, 116.6, 118.2, 123.8, 124.5, 125.2, 125.3, 126.4, 126.7, 127.6, 128.3, 128.5, 130.0, 132.4, 134.0, 134.3, 136.2, 138.2, 139.1, 172.9, 196.5; IR (KBr, cm^{-1}): 2975, 2926, 1761, 1686, 1604, 1453, 1378, 1244, 1123, 10489, 752,664; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1808.

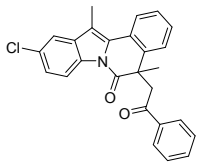
10-fluoro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ba)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded

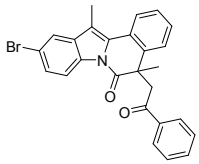
3aa. White solid; 60.7 mg, 77% yield; m.p. 219-220 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.63 (s, 3H), 4.06 (d, *J* = 18.2 Hz, 1H), 4.30 (d, *J* = 18.2 Hz, 1H), 7.06 (td, *J* = 2.5, 9.0 Hz, 1H), 7.22−7.28 (m, 3H), 7.31-7.35 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.4Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 8.05 (d, *J* = 7.9 Hz, 1H), 8.52 (dd, *J* = 4.8, 8.9 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.5, 48.7, 114.0 (d, J_F = 24.0 Hz), 112.8 (d, J_F = 24.4 Hz), 113.7 (d, J_F = 4.1 Hz), 117.7 (d, J_F = 8.9 Hz), 124.6, 125.5, 126.1, 126.9, 128.0, 128.0, 128.5, 130.6, 131.5, 133.3, 133.8 (d, J_F = 9.4 Hz), 136.1, 139.3, 160.2 (d, J_F = 239.1 Hz), 172.8, 196.4; IR (KBr, cm^{-1}): 2923, 2852, 1685, 1596, 1489, 1465, 1449, 1395, 1380, 1284, 1008, 951, 756, 690; HRMS (ESI) for $C_{26}H_{21}FNO_2^+$ $[M+H]^+$ calcd. 398.1551, found 398.1556.

10-chloro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ca)



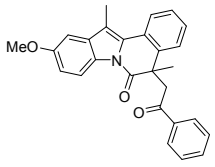
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ca**. White solid; 74.3 mg, 90% yield; m.p. 204-206 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.63 (s, 3H), 2.61 (s, 3H), 4.06 (d, *J* = 18.2 Hz,1H), 4.28 (d, *J* = 18.2 Hz, 1H), 7.20−7.33 (m, 4H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.86 (d, *J* = 7.4 Hz, 2H), 8.03 (d, *J* = 7.9 Hz, 1H), 8.49 (d, *J* =8.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 45.5, 48.6, 113.2, 117.6, 118.0, 124.6, 125.3, 125.5, 125.9, 126.9, 128.0, 128.1, 128.5, 129.6, 131.3, 132.6, 133.3, 133.9, 136.0, 139.2, 172.9, 196.4; IR (KBr, cm^{-1}): 2924, 2854, 1684, 1599, 1446, 1377, 1365, 1274, 1078, 1006, 750, 689, 660; HRMS (ESI) for $C_{26}H_{21}ClNO_2^+$ $[M+H]^+$ calcd.414.1255, found 414.1259.

10-bromo-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3da)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3da**. White solid; 71.3 mg, 78% yield; m.p. 185-187 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.64 (s, 3H), 4.06 (d, *J* = 18.2 Hz, 1H), 4.29 (d, *J* = 18.2 Hz, 1H), 7.22−7.28 (m, 2H), 7.32−7.37 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.44 (dd, *J* = 1.8, 8.7 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.72 (d, *J* = 1.8 Hz, 1H), 7.87 (d, *J* = 7.4 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.43 (d, *J* = 8.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.5, 45.6, 48.7, 113.2, 117.4, 118.0, 121.1, 124.6, 125.6, 126.0, 126.9, 128.0, 128.1, 128.5, 131.2, 133.0, 133.4, 134.3, 136.1, 139.3, 172.9, 196.4; IR (KBr, cm^{-1}): 2923, 2853, 1685, 1599, 1447, 1372, 1274, 1216, 945, 753, 691; HRMS (ESI) for $C_{26}H_{21}BrNO_2^+$ $[M+H]^+$ calcd.458.0750, found 458.0757.

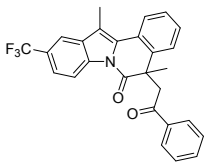
10-methoxy-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ea)



Purification by flash chromatography (PE/EA=20:1-5:1) afforded **3ea**. White solid; 67.8 mg, 83% yield; m.p. 209-210 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.63 (s, 3H), 2.64 (s, 3H), 3.88 (s, 3H), 4.04 (d, *J* = 18.2 Hz, 1H), 4.29 (d, *J* = 18.2 Hz, 1H), 6.96 (dd, *J* =

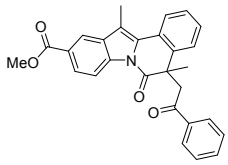
2.5, 8.9 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 7.18−7.26 (m, 2H), 7.29-7.33 (m, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.86-7.88 (m, 2H), 8.03 (d, *J* = 8.0 Hz, 1H), 8.46 (d, *J* = 8.9 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.6, 45.4, 48.5, 55.7, 101.5, 113.4, 114.0, 117.4, 124.5, 125.3, 126.4, 126.8, 127.6, 128.0, 128.5, 129.0, 130.7, 133.2, 133.6, 136.2, 139.2, 156.9, 172.5, 196.4; IR (KBr, cm^{-1}): 2984, 2916, 2849, 1741, 1688, 1603, 1468, 1448, 1375, 1242, 1047; HRMS (ESI) for $C_{27}H_{24}NO_3^+$ [M+H] $^+$ calcd.410.1751, found 410.1755

5,12-dimethyl-5-(2-oxo-2-phenylethyl)-10-(trifluoromethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3fa)



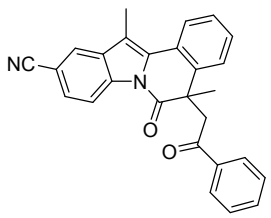
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3fa**. White solid; 62.7 mg, 70% yield; m.p. 186-188 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.66 (s, 3H), 2.71 (s, 3H), 4.10 (d, *J* = 18.2 Hz, 1H), 4.31 (d, *J* = 18.2 Hz, 1H), 7.23−7.30 (m, 2H), 7.34-7.42 (m, 3H), 7.50-7.55 (m, 1H), 7.60 (dd, *J* =1.2, 8.6 Hz, 1H), 7.87-7.89 (m, 3H), 8.08 (d, *J* = 7.9 Hz, 1H), 8.67 (d, *J* = 8.6 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.7, 48.7, 113.8, 115.6 (q, J_F = 4.1 Hz), 116.8, 122.0 (q, J_F = 3.5 Hz), 124.6, 124.8 (q, J_F = 270.3 Hz), 125.7, 125.8, 126.1 (q, J_F = 31.7 Hz), 127.0, 128.0, 128.3, 128.6, 131.7, 132.3, 133.4, 135.8, 135.9, 139.1, 173.2, 196.4; IR (KBr, cm^{-1}): 2971, 2926, 2868, 1686, 1598, 1448, 1394, 1326, 1271, 1118, 1051, 754, 689; HRMS (ESI) for $C_{27}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 448.1519, found 448.1524.

Methyl5,12-dimethyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-10 –carboxylate (3ga)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ga**. White solid; 66.0 mg, 76% yield; m.p. 230-231 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.66 (s, 3H), 2.73 (s, 3H), 3.96 (s, 3H), 4.09 (d, *J* = 18.2 Hz, 1H), 4.31 (d, *J* = 18.2 Hz, 1H), 7.23−7.29 (m, 2H), 7.33-7.42 (m, 3H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.88 (d, *J* = 7.4 Hz, 2H), 8.07 (t, *J* = 7.2 Hz, 2H), 8.35 (s, 1H), 8.60 (d, *J* = 8.6 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.7, 48.7, 52.1, 114.3, 116.3, 120.5, 124.6, 125.6, 125.7, 126.0, 126.7, 127.0, 128.0, 128.1, 128.5, 131.2, 132.4, 133.4, 136.1, 137.0, 139.1, 167.5, 173.2, 196.4; IR (KBr, cm^{-1}): 2923, 2852, 1762, 1685, 1658, 1605, 1448, 1374, 1247, 1107, 946, 915, 690; HRMS (ESI) for $C_{28}H_{24}NO_4^+$ [M+H] $^+$ calcd. 438.1700, found 438.1705.

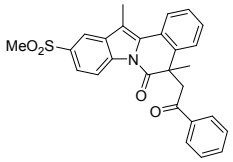
5,12-dimethyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-10-carbonitrile (3ha)



Purification by flash chromatography (PE/EA=20:1-5:1) afforded **3ha**. White solid; 67.8 mg, 84% yield; m.p. 235-238 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.67 (s, 3H), 2.70 (s, 3H), 4.13 (d, *J* = 18.3 Hz, 1H), 4.31 (d, *J* = 18.3 Hz, 1H), 7.30-7.31 (m, 2H), 7.37-7.44 (m, 3H), 7.53−7.57 (m, 1H), 7.61 (dd, *J* = 1.6, 8.5 Hz, 1H), 7.88-7.90 (m, 2H), 7.93 (d, *J* = 1.0 Hz,

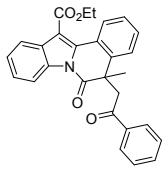
1H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.66 (d, *J* = 8.5 Hz,1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 45.7, 48.9, 107.1, 113.2, 117.3, 119.8, 123.0, 124.7, 125.5, 127.1, 128.0, 128.4, 128.6, 128.6, 132.2, 132.6, 133.5, 135.8, 136.1, 139.2, 173.3, 196.4; IR (KBr, cm^{-1}): 2972, 2924, 2869, 2225, 1684, 1600, 1457, 1362, 1242, 1217, 948, 756, 690; HRMS (ESI) for $C_{27}H_{21}N_2O_2^+$ $[M+H]^+$ calcd. 405.1598, found 405.1603.

5,12-dimethyl-10-(methylsulfonyl)-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ia)



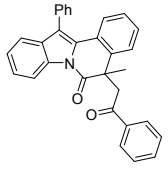
Purification by flash chromatography (PE/EA=5:1-2:1) afforded **3ia**. White solid; 73.1 mg, 80% yield; m.p. 262-264 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.69 (s, 3H), 2.75 (s, 3H), 3.12 (s, 3H), 4.14 (d, *J* = 18.3 Hz, 1H), 4.32 (d, *J* = 18.3 Hz, 1H), 7.30-7.33 (m, 2H), 7.37-7.44 (m, 3H), 7.53−7.57 (m, 1H), 7.88-7.92 (m, 3H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 1.5 Hz, 1H), 8.75 (d, *J* = 8.7 Hz,1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 30.5, 45.0, 45.7, 48.9, 113.9, 117.3, 118.4, 123.8, 124.7, 125.6, 125.8, 127.1, 128.0, 128.6, 128.6, 132.5, 132.7, 133.6, 135.7, 135.8, 136.8, 139.1, 173.4, 196.5; IR (KBr, cm^{-1}): 2988, 2926, 1761, 1684, 1599, 1549, 1452, 1369, 1244, 1147, 1048, 757, 691; HRMS (ESI) for $C_{27}H_{24}NO_2S^+$ $[M+H]^+$ calcd. 458.1421, found 458.1417.

Ethyl5-methyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-12-carboxylate (3ja)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ja**. White solid; 73.4 mg, 84% yield; m.p. 97-98 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.50 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 3H), 4.10 (d, *J* = 18.2 Hz, 1H), 4.29 (d, *J* = 18.2 Hz, 1H), 4.50-4.62 (m, 2H), 7.21−7.23 (m, 1H), 7.26-7.33 (m, 2H), 7.37-7.42 (m, 4H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.98-8.02 (m, 1H), 8.52-8.55 (m, 1H), 8.59-8.62 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 14.3, 30.2, 46.0, 48.1, 61.1, 110.2, 116.5, 121.0, 123.5, 123.8, 124.9, 125.9, 126.7, 128.0, 128.4, 128.5, 128.9, 130.1, 133.4, 134.2, 135.9, 137.1, 140.1, 165.8, 173.5, 196.0; IR (KBr, cm^{-1}): 3063, 2979, 2931, 1706, 1582, 1550, 1449, 1332, 1250, 1150, 1113, 1034, 755, 689; HRMS (ESI) for $C_{28}H_{24}NO_4^+$ $[M+H]^+$ calcd. 438.1700, found 438.1706.

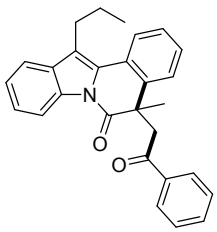
5-methyl-5-(2-oxo-2-phenylethyl)-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (3ka)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ka**. White solid; 77.0 mg, 87% yield; m.p. 88-90 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.71 (s, 3H), 4.08 (d, *J* = 18.1 Hz, 1H), 4.34 (d, *J* = 18.1 Hz, 1H), 6.93-6.97 (m, 1H), 7.13 (td, *J* = 1.2, 7.3, Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.24-7.33 (m, 2H), 7.36-7.42 (m, 3H), 7.47-7.57 (m, 7H), 7.89-7.91 (m, 2H), 8.61 (d, *J* = 8.2 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 30.5, 45.8, 48.3, 116.5, 119.3, 120.1, 124.2, 124.2, 125.2, 125.6, 125.7, 126.3, 127.9, 128.0, 128.2, 128.5, 129.1, 129.8, 130.3, 132.3, 133.2, 134.3, 134.3, 136.1, 139.2,

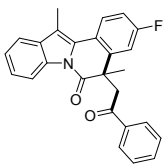
173.2, 196.3; IR (KBr, cm^{-1}): 3061, 2975, 2926, 1734, 1686, 1604, 1448, 1362, 1234, 1007, 944, 753, 690;HRMS (ESI) for $C_{31}H_{24}NO_2^+$ $[M+H]^+$ calcd. 442.1802, found 442.1808.

5-methyl-5-(2-oxo-2-phenylethyl)-12-propylindolo[2,1-a]isoquinolin-6(5H)-one (3la)



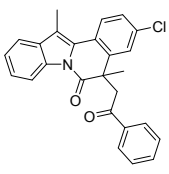
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ea**. White solid; 68.1 mg, 84% yield; m.p. 140-143 °C; **^{1}H NMR (400MHz, $CDCl_3$)** δ (ppm) = 1.16 (t, *J* = 7.3 Hz, 3H), 1.62 (s, 3H), 1.82-1.91 (m, 2H), 3.11 (t, *J* = 7.8 Hz, 2H), 4.07 (d, *J* = 18.2 Hz, 1H), 4.32 (d, *J* = 18.2 Hz, 1H), 7.19-7.26 (m, 2H), 7.32-7.41 (m, 5H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.62 (d, *J* = 6.8 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 8.58 (d, *J* = 8.3 Hz,1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 14.6, 22.3, 27.4, 30.6, 45.6, 48.2, 116.6, 118.4, 119.6, 123.9, 124.4, 125.1, 125.4, 126.1, 126.9, 127.8, 128.0, 128.5, 129.5, 132.2, 133.3, 134.4, 136.1, 139.0, 173.0, 196.3; IR (KBr, cm^{-1}): 3063, 2968, 2924, 1734, 1685, 1604, 1448, 1362, 1234, 1007, 944, 753, 690; HRMS (ESI) for $C_{28}H_{26}NO_2^+$ $[M+H]^+$ calcd. 408.1958, found 408.1956.

3-fluoro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ma)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ma**. White solid; 61.0 mg, 77% yield; m.p. 188-190 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.62 (s, 3H), 2.64 (s, 3H), 3.95 (d, *J* = 18.3 Hz, 1H), 4.35 (d, *J* = 18.3 Hz 1H), 6.96 (dd，*J* = 2.6， 9.9 Hz, 1H), 7.03 (td， *J* = 2.6, 8.7 Hz, 1H), 7.32-7.41 (m, 4H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.58-7.60 (m, 1H), 7.86-7.88 (m, 2H), 8.03 (dd, *J* = 5.7 8.9 Hz, 1H), 8.54-8.57 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.4, 30.4, 45.8 (d, J_F = 1.1 Hz), 48.5, 111.6 (d, J_F = 22.6 Hz), 113.7 (d, J_F = 1.7 Hz), 114.2 (d, J_F = 21.6 Hz), 116.5, 118.3, 122.9 (d, J_F = 3.1 Hz), 124.0, 125.4, 127.3 (d, J_F = 8.2 Hz), 128.0, 128.5, 129.2, 132.4, 133.4, 134.2, 136.0, 141.8 (d, J_F = 6.7 Hz), 162.0 (d, J_F = 247.0 Hz), 172.2, 196.2; IR (KBr, cm^{-1}): 3063, 2968, 2924, 2869, 1685, 1600, 1595, 1453, 1371, 1343, 1217, 1007, 760, 689; HRMS (ESI) for $C_{26}H_{21}FNO_2^+$ $[M+H]^+$ calcd. 398.1551, found 698.1553.

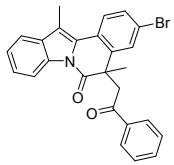
3-chloro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3na)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3na**. White solid; 69.4 mg, 84% yield; m.p. 131-132 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.64 (s, 3H), 2.66 (s, 3H), 3.97 (d, *J* = 18.3 Hz, 1H), 4.35 (d, *J* = 18.3 Hz 1H), 7.23 (t，*J* = 3.2 Hz, 1H), 7.30 (dd， *J* = 2.1, 8.6 Hz, 1H), 7.34-7.37 (m, 2H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.59-7.62 (m, 1H), 7.88-7.90 (m, 2H), 7.99 (d, *J* = 8.6 Hz, 1H), 8.84-8.56 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 45.6, 48.7, 114.7, 116.6, 118.4, 124.1, 124.8, 125.1, 125.7, 126.6, 127.2, 128.1, 128.6, 129.1,

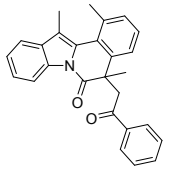
132.3, 133.3, 133.5, 134.4, 136.0, 141.1, 172.2, 196.2; IR (KBr, cm^{-1}): 3062, 2973, 2926, 2869, 1684, 1598, 1452, 1384, 1222, 1007, 755, 688; HRMS (ESI) for $C_{26}H_{21}ClNO_2^+$ $[M+H]^+$ calcd. 414.1255, found 414.1262.

3-bromo-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3oa)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3oa**. White solid; 84.3 mg, 92% yield; m.p. 201-202 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.66 (s, 3H), 2.66 (s, 3H), 4.00 (d, *J* = 18.3 Hz, 1H), 4.38 (d, *J* = 18.3 Hz 1H), 7.35-7.48 (m, 6H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.62-7.64 (m, 1H), 7.91-7.95 (m, 3H), 8.59-8.61 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 30.4, 45.6, 48.6, 114.8, 116.6, 118.4, 121.4, 124.1, 125.4, 125.7, 126.7, 127.7, 128.0, 128.5, 129.1, 130.1, 132.2, 133.4, 134.3, 135.9, 141.3, 172.1, 196.2; IR (KBr, cm^{-1}): 3062, 2972, 2925, 2868, 1732, 1685, 1597, 1451, 1383, 1341, 1242, 1217, 1007, 653, 688; HRMS (ESI) for $C_{26}H_{21}BrNO_2^+$ $[M+H]^+$ calcd. 458.0750, found 458.0757.

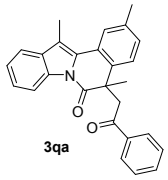
1,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3pa)

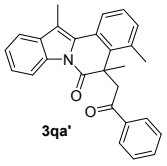


Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3pa**. White solid; 62.9 mg, 80% yield; m.p. 160-161 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.44 (s, 3H), 2.37 (s, 3H), 2.50 (s, 3H), 4.00 (d, *J* = 18.1 Hz, 1H), 4.20 (d, *J* = 18.1 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 1H), 7.33-7.40 (m, 2H), 7.43 (t, *J* = 7.9 Hz, 2H), 7.53-7.60 (m, 2H), 7.95 (d, *J* = 7.2 Hz, 2H), 8.40-8.42 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 13.0, 22.1, 28.3, 46.0, 47.5, 115.7, 115.8, 118.3, 120.5, 123.7, 125.5, 125.6, 128.0, 128.2, 128.5, 130.2, 130.9, 132.6, 133.2, 135.3, 135.6, 136.4, 139.5, 172.2, 196.1; IR (KBr, cm^{-1}): 3062, 2968, 2923, 2868, 1734, 1687, 1599, 1449, 1352, 1216, 1060, 1007, 749, 691; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1807.

2,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3qa) (major)

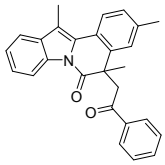
and 4,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3qa') (minor)





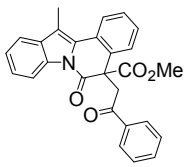
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **mixture of 3qa and 3qa'**. White solid; 66.8 mg, 85% yield; m.p. 171-173 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.62 (s, 3H), 1.75 (s, 0.75H), 2.38 (s, 3H), 2.52 (s, 0.75H), 2.66 (s, 0.75H), 2.69 (s, 3H), 4.04 (d, *J* = 18.2 Hz, 1H), 4.29 (d, *J* = 18.2 Hz, 1H), 4.42 (d, *J* = 18.8 Hz, 0.25H), 4.58 (d, *J* = 18.7 Hz, 0.25H), 7.03 (d, *J* = 8.2 Hz, 1.25H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 0.25H), 7.32-7.40 (m, 5H), 7.50 (t, *J* = 7.4 Hz, 1.25H), 7.60-7.62 (m, 1.25H), 7.86-7.89 (m, 3.5H), 7.97 (d, *J* = 7.8 Hz, 0.25H), 8.54-8.59 (m, 1.25H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 12.0, 21.4, 23.8, 26.5, 30.6, 45.3, 46.9, 47.0, 48.4, 113.7, 114.0, 116.5, 116.6, 118.2, 123.8, 123.9, 124.4, 124.4, 125.2, 125.3, 125.9, 126.2, 126.7, 127.4, 127.9, 128.0, 128.4, 128.5, 128.7, 130.0, 130.2, 132.4, 132.6, 132.8, 134.0, 134.1, 134.3, 135.8, 136.1, 136.2, 136.4, 173.1, 173.6, 196.4, 196.7; IR (KBr, cm^{-1}): 3061, 2973, 2923, 2869, 1735, 1685, 1599, 1452, 1384, 1217, 1007, 753, 689; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1806.

3,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ra)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ra**. White solid; 73.6 mg, 94% yield; m.p. 154-155 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.62 (s, 3H), 2.27 (s, 3H), 2.64 (s, 3H), 4.03 (d, *J* = 18.2 Hz, 1H), 4.30 (d, *J* = 18.2 Hz, 1H), 7.05 (s, 1H), 7.12 (d, *J* = 8.1 Hz, 1H), 7.30-7.38 (m, 4H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.56-7.58 (m, 1H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 1H), 8.56-8.58 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.4, 21.4, 30.6, 45.5, 48.5, 113.3, 116.5, 118.1, 123.7, 123.8, 125.0, 125.1, 125.3, 127.8, 128.0, 128.4, 130.1, 132.5, 133.2, 134.2, 136.2, 137.5, 139.1, 173.0, 196.3; IR (KBr, cm^{-1}): 3059, 3032, 2973, 2924, 1734, 1684, 1600, 1453, 1372, 1217, 1007, 755, 689; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ $[M+H]^+$ calcd. 394.1802, found 394.1805.

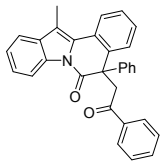
Methyl 12-methyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-5-carboxylate (3ra)



Purification by flash chromatography (PE/EA=10-5:1) afforded **3sa**. White solid; 50.9 mg, 60% yield; m.p. 242-244 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 2.70 (s, 3H), 3.57 (s, 3H), 4.54 (d, *J* = 18.6 Hz, 1H), 4.61 (d, *J* = 18.6 Hz, 1H), 7.20-7.24 (m, 1H), 7.35-7.40 (m, 6H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.61-7.63 (m, 1H), 7.89 (d, *J* = 7.4 Hz, 2H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.56-8.58 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.7, 46.7, 53.5, 56.2, 115.5, 116.8, 118.5, 124.3, 125.3, 125.4, 125.8, 127.6, 127.6, 128.1, 128.1, 128.5, 129.8, 132.4, 133.4, 134.5, 135.9, 166.7, 170.4, 195.6; IR (KBr, cm^{-1}): 3064, 2954, 2929, 1743, 1686, 1599, 1453, 1400, 1228, 1180, 750, 690; HRMS

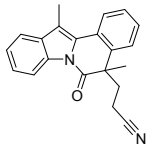
(ESI) for $C_{27}H_{22}NO_4^+$ [M+H] $^+$ calcd. 424.1543, found 424.1542.

12-methyl-5-(2-oxo-2-phenylethyl)-5-phenylindolo[2,1-a]isoquinolin-6(5H)-one (3ta)



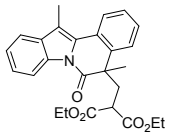
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **3ta**. White solid; 48.5 mg, 55% yield; m.p. 258-260 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 2.68 (s, 3H), 4.42 (d, *J* = 17.9 Hz, 1H), 4.86 (d, *J* = 17.9 Hz, 1H), 7.15-7.25 (m, 7H), 7.28-7.33 (m, 2H), 7.36-7.43 (m, 3H), 7.51-7.58 (m, 2H), 7.94 (d, *J* = 7.3 Hz, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.47-8.49 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 47.9, 53.8, 114.6, 116.5, 118.3, 123.9, 125.4, 125.5, 126.5, 127.1, 127.2, 127.5, 127.7, 127.9, 128.1, 128.6, 128.8, 130.0, 132.4, 133.3, 134.6, 136.4, 137.7, 142.4, 170.5, 196.2; IR (KBr, cm^{-1}): 3062, 2926, 2867, 1687, 1599, 1451, 1369, 1339, 1217, 1175, 906, 748, 691; HRMS (ESI) for $C_{31}H_{24}NO_2^+$ [M+H] $^+$ calcd. 442.1802, found 442.1800.

3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)propanenitrile (5aa)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **5aa**. Colorless liquid; 39.1 mg, 62% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.69 (s, 3H), 1.93-2.04 (m, 1H), 2.07-2.15 (m, 1H), 2.27-2.35 (m, 1H), 2.65 (s, 3H), 2.78-2.85 (m, 1H), 7.35-7.48 (m, 5H), 7.59-7.61 (m, 1H), 8.03 (d, *J* = 7.4 Hz, 1H), 8.55-8.57 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.4, 13.5, 29.1, 36.7, 47.9, 115.2, 116.6, 118.5, 118.7, 124.5, 125.4, 125.9, 126.1, 126.7, 127.8, 128.4, 129.0, 132.4, 134.0, 136.1, 171.1; IR (KBr, cm^{-1}): 3065, 2976, 2929, 2871, 2247, 1690, 1604, 1452, 1396, 1336, 1242, 1211, 755; HRMS (ESI) for $C_{21}H_{19}N_2O^+$ [M+H] $^+$ calcd. 315.1492, found 315.1494.

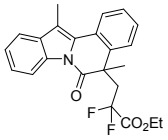
Diethyl 2-((5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl) methyl)malonate (5ab)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **5ab**. White solid; 64.1 mg, 74% yield; m.p. 85-86 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.97-1.04 (m, 6H), 1.71 (s, 3H), 2.65 (s, 3H), 2.69 (dd, *J* = 6.3, 14.4 Hz, 1H), 3.01 (dd, *J* = 6.9, 14.4 Hz, 1H), 3.14 (t, *J* = 6.8 Hz, 1H), 3.68-3.80 (m, 2H), 3.81-3.89 (m, 1H), 3.91-3.99 (m, 1H), 7.32-7.42 (m, 4H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.57-7.59 (m, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 8.57 (d, *J* = 7.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.4, 13.5, 13.6, 29.3, 39.6, 47.2, 48.7, 61.4, 114.4, 116.6, 118.3, 124.2, 125.0, 125.6, 126.6, 126.7, 127.3, 127.8, 129.4, 132.3, 134.1, 136.9, 168.7, 171.5; IR (KBr, cm^{-1}): 2981,2935, 1732, 1692, 1452, 1369, 1334, 1236, 1155, 1026, 860, 755; HRMS (ESI) for $C_{26}H_{28}NO_5^+$ [M+H] $^+$ calcd. 434.1962, found 434.1961.

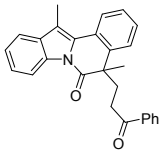
Ethyl 3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)-2,2-

Difluoropropanoate (5ac)



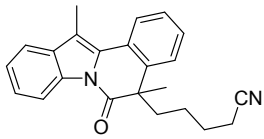
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **5ac**. White solid; 57.6 mg, 73% yield; m.p. 86-87 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.12 (t, *J* = 7.1 Hz, 3H), 1.71 (s, 3H), 2.66 (s, 3H), 2.90-3.02 (m, 1H), 3.40 (q, *J* = 14.7 Hz, 1H), 3.84-3.96 (m, 2H), 7.33-7.44 (m, 5H), 7.59-7.61 (m, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.60-8.62 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.6, 13.6, 31.4, 44.5 (q, J_F = 23.2 Hz), 62.9, 114.7 (dd, J_F = 3.7, 249.3 Hz), 114.9, 116.8, 118.5, 124.4, 125.1, 125.9, 126.3, 127.2, 127.4, 127.6, 129.4, 132.5, 134.3, 135.7, 163.5 (t, J_F = 32.0 Hz), 171.2; **^{19}F NMR (376 MHz, CDCl3)** δ(ppm) = -99.09 (d, *J* = 265.6 Hz, 1F), -103.94 (d, *J* = 265.6 Hz, 1F); IR (KBr, cm^{-1}): 3066, 2983, 2938, 2873, 1766, 1692, 1452, 1374, 1337, 1208, 1064, 1019, 755;HRMS (ESI) for $C_{23}H_{21}F_2NO_3^+$ [M+H] $^+$ calcd. 398.1562, found 398.1565.

5,12-dimethyl-5-(3-oxo-3-phenylpropyl)indolo[2,1-a]isoquinolin-6(5H)-one (5ad)



Purification by flash chromatography (PE/EA=20:1-10:1) afforded **5ad**. White solid; 66.8 mg, 85% yield; m.p. 86-87 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.72 (s, 3H), 2.43-2.54 (m, 2H), 2.64 (s, 3H), 2.73-2.90 (m, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.34-7.49 (m, 6H), 7.58-7.60 (m, 1H), 7.70-7.72 (m, 2H), 7.99-8.01 (m, 1H); 8.61-8.63 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.4, 29.0, 34.3, 35.8, 48.0, 114.4, 116.5, 118.4, 124.2, 125.1, 125.7, 126.2, 126.6, 127.3, 127.9, 128.2, 128.3, 129.6, 132.4, 132.9, 134.1, 136.4, 137.8, 172.4, 199.0; IR (KBr, cm^{-1}): 3062, 2974, 2929, 2869, 1687, 1599, 1541, 1365, 1336, 1212, 754, 691; HRMS (ESI) for $C_{27}H_{24}NO_2^+$ [M+H] $^+$ calcd. 394.1802, found 394.1807.

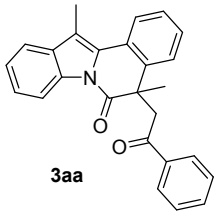
5-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)pentanenitrile (5ae)



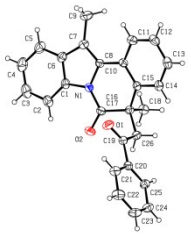
Purification by flash chromatography (PE/EA=20:1-10:1) afforded **5ae**. White solid; 28.0 mg, 82% yield; m.p. 47-48 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.02-1.14 (m, 2H), 1.45-1.60 (m, 2H), 1.67 (s, 3H), 1.91-1.98 (m, 1H), 2.08-2.24 (m, 2H), 2.35-2.42 (m, 1H), 2.66 (s, 3H), 7.35-7.44 (m, 5H), 7.59-7.61 (m, 1H), 8.01-8.05 (m, 1H); 8.58-8.60 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 11.5, 16.8, 24.4, 25.4, 29.0, 41.4, 48.3, 114.3, 116.6, 118.4, 119.4, 124.2, 125.1, 125.7, 126.2, 126.5, 127.2, 128.1, 129.6, 132.4, 134.0, 138.0, 172.7; IR (KBr, cm^{-1}): 3063, 2932, 2866, 2313, 1761, 1690, 1600, 1452, 1366, 1336, 1244, 756; HRMS (ESI) for $C_{23}H_{23}N_2O^+$ [M+H] $^+$calcd. 343.1805, found 343.1803.

6. X-Ray Crystallographic Data of 3aa

The crystal structure **3aa** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: CCDC 1892795.



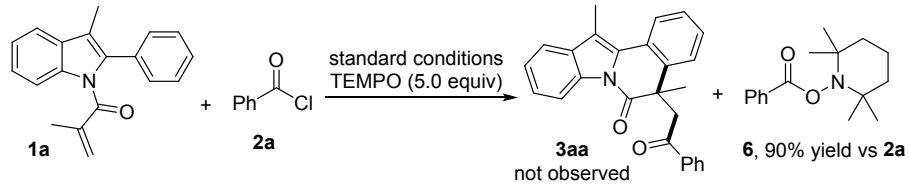
3aa



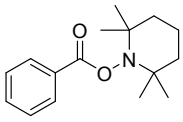
Bond precision:	C-C = 0.0022 A		Wavelength= 1.54184
Cell:	a=14.7360(8)	b=11.6168(7)	c=11.8487(7)
	alpha=90	beta=108.619 (6)	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	1922.2(2)		1922.16(19)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2ybc		-P 2ybc
Moiety formula	C26 H21 N O2		C26 H21 N O2
Sum formula	C26 H21 N O2		C26 H21 N O2
Mr	379.44		379.44
Dx,g cm-3	1.311		1.311
Z	4		4
Mu (mm-1)	0.652		0.0.652
F000	800.0		800.0
F000’	802.29		
h,k,lmax	17,13,14		17,13,14
Nref	3394		3303
Tmin,Tmax	0.875,0.913		0.907,1.000
Tmin’	0.872		
Correction method= # Reported T Limits: Tmin=0.907 Tmax=1.000			
AbsCorr = MULTI-SCAN			
Data completeness= 0.973			Theta(max)= 66.590
R(reflections)= 0.0375(2874)			wR2(reflections)= 0.1017(3303)
S = 1.070		Npar= 264	

7. Mechanistic Studies

7.1 Radical trapping experiments



The radical trapping experiments were conducted with **1a** and **2a** under the standard conditions with TEMPO (5.0 equiv.) as the radical scavenger. The reaction could be terminated completely, while TEMPO-trapped product **6** was observed in 90% yield. The results suggest an acyl radical pathway.



Purification by flash chromatography (PE/EA = 30:1) afforded **6**. 94.0 mg, White solid; 90% yield; m.p. 66-67 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.12 (s, 6H), 1.28 (s, 6H), 1.46 (d, *J* = 12.0 Hz, 1H), 1.57-1.82 (m, 5H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.0 Hz, 1H), 8.08 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 14.7, 18.5, 29.7, 36.7, 58.0, 126.2, 127.2, 127.4, 130.6, 164.0; IR (KBr, cm^{-1}): 2976, 2940, 1741, 1599, 1452, 1364, 1253, 1177; 1083, 1062, 913, 717, 650; HRMS (ESI) for $C_{16}H_{24}NO_2^+$ [M+H] $^+$calcd. 262.1802, found 262.1797.

7.2 Stern-Volmer fluorescence quenching experiments

Stern-Volmer fluorescence quenching experiments were run with freshly prepared solutions of 0.1 mM *fac*-Ir(ppy)$_3$ in degassed dry CH_3CN added the appropriate amount of a quencher in a screw-top quartz cuvette at room temperature. The solutions were irradiated at 395 nm and fluorescence was measured from 450 nm to 650 nm. Control experiments showed that the excited state * *fac*-Ir(ppy)$_3$ was mainly quenched by benzoyl chloride **2a**.

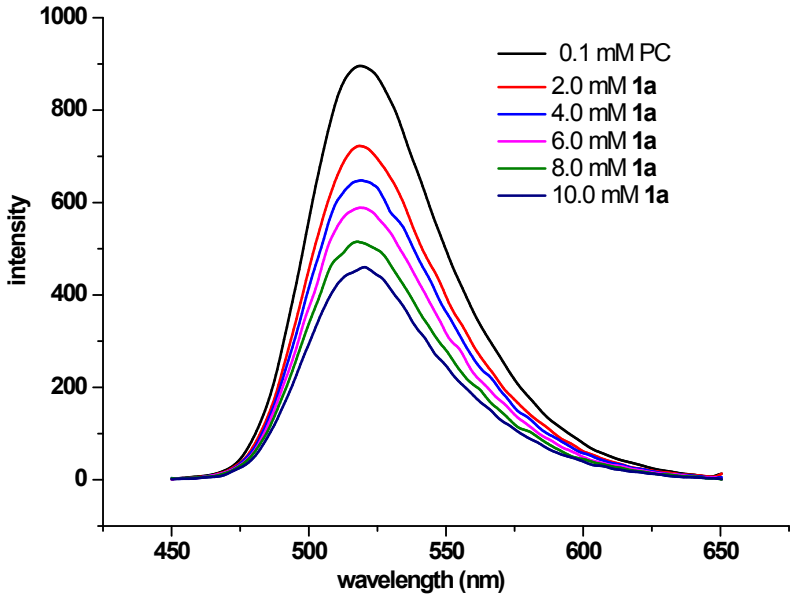


Figure S1. Fluorescence quenching experiments date with *fac*-Ir(ppy)$_3$ and variable **1a** (mM)

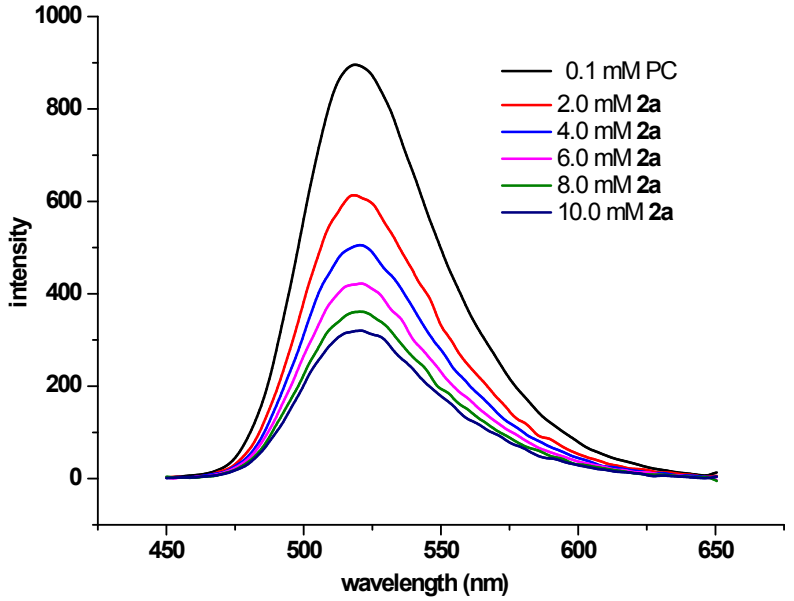


Figure S2. Fluorescence quenching experiments date with *fac*-Ir(ppy)$_3$ and variable **2a** (mM)

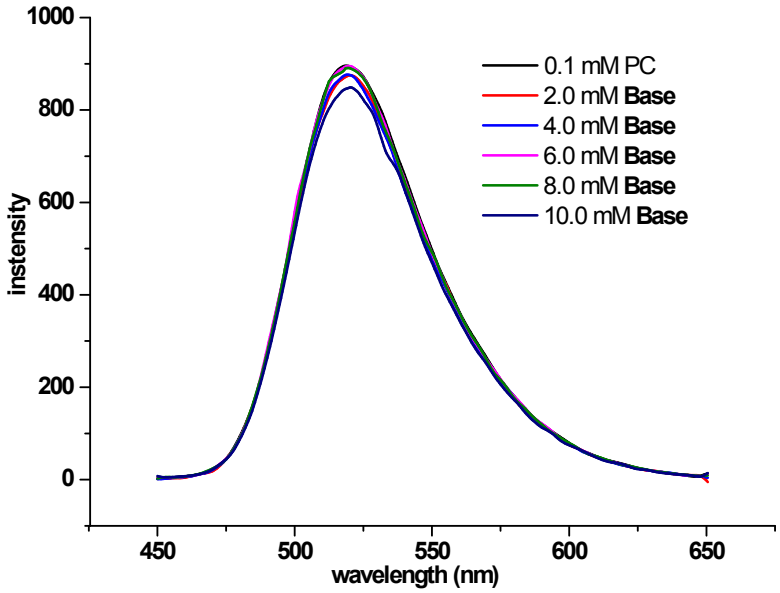


Figure S3. Fluorescence quenching experiments date with *fac*-Ir(ppy)$_3$ and variable 2,4,6-collidine (Base, mM)

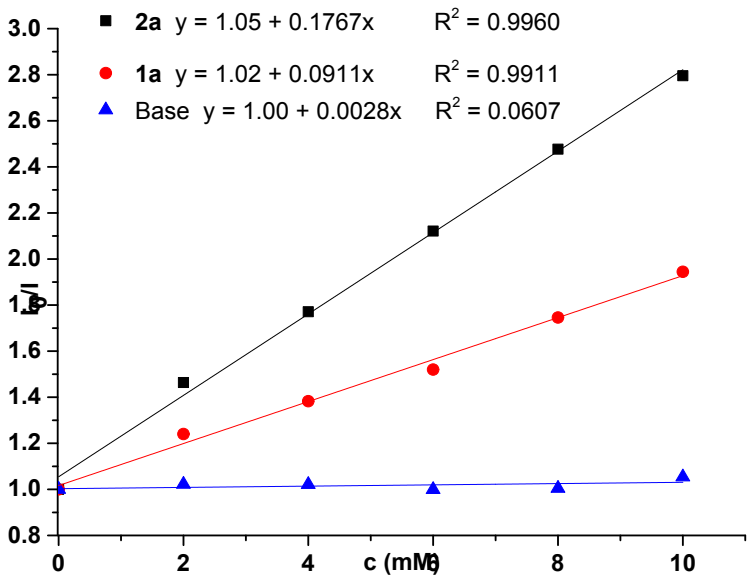


Figure S4. Stern-Volmer plots of *fac*-Ir(ppy)$_3$ with different quenchers

7.3 Measurement of quantum yield

According to the procedure of Yoon, [8] the photon flux of the LED was determined by standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (2.21 g) in 30 mL of a 0.05 M H_2SO_4 solution. A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (50 mg) and sodium acetate (11.25 g) in 50 mL of a 0.5 M solution H_2SO_4. Both solutions were stored in the dark. To determine the photon flux of the LEDs, the ferrioxalate solution (2.0 mL) was placed in a cuvette and irradiated for 90 s at λ_{max} = 420 nm. After irradiation, the phenanthroline solution (0.35 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 h to allow the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was measured at 510 nm. A nonirradiated sample was also prepared and the absorbance at 510 nm was measured. Conversion was calculated using eq. 1.

$$\text{mol } Fe^{2+} = \frac{V \cdot \Delta A}{l \cdot \varepsilon} \qquad (1)$$

where V is the total volume (0.00235 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.00 cm), and ε is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 L mol^{-1} cm^{-1}).

$$photo\ flux = \frac{mol\ Fe^{2+}}{\Phi \cdot t \cdot f} \qquad (2)$$

where Φ is the quantum yield for the ferrioxalate actinometer (1.12 at λ_{ex} = 420 nm), t is the irradiation time (90 s), and f is the fraction of light absorbed at λ_{ex} = 420 nm by the ferrioxalate actinometer. This value is calculated using eq. 3 where A (420 nm) is the absorbance of the ferrioxalate solution at 420 nm.

$$f = 1 - 10^{-A(420\ nm)} \qquad (3)$$

$$mol\ Fe^{2+} = \frac{V \cdot \Delta A}{l \cdot \varepsilon} = \frac{0.00235\ L \cdot 0.763}{1cm \cdot 11100\ L\ mol^{-1}\ cm^{-1}} = 1.62 \times 10^{-7}\ mol$$

$$photo\ flux = \frac{mol\ Fe^{2+}}{\Phi \cdot t \cdot f} = \frac{1.62 \times 10^{-7}}{1.12 \cdot 90 \cdot 1} = 1.61 \times 10^{-9}\ einstein \cdot s^{-1}$$

Determination of the reaction quantum yield at 420 nm and quantum yield measurement was performed in an oven-dried 20 mL quartz vial with a magnetic

stirring bar. Acyl chloride **2a** (0.4 mmol) and 2,4,6-collidine (0.25 mmol) were added to a solution of substrate **1a** (0.2 mmol) and photocatalyst *fac*-Ir(ppy)$_3$ (3 mol%) in dry CH_3CN (4 mL) at room temperature. The mixture was degassed by three cycles of freeze-pump-thaw and then irradiated in Parallel Light Reactor (WP-TEC-1020) for for 18000 s (5.0 h). The reaction mixture was concentrated under reduced pressure, and the resulting mixture was rapid filtered by flash column chromatography on silica gel. The crude yield of the product **3aa** was determined by ^{1}H NMR based on a 1,3,5-trimethoxybenzene standard and the final yield was 25% (5.0 x 10^{-5} mol). The reaction quantum yield (Φ) was determined using eq. 4, where the photon flux is $1.61 \cdot 10^{-9}$ E s^{-1} (determined by actinometry as described above), t is the reaction time (18000 s) and f is the fraction of incident light absorbed by the reaction mixture, determined using eq. 3 (A >3 indicating that the fraction of light absorbed is >0.999).

Φ = Mole number for product/Mole number for absorption of photons

$$\Phi = \frac{Mol\ product}{flux * t * f} = \frac{Mol\ product}{flux * t * f} = 1.73 \qquad \text{(eq.4)}$$

We calculated the quantum yield of the model reaction of **1a** with **2a** to be 1.73. This result shows that the reaction contains radical chain propagation process.

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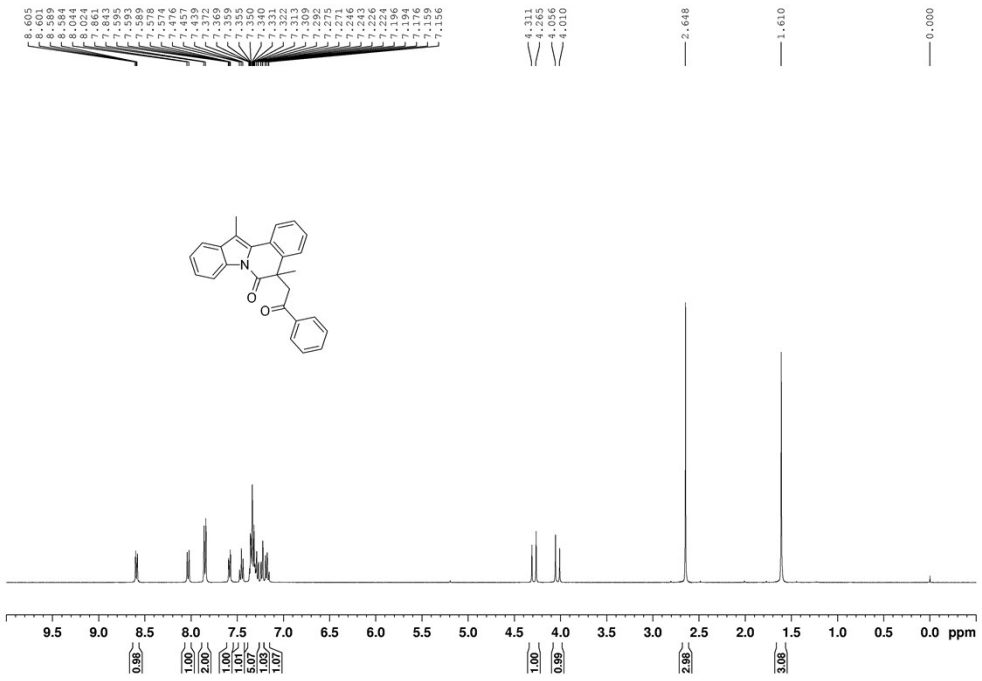
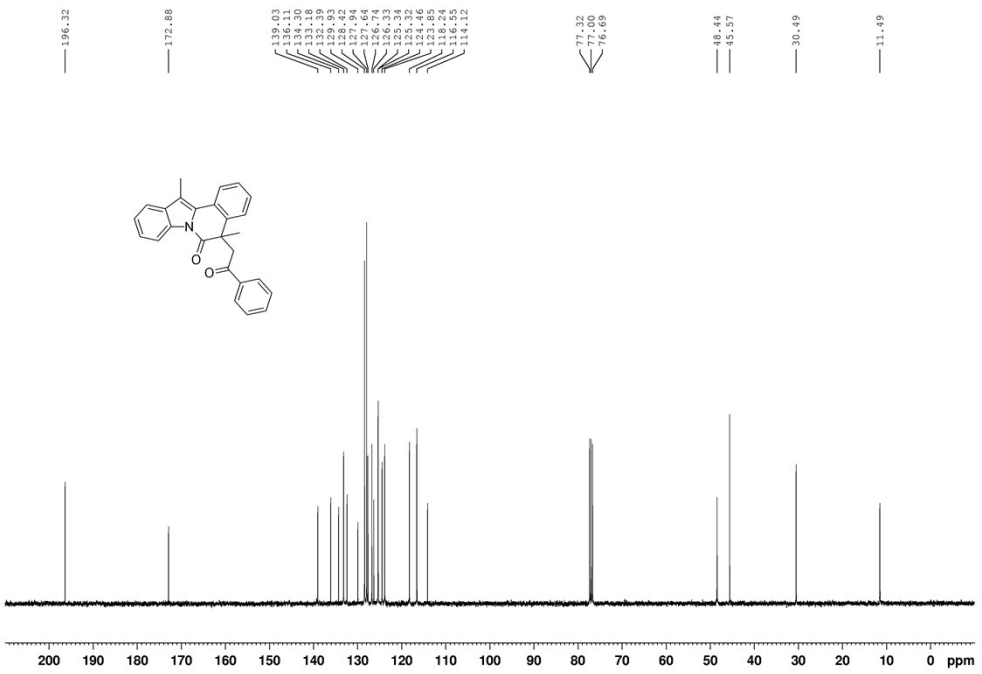
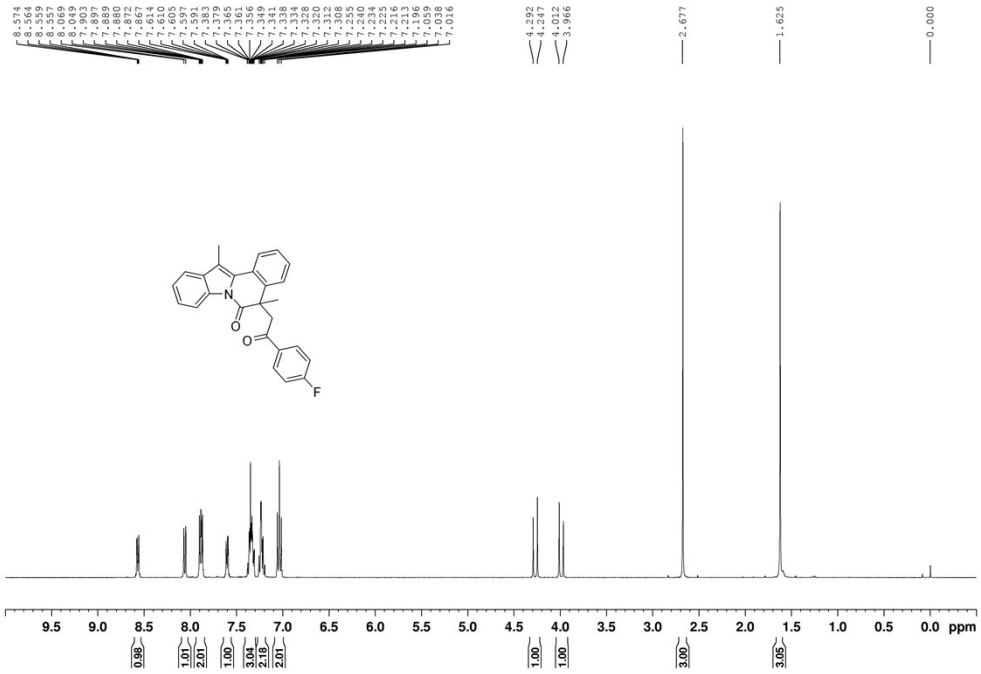
8. NMR Data of Products

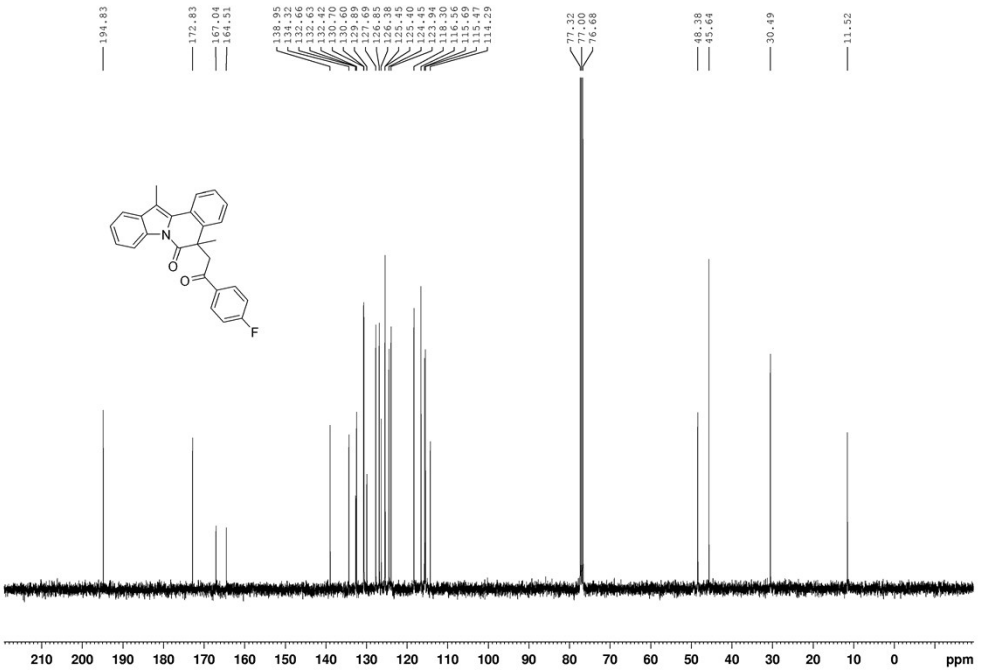
5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3aa)





5-(2-(4-fluorophenyl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ab)





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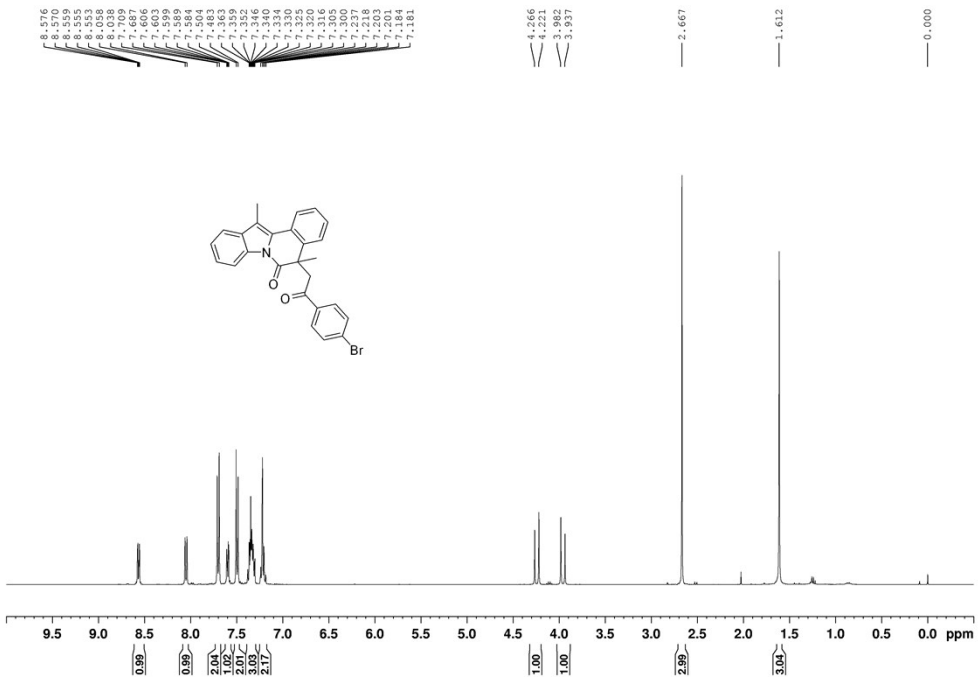
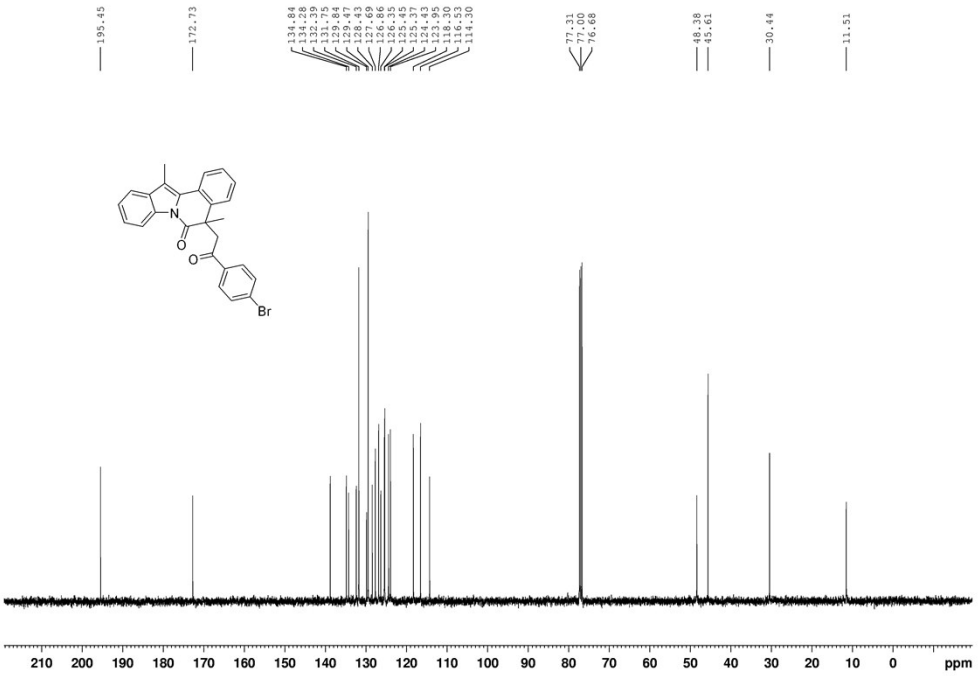
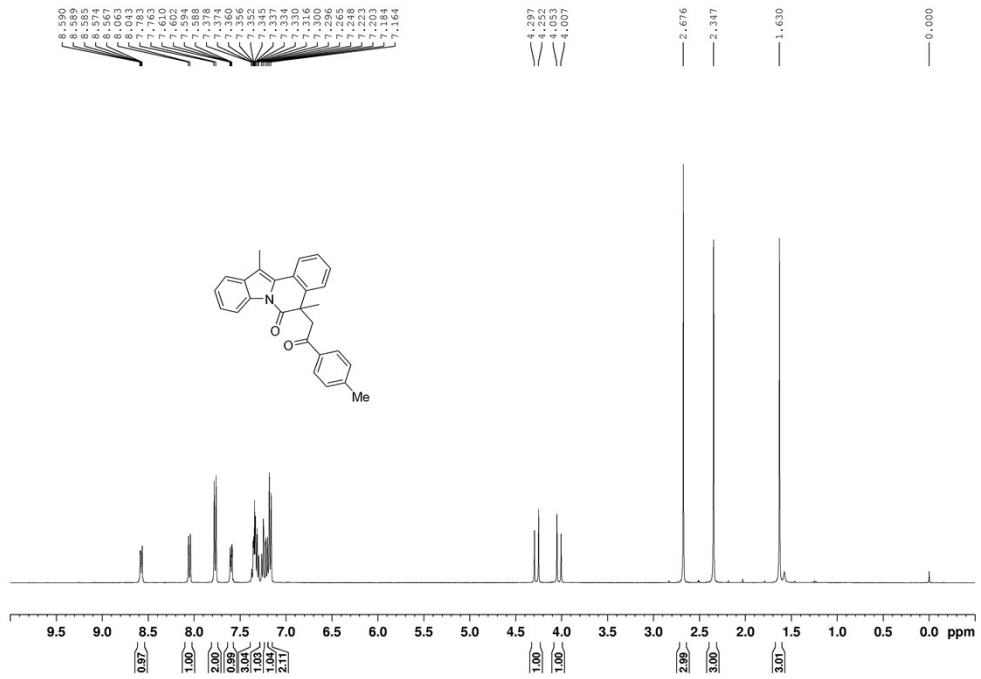
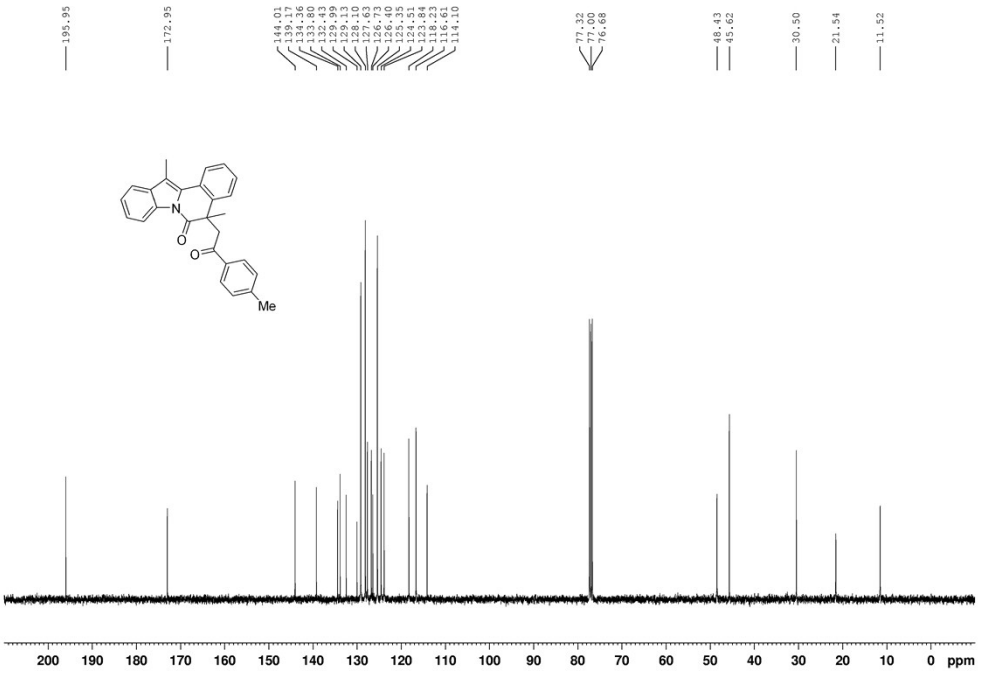




5,12-dimethyl-5-(2-oxo-2-(p-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ad)





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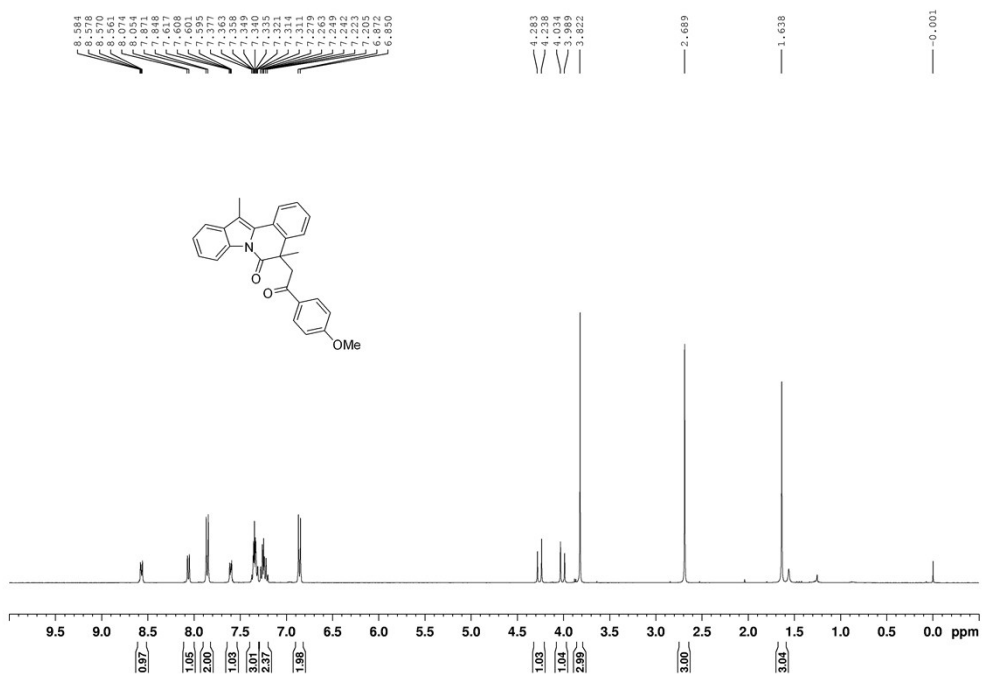

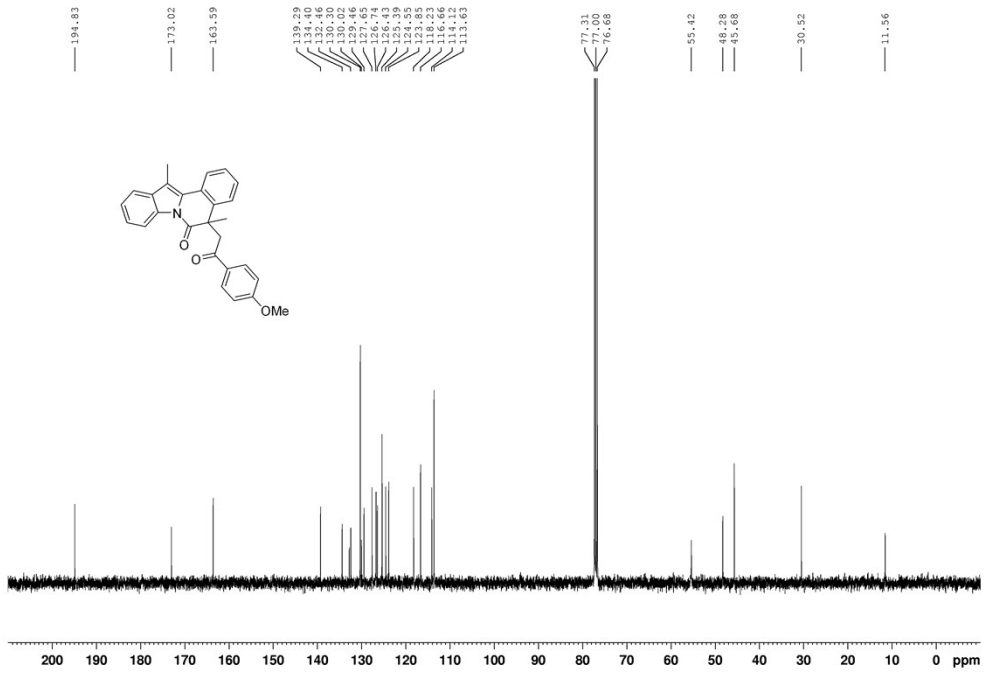

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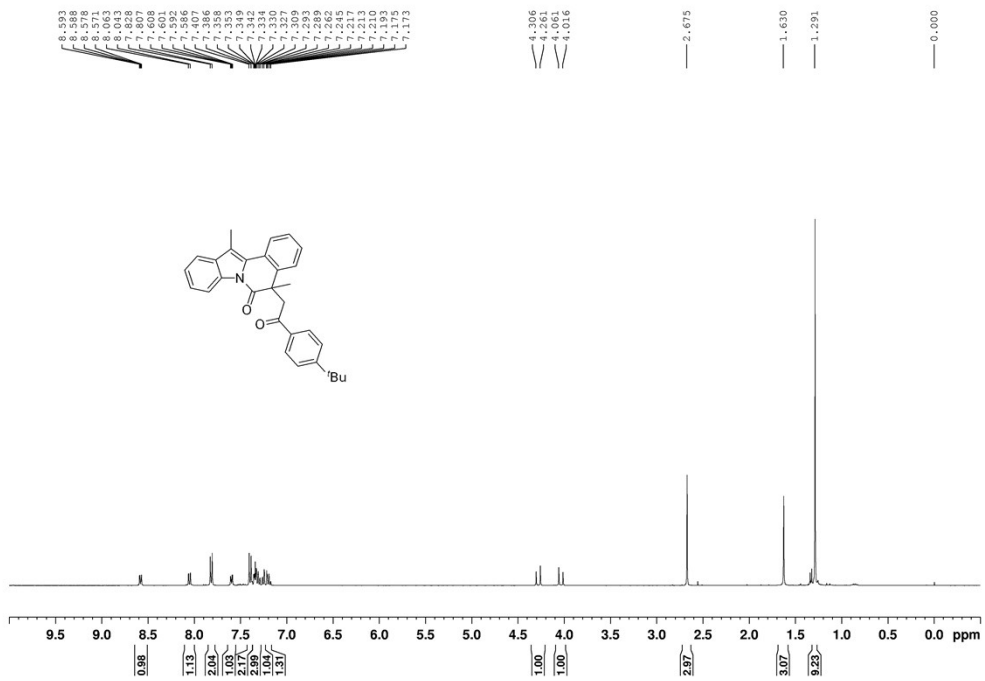

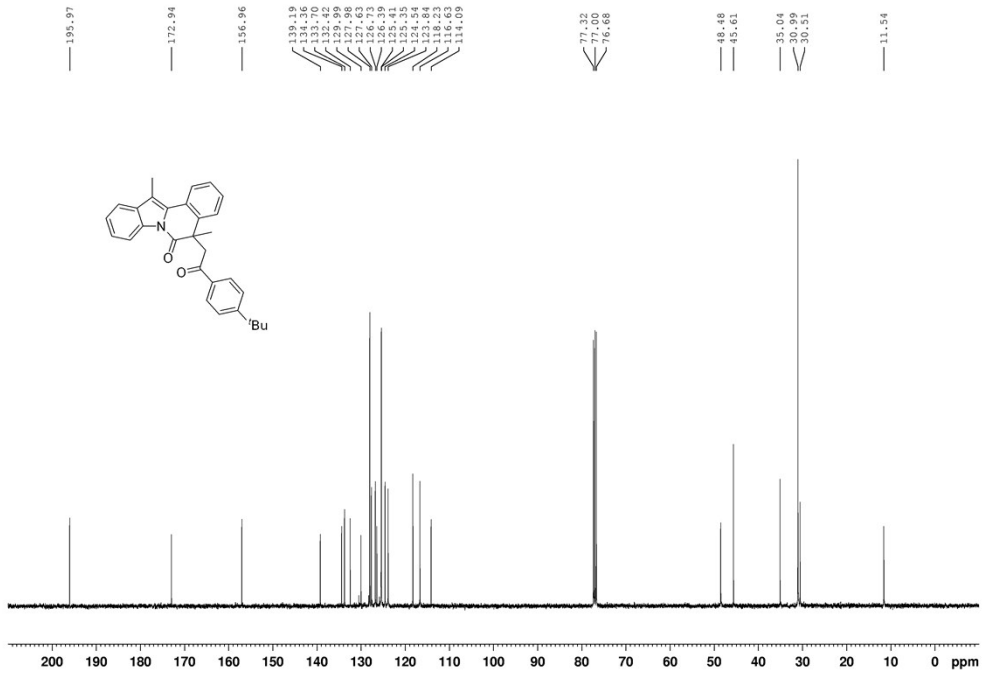

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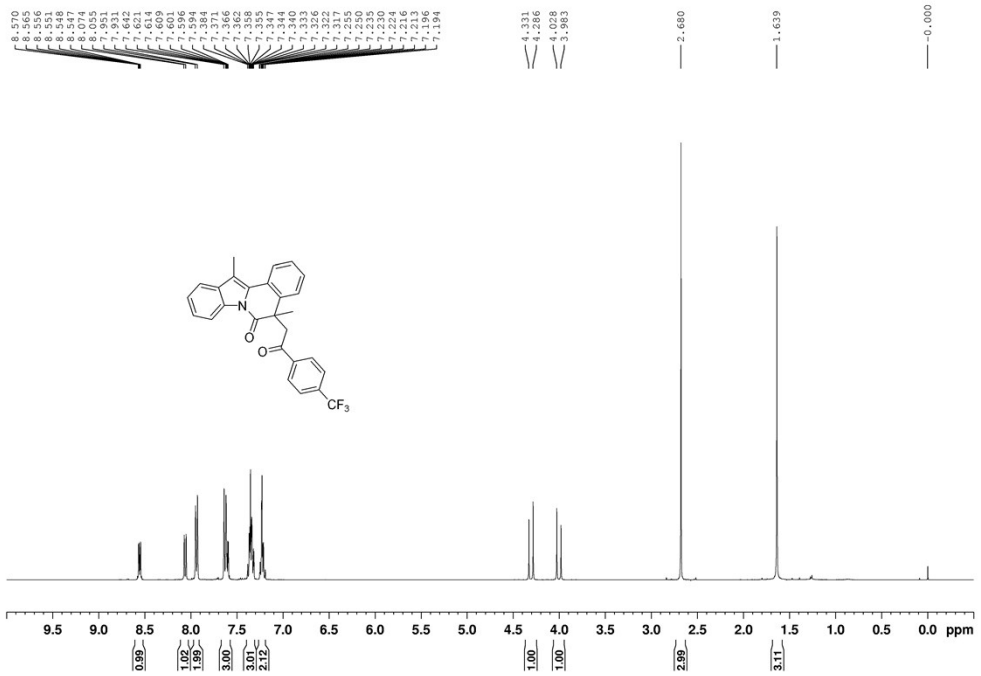
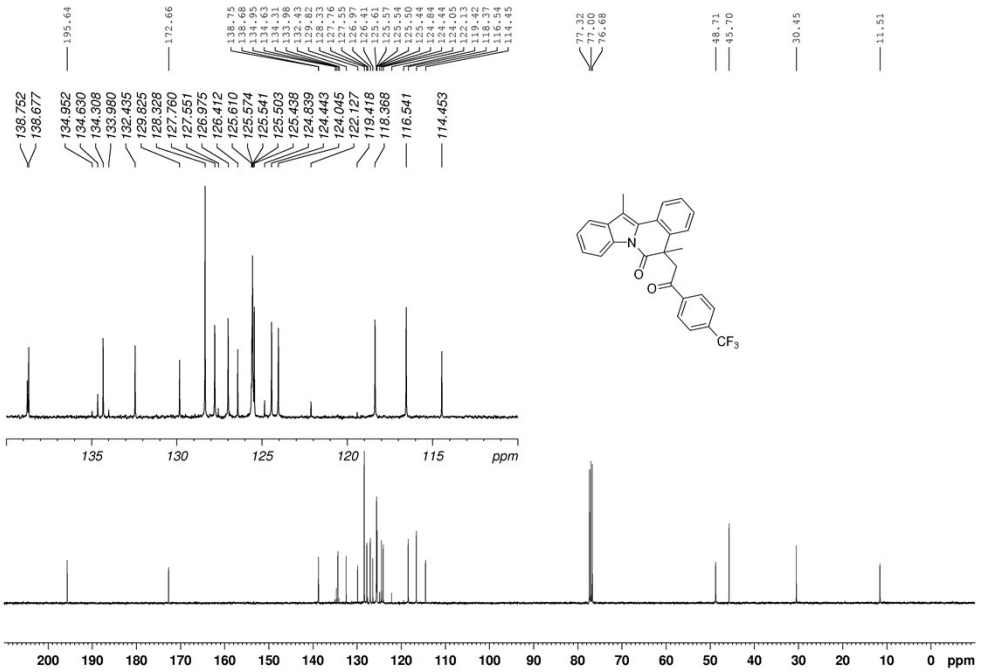
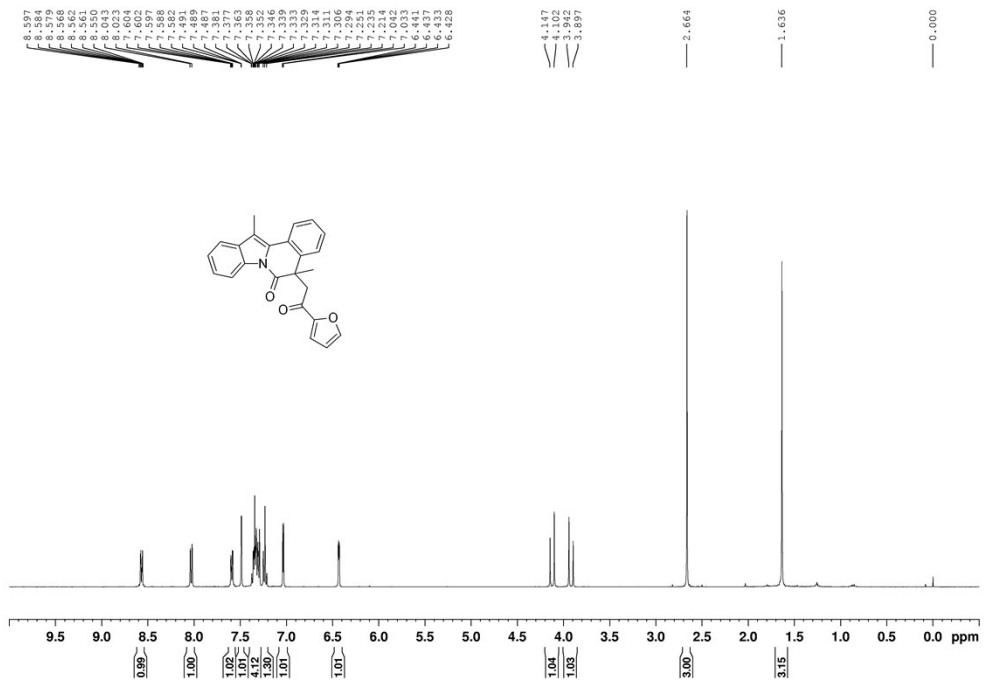
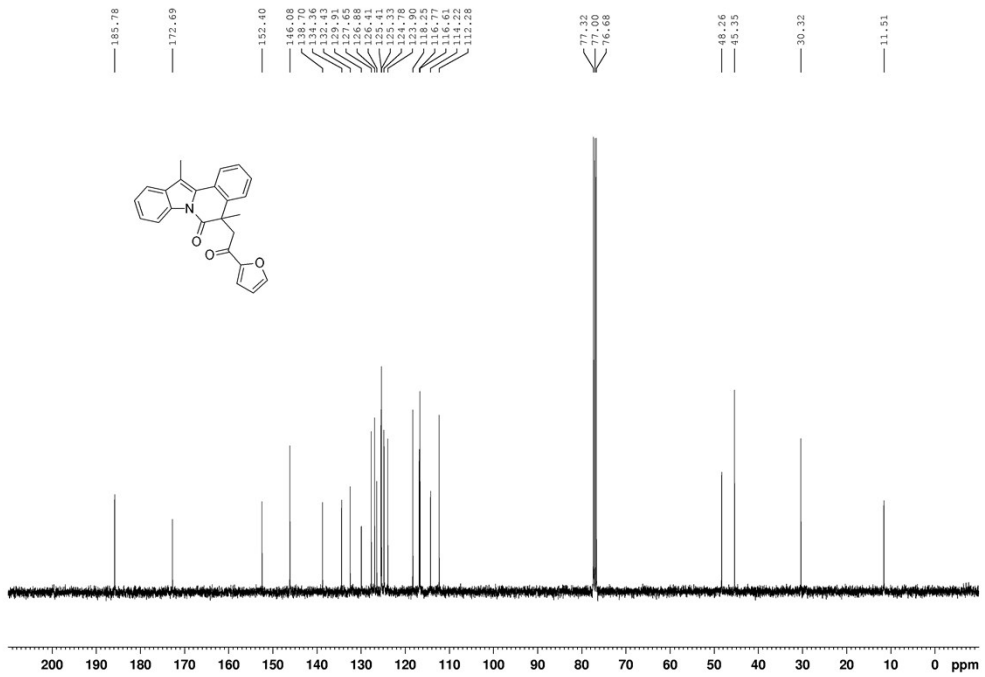


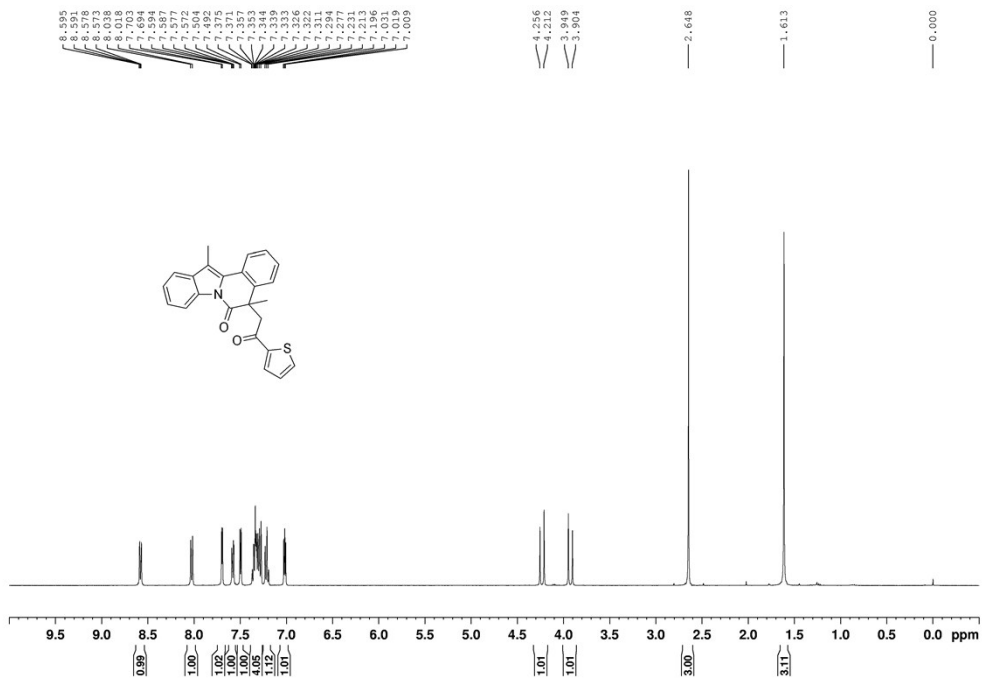


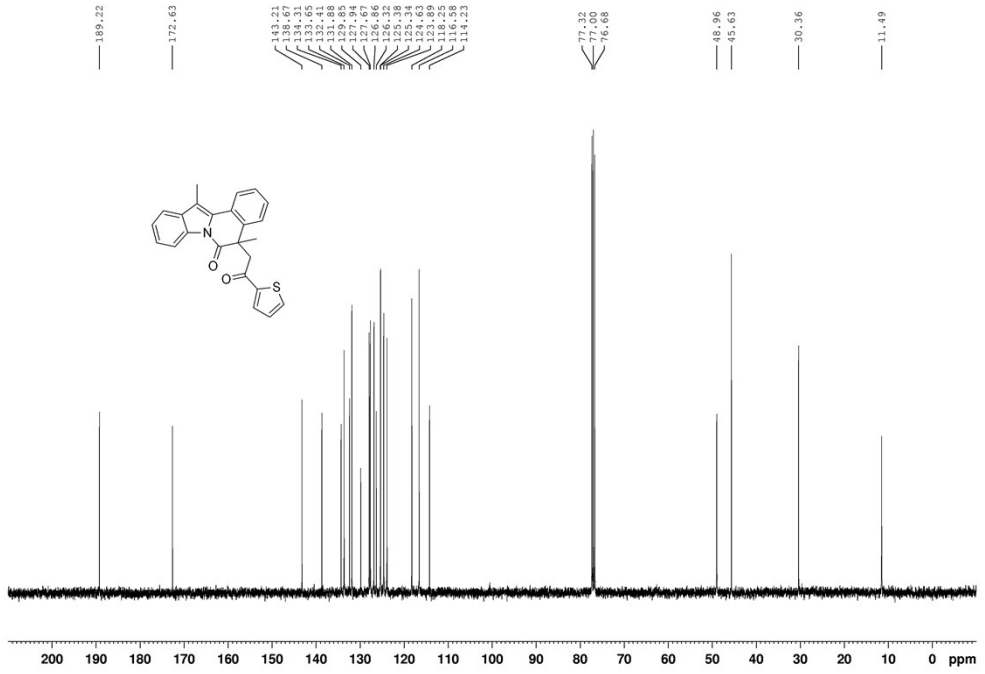
5-(2-(furan-2-yl)-2-oxoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3ah)



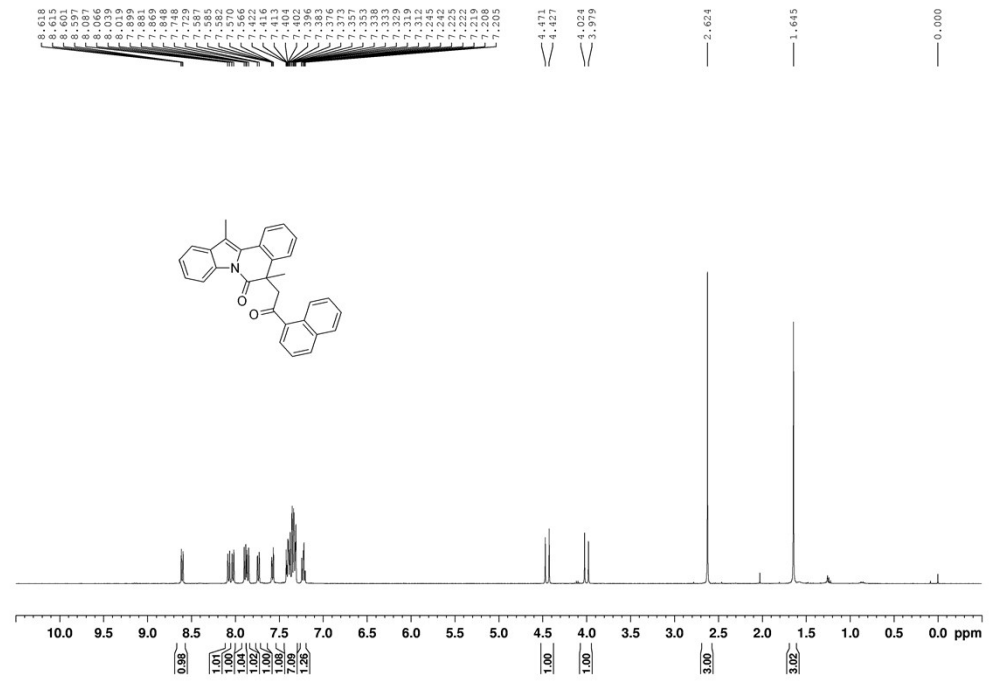


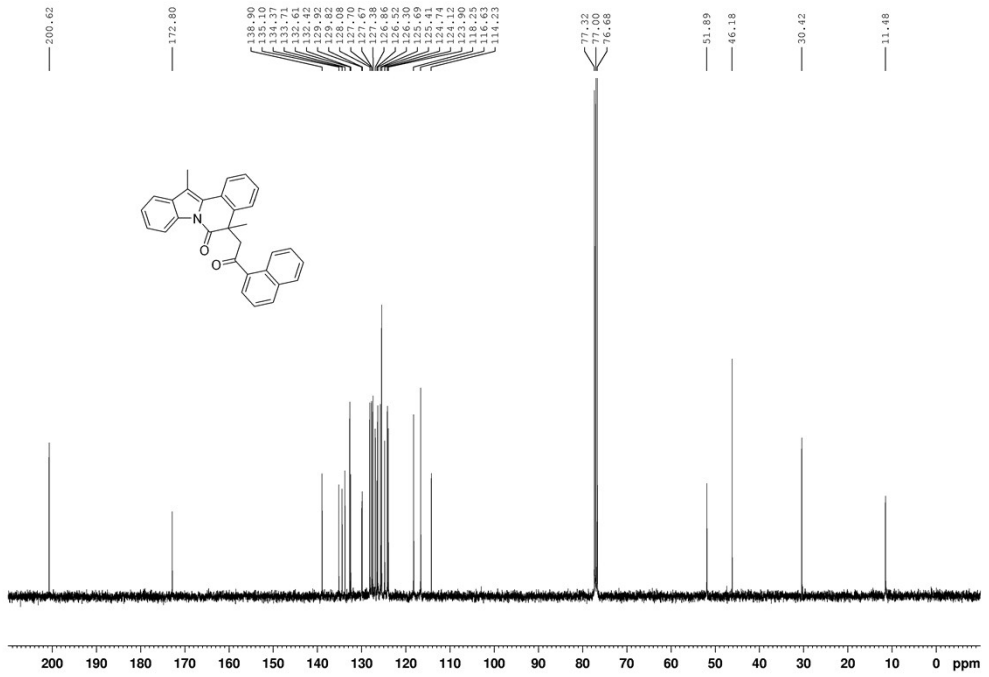
5,12-dimethyl-5-(2-oxo-2-(thiophen-2-yl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ai)



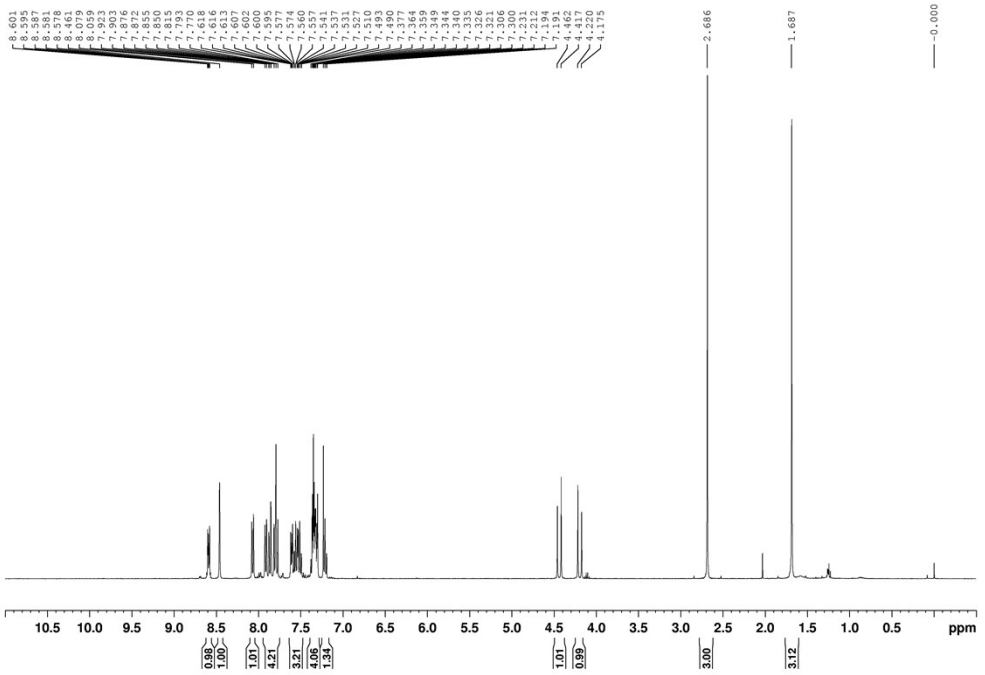


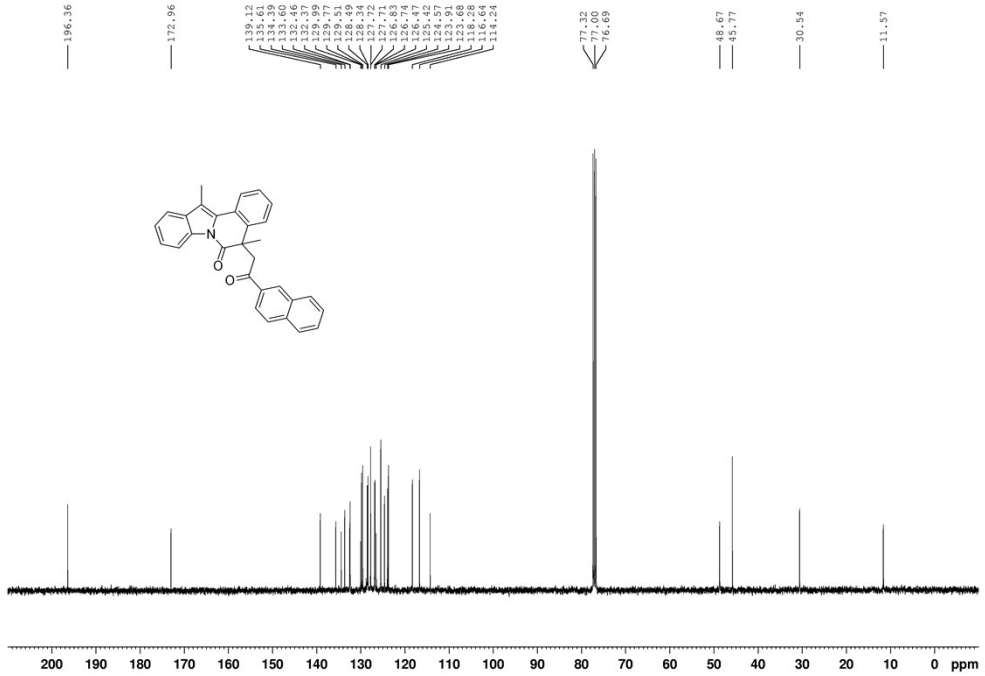
5,12-dimethyl-5-(2-(naphthalen-1-yl)-2-oxoethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3aj)



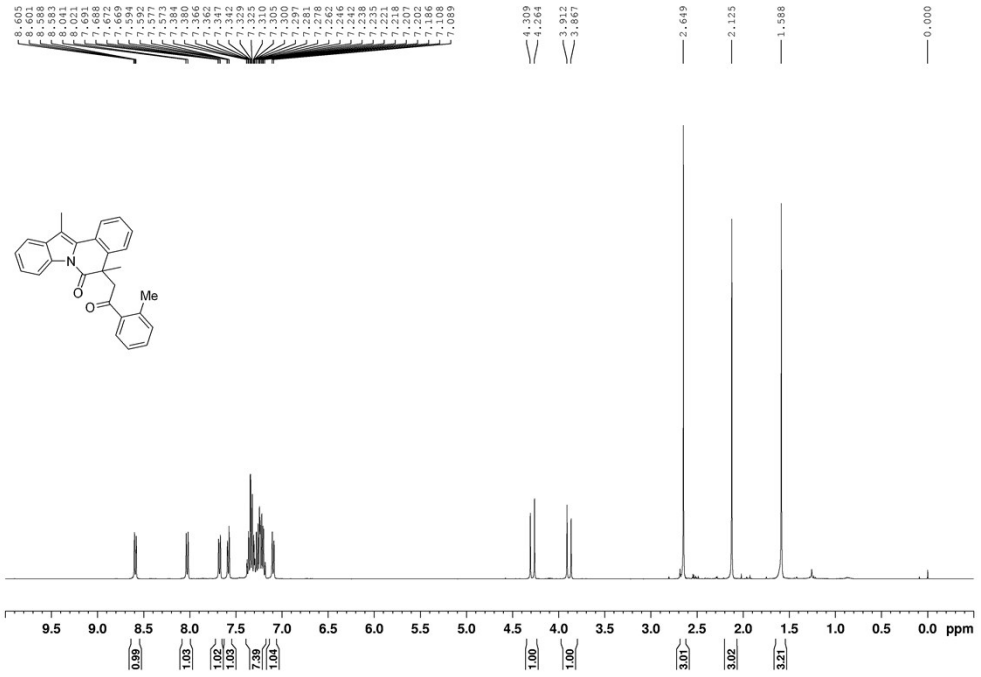


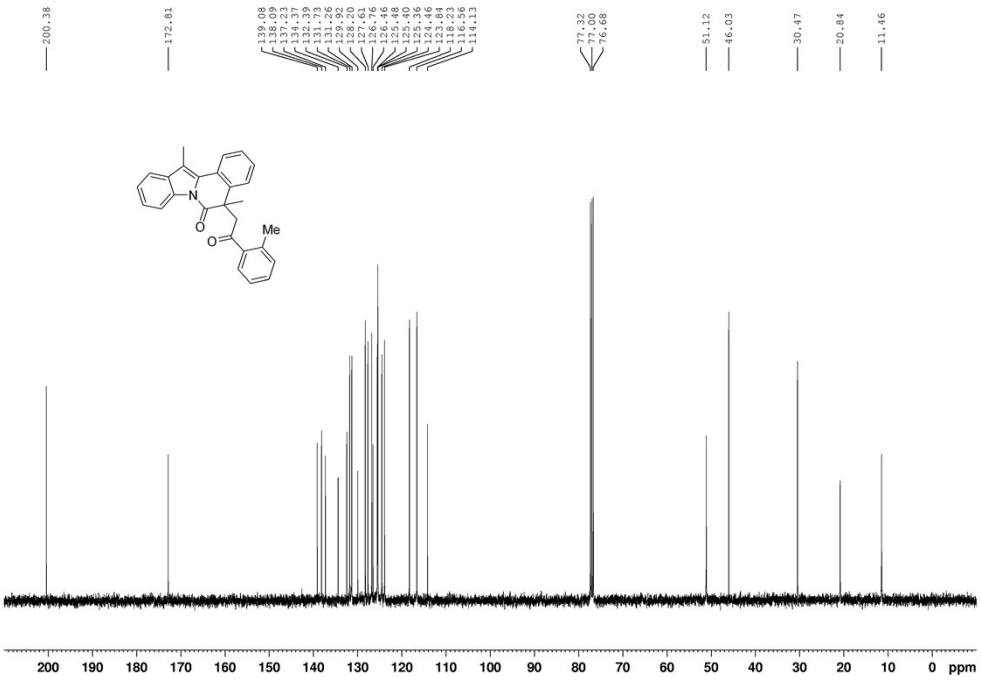
5,12-dimethyl-5-(2-(naphthalen-2-yl)-2-oxoethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ak)



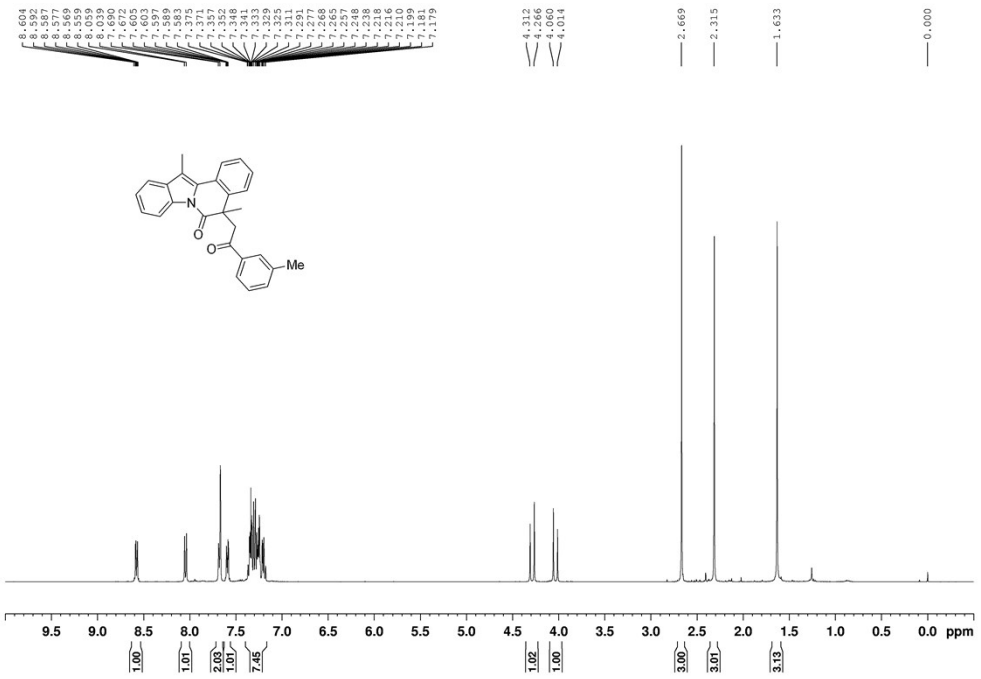


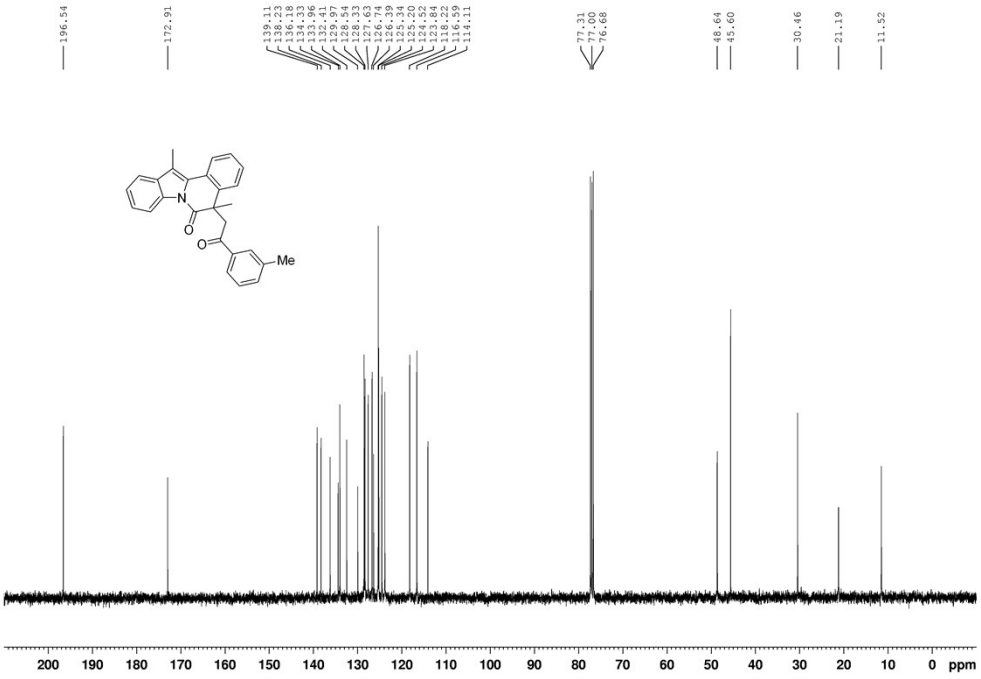
5,12-dimethyl-5-(2-oxo-2-(o-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3al)





5,12-dimethyl-5-(2-oxo-2-(m-tolyl)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3am)





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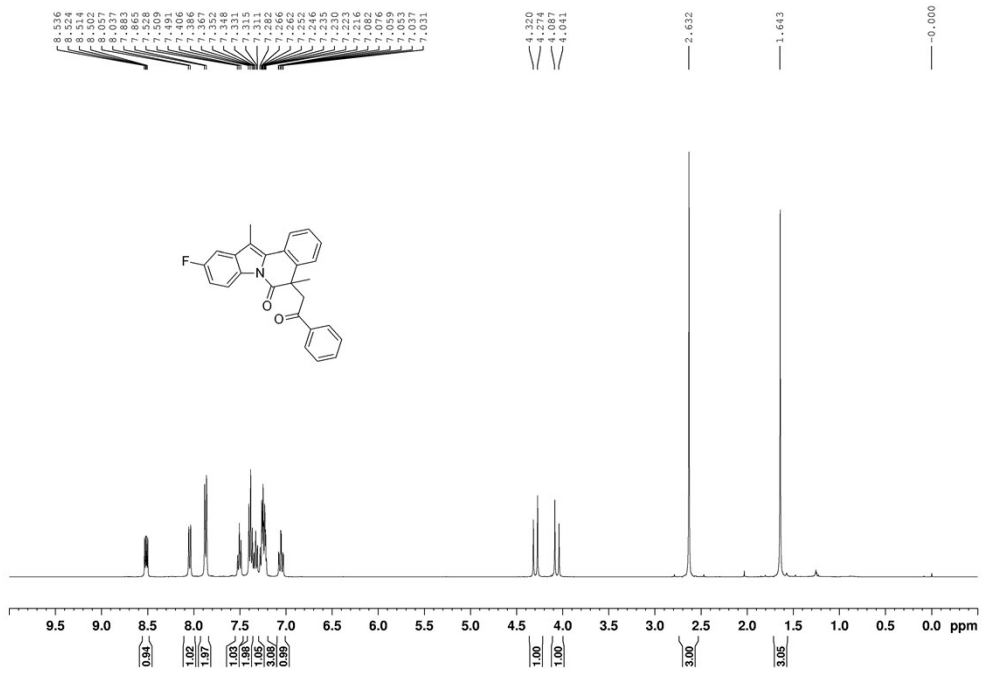

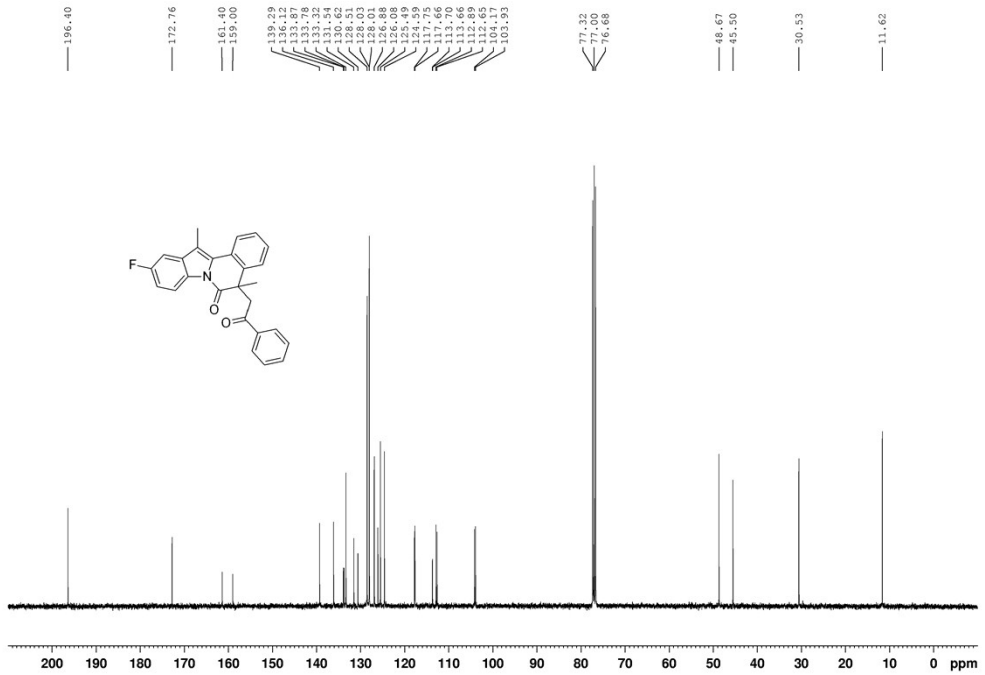

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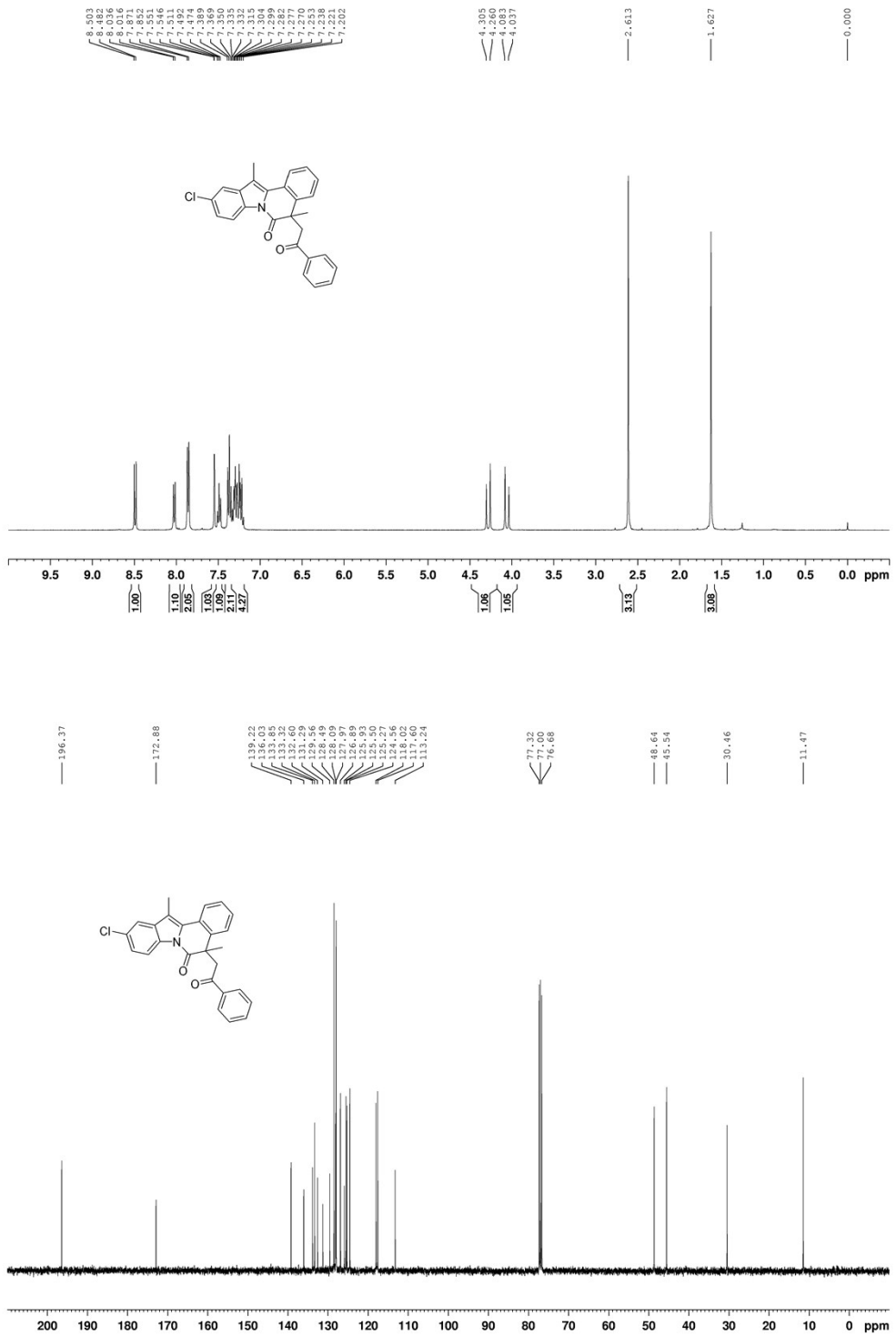
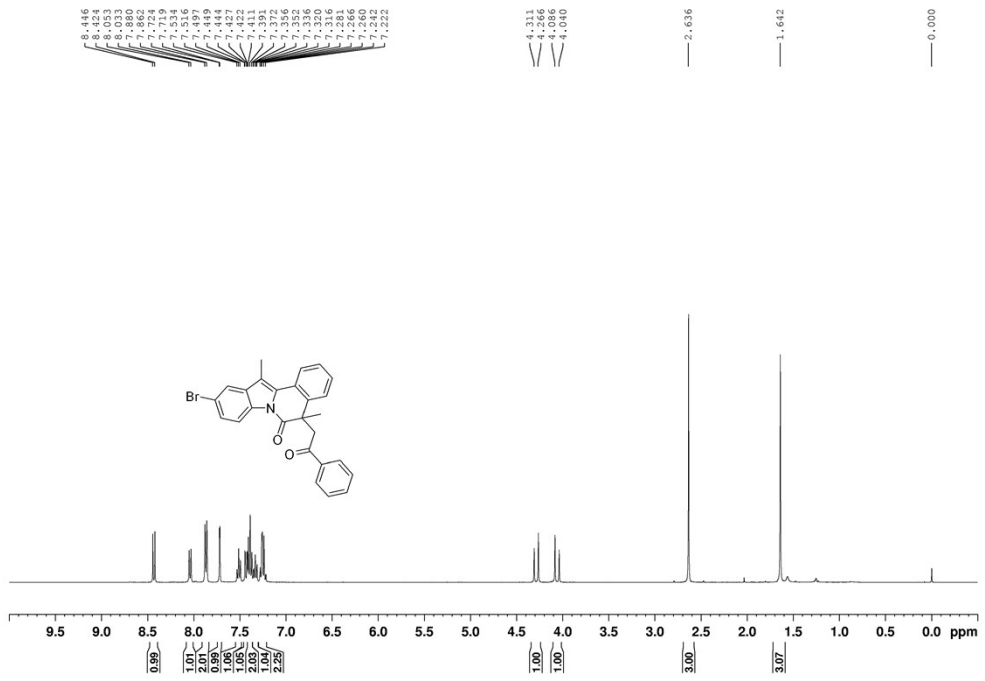
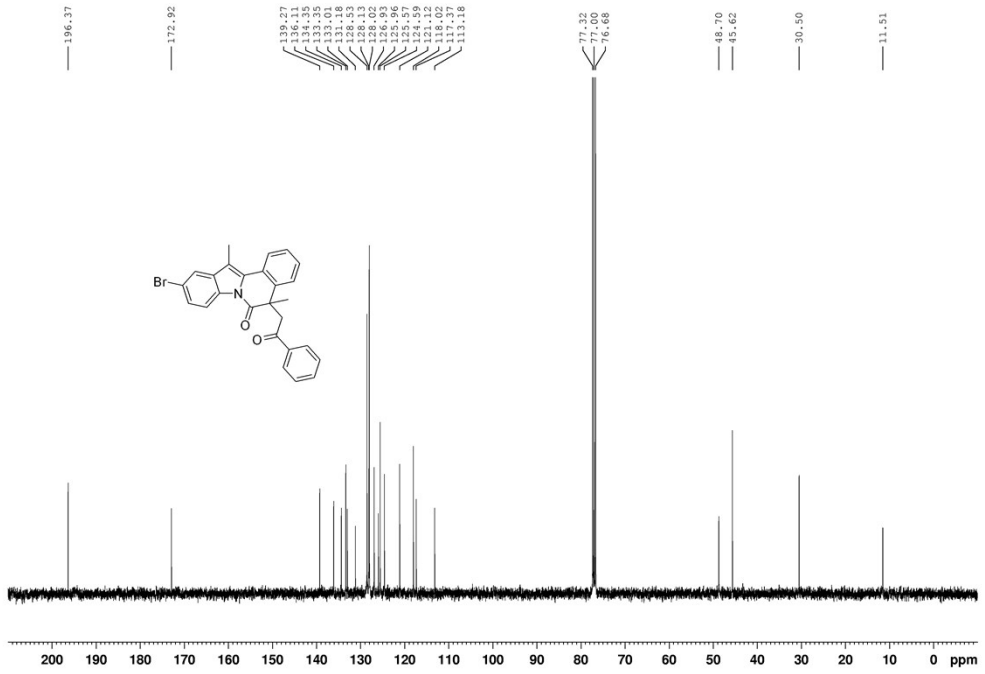


10-bromo-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3da)





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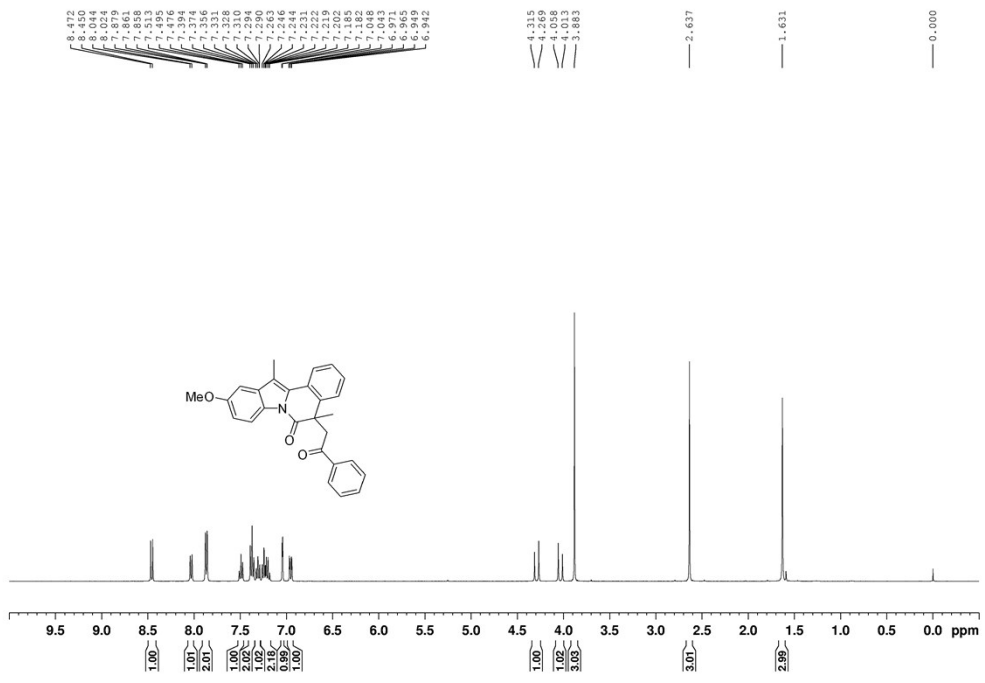

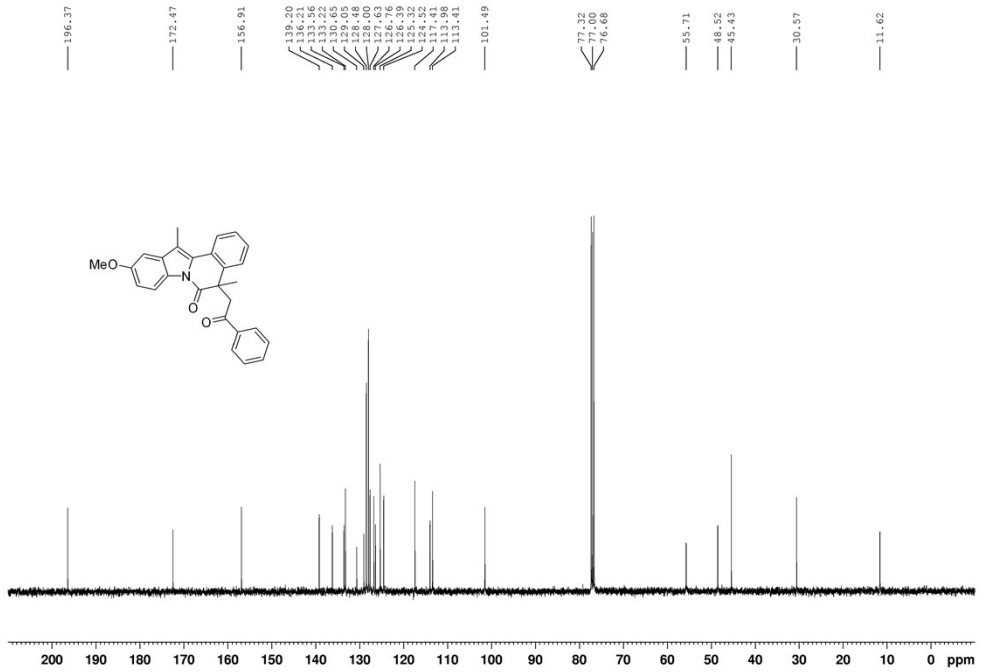

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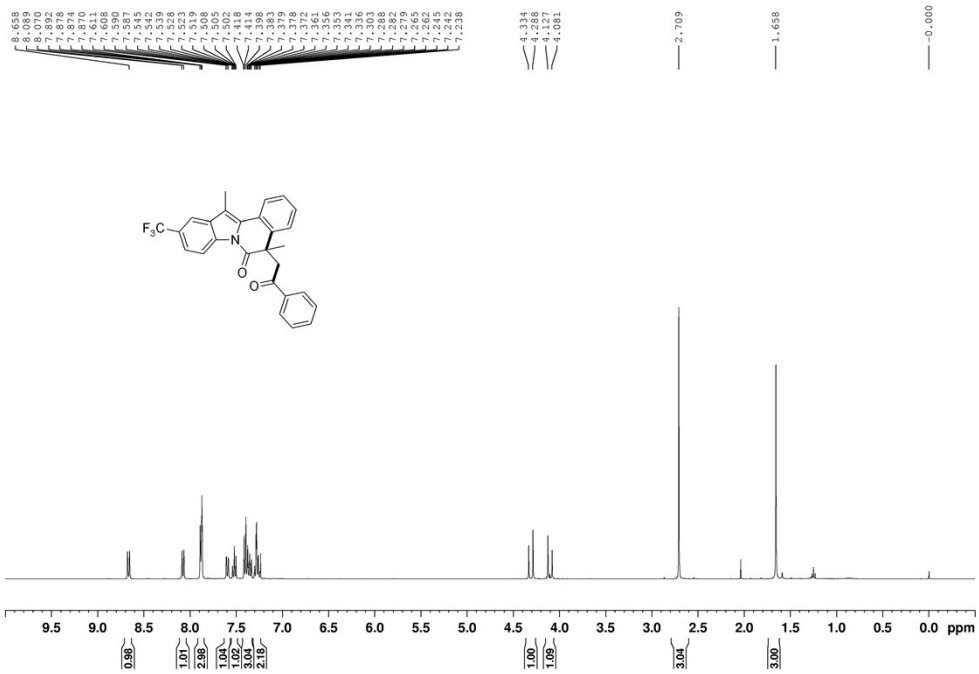

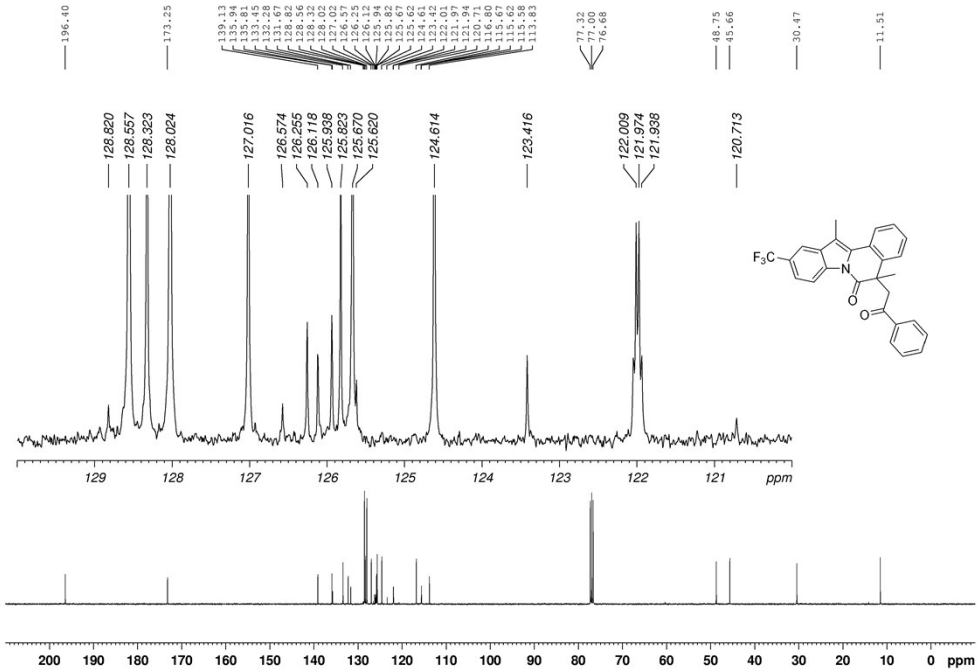

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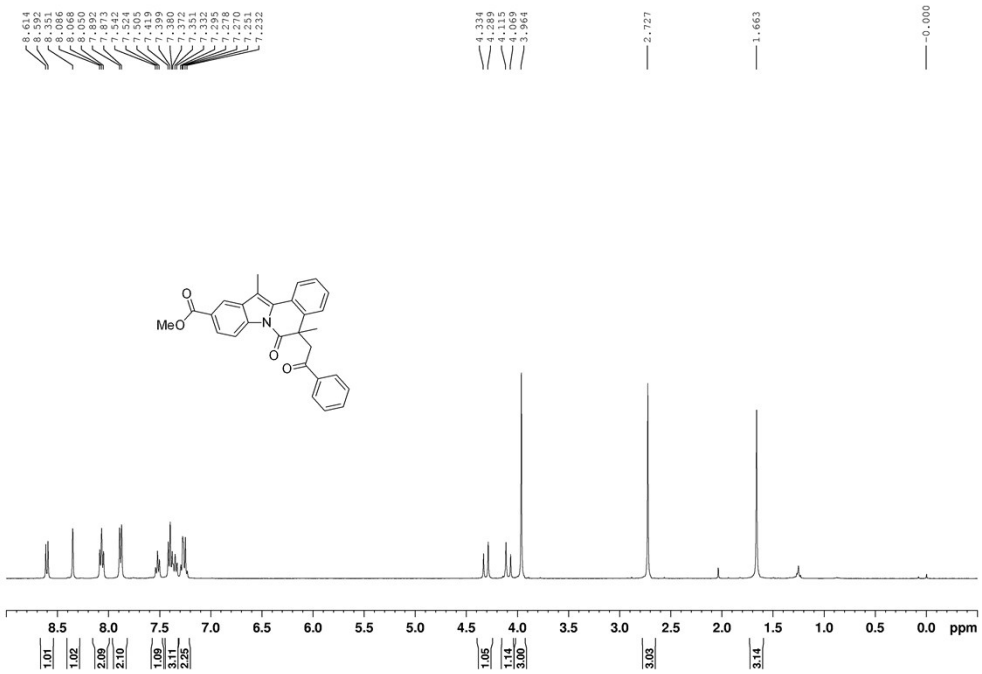
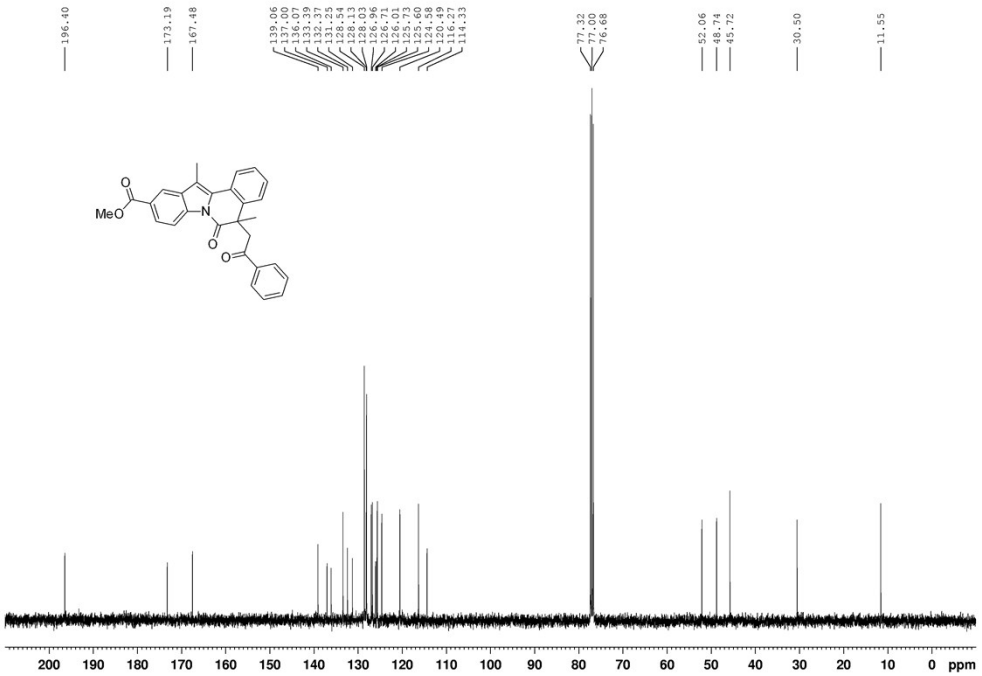
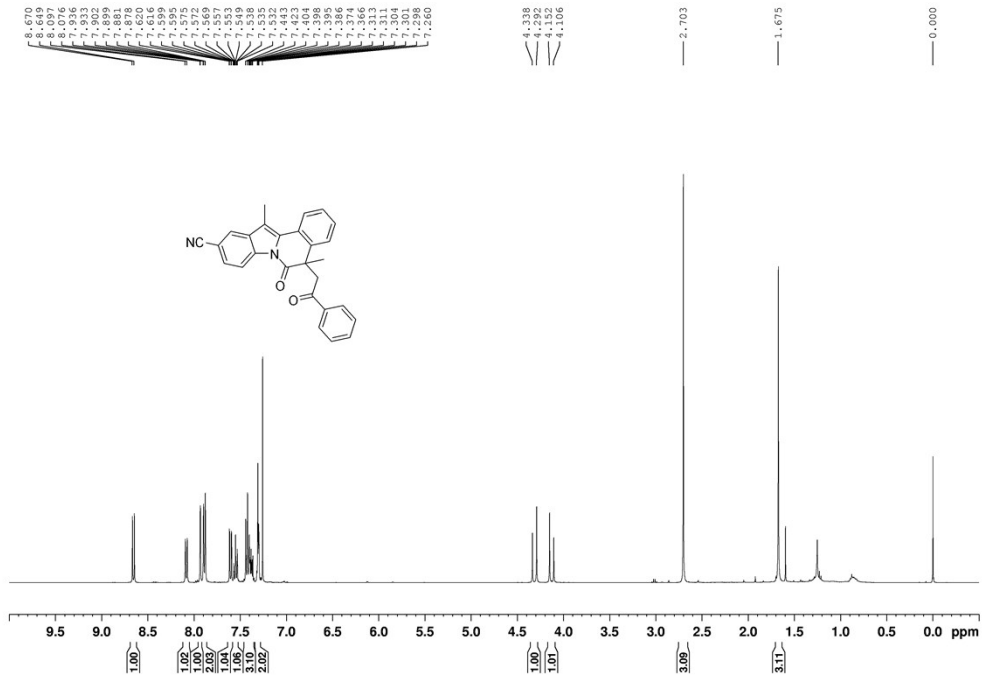
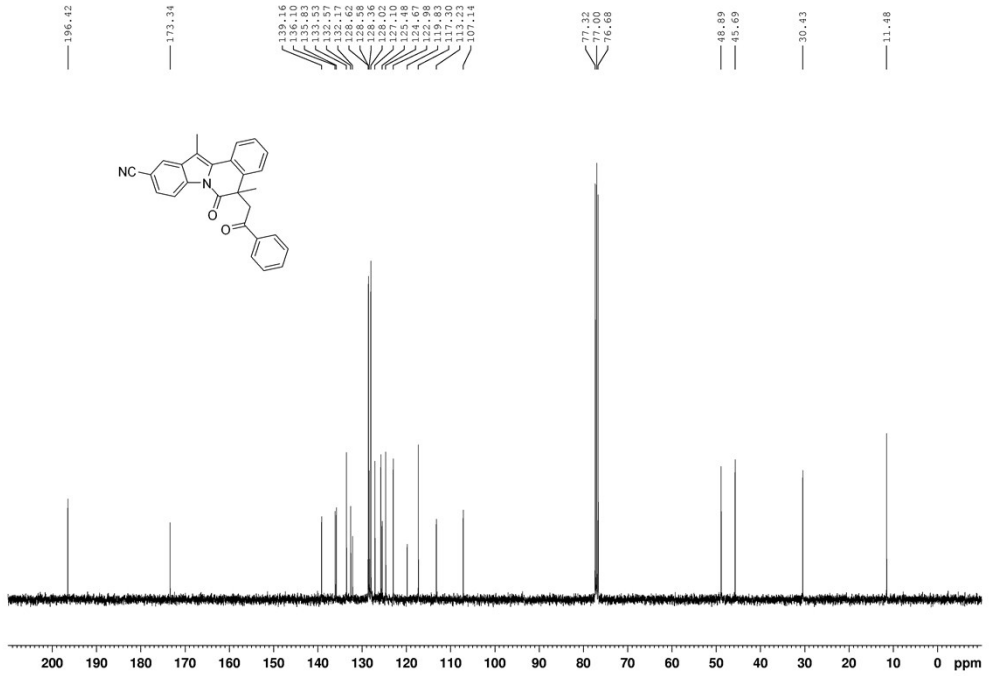


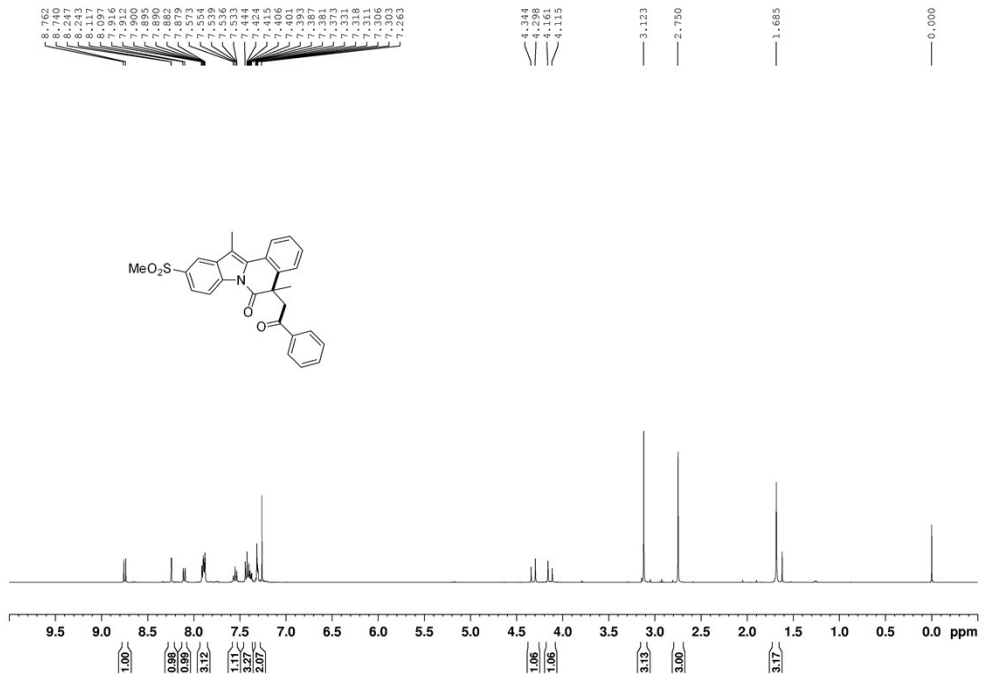


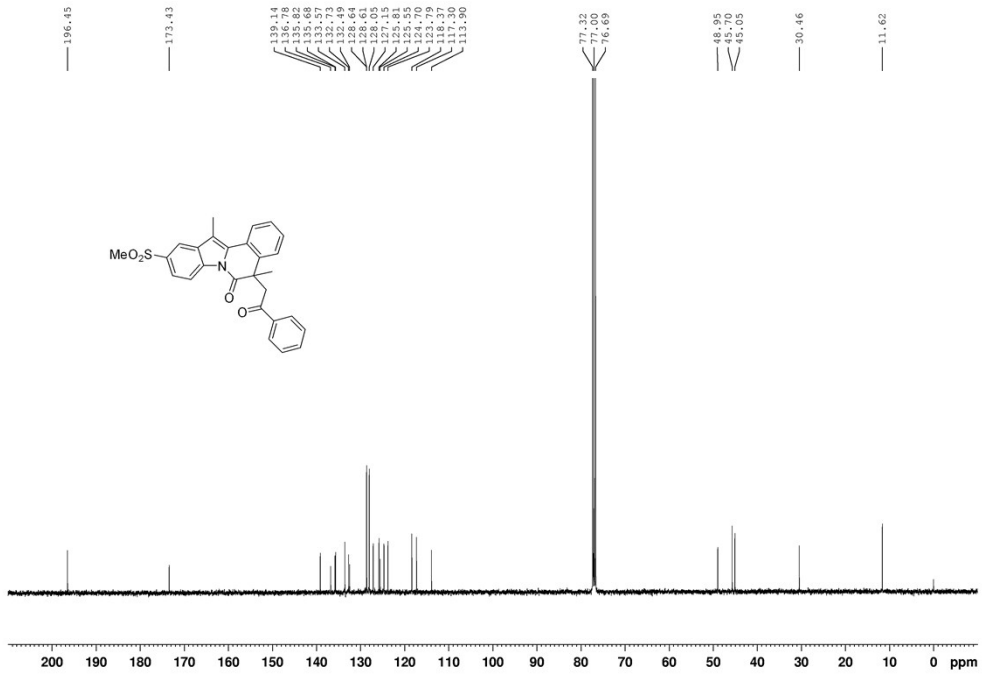
5,12-dimethyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-10-carbonitrile (3ha)





5,12-dimethyl-10-(methylsulfonyl)-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ia)





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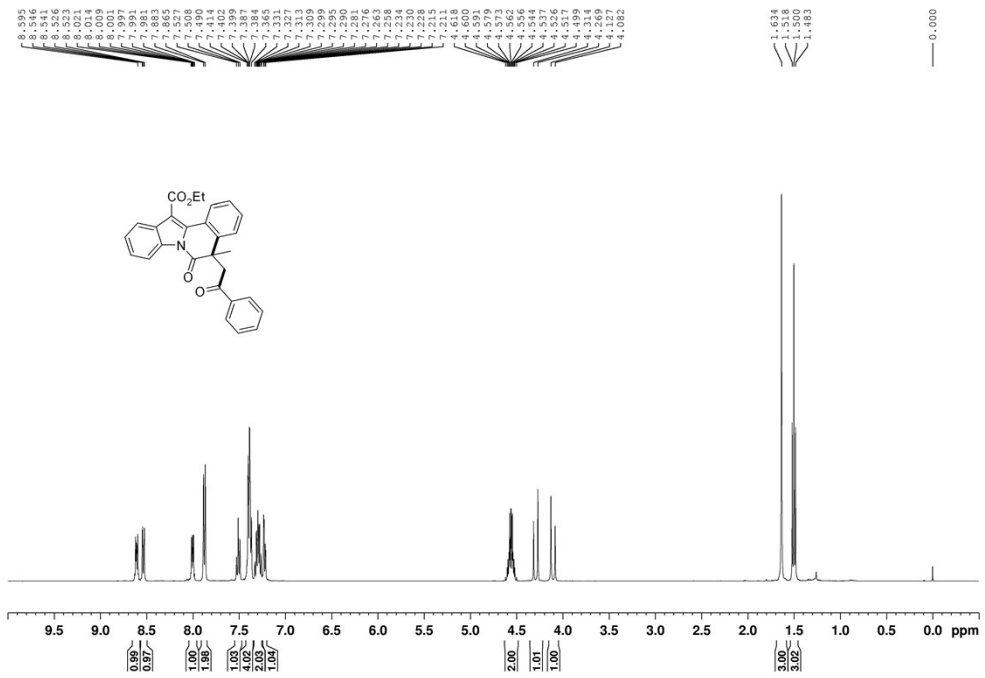

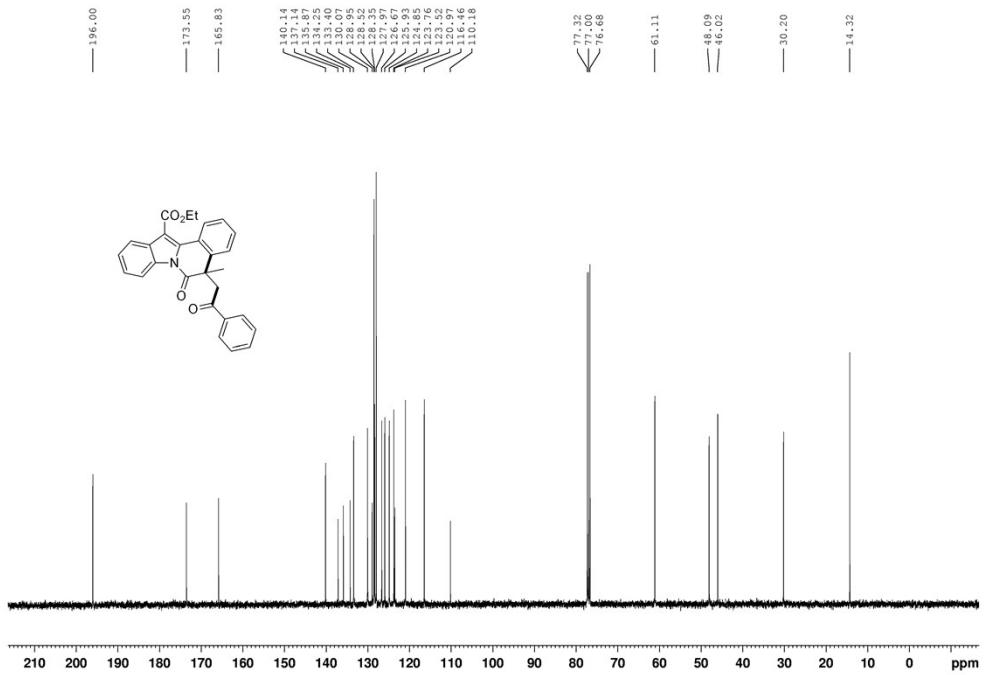

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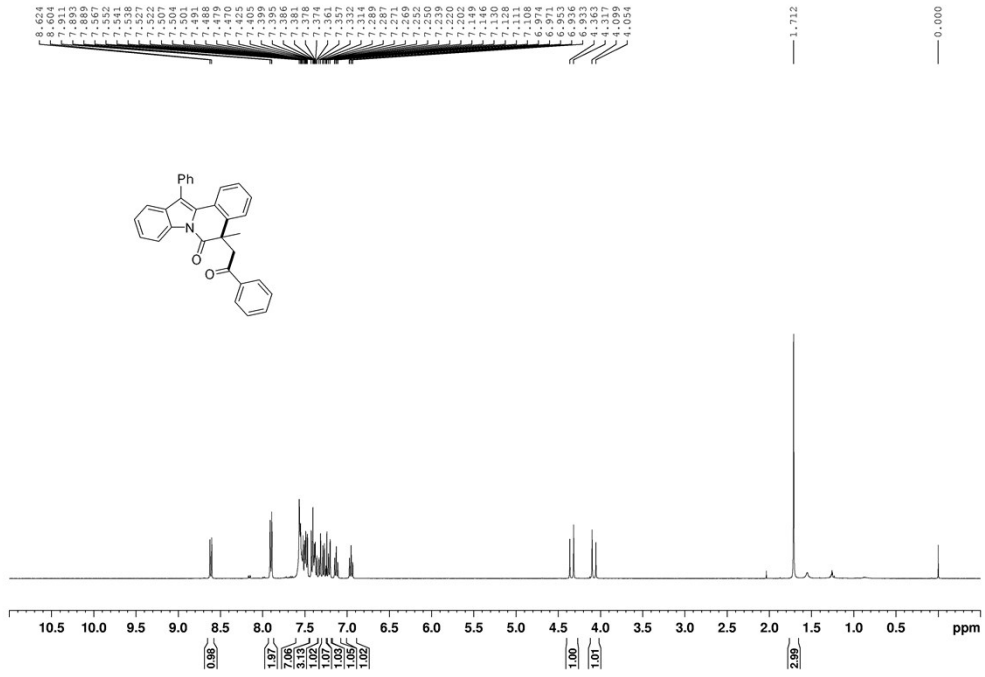

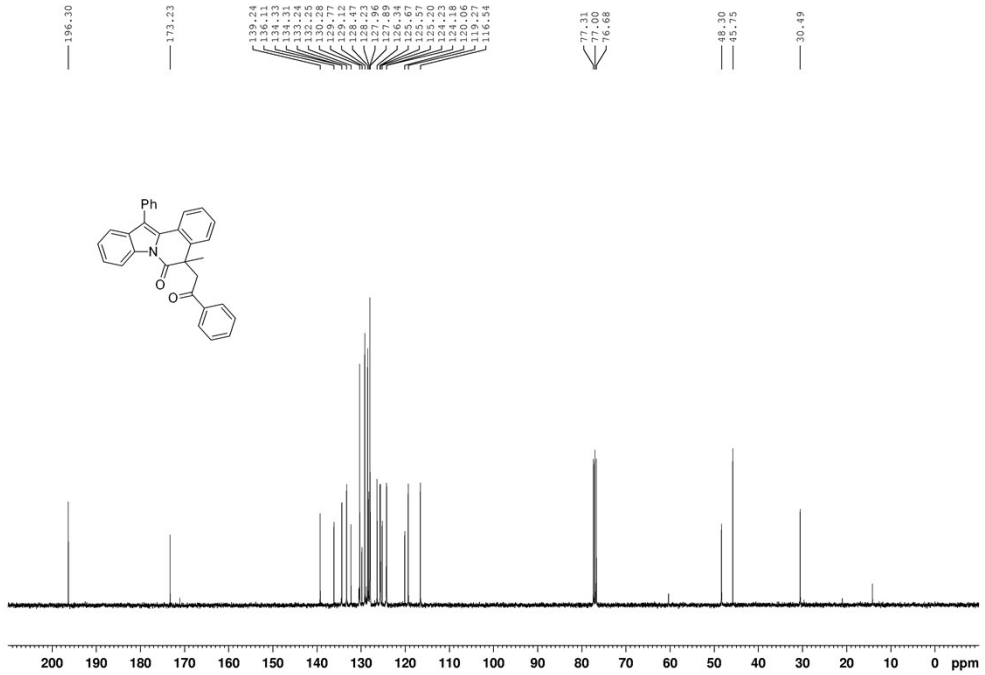

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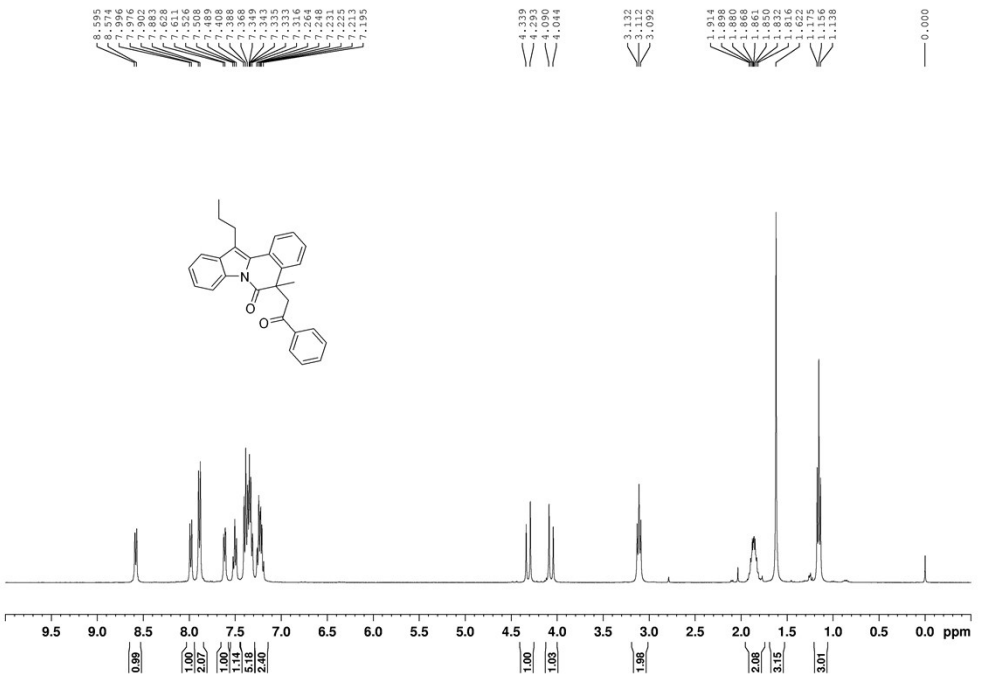
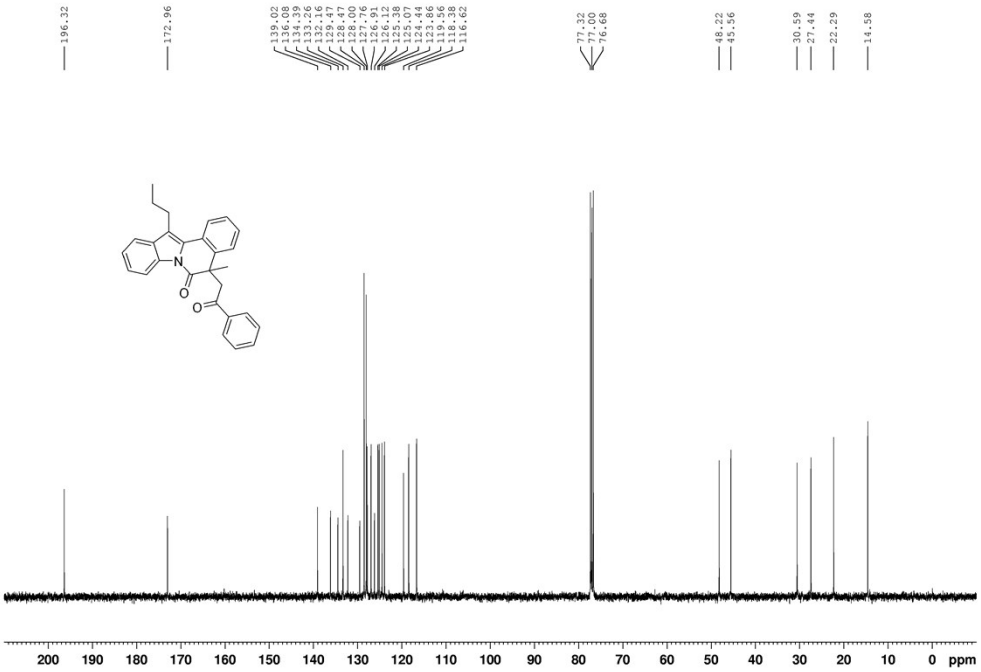
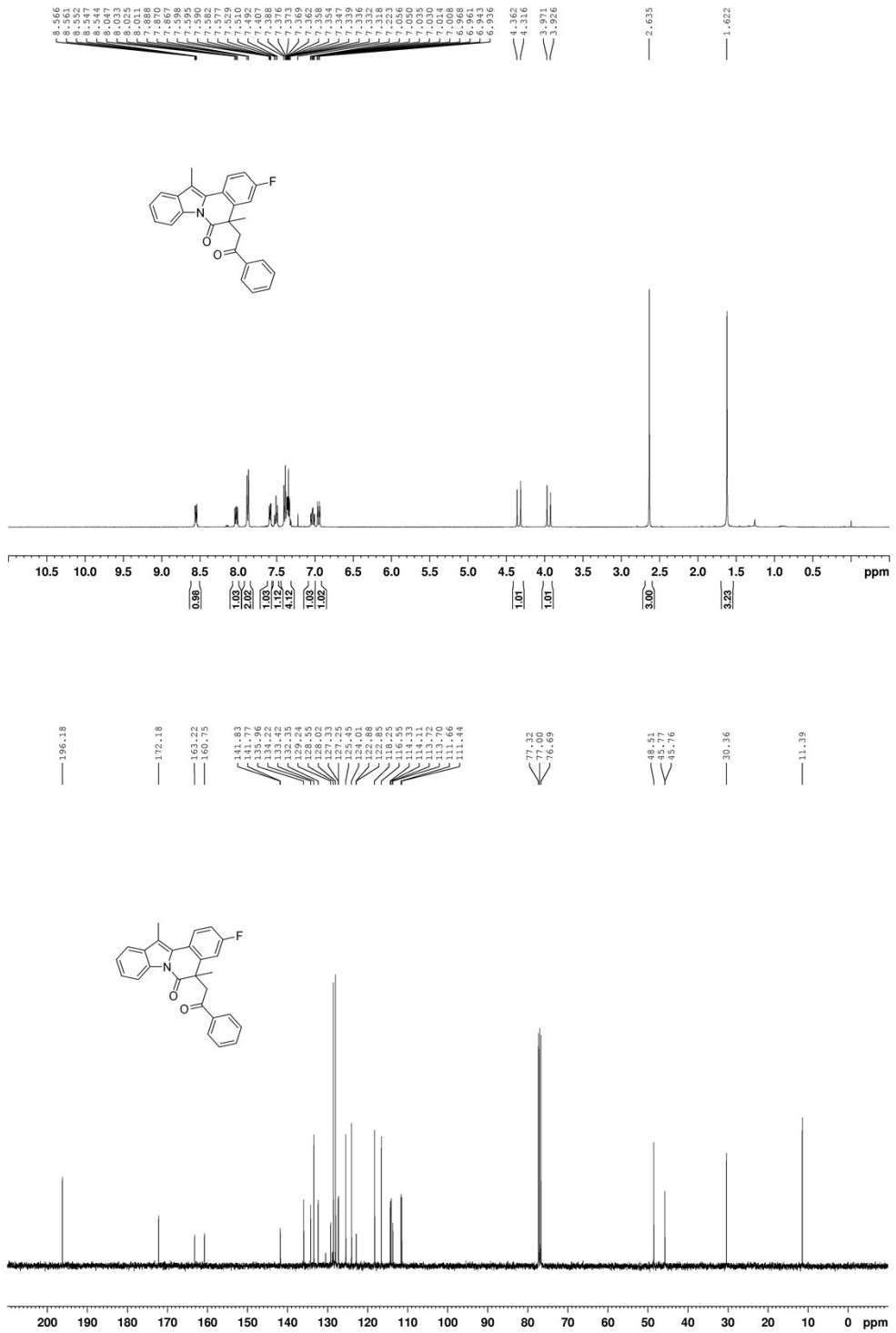
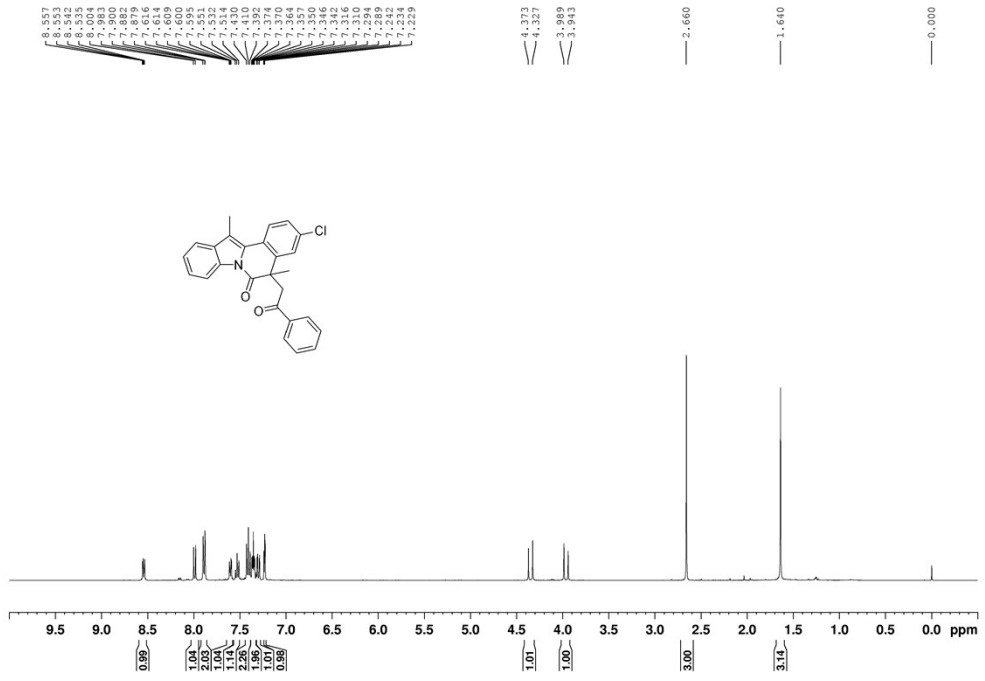


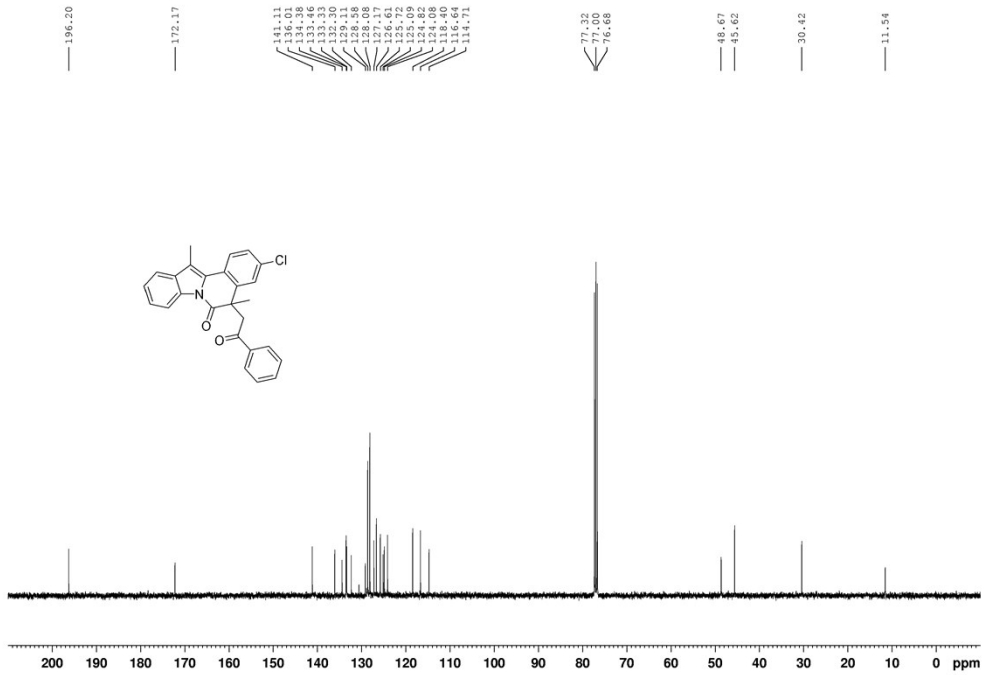


3-fluoro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ma)

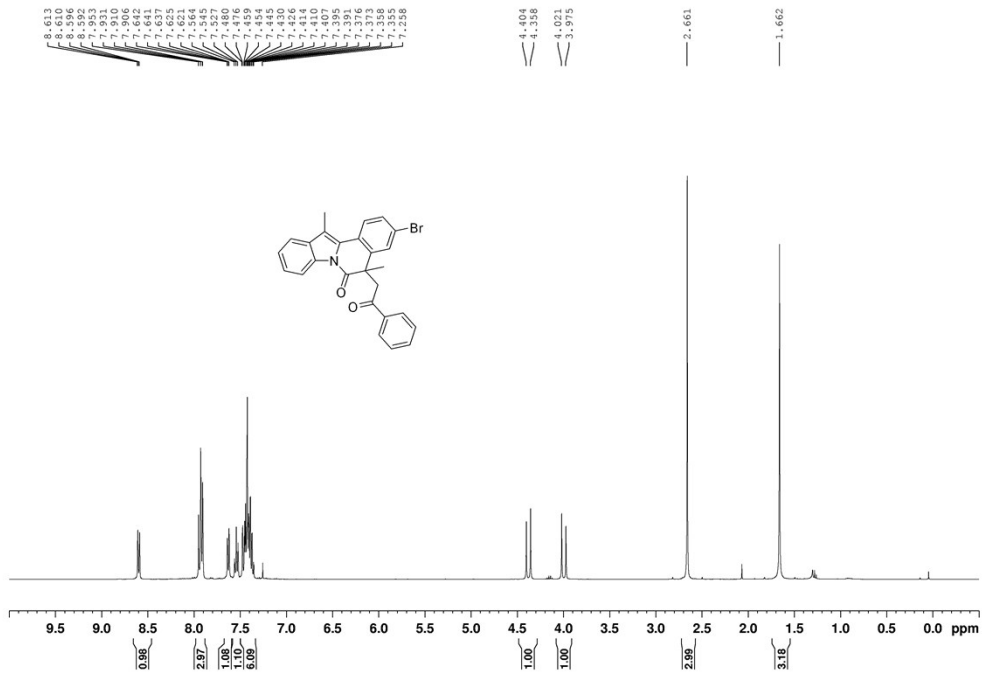


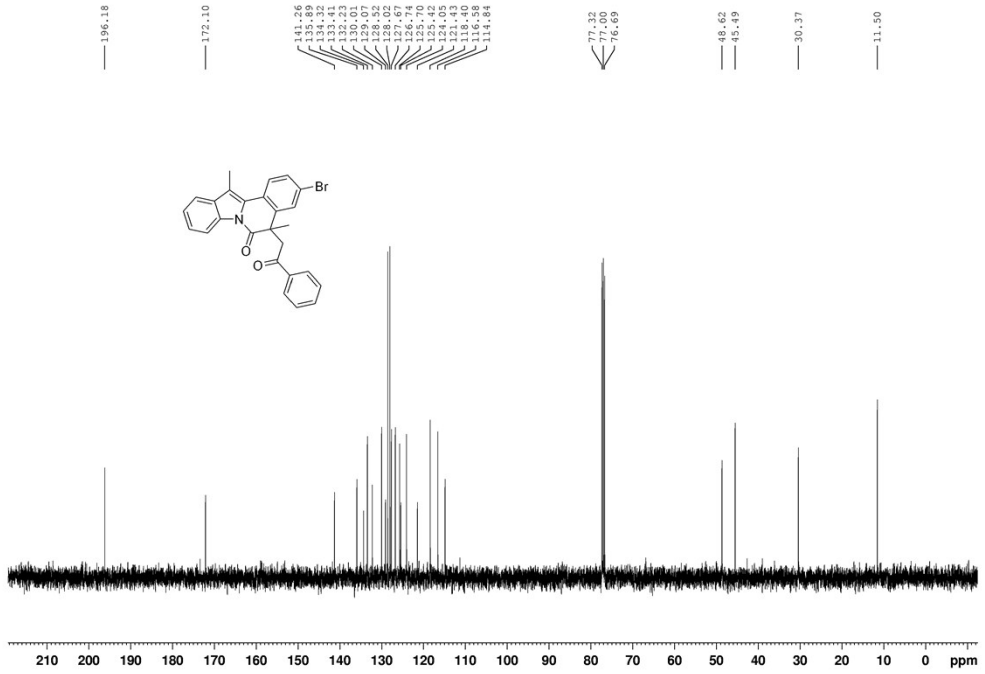
3-chloro-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3na)



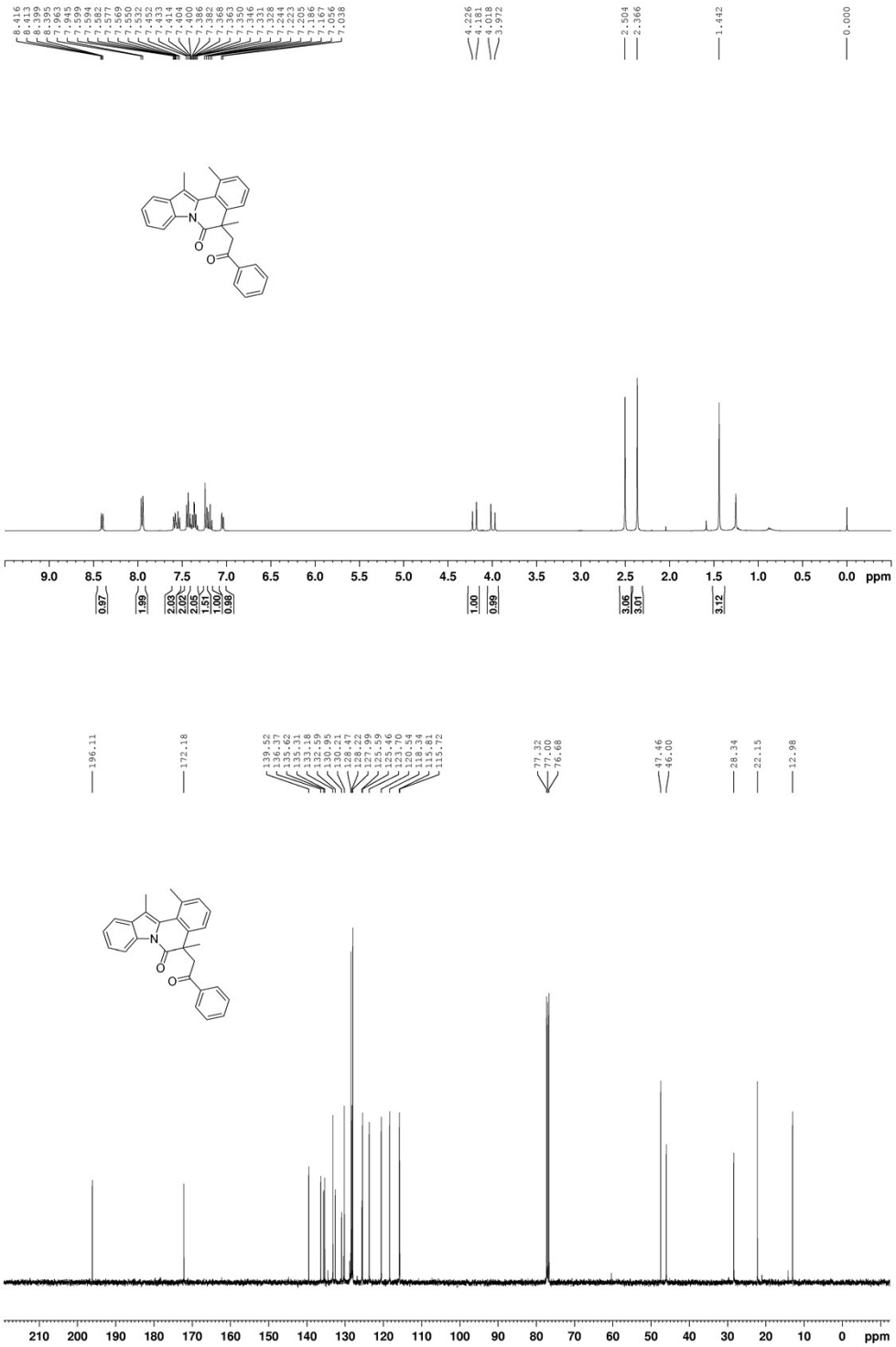


3-bromo-5,12-dimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3oa)

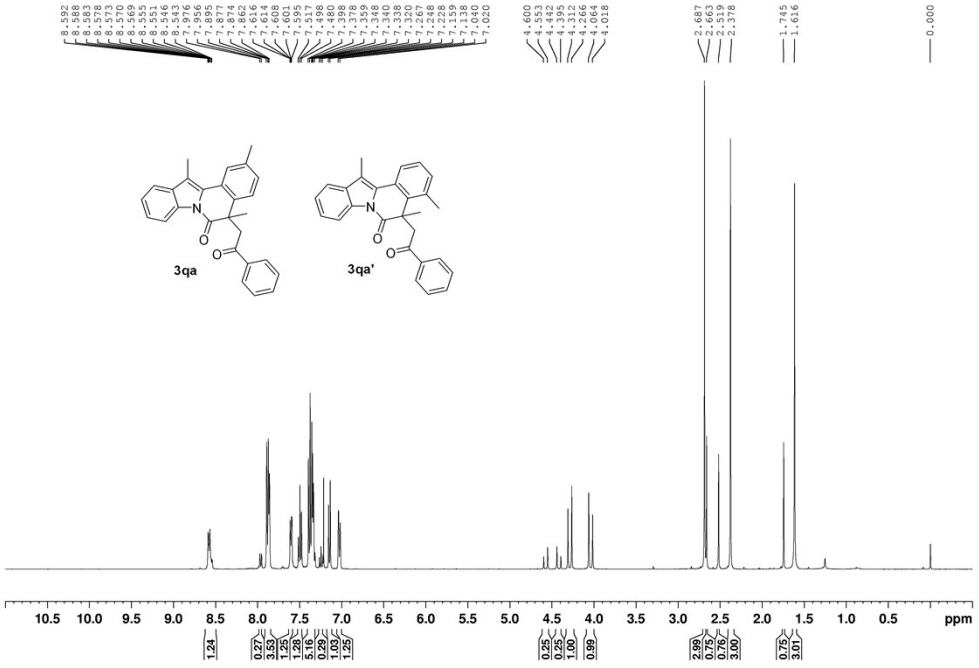


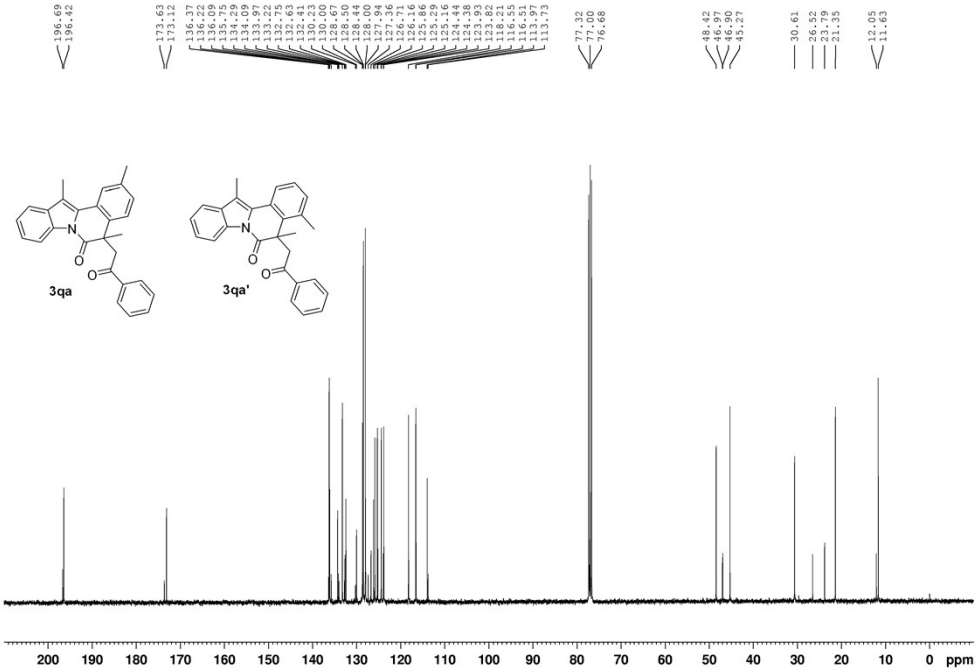


1,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3pa)

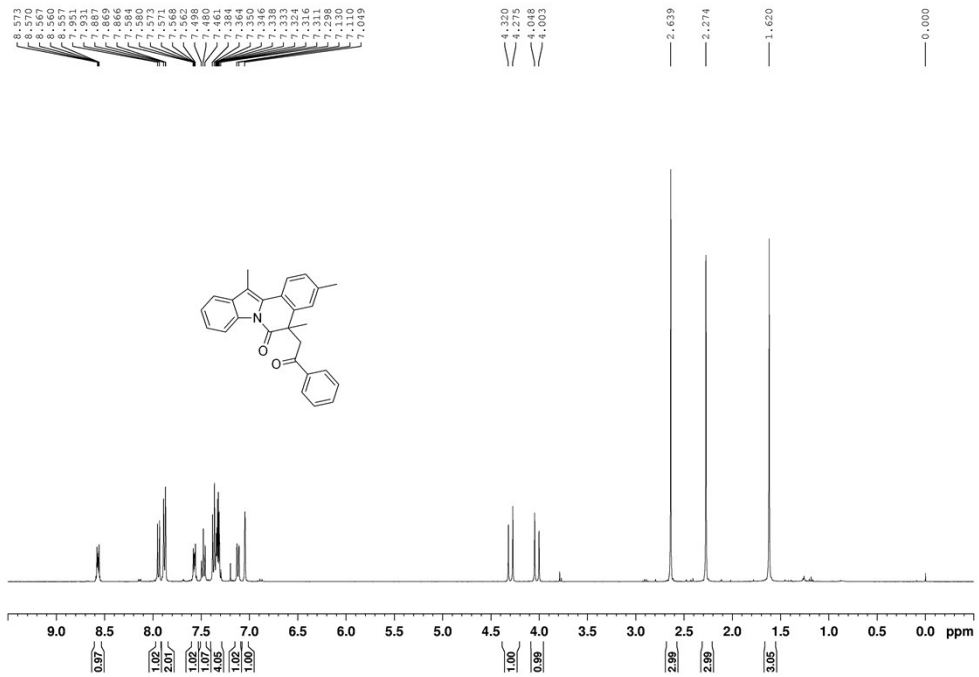


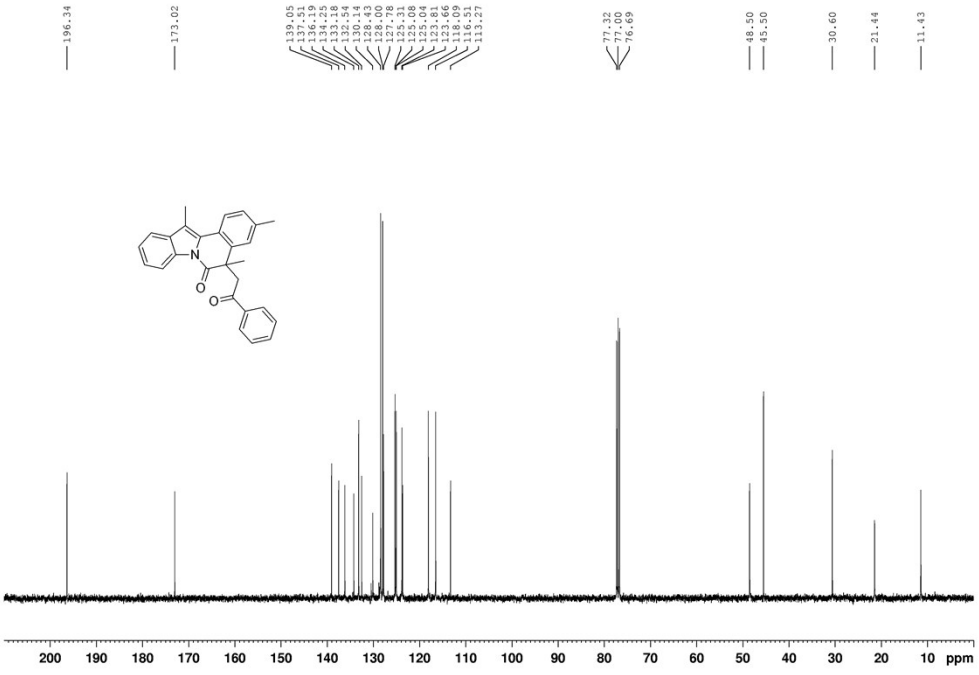
2,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3qa) (major)
and 4,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3qa') (minor)



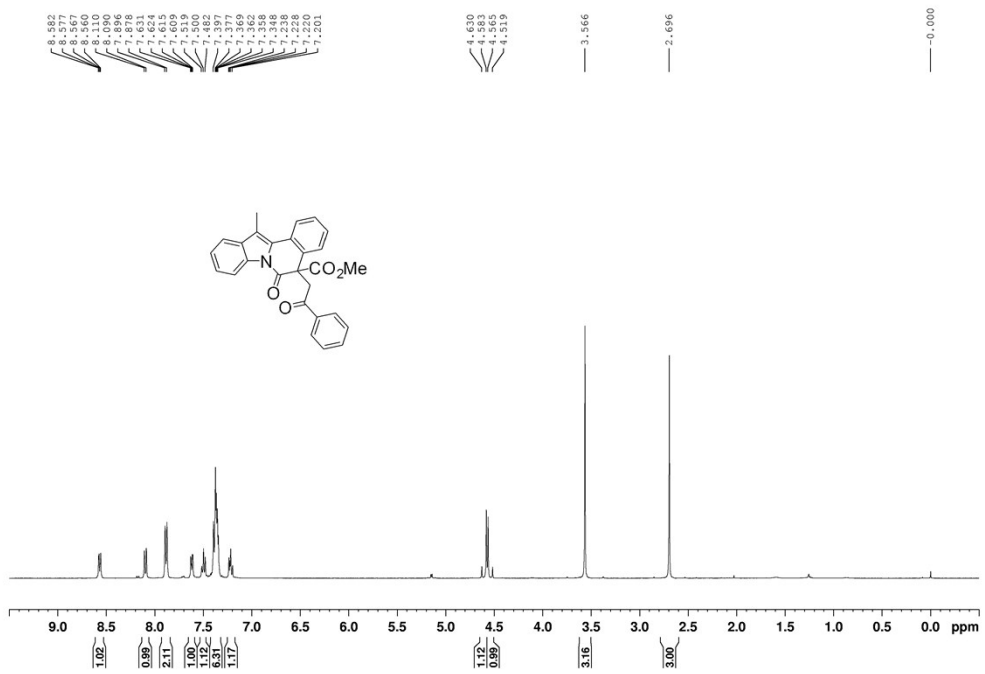


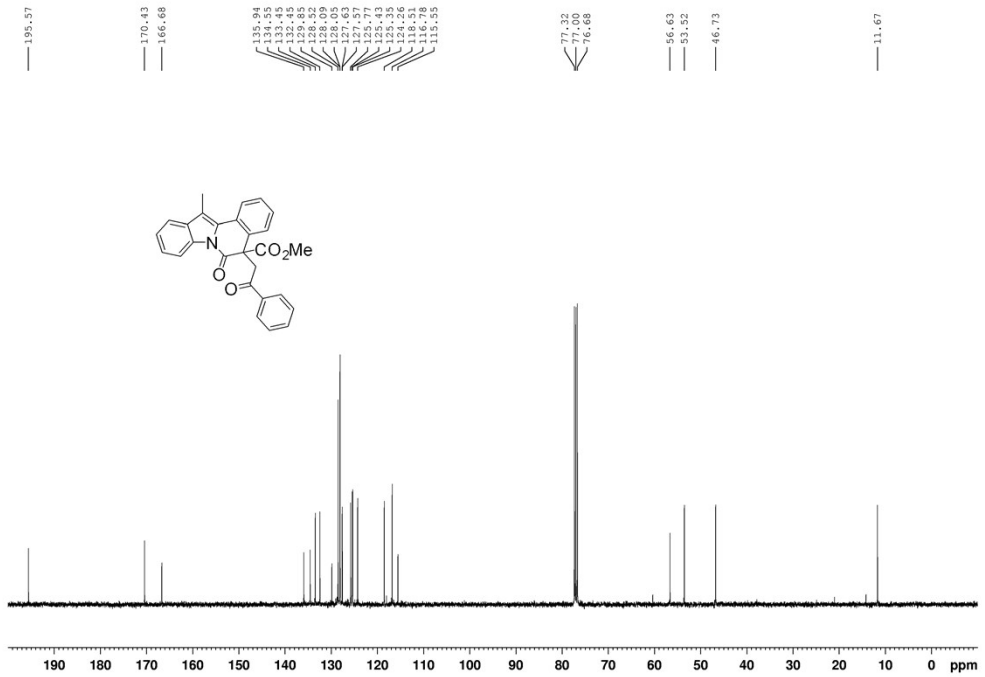
3,5,12-trimethyl-5-(2-oxo-2-phenylethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3ra)





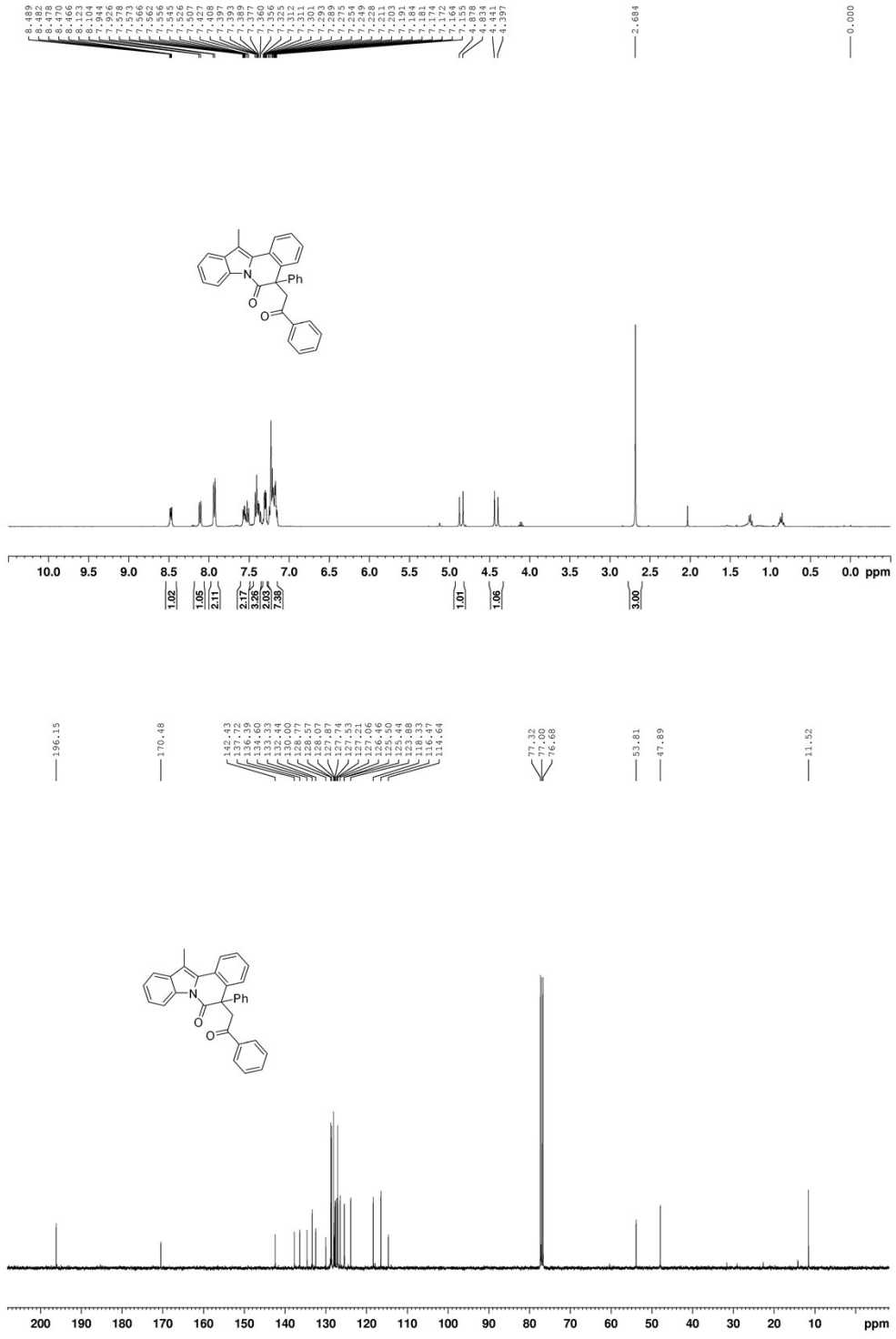
Methyl 12-methyl-6-oxo-5-(2-oxo-2-phenylethyl)-5,6-dihydroindolo[2,1-a]isoquinoline-5-carboxylate (3sa)





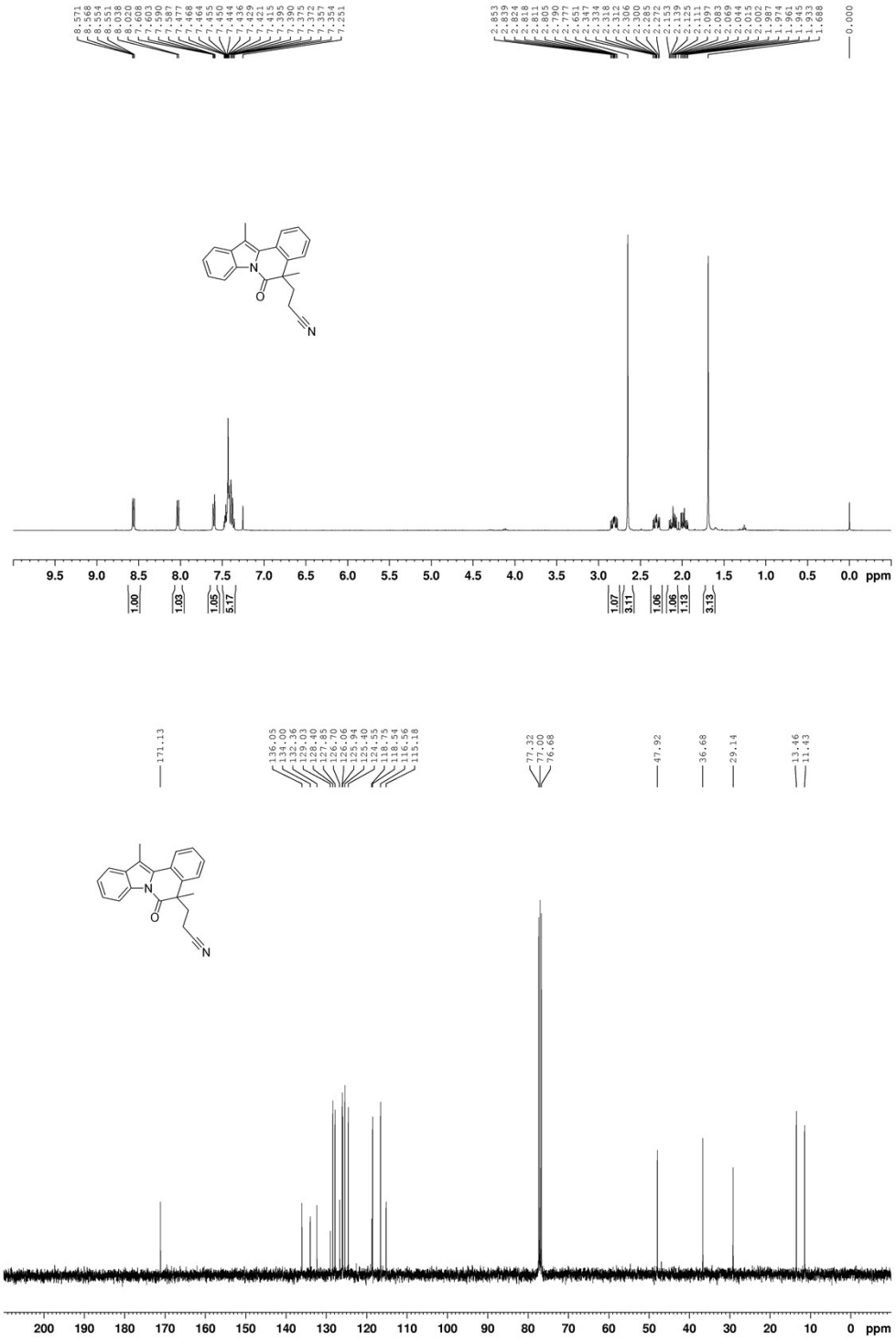
12-methyl-5-(2-oxo-2-phenylethyl)-5-phenylindolo[2,1-a]isoquinolin-6(5H)-one

(3ta)



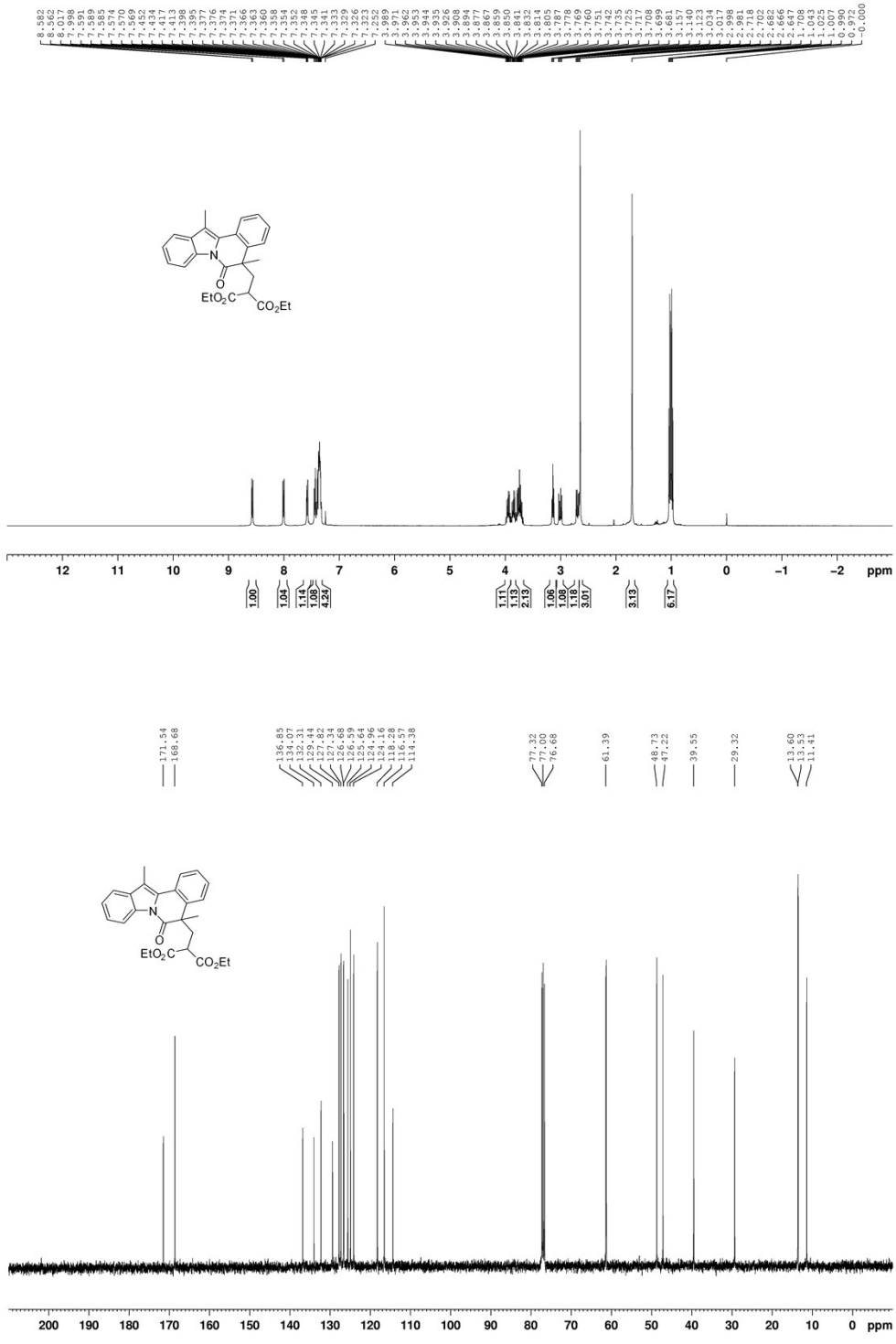
3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)propanenitrile

(5aa)

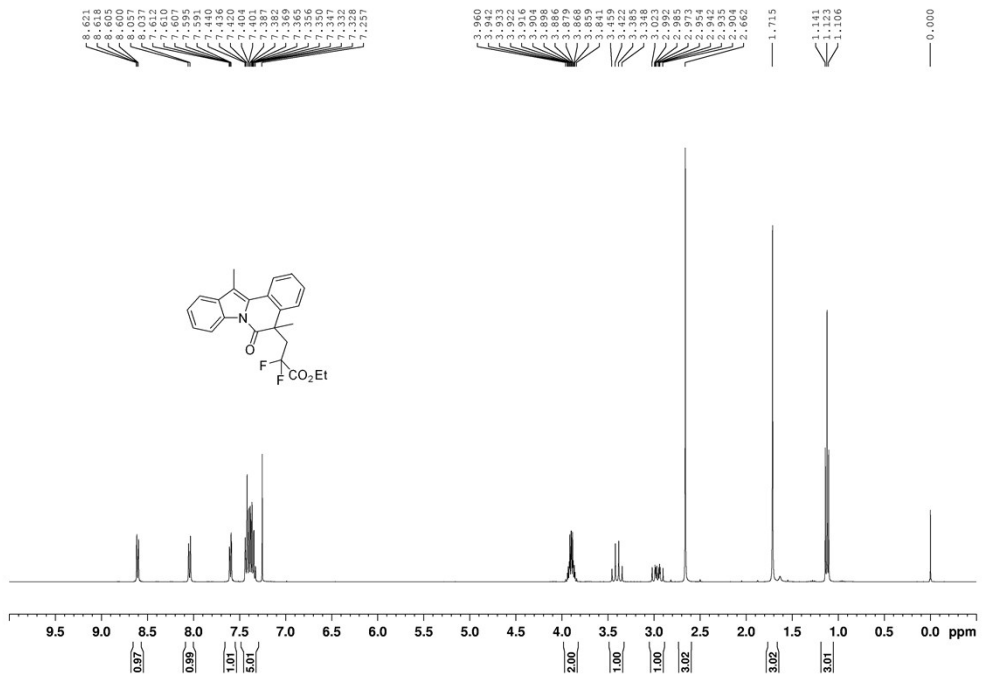


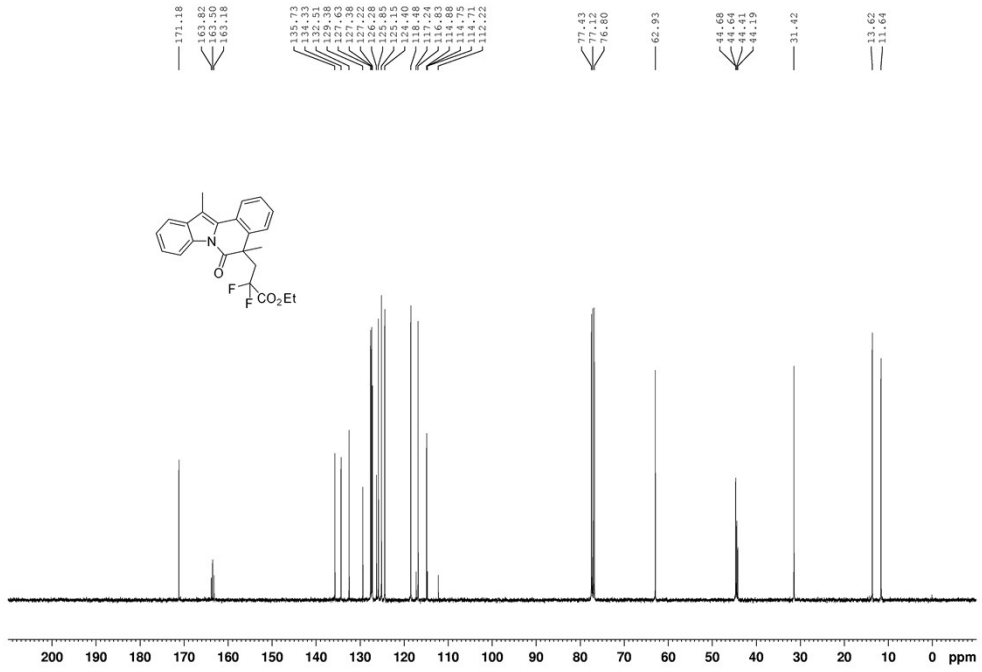
Diethyl 2-((5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)

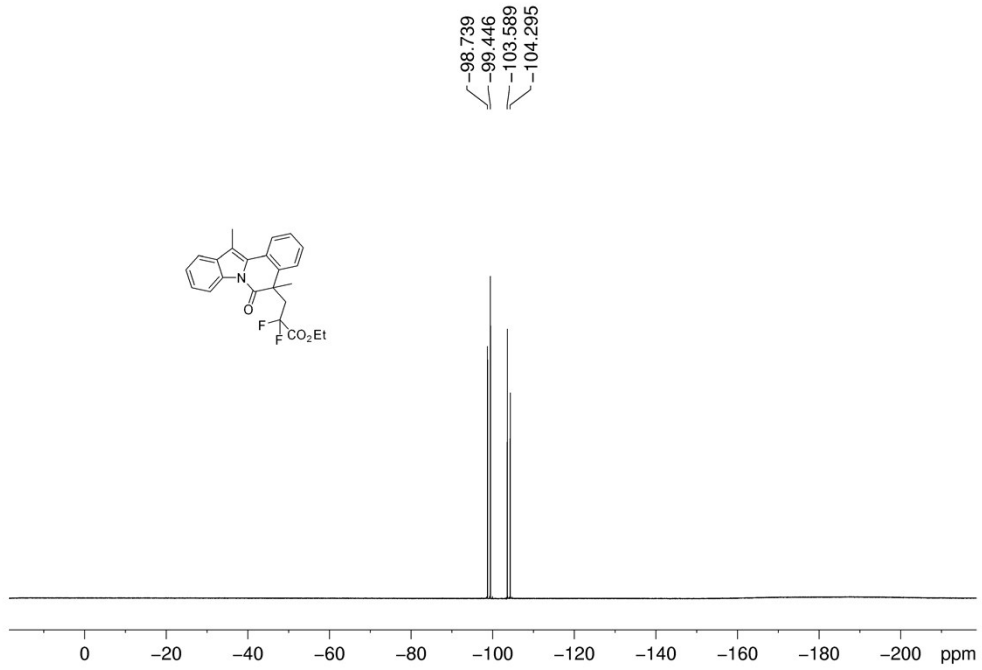
methyl)malonate (5ab)



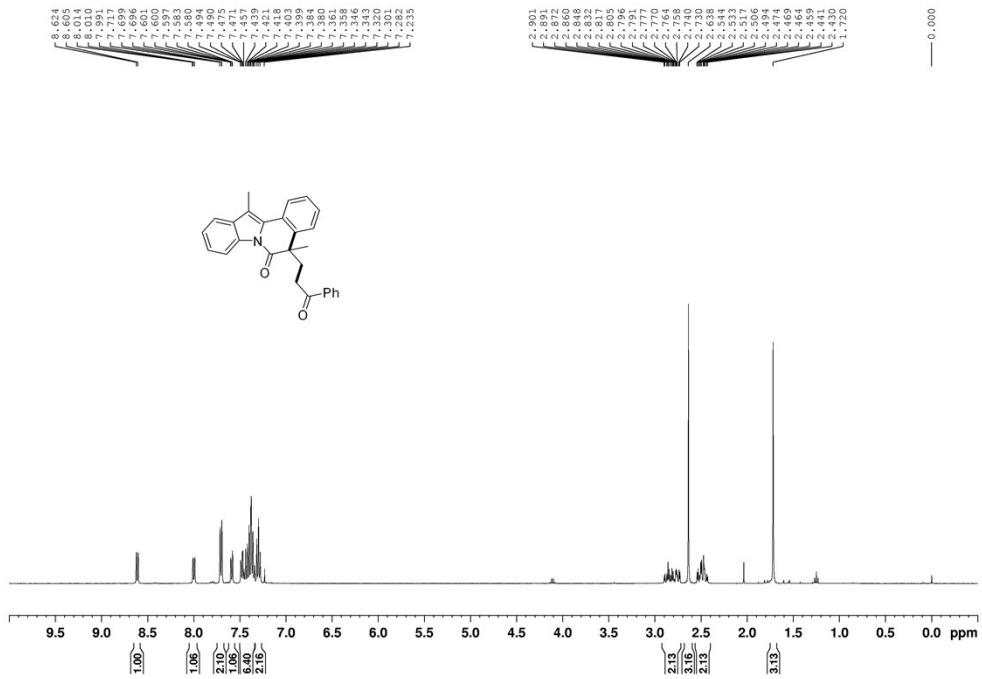
Ethyl 3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)-2,2-Difluoropropanoate (5ac)

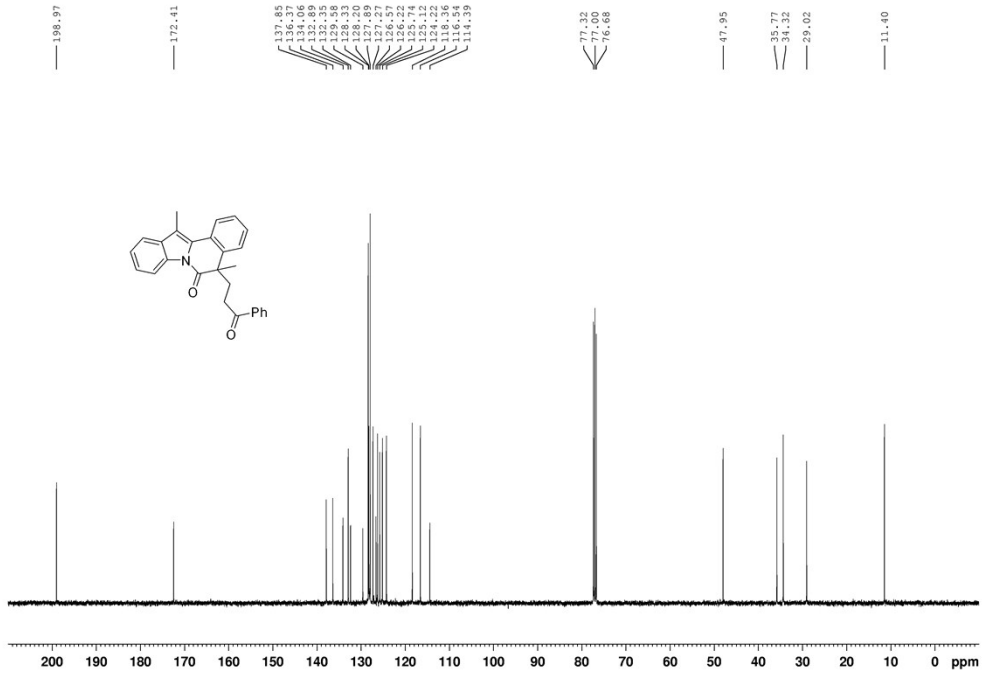




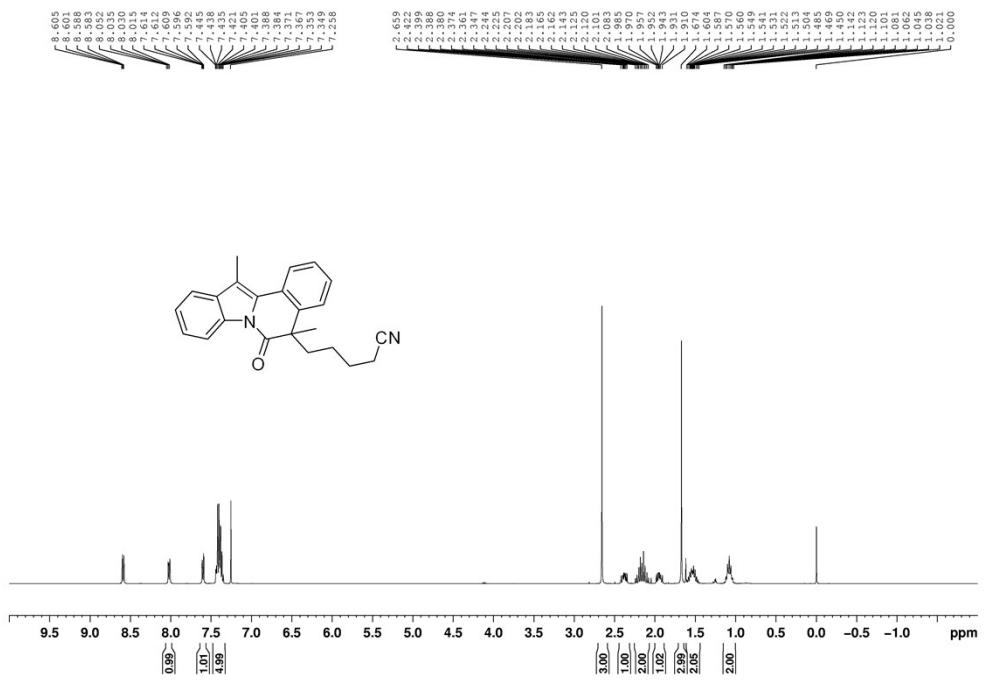


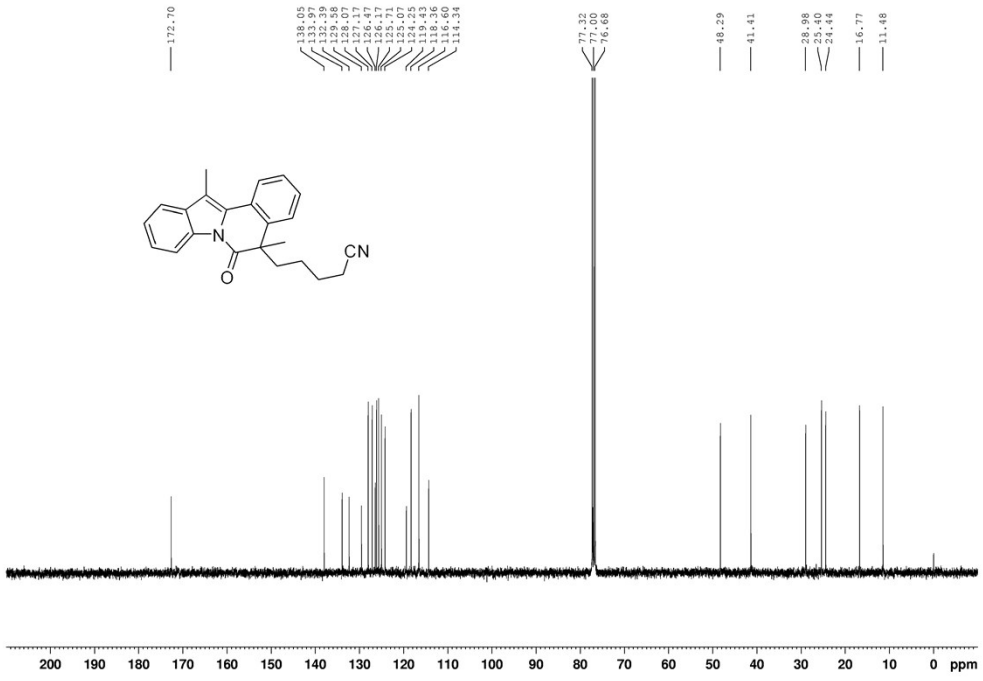
5,12-dimethyl-5-(3-oxo-3-phenylpropyl)indolo[2,1-a]isoquinolin-6(5H)-one (5ad)



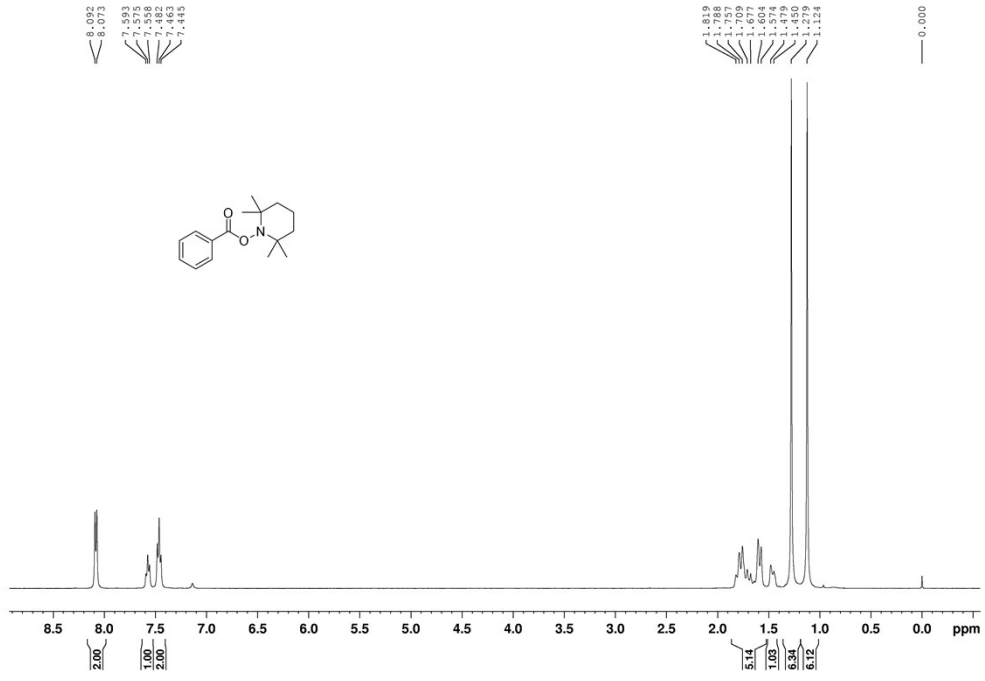


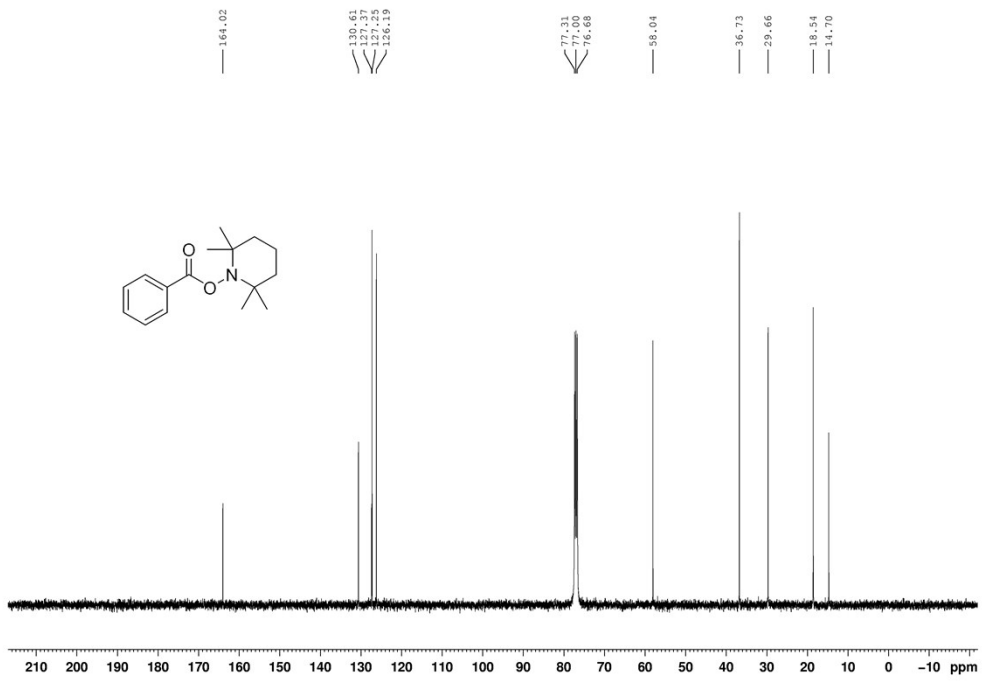
5-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)pentanenitrile (5ae)





2,2,6,6-tetramethylpiperidin-1-yl benzoate (6)

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