Visible-light-induced decarboxylative cascade cyclization of acryloylbenzamides with *N*-hydroxyphthalimide esters via EDA complexes

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Supporting Information

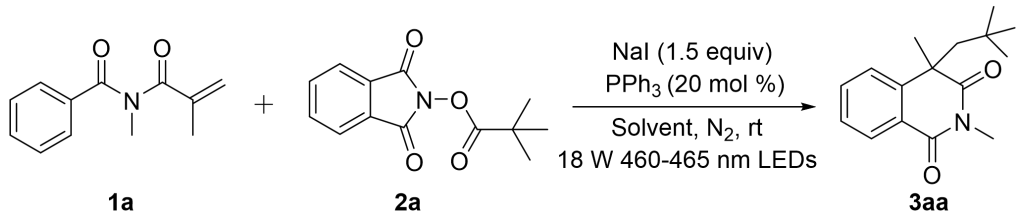
Contents

1. General Information

Unless otherwise indicated, all reagents were purchased from commercial distributors and used without further purification. ^{1}H NMR and ^{13}C NMR were recorded at 400 MHz and 500 MHz, 100 MHz and 125 MHz, respectively, using tetramethylsilane as an internal reference. High-resolution mass spectra (HRMS) were measured on a quadrupole time-of-flight (Q-TOF) mass spectrometer instrument with an electrospray ionization (ESI) source. UV-Vis spectra were obtained using a UV-5500 spectrometer. Melting points were uncorrected. Blue Led light were purchased from Ouying Lighting Co., Ltd. (18 W/5313 A/460-465 nm), The distance between the light source and the irradiation instrument is 8 cm. Flash column chromatography was performed over silica gel 200-300 mesh. Thin-layer chromatography (TLC) was carried out with silica gel GF254 plates. *N*-methacryloylbenzamides **1** and *N*-hydroxyphthalimide esters **2** were prepared according to the previous reported protocols.[1-2]

2. Optimization of the Reaction Conditions

Table S1. Screening of solvents[a]

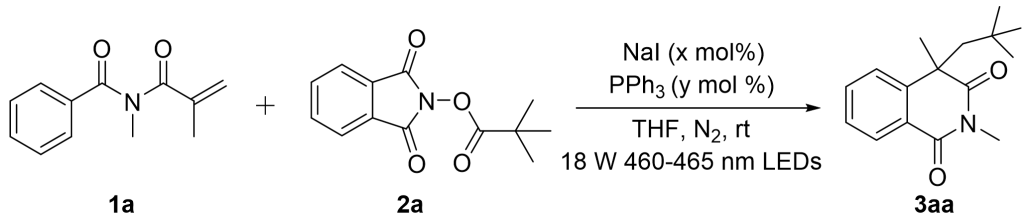


1a **2a** **3aa**

Entry	I source	P source	Solvent	Yield (%)[b]
1	NaI	PPh_3	DCM	trace
2	**NaI**	PPh_3	**THF**	**86**
3	NaI	PPh_3	Acetone	81
4	NaI	PPh_3	MeCN	72
5	NaI	PPh_3	Dioxane	trace
6	NaI	PPh_3	MeOH	trace
7	NaI	PPh_3	DMF	79
8	NaI	PPh_3	DMSO	82

[a] Reaction condition: **1a** (0.2 mmol), **2a** (0.3 mmol), NaI (0.3 mmol), PPh_3 (20 mol %), solvent (2 mL), under irradiation of 18 W blue LEDs for 17 h. [b] Isolated yields based on **1a**.

Table S2. Screening of catalytic system and others[a]



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

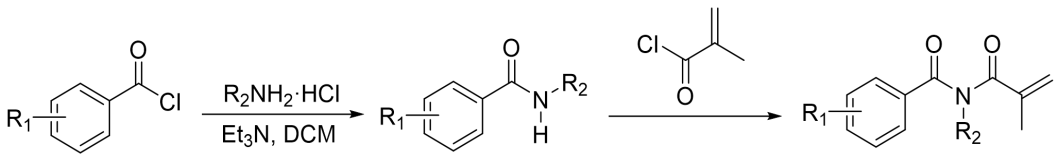
Entry	I source	P source	Solvent	Yield (%)[b]
1	KI	PPh_3	THF	trace
2	NH_4I	PPh_3	THF	26
3	$^nBu_4NI$	PPh_3	THF	74
4	NaI	PCy_3	THF	22
5	NaI	$P(C_6F_5)_3$	THF	trace
6[c]	NaI	PPh_3	THF	83
7[d]	NaI	PPh_3	THF	92
8[d,e]	NaI	PPh_3	THF	79
8[d,f]	NaI	PPh_3	THF	68
10[d,g]	NaI	PPh_3	THF	89
11[d,h]	NaI	PPh_3	THF	47
12[i]	NaI	PPh_3	THF	42
13[j]	NaI	PPh_3	THF	90
14[k]	NaI	PPh_3	THF	0
15[l]	NaI	PPh_3	THF	0
16[m]	NaI	PPh_3	THF	0

[a] Reaction condition: **1a** (0.2 mmol), **2a** (0.3 mmol), NaI (1.5 equiv), PPh_3 (20 mol %), THF (2 mL), under irradiation of 18 W blue LEDs for 17 h. [b] Isolated yields based on **1a**. [c] NaI (1 equiv.). [d] NaI (1.2 equiv.). [e] PPh_3 (10 mol %). [f] **2a** (0.2 mmol). [g] **2a** (0.4 mmol). [h] 18 W white LEDs. [i] NaI (0.2 equiv), 17 hrs. [j] NaI (0.2 equiv), 72 hrs. [k] Without blue LEDs. [l] Without NaI. [m] Without PPh_3.

3. General Procedures for Synthesis of Starting Materials

Synthesis of acryloylbenzamides 1. The acyl chloride (1 equiv.) was dissolved in CH_2Cl_2 (2 M). Amine hydrochloride (2 equiv.) and Et_3N (2 equiv.) were added and the mixture was stirred at 0 °C until consumption of acyl chloride. The corresponding amide was isolated after addition of 5 mL of saturated Na_2CO_3 solution and extraction with CH_2Cl_2. It was used without any purification in the next step. A round bottom flask was charged with amide (1.0 equiv.), DMAP (0.1 equiv.), Et_3N (2 equiv.) in CH_2Cl_2 (0.5 M). Then, acryloyl chloride (2 equiv.) was added slowly to the reaction mixture at 0 °C. After that, the residue was stirred at room temperature for 4-6 hrs.

The reaction was completed by TLC monitoring, the organic phase was separated, dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel affording the corresponding product.

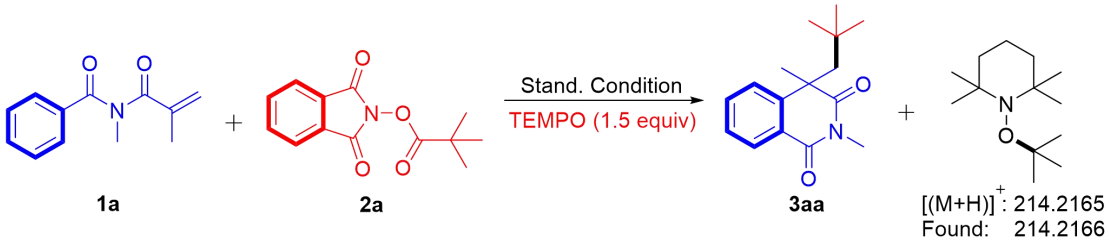


Scheme S1. Synthesis of acryloylbenzamides 1

Synthesis of *N*-hydroxyphthalimide esters 2. The corresponding alkyl carboxylic acid (10 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (11 mmol, 1.1 equiv.), and 4-dimethylaminopyridine (1.0 mmol, 10 mol %) were mixed in a flask with a magnetic stirring bar. Dry CH_2Cl_2 (40 mL) was added. Then a solution of *N*,*N*′-dicyclohexylcarbodiimide (11.0 mmol, 1.1 eq.) in CH_2Cl_2 (15 mL) was added slowly at room temperature. The reaction mixture was monitored by TLC at room temperature. After completed, the white precipitate was filtered off and the solution was concentrated under vacuum. The corresponding redox active esters were purified by column chromatography on silica gel (CH_2Cl_2 or petroleum ether/ethyl acetate as eluent).

Scheme S2. Synthesis of *N*-hydroxyphthalimide esters 2

4. Radical Trapping Experiments



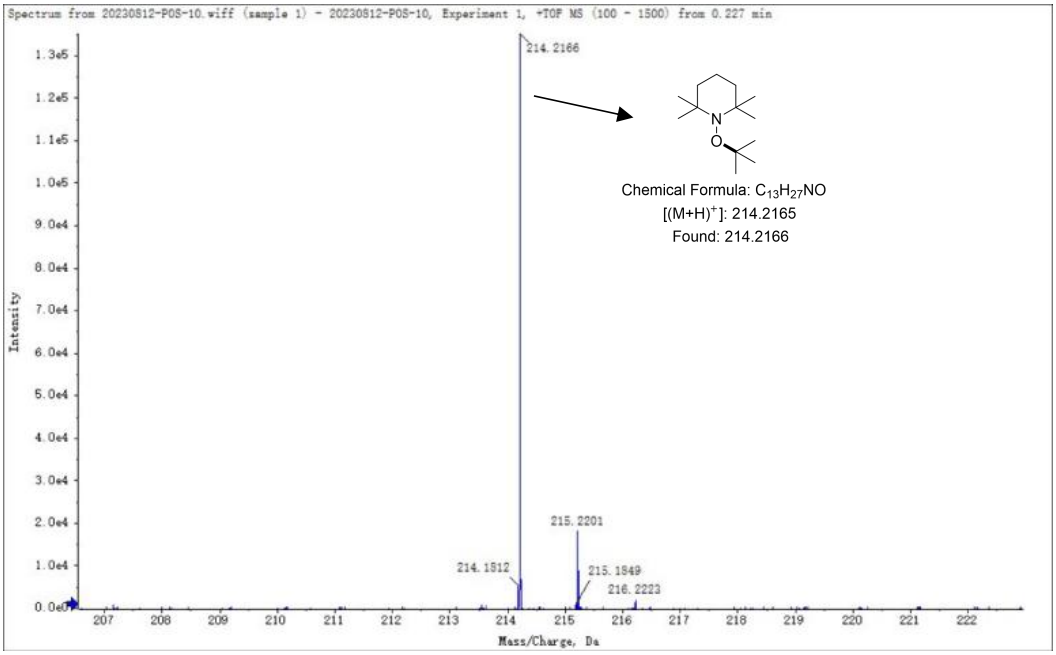
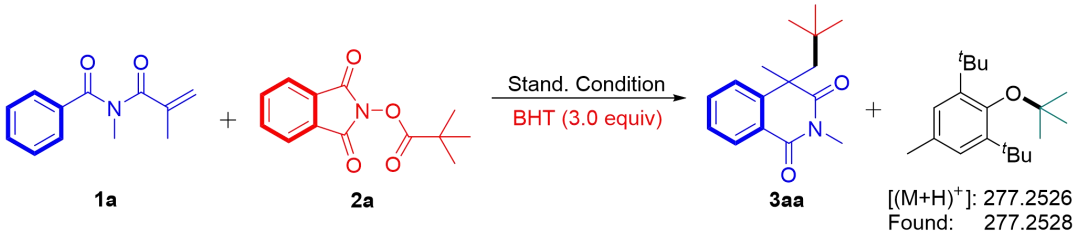


Figure S1. HR-MS Spectra of TEMPO-adduct.



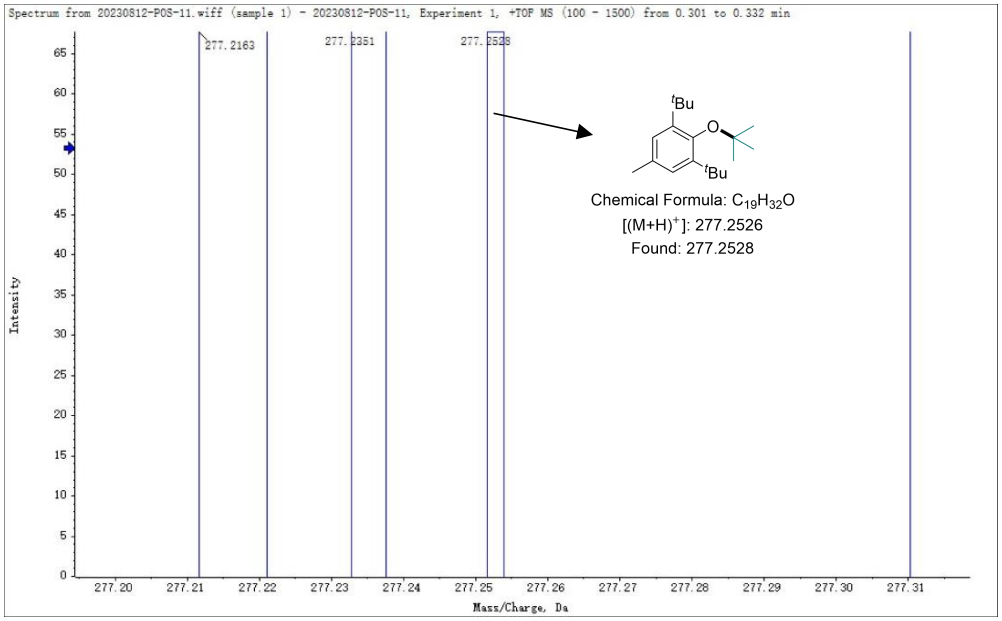
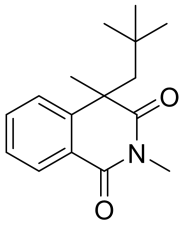


Figure S2. HR-MS Spectra of BHT-adduct.

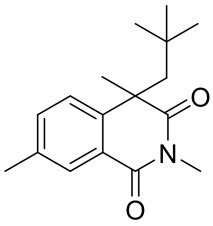
5. Characterization Data

2,4-Dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3aa)



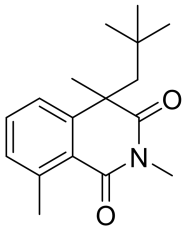
Yield 92% (47.5 mg); white solid; mp 90.1-91.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J*=7.9, 1.5 Hz, 1H), 7.59 (td, *J*=7.6, 1.5 Hz, 1H), 7.47-7.39 (m, 2H), 3.37 (s, 3H), 2.49 (d, *J*=14.3 Hz, 1H), 2.02 (d, *J*=14.3 Hz, 1H), 1.58 (s, 3H), 0.53 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.83, 164.57, 144.14, 133.41, 128.98, 127.35, 126.86, 124.39, 55.48, 46.06, 33.62, 32.01, 30.73, 27.30.

2,4,7-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ab)



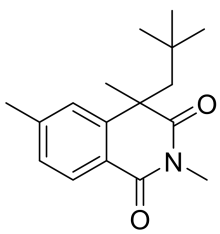
Yield 94% (51.5 mg); white solid; mp 95.3-97.6 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.05-8.01 (m, 1H), 7.41-7.34 (m, 1H), 7.32 (d, *J*=8.0 Hz, 1H), 3.35 (d, *J*=1.1 Hz, 3H), 2.46 (dd, *J*=14.3, 1.0 Hz, 1H), 2.40 (s, 3H), 1.98 (dd, *J*=14.3, 0.9 Hz, 1H), 1.53 (d, *J*=1.1 Hz, 3H), 0.52 (d, *J*=1.2 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.01, 164.71, 141.21, 137.16, 134.48, 128.93, 126.79, 124.11, 55.35, 45.76, 33.63, 31.97, 30.74, 27.27, 21.08.

2,4,8-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ac)



Yield 85% (46.6 mg); white solid; mp 86.6-89.0 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 (td, *J*=7.7, 1.2 Hz, 1H), 7.33 (d, *J*=7.9 Hz, 1H), 7.22-7.18 (m, 1H), 3.34 (d, *J*=1.4 Hz, 3H), 2.79 (s, 3H), 2.48 (dd, *J*=14.3, 1.3 Hz, 1H), 1.99 (dd, *J*=14.3, 1.2 Hz, 1H), 1.57 (d, *J*=1.4 Hz, 3H), 0.54 (d, *J*=1.5 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.55, 165.10, 145.54, 142.56, 132.22, 131.30, 125.24, 122.79, 55.90, 45.99, 34.05, 32.03, 30.74, 27.27, 24.34.

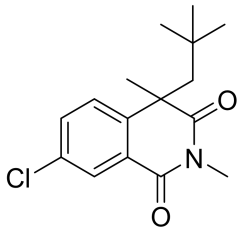
2,4,6-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ad)



Yield 65% (35.4 mg); white solid; mp 124.1-126.1 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (d, *J*=7.8 Hz, 1H), 7.21 (d, *J*=8.4 Hz, 2H), 3.35 (d, *J*=1.4 Hz, 3H), 2.50-2.46 (m, 1H), 2.43 (s, 3H), 2.00 (dd, *J*=14.2, 1.1 Hz, 1H), 1.56 (d, *J*=1.3 Hz, 3H), 0.53 (d,

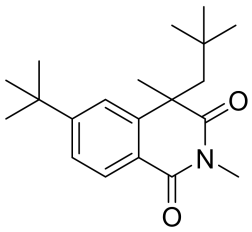
J=1.4 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.00, 164.59, 144.16, 144.09, 129.01, 128.45, 127.25, 121.93, 55.43, 45.98, 33.59, 32.03, 30.74, 27.21, 22.04.

7-Chloro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ae)



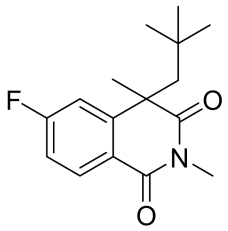
Yield 75% (44.0 mg); white solid; mp 105.2-107.1 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (dd, *J*=2.4, 1.2 Hz, 1H), 7.54 (ddd, *J*=8.6, 2.4, 1.1 Hz, 1H), 7.39 (d, *J*=8.4 Hz, 1H), 3.36 (d, *J*=1.2 Hz, 3H), 2.49 (dd, *J*=14.3, 1.1 Hz, 1H), 1.98 (d, *J*=14.4 Hz, 1H), 1.57-1.56 (m, 0H), 1.55 (d, *J*=1.1 Hz, 3H), 1.23 (s, 0H), 0.57 (d, *J*=1.1 Hz, 1H), 0.54 (d, *J*=1.2 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.51, 163.64, 142.77, 133.85, 133.81, 128.87, 128.78, 126.18, 55.65, 46.14, 33.84, 32.28, 31.06, 27.72.

6-(*tert*-Butyl)-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3af)



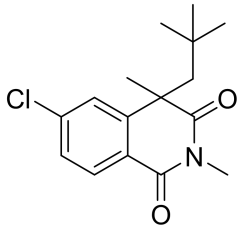
Yield 74% (46.5 mg); white solid; mp 138.7-141.6 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17-8.14 (m, 1H), 7.43 (d, *J*=8.0 Hz, 2H), 3.35 (d, *J*=1.4 Hz, 3H), 2.51 (d, *J*=14.3 Hz, 1H), 2.02 (d, *J*=14.3 Hz, 1H), 1.57 (s, 3H), 1.33 (d, *J*=1.4 Hz, 9H), 0.51 (d, *J*=1.5 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.43, 164.74, 157.12, 143.76, 129.08, 124.90, 124.00, 122.10, 55.54, 46.49, 35.60, 33.99, 32.20, 31.35, 30.98, 27.43.

6-Fluoro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ag)



Yield 90% (49.8 mg); white solid; mp 170.6-172.0 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.27 (ddd, *J*=9.6, 5.8, 1.2 Hz, 1H), 7.14-7.08 (m, 2H), 3.35 (d, *J*=1.3 Hz, 3H), 2.50 (dd, *J*=14.3, 1.3 Hz, 1H), 1.95 (dd, *J*=14.4, 1.2 Hz, 1H), 1.57 (d, *J*=1.4 Hz, 3H), 0.55 (d, *J*=1.4 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.26, 167.11, 165.08, 163.58, 147.28, 132.02, 120.92, 55.60, 46.28, 33.58, 32.05, 30.71, 27.31.

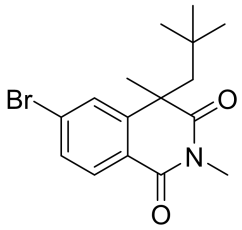
6-Chloro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ah)



Yield 58% (34.1 mg); white solid; mp 184.2-185.0 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.18 (dd, *J*=8.5, 1.2 Hz, 1H), 7.44-7.37 (m, 2H), 3.35 (d, *J*=1.3 Hz, 3H), 2.50 (dd, *J*=14.4, 1.2 Hz, 1H), 1.97 (dd, *J*=14.4, 1.0 Hz, 1H), 1.57 (d, *J*=1.2 Hz, 3H),

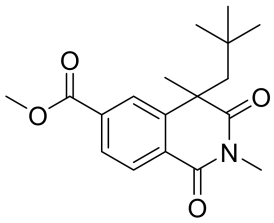
0.55 (d, *J*=1.3 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.85, 163.43, 145.63, 139.87, 130.38, 127.75, 126.76, 122.66, 55.24, 45.87, 33.26, 31.79, 30.50, 27.11.

6-Bromo-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ai)



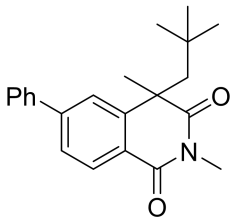
Yield 67% (44.9 mg); white solid; mp 167.2-168.6 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.60 – 7.53 (m, 2H), 3.35 (d, *J* = 1.0 Hz, 3H), 2.50 (dd, *J* = 14.5, 1.0 Hz, 1H), 1.99 – 1.95 (m, 1H), 1.57 (d, *J* = 1.0 Hz, 3H), 0.55 (d, *J* = 1.1 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.30, 164.08, 146.21, 131.17, 130.90, 130.30, 129.05, 123.56, 55.73, 46.34, 33.78, 32.31, 31.02, 27.64.

Methyl 2,4-dimethyl-4-neopentyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinoline-6-carboxylate (3aj)



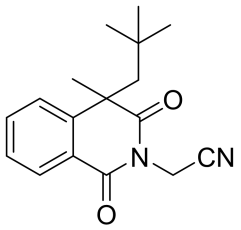
Yield 95% (60.1 mg); white solid; mp 121.1-123.0 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.32 (dd, *J*=8.2, 1.4 Hz, 1H), 8.13 (d, *J*=1.6 Hz, 1H), 8.04 (dd, *J*=8.2, 1.6 Hz, 1H), 3.96 (d, *J*=1.4 Hz, 3H), 3.38 (d, *J*=1.4 Hz, 3H), 2.52 (dd, *J*=14.4, 1.4 Hz, 1H), 2.09 (dd, *J*=14.4, 1.3 Hz, 1H), 1.61 (d, *J*=1.4 Hz, 3H), 0.52 (d, *J*=1.5 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.10, 165.91, 163.57, 144.07, 134.08, 129.04, 128.10, 127.72, 127.43, 55.16, 52.56, 45.93, 33.29, 31.77, 30.52, 27.22.

2,4-Dimethyl-4-neopentyl-6-phenylisoquinoline-1,3(2*H*,4*H*)-dione (3ak)



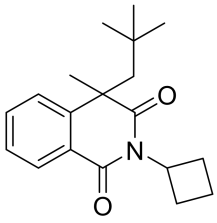
Yield 93% (62.4 mg); white solid; mp 90.9-92.5 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.6 Hz, 1H), 7.65 – 7.59 (m, 4H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.40 (m, 1H), 3.40 (s, 3H), 2.56 (d, *J* = 14.4 Hz, 1H), 2.11 (d, *J* = 14.4 Hz, 1H), 1.63 (s, 3H), 0.58 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.09, 164.64, 146.38, 144.71, 140.17, 129.83, 129.40, 128.85, 127.65, 126.60, 125.76, 123.42, 55.68, 46.47, 33.94, 32.29, 31.07, 27.55.

2-(4-Methyl-4-neopentyl-1,3-dioxo-3,4-dihydroisoquinolin-2(1*H*)-yl)acetonitrile (3al)



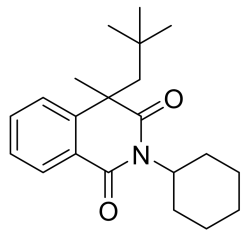
Yield 80% (45.5 mg); white solid; mp 165.1-167.3 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.27 (dd, *J*=7.9, 1.5 Hz, 1H), 7.66 (td, *J*=7.7, 1.5 Hz, 1H), 7.51-7.44 (m, 2H), 4.94-4.84 (m, 2H), 2.54 (d, *J*=14.4 Hz, 1H), 2.08 (d, *J*=14.5 Hz, 1H), 1.62 (s, 3H), 0.55 (d, *J*=1.1 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.82, 163.30, 144.12, 134.66, 129.66, 128.09, 127.48, 123.50, 114.60, 55.44, 46.97, 34.00, 32.31, 31.11, 27.91.

2-Cyclobutyl-4-methyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3am)



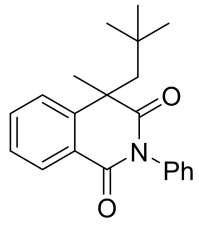
Yield 76% (45.3 mg); white solid; mp 92.7-94.2 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.20 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.55 (td, *J* = 7.7, 1.5 Hz, 1H), 7.42 – 7.36 (m, 2H), 5.19 (p, *J* = 8.9 Hz, 1H), 2.79 (dp, *J* = 12.0, 9.5 Hz, 2H), 2.48 (d, *J* = 14.3 Hz, 1H), 2.35 – 2.26 (m, 2H), 1.99 – 1.87 (m, 2H), 1.82 – 1.71 (m, 1H), 1.55 (s, 3H), 0.53 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.71, 164.63, 143.71, 132.88, 128.61, 127.01, 126.52, 124.82, 54.89, 47.88, 46.11, 33.48, 31.79, 30.65, 27.85, 27.80, 15.40.

2-Cyclohexyl-4-methyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3an)



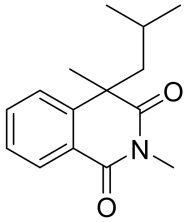
Yield 75% (48.8 mg); white solid; mp 96.2-98.3 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.54 (tt, *J*=8.2, 1.3 Hz, 1H), 7.42-7.36 (m, 2H), 4.81 (tt, *J*=12.2, 3.8 Hz, 1H), 2.54-2.48 (m, 1H), 2.39 (qd, *J*=12.5, 3.7 Hz, 2H), 1.98 (d, *J*=14.3 Hz, 1H), 1.86-1.78 (m, 2H), 1.68-1.62 (m, 2H), 1.62-1.56 (m, 1H), 1.54-1.52 (m, 3H), 1.36 (qq, *J*=13.4, 3.8, 3.3 Hz, 2H), 1.29-1.18 (m, 1H), 0.54 (d, *J*=1.1 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.61, 164.43, 143.69, 132.76, 128.76, 126.98, 126.57, 124.75, 54.41, 53.64, 46.13, 33.98, 31.77, 30.78, 28.61, 28.47, 26.35, 26.30, 25.30.

4-Methyl-4-neopentyl-2-phenylisoquinoline-1,3(2*H*,4*H*)-dione (3ao)



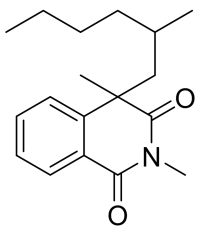
Yield 82% (52.7 mg); white solid; mp 159.2-160.3 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.29 (dd, *J*=7.9, 1.5 Hz, 1H), 7.65 (td, *J*=7.6, 1.5 Hz, 1H), 7.56-7.41 (m, 5H), 7.18 (dd, *J*=8.2, 1.3 Hz, 2H), 2.59 (d, *J*=14.4 Hz, 1H), 2.11 (d, *J*=14.4 Hz, 1H), 1.69 (s, 3H), 0.68 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.35, 164.28, 143.93, 135.47, 134.54, 133.45, 129.17, 129.10, 128.40, 128.04, 127.25, 126.94, 124.13, 123.72, 54.53, 46.59, 34.02, 31.2, 30.83.

4-Isobutyl-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ba)



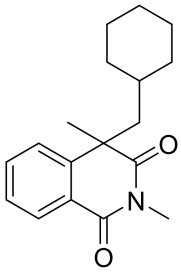
Yield 70% (34.5 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (dt, *J*=8.0, 1.4 Hz, 1H), 7.65-7.59 (m, 1H), 7.44-7.38 (m, 2H), 3.37 (d, *J*=1.3 Hz, 3H), 2.31 (ddd, *J*=13.9, 8.1, 1.2 Hz, 1H), 1.92 (ddd, *J*=14.0, 5.1, 1.2 Hz, 1H), 1.56 (d, *J*=1.4 Hz, 3H), 1.18 (dtdd, *J*=8.2, 6.6, 5.1, 1.4 Hz, 1H), 0.61 (dd, *J*=6.7, 1.3 Hz, 3H), 0.57 (dd, *J*=6.7, 1.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.99, 164.59, 143.91, 133.88, 128.96, 127.29, 125.90, 124.72, 51.04, 46.99, 31.71, 27.28, 25.65, 24.04, 22.42.

2,4-Dimethyl-4-(2-methylhexyl)isoquinoline-1,3(2*H*,4*H*)-dione (3ca)



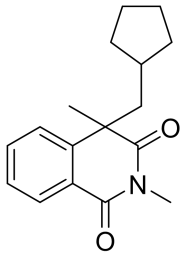
Yield 71% (41.0 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (ddd, *J*=8.1, 3.1, 1.3 Hz, 1H), 7.65-7.57 (m, 1H), 7.44-7.36 (m, 2H), 3.37 (s, 3H), 2.35 (dd, *J*=14.0, 5.8 Hz, 1H), 2.22 (dd, *J*=14.0, 8.4 Hz, 0H), 2.00 (dd, *J*=14.0, 3.0 Hz, 0H), 1.79 (dd, *J*=13.9, 6.1 Hz, 1H), 1.58 (d, *J*=5.5 Hz, 3H), 1.14-0.87 (m, 3H), 0.76 (dt, *J*=8.7, 6.9 Hz, 3H), 0.55 (d, *J*=6.1 Hz, 1H), 0.40 (d, *J*=6.6 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.86, 176.63, 164.37, 164.32, 143.89, 143.54, 133.60, 133.53, 128.64, 127.03, 127.01, 125.73, 125.61, 124.57, 124.46, 50.24, 49.02, 46.91, 46.56, 37.52, 36.53, 31.22, 30.51, 30.07, 29.75, 28.56, 28.42, 27.04, 26.96, 22.54, 22.51, 20.57, 19.39, 13.83, 13.81.

4-(Cyclohexylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3da)



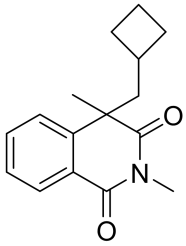
Yield 80% (45.7 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (dd, *J*=7.9, 1.5 Hz, 1H), 7.62 (td, *J*=7.6, 1.4 Hz, 1H), 7.45-7.38 (m, 2H), 3.38 (t, *J*=1.2 Hz, 3H), 2.32 (ddd, *J*=14.2, 7.5, 1.5 Hz, 1H), 1.89 (ddd, *J*=14.1, 4.7, 1.4 Hz, 1H), 1.55 (d, *J*=1.5 Hz, 3H), 1.51-1.42 (m, 3H), 1.26-1.21 (m, 1H), 1.17-1.10 (m, 1H), 1.00-0.68 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.03, 164.67, 144.03, 133.89, 128.98, 127.28, 125.87, 124.62, 49.67, 46.76, 34.98, 34.39, 33.07, 31.87, 27.33, 26.15, 26.12, 26.07.

4-(Cyclopentylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ea)



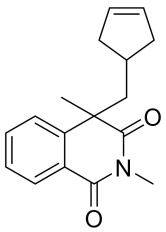
Yield 71% (38.6 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26-8.21 (m, 1H), 7.61 (td, *J*=7.6, 1.5 Hz, 1H), 7.41 (t, *J*=7.5 Hz, 2H), 3.37 (s, 3H), 2.37 (dd, *J*=13.8, 7.3 Hz, 1H), 2.03 (dd, *J*=13.8, 5.1 Hz, 1H), 1.60 (s, 3H), 1.49-1.33 (m, 3H), 1.30-1.14 (m, 4H), 0.93 (dq, *J*=12.0, 8.7 Hz, 1H), 0.73 (ddt, *J*=12.1, 9.0, 4.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.00, 164.64, 144.09, 133.84, 128.84, 127.29, 125.86, 124.81, 49.59, 47.48, 37.49, 33.69, 32.40, 30.38, 27.29, 25.01, 24.73.

4-(Cyclobutylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3fa)



Yield 43% (22.0 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (dd, *J*=7.9, 1.4 Hz, 1H), 7.64-7.59 (m, 1H), 7.44-7.38 (m, 2H), 3.35 (d, *J*=1.0 Hz, 3H), 2.34 (dd, *J*=13.5, 7.9 Hz, 1H), 1.95 (dd, *J*=13.5, 6.3 Hz, 1H), 1.77 (dt, *J*=15.0, 7.7 Hz, 1H), 1.67 (qd, *J*=6.7, 6.2, 4.2 Hz, 1H), 1.63-1.49 (m, 6H), 1.48-1.40 (m, 1H), 1.26 (t, *J*=10.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.76, 164.65, 143.79, 133.84, 128.75, 127.32, 125.75, 124.88, 51.45, 46.96, 32.99, 29.03, 28.60, 28.50, 27.30, 18.80.

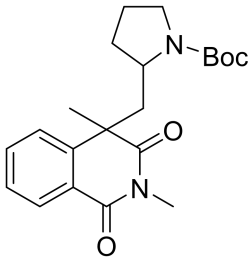
4-(Cyclopent-3-en-1-ylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ga)



Yield 70% (37.6 mg); yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (dd, *J*=8.1, 1.6 Hz, 1H), 7.65-7.60 (m, 1H), 7.42 (ddd, *J*=7.1, 6.1, 1.2 Hz, 2H), 5.50-5.40 (m, 2H), 3.38 (s, 3H), 2.51 (dd, *J*=13.7, 7.6 Hz, 1H), 2.15-2.04 (m, 2H), 1.90-1.79 (m, 2H), 1.77-1.67 (m, 1H), 1.64 (s, 3H), 1.59-1.51 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.90, 164.56, 143.83,

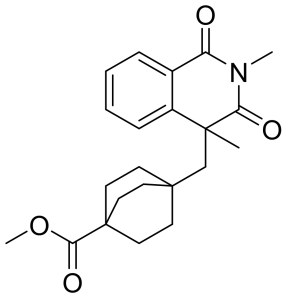
133.91, 129.90, 129.89, 128.89, 127.42, 125.86, 124.87, 49.92, 47.54, 39.48, 38.50, 35.81, 29.93, 27.31.

***tert*-Butyl-2-((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)-pyrrolidine-1-carboxylate (3ha)**



Yield 69% (51.0 mg); white solid; mp 106.7.1-108.8 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25-8.21 (m, 1H), 7.61 (t, *J*=7.6 Hz, 1H), 7.42 (t, *J*=7.5 Hz, 2H), 3.35 (s, 3H), 3.05 (dt, *J*=11.7, 6.1 Hz, 1H), 2.11-1.72 (m, 1H), 1.60 (s, 4H), 1.45 (t, *J*=14.3 Hz, 4H), 1.34 (s, 11H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.04, 164.30, 154.41, 143.55, 134.04, 133.52, 132.57, 128.90, 127.15, 124.96, 123.32, 45.76, 28.30, 27.07.

Methyl4-((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)bicyclo[2.2.2]octane-1-carboxylate (3ia)



Yield 57% (42.1 mg); white solid; mp 154.1-155.7 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (dd, *J*=8.3, 1.5 Hz, 1H), 7.59 (td, *J*=7.5, 1.5 Hz, 1H), 7.42 (t, *J*=7.3 Hz, 2H), 3.53 (s, 3H), 3.37 (s, 3H), 2.41 (d, *J*=14.5 Hz, 1H), 1.96 (d, *J*=14.5 Hz, 1H), 1.53 (s, 3H), 1.52-1.46 (m, 6H), 1.05-0.93 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.19, 176.68, 164.43, 144.13, 133.53, 129.08, 127.47, 126.61, 124.12, 53.48, 51.67, 45.51, 38.16, 33.99, 32.00, 31.25, 28.39, 27.36.

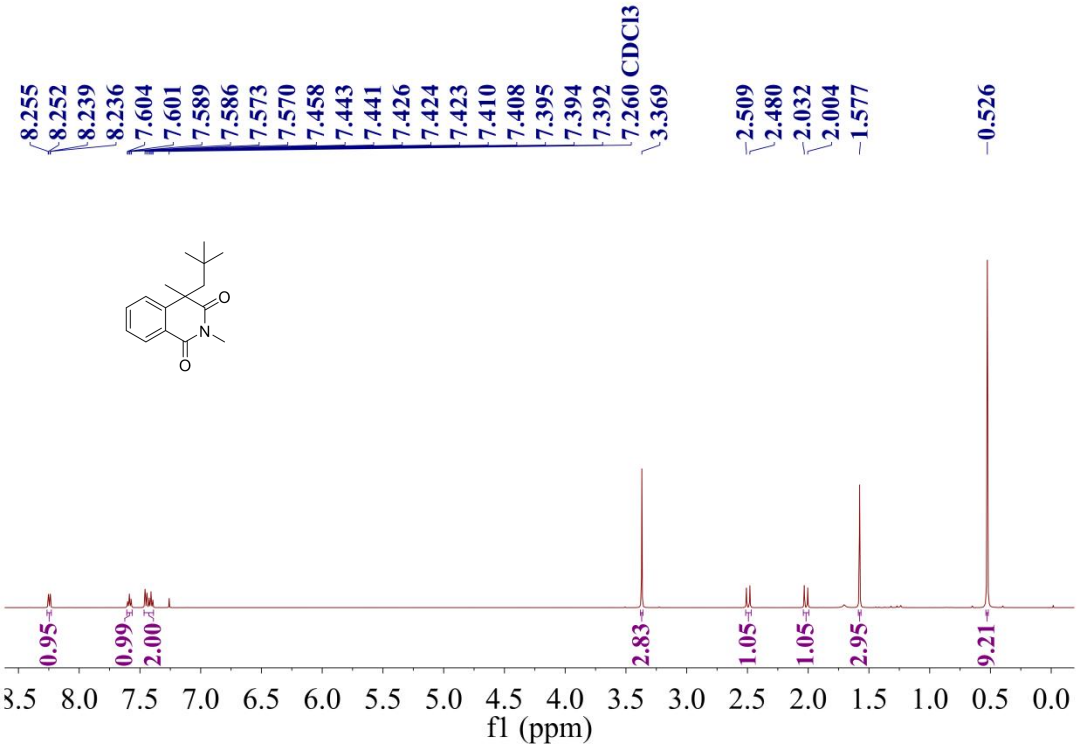
6. References

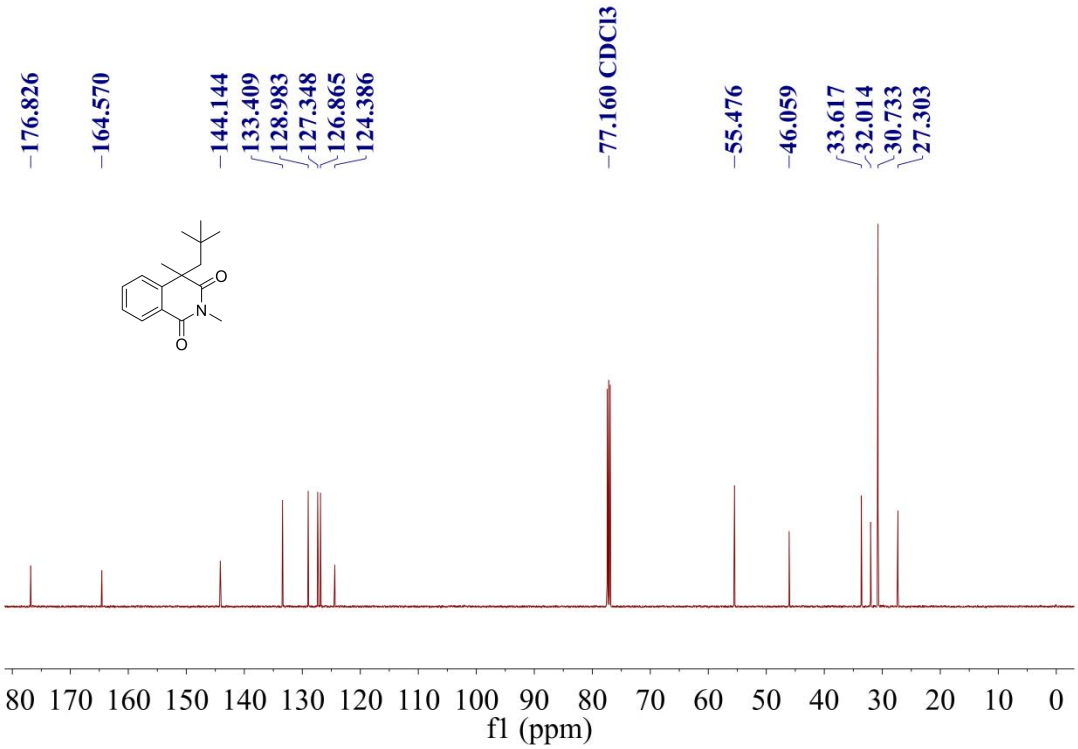
[1] Kong, W.; Casimiro, M.; Fuentes, N.; Merino, E.; Nevado, C., *Angew. Chem. Int. Ed.* **2013,** *52*, 13086-13090.

[2] Fu, M.-C.; Shang, R.; Zhao, B.; Wang, B.; Fu, Y., *Science* **2019,** *363*, 1429-1434.

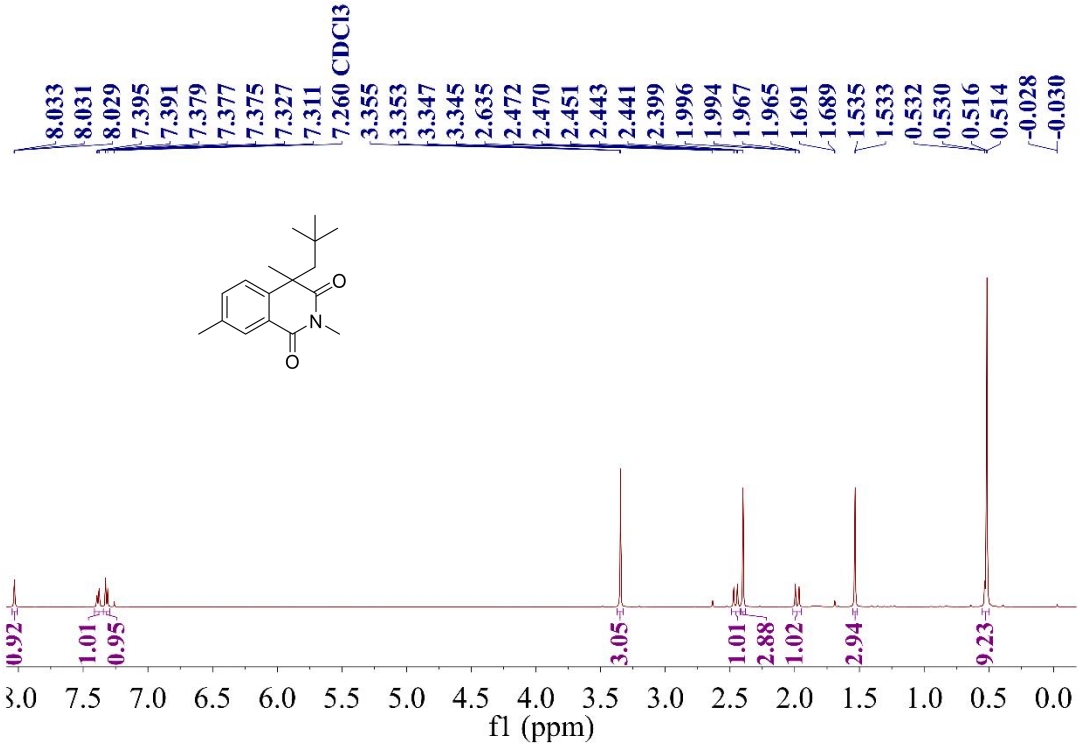
7. NMR Spectra of Products

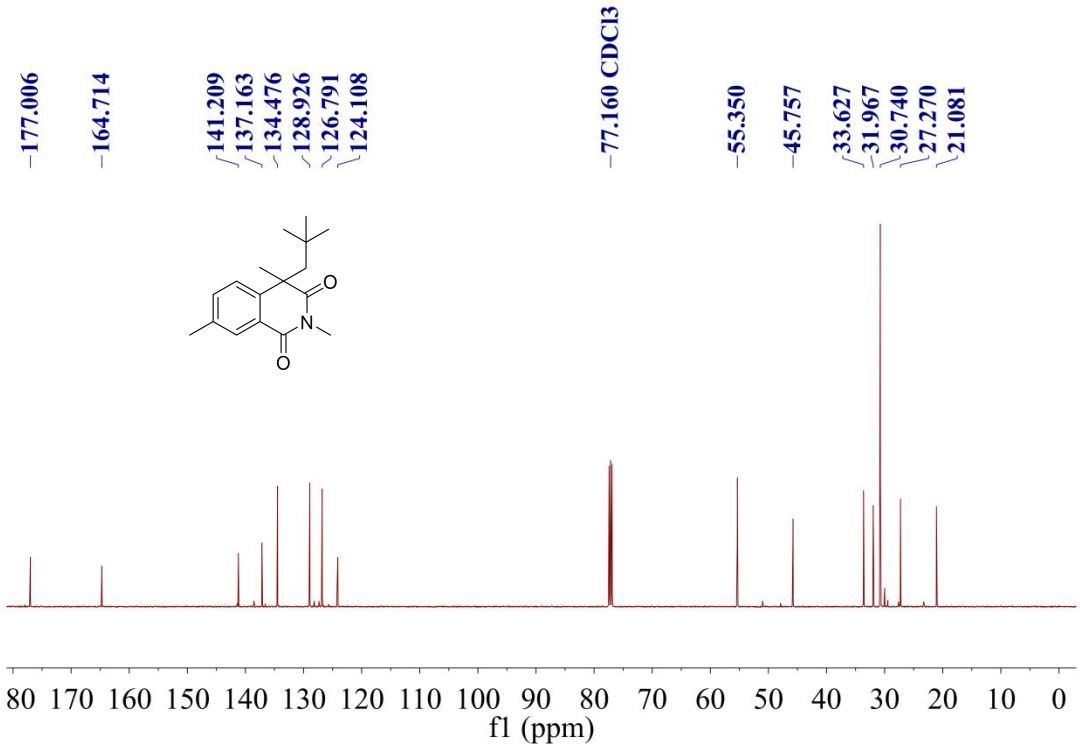
2,4-Dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3aa)



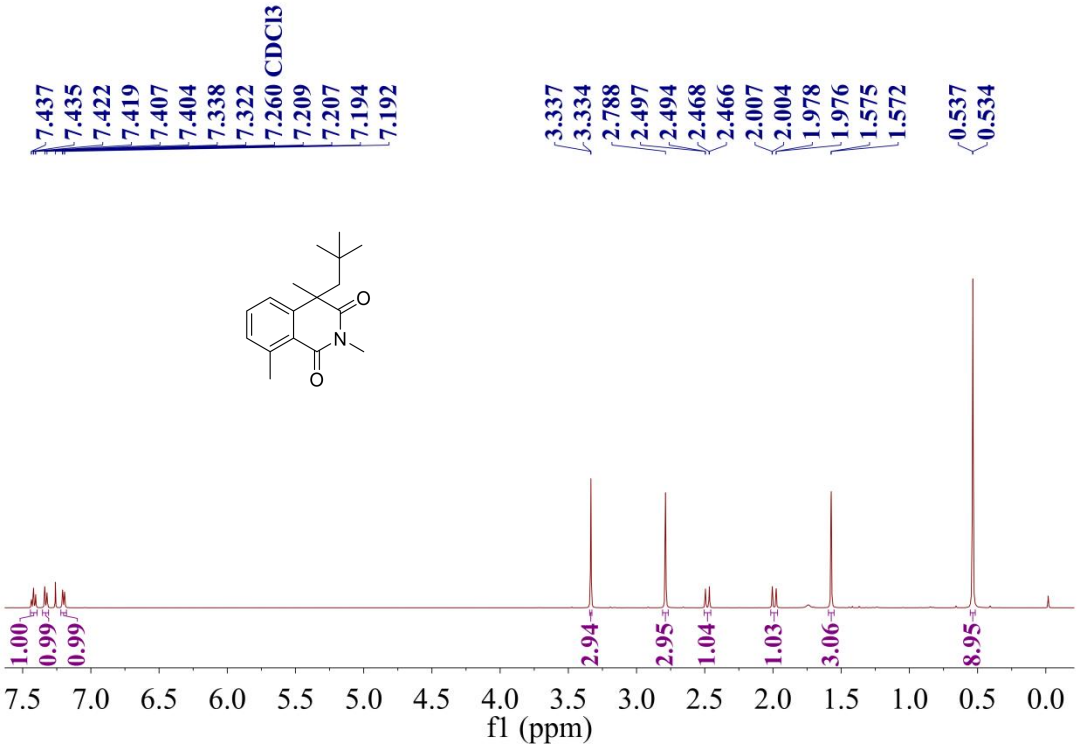


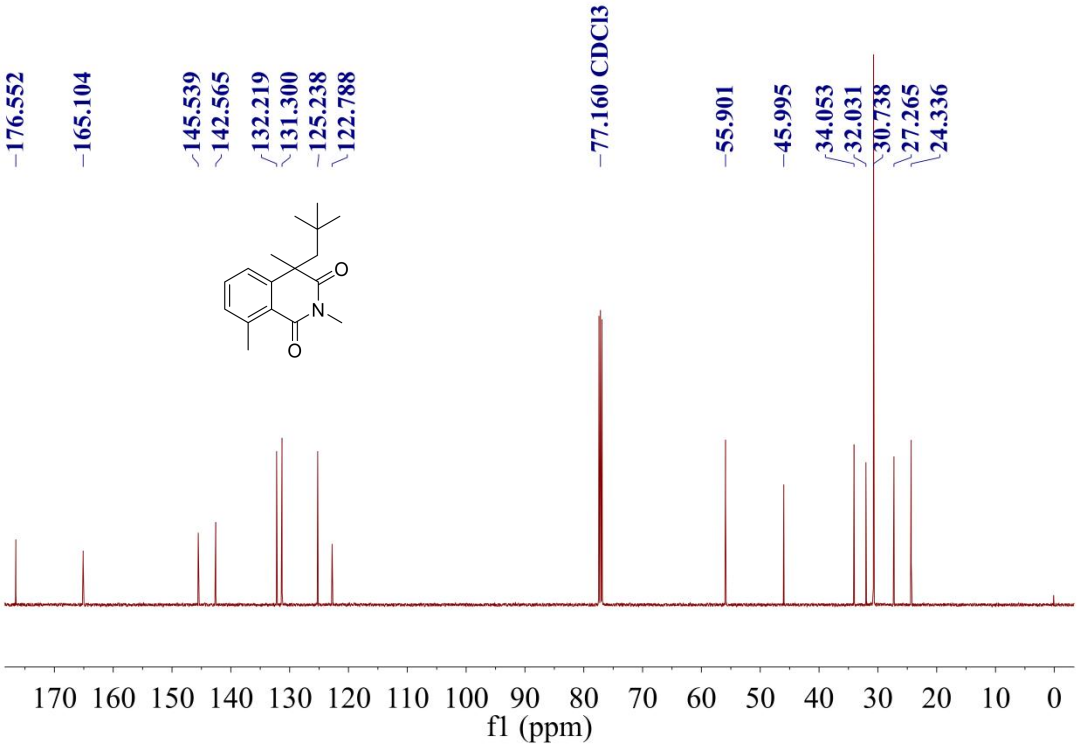
2,4,7-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ab)



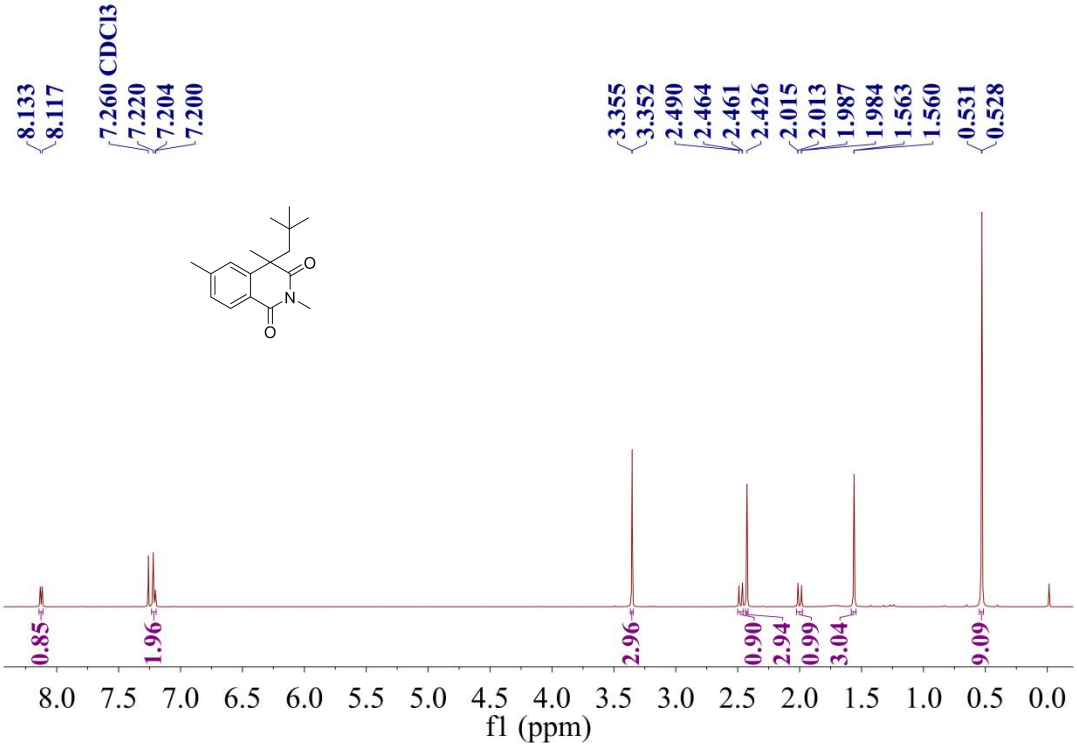


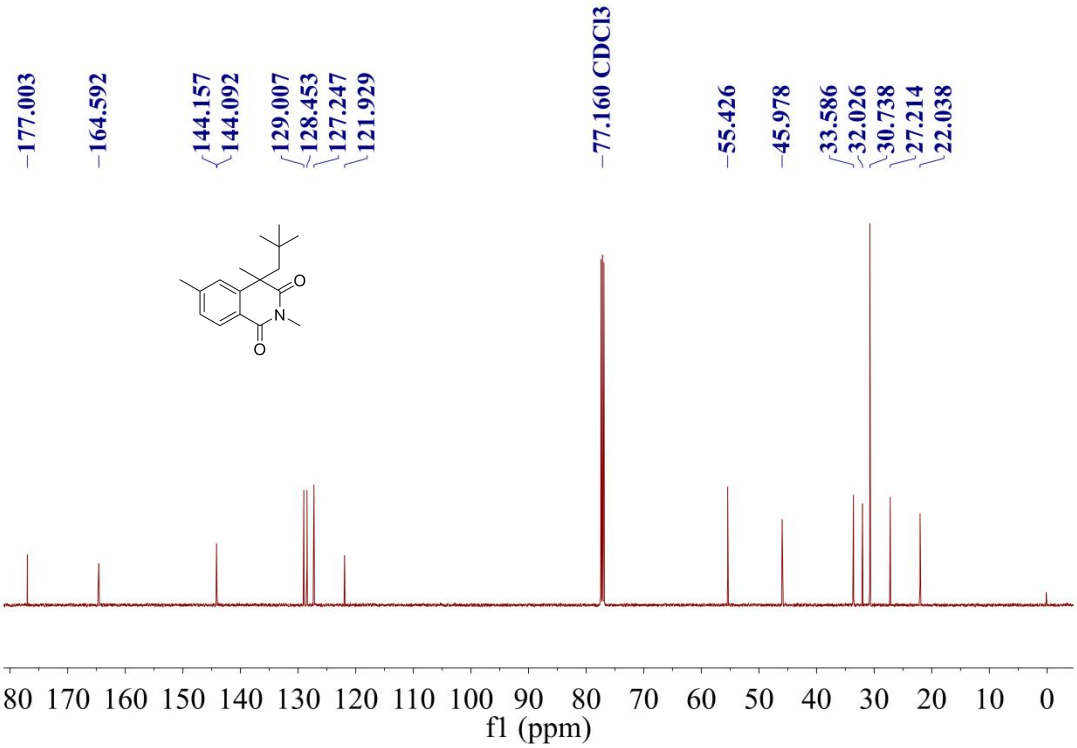
2,4,8-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ac)



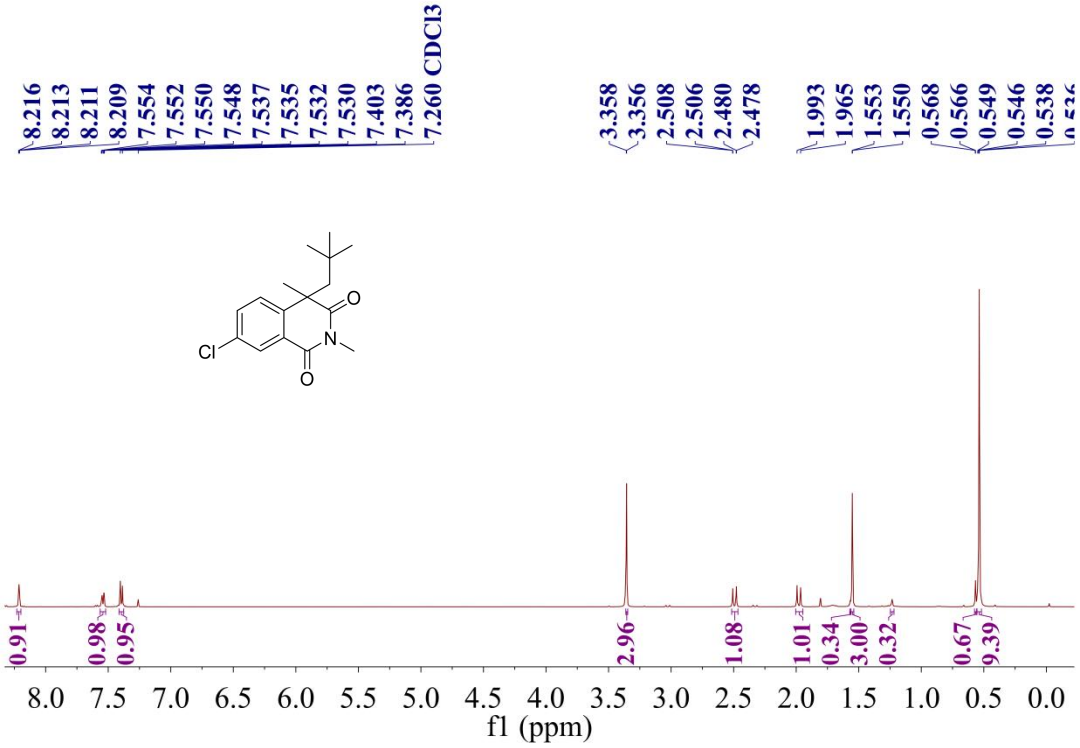


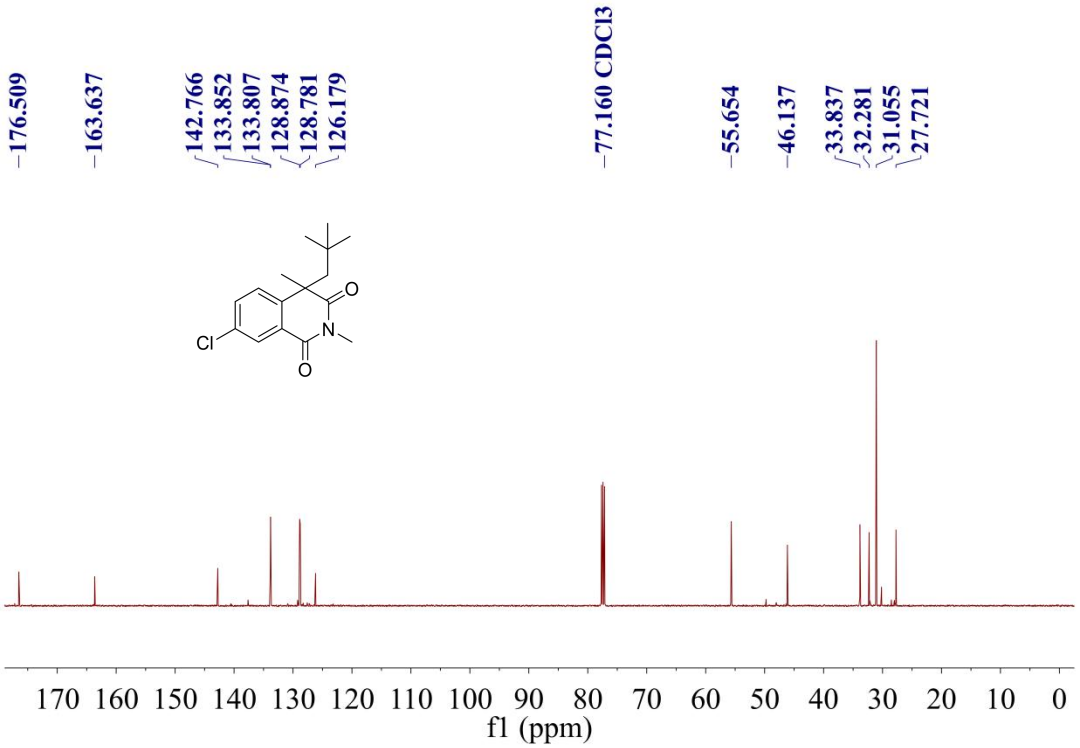
2,4,6-Trimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ad)



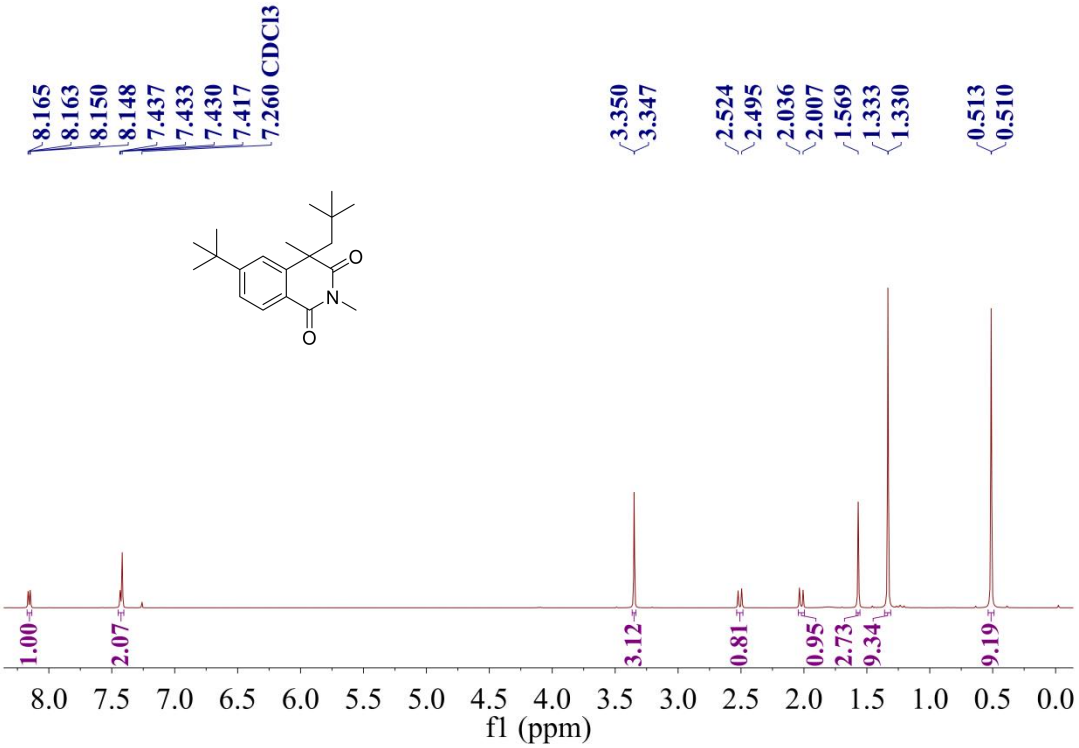


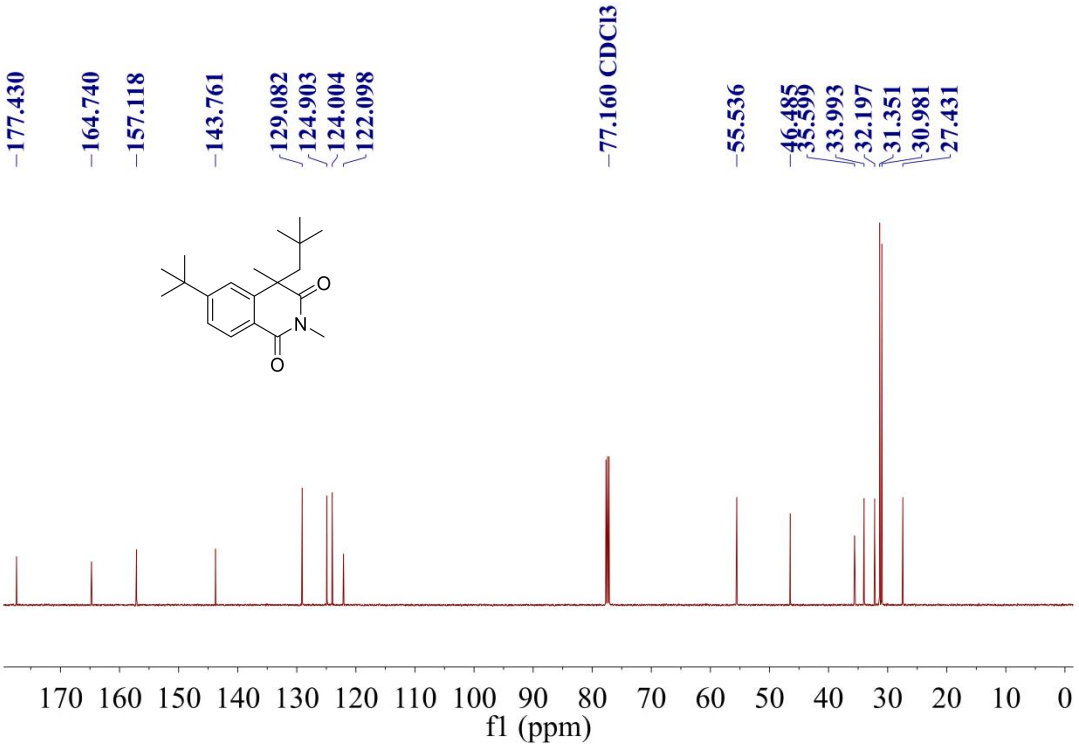
7-Chloro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ae)



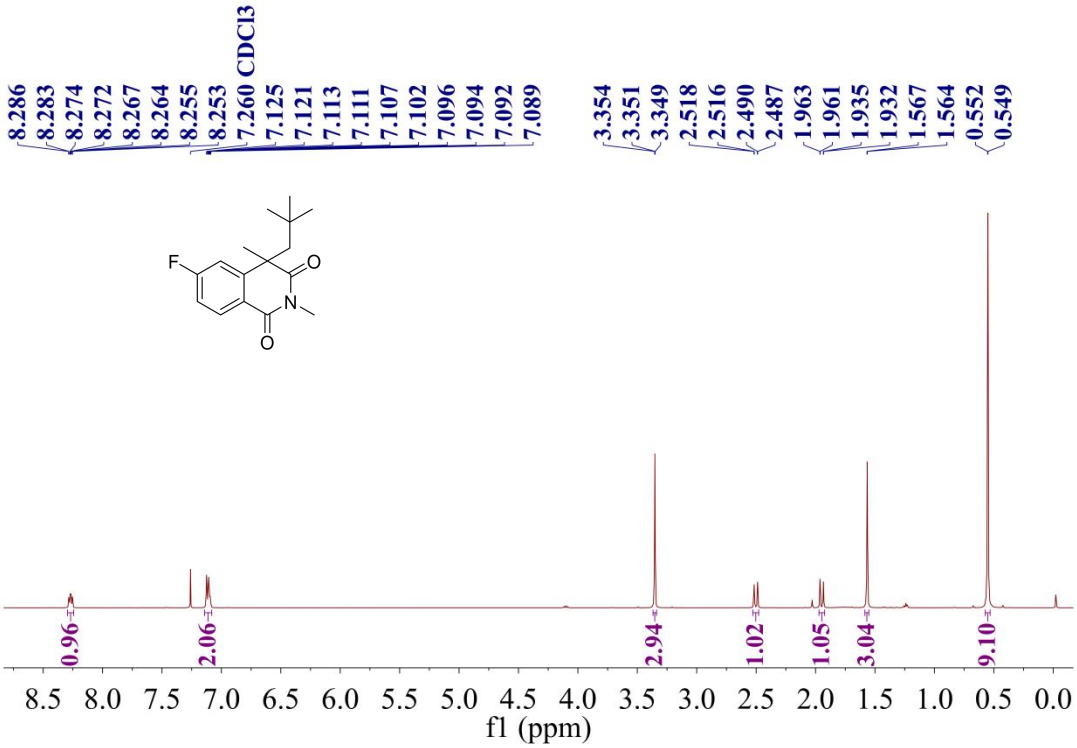


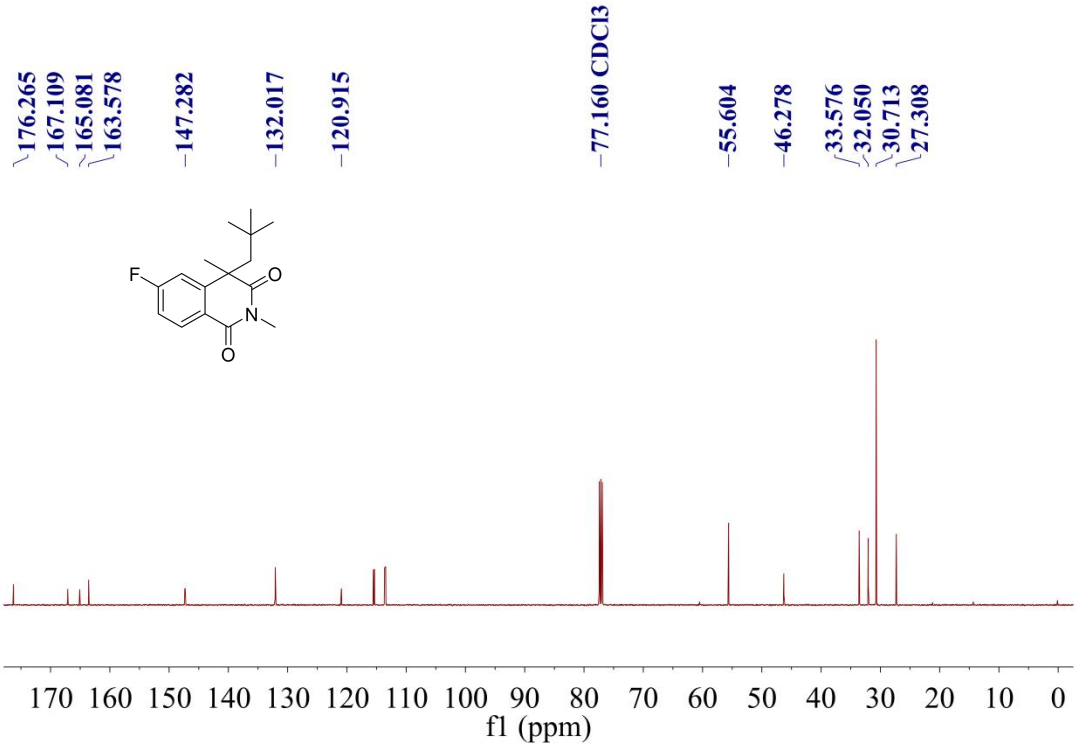
6-(*tert*-Butyl)-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3af)

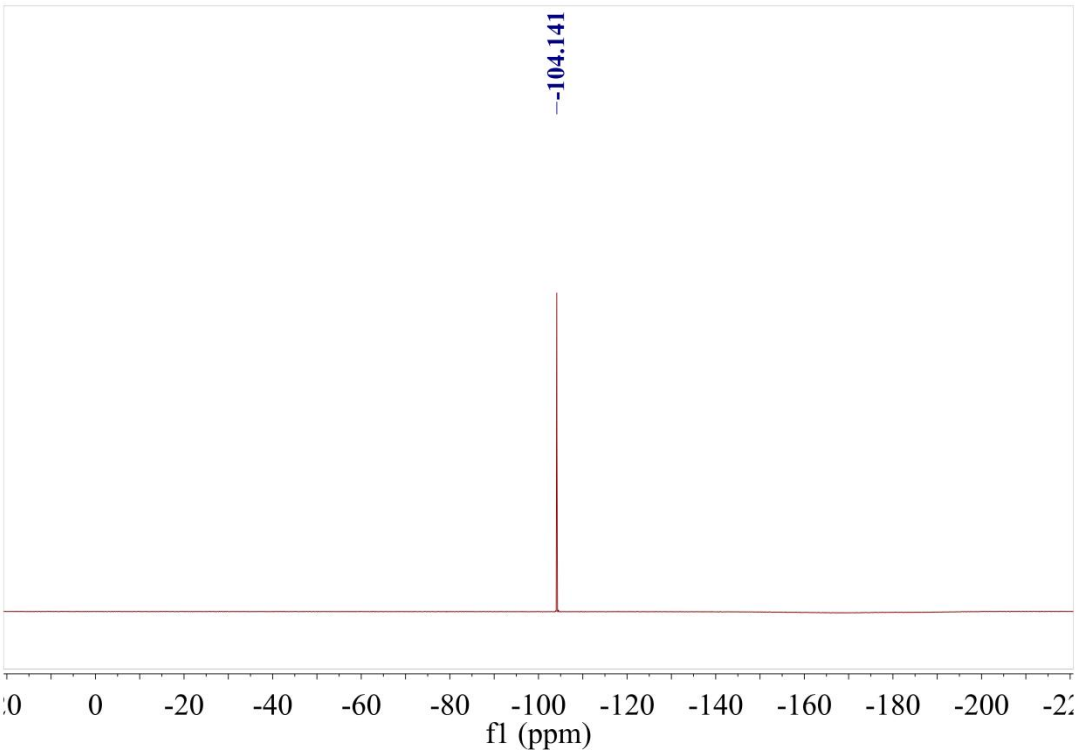




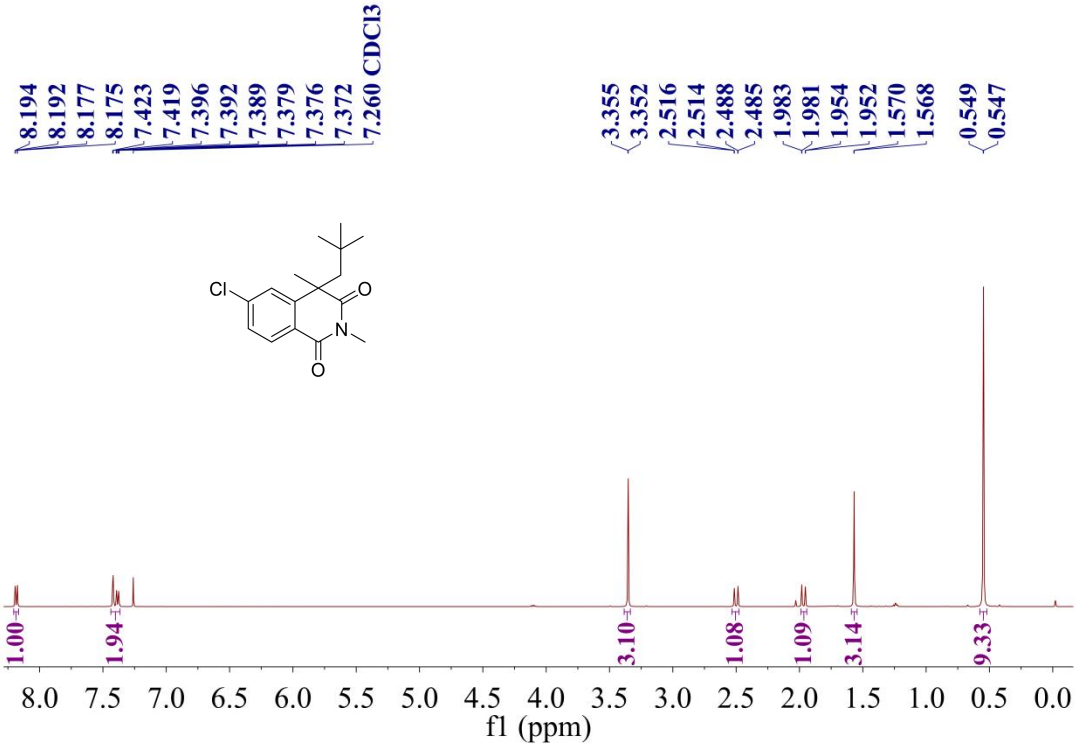
6-Fluoro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ag)

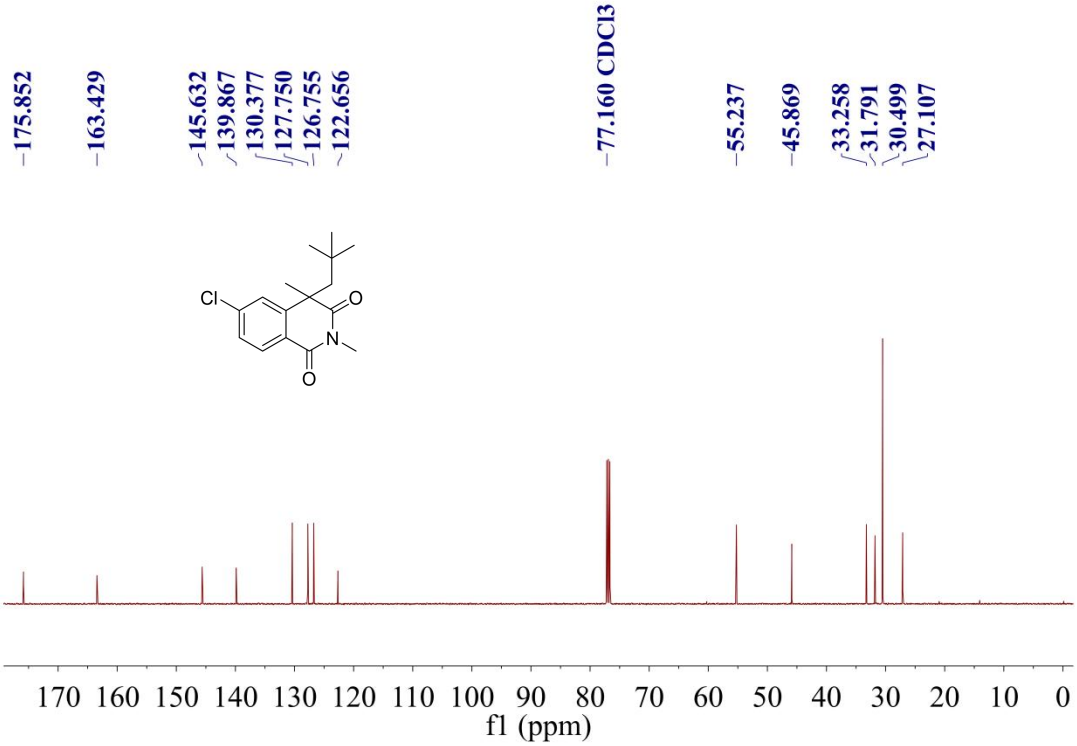




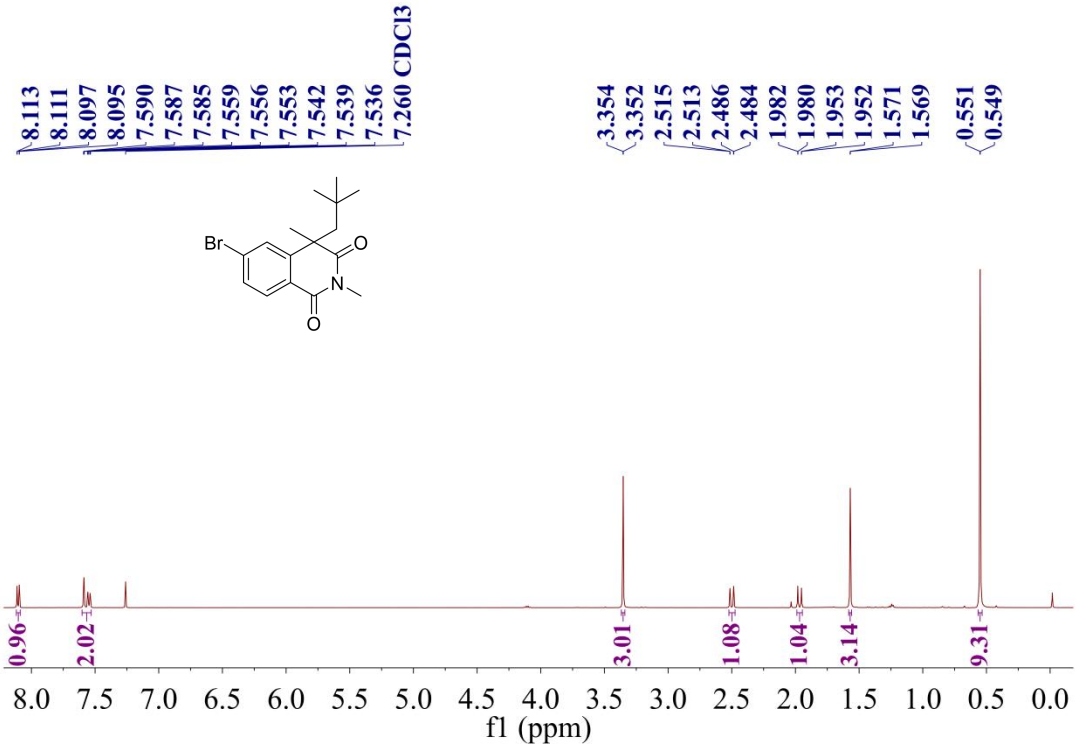

-104.141
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

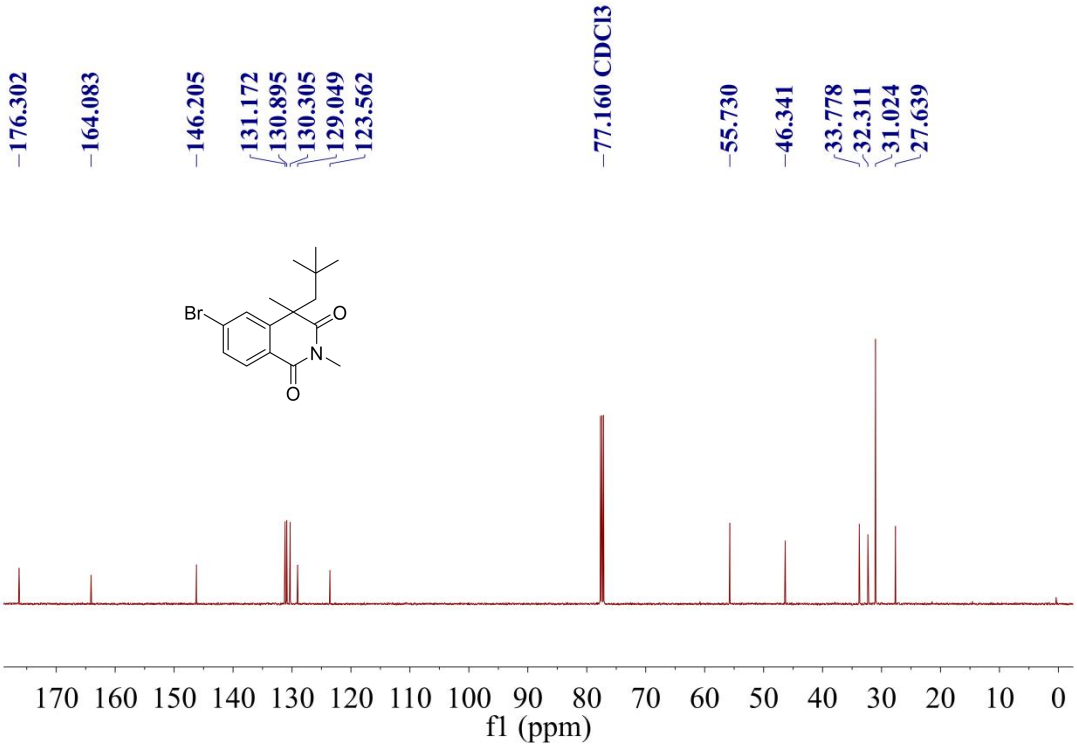
6-Chloro-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ah)



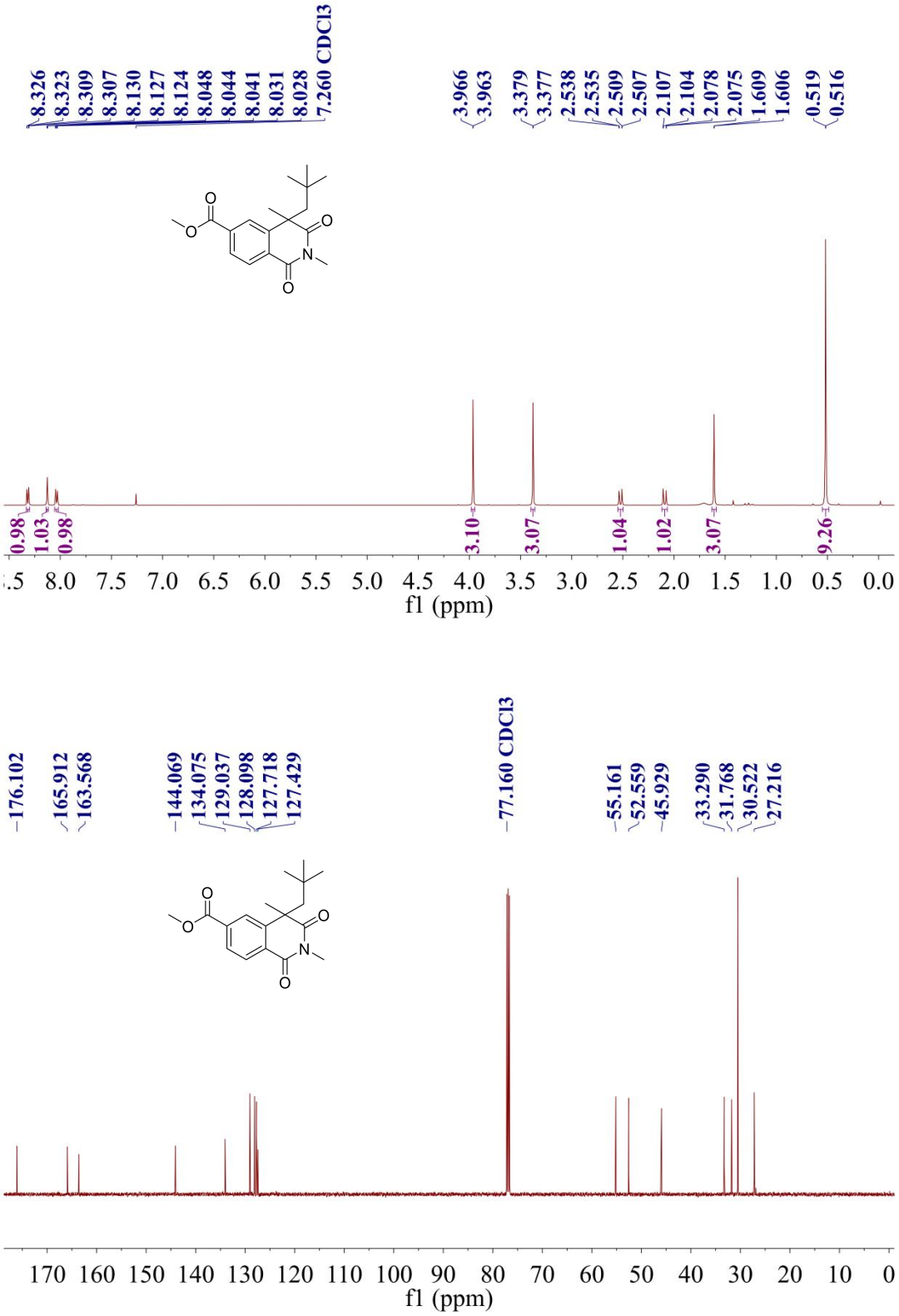


6-Bromo-2,4-dimethyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3ai)

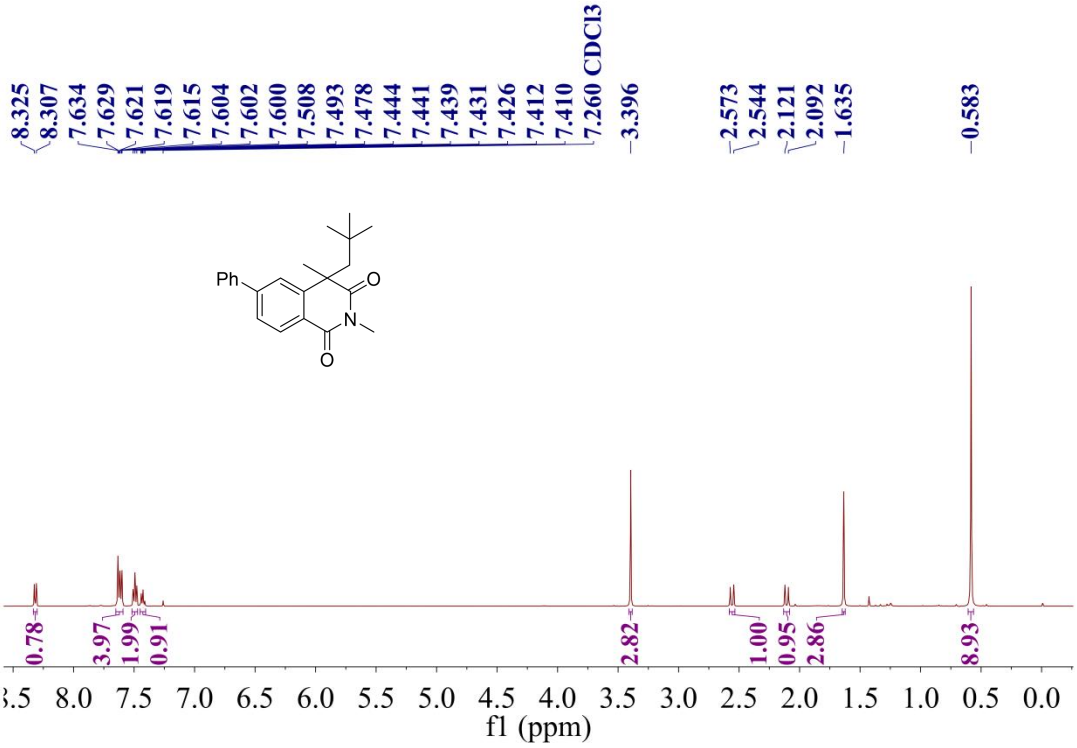


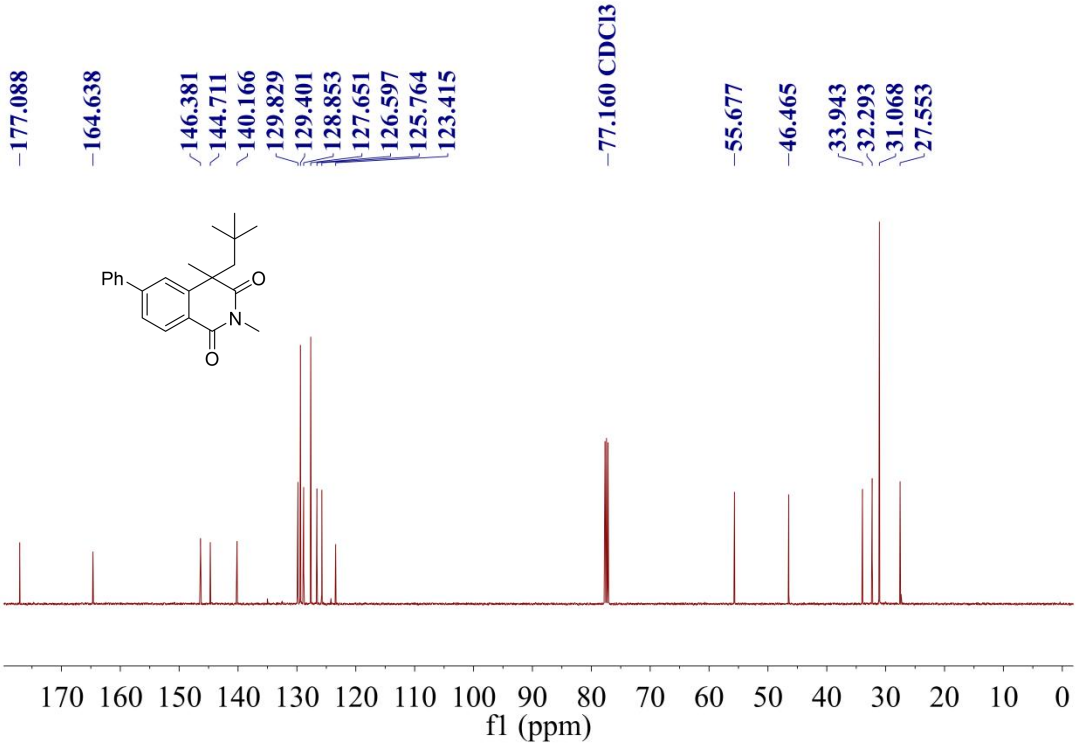


Methyl 2,4-dimethyl-4-neopentyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinoline-6-carboxylate (3aj)

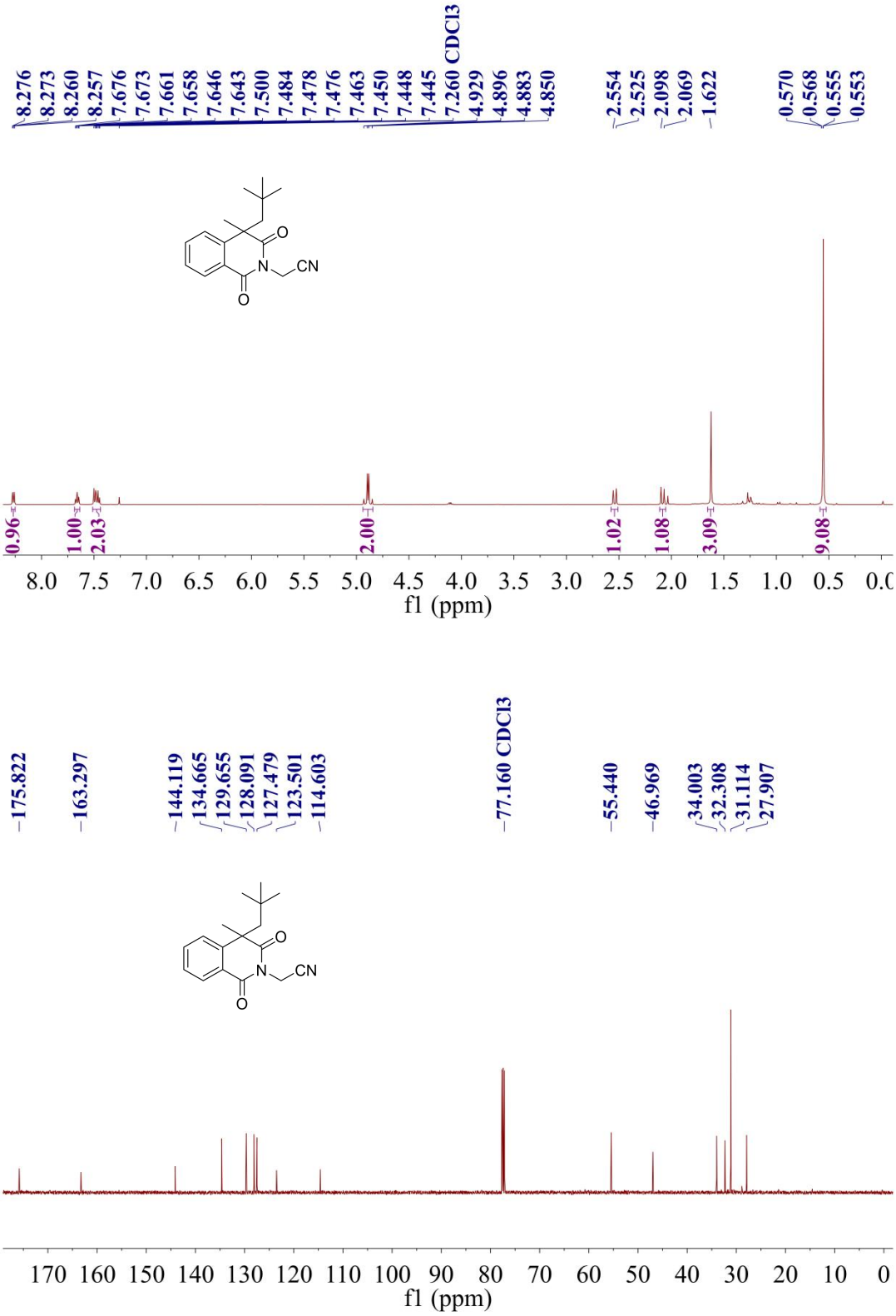


2,4-Dimethyl-4-neopentyl-6-phenylisoquinoline-1,3(2*H*,4*H*)-dione (3ak)

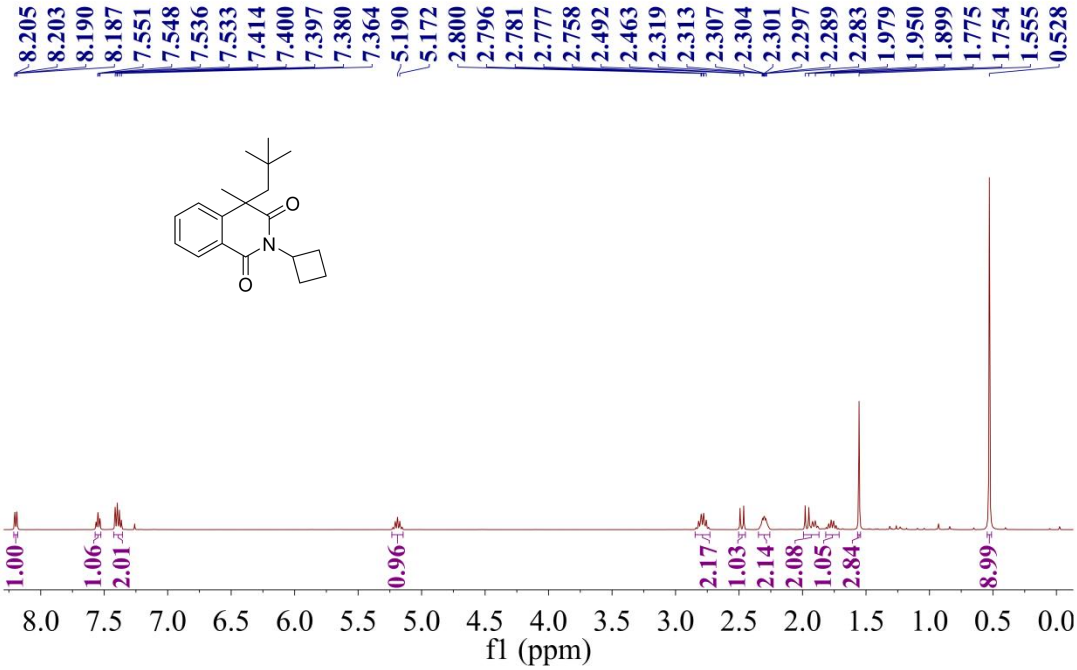


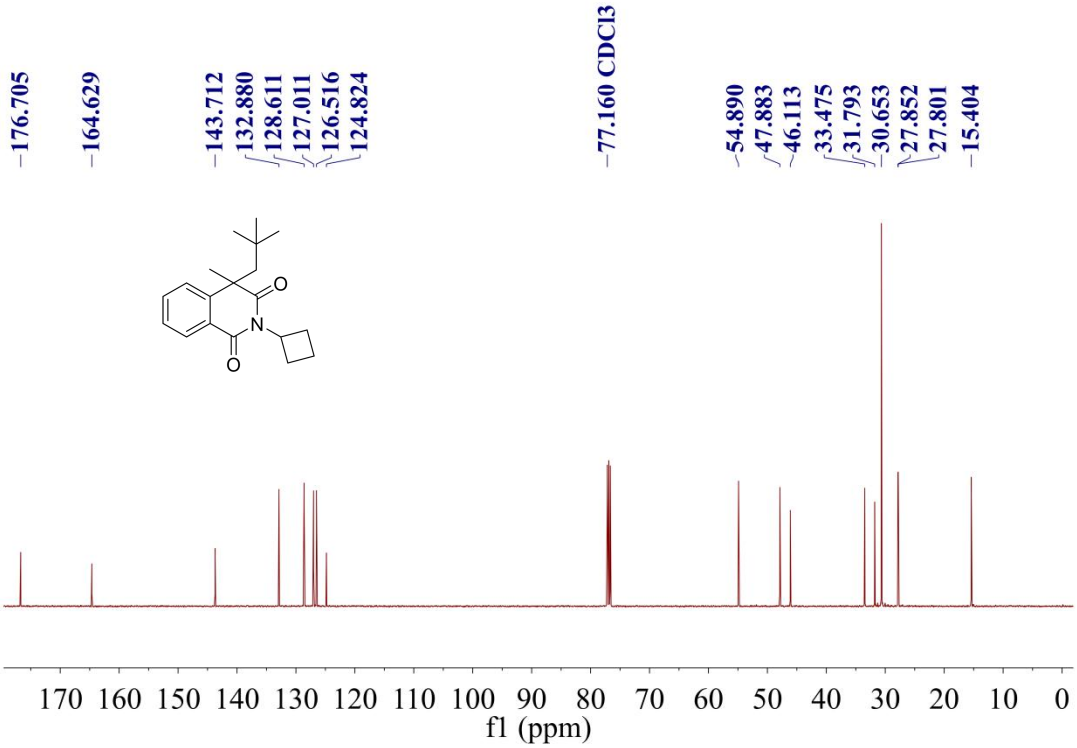


2-(4-Methyl-4-neopentyl-1,3-dioxo-3,4-dihydroisoquinolin-2(1*H*)-yl)acetonitrile (3al)

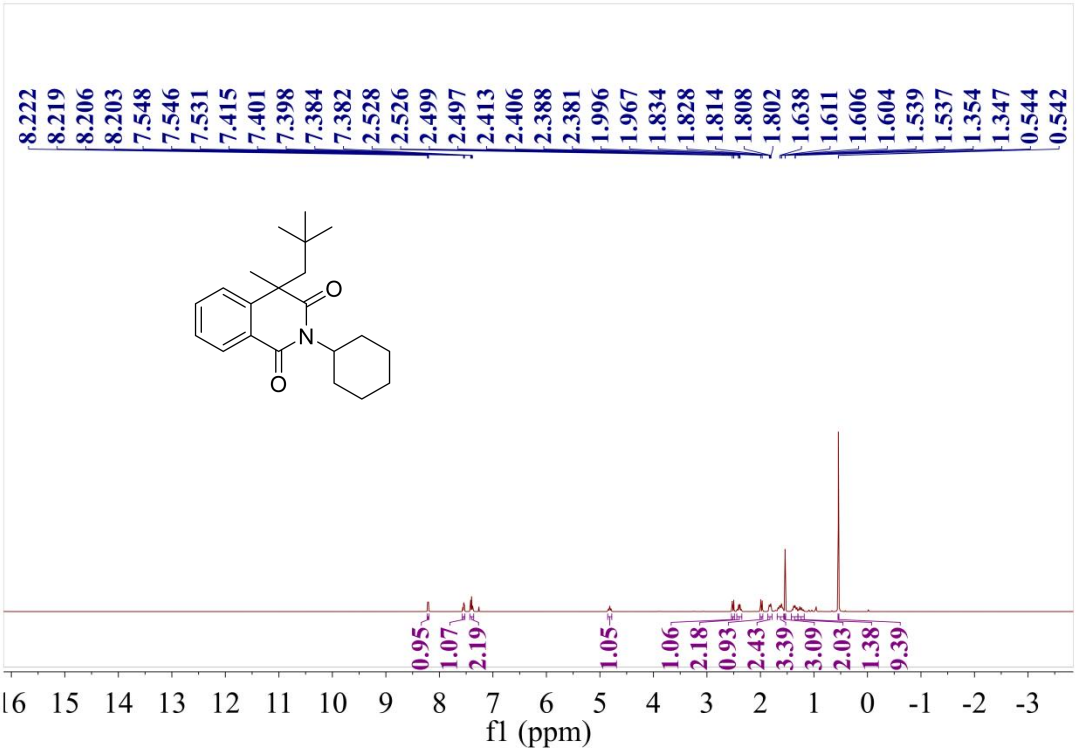


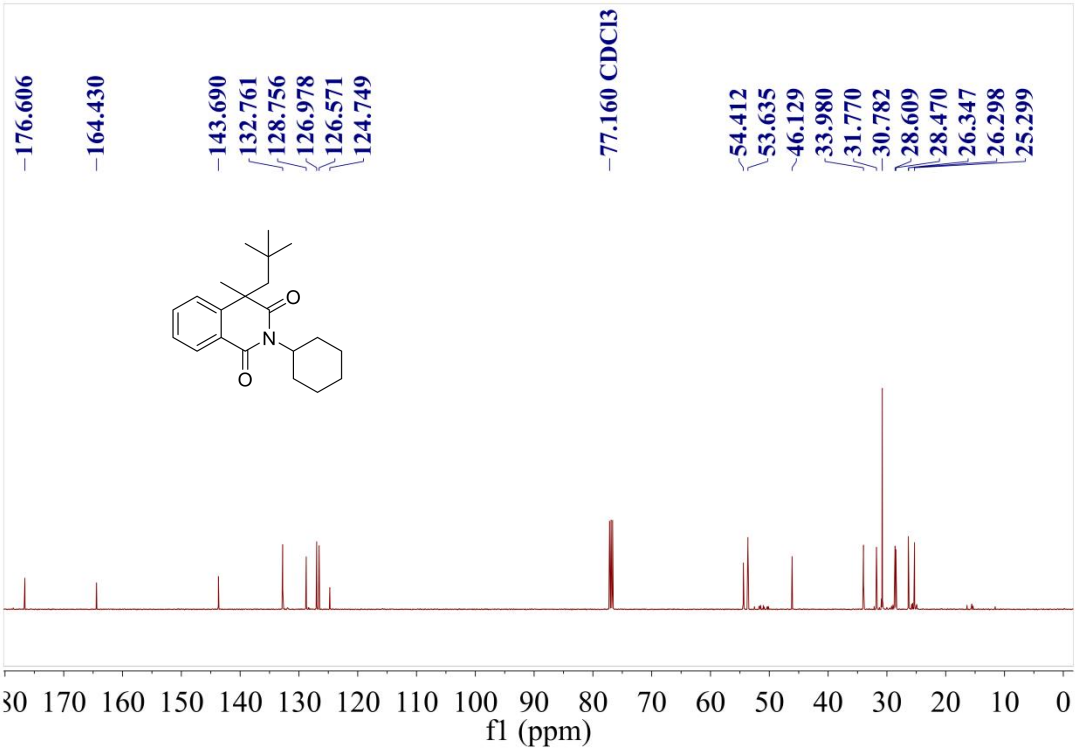
2-Cyclobutyl-4-methyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3am)



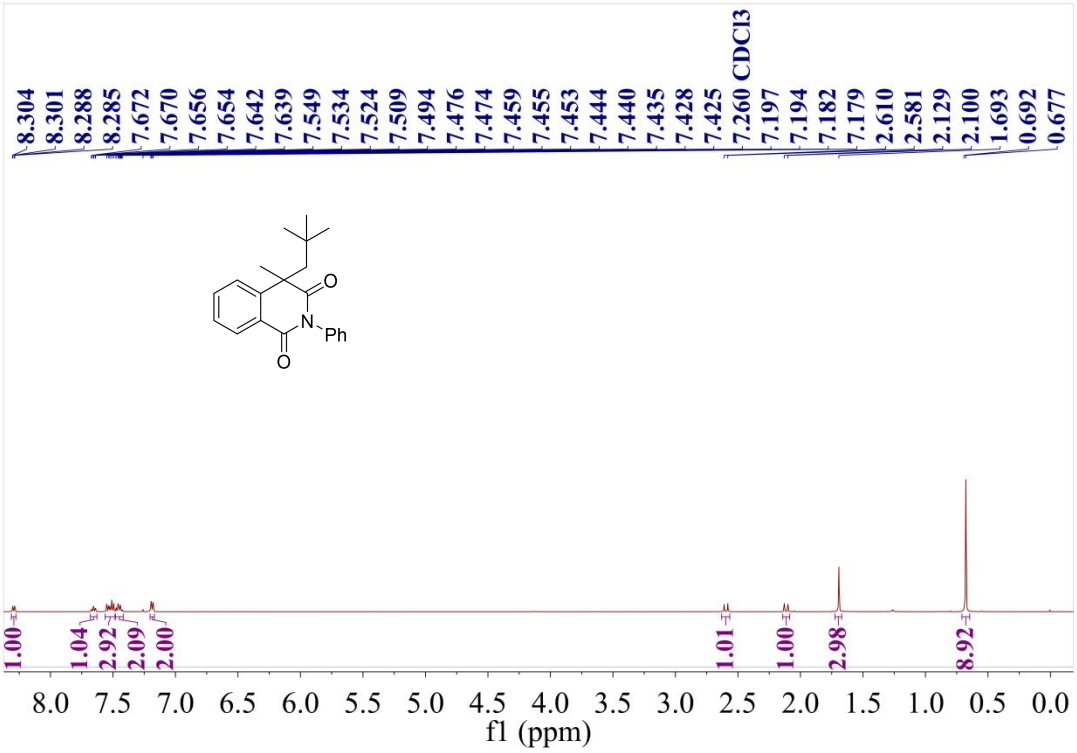


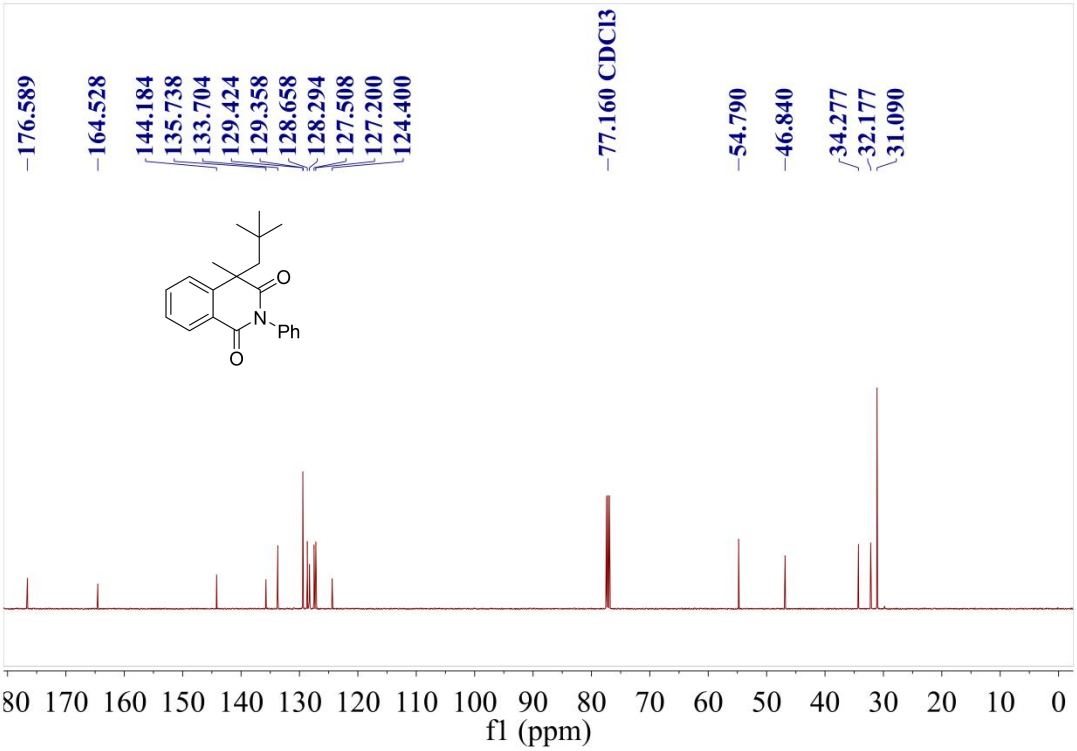
2-Cyclohexyl-4-methyl-4-neopentylisoquinoline-1,3(2*H*,4*H*)-dione (3an)



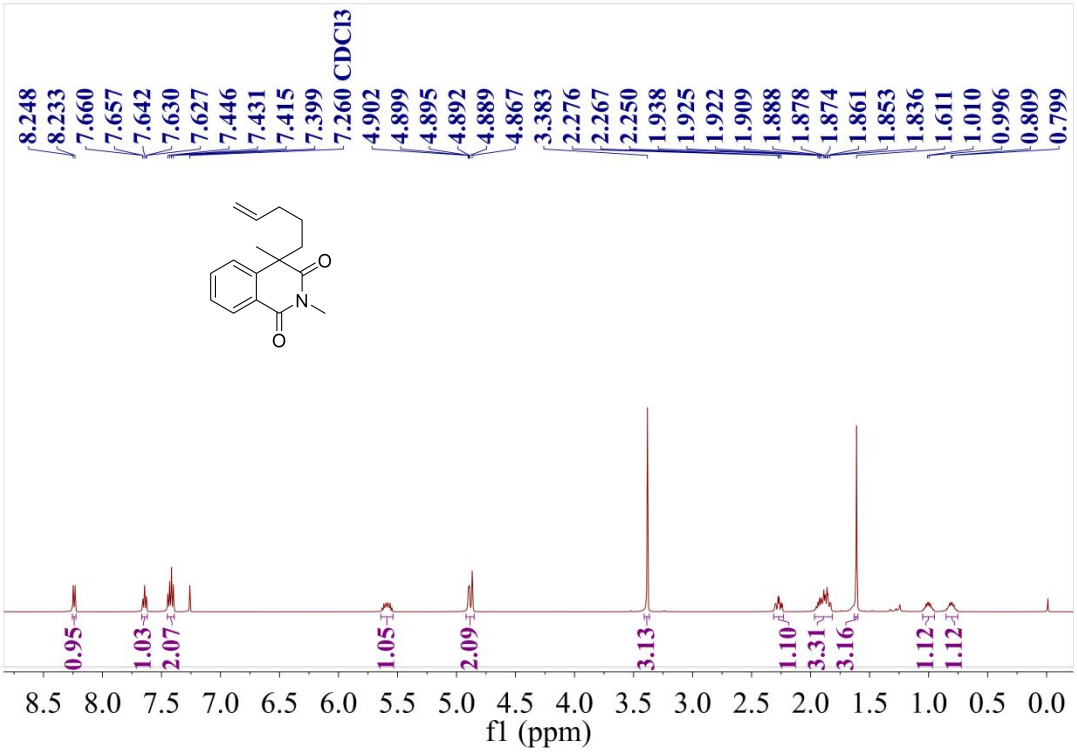


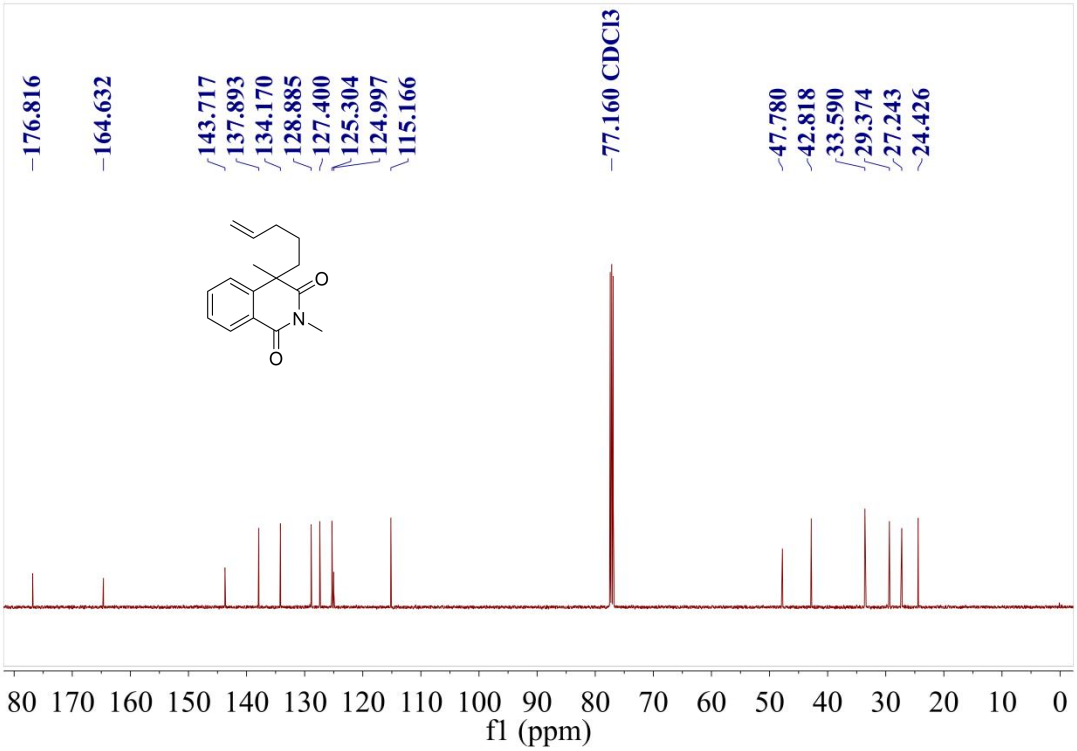
4-Methyl-4-neopentyl-2-phenylisoquinoline-1,3(2*H*,4*H*)-dione (3ao)



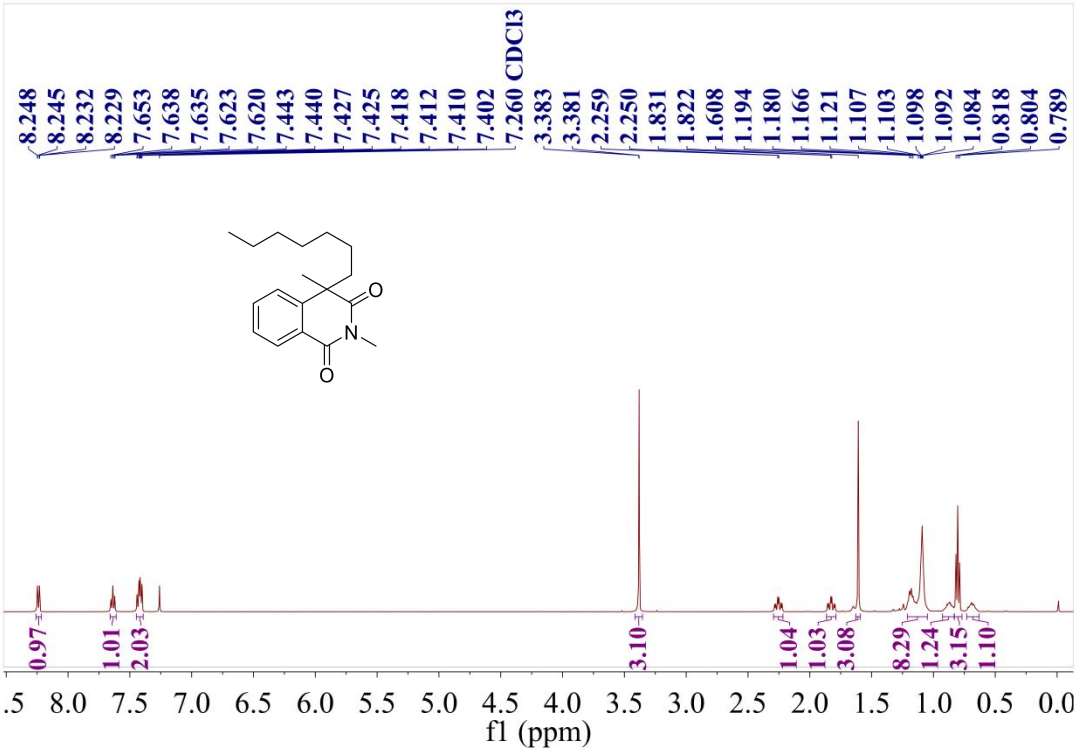


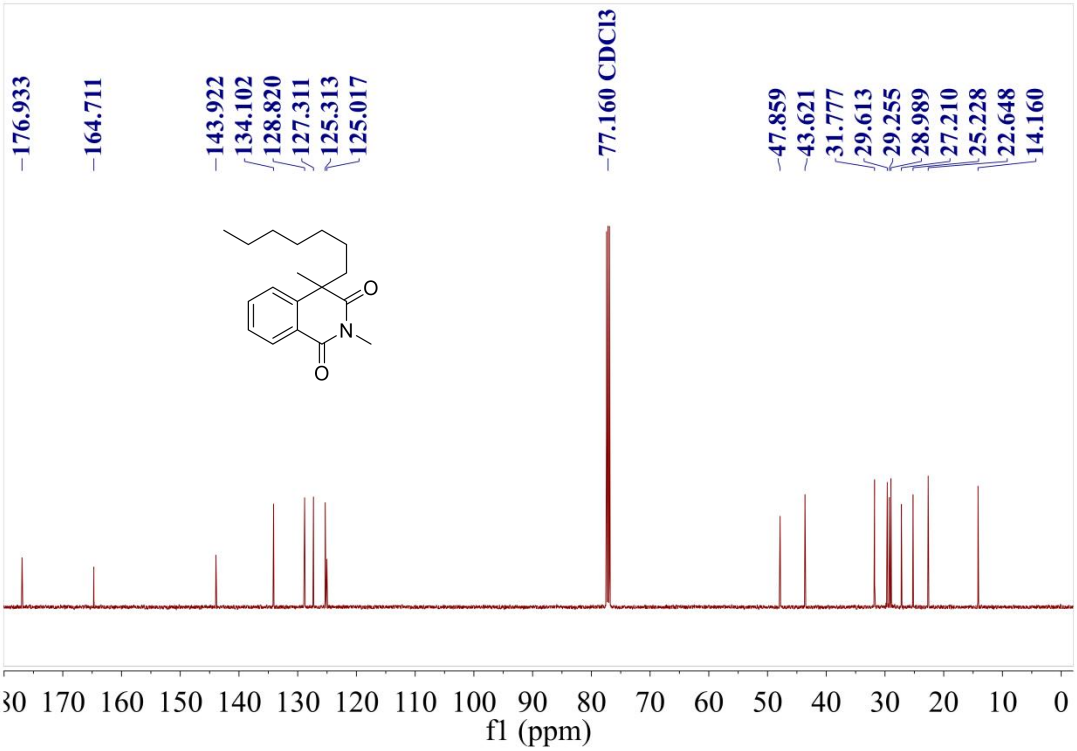
2,4-dimethyl-4-(pent-4-en-1-yl)isoquinoline-1,3(2*H*,4*H*)-dione (3ba)



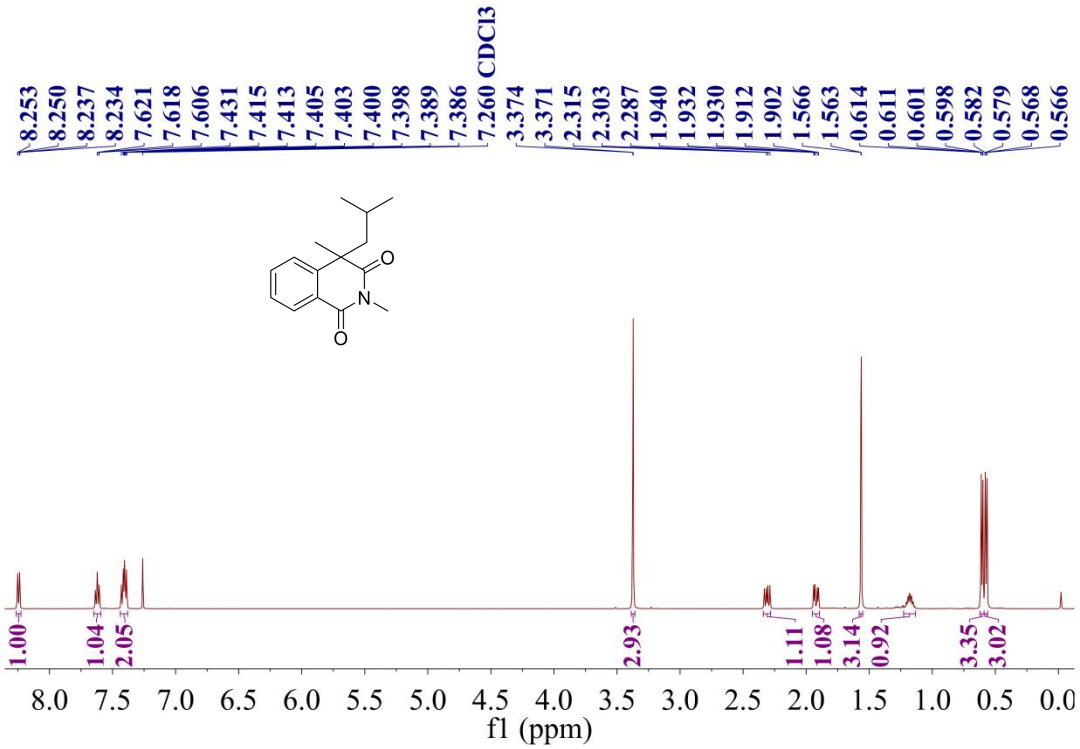


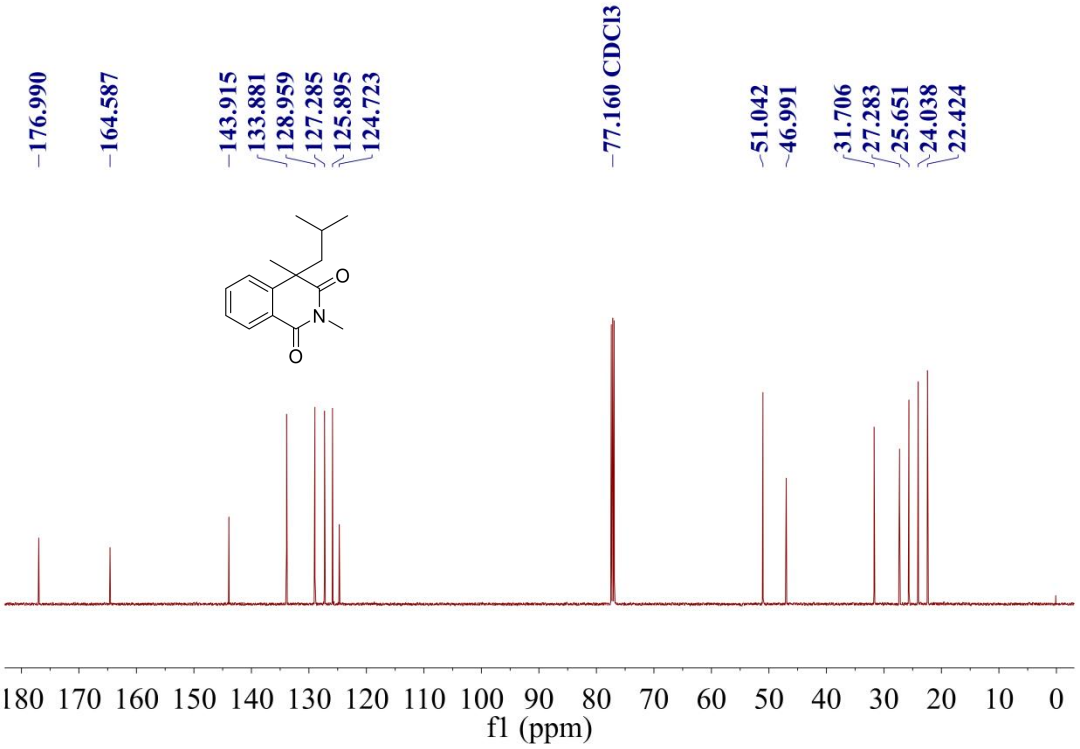
4-heptyl-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ca)



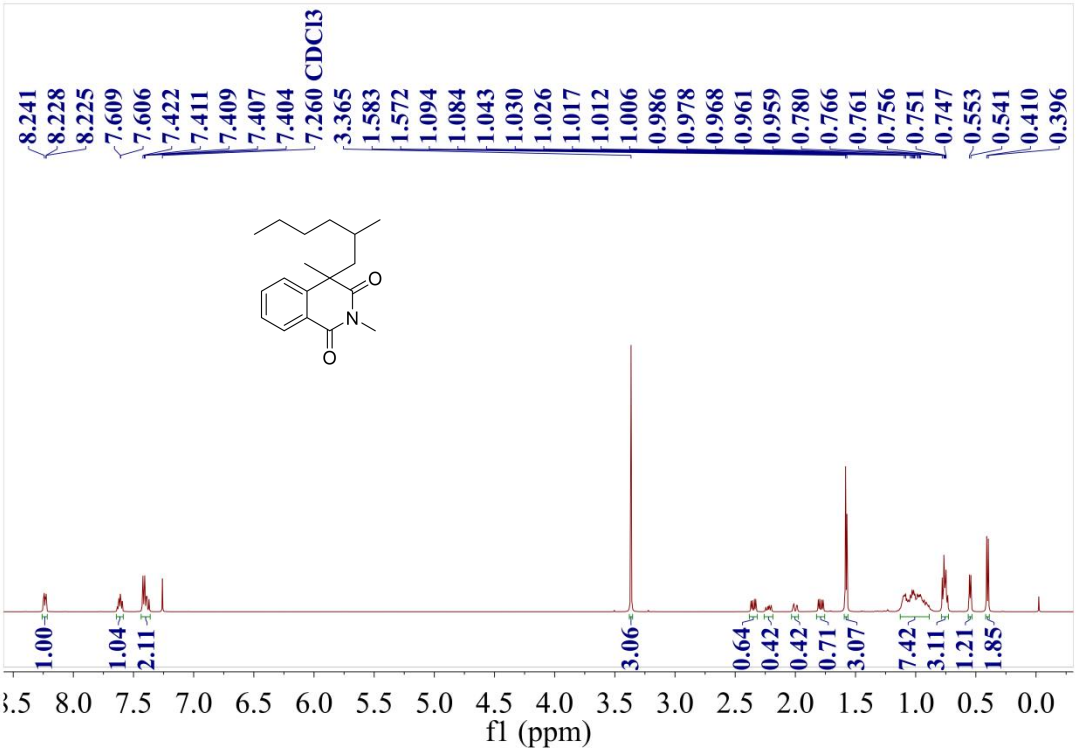


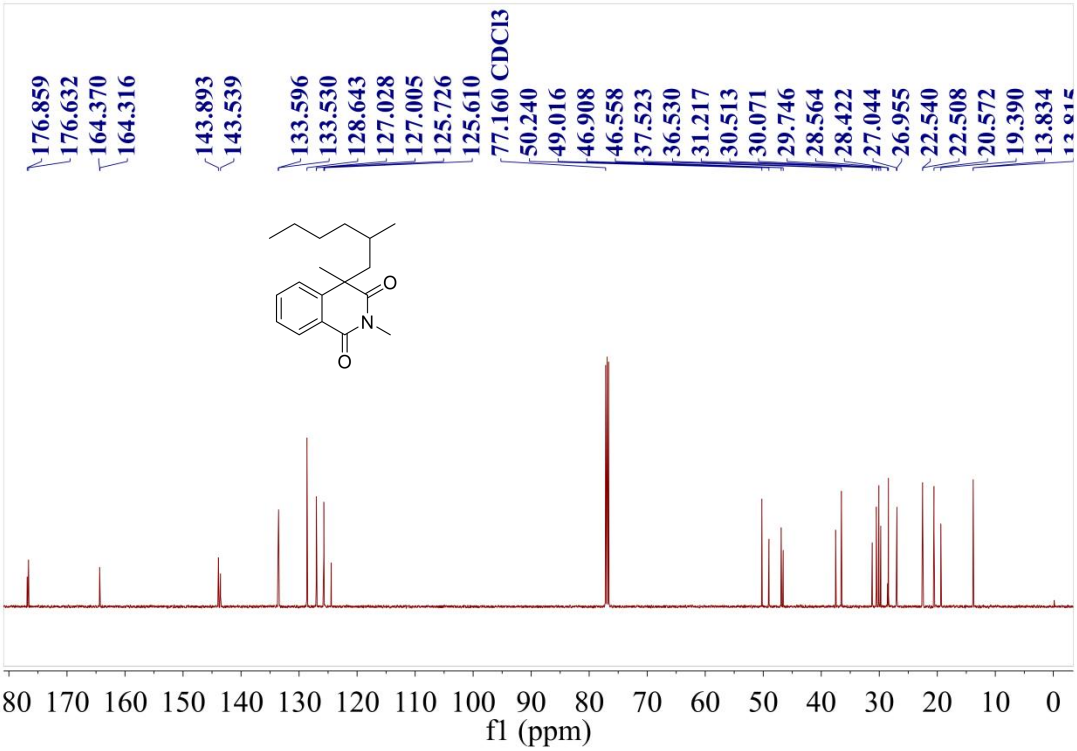
4-Isobutyl-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3da)



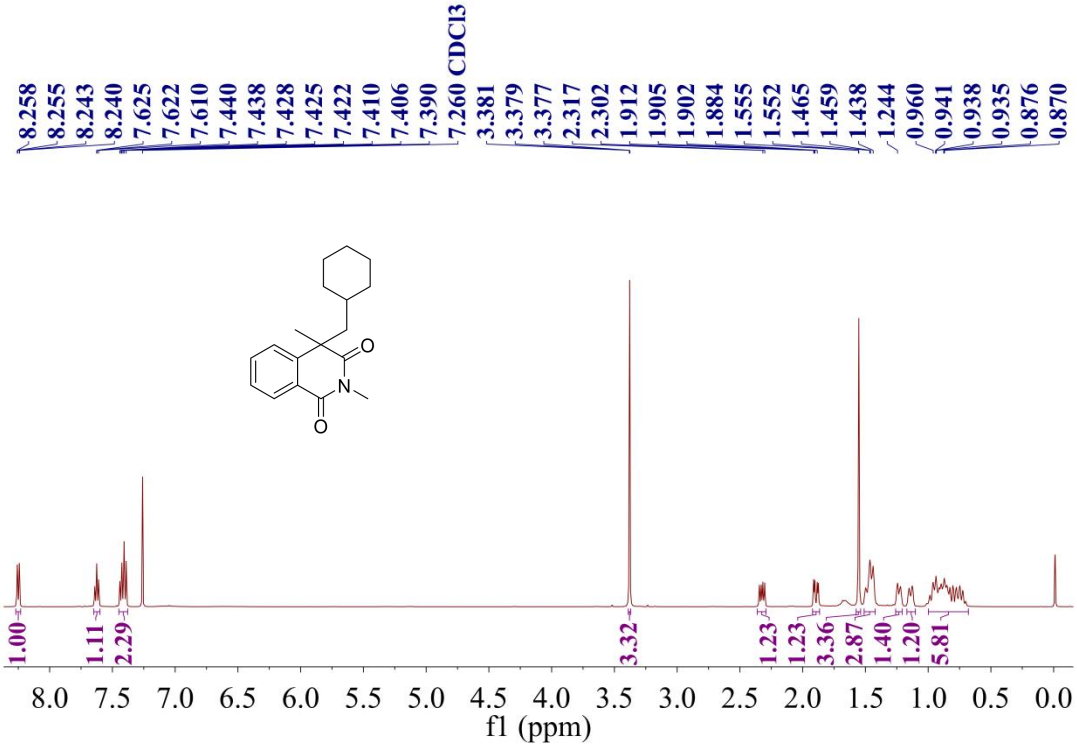


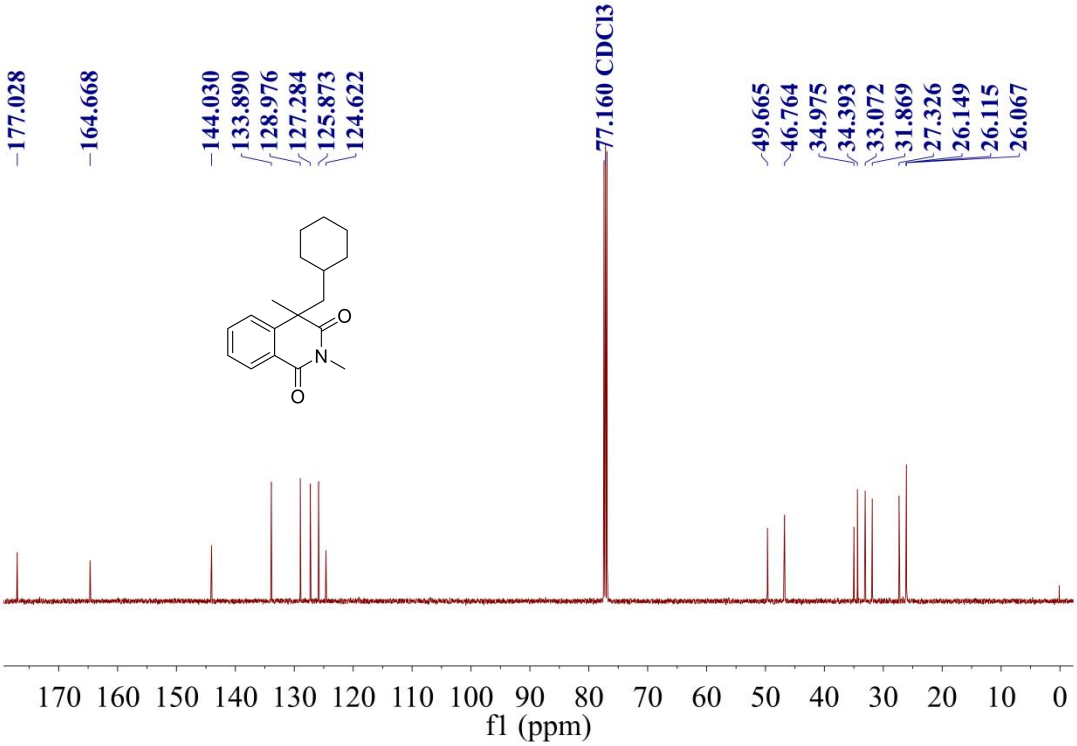
2,4-Dimethyl-4-(2-methylhexyl)isoquinoline-1,3(2*H*,4*H*)-dione (3ea)



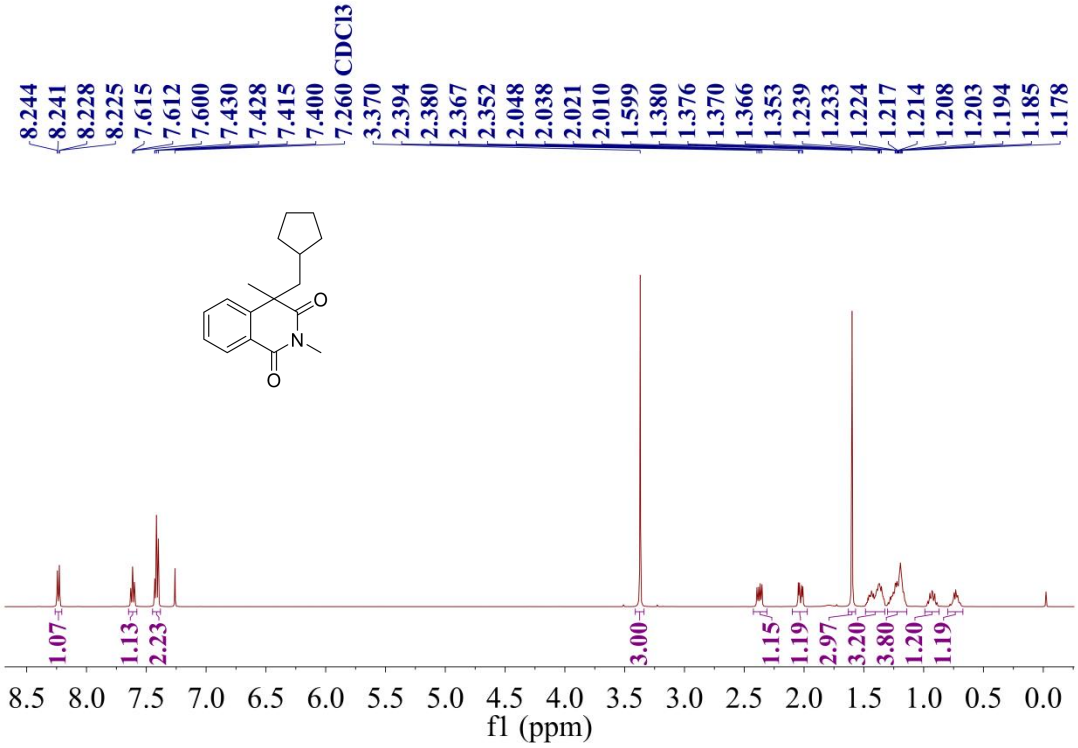


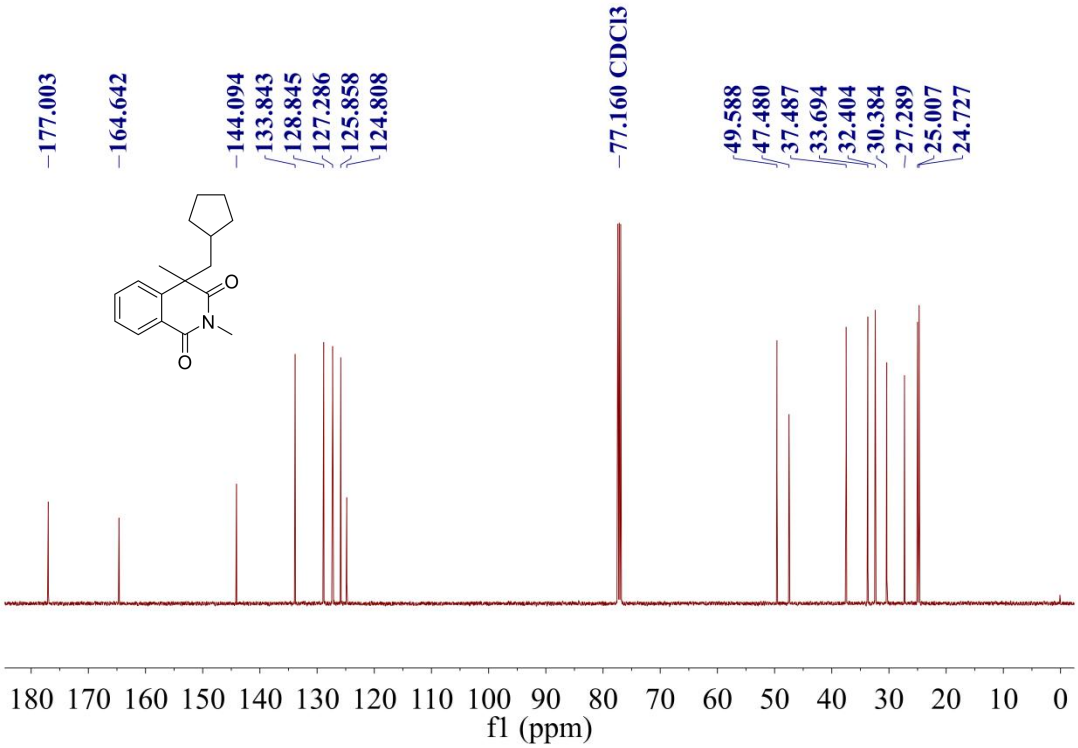
4-(Cyclohexylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3fa)



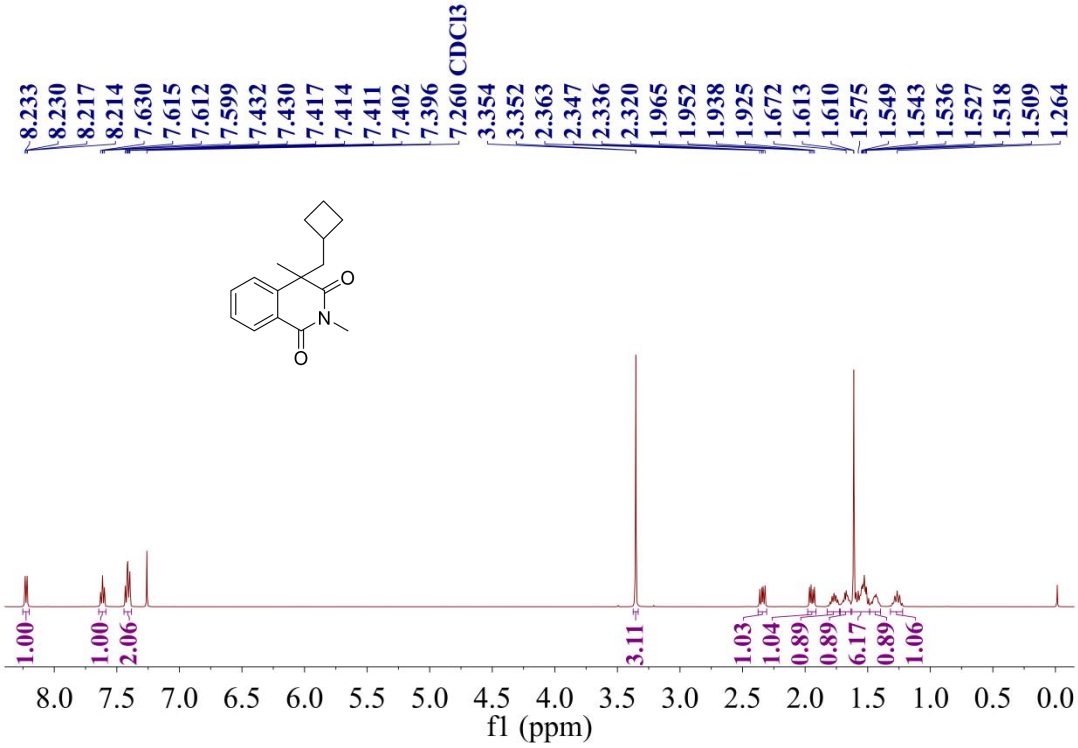


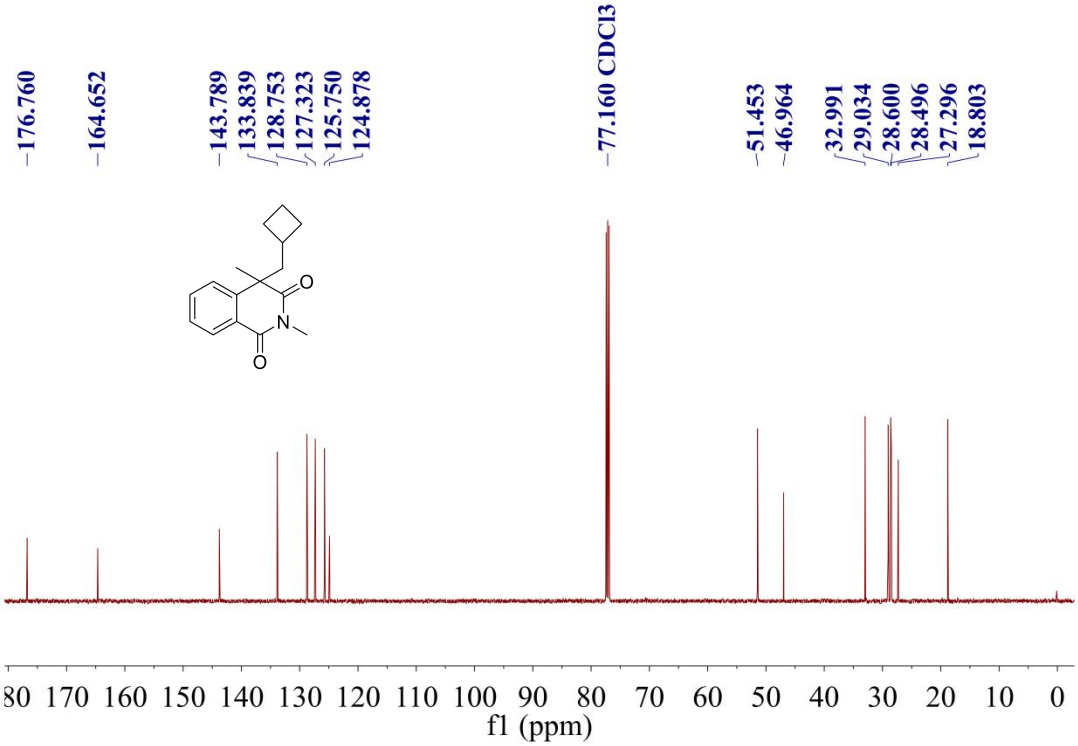
4-(Cyclopentylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ga)



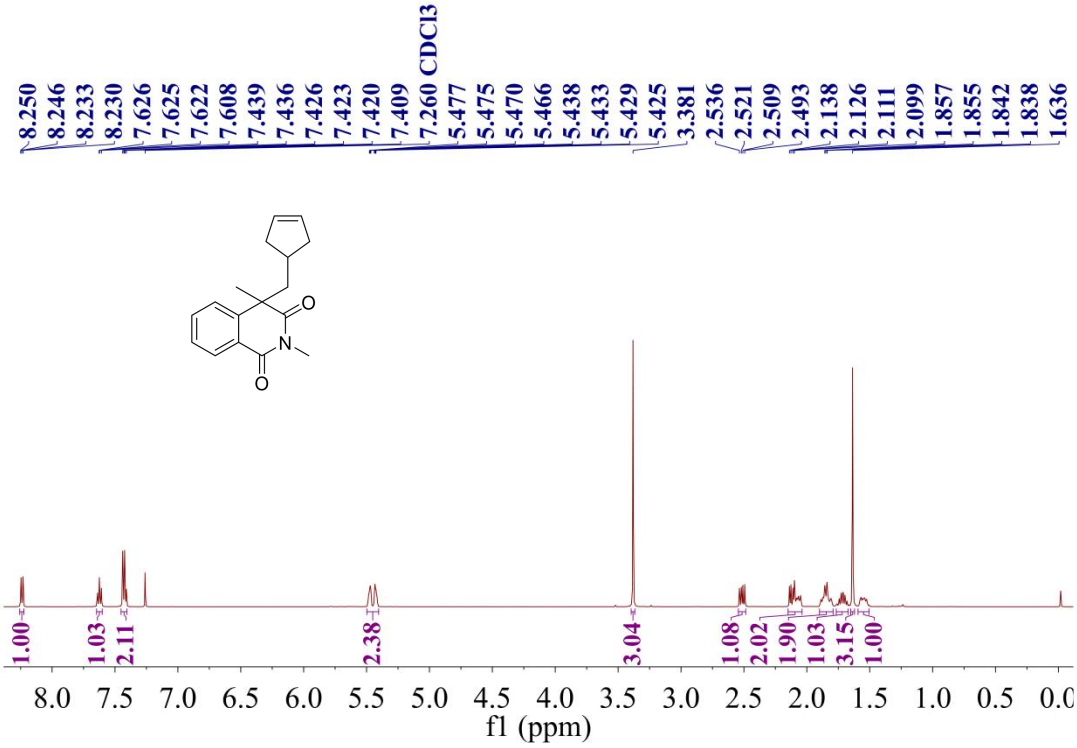


4-(Cyclobutylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ha)





4-(Cyclopent-3-en-1-ylmethyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3ia)



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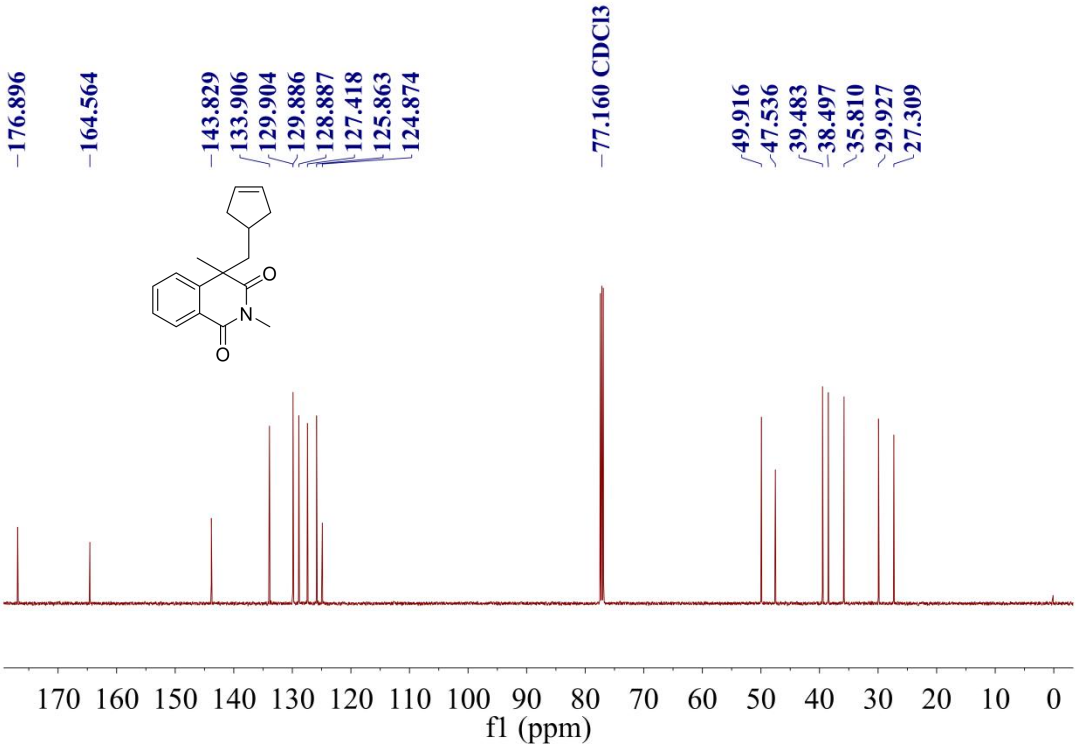
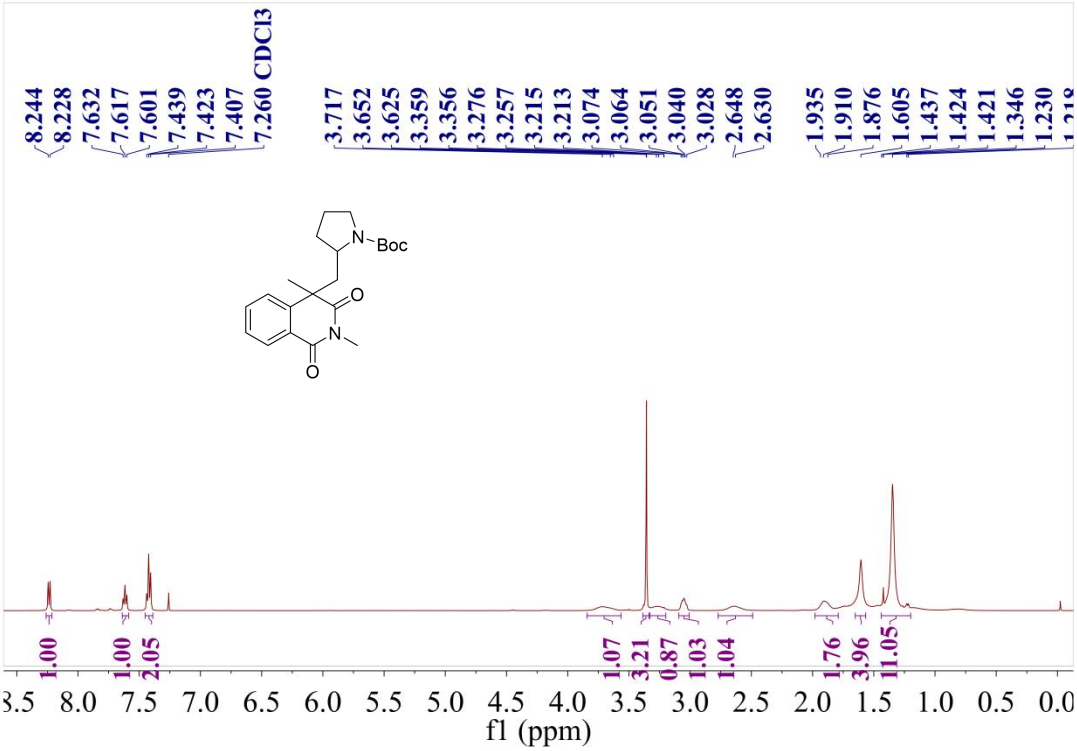
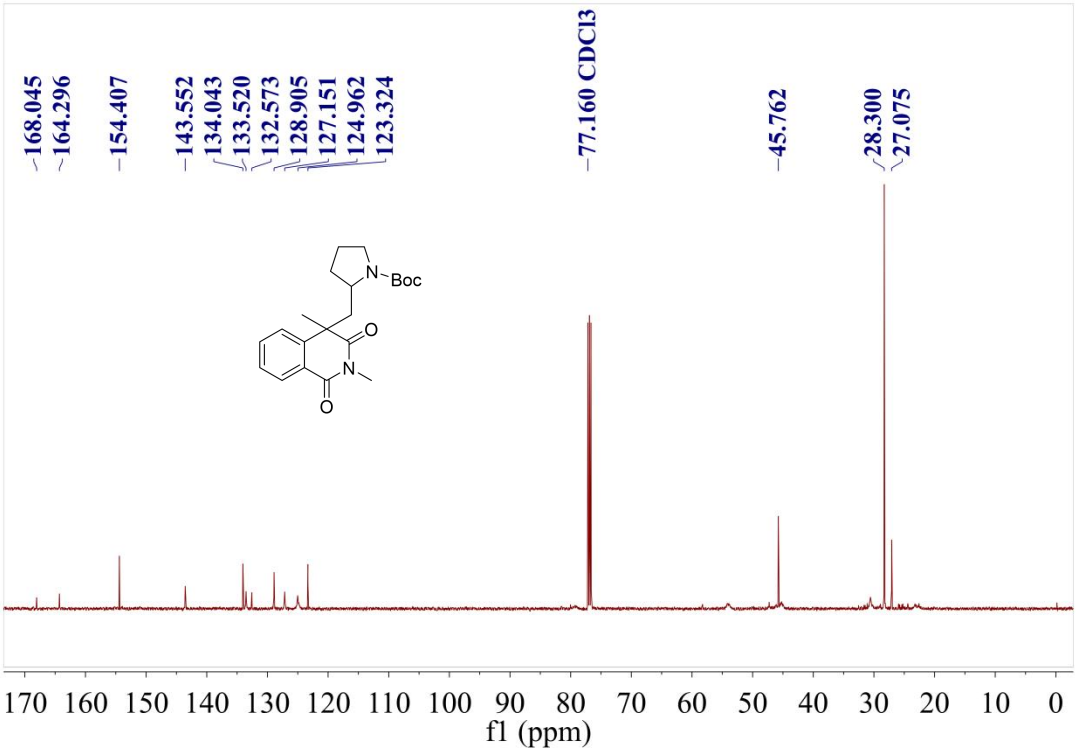


***tert*-Butyl-2-((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)-pyrrolidine-1-carboxylate (3ja)**





Methyl4-((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)bicyclo[2.2.2]octane-1-carboxylate (3ka)