Supporting Information

Base-promoted Aerobic Oxidation of *N*-Alkyl Iminium Salts Derived from Isoquinolines and Related Heterocycles

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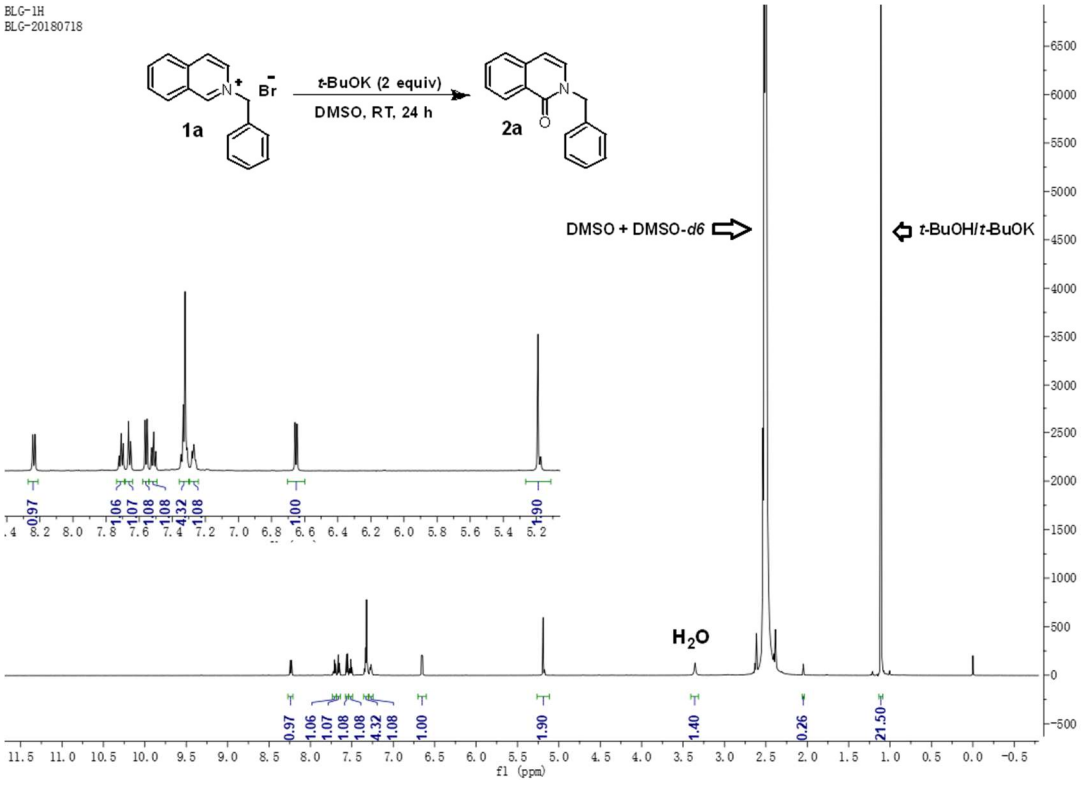
1 General information

Unless otherwise noted, commercially available reagents were used as received. All solvents for chromatographic separations were distilled before use. Solvents for the water-free reactions were dried with standard procedures and stored with Schlenk flasks over molecular sieves. Column chromatography was carried out with 200−300 mesh silica gel. Thin-layer chromatography (TLC) was performed on glass-backed silica plates. UV light, I_2, and solutions of 2, 4-dinitrophenylhydrazine were used to visualize products. Concentrating a solution under reduced pressure refers to distillation using a rotary evaporator attached to a vacuum pump (3 – 10 mmHg). Products obtained as solids or high boiling oils were dried under vacuum (1 – 3 mmHg). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 600 or AV 400 NMR spectrometer at 293 K and the chemical shifts (δ) were internally referenced by the residual solvent signals relative to tetramethylsilane ($CDCl_3$ at 7.26 ppm for ^{1}H, and at 77.00 ppm for ^{13}C; DMSO-d_6 at 2.50 ppm for ^{1}H, and at 39.50 ppm for ^{13}C). Data are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration). High-Resolution Mass Spectrometry (HRMS) for accurate mass measurements was performed on a mass spectrometer of Waters Synapt-G2, Bruker FT-ICR SolariX or Agilent LCMS TOF 6224. All the known products were confirmed by comparison with spectroscopic analysis of the authentic samples. The yields in the text refer to isolated yields of compounds.

2 Component analysis of the final reaction mixture with NMR spectra

2.1 The NMR spectrum of the reaction mixture of 1a without quench in advance

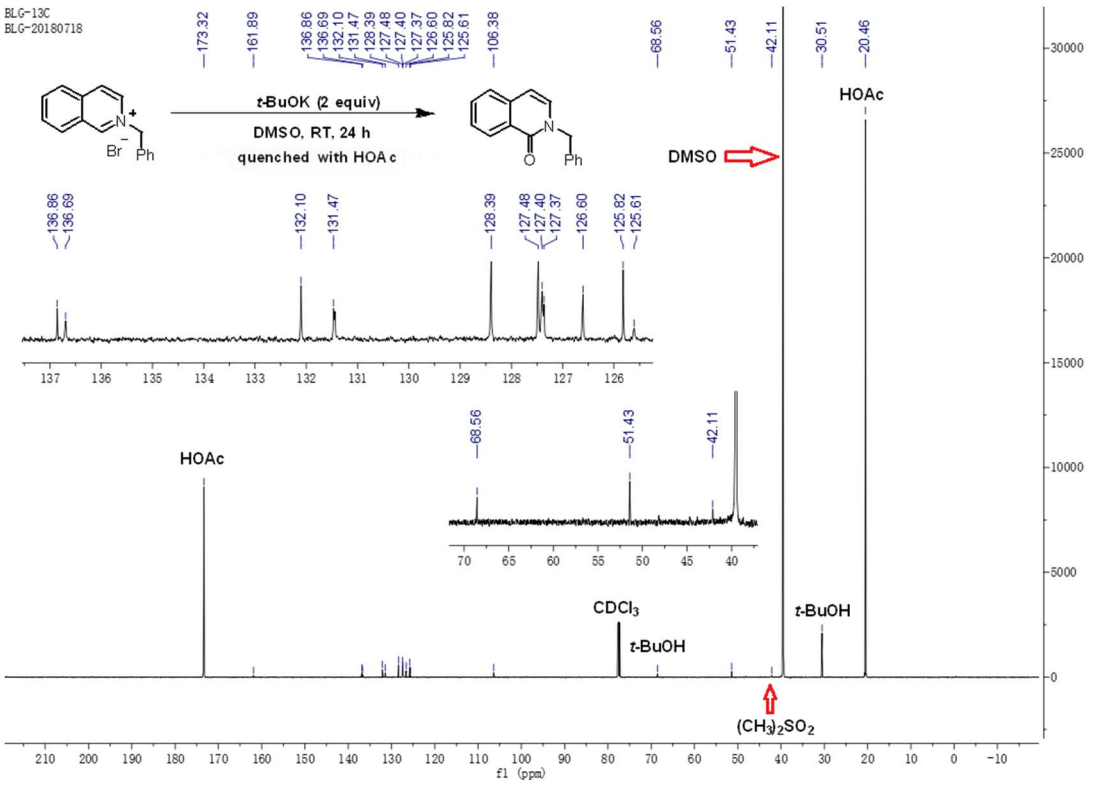
Figure S1. The ^{1}H NMR spectrum of reaction solution of **1a**



After the reaction was complete, an aliquot of the mixture was transferred to a NMR tube, diluted with DMSO-d_6, and submitted to record NMR spectra. The assigned signals of H_2O, *t*-BuOH and DMSO are as indicated, respectively. The signals in the expanded region (5.0 – 8.5 ppm) are assigned to **2a**. The spectrum clearly showed that **1a** was completely converted to **2a**.

2.2 The NMR spectrum of the reaction mixture of 1a quenched with HOAc

Figure S2. The ^{13}C NMR spectrum of reaction solution of **1a**



The sample of this spectrum is taken from the same reaction system as that of the previous spectrum (Figure S1). After the reaction was complete, it was quenched with excess of HOAc (about 1 mL). An aliquot of the mixture was transferred to a NMR tube, diluted with $CDCl_3$, and submitted to record NMR spectra. The assigned signals of HOAc, t-BuOH, DMSO and dimethyl sulfone are as indicated, respectively. The rest of signals (105 – 165 ppm, 51.4 ppm) are assigned as that of **2a**. The signal intensity of dimethyl sulfone was much weaker than that of **2a**, which demonstrated that the substrate was more susceptible to be oxidized than DMSO.

2.3 The NMR spectra of the isolated products from the reaction of 1r

Figure S3. The ^{1}H NMR spectrum of the isolated products from the reaction of **1r**

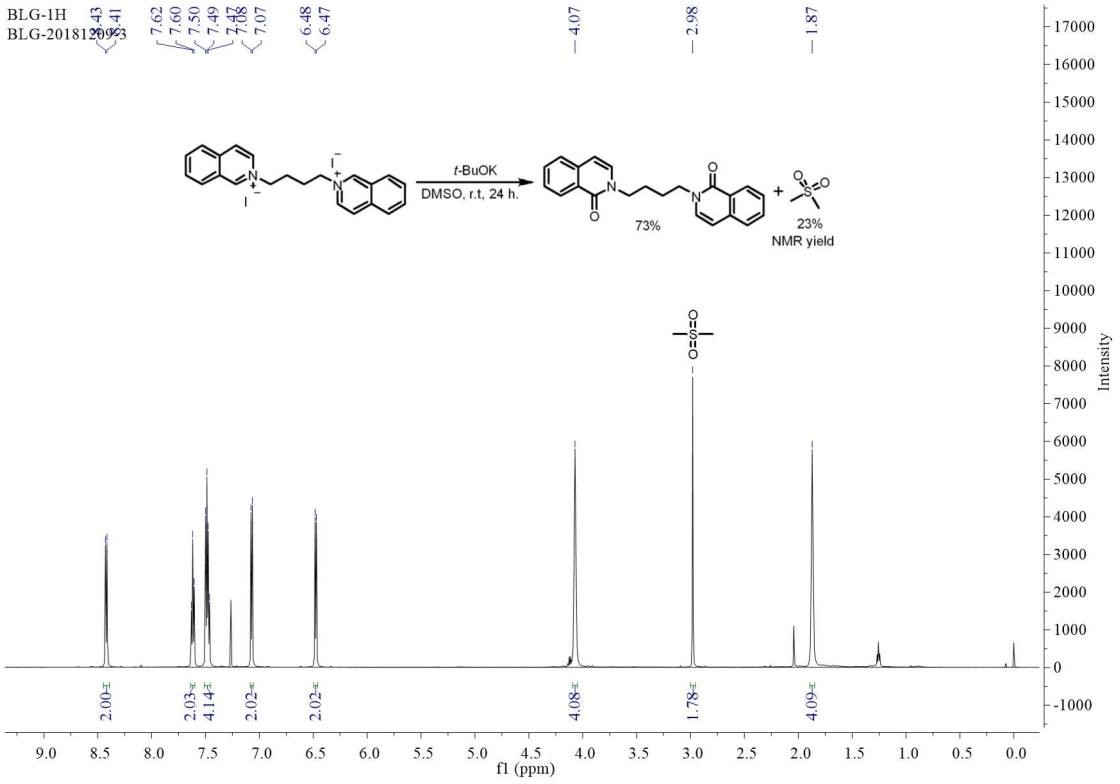
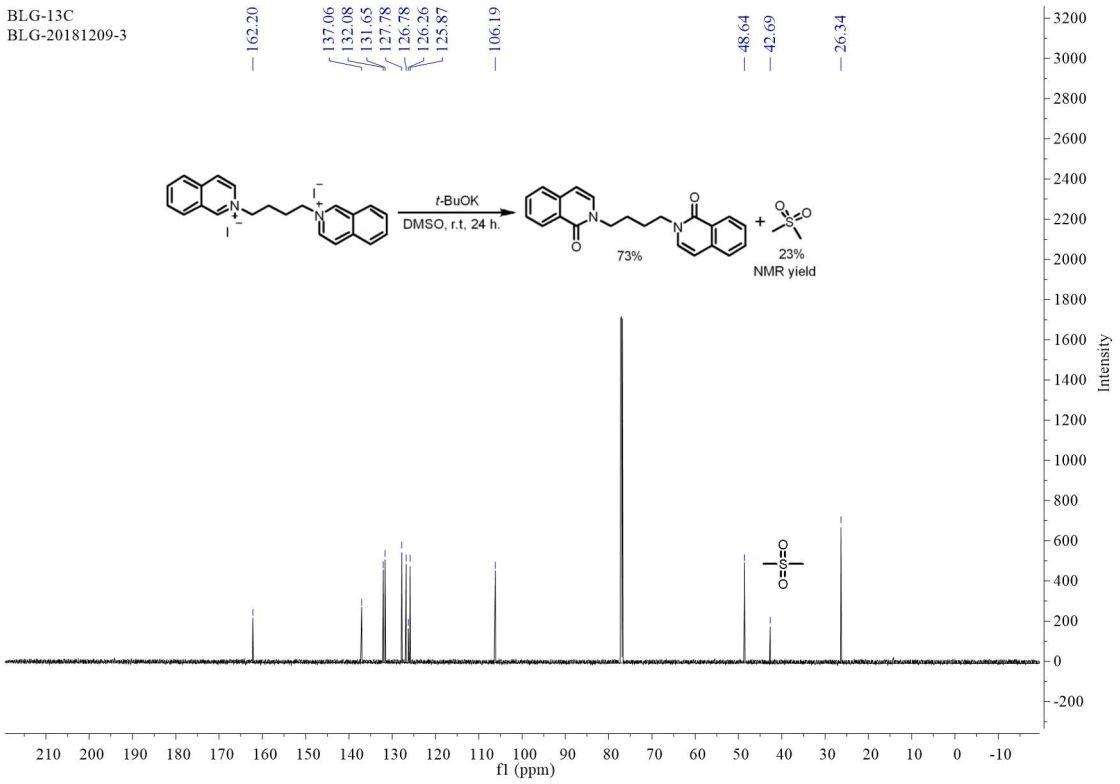


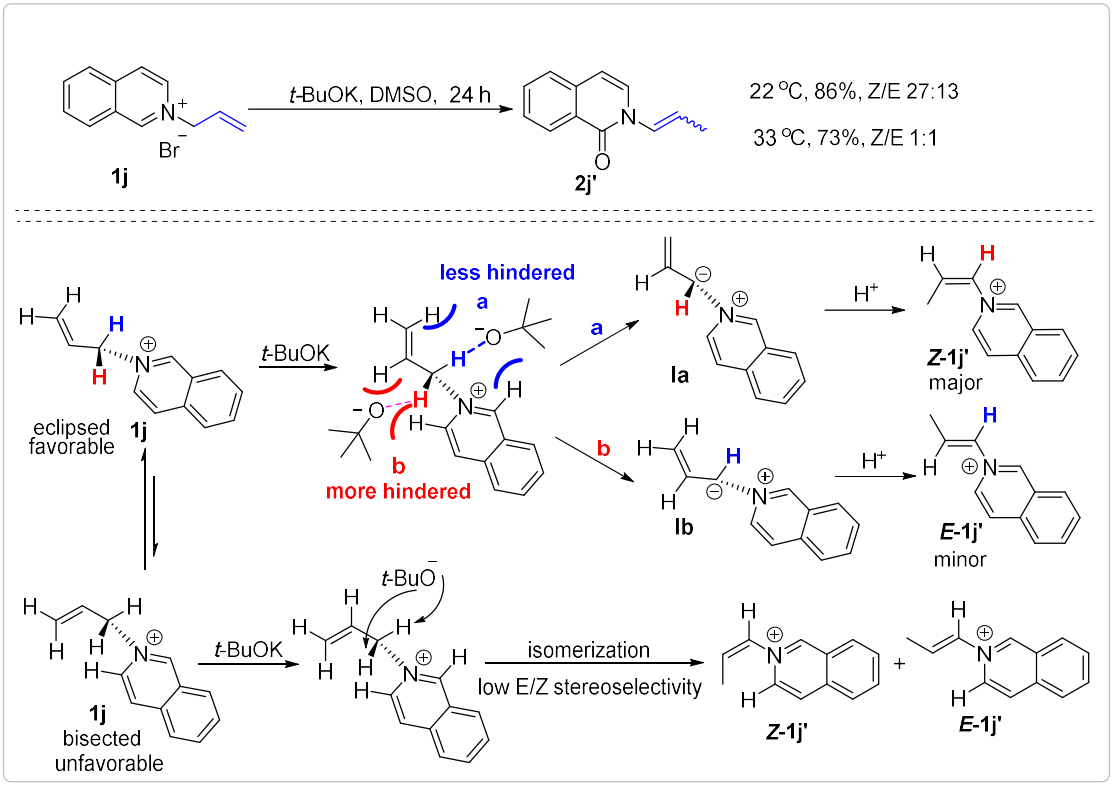
Figure S4. The ^{13}C NMR spectrum of the isolated products from the reaction of **1r**



The signals of dimethyl sulfone are assigned as indicated.[1] The yield of dimethyl sulfone was calculated from the integration of H signals relative to that of **2r**. Dimethyl sulfone was finally removed by washing the mixture solution in EtOAc with water.

3 Explanation of the stereoselectivity for the formation of 2j'

Figure S5. The stereoselectivity for the formation of **2j'**

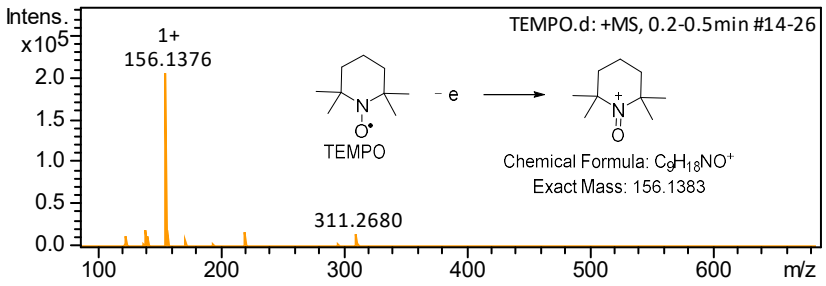


There are two families of conformations available to the terminal alkene derivative **1j**, i.e., favorable eclipsed and unfavorable bisected conformations. The deprotonation/protonation of favorable eclipsed **1j** from the less hindered direction generates (*Z*)**-1j'** as the major configurational isomer, that is then oxidized into (*Z*)-**2j'**.[2]

4 Mechanistic insights by high resolution mass spectroscopy (HRMS)

4.1 ESI-MS spectrum of TEMPO

Figure S6. ESI-MS spectrum of TEMPO

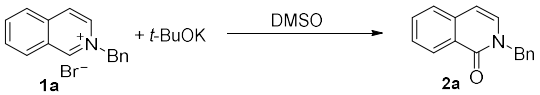


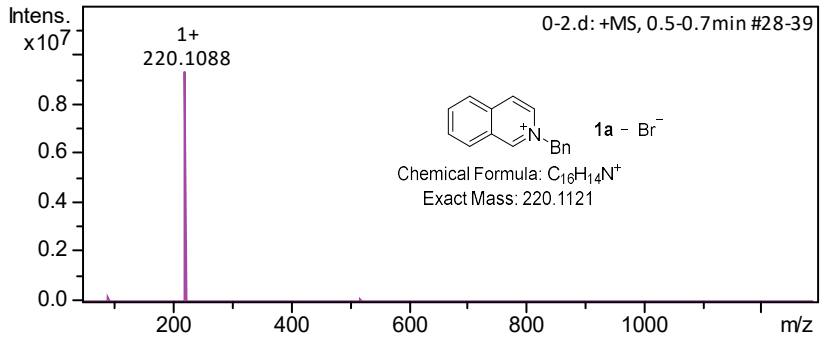
Meas. m/z	#	Ion Formula	m/z	Adduct	err [ppm]
156.1376	1	C9H18NO	156.1383	M+H	4.5

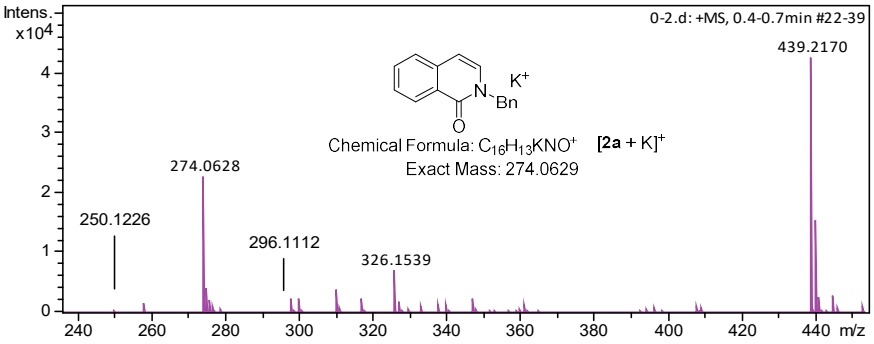
When the sample of TEMPO was recorded, the peak at m/z=375.24 was not detected.

4.2 Monitoring the standard reaction with HRMS

Figure S7. ESI-MS spectrum of the reaction mixture of **1a** under standard conditions







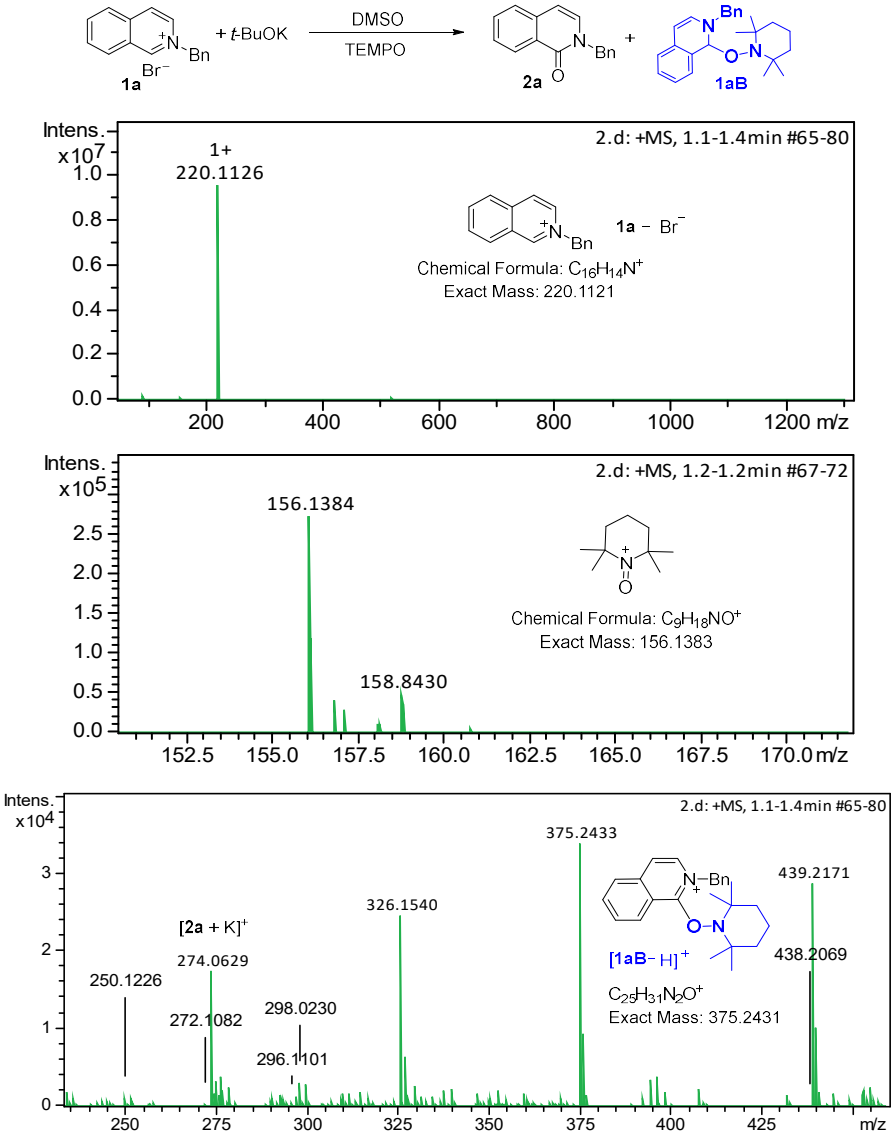
Meas. m/z	#	Ion Formula	Sum Formula	m/z	Adduct	err [ppm]	z
130.0646	1	C9H8N	C9H7N	130.0651	M+H	3.8	1+
250.1226	1	C17H16NO	C17H15NO	250.1226	M+H	0.3	1+

274.0628	1	C16H13KNO	C16H13NO	274.0629	M+K	0.1 1+
296.1112	1	C18H18NOS	C18H17NOS	296.1104	M+H	-2.9 1+
326.1539	1	C23H20NO	C23H19NO	326.1539	M+H	0.1 1+
439.2170	1	C32H27N2	C32H26N2	439.2169	M+H	-0.3 1+

Under standard conditions, the mass peak at m/z=375.24 was not detected in the reaction mixture.

4.3 Monitoring the TEMPO-added reaction with HRMS

Figure S8. ESI-MS spectrum of the reaction mixture of **1a** with the addition of TEMPO



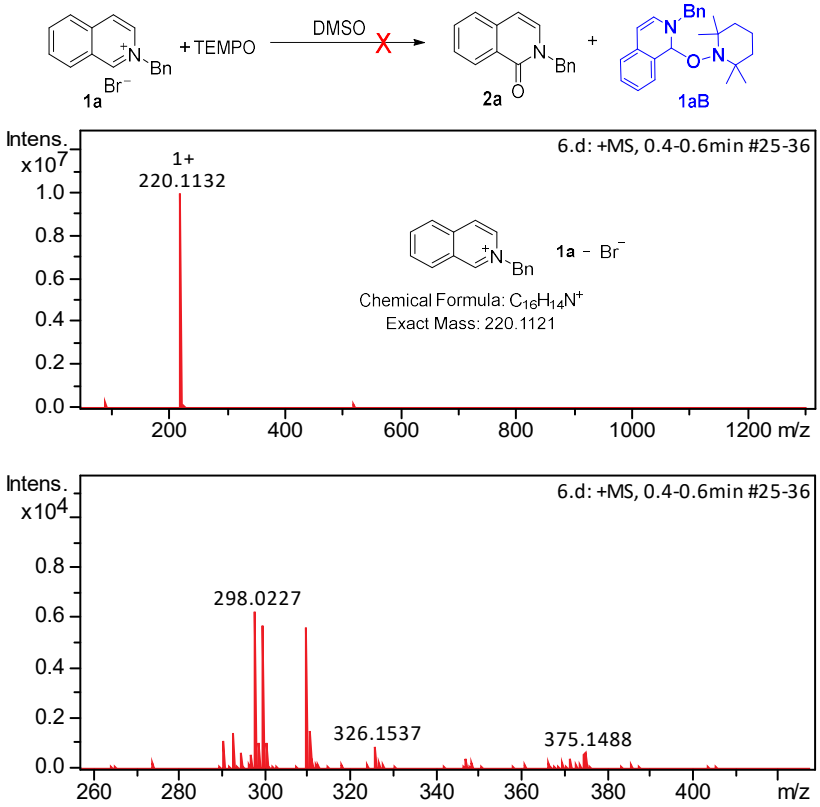
Meas. m/z	#	Ion Formula	Sum Formula	m/z	Adduct	err [ppm]	z
130.0650	1	C9H8N	C9H7N	130.0651	M+H	0.7	1+
156.1383	1	C9H18NO	C9H17NO	156.1383	M+H	-0.2	1+
158.1539	1	C9H20NO	C9H19NO	158.1539	M+H	0.3	1+
220.1126	1	C16H14N	C16H14N	220.1121	M	-2.3	1+
234.1277	1	C17H16N	C17H15N	234.1277	M+H	0.1	1+

250.1226	1	C17H16NO	C17H15NO	250.1226	M+H	0.1	1+
272.1082	1	C11H23KNO2S	C11H23NO2S	272.1081	M+K	-0.5	1+
274.0629	1	C16H13KNO	C16H13NO	274.0629	M+K	-0.0	1+
296.1101	1	C18H18NOS	C18H17NOS	296.1104	M+H	0.9	1+
375.2433	1	C25H31N2O	C25H31N2O	375.2431	M	-0.7	1+
438.2069	1	C32H26N2	C32H25N2	438.2091	M+H	4.9	1+
439.2171	1	C32H27N2	C32H26N2	439.2169	M+H	-0.4	1+
471.2069	1	C32H27N2O2	C32H26N2O2	471.2067	M+H	-0.3	1+
594.3483	1	C41H44N3O	C41H43N3O	594.3479	M+H	-0.6	1+

With the addition of TEMPO to the reaction mixture, a new mass peak at m/z=375.24 was detected, which resulted from a radical intermediate was trapped by TEMPO.

4.4 Monitoring the TEMPO-added reaction with HRMS in the absence of *t*-BuOK

Figure S9. ESI-MS spectrum of the mixture of **1a** and TEMPO

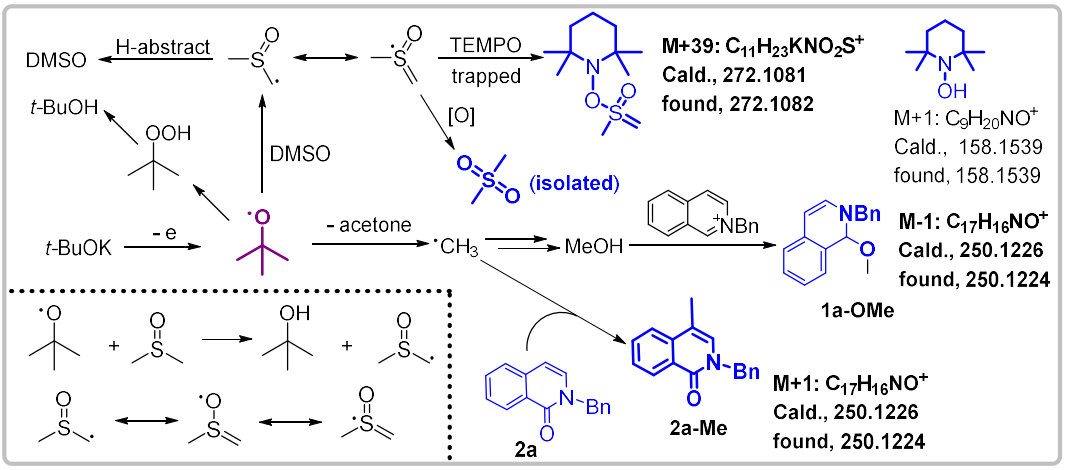


In the absence of *t*-BuOK, the mass peaks of 2a and 1aB were not detected with the addition of TEMPO, which implied that the oxidation of 1a was initiated by *t*-BuOK.

4.5 Experimental proofs to support intermediacy of *tert*-butoxyl radicals

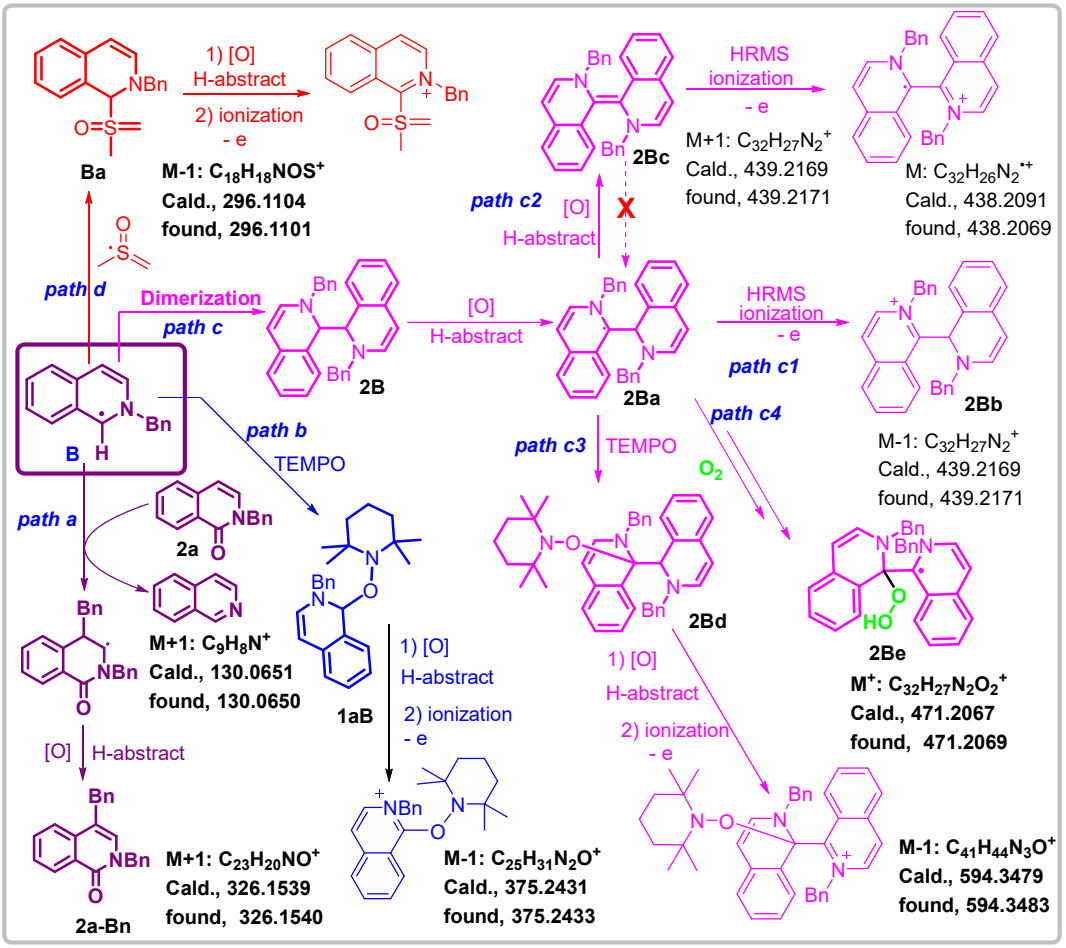
Figure S10. A proposal for the transformation of *tert*-butoxyl radicals leading to

formation of HRMS-identified species

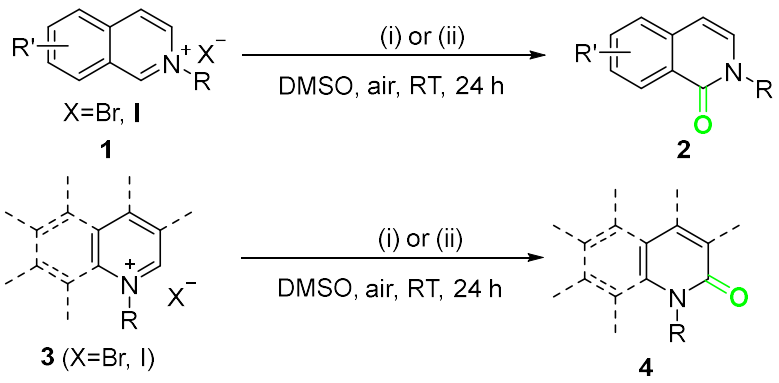


4.6 Experimental proofs to support intermediacy of radical B in Scheme 2

Figure S11. A proposal for the transformation of radical B in Scheme 2 leading to formation of HRMS-identified species



5 General procedures for the oxidation of *N*-alkyl iminium salts 1 & 3

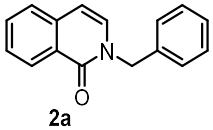


Conditions: (i) *t*-BuOK (2 equiv). (ii) UHP (1.5 equiv), Cs_2CO_3 (1.5 equiv)

Procedure (i), through the *t*-BuOK-promoted aerobic oxidation. To the mixture of *N*-alkyl iminium salt **1** or **3** (0.3 mmol) and potassium *tert*-butoxide (67 mg, 0.6 mmol) in 5 mL reaction flask was added dimethyl sulfoxide (1.5 mL). The mixture was continually stirred at room temperature until **1** or **3** was consumed as indicated by TLC (typically, for 24 h). Then it was diluted with water (5 mL), and extracted with ethyl acetate (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to give the desired product **2** (for **1**) or **4** (for **3**).

Procedure (ii), through the UHP-mediated oxidation. To the mixture of *N*-alkyl iminium salt **1** or **3** (0.3 mmol), cesium carbonate (147 mg, 0.45 mmol) and urea hydrogen peroxide (42 mg, 0.45 mmol) in 5 mL flask was added dimethyl sulfoxide (1.5 mL). The mixture was continually stirred at room temperature until **1** or **3** was consumed as indicated by TLC (typically, for 24 h). Then it was diluted with water (5 mL), and extracted with ethyl acetate (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to give the desired product **2** (for **1**) or **4** (for **3**).

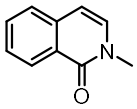
***N*-benzylisoquinolin-1(*2H*)-one (2a)[3]**



2a

The reaction was performed according to Procedure (i). Yellow solid (67 mg, 95%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.34 – 7.27 (m, 5H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.46 (d, *J* = 7.4 Hz, 1H), 5.21 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 137.0, 136.9, 132.2, 131.3, 128.8, 128.1, 128.0, 127.8, 126.9, 126.4, 125.9, 106.4, 51.7.

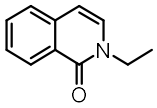
2-methylisoquinolin-1(*2H*)-one (2b) [3]



2b

The reaction was performed according to Procedure (i). Yellow oil (40 mg, 84%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.54 – 7.44 (m, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.48 (d, *J* = 7.2 Hz, 1H), 3.60 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.6, 137.1, 132.4, 132.0, 127.6, 126.8, 126.1, 125.8, 106.0, 36.9.

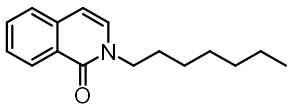
***N*-ethylisoquinolin-1(*2H*)-one (2c)**[4]



2c

The reaction was performed according to Procedure (i). Yellow oil (47 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.51–7.44 (m, 2H), 7.06 (d, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.3 Hz, 1H), 4.05 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 137.0, 132.0, 131.1, 127.8, 126.7, 126.4, 125.8, 106.2, 44.2, 14.5.

***N*-heptylisoquinolin-1(*2H*)-one (2d)** [3]

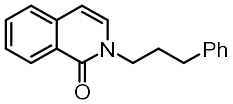


2d

The reaction was performed according to Procedure (i). Yellow oil (69 mg, 94%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.47 (d, *J* = 7.3 Hz, 1H), 3.98 (t, *J* = 7.4 Hz, 2H), 1.81 – 1.73 (m, 2H), 1.39 – 1.23 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 137.0, 131.9, 131.7, 127.8, 126.7, 126.4, 125.8, 105.8, 49.4, 31.7, 29.3, 29.0, 26.7, 22.5,

14.0.

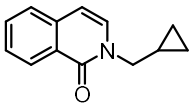
***N*-(3-phenylpropyl) isoquinolin-1(*2H*)-one (2e)** [3]



2e

The reaction was performed according to Procedure (i). Light yellow oil (71 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.52–7.44 (m, 2H), 7.31 – 7.24 (m, 2H), 7.23–7.25 (m, 3H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 7.3 Hz, 1H), 4.02(t, *J*= 7.7 Hz, 2H), 2.71 (t, *J* = 7.7 Hz, 2H), 2.23 – 2.02 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 141.0, 137.0, 132.0, 131.6, 128.5, 128.3, 127.8, 126.8, 126.4, 126.1, 125.8, 106.0, 49.0, 33.0, 30.6.

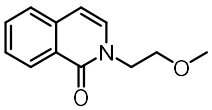
***N*-(cyclopropylmethyl)isoquinolin-1(*2H*)-one (2f)** [3]



2f

The reaction was performed according to Procedure (i). Light yellow oil (45 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.3 Hz, 1H), 3.88 (d, *J* = 7.1 Hz, 2H), 1.32 – 1.21 (m, 1H), 0.61 – 0.56 (m, 2H), 0.43 – 0.38 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 137.0, 132.0, 131.4, 127.9, 126.6, 126.4, 125.8, 105.8, 53.1, 10.8, 3.8.

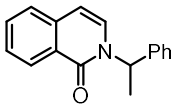
***N*-allylisoquinolin-1(2H)-one (2g)**[5]



2g

The reaction was performed according to Procedure (i). Yellow oil (46 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 6.47 (d, *J* = 7.3 Hz, 1H), 4.19 (t, *J* = 5.1 Hz, 2H), 3.72 (t, *J* = 5.1 Hz, 2H), 3.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 137.2, 132.9, 132.1, 127.8, 126.6, 126.2, 125.8, 105.4, 70.8, 59.0, 49.3.

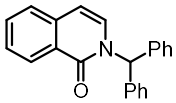
***N*-(1-phenylethyl) isoquinolin-1(*2H*)-one (2h)** [3]



2h

The reaction was performed according to Procedure (i). Light yellow oil (57 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.0 Hz, 1H), 7.69 – 7.57 (m, 1H), 7.53 – 7.42 (m, 2H), 7.38–7.32(m, 4H), 7.31–7.27 (m, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.56 (q, *J* = 7.1 Hz, 1H), 6.43 (d, *J* = 7.5 Hz, 1H), 1.75 (d, *J* = 7.1 Hz,3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 140.6, 136.6, 132.2, 128.8, 128.2, 128.0, 127. 8, 127.4, 126.8, 126.1, 125.8, 106.5, 52.1, 18.8.

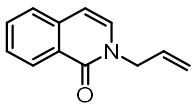
_N_-benzhydrylisoquinolin-1(_2H_)-one (2i) [3]



2i

The reaction was performed according to Procedure (ii). Yellow solid (55 mg, 59%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.0 Hz, 1H), 7.64–7.60 (m, 2H), 7.50–7.45 (m, 2H), 7.36–7.27 (m, 6H), 7.20 (d, *J* = 7.3 Hz, 4H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.44 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 139.2, 136.7, 132.4, 129.7, 128.8, 128.8, 128.4, 127.9, 126.9, 126.1, 125.9, 105.9, 61.7.

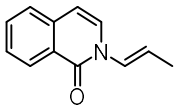
_N_-allylisoquinolin-1(_2H_)-one (2j)[5]



2j

The reaction was performed according to Procedure (ii). Light yellow oil (48 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.50 (d, *J* = 7.3 Hz, 1H), 6.01 – 5.93 (m, 1H), 5.24 (d, *J* = 10.3 Hz, 1H), 5.20 (d, *J* = 17.1 Hz, 1H), 4.64 (d, *J* = 5.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 137.1, 132.9, 132.2, 131.1, 128.0, 126.8, 126.3, 125.9, 118.0, 106.2, 50.7.

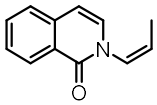
(_E_)-2-(prop-1-en-1-yl)isoquinolin-1(2H)-one [(E)-2j'][22]



(*E*)-2j'

The reaction was performed according to Procedure (i). White solid (13 mg, 23%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.48 (dd, *J* = 13.9, 7.6 Hz, 1H), 7.38 (dd, *J* = 14.3, 1.1 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 6.51 (d, *J* = 7.5 Hz, 1H), 5.82 – 5.70 (m, 1H), 1.89 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 136.4, 132.4, 128.2, 127.9, 127.5, 127.0, 125.9, 115.9, 106.8, 15.4. HRMS (ESI-TOF) calcd for $C_{12}H_{11}NNaO$ $[M + Na]^+$: 208.0733; found 208.0736.

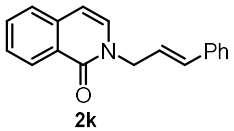
(*Z*)-2-(prop-1-en-1-yl)isoquinolin-1(2H)-one [(Z)-2j'][22]



(*Z*)-2j'

The reaction was performed according to Procedure (i). The R_f value of **(**Z**)-2j'** and **2j** was same as 0.20 (PE/EA = 20:3). The two constitutional isomers were difficult to be separated, and obtained as a mixed yellow oil in a ratio of 3.3 to 1 (35 mg, 63% total yield of two isomers). **(**Z**)-2j'**, major isomer. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.66 – 7.57 (m, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.48 (dd, *J* = 11.7, 4.5 Hz, 1H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.80 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.50 (d, *J* = 7.4 Hz, 1H), 1.73 (dd, *J* = 7.1, 1.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 137.0, 132.4, 131.7, 128.6, 128.0, 126.9, 125.9, 122.3, 118.0, 105.7, 12.3. HRMS (ESI-TOF) calcd for $C_{12}H_{11}NNaO$ $[M + Na]^+$: 208.0733; found 208.0729. **2j**, minor isomer. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.50 (d, *J* = 7.3 Hz, 1H), 6.01 – 5.93 (m, 1H), 5.24 (d, *J* = 10.3 Hz, 1H), 5.20 (d, *J* = 17.1 Hz, 1H), 4.64 (d, *J* = 5.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 137.1, 132.9, 132.2, 131.1, 128.0, 126.8, 126.3, 125.9, 118.0, 106.2, 50.7.

***N*-cinnamylisoquinolin-1(*2H*)-one (2k)**

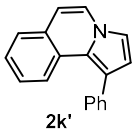


2k

The reaction was performed according to Procedure (ii). TLC: R_f = 0.40 (PE/EA = 10:1).

Yellow solid (58 mg, 74%), m. p. 83–84 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.52 – 7.46 (m, 2H), 7.36 (d, *J* = 7.3 Hz, 2H), 7.31–7.27 (m, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 15.9 Hz, 1H), 6.50 (d, *J* = 7.4 Hz, 1H),6.37-6.31(m,1H) , 4.80 (dd, *J* = 6.4, 1.1 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 137.1, 136.2, 133.6, 132.2, 131.0, 128.6, 127.99, 127.97, 126.9, 126.6, 126.4, 125.9, 124.2, 106.4, 50.3. HRMS (ESI-TOF) calcd for $C_{18}H_{16}NO$ $[M + H]^+$: 262.1226; found 262.1224.

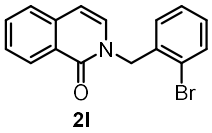
1-phenylpyrrolo [2, 1-a] isoquinoline (2k')



2k'

The reaction was performed according to Procedure (i). TLC: R_f = 0.70 (PE/EA = 10:1). Yellow oil (17 mg, 23%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.73 (d, *J* = 7.3 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 6.8 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.72 (d, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.2, 129.0, 127.4, 126.6, 125.9, 125.85, 125.78, 125.6, 124.4, 123.7, 121.4, 118.5, 113.6, 113.5, 110.2. HRMS (ESI-TOF) calcd for $C_{18}H_{14}N$ $[M + H]^+$: 244.1121; found 244.1112.

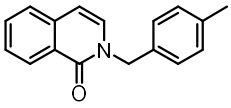
***N*-(2-bromobenzyl) isoquinolin-1(*2H*)-one (2l)[6]**



2l

The reaction was performed according to Procedure (i). White solid (70 mg, 74%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.55–7.48 (m, 2H), 7.25–7.21 (m, 1H), 7.18–7.12 (m, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 7.4 Hz, 1H), 5.33 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 137.1, 136.0, 133.0, 132.4, 131.5, 129.5, 129.3, 128.1, 127.9, 127.0, 126.3, 126.0, 123.4, 106.5, 51.6.

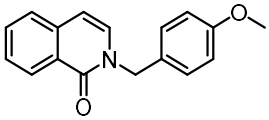
***N*-(4-methylbenzyl) isoquinolin-1(2H)-one (2m)[6]**



2m

The reaction was performed according to Procedure (i). White solid (57 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.6 Hz, 1H), 7.65–7.58 (m, 1H), 7.51 – 7.45 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.4 Hz, 1H), 6.46 (d, *J* = 7.4 Hz, 1H), 5.18 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 137.6, 137.0, 134.0, 132.2, 131.2, 129.5, 128.10, 128.06, 126.8, 126.4, 125.9, 106.3, 51.4, 21.1.

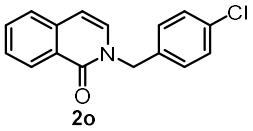
***N*-(4-methoxybenzyl) isoquinolin-1(*2H*)-one (2n) [6]**



2n

The reaction was performed according to Procedure (i). White solid (72 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 – 8.40 (m, 1H), 7.64 (m, 1H), 7.51 – 7.46 (m, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.08 (d, *J* = 7.4 Hz, 1H), 6.89 – 6.84 (m, 2H), 6.46 (d, *J* = 7.4 Hz, 1H), 5.15 (s, 2H), 3.78 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 159.3, 137.0, 132.1, 131.2, 129.5, 129.1, 128.1, 126.8, 126.4, 125.9, 114.2, 106.3, 55.3, 51.2.

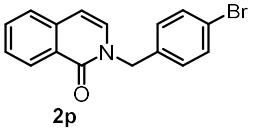
***N*-(4-chlorobenzyl) isoquinolin-1(*2H*)-one (2o) [6]**



2o

The reaction was performed according to Procedure (i). White solid (73 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (d, *J* = 7.9 Hz, 1H), 7.54–7.47 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.33–7.23 (m, 4H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 7.4 Hz, 1H), 5.18 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 136.9, 135.4, 133.8, 132.4, 131.1, 129.3, 129.0, 128.1, 127.1, 126.3, 126.0, 106.7, 51.2.

***N*-(4-bromobenzyl) isoquinolin-1(*2H*)-one (2p) [6]**

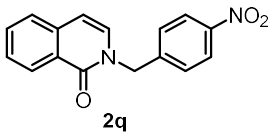


2p

The reaction was performed according to Procedure (i). White solid (90 mg, 95%). ^{1}H

NMR (600 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.52–7.47 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.49 (d, *J* = 7.4 Hz, 1H), 5.16 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 137.0, 136.0, 132.4, 131.9, 131.1, 129.6, 128.1, 127.0, 126.3, 126.0, 121.9, 106.6, 51.3.

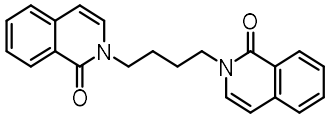
_N_-(4-nitrobenzyl) isoquinolin-1(_2H_)-one (2q)[7]



2q

The reaction was performed according to Procedure (ii). Yellow solid (59 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.73 – 7.63 (m, 2H), 7.57 – 7.50 (m, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 7.4 Hz, 1H), 5.30 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 147.6, 144.2, 137.0, 132.6, 131.0, 128.5, 128.1, 127.3, 126.2, 126.1, 124.0, 107.1, 51.6.

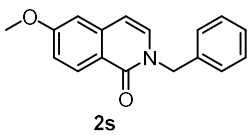
2,2'-(butane-1,4-diyl)bis(isoquinolin-1(2H)-one) (2r) [3]



2r

The reaction was performed according to Procedure (i), and 134 mg of t-BuOK (1.2 mmol) and 3 mL of DMSO were used. Initially, 83 mg of light yellow solid was isolated. The ^{1}H NMR spectrum showed that the sample contained the target compound (**2r**) and 30% of dimethyl sulfone (δ singlet at 2.98 ppm in ^{1}H NMR, 42.7 ppm in ^{13}C NMR),[1] where the ratio value was based on the integration of H signal relative to that of **2r**. The calculated yield of dimethyl sulfone was 23%. After the sample was dissolved in ethyl acetate, fully washed with water, and concentrated in vacuum. 75 mg of **2r** was obtained as a light yellow solid (73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 7.1Hz, 2H), 7.53–7.44 (m, 4H), 7.07 (d, *J* = 7.3 Hz, 2H), 6.48 (d, *J* = 7.3 Hz, 2H), 4.07 (s, 4H), 1.87 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 137.1, 132.1, 131.7, 127.8, 126.8, 126.3, 125. 9, 106.2, 48.7, 26.3.

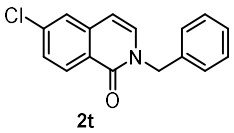
_N_-benzyl-6-methoxyisoquinolin-1(2H)-one (2s)[8]



2s

The reaction was performed according to Procedure (i). Light yellow solid (69 mg, 87%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.28 (m, 5H), 7.09 – 7.02 (m, 2H), 6.85 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 7.4 Hz, 1H), 5.20 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.8, 162.0, 139.1, 137.1, 132.0, 130.2, 128.8, 128.0, 127.8, 120.3, 116.3, 106. 9, 106.1, 55.4, 51.5.

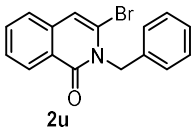
***N*-benzyl-6-chloroisoquinolin-1(*2H*)-one (2t)**



2t

The reaction was performed according to Procedure (i). TLC: R_f = 0.50 (PE/EA = 5:1). White solid (76 mg, 94%), m. p. 72 – 74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.6 Hz, 1H), 7.48 (s, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.38 – 7.28 (m, 5H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 7.3 Hz, 1H), 5.20 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.7, 138.8, 138.2, 136.6, 132.7, 130.0, 128.9, 128.01, 127.97, 127.4, 125.2, 124.7, 105.3, 51.8. HRMS (ESI-TOF) calcd for $C_{16}H_{13}ClNNaO$ $[M + Na]^+$: 292.0500; found 292.0500.

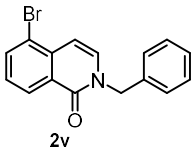
***N*-benzyl-3-bromoisoquinolin-1(*2H*)-one (2u)**



2u

The reaction was performed according to Procedure (i). TLC: R_f = 0.35 (PE/EA = 5:1). **2u** was obtained as a light white solid (45 mg, 48%). m. p. 134 – 136°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.69 (m, 1H), 7.58 – 7.51 (m, 1H), 7.38 – 7.27 (m, 6H), 5.19 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.4, 136.3, 135.5, 133.0, 131.8, 129.0, 128.5, 128.2, 128.1, 127.9, 126.6, 125.9, 100.2, 51.8. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrNO$ $[M + H]^+$: 314.0175; found 314.0179. In addition, 18 mg of **2a** (25% yield) was obtained.

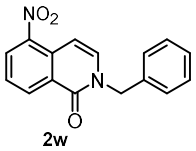
***N*-benzyl-5-bromoisoquinolin-1(*2H*)-one (2v)[6]**



2v

The reaction was performed according to Procedure (i). **2v** was obtained as a white solid (65 mg, 69 %). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.87 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.37 – 7.27 (m, 6H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 5.21 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.5, 136.5, 136.4, 136.0, 132.5, 128.9, 128.0, 127.9, 127.8, 127.4, 120.6, 105.0, 51.9. In addition, 8 mg of **2a** (11% yield) was obtained.

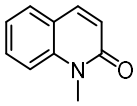
_N_-benzyl-5-nitroisoquinolin-1(_2H_)-one (2w) [6]



2w

The reaction was performed according to Procedure (i). Yellow solid (23 mg, 27%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (d, *J* = 7.8 Hz, 1H), 8.40 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.27 (m, 7H), 7.30 (t, *J* = 21.7 Hz, 3H), 5.23 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.7, 144.8, 135.9, 134.9, 134.5, 130.8, 129.3, 129.0, 128.3, 128.3, 128.1, 125.8, 100.9, 52.1.

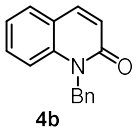
_N_-methylquinolin-2(_1H_)-one (4a) [3]



4a

The reaction was performed according to Procedure (i). Yellow solid (39 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 9.4 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 9.4 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 140.0, 138.9, 130.6, 128.7, 122.1, 121.7, 120.7, 114.1, 29.4.

_N_-benzylquinolin-2(_1H_)-one (4b) [3]

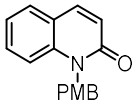


4b

The reaction was performed according to Procedure (i). Yellow oil (54 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 9.5 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 7.8

Hz, 1H), 7.31 – 7.24 (m, 3H), 7.22 (t, *J* = 6.6 Hz, 3H), 7.17 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 9.5 Hz, 1H), 5.55 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.5, 139.6, 139.5, 136.4, 130.6, 128.8, 128.8, 127.3, 126.6, 122.2, 121.7, 121.0, 115.1, 45.9.

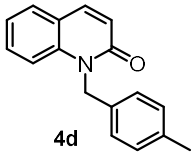
***N*-(4-methoxybenzyl) quinolin-2(*1H*)-one (4c)[9]**



4c

The reaction was performed according to Procedure (i). Light yellow solid (64 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 9.5 Hz, 1H), 7.55 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.20 – 7.15 (m, 3H), 6.84 – 6.81 (m, 2H), 6.79 (d, *J* = 9.5 Hz, 1H), 5.49 (s, 2H), 3.75 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.5, 158.8, 139.5, 139.4, 130.5, 128.8, 128.5, 128.0, 122.1, 121.8, 121.0, 115.0, 114.2, 55.2, 45.4.

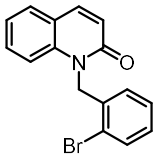
***N*-(4-methylbenzyl) quinolin-2(*1H*)-one (4d)**



4d

The reaction was performed according to Procedure (i). TLC: R_f = 0.45 (PE/EA = 20:3). Light yellow solid (56 mg, 75%), m. p. 130–132 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 9.5 Hz, 1H), 7.54 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.45 – 7.37 (m, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 2H),7.09(d, J = 8.2 Hz, 2H), 6.79 (d, *J* = 9.5 Hz, 1H), 5.51 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.5, 139.6, 139.4, 136.9, 133.4, 130.6, 129.4, 128.8, 126.6, 122.1, 121.7, 121.0, 115.1, 45.7, 21.0. HRMS (ESI-TOF) calcd for $C_{17}H_{15}NNaO$ $[M + Na]^+$: 272.1046; found 272.1045.

***N*-(2-bromobenzyl) quinolin-2(*1H*)-one (4e)**

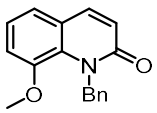


4e

The reaction was performed according to Procedure (i). TLC: R_f = 0.55 (PE/EA = 20:3). Yellow solid (57 mg, 60%), m. p. 132–135 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 9.5 Hz, 1H), 7.66 – 7.54 (m, 2H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14 –

7.08 (m, 2H), 7.04 (d, *J* = 8.5 Hz, 1H), 6.81 (d, *J* = 9.5 Hz, 1H), 6.74 – 6.68 (m, 1H), 5.59 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 139.8, 139.3, 134.8, 132.9, 130.9, 128.9, 128.8, 127.8, 127.0, 122.6, 122.4, 121.6, 120.9, 114.98, 46.4. HRMS (ESI-TOF) calcd for $C_{16}H_{12}BrNNaO$ $[M + Na]^+$: 335.9994; found 335.9995.

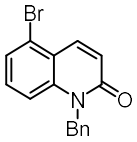
_N_-benzyl-8-methoxyquinolin-2(*1H*)-one (4f)



4f

The reaction was performed according to Procedure (i). TLC: R_f = 0.35 (PE/EA = 4:1). Light yellow solid (70 mg, 88%), m. p. 108–109 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 9.4 Hz, 1H), 7.25 – 7.23 (m, 2H), 7.17 – 7.07 (m, 5H), 6.97 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.78 (d, *J* = 9.4 Hz, 1H), 5.89 (s, 2H), 3.57 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 148.3, 139.8, 139.4, 130.8, 128.1, 126.1, 125.8, 123.2, 122.9, 122.0, 121.9, 114.1, 56.5, 49.8. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO_2$ $[M + H]^+$: 266.1176; found 226.1176.

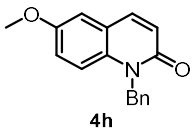
_N_-benzyl-5-bromoquinolin-2(*1H*)-one (4g)



4g

The reaction was performed according to Procedure (ii). TLC: R_f = 0.35 (PE/EA = 5:1). **L**ight yellow solid (67 mg, 71%), m. p. 136–138 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 9.8 Hz, 1H), 7.43 (dd, *J* = 6.5, 2.0 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.21 (m, 3H), 7.18 (d, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 9.8 Hz, 1H), 5.55 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 140.8, 138.2, 136.0, 130.9, 128.9, 127.4, 126.5, 123.8, 122.8, 120.0, 114.8, 46.3. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrNO$ $[M + H]^+$: 314.0175; found 314.0175.

_N_-benzyl-6-methoxyquinolin-2(*1H*)-one (4h)



4h

The reaction was performed according to Procedure (i). TLC: R_f = 0.20 (PE/EA = 2:1). Light yellow solid (71 mg, 89%), m. p. 106–108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d,

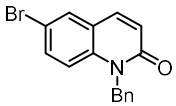
J = 9.5 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.24 – 7.15 (m, 4H), 7.02 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 6.81 (d, *J* = 9.5 Hz, 1H), 5.53 (s, 2H), 3.80 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 154.8, 139.0, 136.5, 134.0, 128.8, 127.2, 126.6, 122.2, 121.7, 119.2, 116.4, 110.7, 55.7, 46.0. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO_2$ [M + H] $^+$: 266.1176; found 266.1174.

_N_-benzyl-6-methylquinolin-2(*1H*)-one (4i)

4i

The reaction was performed according to Procedure (i). TLC: R_f = 0.40 (PE/EA = 5:1). Light yellow solid (65 mg, 87%), m. p. 102–104 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68–7.63(m, 1H), 7.32 (s, 1H), 7.29–7.24 (m, 2H), 7.20 (t, *J* = 7.0 Hz, 4H), 7.13 (d, *J* = 8.6 Hz, 1H), 6.77 (d, *J* = 9.5 Hz, 1H), 5.52 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) 162.4, 139.4, 137.5, 136.5, 131.9 , 131.8, 128.8, 128.6, 127.2, 126.6, 121.60, 121.0, 115.0, 45.9, 20.5. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO$ [M + H] $^+$: 250.1226; found 250.1224.

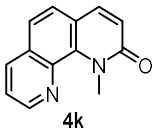
_N_-benzyl-6-bromoquinolin-2(*1H*)-one (4j)



4j

The reaction was performed according to Procedure (i). TLC: R_f = 0.18 (PE/EA = 20:3). Yellow solid (70 mg, 74%), m. p. 138–140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 2.2 Hz, 1H), 7.65 (d, *J* = 9.5 Hz, 1H), 7.48 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 2H), 7.13 (d, *J* = 9.0 Hz, 1H), 6.82 (d, *J* = 9.5 Hz, 1H), 5.52 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 138.5, 138.3, 135.9, 133.3, 131.0, 128.9, 127.5, 126.5, 123.0, 122.4, 116. 8, 115.0, 46.0. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrNO$ [M + H] $^+$:314.0175; found 314.0176.

_N_-methyl-1,10-phenanthrolin-2(*1H*)-one (4k)[10]

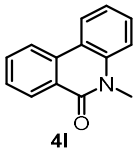


4k

The reaction was performed according to Procedure (i). Light white solid (47 mg, 74%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (d, *J* = 3.6 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.56 (q, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 8.1, 4.0 Hz, 1H), 6.91 (d, *J* = 9.2 Hz, 1H), 4.48 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 147.1, 140.2, 139.0, 137.9, 136.1, 130.1, 126.7, 122.4, 122.2, 121.8, 120.4, 37.8.

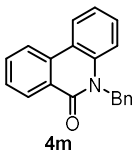
***N*-methylphenanthridin-6(*5H*)-one (4l)[5]**



4l

The reaction was performed according to Procedure (i). White solid (25 mg, 80%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (d, *J* = 7.9 Hz, 1H), 8.35 – 8.20 (m, 2H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 138.1, 133.6, 132.4, 129.6, 128.9, 127.9, 125.6, 123.2, 122.4, 121.6, 119.3, 115.0, 30.0.

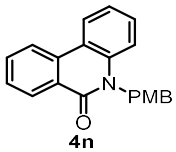
***N*-benzylphenanthridin-6(*5H*)-one (4m)[5]**



4m

The reaction was performed according to Procedure (i). White solid (23 mg, 54%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 7.9, 1H), 8.35 – 8.25 (m, 2H), 7.86 – 7.75 (m, 1H), 7.66–7.59 (m, 1H), 7.42 – 7.36 (m, 1H), 7.34 – 7.18 (m, 7H), 5.67 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 137.4, 136.6, 133.9, 132.7, 129.6, 129.2, 128.8, 128.0, 127.2, 126.6, 125.5, 123.3, 122.6, 121.7, 119.6, 116.0, 46.5.

***N*-(4-methoxybenzyl) phenanthridin-6(*5H*)-one (4n)[5]**

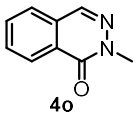


4n

The reaction was performed according to Procedure (i). White solid (30 mg, 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.0 Hz, 1H), 8.28 (t, *J* = 8.7 Hz, 2H), 7.80 – 7.75 (m, 1H), 7.63–7.58 (m, 1H), 7.42 – 7.37 (m, 1H), 7.42– 7.38(m, 1H), 7.27 – 7.24 (m, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.60 (s, 2H), 3.74 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 158.8, 137.4, 133.9, 132.6, 129.5, 129.1, 128.7, 128.00, 127.96,

125.6, 123.3, 122.5, 121.7, 119.6, 116.0, 114.3, 55.3, 45.9.

***N*-methylphthalazin-1(2H)-one (4o)[5]**



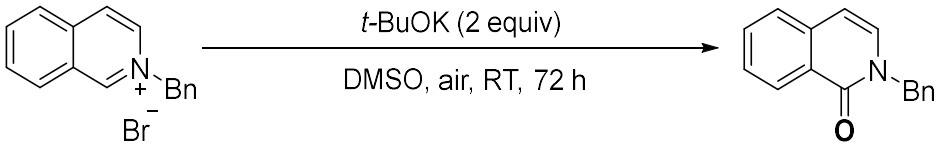
4o

The reaction was performed according to Procedure (i). Light yellow solid (28 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 7.6 Hz, 1H), 8.15 (s, 1H), 7.85–7.75 (m, 2H), 7.70 (d, *J* = 7.4 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.7, 137.6, 132.9, 131.6, 129.8, 127.8, 126.5, 126.0, 39.4.

6 Scale-up of the reaction and synthetic transformations of isoquinolinone

6.1 Scale-up syntheses of 2a

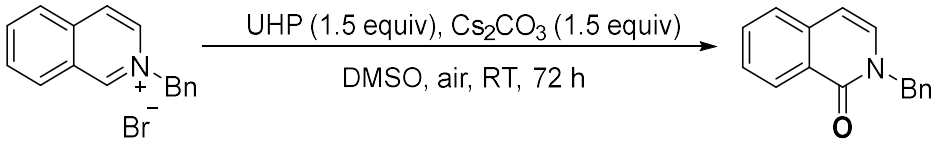
(i) Preparation through the *t*-BuOK-promoted aerobic oxidation



1a (1.80 g, 6 mmol) **2a** (1.32 g, 93%)

To the mixture of *N*-benzylisoquinolin-2-ium bromide **1a** (1.80 g, 6.0 mmol) and potassium *tert*-butoxide (1.35 g, 12.0 mmol) in a 100 mL flask was added DMSO (30 mL) with stirring. The reaction mixture was continually stirred in air at room temperature until **1a** was consumed as indicated by TLC (ca 72 h). Then it was diluted with ethyl ester (70 mL) and water (70 mL), and extracted with EtOAc (3 × 70 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=5:1) to provide *N*-benzylisoquinolin-1(2*H*)-one **2a** as a yellow solid (1.32 g, 93% yield).

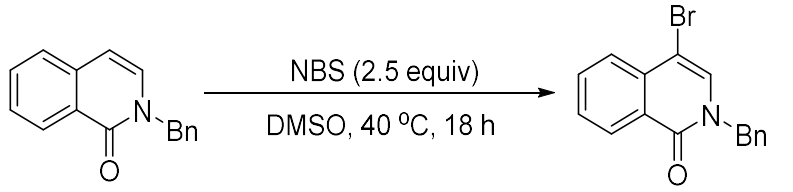
(ii) Preparation through the UHP-mediated oxidation



1a (1.80 g, 6 mmol) **2a** (1.22 g, 86%)

To the mixture of *N*-benzylisoquinolin-2-ium bromide **1a** (1.80 g, 6.0 mmol), cesium carbonate (2.93 g, 9.0 mmol) and urea hydrogen peroxide (847 mg, 9.0 mmol) in a 100 mL reaction flask was added DMSO (30 mL) with stirring. The reaction mixture was continually stirred in air at room temperature until **1** was consumed as indicated by TLC (ca 24 h). Then it was diluted with ethyl ester (70 mL) and water (70 mL), and extracted with EtOAc (3 × 70 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=5:1) to provide *N*-benzylisoquinolin-1(2*H*)-one **2a** as a yellow solid (1.22 g, 86%).

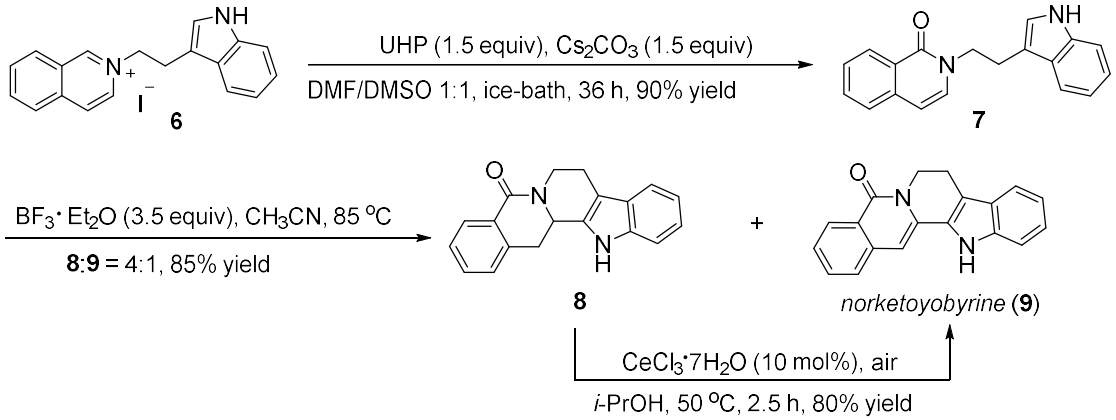
6.2 Bromination of 2a with *N*-bromosuccinimide



2a **5** (93% yield)

A 10 mL reaction flask was charged with the solution of *N*-benzylisoquinolin-1(2*H*)-one **2a** (71 mg, 0.3 mmol) and NBS (133 mg, 0.75 mmol) in DMSO (1.5 mL). The reaction mixture was continually stirred at 40 °C until **2a** was consumed as indicated by TLC (ca 18 h). Then it was diluted with ethyl acetate (5 mL) and water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic phase was washed with water and saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate= 5:1) to provide *N*-benzyl-4-bromoisoquinolin-1(2*H*)-one **5** as a white solid (87 mg, 93%).[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.69 – 7.60 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.26 (m, 3H), 7.25 – 7.20 (m, 3H), 5.12 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.4, 136.3, 135.47, 133.0, 131.8, 129.0, 128.5, 128.15, 128.10, 127.9, 126.6, 125.9, 100.2, 51.8.

6.3 Total synthesis of norketoyobyrine (9)



Oxidation of iminium salt 6. To a 100 mL flask was charged with 2-(2-(1*H*-indol-3-yl)ethyl)isoquinolin-2-ium iodide **6** (800 mg, 2 mmol), cesium carbonate (977 mg, 3.0 mmol) and UHP (282 mg, 3.0 mmol), and cooled in an ice-bath. Then DMSO (7.5 mL) and DMF (7.5 mL) was added with stirring. The reaction mixture was continually stirred in an ice-bath until **6** was consumed as indicated by TLC (ca 36 h). It was diluted with ethyl acetate (15 mL) and water (15 mL), and extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with water and saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=2:1) to provide 2-(2-(1*H*-indol-3-yl)ethyl)isoquinolin-1(2*H*)-one **7** as a yellow solid (519 mg, 90% yield), m. p. 120–130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.0 Hz, 1H), 8.04 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.43 – 7.33 (m, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.94 (s, 1H), 6.78 (d, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.3 Hz, 1H), 4.30 (t, *J* = 7.3 Hz, 2H), 3.42 – 3.14 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 137.2, 136.4, 132.1, 132.0, 127.8, 127.3, 126.6, 126.3, 125.8, 122.5, 122.2, 119.6, 118.7, 112.4, 111.2, 105.4, 50.3, 25.0. HRMS (ESI-TOF) calcd for $C_{19}H_{16}N_2NaO$ $[M + Na]^+$: 311.1155; found 311.1153.

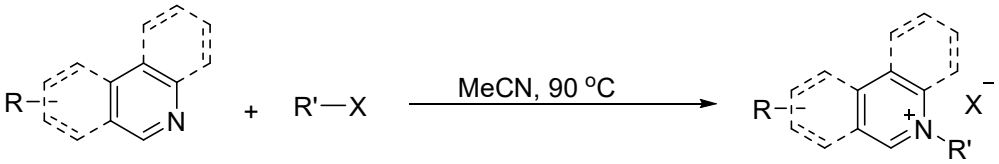
Cyclization of isoquinolone 7. A 10 mL screwtop pressure Schlenk tube was charged with the solution of 2-(2-(1*H*-indol-3-yl)ethyl)isoquinolin-1(2*H*)-one **7** (29 mg, 0.1 mmol) in CH_3CN (2 mL). $BF_3{\cdot}Et_2O$ (43 µL , 0.35 mmol) was added with stirring. The tube

was sealed with a screw stopper, and stirred for 48 h at 85 °C. After cooling it to RT, the mixture was diluted with dichloromethane (5 mL) and water (5 mL), extracted with dichloromethane (3 × 5 mL). The organic combined phase was dried over anhydrous $CaCl_2$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (PE/DCM =1:10) to provide 24 mg of yellow solid. ^{1}H NMR spectrum indicated that it constituted of dihydronorketoyobyrine **8** and norketoyobyrine **9** in a ratio of 4 to 1. Thus, the total yield of the two compounds was 85%. Dihydronorketoyobyrine **8** (major),[11] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 6.9 Hz, 1H), 7.47 (t, *J* = 6.3 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.13 – 7.06 (m, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 5.15 – 4.94 (m, 2H), 3.60 (dd, *J* = 15.8, 3.8 Hz, 1H), 2.96 (dd, *J* = 12.4, 3.1 Hz, 2H), 2.89 (d, *J* = 11.7 Hz, 1H), 2.82 – 2.69 (m, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.8, 136.9, 136.3, 133.6, 131.9, 128.8, 127.8, 127.2, 127.1, 126.1, 121.2, 118.6, 117.9, 111.1, 107.3, 51.6, 39.0, 34.2, 20.6. Norketoyobyrine **9** (minor),[12] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.71 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 5.6 Hz, 1H), 7.58 (d, *J* = 5.3 Hz, 1H), 7.41 (br.s, 2H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.12 - 7.06 (m, 2H), 4.41 (t, *J* = 6.5 Hz, 2H), 3.10 (t, *J* = 6.6 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.2, 138.0, 136.1, 132.6, 132.3, 128.1, 127.5, 126.07, 125.9, 125.5, 124.5, 123.5, 119.4, 119.1, 112.5, 111.6, 99.0, 40.4, 19.3.

Oxidation of 3, 4-dihydroisoquinolin-1(2*H*)-one 8. To a 10 mL flask was added the mixture of **8** and **9** (29 mg, ratio 4:1, 0.1 mmol) in *i*-PrOH (4 mL). The flask was put in an oil-bath at 50 °C and stirred until the solid was completely dissolved. Then $CeCl_3 \cdot 7H_2O$ (0.01 mmol, 4 mg) was added. The reaction mixture was stirred until **8** was consumed as indicated by TLC (ca 2.5 h). It was neutralized to pH 8−9 with saturated $NaHCO_3$, and completely extracted with EtOAc (8 × 3 mL). The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/CH_2Cl_2 = 1:5) to give norketoyobyrine **9** as a yellow solid (23 mg, 80%).[12] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (s, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 7.75 – 7.67 (m, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 8.1

Hz, 0H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.11 – 7.03 (m, 2H), 4.40 (t, *J* = 6.6 Hz, 2H), 3.09 (t, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.7, 138.5, 136.6, 133.1, 132.8, 128.6, 128.0, 126.6, 126.4, 126.0, 125.0, 124.0, 120.0, 119.6, 113.0, 112.1, 99.5, 40.9, 19.8.

7. Preparation of *N*-alkyl iminium salts 1 and 3



S1 or **S3**

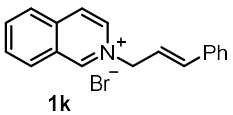
X = Br, I

1 or **3**

N-alkyl iminium salts 1a–1c,[13–15] 1d–1e,[3] 1f–1h,[5] 1i,[3] 1j,[5] 1l,[5] 1m–1q,[16] 1t,[16] 1w,[16] 3a,[18] 3h,[20] 3i,[21] 3k,[19] and 3l–3o[5] were prepared according to literature procedures. Others were synthesized as the following general procedure.

An oven-dried flask was charged with CH_3CN (10 mL), aromatic azine **1** or **3** (3 mmol) and alkyl halide (3 mmol). The reaction mixture was refluxed until the azine was consumed as indicated by TLC. Then it was cooled to room temperature, and concentrated under reduced pressure. The residue was diluted with diethyl ether, and the iminium salt was precipitated quickly. The solid was washed with diethyl ether to give purified **1** or **3**. If the iminium salt could not be precipitated, the residue was thoroughly washed with diethyl ether by ultrasonic vibration. Normally, washing three times will lead to the purified salt.

***N*-cinnamylisoquinolin-2-ium bromide (1k)**

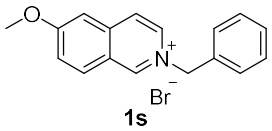


1k

Brown oil (812 mg, 83%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.89 (d, *J* = 6.7 Hz, 1H), 8.67 (d, *J* = 6.8 Hz, 1H), 8.58 (d, J = 8.3 Hz, 1H), 8.40 (d, *J* = 8.2 Hz, 1H), 8.29 (t, *J* = 7.6 Hz, 1H), 8.10 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 15.8 Hz, 1H), 6.78 – 6.72 (m, 1H), 5.63 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.5, 137.6, 137.4, 137.1, 135.8, 135.3, 131.7,

131.0, 129.2, 129.1, 127.8, 127.4, 126.5, 122.8, 62.6. HRMS (ESI-TOF) calcd for $C_{18}H_{16}N$ [M-Br] $^{+}$:246.1227; found 246.1278.

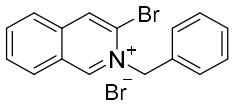
***N*-benzyl-6-methoxyisoquinolin-2-ium bromide (1s)**



1s

White solid (173 mg, 86%), m. p. 148–150 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.07 (s, 1H), 8.73 (d, *J* = 6.6 Hz, 1H), 8.43 (d, *J* = 9.1 Hz, 1H), 8.38 (d, *J* = 6.8 Hz, 1H), 7.78 (s, 1H), 7.71 – 7.66 (m, 1H), 7.57 (d, *J* = 6.5 Hz, 2H), 7.50 – 7.38 (m, 3H), 5.91 (s, 2H), 4.06 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.3, 148.7, 140.5, 135.6, 135.1, 133.0, 129.6, 129.2, 124.8, 124.5, 123.2, 106.5, 63.1, 57.2. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO$ [M-Br] $^{+}$:250.1226; found 250.1225.

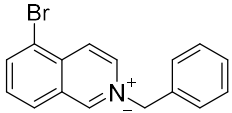
***N*-benzyl-3-bromoisoquinolin-2-ium bromide (1u)**



1u

Pink solid (405 mg, 89%), m. p. > 250 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.59–10.40 (m, 1H), 9.46 (d, *J* = 8.1 Hz, 1H), 8.65 (d, *J* = 8.2 Hz, 1H), 8.47 – 8.30 (m, 2H), 8.23–8.15 (m, 1H), 7.70 (s, 2H), 7.47 (d, *J* = 7.6 Hz, 3H), 6.02 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.6, 139.4, 136.5, 134.4, 132.6, 132.3, 129.9, 129.6, 129.6, 129.6, 128.1, 126.5, 122.5, 63.8. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN$ [M-Br] $^{+}$:298.0226; found 298.0225.

***N*-benzyl-5-bromoisoquinolin-2-ium bromide (1v)**

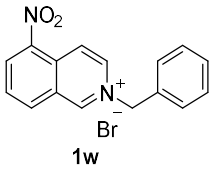


1v

White solid (651 mg, 86%), m. p. 122–124 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.48 (d, *J* = 4.2 Hz, 1H), 8.95 (d, *J* = 7.0 Hz, 1H), 8.64 – 8.59 (m, 3H), 8.01 (t, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.48 – 7.44 (m, 3H), 6.08 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 151.5, 141.0, 136.9, 136.4, 134.5, 132.7, 131.4, 129.8, 129.7, 129.4, 129.3, 129.2, 125.7, 121.3, 63.8. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN$ [M-Br] $^{+}$:298.0226; found

298.0221.

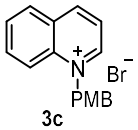
***N*-benzyl-5-nitroisoquinolin-2-ium bromide (1w)**



1w

Yellow solid (963 mg, 93%), m. p. 202–204 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.63 (s, 1H), 9.09 – 9.03 (m, 2H), 9.00 (d, *J* = 7.2 Hz, 1H), 8.96 (d, *J* = 8.3 Hz, 1H), 8.28 (t, *J* = 8.0 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.49 – 7.45 (m, 3H), 6.10 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 151.8, 144.7, 138.3, 137.9, 134.9, 134.7, 134.3, 131.2, 129.9, 129.7, 129.6, 128.8, 122.7, 64.1. HRMS (ESI-TOF) calcd for $C_{16}H_{13}N_2O_2$ [M-Br] $^{+}$:265.0972; found 265.0970.

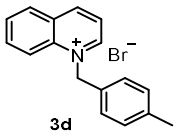
***N*-(4-methoxybenzyl)quinolin-1-ium bromide (3c)**



3c

Gray solid (862 mg, 87%), m. p. 180–182 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.79 (d, *J* = 5.7 Hz, 1H), 9.39 (d, *J* = 8.3 Hz, 1H), 8.64 (d, *J* = 9.0 Hz, 1H), 8.54 – 8.50 (m, 1H), 8.31 –8.27 (m, 1H), 8.26 – 8.22 (m, 1H), 8.03 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.34 (s, 2H), 3.73 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.1, 150.4, 148.4, 138.0, 136.1, 131.3, 130.4, 130.4, 129.9, 125.9, 122.9, 119.8, 115.0, 60.0, 55.7. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO$ [M-Br] $^{+}$:250.1226; found 250.1227.

***N*-(4-methylbenzyl)quinolin-1-ium bromide (3d)**

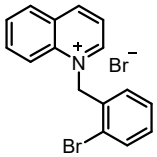


3d

White solid (858 mg, 91%), m. p. 114–116 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.85 (d, *J* = 5.4 Hz, 1H), 9.42 (d, *J* = 8.3 Hz, 1H), 8.58 (d, *J* = 9.0 Hz, 1H), 8.54 (d, *J* = 8.1 Hz, 1H), 8.32 (dd, *J* = 8.2, 5.9 Hz, 1H), 8.23 (t, *J* = 7.9 Hz, 1H), 8.03 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 6.39 (s, 2H), 2.27 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.7, 148.5, 138.8, 138.0, 136.2, 131.31, 130.4, 130.4, 130.1, 128.0,

122.9, 119.8, 60.2, 21.1. HRMS (ESI-TOF) calcd for $C_{17}H_{16}N$ [M-Br] $^{+}$:234.1277; found 234.1278.

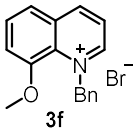
***N*-(2-bromobenzyl)quinolin-1-ium bromide (3e)**



3e

Purple solid (887 mg, 78%), m. p. 118–120 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.65 (d, *J* = 5.6 Hz, 1H), 9.50 (d, *J* = 8.3 Hz, 1H), 8.61 (d, *J* = 8.1 Hz, 1H), 8.36 – 8.23 (m, 3H), 8.08 (t, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.43 (s, 2H). 13C NMR (151 MHz, DMSO-d_6) δ 150.9, 149.2, 138.3, 136.62, 133.8, 133.1, 131.5, 131.4, 130.6, 130.3, 129.5, 129.1, 123.1, 122.8, 119.3, 60.6. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN$ [M-Br] $^{+}$:298.0226; found 298.0230.

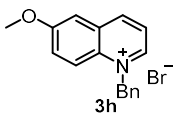
***N*-benzyl-8-methoxyquinolin-1-ium bromide (3f)**



3f

Yellow solid (860 mg, 87%), m. p. 138–140 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.75 – 9.60 (m, 1H), 9.40 – 9.34 (m, 1H), 8.28 (dd, *J* = 8.2, 5.9 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.94 (td, *J* = 8.0, 2.7 Hz, 1H), 7.73 (d, *J* = 2.7 Hz, 1H), 7.34 (t, *J* = 8.0, 4.7 Hz, 3H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.55 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 153.0, 150.7, 148.9, 136.6, 132.7, 131.1, 129.3, 128.5, 126.6, 123.1, 123.1, 120.3, 117.3, 65.8, 57.5. HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO$ [M-Br] $^{+}$:250.1226; found 250.1229.

***N*-benzyl-6-methoxyquinolin-1-ium bromide (3h)**

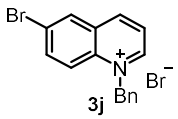


3h

Green solid (941 mg, 95%), m. p. 210–212 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.62 (d, *J* = 5.7 Hz, 1H), 9.23 (d, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 9.7 Hz, 1H), 8.27 – 8.21 (dd, *J* = 8.4, 5.8 Hz, 1H), 7.96 (d, *J* = 2.7 Hz, 1H), 7.85 (dd, *J* = 9.7, 2.8 Hz, 1H), 7.44 – 7.28 (m, 5H), 6.39 (s, 2H), 3.99 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.7, 147.9, 146.7, 134.5, 133.7, 132.5, 129.6, 129.2, 128.2, 127.7, 123.2, 121.5, 109.0, 60.4, 56.9. HRMS (ESI-

TOF) calcd for $C_{17}H_{16}NO$ [M-Br] $^{+}$:250.1226; found 250.1225.

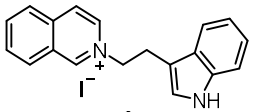
_N_-benzyl-6-bromoquinolin-1-ium bromide (3j)



3j

Gray solid (1.0 g, 88%), m. p. > 250 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.90 – 9.77 (m, 1H), 9.33 (d, *J* = 8.4 Hz, 1H), 8.87 (d, *J* = 2.1 Hz, 1H), 8.49 (d, *J* = 9.4 Hz, 1H), 8.39 – 8.30 (m, 2H), 7.44 – 7.31 (m, 5H), 6.42 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 149.3, 145. 6, 136.6, 135.0, 132.0, 131.0, 129.5, 127.5, 127.2, 125.7, 122.0, 121.5, 119.9, 58.5. HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN$ [M-Br] $^{+}$:298.0226; found 298.0223.

2-(2-(1*H*-indol-3-yl)ethyl)isoquinolin-2-ium iodide (6)



6

Yellow solid (305 mg, 76%), m. p. 240–245 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.91 (s, 1H), 9.92 (s, 1H), 8.76 (d, *J* = 6.6 Hz, 1H), 8.56 (d, *J* = 6.7 Hz, 1H), 8.38 (d, *J* = 8.3 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H), 8.24 (t, *J* = 7.5 Hz, 1H), 8.04 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.14 – 7.03 (m, 2H), 6.93 (t, *J* = 7.4 Hz, 1H), 4.99 (t, *J* = 7.2 Hz, 2H), 3.50 (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.3, 137.4, 137.3, 136.7, 135.4, 131.6, 130.7, 127.7, 127.5, 127.2, 126.1, 124.4, 121.8, 119.0, 118.5, 112.0, 109.0, 61.9, 27.2. HRMS (ESI-TOF) calcd for $C_{19}H_{17}N_2$ [M-I^-]$^{+}$: 273.1386; found 273.1379.

8 Reference

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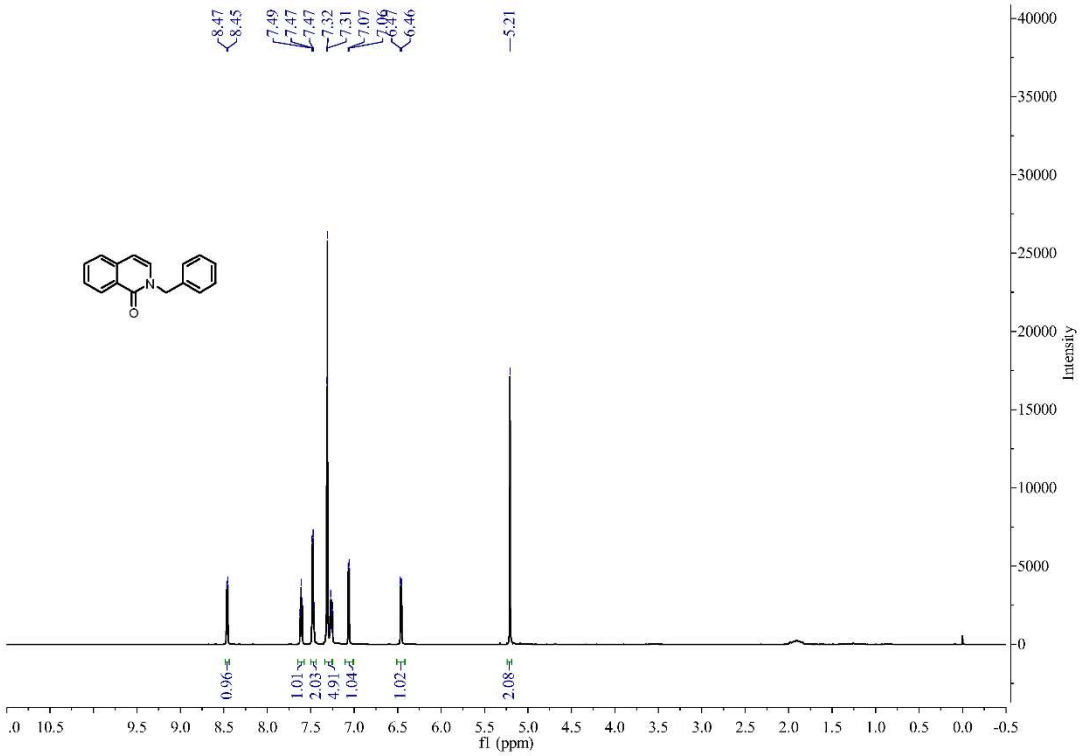
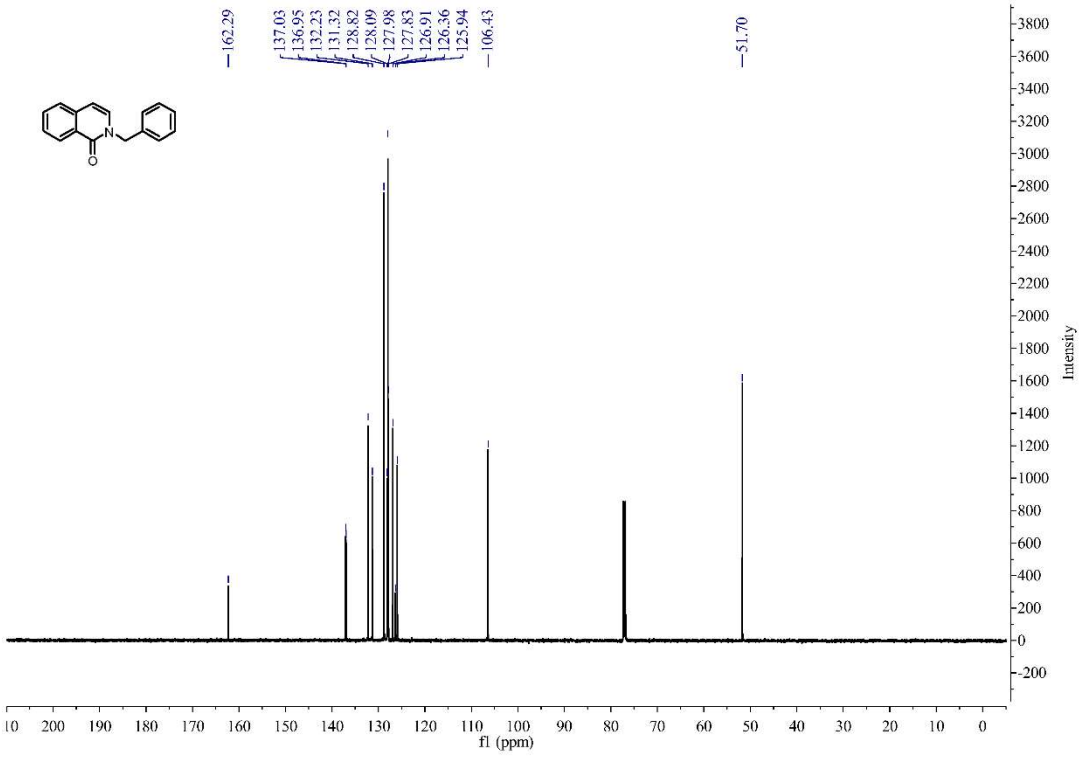
9 NMR spectra

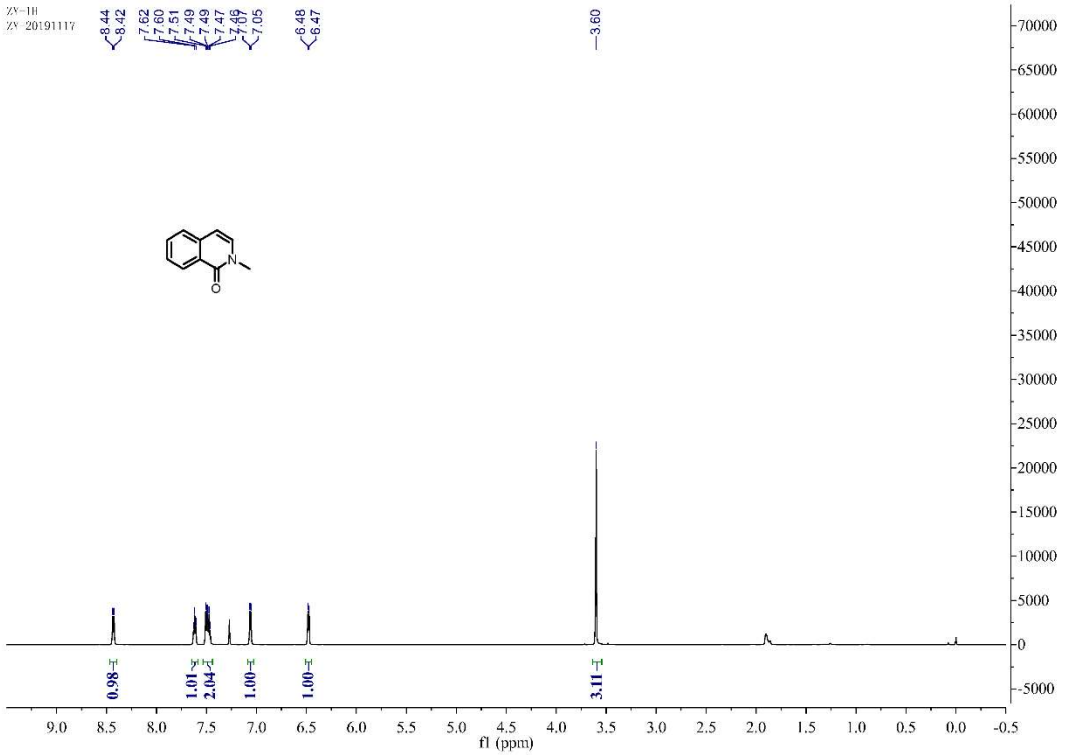
9.1 Spectra of compounds 2a–2w

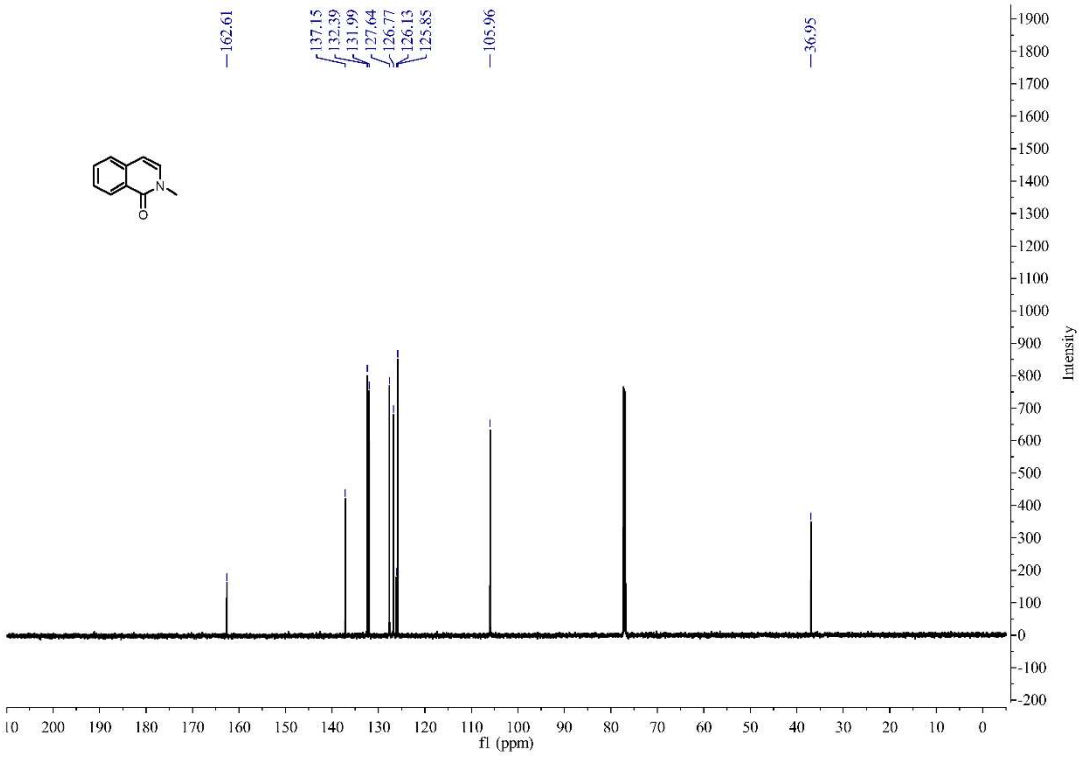
N-benzylisoquinolin-1(*2H*)-one (2a)



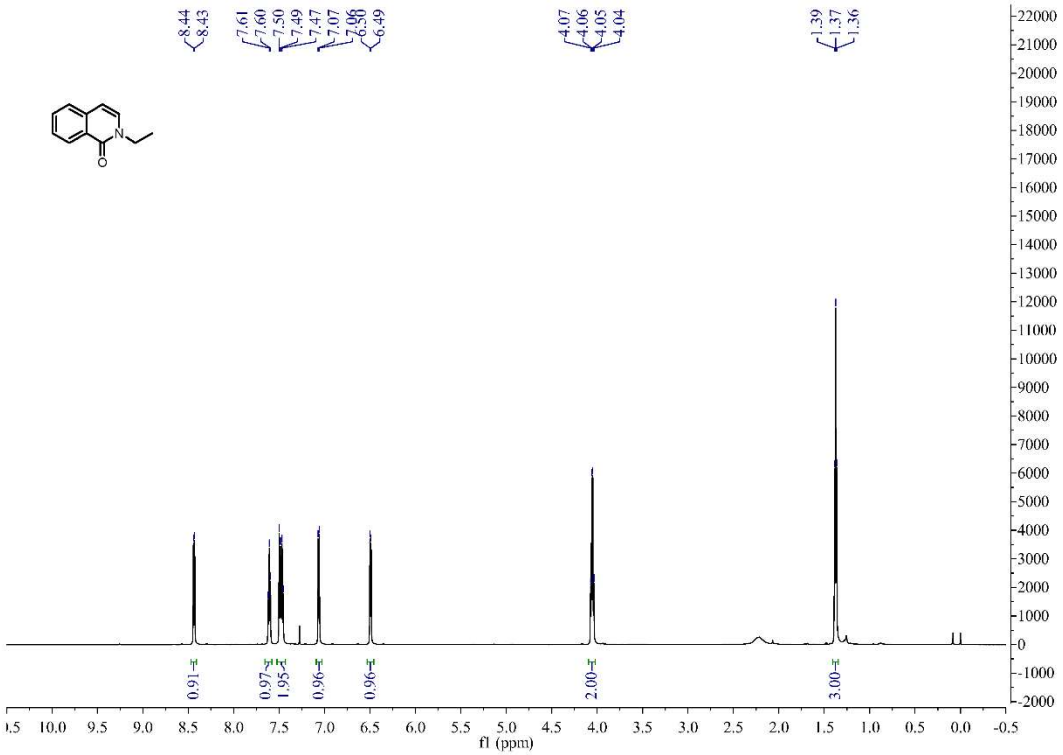


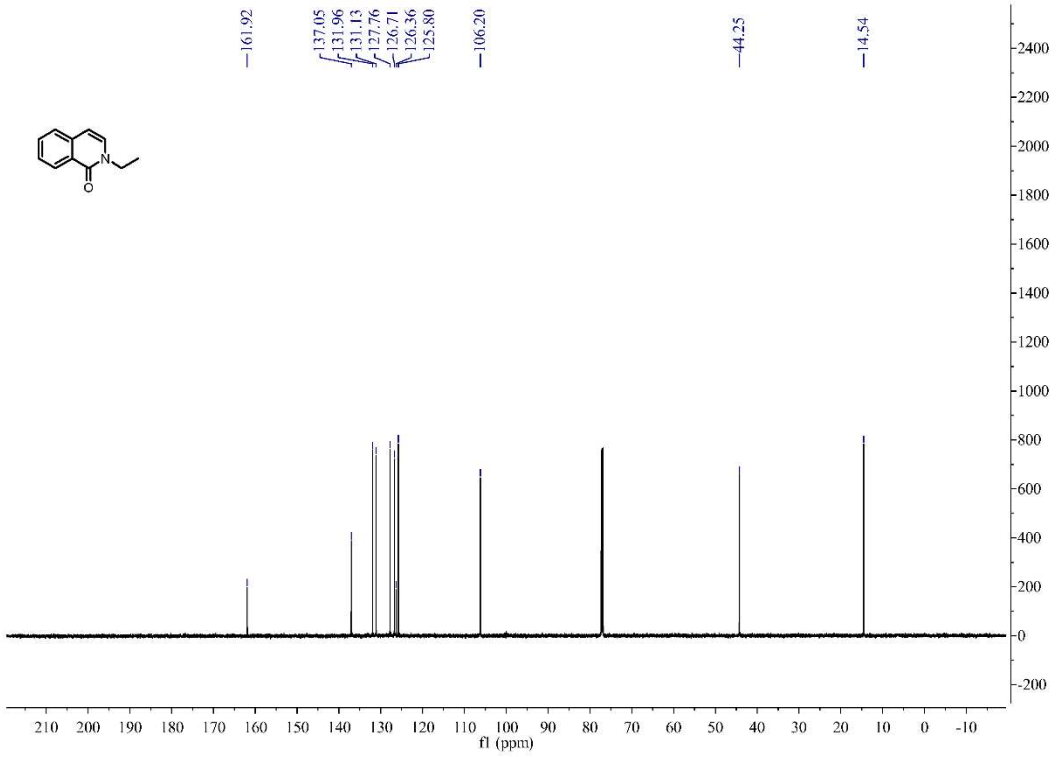
2-methylisoquinolin-1(*2H*)-one (2b)





***N*-ethylisoquinolin-1(*2H*)-one (2c)**





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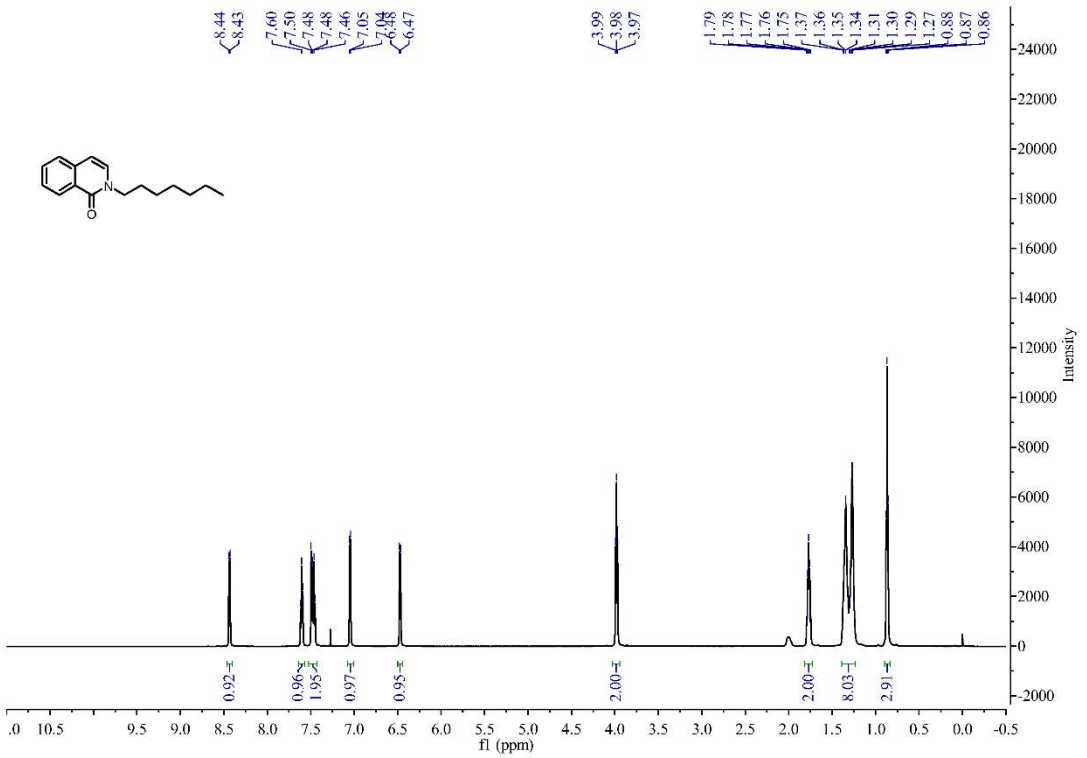

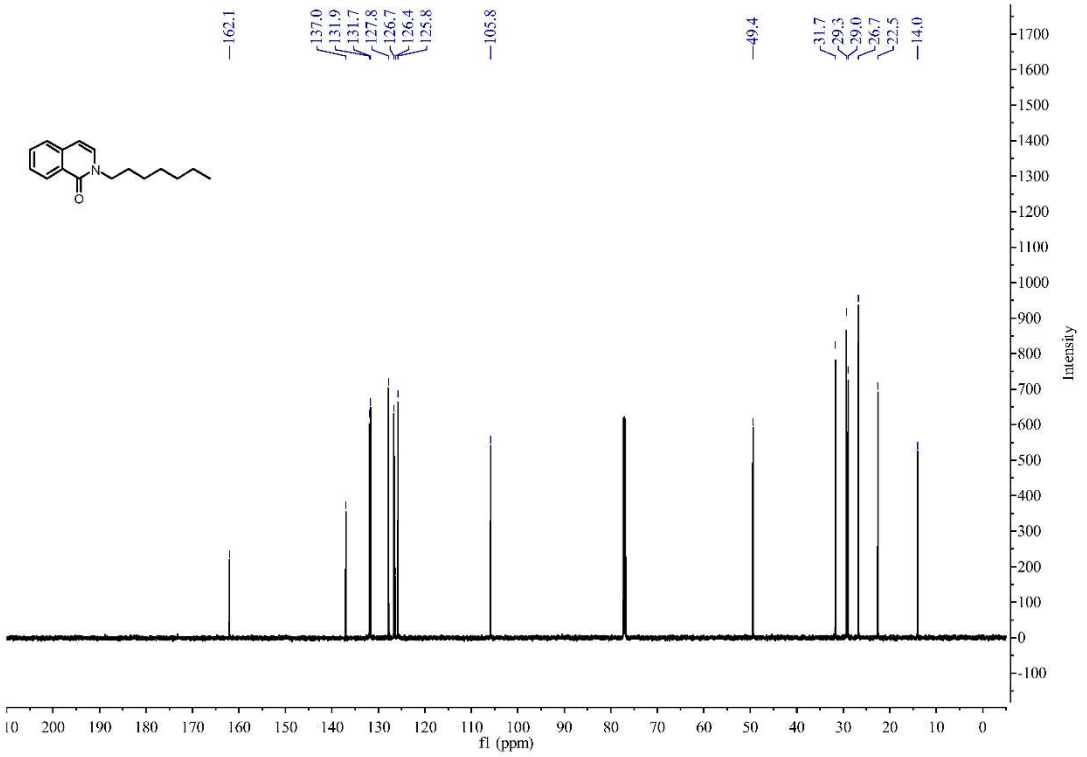

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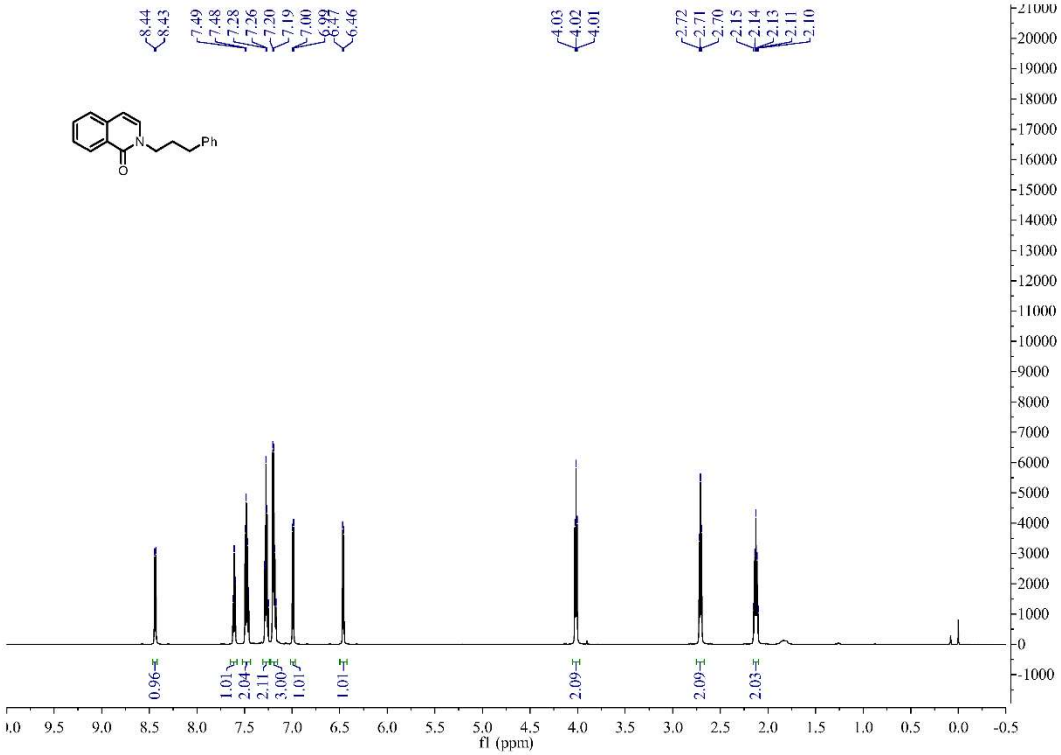

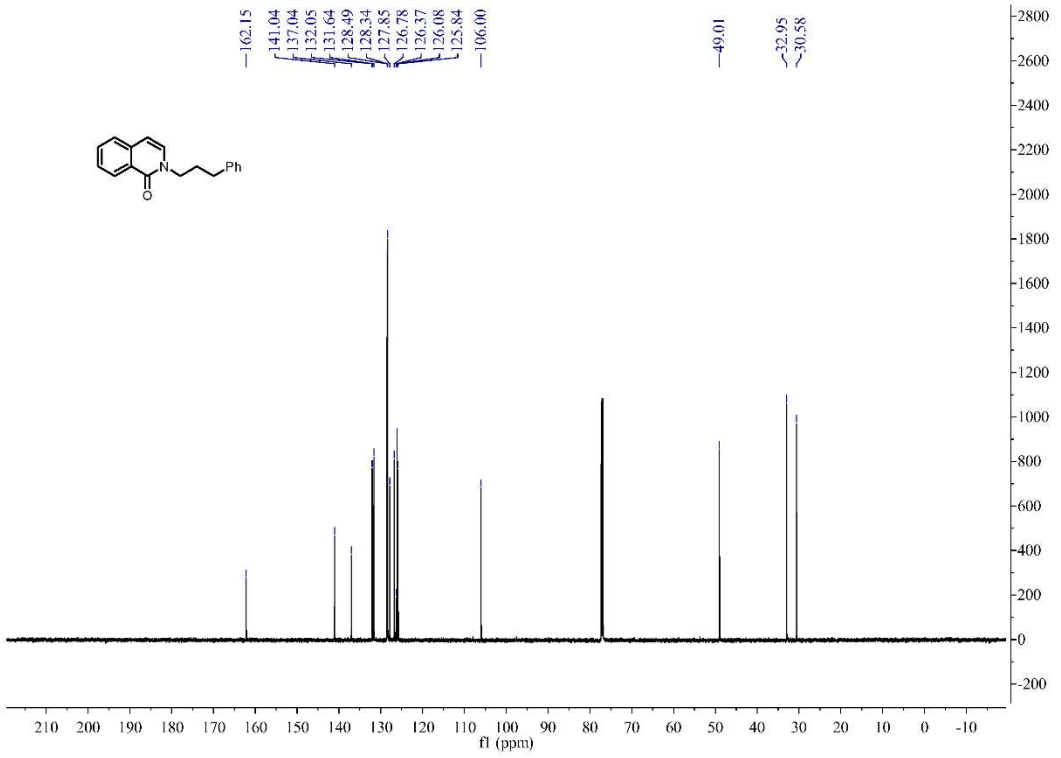

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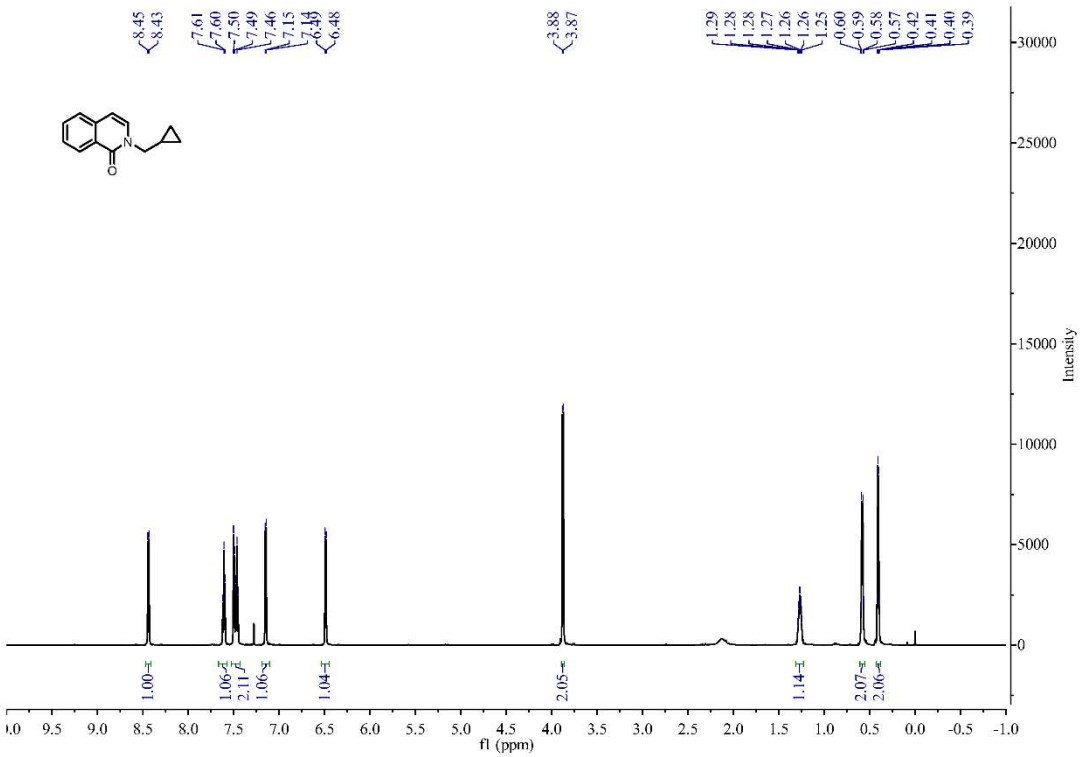
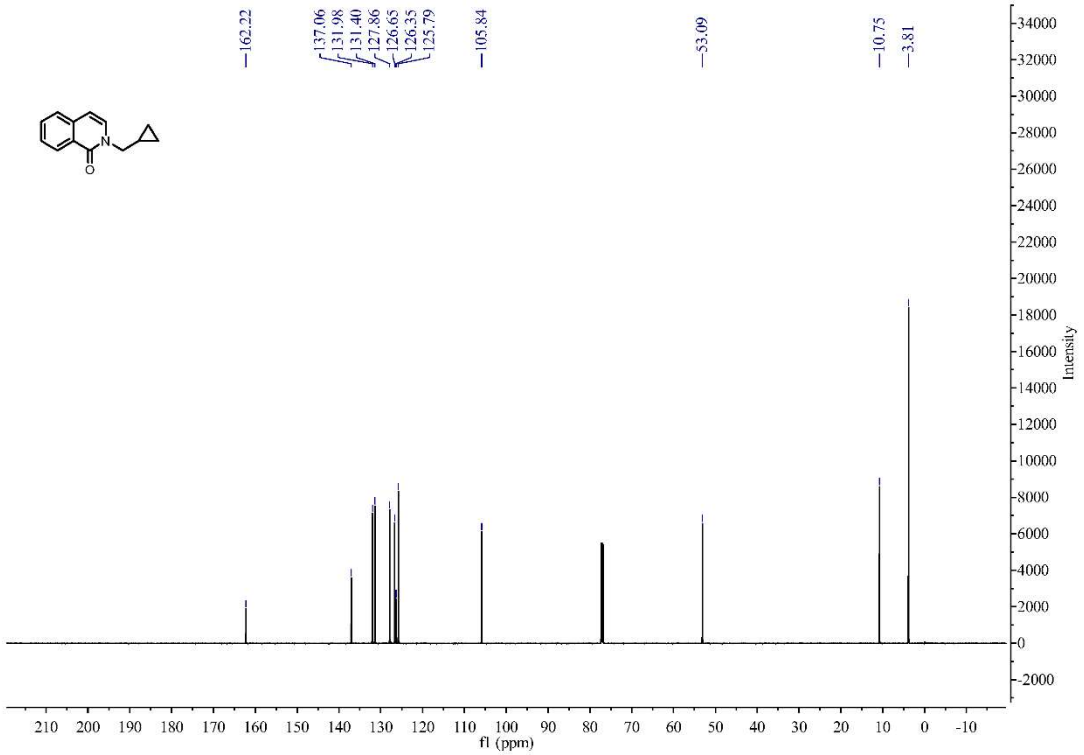
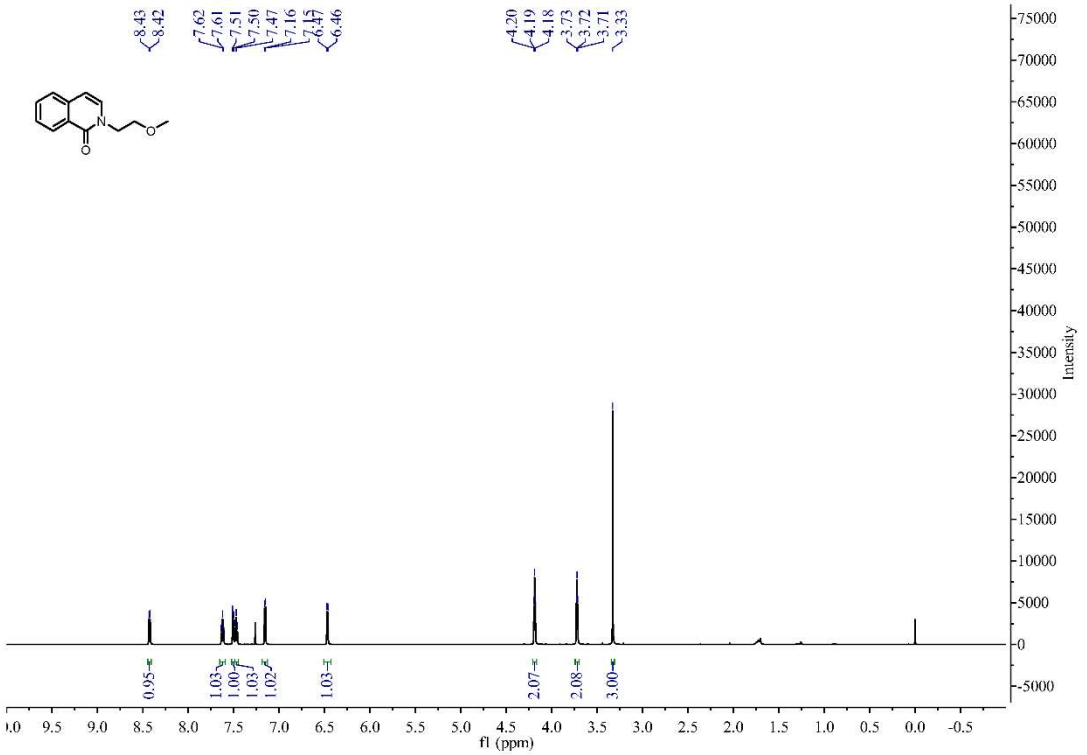
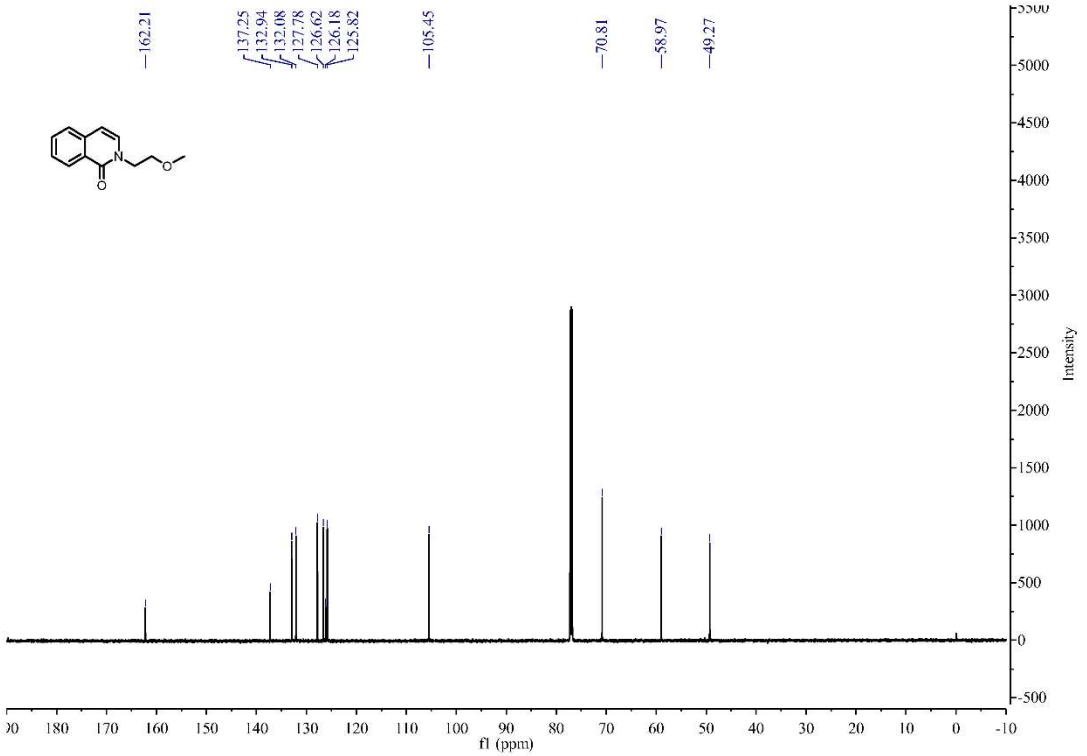




***N*-allylisoquinolin-1(2H)-one (2g)**





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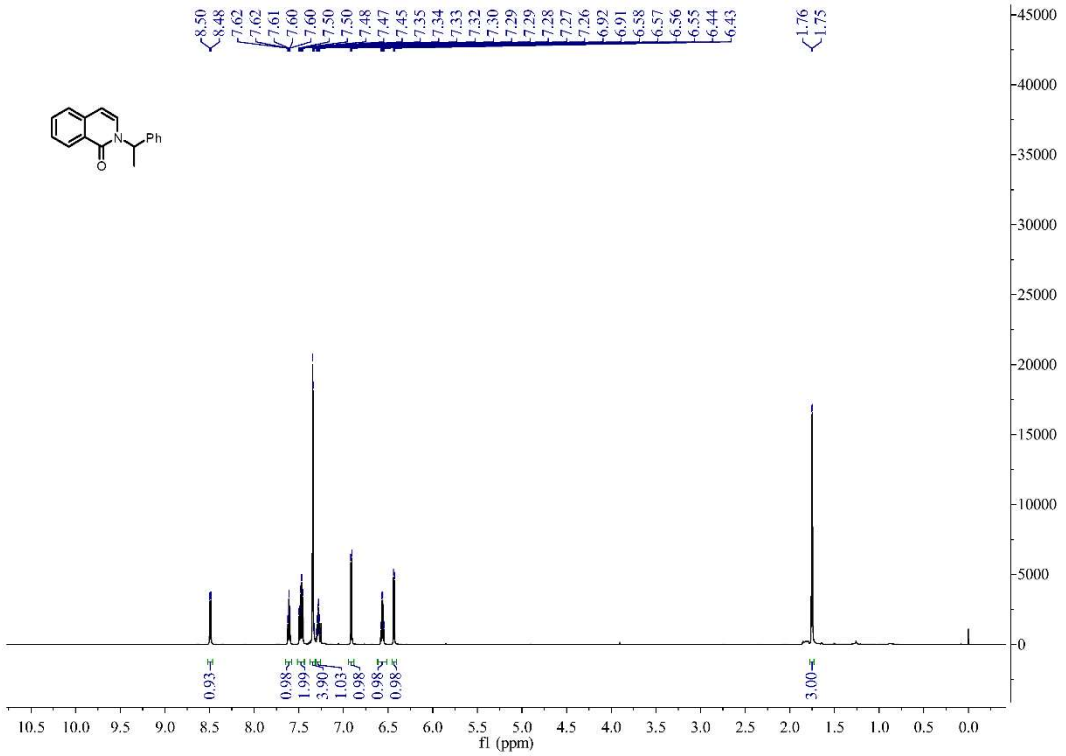

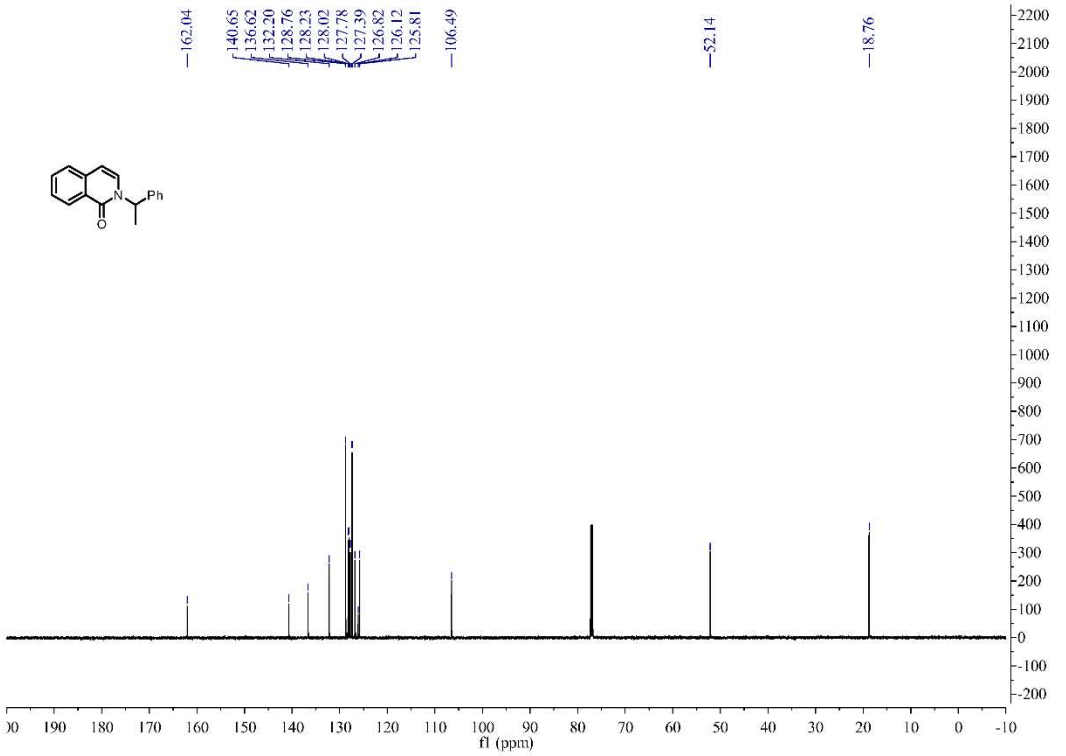

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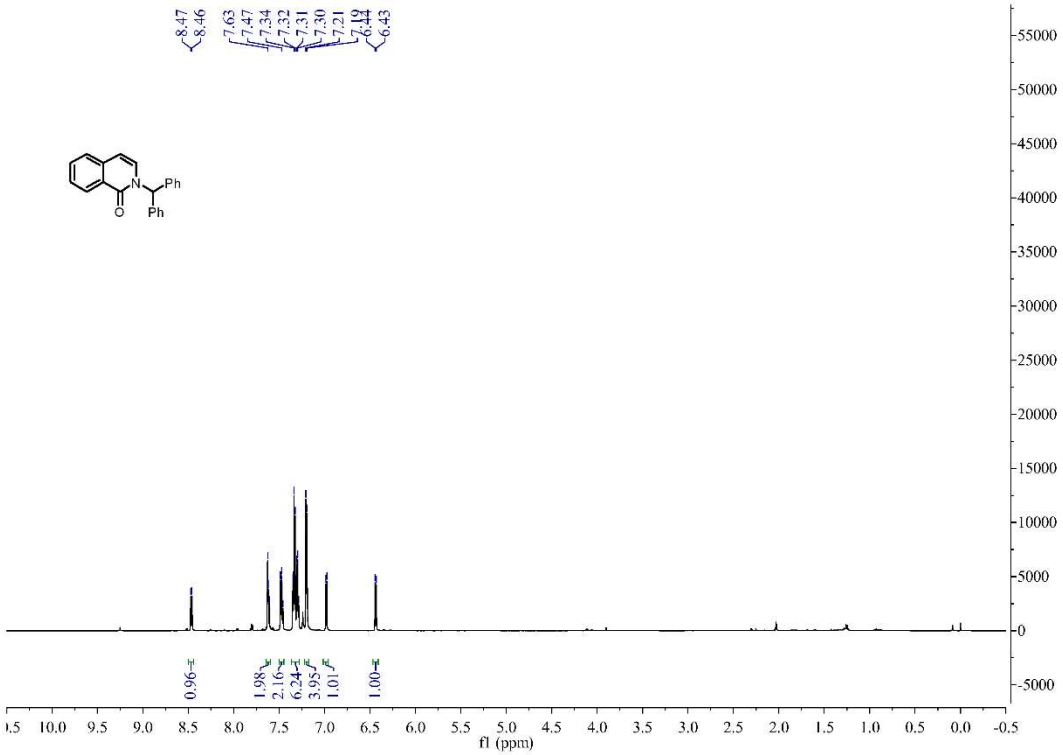

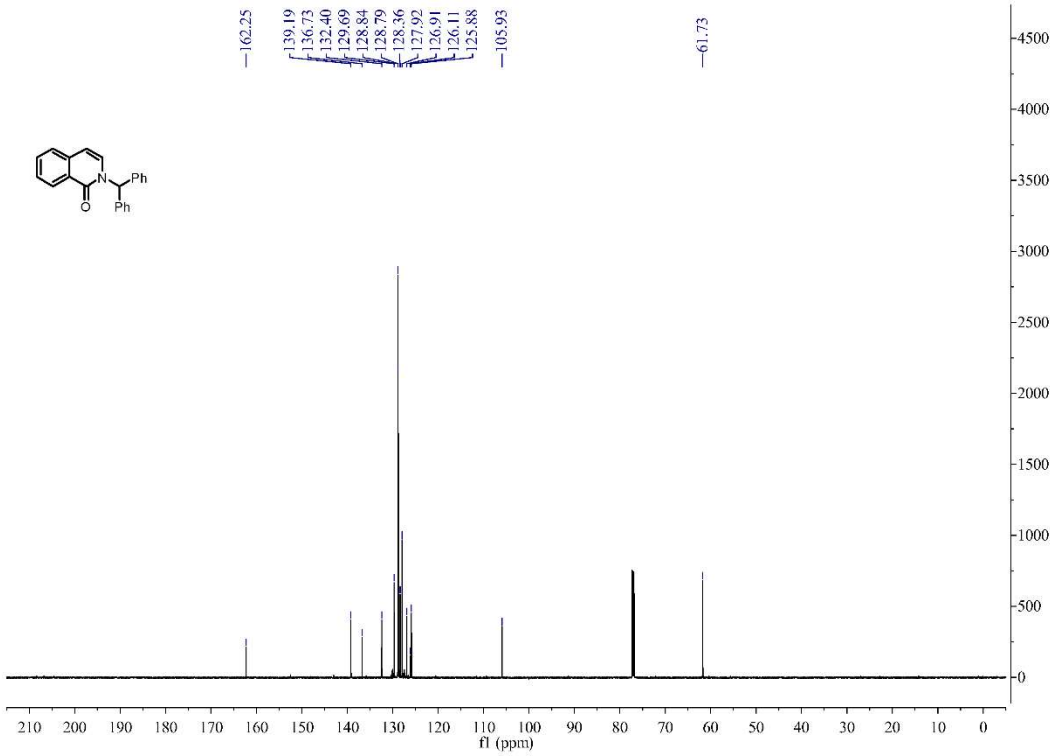

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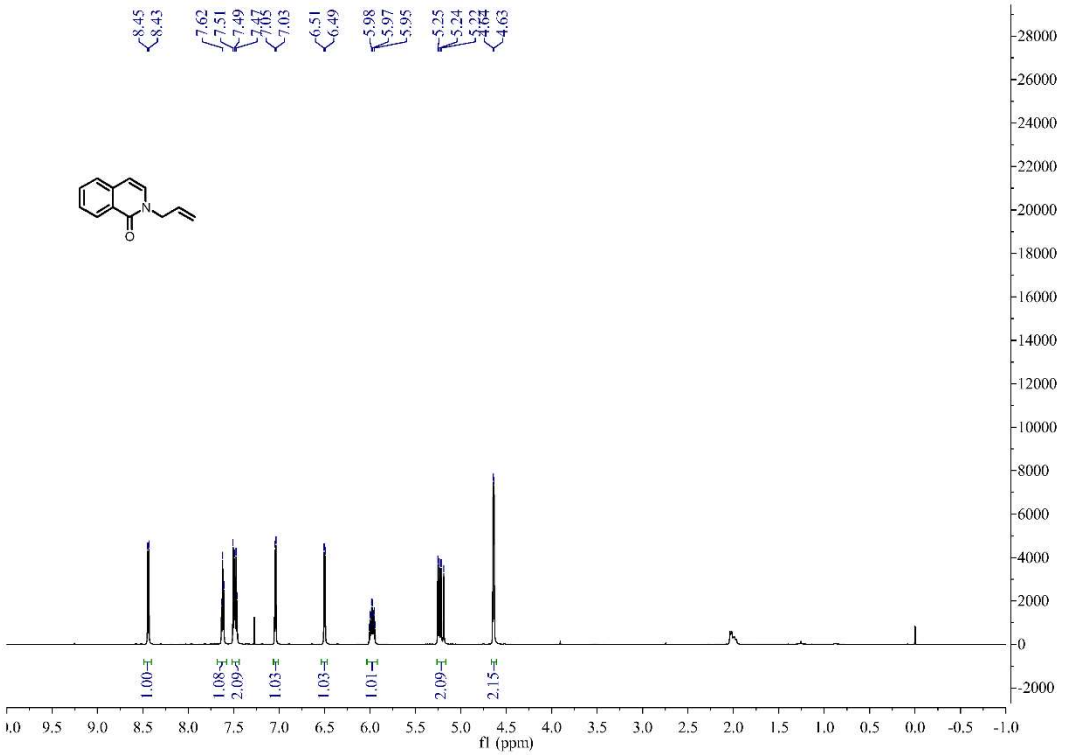
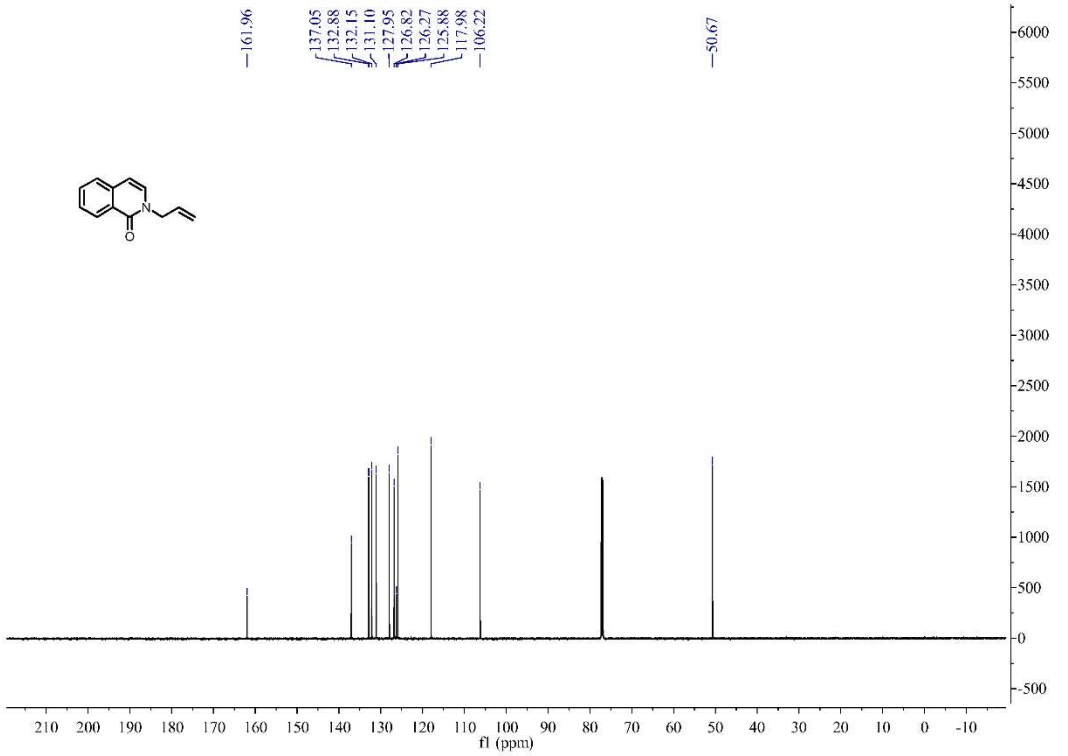
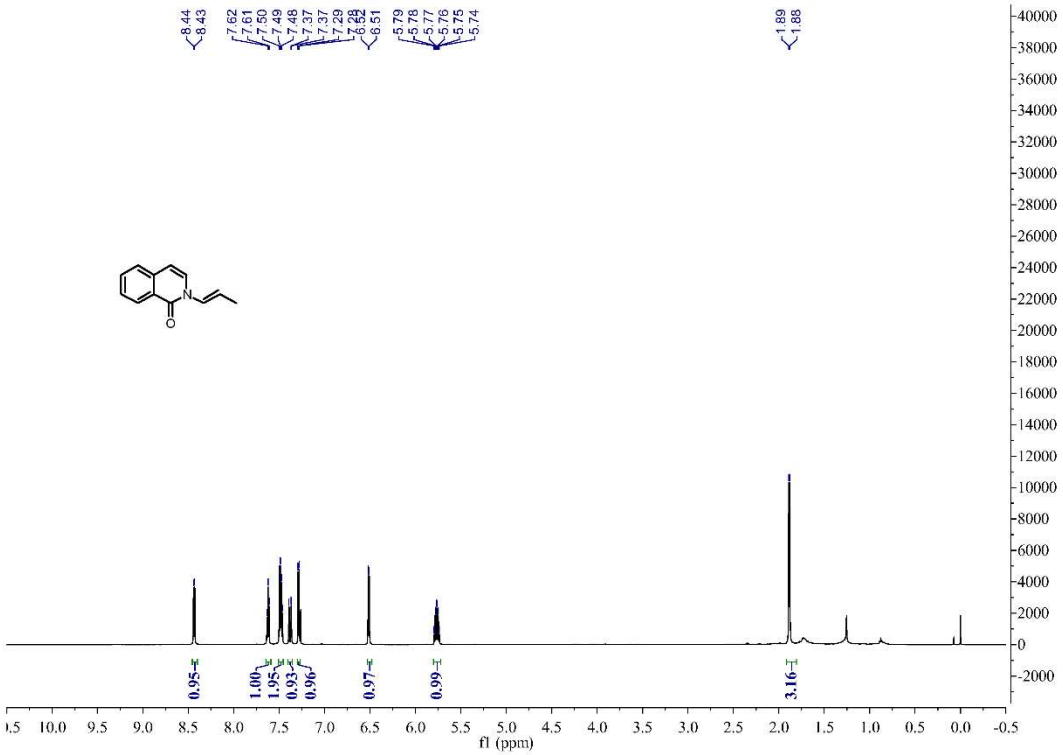
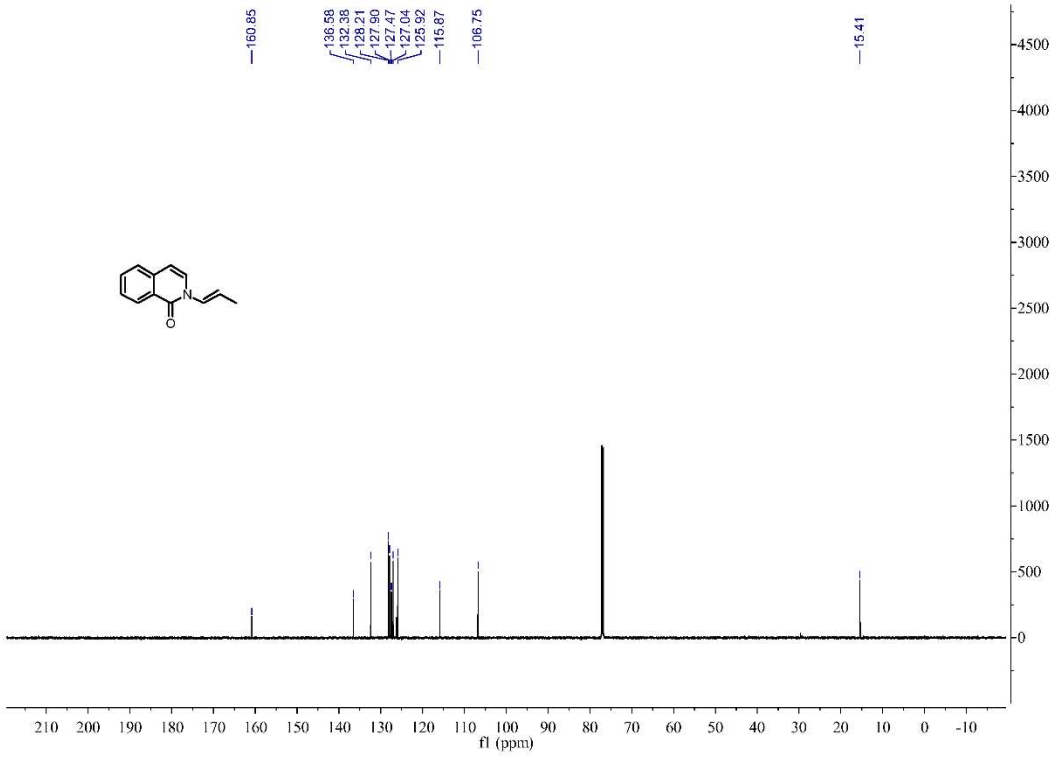




(*E*)-2-(prop-1-en-1-yl)isoquinolin-1(2*H*)-one (*E*)-2j'





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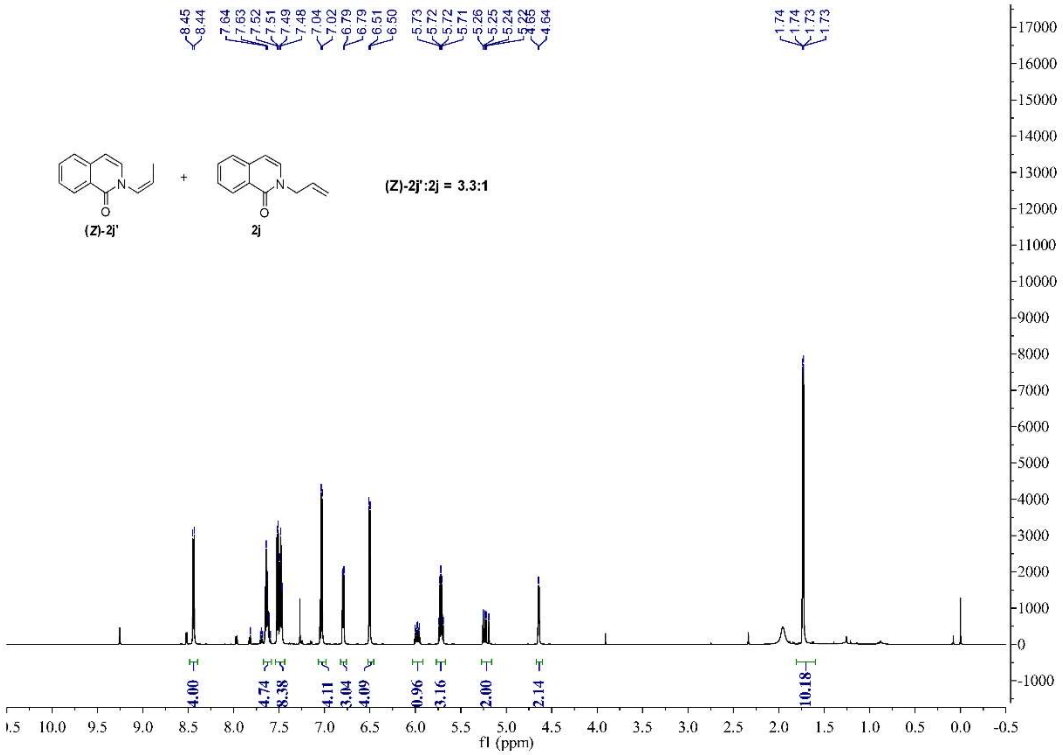
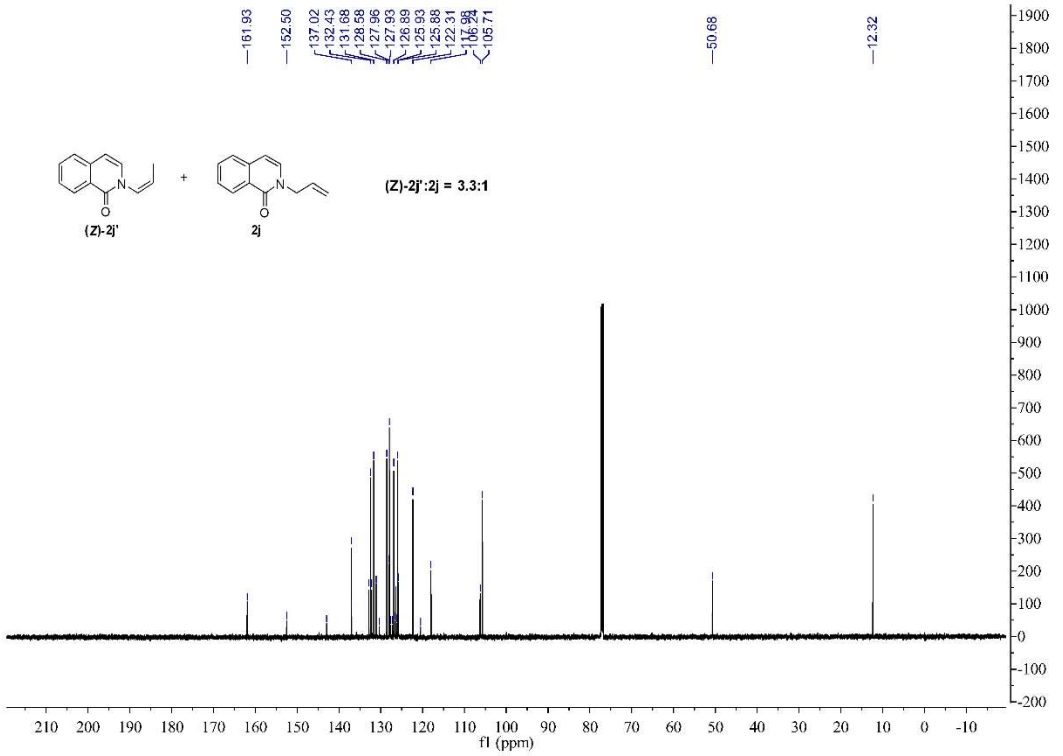
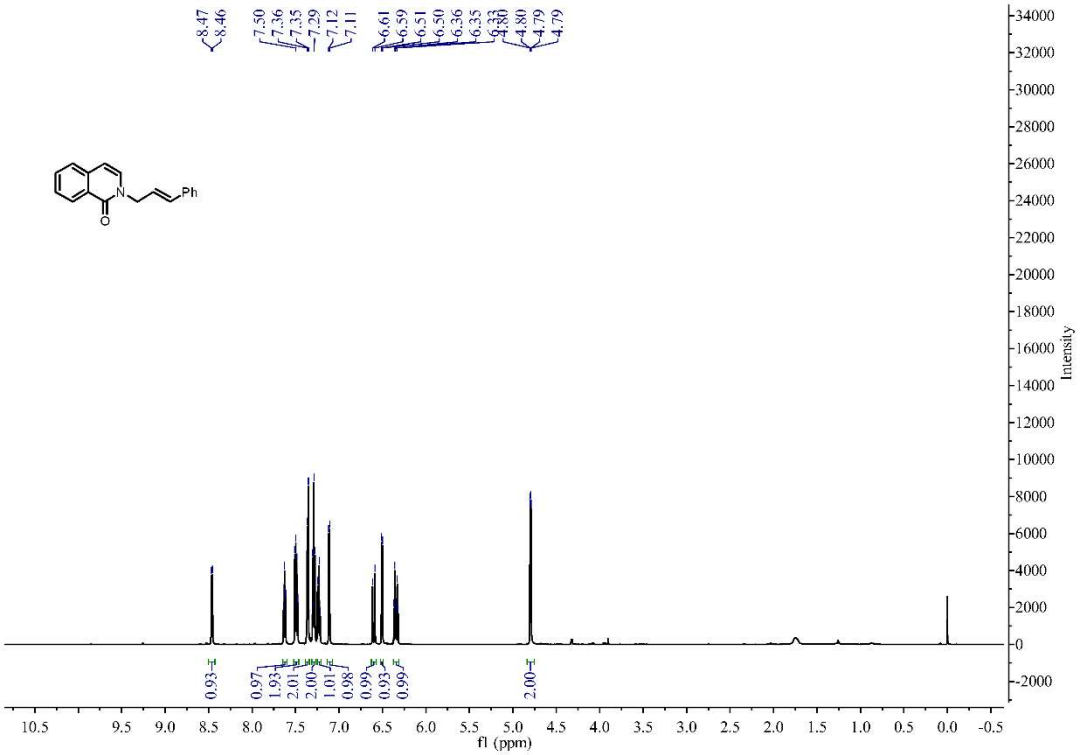
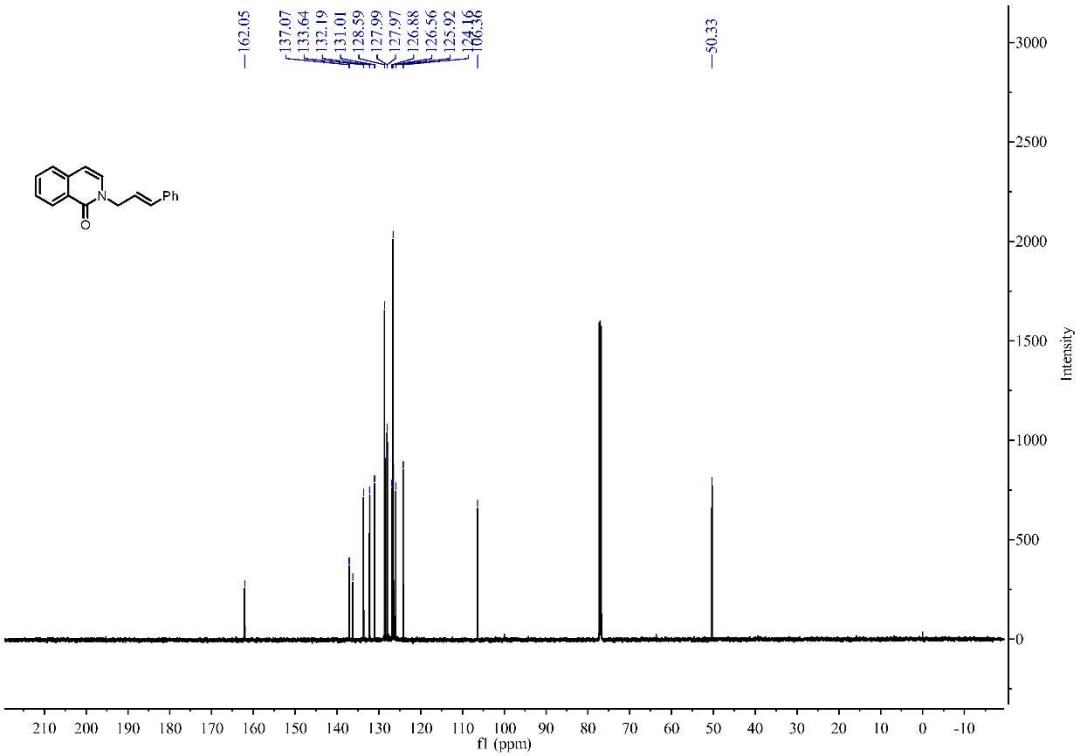


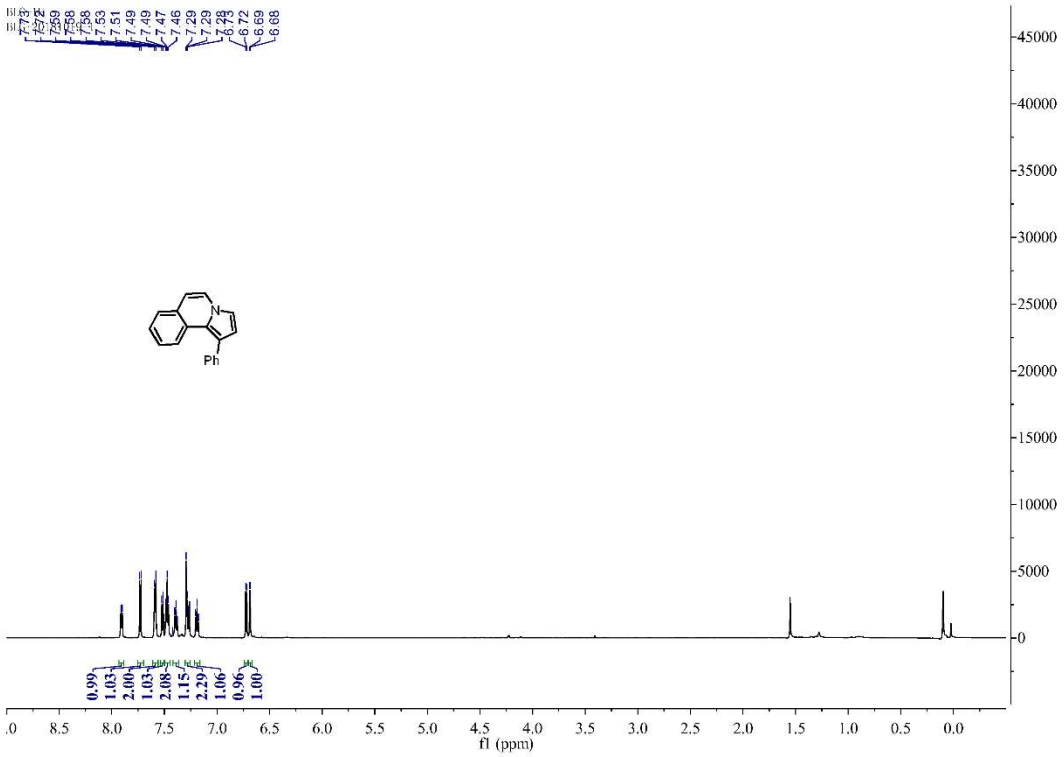


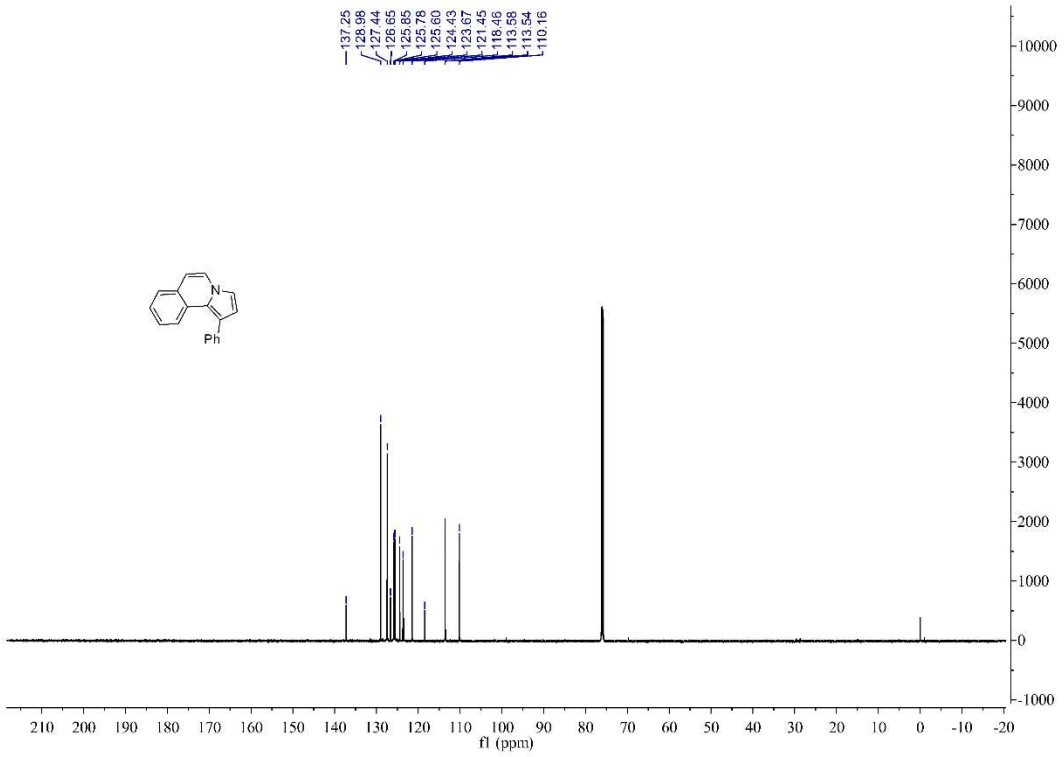
***N*-cinnamylisoquinolin-1(*2H*)-one (2k)**



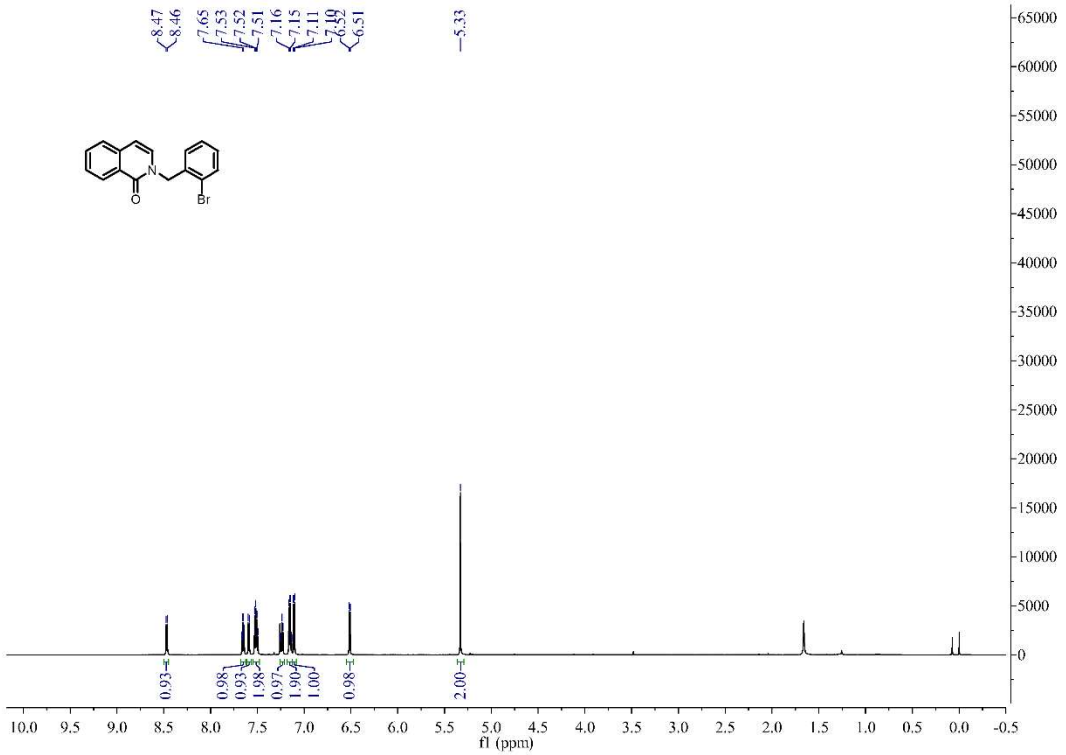


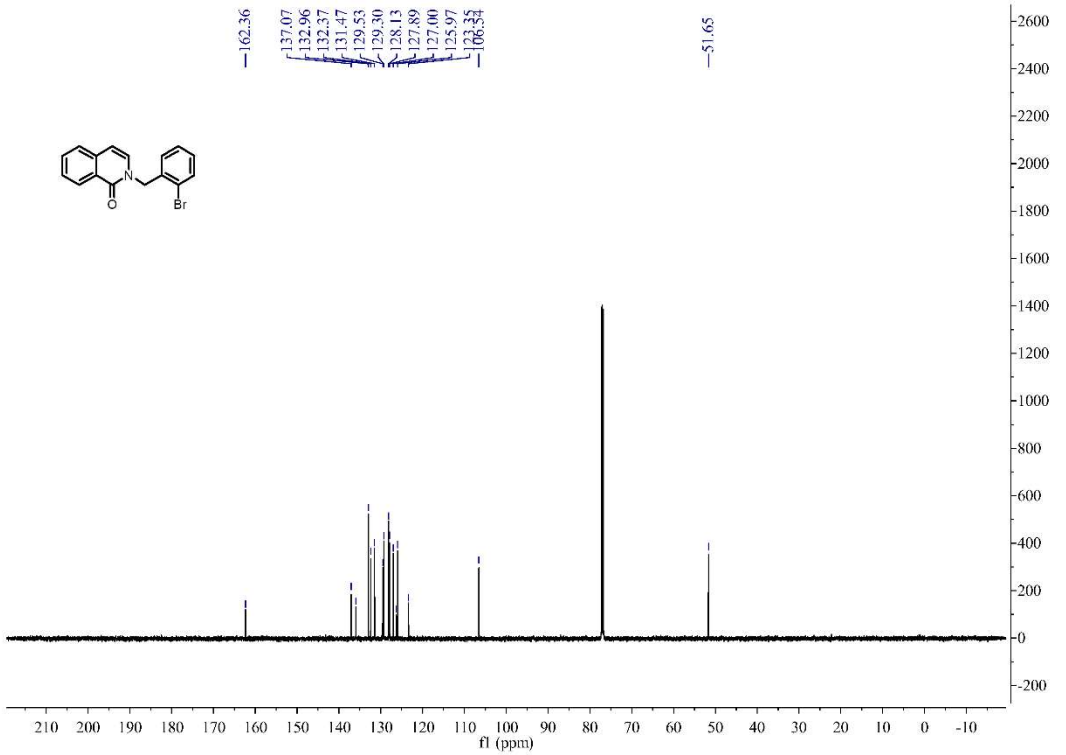
1-phenylpyrrolo[2,1-a]isoquinoline (2k')



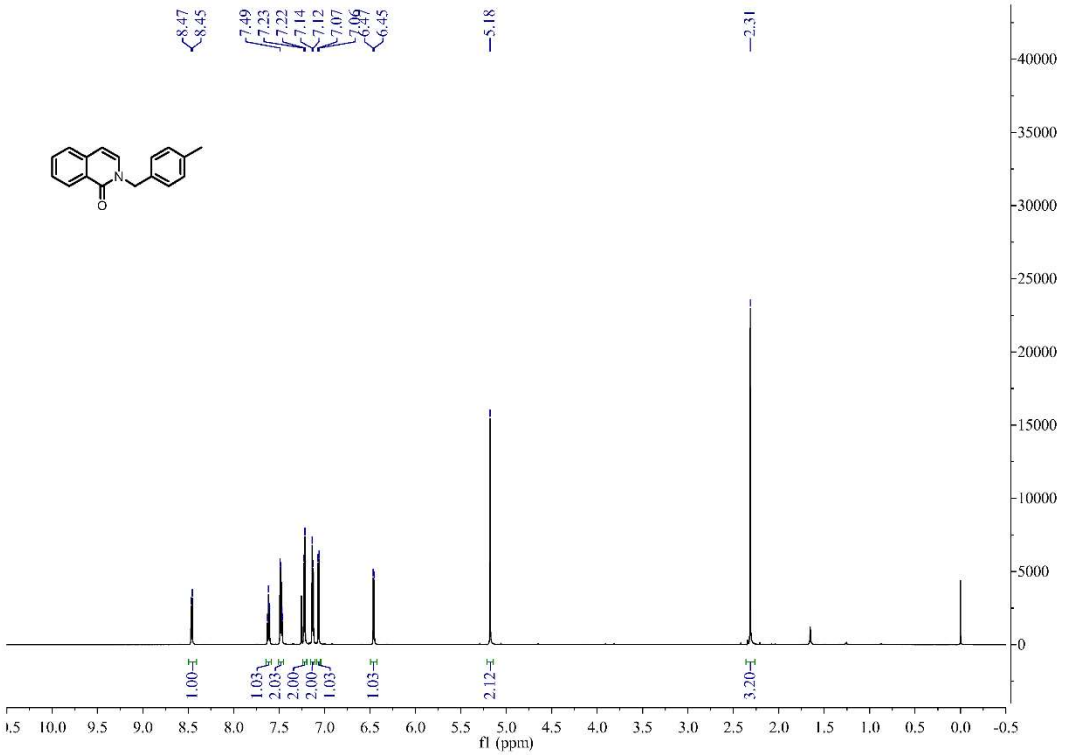


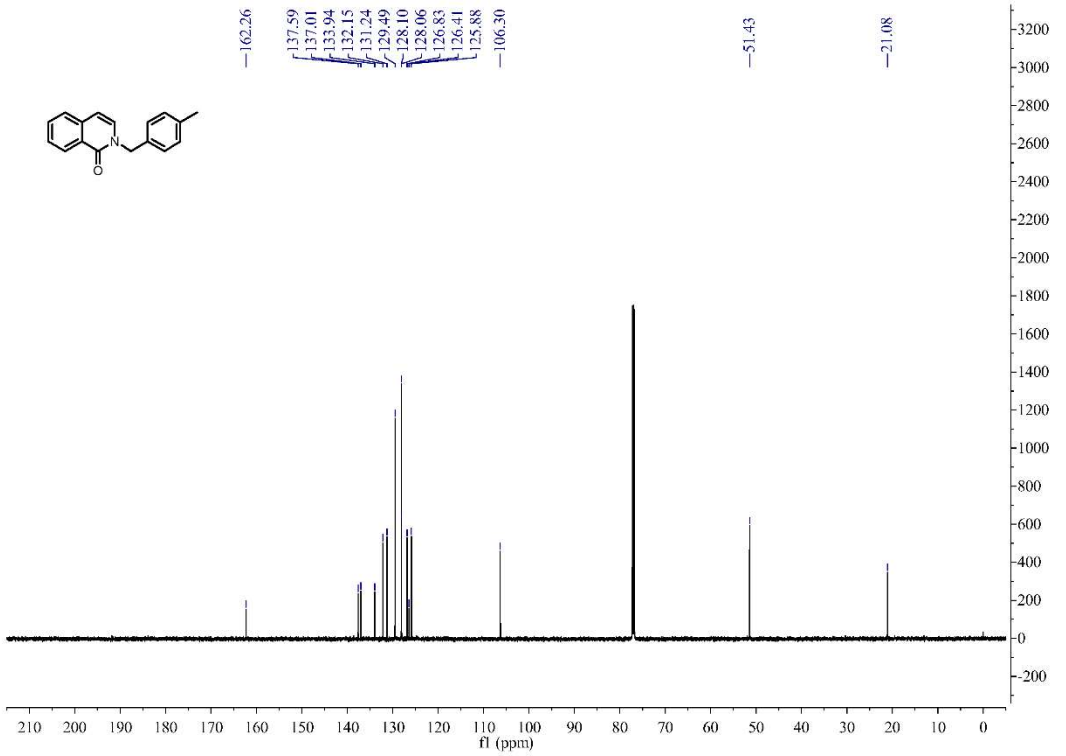
***N*-(2-bromobenzyl) isoquinolin-1(*2H*)-one (2l)**



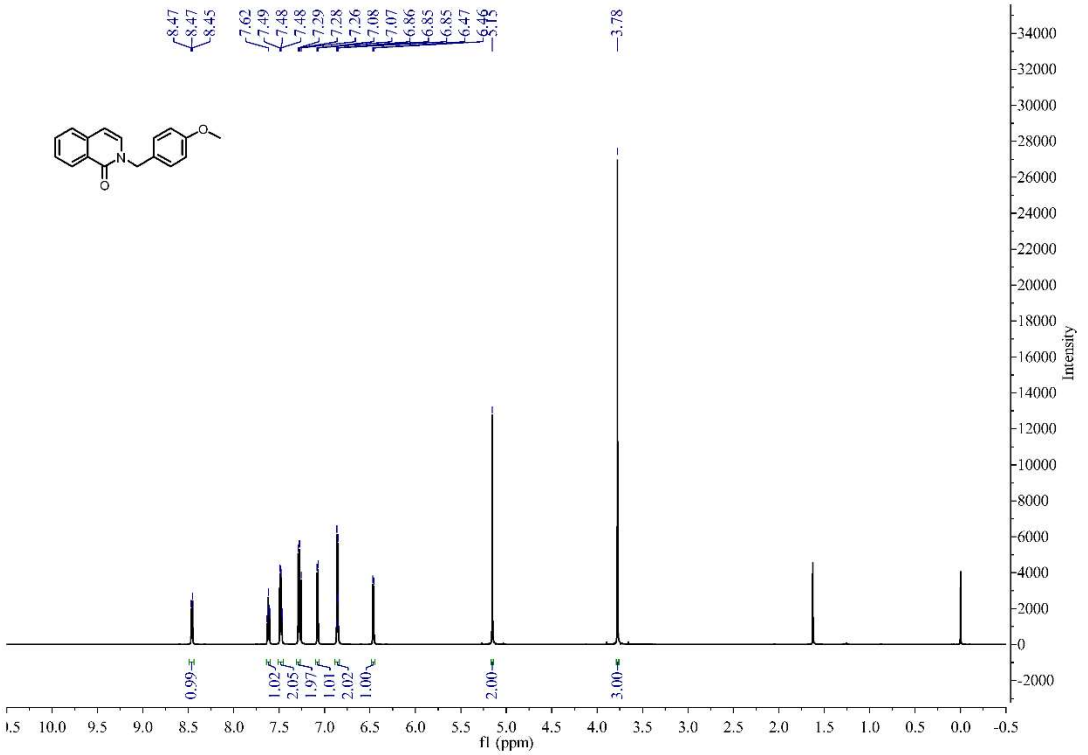


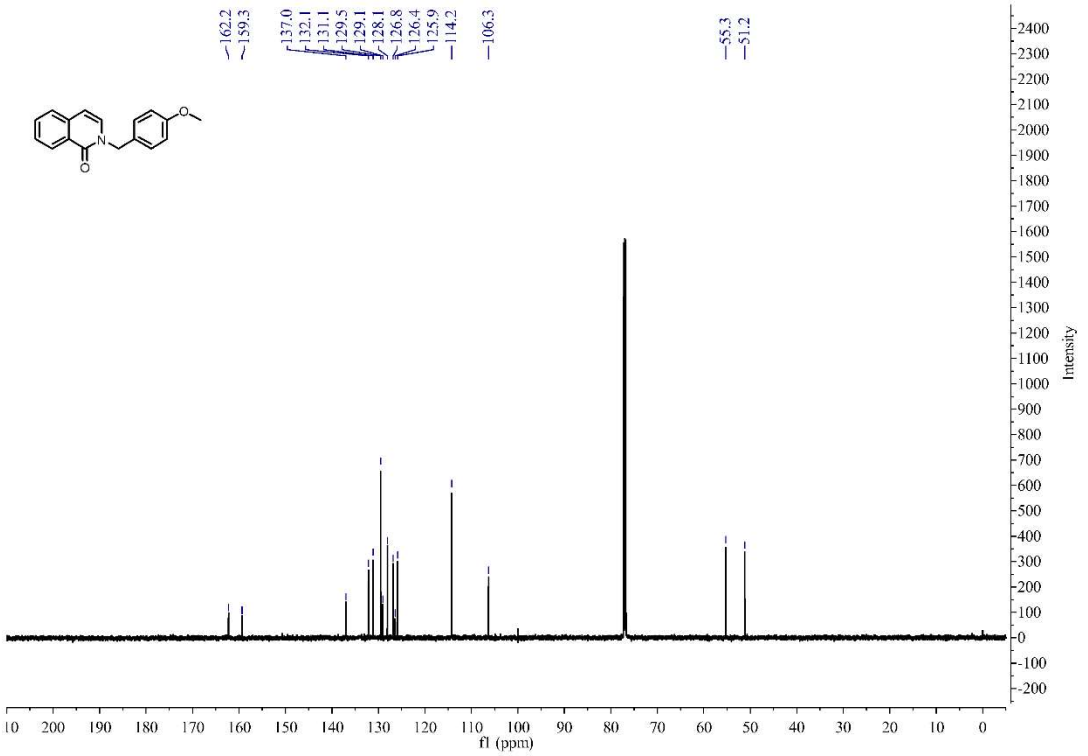
***N*-(4-methylbenzyl) isoquinolin-1(2H)-one (2m)**



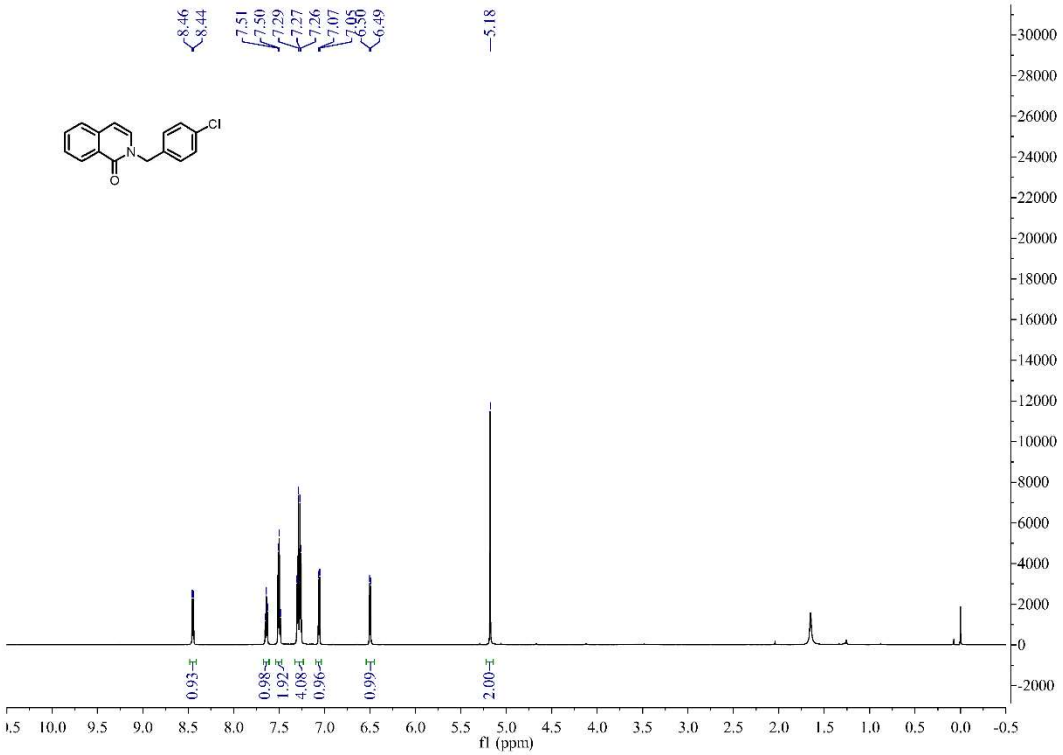


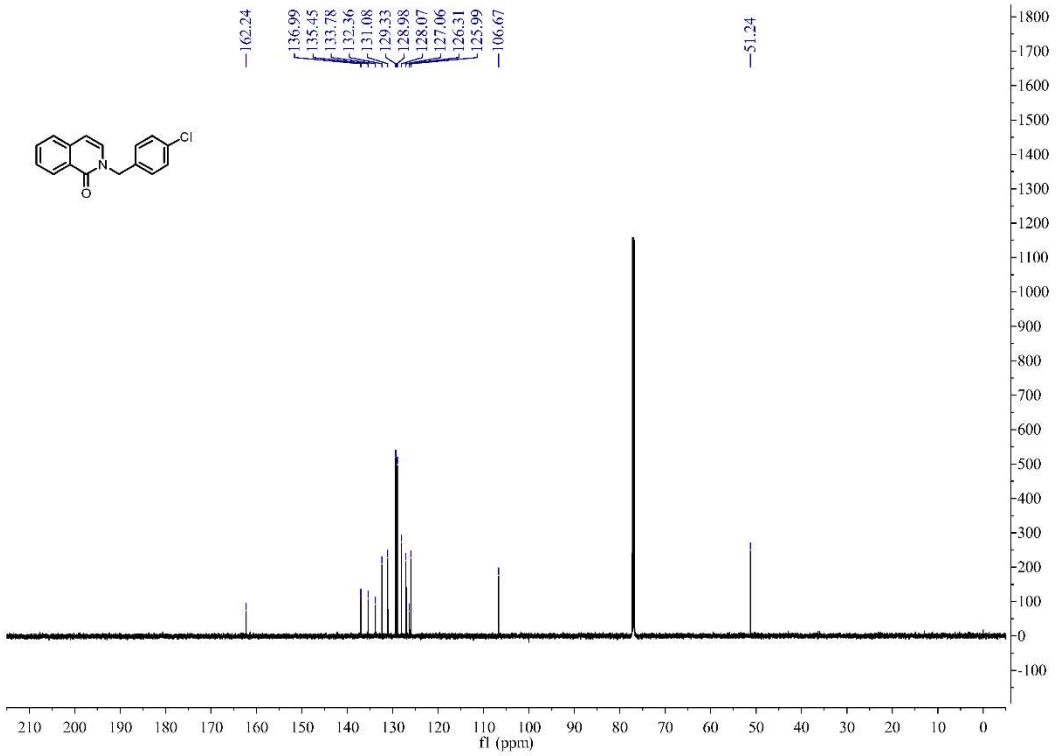
_N_-(4-methoxybenzyl) isoquinolin-1(_2H_)-one (2n)



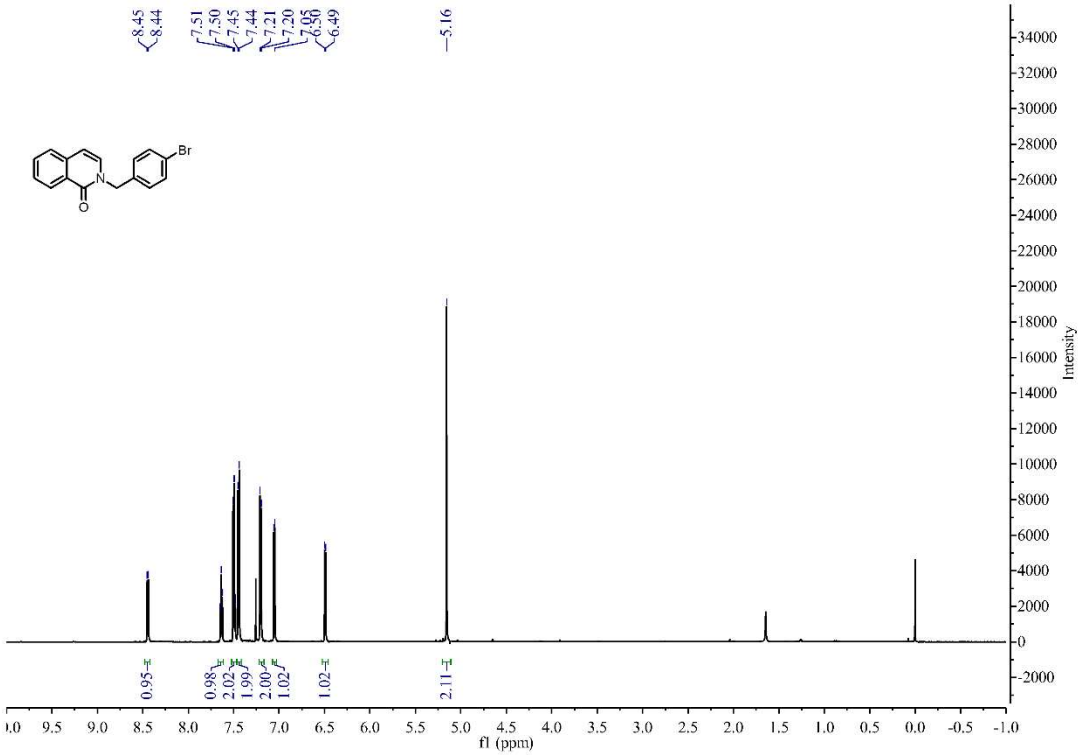


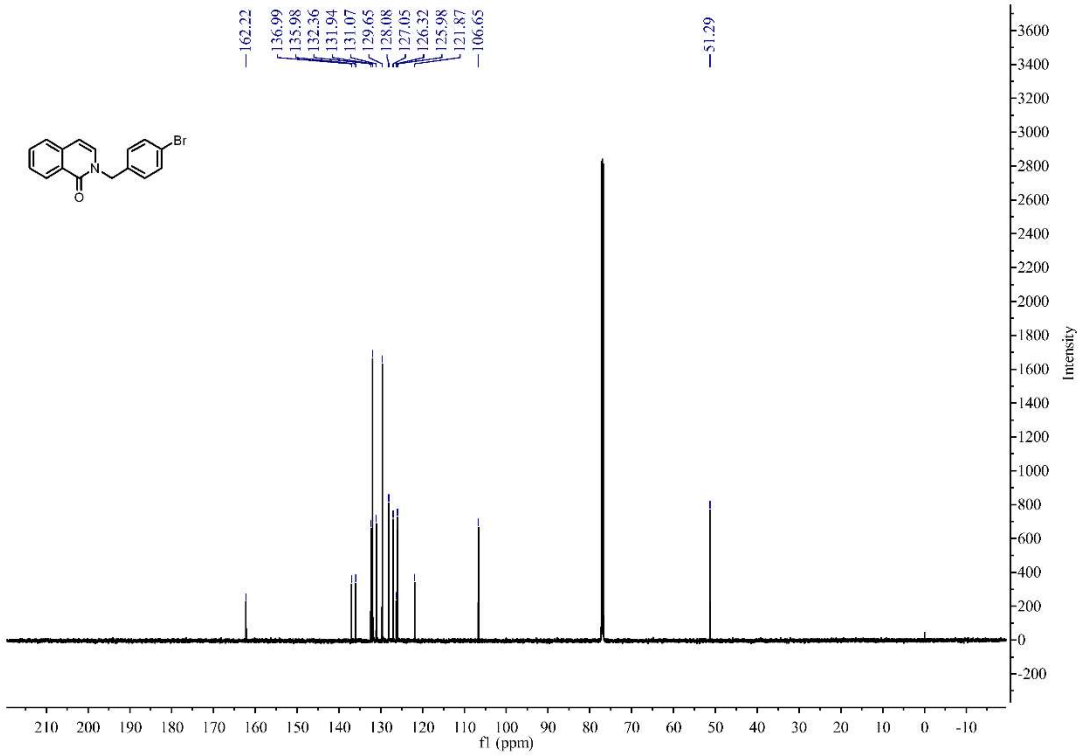
***N*-(4-chlorobenzyl) isoquinolin-1(*2H*)-one (2o)**



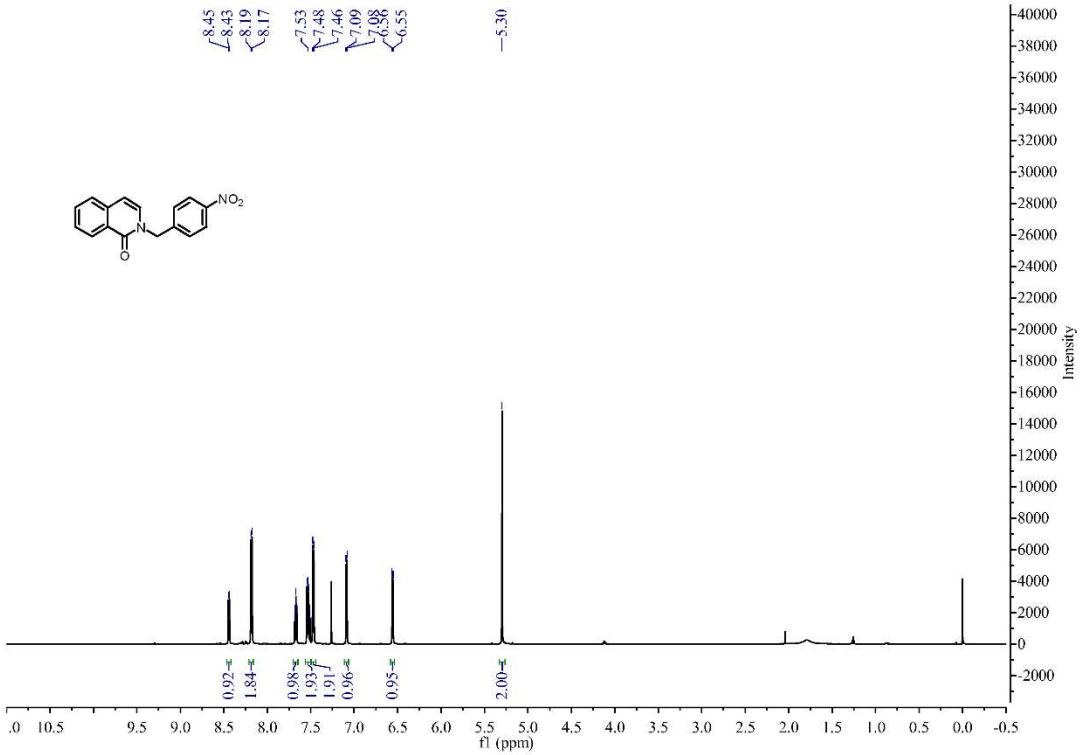


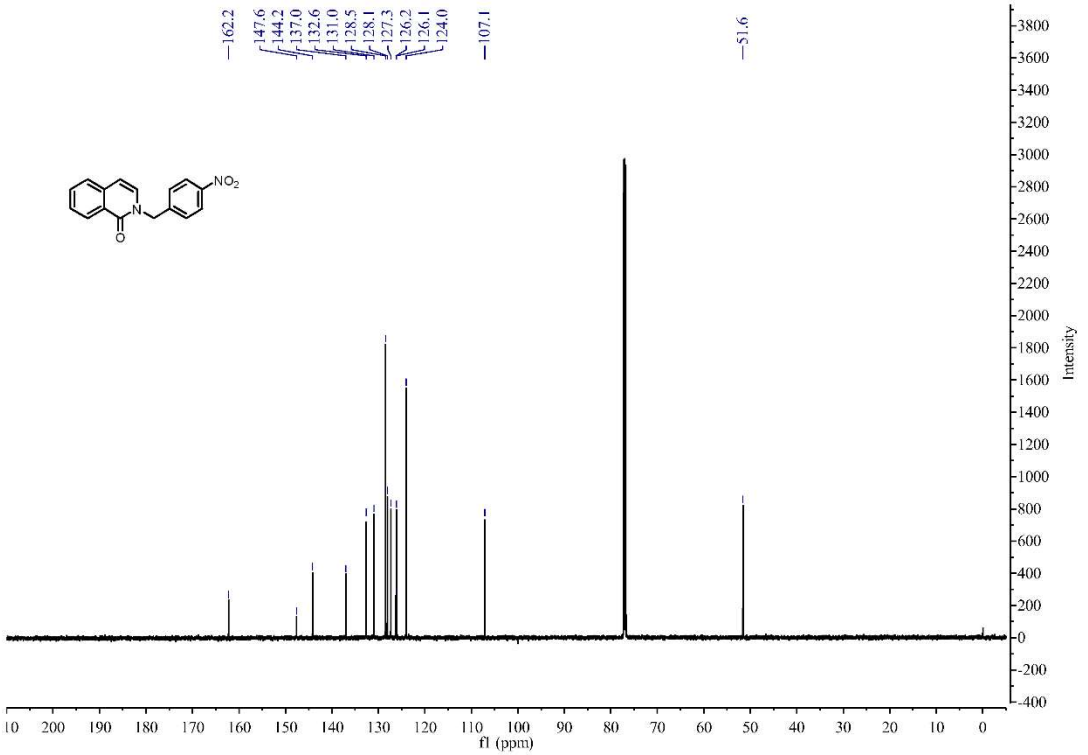
***N*-(4-bromobenzyl) isoquinolin-1(*2H*)-one (2p)**



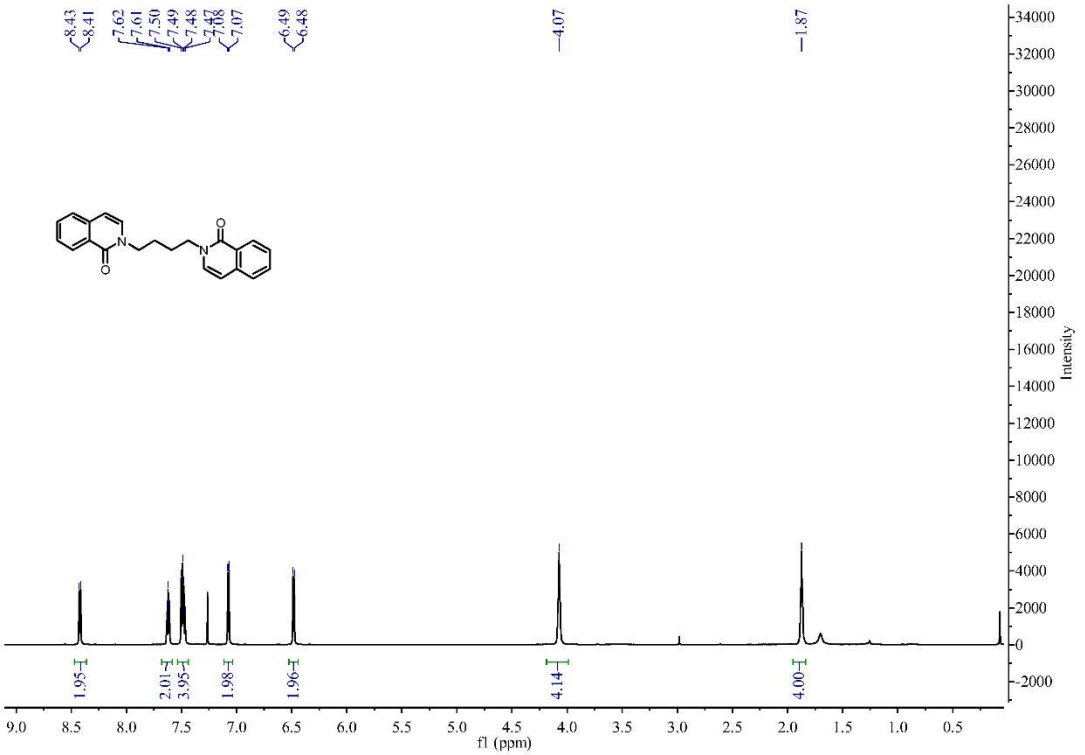


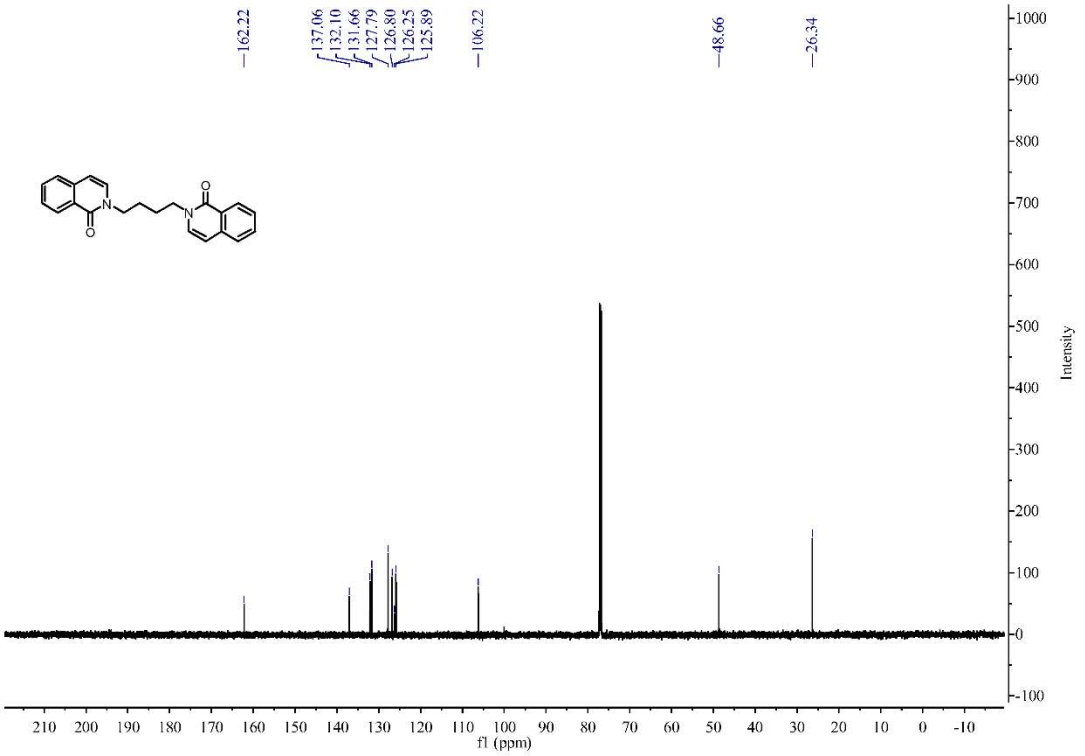
***N*-(4-nitrobenzyl) isoquinolin-1(*2H*)-one (2q)**



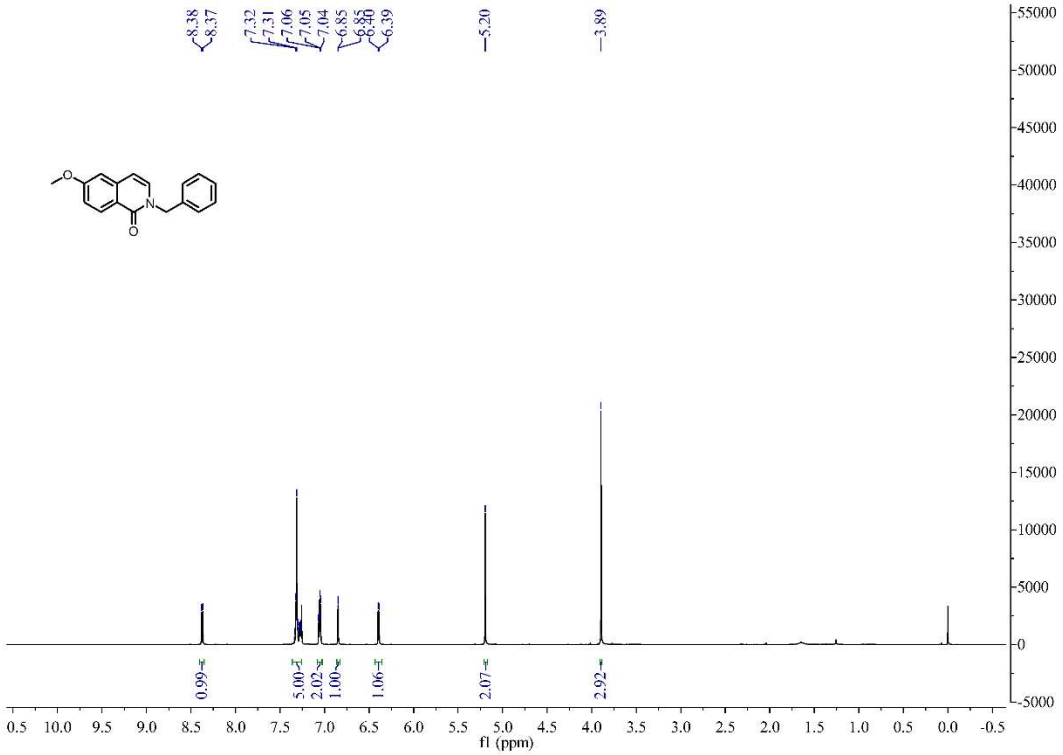


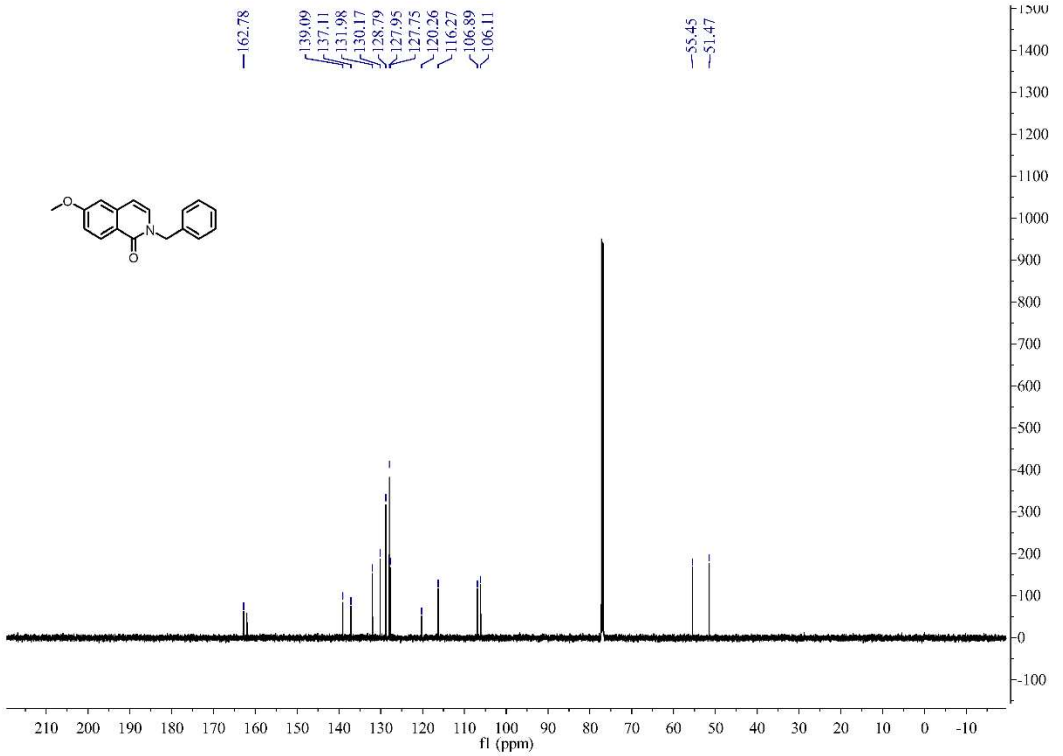
2,2'-(butane-1,4-diyl)bis(isoquinolin-1(2H)-one) (2r)



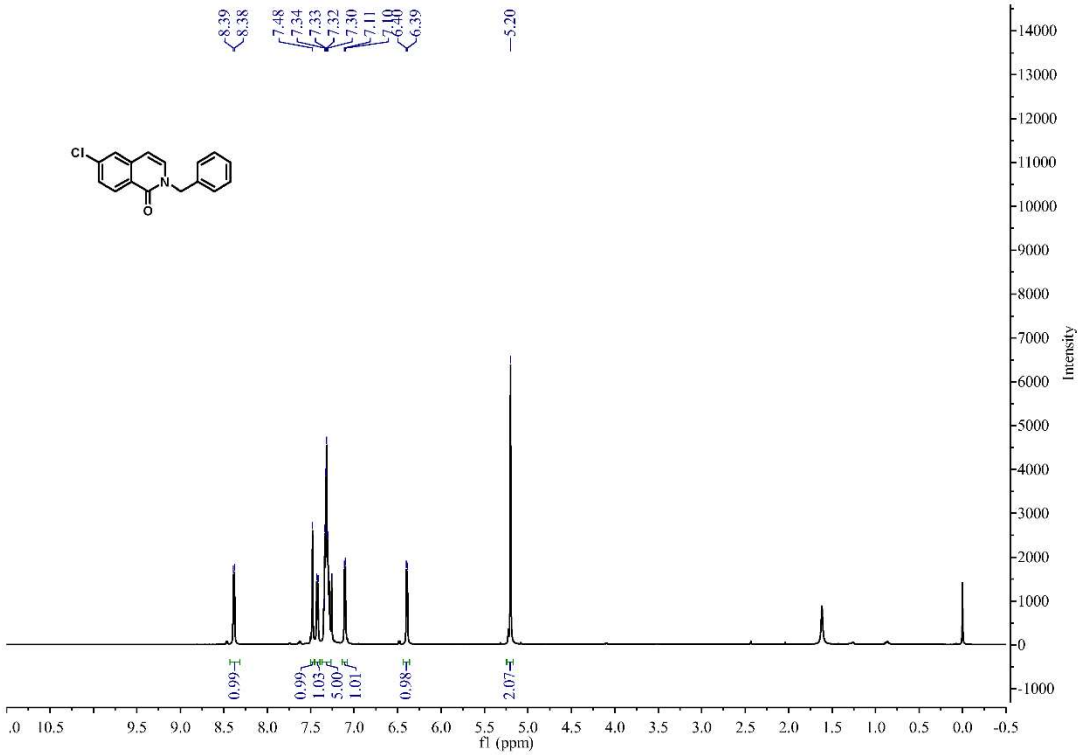


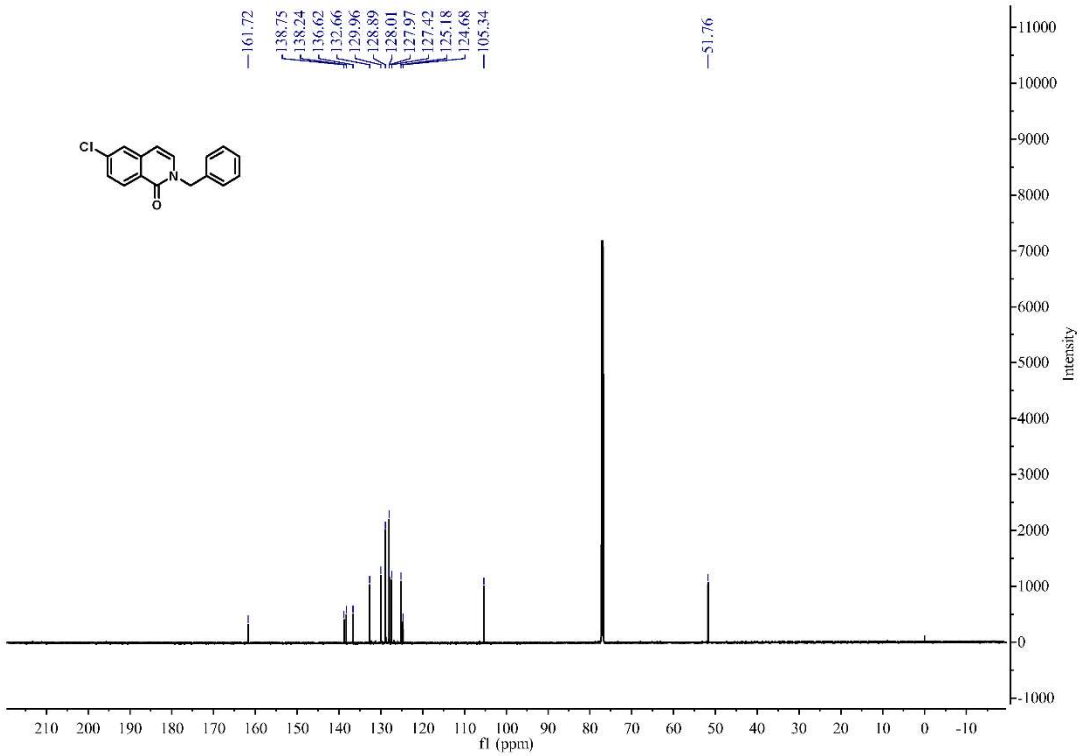
***N*-benzyl-6-methoxyisoquinolin-1(2H)-one (2s)**



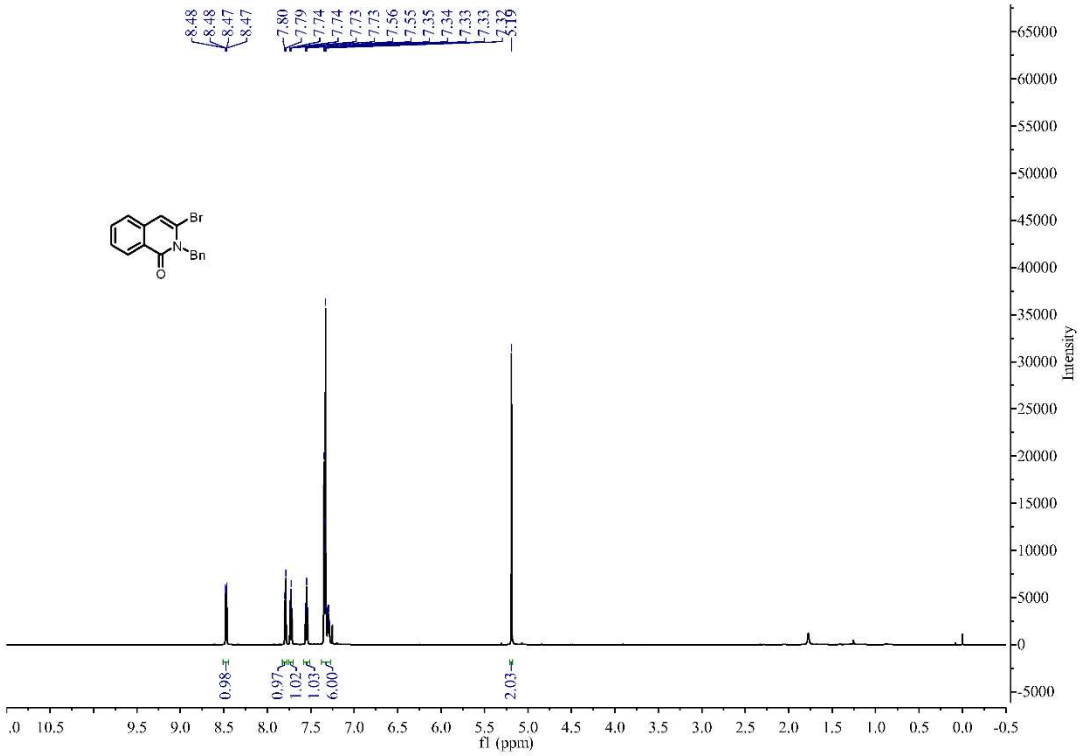


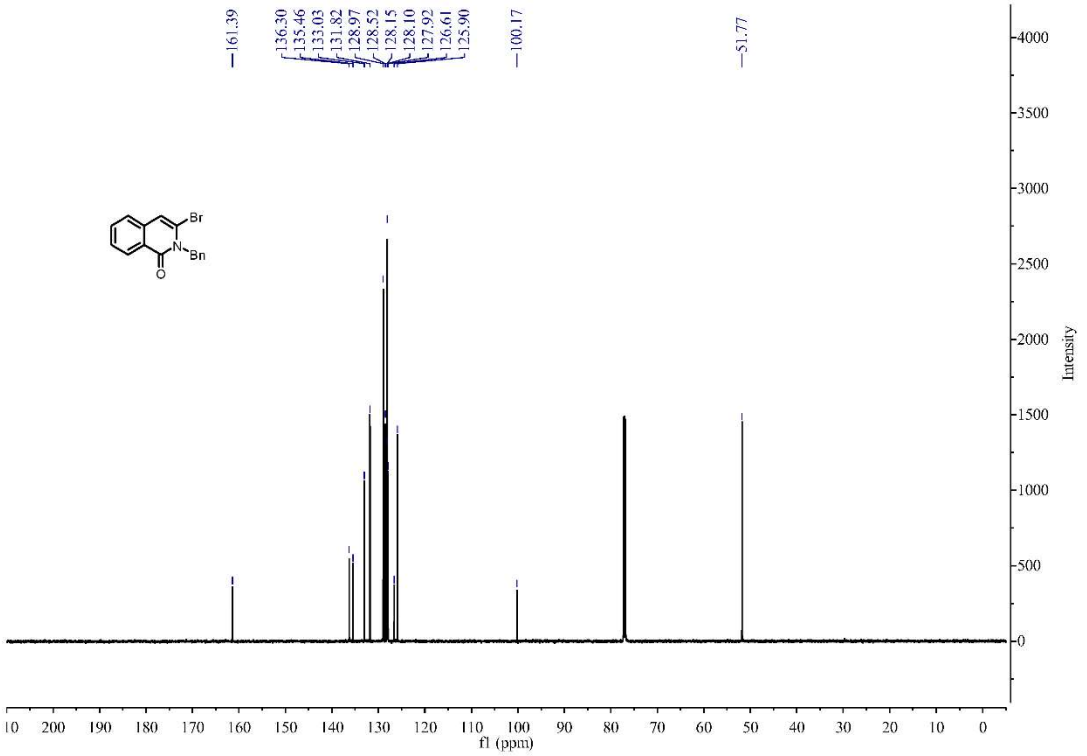
***N*-benzyl-6-chloroisoquinolin-1(*2H*)-one (2t)**



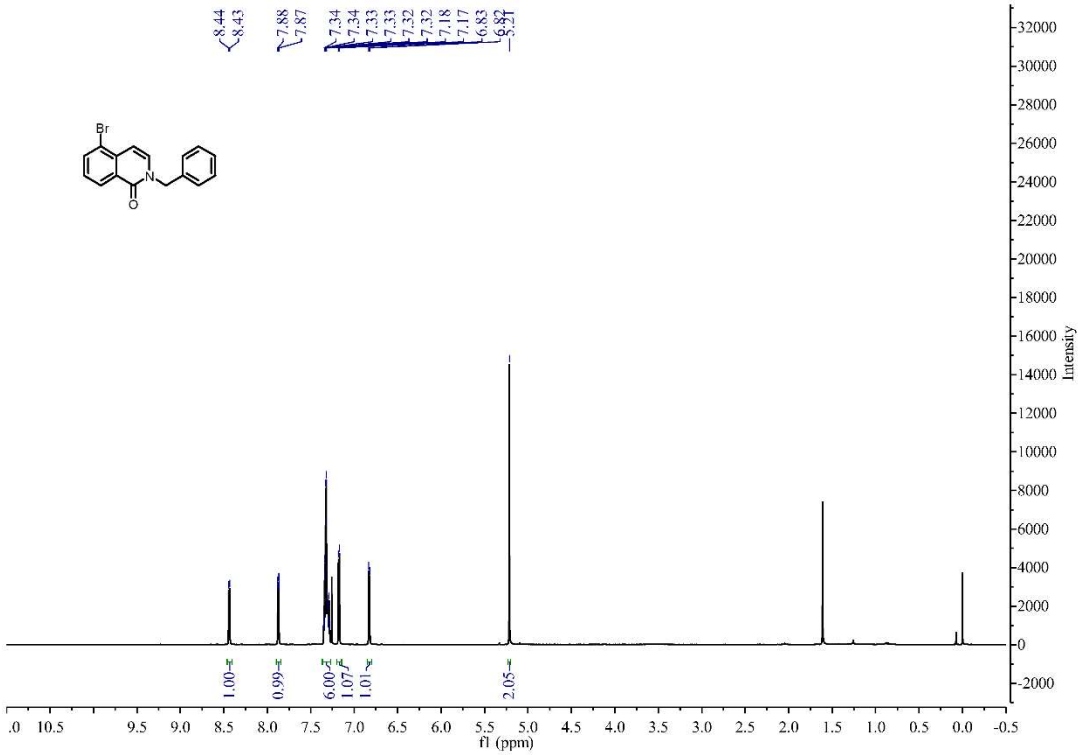


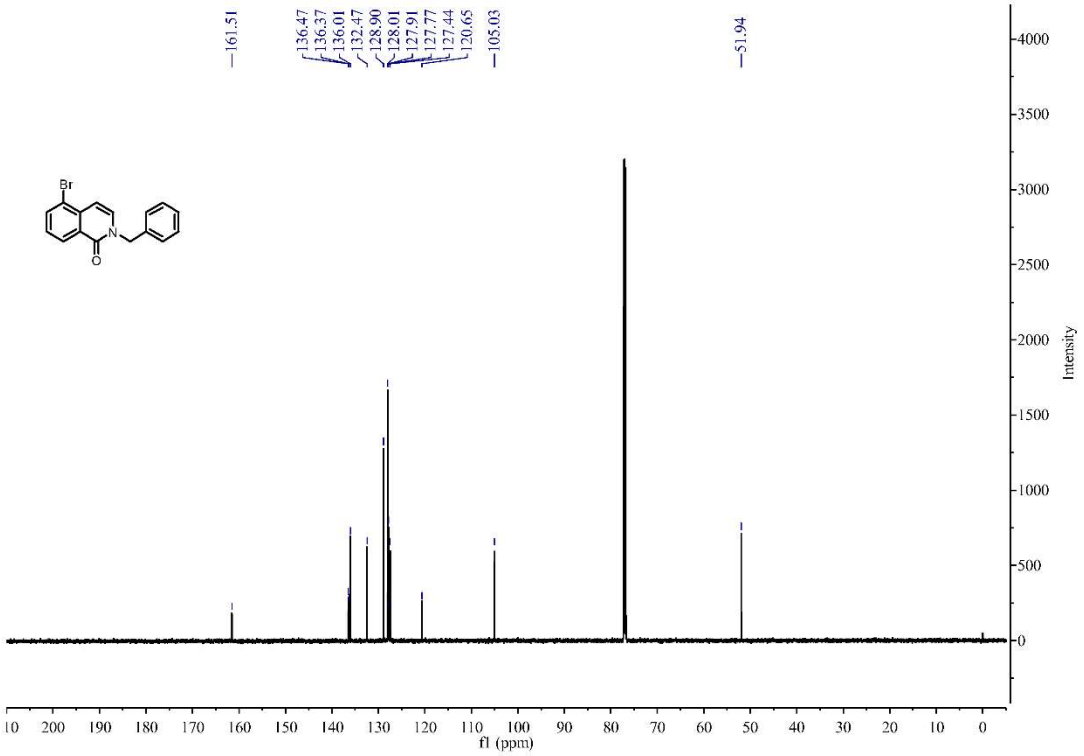
***N*-benzyl-3-bromoisoquinolin-1(*2H*)-one (2u)**



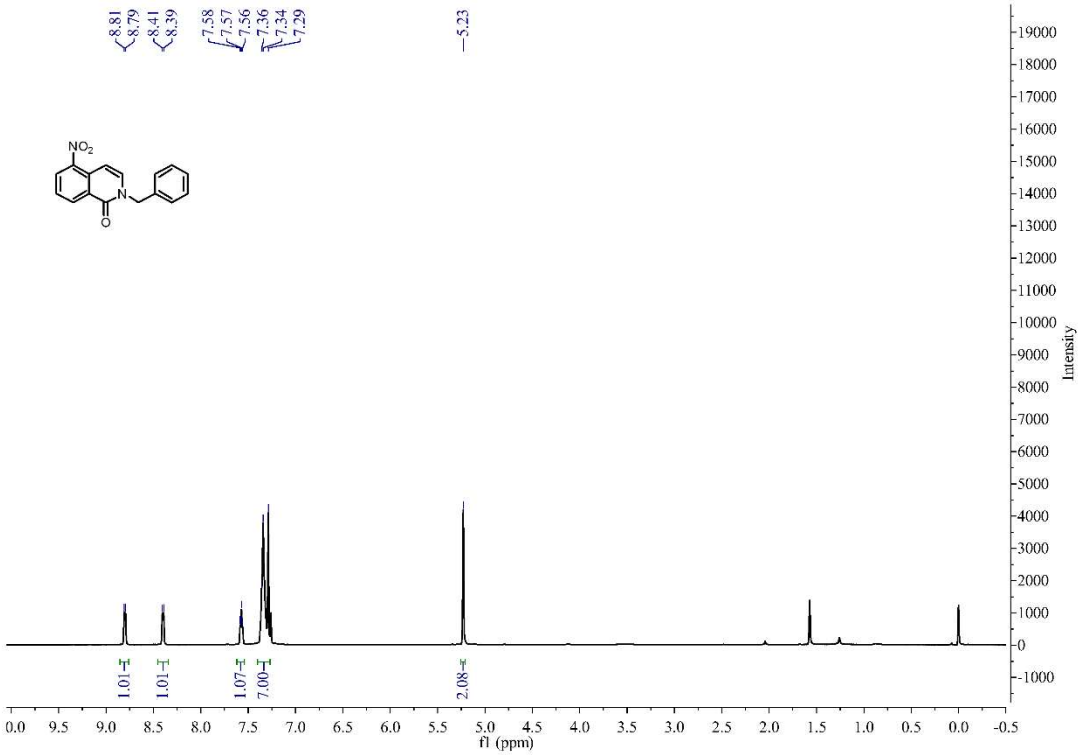


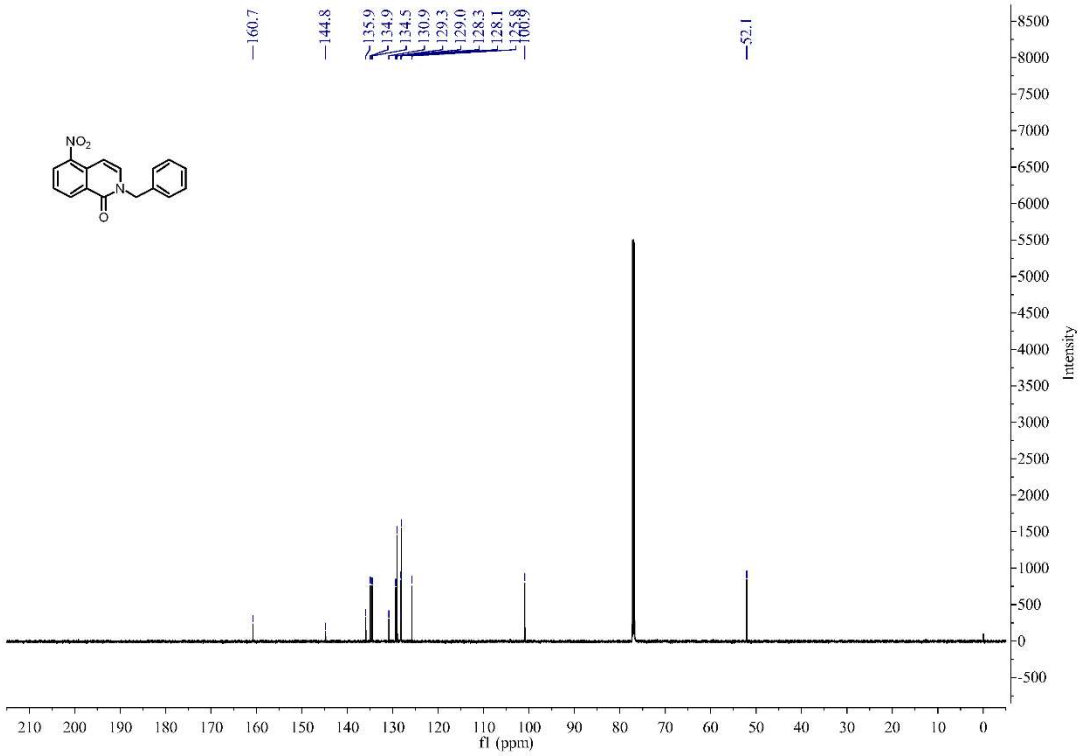
***N*-benzyl-5-bromoisoquinolin-1(*2H*)-one (2v)**





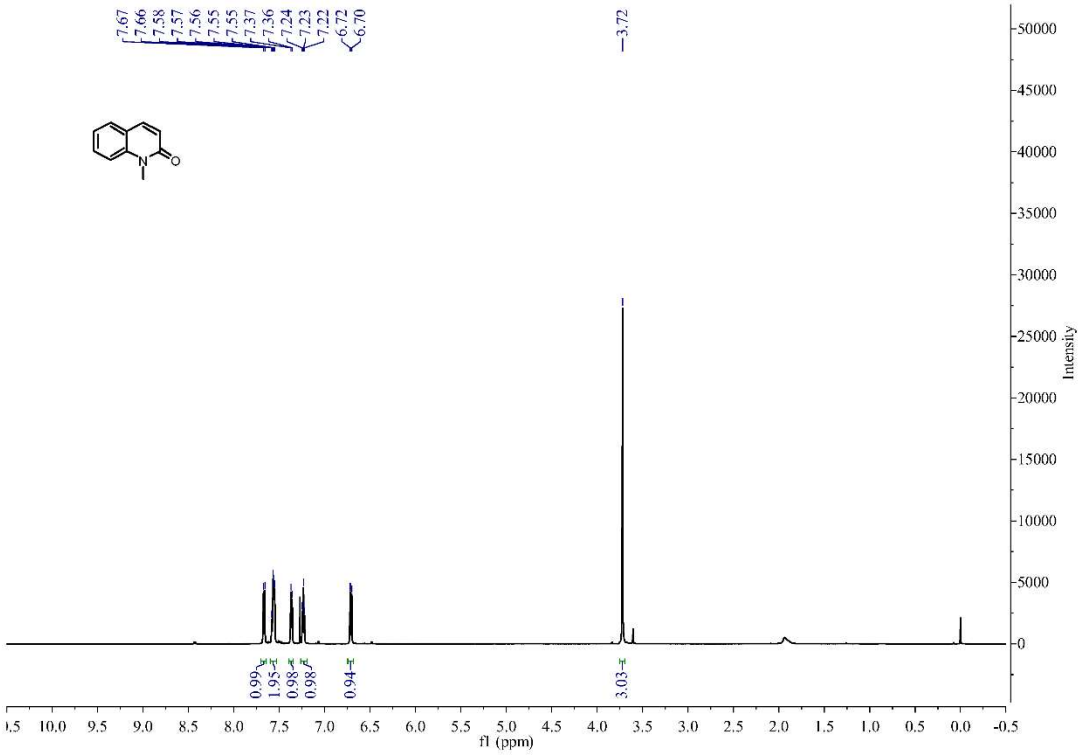
***N*-benzyl-5-nitroisoquinolin-1(*2H*)-one (2w)**

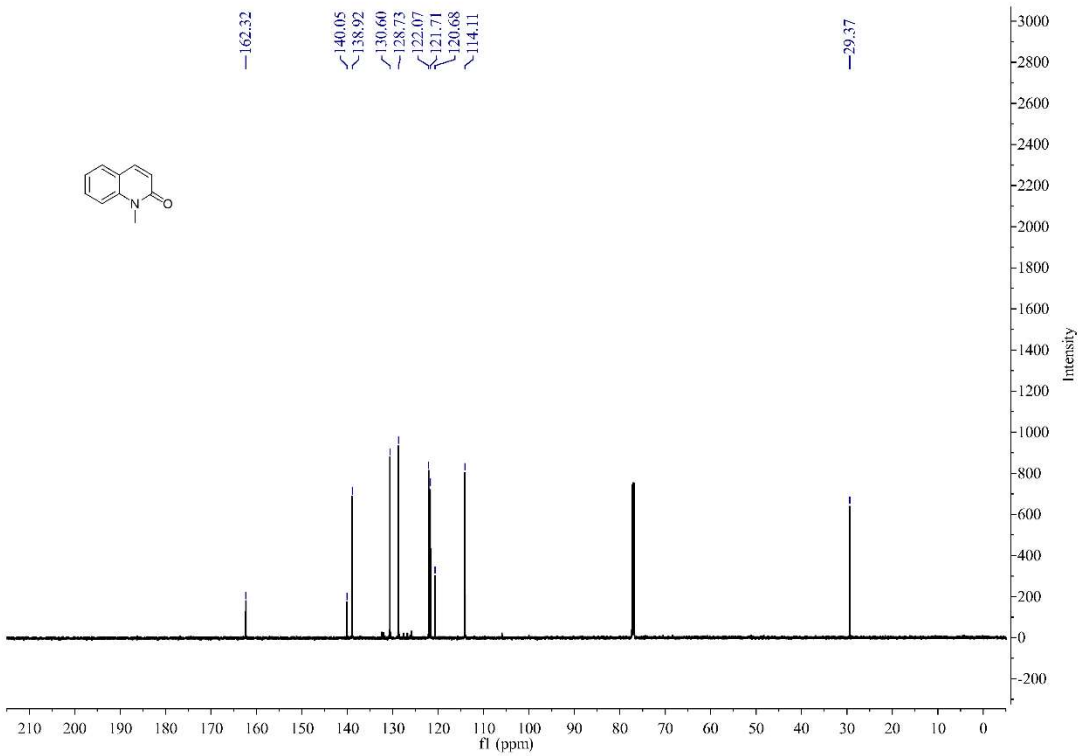




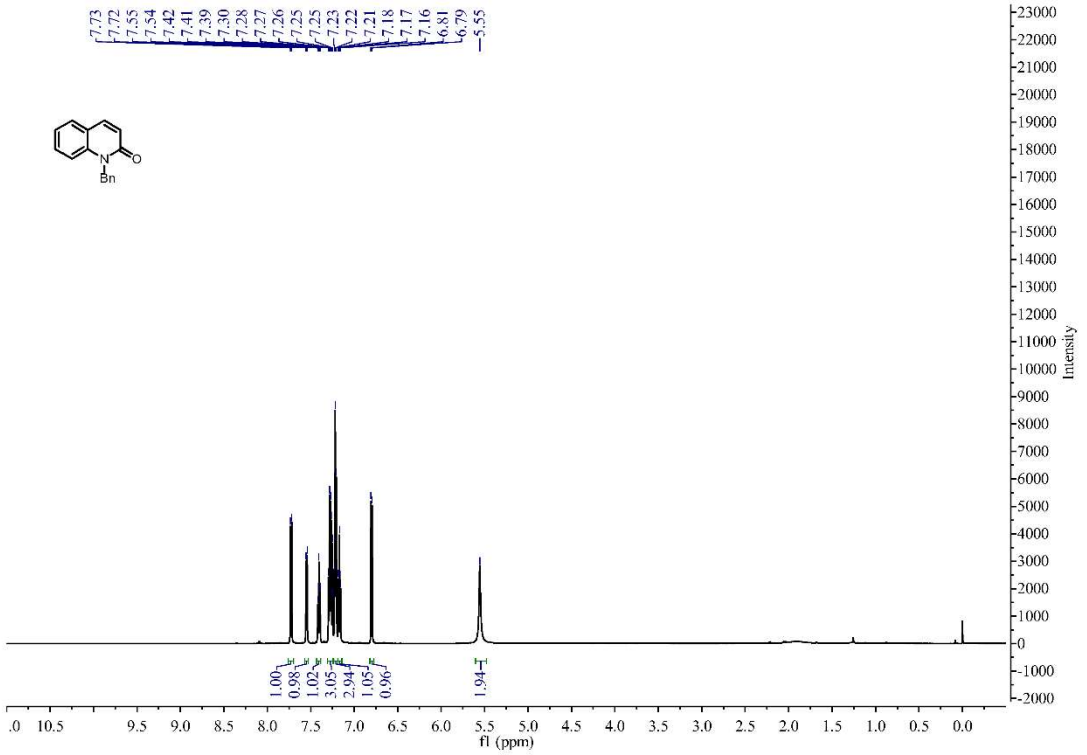
9.2 Spectra of compounds 4a–4o

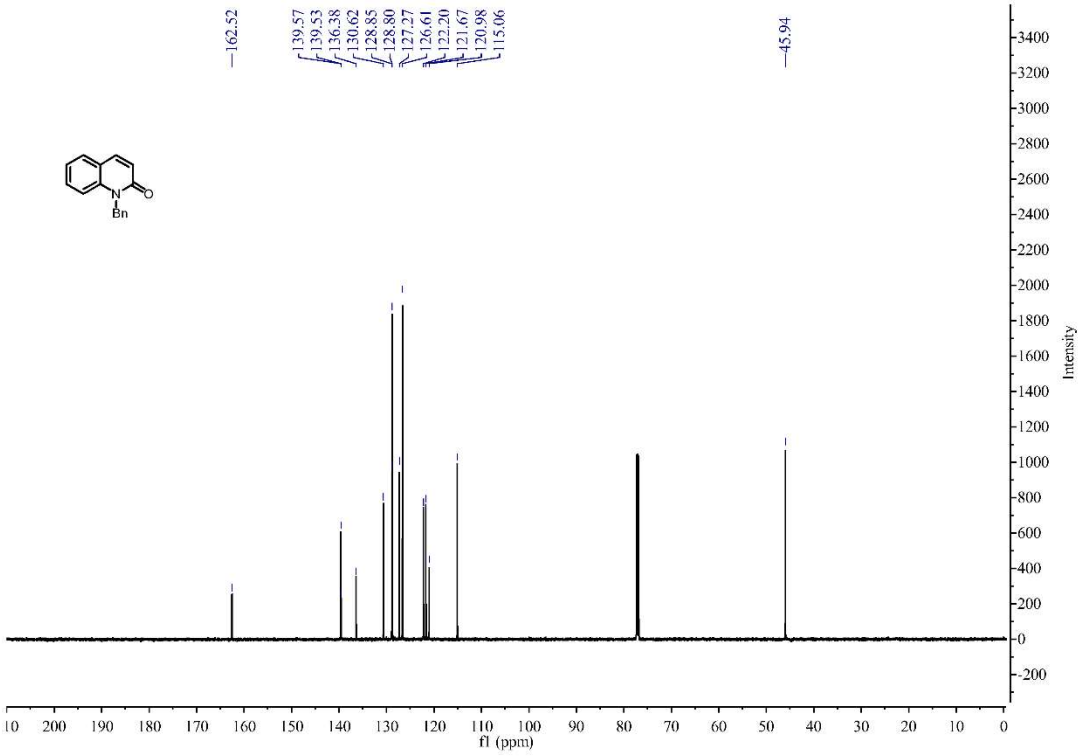
N-methylquinolin-2(*1H*)-one (4a)



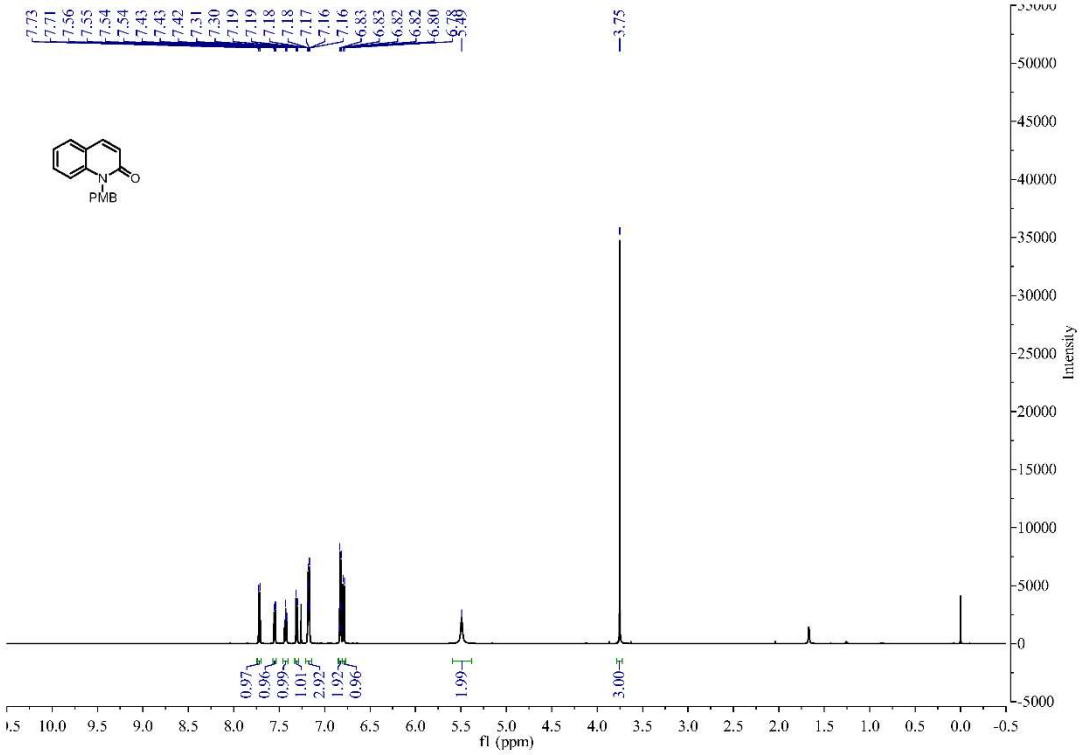


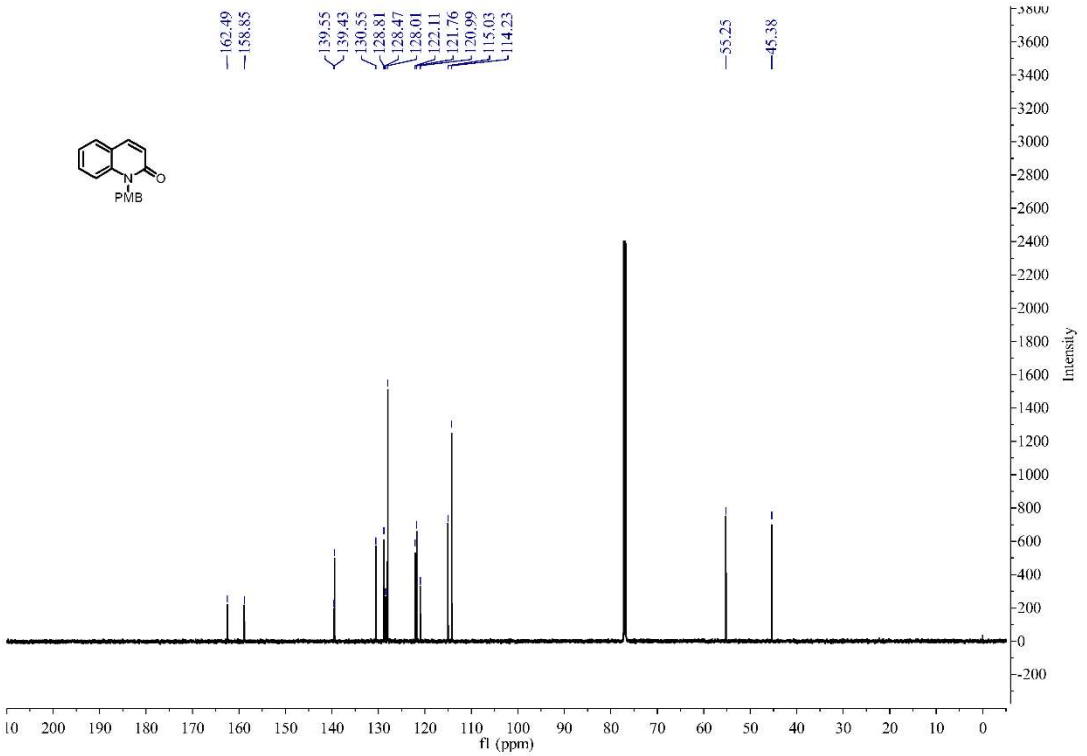
***N*-benzylquinolin-2(*1H*)-one (4b)**



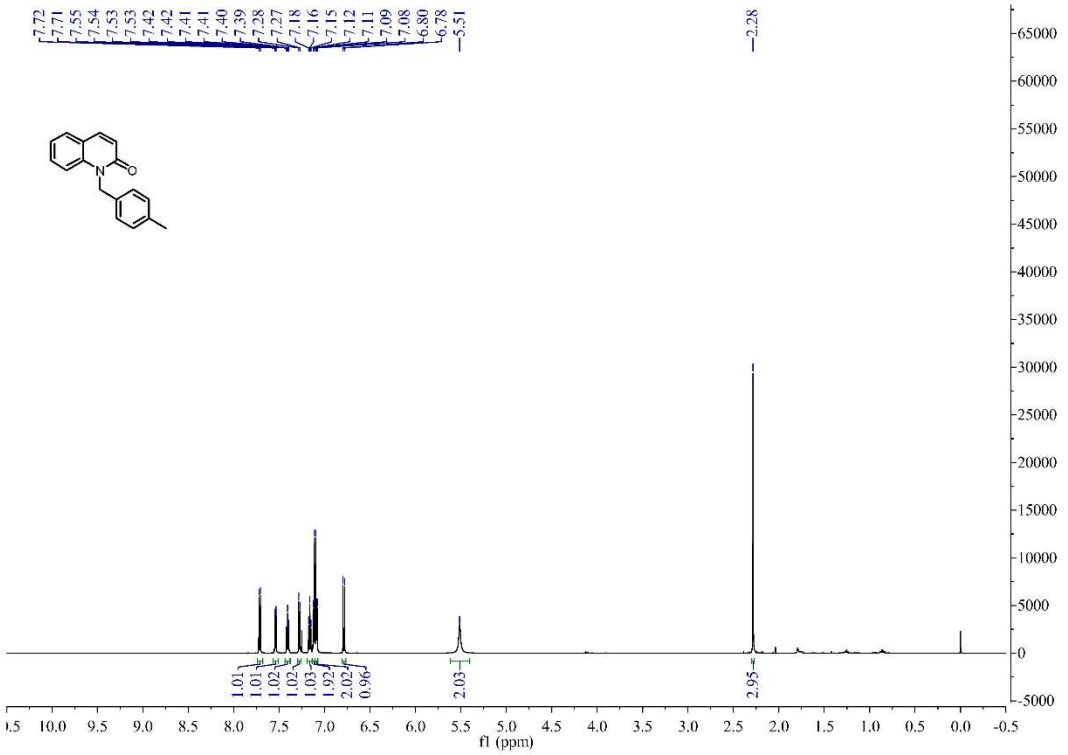


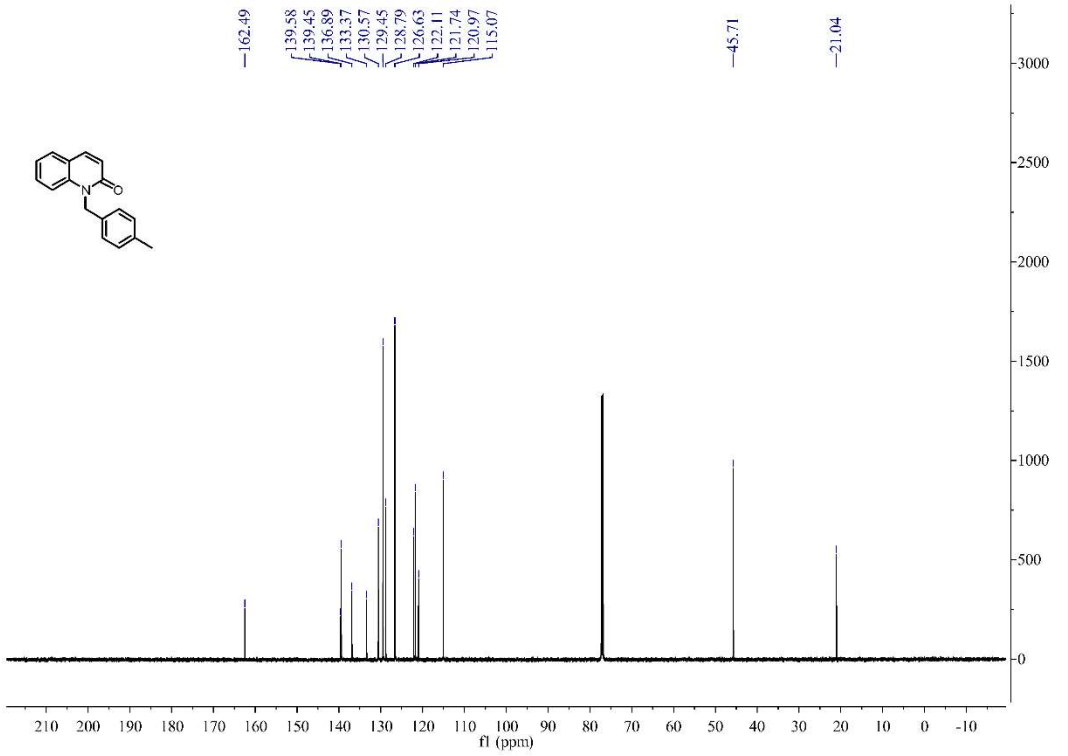
_N_-(4-methoxybenzyl) quinolin-2(_1H_)-one (4c)



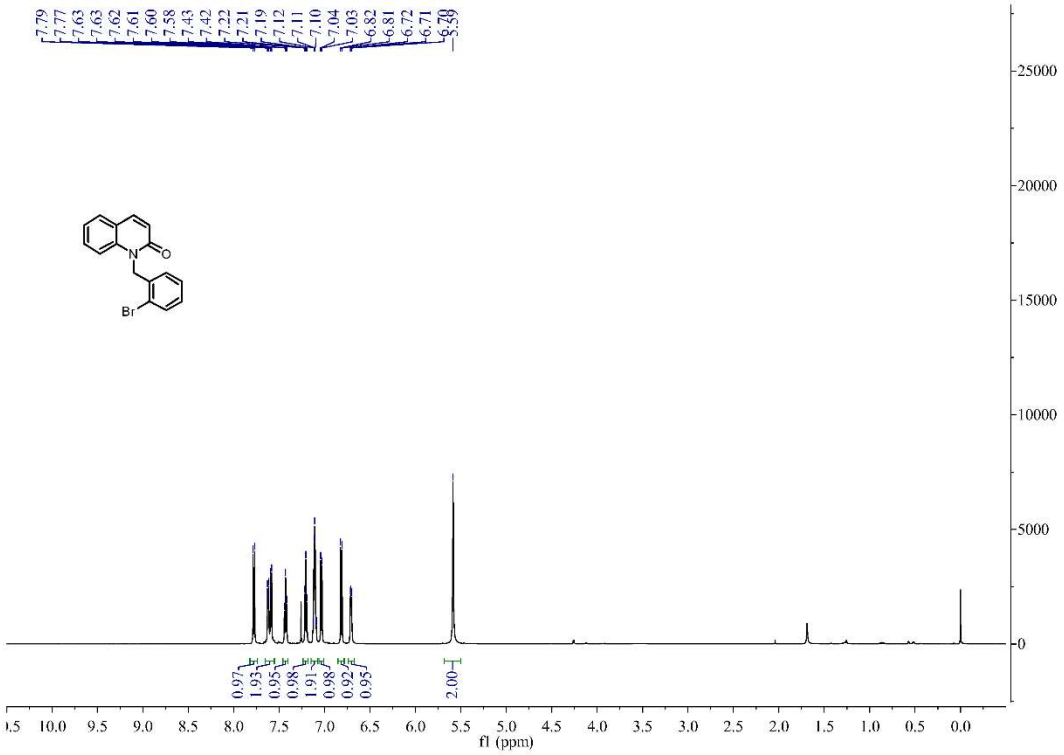


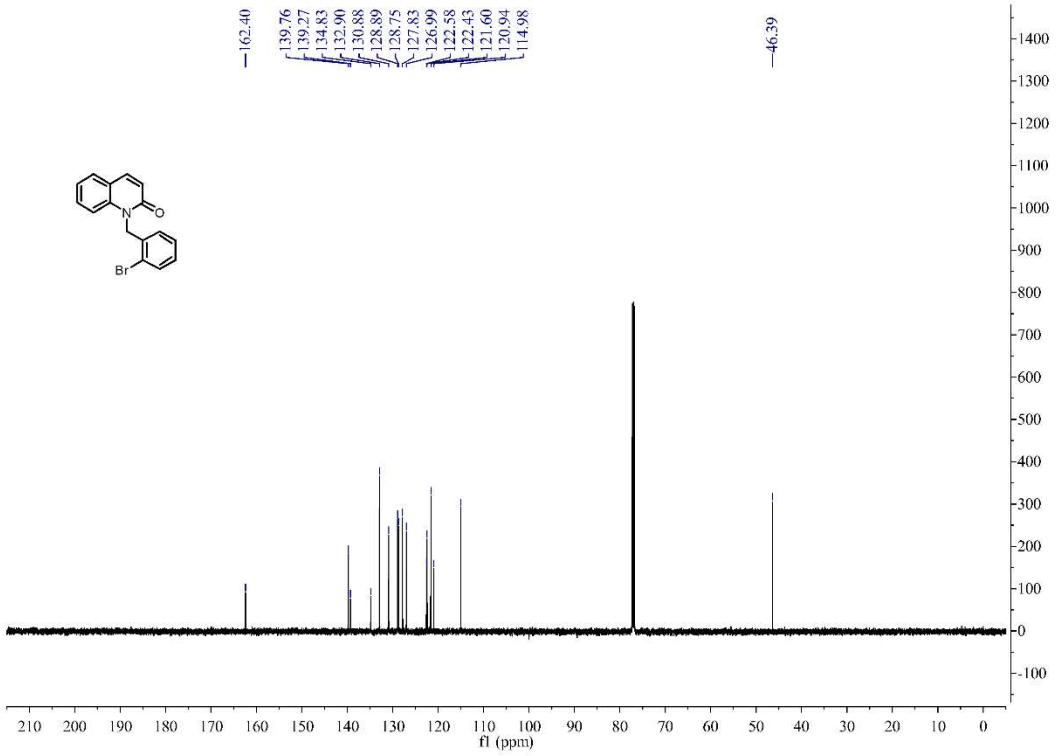
_N_-(4-methylbenzyl) quinolin-2(_1H_)-one (4d)



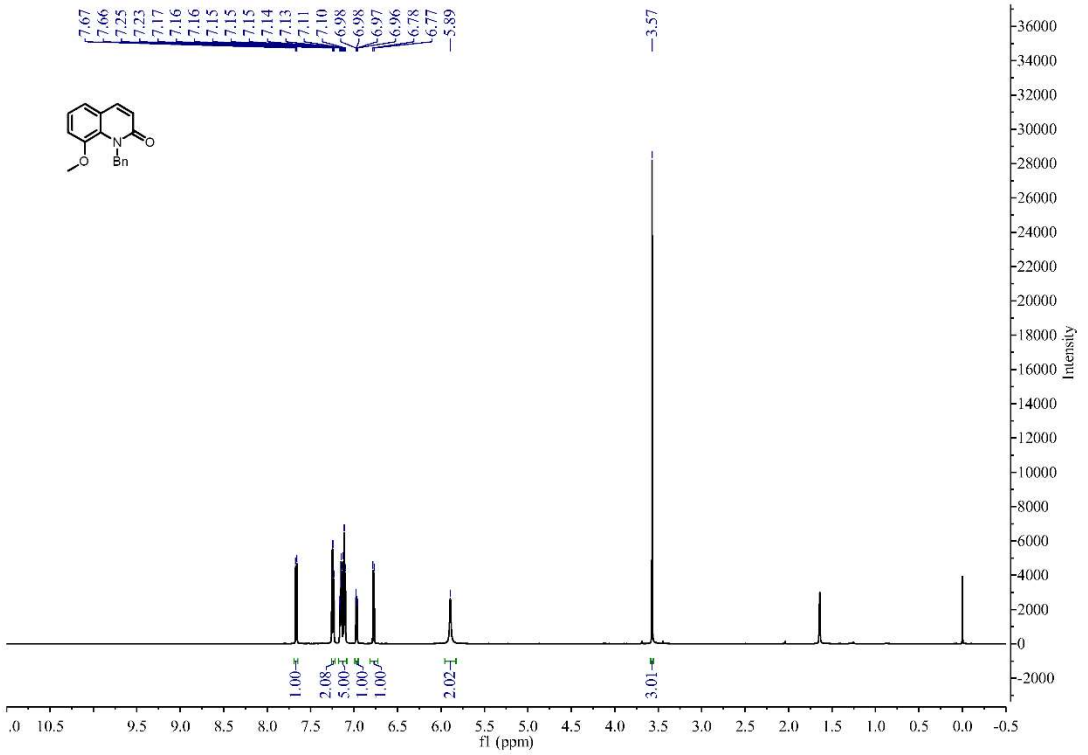


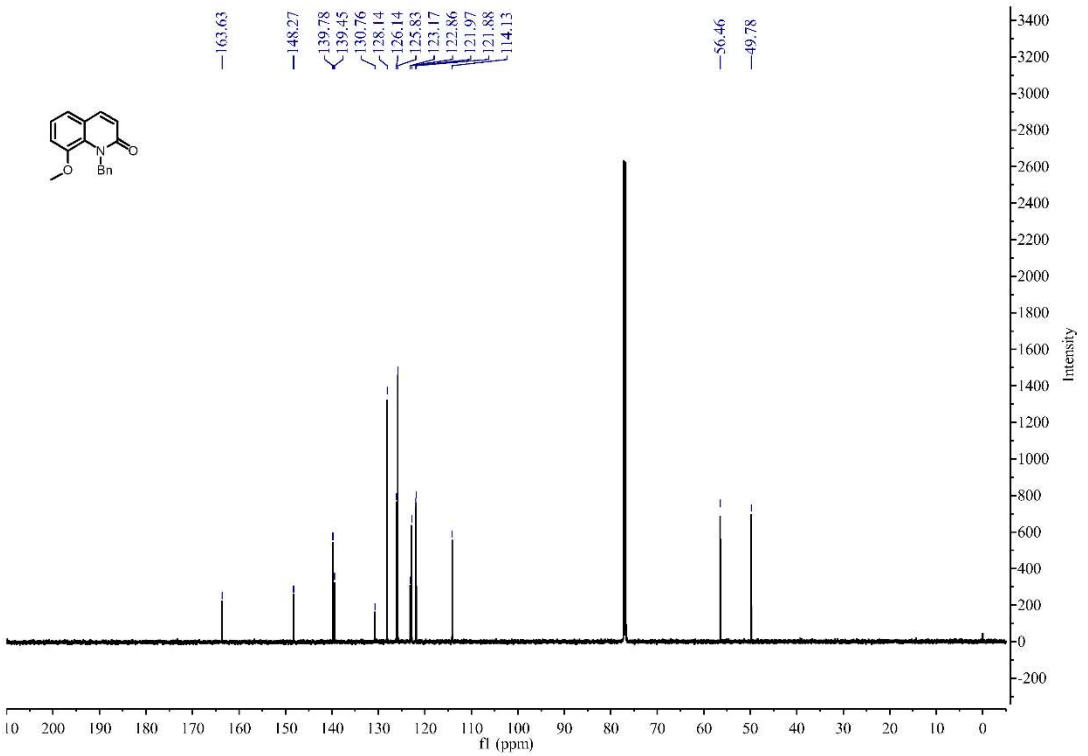
_N_-(2-bromobenzyl) quinolin-2(_1H_)-one (4e)



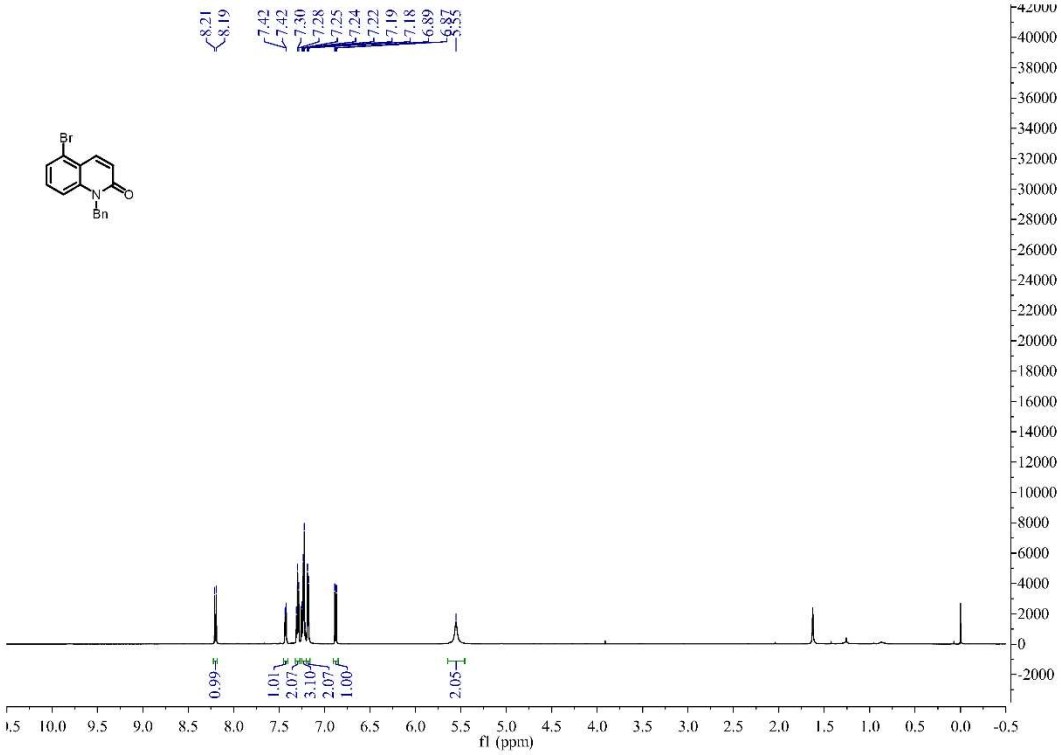


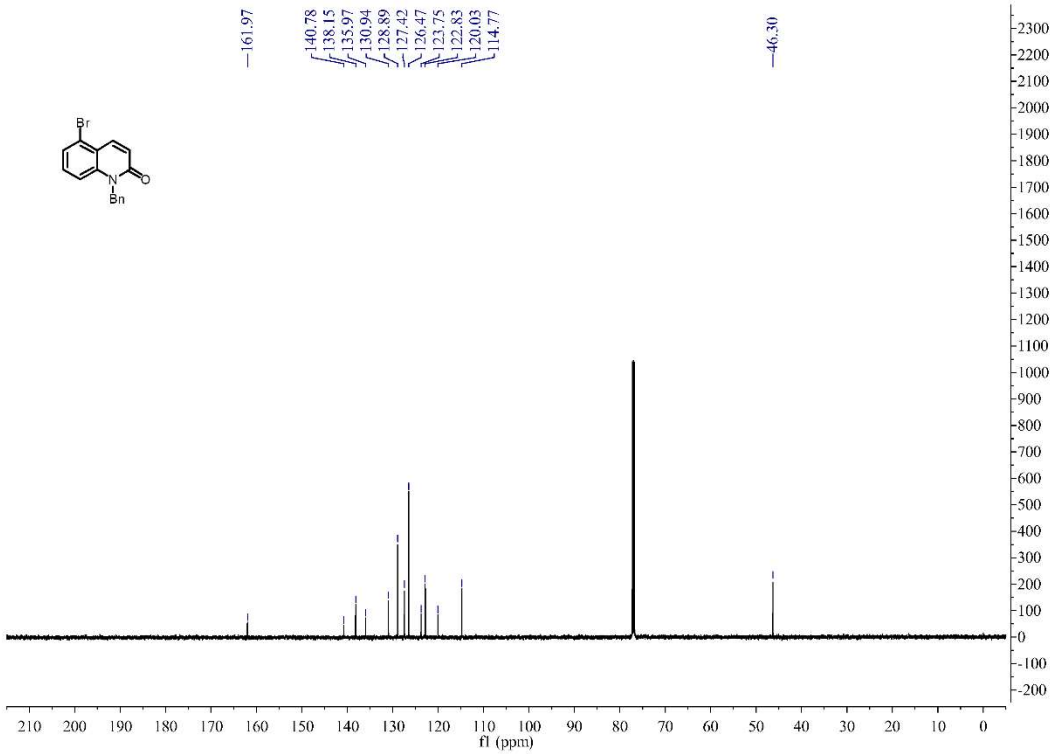
***N*-benzyl-8-methoxyquinolin-2(*1H*)-one (4f)**



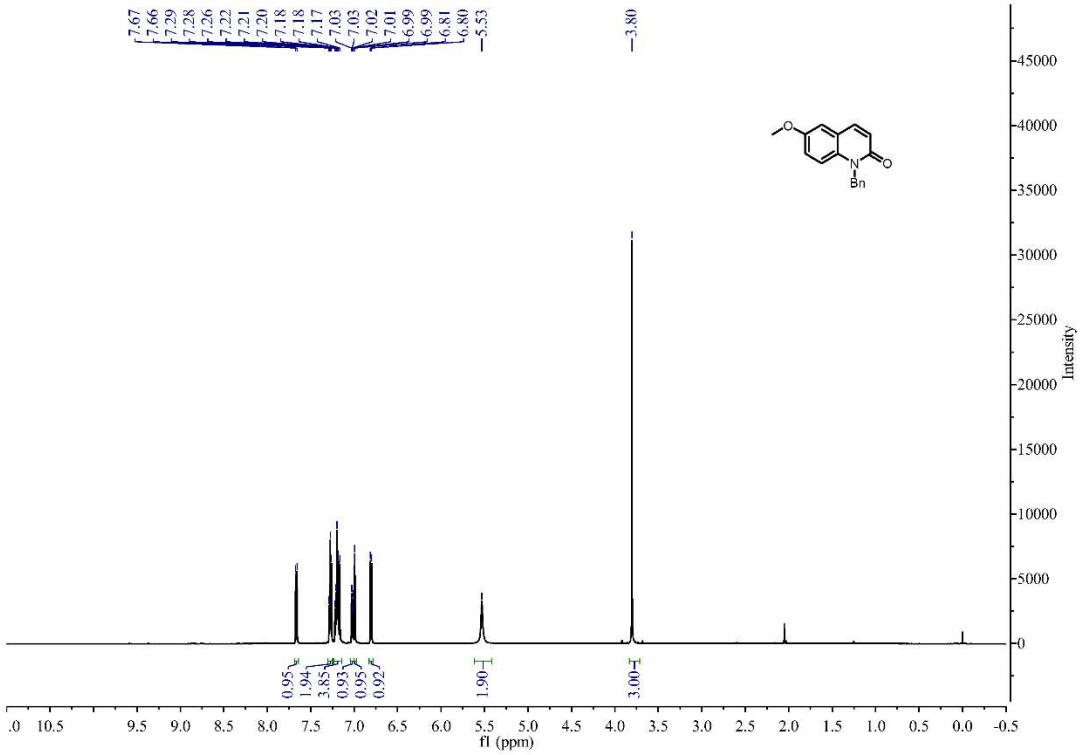


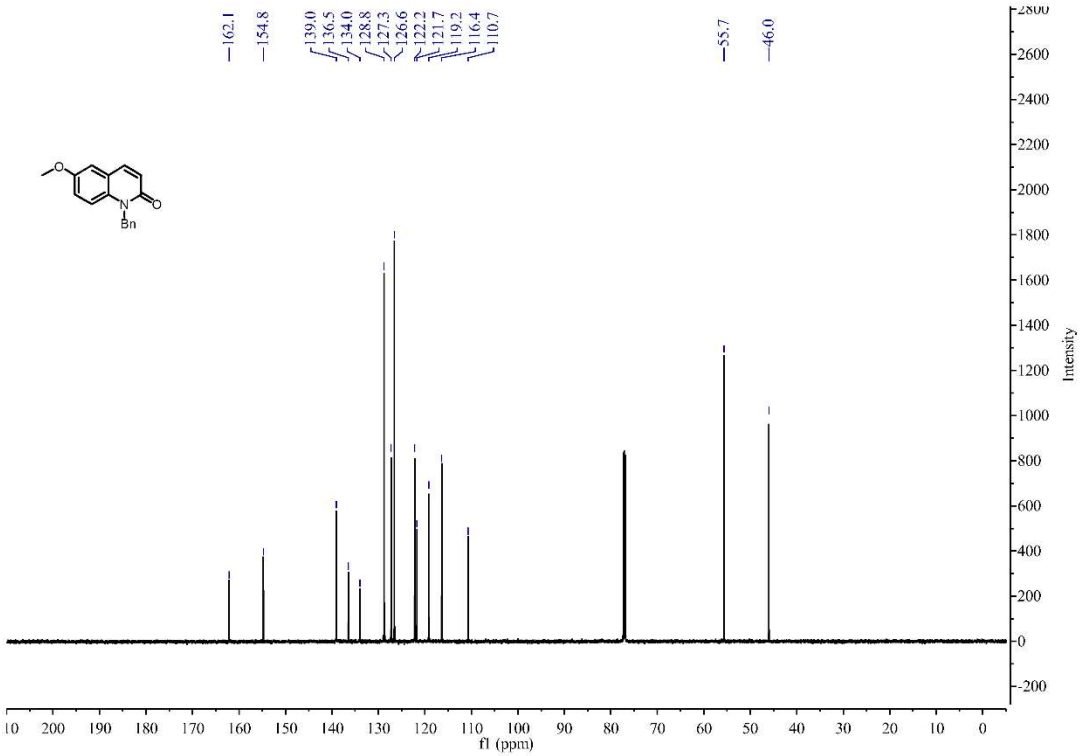
***N*-benzyl-5-bromoquinolin-2(*1H*)-one (4g)**



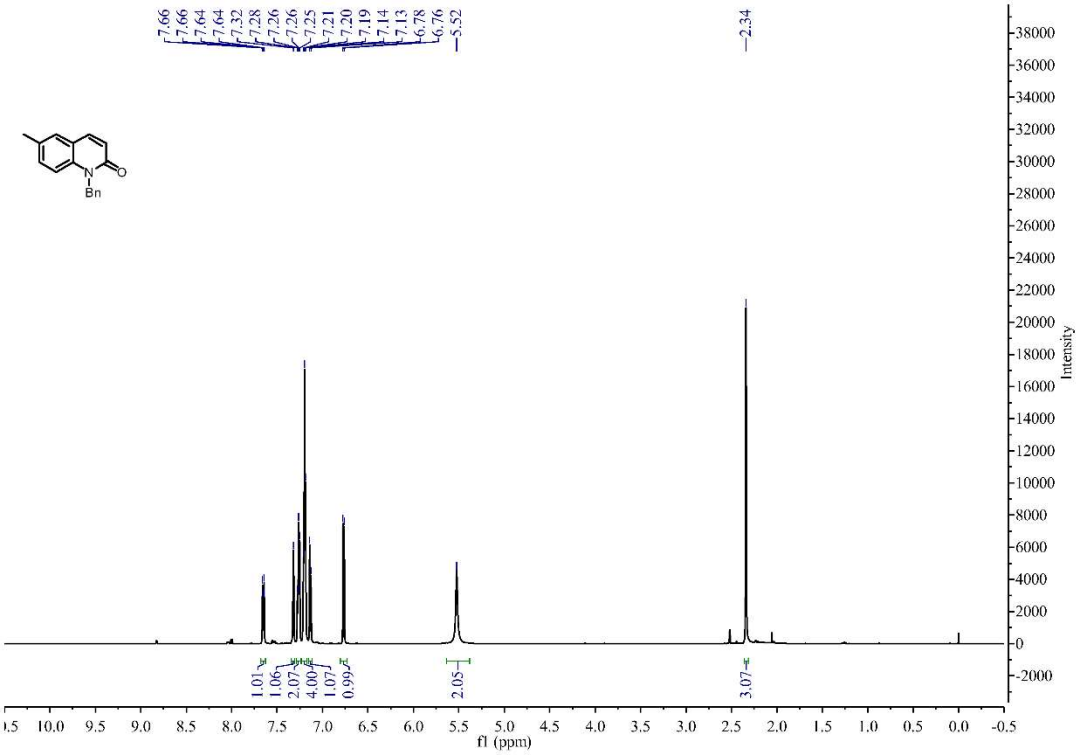


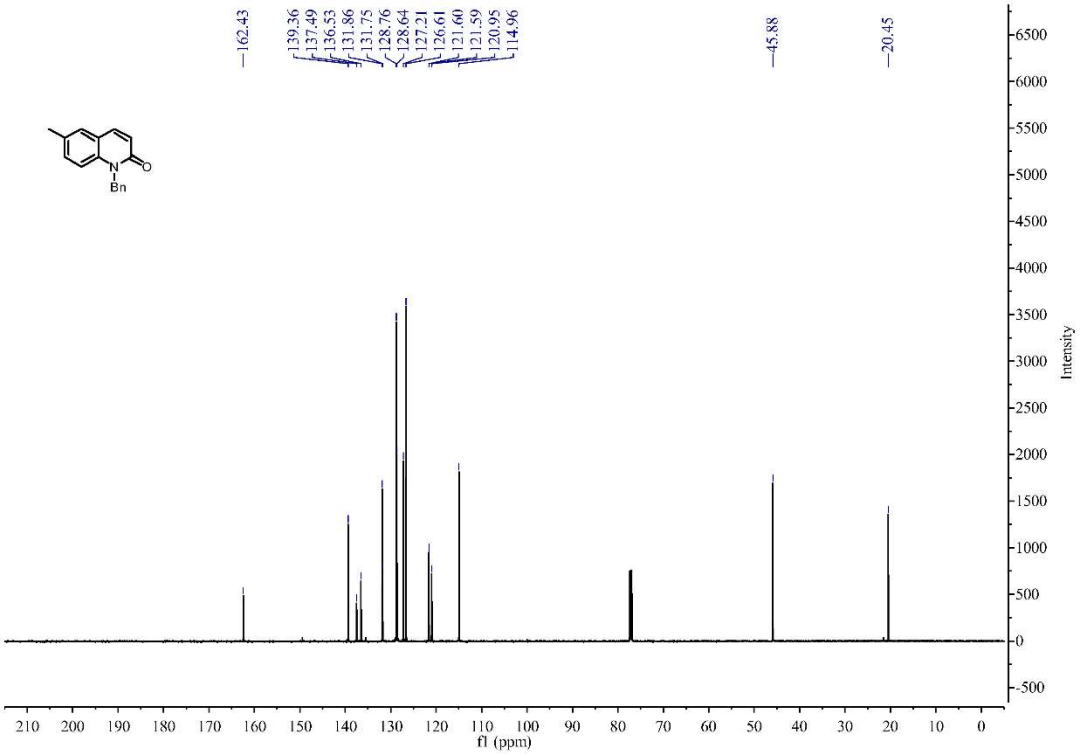
_N_-benzyl-6-methoxyquinolin-2(_1H_)-one (4h)



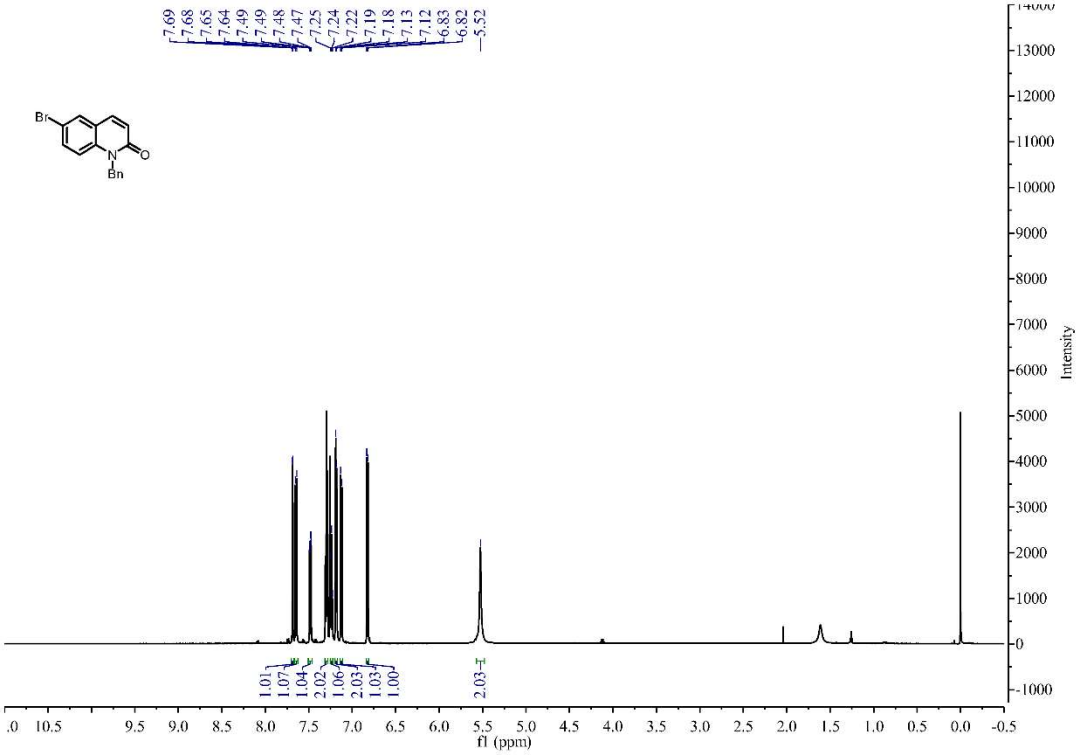


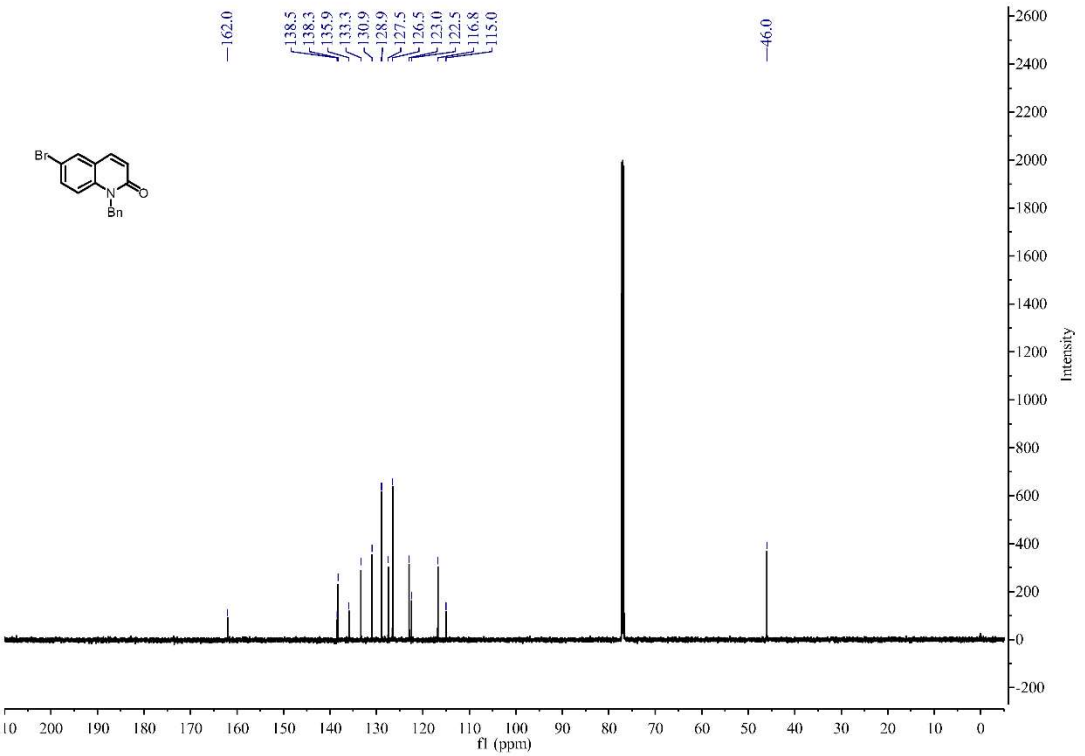
***N*-benzyl-6-methylquinolin-2(*1H*)-one (4i)**



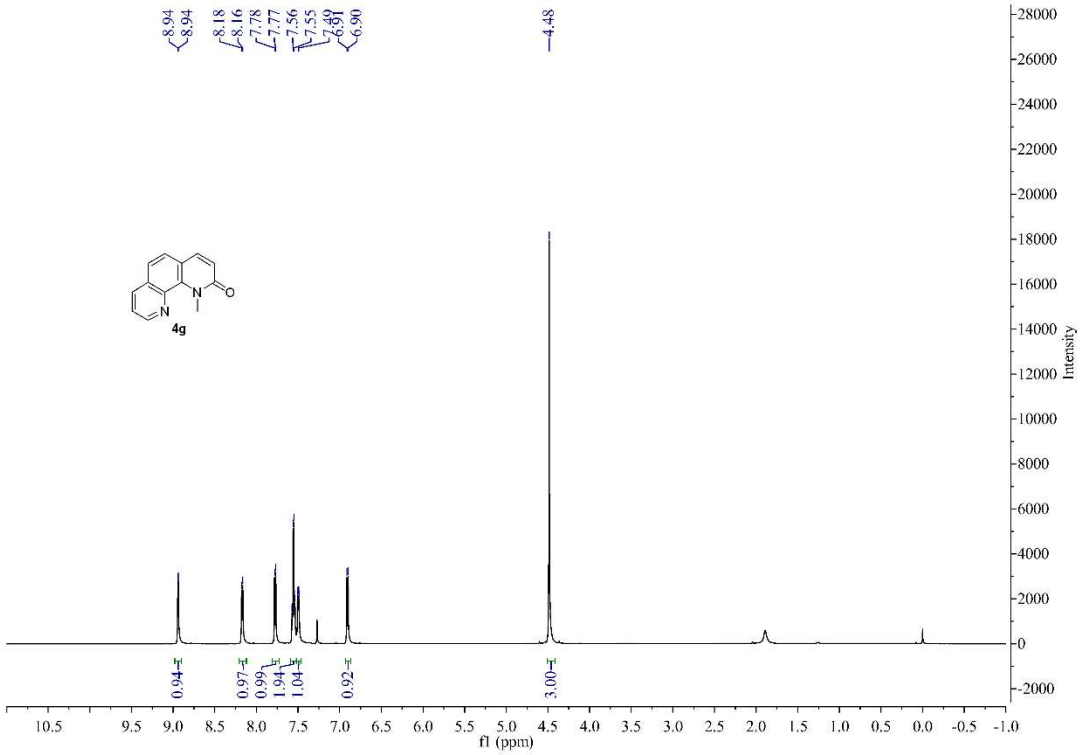


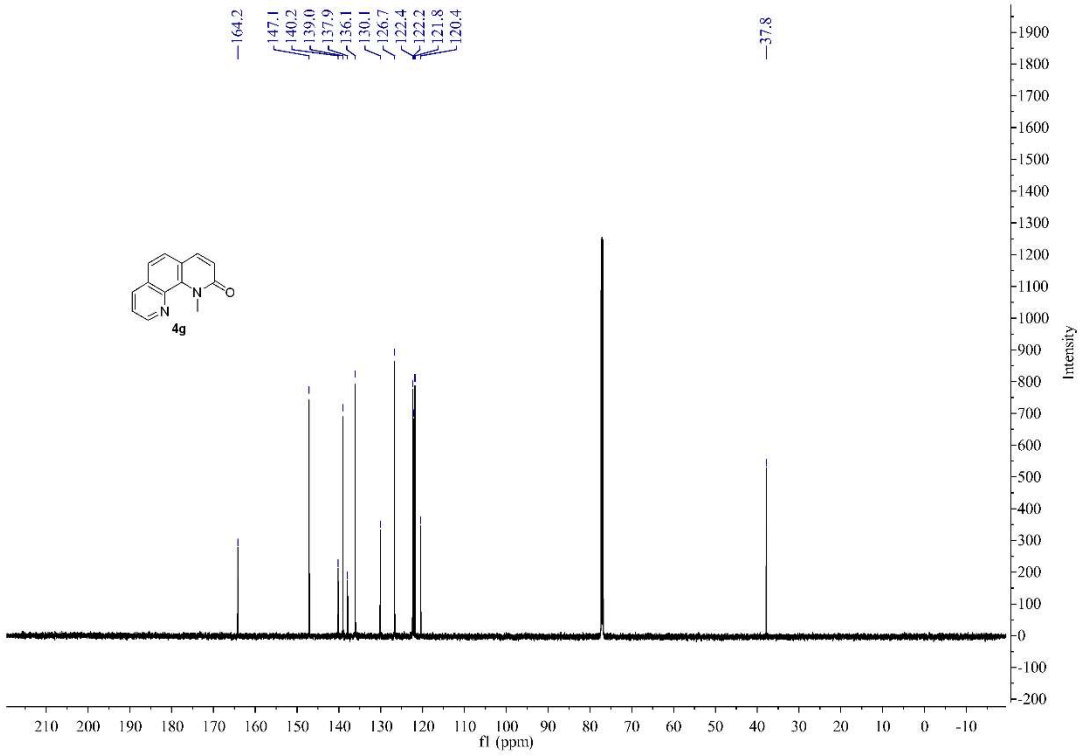
***N*-benzyl-6-bromoquinolin-2(*1H*)-one (4j)**



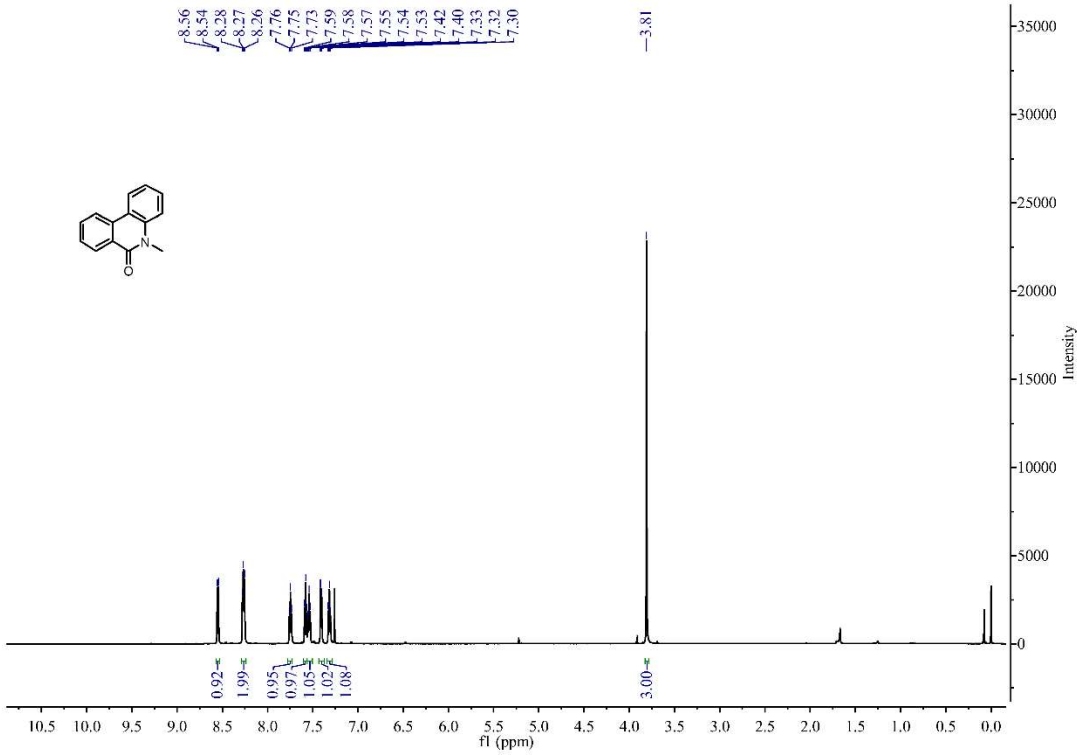


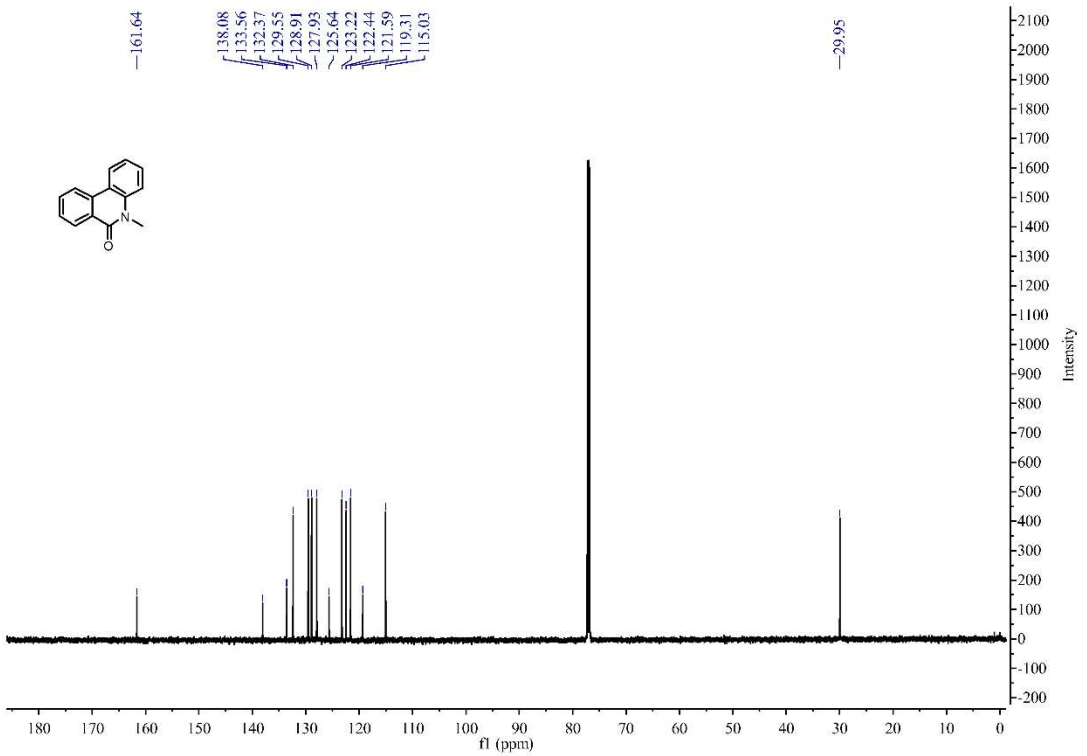
***N*-methyl-1,10-phenanthrolin-2(*1H*)-one (4k)**



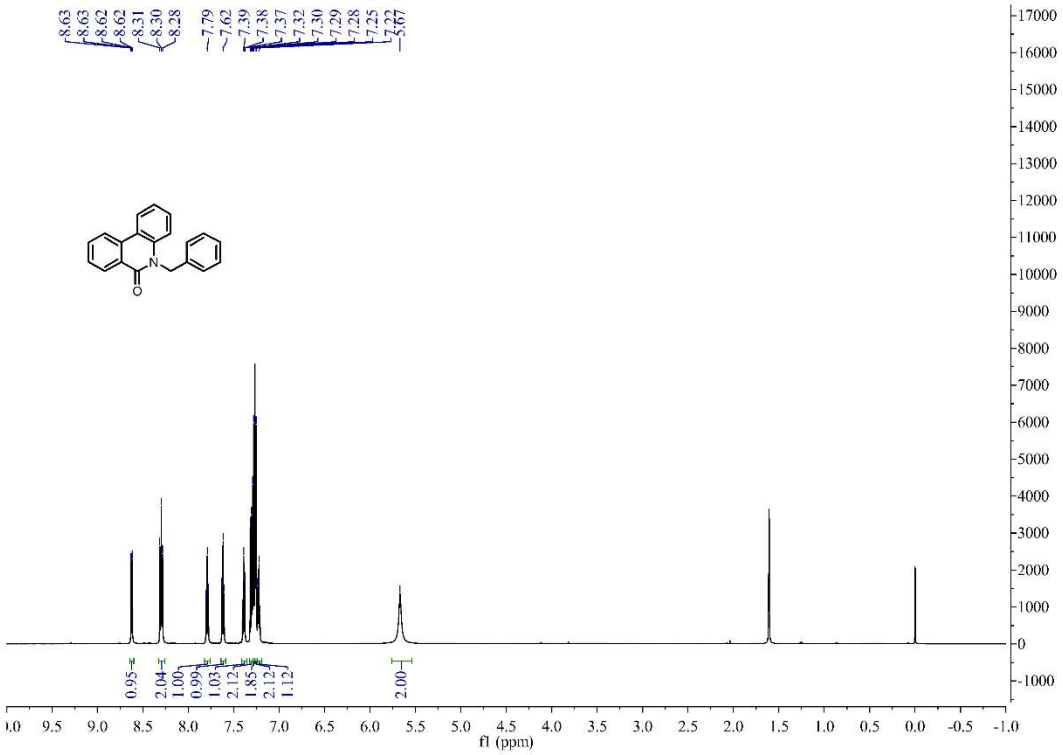


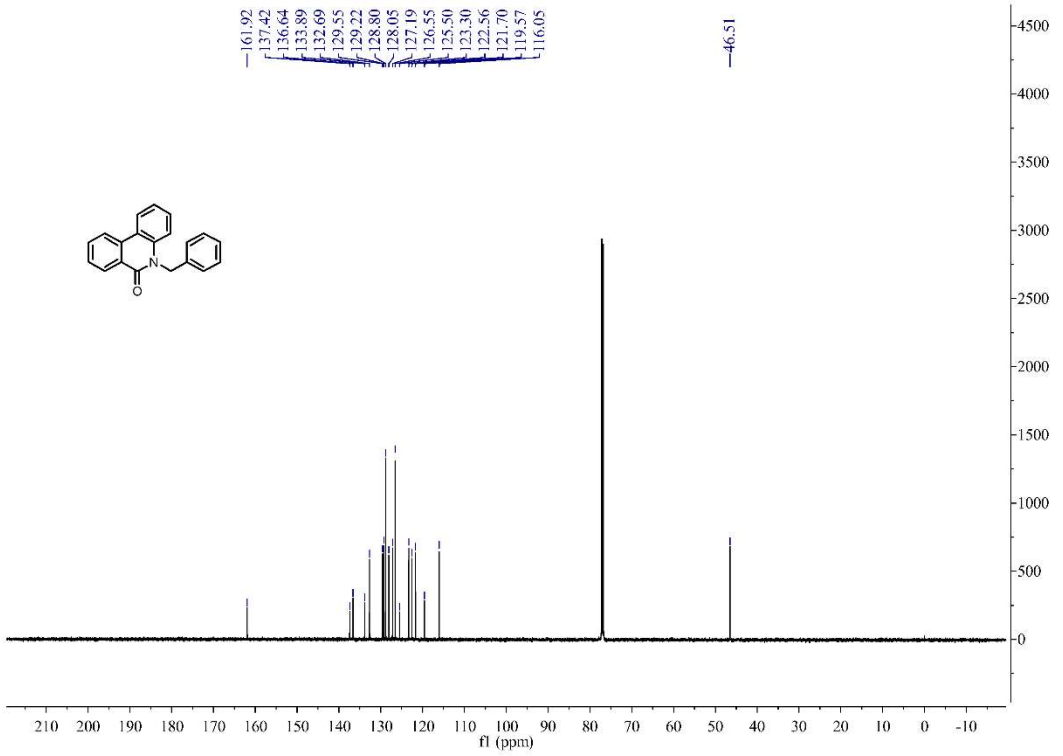
_N_-methylphenanthridin-6(_5H_)-one (4l)



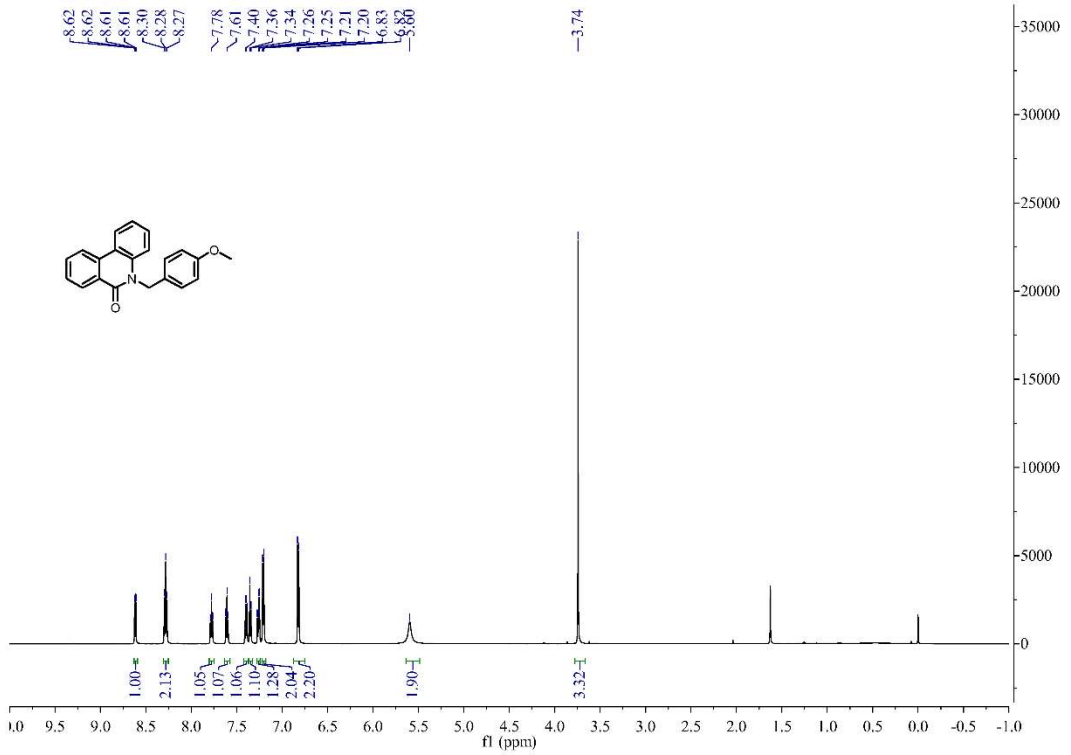


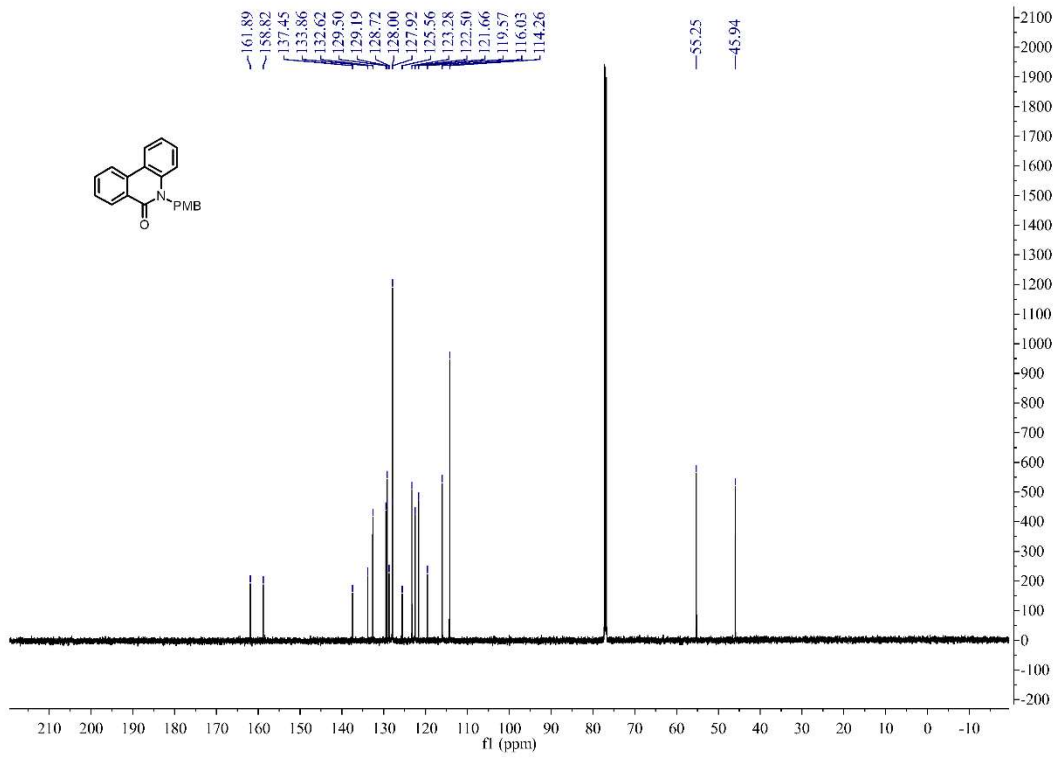
***N*-benzylphenanthridin-6(*5H*)-one (4m)**



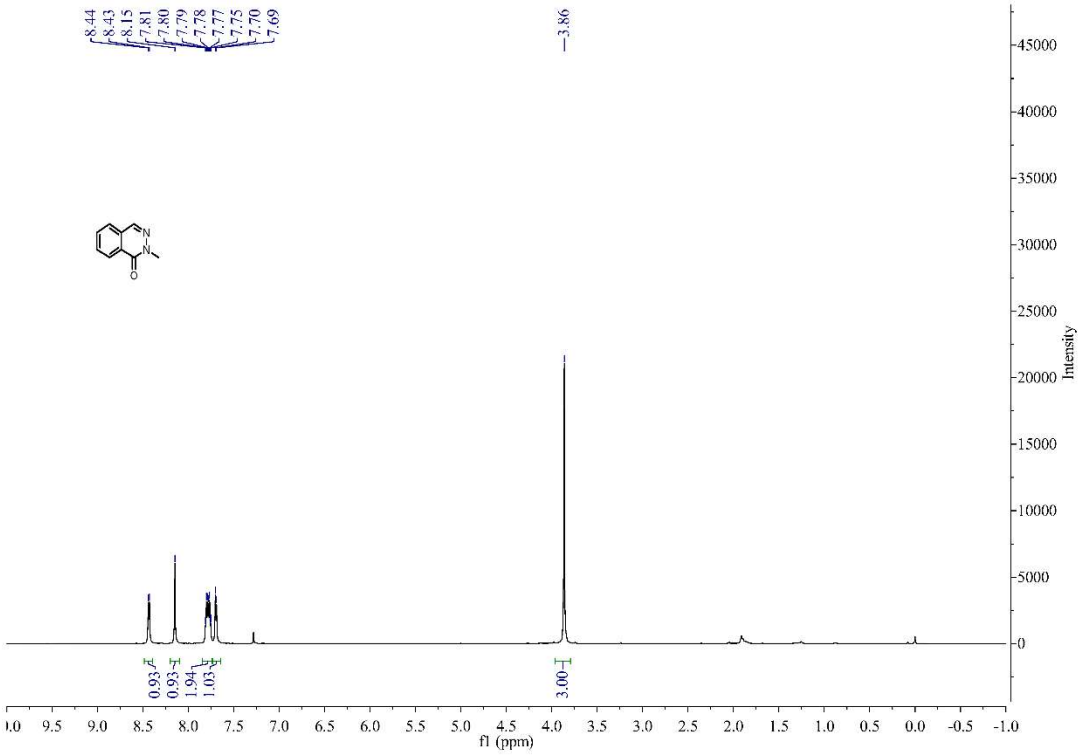


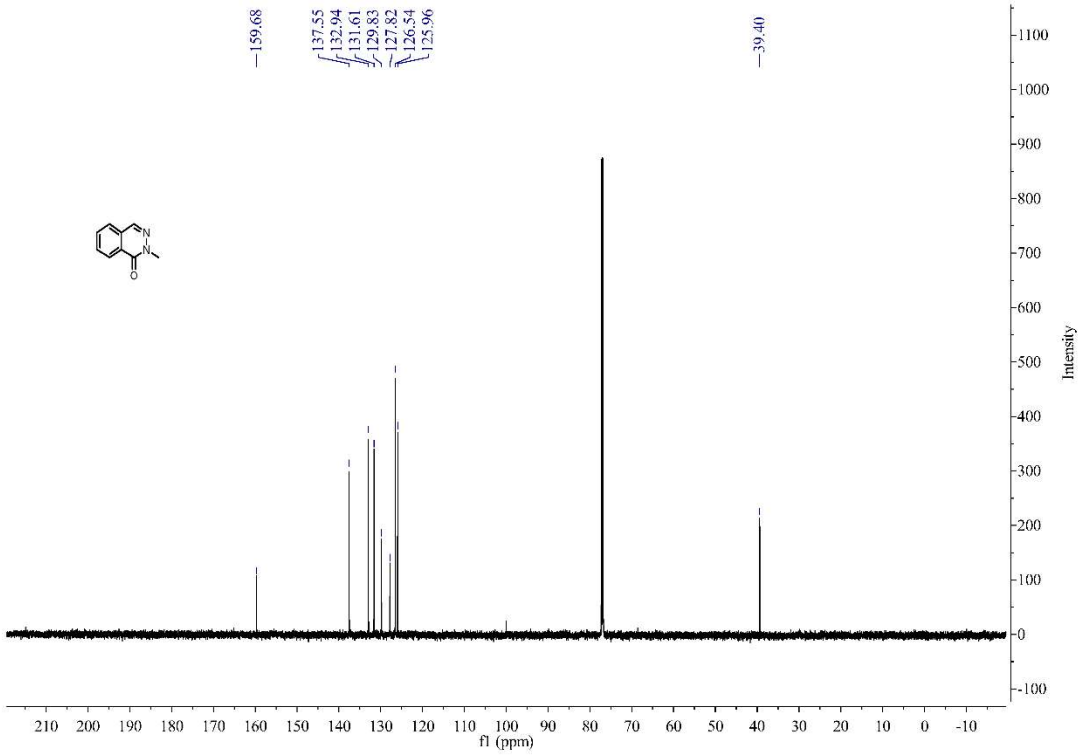
***N*-(4-methoxybenzyl) phenanthridin-6(*5H*)-one (4n)**





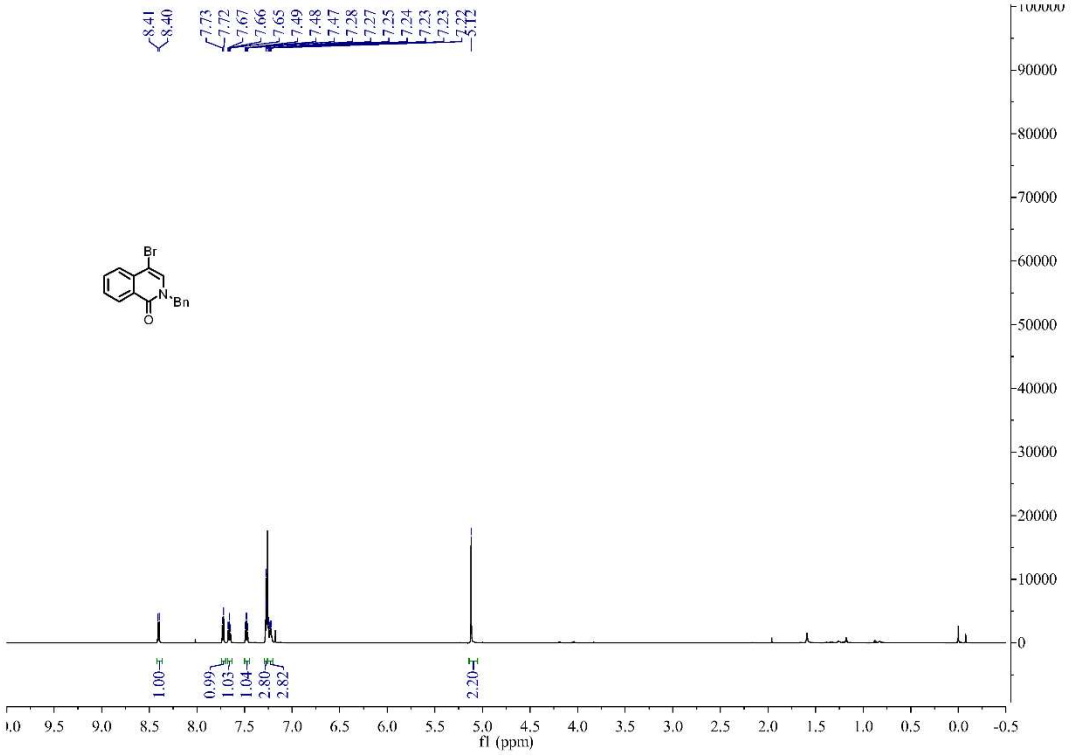
***N*-methylphthalazin-1(2H)-one (4o)**

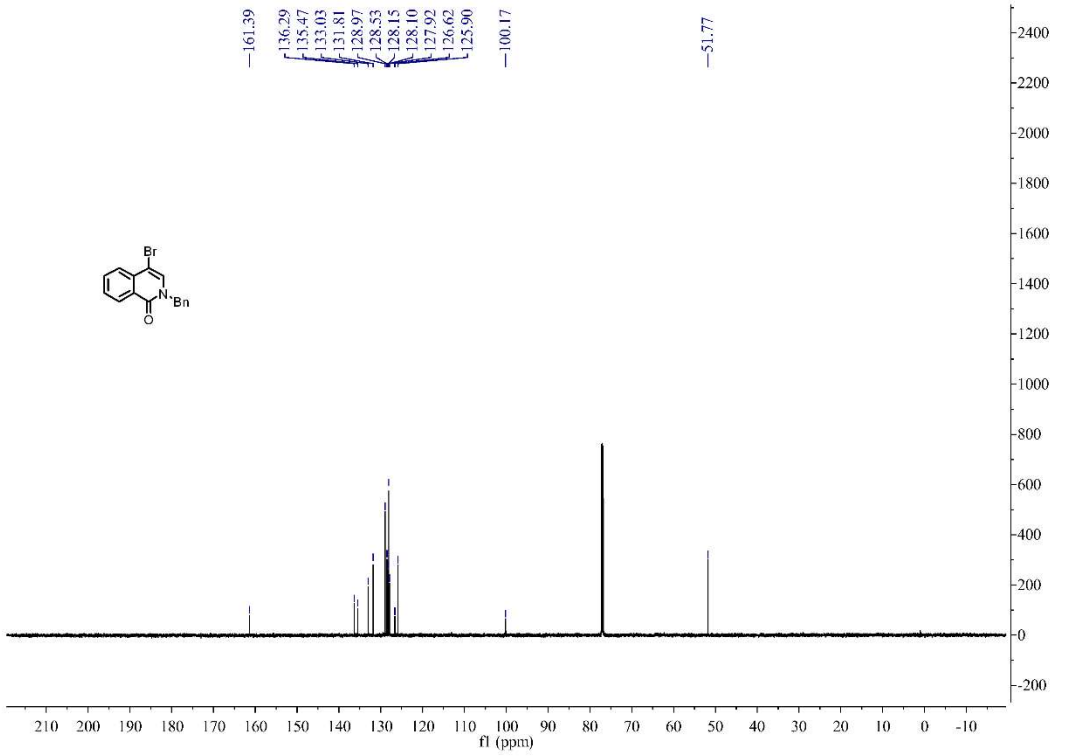




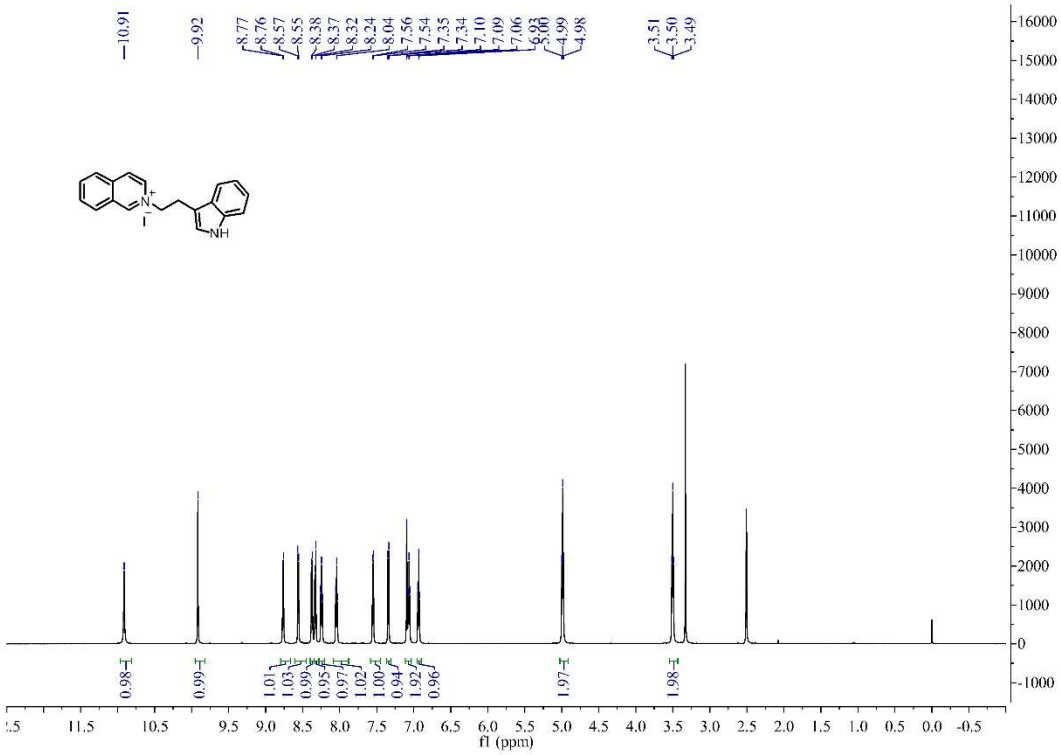
9.3 Spectra of compounds 5–9

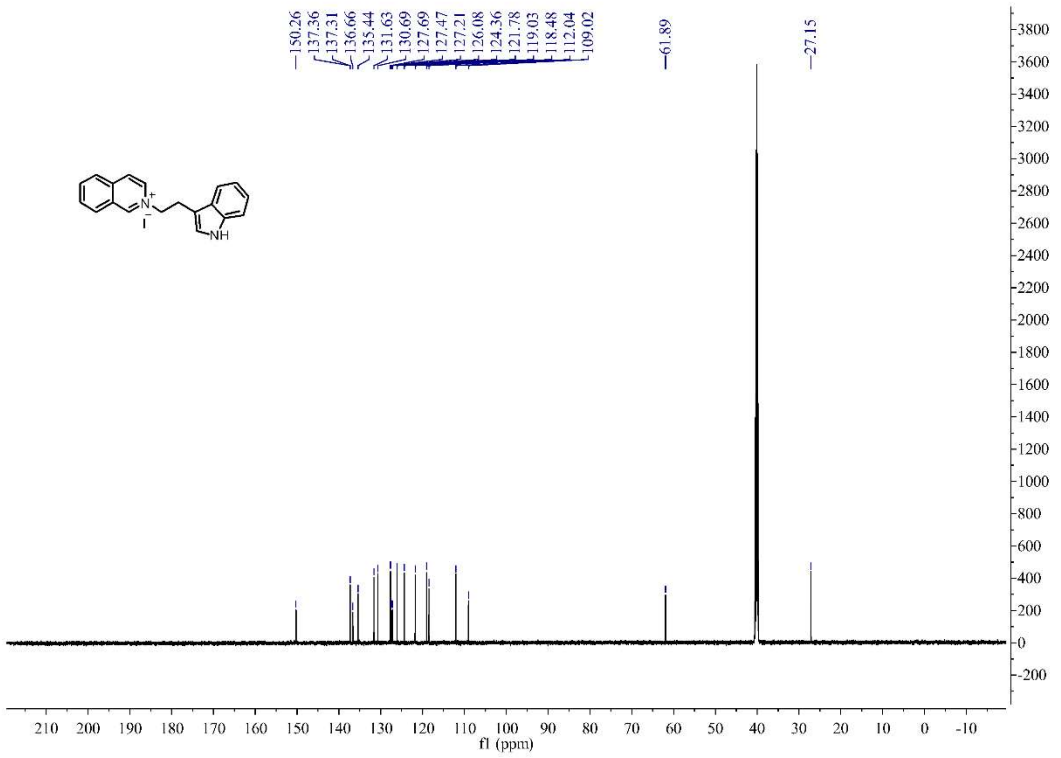
2-benzyl-4-bromoisoquinolin-1(2H)-one 5



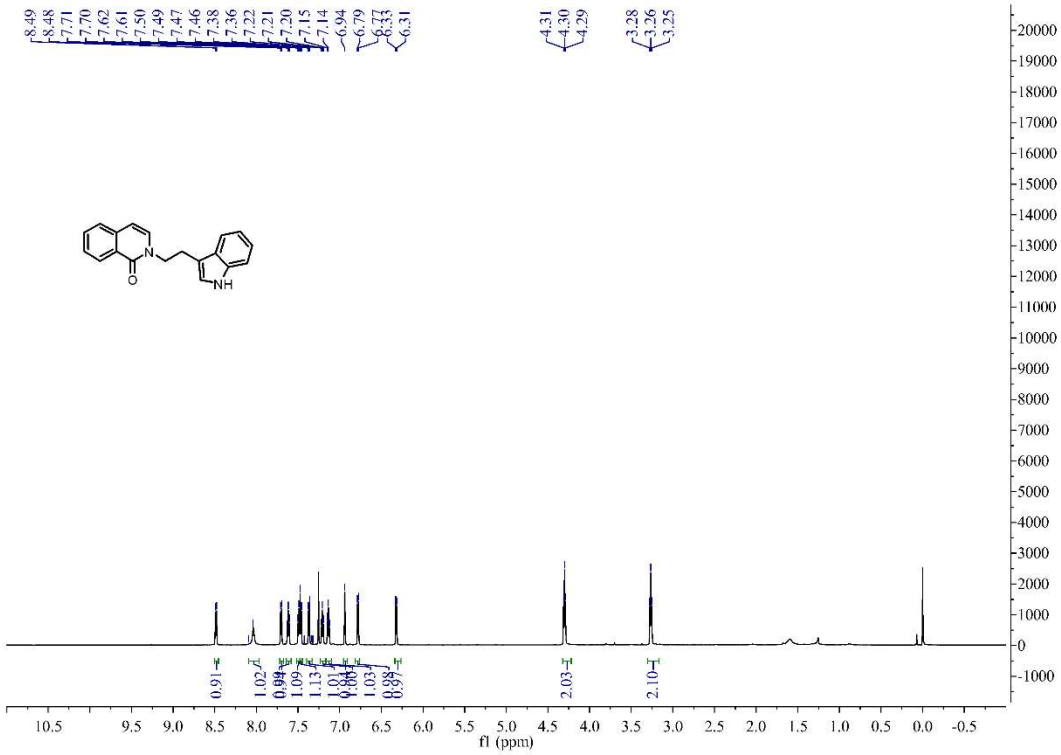


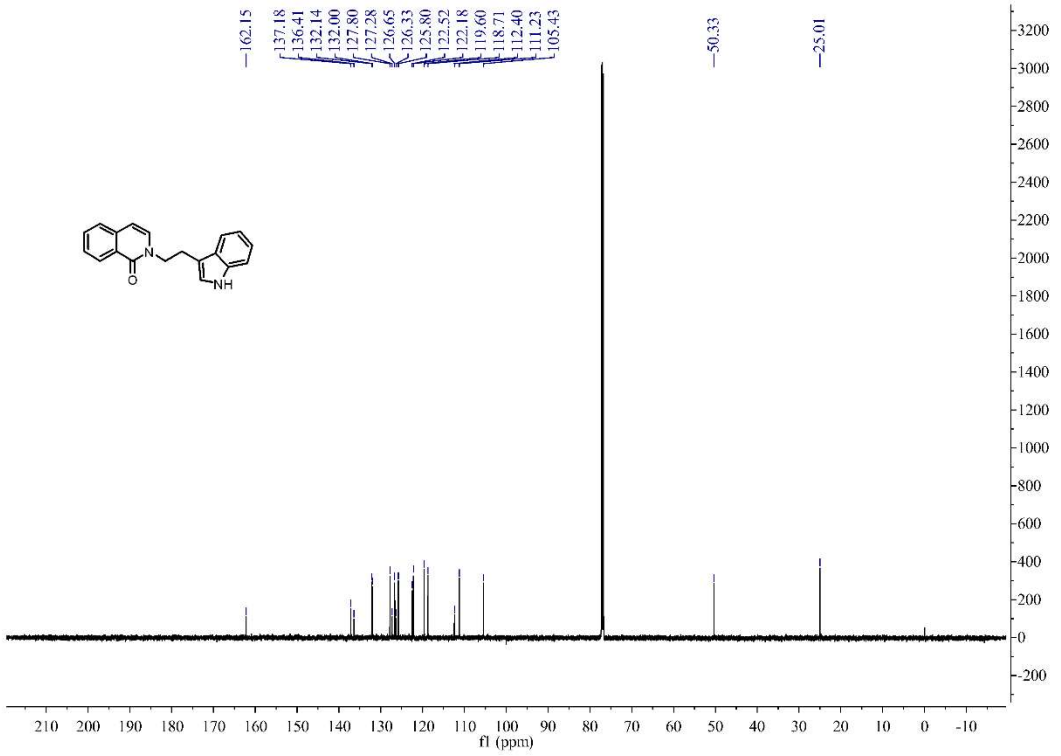
2-(2-(1H-indol-3-yl)ethyl)isoquinolin-2-ium 6



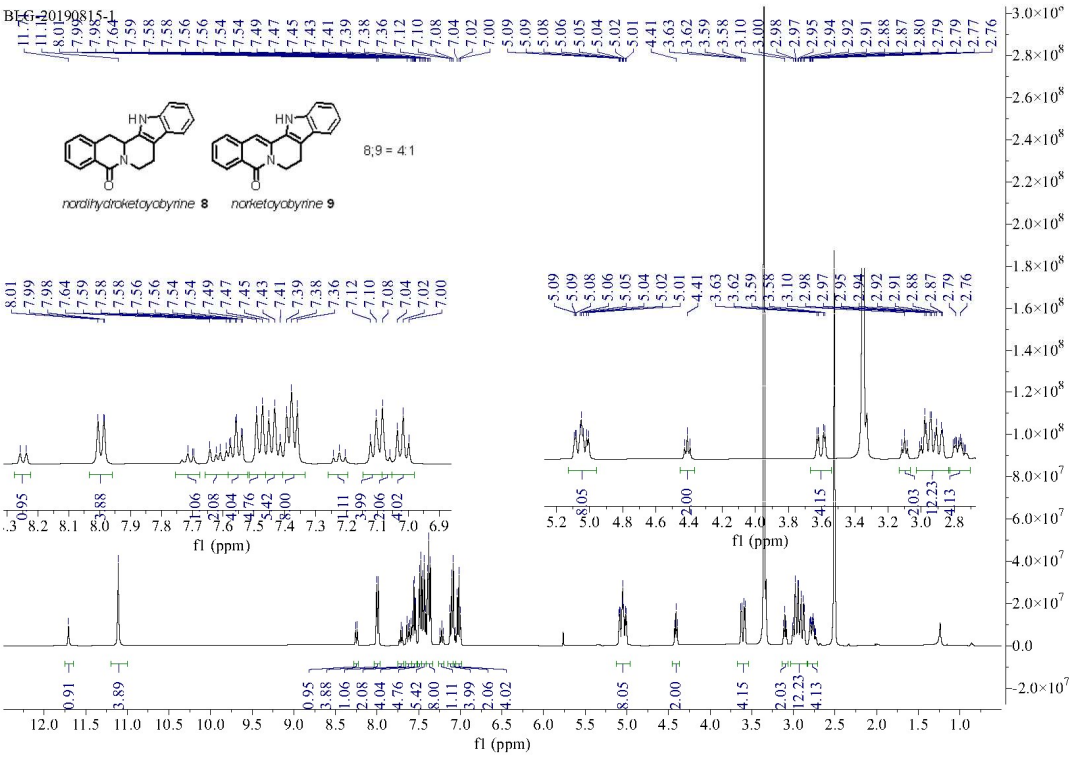


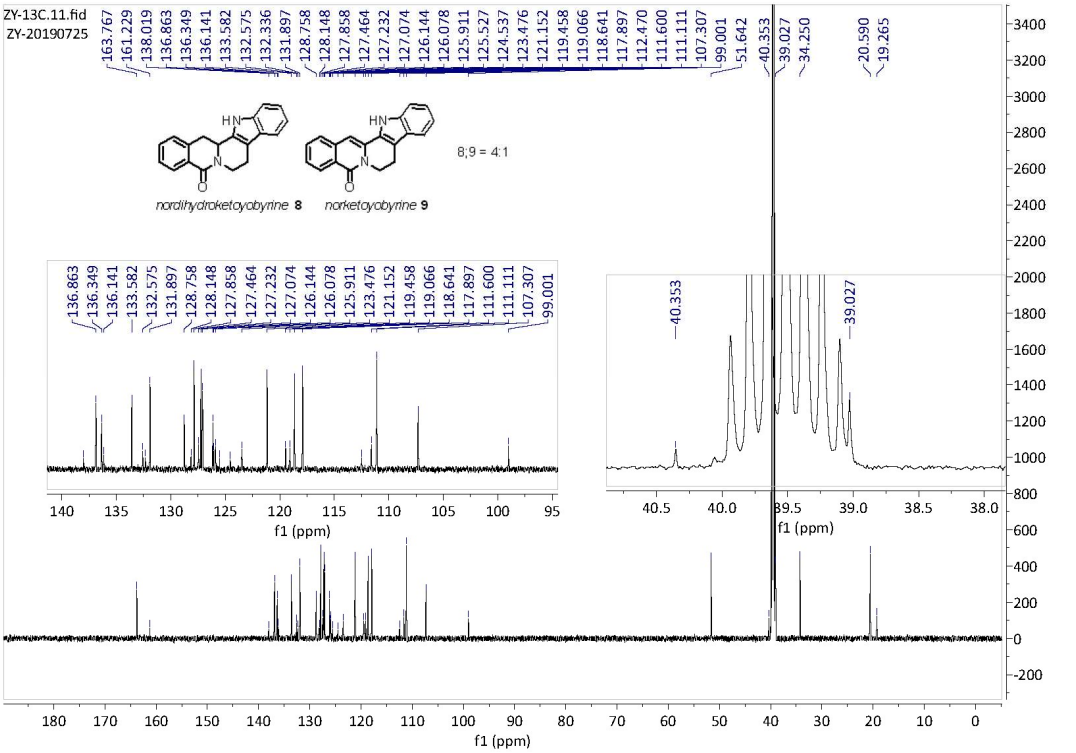
2-(2-(1H-indol-3-yl)ethyl)isoquinolin-1(2H)-one 7



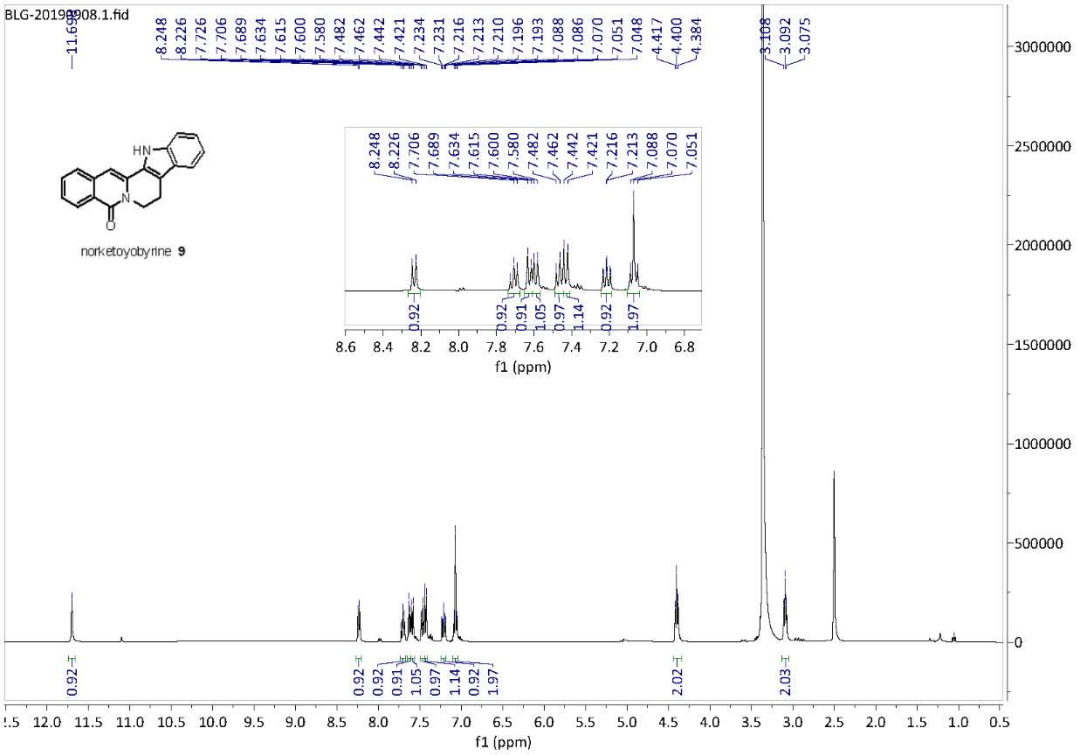


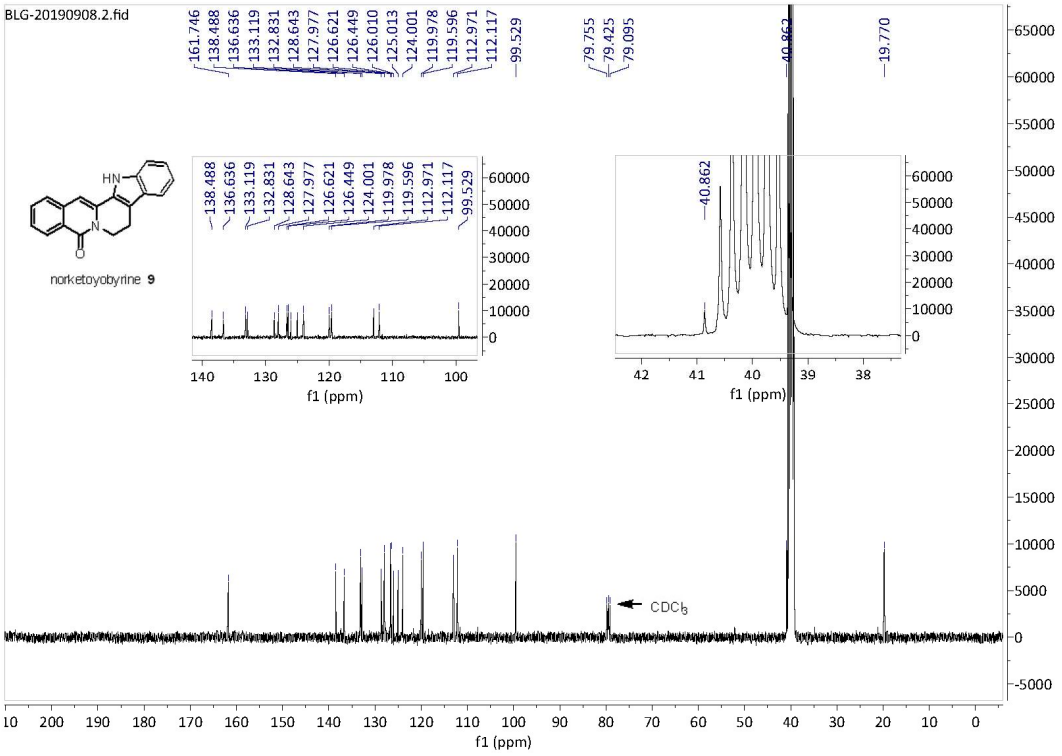
***Dihydronorketoyobyrine* 8 : *Norketoyobyrine* 9 = 4:1**





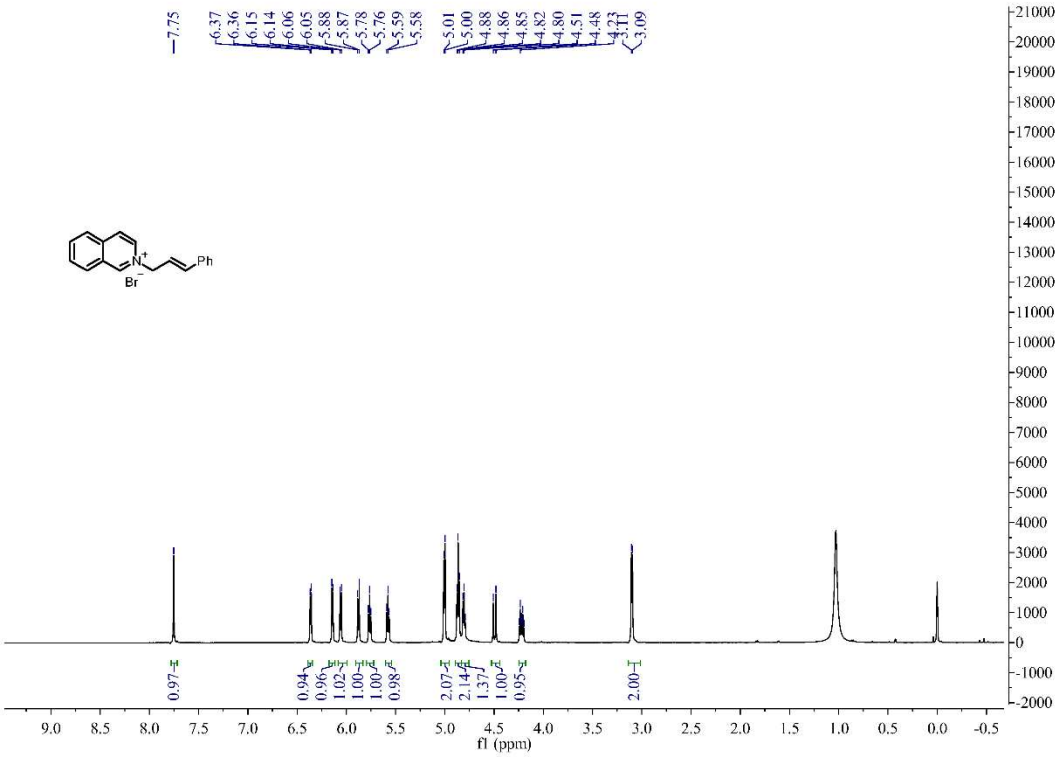
***Norketoyobyrine* 9**

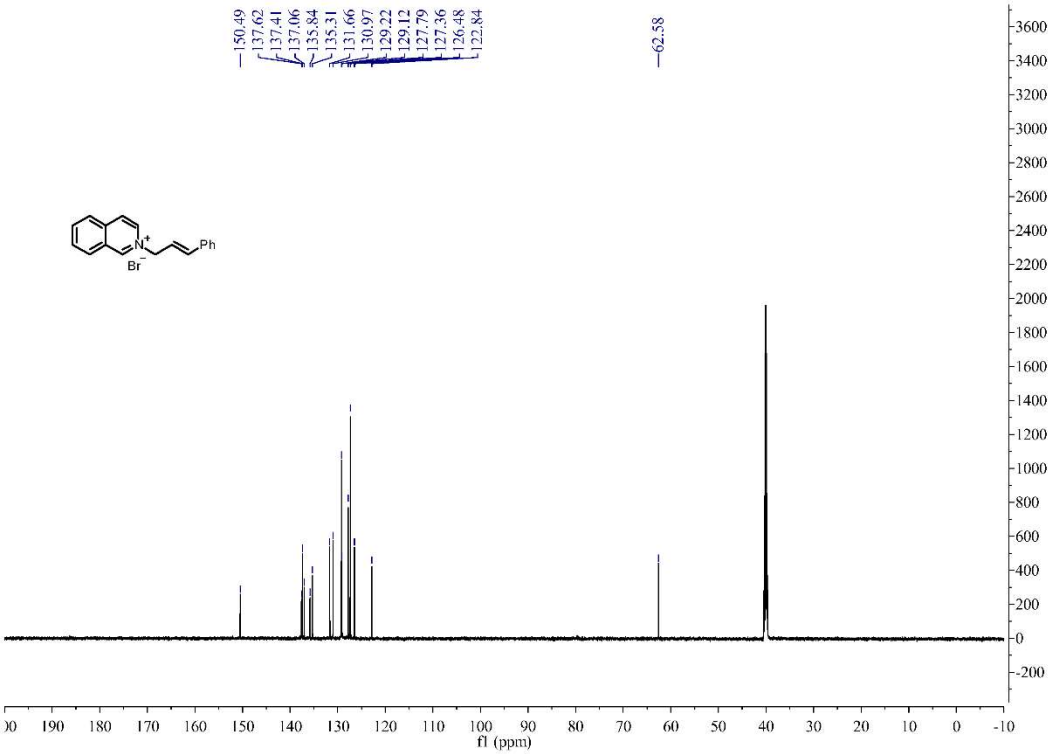




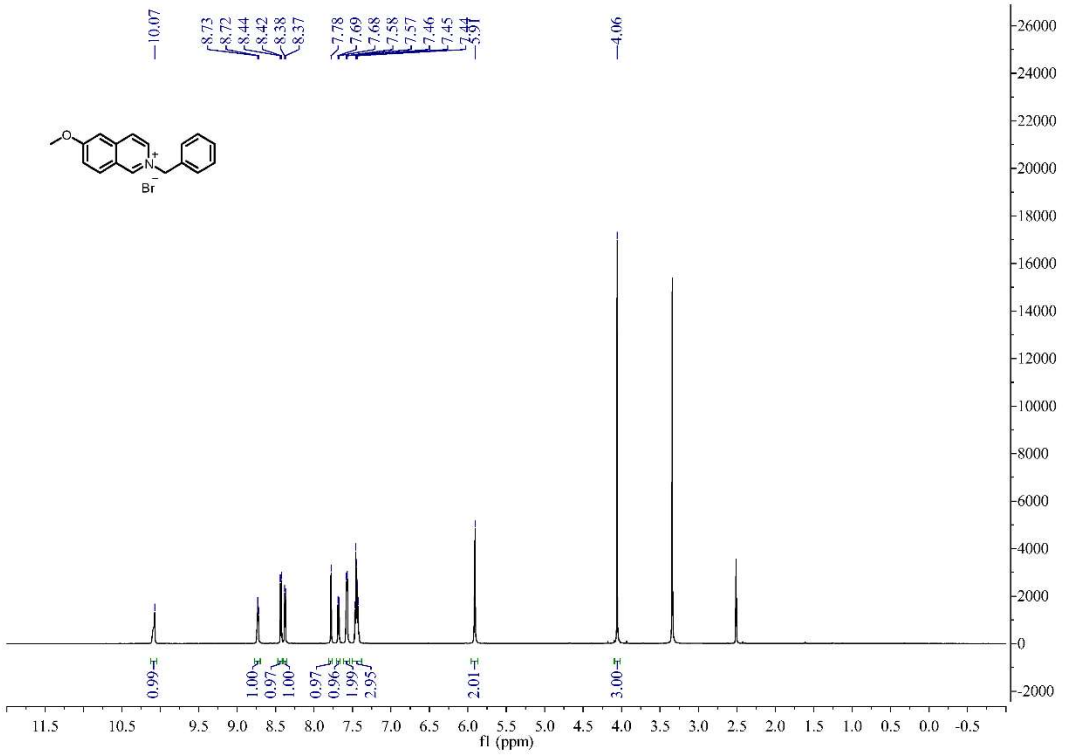
9.4 Spectra for the new compounds of substrates 1 & 3

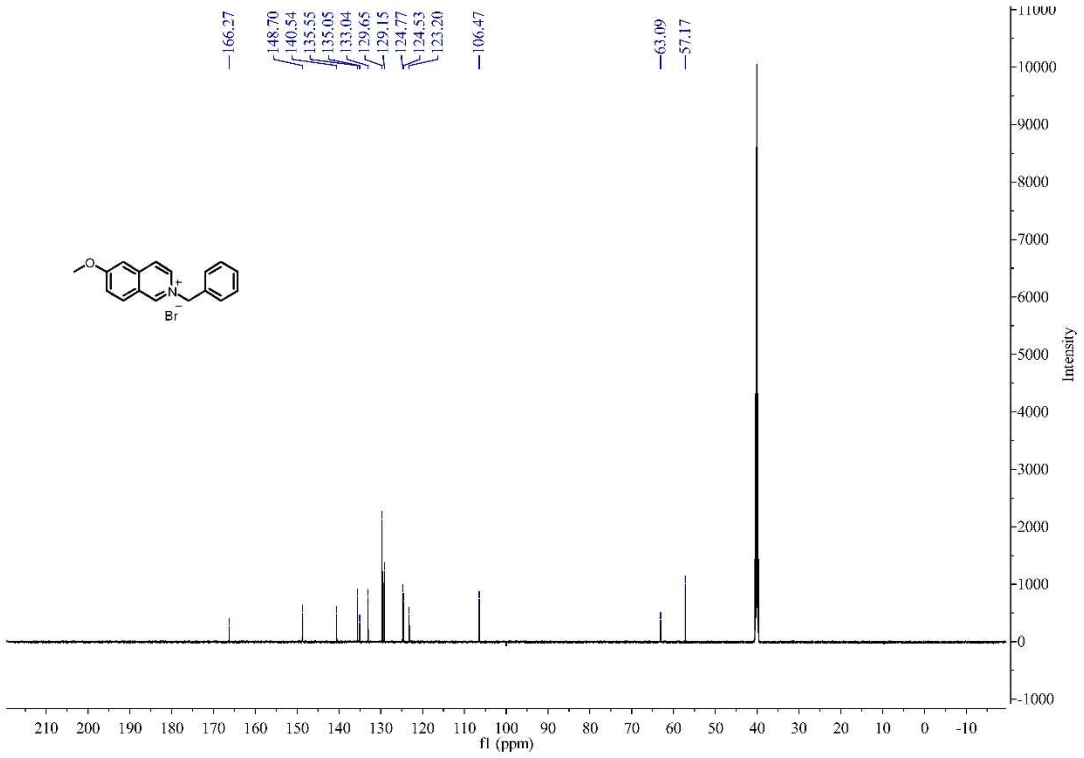
N-cinnamylisoquinolin-2-ium bromide (1k)



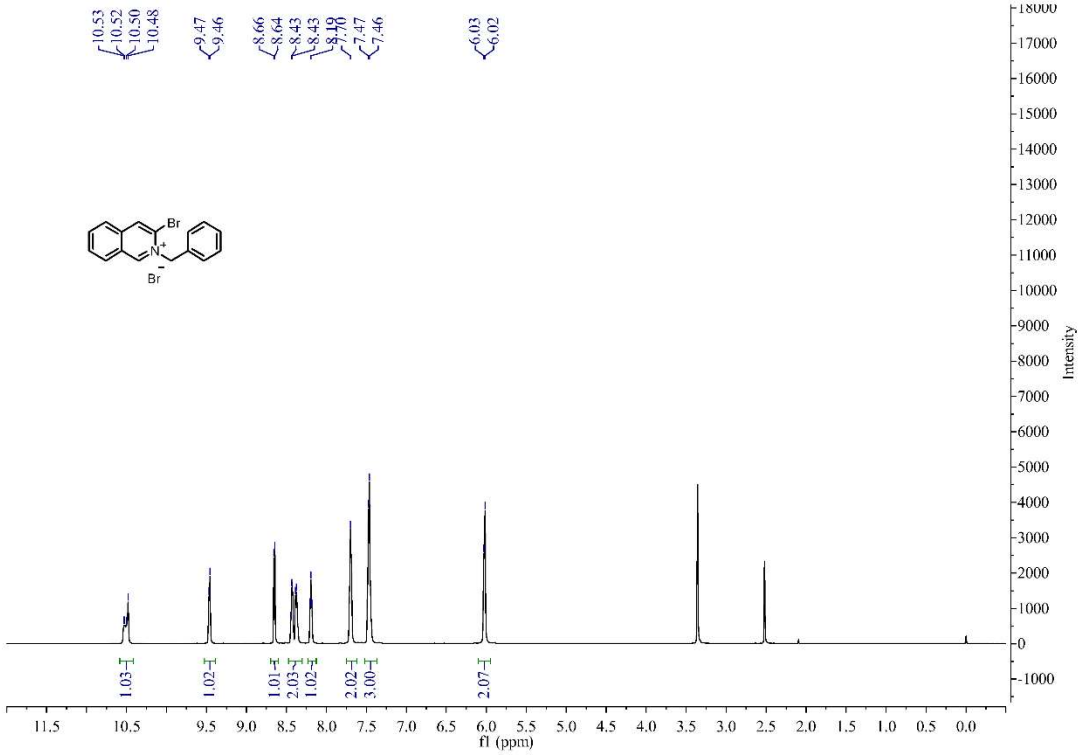


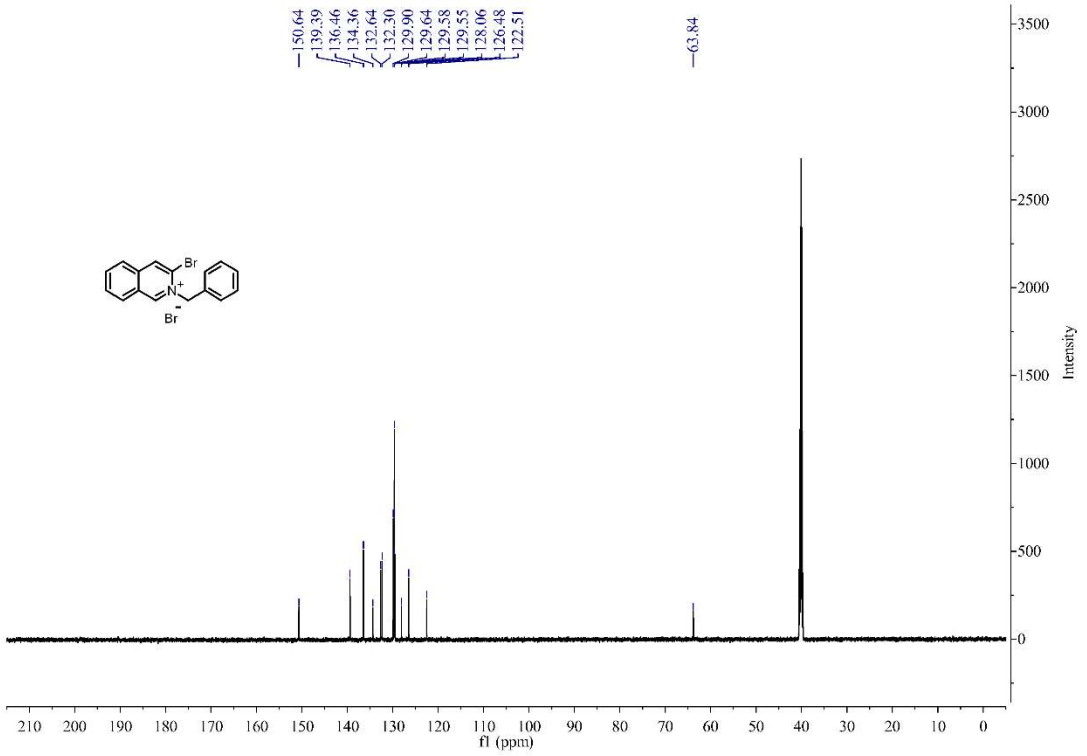
***N*-benzyl-6-methoxyisoquinolin-2-ium bromide (1s)**



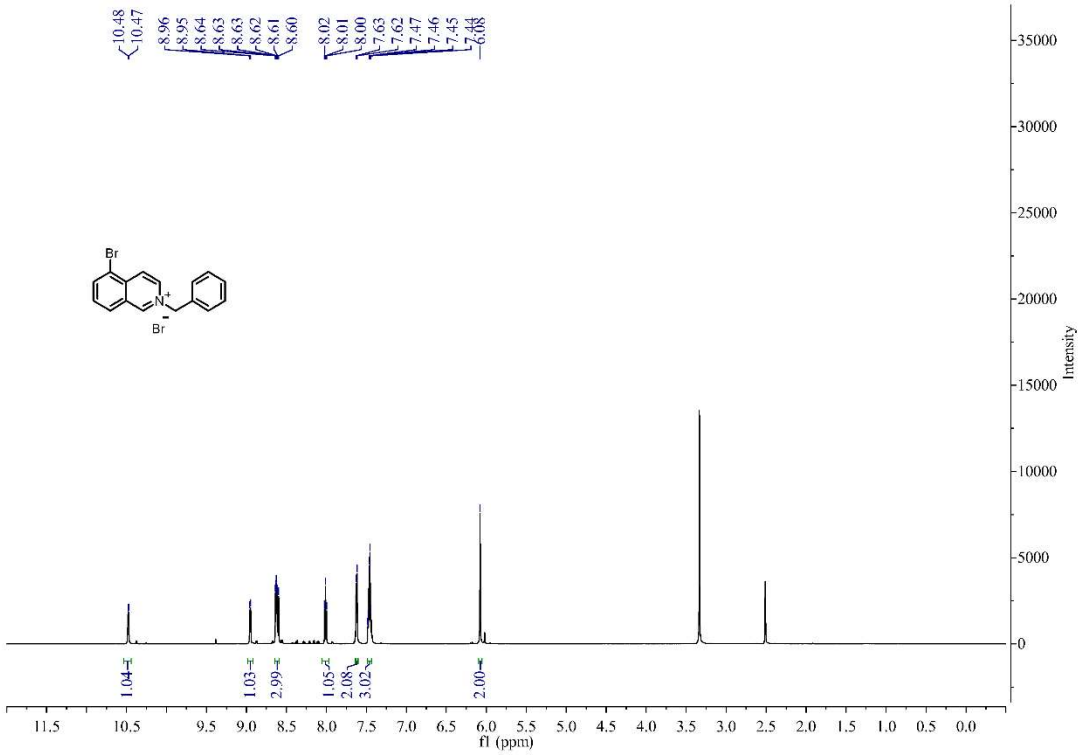


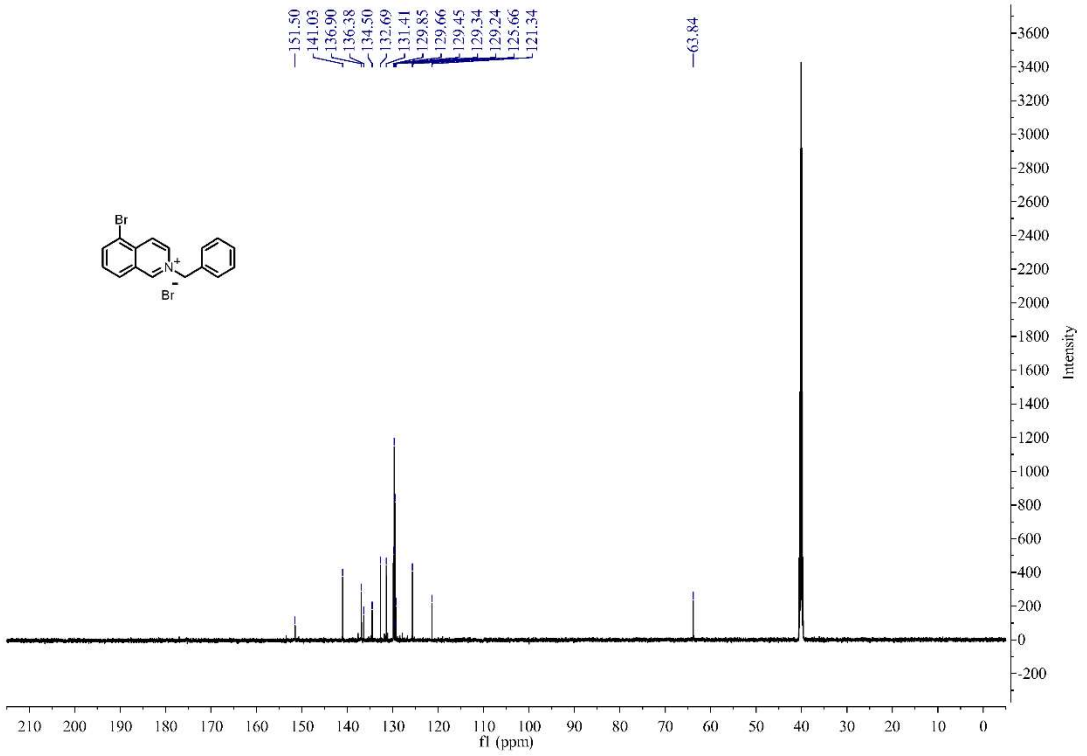
***N*-benzyl-3-bromoisoquinolin-2-ium bromide (1u)**





***N*-benzyl-5-bromoisoquinolin-2-ium bromide (1v)**





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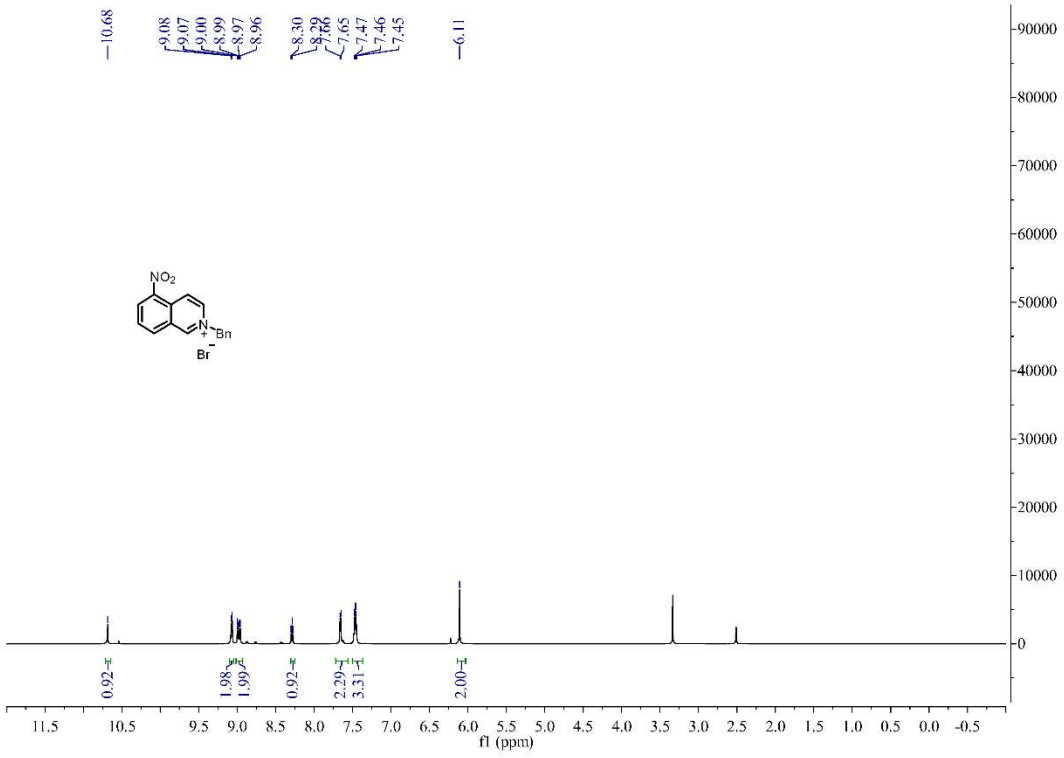
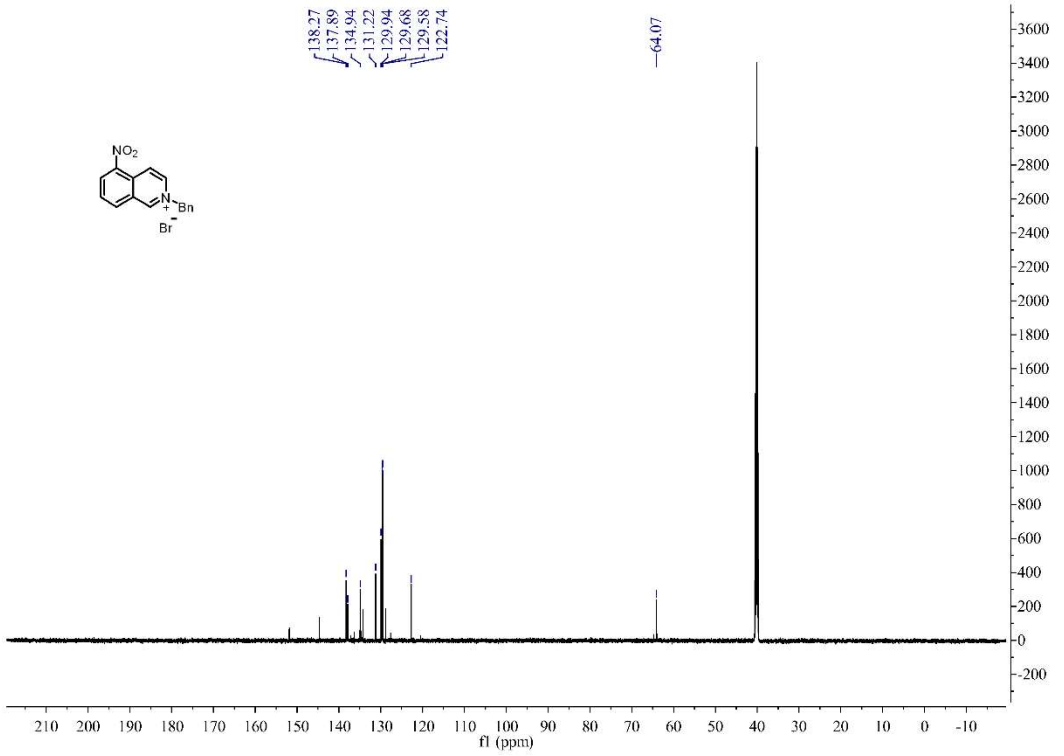
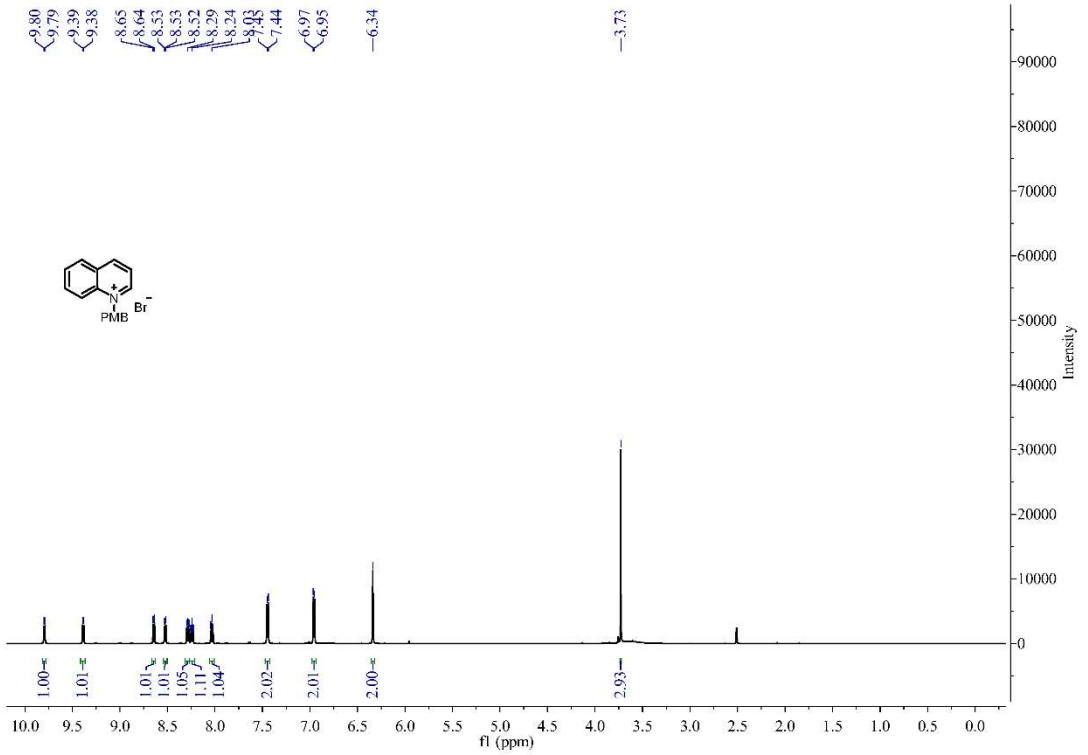
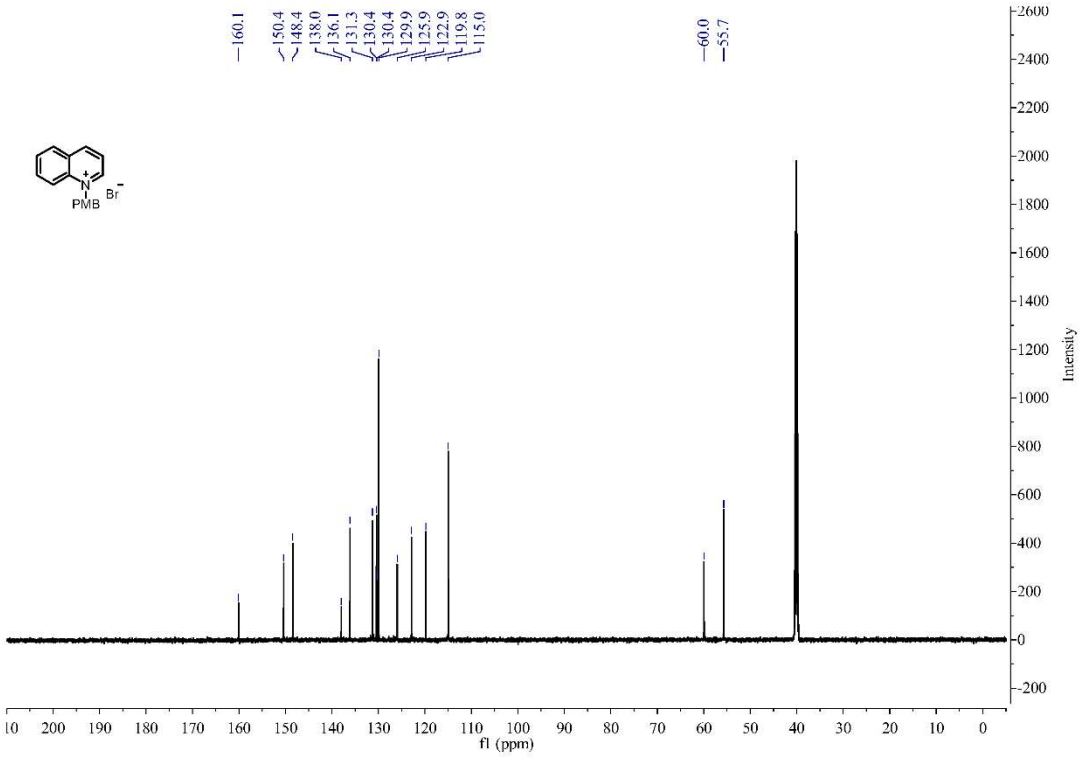


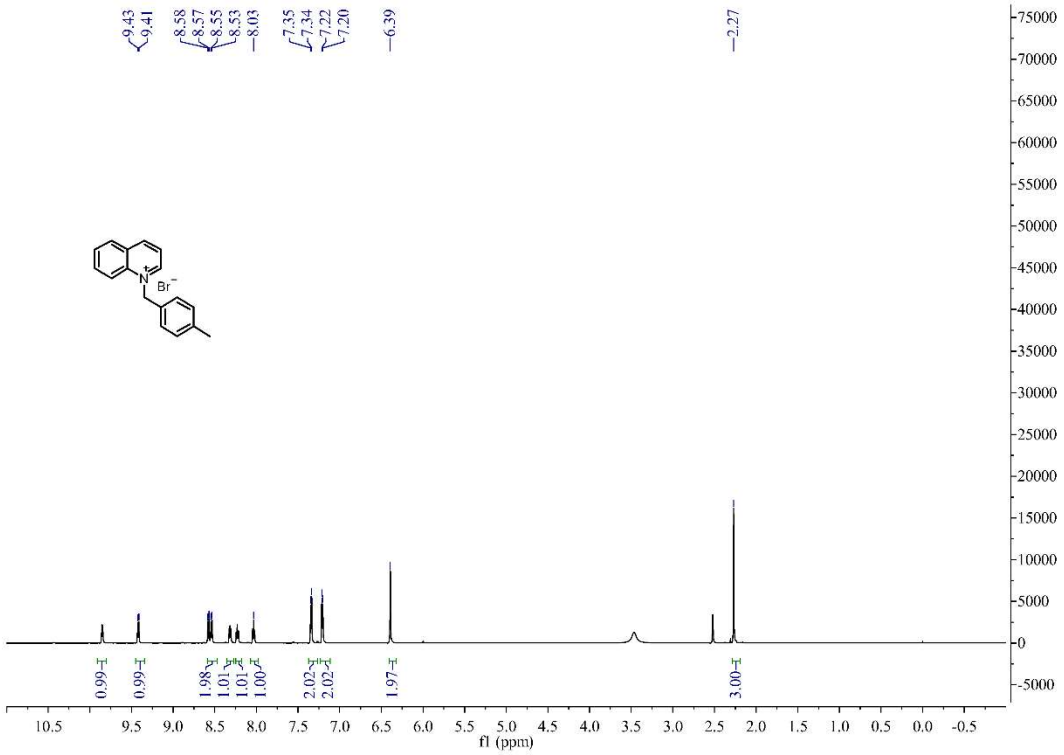


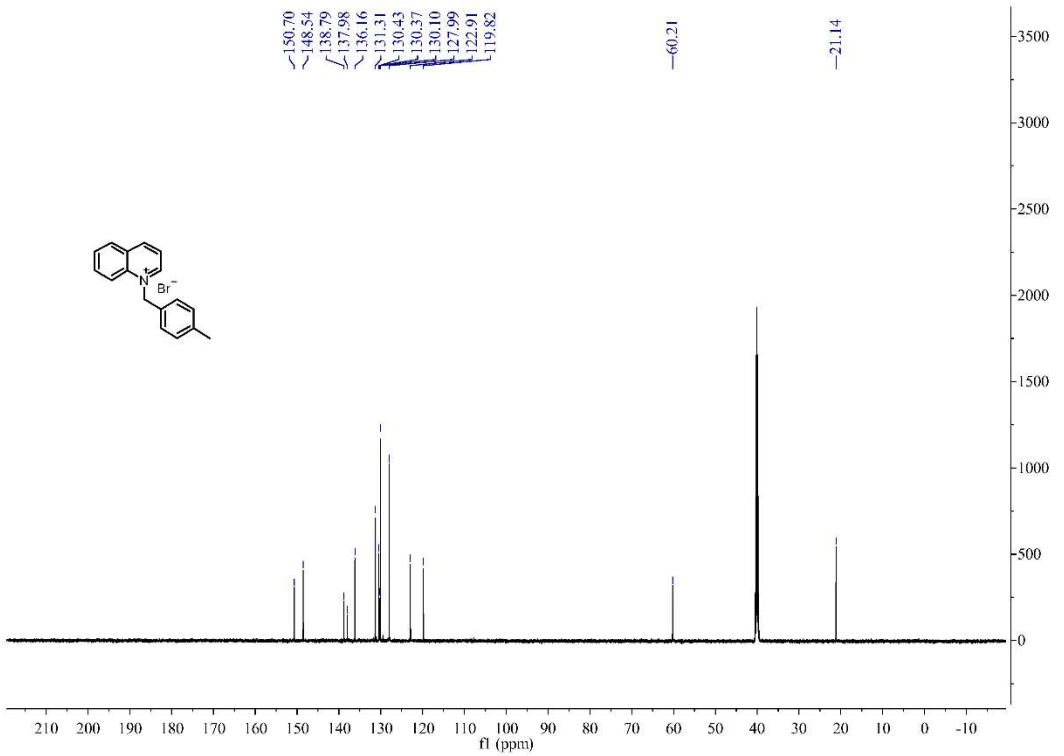
_N_-(4-methoxybenzyl)quinolin-1-ium bromide (3c)



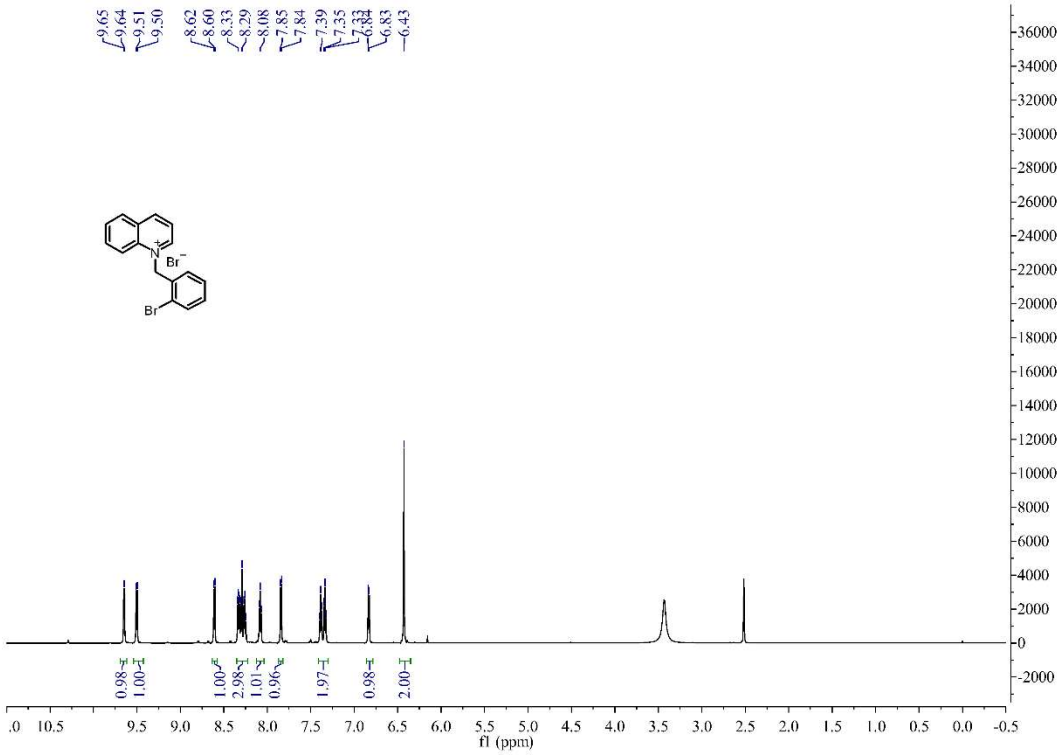


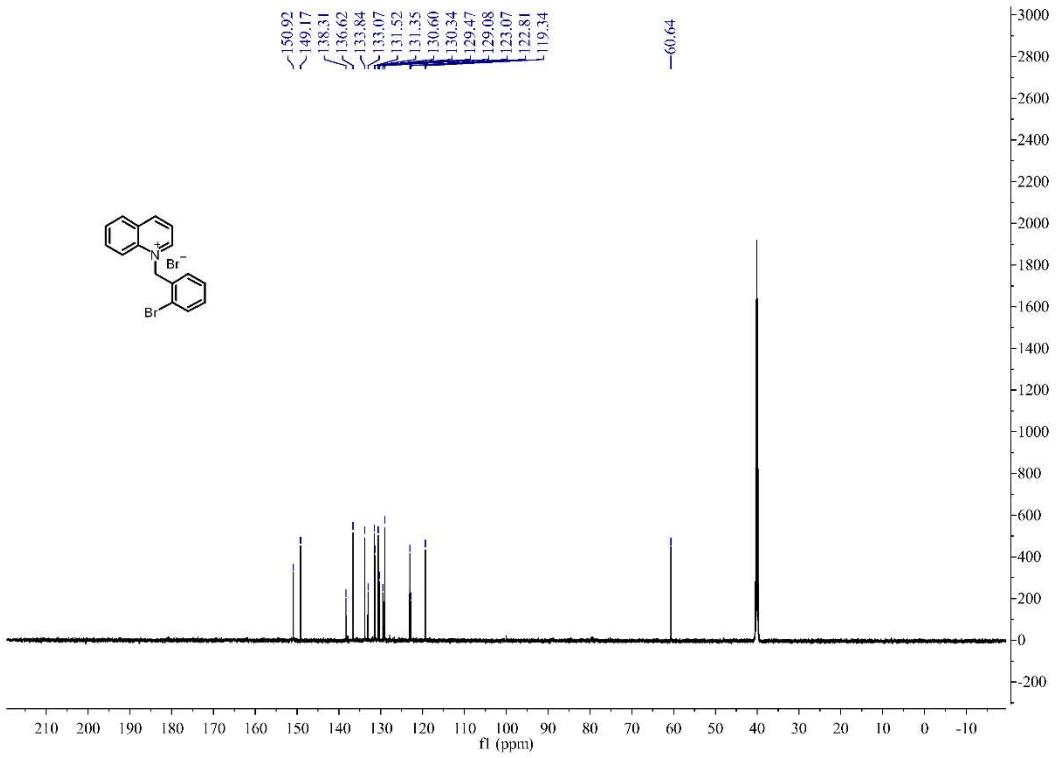
***N*-(4-methylbenzyl)quinolin-1-ium bromide (3d)**



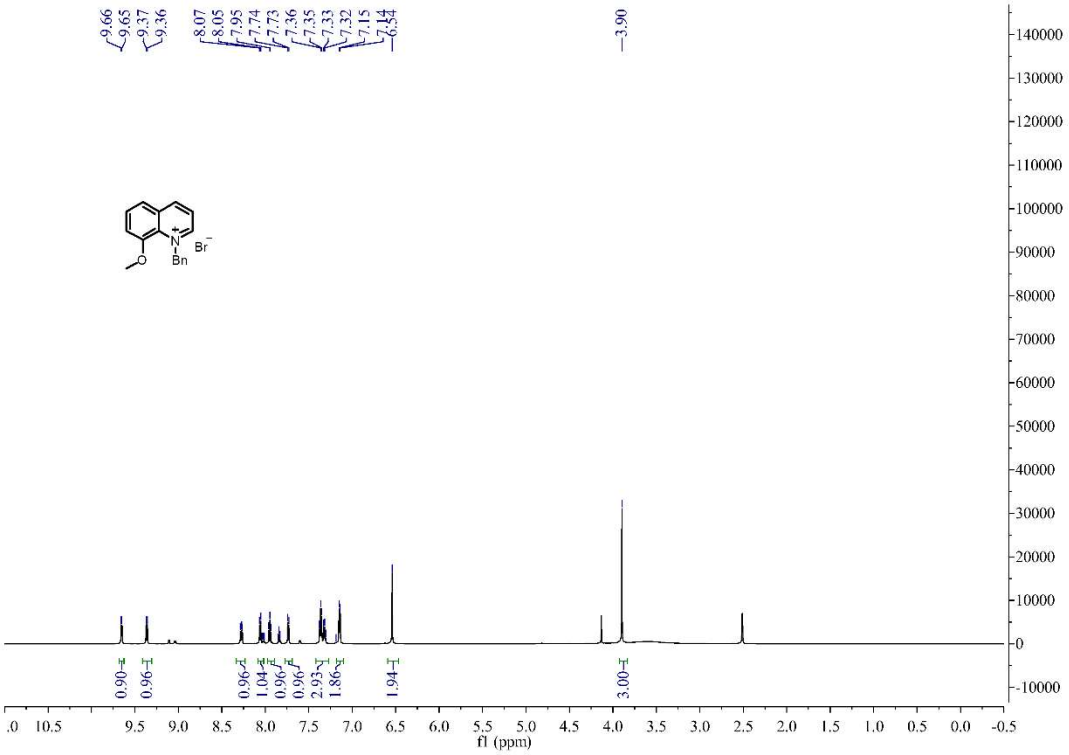


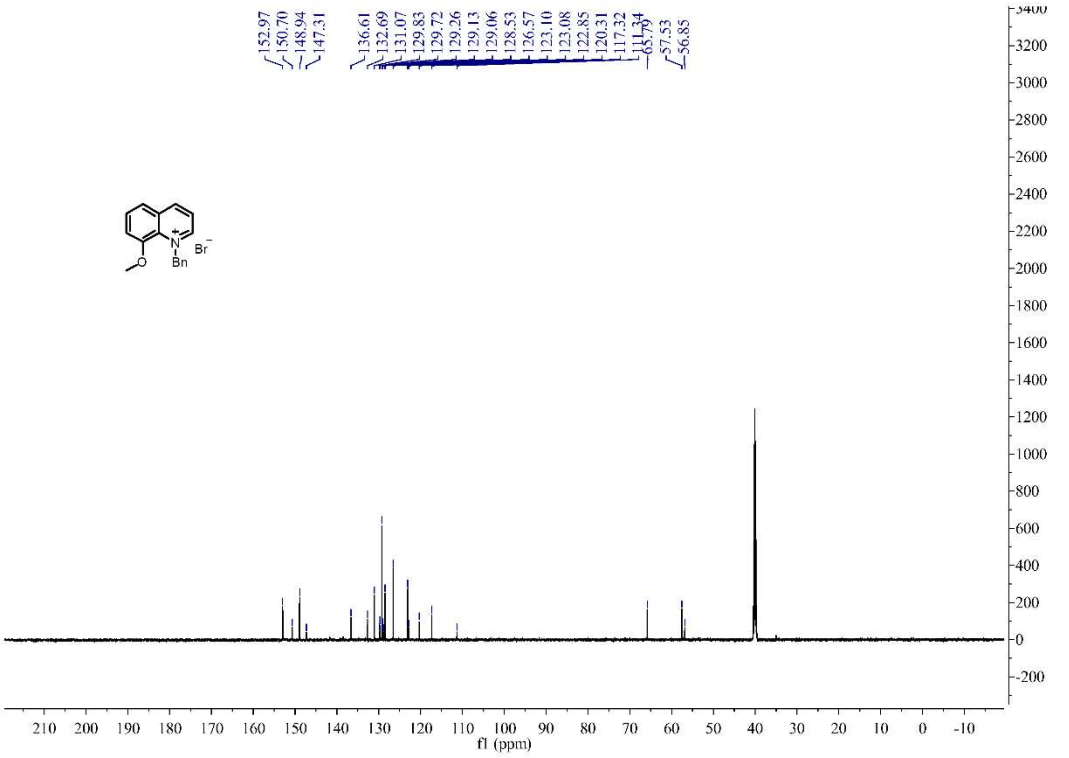
_N_-(2-bromobenzyl)quinolin-1-ium bromide (3e)



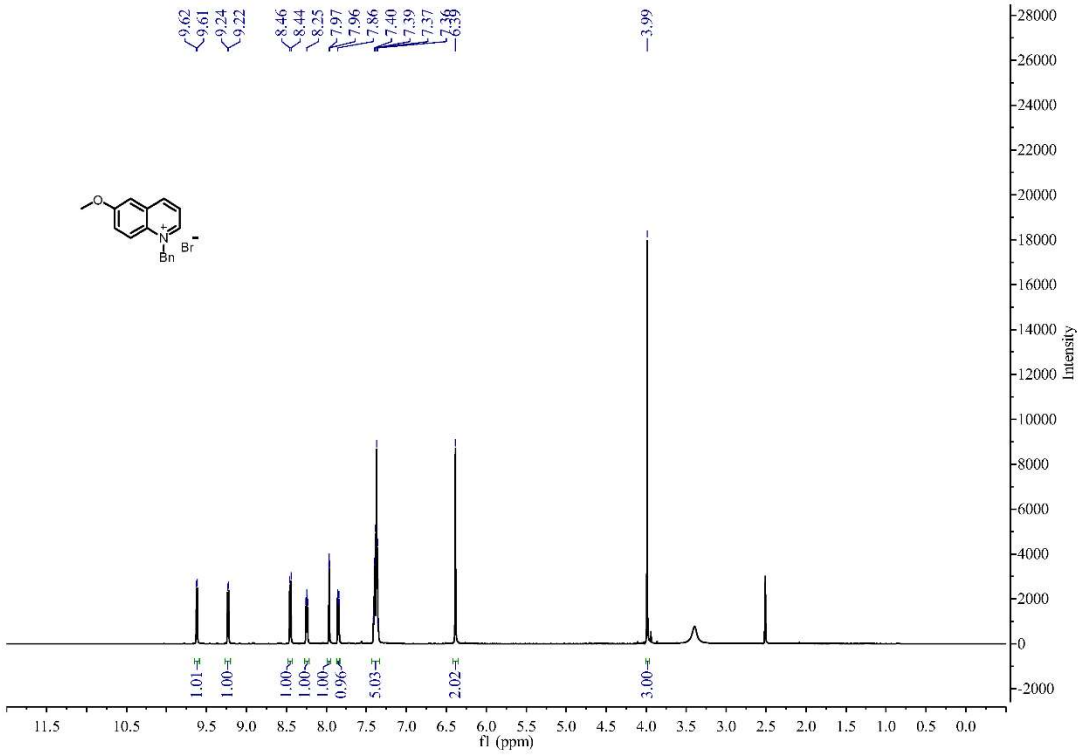


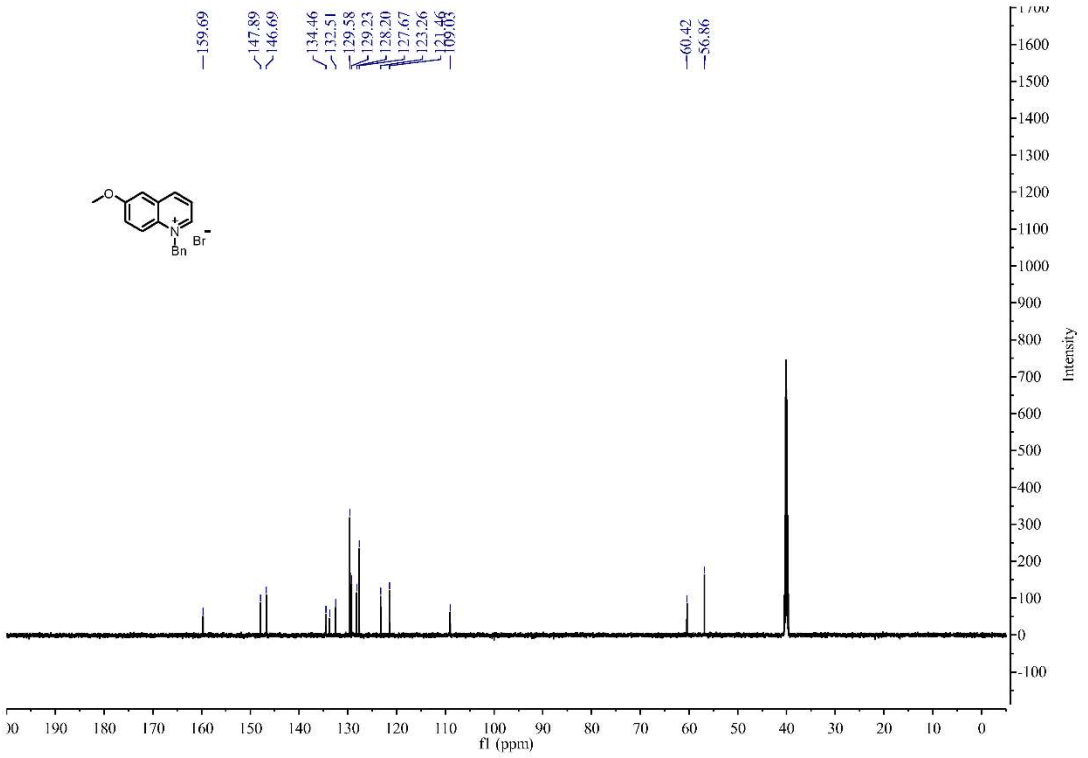
***N*-benzyl-8-methoxyquinolin-1-ium bromide (3f)**





***N*-benzyl-6-methoxyquinolin-1-ium bromide (3h)**





N-benzyl-6-bromoquinolin-1-ium bromide (3j)