Supporting Information

Expedient Delivery of Quinolinones via Traceless N-Nitroso Enabled Oxidative Heck/Amidation Cascade

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A. General Information

^{1}H and ^{13}C NMR spectra were recorded on BRUKER DRX-400 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); dt (doublets of triplet); dq (doublets of quartet). Coupling constants are reported as a J value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.0, triplet). Gas chromatograph mass spectra were obtained with a SHIMADZU model GCMS–QP 5000 spectrometer. HRMS was carried out on a MAT 95XP (Thermo).

B. General procedure:

1) Synthesis of N-Nitrosamine Substrates:

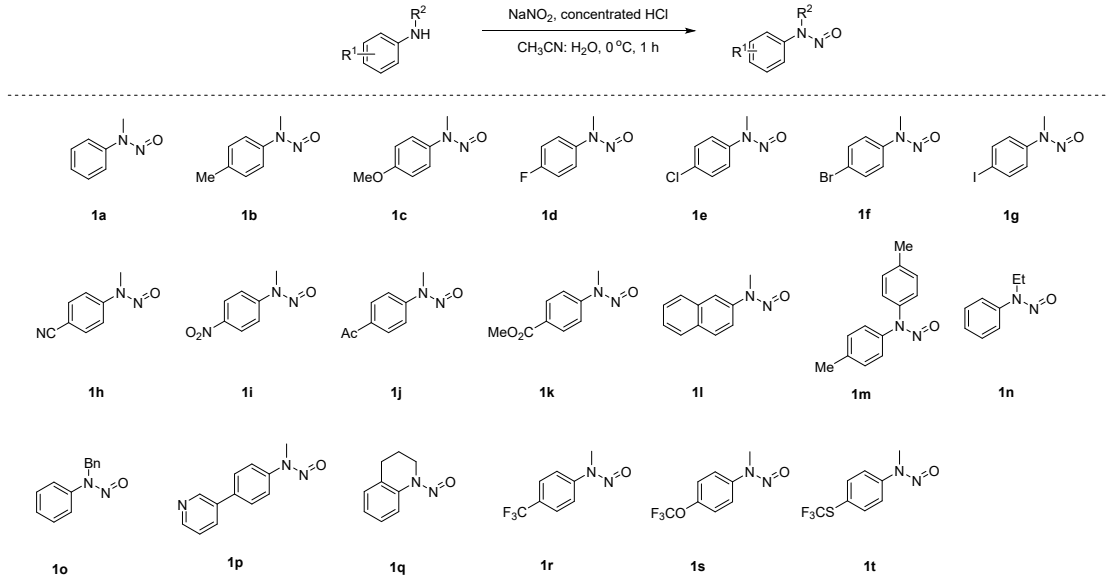


Figure S1. Synthesis of N-Nitrosamine Substrates.

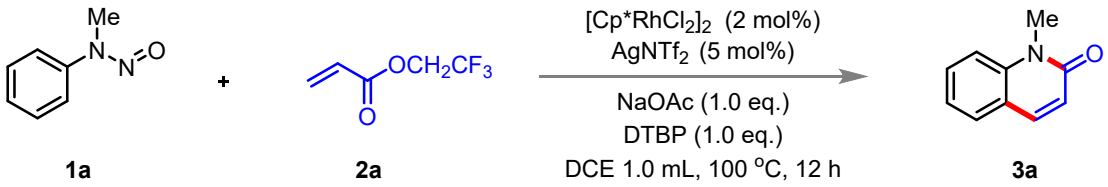
A mixture of aniline (e.g., N-methylaniline, 1.07 g, 10 mmol), concentrated HCl (1.3 ml, 5 equiv.) and ice (5 g) was placed in a round bottomed flask and stirred at low temperature. To this mixture was added an aqueous solution (13 mL) of $NaNO_2$ (0.7 g, 10 mmol) over the course of 5 to 10 min. The reaction was allowed to proceed for at least 1 h. The mixture was then extracted with DCM. The organic phase was washed with saturated brine solution, dried and dehydrated, and the solvent was removed under reduced pressure.[1]

2) General procedure for N-NO as traceless, internal oxidizing DG enabled oxidative Heck & amidation cascade:

An oven-dried 10 mL Schlenk Tube was charged with N-nitroso anilines **1** (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.3 mmol) in sequence, followed by adding acrylate **2** (0.3 mmol) in DCE (1.0 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired annulation products **3**.

3) Investigation of reaction conditions:

a) Standard conditions:



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

Figure S2. Standard conditions

After extensive investigations of this oxidative Heck and amidation cascade, the optimal condition is: N-nitroso aniline **1a** (0.2 mmol), acrylate **2a** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol), DTBP (0.2 mmol), DCE 1.0 mL.

b) Investigation of acrylic acid derivatives:

We also investigated an array of acrylic acid derivatives for this oxidative Heck and amidation cascade, as summarized in **Figure S3**, sterically hindered *tert*-butyl acrylate **2d**, exhibited comparable efficiency compared to **2a**, while methyl acrylate **2b**, ethyl acrylate **2c**, acrylic acid **2e**. Intriguingly, highly steric hindered acrylate **2f** showed no reactivity for this oxidative Heck cascade. Notably, acrylate anhydride **2g** and **2h**, acryloyl chloride **2i**, N-(*tert*-butyl)acrylamide **2j** could not serve as amenable substrates for this quinolinone synthesis.

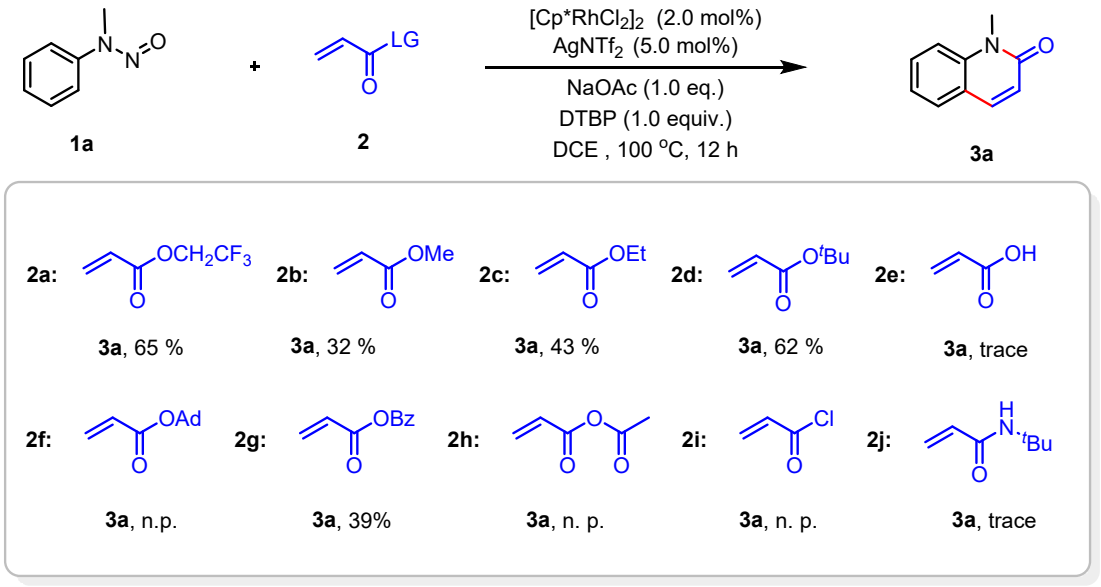
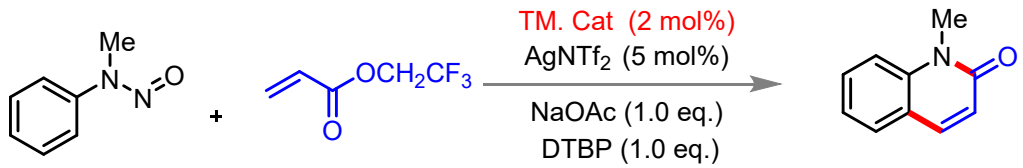


Figure S3. Effect of acrylic acid derivatives for this oxidative Heck cascade

c) Evaluation of metal catalysts:

As depicted in **Figure S4**, metal catalyst candidates investigation revealed that Rh(III) gave optimal result for this oxidative Heck/amidation enabled by N-nitroso aniline as the traceless, internal oxidizing directing groups. However Ru(II) exhibited low yield, while other metal salts including Pd(II), Ir(III), Co(III) and Co(II) showed no catalytic efficiency.



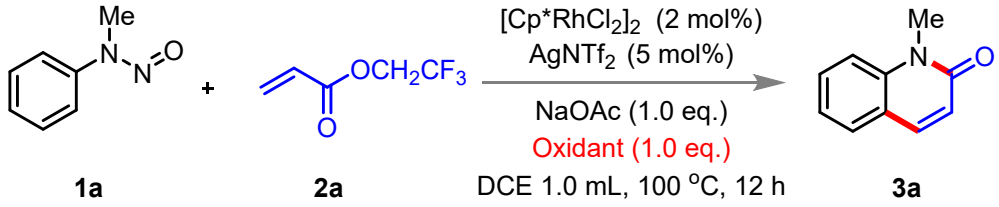
1a **2a** **3a**

Entry	Variation of standard conditions	Yield (%)
1	$[Cp^*RhCl_2]_2$	**72**
2	$[Cp^*IrCl_2]_2$ instead of $[Cp^*RhCl_2]_2$	n. p.
3	$[Ru(p\text{-cymene})Cl_2]_2$ instead of $[Cp^*RhCl_2]_2$	22
4	$Pd(OAc)_2$ instead of $[Cp^*RhCl_2]_2$	n. p.
5	$[Cp^*Co(CO)I_2]$ instead of $[Cp^*RhCl_2]_2$	n. p.
6	$Co(NTf_2)_2$ instead of $[Cp^*RhCl_2]_2$	n. p.
7	without $[Cp^*RhCl_2]_2$	n. p.

Figure S4. Effect of various catalysts for this oxidative Heck cascade

d) Evaluation of Oxidant:

Extensive investigation of various oxidant for this oxidative Heck/amidation cascade for the quinolinone **3a** synthesis enabled by N-nitroso aniline **1a** with acrylate **2a** indicated that DTBP gave the optimal result (**Figure S5**). Control experiment showed that the addition of DTBP improve the efficiency, significantly, the absence of DTBP under N_2 atmosphere led to only trace amount of the desired quinolinone **3a**. Notably, 30% H_2O_2 solution gave a slightly lower yield. However, Na_2CO_3•$1.5H_2O_2$ and TBHP delivered no desired quinolinone product **3a**.



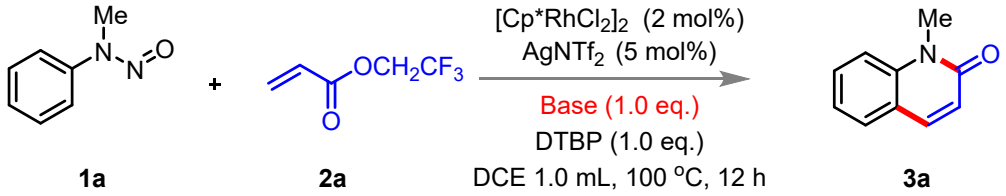
1a **2a** **3a**

Entry	Variation of standard conditions	Yield (%)
1	DTBP	**72**
2	without DTBP, under air	55
3	without DTBP, under N_2 atmosphere	trace
4	$Cu(OAc)_2$ (1.0 equiv.) instead of DTBP	70
5	$Cu(OAc)_2$ (30 mol%), air instead of DTBP	61
6	$Na_2CO_3 \cdot 1.5\ H_2O_2$ instead of DTBP	trace
7	TBHP instead of DTBP	n. p.
8	30% H_2O_2 instead of DTBP	32

Figure S5. Effect of oxidants for this oxidative Heck cascade

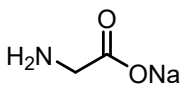
e) Evaluation of Base:

Various base metal carboxylates were investigated, as depicted in **Figure S6**, the carboxylate played a crucial role for this oxidative Heck/amidation cascade for the quinolinone **3a** synthesis. Control experiment indicated that no desired product 3a was observed, in the absence of sodium carboxylate. Electron-deficient CF_3CO_2Na or sterically hinderance $MesCO_2Na$ or PivONa gave lower efficiency. Sodium carbonate could also deliver to the desired quinolinone **3a** in moderated yield. Control experiments sodium cationic ion exhibited a crucial role for this oxidative Heck cascade, and cesium acetate, potassium acetate afforded no desired product. Amino acid derived sodium salt or that contained coordinating effect, eg., sodium isonicotinate gave no desired quinolinone product **3a**.

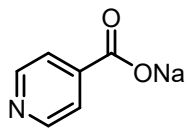


1a **2a** **3a**

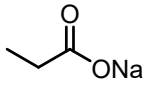
Entry	Variation of standard conditions	Yield (%)
1	NaOAc	**72**
2	Without NaOAc	n. p.
3	CF_3CO_2Na instead of NaOAc	33
4	$MesCO_2Na$ instead of NaOAc	27
5	PivONa instead of NaOAc	47
6	Na_2CO_3 instead of NaOAc	43
7	CsOAc instead of NaOAc	n. p.
8	KOAc instead of NaOAc	n. p.
9	sodium glycinate instead of NaOAc	n. p.
10	sodium isonicotinate instead of NaOAc	n. p.
11	sodium propionate instead of NaOAc	32



sodium glycinate



sodium isonicotinate

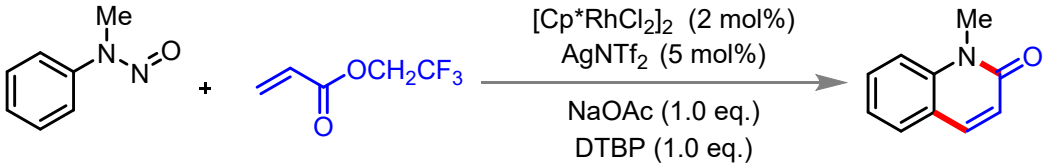


sodium propionate

Figure S6. Effect of base for this oxidative Heck cascade

f) Evaluation of acid:

As depicted in **Figure S7**, addition of acids gave inferior yields for the formation of quinolinone product **3a**, while the use of PivOH or 1-$AdCO_2H$ as the solvent led to totally shut down of this oxidative Heck and amidation cascade.



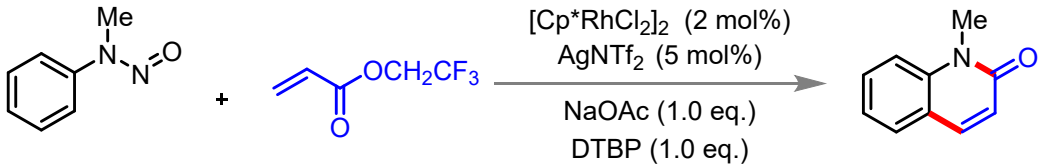
1a **2a** **3a**

Entry	Addition of acid	Yield (%)
1	None	**72**
2	HOTf	45
3	HOTs	34
4	HOAc	52
5	PivOH	n. p.
6	$AdCO_2H$	n. p.

Figure S7. Effect of acids for this oxidative Heck cascade

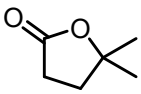
g) Evaluation of solvent:

As summarized in **Figure S8**, solvent screening revealed that DCE was optimal, acetic acid and TFE were also amenable solvent for this oxidative Heck/amidation cascade. Other solvents including THF, ^{t}BuOH, 5,5-Dimethyl-dihydro-furan-2-one, L-Methyl Lactate gave no desired product **3a**.

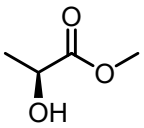


1a **2a** **3a**

Entry	Solvent	Yield (%)
1	DCE	**72**
2	AcOH	58
3	TFE	44
4	THF	n. p.
5	^{t}BuOH	n. p.
6	5,5-Dimethyl-dihydro-furan-2-one	n. p.
7	L-Methyl Lactate	n. p.



5,5-Dimethyl-dihydro-furan-2-one



L-Methyl Lactate

Figure S8. Effect of solvents for this oxidative Heck cascade

C. Preliminary mechanism studies:

1) H/D exchange experiments

An oven-dried 10 mL Schlenk Tube was charged with N-nitroso aniline **1a** (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.2 mmol) in sequence, rinsed with nitrogen three times, followed by adding CD_3OD (0.1 mL) and DCE (1.0 mL) through syringe. The mixture wasstirred at 100 °C for 12 h and then diluted with 3 mL of CH_2Cl_2. The solution was filtered through a celite pad and washed with 15-20 mL of CH_2Cl_2. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 20/1, v/v) to provide **$[D_n]$-1a**. The deuterated ratio was calculated from ^1H NMR analysis (**Figure S9**).

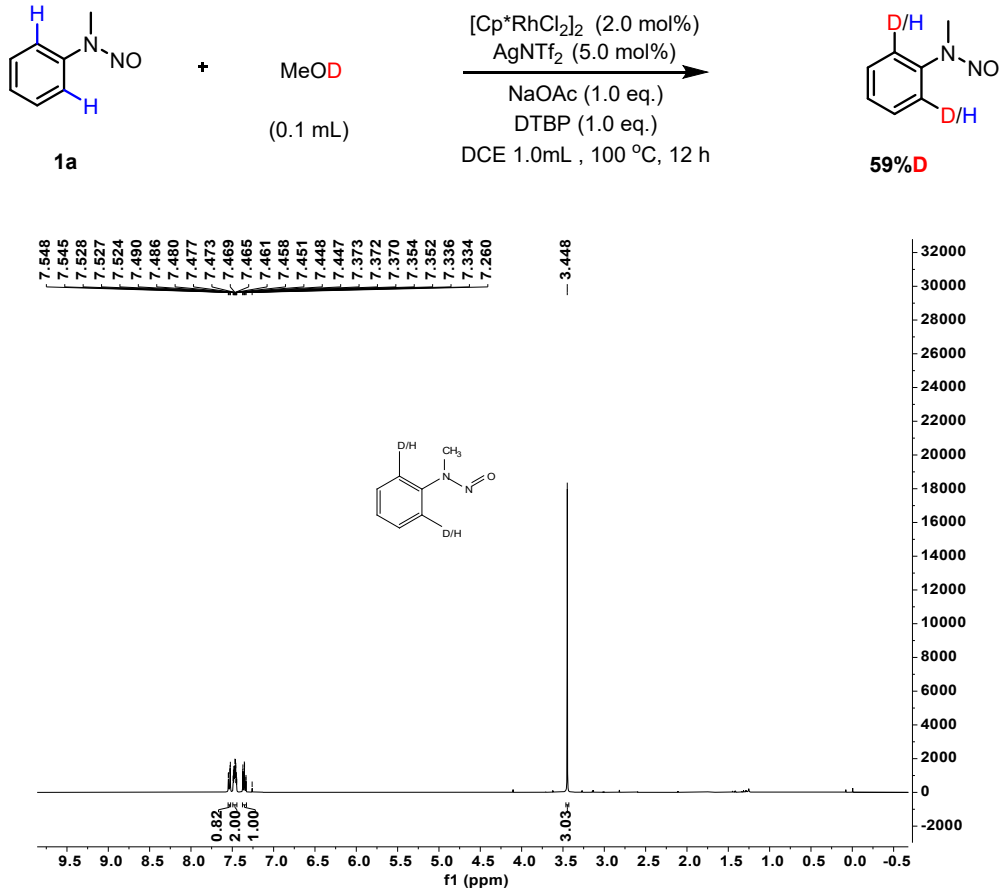


Figure S9. H/D exchange experiments

2) Competing experiments

To a 20 mL test tube with a stirring bar, N-methylnitrous amide **1b** (0.2 mmol) and **1c** (0.2 mmol), acrylate **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol), DTBP (0.2 mmol), DCE (1.0 mL) were added under air, and the mixture was stirred at 100 °C for 12 hours. After cooling down, the volatiles were removed and the mixture was purified by flash chromatography of silica gel. The product **3b** and **3d** were isolated and combined. The ratio of **3b**/**3d** = 3/(3,75-3.00) = 4.0 was determined by ^{1}H NMR analysis (**Figure S10**). These observations supported a base-assisted internal electrophile-type substitution (BIES) mechanism.

For weak coordination enabled C-H functionalization that proceed via BIES mechanism: a) Q. Bu, T. Rogge, V. Kotek, L. Ackermann, *Angew. Chem., Int. Ed.*, 2018, **57**, 765–768; b) I. Choi, A. M. Messinis, L. Ackermann, *Angew. Chem., Int. Ed.*, 2020, **59**, 12534–12540; c) T. Rogge, J. C. A. Oliveira, R. Kuniyil, L. Hu, L. Ackermann, *ACS Catal.*, 2020, **10**, 10551−10558; d) U. Dhawa, C. Tian, W. Li, L. Ackermann, *ACS Catal.*, 2020, **10**, 6457−6462.

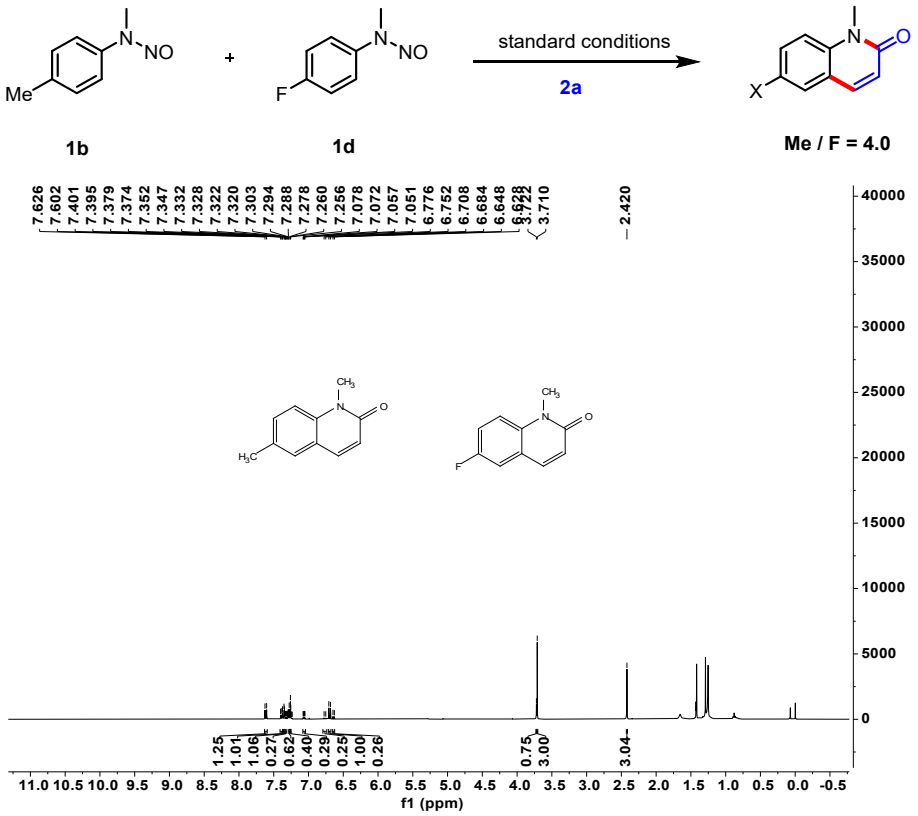


Figure S10. Competing experiments

3) Proposed pathways

To obtain some insight, we conducted the following experiments to elucidate which pathway might be involved for the quinolinone synthesis via oxidative Heck and amidation cascade (**Figure S11**):

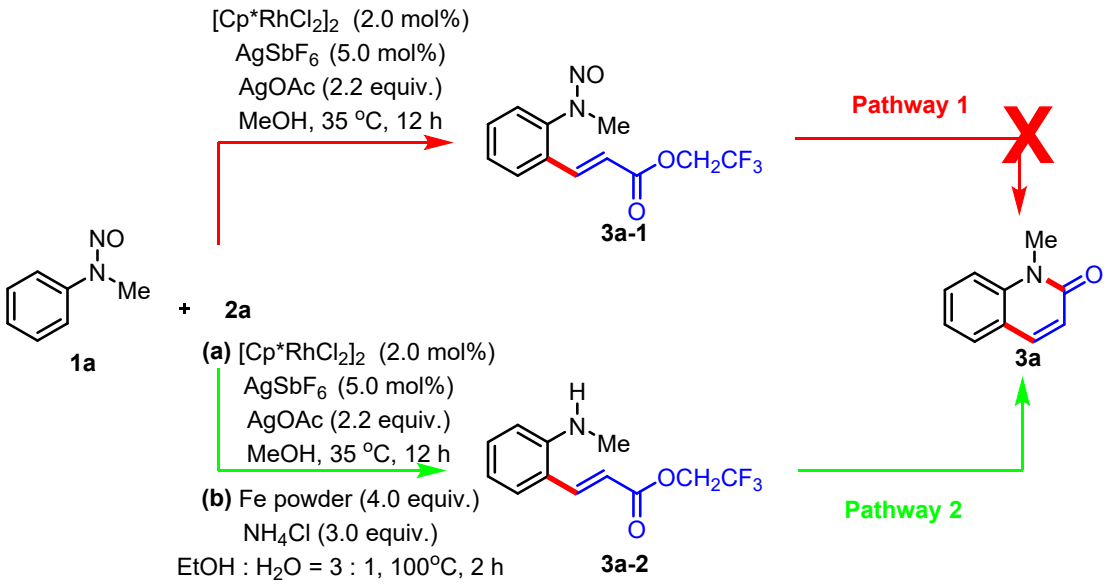


Figure S11. Possible pathways for the quinolinones delivery via oxidative Heck cascade

a) To explore the reaction pathway I, the following two possible intermediates were prepared in advance, to our surprise, ortho-olefinated N-nitrosoaniline **3a-1** exhibited no reactivity for the generation of **3a** under standard Rh(III) catalysis.

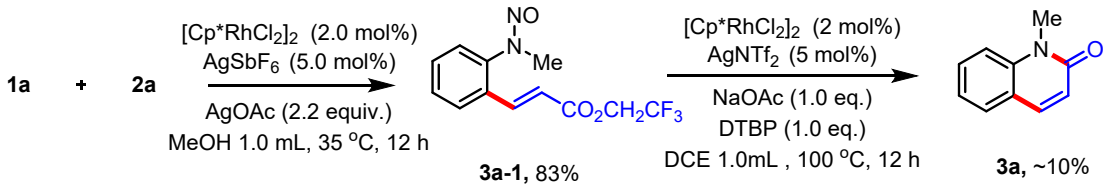


Figure S12. Pathway I

Specific operations are as follows: An oven-dried 10 mL Schlenk Tube was charged with N-nitroso aniline **1a** (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgSbF_6$

(0.01 mmol), AgOAc (0.44 mmol) in sequence, rinsed with nitrogen three times, followed by adding acrylate **2a** (0.3 mmol) in MeOH (1.0 mL) through syringe. The resulting reaction mixture was stirred at 35 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the product **3a-1**.[2]

When **3a-1** is used as the reaction substrate, only trace amounts of the target product are generated, so **3a-1** cannot be used as an intermediate in this reaction. Intriguingly, when performing reduction reaction of **3a-1** to the possible intermediate **3a-2**, quinolinone **3a** was obtained in high yield, mediated by iron powder or CuCl. It was speculated that a reduction followed by intramolecular amidation cascade proceed smoothly, which might be catalyzed by the oxidized Cu(II) or Fe(II or III) salt.

Further treatment of the pre-synthesized ortho-olefin aniline **3a-2** under the standard conditions led to the desired quinolinone **3a** in good efficiency.

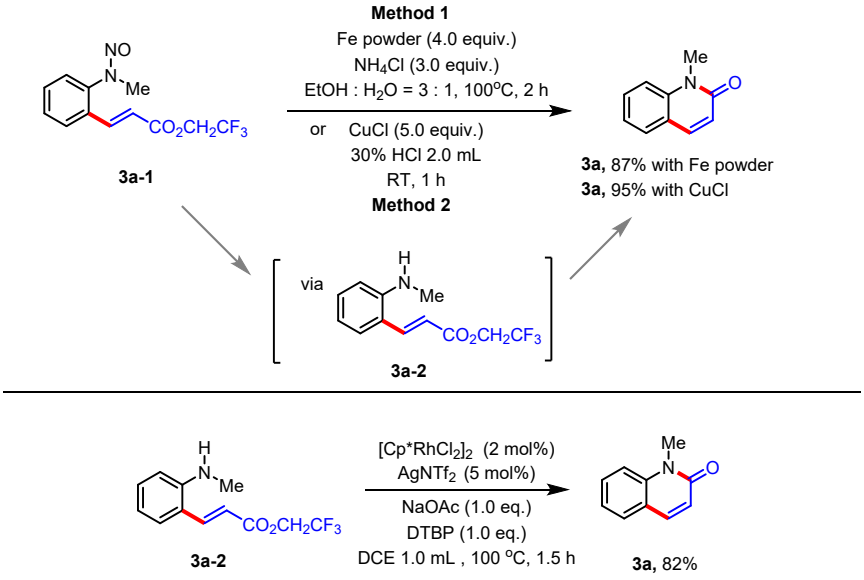


Figure S13. Pathway II

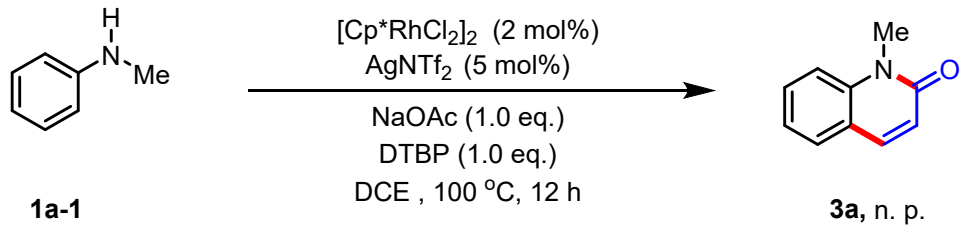
Specific operations are as follows**:**

Method 1: An oven-dried 10 mL Schlenk Tube was charged with acrylate **3a-1** (0.2 mmol), Fe powder (0.8 mmol), NH_4Cl (0.6 mmol) in sequence, followed by adding EtOH (1.5 mL) and H_2O (0.5 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 2 h and then diluted with CH_2Cl_2 and filtered through diatomite.

Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the product **3a**.[3]

Method 2: An oven-dried 10 mL Schlenk Tube was charged with acrylate **3a-1** (0.2 mmol), CuCl (1.0 mmol) in sequence, followed by adding 30% HCl (2.0 mL) through syringe. The resulting reaction mixture was stirred at room temperature for 1 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the product **3a**.[4]

b) Meanwhile, the use of N-Me aniline **1a-1** under the standard condition via Rh(III) catalysis, no desired quinolinone product **3a** was obtained, with starting material **1a-1** fully recovered.



1a-1 **3a,** n. p.

Figure S14. N-Me Aniline as the substrate

c) Proposed mechanism

According to the literature and experimental observations, it was proposed that catalytically reactive Rh(III) species A was generated from Rh(III) pre-catalyst and AgNTf2 as the halide scavenger (Figure S15). Subsequently, N-nitroso serve as the key directing group to Rh(III) catalyst to facilitate the reversible *ortho* C–H cleavage. Further olefin coordination and migratory insertion gave rhodium species **D**, in which nitroso functionality is a bonding ligand on Rh(III) intermediate. Subsequently, β-H elimination and treatment of the in situ formed HOAc of **D** led to release of nitroso group to give aniline **3a-2**. Then, a facile intramolecular amidation of **3a-2** proceed smoothly, affording quinolinone products. Further oxidation of the released Rh(I) species to Rh(III) with DTBP, finished the whole catalytic cycle.

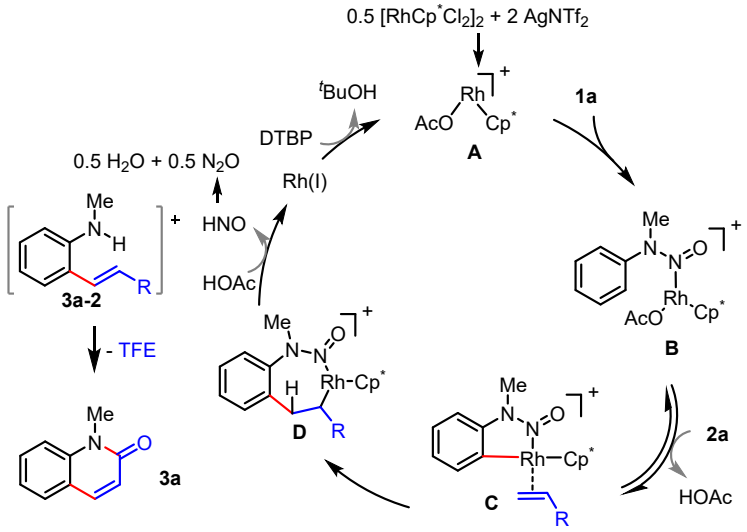


Figure S15. Proposed mechanism

D. Synthetic applications

1) Site-selective C-H activation: N-H quinolinone and C2-Cl quinoline synthesis

As summarized in **Figure S15**, N–H quinolinone and C2–Cl quinoline could be readily obtained via N-nitroso anilines enabled site-selective C–H activation.

Step 1: A solution of **3o** (0.2 mmol) in a 47% aqueous hydrobromic acid solution (2.0 mL) was heated under reflux. After 2h the solution was allowed to cool to room temperature and then neutralised with 1 M NaOH solution. The aqueous solution was extracted twice with CH_2Cl_2. The filtrate was concentrated and the residue was purified by column chromatography on silica gel to give quinolinone **3o-1**, which is a receptor antagonist for corticotropin releasing factor (CRF).[5]

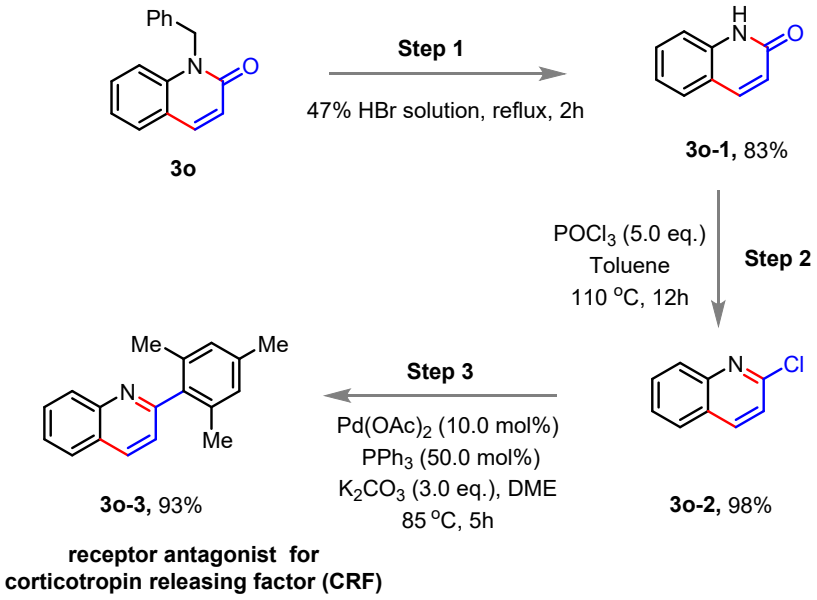


Figure S15. Site-selective C–H activation: N–H quinolinone and C2–Cl quinoline synthesis

Step 2: An oven-dried 10 mL Schlenk Tube was charged with quinolinone **3o-1** (0.2 mmol), in sequence, followed by adding phosphorus oxychloride (1.0 mmol) in toluene (3.0 mL) through syringe. The resulting reaction mixture was was refluxed under argon for 12 h. After completion of the reaction, the mixture was carefully

quenched with water and basified with aqueous NH_4OH. The reaction mixture was extracted with EtOAc, dried over Na_2SO_4. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired produce **3o-2**.[6]

Step 3: An oven-dried 10 mL Schlenk Tube was charged with 2-chloroquinoline **3o-2** (0.2 mmol), 2,4,6-Trimethyl-phenylboronic acid (0.3 mmol), $Pd(OAc)_2$ (0.02 mmol), PPh_3 (0.1 mmol), K_2CO_3 (0.6 mmol) in sequence, followed by adding DME (4.0 mL) and H_2O (1.0 mL) through syringe. The resulting reaction mixture was was refluxed under argon for 5h and then the reaction mixture was diluted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with water followed by saturated brine. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired produce **3o-3**.[7]

2) Concise synthesis of Flucarbril drug and analogues in 1 step:

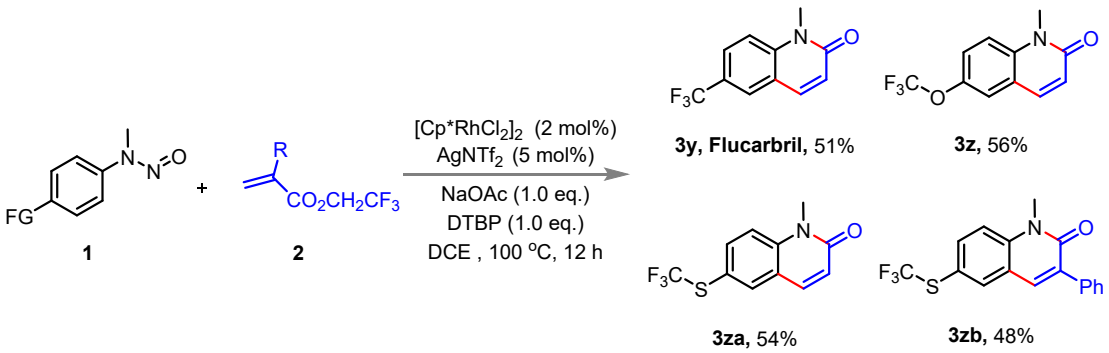


Figure S16. Synthesis of Flucarbril drug and analogues

Procedure:

An oven-dried 10 mL Schlenk Tube was charged with N-nitroso anilines (**1r, 1s, 1t**) (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.2 mmol) in sequence, followed by adding acrylate **2** (0.3 mmol) in DCE (1.0 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired Flucarbril drug **3y,** and its analogues **3z, 3za, 3zb**.

3) Synthesis of daurine analog

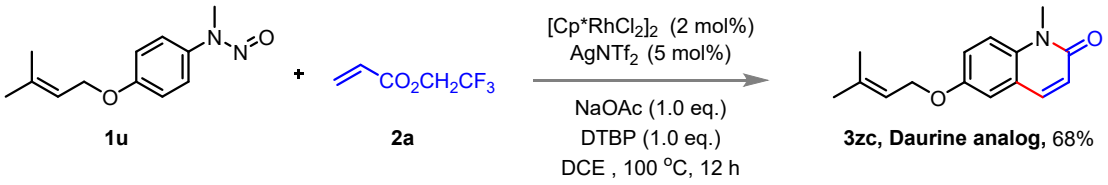


Figure S17. Synthesis of daurine analog

Procedure:

An oven-dried 10 mL Schlenk Tube was charged with methyl N-methyl-N-(4-((3-methylbut-2-en-1-yl)oxy)phenyl)nitrous amide (**1u**) (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.2 mmol) in sequence, followed by adding acrylate **2a** (0.3 mmol) in DCE (1.0 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the daurine analog **3zc**.

5) Synthesis of Cilostamide

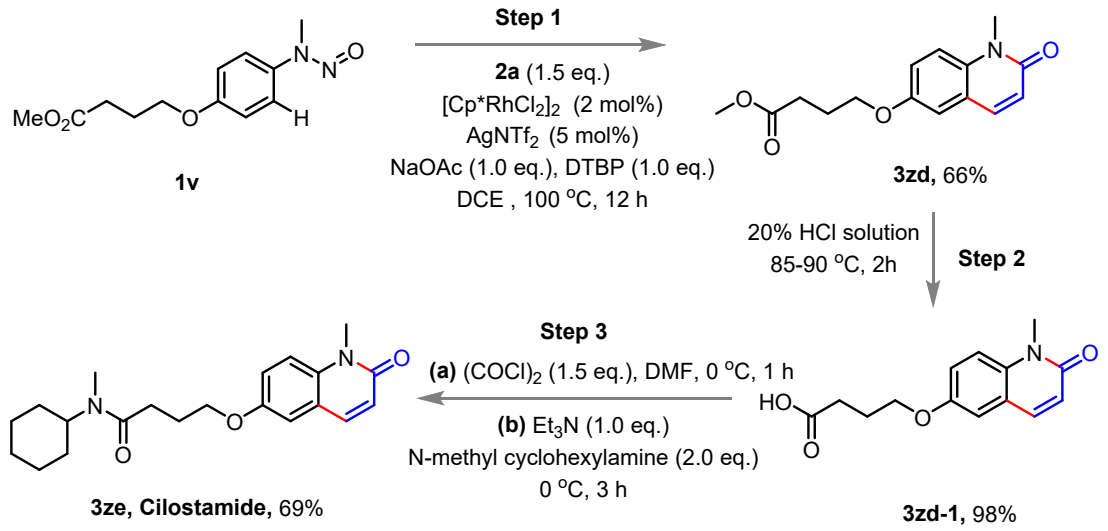


Figure S18. Synthesis of cilostamide

Procedure:

Step 1: An oven-dried 10 mL Schlenk Tube was charged with methyl 4-(4-(methyl(nitroso)amino)phenoxy)butanoate (**1u**) (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004

mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.2 mmol) in sequence, followed by adding acrylate **2a** (0.3 mmol) in DCE (1.0 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired produce **3zd**.

Step 2: A suspension of 0.5 mmol Methyl 4-((1-methyl-2-oxo-1,2-dihydroquinolin -6-yl)oxy) butanoate (**3zd**) in 2.0 ml of 20% HC1 solution was stirred at 85-90°C for 2 h, then cooled. The precipitated crystals were collected by filtration and washed with water gave produce **3zd-1**.

Step 3 : Oxalyl chloride (1.5 mmol) was added dropwise to a solution of 0.5 mmol 4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanoic acid in 3.0 ml of DMF with stirring and ice-water cooling, and the reaction mixture was stirred at room temperature for 1 h. Next, Et_3N (0.5 mmol) was added dropwise with stirring and ice-water cooling, then N-methyl cyclohexylamine (1.0 mmol) was added, and the whole mixture was stirred at room temperature for 3 h and then diluted with CH2Cl2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the **Cilostamide 3ze**.[9]

6) Concise delivery of Aripiprazole analog

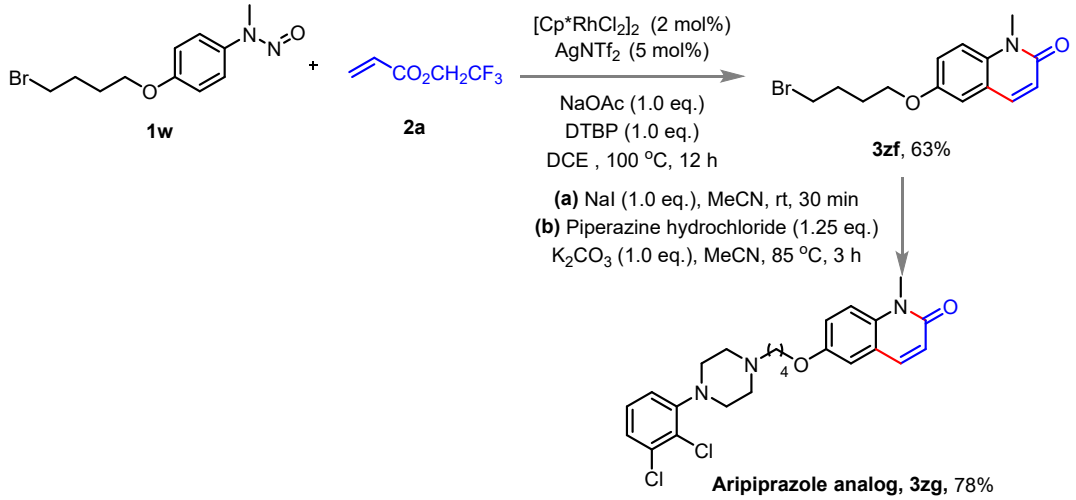


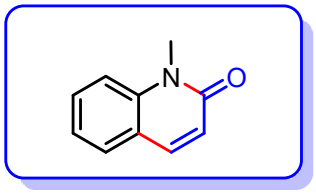
Figure S20. Synthesis of Aripiprazole analog

Procedure:

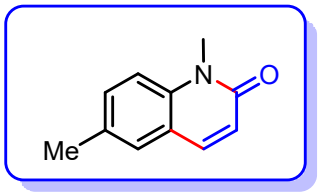
An oven-dried 10 mL Schlenk Tube was charged with N-(4-(4-bromobutoxy)phenyl)-N-methylnitrous amide (**1w**) (0.2 mmol), $[RhCp^*Cl_2]_2$ (0.004 mmol), $AgNTf_2$ (0.01 mmol), NaOAc (0.2 mmol) and DTBP (0.2 mmol) in sequence, followed by adding acrylate **2a** (0.3 mmol) in DCE (1.0 mL) through syringe. The resulting reaction mixture was stirred at 100 ℃ for 12 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the daurine analog **3zf**.

An oven-dried 10 mL Schlenk Tube was charged with 6-(4-bromobutoxy)-1-methylquinolin-2(1H)-one (**3zf**) (0.2 mmol), NaI (0.2 mmol) in sequence, followed by adding MeCN (1.0 mL) through syringe. The resulting reaction mixture was stirred at room temperature for 30 min and then added 1-(2,3-Dichlorophenyl)piperazine hydrochloride (0.25 mmol) and K_2CO_3 (0.2 mmol) with MeCN (1.0 mL). The resulting reaction mixture was stirred at 85 ℃ for 3 h and then diluted with CH_2Cl_2 and filtered through diatomite. Removing the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the daurine analog **3zg**.[10]

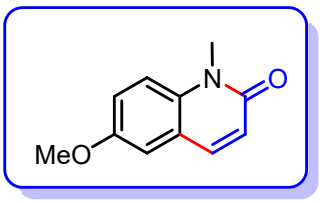
E. Analytical data for the obtained products



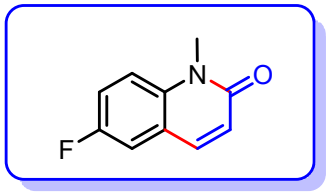
1-Methylquinolin-2(1*H*)-one (3a), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 9.6 Hz, 1H), 7.59-7.54 (m, 2H), 7.36 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 7.25-7.21 (m, 1H), 6.71 (d, J = 9.6 Hz, 1H), 3.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.3, 140.0, 138.9, 130.6, 128.7, 122.0, 121.6, 120.6, 114.1, 29.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_9NO$: 159.0684, Found: 159.0689.



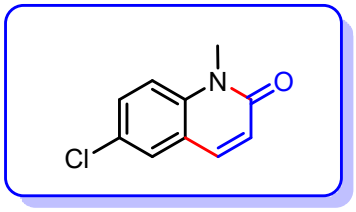
1,6-Dimethylquinolin-2(1*H*)-one (3b), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 9.2 Hz, 1H), 7.40-7.34 (m, 2H), 7.26 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 9.6 Hz, 1H), 3.70 (s, 3H) , 2.42 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.3, 138.7, 138.0, 131.8, 131.6, 128.5, 121.7, 120.6, 114.0, 29.4, 20.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}NO$: 173.0841, Found: 173.0837.



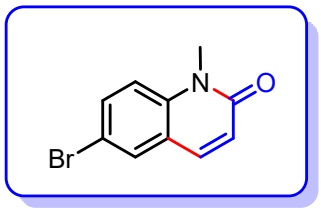
6-Methoxy-1-methylquinolin-2(1*H*)-one (3c), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 9.2 Hz, 1H), 7.30 (d, J = 9.2 Hz, 1H), 7.36 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 6.73 (d, J = 9.6 Hz, 3H) , 3.87 (s, 3H) , 3.71 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.0, 154.7, 138.4, 134.6, 122.3, 121.4, 119.2, 115.4, 110.5, 55.7, 29.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}NO_2$: 189.0790, Found: 189.0796.



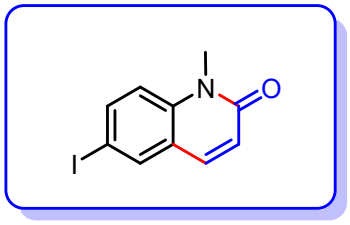
6-Fluoro-1-methylquinolin-2(1*H*)-one (3d), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 9.2 Hz, 1H), 7.28-7.16 (m, 3H), 6.64 (d, *J* = 9.6 Hz, 1H), 3.65 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.9, 157.8 (d, *J* = 241.0 Hz), 137.9 (d, *J* = 3.0 Hz), 136.7, 127.2, 123.2, 118.3 (d, *J* = 24.0 Hz), 115.7 (d, *J* = 8.0 Hz), 113.7 (d, *J* = 22.0 Hz), 27.7. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -121.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8FNO$: 162.0355, Found: 162.0358.



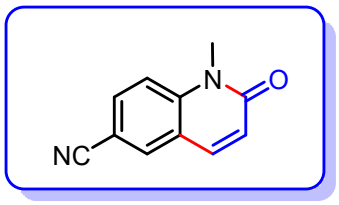
6-Chloro-1-methylquinolin-2(1*H*)-one (3e), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 9.6 Hz, 1H), 7.52-7.48 (m, 2H), 7.28 (d, *J* = 8.8 Hz, 1H), 6.73 (d, *J* = 9.6 Hz, 1H), 3.69 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.9, 138.5, 137.7, 130.5, 127.7, 127.5, 123.0, 121.6, 115.5, 29.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8ClNO$: 193.0294, Found: 193.0290.



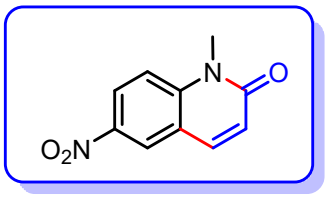
6-Bromo-1-methylquinolin-2(1*H*)-one (3f), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 2.4 Hz, 1H), 7.64 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.24 (d, *J* = 9.2 Hz, 1H), 6.73 (d, *J* = 9.2 Hz, 1H), 3.70 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.9, 139.0, 137.7, 133.3, 130.9, 123.0, 122.2, 115.9, 114.9, 29.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8BrNO$: 236.9789, Found: 236.9795.



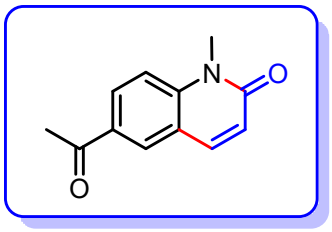
6-Iodo-1-methylquinolin-2(1*H*)-one (3g), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 2.4 Hz, 1H), 7.81 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.56 (d, *J* = 9.6 Hz, 1H), 7.12 (d, *J* = 9.2 Hz, 1H), 6.71 (d, *J* = 9.6 Hz, 1H), 3.68 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.9, 139.6, 139.0, 137.6, 137.0, 122.8, 122.7, 116.1, 84.9, 29.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8INO$: 284.9651, Found: 284.9657.



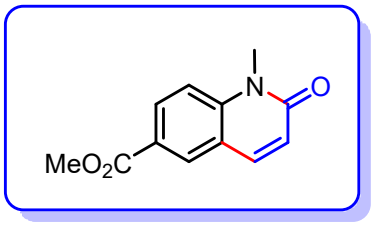
1-Methyl-2-oxo-1,2-dihydroquinoline-6-carbonitrile (3h), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.0 Hz, 1H), 7.79 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.67 (d, *J* = 9.6 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 6.81 (d, *J* = 9.6 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.4, 144.0, 137.9, 133.1, 133.1, 123.7, 121.0, 120.7, 115.1, 106.2, 29.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_8N2O$: 184.0637, Found: 184.0642.



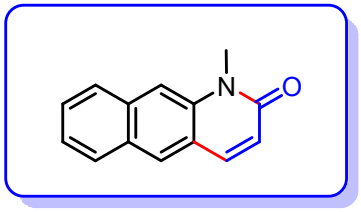
1-Methyl-6-nitroquinolin-2(1*H*)-one (3i), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.0 Hz, 1H), 7.79 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.67 (d, *J* = 9.6 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 6.81 (d, *J* = 9.6 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.9, 144.0, 142.2, 138.5, 125.3, 124.5, 124.0, 120.1, 114.8, 30.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8N_2O_3$: 204.0535, Found: 204.0529.



6-Acetyl-1-methylquinolin-2(1*H*)-one (3j), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.13 (m, 2H), 7.74 (d, J = 9.6 Hz, 1H), 7.41 (dd, J = 0.8, 9.6 Hz, 1H), 6.75 (d, J = 9.2 Hz, 1H), 3.74 (s, 3H), 2.65 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 196.3, 162.2, 143.0, 139.2, 131.0, 130.2, 129.7, 122.6, 120.0, 114.3, 29.7, 26.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}NO_2$: 201.2250, Found: 201.2245.

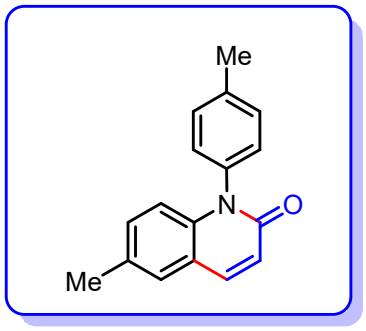


Methyl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3k), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 2.0 Hz, 1H), 8.21 (dd, J = 2.0 Hz, 9.2 Hz, 1H), 7.73 (d, J = 9.5 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 6.76 (d, J = 9.2 Hz, 1H), 3.96 (s, 3H), 3.74 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 166.2, 162.3, 143.0, 139.1, 131.4, 130.8, 124.0, 122.5, 120.1, 114.1, 52.3, 29.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}NO_3$: 217.0739, Found: 217.0744.

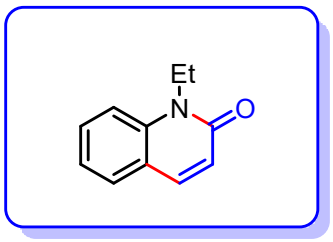


1-Methylbenzo[*g*]quinolin-2(1*H*)-one (3l), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.91-7.88 (m, 2H), 7.77 (d, J = 9.6 Hz, 1H), 7.64 (s, 1H), 7.57-7.52 (m, 1H), 7.47-7.43 (m, 1H), 6.71 (d, J = 9.6 Hz, 1H), 3.77 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 162.4, 138.9, 137.4, 134.2, 128.7, 128.4, 128.0, 127.7, 127.4, 125.0, 122.3, 121.0,

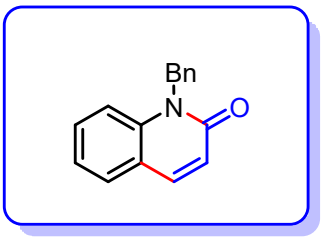
110.3, 29.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}NO$: 209.0841, Found: 209.0837.



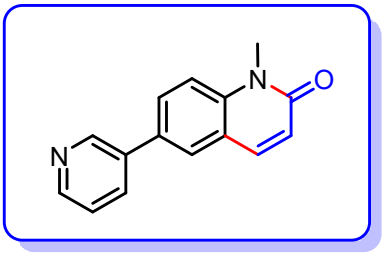
6-Methyl-1-(*p*-tolyl)quinolin-2(1*H*)-one (3m), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 9.6 Hz, 1H), 7.40-7.37 (m, 3H), 7.16-7.12 (m, 3H), 6.76 (d, J = 9.6 Hz, 1H), 6.59 (d, J = 8.8 Hz, 1H), 2.46 (s, 3H), 2.39 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.4, 145.2, 139.5, 138.8, 135.1, 131.8, 131.4, 130.8, 128.5, 128.0, 122.2, 120.3, 116.0, 21.3, 20.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}NO$: 249.1154, Found: 249.1160.



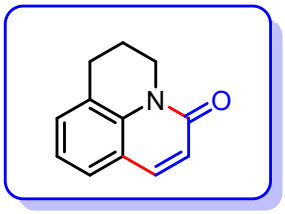
1-Ethylquinolin-2(1*H*)-one (3n), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 9.2 Hz, 1H), 7.58-7.54 (m, 2H), 7.40-7.38 (m, 1H), 7.21 (td, J = 1.2, 7.2 Hz, 1H), 6.70 (d, J = 9.2 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.9, 138.9, 130.5, 129.0, 124.1, 121.9, 121.7, 121.0, 114.0, 37.2, 12.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}NO$: 173.0841, Found: 173.0847.



1-Benzylquinolin-2(1*H*)-one (3o), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 9.2 Hz, 1H), 7.56 (dd, J = 1.6, 7.6 Hz, 1H), 7.44-7.40 (m, 1H), 7.32-7.16 (m, 7H), 6.81 (d, J = 9.2 Hz, 1H), 5.57 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ. 162.5, 139.6, 139.4, 136.3, 130.6, 128.8, 128.8, 127.2, 126.5, 122.2, 121.6, 120.9, 115.0, 45.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}NO$: 235.0997, Found: 235.0992.

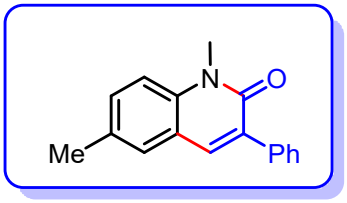


1-Methyl-6-(pyridin-3-yl)quinolin-2(1*H*)-one (3p), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 2.0 Hz, 1H), 8.54-8.52 (m, 1H), 7.84-7.81 (m, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.35-7.18 (m, 4H), 6.75 (d, J = 9.6 Hz, 1H), 3.71 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.2, 150.9, 147.8, 139.9, 138.8, 138.5, 130.5, 128.6, 124.7, 122.0, 121.6, 120.8, 120.6, 114.0, 29.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}N_2O$: 236.0950, Found: 236.0953.

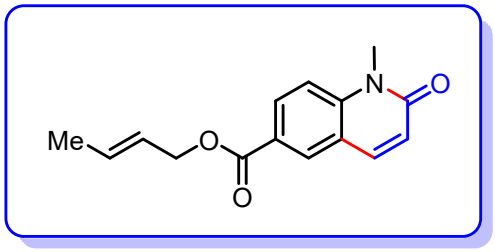


2,3-Dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinolin-5-one (3q), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 9.2 Hz, 1H), 7.39 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.30 (dd, J = 1.2 Hz, 6.4 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 9.6 Hz, 1H), 4.21-4.18 (m, 2H), 2.98 (t, J = 6.4 Hz, 2H), 2.12 (dt, J = 6.0 Hz, 12.0 Hz, 2H). **^{13}C NMR (100 MHz,**

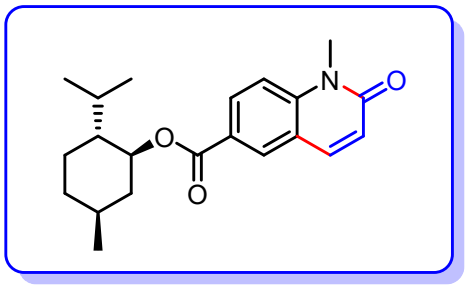
$CDCl_3$) δ 162.0, 138.9, 136.7, 129.9, 126.6, 124.9, 121.8, 121.3, 120.5, 42.2, 27.6, 20.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}NO$: 185.0841, Found: 185.0835.



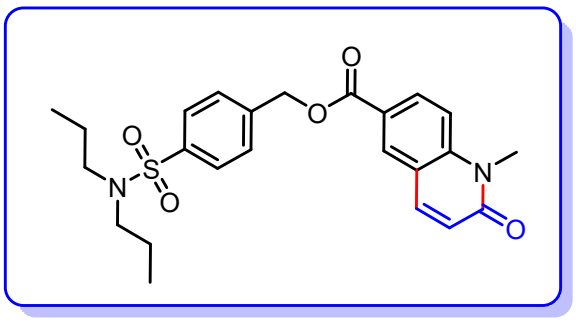
1,6-dimethyl-3-phenylquinolin-2(1*H*)-one (3r), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.72-7.68 (m, 2H), 7.45-7.36 (m, 5H), 7.27 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H), 2.43 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.4, 137.6, 136.9, 136.6, 132.4, 131.7, 131.5, 129.0, 128.6, 128.1, 127.9, 120.7, 113.9, 29.9, 20.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}NO$: 249.1154, Found: 249.1154.



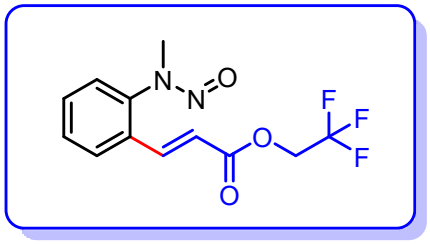
(*E*)-But-2-en-1-yl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 2.0 Hz, 1H), 8.21 (dd, J = 2.0 Hz, 8.8 Hz, 1H), 7.72 (d, J = 9.6 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 9.6 Hz, 1H), 5.95 – 5.86 (m, 1H), 5.77 – 5.70 (m, 1H), 4.78 (d, J = 6.8 Hz, 2H), 3.74 (s, 3H), 1.77 (d, J = 6.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 165.5, 162.3, 143.0, 139.1, 131.7, 131.4, 130.8, 125.0, 124.2, 122.5, 120.1, 114.1, 65.9, 29.7, 17.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}NO_3$: 257.1052, Found: 257.1051.



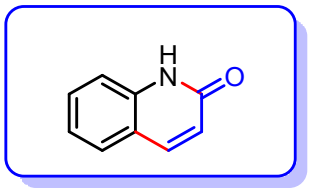
(1*R*, 2*S*, 5*R*)-2-Isopropyl-5-methylcyclohexyl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3w), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 2.0 Hz, 1H), 8.22 (dd, J =2.0 Hz, 8.8 Hz, 1H), 7.75 (d, J = 9.6 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 9.6 Hz, 1H), 4.98 (td, J = 4.5 Hz, 10.8 Hz, 1H), 3.75 (s, 3H), 2.51-2.47 (m, 1H), 2.38-2.30 (m, 1H), 2.25-2.19 (m, 1H), 1.53 (d, J = 4.8 Hz, 3H), 1.49 (d, J = 2.8 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.8 Hz, 2H), 0.94 (dd, J = 4.8 Hz, 6.8 Hz, 6H), 0.81 (d, J = 6.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 65.2, 162.4, 142.8, 139.2, 131.4, 130.7, 124.7, 122.4, 120.1, 114.1, 75.2, 47.3, 41.0, 34.3, 31.5, 29.7, 26.6, 23.7, 22.0, 20.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{27}NO_3$: 341.1991, Found: 341.1987.



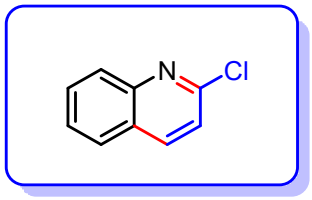
4-(*N*,*N*-dipropylsulfamoyl)benzyl1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3x), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 2.0 Hz, 1H), 8.22 (dd, J = 2.0 Hz, 8.8 Hz, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 9.6 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.8 Hz, 1H), 6.74 (d, J = 9.6 Hz, 1H), 5.43 (s, 2H), 3.72 (s, 3H), 3.08 – 3.04 (m, 4H), 1.54 (q, J = 7.6 Hz, 4H), 0.85 (t, J = 7.6 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3, 162.2, 143.2, 140.3, 140.0, 139.0, 131.4, 130.9, 128.2, 127.3, 123.3, 122.5, 120.1, 114.3, 65.7, 50.1, 29.7, 22.0, 11.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}N_2O_5S$: 456.1719, Found: 456.1720.



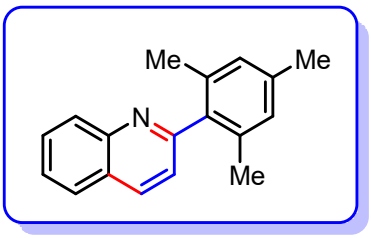
2,2,2-Trifluoroethyl (*E*)-3-(2-(methyl(nitroso)amino)phenyl)acrylate (3a-1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 1.6 Hz, 7.6 Hz, 1H), 7.65 (d, J = 16.0 Hz, 1H), 7.59-7.55 (m, 1H), 7.53-7.48 (m,1H), 7.35 (dd, J = 1.4 Hz, 7.6 Hz, 1H), 6.49 (d, J = 15.9 Hz, 1H), 4.57 (q, J = 8.4 Hz, 2H), 3.42 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.5, 147.3, 141.8, 131.5, 129.9, 129.3, 127.4, 124.4 (q, J = 250 Hz), 119.1, 117.8, 60.5 (q, J = 37 Hz), 38.6, 35.7. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -73.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}F_3N_2O_3$: 288.0722, Found: 288.0730.



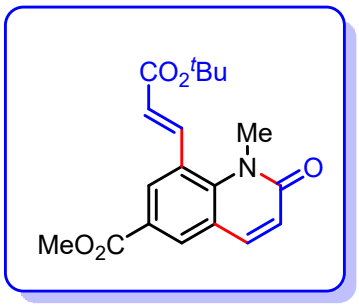
Quinolin-2(1H)-one (3o-1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.57 (s, 1H), 7.82 (d, *J* = 9.6 Hz, 1H), 7.57 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 7.54-7.50 (m, 1H), 7.46 (dd, *J* = 1.2 Hz, 8.4 Hz, 1H), 7.24-7.20 (m, 1H), 6.73 (d, *J* = 9.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.7, 141.1, 138.5, 130.7, 127.7, 122.7, 121.3, 119.9, 116.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for C_9H_7NO: 145.0528, Found: 145.0531.



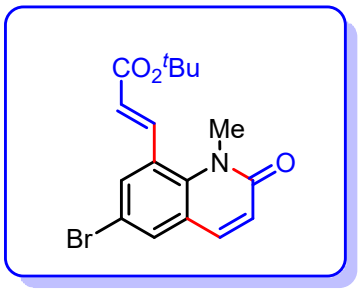
2-Chloroquinoline (3o-2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 8.03 (dd, *J* = 1.2 Hz, 8.8 Hz, 1H), 7.82 (dd, *J* = 1.2 Hz, 8.4 Hz, 1H), 7.76-7.72 (m, 1H), 7.58-7.54 (m, 1H), 7.39 (d, *J* = 8.8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 150.6, 147.8, 138.9, 130.6, 128.5, 127.5, 127.0, 126.8, 122.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for C_9H_6ClN: 163.0189, Found: 163.0193.



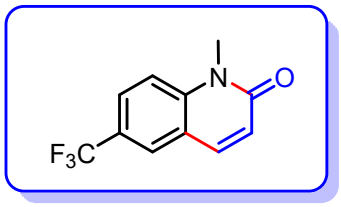
2-Mesitylquinoline (3o-3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.88 (dd, J = 8.4, 1.4 Hz, 1H), 7.76-7.72 (m, 1H), 7.59-7.55 (m, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.98 (s, 2H), 2.35 (s, 3H), 2.06 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.6, 148.1, 137.8, 137.5, 136.1, 135.5, 129.4, 129.4, 128.3, 127.5, 126.6, 126.3, 122.8, 77.3, 77.0, 76.7, 21.0, 20.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{17}N$: 247.1361, Found: 247.1355.



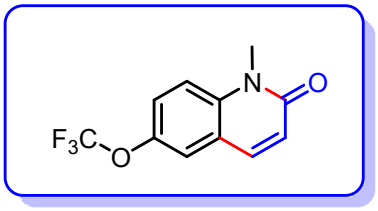
Methyl (*E*)-8-(3-(*tert*-butoxy)-3-oxoprop-1-en-1-yl)-1-methyl-2-oxo-1,2-dihydro-quinoline-6-carboxylate (3f-1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (dd, J = 2.0 Hz, 7.6 Hz, 2H), 8.07 (d, J = 15.6 Hz, 1H), 7.71 (d, J = 9.6 Hz, 1H), 6.76 (d, J = 9.2 Hz, 1H), 6.29 (d, J = 15.6 Hz, 1H), 3.96 (s, 3H), 3.80 (s, 3H), 1.55 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 177.3, 165.7, 165.3, 163.9, 142.9, 139.6, 132.9, 131.5, 124.5, 124.2, 122.8, 122.4, 121.9, 81.2, 52.4, 37.7, 28.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}NO_5$: 343.1420, Found: 343.1426.



***tert*-Butyl (*E*)-3-(6-bromo-1-methyl-2-oxo-1,2-dihydroquinolin-8-yl)acrylate (3k-1), ^{1}H NMR (400 MHz, $CDCl_3$) δ** 8.02 (d, J = 15.6 Hz, 1H), 7.63 (s, 2H), 7.57 (d, J = 9.6 Hz, 1H), 6.74 (d, J = 9.6 Hz, 1H), 6.20 (d, J = 15.6 Hz, 1H), 3.75 (s, 3H), 1.54 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 196.4, 162.3, 143.1, 139.2, 131.1, 130.3, 129.7, 122.6, 120.1, 114.3, 106.0, 102.9, 29.8, 29.7, 26.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}BrNO_3$: 363.0470, Found: 363.0473.

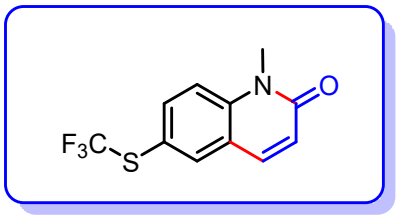


Methyl-6-(trifluoromethyl)quinolin-2(1*H*)-one (3y), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 2.4 Hz, 1H), 7.78 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.71 (d, J = 9.2 Hz, 1H),7.46 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 9.6 Hz, 1H), 3.75 (s, 3H), **^{13}C NMR (100 MHz, $CDCl_3$) δ** 162.1, 142.1, 138.5, 127.0 (q, J = 3.0 Hz), 126.0 (q, J = 4.0 Hz), 126.0, 123.3, 120.6, 120.2, 117.9, 114.7, 29.7. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -61.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_8F_3NO$: 227.0558, Found: 227.0563.

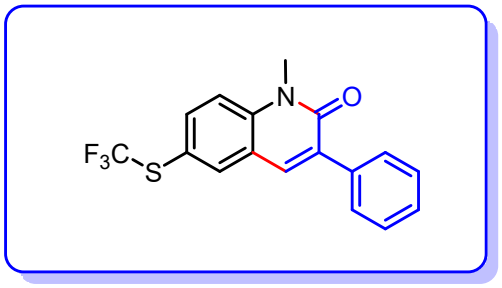


1-Methyl-6-(trifluoromethoxy)quinolin-2(1*H*)-one (3z), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 9.6 Hz, 1H), 7.41 (d, J = 13.6 Hz, 3H), 6.78 (d, J = 9.6 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 162.0, 143.7, 138.6, 138.0, 124.2, 123.7,

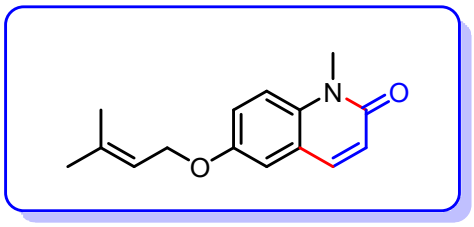
123.4, 121.7, 121.2, 118.0 (q, J = 117.0 Hz), 29.67. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -58.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_8F_3NO_2$: 243.0507, Found: 243.0511.



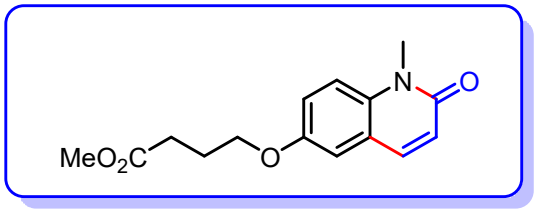
1-Methyl-6-((trifluoromethyl)thio)quinolin-2(1*H*)-one (3za), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 2.0 Hz, 1H), 7.74 (dd, J = 2.0 Hz, 6.8 Hz, 1H), 7.60 (d, J = 9.6 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 6.70 (d, J = 9.2 Hz, 1H), 3.67 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 162.1, 141.7, 138.2, 137.9, 137.1, 128.0, 123.1, 121.3, 117.2 (q, J = 2.0 Hz), 115.39, 29.7. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -43.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_8F_3NOS$: 259.0279, Found: 259.0284.



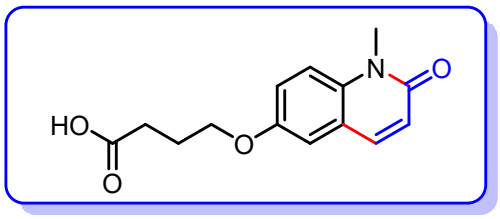
1-Methyl-3-phenyl-6-((trifluoromethyl)thio)quinolin-2(1*H*)-one (3zb), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 2.0 Hz, 1H), 7.82-7,79 (m, 2H), 7.72–7.68 (m, 2H), 7.48 – 7.39 (m, 4H), 3.81 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 161.4, 141.1, 137.5, 137.1, 136.1, 135.8, 133.9, 128.9, 128.5, 128.3, 121.4, 117.2 (q, J = 2.0 Hz), 115.2, 30.2. **^{19}F NMR (376 MHz, $CDCl_3$) δ** -43.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{12}F_3NOS$: 335.0592, Found: 335.0587.



1-Methyl-6-((3-methylbut-2-en-1-yl)oxy)quinolin-2(1*H*)-one (3zc), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 9.6 Hz, 1H), 7.29 (d, *J* = 9.2 Hz, 1H), 7.20 (dd, *J* = 2.8 Hz, 9.2 Hz, 1H), 7.02 (d, *J* = 2.8 Hz, 1H), 6.71 (d, *J* = 9.6 Hz, 1H), 5.55–5.47 (m, 1H), 4.56 (d, *J* = 6.8 Hz, 2H), 3.70 (s, 3H), 1.81 (d, *J* = 1.6 Hz, 3H), 1.77 (d, *J* = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 162.0, 153.9, 138.7, 138.5, 134.6, 122.3, 121.4, 119.9, 119.3, 115.4, 111.5, 65.3, 29.5, 25.8, 18.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}NO_2$: 243.1259, Found: 243.1256.

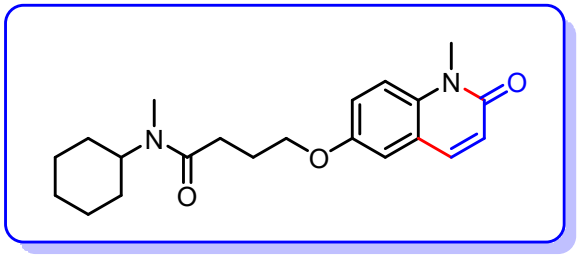


Methyl 4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanoate (3zd), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 9.6 Hz, 1H), 7.28 (d, J = 9.2 Hz, 1H), 7.16 (dd, J = 2.8 Hz, 9.2 Hz, 1H), 6.99 (d, J = 2.8 Hz, 1H), 6.70 (d, J = 9.2 Hz, 1H), 4.06 (t, J = 6.0 Hz, 2H), 3.70 (s, 3H), 3.69 (s, 3H), 2.56 (t, J = 7.2 Hz, 2H), 2.19 – 2.10 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 173.5, 161.8, 153.8, 138.3, 134.6, 122.2, 121.3, 119.5, 119.5, 115.3, 111.3, 67.2, 51.6, 30.4, 29.4, 24.5, 21.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}NO_4$: 275.1158, Found: 275.1156.

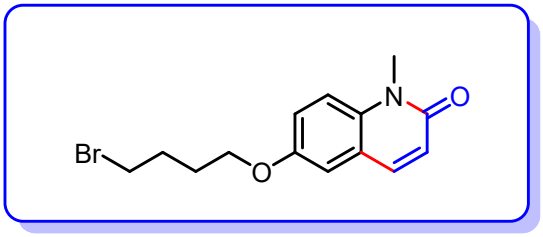


4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanoic acid (3zd-1), ^{1}H NMR (400 MHz, DMSO-d6) δ 12.17 (s, 1H), 7.83 (d, *J* = 9.6 Hz, 1H), 7.45 (d, *J* = 9.2 Hz,

1H), 7.31 – 7.21 (m, 2H), 6.60 (d, *J* = 9.6 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 3.59 (s, 3H), 2.41 (t, *J* = 7.2 Hz, 2H), 1.97 (p, *J* = 6.8 Hz, 2H). **^{13}C NMR (100 MHz, DMSO-d6)** ***δ*** 174.1, 160.72, 153.4, 138.7, 134.3, 121.6, 120.9, 120.0, 116.0, 111.4, 67.1, 30.1, 29.1, 24.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}NO_4$: 261.1001, Found: 261.1005.

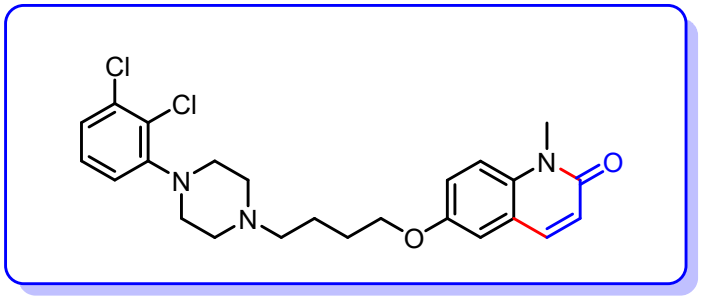


N*-cyclohexyl-*N*-methyl-4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy) butanamide (3ze), ^{1}H NMR (400 MHz, $CDCl_3$)** ***δ 7.52 (d, *J* = 9.6 Hz, 1H), 7.22 (dd, *J* = 1.6 Hz, 9.2 Hz, 1H), 7.14-7.10 (m, 1H), 6.96 (d, *J* = 2.8 Hz, 1H), 6.64 (d, *J* = 9.6 Hz, 1H), 4.43–3.47 (m, 1H), 4.03 (t, *J* = 6.0 Hz, 2H), 3.63 (s, 3H), 2.76 (d, *J* = 10.8 Hz, 3H), 2.47 (m, 2H), 2.11 (m, 2H), 1.81–1.50 (m, 6H), 1.24–1.16 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 171.6, 161.9, 154.0, 138.4, 134.5, 122.3, 121.4, 119.5, 115.3, 111.4 (d, *J* = 2.0 Hz), 67.8 (d, *J* = 8.0 Hz), 54.4 (d, *J* = 414.0 Hz), 30.9, 30.1 (d, *J* = 28.0 Hz), 29.7 (d, *J* = 5.0 Hz), 29.4 (d, *J* = 10.0 Hz), 25.7 (d, *J* = 16.0 Hz), 25.5 (d, *J* = 30.0 Hz), 24.9 (d, *J* = 31.0 Hz). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{28}N_2O_3$: 356.2100, Found: 356.2103.



6-(4-Bromobutoxy)-1-methylquinolin-2(1*H*)-one (3zf), ^{1}H NMR (400 MHz, $CDCl_3$) ***δ*** 7.58 (d, *J* = 9.6 Hz, 1H), 7.28 (d, *J* = 9.2 Hz, 1H), 7.16 (dd, *J* = 2.9 Hz, 9.4 Hz, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 6.71 (d, *J* = 9.6 Hz, 1H), 4.03 (t, *J* = 6.0 Hz, 2H), 3.70 (s, 3H), 3.27 (t, *J* = 6.8 Hz, 2H), 2.08 – 2.00 (m, 2H), 1.97–1.90 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** ***δ*** 161.9, 153.9, 138.3, 134.6, 122.3, 121.3, 119.5, 115.4, 111.3,

67.2, 30.1, 29.6, 29.5, 6.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}BrNO_2$: 309.0364, Found: 309.0370.



6-(4-(4-(2,3-Dichlorophenyl)piperazin-1-yl)butoxy)-1-methylquinolin-2(1*H*)-one (3zg), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 9.6 Hz, 1H), 7.28 (d, J = 9.2 Hz, 1H), 7.21 (dd, J = 1.6 Hz, 8.0 Hz, 1H), 7.18–7.13 (m, 2H), 6.98 (d, J = 2.8 Hz, 1H), 6.91 (dd, J = 1.7 Hz, 7.6 Hz, 1H), 6.69 (d, J = 9.6 Hz, 1H), 4.45–4.41 (m, 2H), 4.03-4.00 (m, 4H), 3.68 (s, 3H), 3.29-3.21 (m, 4H), 2.99 (t, J = 5.2 Hz, 2H), 2.06-2.00 (m, 3H), 1.95-1.90 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.9, 153.9, 149.9, 138.3, 134.5, 134.2, 127.8, 127.6, 125.6, 122.2, 121.3, 119.5, 118.9, 115.4, 111.2, 77.3, 77.0, 76.7, 67.1, 51.8, 50.2, 49.9, 39.7, 30.0, 29.6, 29.5, 6.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{27}Cl_2N_3O_2$: 459.1480, Found: 459.1483.

F. References

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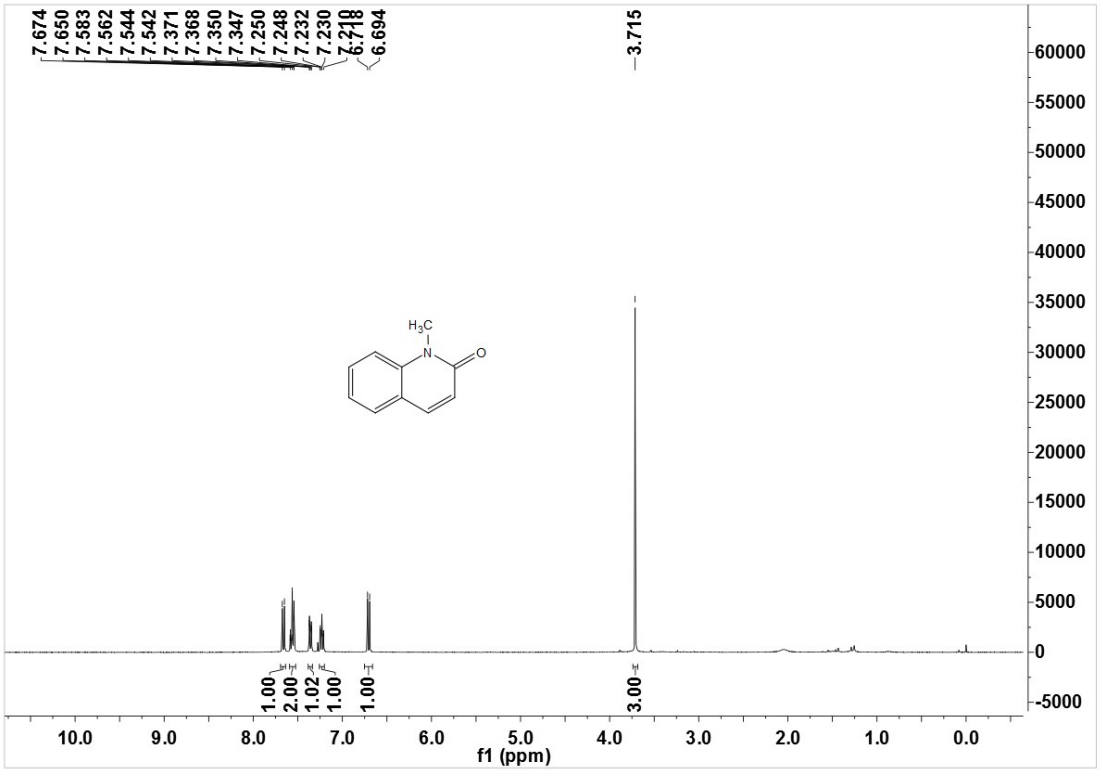
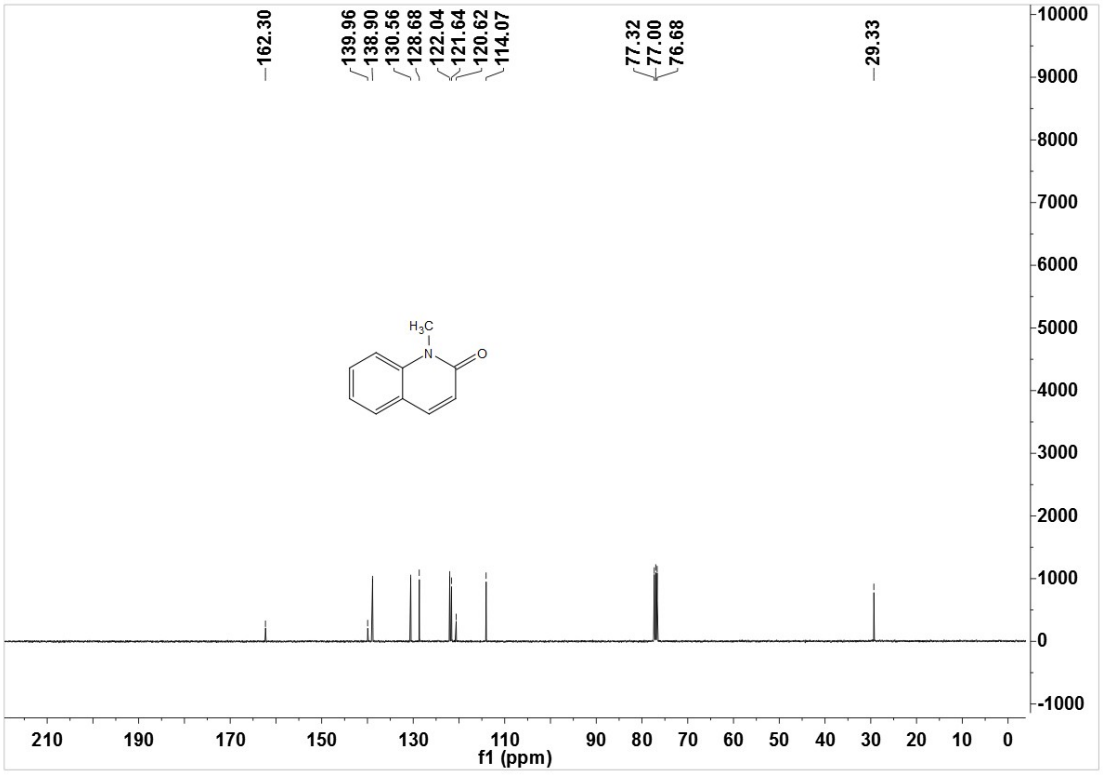
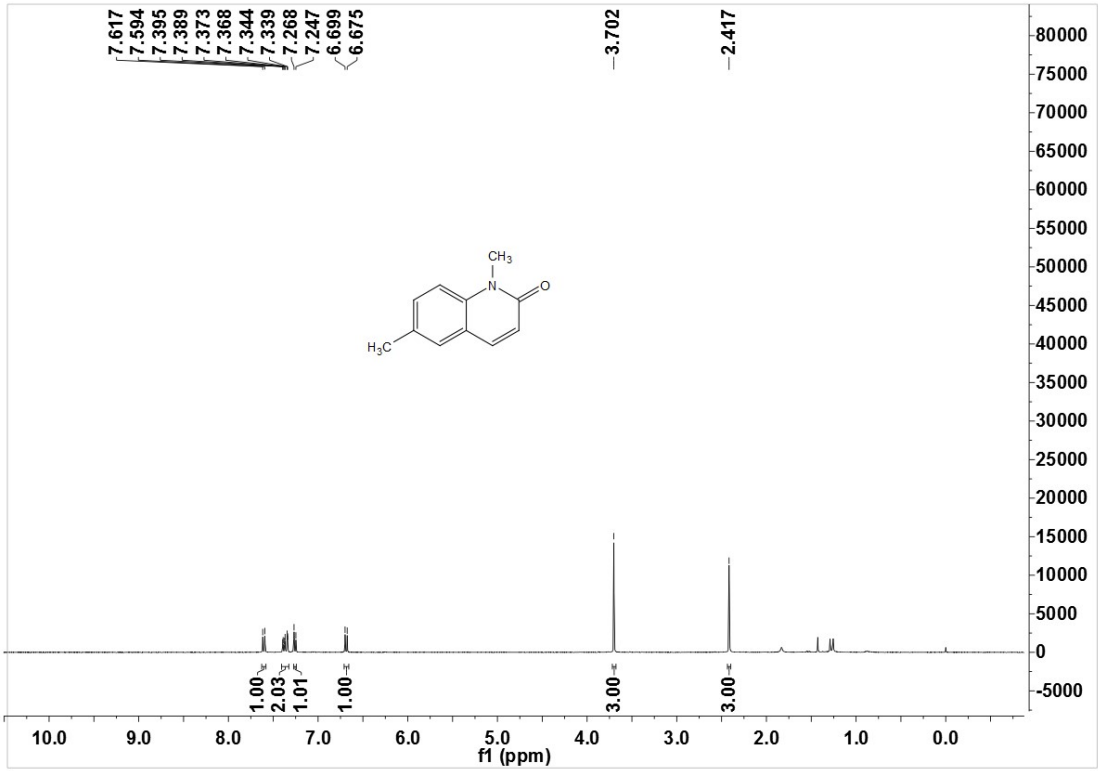
G. NMR spectra

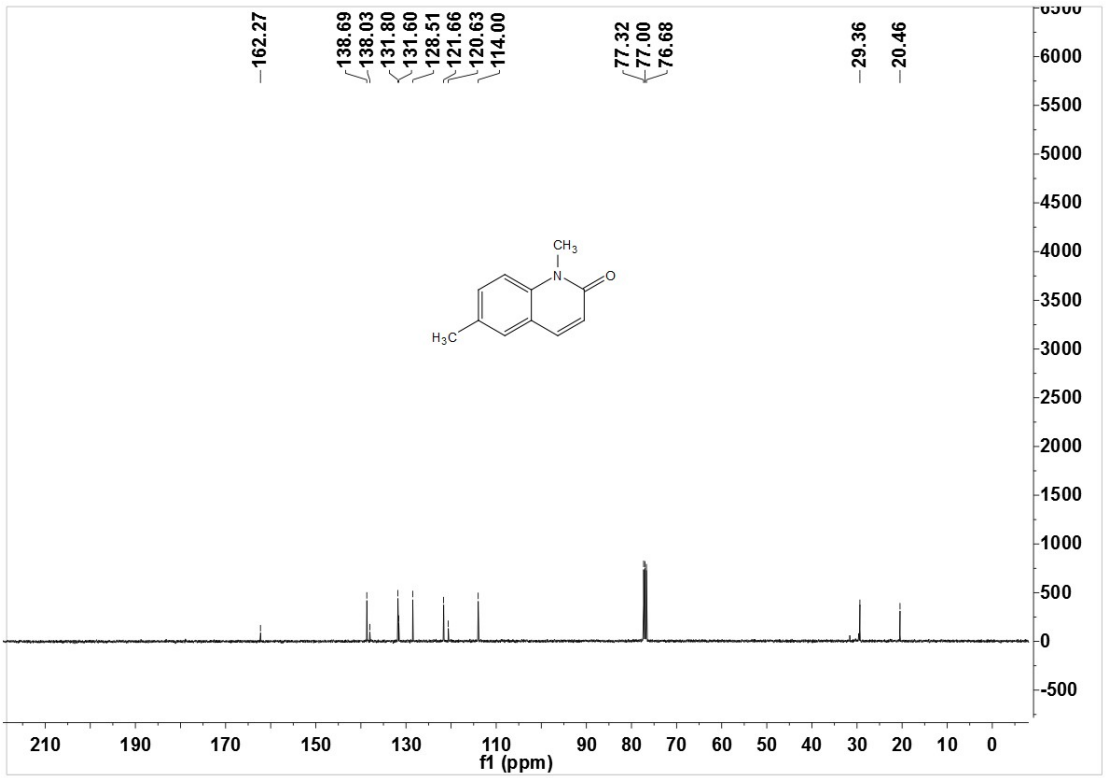
1-Methylquinolin-2(1*H*)-one (3a)



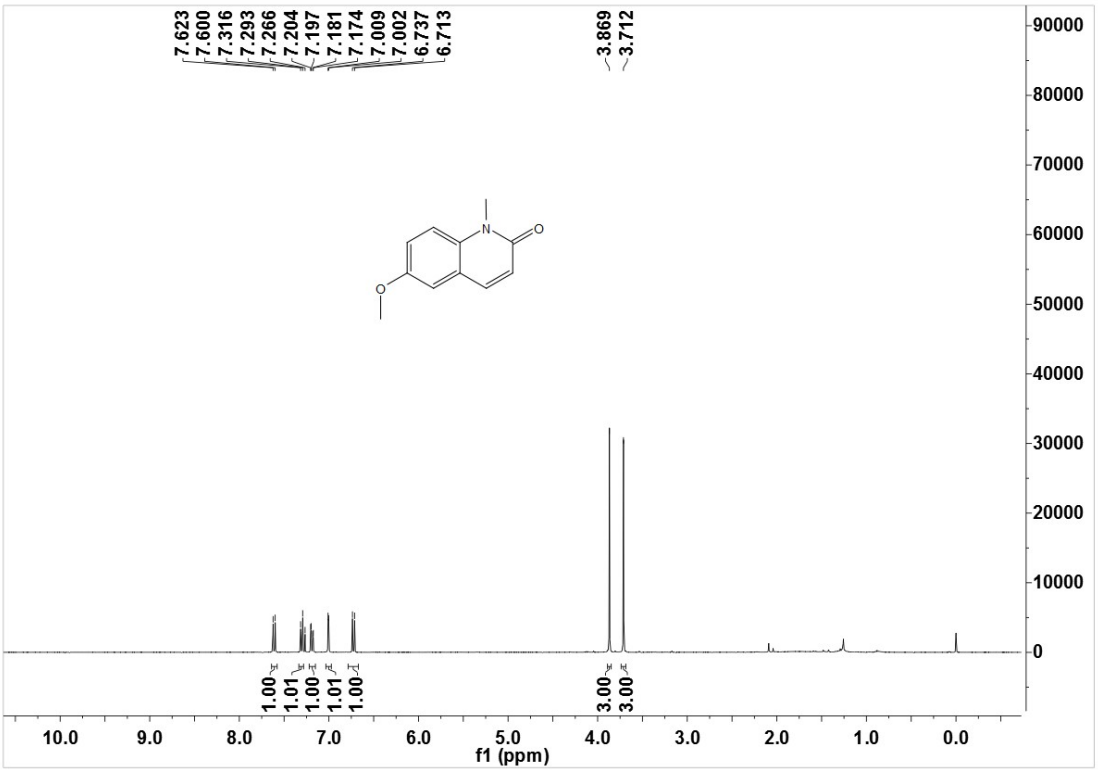


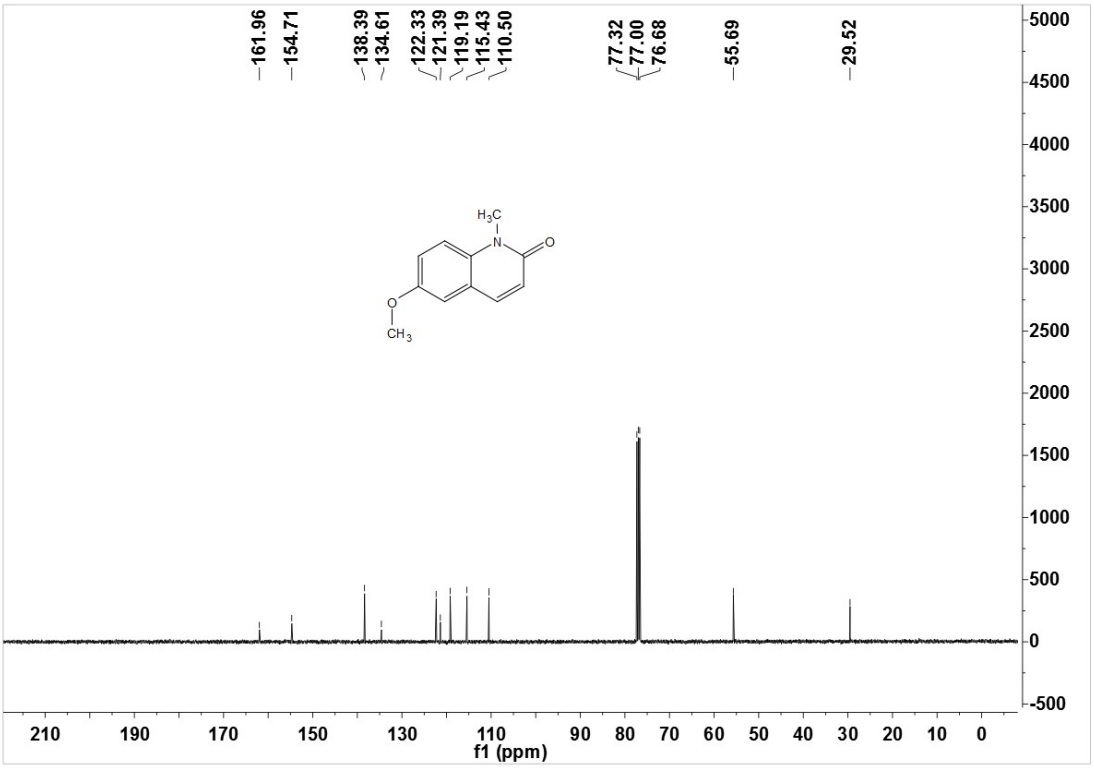
1,6-Dimethylquinolin-2(1*H*)-one (3b)



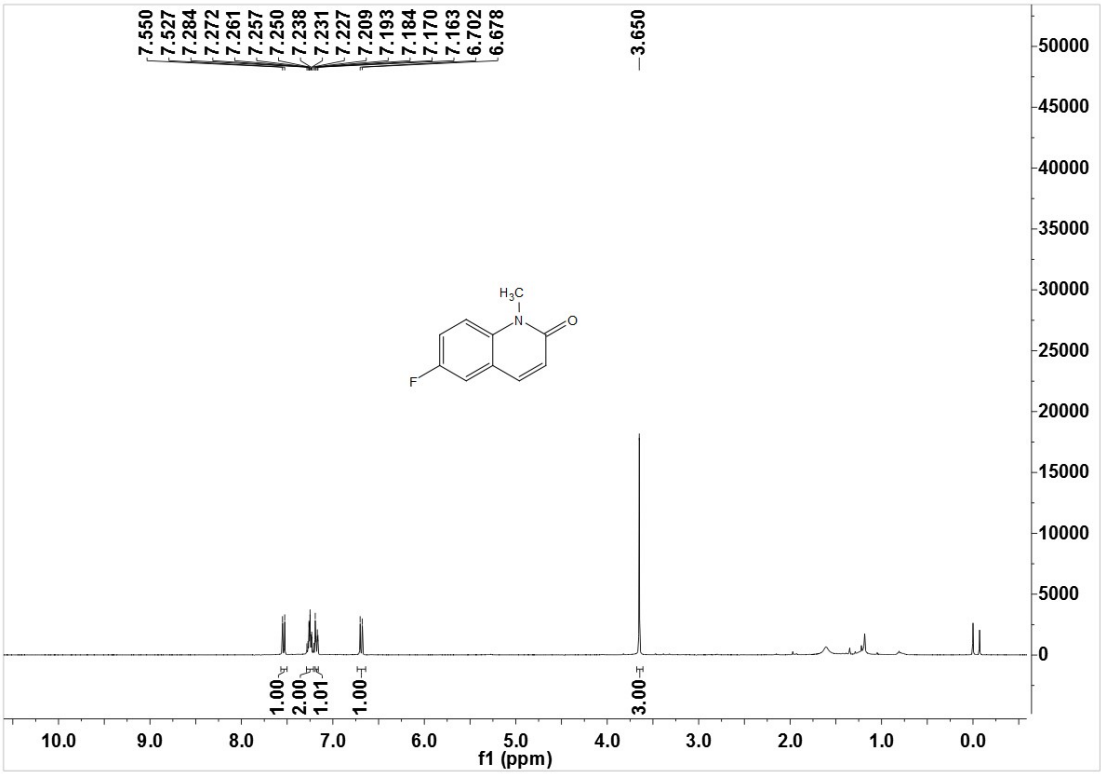


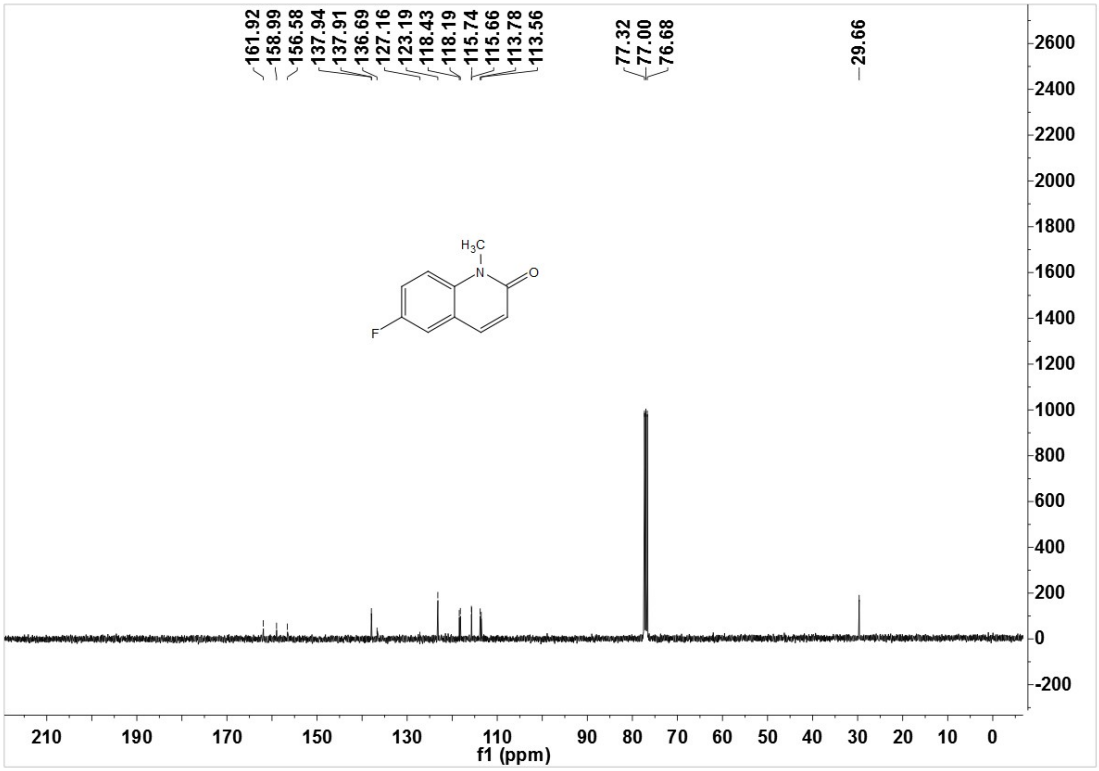
6-Methoxy-1-methylquinolin-2(1*H*)-one (3c)

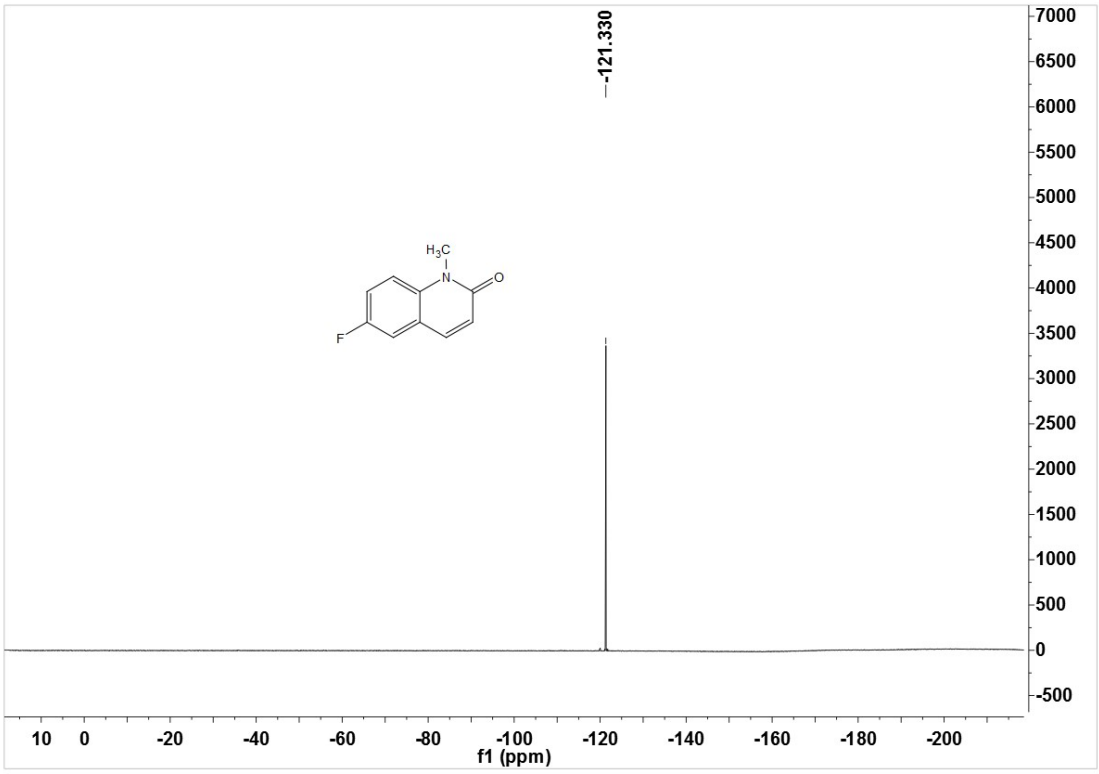




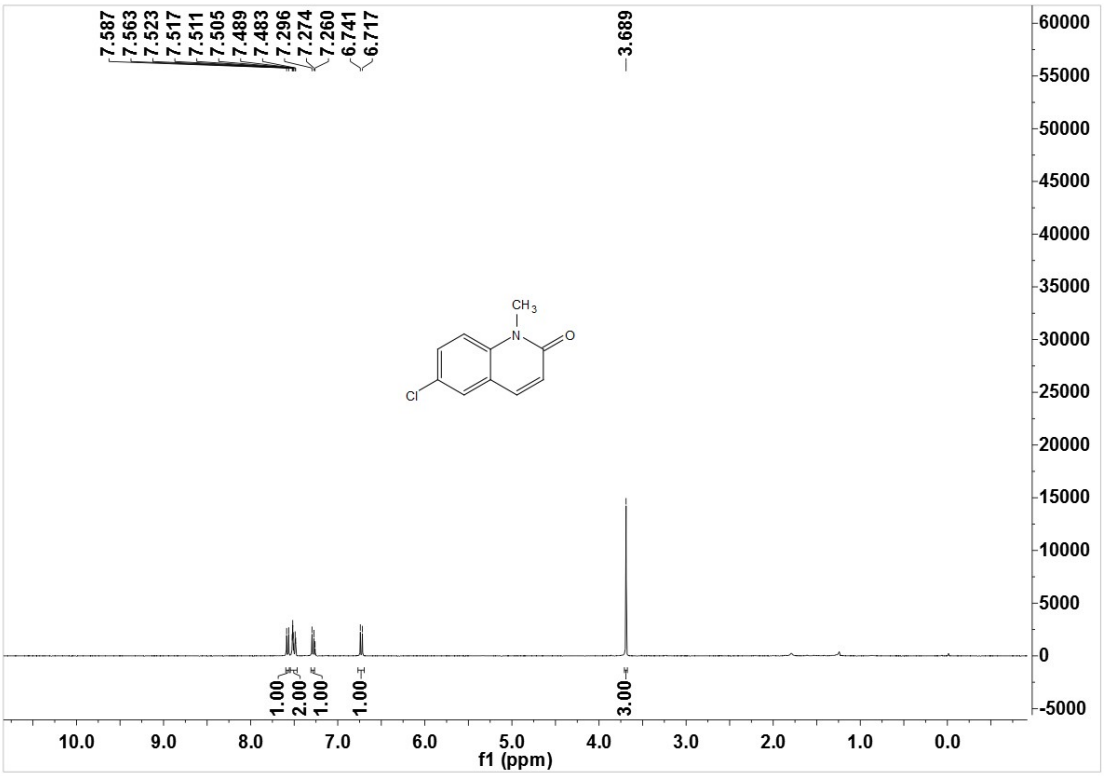
6-Fluoro-1-methylquinolin-2(1*H*)-one (3d)

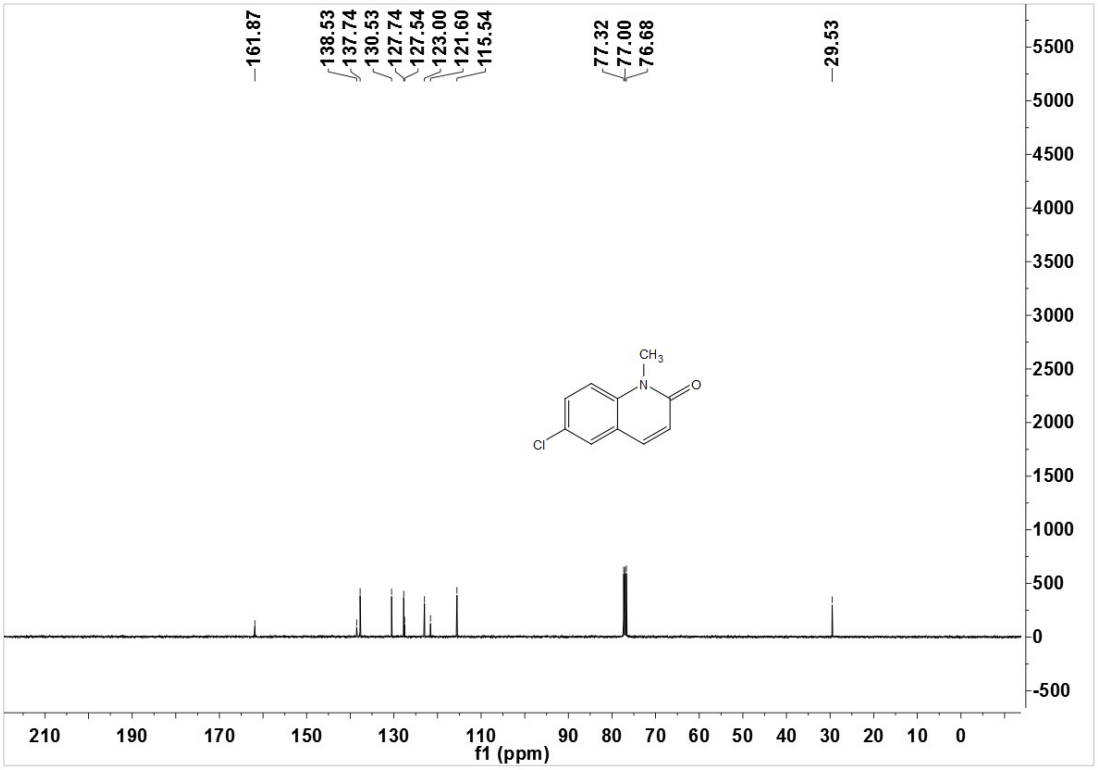




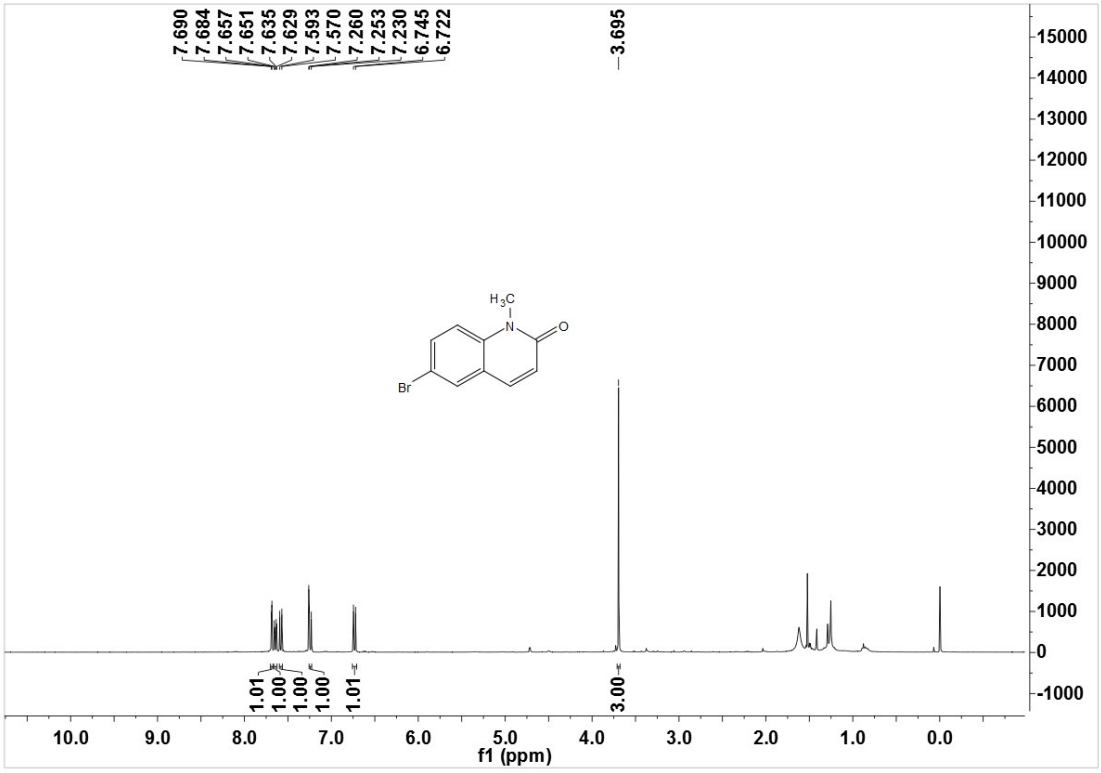


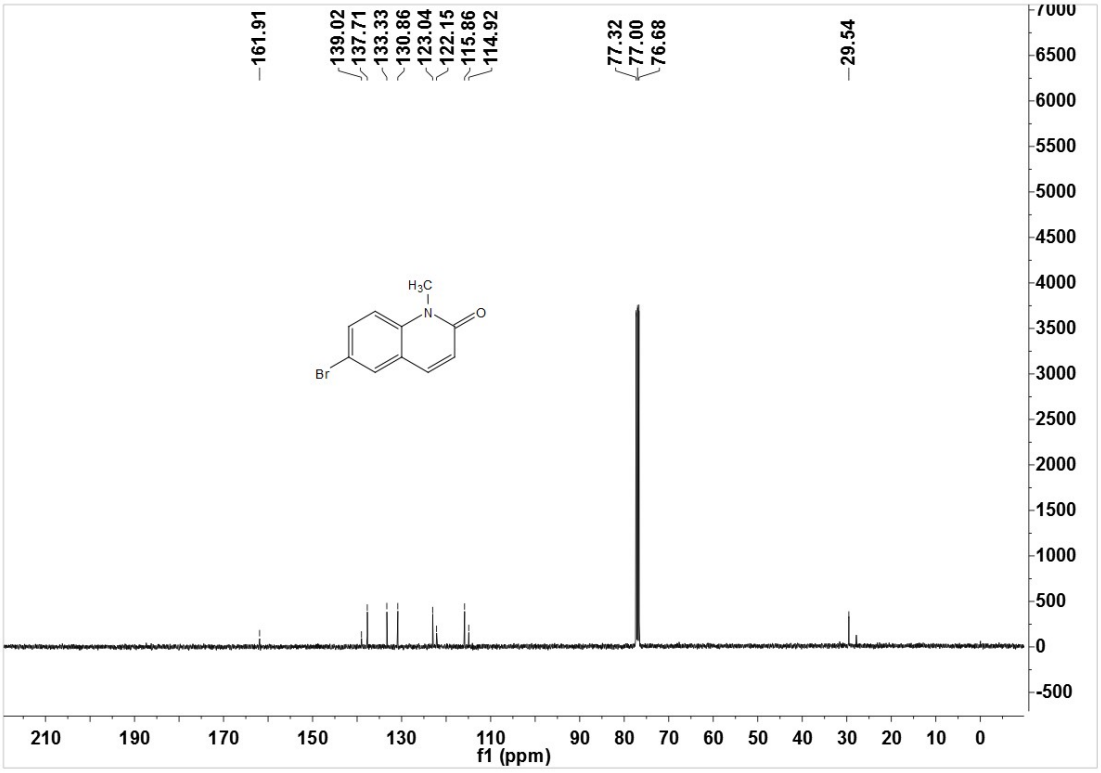
6-Chloro-1-methylquinolin-2(1*H*)-one (3e)



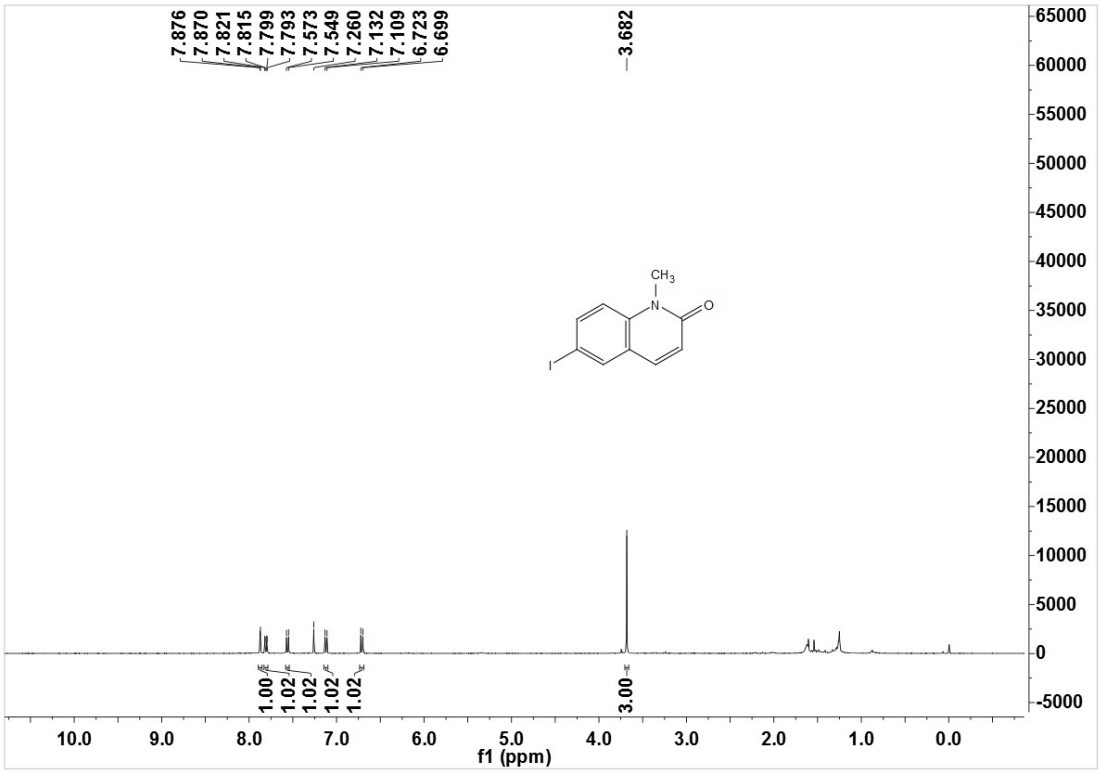


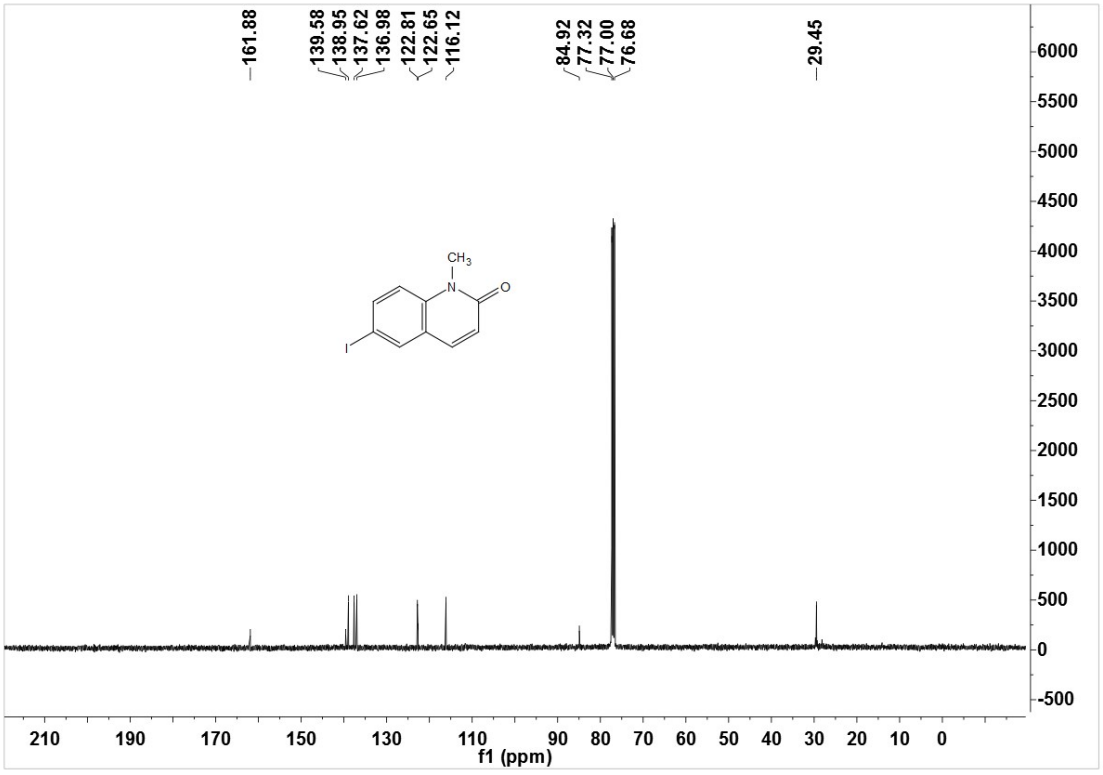
6-Bromo-1-methylquinolin-2(1*H*)-one (3f)



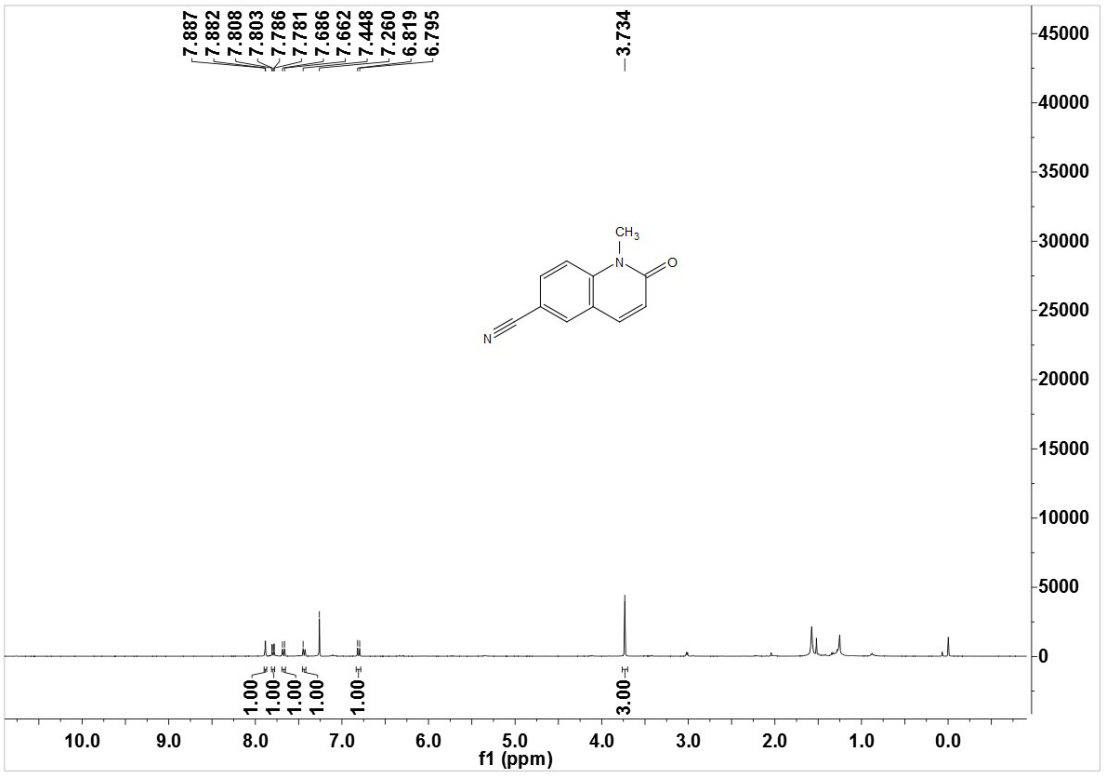


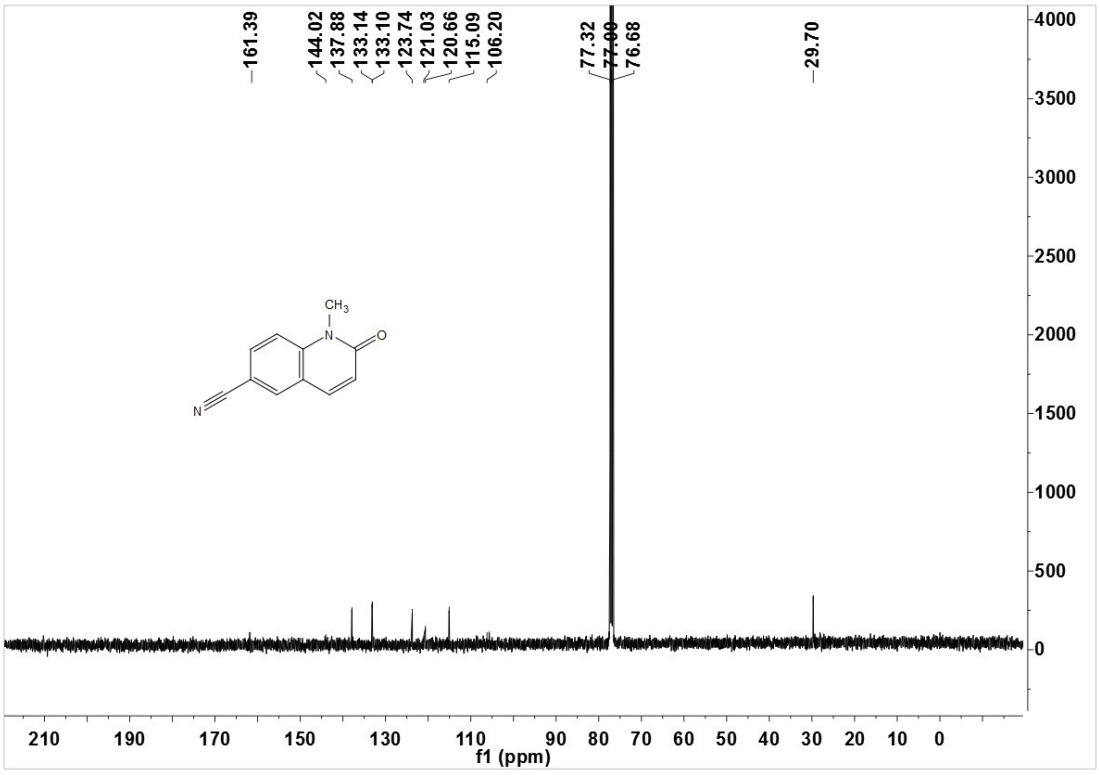
6-Iodo-1-methylquinolin-2(1*H*)-one (3g)



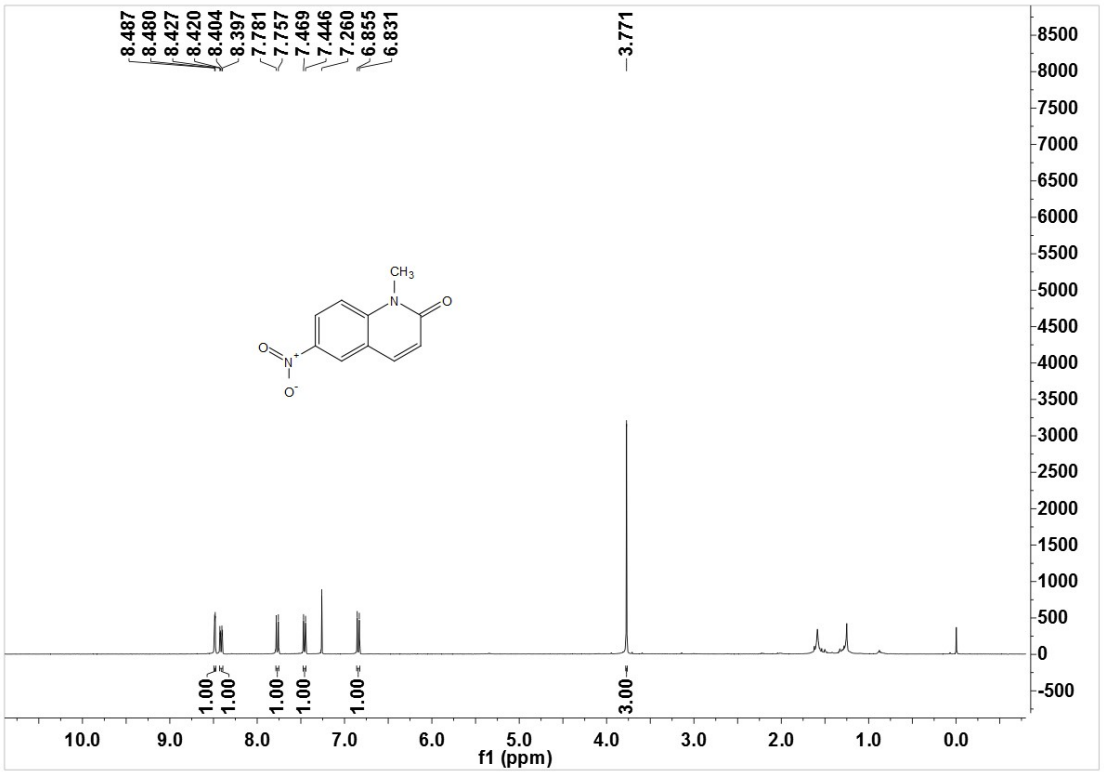


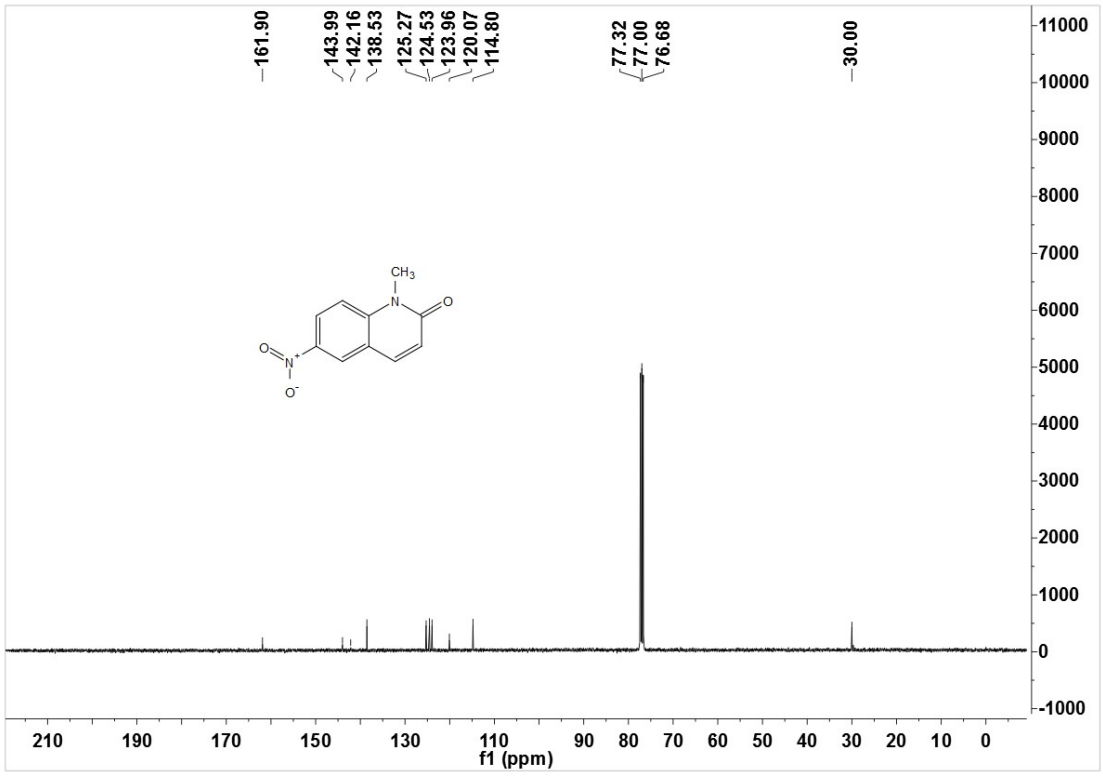
1-Methyl-2-oxo-1,2-dihydroquinoline-6-carbonitrile (3h)



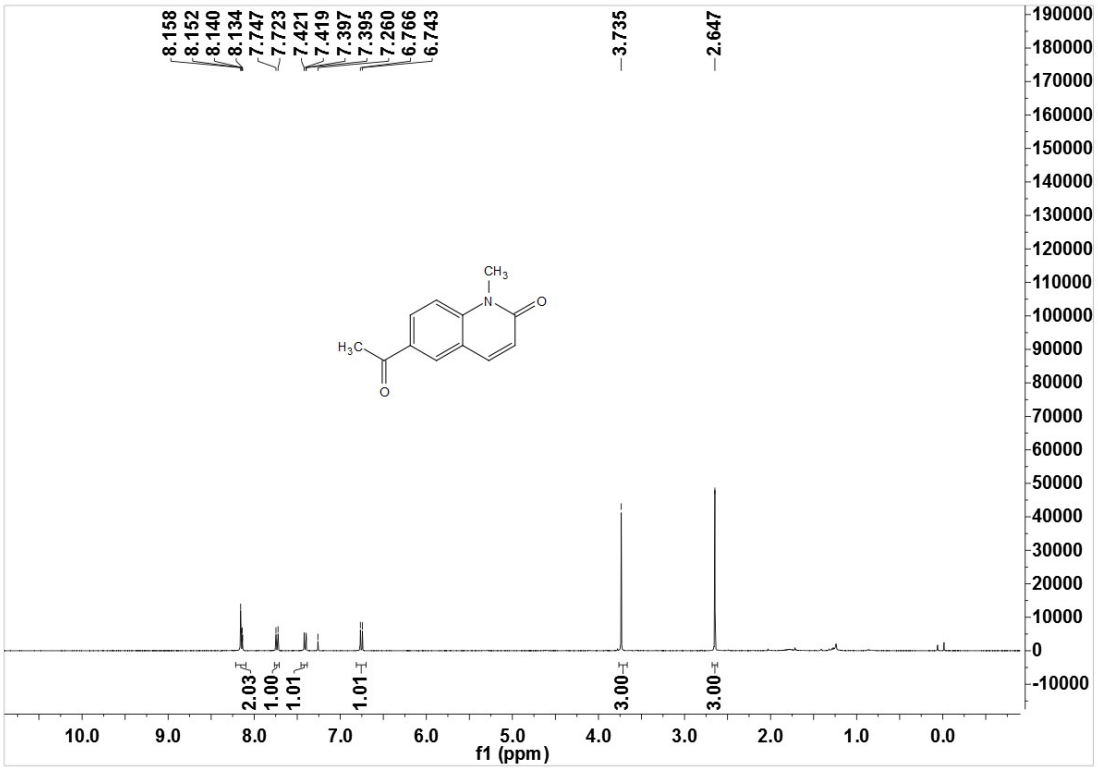


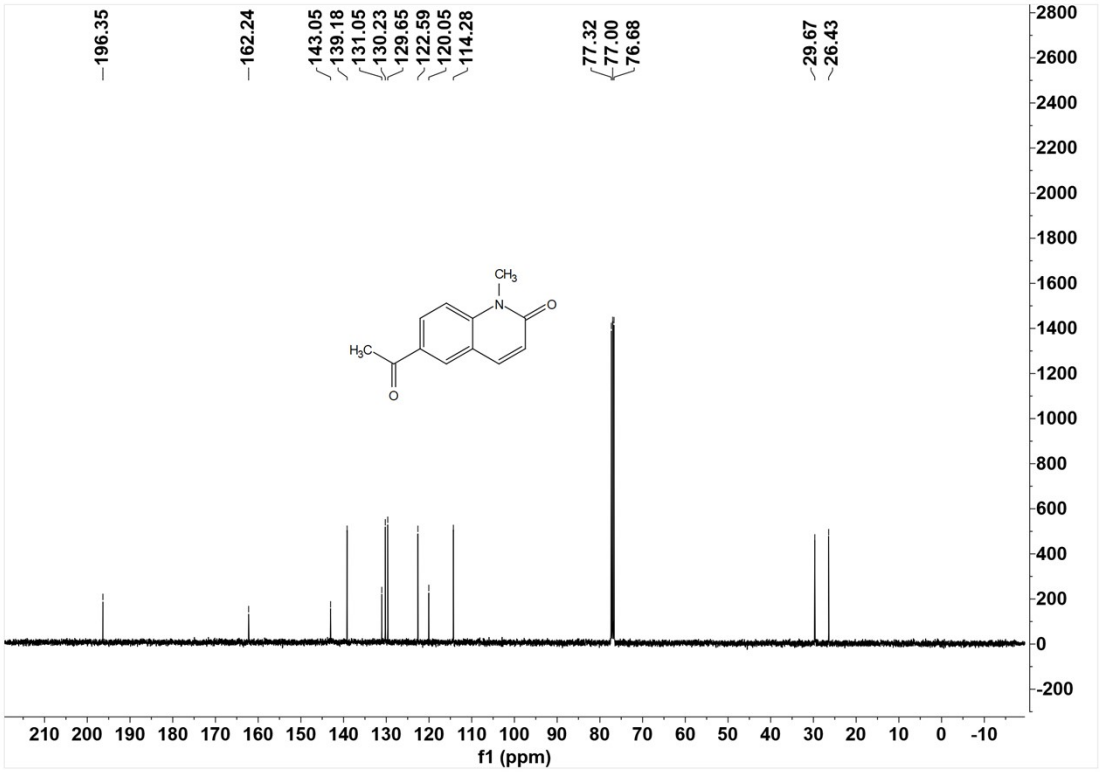
1-Methyl-6-nitroquinolin-2(1*H*)-one (3i)



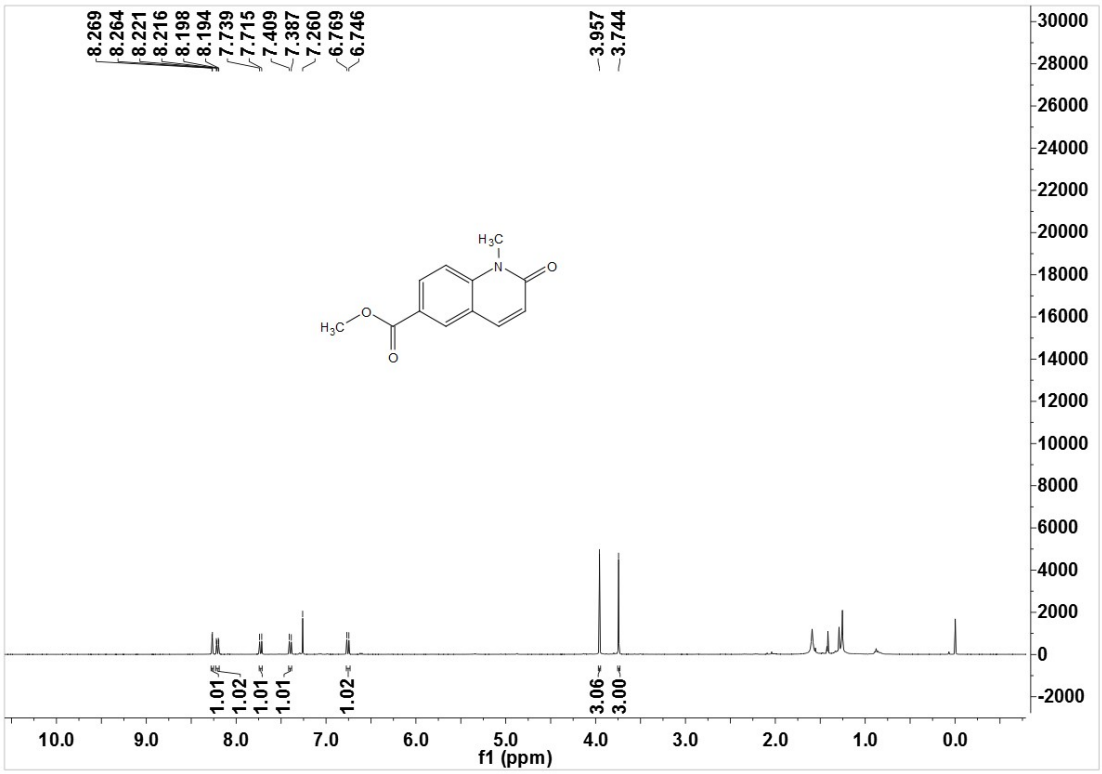


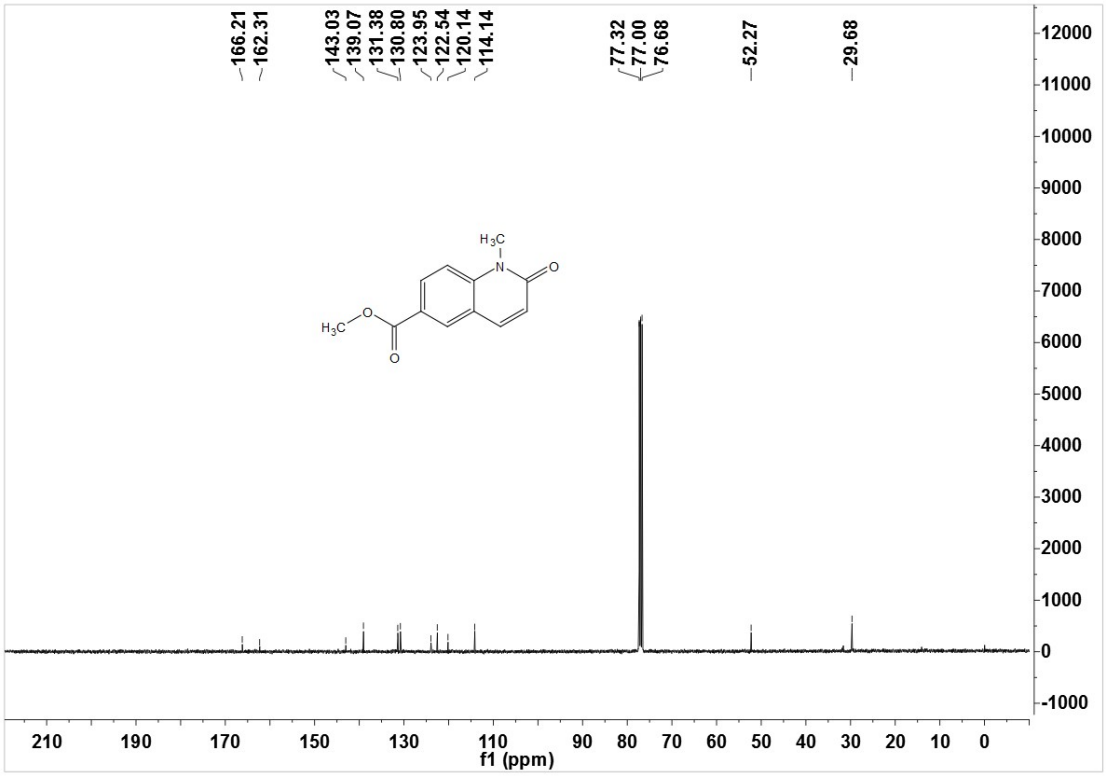
6-Acetyl-1-methylquinolin-2(1*H*)-one (3j)



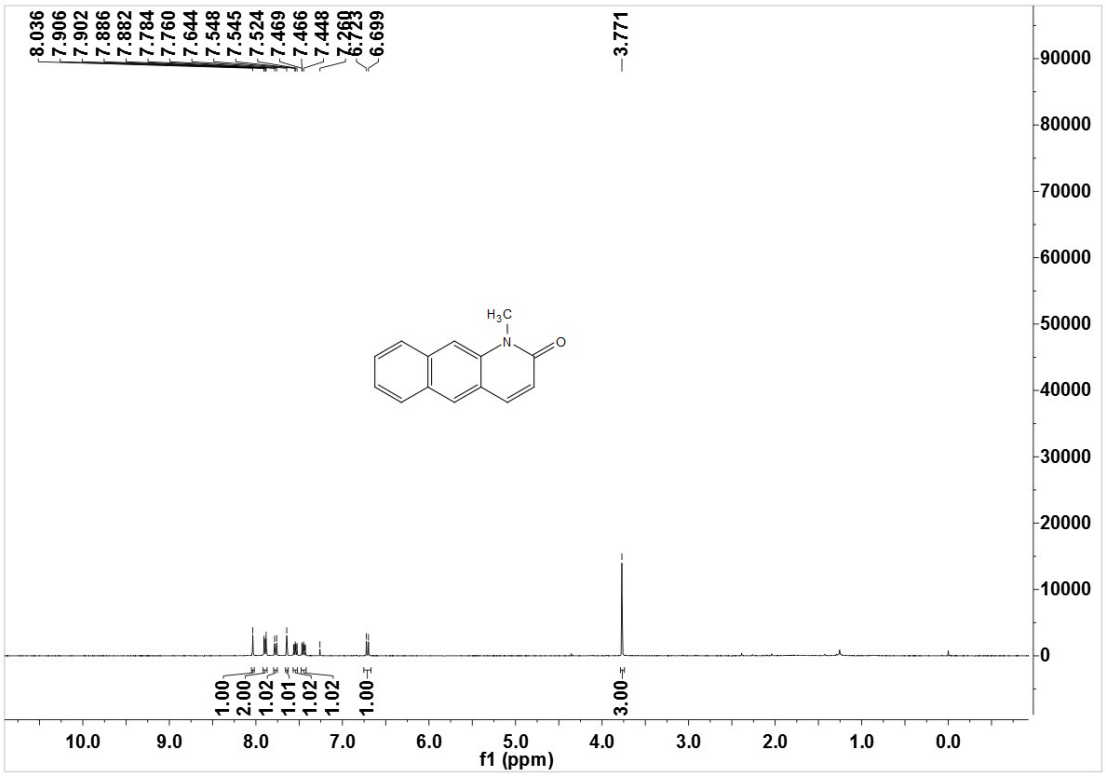


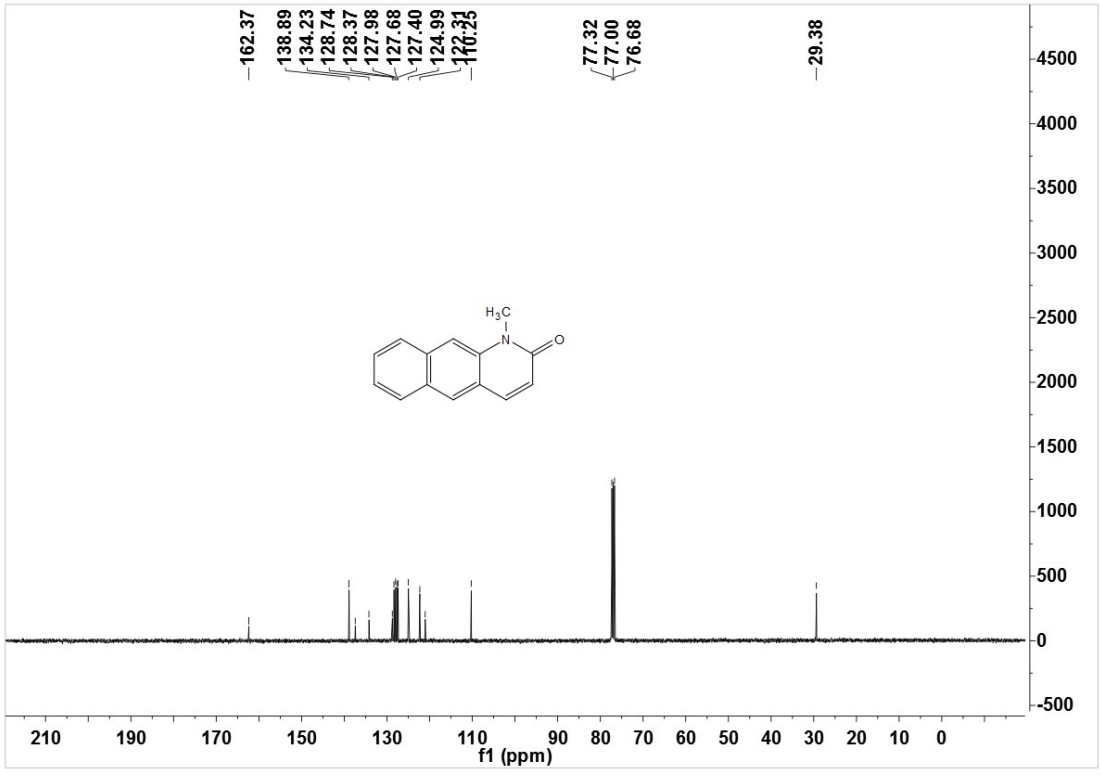
Methyl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3k)



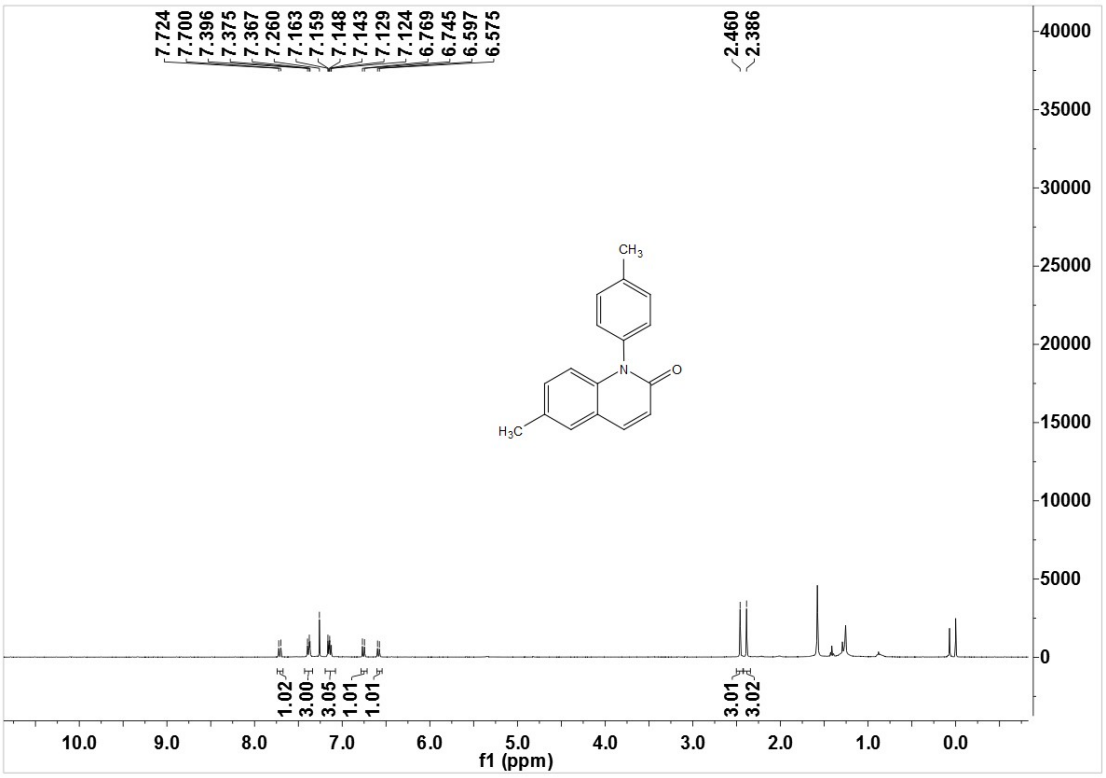


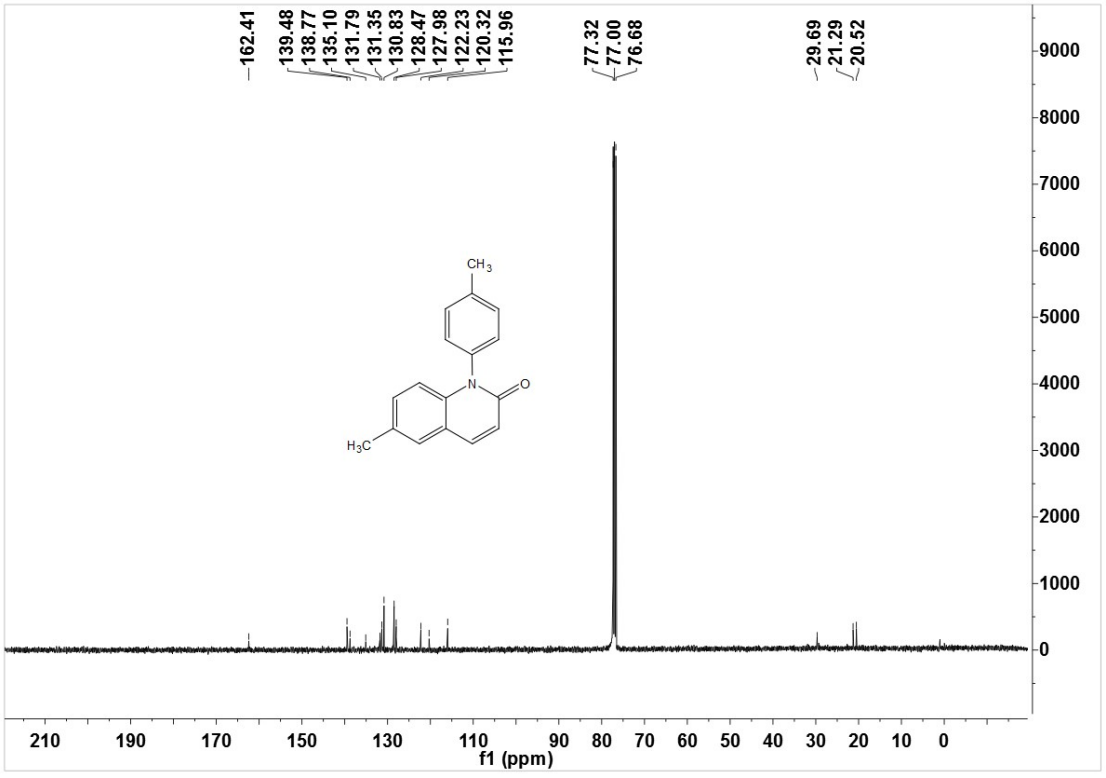
1-Methylbenzo[*g*]quinolin-2(1*H*)-one (3l)



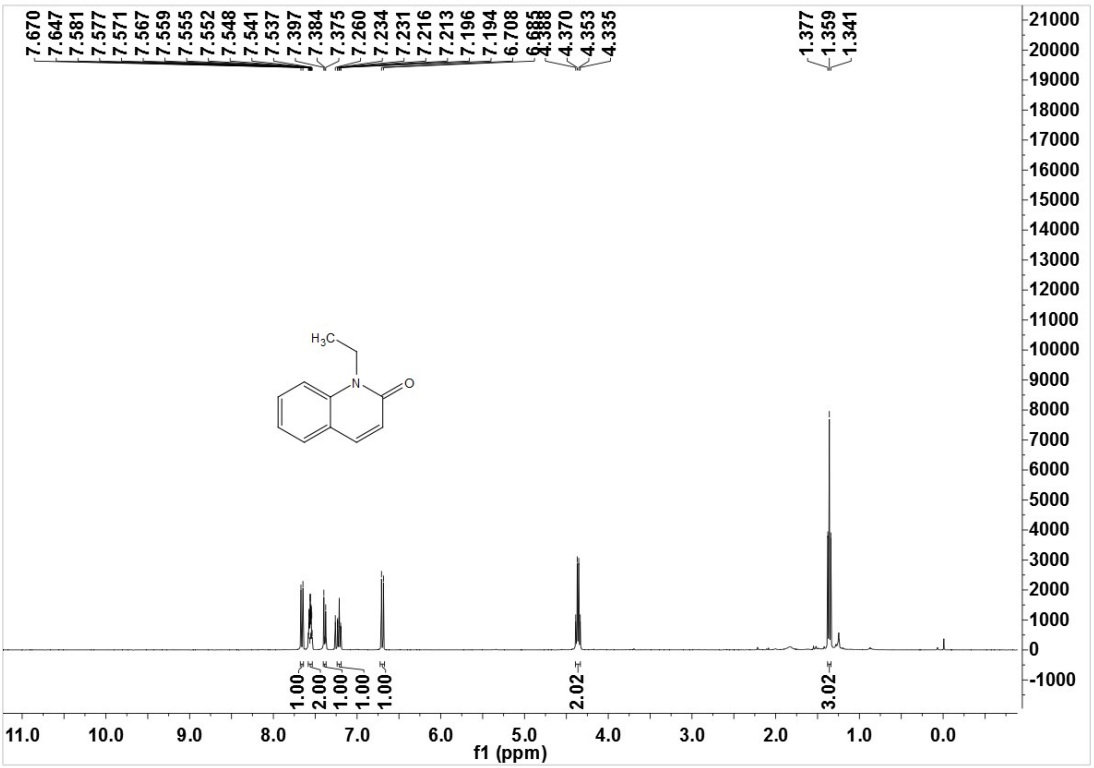


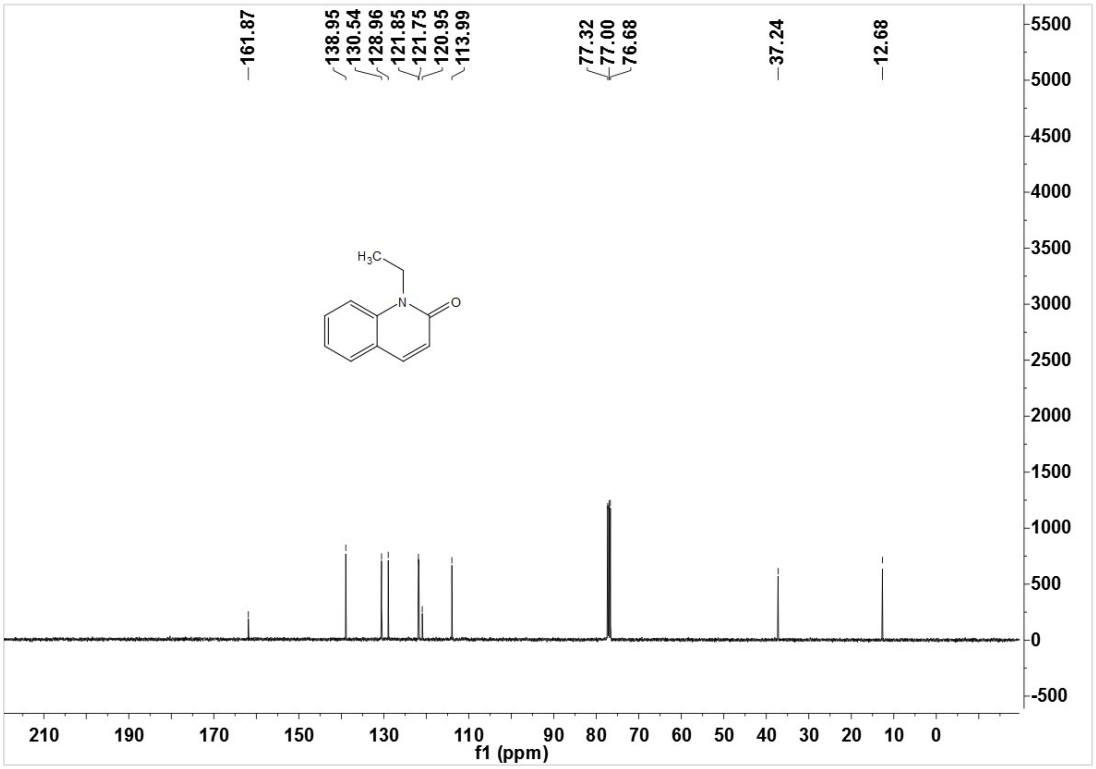
6-Methyl-1-(*p*-tolyl)quinolin-2(1*H*)-one (3m)



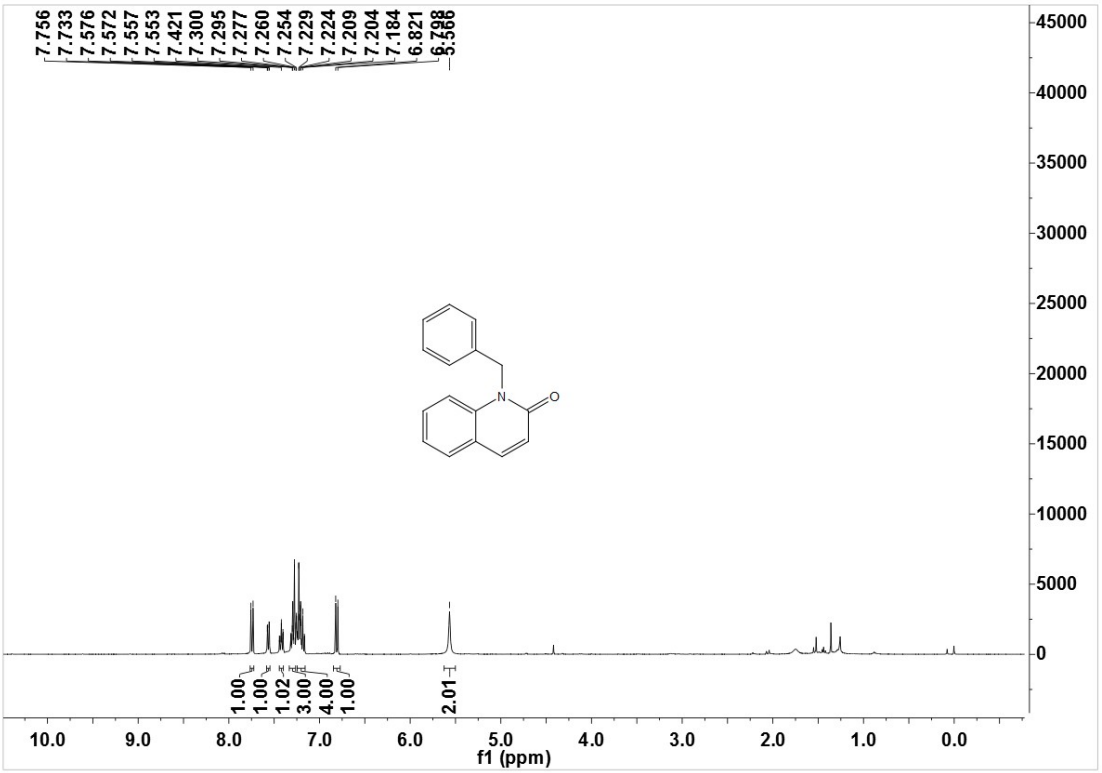


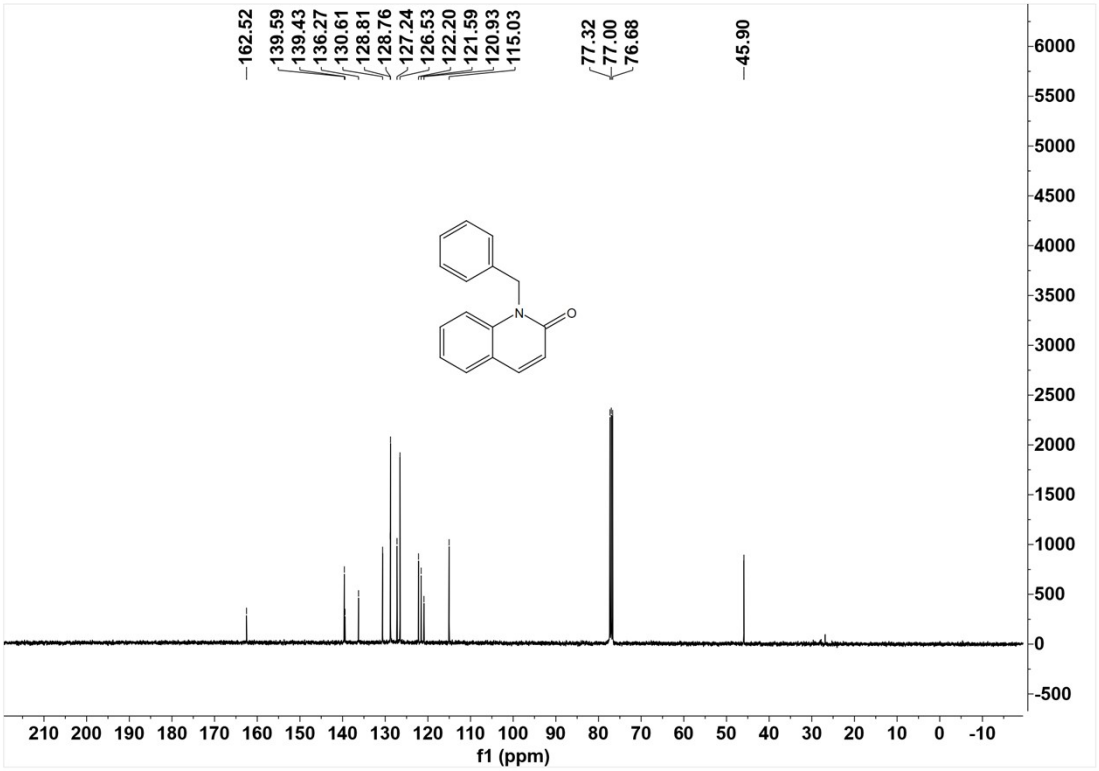
1-Ethylquinolin-2(1*H*)-one (3n)



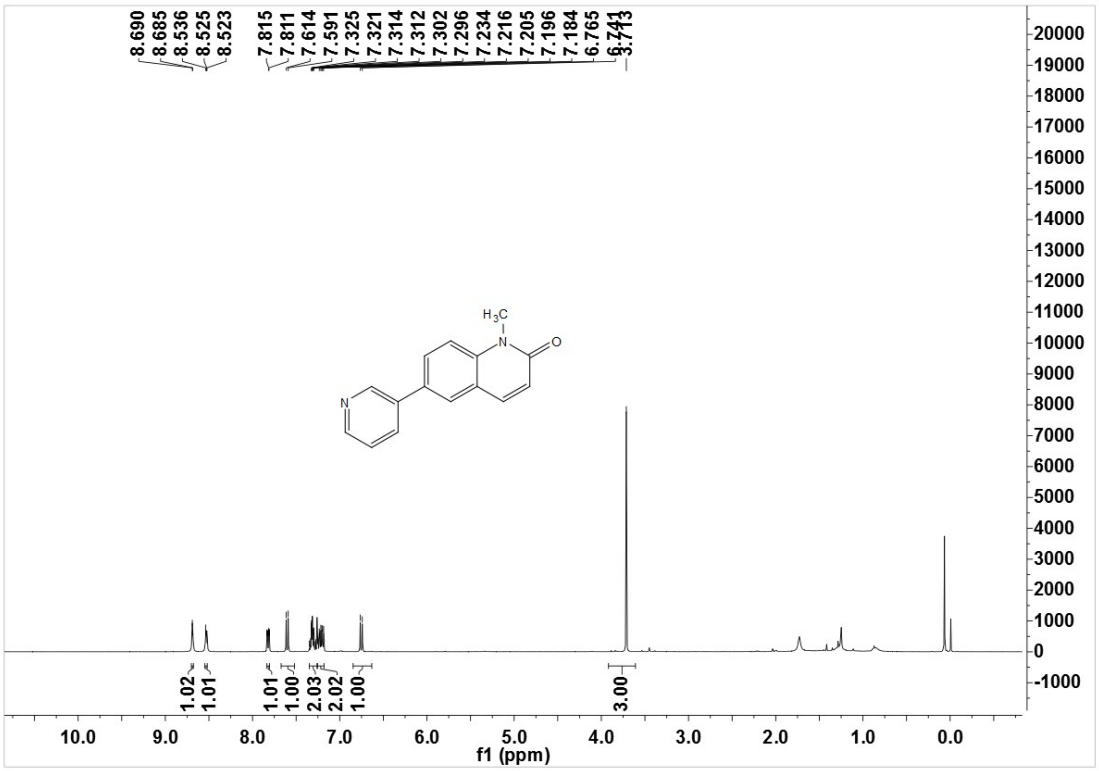


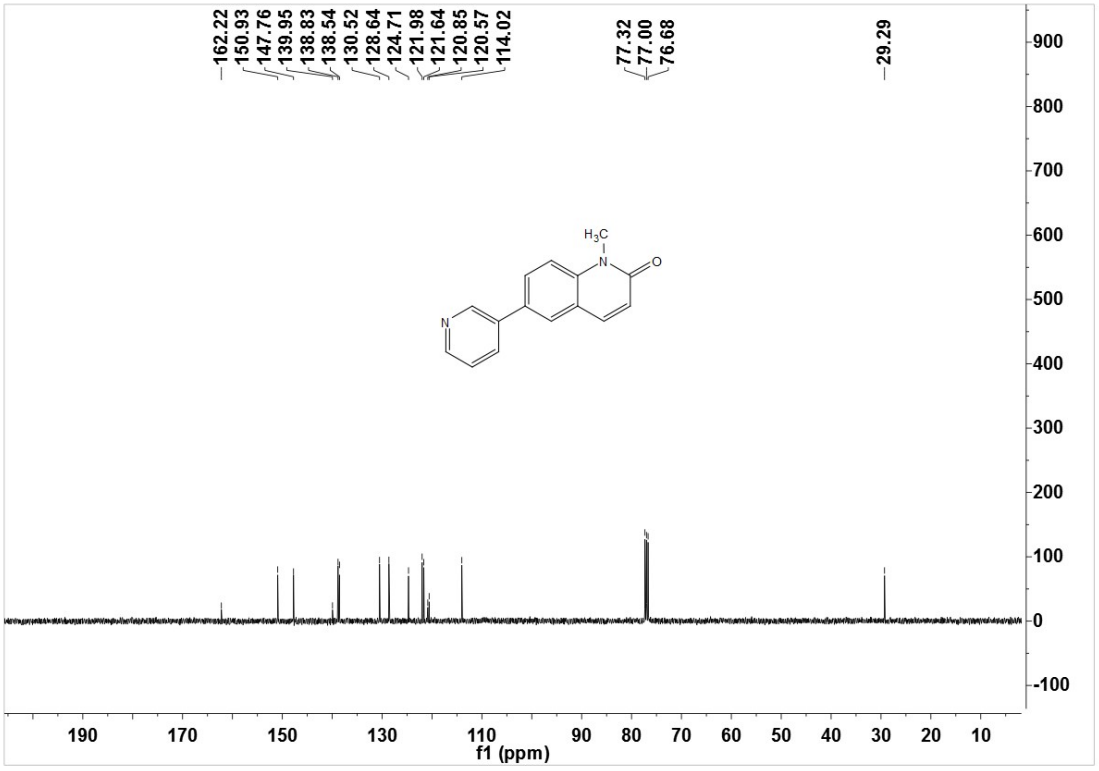
1-Benzylquinolin-2(1*H*)-one (3o)



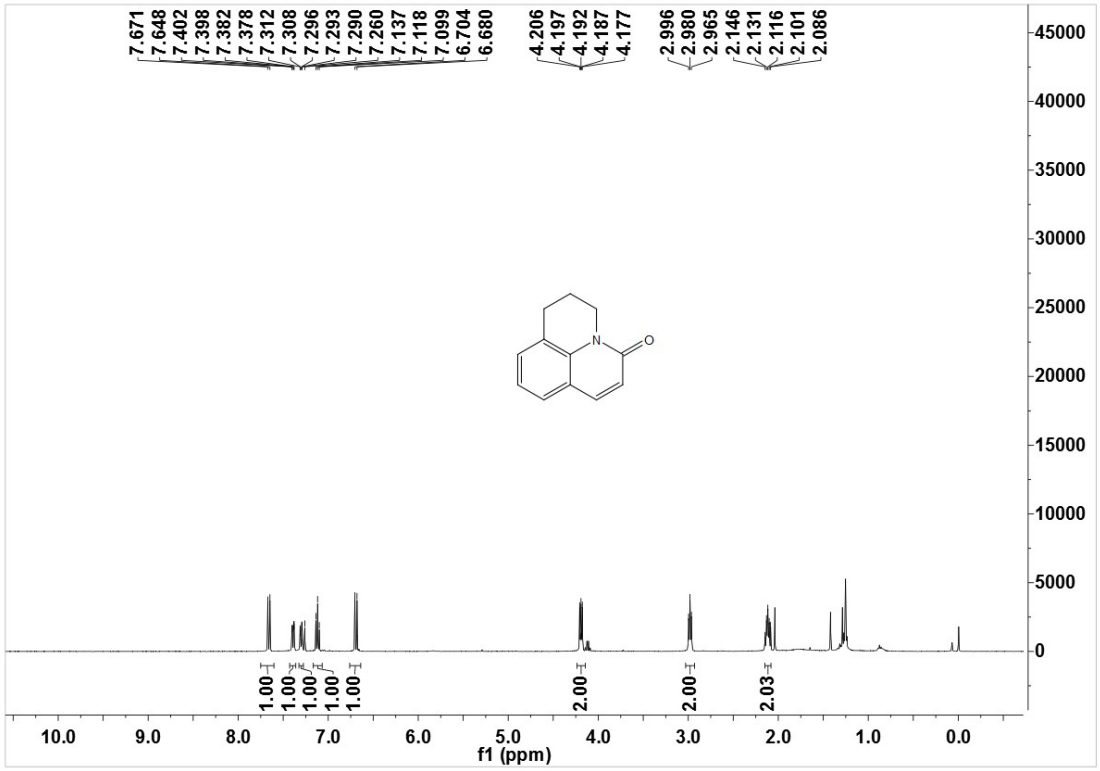


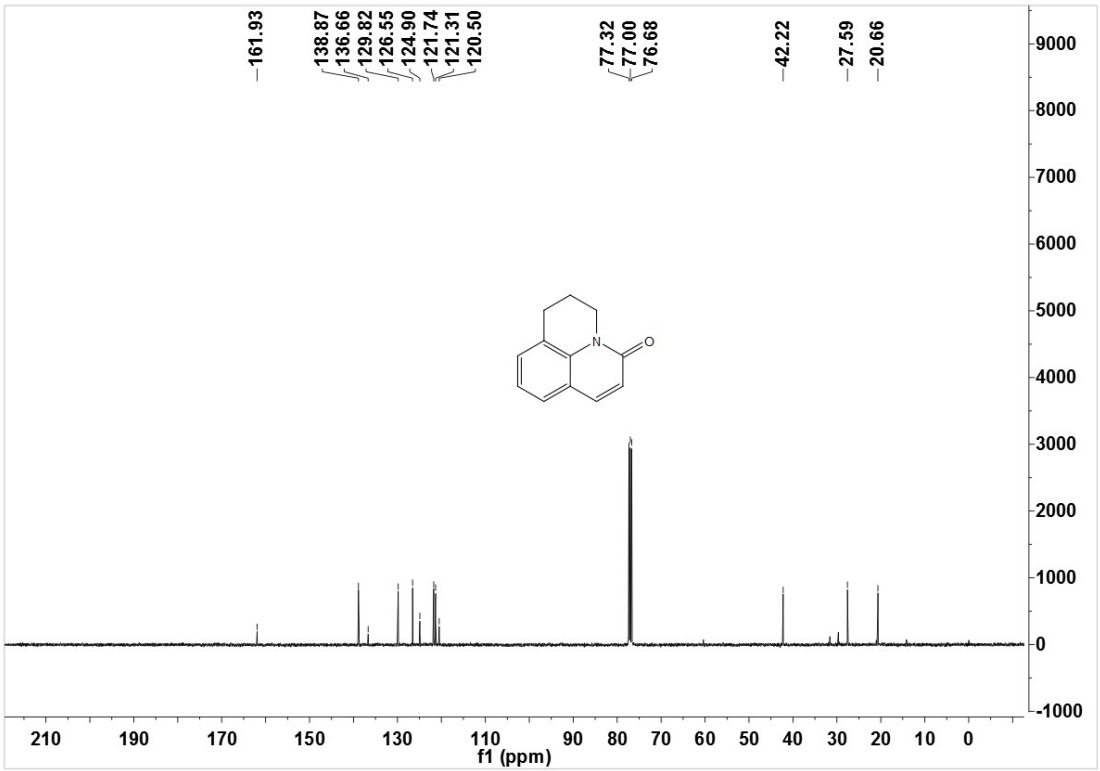
1-Methyl-6-(pyridin-3-yl)quinolin-2(1*H*)-one (3p)



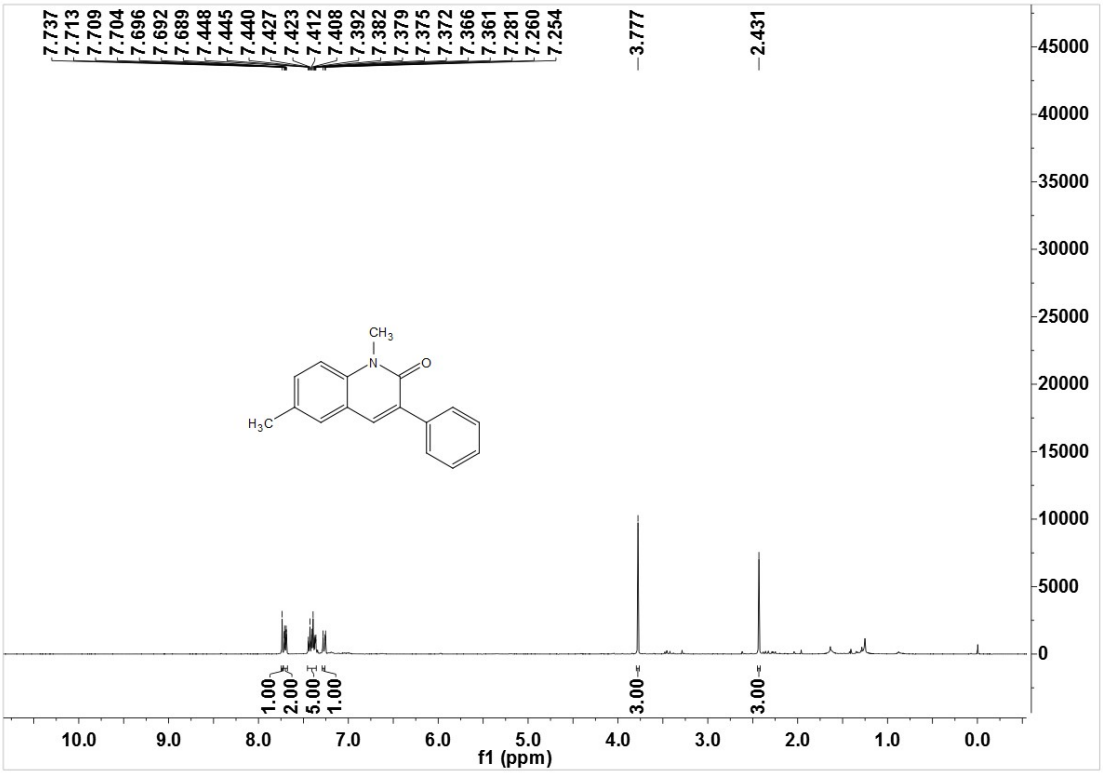


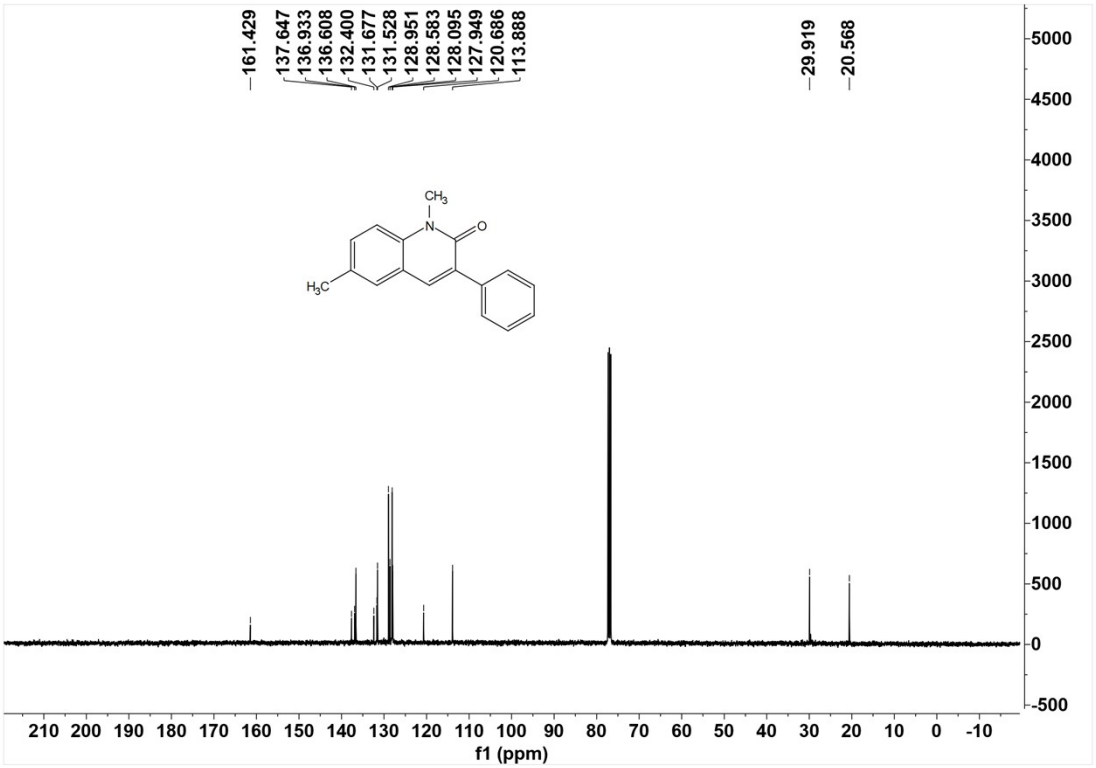
2,3-Dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinolin-5-one (3q)



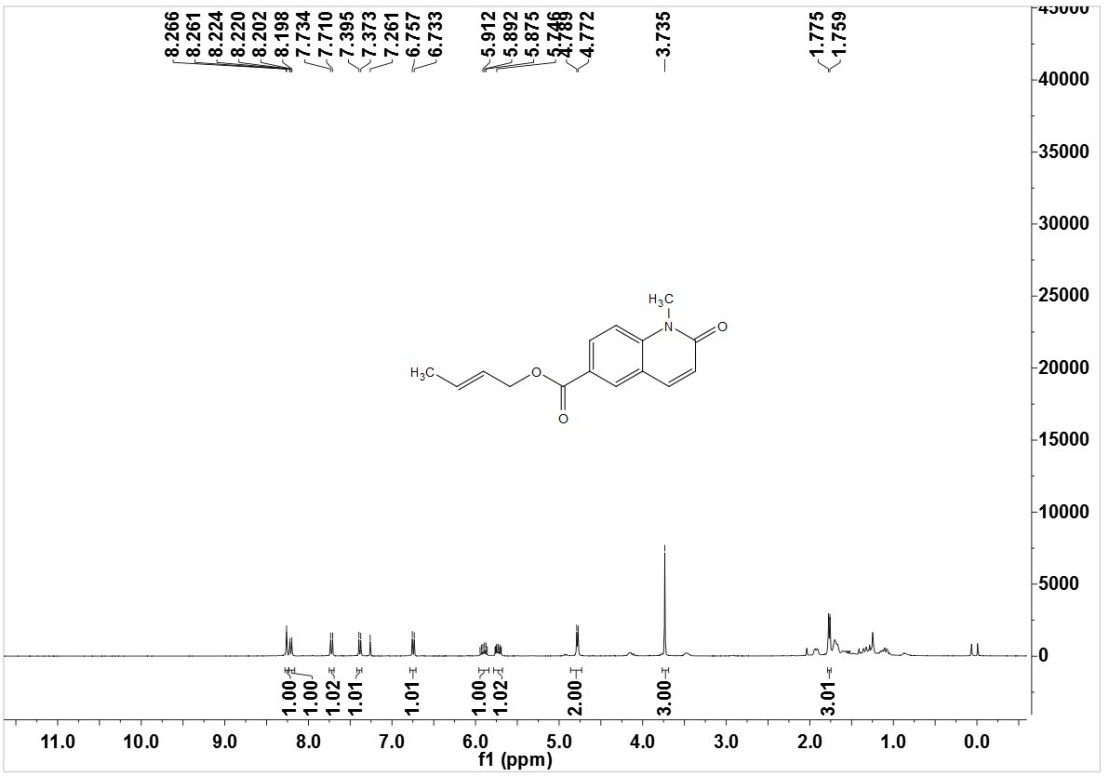


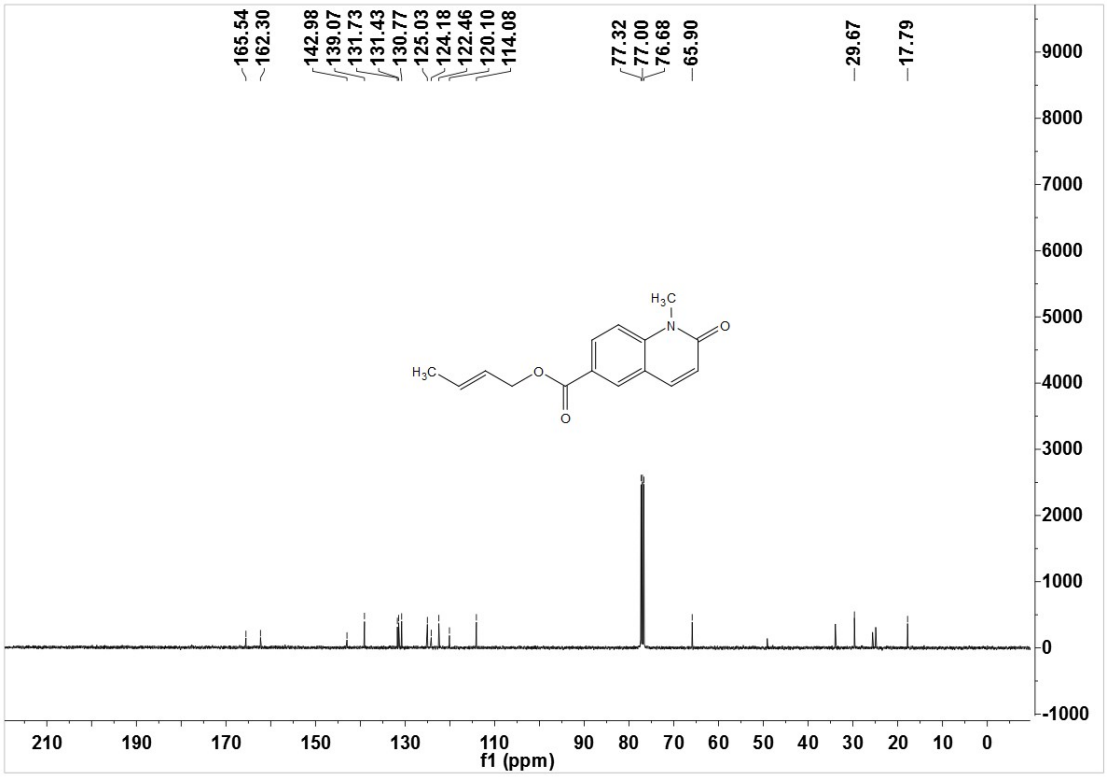
1,6-dimethyl-3-phenylquinolin-2(1*H*)-one (3r)



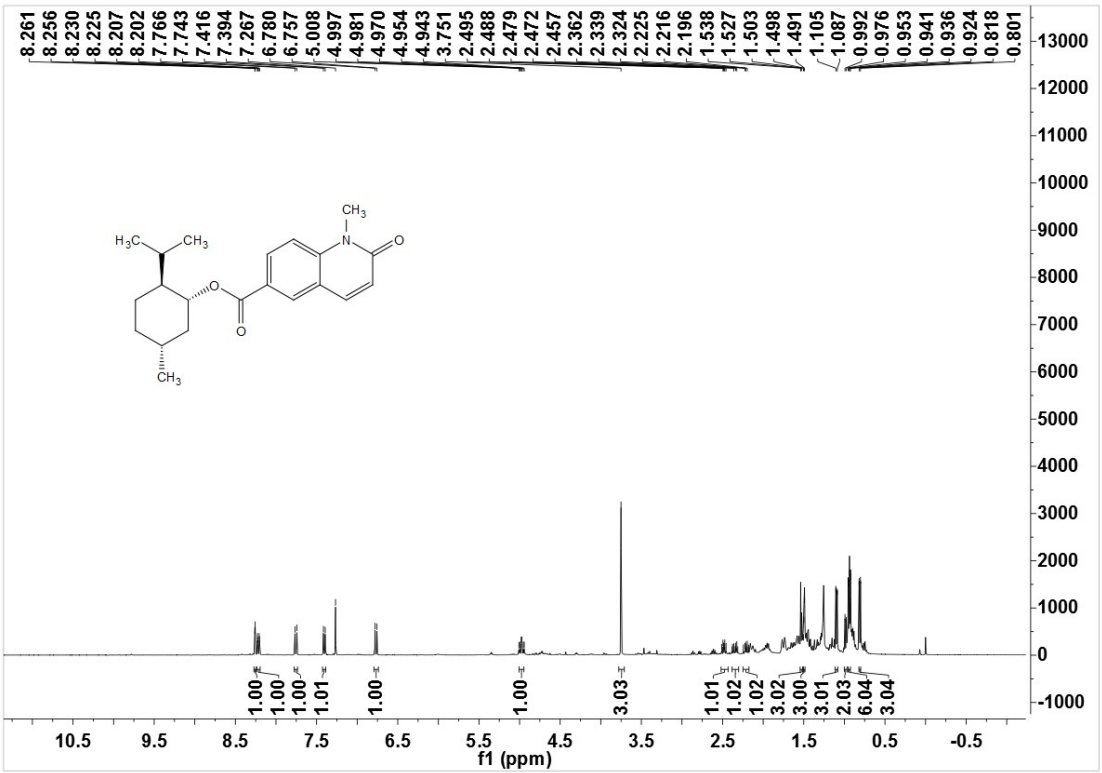


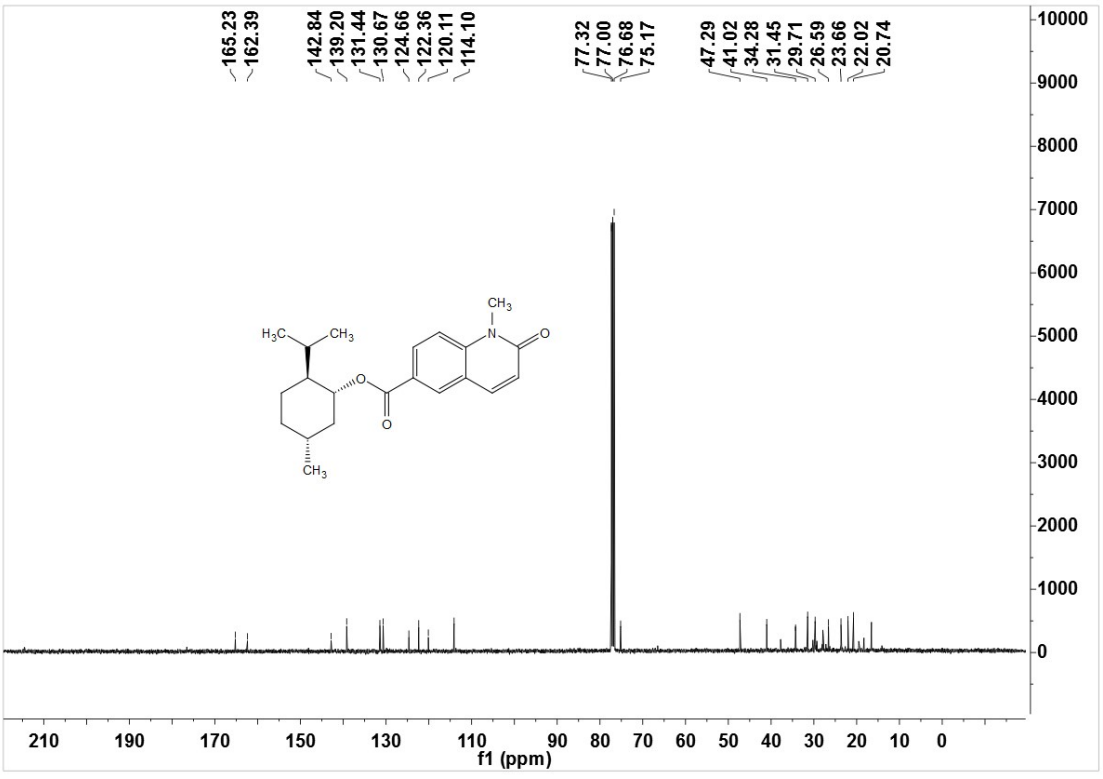
(*E*)-But-2-en-1-yl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3v)



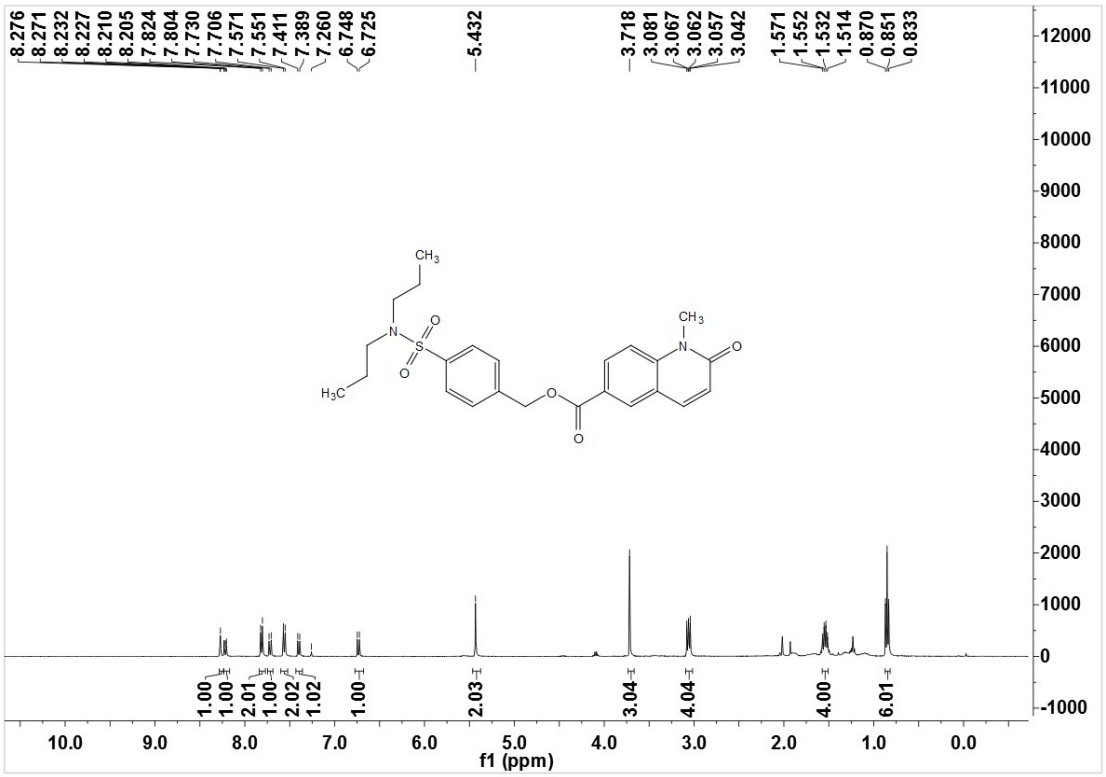


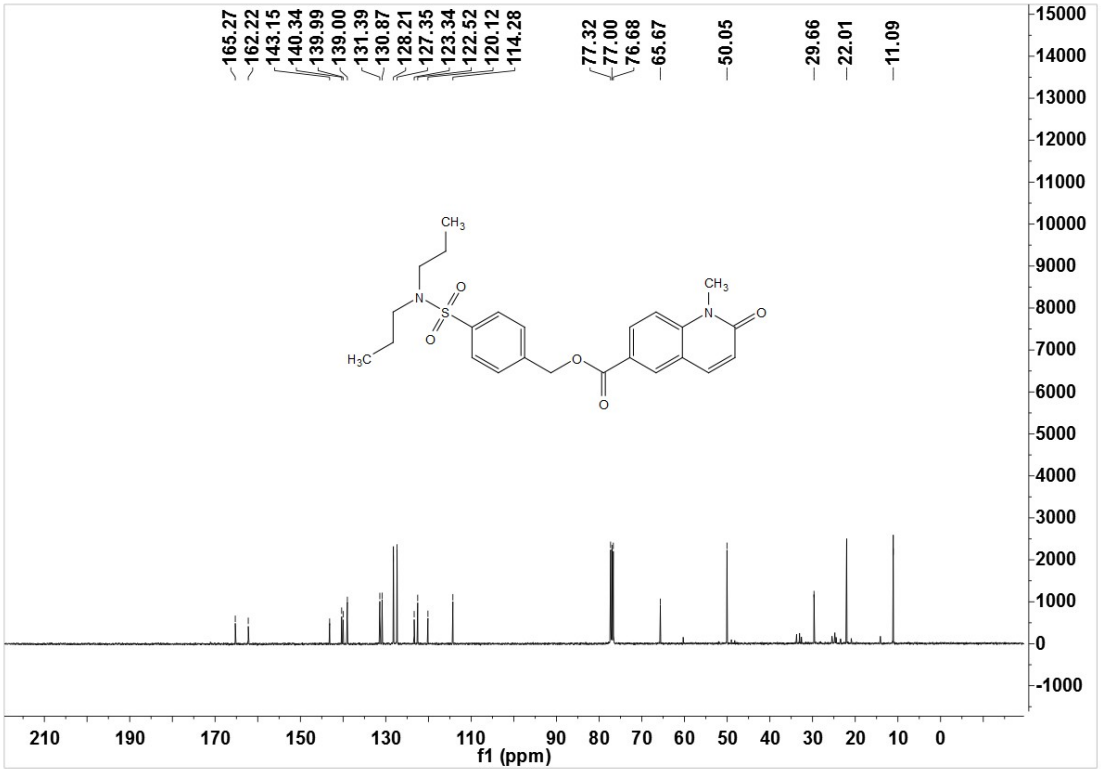
(1*R*, 2*S*, 5*R*)-2-Isopropyl-5-methylcyclohexyl 1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3w)



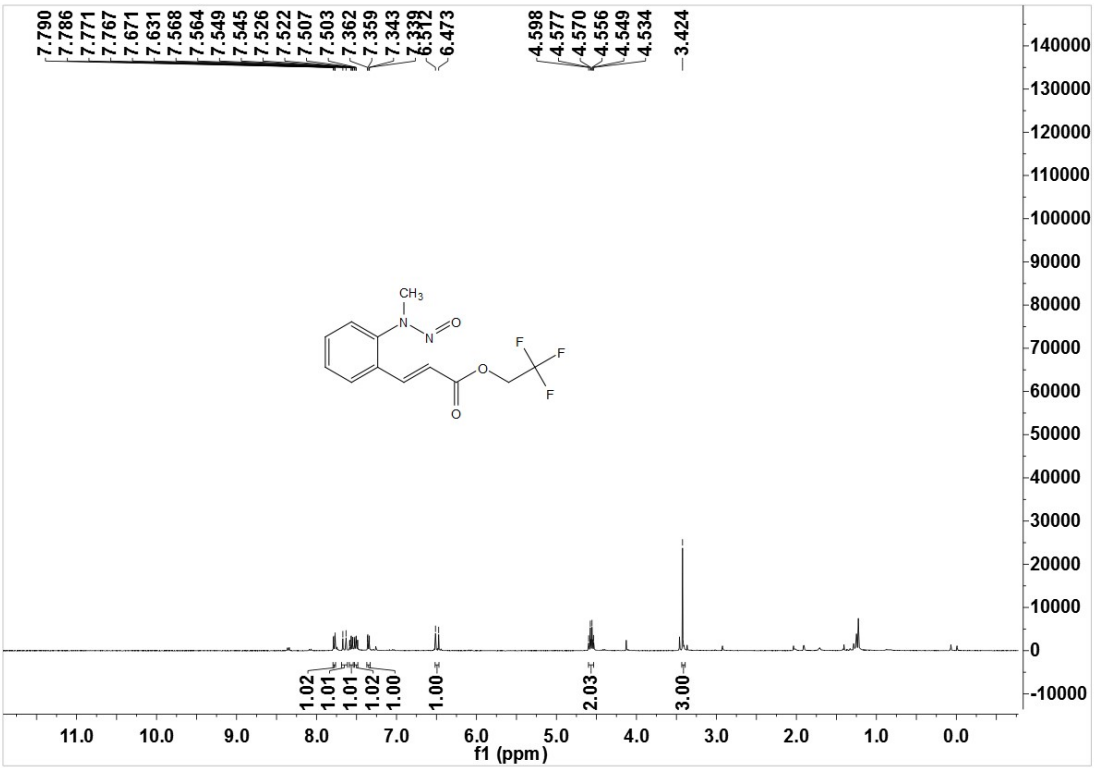


4-(*N*,*N*-dipropylsulfamoyl)benzyl1-methyl-2-oxo-1,2-dihydroquinoline-6-carboxylate (3x)





2,2,2-Trifluoroethyl (*E*)-3-(2-(methyl(nitroso)amino)phenyl)acrylate (3a-1)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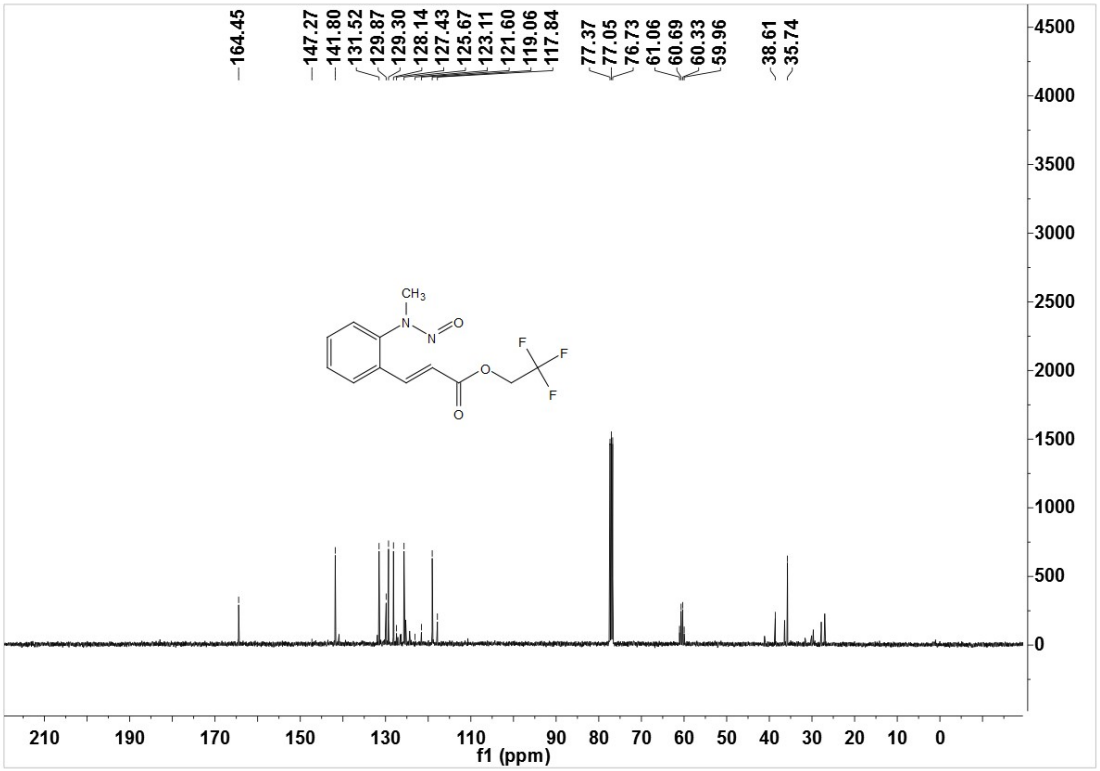
7.786
7.771
7.767
7.671
7.631
7.568
7.564
7.549
7.545
7.526
7.522
7.507
7.503
7.362
7.359
7.343
6.512
6.473
4.598
4.577
4.570
4.556
4.549
4.534
3.424
1.02
1.01
1.01
1.02
1.00
1.00
2.03
3.00
f1 (ppm)


164.45
147.27
141.80
131.52
129.87
129.30
128.14
127.43
125.67
123.11
121.60
119.06
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77.05
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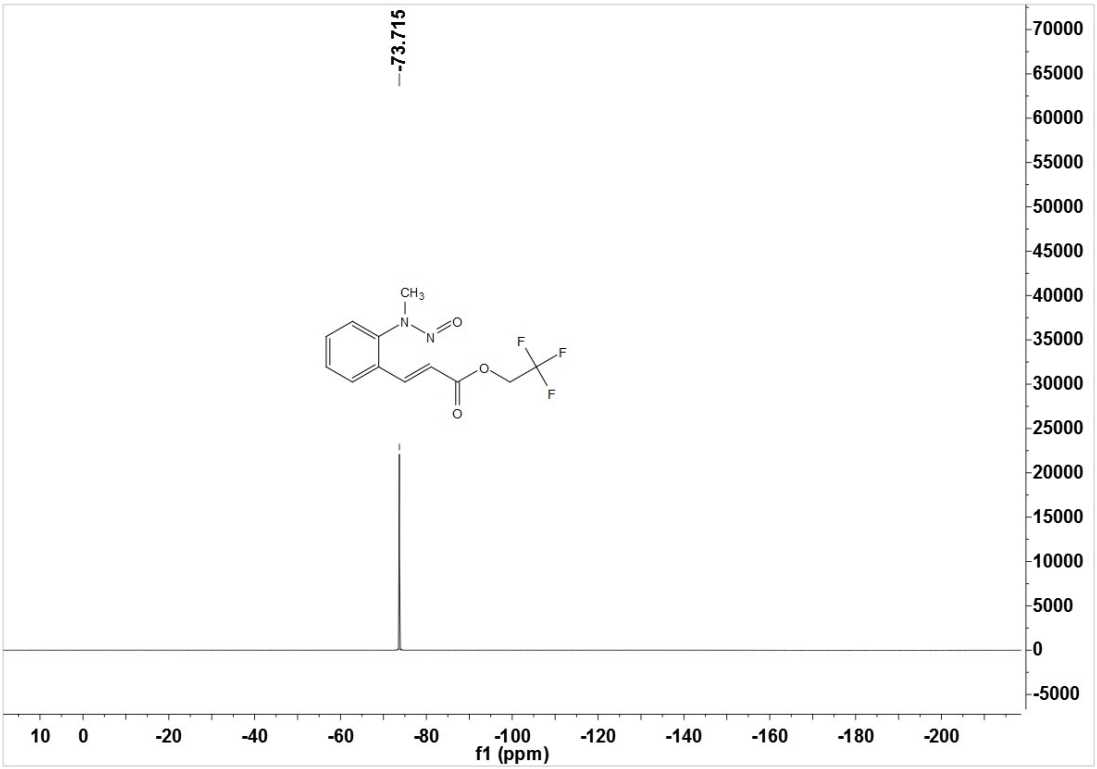
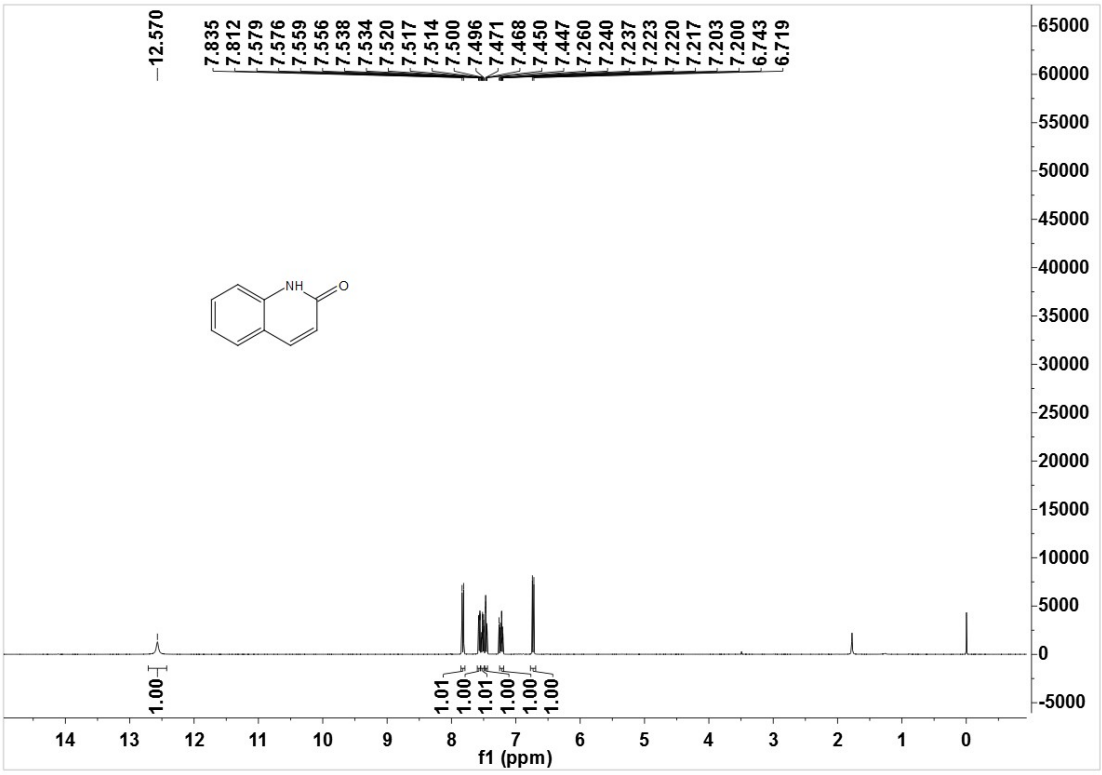
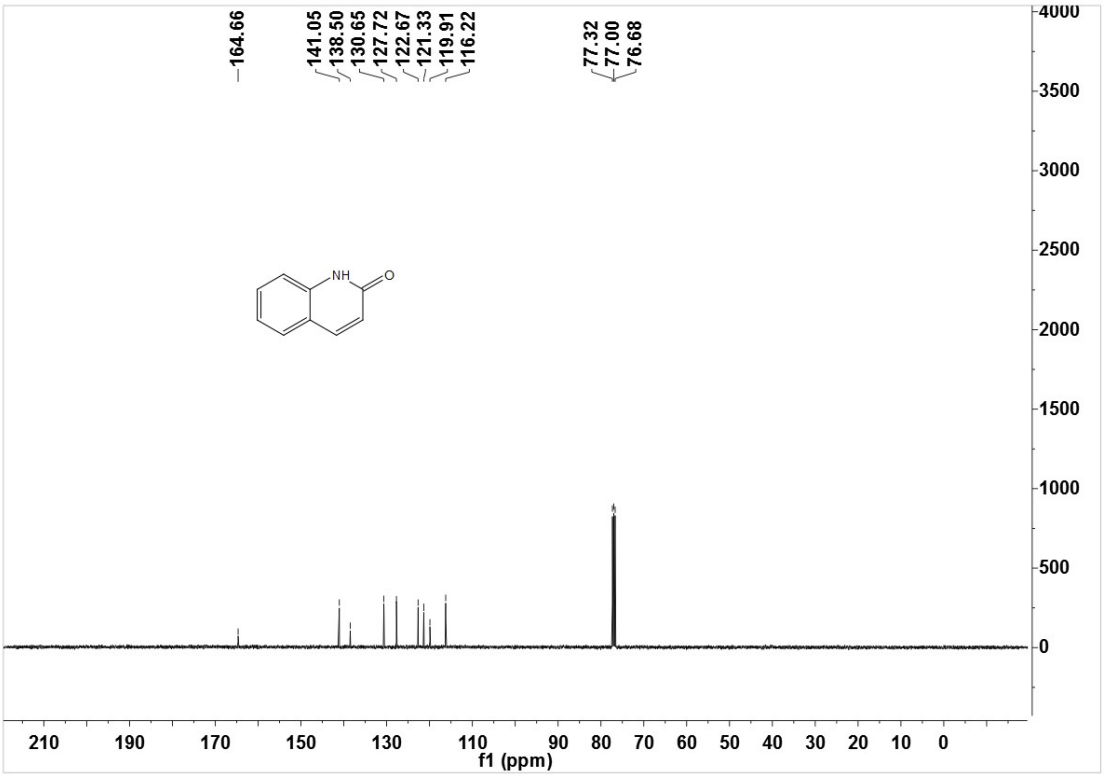
61.06
60.69
60.33
59.96
38.61
35.74
f1 (ppm)

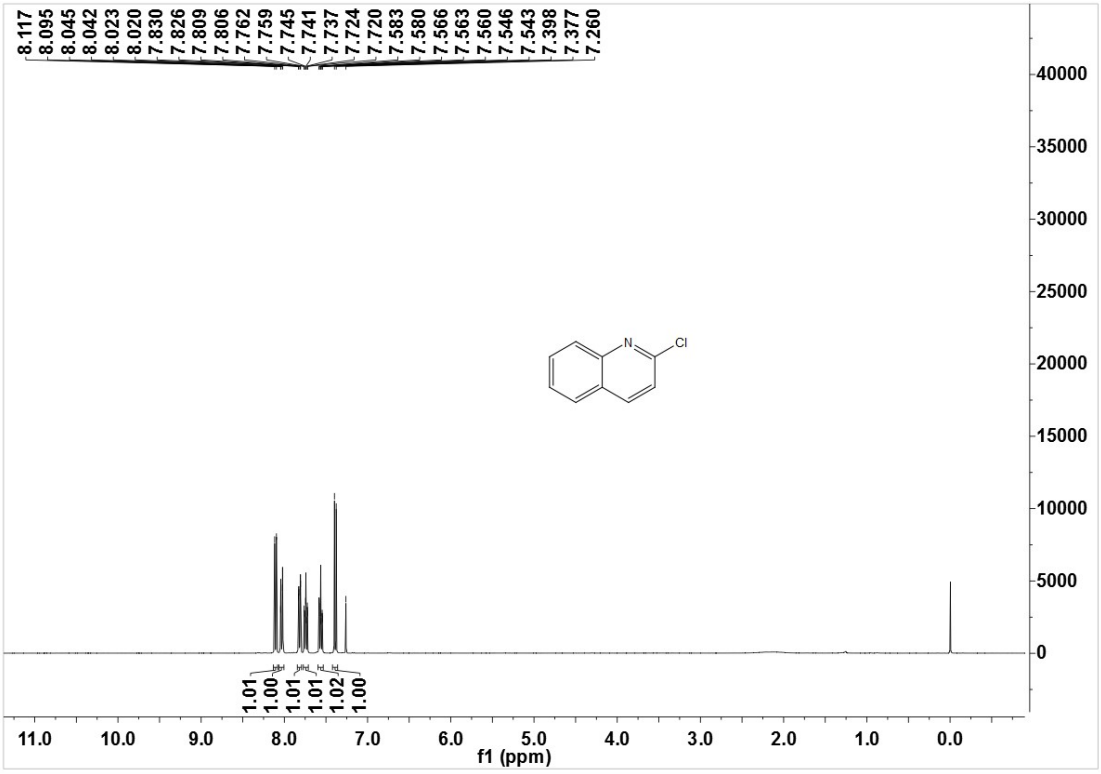


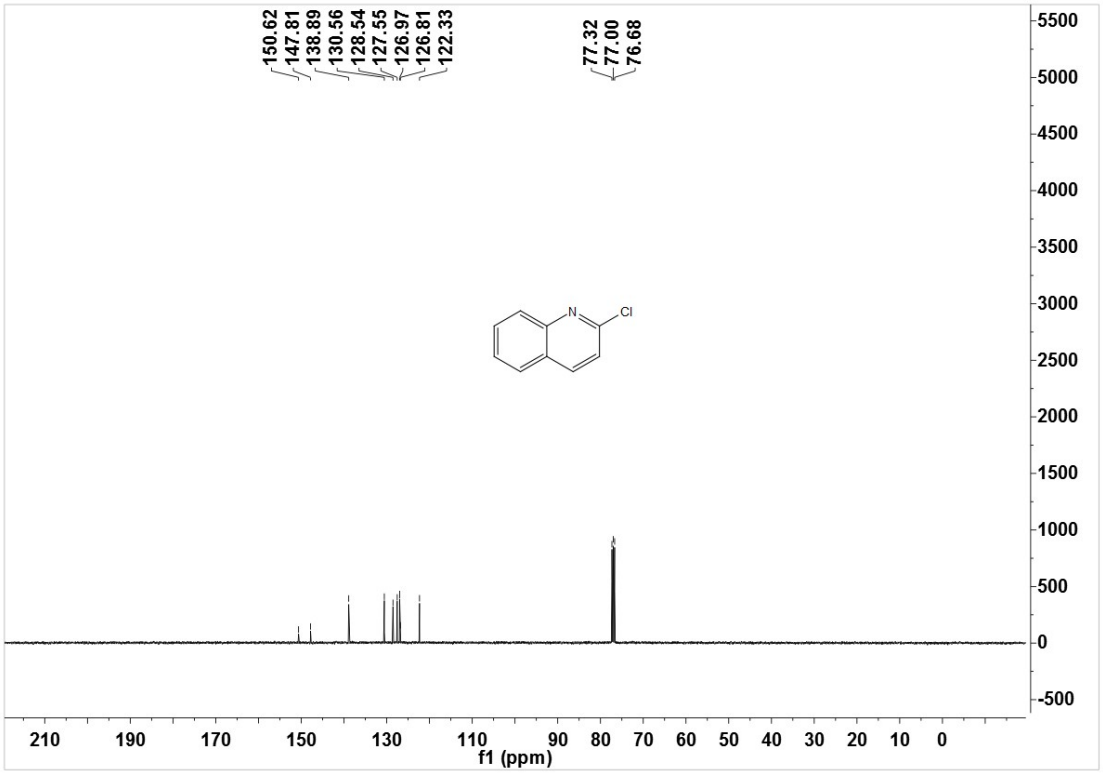
Quinolin-2(1*H*)-one (3o-1)



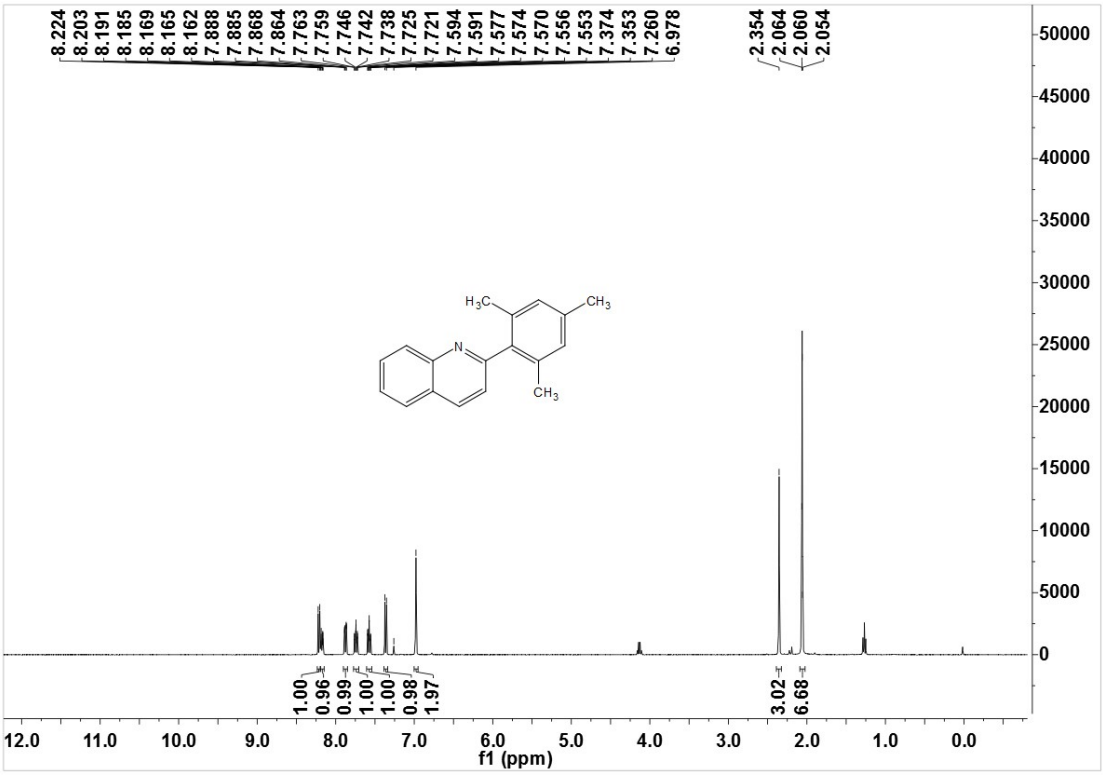


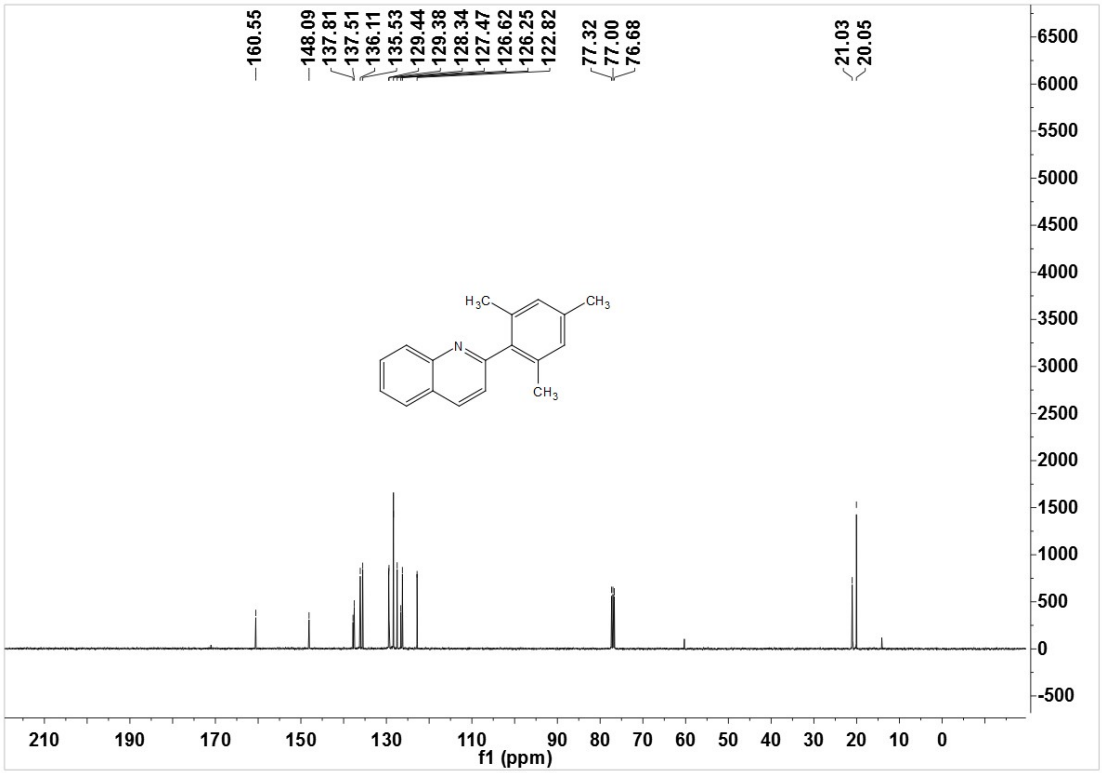
2-Chloroquinoline (3o-2)



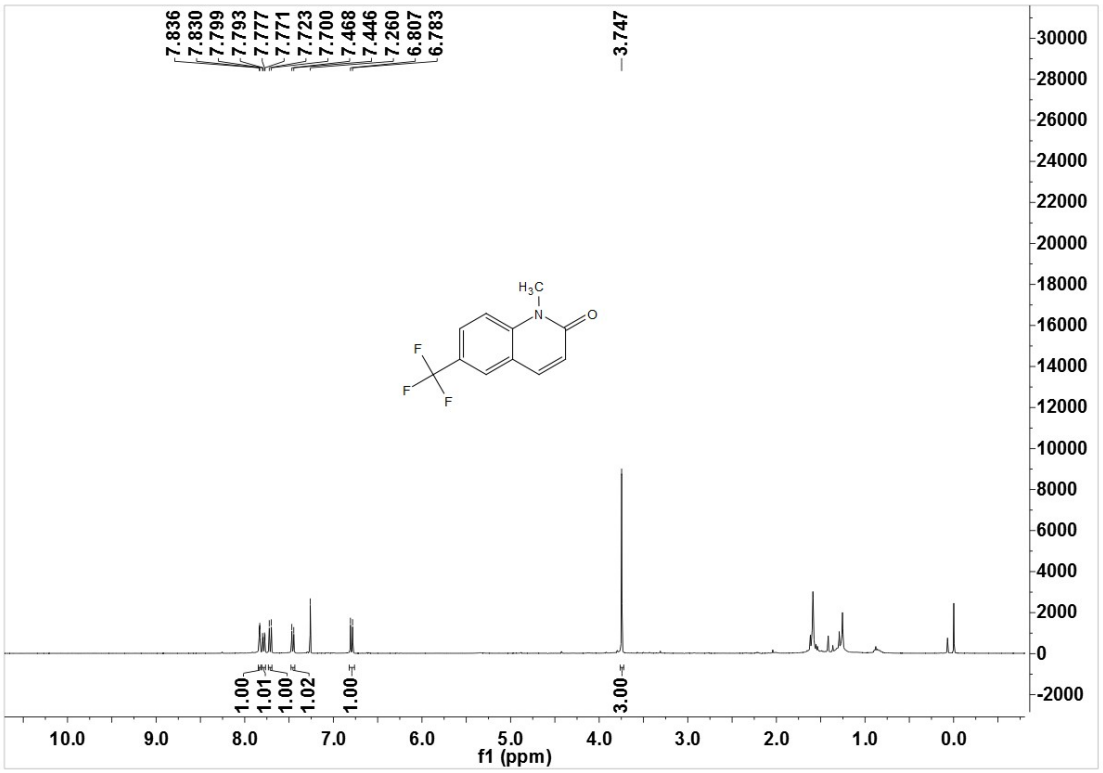


2-Mesitylquinoline (3o-3)





Methyl-6-(trifluoromethyl)quinolin-2(1*H*)-one (3y)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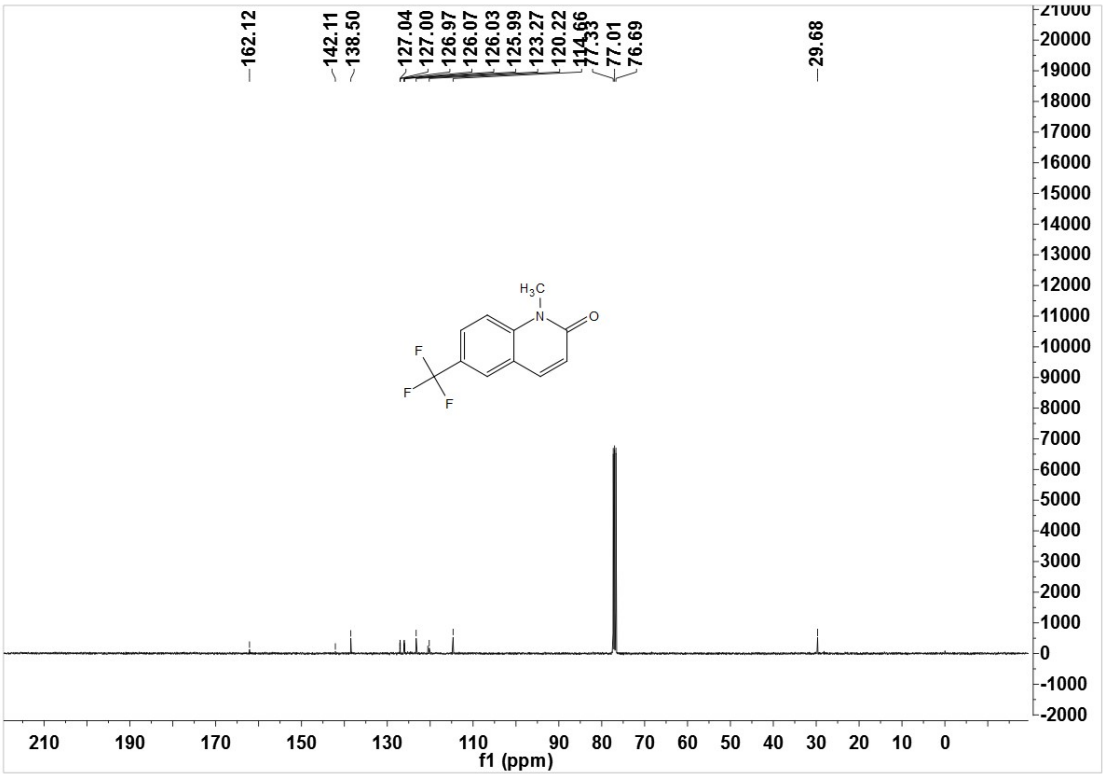
7.830
7.799
7.793
7.777
7.771
7.723
7.700
7.468
7.446
7.260
6.807
6.783
3.747
1.00
1.01
1.00
1.02
1.00
3.00
f1 (ppm)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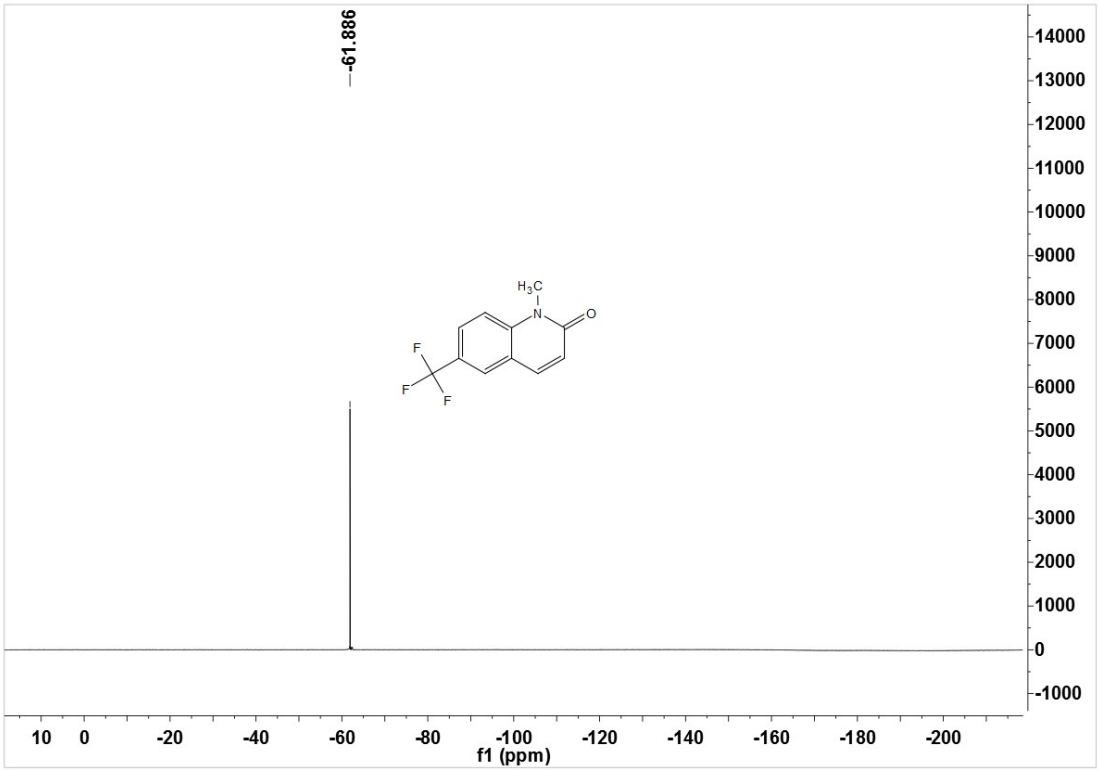
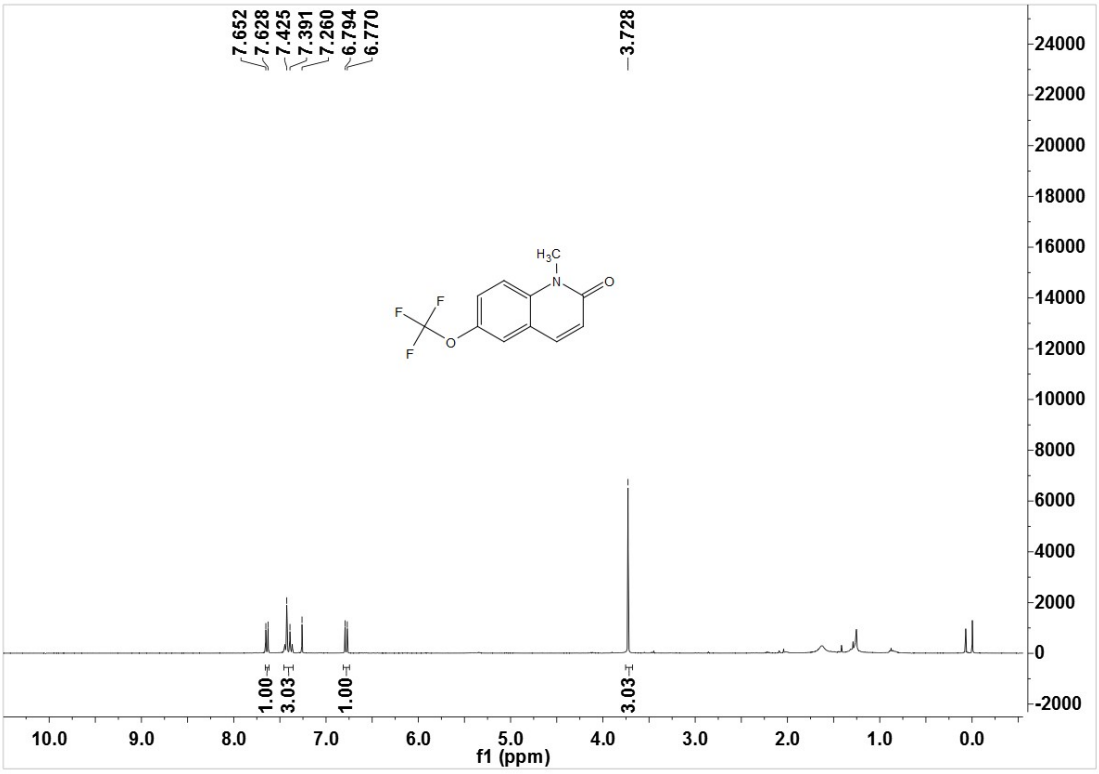
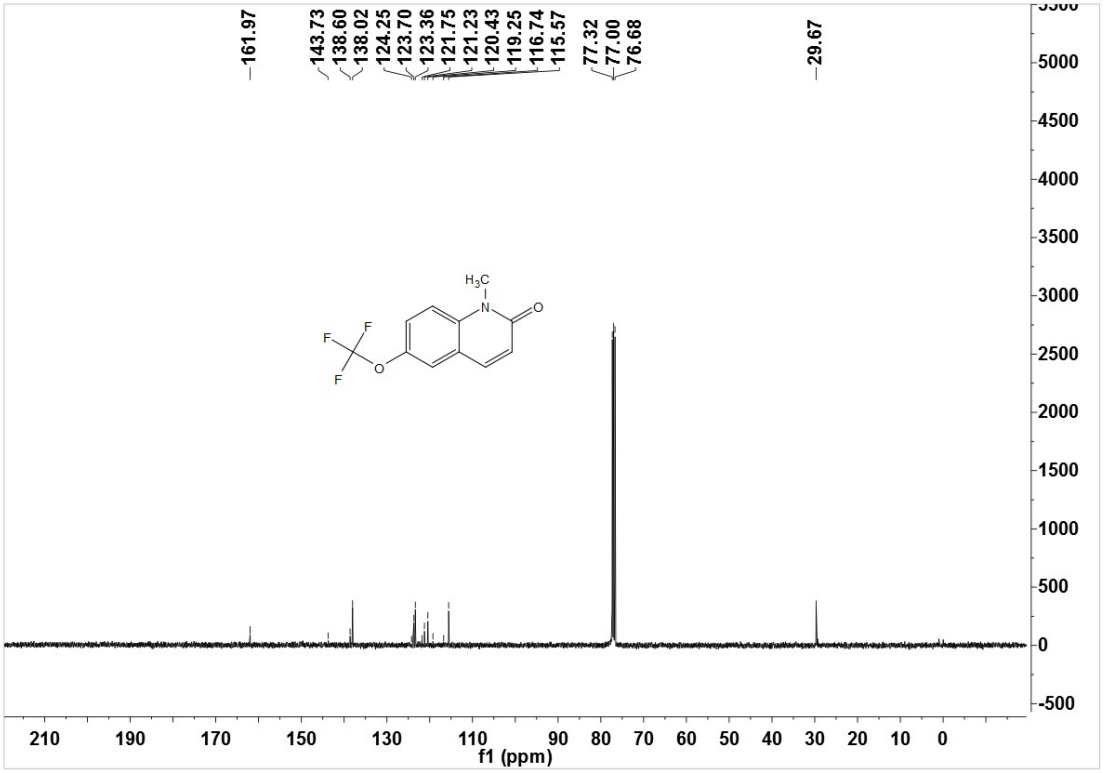
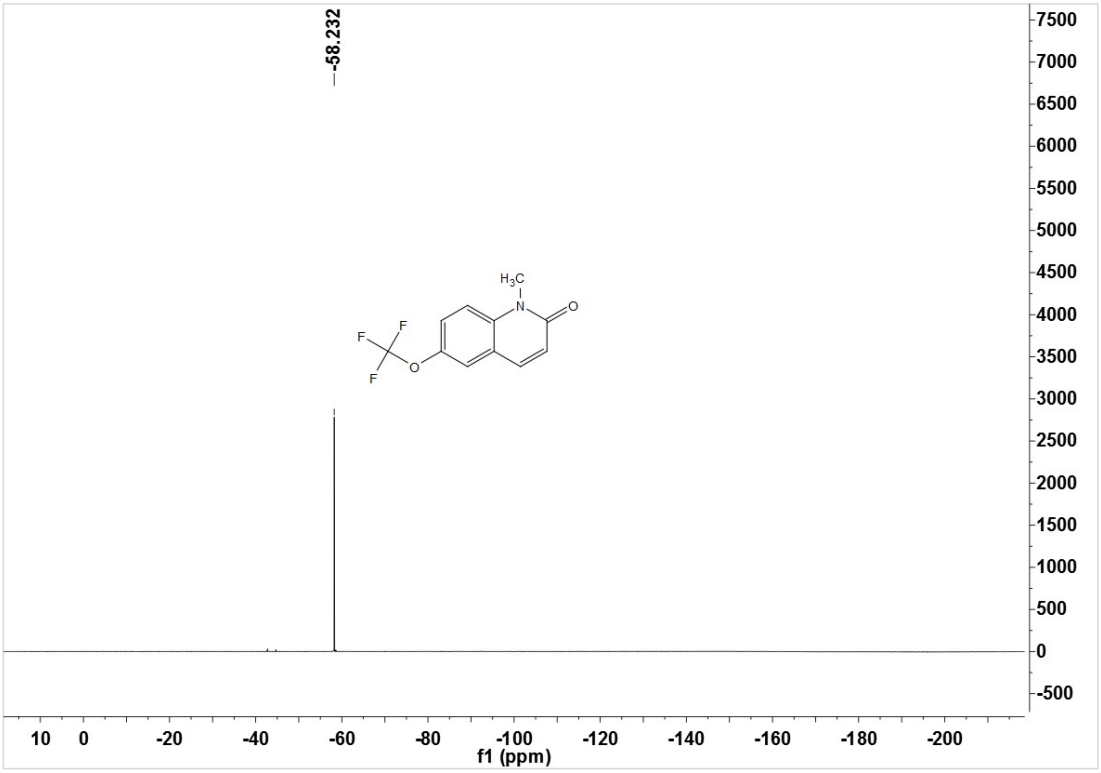
142.11
138.50
127.04
127.00
126.97
126.07
126.03
125.99
123.27
120.22
114.66
77.33
77.01
76.69
29.68
f1 (ppm)



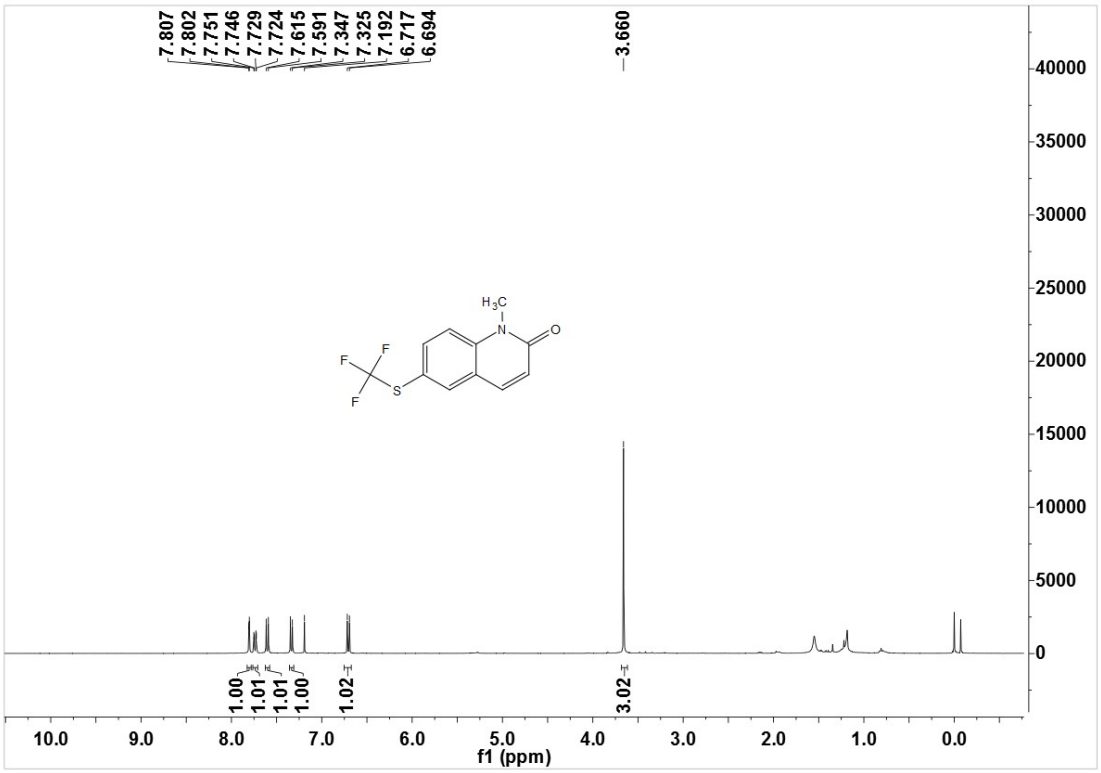
1-Methyl-6-(trifluoromethoxy)quinolin-2(1*H*)-one (3z)

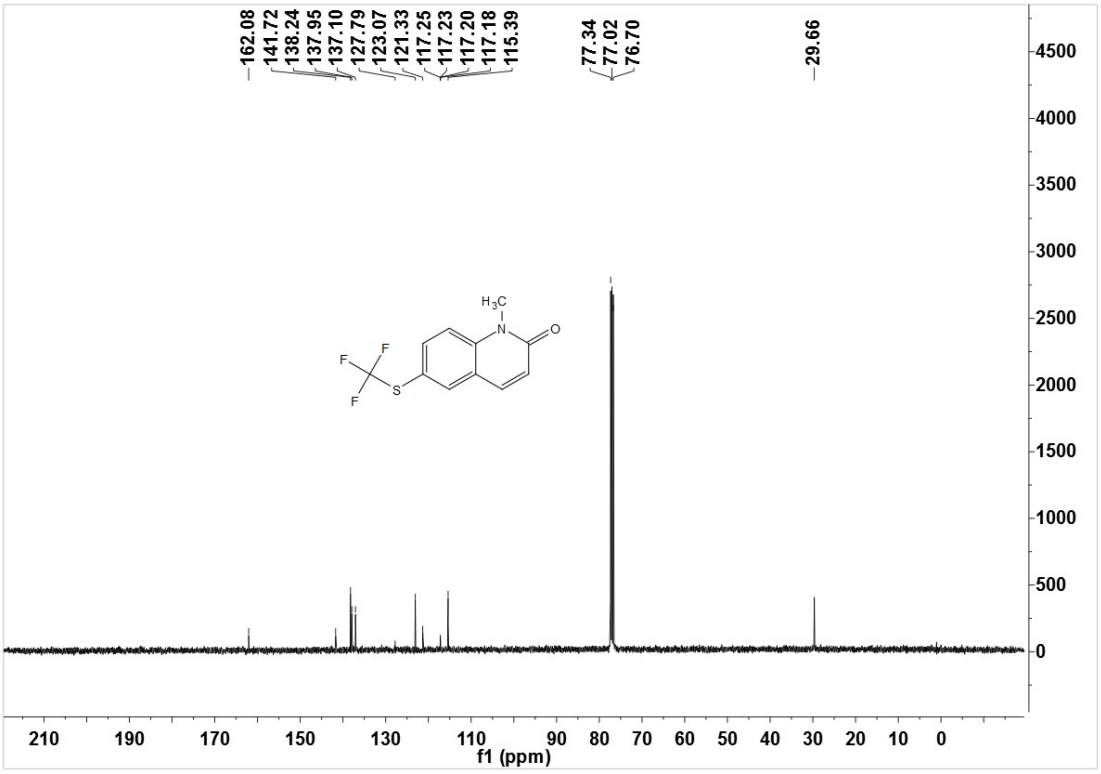


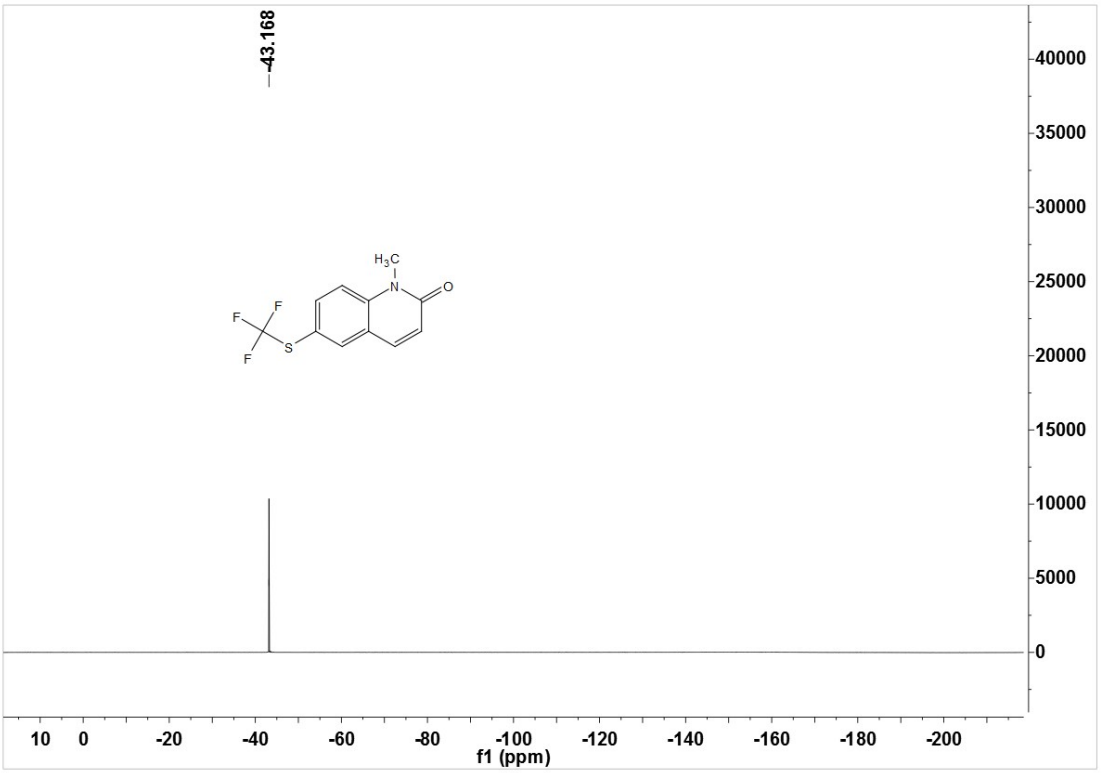

161.97
143.73
138.60
138.02
124.25
123.70
123.36
121.75
121.23
120.43
119.25
116.74
115.57
77.32
77.00
76.68
29.67
H3C
N
O
F
F
F
O
f1 (ppm)


-58.232
H3C
N
O
F
F
F
O
f1 (ppm)

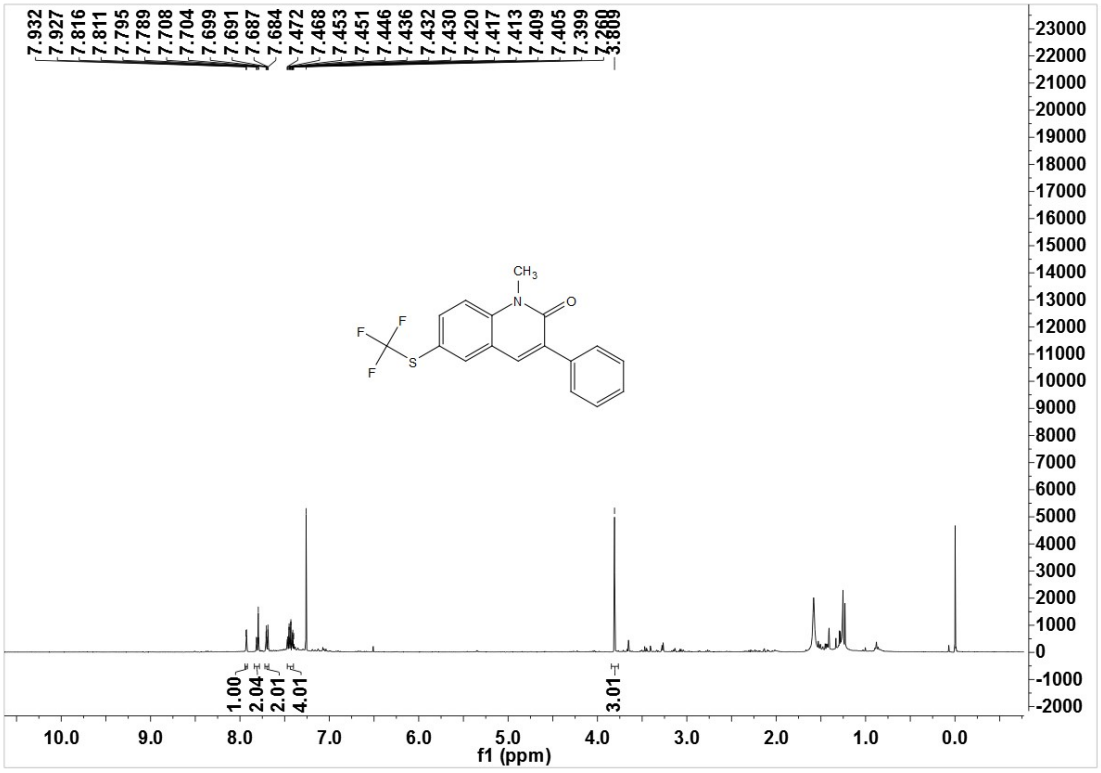
1-Methyl-6-((trifluoromethyl)thio)quinolin-2(1*H*)-one (3za)

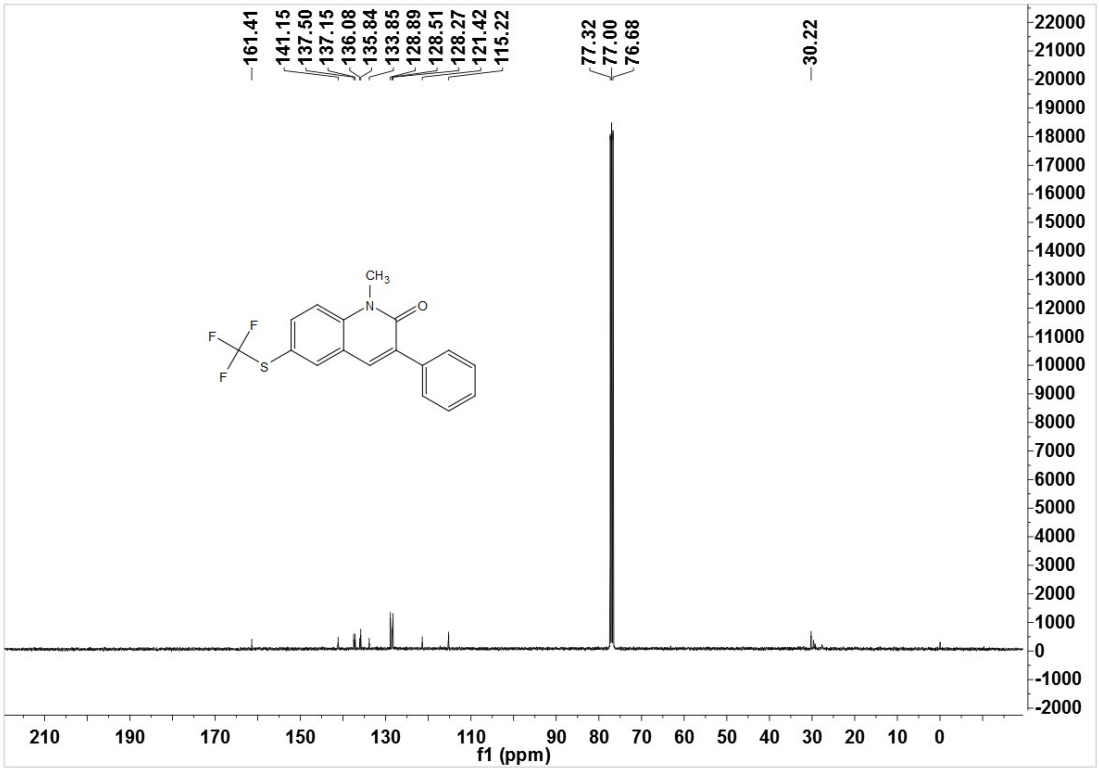


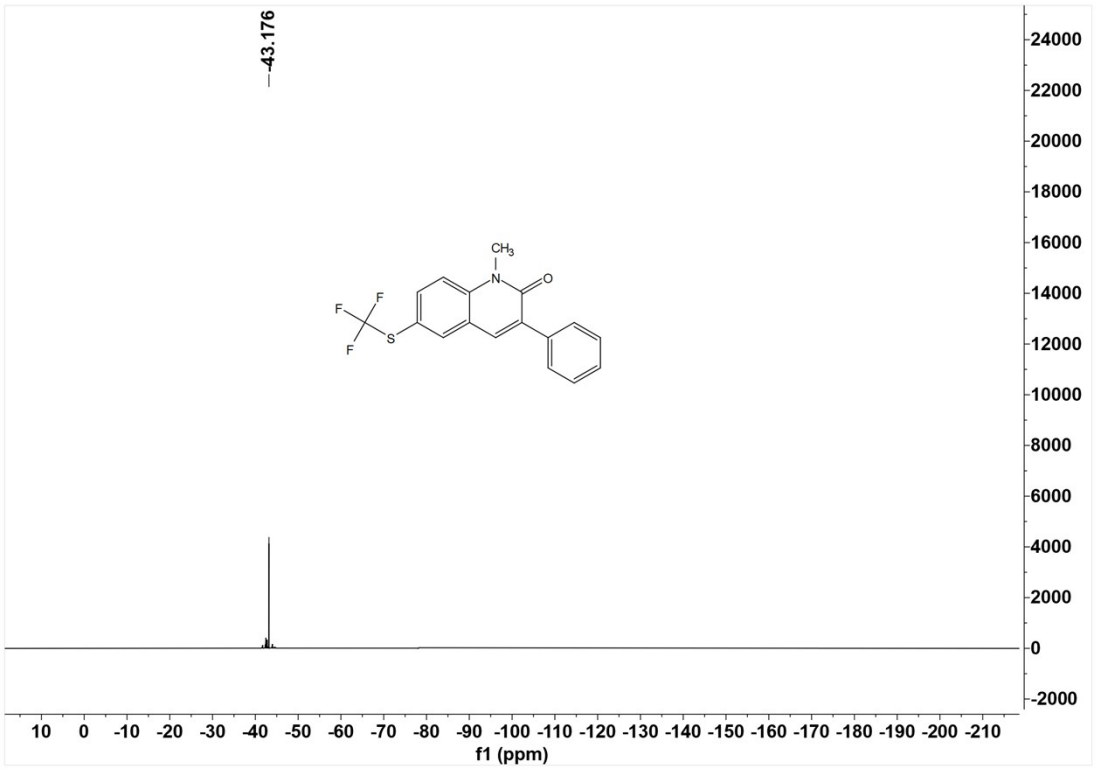




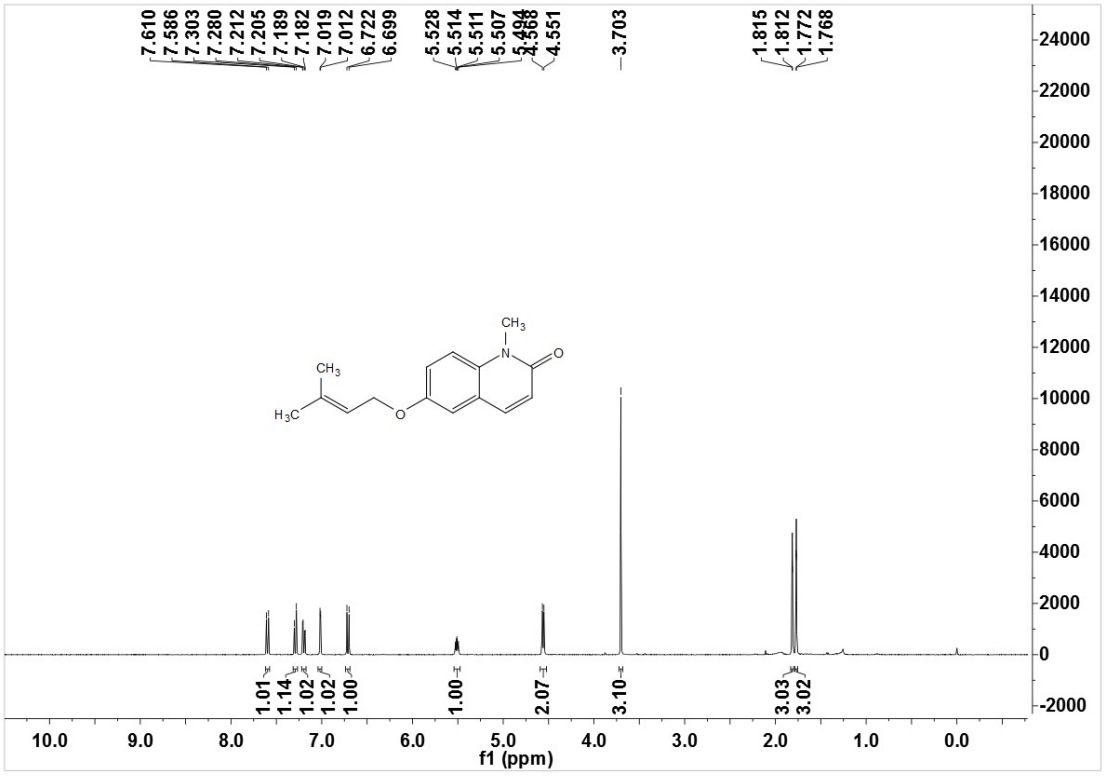
1-Methyl-3-phenyl-6-((trifluoromethyl)thio)quinolin-2(1*H*)-one (3zb)

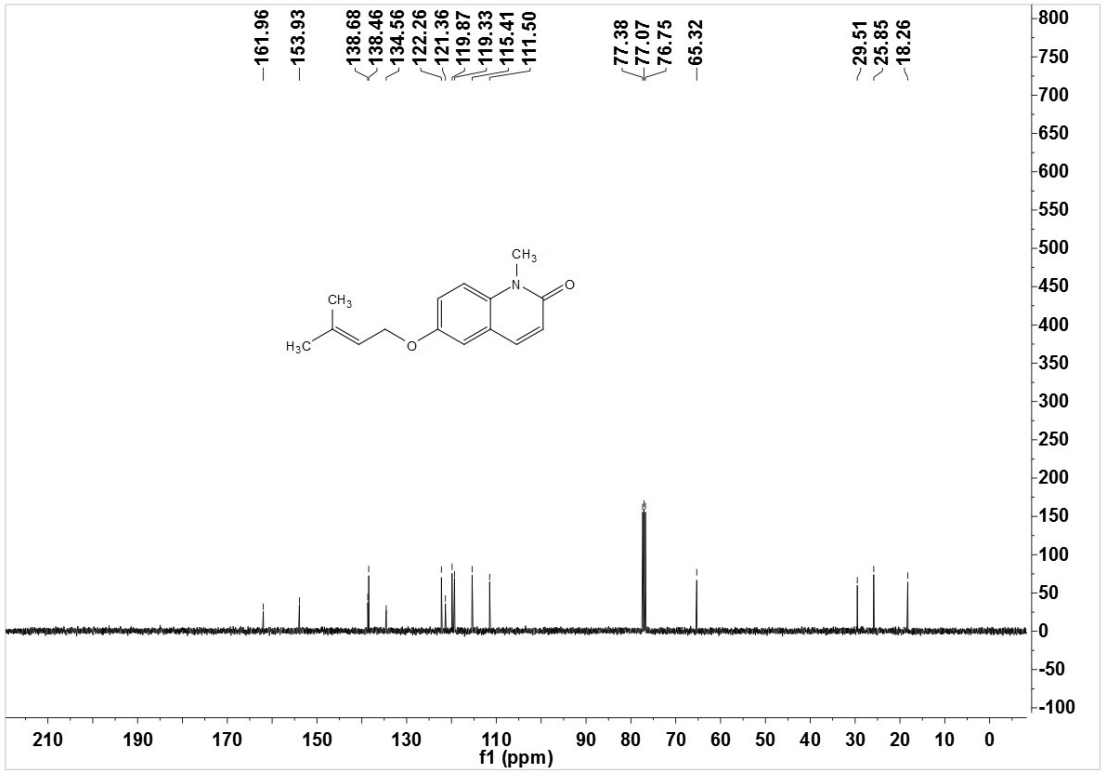




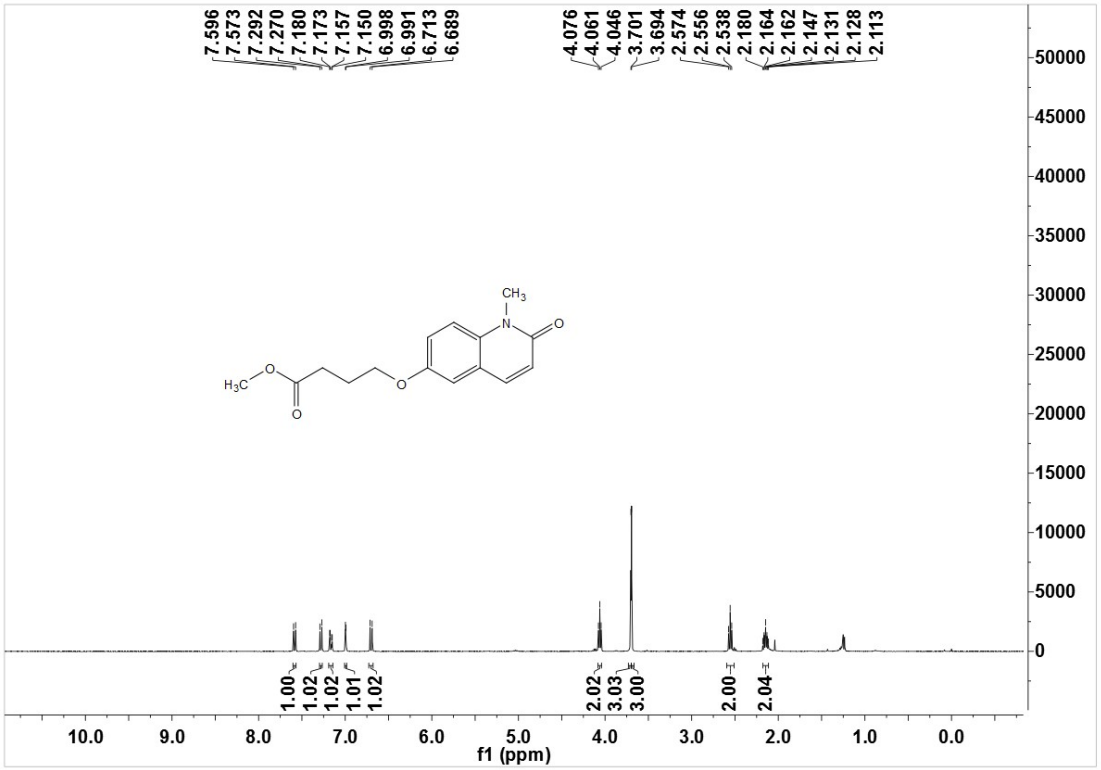


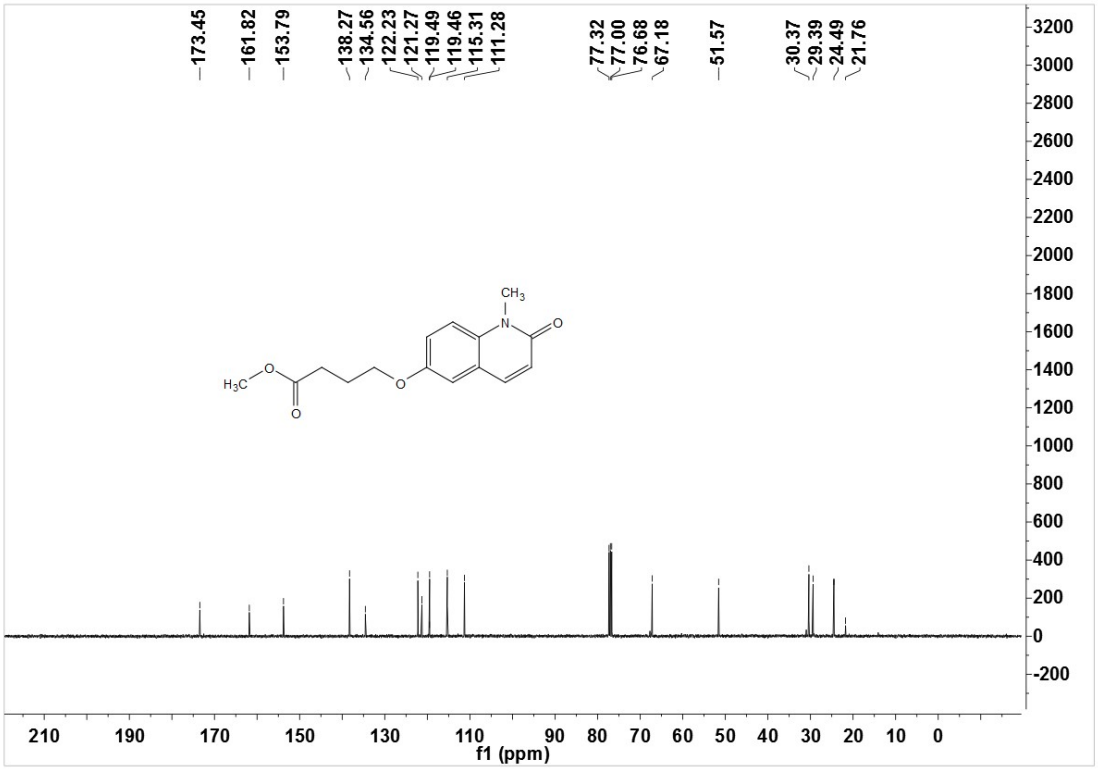
1-Methyl-6-((3-methylbut-2-en-1-yl)oxy)quinolin-2(1*H*)-one (3zc)



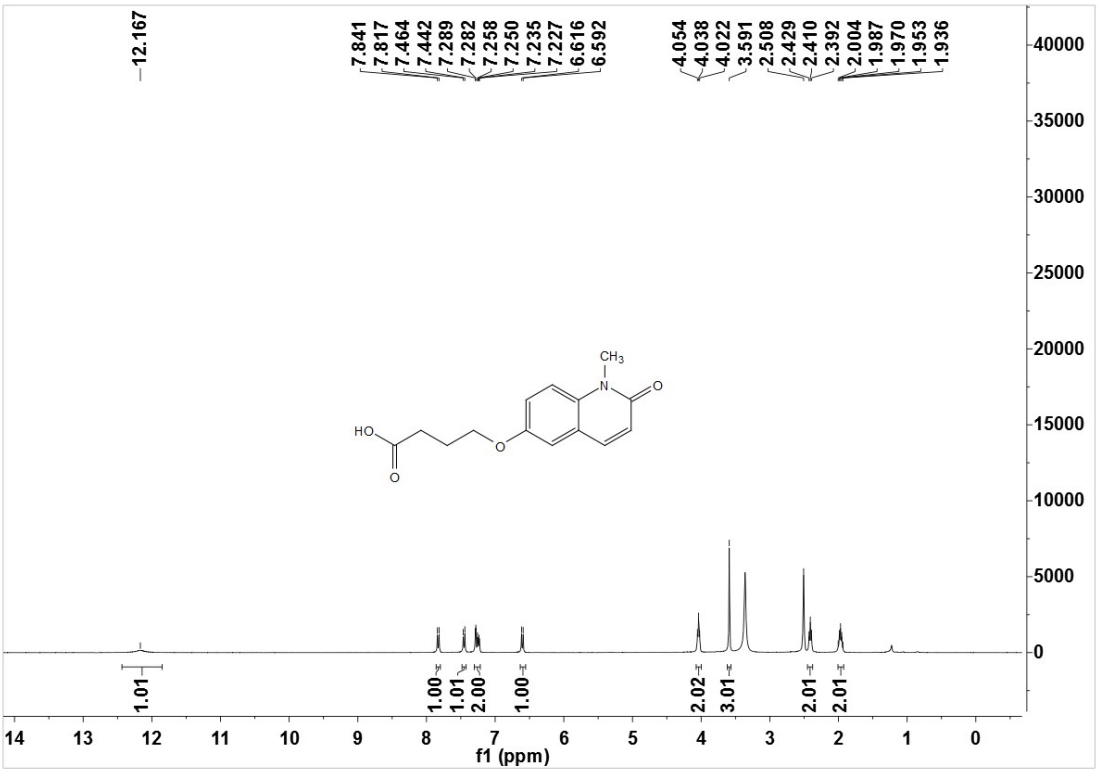


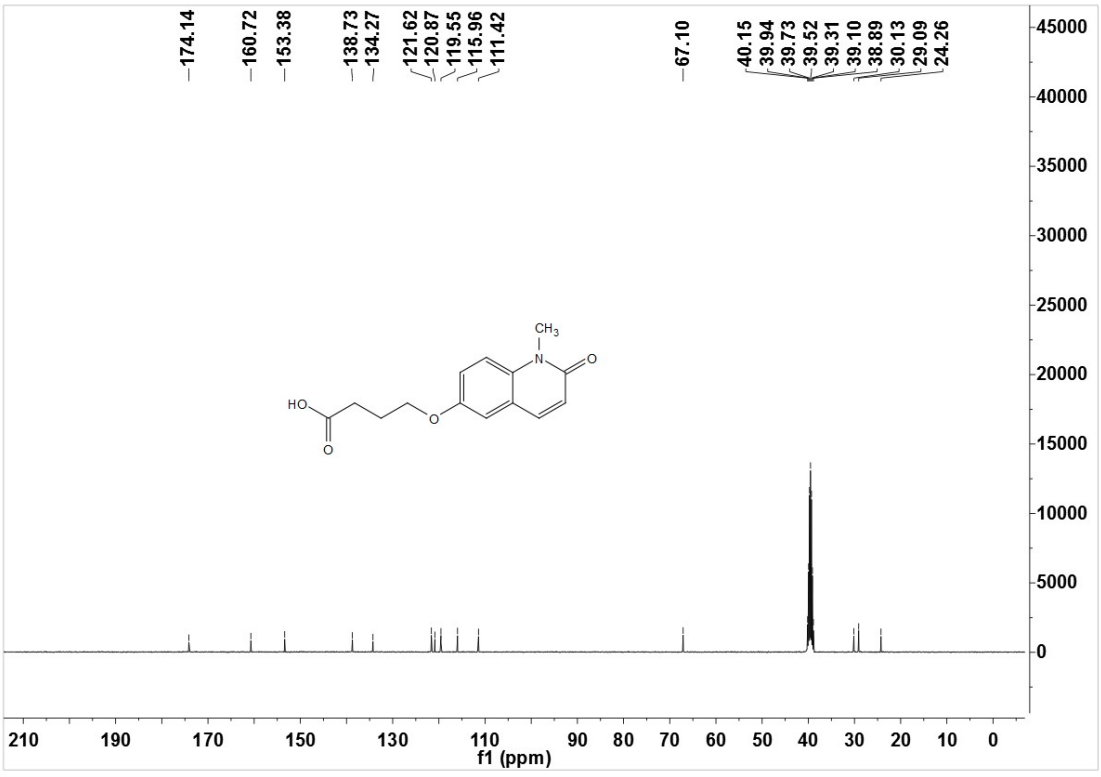
Methyl 4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanoate (3zd)



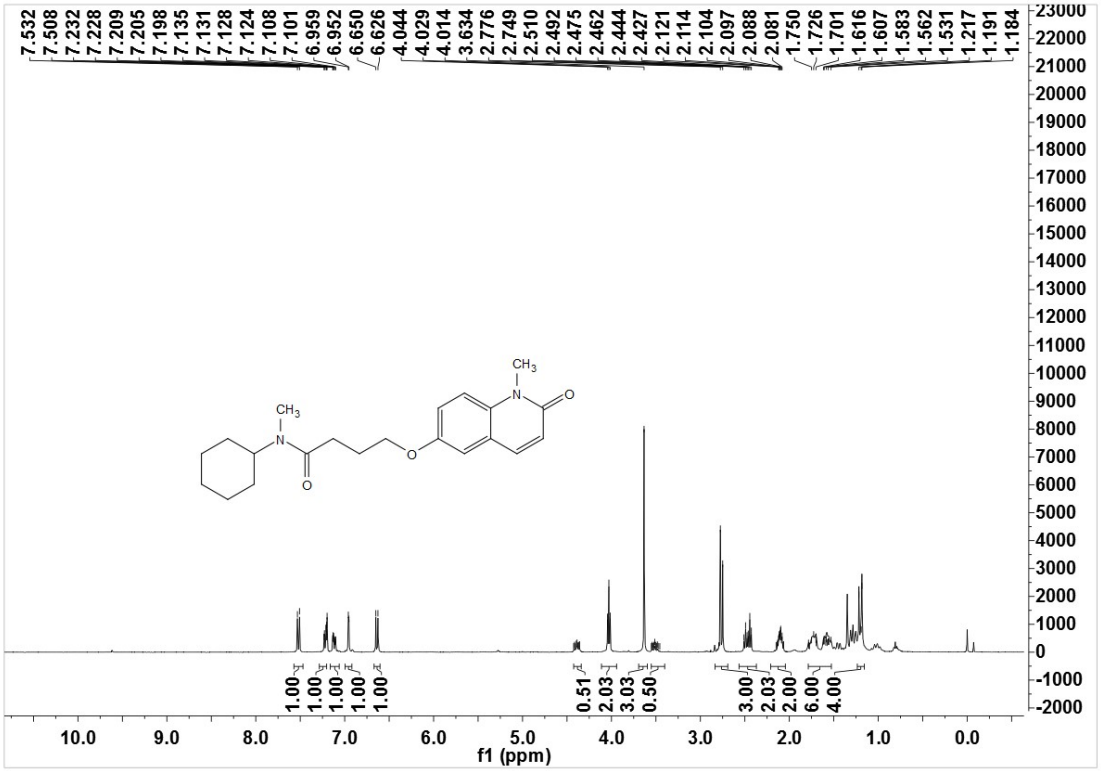


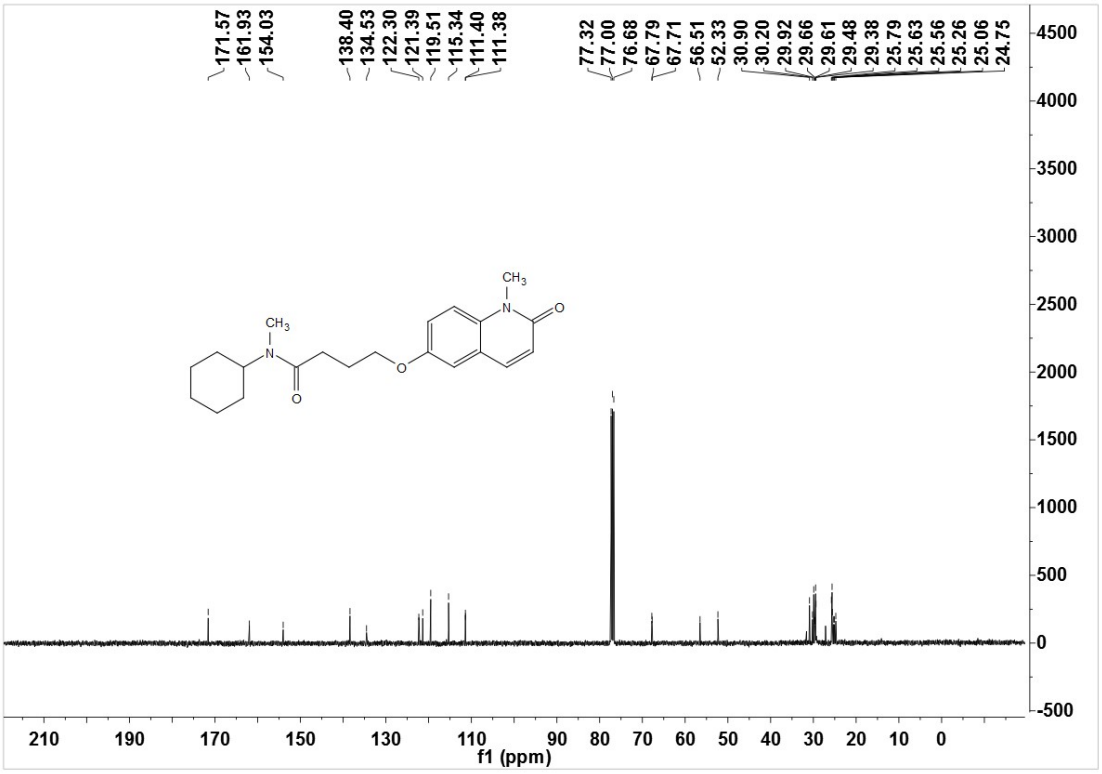
4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanoic acid (3zd-1)



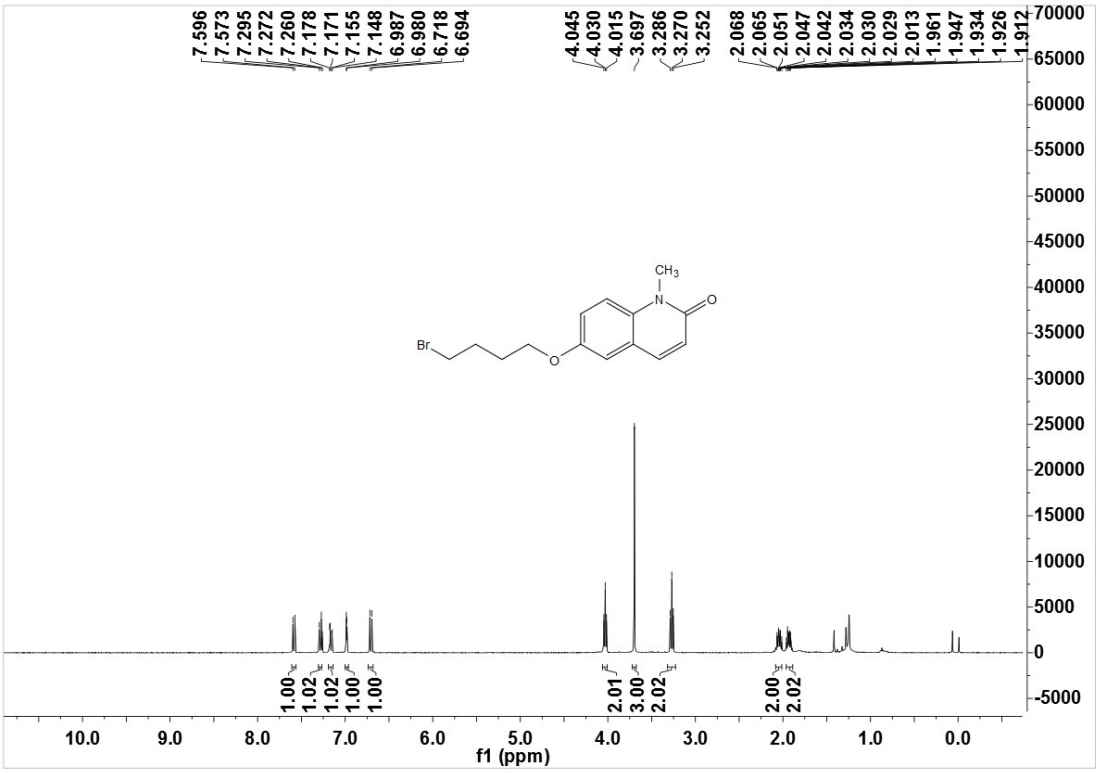


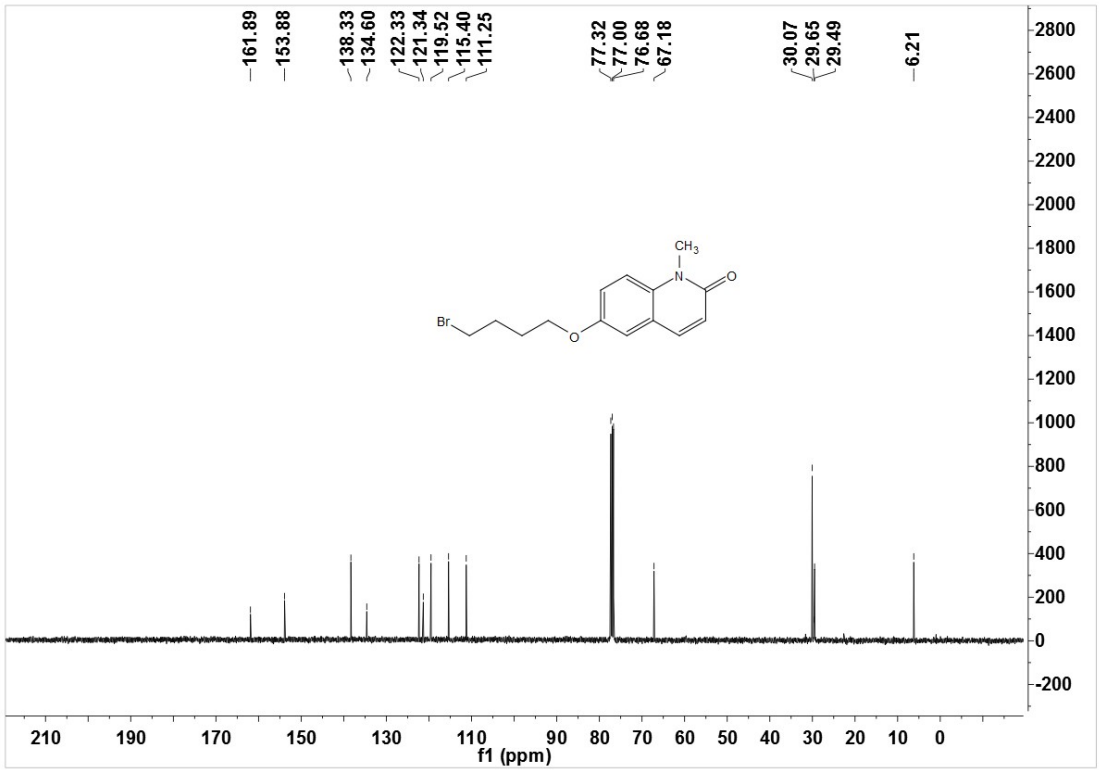
_N_-cyclohexyl-_N_-methyl-4-((1-methyl-2-oxo-1,2-dihydroquinolin-6-yl)oxy)butanamide (3ze)



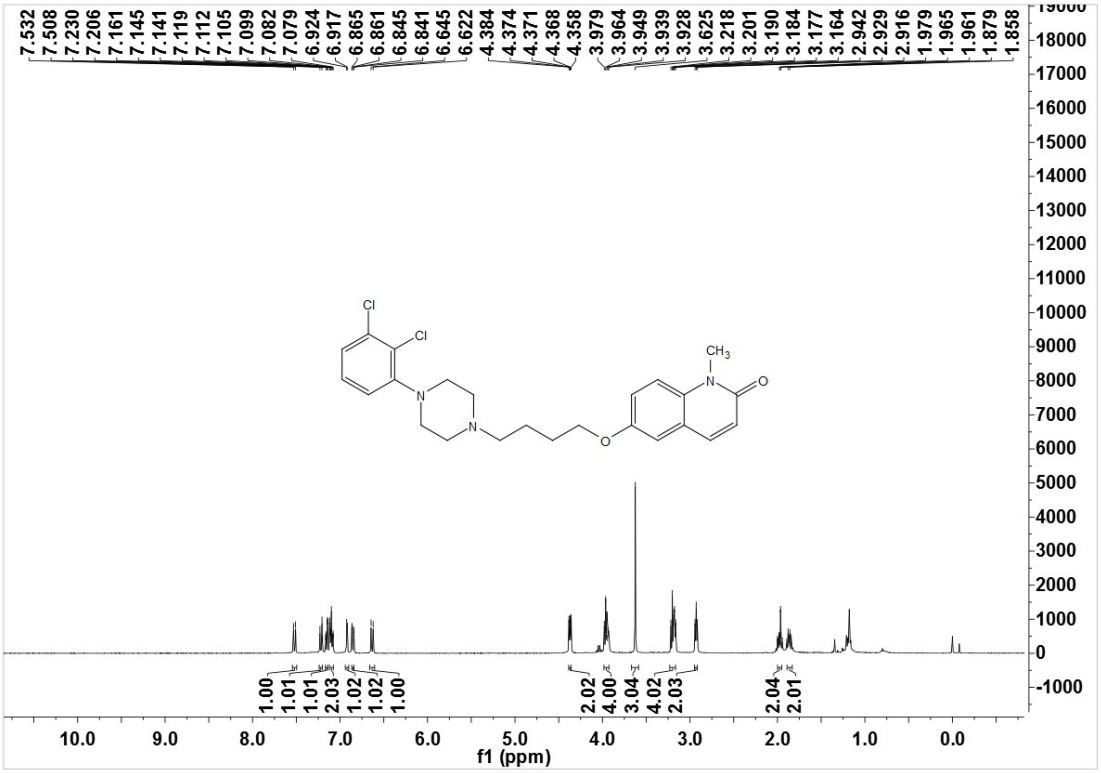


6-(4-Bromobutoxy)-1-methylquinolin-2(1*H*)-one (3zf)





6-(4-(4-(2,3-Dichlorophenyl)piperazin-1-yl)butoxy)-1-methylquinolin-2(1H)-one (3zg)


7.532
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7.145
7.141
7.119
7.112
7.105
7.099
7.082
7.079
6.924
6.917
6.865
6.861
6.845
6.841
6.645
6.622
4.384
4.374
4.371
4.368
4.358
3.979
3.964
3.949
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3.928
3.625
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3.201
3.190
3.184
3.177
3.164
2.942
2.929
2.916
1.979
1.965
1.961
1.879
1.858
Cl
Cl
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N
O
CH3
N
O
1.00
1.01
1.01
2.03
1.02
1.02
1.00
2.02
4.00
3.04
4.02
2.03
2.04
2.01
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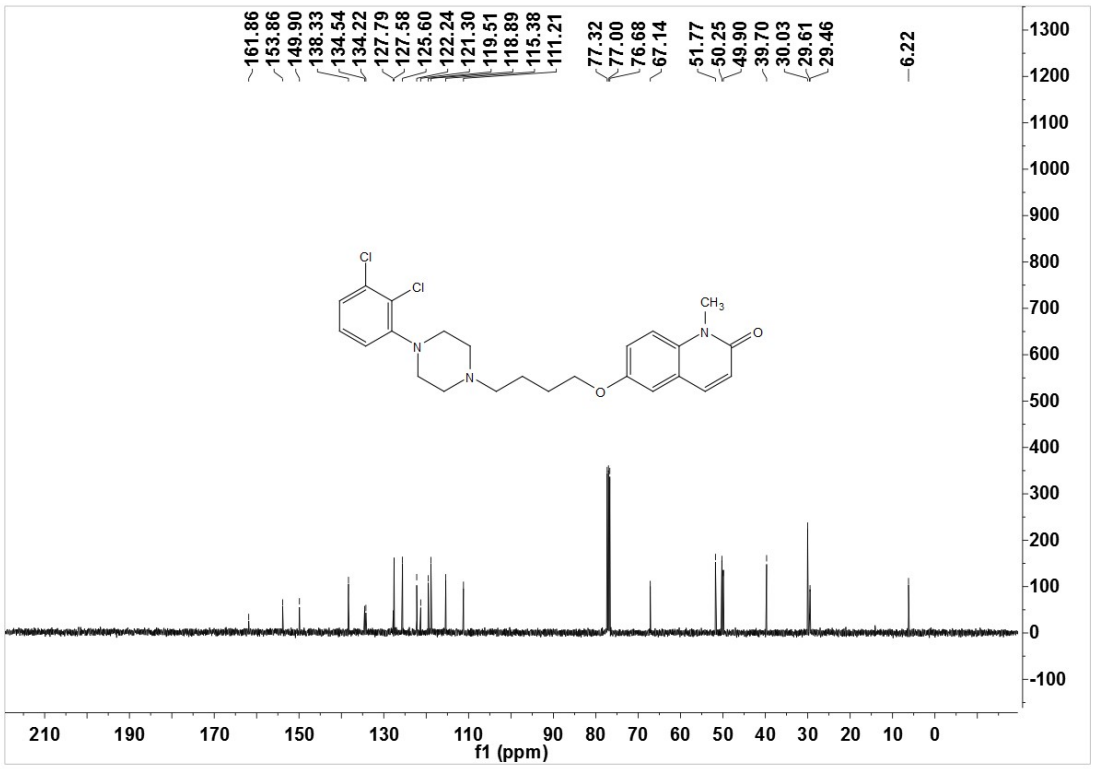
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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138.33
134.54
134.22
127.79
127.58
125.60
122.24
121.30
119.51
118.89
115.38
111.21
77.32
77.00
76.68
67.14
51.77
50.25
49.90
39.70
30.03
29.61
29.46
6.22
Cl
Cl
N
N
O
CH3
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)