Supporting Information

Divergent synthesis of nitrogen heterocycles via H_2O-mediated hydride transfer reactions

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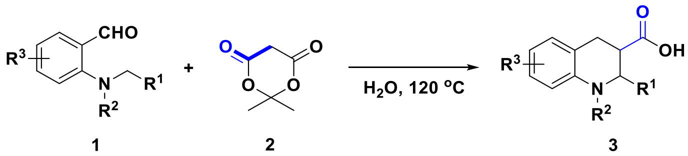
1. General Information

Unless otherwise noted, all reagents and solvents were purchased from the commercial sources and used as received. Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm. The products were purified by flash column chromatography (200-300 mesh silica gel) eluted with the gradient of petroleum ether and ethyl acetate. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker 500 MHz NMR spectrometer ($CDCl_3$ or DMSO-d_6 solvent). The chemical shifts were reported in parts per million (ppm), downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet) or dimethyl sulfoxide-d_6 (δ 2.54, singlet). Multiplicities were afforded as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet) or m (multiplets). The number of protons for a given resonance is indicated by nH. Coupling constants were reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) was referenced to the appropriate residual solvent peak. High resolution mass spectral analysis (HRMS) was performed on Waters XEVO G2 Q-TOF. *o*-Fluorobenzaldehydes, Meldrum's acid, 4-hydroxy-6-methyl-2H-pyran-2-one, and 4-hydroxycoumarin were purchased from adamas-beta.

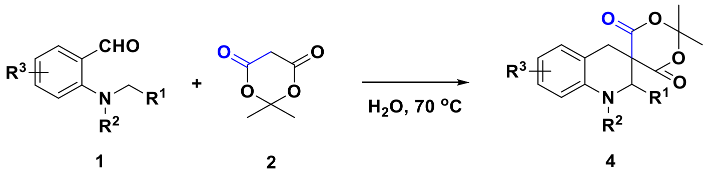
2. General Procedure

2.1 General Procedure for construction of the 3-carboxyl tetrahydroquinolines 3



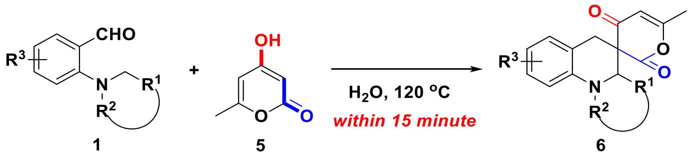
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the desired 3-carboxyl tetrahydroquinolines **3a-l**.

2.2 General Procedure for construction of the spirocyclic tetrahydroquinolines 4



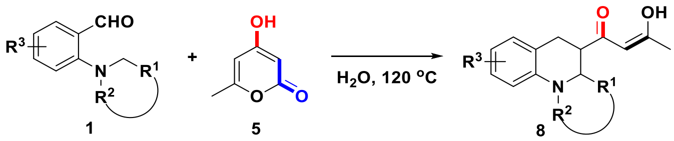
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 70 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the desired spirocyclic tetrahydroquinolines **4a-j**.

2.3 General Procedure for construction of the spirocyclic tetrahydroquinolines 6



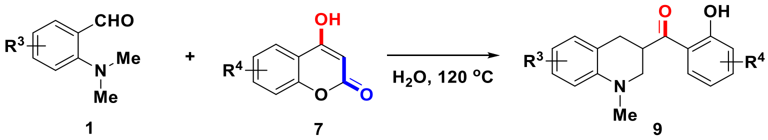
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), 4-hydroxy-6-methyl-2H-pyran-2-one **5** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C within 15 minute. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the desired spirocyclic tetrahydroquinolines **6a-g**.

2.4 General Procedure for construction of the 3-acyl substituted tetrahydroquinolines 8



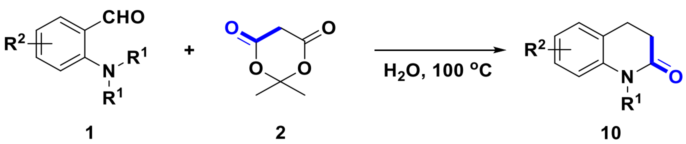
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), 4-hydroxy-6-methyl-2H-pyran-2-one **5** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the 3-acyl substituted tetrahydroquinolines **8a-j**.

2.5 General Procedure for construction of the 3-acyl substituted tetrahydroquinolines 9



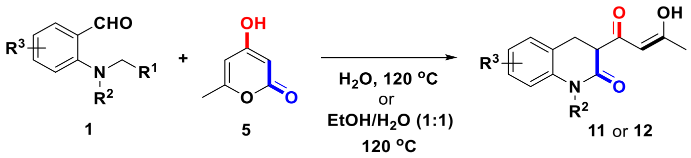
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), 4-hydroxycoumarin **7** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the 3-acyl substituted tetrahydroquinolines **9a-i**.

2.6 General Procedure for construction of 3,4-unsubstituted 3,4-dihydroquinolin-2(1*H*)-ones 10



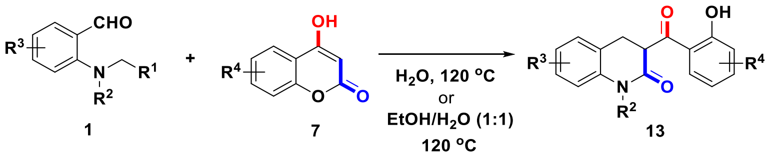
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 100 °C for 1~4 h. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3,4-unsubstituted 3,4-dihydroquinolin-2(1*H*)-ones **10a-m**.

2.7 General Procedure for construction of the 3-substituted 3,4-dihydroquinolin-2(1*H*)-ones 11 or 12



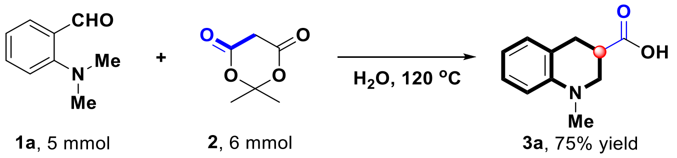
A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), 4-hydroxy-6-methyl-2H-pyran-2-one **5** (0.12 mmol), and H_2O (1.0 mL) or (H_2O (1.0 mL) and EtOH (1 mL)). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3-substituted 3,4-dihydroquinolin-2(1*H*)-ones **11a-f (12,** R^3 = Electron withdrawing groups**)**.

2.8 General Procedure for construction of the 3-substituted 3,4-dihydroquinolin-2(1*H*)-ones 13



A sealed tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), 4-hydroxycoumarin **7** (0.2 mmol), and H_2O (2.0 mL) or (H_2O (1.0 mL) and EtOH (1 mL)). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3-substituted 3,4-dihydroquinolin-2(1*H*)-ones **13a-j**.

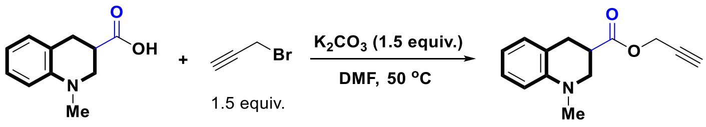
2.9 General Procedure for Large-scale Synthesis of β-amino acid 3a



A sealed tube was charged with *ortho*-amino benzaldehyde **1a** (5 mmol), Meldrum's acid **2** (6 mmol), and H_2O (50.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (50 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the desired β-amino acid **3a** in 75% yield (716 mg).

2.10 The Application of the β-Amino Acid Derivatives

(a) General Procedure for Synthesis of Terminal Alkyne Substituted Ester 14a

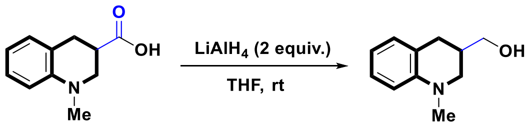


3a

14a, 95% yield

A tube was charged with **3a** (0.1 mmol), propargyl bromide (0.15 mmol), K_2CO_3 (0.15 mmol), and commercially available DMF (1.0 mL) under air. The mixture was stirred at 50 °C. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the terminal alkyne substituted ester **14a** in 95% yield.

(b) General Procedure for Synthesis of Amino Alcohol 15a



3a

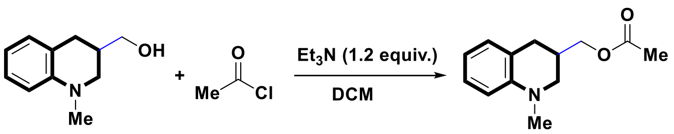
15a, 92% yield

amino alcohol

A tube was charged with **3a** (0.1 mmol), $LiAlH_4$ (0.2 mmol), and distilled THF (1.0 mL) under air. The mixture was stirred at room temperature. Upon completion of the reaction as indicated by TLC analysis, H_2O was added dropwise and the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:15) to afford the amino alcohol **15a** in 92% yield.

2.11 Synthesis of Analogue of MT2 Melatonin Receptor Agonist

(a) General Procedure for Synthesis of Analogue of MT2 Melatonin Receptor Agonist 16a

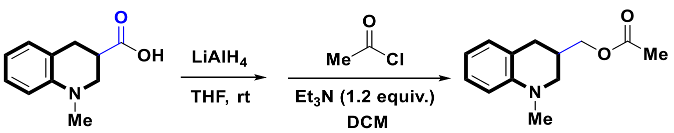


15a

16a, 95% yield

A tube was charged with **15a** (0.1 mmol), acetylchloride (0.3 mmol), Et_3N (0.12 mmol), and distilled DCM (1.0 mL). The mixture was stirred at room temperature. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the analogue of MT2 melatonin receptor agonist **16a** in 95% yield.

(b) General Procedure for "One-pot" Synthesis of Analogue of MT2 Melatonin Receptor Agonist 16a



3a

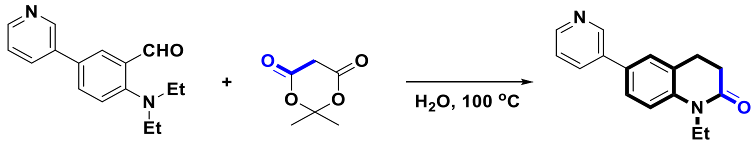
16a, 90% yield

A tube was charged with **3a** (0.1 mmol), $LiAlH_4$ (0.2 mmol), and distilled THF (1.0 mL) under air.

The mixture was stirred at room temperature. Upon completion of the reaction as indicated by TLC analysis, H_2O was added dropwise and the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly used without purification.

A tube was charged with the above residue, acetylchloride (0.3 mmol), Et_3N (0.12 mmol), and distilled DCM (1.0 mL). The mixture was stirred at room temperature. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the analogue of MT2 melatonin receptor agonist **16a** in 90% yield.

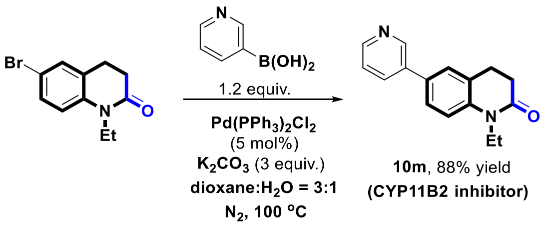
2.12 General Procedure for Synthesis of Inhibitor of Aldosterone Synthase (CYP11B2)



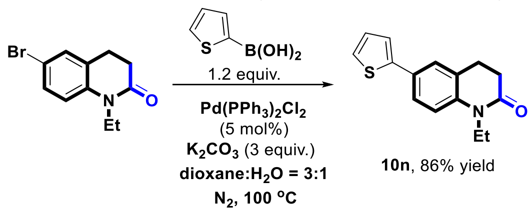
1m **2** **10m**, 78% yield

A sealed tube was charged with *ortho*-amino benzaldehyde **1m** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 100 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:2) to afford the inhibitors of aldosterone synthase **10m** in 78% yield.

2.13 General Procedure for Synthesis of Inhibitor of Aldosterone Synthase (CYP11B2) and Its Analogue



A sealed tube was charged with brominated 3,4-dihydroquinolin-2(1*H*)-one (0.1 mmol), 3-pyridylboronic acid (0.12 mmol), $Pd(PPh_3)_3Cl_2$ (5 mol%), K_2CO_3 (3 equiv.), dioxane (1.5 mL), and H_2O (0.5 mL). The mixture was stirred at 100 °C under N_2 atmosphere. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:2) to afford the inhibitors of aldosterone synthase **10m** in 88% yield.

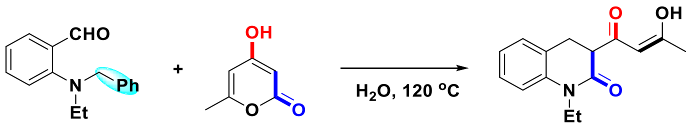


A sealed tube was charged with brominated 3,4-dihydroquinolin-2(1*H*)-one (0.1 mmol), 2-

thiopheneboronic acid (0.12 mmol), $Pd(PPh_3)_3Cl_2$ (5 mol%), K_2CO_3 (3 equiv.), dioxane (1.5 mL), and H_2O (0.5 mL). The mixture was stirred at 100 °C under N_2 atmosphere. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the inhibitors of aldosterone synthase **10n** in 86% yield.

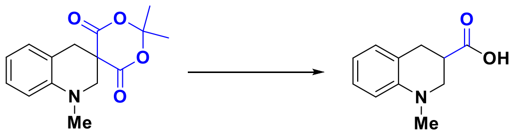
3. Mechanistic Studies

3.1 The Studies of the Reaction Process and the Role of Hydrogen Bonding Interaction



1c 5 11a, 81% yield

A sealed tube was charged with *ortho*-amino benzaldehyde **1c** (0.1 mmol), 4-hydroxy-6-methyl-2H-pyran-2-one **5** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3-substituted 3,4-dihydroquinolin-2(1*H*)-one **11a** in 81% yield. The result indicated that the α-C(sp^3)-H of benzyl group transferred preferentially in the reaction.

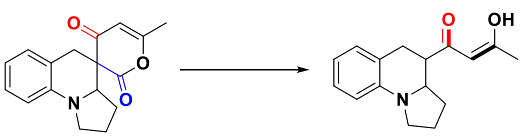


4a

1. toluene, 120 °C: NR
2. H_2O, 120 °C, 1 h: **3a**, 88% yield

A sealed tube was charged with spirocyclic tetrahydroquinoline **4a** (0.1 mmol) and toluene (1.0 mL). The mixture was stirred at 120 °C. No reaction occurred by monitoring the reaction system.

A sealed tube was charged with spirocyclic tetrahydroquinoline **4a** (0.1 mmol) and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3-substituted 3,4-dihydroquinolin-2(1H)-one **3a** in 88% yield.



6a

1. toluene, 120 °C: NR
2. H_2O, 120 °C, 2 h: **8a**, 82% yield, dr > 20:1

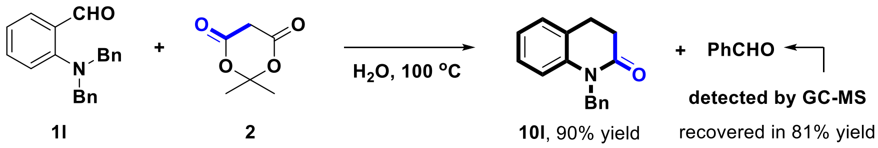
A sealed tube was charged with spirocyclic tetrahydroquinoline **6a** (0.1 mmol) and toluene (1.0 mL). The mixture was stirred at 120 °C. No reaction occurred by monitoring the reaction system.

A sealed tube was charged with spirocyclic tetrahydroquinoline **6a** (0.1 mmol) and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:50) to afford the 3-substituted 3,4-dihydroquinolin-2(1*H*)-one **8a** in 88% yield.

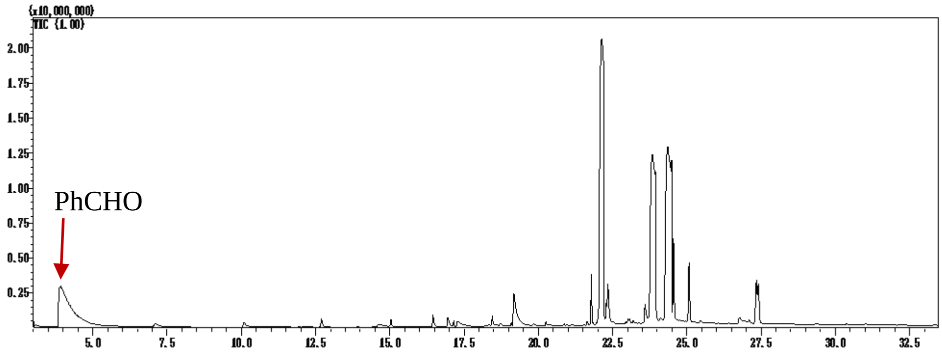
The control experiments confirmed the intramolecular hydrolysis/decarboxylation process. In addition, the significance of hydrogen bonding interaction also was proved by comparing toluene and H_2O as reaction medium.

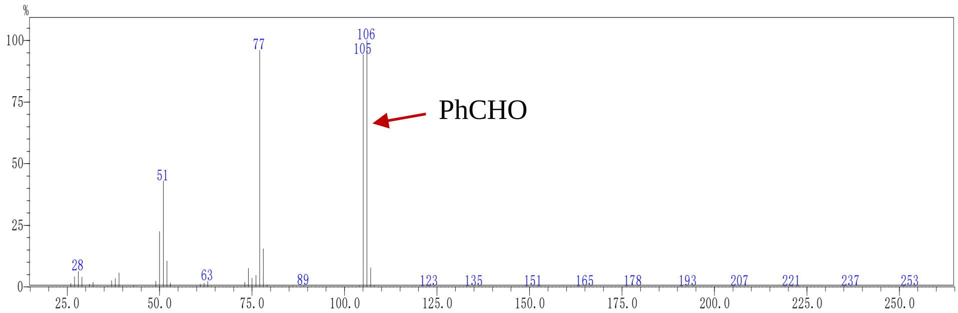
3.2 The Studies of the Hydrolysis-involved *N*-Dealkylation Process

(a) Recovery of benzaldehyde



A sealed tube was charged with *ortho*-amino benzaldehyde **1m** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 100 °C. Upon completion of the reaction, the reaction system was detected by GC-MS. As a result, PhCHO was detected by GC-MS which certified our proposed *N*-dealkylation process.

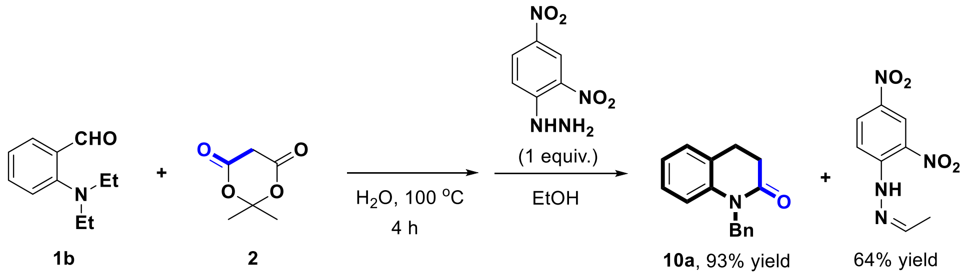




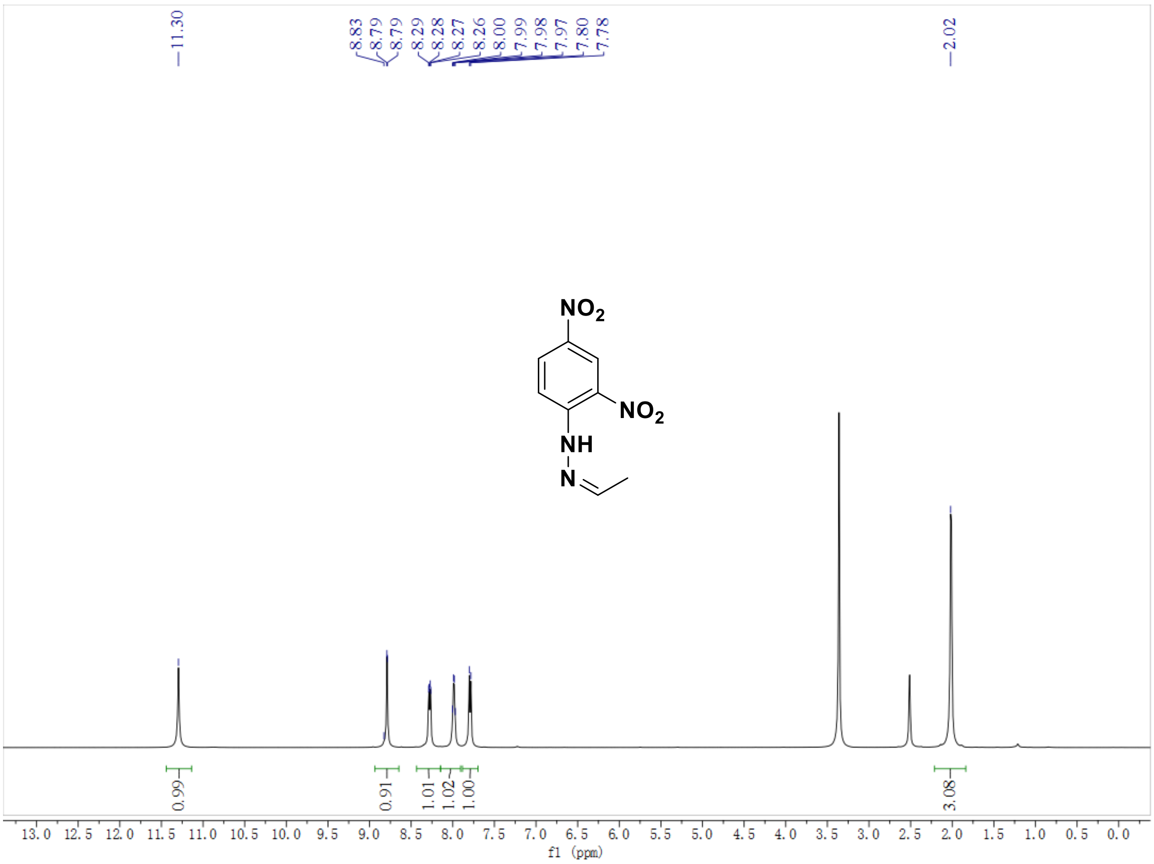
Conditions: gas chromatograph-mass spectrometer (GC-MS, QP 2010, Shimadzu, Japan), equipped with RTX-5MS column (30 m, 0.25 m film thickness, 0.25 mm i. d, Agilent Technologies, USA). Helium was used as a carrier gas at a flow rate of 7.0 mL/min. The column temperature was programmed as follows: 80 °C (2 min), raised to 260 °C at a rate of 7 °C/min held for 2 min. Temperatures of the injection port and interface were set at 260 °C and 280 °C, respectively. The mass spectrometer was operated in electron impact (EI) mode at 70 eV.

In addition, the released PhCHO could be isolated by preparative chromatography in 81% yield.

(b) Recovery of acetaldehyde

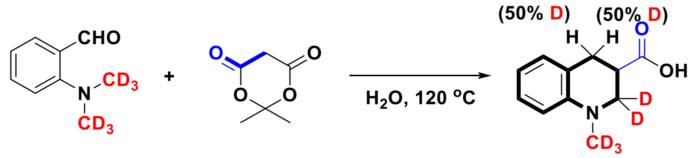


A Schlenk tube was charged with *ortho*-amino benzaldehyde **1** (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 100 °C for 4 h. Then 2, 4-dinitrophenylhydrazine (0.1 mmol in 1.0 mL of EtOH) was injected in the Schlenk tube. The mixture was stirred at 100 °C for 8 h. Then the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3,4-unsubstituted 3,4-dihydroquinolin-2(1*H*)-one **10a** and 1-(2,4-dinitrophenyl)-2-ethylidenehydrazine.



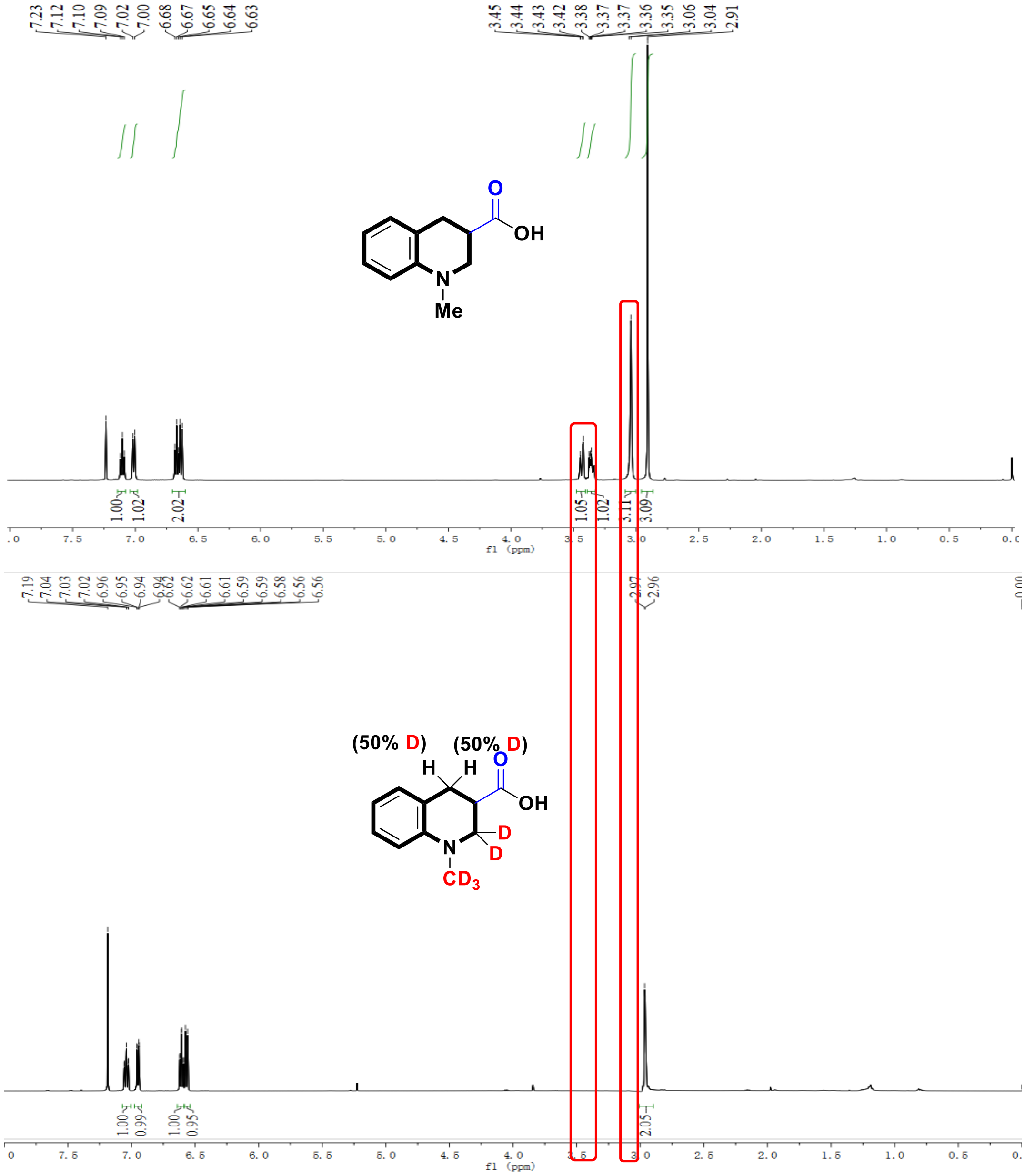
Recovery of benzaldehyde and acetaldehyde certified our proposed *N*-dealkylation process.

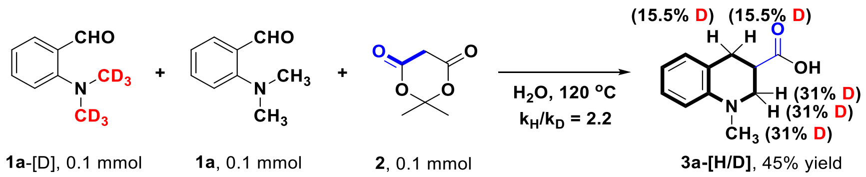
3.3 Isotope-labeling Experiments



A sealed tube was charged with *ortho*-amino benzaldehyde **1a**-[D] (0.1 mmol), Meldrum's acid **2** (0.12 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the desired β-amino acid **3a**-[D] in 75% yield.

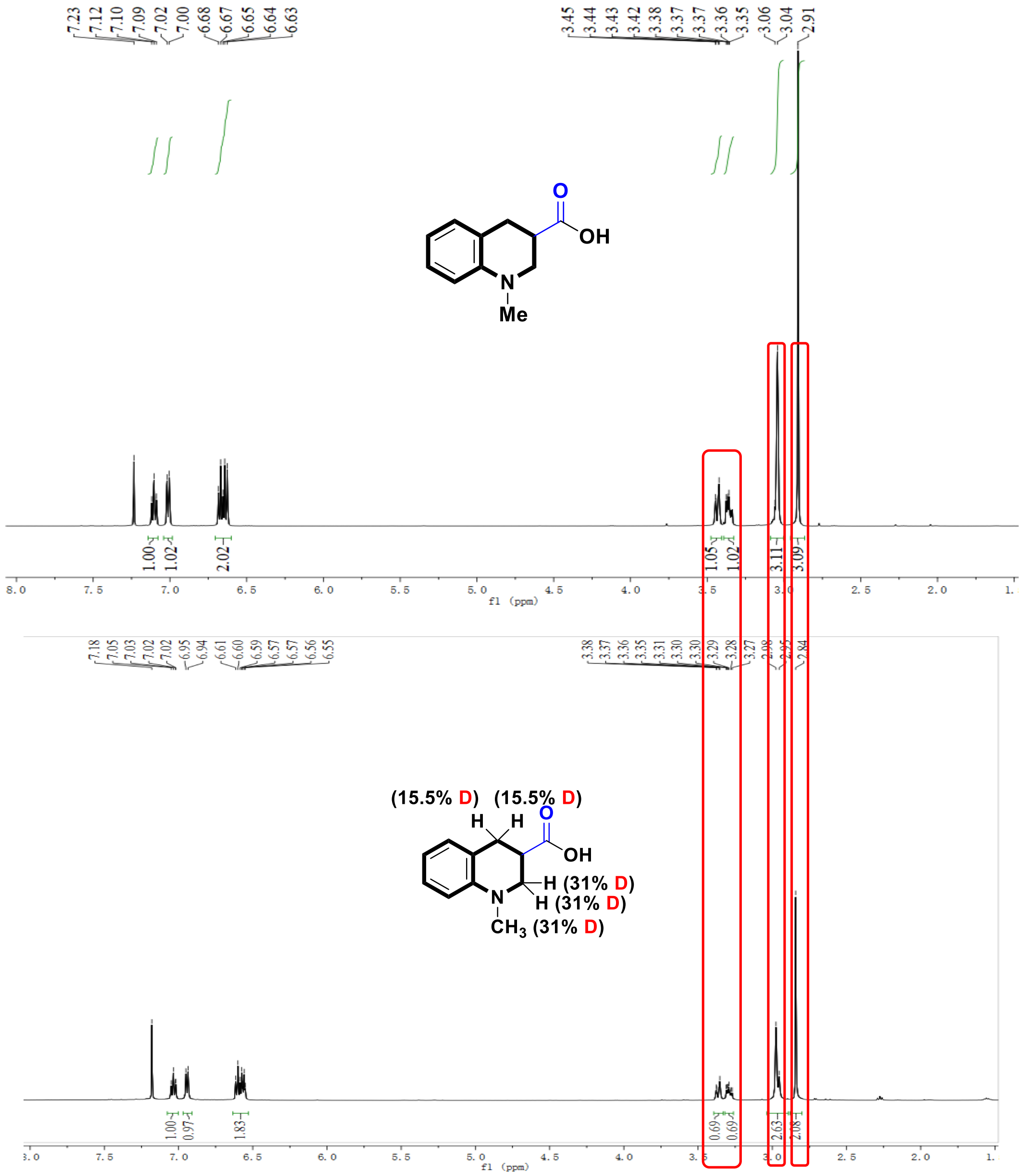
When **1a**-[D] was used, the observation of the deuteration (50%) at the benzyl position by ^{1}H NMR fully corroborated the occurrence of [1,5]-hydride transfer.

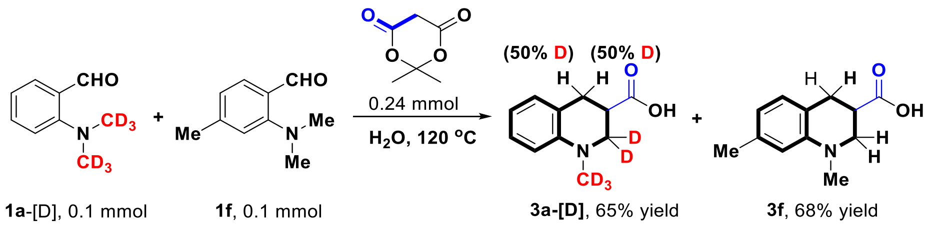




A sealed tube was charged with *ortho*-amino benzaldehyde **1a** (0.1 mmol), **1a**-[D] (0.1 mmol), Meldrum's acid **2** (0.1 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL ×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the desired β-amino acid **3a**-[H/D] in 45% yield.

A deuterium kinetic isotope effect (DKIE) of 2.2 was obtained through competitive reaction between substrates **1a** and **1a**-[D], implying that the [1,5]-hydride transfer process might be involved in the rate-determining step.

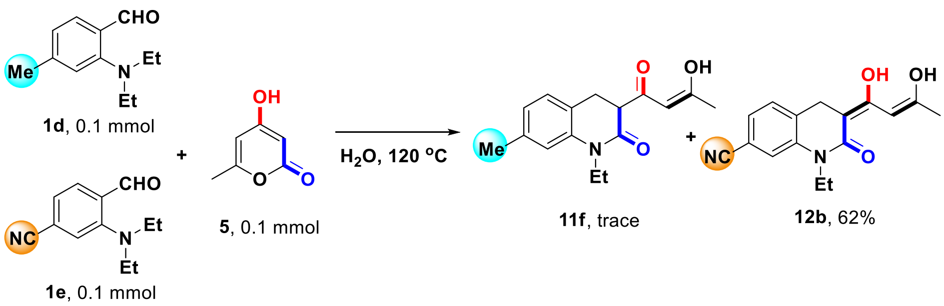




A sealed tube was charged with *ortho*-amino benzaldehyde **1a** (0.1 mmol), **1f** (0.1 mmol), Meldrum's acid **2** (0.24 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the desired β-amino acid **3a**-[D] in 65% yield and **3f** in 68%.

The reaction between **1a**-[D], **1f**, and Meldrum's acid demonstrated it was an intramolecular hydride transfer reaction.

3.4 Competing reaction

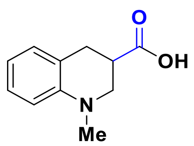


A sealed tube was charged with *ortho*-amino benzaldehydes **1d** (0.1 mmol), **1e** (0.1 mmol), 4-hydroxy-6-methyl-2H-pyran-2-one **5** (0.1 mmol), and H_2O (1.0 mL). The mixture was stirred at 120 °C. Upon completion of the reaction as indicated by TLC analysis, the resulting solution was extracted with DCM (5 mL×3). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:20) to afford the 3-substituted 3,4-dihydroquinolin-2(1*H*)-one **12b** in 62% yield.

The result indicated that the electron-withdrawing group (CN) substituted 2-(diethylamino)benzaldehyde **1e** reacted faster with **5**, which might be due to the increased electrophilicity of aldehyde group of **1e** and stability of the product **12b** with π-conjugate system.

4. Characterization of Products

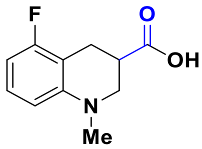
1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (80% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.67 (s, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.71 – 6.60 (m, 2H), 3.46-3.40 (m, 1H), 3.39 – 3.33 (m, 1H), 3.07-3.00 (m, 3H), 2.91 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.8, 145.9, 129.1, 127.5, 120.8, 117.2, 111.5, 52.1, 39.2, 38.5, 29.9. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{14}NO_2$: 192.1019, found: 192.1010.

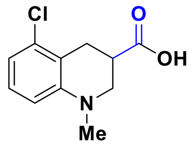
5-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (70% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (dd, *J* = 15.2, 7.9 Hz, 1H), 6.39 – 6.28 (m, 2H), 3.39-3.32 (m, 1H), 3.30-3.25 (m, 1H), 3.06-2.98 (m, 1H), 2.97-2.91 (m, 1H), 2.89 – 2.80 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.7, 161.1 (d, *J* = 240.0 Hz), 147.4 (d, *J* = 7.6 Hz), 127.61 (d, *J* = 10.7 Hz), 107.9 (d, *J* = 21.2 Hz), 106.82 (d, *J* = 2.3 Hz), 103.6 (d, *J* = 22.5 Hz), 51.7, 39.6, 37.6, 22.6 (d, *J* = 6.0 Hz). **^{19}F NMR** (470 MHz, DMSO) δ **–** 118.49. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}FNO_2$: 210.0925, found: 210.0918.

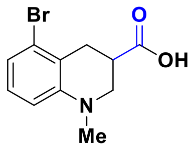
5-chloro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (72% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (t, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 3.44 (dd, *J* = 11.2, 2.9 Hz, 1H), 3.40 – 3.32 (m, 1H), 3.18 (dd, *J* = 16.2, 5.0 Hz, 1H), 3.06 (m, 1H), 3.00 (dd, *J* = 16.2, 8.9 Hz, 1H), 2.93 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.2, 147.4, 134.5, 127.6, 118.7, 117.80, 109.8, 51.7, 39.7, 38.3, 27.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}ClNO_2$: 226.0629, found: 226.0621.

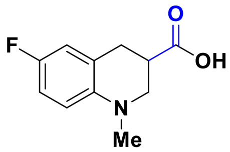
5-bromo-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (73% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 12.59 (s, 1H), 6.95 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 3.39 (dd, *J* = 11.3, 3.0 Hz, 1H), 3.26 (dd, *J* = 11.2, 8.0 Hz, 1H), 2.93 (dd, *J* = 12.5, 4.9 Hz, 2H), 2.90 – 2.77 (m, 4H). **^{13}C NMR** (125 MHz, DMSO) δ 174.6, 148.4, 128.6, 125.2, 120.5, 120.3, 110.9, 51.9, 39.6, 38.0, 30.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}BrNO_2$: 270.0124, found: 270.0112.

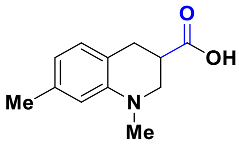
6-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (66% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 6.83 (m, 1H), 6.79 (dd, J = 8.9, 2.9 Hz, 1H), 6.58 (dd, J = 8.9, 4.7 Hz, 1H), 3.46 – 3.39 (m, 1H), 3.38 – 3.30 (m, 1H), 3.13 – 3.00 (m, 3H), 2.91 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.2, 155.6 (d, J = 235.0 Hz), 142.5 (d, J = 2.5 Hz), 122.5 (d, J = 7.5 Hz), 115.5 (d, J = 22.5 Hz), 113.6 (d, J = 21.3 Hz), 112.5 (d, J = 7.5 Hz), 52.3, 39.8, 38.5, 29.8. **^{19}F NMR** (470 MHz, DMSO) δ – 109.57. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}FNO_2$: 210.0925, found: 210.0916.

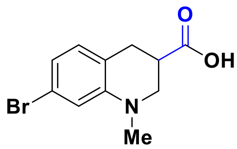
1,7-dimethyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (73% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.15 (s, 1H), 6.90 (d, J = 7.5 Hz, 1H), 6.50 (d, J = 7.5 Hz, 1H), 6.46 (s, 1H), 3.41 (dd, J = 11.6, 3.1 Hz, 1H), 3.33 (dd, J = 11.1, 8.9 Hz, 1H), 3.08 – 2.96 (m, 3H), 2.90 (s, 3H), 2.28 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.8, 145.7, 137.1, 129.0, 118.1, 117.9, 112.3, 52.2, 39.3, 38.7, 29.6, 21.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{12}H_{16}NO_2$: 206.1176, found: 206.1182.

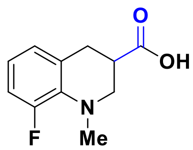
7-bromo-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (71% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 12.51 (s, 1H), 6.89 (d, J = 7.2 Hz, 1H), 6.68 (s, 2H), 3.41 (s, 1H), 3.30 – 3.24 (m, 1H), 2.87 (d, J = 16.4 Hz, 5H), 2.82 – 2.74 (m, 1H). **^{13}C NMR** (125 MHz, DMSO) δ 174.7, 147.7, 130.7, 120.6, 120.5, 118.6, 113.2, 51.9, 39.0, 37.7, 29.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}BrNO_2$: 270.0124, found: 270.0118.

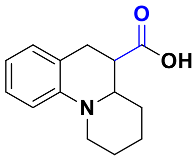
8-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (68% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.55 (s, 1H), 6.90 (dd, *J* = 16.3, 7.6 Hz, 2H), 6.80 (dt, *J* = 12.6, 6.4 Hz, 1H), 3.50 – 3.43 (m, 1H), 3.27 – 3.19 (m, 1H), 3.06 (d, *J* = 8.0 Hz, 2H), 3.01 (s, 3H), 2.98 (d, *J* = 7.8 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.4, 154.4 (d, *J* = 242.5 Hz), 135.1 (d, *J* = 10.0 Hz), 127.2 (d, *J* = 2.5 Hz), 124.9 (d, *J* = 2.5 Hz), 120.4 (d, *J* = 7.5 Hz), 114.3 (d, *J* = 21.3 Hz), 53.8, 42.9, 35.5, 29.9. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **–** 123.48. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{11}H_{12}FNNaO_2$: 232.0744, found: 232.0746.

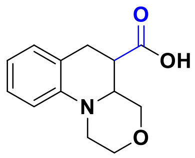
2,3,4,4a,5,6-hexahydro-1H-pyrido[1,2-a]quinoline-5-carboxylic acid (3i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (70% yield, dr 6:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 – 7.02 (m, 1H), 6.98 (d, *J* = 7.1 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.69 (t, *J* = 7.3 Hz, 1H), 4.04 – 3.95 (m, 1H), 3.47 – 3.34 (m, 1H), 3.07 – 2.92 (m, 3H), 2.87 – 2.74 (m, 1H), 1.68 – 1.35 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.6, 144.3, 129.9, 128.9, 127.6, 122.8, 122.1, 118.7, 117.9, 113.7, 113.2, 58.1, 57.3, 48.9, 48.5, 45.9, 42.8, 30.9, 29.7, 27.4, 26.6, 24.5, 24.5, 23.3. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{14}H_{17}NNaO_2$: 254.1151, found: 254.1150.

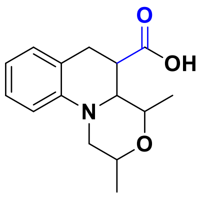
1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinoline-5-carboxylic acid (3j)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (68% yield, dr 12:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.71 (t, *J* = 7.0 Hz, 2H), 3.94 (d, *J* = 10.8 Hz, 2H), 3.65 (t, *J* = 11.4 Hz, 1H), 3.54 (d, *J* = 12.3 Hz, 1H), 3.33 (t, *J* = 10.5 Hz, 1H), 3.25 (t, *J* = 9.0 Hz, 1H), 3.02 (dd, *J* = 15.4, 10.1 Hz, 1H), 2.98 – 2.93 (m, 1H), 2.89 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.63 (dd, *J* = 14.7, 9.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.8, 145.4, 128.9, 127.6, 122.7, 119.0, 112.3, 70.3, 66.8, 56.2, 46.7, 41.9, 30.1. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{13}H_{15}NNaO_3$: 256.0944, found: 256.0940.

2,4-dimethyl-1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinoline-5-carboxylic acid (3k)

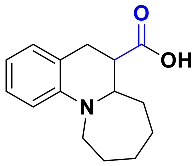


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (72% yield, dr 1.3:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.53 (s, 2H), 7.13 (dd, J = 14.1, 6.8 Hz, 2H), 7.03 (d, J = 7.4 Hz, 2H), 6.87 (d, J = 8.3 Hz, 1H), 6.82 (t, J = 7.3 Hz, 1H), 6.74 (t, J = 7.3 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 3.89 – 3.75

(m, 4H), 3.71 (dd, J = 11.8, 2.3 Hz, 1H), 3.58 (dd, J = 12.9, 1.9 Hz, 1H), 3.45 (dd, J = 9.3, 6.2 Hz, 1H), 3.24 (dd, J = 9.3, 4.9 Hz, 1H), 3.18 – 2.99 (m, 4H), 2.92 – 2.70 (m, 5H), 2.49 (t, J = 11.3 Hz, 1H), 1.31 (d, J = 6.2 Hz, 4H), 1.25 (d, J = 6.2 Hz, 5H), 1.22 (d, J = 6.2 Hz, 3H), 1.16 (d, J = 6.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.1, 176.7, 145.9, 145.1, 129.7, 127.9, 127.7, 127.3, 125.5, 122.4, 120.3, 118.7, 113.9, 112.3, 75.0, 73.5, 70.9, 70.0, 62.2, 61.4, 53.8, 53.5, 43.5, 39.2, 29.9, 28.8, 19.2, 18.9, 18.3, 17.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{20}NO_3$: 262.1438, found: 262.1430.

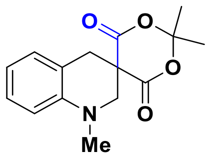
5,6,6a,7,8,9,10,11-octahydroazepino[1,2-a]quinoline-6-carboxylic acid (3l)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (74% yield, dr 1:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.95 (dd, J = 152.3, 105.5 Hz, 1H), 7.13 – 6.98 (m, 2H), 6.65 – 6.54 (m, 2H), 3.91 (m, 1H), 3.82 (m, 2H), 3.26 – 3.13 (m, 1H), 3.13 – 2.98 (m, 2H), 2.94 – 2.83 (m, 1H), 2.81 – 2.74 (m, 1H), 2.08 (m, 1H), 1.85 – 1.73 (m, 1H), 1.72 – 1.53 (m, 5H), 1.46 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.5, 179.3, 143.8, 143.3, 129.6, 129.1, 127.5, 127.4, 118.5, 118.3, 115.5, 115.3, 110.4, 110.0, 59.0, 58.9, 49.7, 49.3, 42.2, 41.7, 34.8, 30.7, 27.1, 26.5, 26.4, 26.2, 25.9, 25.9, 25.7, 24.9. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{15}H_{19}NNaO_2$: 268.1308, found: 268.1310.

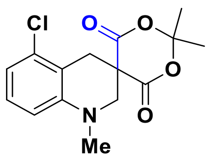
1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (93% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (t, J = 7.1 Hz, 1H), 7.04 (d, J = 6.7 Hz, 1H), 6.77-6.73 (m, 2H), 3.59 (s, 2H), 3.33 (s, 2H), 3.00 (s, 3H), 1.79 (s, 3H), 1.78 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.5, 144.7, 128.4, 127.6, 119.3, 117.8, 111.9, 105.2, 57.2, 47.4, 39.6, 34.4, 29.5, 28.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{18}NO_4$: 276.1230, found: 276.1224.

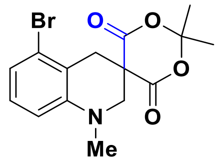
5-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (90% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (t, J = 8.1 Hz, 1H), 6.82 (d, J = 7.9 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 3.58 (s, 2H), 3.35 (s, 2H), 3.02 (s, 3H), 1.81 (s, 3H), 1.81 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.2, 146.1, 133.9, 127.7, 118.5, 117.4, 110.5, 105.4, 56.9, 47.1, 40.1, 31.8, 29.7, 28.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}ClNO_4$: 310.0841, found: 310.0849.

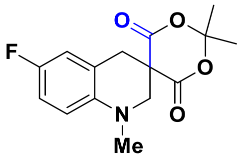
5-bromo-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (83% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13-6.97 (m, 2H), 6.71 (d, J = 6.8 Hz, 1H), 3.61 (s, 2H), 3.37 (s, 2H), 3.05 (s, 3H), 1.85 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.1, 146.2, 128.2, 124.8, 121.8, 118.9, 111.2, 105.4, 57.0, 47.5, 40.1, 34.7, 29.7, 28.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}BrNO_4$: 354.0335, found: 354.0331.

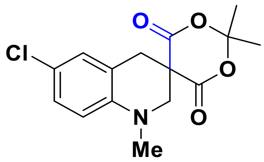
6-fluoro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (72% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (t, J = 8.5 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.65 (dd, J = 8.8, 4.6 Hz, 1H), 3.56 (s, 2H), 3.31 (s, 2H), 2.98 (s, 3H), 1.81 (s, 3H), 1.78 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.34, 155.7 (d, J = 236.3 Hz), 141.20 (d, J = 1.7 Hz), 121.08 (d, J = 7.3 Hz), 114.9 (d, J = 23.7 Hz), 113.8 (d, J = 22.5 Hz), 113.08 (d, J = 7.7 Hz), 105.3, 57.8, 47.6, 40.1, 33.9, 29.6, 28.4. **^{19}F NMR** (470 MHz, $CDCl_3$) δ – 127.18. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}FNO_4$: 294.1136, found: 294.1130.

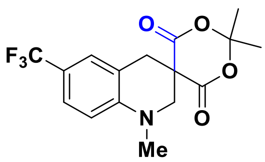
6-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (82% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, J = 8.7 Hz, 1H), 6.94 (s, 1H), 6.56 (d, J = 8.7 Hz, 1H), 3.51 (s, 2H), 3.21 (s, 2H), 2.92 (s, 3H), 1.73 (s, 3H), 1.71 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.2, 142.2, 127.1, 126.4, 121.4, 119.7, 112.1, 104.3, 56.1, 45.9, 38.7, 33.0, 28.5, 27.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}ClNO_4$: 310.0841, found: 310.0847.

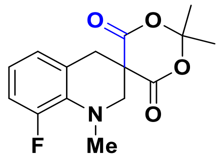
1,2',2'-trimethyl-6-(trifluoromethyl)-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (84% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 1H), 7.26 (s, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 3.66 (s, 2H), 3.33 (s, 2H), 3.05 (s, 3H), 1.80 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.0, 146.8, 125.5 (q, *J* = 3.7 Hz), 125.0 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 268.8 Hz), 123.8, 121.7, 118.8 (q, *J* = 32.5 Hz), 118.3, 111.0, 105.4, 56.4, 46.0, 39.5, 34.6, 29.4, 28.5. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **-** 60.94. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{17}F_3NO_4$: 344.1104, found: 344.1119.

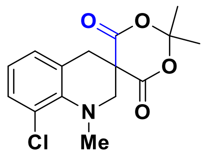
8-fluoro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (62% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 – 6.86 (m, 2H), 6.80 (d, *J* = 6.5 Hz, 1H), 3.66 (s, 2H), 3.36 (s, 2H), 3.11 (s, 3H), 1.86 (s, 3H), 1.77 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.8, 153.6 (d, *J* = 242.5 Hz), 133.4 (d, *J* = 10.0 Hz), 124.7 (d, *J* = 3.75 Hz), 124.1 (d, *J* = 3.75 Hz), 120.1 (d, *J* = 7.5 Hz), 114.1 (d, *J* = 21.3 Hz), 105.3, 60.1, 45.4, 43.7, 33.3, 29.7, 28.3. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **–** 124.33. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{15}H_{16}FNNaO_4$: 316.0956, found: 316.0959.

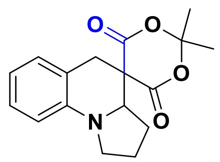
8-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (55% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.3 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 2H), 3.44 (s, 2H), 3.12 (s, 3H), 1.92 (s, 3H), 1.80 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.0, 142.7, 128.9, 127.3, 126.4, 125.6, 122.3, 105.5, 60.7, 46.1, 44.3, 33.4, 29.8, 28.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}ClNO_4$: 310.0841, found: 310.0849.

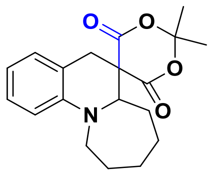
2',2'-dimethyl-1,2,3,3a-tetrahydro-5H-spiro[pyrrolo[1,2-a]quinoline-4,5'-[1,3]dioxane]-4',6'-dione (4i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (70% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 3.96 (t, *J* = 7.4 Hz, 1H), 3.62 (t, *J* = 8.2 Hz, 1H), 3.55 (d, *J* = 16.2 Hz, 1H), 3.30 (q, *J* = 8.1 Hz, 1H), 3.13 (d, *J* = 16.2 Hz, 1H), 2.19 (dd, *J* = 7.1, 4.1 Hz, 1H), 1.99 (dd, *J* = 17.8, 8.3 Hz, 2H), 1.76 (d, *J* = 13.8 Hz, 6H), 1.68 (dd, *J* = 19.9, 9.9 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.1, 164.1, 143.1, 128.2, 127.8, 116.9, 116.1, 111.5, 104.7, 64.7, 47.9, 47.3, 36.5, 29.9, 28.5, 28.1, 23.1. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{20}NO_4$: 302.1387, found: 302.1381.

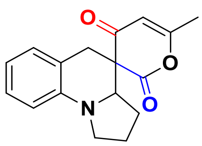
2',2'-dimethyl-6a,7,8,9,10,11-hexahydro-5H-spiro[azepino[1,2-a]quinoline-6,5'-[1,3]dioxane]-4',6'-dione (4j)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (82% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 3.63 (dd, *J* = 12.3, 4.0 Hz, 1H), 3.54 – 3.45 (m, 2H), 3.41 (m, 1H), 3.20 (d, *J* = 17.0 Hz, 1H), 1.99 – 1.87 (m, 3H), 1.84 – 1.77 (m, 4H), 1.76 – 1.67 (m, 4H), 1.62 (m, 1H), 1.47 (dd, *J* = 22.8, 11.2 Hz, 1H), 1.41 – 1.29 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.4, 166.6, 146.2, 128.6, 126.8, 119.7, 118.3, 115.1, 104.9, 67.6, 50.6, 50.4, 32.8, 30.7, 30.5, 29.5, 28.3, 27.7, 26.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{19}H_{24}NO_4$: 330.1700, found: 330.1705.

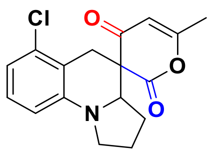
6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (77% yield, dr 5:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 13.7, 6.1 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.64 (dd, *J* = 13.5, 6.3 Hz, 1H), 6.57 (t, *J* = 6.6 Hz, 1H), 5.71 (s, 1H), 3.77 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.56 (td, *J* = 8.6, 2.5 Hz, 1H), 3.47 (d, *J* = 16.4 Hz, 1H), 3.31 (dt, *J* = 15.6, 7.9 Hz, 1H), 2.96 (d, *J* = 16.4 Hz, 1H), 2.17 (d, *J* = 4.9 Hz, 3H), 2.13 – 2.06 (m, 1H), 2.06 – 1.99 (m, 1H), 1.99 – 1.90 (m, 1H), 1.64 – 1.53 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.7, 168.47, 165.7, 143.2, 128.4, 127.6, 118.3, 116.1, 111.2, 106.1, 63.7, 53.8, 47.6, 36.5, 27.9, 23.4, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{18}NO_3$: 284.1281, found: 284.1289.

6'-chloro-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6b)

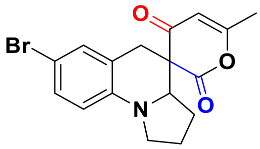


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (85% yield, dr 5:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (d, *J* = 6.5 Hz, 1H), 6.73 (d, *J* = 7.7 Hz, 1H), 6.50 (d, *J* = 7.1 Hz, 1H), 5.67 (d, *J* = 88.0 Hz, 1H), 3.71-3.61 (m, 1H), 3.60-3.50 (m, 1H), 3.40 – 3.16 (m, 3H), 2.21 (s, 3H), 2.18-2.08 (m, 1H), 2.07-2.00 (m, 1H), 2.00-1.90 (m, 1H), 1.67-1.55 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ

193.1, 168.5, 165.8, 144.3, 133.9, 127.7, 116.9, 116.8, 109.7, 106.3, 63.5, 54.1, 47.7, 33.3, 27.9, 23.4, 20.5. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{17}H_{16}ClNNaO_3$: 340.0711, found: 340.0714.

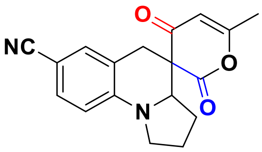
7'-bromo-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (70% yield, dr 4:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.1 Hz, 1H), 7.12 (d, *J* = 31.5 Hz, 1H), 6.45 (d, *J* = 8.3 Hz, 1H), 5.65 (d, *J* = 87.3 Hz, 1H), 3.96 – 3.69 (m, 1H), 3.53 (t, *J* = 7.9 Hz, 1H), 3.41 (dd, *J* = 29.5, 16.3 Hz, 1H), 3.34 – 3.20 (m, 1H), 2.97 (dd, *J* = 53.7, 16.3 Hz, 1H), 2.21 (s, 3H), 2.15 – 2.07 (m, 1H), 2.00 – 1.90 (m, 1H), 1.75 – 1.64 (m, 1H), 1.57 (dd, *J* = 19.3, 10.0 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.2, 168.5, 165.5, 142.2, 130.8, 130.2, 120.4, 112.7, 107.9, 106.1, 63.7, 53.4, 47.6, 35.9, 27.9, 23.3, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}BrNO_3$: 362.0386, found: 362.0386.

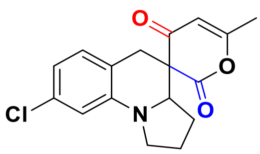
6-methyl-2,4-dioxo-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-7'-carbonitrile (6d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:30) afforded the product (70% yield, dr 4:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (dd, *J* = 29.8, 7.6 Hz, 1H), 6.91 (t, *J* = 9.2 Hz, 1H), 6.77 (s, 1H), 5.77 (s, 1H), 3.79 – 3.71 (m, 1H), 3.56 (t, *J* = 8.6 Hz, 1H), 3.48 (d, *J* = 16.9 Hz, 1H), 3.30 (dd, *J* = 16.5, 8.2 Hz, 1H), 2.98 (d, *J* = 16.9 Hz, 1H), 2.21 (d, *J* = 17.7 Hz, 3H), 2.13 (m, 2H), 2.00 (dd, *J* = 17.8, 9.9 Hz, 1H), 1.66 – 1.53 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.8, 168.7, 165.6, 143.2, 128.9, 123.8, 119.5, 113.7, 110.9, 106.2, 63.7, 52.9, 47.5, 35.9, 27.9, 23.3, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}N_2O_3$: 309.1234, found: 309.1236.

8'-chloro-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6e)

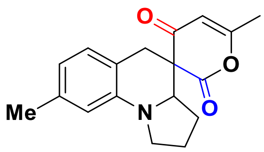


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (73% yield, dr 5:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (dd, *J* = 33.3, 7.5 Hz, 1H), 6.67 – 6.56 (m, 1H), 6.55 (s, 1H), 5.64 (d, *J* = 92.0 Hz, 1H), 3.85 (dd, *J* = 81.5, 6.6 Hz, 1H), 3.53 (t, *J* = 7.8 Hz, 1H), 3.38 (t, *J* = 12.9 Hz, 1H), 3.33 – 3.21 (m, 1H), 3.00 (dd, *J* = 54.9, 16.1 Hz, 1H), 2.20 (s, 3H), 2.08 (dd, *J* = 16.7, 10.4 Hz, 2H), 1.99 (d, *J* =

7.8 Hz, 1H), 1.61 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.4, 168.5, 165.5, 144.0, 133.1, 129.2, 116.6, 115.8, 110.9, 106.1, 63.3, 53.4, 47.6, 36.2, 27.9, 23.4, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}ClNO_3$: 318.0891, found: 318.0898.

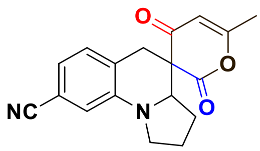
6,8'-dimethyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (75% yield, dr 4:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (dd, *J* = 35.7, 7.3 Hz, 1H), 6.48 (t, *J* = 11.0 Hz, 1H), 6.42 (s, 1H), 5.72 (s, 1H), 3.82 – 3.75 (m, 1H), 3.57 (t, *J* = 8.2 Hz, 1H), 3.42 (t, *J* = 13.8 Hz, 1H), 3.39 – 3.26 (m, 1H), 2.95 (d, *J* = 16.3 Hz, 1H), 2.31 (s, 3H), 2.20 (s, 3H), 2.14-2.05 (m, 1H), 2.05-2.00 (m, 1H), 1.99 – 1.90 (m, 1H), 1.62-1.60 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.8, 168.3, 165.6, 142.9, 137.2, 128.2, 117.1, 115.2, 111.9, 106.1, 63.6, 54.0, 47.5, 36.4, 27.9, 23.4, 21.7, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{20}NO_3$: 298.1438, found: 298.1432.

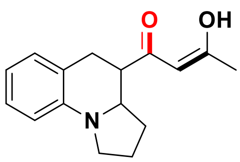
6-methyl-2,4-dioxo-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-8'-carbonitrile (6g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (81% yield, dr 5:1) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 29.9, 7.5 Hz, 1H), 6.91 (t, *J* = 9.2 Hz, 1H), 6.77 (s, 1H), 5.68 (d, *J* = 90.2 Hz, 1H), 3.96 – 3.70 (m, 1H), 3.56 (t, *J* = 8.5 Hz, 1H), 3.45 (dd, *J* = 32.9, 16.7 Hz, 1H), 3.29 (dt, *J* = 15.4, 7.8 Hz, 1H), 3.04 (dd, *J* = 52.8, 16.7 Hz, 1H), 2.23 (s, 3H), 2.17 – 2.05 (m, 2H), 2.05 – 1.94 (m, 1H), 1.72 – 1.58 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.8, 168.7, 165.6, 143.2, 128.9, 123.8, 119.8, 119.5, 113.7, 110.9, 106.2, 63.7, 52.9, 47.5, 35.9, 27.9, 23.3, 20.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}N_2O_3$: 309.1234, found: 309.1238.

(Z)-1-(1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8a)

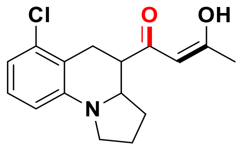


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (75% yield, dr >20:1, tr 15:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.70 (s, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 7.0 Hz, 1H), 6.62 (t, *J* = 7.0 Hz, 1H), 6.49 (d, *J* = 7.9 Hz, 1H), 5.61 (s, 1H), 3.65 – 3.52 (m, 1H), 3.46 (t, *J* = 8.8 Hz, 1H), 3.25 (q, *J* = 8.4 Hz, 1H), 3.09 (t, *J* = 14.0 Hz, 1H), 2.87 (d, *J* = 15.6 Hz, 1H), 2.21-2.17 (m, 2H), 2.136 (s, 3H), 2.03-

1.93 (m, 1H), 1.58 – 1.44 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 195.2, 191.8, 143.8, 128.5, 127.6, 120.3, 115.2, 110.3, 100.2, 59.8, 47.2, 46.5, 32.6, 31.7, 25.0, 23.9. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{20}NO_2$: 258.1489, found: 258.1483.

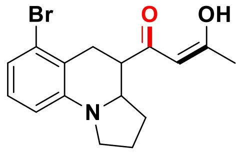
(Z)-1-(6-chloro-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (83% yield, dr >20:1, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.63 (s, 1H), 7.00 (t, *J* = 7.9 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.34 (d, *J* = 8.1 Hz, 1H), 5.59 (s, 1H), 3.49 (dd, *J* = 14.4, 9.7 Hz, 1H), 3.38 (t, *J* = 9.0 Hz, 1H), 3.28 – 3.15 (m, 2H), 2.87 – 2.77 (m, 1H), 2.16 (dd, *J* = 11.5, 6.6 Hz, 2H), 2.09 (d, *J* = 18.4 Hz, 4H), 1.96 (dd, *J* = 19.9, 8.9 Hz, 1H), 1.54 – 1.43 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.5, 191.9, 145.1, 134.1, 127.8, 118.1, 115.9, 108.8, 100.2, 59.2, 47.3, 46.4, 31.6, 29.9, 24.9, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{19}ClNO_2$: 292.1099, found: 292.1091.

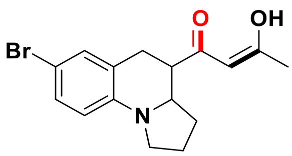
(Z)-1-(6-bromo-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (78% yield, dr 4:1, tr 15:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.65 (s, 1H), 6.93 (t, *J* = 7.7 Hz, 1H), 6.83 (t, *J* = 10.7 Hz, 1H), 6.38 (t, *J* = 8.4 Hz, 1H), 5.59 (s, 1H), 3.50-3.45 (m, 1H), 3.37 (t, *J* = 9.0 Hz, 1H), 3.25-3.20 (m, 1H), 3.15 (d, *J* = 16.0 Hz, 1H), 2.86 – 2.80 (m, 1H), 2.15-2.10 (m, 1H), 2.11-2.03 (m, 4H), 1.99 – 1.89 (m, 2H), 1.55 – 1.43 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.4, 192.0, 145.1, 128.3, 125.0, 119.6, 119.1, 109.4, 100.3, 59.2, 47.3, 46.6, 32.9, 31.6, 25.1, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{19}BrNO_2$: 336.0594, found: 336.0590.

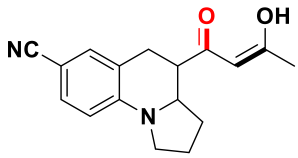
(Z)-1-(7-bromo-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (68% yield, dr >20:1, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.66 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.13 (s, 1H), 6.32 (d, *J* = 8.4 Hz, 1H), 5.59 (s, 1H), 3.54 (d, *J* = 2.2 Hz, 1H), 3.40 (t, *J* = 8.8 Hz, 1H), 3.19 (q, *J* = 8.4 Hz, 1H), 3.04 (t, *J* = 14.1 Hz, 1H), 2.81 (d, *J* = 15.7 Hz, 1H), 2.24 – 2.05 (m, 6H), 1.99 (dd, *J* = 19.1, 9.1 Hz, 1H), 1.57 – 1.41 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.7, 191.8, 142.7, 130.8, 130.1, 122.3, 111.7, 106.7, 100.2, 59.8, 47.3, 46.1, 32.2, 31.7, 24.9, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{19}BrNO_2$: 336.0594, found: 336.0598.

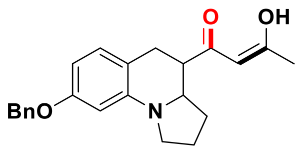
(Z)-4-(3-hydroxybut-2-enoyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-7-carbonitrile (8e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (63% yield, dr >20:1, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.63 (s, 1H), 7.06 (d, *J* = 7.1 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.62 (s, 1H), 5.61 (s, 1H), 3.58 (t, *J* = 9.9 Hz, 1H), 3.43 (t, *J* = 8.9 Hz, 1H), 3.20 (q, *J* = 8.3 Hz, 1H), 3.07 (t, *J* = 14.3 Hz, 1H), 2.88 (d, *J* = 16.2 Hz, 1H), 2.25 – 2.14 (m, 2H), 2.12 (d, *J* = 12.2 Hz, 4H), 2.06 – 1.93 (m, 1H), 1.58 – 1.45 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.2, 191.8, 143.9, 128.9, 125.5, 119.9, 118.6, 112.5, 110.9, 100.3, 59.8, 47.2, 45.6, 32.5, 31.7, 24.9, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{19}N_2O_2$: 283.1441, found: 283.1448.

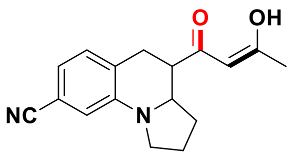
(Z)-1-(8-(benzyloxy)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (62% yield, dr 10:1, tr 11:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) 15.69 (s, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.41 (dd, *J* = 10.2, 4.7 Hz, 2H), 7.35 (dd, *J* = 8.3, 6.3 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.26 (dd, *J* = 8.1, 2.4 Hz, 1H), 6.14 (d, *J* = 2.4 Hz, 1H), 5.60 (s, 1H), 5.07 (s, 2H), 3.57 (td, *J* = 10.1, 5.1 Hz, 1H), 3.41 (td, *J* = 8.9, 1.4 Hz, 1H), 3.22 (td, *J* = 9.4, 7.5 Hz, 1H), 3.06 – 2.94 (m, 1H), 2.83 (dd, *J* = 15.4, 3.8 Hz, 1H), 2.21 – 2.14 (m, 2H), 2.13 (s, 3H), 2.09 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.02 – 1.91 (m, 1H), 1.55-1.43 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.2, 190.7, 157.8, 143.6, 136.5, 127.9, 127.5, 126.8, 126.6, 126.5, 112.4, 99.6, 99.1, 96.7, 68.9, 58.6, 46.1, 45.8, 30.9, 30.7, 23.9, 22.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{23}H_{26}NO_3$: 364.1907, found: 364.1903.

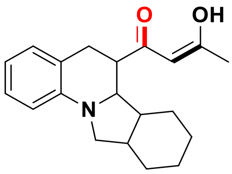
(Z)-4-(3-hydroxybut-2-enoyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-8-carbonitrile (8g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (76% yield, dr >20:1, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.63 (s, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 6.62 (s, 1H), 5.61 (s, 1H), 3.63 – 3.54 (m, 1H), 3.43 (t, *J* = 8.9 Hz, 1H), 3.20 (dd, *J* = 17.3, 8.6 Hz, 1H), 3.12 – 3.02 (m, 1H), 2.88 (d, *J* = 16.1 Hz, 1H), 2.26 – 2.08 (m, 6H), 2.00 (dd, *J* = 12.5, 5.9 Hz, 1H), 1.60 – 1.43 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.2, 191.8, 143.9, 128.9, 125.6, 119.9, 118.6, 112.5, 110.9, 100.3, 59.8, 47.2, 45.6, 32.5, 31.7, 24.9, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{19}N_2O_2$: 283.1441, found: 283.1446.

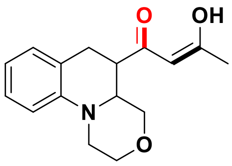
(Z)-1-(5,6,6a,6b,7,8,9,10,10a,11-decahydroisoindolo[2,1-a]quinolin-6-yl)-3-hydroxybut-2-en-1-one (8h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (60% yield, dr 1:0.6, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.6 (s, 1H), 15.5 (s, 1H), 7.02 (t, *J* = 7.0 Hz, 2H), 6.92 (d, *J* = 6.7 Hz, 2H), 6.47 (dd, *J* = 15.7, 7.6 Hz, 2H), 6.33 (ddd, *J* = 22.9, 15.3, 8.2 Hz, 2H), 5.52 (s, 1H), 5.12 (s, 1H), 3.66 (dd, *J* = 20.8, 11.4 Hz, 1H), 3.42 (q, *J* = 8.3 Hz, 1H), 3.36 – 3.25 (m, 1H), 3.21 (t, *J* = 6.8 Hz, 1H), 3.18 – 3.13 (m, 1H), 3.11 – 2.96 (m, 2H), 2.86 (ddd, *J* = 39.0, 24.7, 10.8 Hz, 2H), 2.74 – 2.60 (m, 2H), 2.12 – 1.98 (m, 5H), 1.97 – 1.81 (m, 5H), 1.78 – 1.68 (m, 2H), 1.68 – 1.54 (m, 4H), 1.46 (dt, *J* = 18.7, 9.6 Hz, 2H), 1.36 – 1.15 (m, 5H), 1.08 (dd, *J* = 18.8, 9.7 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.6, 194.2, 192.8, 192.5, 191.3, 191.1, 190.9, 190.6, 143.7, 143.2, 142.7, 127.6, 127.6, 127.3, 127.3, 126.7, 126.5, 126.5, 126.4, 119.1, 118.9, 117.4, 117.1, 114.0, 113.8, 113.8, 113.5, 109.3, 108.5, 108.5, 108.0, 99.7, 99.5, 99.2, 99.0, 63.2, 62.6, 58.0, 57.4, 52.8, 52.4, 50.9, 50.3, 49.8, 46.4, 44.9, 42.7, 42.5, 42.4, 38.8, 38.7, 36.4, 35.6, 32.7, 32.6, 30.7, 30.3, 28.1, 27.9, 27.8, 27.6, 26.8, 24.9, 24.7, 24.7, 24.7, 24.6, 24.4, 24.2, 24.1, 24.0, 23.9, 23.1, 20.4, 20.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{20}H_{26}NO_2$: 312.1958, found: 312.1952.

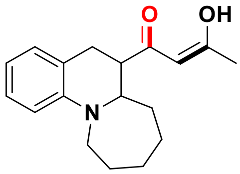
(Z)-1-(1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinolin-5-yl)-3-hydroxybut-2-en-1-one (8i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (66% yield, dr >20:1, tr 19:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$)δ 15.6 (s, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.78 (t, *J* = 7.3 Hz, 1H), 5.58 (s, 1H), 5.32 (s, 1H), 4.07 – 3.99 (m, 1H), 3.94 (d, *J* = 8.7 Hz, 1H), 3.70 (ddd, *J* = 18.9, 13.8, 8.3 Hz, 2H), 3.39 – 3.26 (m, 2H), 3.11 (dd, *J* = 15.8, 11.5 Hz, 1H), 3.01 (td, *J* = 11.9, 3.5 Hz, 1H), 2.86 (dd, *J* = 15.8, 5.1 Hz, 1H), 2.57 – 2.50 (m, 1H), 2.25 (d, *J* = 3.2 Hz, 1H), 2.12 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.8, 192.7, 192.5, 192.4, 145.3, 145.1, 129.4, 129.2, 127.5, 127.5, 122.6, 122.4, 118.7, 112.9, 112.3, 100.2, 99.9, 76.8, 70.2, 68.4, 66.9, 66.9, 66.1, 56.5, 56.3, 54.2, 48.2, 46.6, 44.8, 42.7, 31.4, 28.7, 25.3, 25.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{20}NO_3$: 274.1438, found: 274.1434.

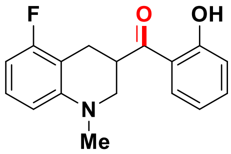
(Z)-3-hydroxy-1-(5,6,6a,7,8,9,10,11-octahydroazepino[1,2-a]quinolin-6-yl)but-2-en-1-one (8j)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (68% yield, dr 10:1, tr 11:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.57 (s, 1H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.94 (d, *J* = 7.0 Hz, 1H), 6.50 (t, *J* = 7.4 Hz, 2H), 5.57 (s, 1H), 3.89 – 3.77 (m, 1H), 3.63 (d, *J* = 10.7 Hz, 1H), 3.18 – 3.07 (m, 1H), 3.02 (t, *J* = 14.8 Hz, 1H), 2.88 (d, *J* = 13.1 Hz, 1H), 2.66 (d, *J* = 15.8 Hz, 1H), 2.03 (s, 3H), 1.50 (m, 4H), 1.30 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.6, 190.9, 142.4, 128.5, 126.5, 117.3, 114.1, 108.9, 98.0, 59.0, 48.6, 42.8, 29.5, 25.3, 25.2, 24.9, 24.2, 23.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{24}NO_2$: 286.1802, found: 286.1809.

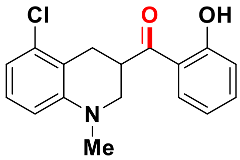
(5-fluoro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (71% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.30 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.10 – 7.05 (m, 1H), 7.04 (t, *J* = 6.2 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.47 – 6.40 (m, 2H), 3.96 – 3.87 (m, 1H), 3.48 – 3.41 (m, 1H), 3.39 (m, 1H), 3.18 – 3.11 (m, 1H), 2.96 (s, 3H), 2.91 (dd, *J* = 16.5, 11.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.9, 163.2, 161.5 (d, *J* = 240.0 Hz), 147.3 (d, *J* = 7.5 Hz), 136.8, 129.8, 127.7 (d, *J* = 11.3 Hz), 119.2, 118.9, 118.4, 108.5 (d, *J* = 20.0 Hz), 106.8 (d, *J* = 2.5 Hz), 103.4 (d, *J* = 22.5 Hz), 52.7, 39.7, 39.2, 24.4. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -123.35. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_2$: 286.1238, found: 286.1232.

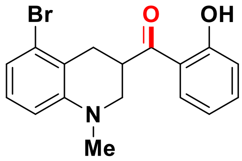
(5-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (75% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.30 (s, 1H), 7.87 – 7.80 (m, 1H), 7.54 – 7.46 (m, 1H), 7.07 – 7.00 (m, 2H), 6.96 – 6.89 (m, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 1H), 3.92 (dd, *J* = 10.7, 5.4 Hz, 1H), 3.44 – 3.38 (m, 1H), 3.38 – 3.34 (m, 1H), 3.21 (m, 1H), 2.99 – 2.90 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.7, 163.2, 147.4, 136.8, 134.4, 129.8, 127.7, 119.3, 119.2, 119.0, 118.5, 117.7, 109.9, 52.8, 39.8, 39.7, 29.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}ClNO_2$: 302.0942, found: 302.0947.

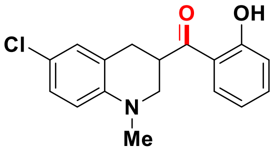
(5-bromo-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (77% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.31 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.49 (dd, J = 11.4, 4.1 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 6.97 – 6.85 (m, 3H), 6.59 (d, J = 7.9 Hz, 1H), 3.96 – 3.87 (m, 1H), 3.44 – 3.32 (m, 2H), 3.23 – 3.13 (m, 1H), 2.99 – 2.90 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.7, 163.2, 147.5, 136.9, 129.8, 128.2, 125.4, 120.9, 120.8, 119.3, 119.0, 118.5, 110.5, 52.8, 40.1, 39.7, 32.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}BrNO_2$: 346.0437, found: 346.0430.

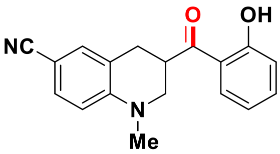
(6-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (80% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.27 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.7 Hz, 1H), 7.07 (dd, J = 8.7, 2.0 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 6.99 (s, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.57 (d, J = 8.7 Hz, 1H), 3.98 – 3.88 (m, 1H), 3.48 – 3.36 (m, 2H), 3.10 (dd, J = 15.9, 11.5 Hz, 1H), 2.92 (d, J = 8.7 Hz, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.7, 163.2, 144.3, 136.9, 129.7, 128.5, 127.3, 122.8, 121.5, 119.2, 119.0, 118.4, 112.4, 53.0, 39.9, 39.3, 31.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}ClNO_2$: 302.0942, found: 302.0951.

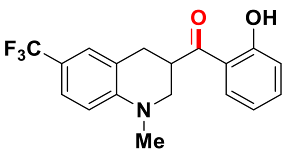
3-(2-hydroxybenzoyl)-1-methyl-1,2,3,4-tetrahydroquinoline-6-carbonitrile (9e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (82% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.20 (s, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.23 (s, 1H), 7.03 (d, J = 8.4 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 6.60 (d, J = 8.6 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.63 (t, J = 11.0 Hz, 1H), 3.48 (d, J = 11.9 Hz, 1H), 3.09 – 2.93 (m, 5H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.1, 163.2, 148.4, 137.1, 132.3, 132.2, 129.7, 120.9, 120.5, 119.4, 119.1, 118.2, 110.4, 97.8, 52.6, 38.9, 31.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}N_2O_2$: 293.1285, found: 293.1273.

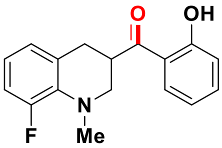
(2-hydroxyphenyl)(1-methyl-6-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-3-yl)methanone (9f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (78% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.18 (s, 1H), 7.74 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.26 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.14 (d, *J* = 6.5 Hz, 1H), 6.94 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.87 – 6.82 (m, 1H), 6.55 (d, *J* = 8.6 Hz, 1H), 3.83 (ddd, *J* = 10.8, 6.5, 4.5 Hz, 1H), 3.52 – 3.44 (m, 1H), 3.35 (ddd, *J* = 11.7, 3.9, 2.3 Hz, 1H), 3.05-2.97 (m, 1H), 2.95 – 2.85 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.5, 163.2, 147.9, 137.0, 129.7, 128.3, 126.1, 125.78 (q, *J* = 3.6 Hz), 125.04 (q, *J* = 268.75 Hz), 124.95 (q, *J* = 3.8 Hz), 120.7, 119.3, 119.1, 118.4, 117.9 (q, *J* = 32.5 Hz), 110.2, 52.7, 39.4, 39.0, 31.8. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -60.80. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}F_3NO_2$: 336.1206, found: 336.1219.

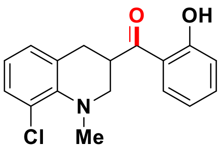
(8-fluoro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (75% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.33 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.92 – 6.83 (m, 2H), 6.77 (dt, *J* = 12.7, 6.4 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.40 (d, *J* = 12.6 Hz, 1H), 3.27 – 3.14 (m, 2H), 3.05 (s, 3H), 2.92 (d, *J* = 15.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.9, 163.2, 154.4 (d, *J* = 242.5 Hz), 136.9, 135.2 (d, *J* = 8.8 Hz), 129.6, 127.7 (d, *J* =3.8 Hz), 124.9 (d, *J* = 2.5 Hz), 120.3 (d, *J* = 8.8 Hz), 119.2, 119.0, 118.5, 114.4 (d, *J* = 21.3 Hz), 55.2, 43.1, 42.9, 37.2, 31.1, 31.0. **^{19}F NMR** (470 MHz, DMSO) δ **–** 123.89. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_2$: 286.1238, found: 286.1230.

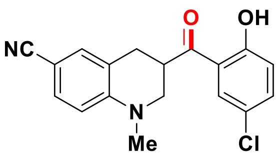
(8-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (61% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.31 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.20 – 7.13 (m, 1H), 7.01 – 6.95 (m, 2H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 7.7 Hz, 1H), 3.91 (t, *J* = 11.1 Hz, 1H), 3.36 (d, *J* = 13.4 Hz, 1H), 3.28 – 3.17 (m, 1H), 3.15 – 3.05 (m, 1H), 2.96 (s, 3H), 2.88 (dd, *J* = 16.9, 4.9 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.8, 163.2, 144.4, 136.8, 129.4, 128.7, 128.3, 127.7, 122.9, 119.3, 119.1, 118.7, 55.2, 43.2, 34.9, 30.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{17}H_{17}ClNO_2$: 302.0942, found: 302.0935.

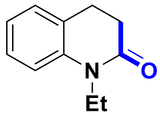
3-(5-chloro-2-hydroxybenzoyl)-1-methyl-1,2,3,4-tetrahydroquinoline-6-carbonitrile (9i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (71% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.12 (s, 1H), 7.78 (s, 1H), 7.49 (d, *J* = 8.9 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.26 (s, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.63 (d, *J* = 8.6 Hz, 1H), 3.90 – 3.81 (m, 1H), 3.63 (t, *J* = 10.9 Hz, 1H), 3.54 – 3.47 (m, 1H), 3.13 – 2.96 (m, 5H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 205.4, 161.7, 148.3, 137.0, 132.4, 132.3, 128.8, 124.1, 120.8, 120.7, 120.4, 118.8, 110.5, 97.9, 52.5, 40.0, 38.9, 31.4. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{18}H_{15}ClN_2NaO_2$: 349.0714, found: 349.0710.

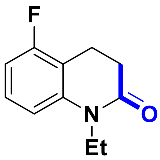
1-ethyl-3,4-dihydroquinolin-2(1H)-one (10a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (93% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.04 – 6.96 (m, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 2.92 – 2.83 (m, 2H), 2.63 (dd, *J* = 8.5, 6.3 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8, 139.6, 127.9, 127.4, 126.5, 122.6, 114.6, 37.3, 31.9, 25.6, 12.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{14}NO$: 176.1070, found: 176.1082.

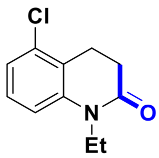
1-ethyl-5-fluoro-3,4-dihydroquinolin-2(1H)-one (10b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (80% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.18 (m, 1H), 6.84 – 6.73 (m, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.00 – 2.86 (m, 2H), 2.63 (dd, *J* = 8.5, 6.6 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.4, 159.8 (d, *J* = 242.5 Hz), 141.3, 128.1 (d, *J* = 10.0 Hz), 113.7 (d, *J* = 21.3 Hz), 110.3, 109.9 (d, *J* = 22.5 Hz), 37.7, 30.9, 17.6, 12.8. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -117.86. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}FNO$: 194.0976, found: 194.0970.

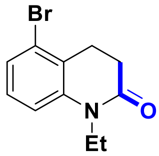
5-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (90% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (t, *J* = 8.1 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.08 – 2.98 (m, 2H), 2.70 – 2.58 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 141.1, 133.3, 127.9, 124.6, 123.7, 113.3, 37.8, 31.0, 22.4, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}ClNO$: 210.0680, found: 210.0689.

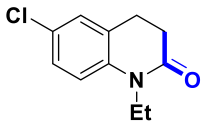
5-bromo-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (75% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 3.5 Hz, 1H), 7.10 (t, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 3.10 – 2.98 (m, 2H), 2.70 – 2.59 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.4, 141.0, 128.3, 126.8, 126.4, 123.8, 113.9, 37.7, 31.2, 25.4, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}BrNO$: 254.0175, found: 254.0185.

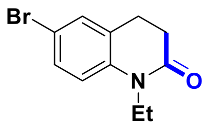
6-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (70% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22-7.19 (m, 1H), 7.15 (d, *J* = 2.4 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 3.97 (q, *J* = 7.1 Hz, 2H), 2.91 – 2.83 (m, 2H), 2.67 – 2.58 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 138.2, 128.3, 127.9, 127.7, 127.3, 115.8, 37.5, 31.6, 25.4, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}ClNO$: 210.0680, found: 210.0689.

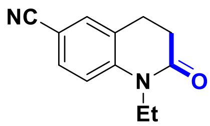
6-bromo-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (92% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.29 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 1H), 3.96 (q, *J* = 7.1 Hz, 2H), 2.90 – 2.83 (m, 2H), 2.67 – 2.59 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 138.7, 130.8, 130.2, 128.7, 116.2, 115.3, 37.4, 31.6, 25.3, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}BrNO$: 254.0175, found: 254.0184.

1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carbonitrile (10g)

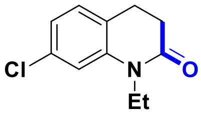


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (62% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.46 (s, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 4.00

(q, *J* = 7.1 Hz, 2H), 3.00 – 2.90 (m, 2H), 2.68 (dd, J = 8.5, 6.4 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 143.5, 132.1, 131.6, 127.4, 118.9, 115.0, 105.8, 37.7, 31.3, 25.3, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{12}H_{13}N_2O$: 201.1022, found: 201.1029.

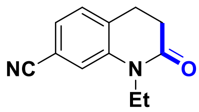
7-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (88% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 7.9 Hz, 1H), 7.03 – 6.94 (m, 2H), 3.95 (q, *J* = 7.1 Hz, 2H), 2.93 – 2.81 (m, 2H), 2.69 – 2.57 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 140.8, 133.1, 128.9, 124.8, 122.4, 114.9, 37.4, 31.7, 25.1, 12.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{13}ClNO$: 210.0680, found: 210.0688.

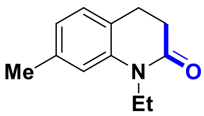
1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-7-carbonitrile (10i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (92% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.29 (t, *J* = 5.7 Hz, 1H), 7.26 (s, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.02 – 2.94 (m, 2H), 2.71 – 2.65 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.1, 140.5, 131.9, 128.9, 126.4, 118.7, 117.5, 111.5, 37.6, 31.1, 25.8, 12.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{12}H_{13}N_2O$: 201.1022, found: 201.1036.

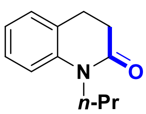
1-ethyl-7-methyl-3,4-dihydroquinolin-2(1H)-one (10j)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (65% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.5 Hz, 1H), 6.86 – 6.79 (m, 2H), 3.98 (q, *J* = 7.1 Hz, 2H), 2.90 – 2.79 (m, 2H), 2.68 – 2.56 (m, 2H), 2.36 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.1, 139.5, 137.2, 127.8, 123.6, 123.3, 115.4, 37.4, 32.2, 25.2, 21.6, 12.9. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{12}H_{16}NO$: 190.1226, found: 190.1212.

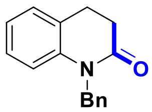
1-propyl-3,4-dihydroquinolin-2(1H)-one (10k)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (82% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.00 (dd, *J* = 7.8, 5.5 Hz, 2H), 3.96 – 3.84 (m, 2H), 2.94 – 2.83 (m, 2H), 2.70 – 2.60 (m, 2H), 1.68 (dd, *J* = 15.4, 7.6 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.2, 139.7, 130.0, 127.4, 126.6, 122.6, 114.9, 43.6, 32.0, 25.6, 20.5, 11.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{12}H_{16}NO$: 190.1226, found: 190.1212.

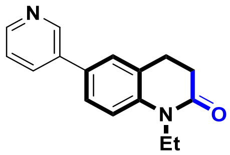
1-benzyl-3,4-dihydroquinolin-2(1H)-one (10l)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (90% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.7 Hz, 3H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 5.20 (s, 2H), 3.05 – 2.95 (m, 2H), 2.81 (dd, *J* = 8.4, 6.3 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.6, 139.9, 137.0, 128.8, 127.9, 127.5, 127.1, 126.4, 122.9, 115.6, 46.2, 31.9, 25.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{16}NO$: 238.1226, found: 238.1218.

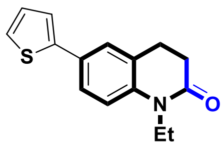
1-ethyl-6-(pyridin-3-yl)-3,4-dihydroquinolin-2(1H)-one (10m)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:2) afforded the product (78% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.58 (d, *J* = 3.1 Hz, 1H), 7.87 (dd, *J* = 6.0, 1.8 Hz, 1H), 7.48 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.18 – 7.08 (m, 1H), 4.03 (dt, *J* = 6.8, 5.0 Hz, 2H), 3.04 – 2.93 (m, 2H), 2.75 – 2.63 (m, 2H), 1.34 – 1.25 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8, 148.1, 147.8, 139.6, 135.9, 134.0, 132.0, 127.3, 126.7, 126.1, 123.7, 115.3, 37.4, 31.8, 25.7, 12.8. **HRMS (ESI):** calcd. for $C_{16}H_{17}N_2O$ $[M+H]^+$: 253.1341, found: 253.1347.

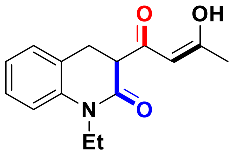
1-ethyl-6-(thiophen-2-yl)-3,4-dihydroquinolin-2(1H)-one (10n)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (86% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 4.5 Hz, 2H), 7.08 – 7.04 (m, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 2.97 – 2.86 (m, 2H), 2.65 (dd, *J* = 8.5, 6.3 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.7, 143.7, 138.9, 129.1, 128.1, 127.0, 125.6, 125.0, 124.5, 122.6, 115.0, 37.4, 31.8, 25.6, 12.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{16}NOS$: 258.0947, found: 258.0959.

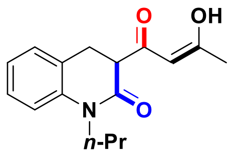
(Z)-1-ethyl-3-(3-hydroxybut-2-enoyl)-3,4-dihydroquinolin-2(1H)-one (11a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (92% yield, tautomerism ratio 5:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.04 (s, 1H), 7.22 – 7.17 (m, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.96 (dd, *J* = 13.4, 7.0 Hz, 2H), 5.57 (s, 1H), 4.02 – 3.87 (m, 2H), 3.46 (t, *J* = 6.8 Hz, 1H), 3.25 (dd, *J* = 15.6, 7.7 Hz, 1H), 2.97 (dd, *J* = 15.6, 5.8 Hz, 1H), 1.95 (s, 3H), 1.21 (dd, *J* = 15.8, 7.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.5, 188.5, 166.9, 138.6, 128.4, 127.8, 124.7, 123.2, 114.7, 99.8, 50.7, 37.9, 28.2, 23.9, 12.6. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{15}H_{17}NNaO_3$: 282.1101, found: 282.1097.

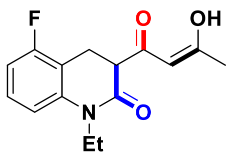
(Z)-3-(3-hydroxybut-2-enoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (11b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (80% yield, tautomerism ratio 5:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.09 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.01 (dd, *J* = 19.4, 7.7 Hz, 2H), 5.64 (s, 1H), 3.98 – 3.85 (m, 2H), 3.55 (t, *J* = 6.5 Hz, 1H), 3.31 (dt, *J* = 16.2, 8.2 Hz, 1H), 3.04 (dd, *J* = 15.6, 5.7 Hz, 1H), 2.02 (s, 3H), 1.69 (dt, *J* = 15.6, 7.7 Hz, 2H), 0.97 (t, *J* = 7.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.6, 188.3, 167.1, 138.7, 128.4, 127.7, 124.8, 123.2, 114.9, 99.8, 50.8, 44.3, 28.2, 23.9, 20.4, 11.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{20}NO_3$: 274.1438, found: 274.1434.

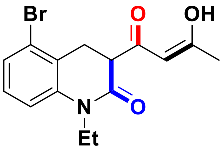
(Z)-3-(3-hydroxybut-2-enoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (11c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (67% yield, tautomerism ratio 6:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.04 (s, 1H), 7.21 (dd, *J* = 14.8, 7.3 Hz, 1H), 6.80 (t, *J* = 8.7 Hz, 2H), 5.66 (s, 1H), 4.00 (m, 2H), 3.55 (t, *J* = 6.2 Hz, 1H), 3.40 (dd, *J* = 16.1, 7.0 Hz, 1H), 3.02 (dd, *J* = 16.1, 5.6 Hz, 1H), 2.03 (s, 3H), 1.27 (d, *J* = 7.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.4, 188.2, 166.5, 160.0 (d, *J* = 242.5 Hz), 140.34 (d, *J* = 6.4 Hz), 128.44 (d, *J* = 9.5 Hz), 112.1 (d, *J* = 21.3 Hz), 110.3 (d, *J* = 8.8 Hz), 110.2 (d, *J* = 11.2 Hz), 99.6, 49.9, 38.3, 23.8, 20.4 (d, *J* = 4.1 Hz), 12.6. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **–** 117.56. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{15}H_{16}FNNaO_3$: 300.1006, found: 300.1006.

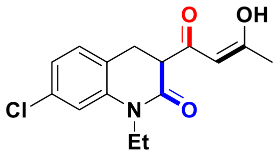
(Z)-5-bromo-1-ethyl-3-(3-hydroxybut-2-enoyl)-3,4-dihydroquinolin-2(1H)-one (11d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (71% yield, tautomerism ratio 6:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.02 (s, 1H), 7.27 (s, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.66 (s, 1H), 3.99 (m, 2H), 3.61 – 3.47 (m, 2H), 3.14 (d, *J* = 12.9 Hz, 1H), 2.03 (s, 3H), 1.30 – 1.24 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.2, 188.2, 166.5, 139.9, 128.6, 127.4, 124.8, 124.1, 114.0, 99.7, 50.2, 38.4, 27.9, 23.9, 12.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}BrNO_3$: 338.0386, found: 338.0389.

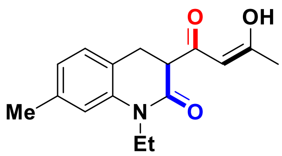
(Z)-7-chloro-1-ethyl-3-(3-hydroxybut-2-enoyl)-3,4-dihydroquinolin-2(1H)-one (11e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (68% yield, tautomerism ratio 6:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.05 (s, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.99 (s, 2H), 5.63 (s, 1H), 3.98 (m, 2H), 3.54 (s, 1H), 3.29 (dd, *J* = 15.5, 6.0 Hz, 1H), 3.02 (dd, *J* = 15.6, 4.3 Hz, 1H), 2.03 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.3, 188.3, 166.7, 139.7, 133.4, 129.4, 123.1, 123.0, 115.0, 99.6, 50.5, 38.1, 27.6, 23.8, 12.5. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{15}H_{17}ClNO_3$: 294.0891, found: 294.0895.

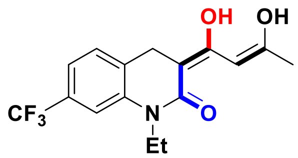
(Z)-1-ethyl-3-(3-hydroxybut-2-enoyl)-7-methyl-3,4-dihydroquinolin-2(1H)-one (11f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (65% yield, tautomerism ratio 6:1) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 15.11 (s, 1H), 7.07 (d, *J* = 7.1 Hz, 1H), 6.83 (d, *J* = 9.4 Hz, 2H), 5.63 (s, 1H), 3.99 (m, 2H), 3.51 (t, *J* = 6.4 Hz, 1H), 3.27 (dd, *J* = 15.6, 7.4 Hz, 1H), 3.00 (dd, *J* = 15.5, 5.5 Hz, 1H), 2.36 (s, 3H), 2.02 (s, 3H), 1.29 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.7, 188.5, 166.9, 138.5, 137.6, 128.2, 123.9, 121.6, 115.4, 99.8, 50.9, 37.9, 27.9, 23.9, 21.6, 12.7. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $C_{16}H_{19}NNaO_3$: 296.1257, found: 296.1258.

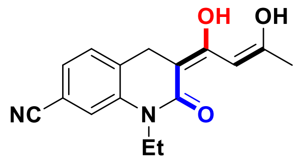
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-7-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (12a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (72% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.81 (s, 1H), 7.31 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.24 (d, *J* = 2.0 Hz, 1H), 6.60 (d, *J* = 8.5 Hz, 1H), 6.08 (d, *J* = 0.6 Hz, 1H), 3.46 (s, 2H), 3.13 (d, *J* = 7.2 Hz, 2H), 2.19 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, DMSO) δ 167.2, 166.1, 161.6, 149.7, 125.9 (q, *J* = 268.8 Hz), 126.4 (q, *J* = 3.8 Hz), 124.8 (q, *J* = 3.8 Hz), 123.7, 115.2 (q, *J* = 31.3 Hz), 108.9, 100.4, 98.8, 37.9, 25.2, 19.8, 14.5. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **–** 62.04. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{17}F_3NO_3$: 328.1155, found: 328.1159.

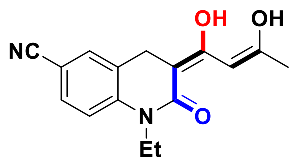
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-7-carbonitrile (12b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (82% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.75 (s, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.90 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.80 (s, 1H), 6.08 (s, 1H), 3.45 (s, 2H), 3.11 (q, *J* = 7.1 Hz, 2H), 2.19 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, DMSO) δ 167.2, 165.9, 161.6, 147.3, 130.1, 129.5, 120.4, 119.4, 111.6, 109.9, 100.4, 98.3, 37.9, 25.5, 19.8, 14.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O_3$: 285.1234, found: 285.1222.

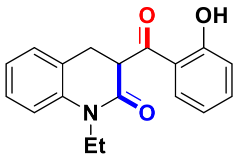
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carbonitrile (12c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (86% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.83 (s, 1H), 7.41 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.19 (d, *J* = 2.0 Hz, 1H), 6.58 (d, *J* = 8.6 Hz, 1H), 6.09 (s, 1H), 3.41 (s, 2H), 3.16 (q, *J* = 7.1 Hz, 2H), 2.20 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, DMSO) δ 167.3, 165.9, 161.8, 150.3, 132.7, 132.3, 124.1, 121.3, 109.5, 100.4, 98.3, 95.8, 37.7, 25.0, 19.8, 14.4. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O_3$: 285.1234, found: 285.1226.

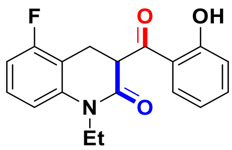
1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (84% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.97 (s, 1H), 7.78 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.48 (m, 1H), 7.35 – 7.27 (m, 1H), 7.18 (d, *J* = 7.0 Hz, 1H), 7.05 (m, 2H), 6.99 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.92 (m, 1H), 4.61 (dd, *J* = 10.4, 6.0 Hz, 1H), 4.10 – 3.95 (m, 2H), 3.50 – 3.40 (m, 1H), 3.09 (dd, *J* = 15.7, 5.9 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.9, 166.6, 162.9, 138.8, 136.8, 130.8, 128.3, 127.9, 124.6, 123.3, 119.4, 119.2, 118.7, 114.9, 48.4, 37.9, 28.9, 12.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{18}NO_3$: 296.1281, found: 296.1275.

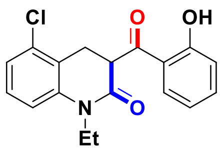
1-ethyl-5-fluoro-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (81% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.91 (s, 1H), 7.80 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.24 (d, *J* = 8.3 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.90 – 6.79 (m, 2H), 4.61 (dd, *J* = 9.5, 6.4 Hz, 1H), 4.03 (dt, *J* = 16.1, 7.2 Hz, 2H), 3.40 (dd, *J* = 16.3, 9.6 Hz, 1H), 3.22 (dd, *J* = 16.3, 6.3 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.4, 166.1, 162.9, 159.9 (d, *J* = 243.8 Hz), 140.4 (d, *J* = 6.3 Hz), 136.9, 130.8, 128.6 (d, *J* = 10.0 Hz), 119.2, 119.2, 118.7, 111.9 (d, *J* = 21.3 Hz), 110.5, 110.4 (d, *J* = 17.5 Hz), 47.6, 38.3, 21.2, 12.7. **^{19}F NMR** (470 MHz, $CDCl_3$) δ **–** 117.44. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}FNO_3$: 314.1187, found: 314.1179.

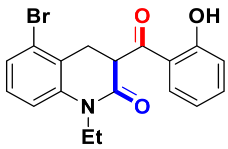
5-chloro-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (82% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.90 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 8.2 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.93 (t, *J* = 7.6 Hz, 1H), 4.59 (dd, *J* = 9.8, 6.2 Hz, 1H), 4.09 – 3.95 (m, 2H), 3.51 (dd, *J* = 16.4, 9.9 Hz, 1H), 3.33 (dd, *J* = 16.4, 6.1 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2, 166.0, 163.0, 140.2, 136.9, 133.6, 130.8, 128.3, 124.3, 123.0, 119.3, 119.2, 118.7, 113.4, 47.8, 38.4, 25.7, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}ClNO_3$: 330.0891, found: 330.0877.

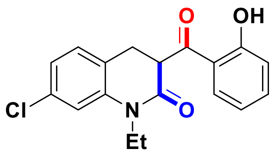
5-bromo-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (91% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.92 (s, 1H), 7.81 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.31 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.16 (t, *J* = 8.1 Hz, 1H), 7.09 – 6.97 (m, 2H), 6.97 – 6.87 (m, 1H), 4.60 (dd, *J* = 10.1, 6.1 Hz, 1H), 4.02 (dt, *J* = 12.0, 7.1 Hz, 2H), 3.52 (dd, *J* = 16.4, 10.1 Hz, 1H), 3.33 (dd, *J* = 16.4, 6.1 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2, 166.2, 162.9, 140.1, 136.9, 130.8, 128.7, 127.5, 124.8, 123.9, 119.3, 119.2, 118.7, 114.2, 47.8, 38.4, 28.6, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}BrNO_3$: 374.0386, found: 374.0377.

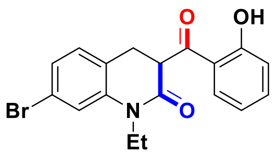
7-chloro-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (83% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.89 (s, 1H), 7.80 – 7.75 (m, 1H), 7.54 – 7.46 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 1.6 Hz, 1H), 7.04 – 6.97 (m, 2H), 6.93 (t, *J* = 7.6 Hz, 1H), 4.60 (dd, *J* = 9.7, 6.1 Hz, 1H), 4.00 (m, 2H), 3.40 (dd, *J* = 15.8, 9.7 Hz, 1H), 3.09 (dd, *J* = 15.9, 6.0 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.4, 166.3, 162.9, 139.9, 136.9, 133.6, 130.7, 129.3, 123.1, 122.8, 119.2, 119.2, 118.8, 115.2, 48.3, 38.2, 28.5, 12.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}ClNO_3$: 330.0891, found: 330.0885.

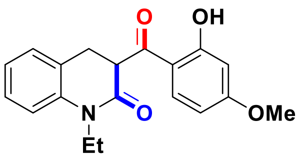
7-bromo-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (74% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.89 (s, 1H), 7.77 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.20 (d, *J* = 1.6 Hz, 1H), 7.17 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.96 – 6.90 (m, 1H), 4.59 (dd, *J* = 9.7, 6.1 Hz, 1H), 4.00 (m, 2H), 3.38 (dd, *J* = 15.8, 9.7 Hz, 1H), 3.07 (dd, *J* = 15.9, 6.0 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.3, 166.3, 163.1, 140.2, 137.0, 129.9, 129.6, 126.1, 123.4, 121.4, 119.2, 118.8, 117.9, 48.3, 38.2, 28.6, 12.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}BrNO_3$: 374.0386, found: 374.0383.

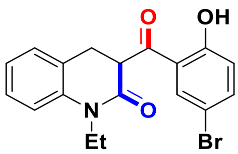
1-ethyl-3-(2-hydroxy-4-methoxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (78% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) 12.47 (s, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.1 Hz, 1H), 7.12 – 6.99 (m, 2H), 6.52 – 6.38 (m, 2H), 4.50 (dd, *J* = 9.9, 6.0 Hz, 1H), 4.02 (dt, *J* = 10.5, 6.7 Hz, 2H), 3.82 (s, 3H), 3.42 (dd, *J* = 15.5, 10.3 Hz, 1H), 3.07 (dd, *J* = 15.7, 5.8 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 199.7, 166.7, 166.5, 166.0, 138.8, 132.4, 128.3, 127.9, 124.8, 123.2, 114.8, 113.6, 108.1, 101.0, 55.7, 48.3, 40.0, 29.1, 12.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{19}H_{20}NO_4$: 326.1387, found: 326.1396.

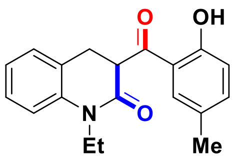
3-(5-bromo-2-hydroxybenzoyl)-1-ethyl-3,4-dihydroquinolin-2(1H)-one (13h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (64% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.91 (s, 1H), 7.86 (d, *J* = 2.3 Hz, 1H), 7.56 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.12 – 7.02 (m, 2H), 6.91 (d, *J* = 8.9 Hz, 1H), 4.52 (dd, *J* = 11.1, 5.8 Hz, 1H), 4.04 (m, 2H), 3.52 – 3.37 (m, 1H), 3.05 (dd, *J* = 15.7, 5.8 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2, 166.2, 161.8, 139.5, 138.6, 132.9, 128.3, 128.1, 124.5, 123.5, 120.8, 120.7, 114.9, 110.8, 48.4, 38.0, 28.7, 12.8. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{18}H_{17}BrNO_3$: 374.0386, found: 374.0390.

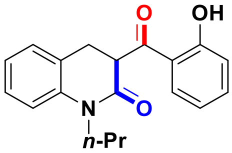
1-ethyl-3-(2-hydroxy-5-methylbenzoyl)-3,4-dihydroquinolin-2(1H)-one (13i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (81% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.82 (s, 1H), 7.53 (s, 1H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.12 – 7.01 (m, 2H), 6.90 (d, *J* = 8.5 Hz, 1H), 4.61 (dd, *J* = 10.5, 6.0 Hz, 1H), 4.04 (m, 2H), 3.45 (dd, *J* = 15.7, 10.5 Hz, 1H), 3.07 (dd, *J* = 15.7, 5.9 Hz, 1H), 2.30 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.8, 166.7, 160.9, 138.8, 137.9, 130.3, 128.3, 128.2, 127.9, 124.7, 123.2, 119.1, 118.5, 114.8, 48.3, 37.9, 29.1, 20.6, 12.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{19}H_{20}NO_3$: 310.1438, found: 310.1433.

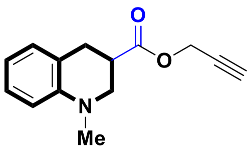
3-(2-hydroxybenzoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (13j)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product (82% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.90 (s, 1H), 7.70 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.01 – 6.94 (m, 2H), 6.93 – 6.89 (m, 1H), 6.87 – 6.81 (m, 1H), 4.54 (dd, *J* = 10.5, 5.9 Hz, 1H), 3.97 – 3.76 (m, 2H), 3.38 (dd, *J* = 15.7, 10.5 Hz, 1H), 3.01 (dd, *J* = 15.7, 5.9 Hz, 1H), 1.67 – 1.58 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.9, 166.8, 162.9, 138.9, 136.8, 130.8, 128.3, 127.9, 124.7, 123.3, 119.5, 119.2, 118.7, 115.1, 48.5, 44.3, 28.9, 20.5, 11.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{19}H_{20}NO_3$: 310.1438, found: 310.1433.

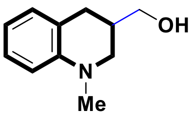
Prop-2-yn-1-yl-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (14a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:50) afforded the product (95% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 – 7.00 (m, 1H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.57 (m, 2H), 4.66 (dd, *J* = 2.4, 1.0 Hz, 2H), 3.37 (m, 1H), 3.28 (m, 1H), 2.97 (dd, *J* = 9.6, 3.4 Hz, 3H), 2.84 (s, 3H), 2.42 (t, *J* = 2.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.7, 144.8, 128.0, 126.4, 119.6, 115.9, 110.2, 76.5, 74.0, 51.2, 51.1, 38.1, 37.5, 29.1. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{14}H_{16}NO_2$: 230.1176, found: 230.1180.

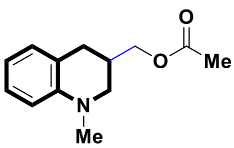
(1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)methanol (15a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (92% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (m, 1H), 6.98 (dd, *J* = 7.1, 0.7 Hz, 1H), 6.66 – 6.59 (m, 2H), 3.69 (dd, *J* = 10.6, 5.8 Hz, 1H), 3.60 (dd, *J* = 10.6, 7.5 Hz, 1H), 3.32 (m, 1H), 3.09 – 2.99 (m, 1H), 2.89 (s, 3H), 2.85 (dd, *J* = 16.0, 5.4 Hz, 1H), 2.55 (dd, *J* = 15.9, 8.9 Hz, 1H), 2.29 – 2.21 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.6, 129.2, 127.2, 121.6, 116.6, 111.1, 65.5, 53.5, 39.3, 35.2, 30.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{11}H_{16}NO$: 178.1226, found: 178.1220.

(1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl acetate (16a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:20) afforded the product

(90% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 11.4, 4.0 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.61 (dd, *J* = 17.0, 7.8 Hz, 2H), 4.10 (dd, *J* = 11.0, 6.0 Hz, 1H), 4.03 (dd, *J* = 11.0, 7.5 Hz, 1H), 3.27 (m, 1H), 3.01 (dd, *J* = 11.1, 8.6 Hz, 1H), 2.88 (s, 3H), 2.84 (dd, *J* = 15.9, 5.0 Hz, 1H), 2.57 (dd, *J* = 15.9, 9.3 Hz, 1H), 2.39 (m, 1H), 2.08 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.1, 146.3, 129.2, 127.3, 120.9, 116.7, 111.1, 66.4, 53.4, 39.2, 32.3, 30.4, 20.9. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $C_{13}H_{18}NO_2$: 220.1332, found: 220.1345.

5. Crystal Structure and Data

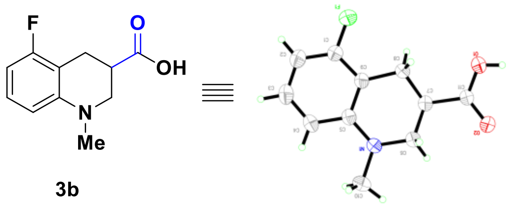
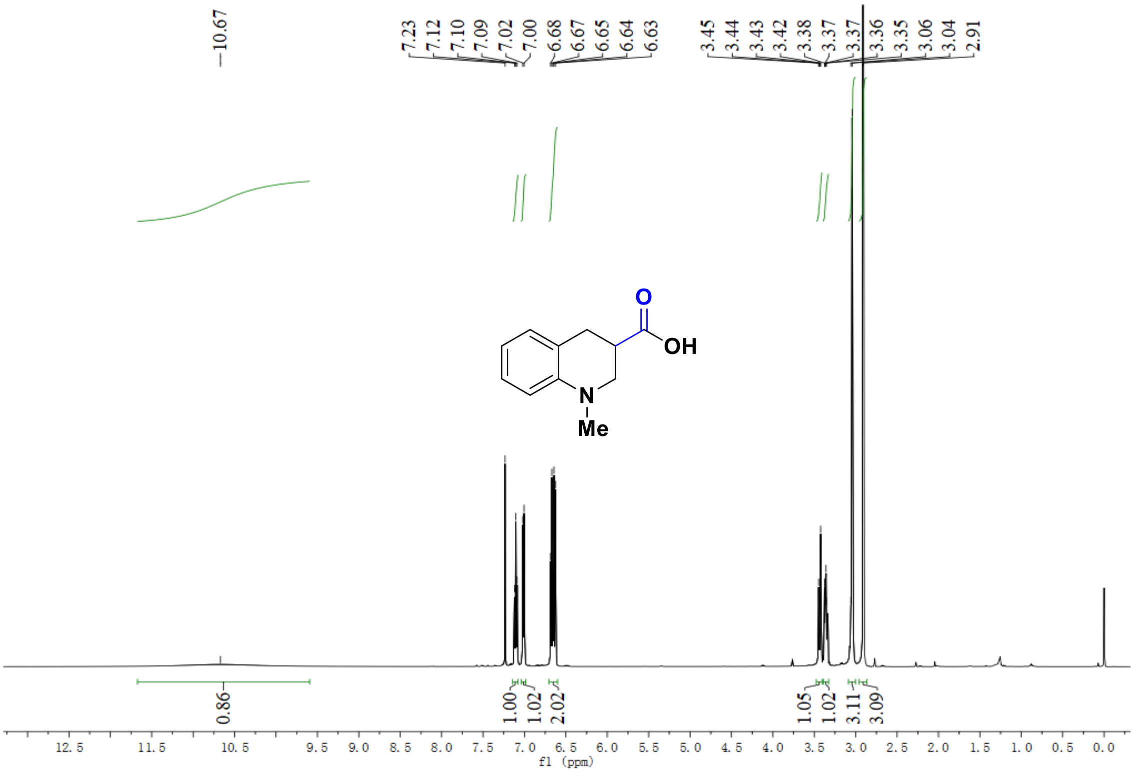


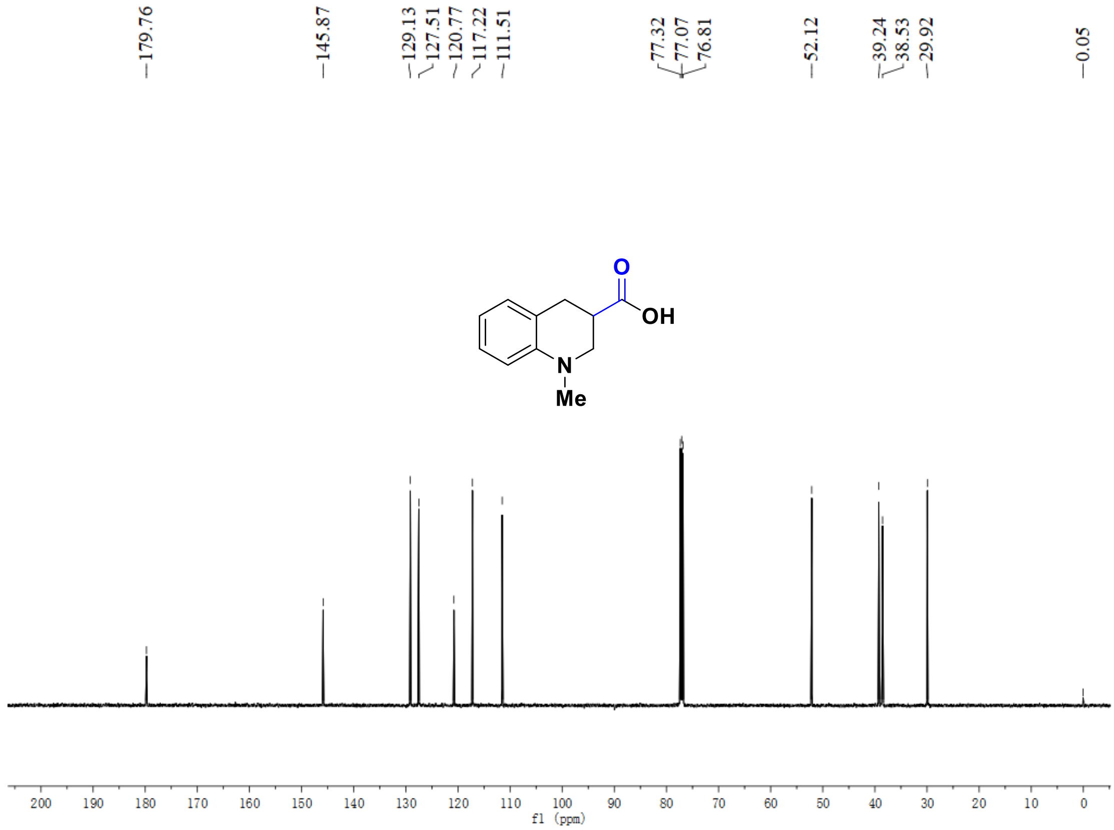
Table 1. Crystal data and structure refinement for **3b**.

Identification code	**3b**
Empirical formula	$C_{11}H_{12}FNO_2$
Formula weight	209.22
Temperature	293(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 5.2503(5) A alpha = 90 deg.
	b = 16.2082(13) A beta = 99.976(13) deg.
	c = 12.1305(19) A gamma = 90 deg.
Volume	1016.7(2) A^3
Z, Calculated density	4, 1.367 Mg/m^3
Absorption coefficient	0.895 mm^-1
F(000)	440
Crystal size	0.120 x 0.120 x 0.110 mm
Theta range for data collection	4.598 to 67.249 deg.
Limiting indices	-4<=h<=6, -18<=k<=19, -14<=l<=14
Reflections collected / unique	3422 / 1817 [R(int) = 0.0298]
Completeness to theta = 67.249	99.4 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1817 / 0 / 138
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0665, wR2 = 0.1672
R indices (all data)	R1 = 0.1142, wR2 = 0.2021
Extinction coefficient	n/a
Largest diff. peak and hole	0.321 and -0.175 e.A^-3

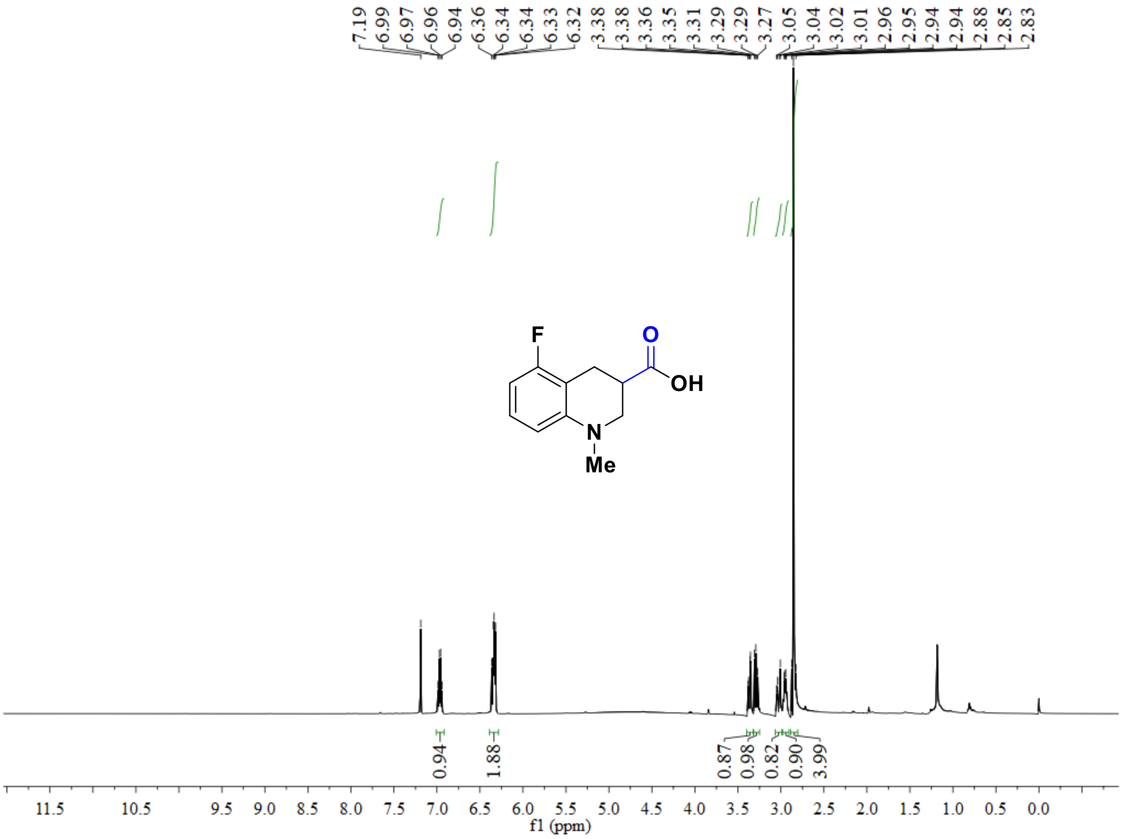
6. ^{1}H and ^{13}C NMR Spectra

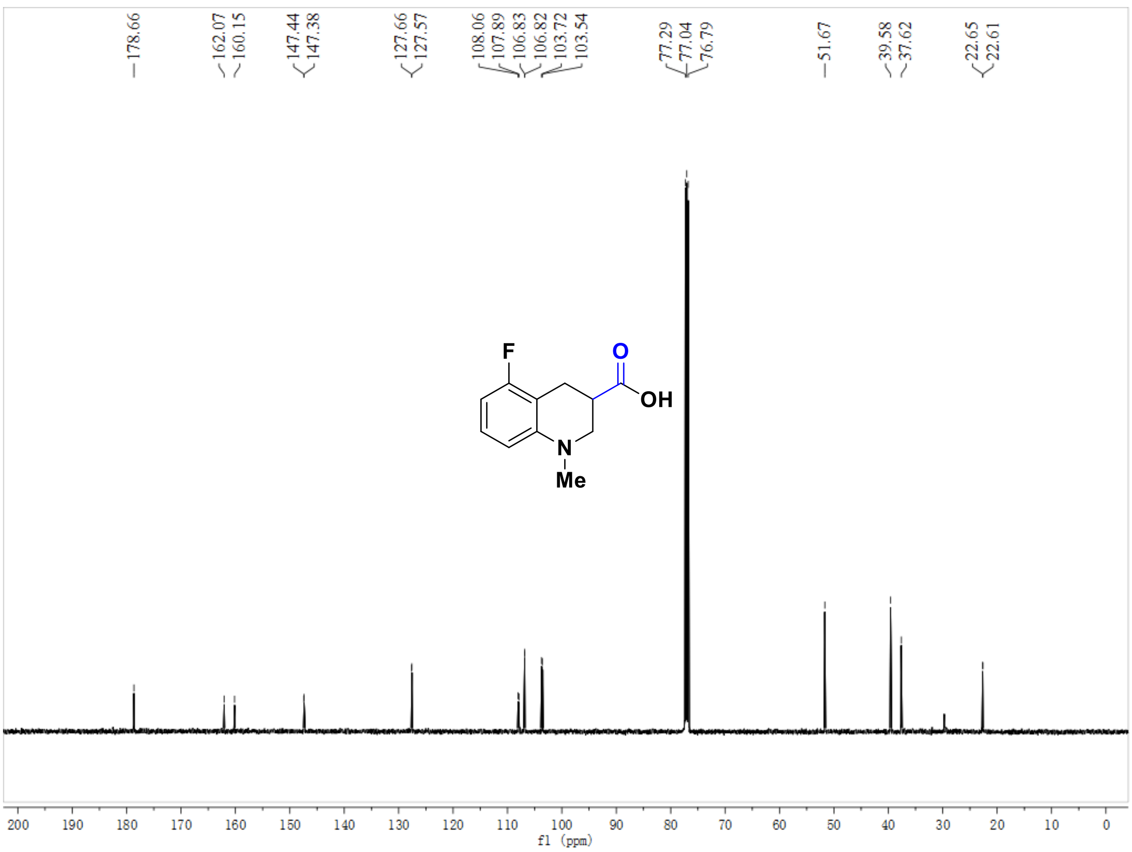
1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3a)

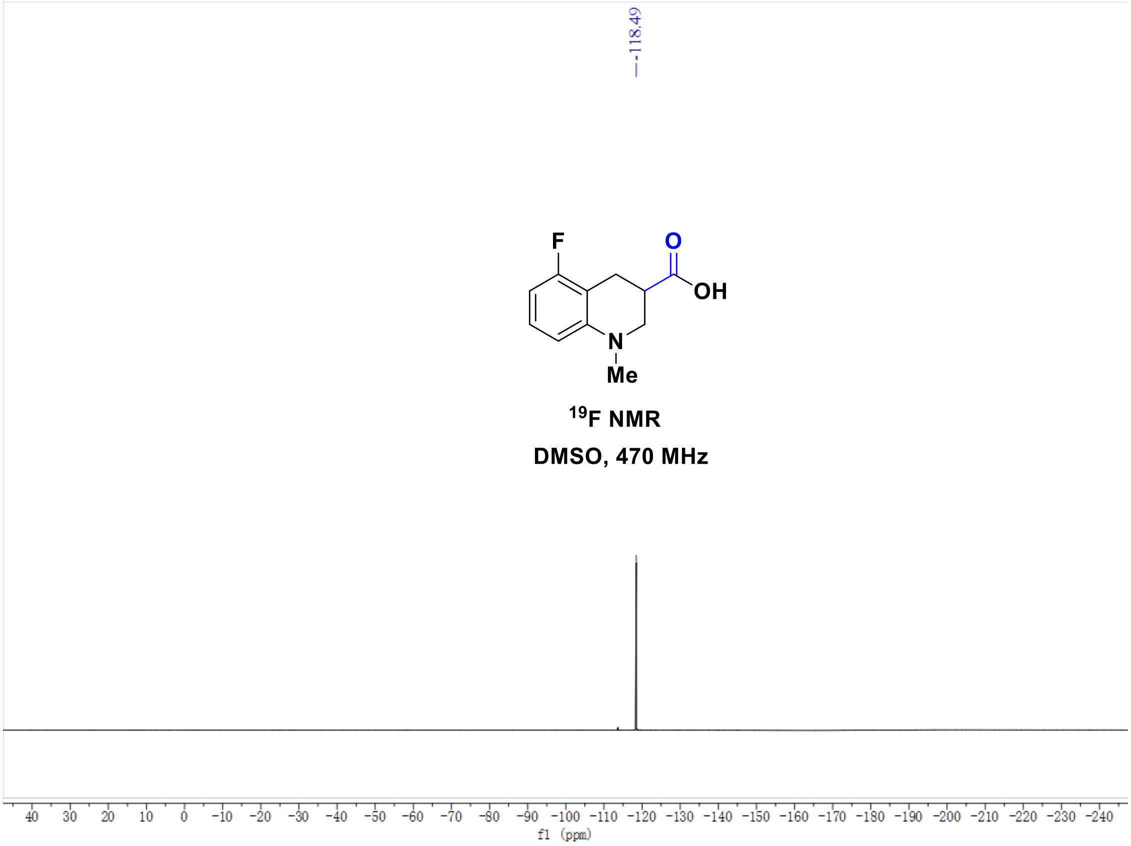




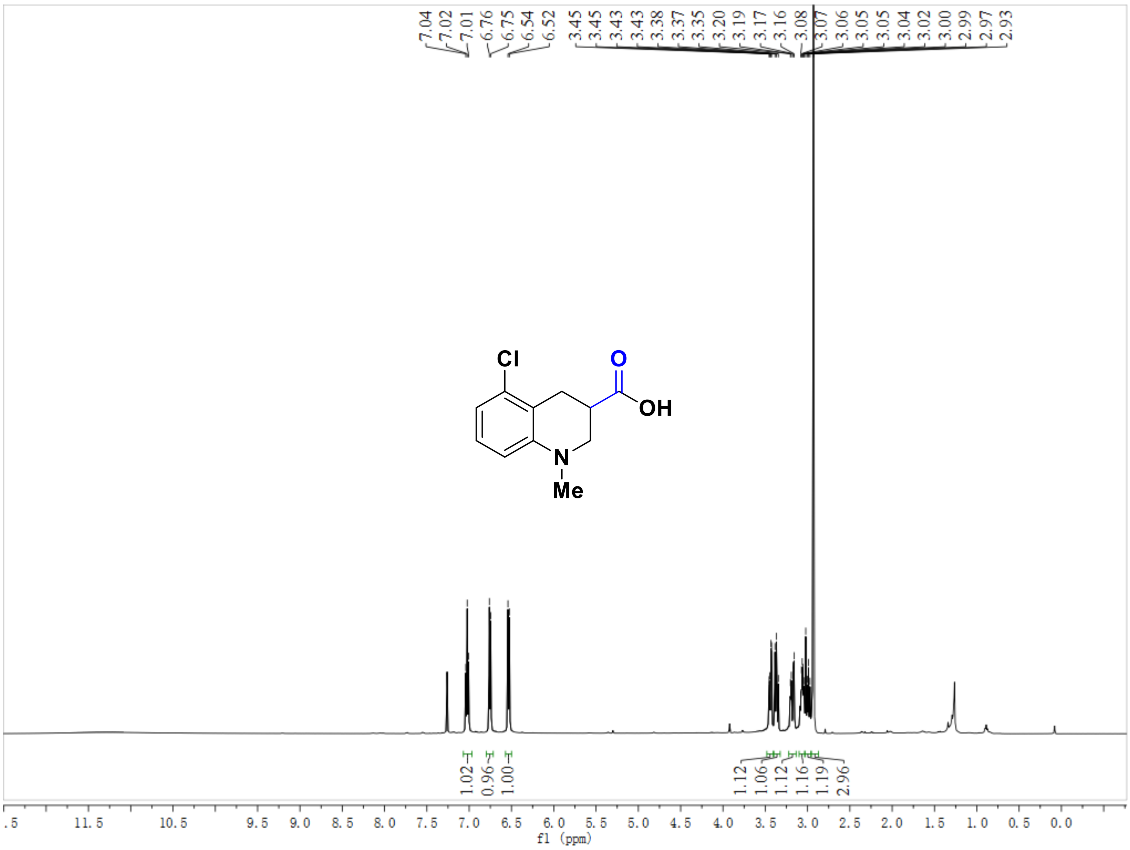
5-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3b)

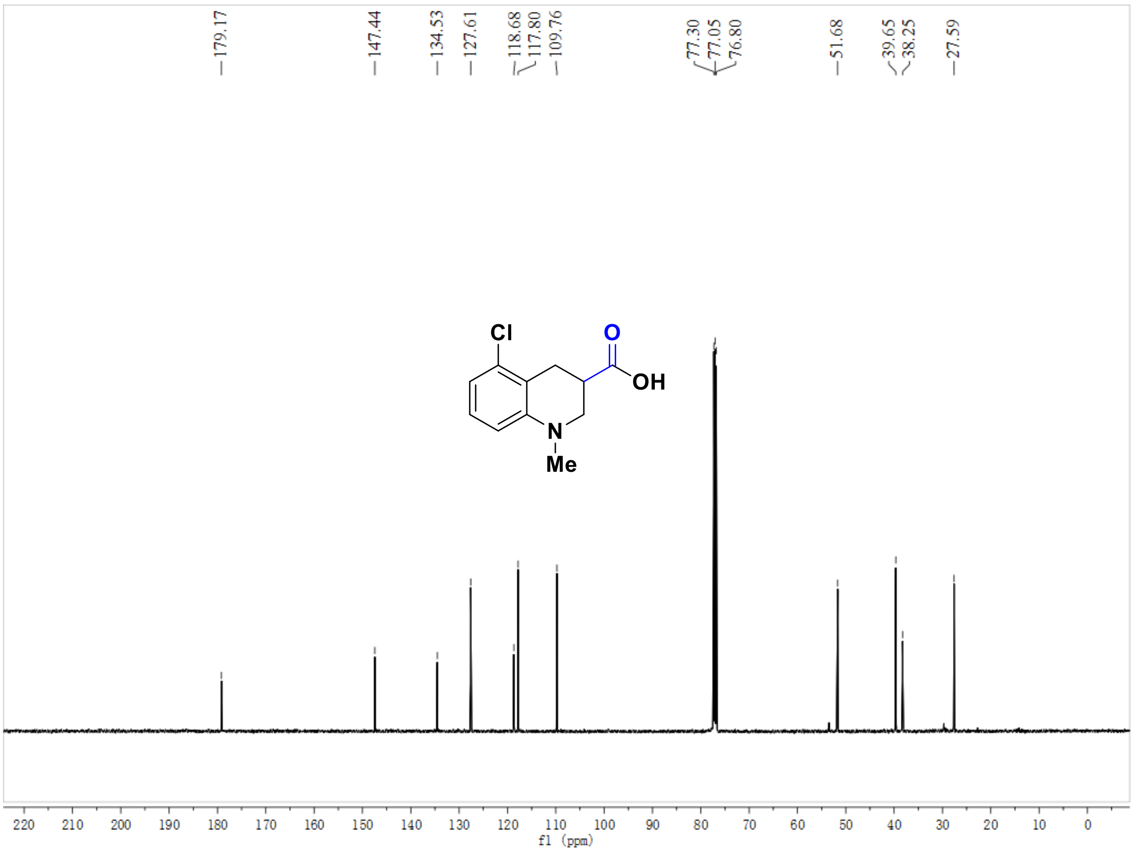




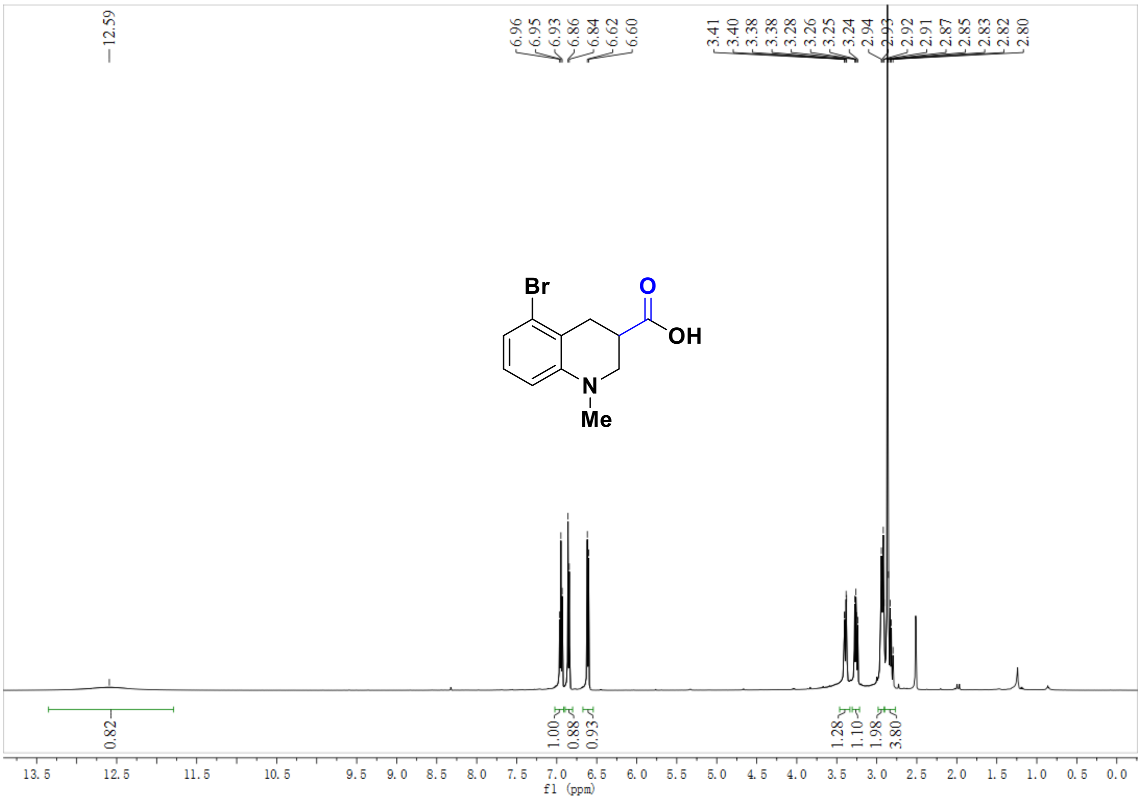

-118.49
F
O
OH
N
Me
19F NMR
DMSO, 470 MHz
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

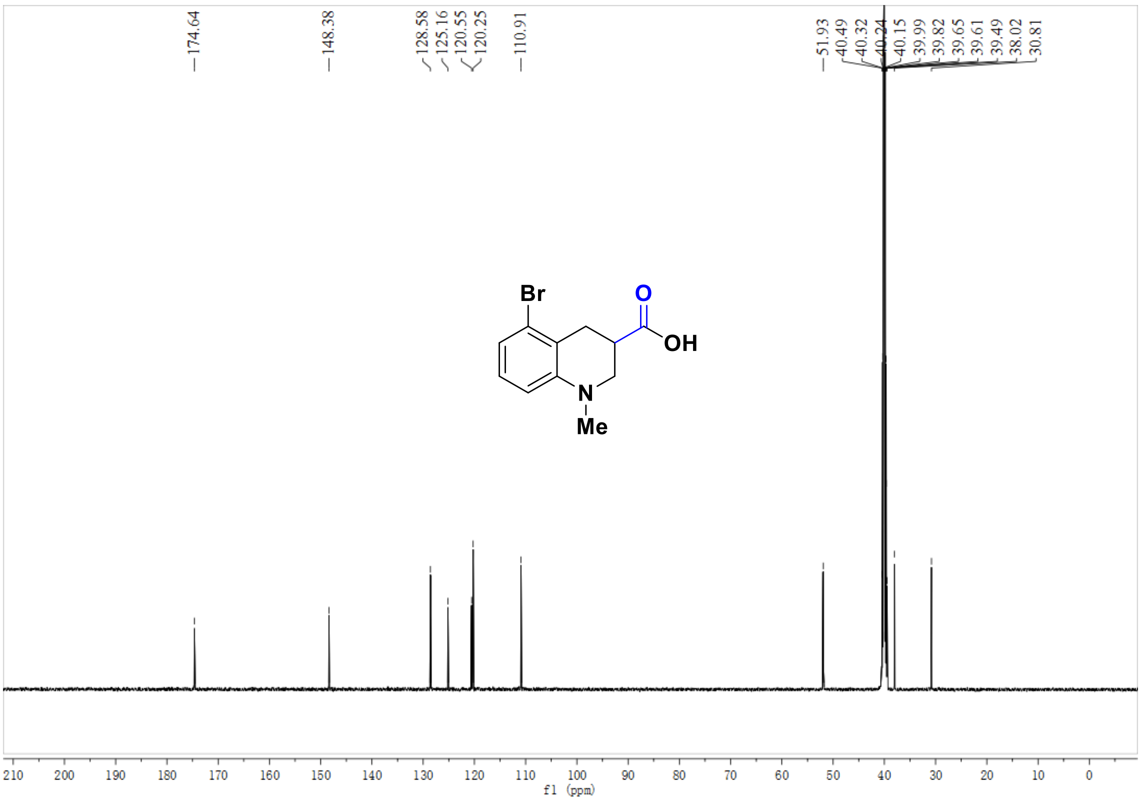
5-chloro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3c)



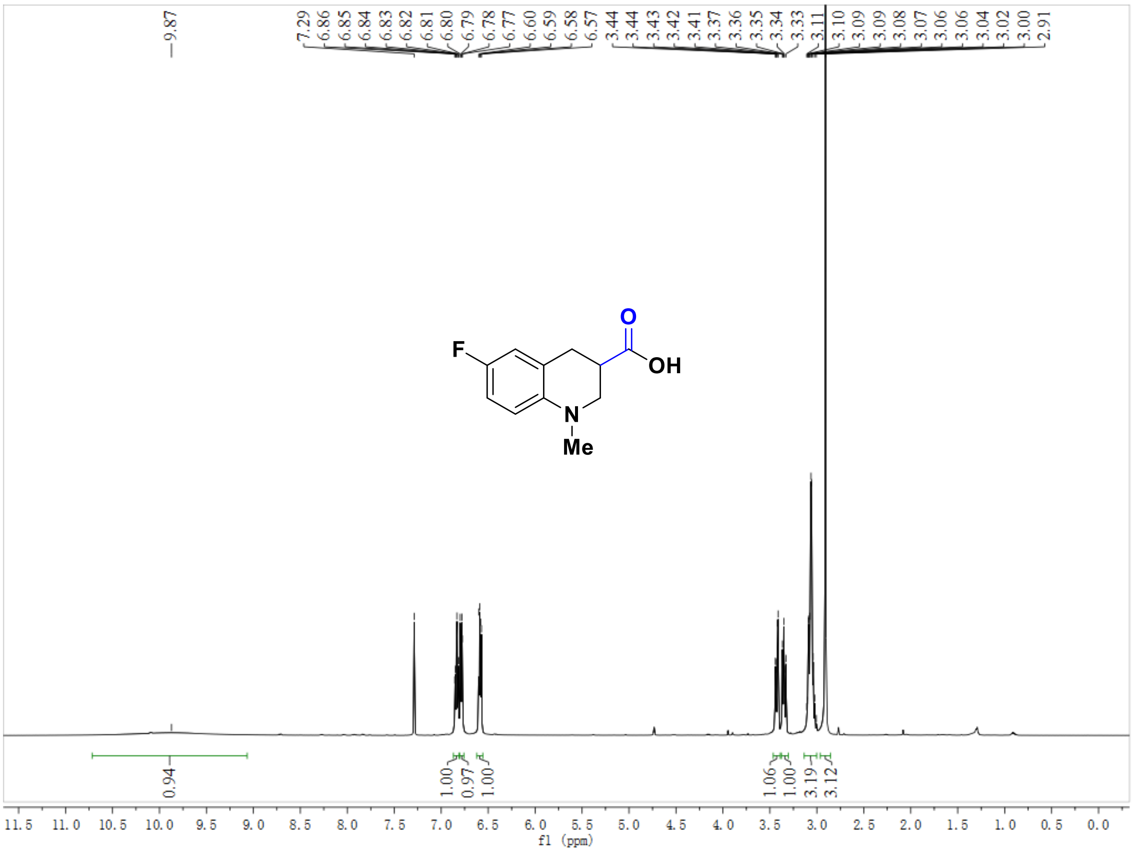


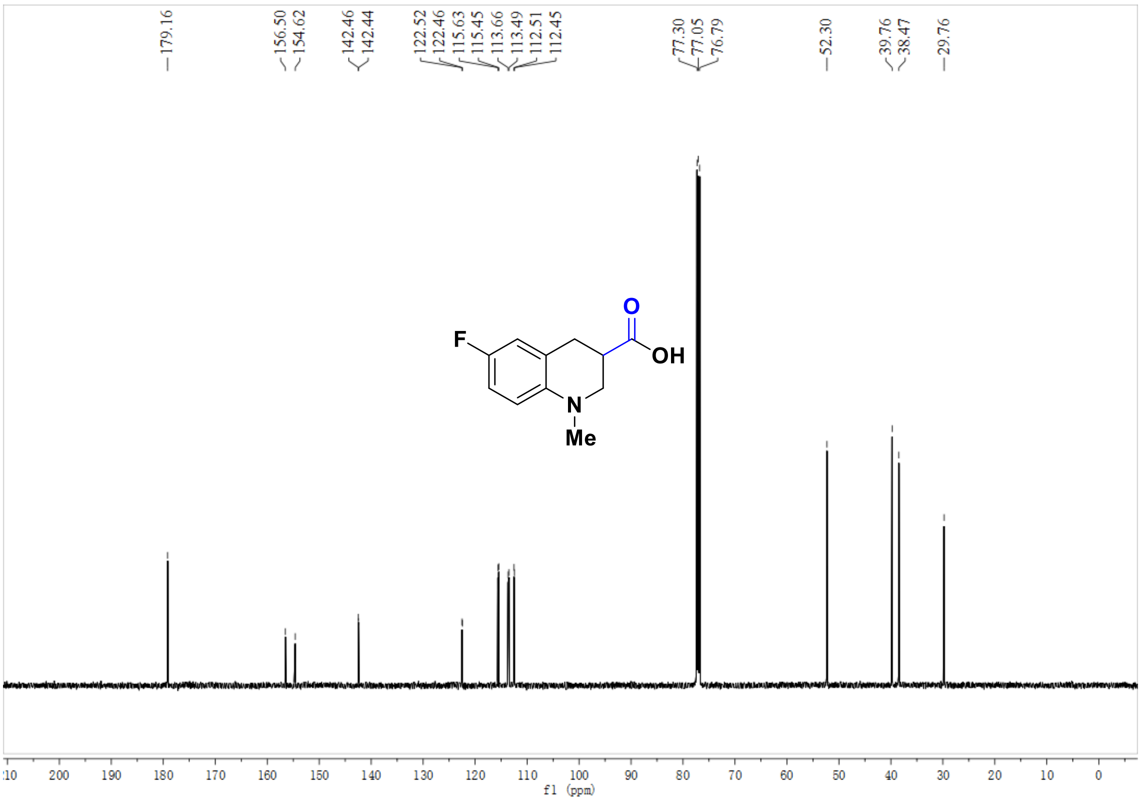
5-bromo-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3d)

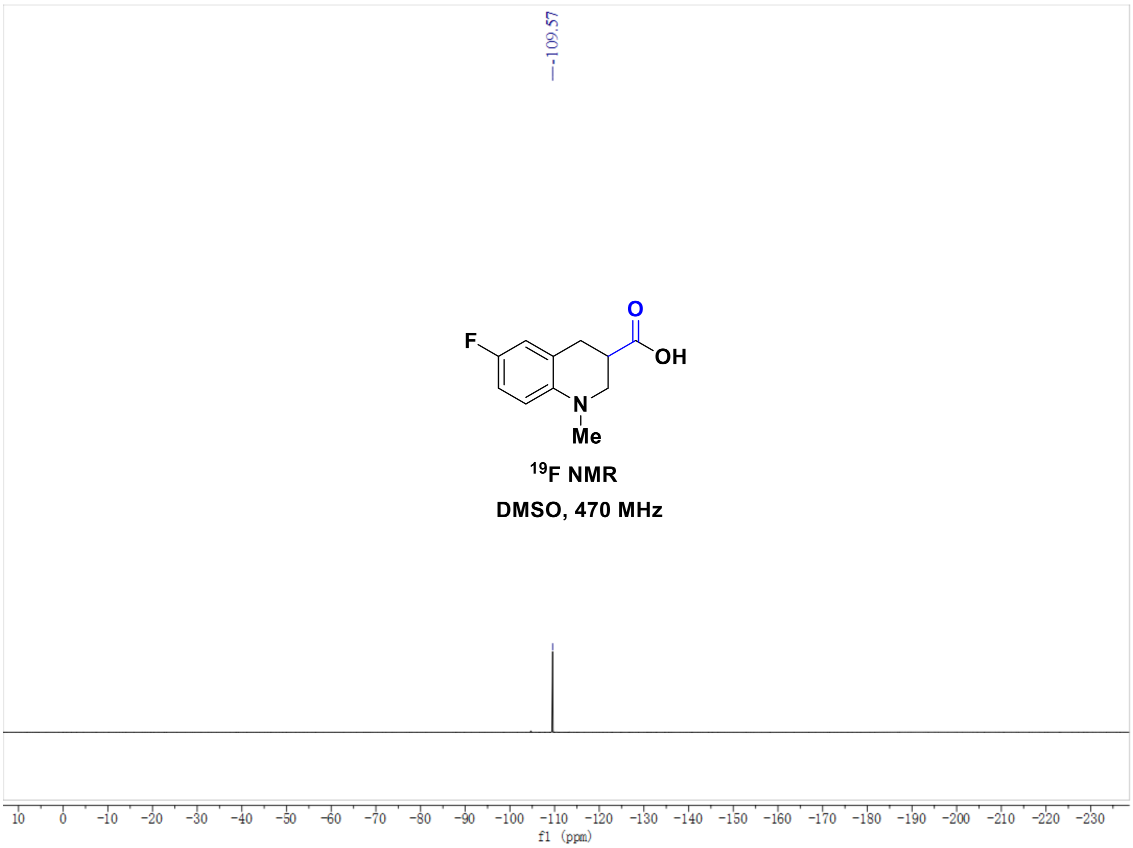




6-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3e)

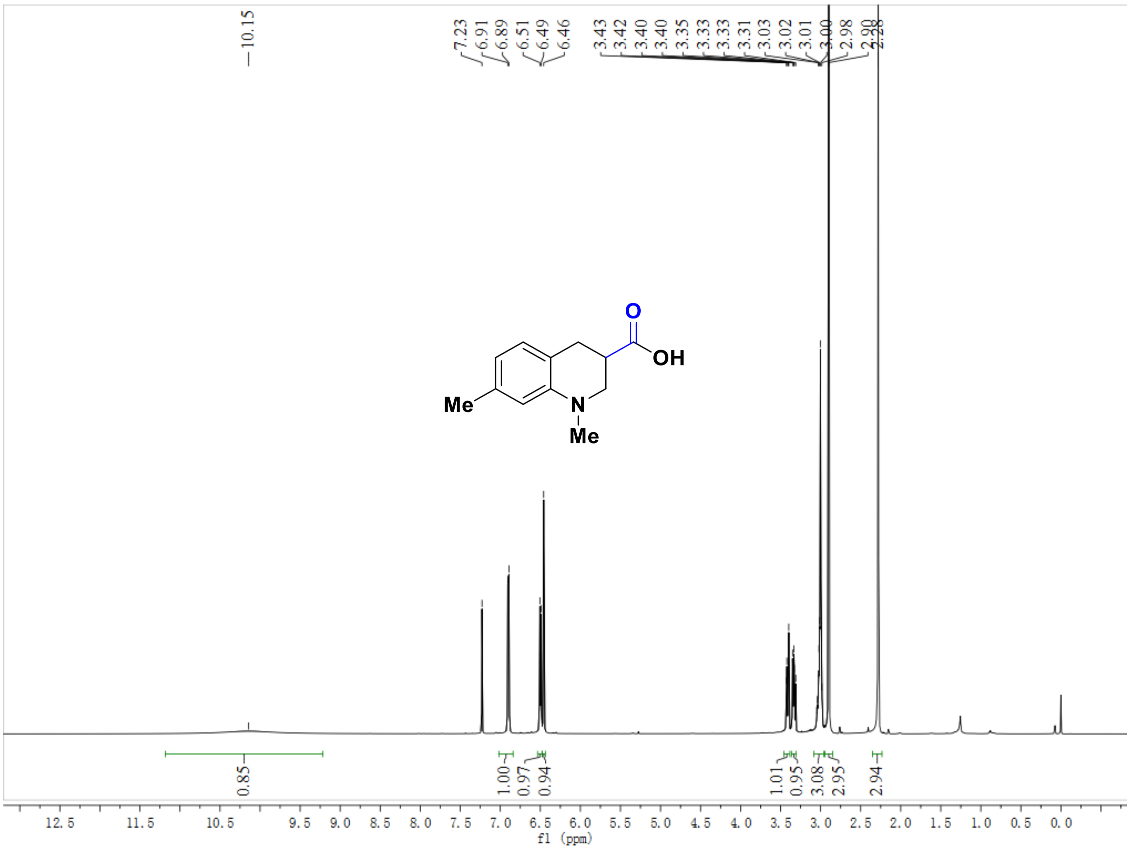


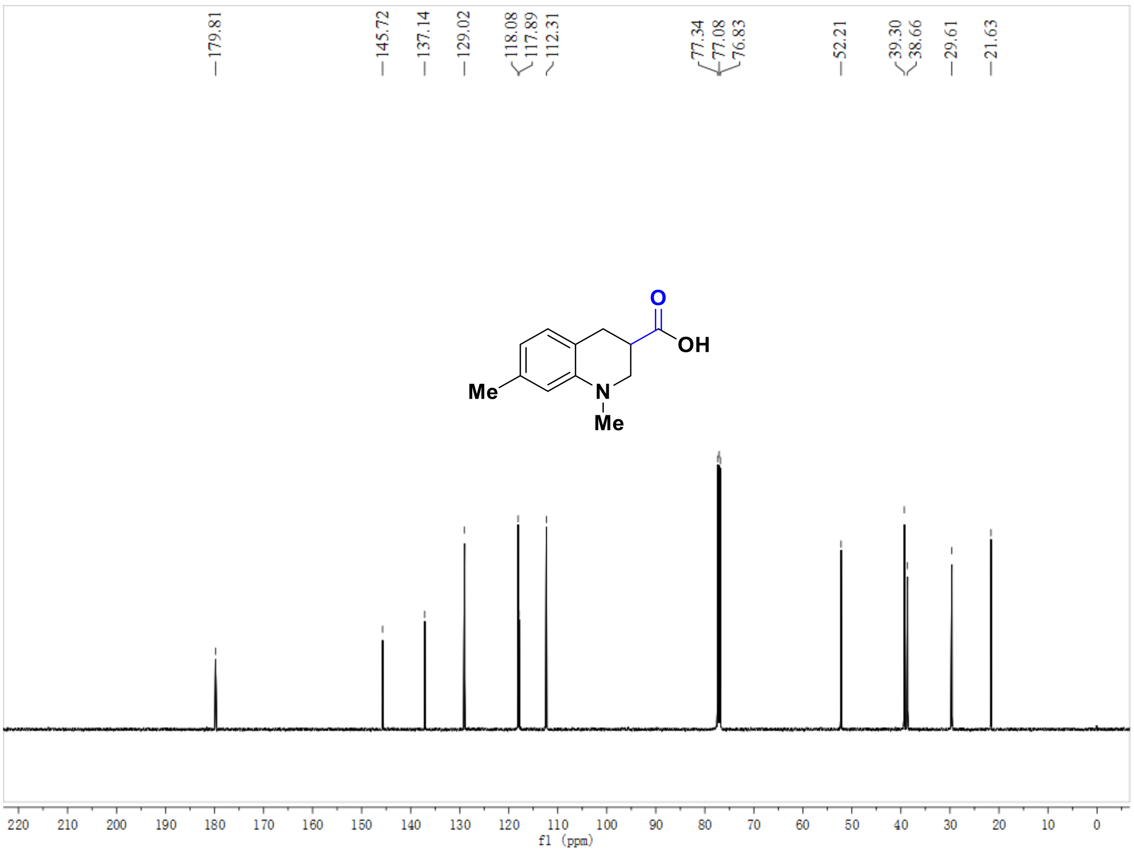




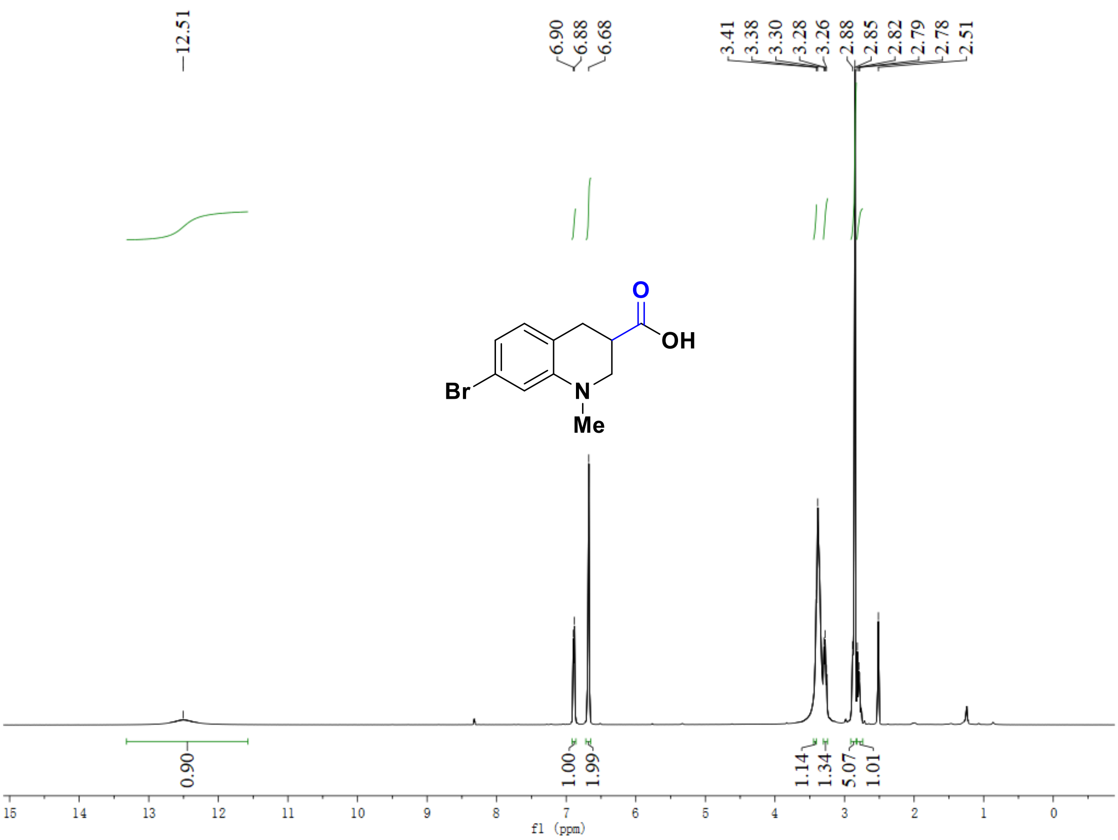
-109.57
F
O
OH
N
Me
19F NMR
DMSO, 470 MHz
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −220 −230
f1 (ppm)

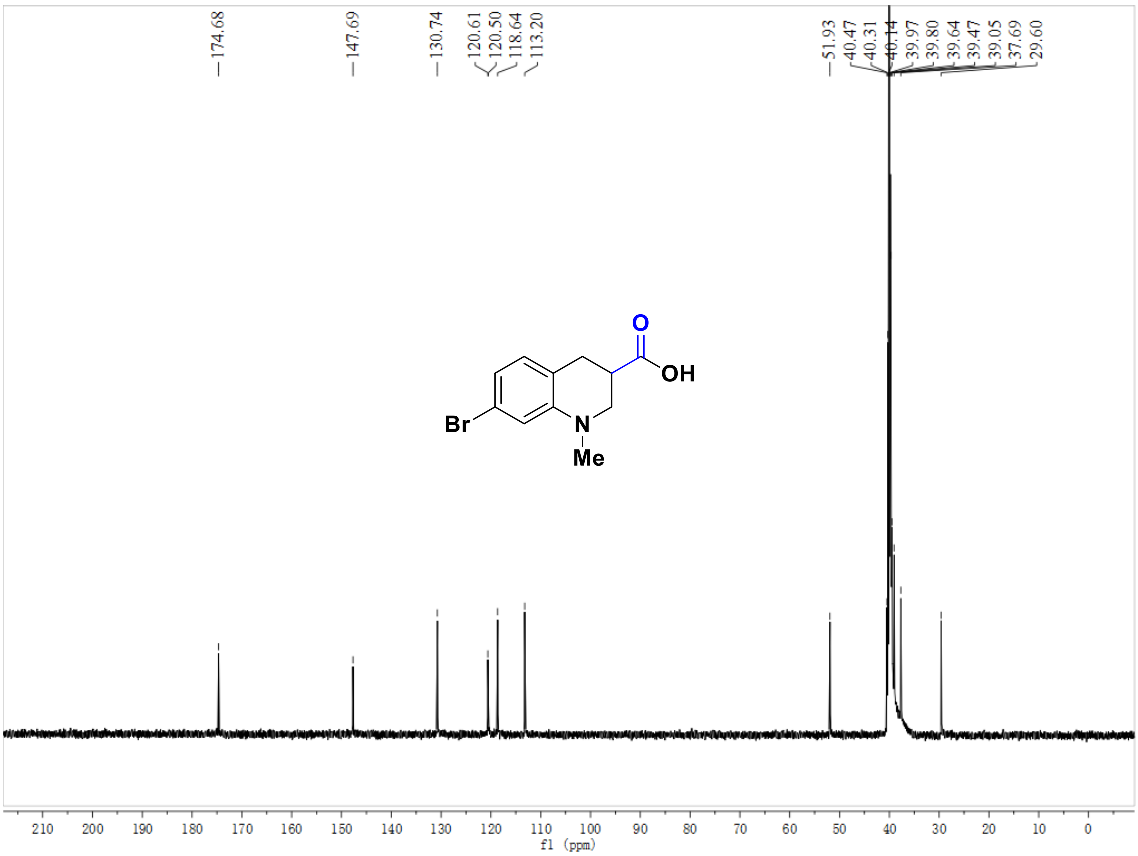
1,7-dimethyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3f)



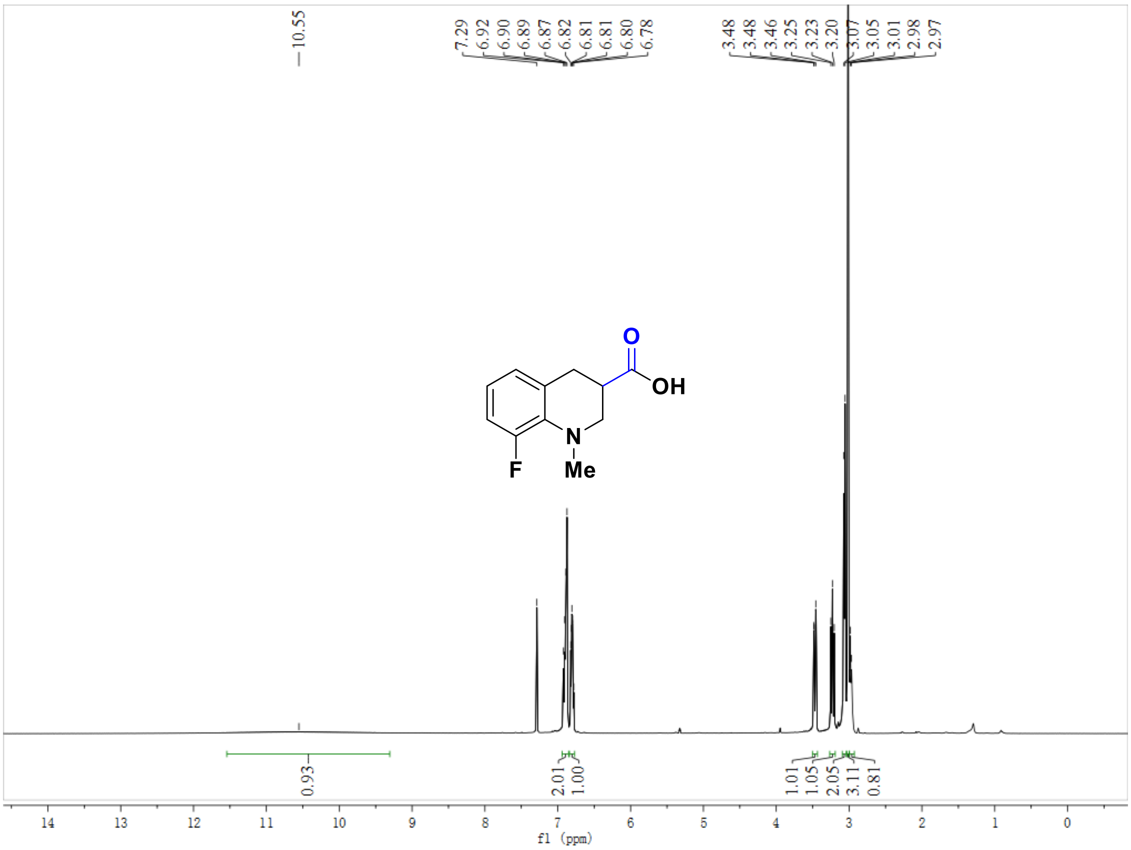


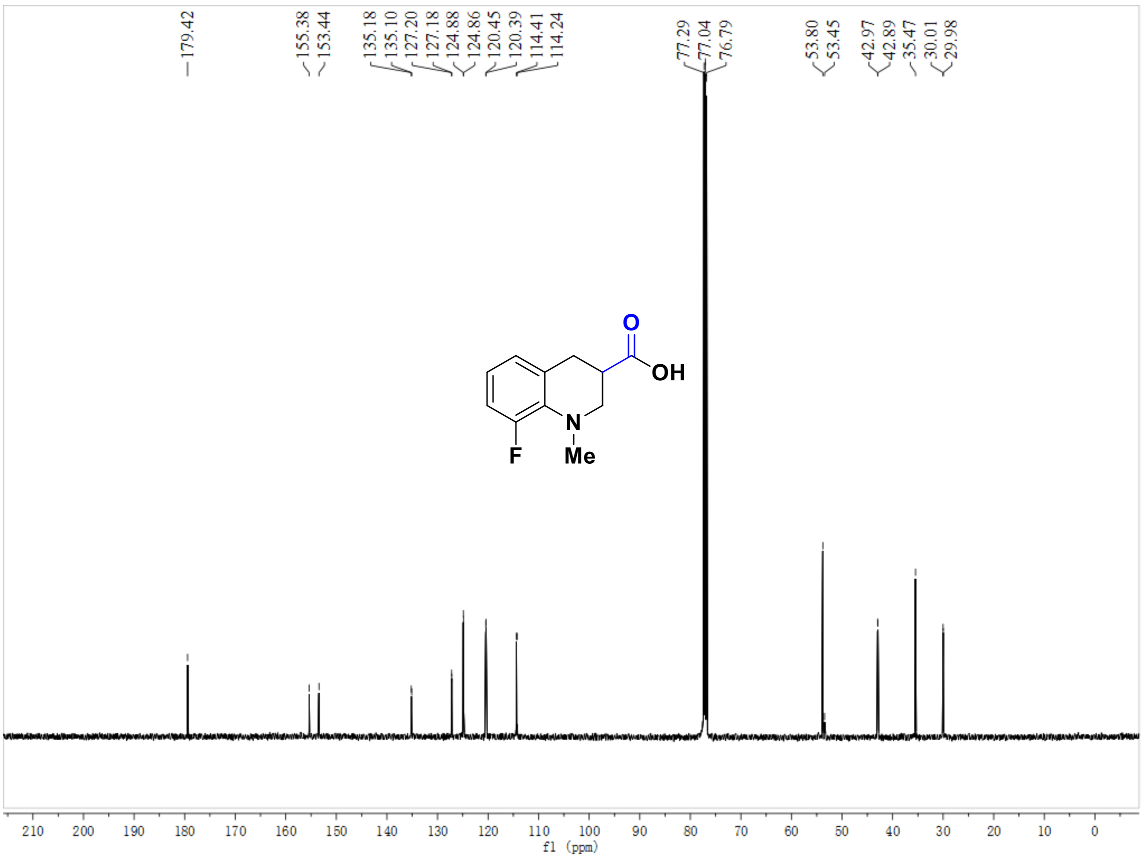
7-bromo-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3g)

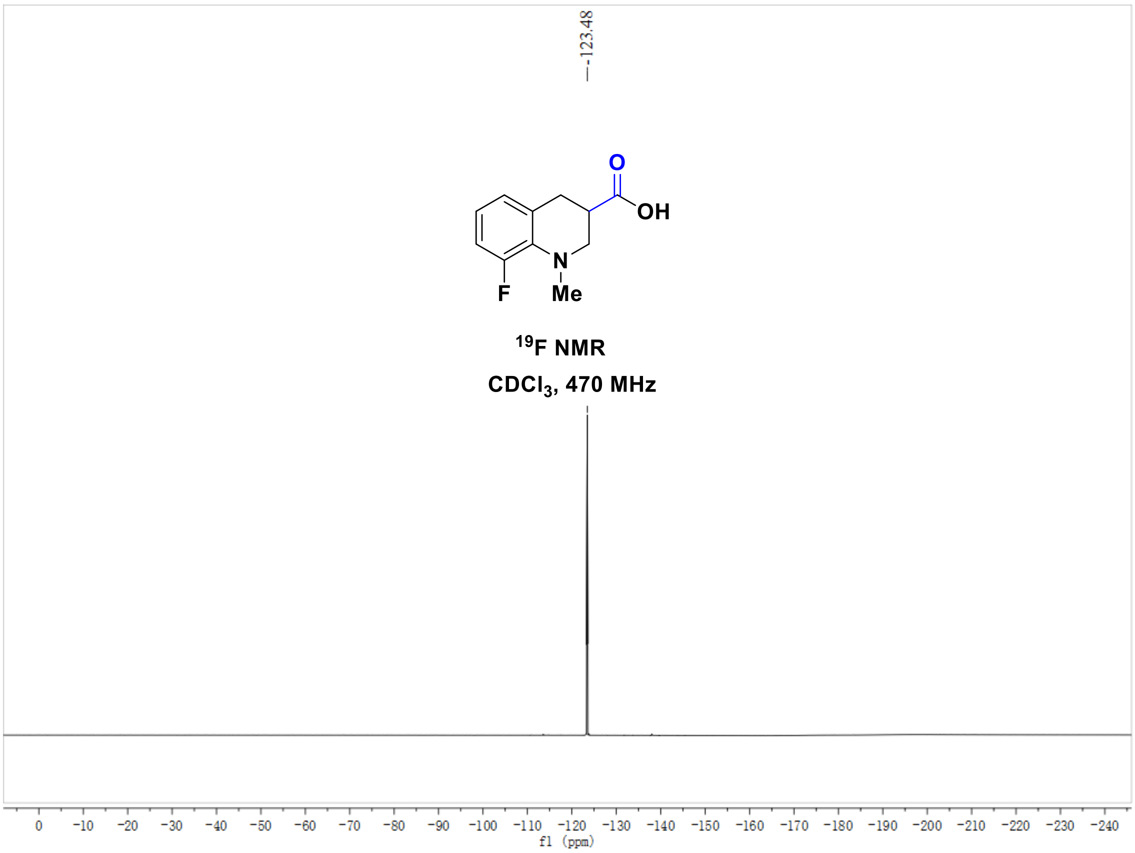




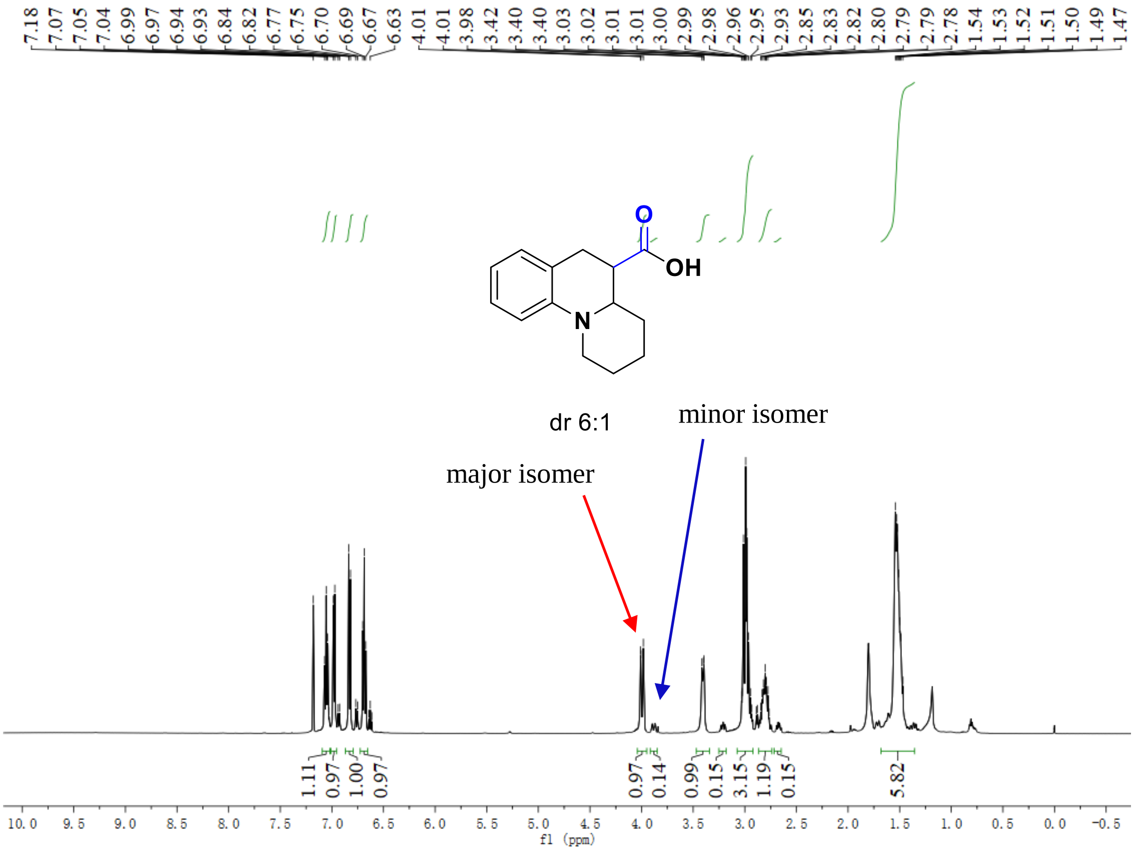
8-fluoro-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (3h)

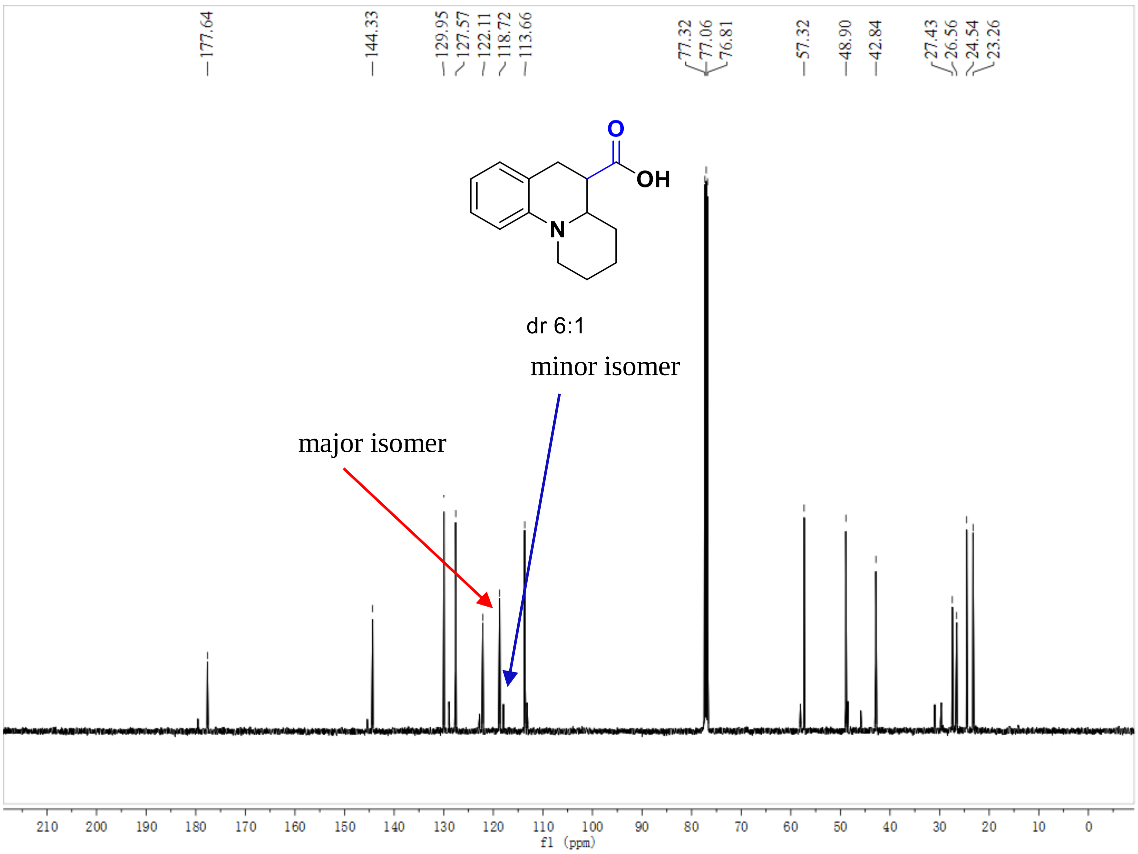




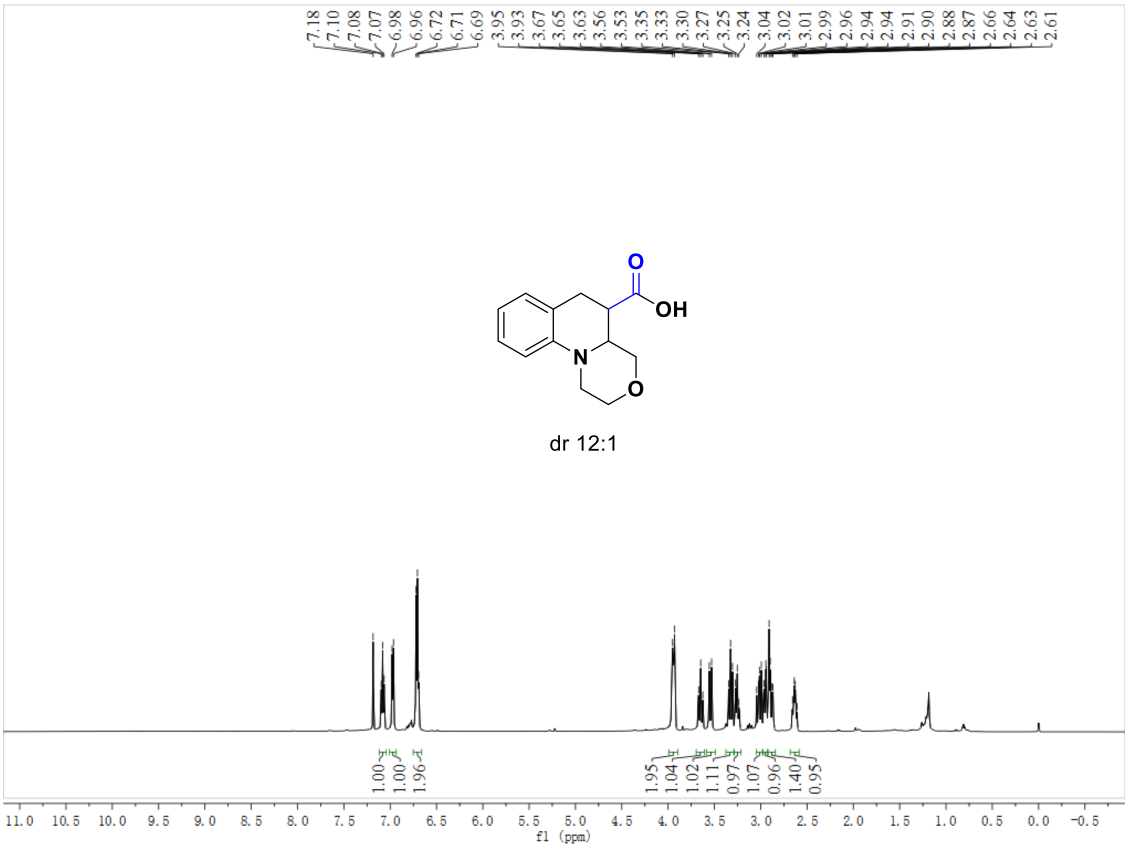

-123.48
O
OH
N
F
Me
19F NMR
CDCl3, 470 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

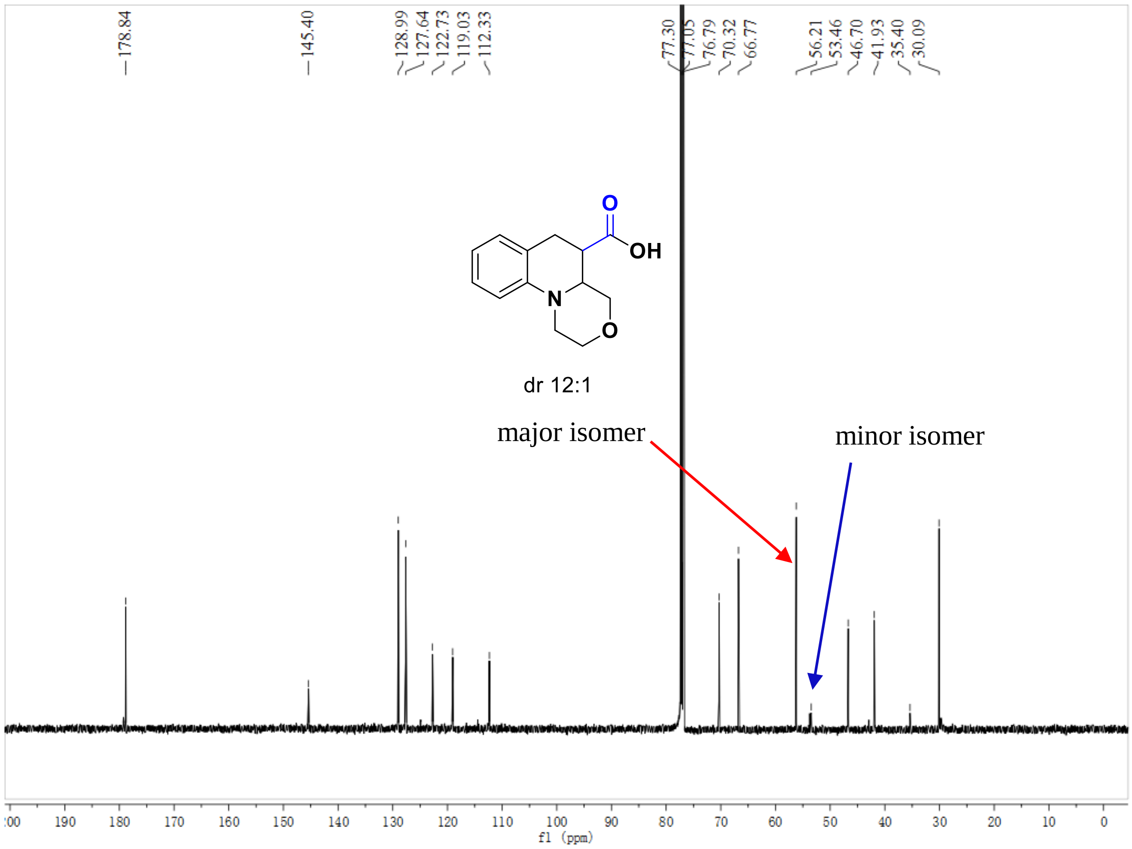
2,3,4,4a,5,6-hexahydro-1H-pyrido[1,2-a]quinoline-5-carboxylic acid (3i)



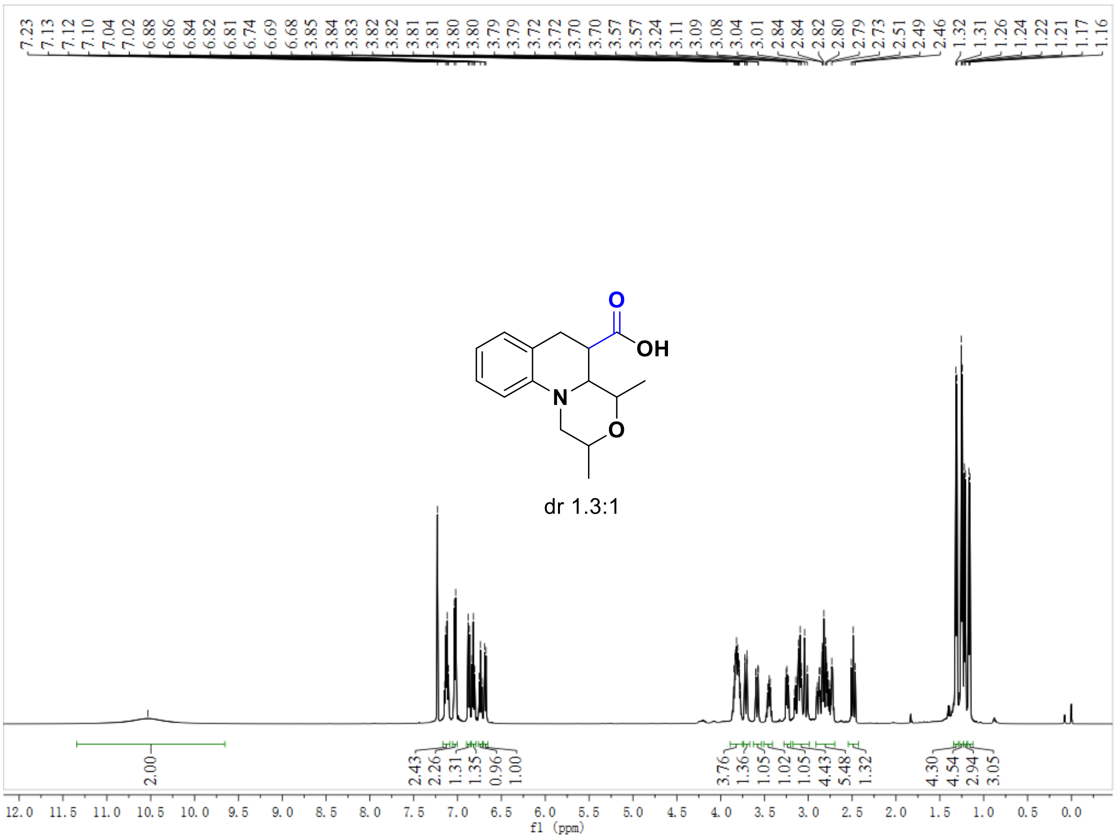


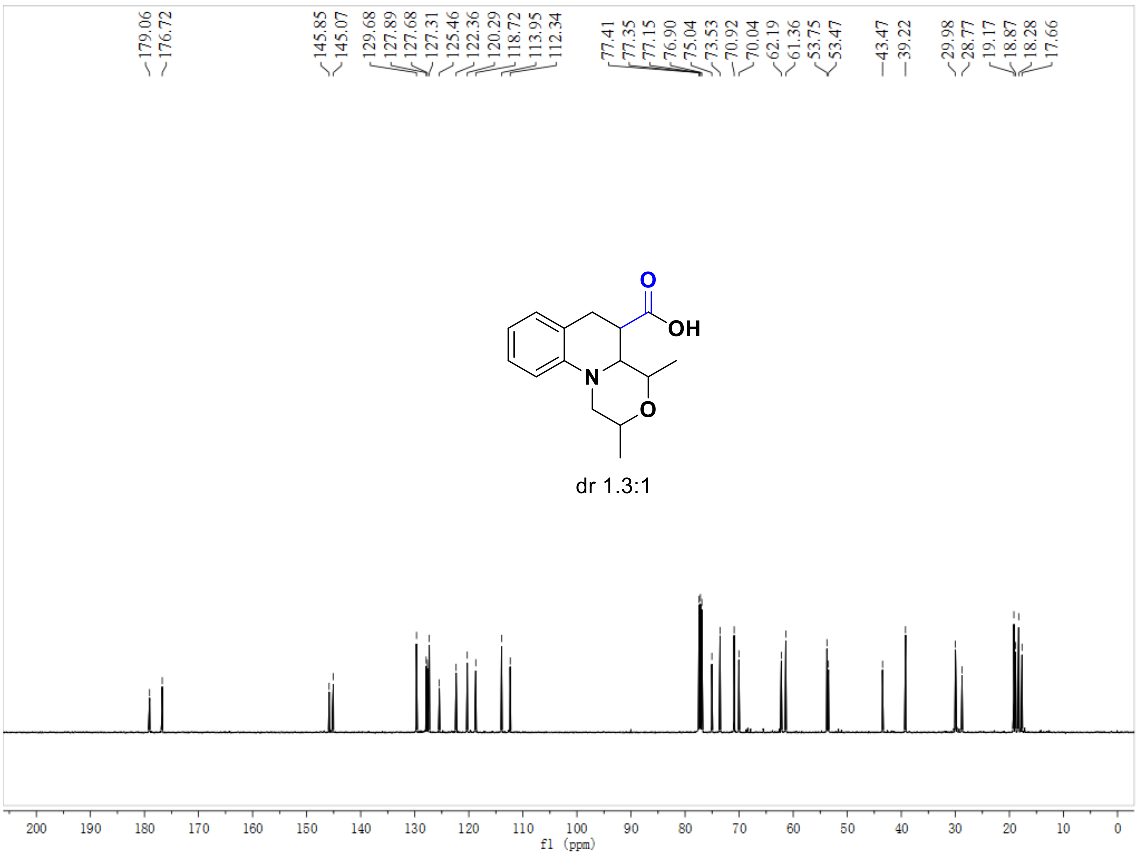
1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinoline-5-carboxylic acid (3j)



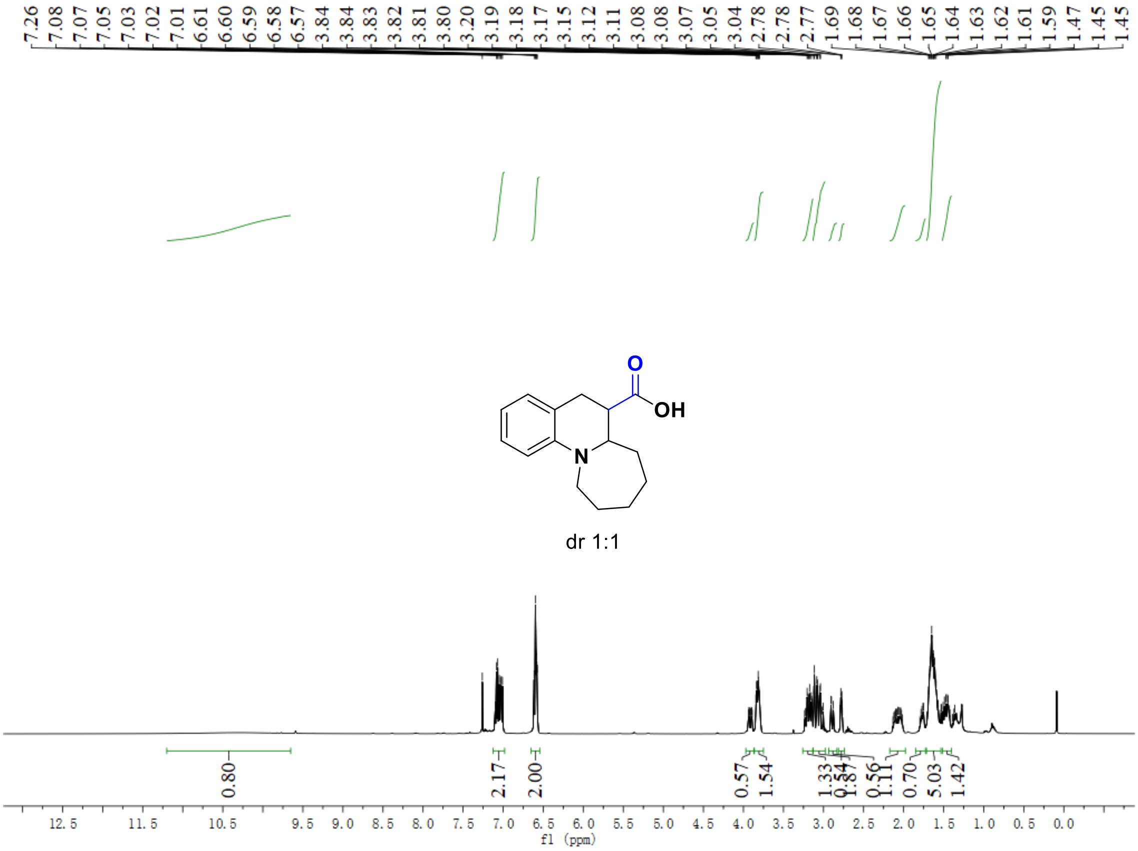


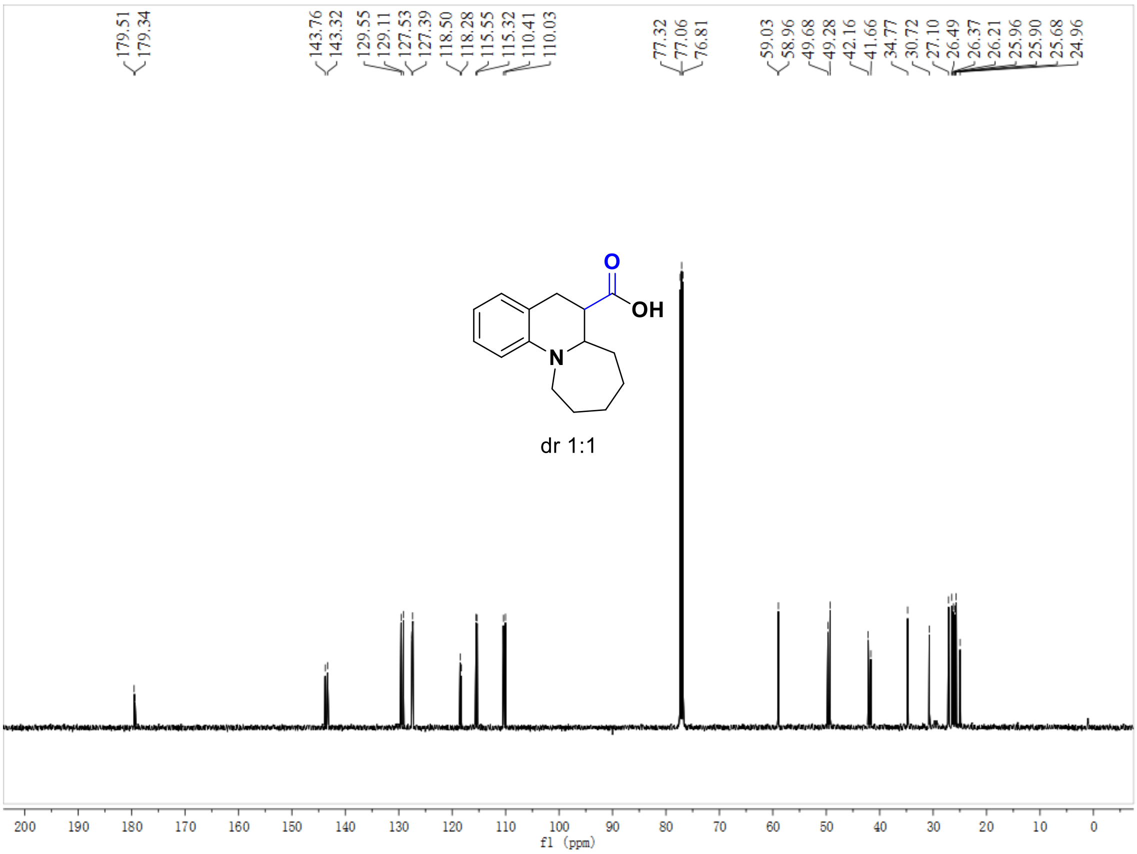
2,4-dimethyl-1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinoline-5-carboxylic acid (3k)



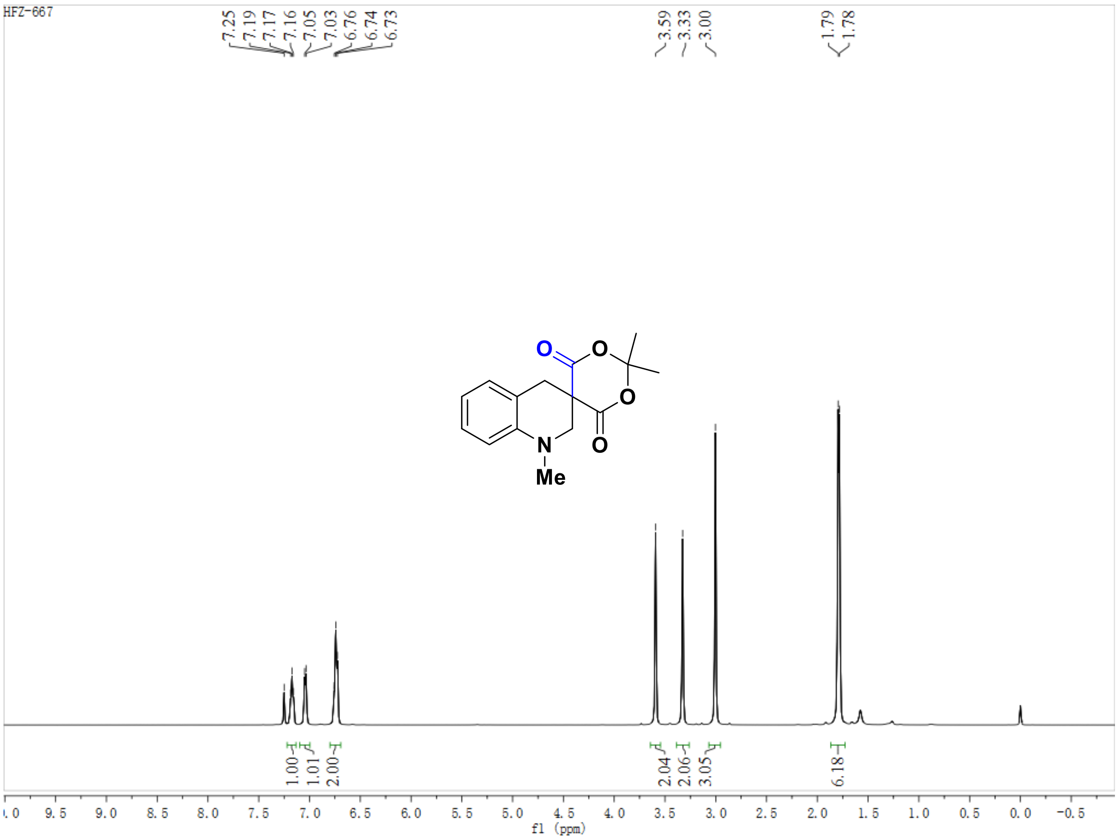


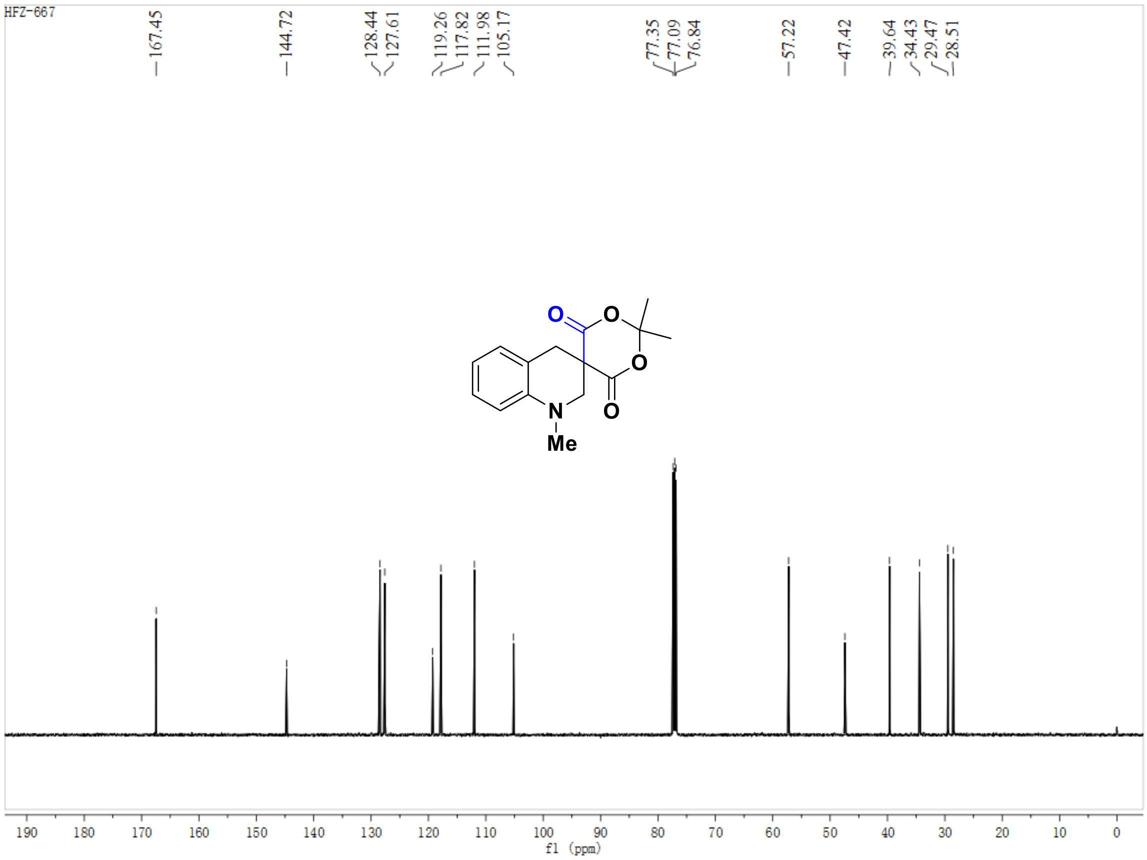
5,6,6a,7,8,9,10,11-octahydroazepino[1,2-a]quinoline-6-carboxylic acid (3l)



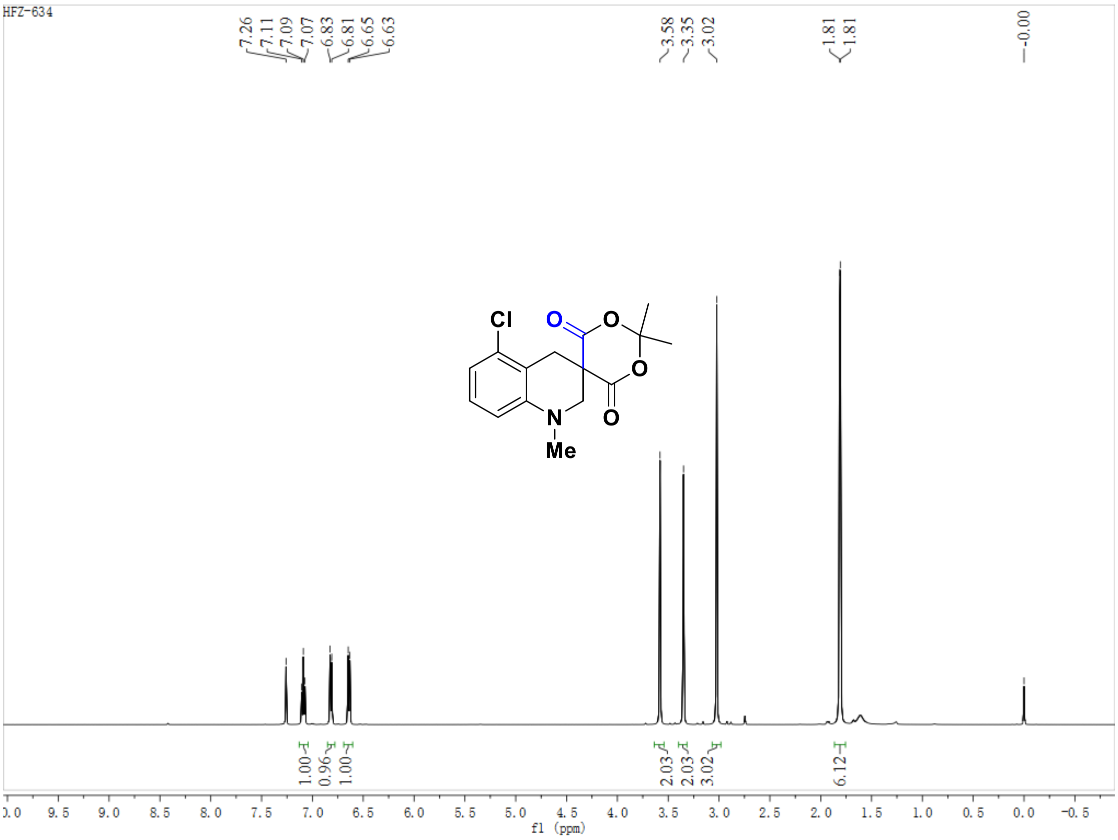


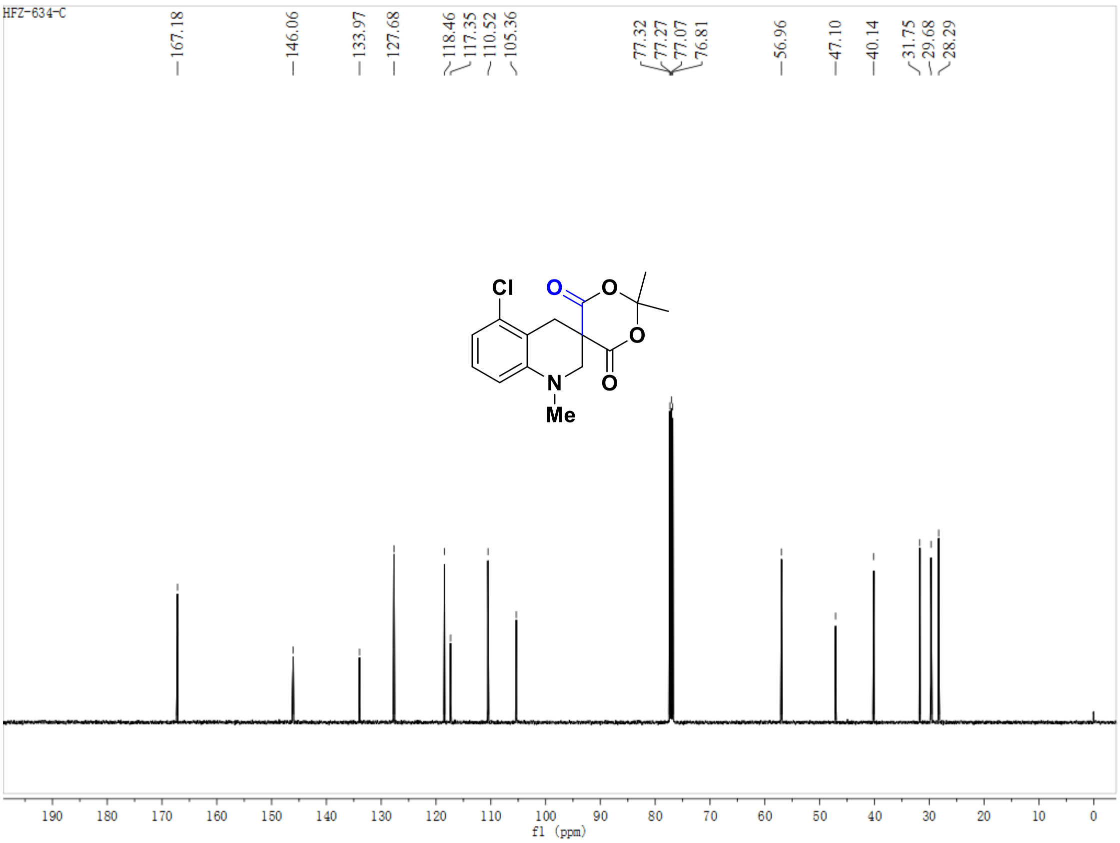
1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4a)



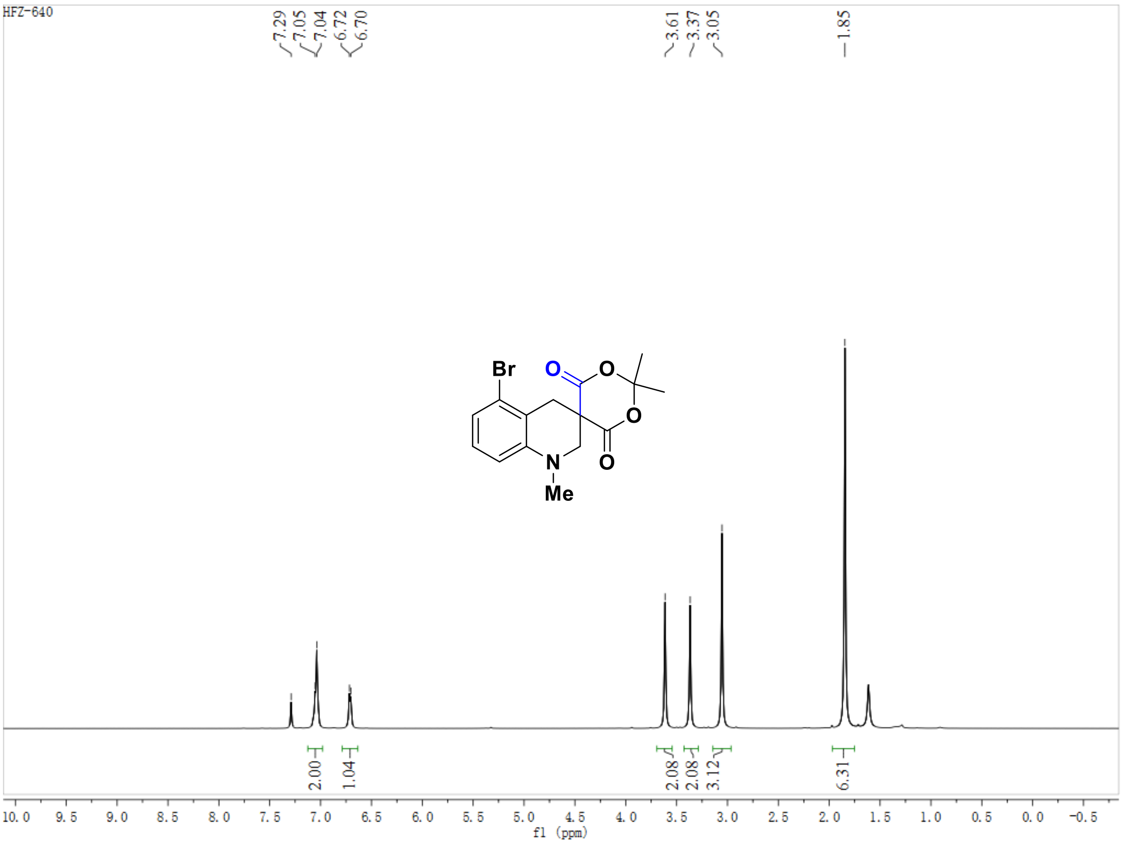


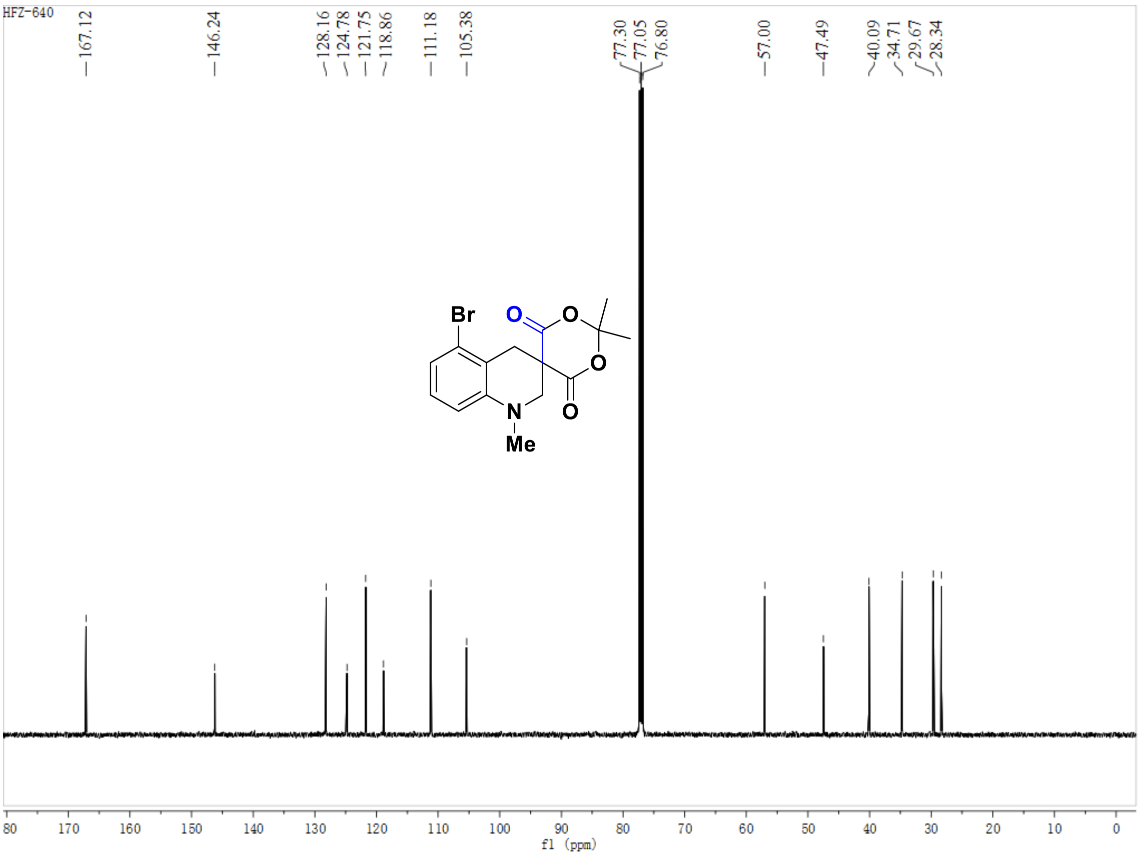
5-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4b)



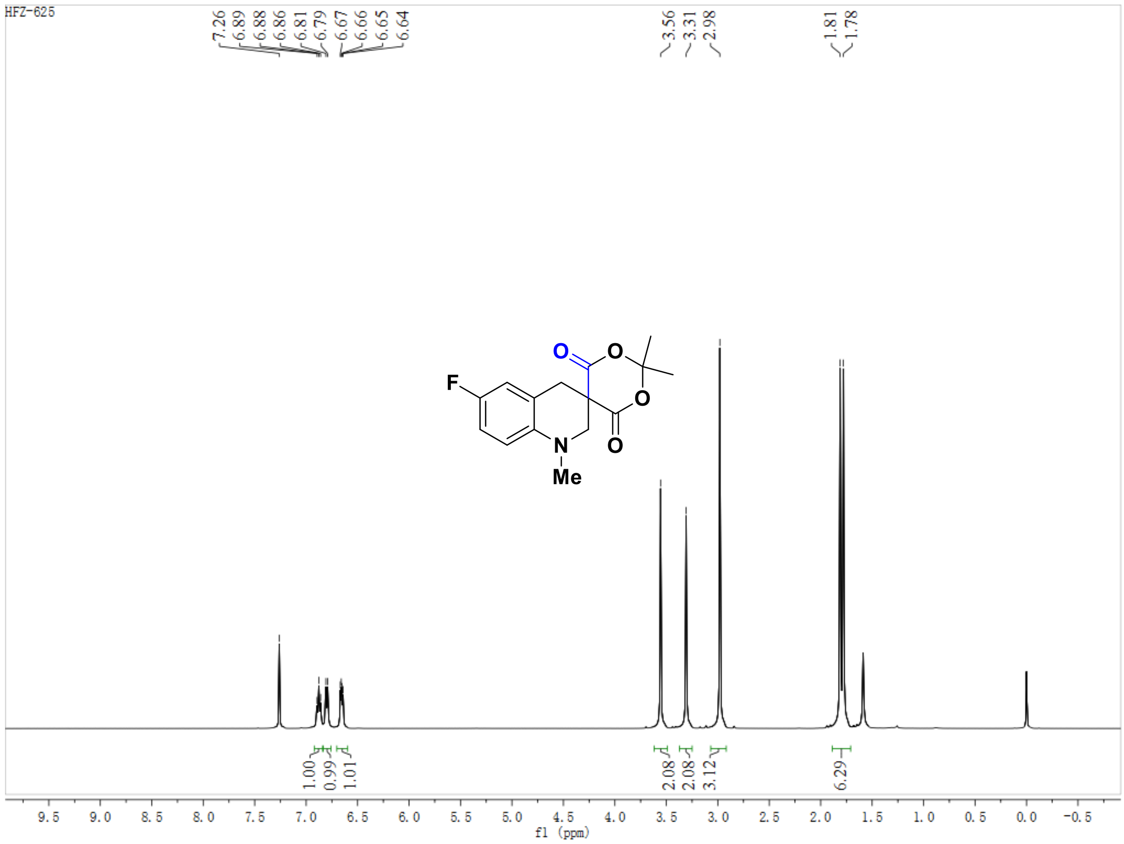


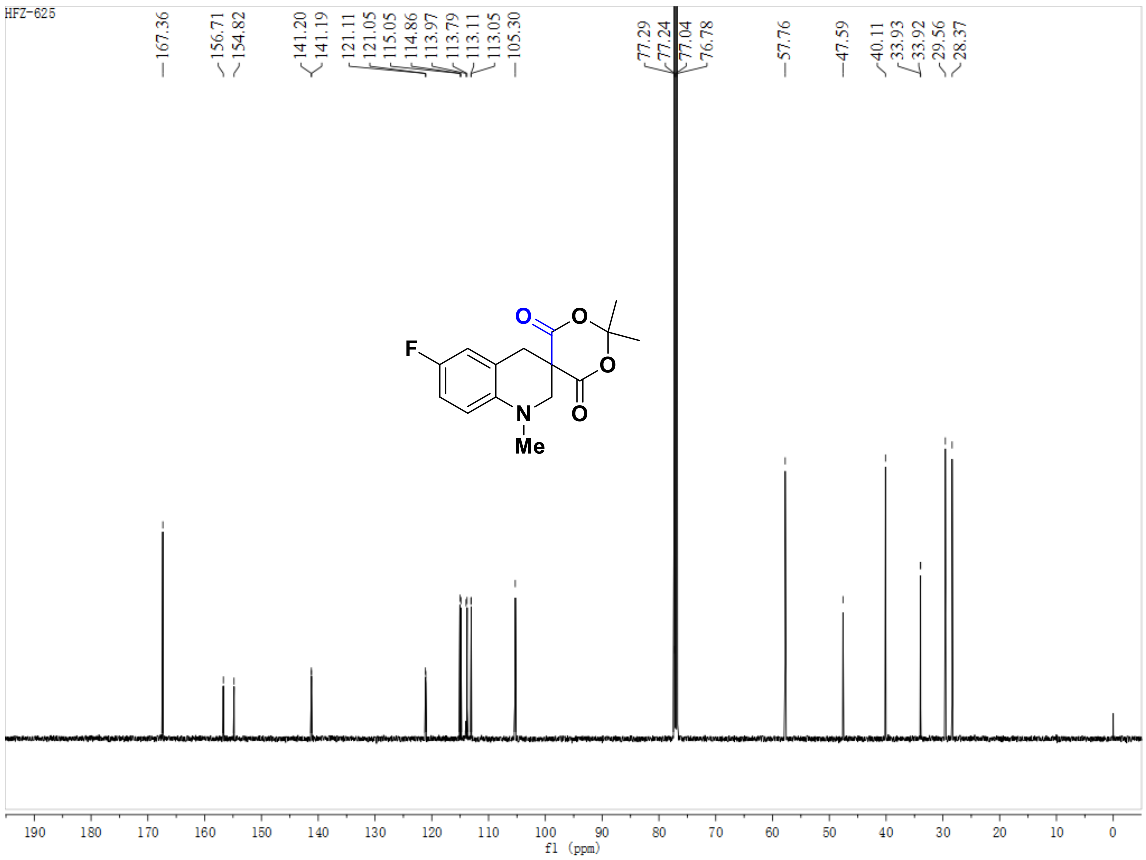
5-bromo-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4c)

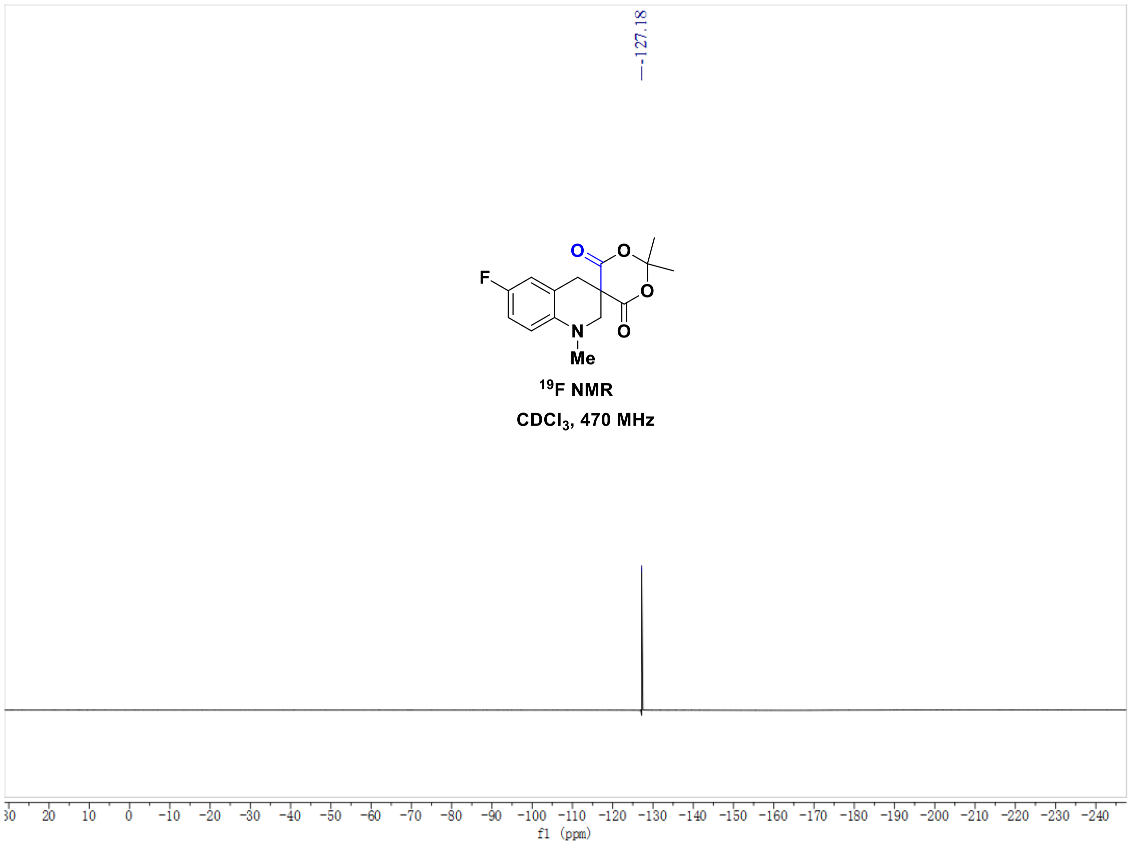




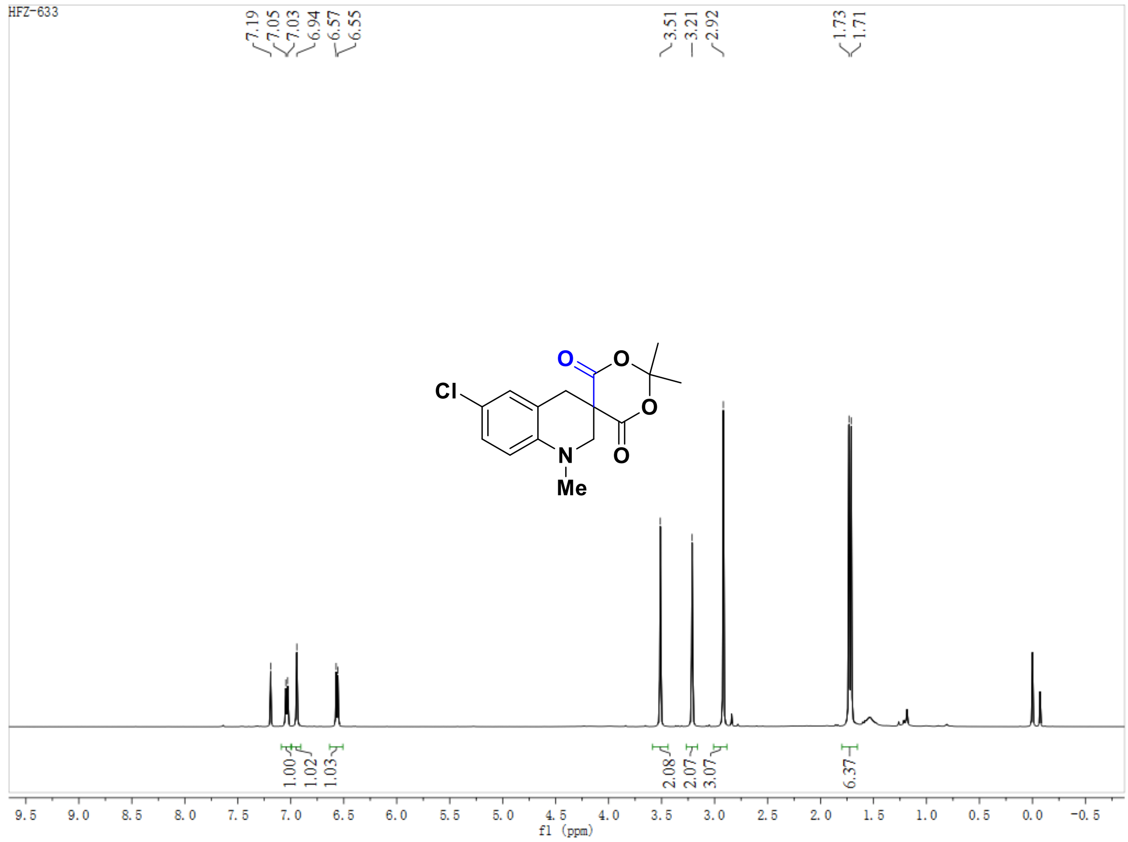
6-fluoro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4d)

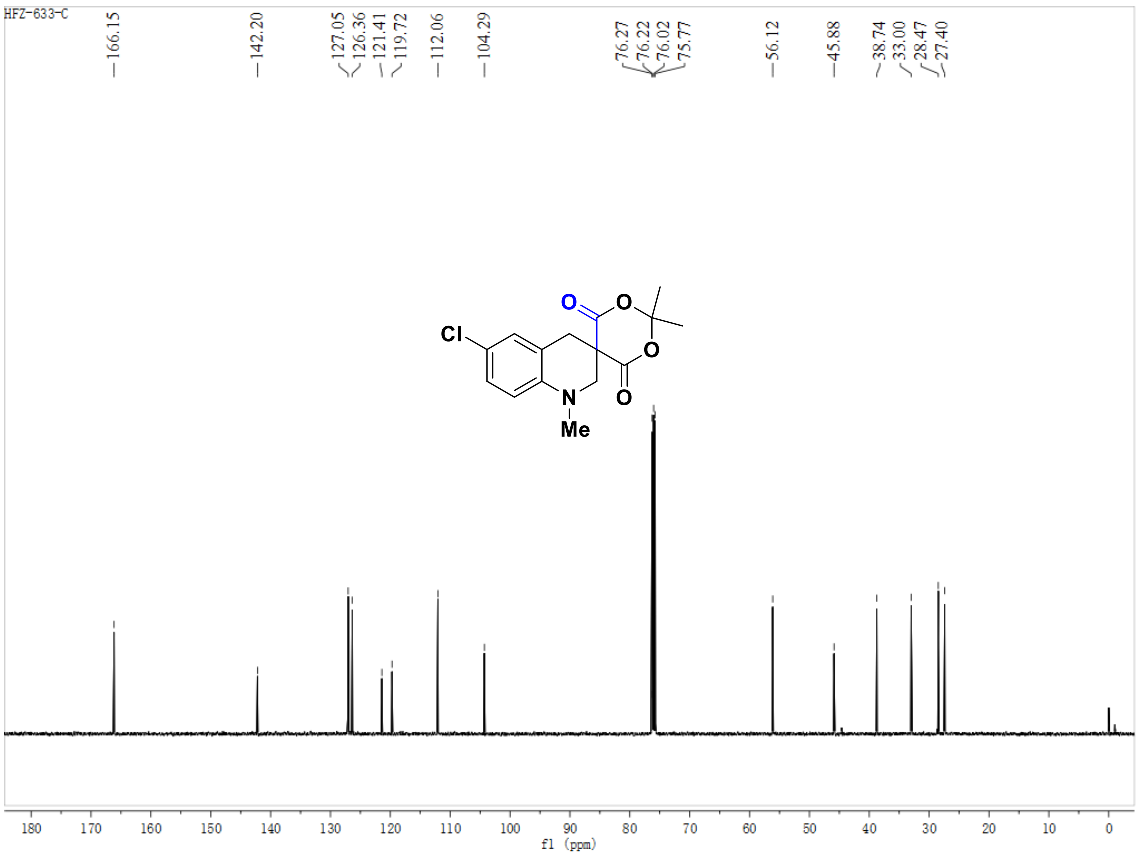




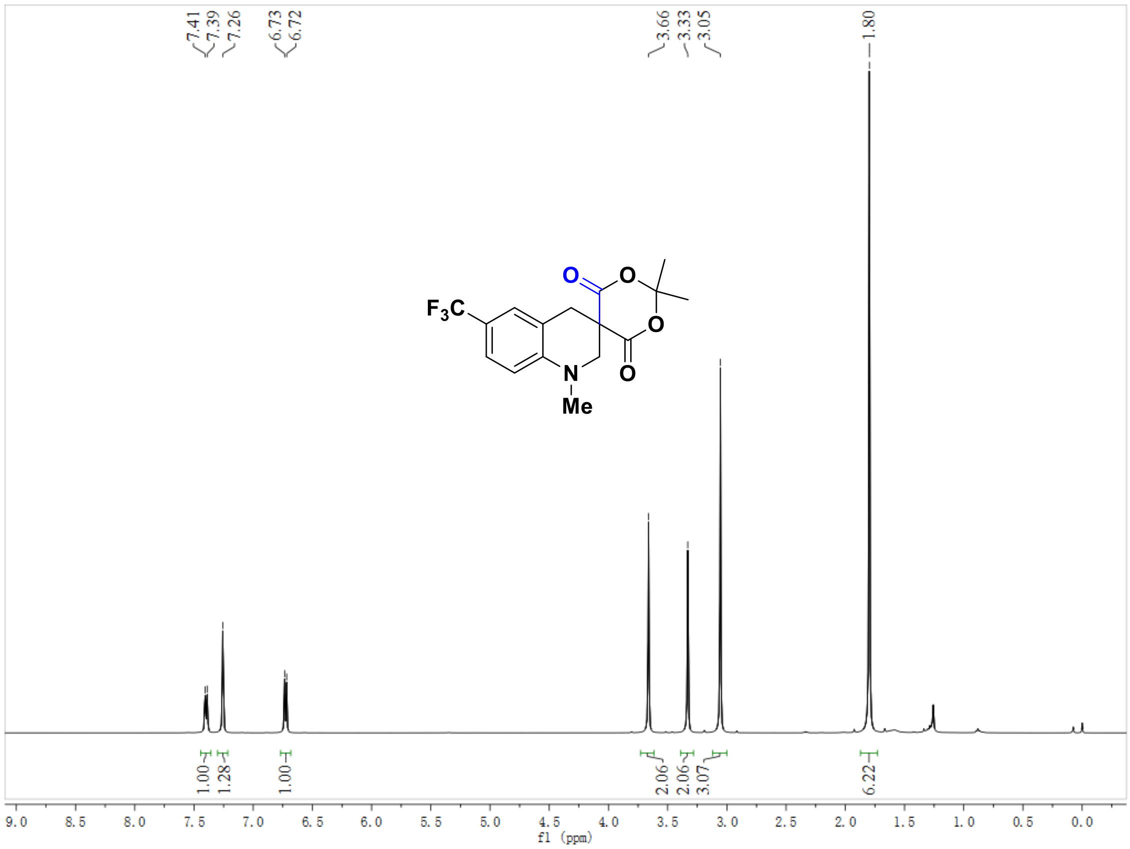

-127.18
F
O
O
O
O
N
Me
19F NMR
CDCl3, 470 MHz
f1 (ppm)

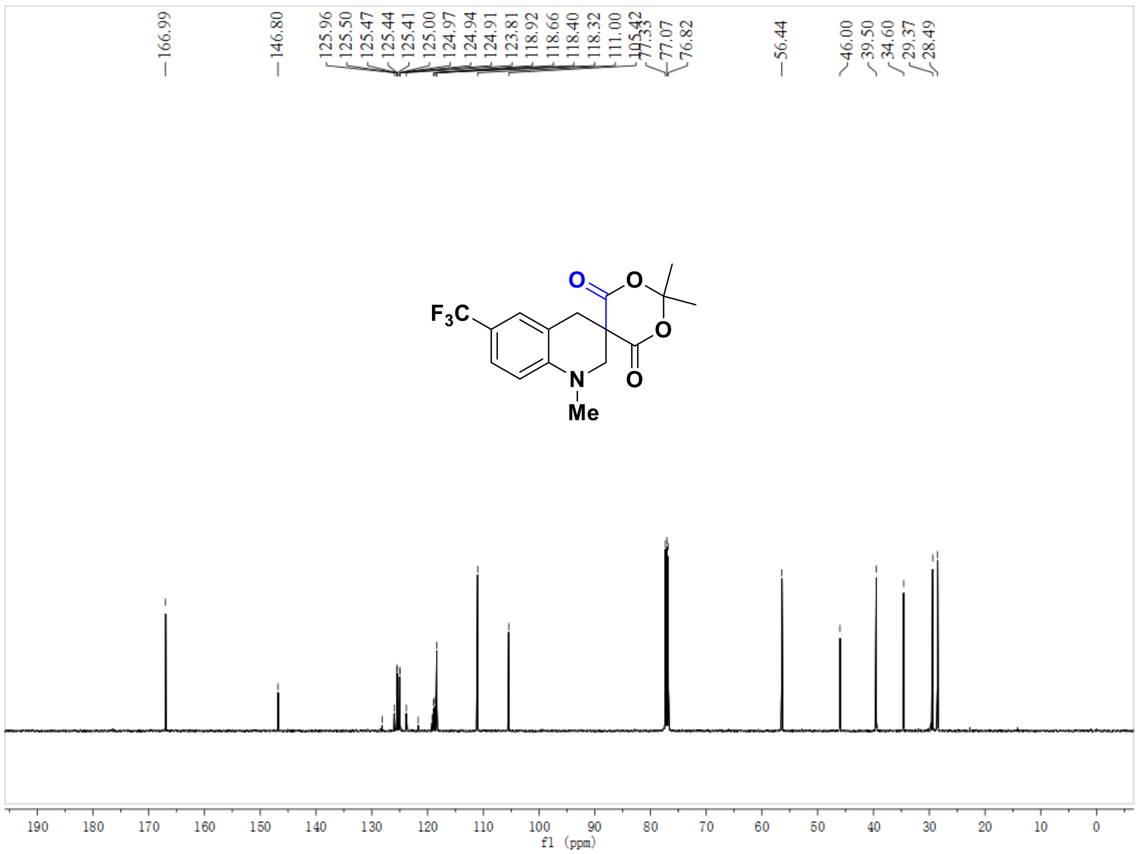
6-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4e)

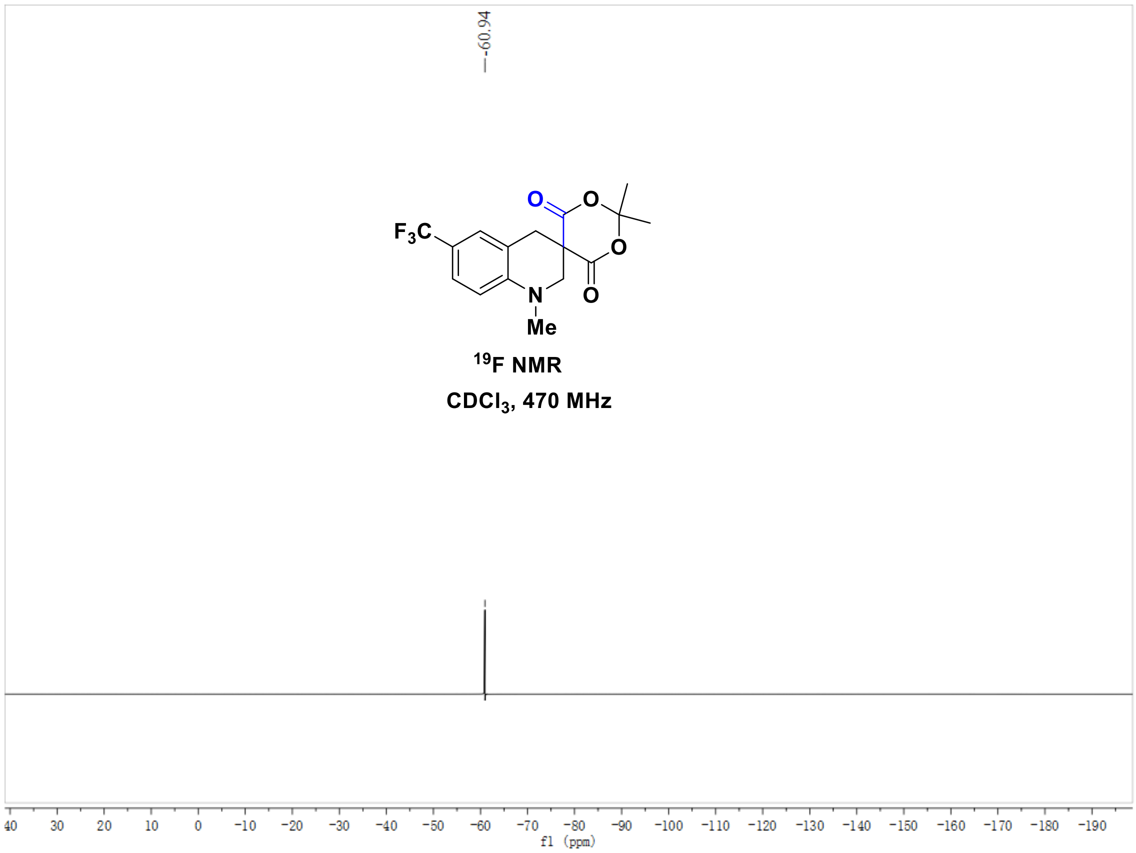




1,2',2'-trimethyl-6-(trifluoromethyl)-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4f)

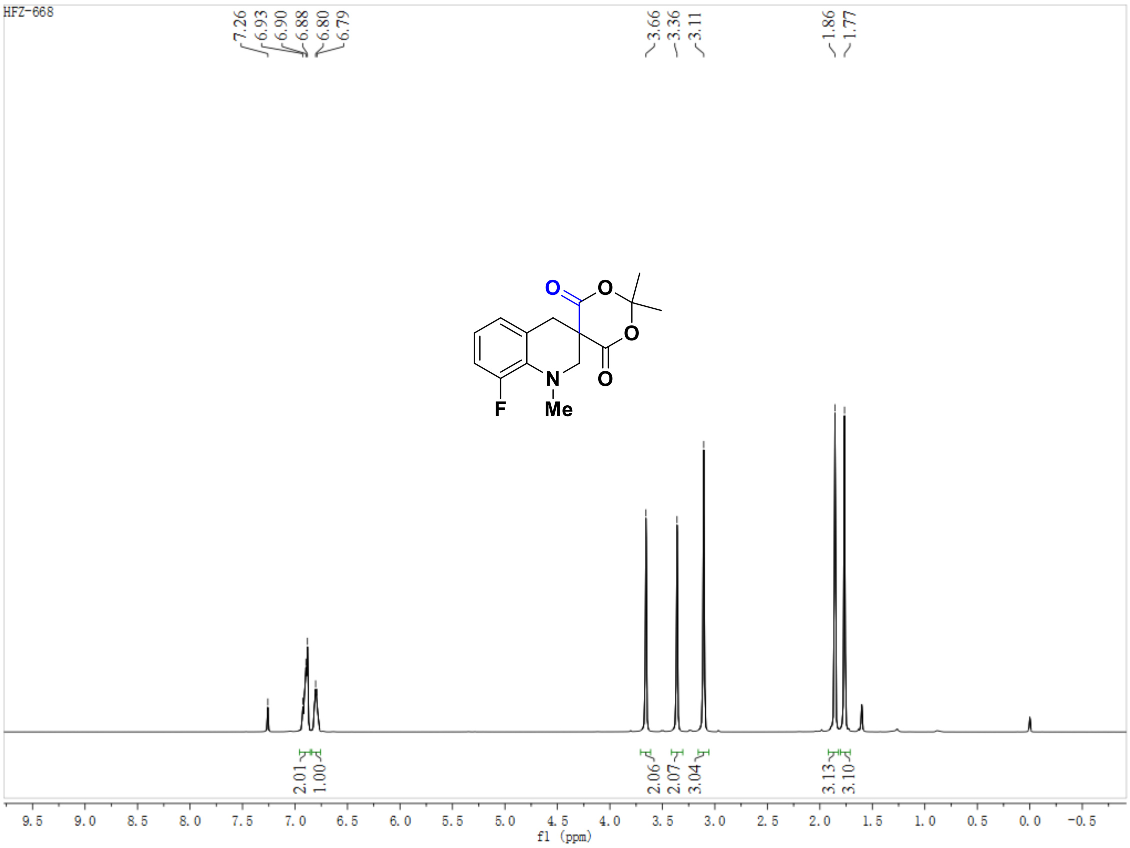


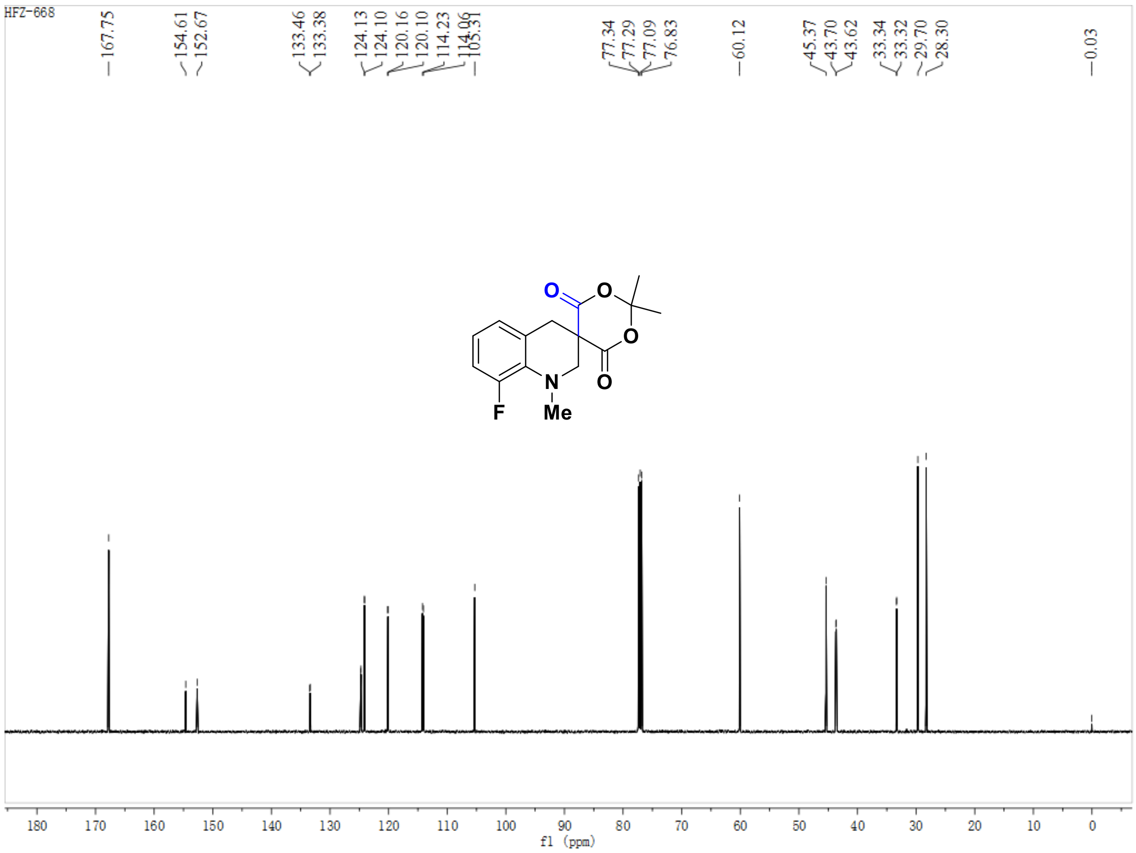


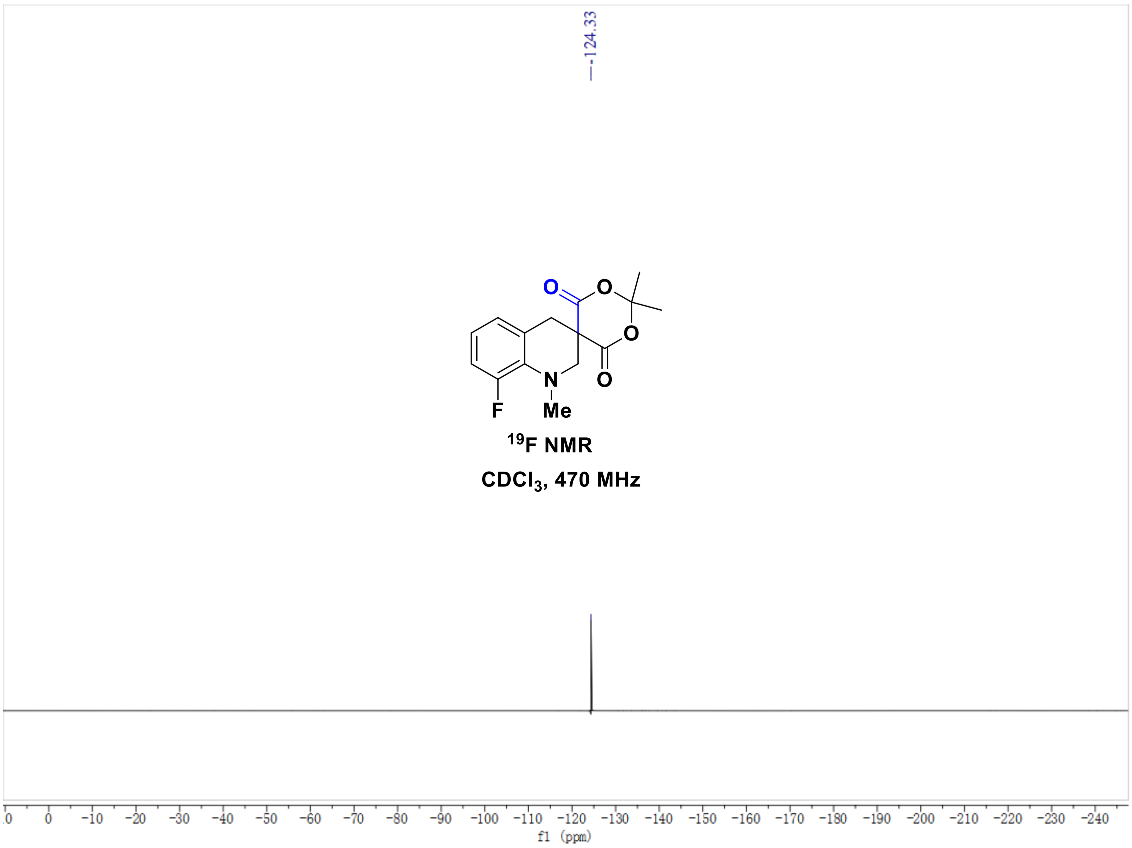


-60.94
F3C
O
O
O
O
N
Me
19F NMR
CDCl3, 470 MHz
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

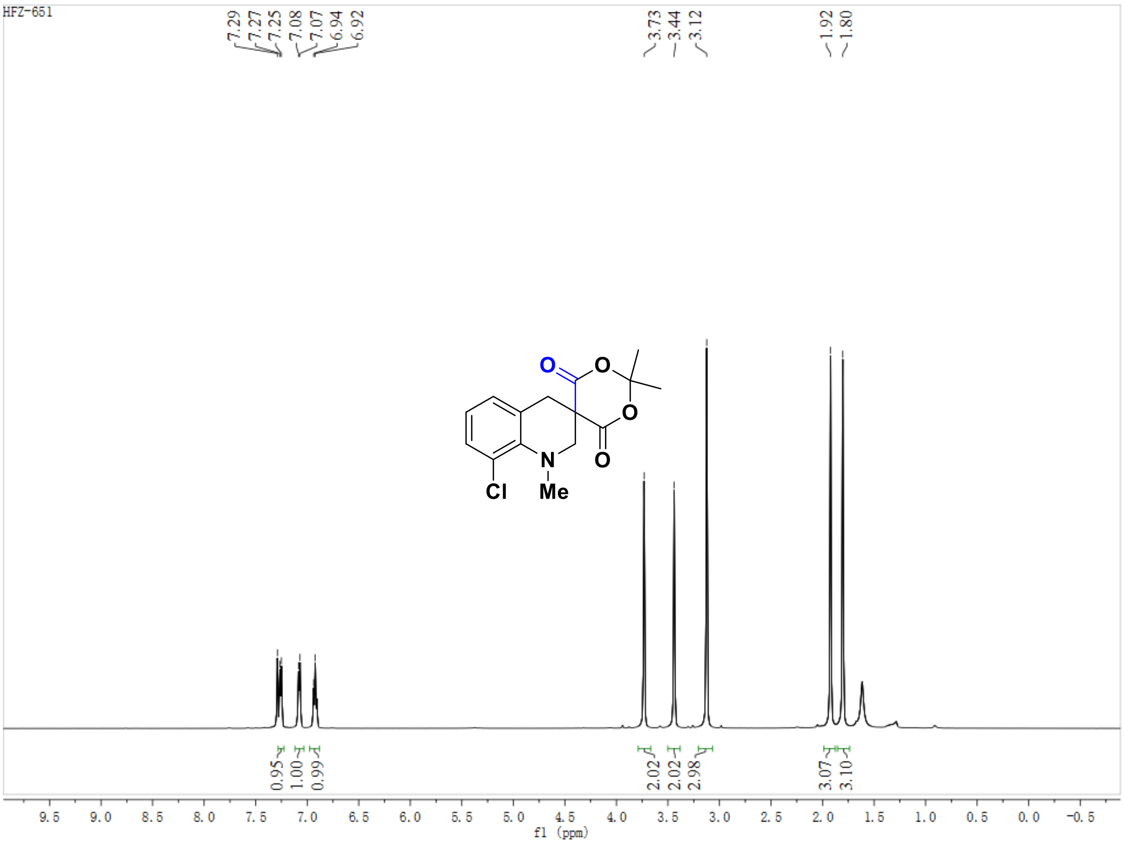
8-fluoro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4g)

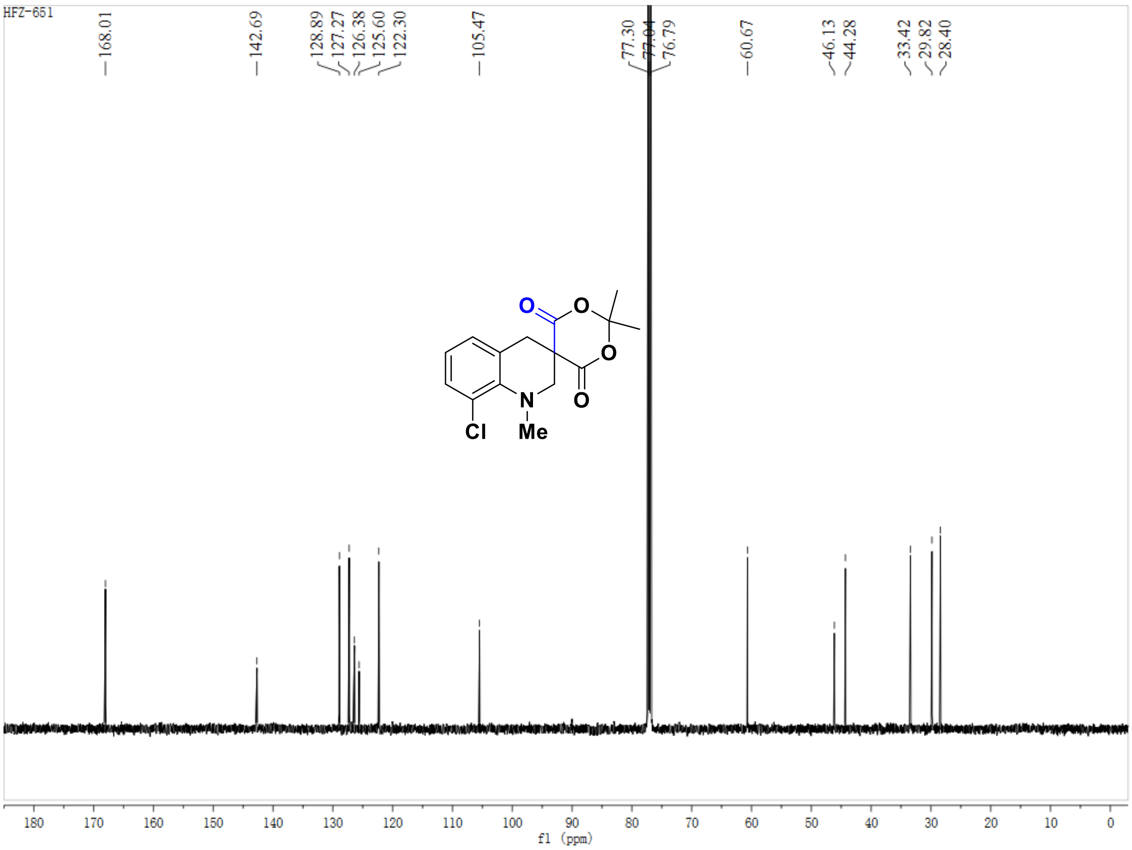




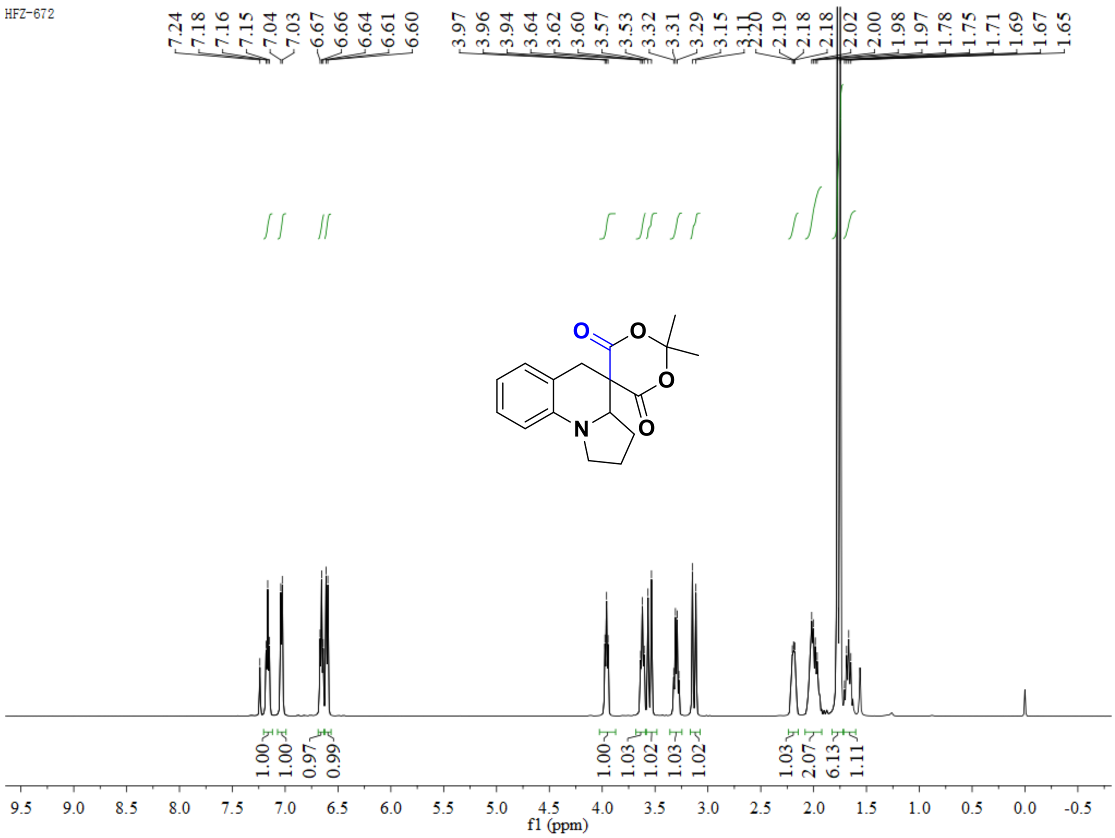

-124.33
O
O
O
O
N
F
Me
19F NMR
CDCl3, 470 MHz
f1 (ppm)

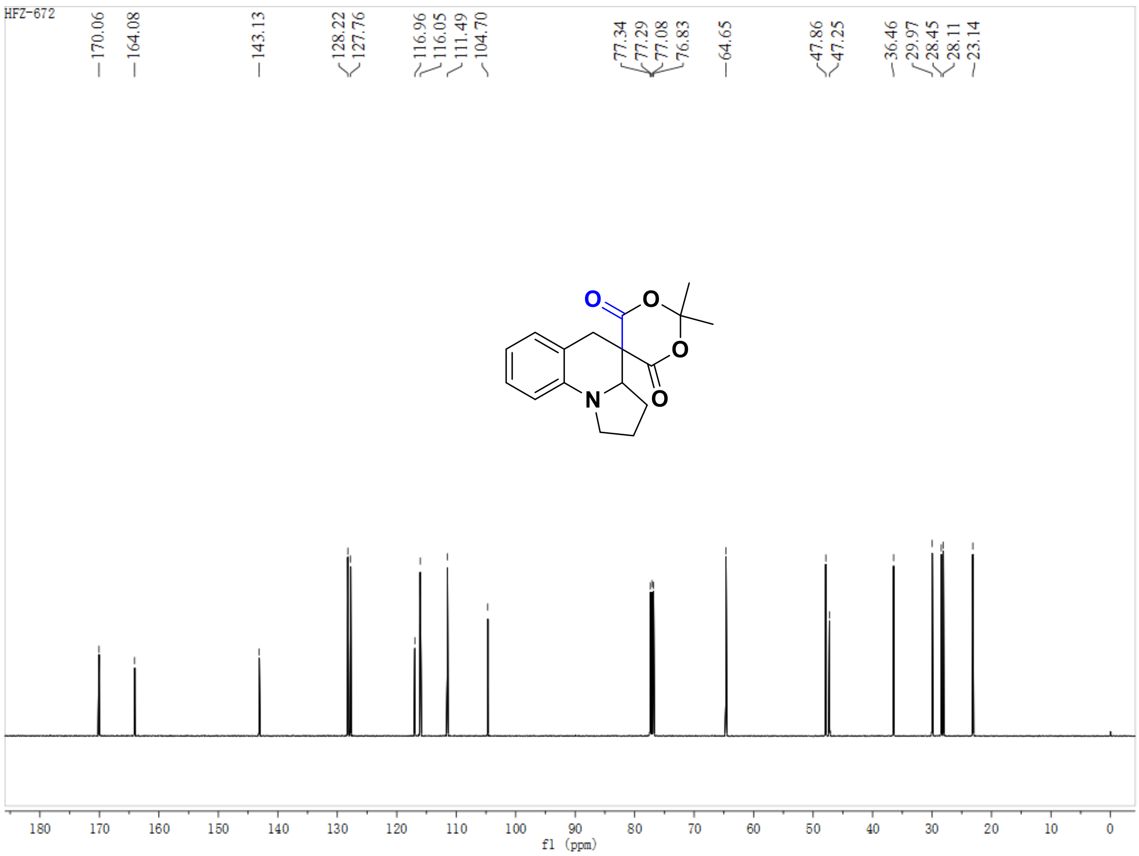
8-chloro-1,2',2'-trimethyl-1,4-dihydro-2H-spiro[quinoline-3,5'-[1,3]dioxane]-4',6'-dione (4h)



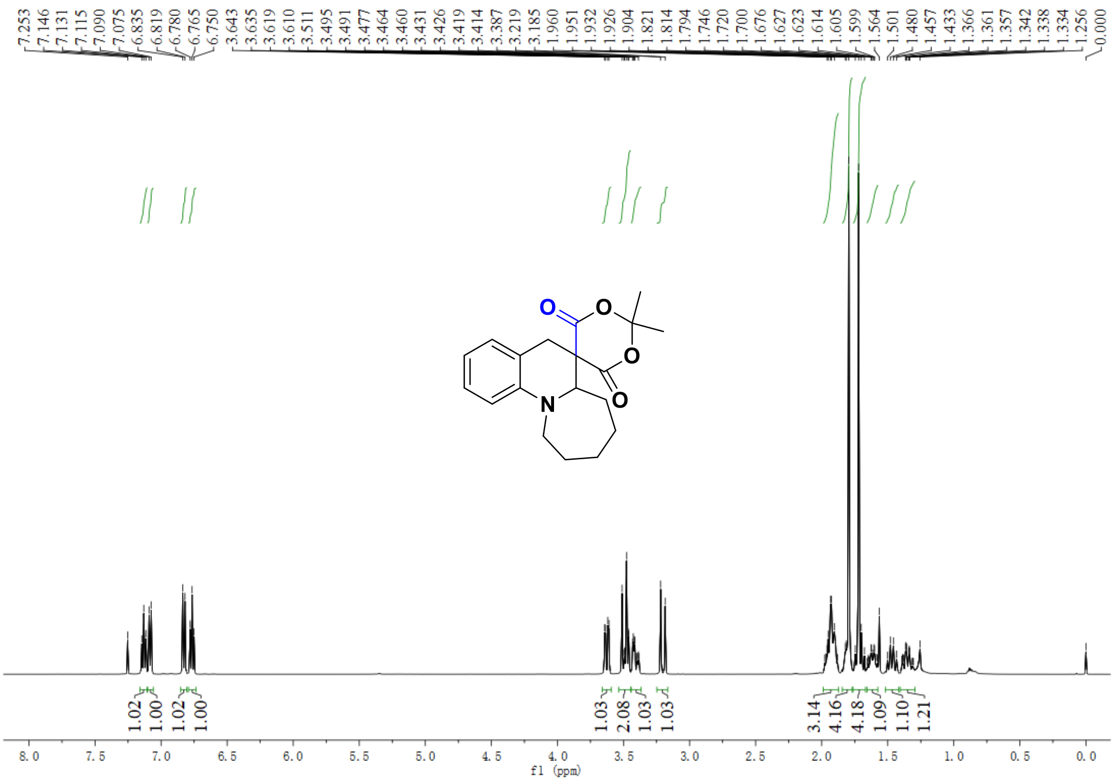


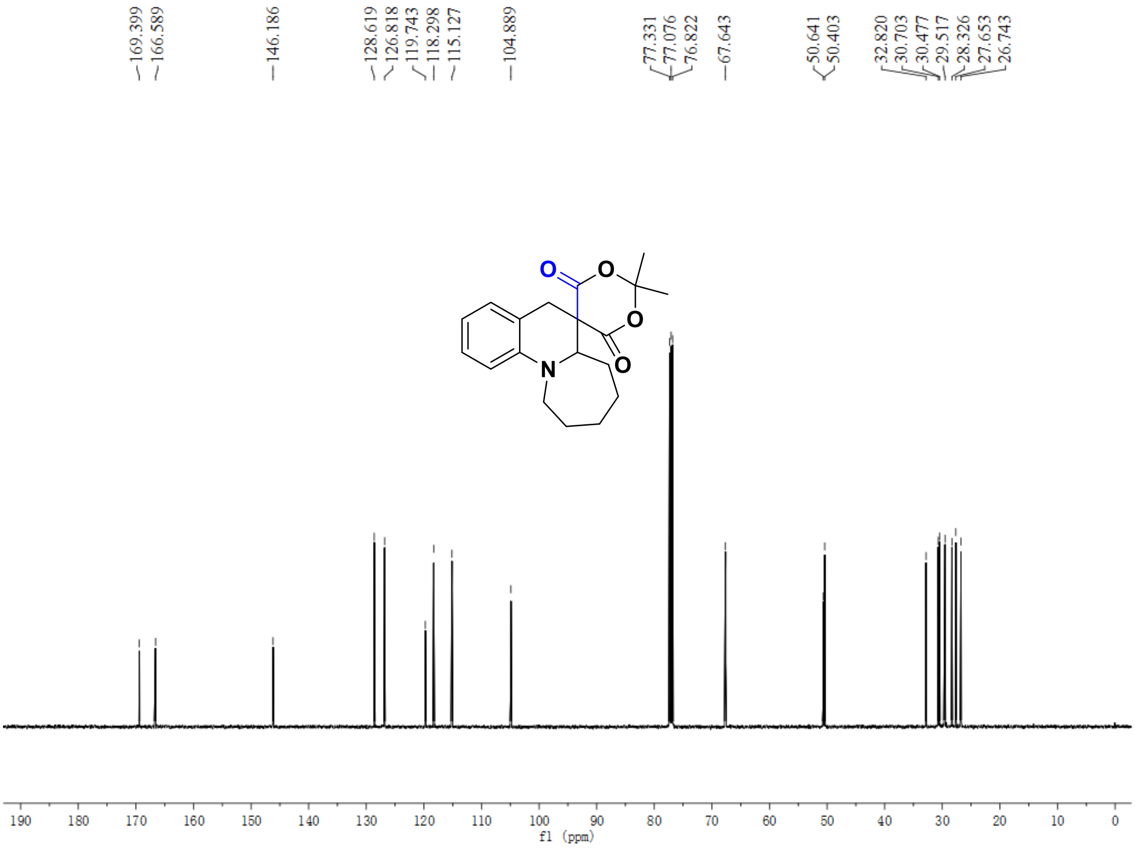
2',2'-dimethyl-1,2,3,3a-tetrahydro-5H-spiro[pyrrolo[1,2-a]quinoline-4,5'-[1,3]dioxane]-4',6'-dione (4i)



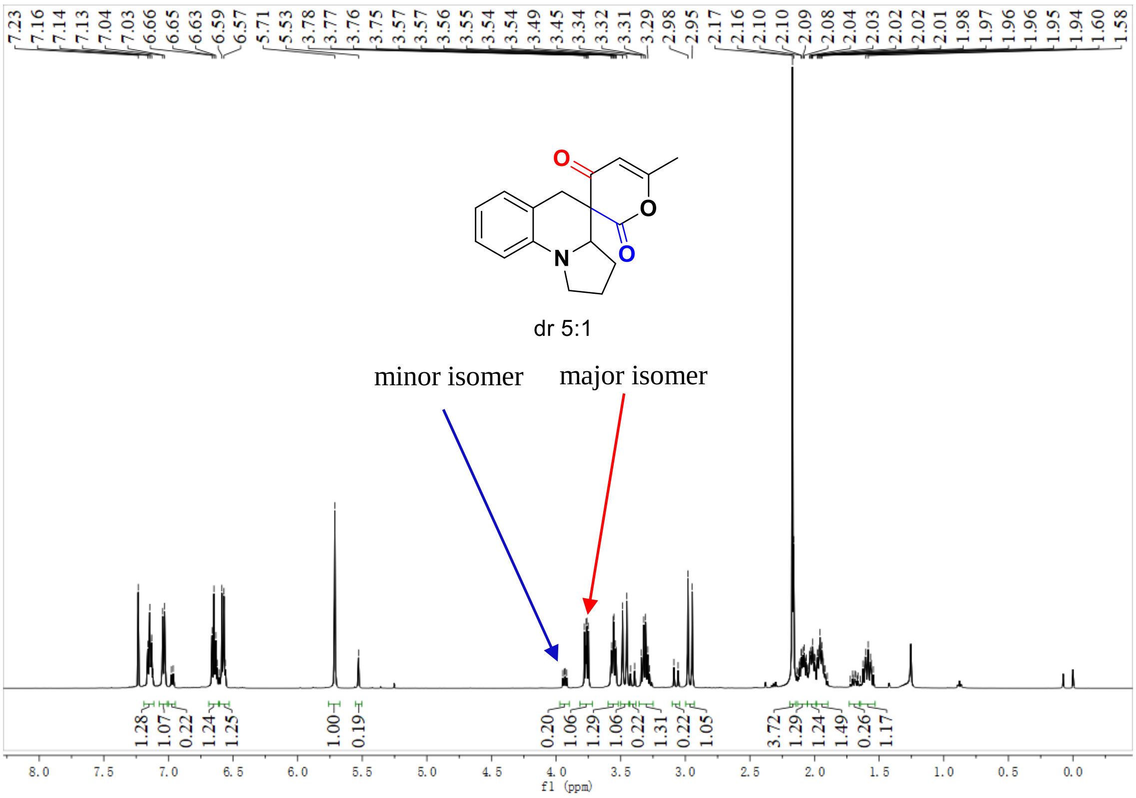


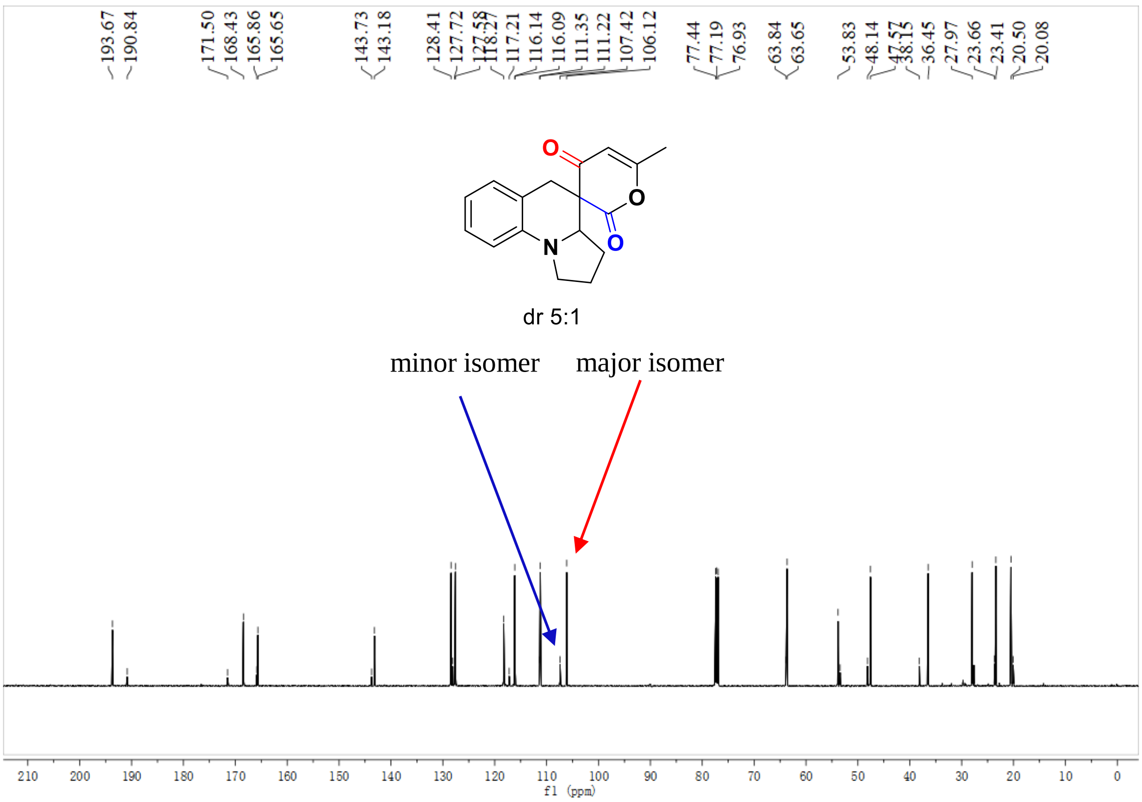
2',2'-dimethyl-6a,7,8,9,10,11-hexahydro-5H-spiro[azepino[1,2-a]quinoline-6,5'-[1,3]dioxane]-4',6'-dione (4j)



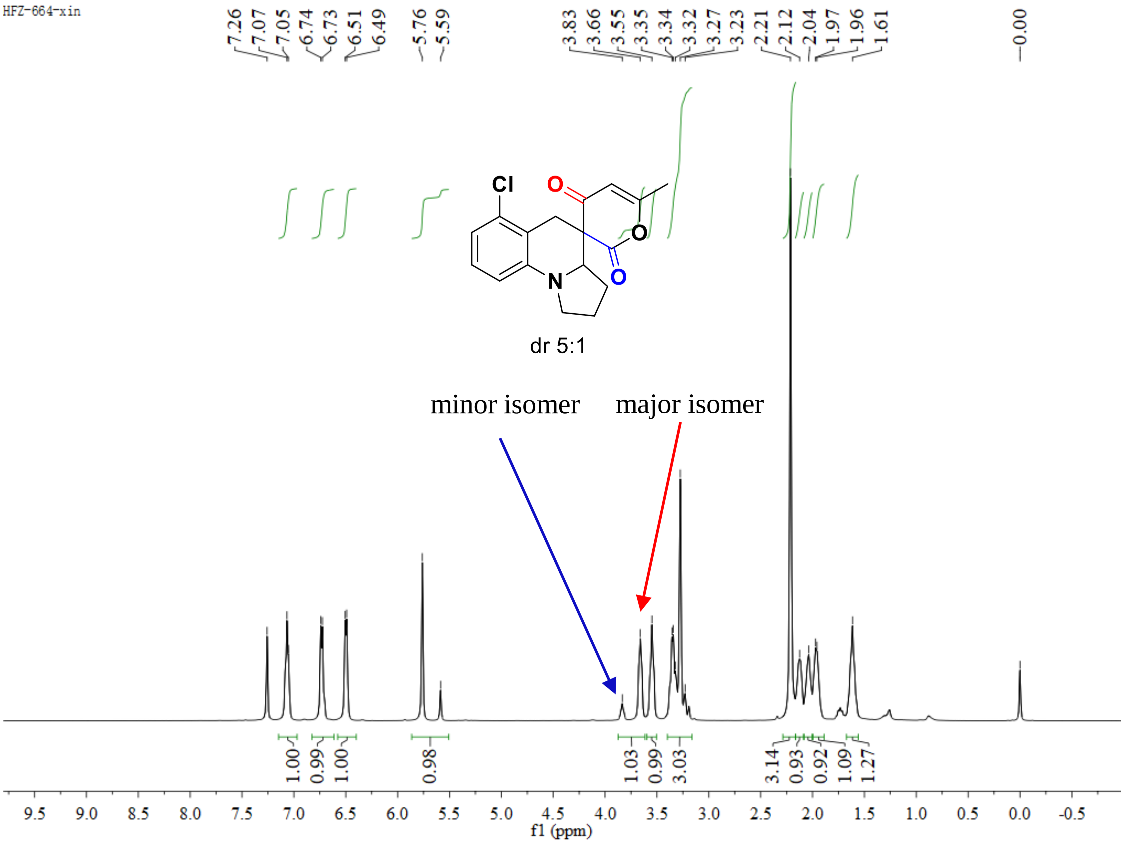


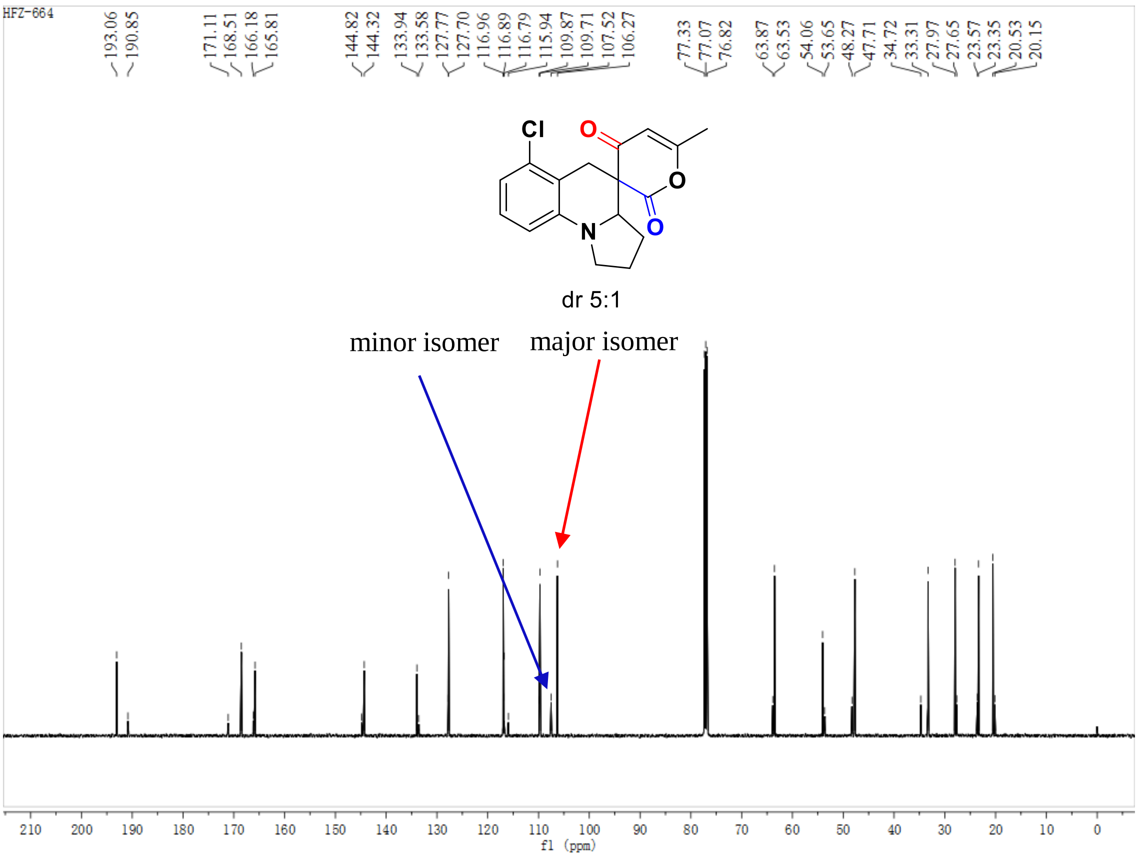
6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6a)



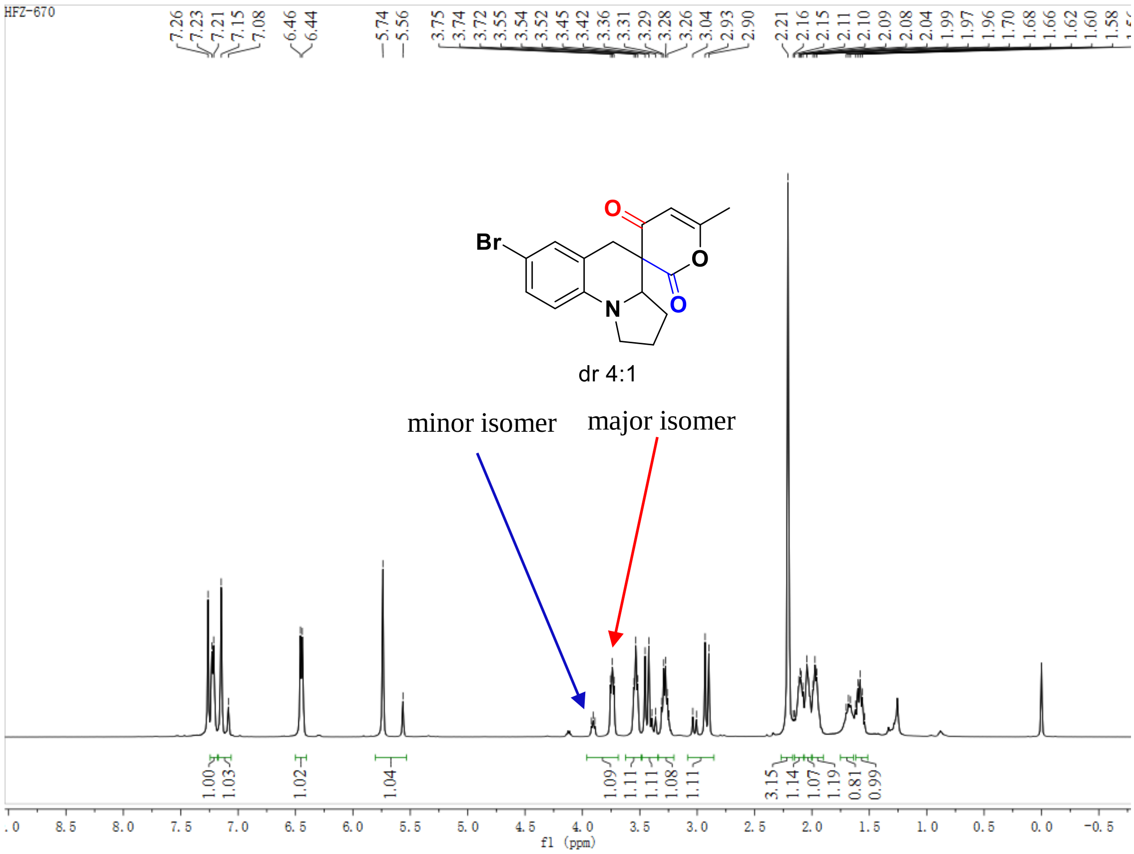


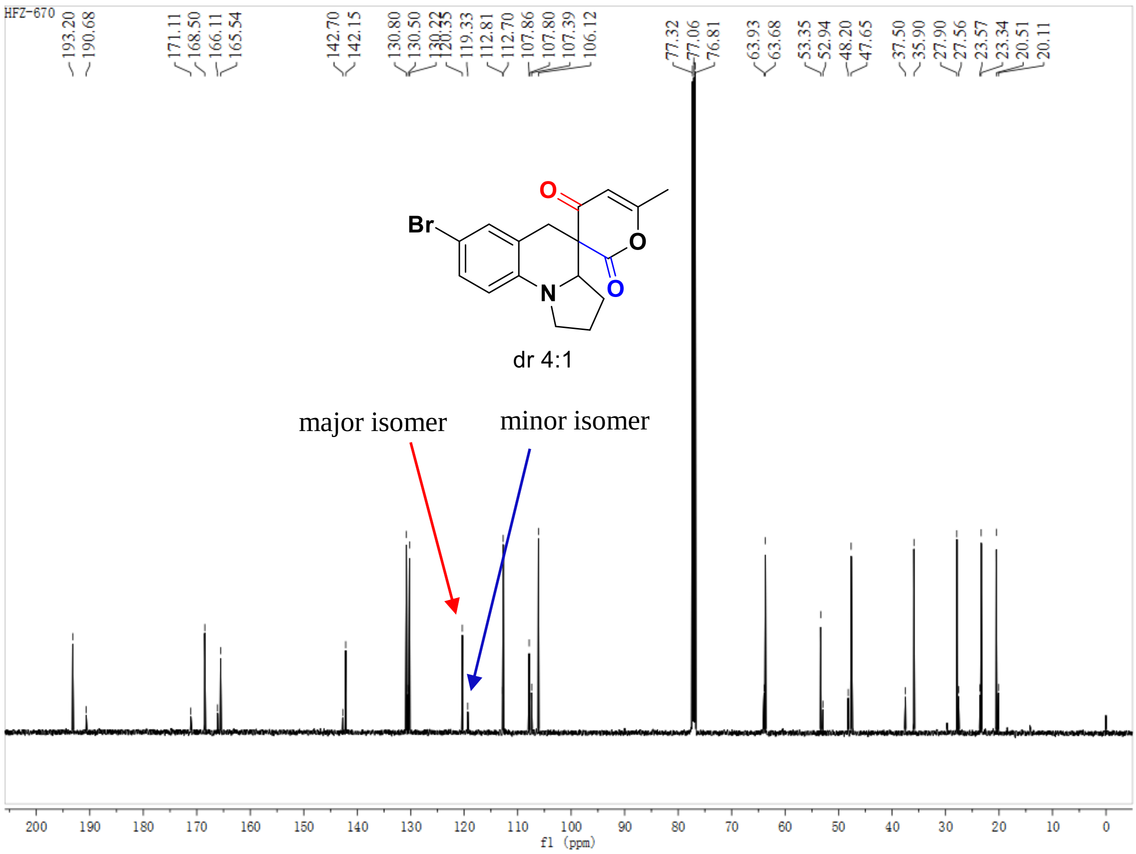
6'-chloro-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6b)



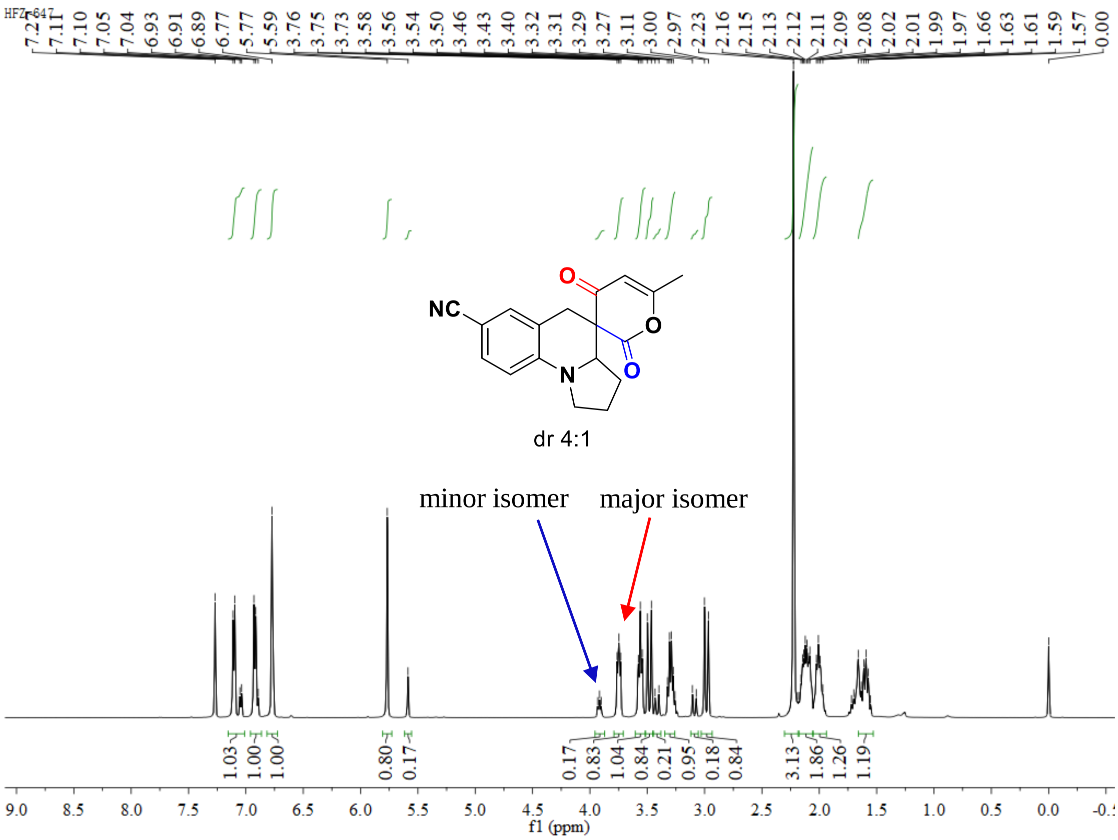


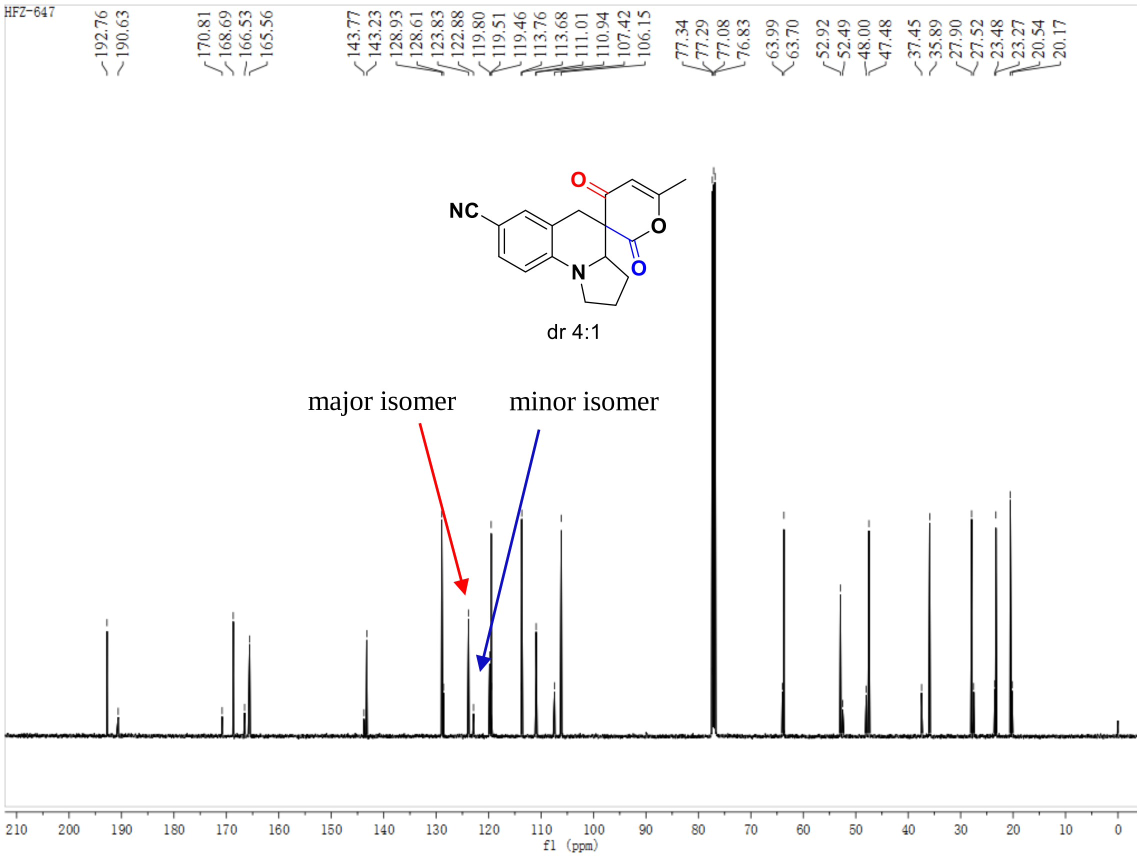
7'-bromo-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6c)



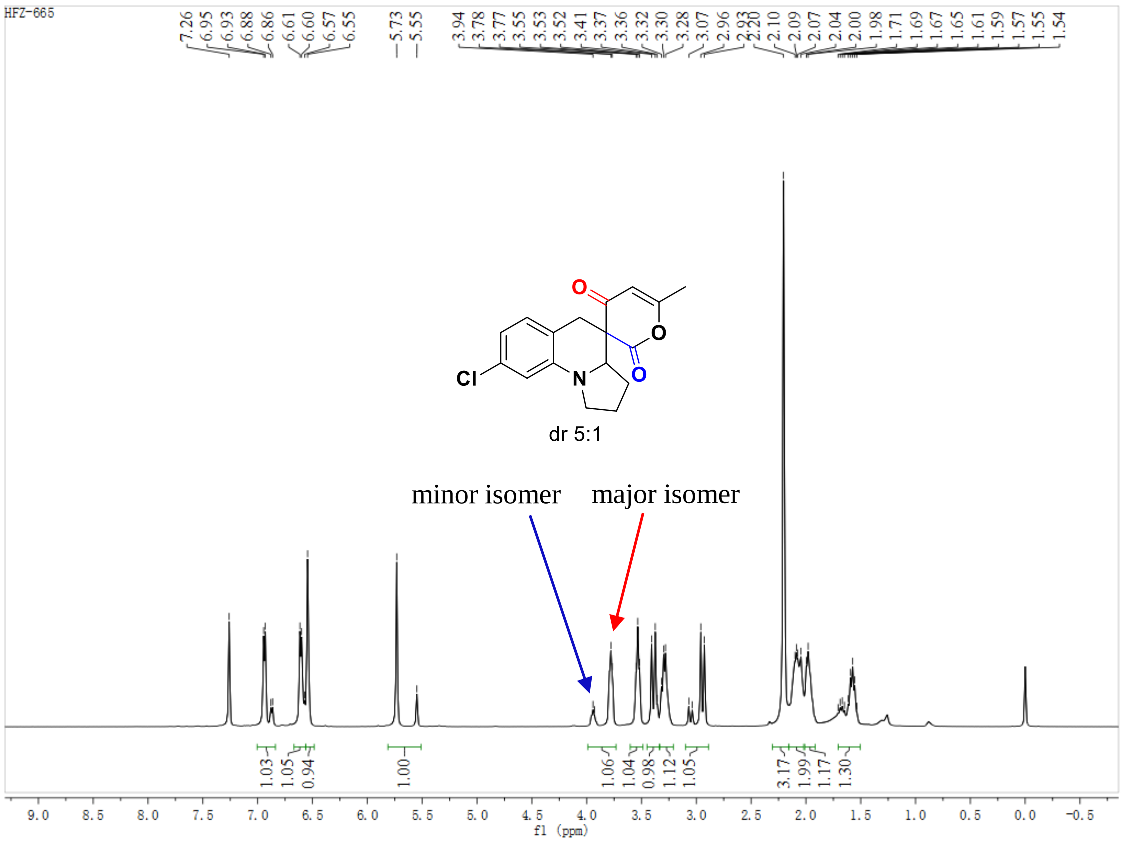


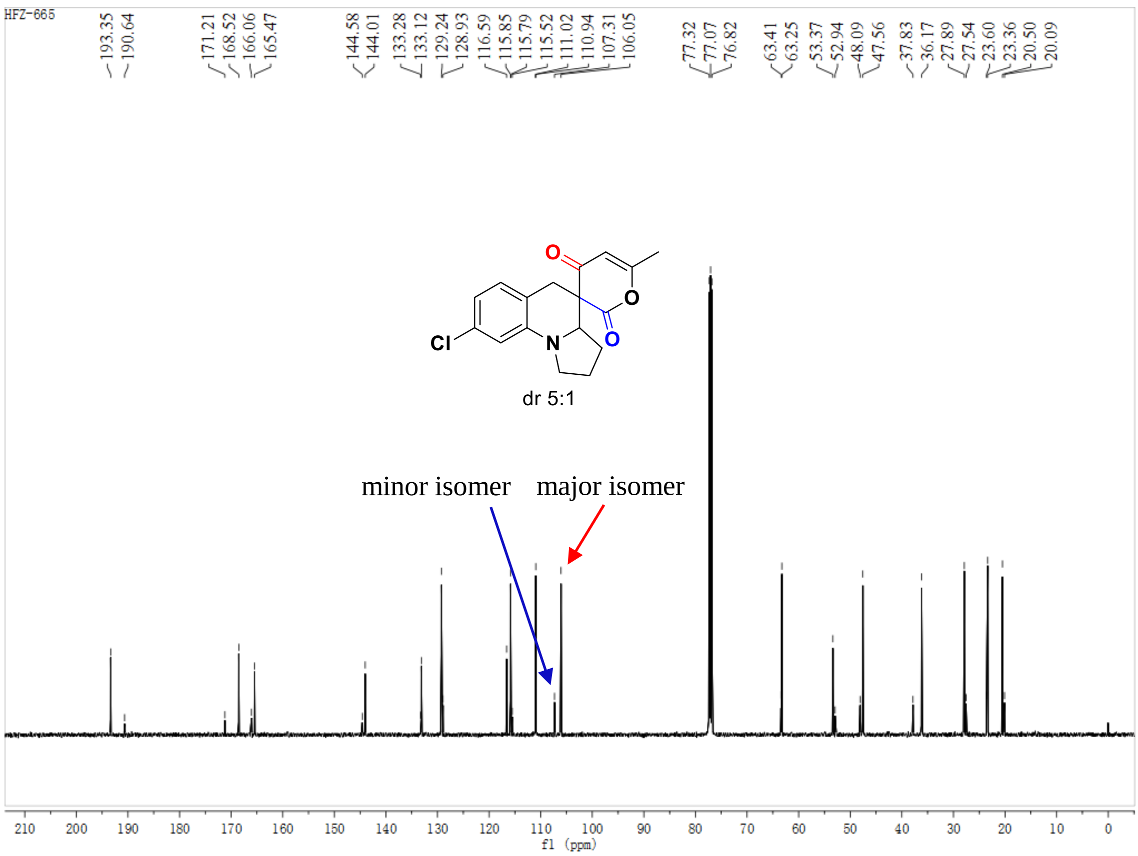
6-methyl-2,4-dioxo-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-7'-carbonitrile (6d)



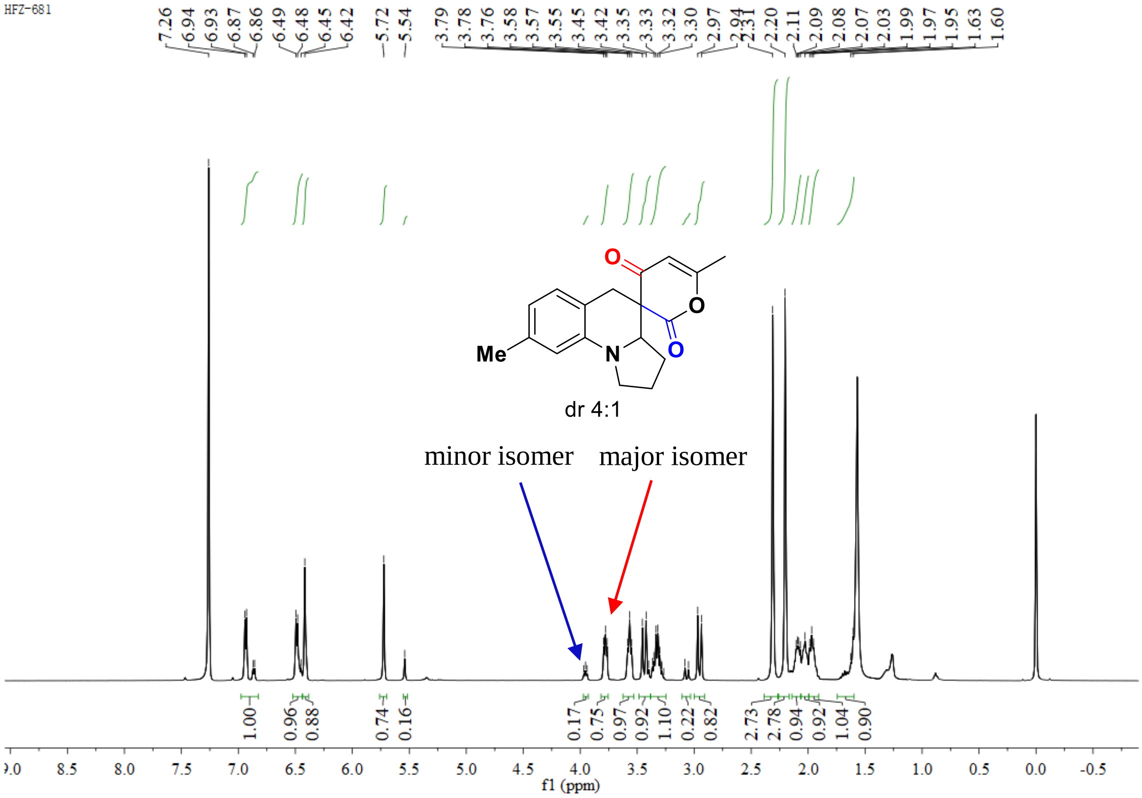


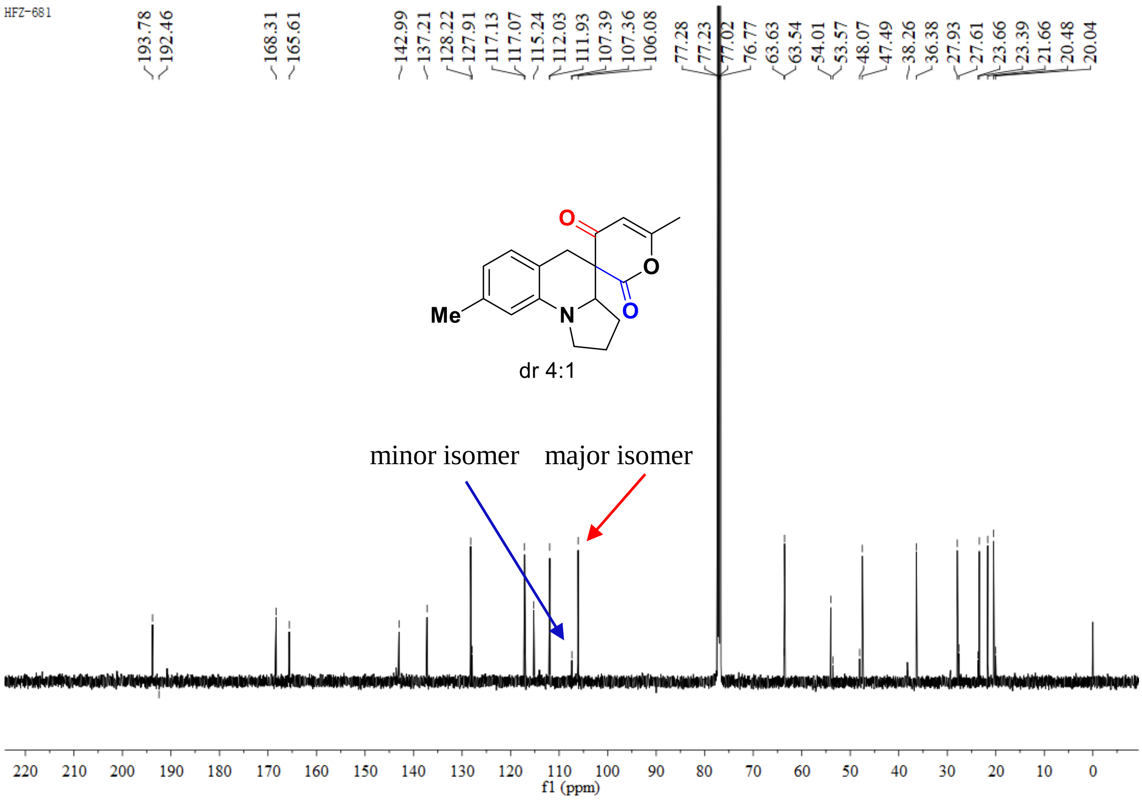
8'-chloro-6-methyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6e)



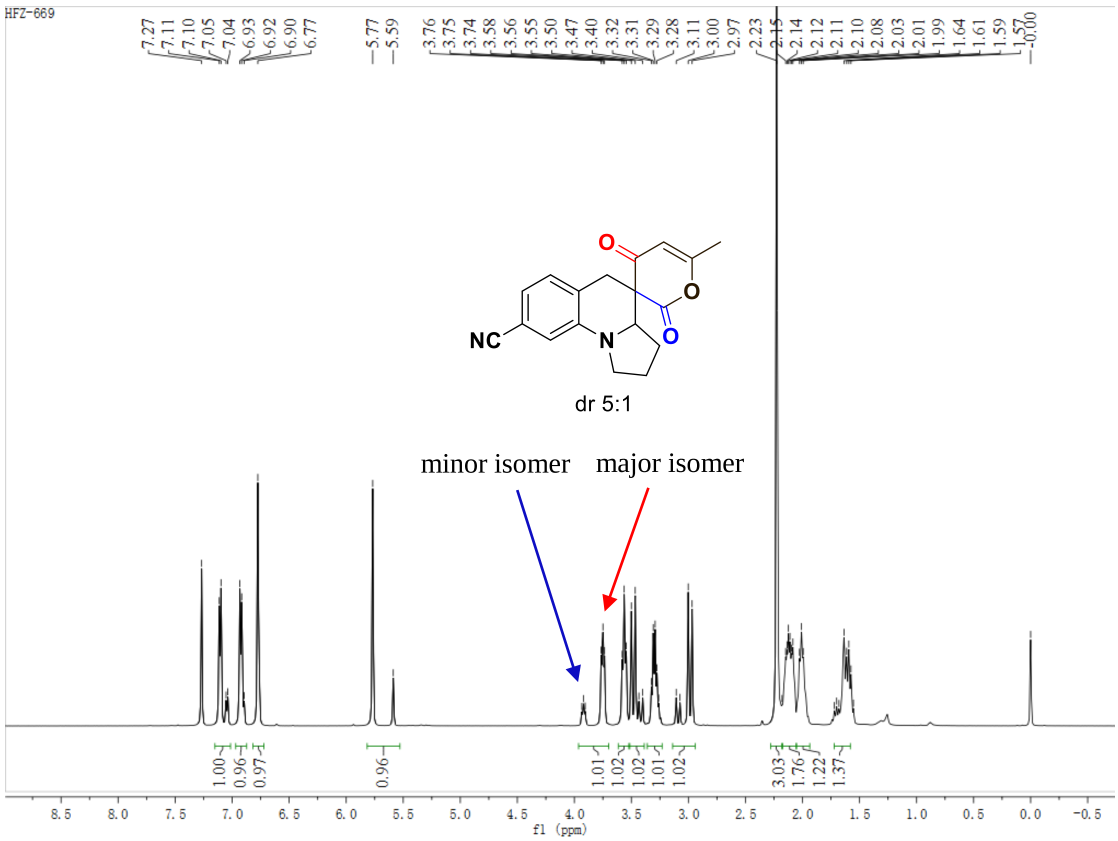


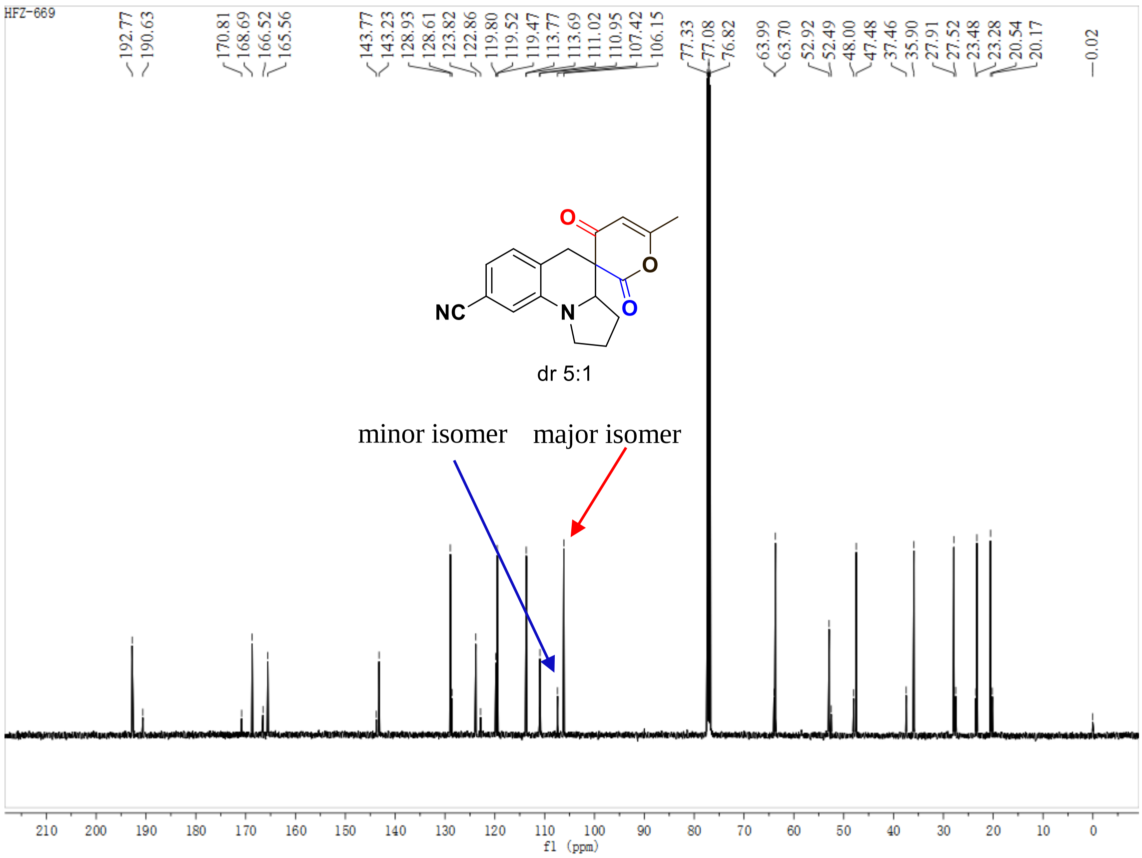
6,8'-dimethyl-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-2,4-dione (6f)



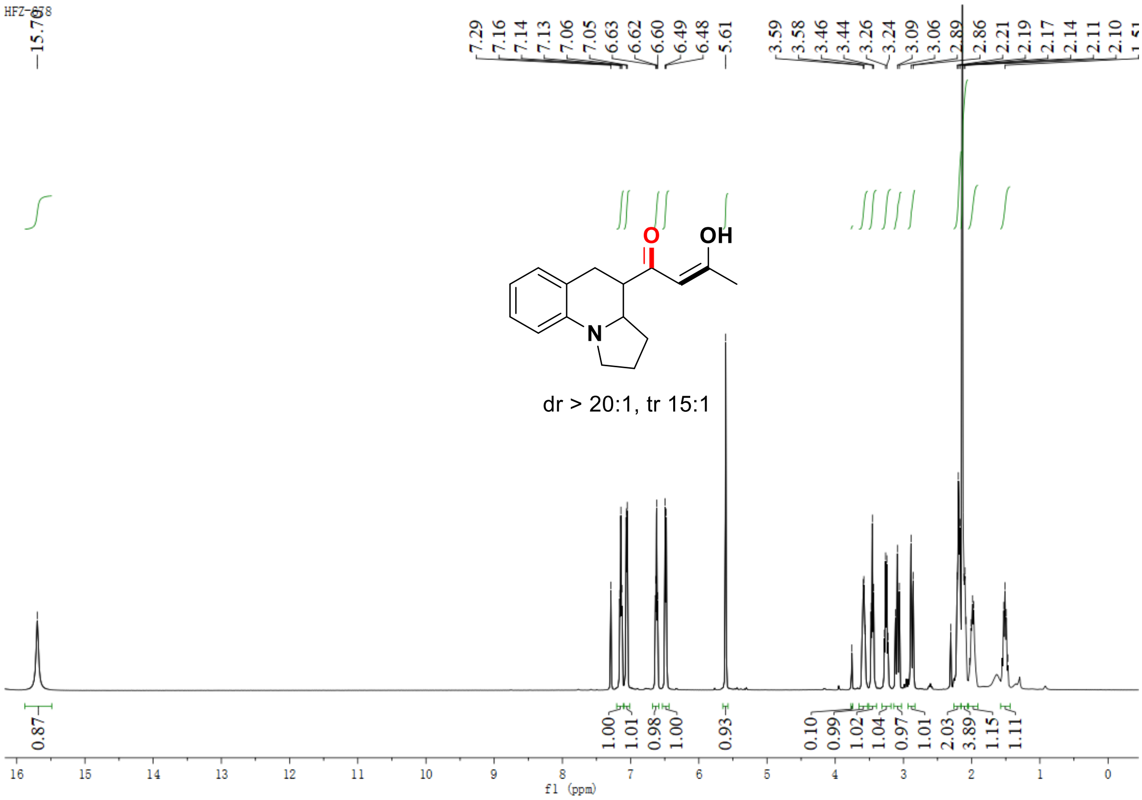


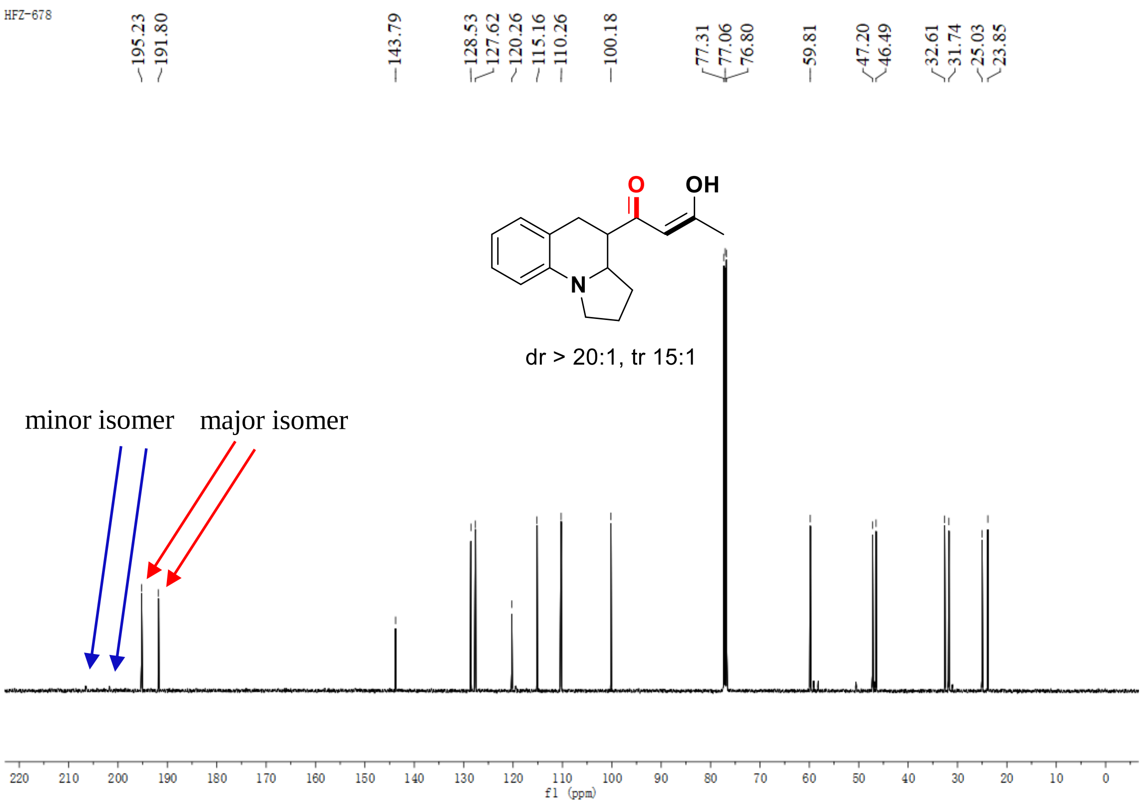
6-methyl-2,4-dioxo-1',2',3',3a'-tetrahydro-2H,4H,5'H-spiro[pyran-3,4'-pyrrolo[1,2-a]quinoline]-8'-carbonitrile (6g)



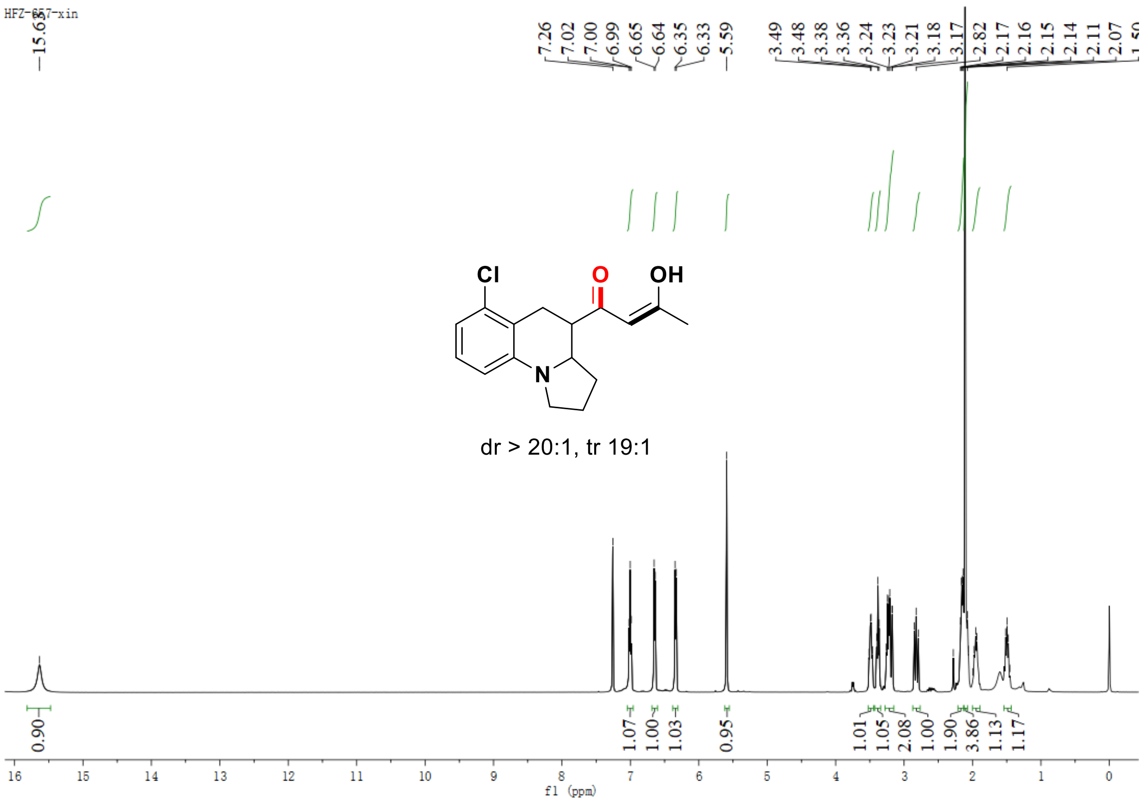


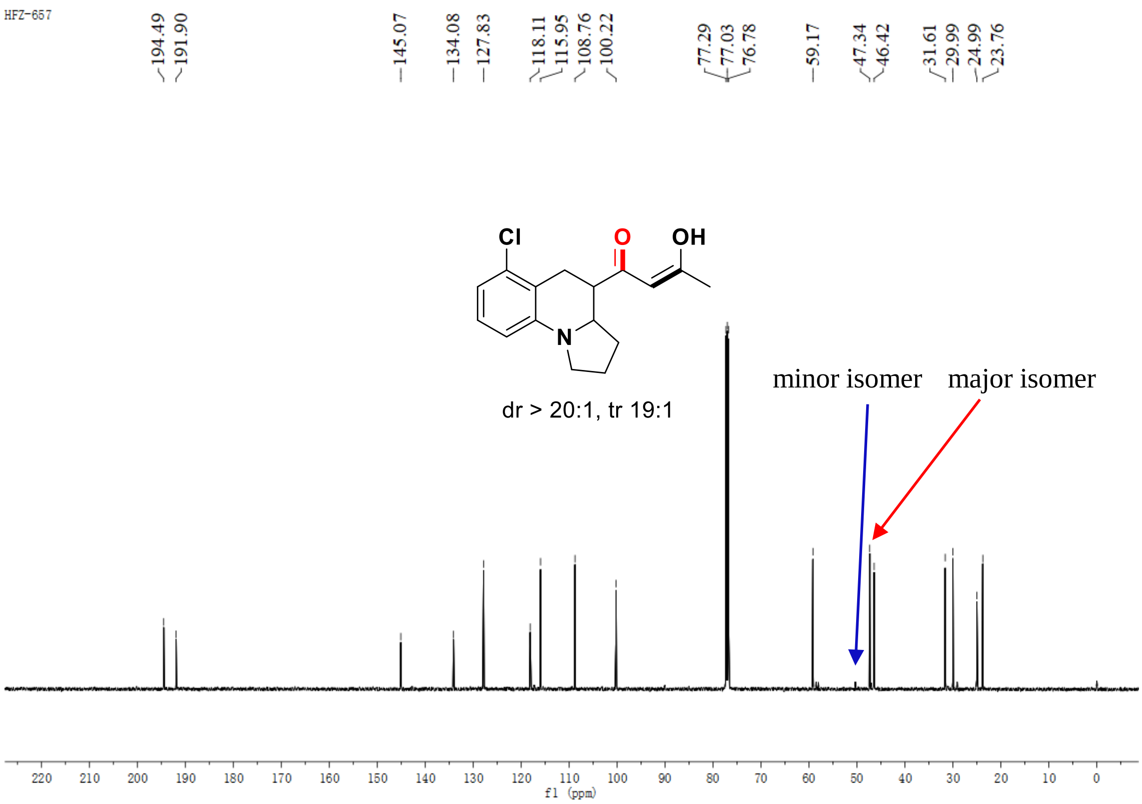
(Z)-1-(1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8a)



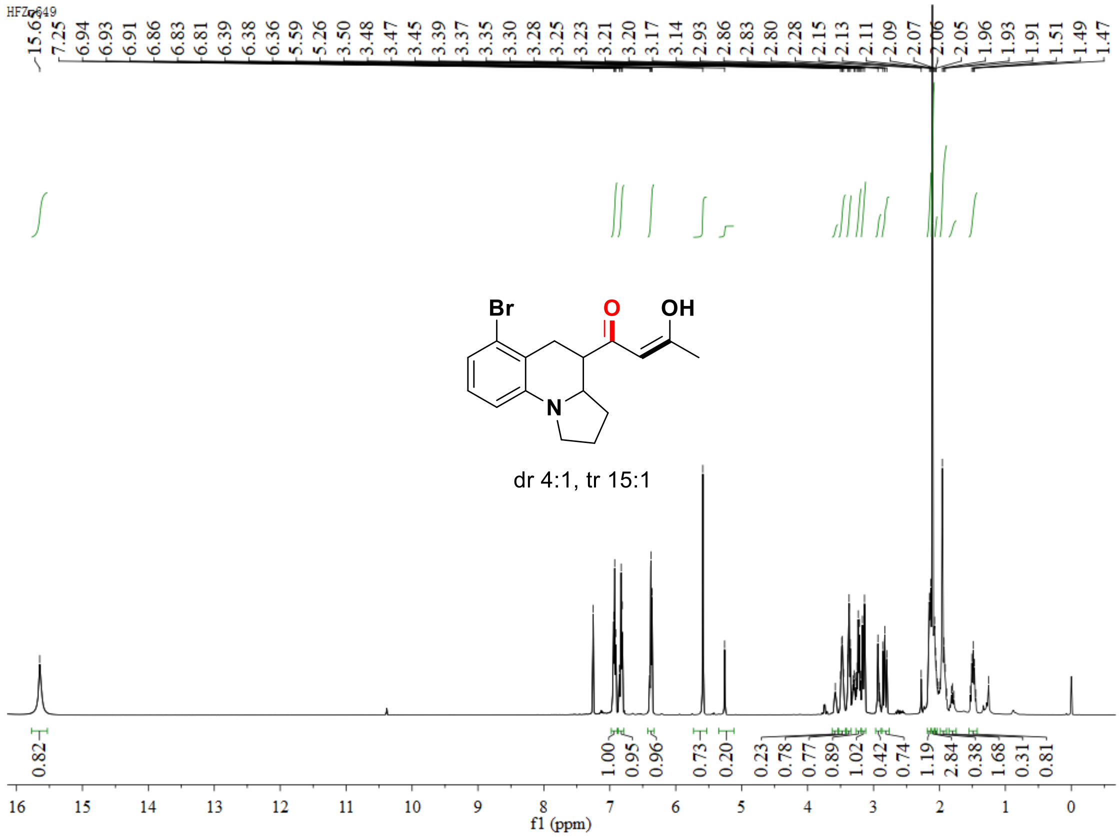


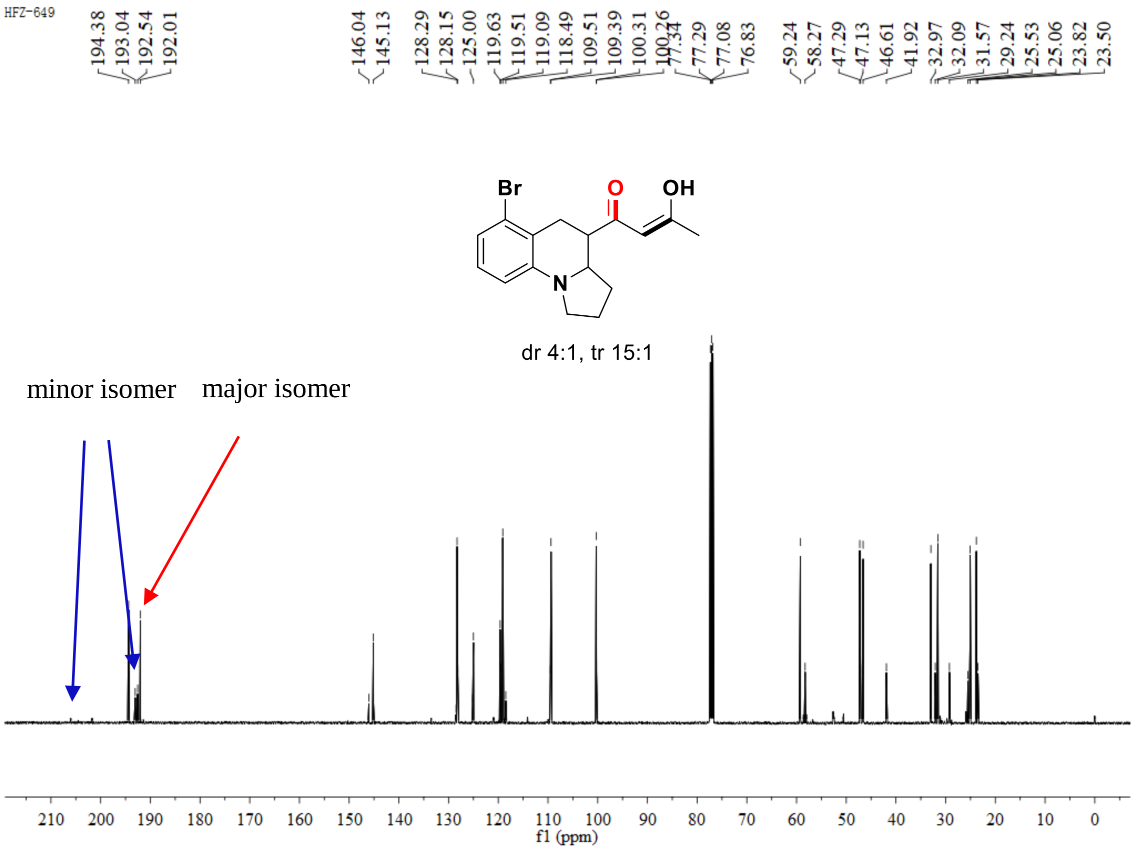
(Z)-1-(6-chloro-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8b)



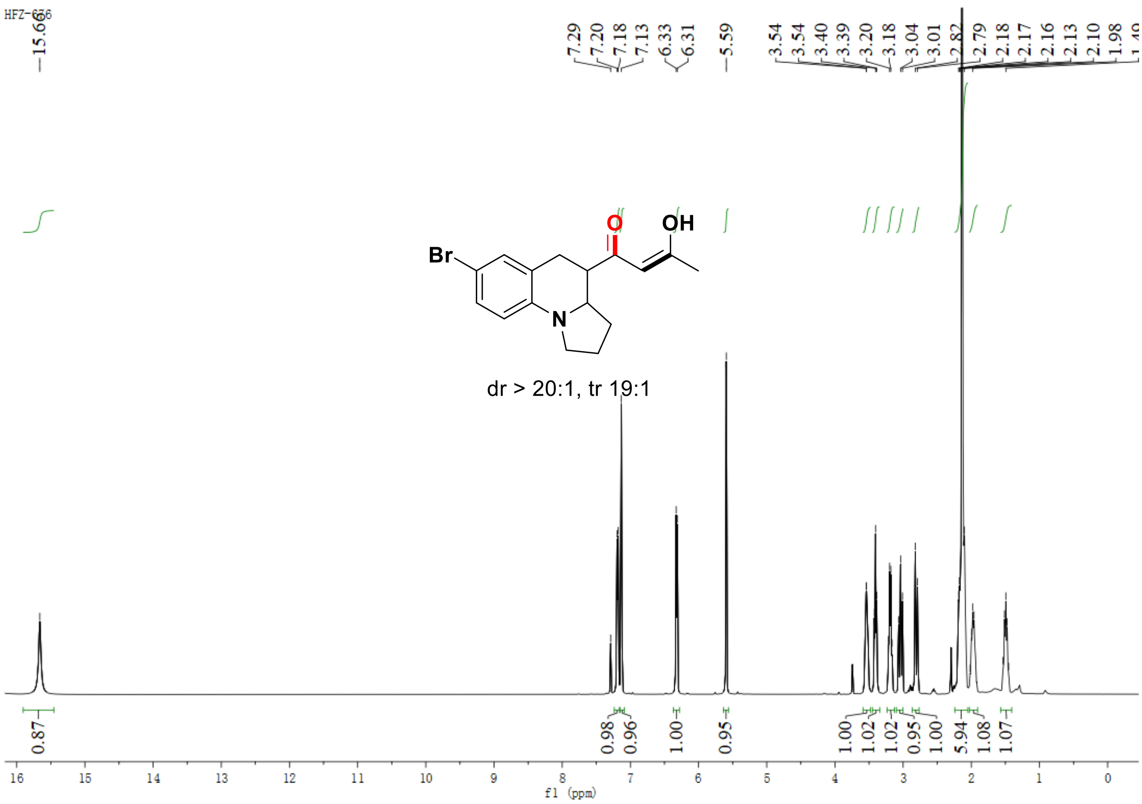


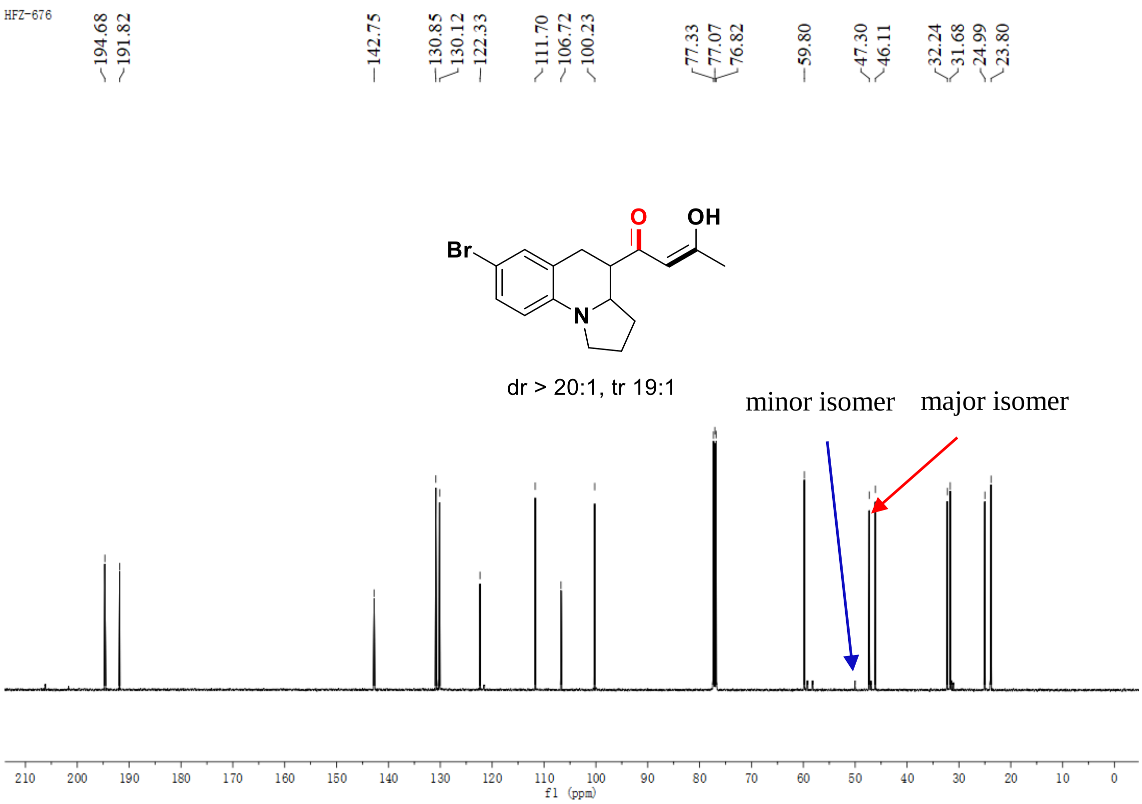
(Z)-1-(6-bromo-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8c)



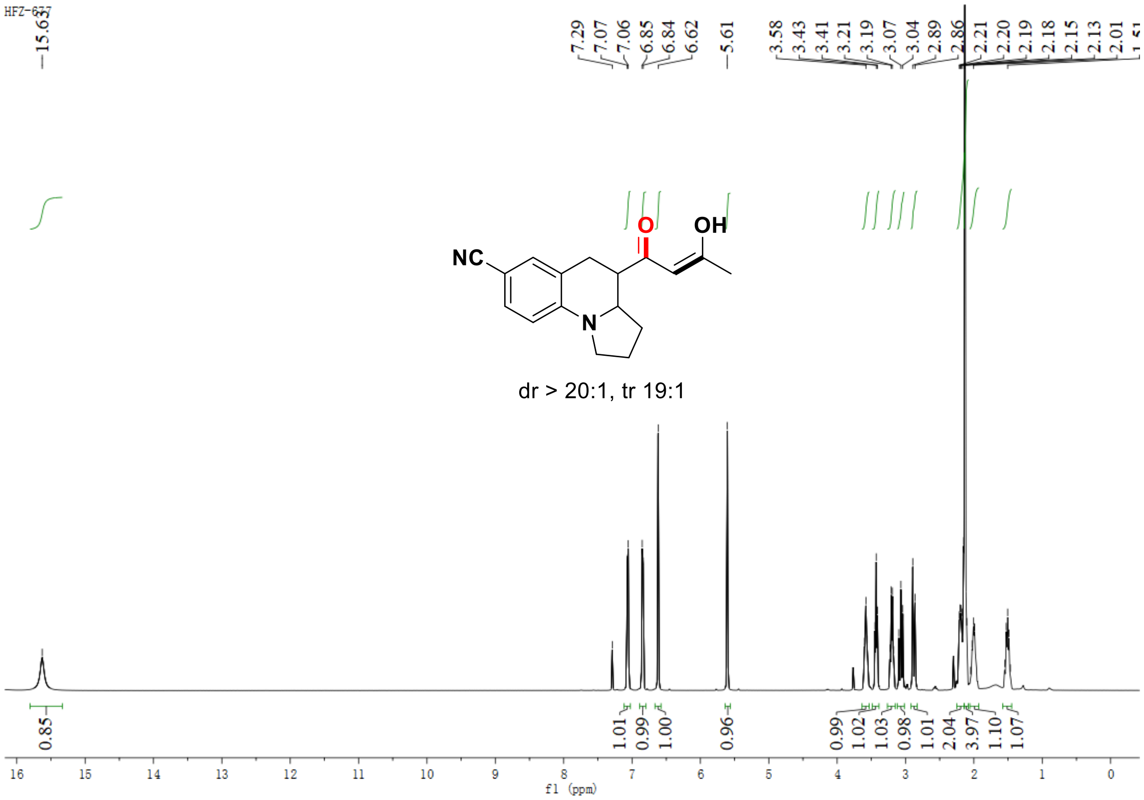


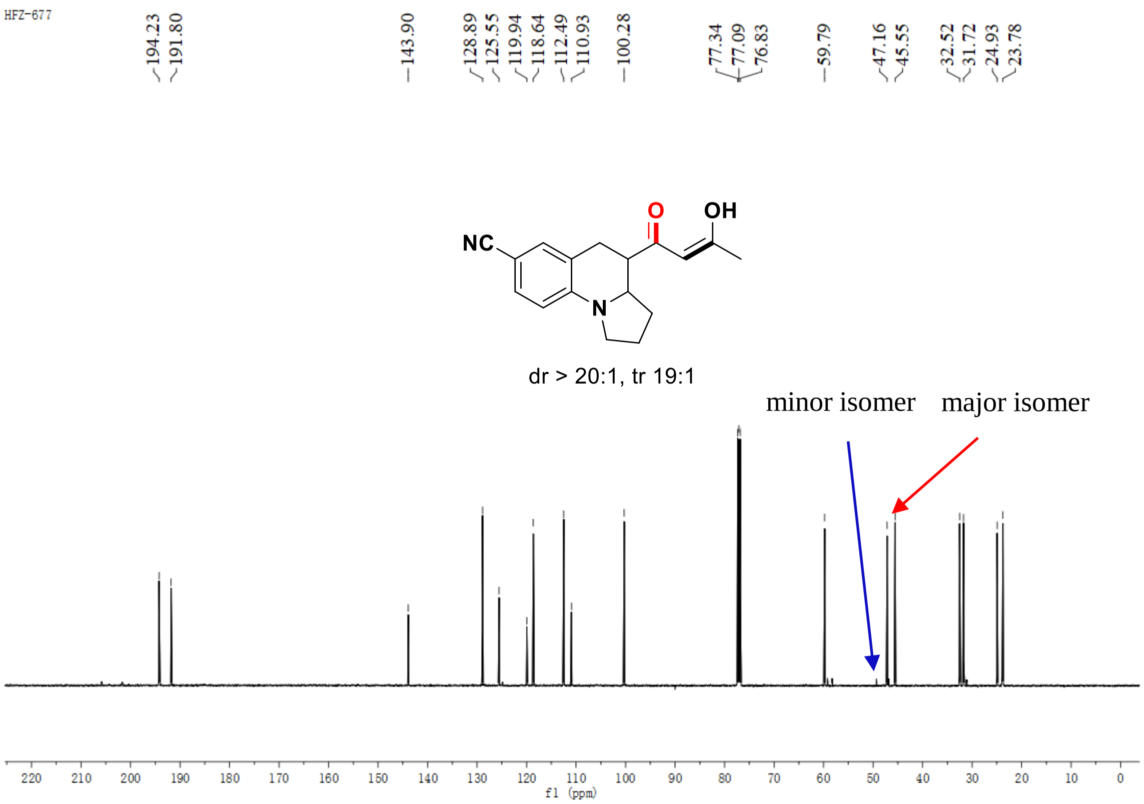
(Z)-1-(7-bromo-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8d)



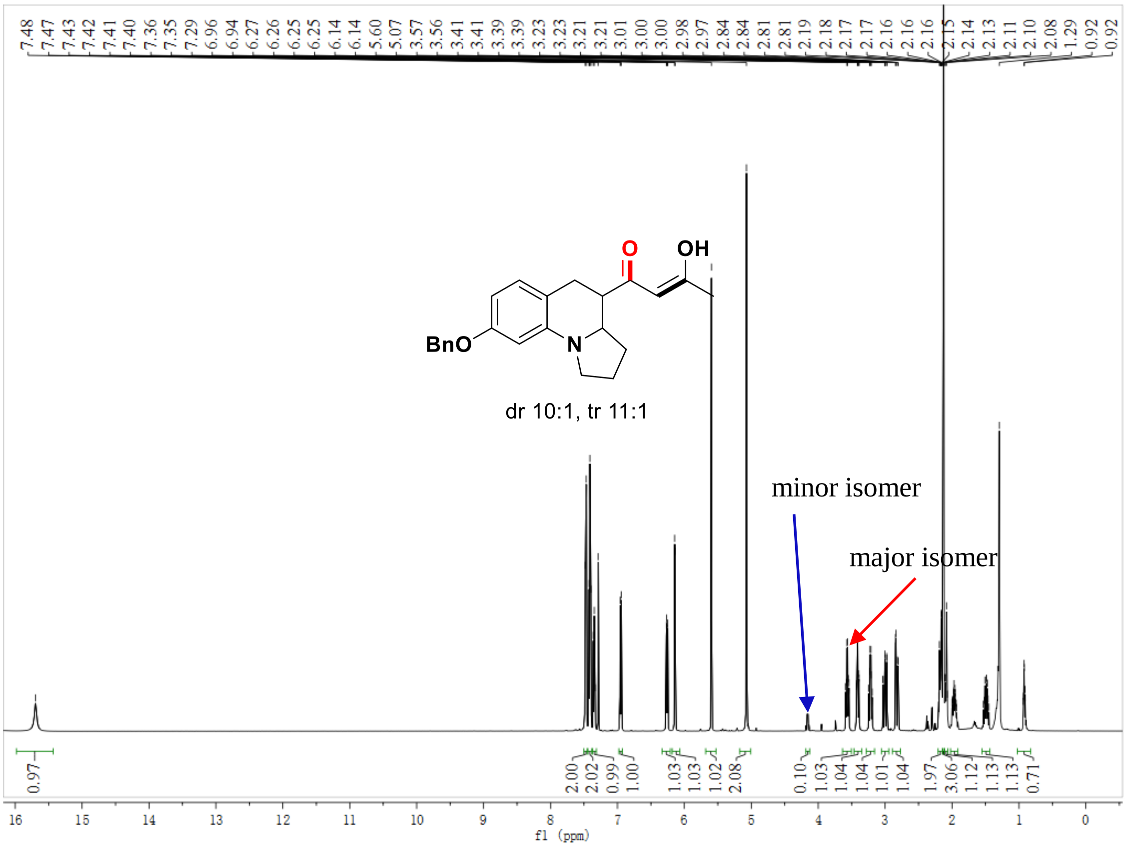


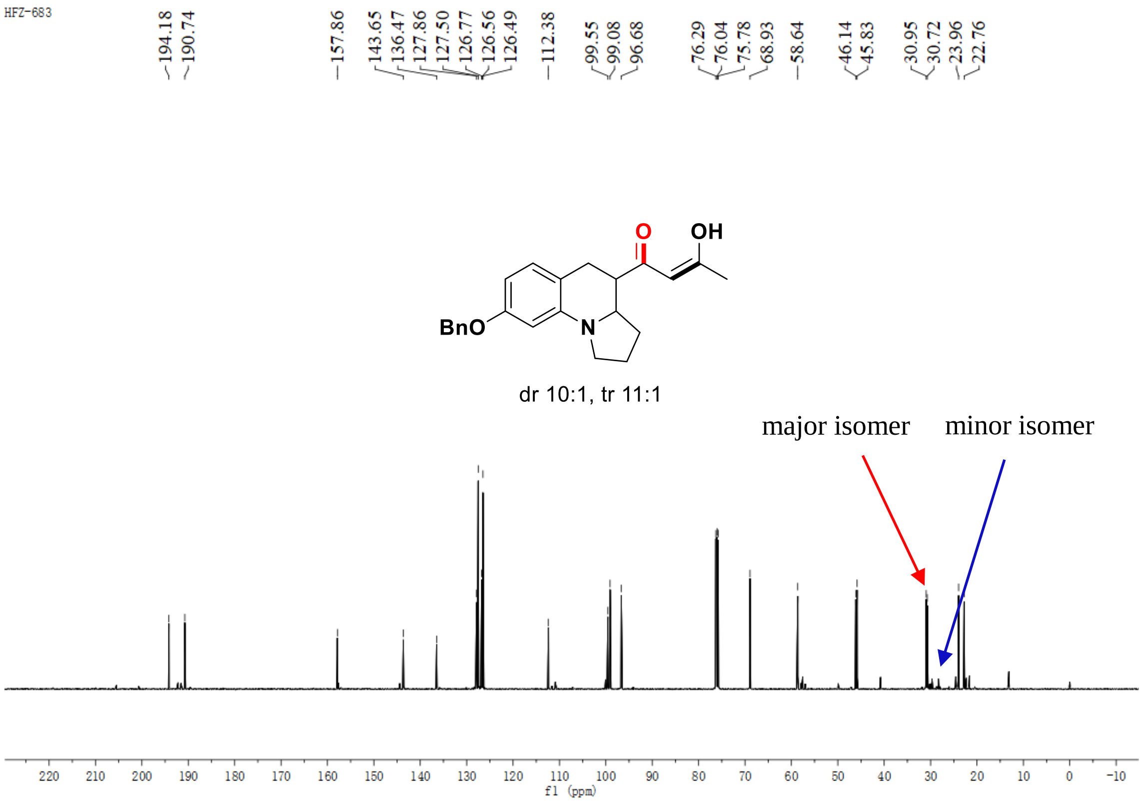
(Z)-4-(3-hydroxybut-2-enoyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-7-carbonitrile (8e)



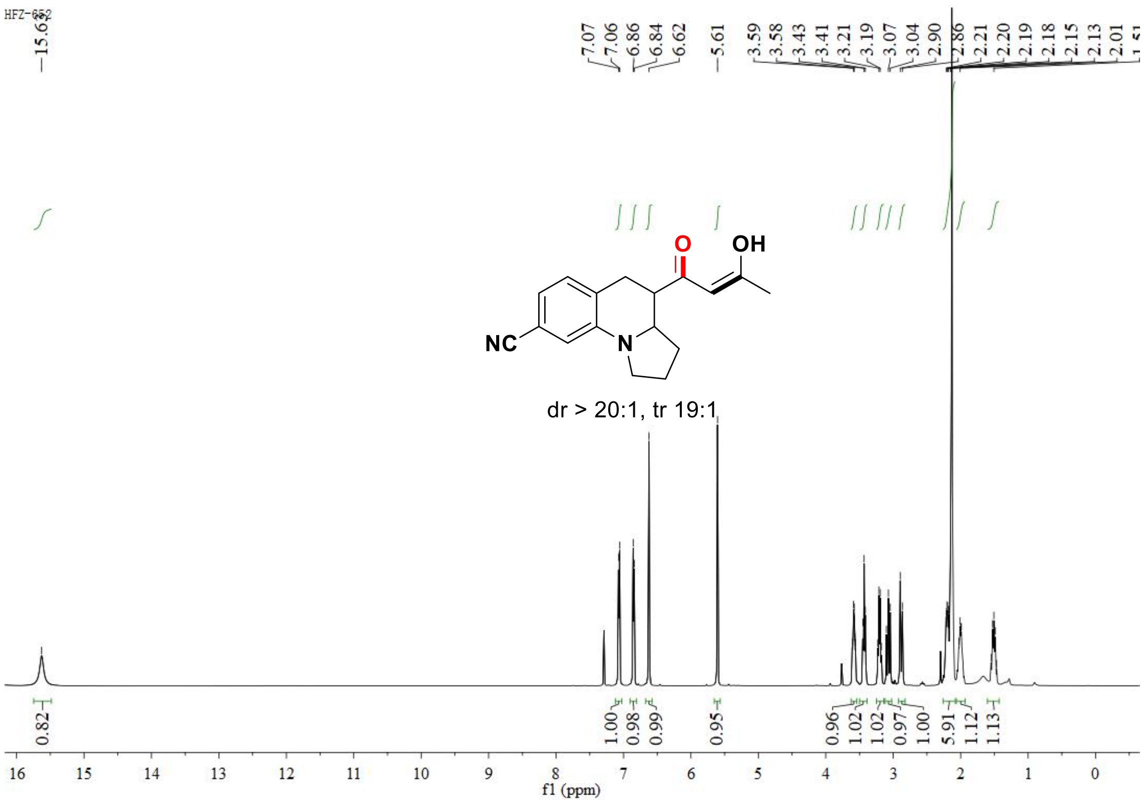


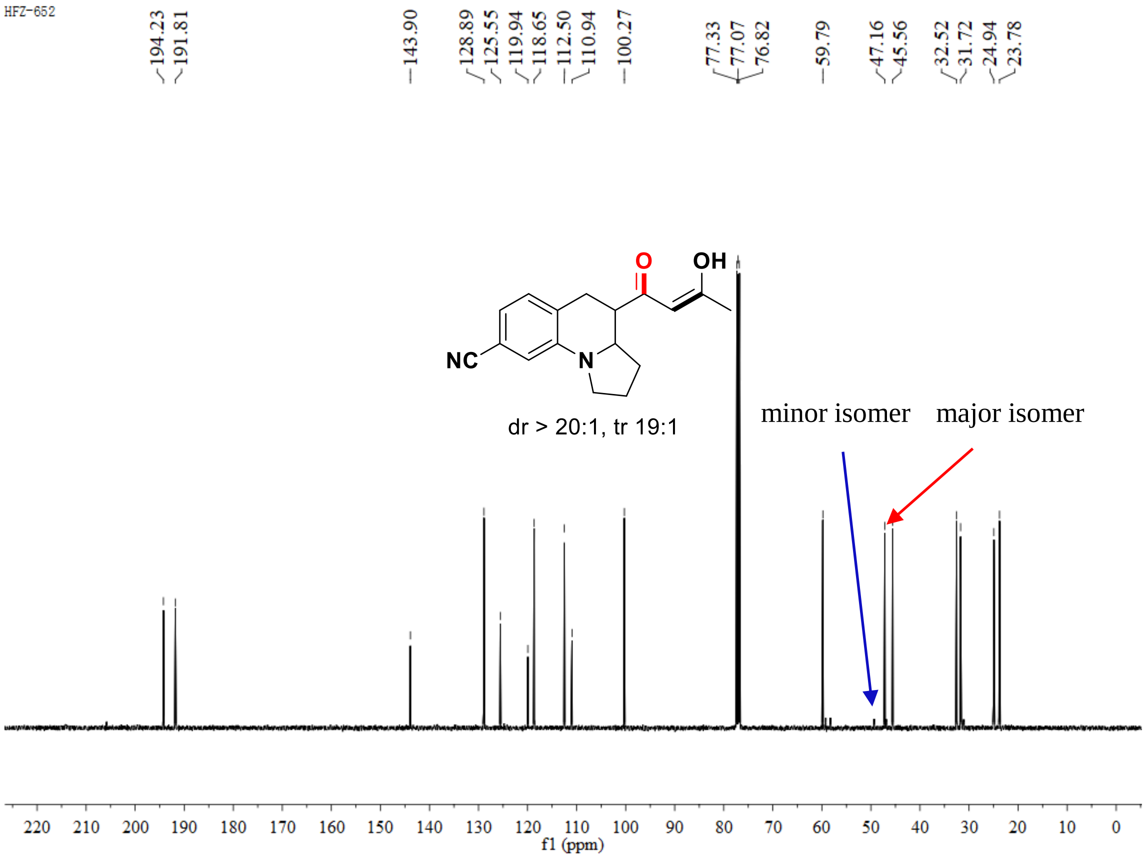
(Z)-1-(8-(benzyloxy)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-3-hydroxybut-2-en-1-one (8f)



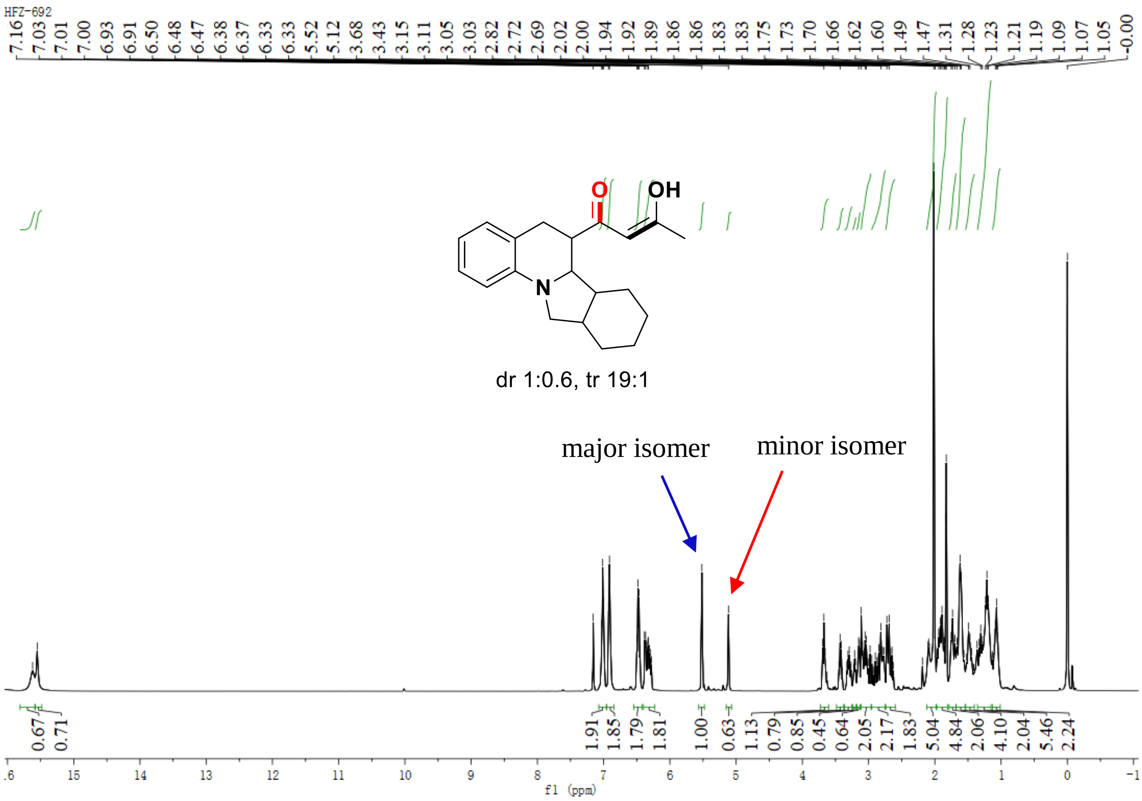


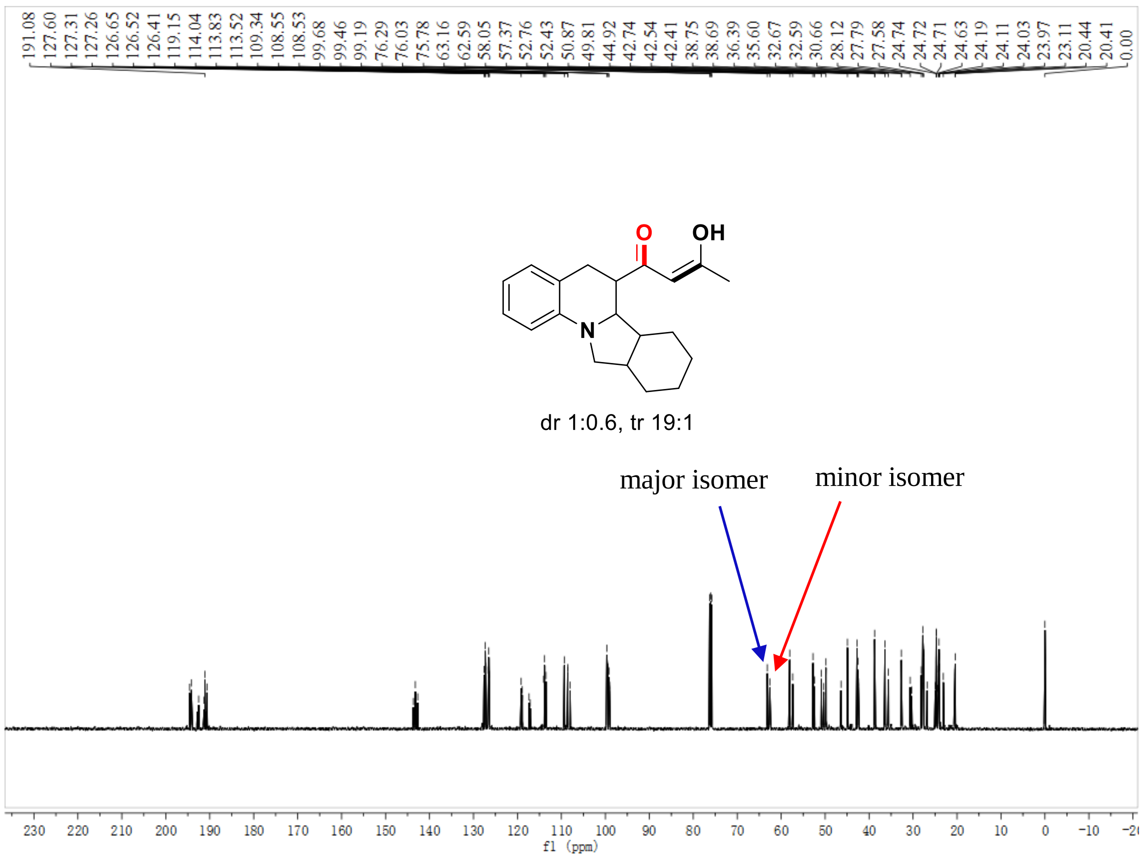
(Z)-4-(3-hydroxybut-2-enoyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-8-carbonitrile (8g)



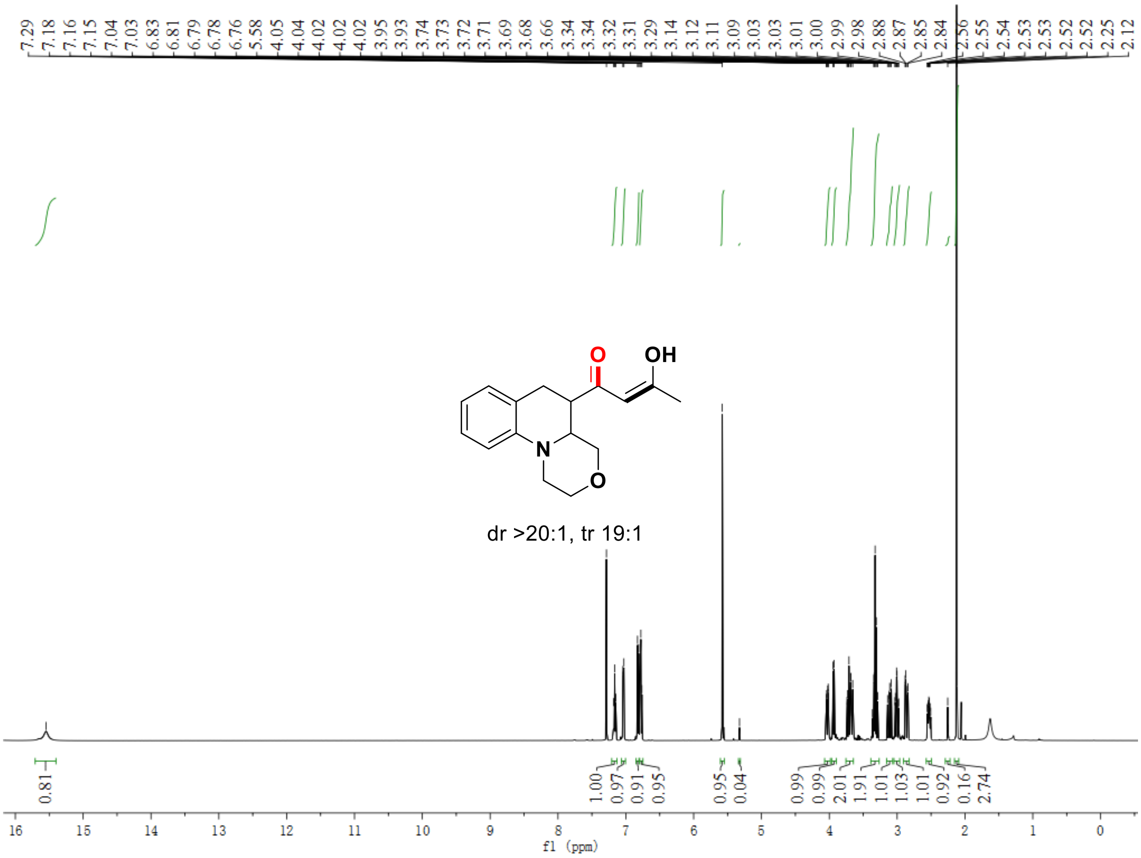


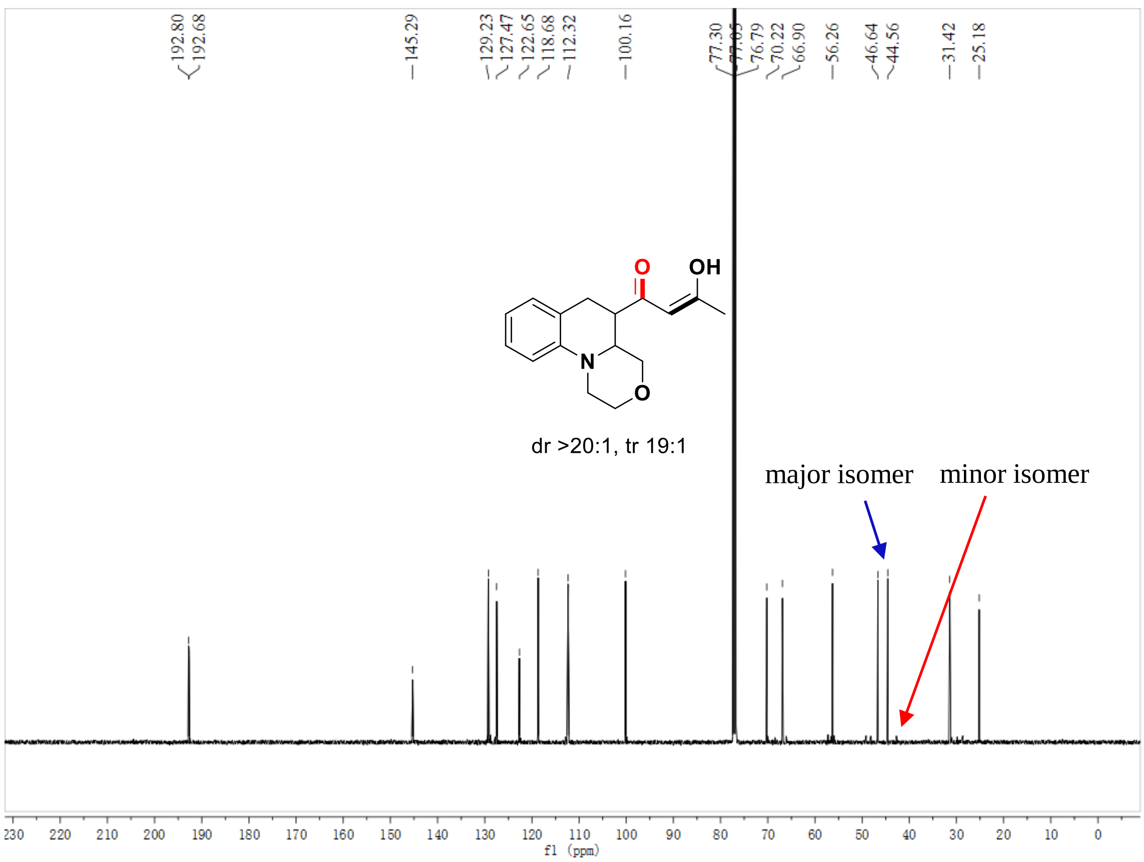
(Z)-1-(5,6,6a,6b,7,8,9,10,10a,11-decahydroisoindolo[2,1-a]quinolin-6-yl)-3-hydroxybut-2-en-1-one (8h)



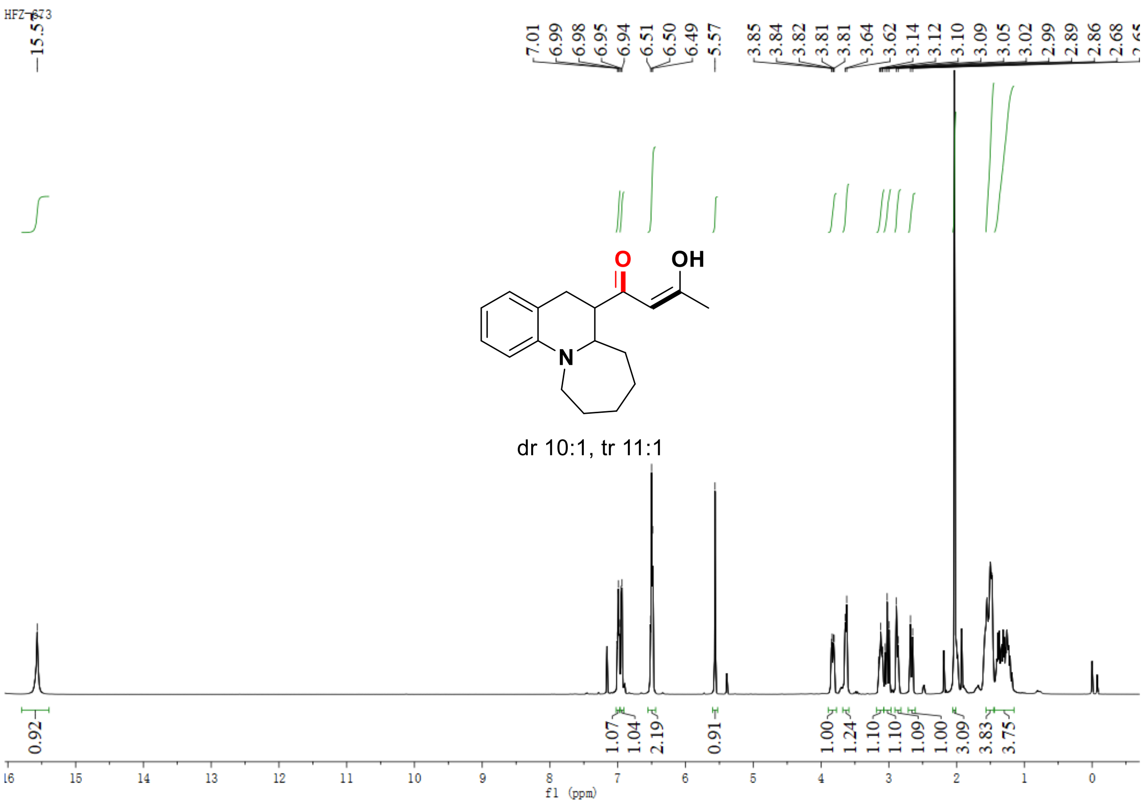


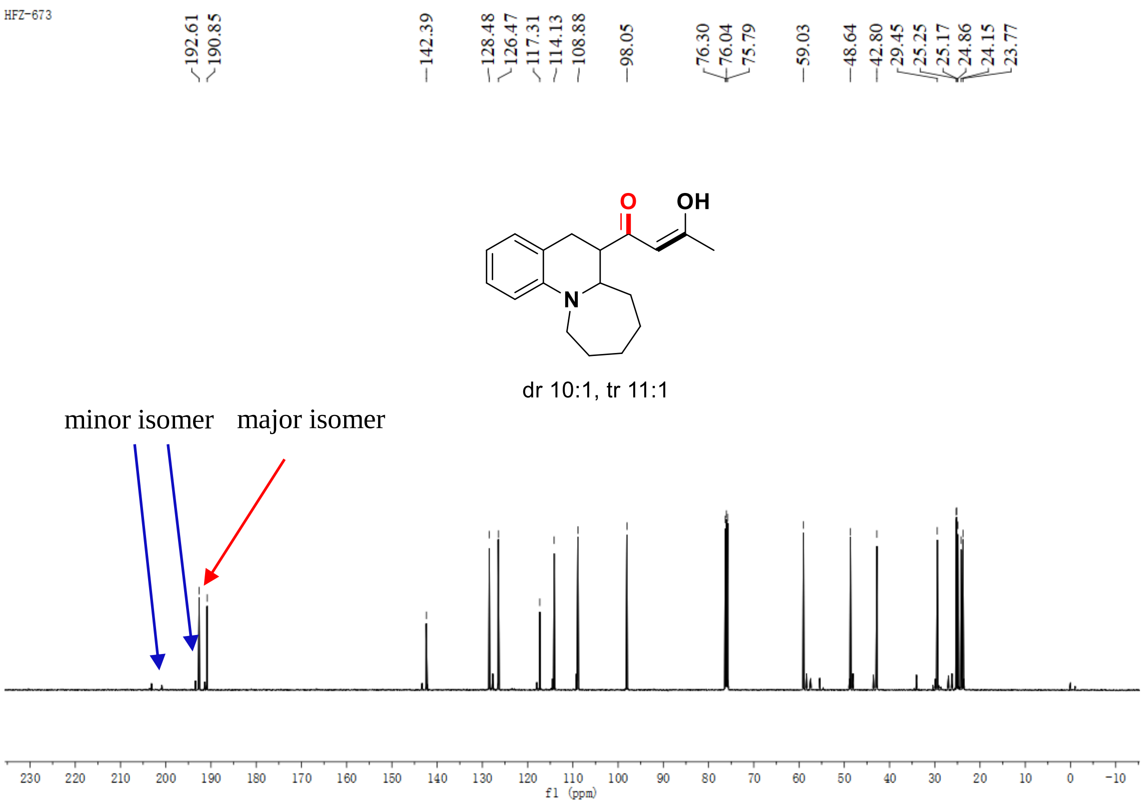
(Z)-1-(1,2,4,4a,5,6-hexahydro-[1,4]oxazino[4,3-a]quinolin-5-yl)-3-hydroxybut-2-en-1-one (8i)



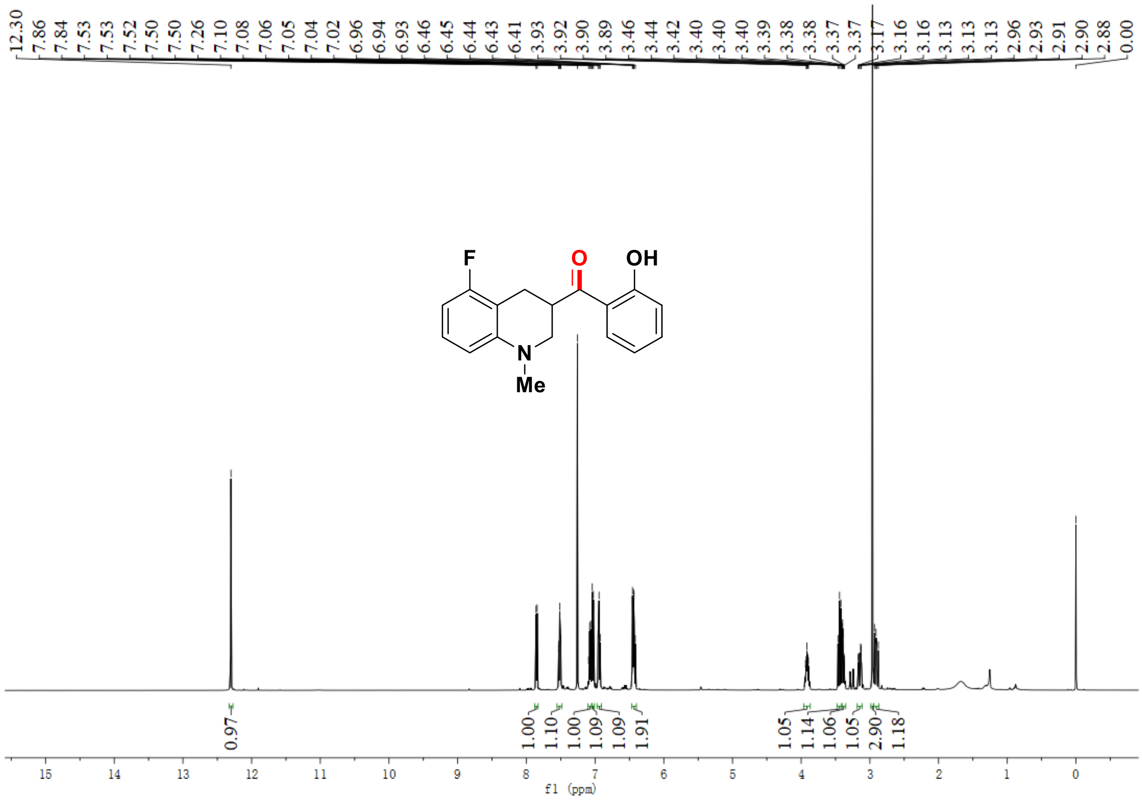


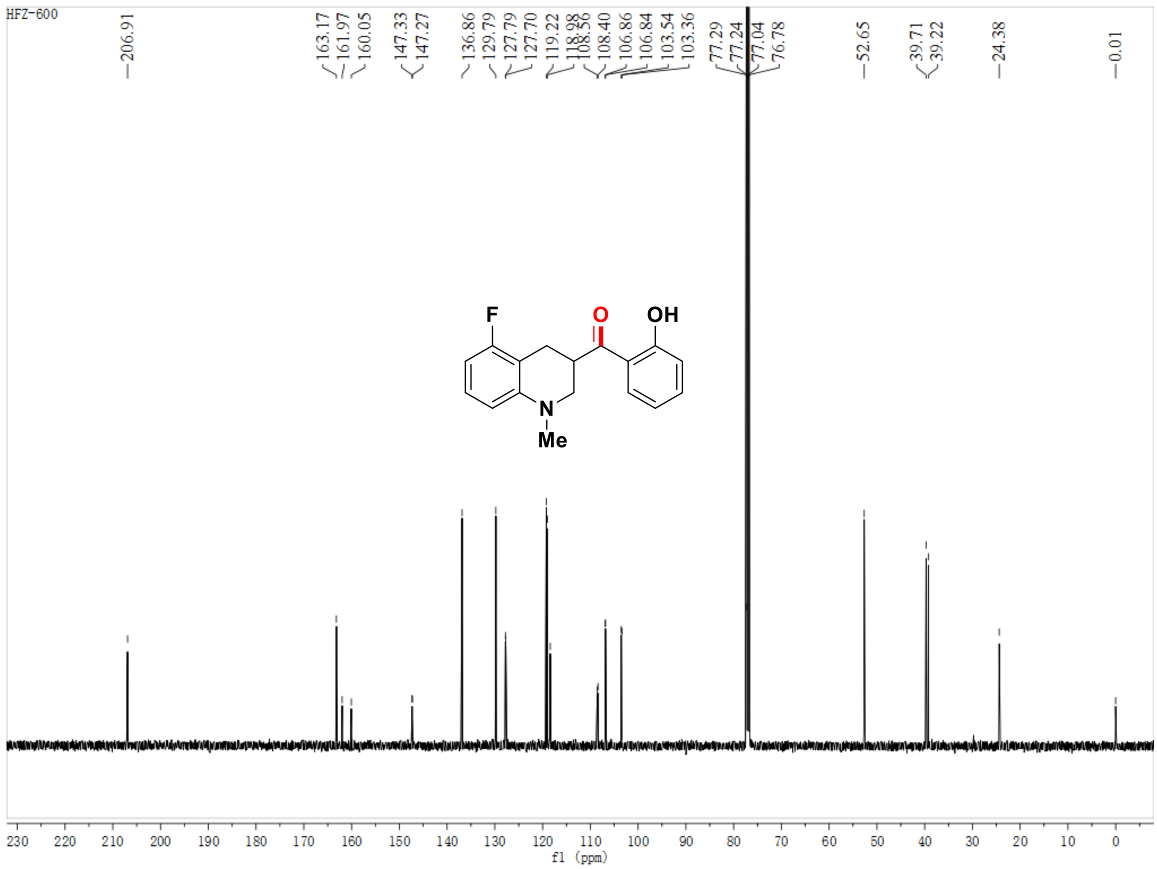
(Z)-3-hydroxy-1-(5,6,6a,7,8,9,10,11-octahydroazepino[1,2-a]quinolin-6-yl)but-2-en-1-one (8j)

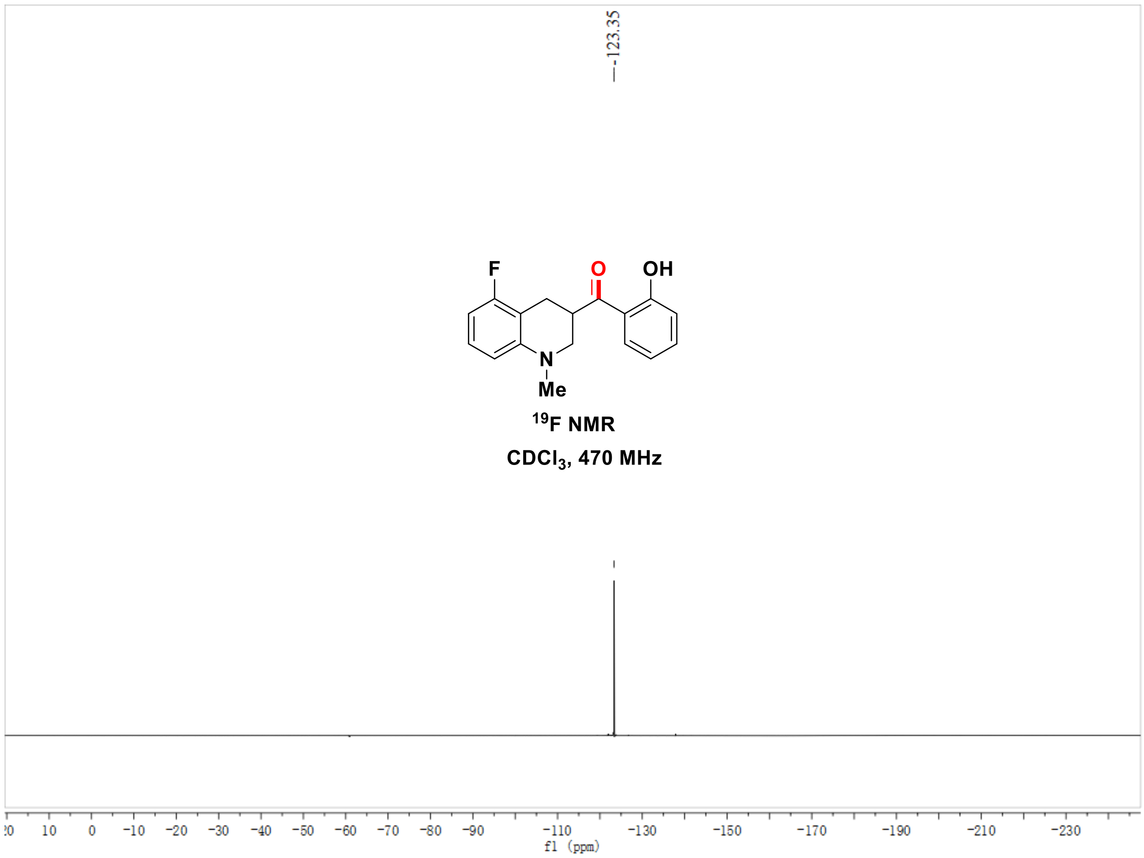




(5-fluoro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9a)







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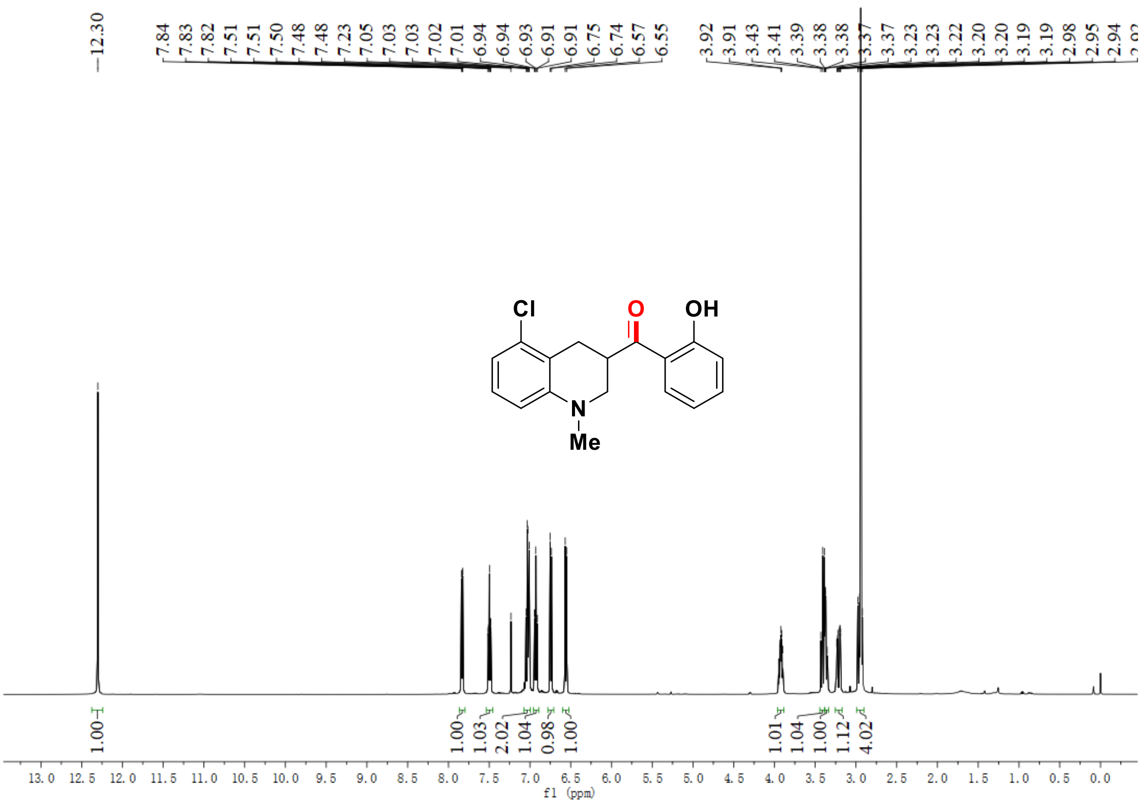
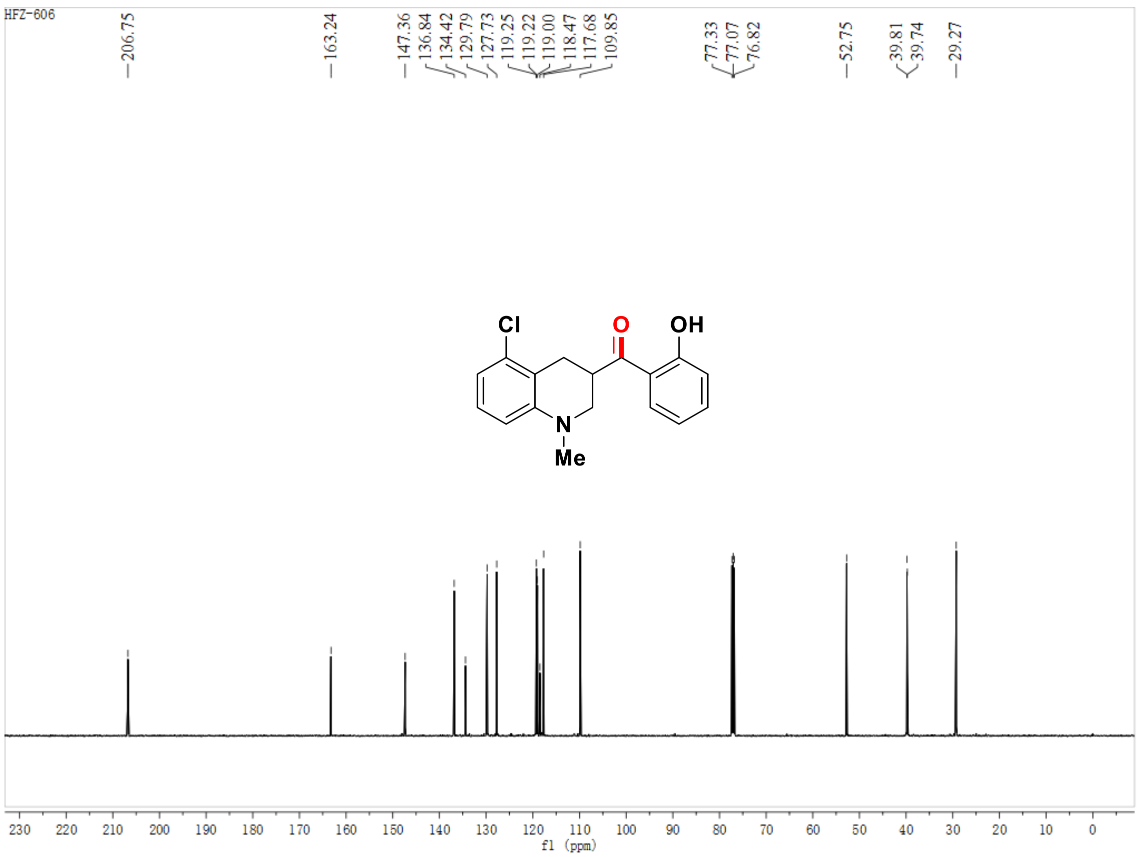
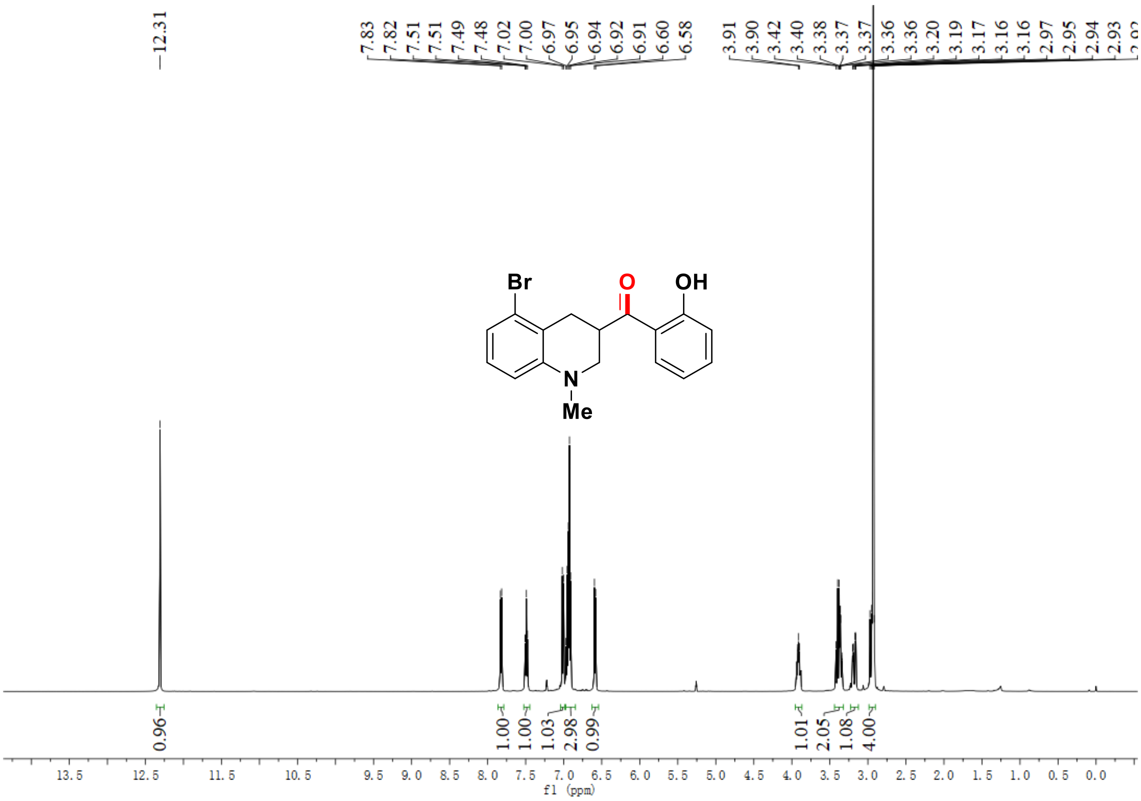
O
OH
N
Me
19F NMR
CDCl3, 470 MHz
f1 (ppm)

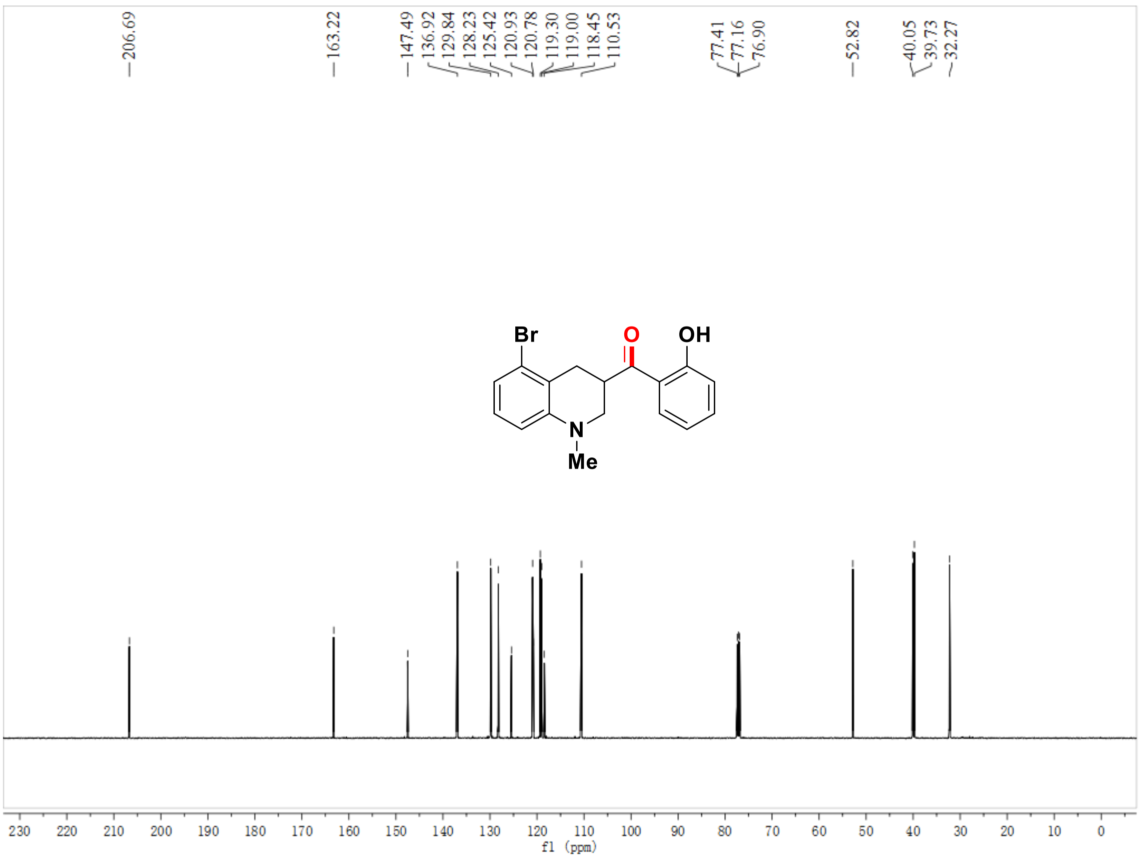
(5-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9b)



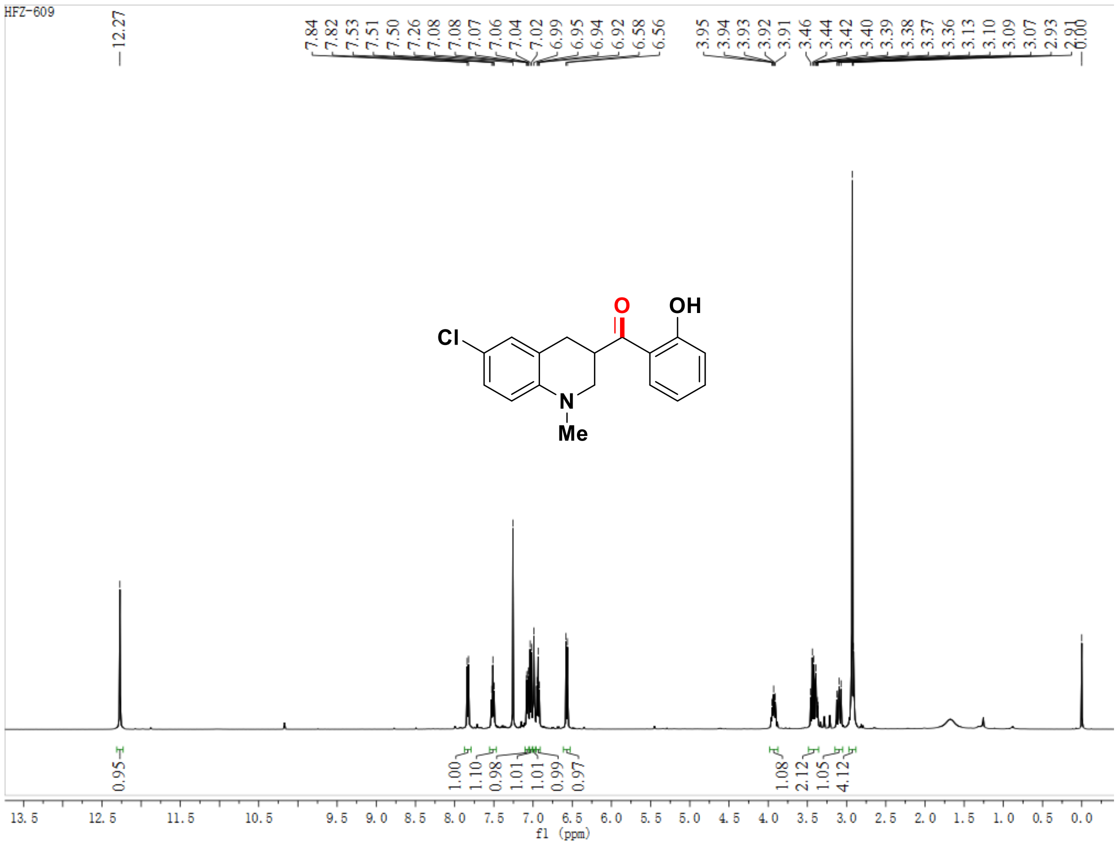


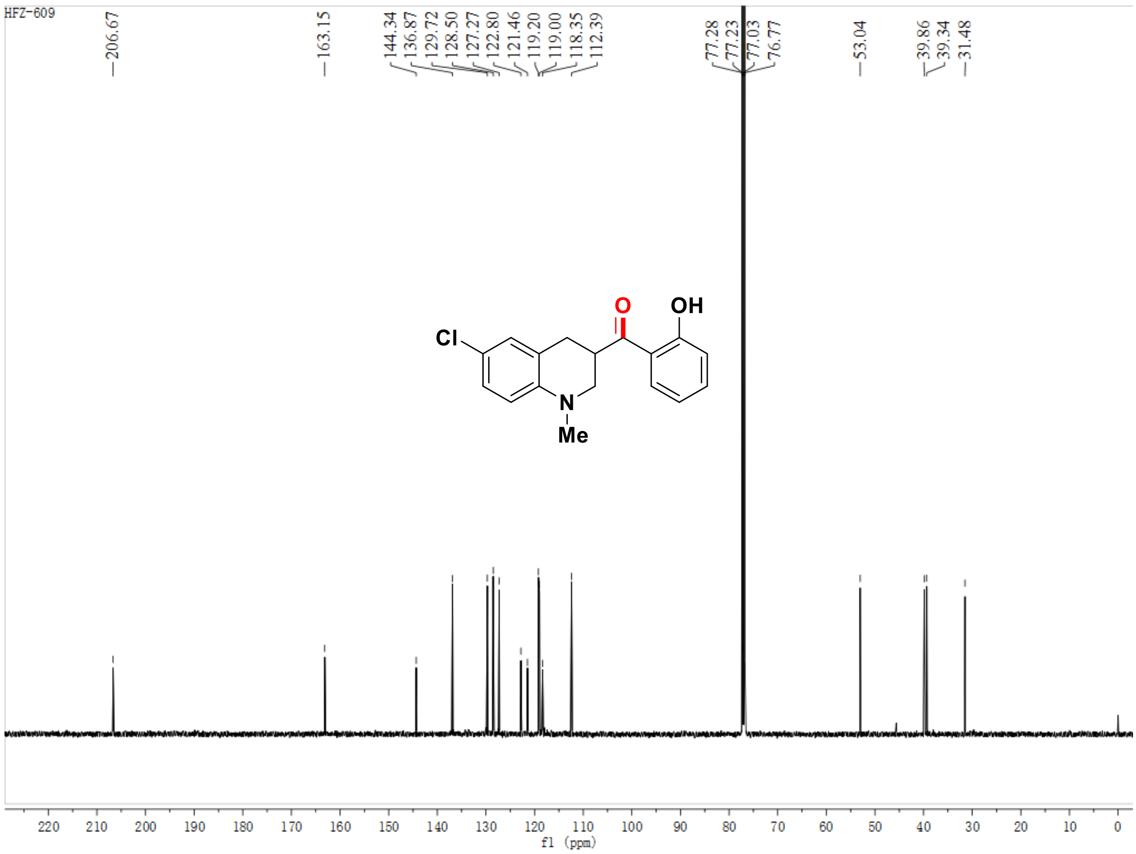
(5-bromo-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9c)



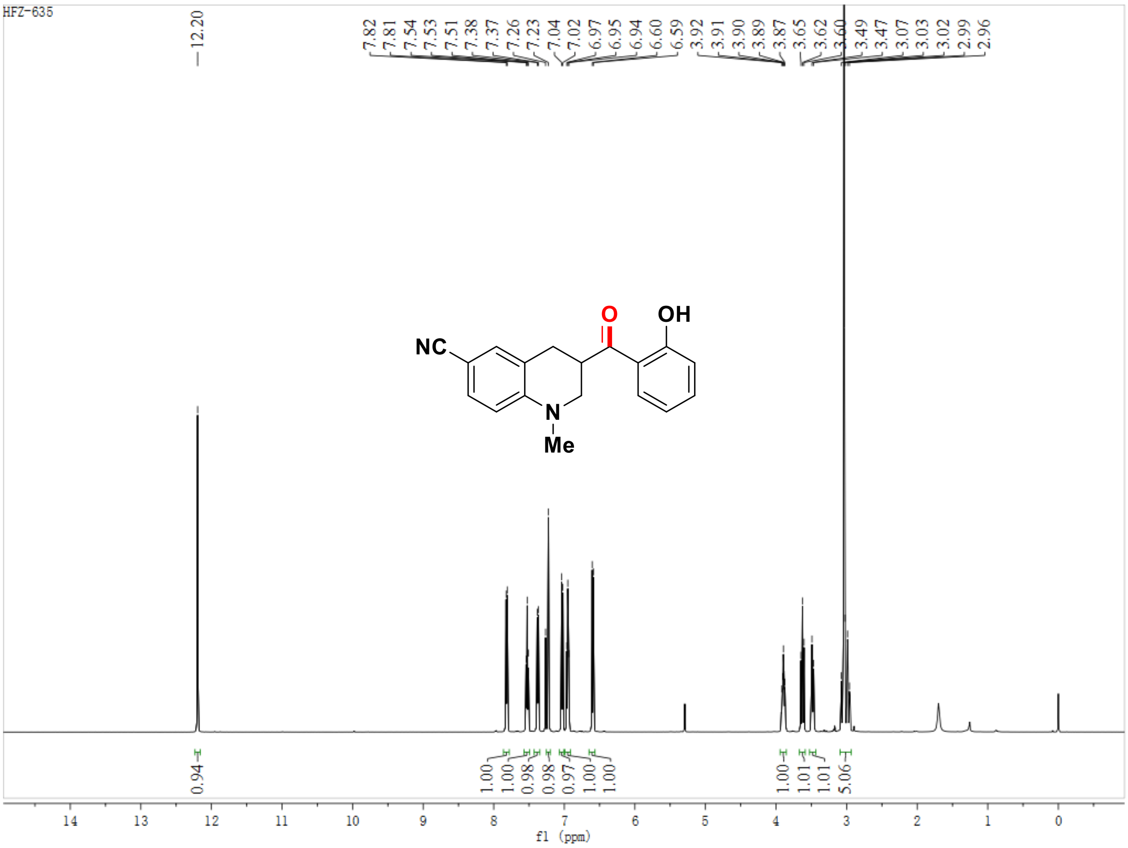


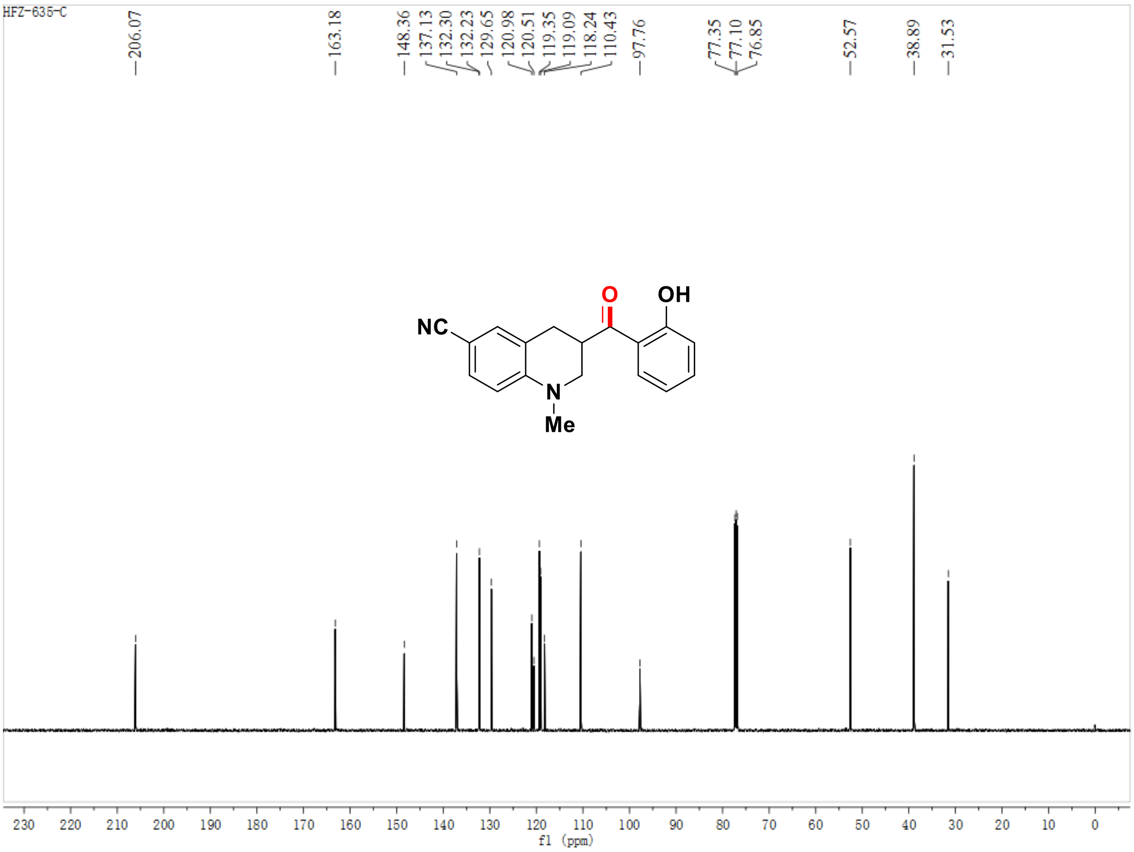
(6-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9d)



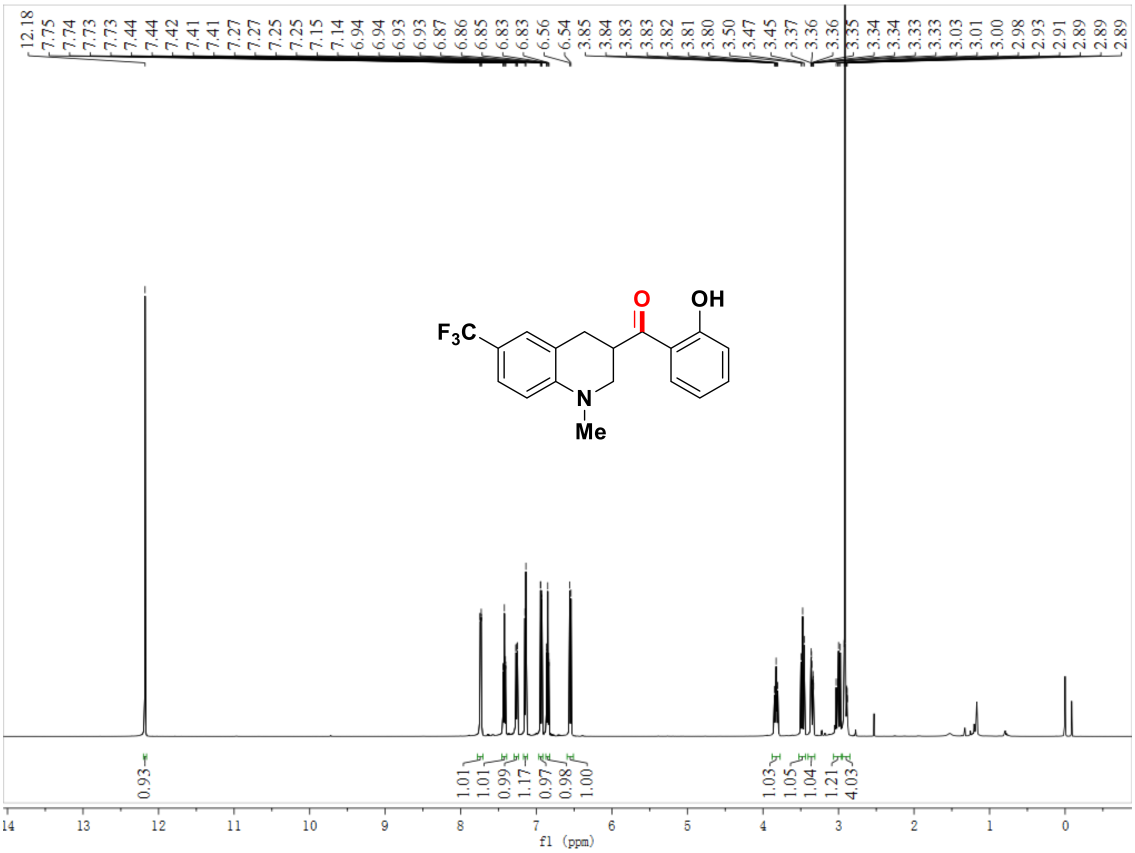


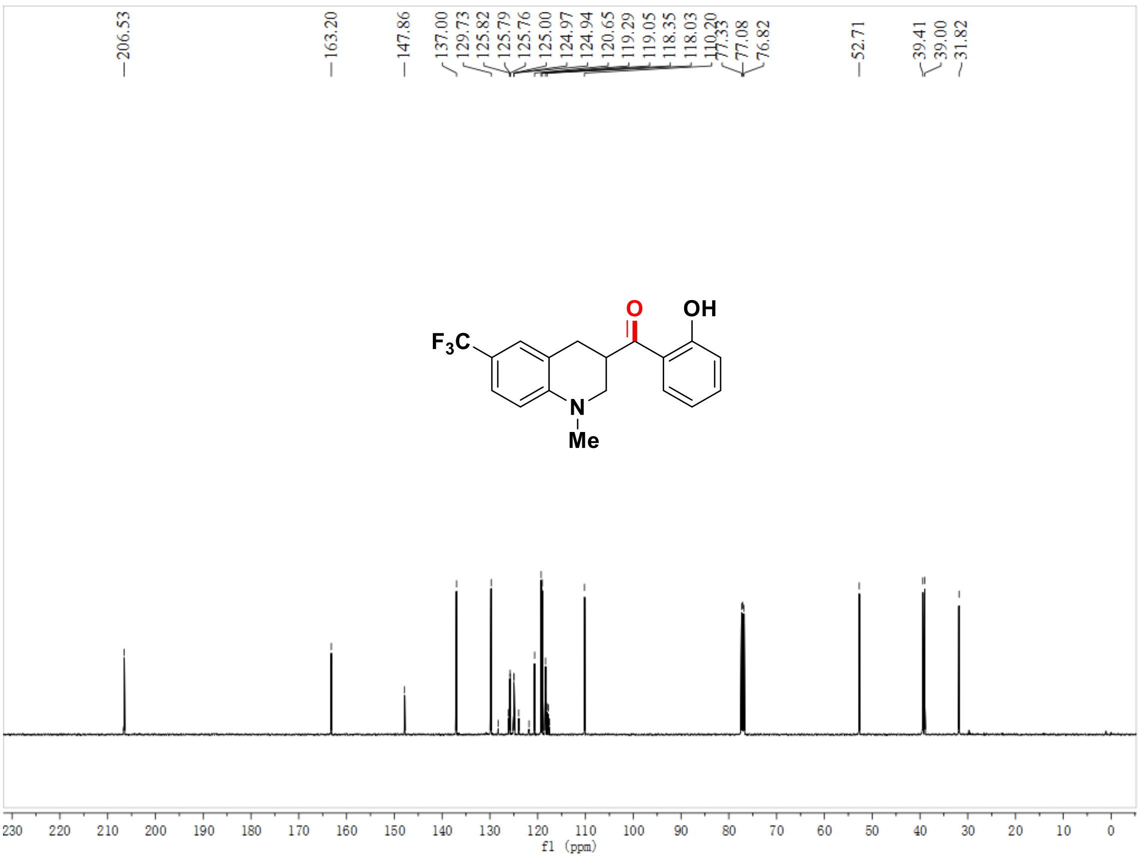
3-(2-hydroxybenzoyl)-1-methyl-1,2,3,4-tetrahydroquinoline-6-carbonitrile (9e)

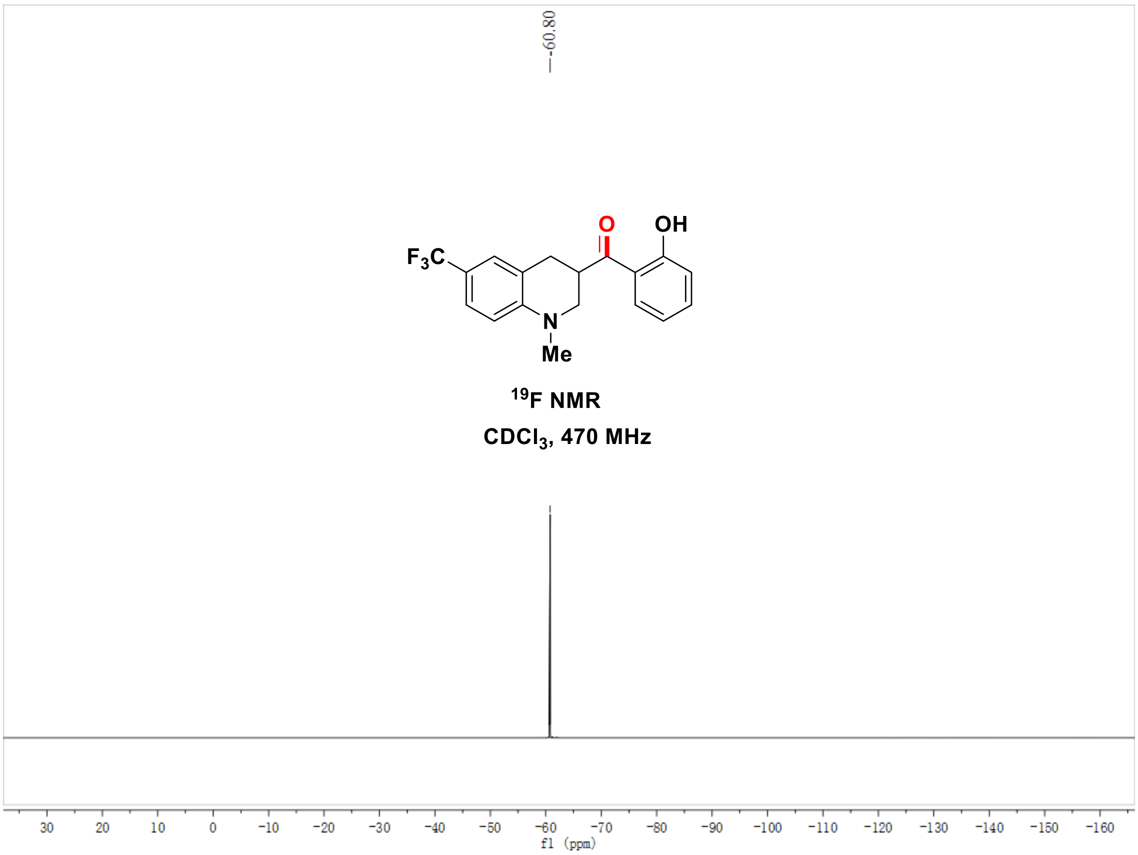




(2-hydroxyphenyl)(1-methyl-6-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-3-yl)methanone (9f)







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CDCl3, 470 MHz
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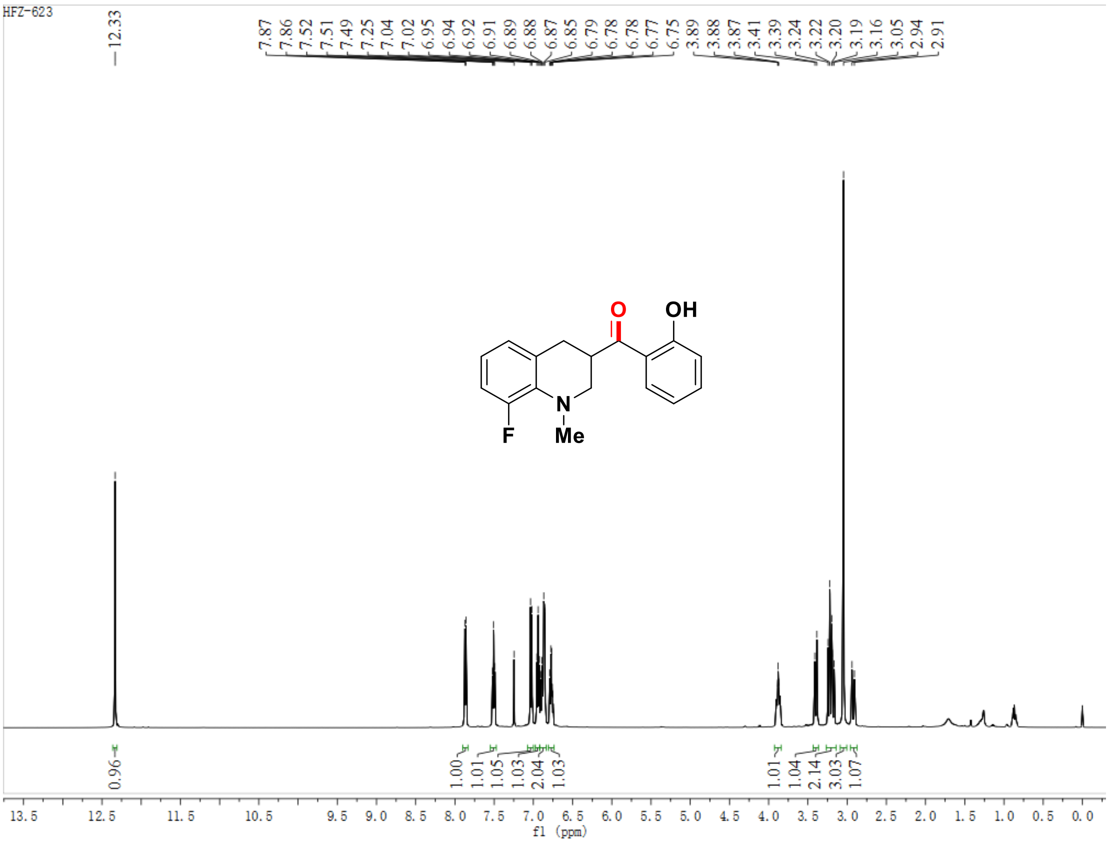
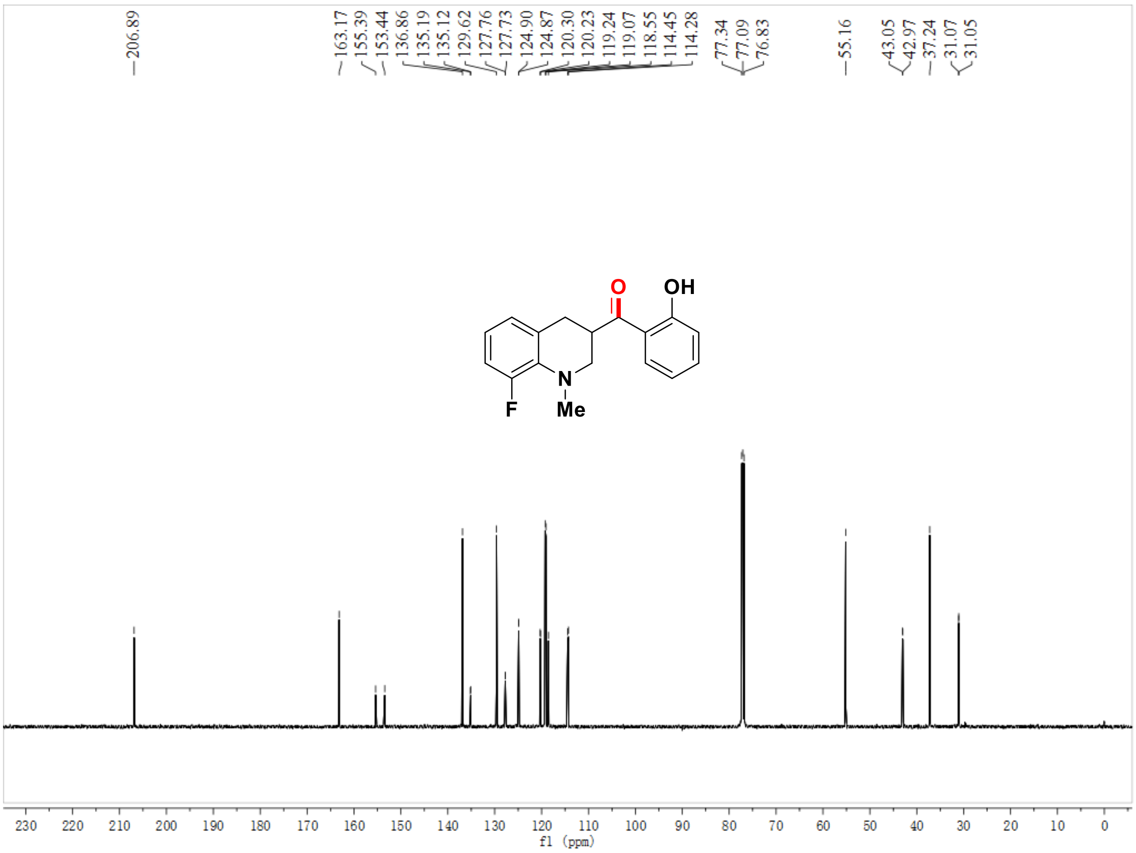
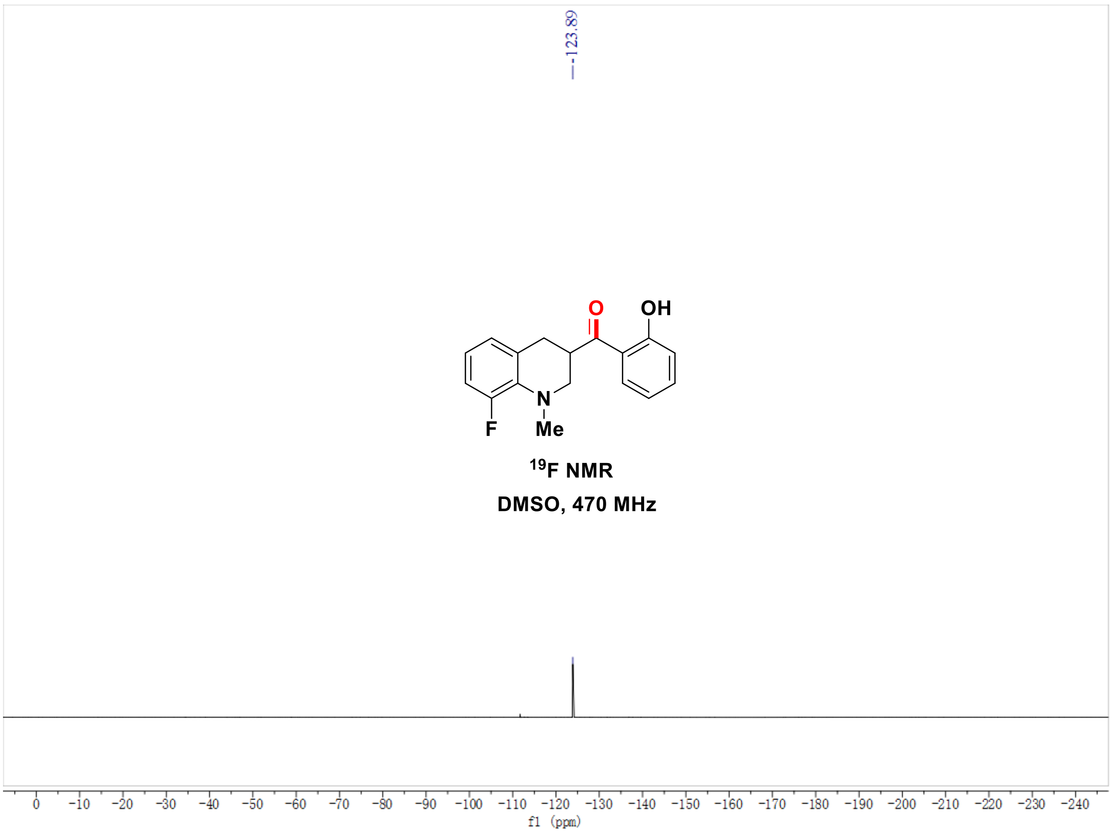
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

(8-fluoro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9g)







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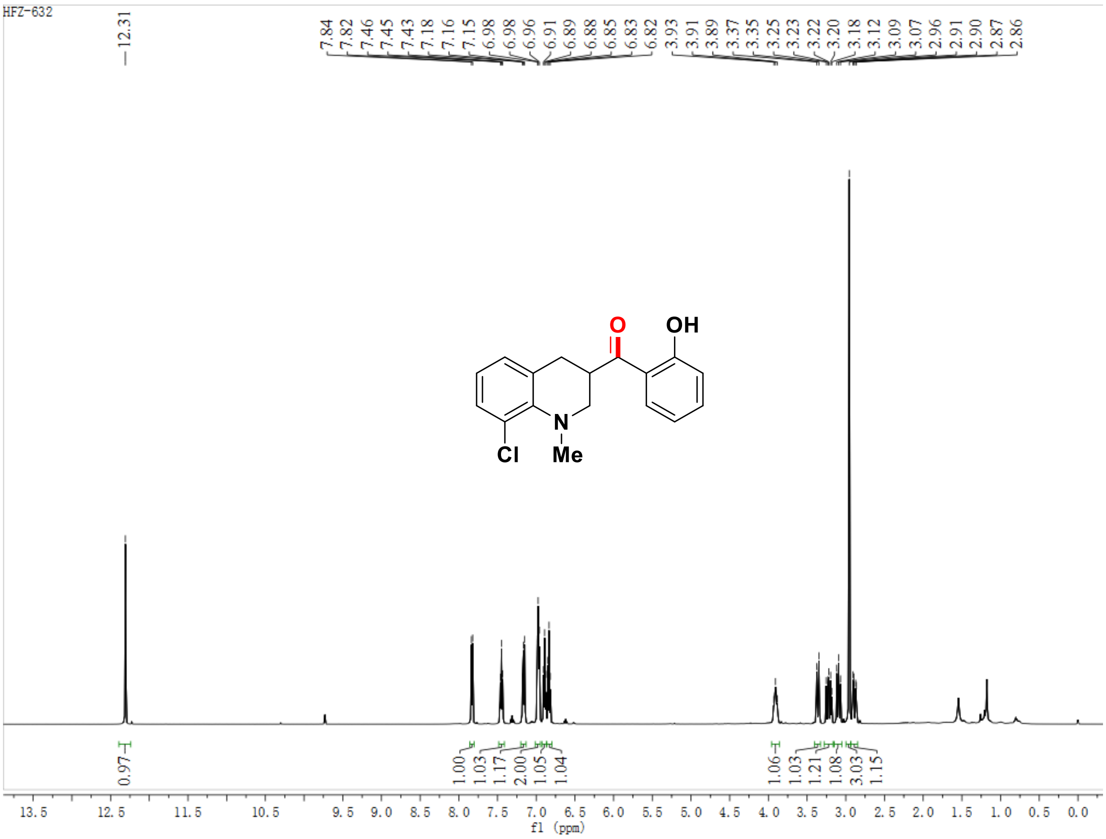
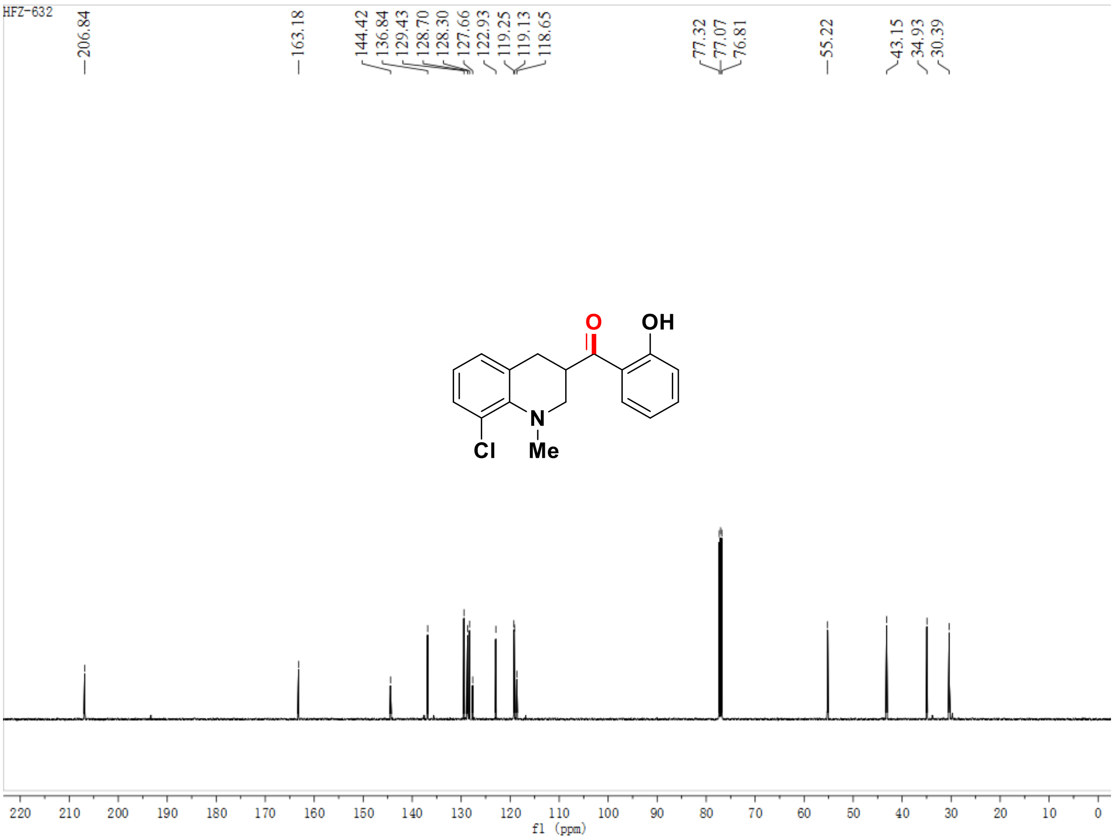
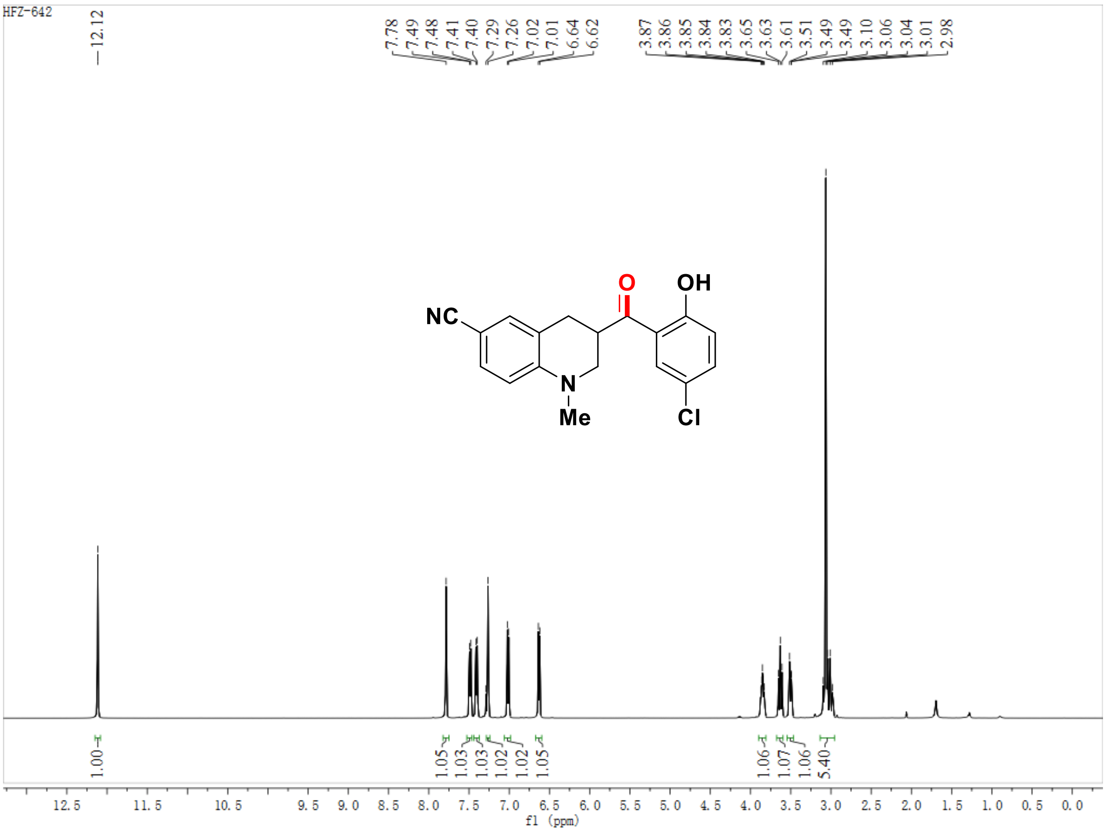
19F NMR
DMSO, 470 MHz
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

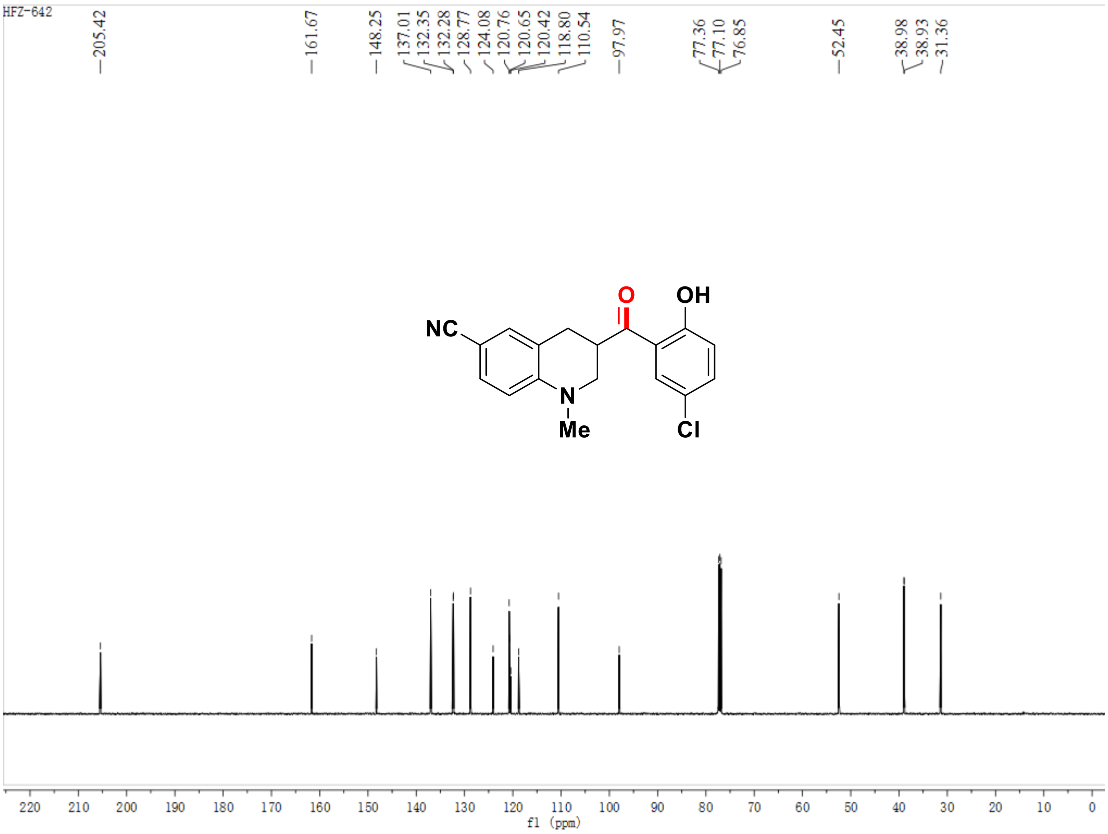
(8-chloro-1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)(2-hydroxyphenyl)methanone (9h)



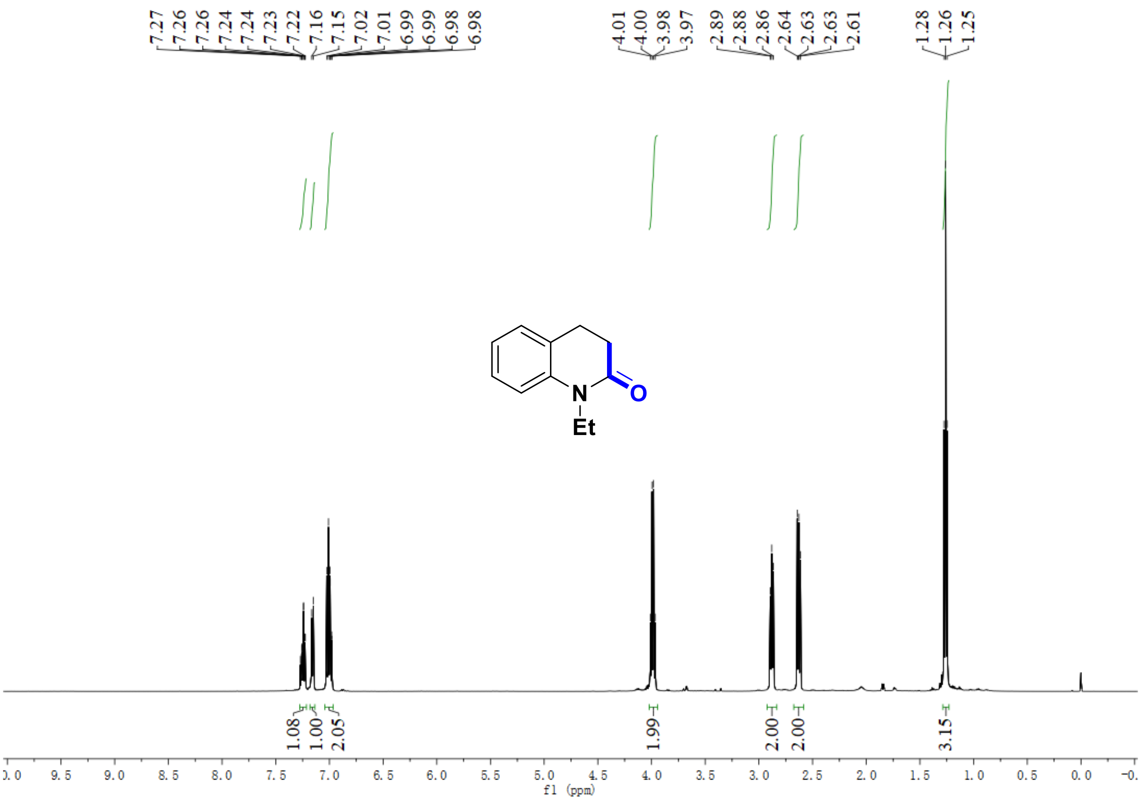


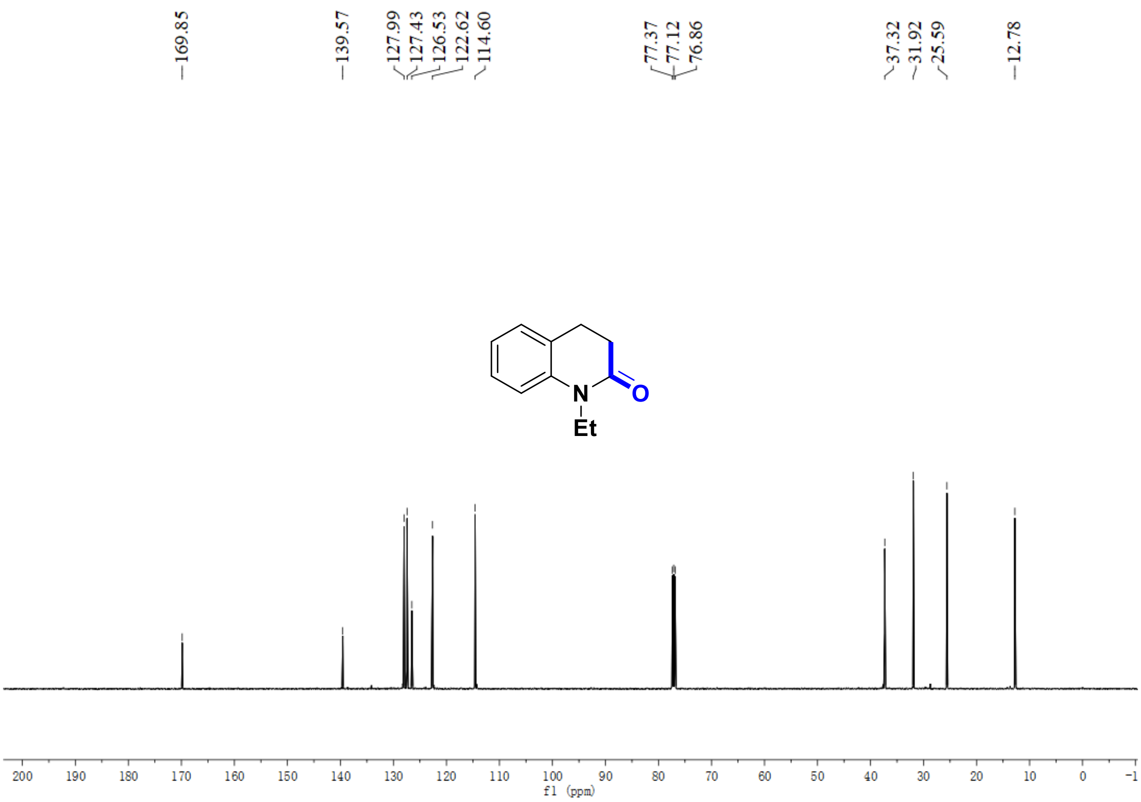
3-(5-chloro-2-hydroxybenzoyl)-1-methyl-1,2,3,4-tetrahydroquinoline-6-carbonitrile (9i)



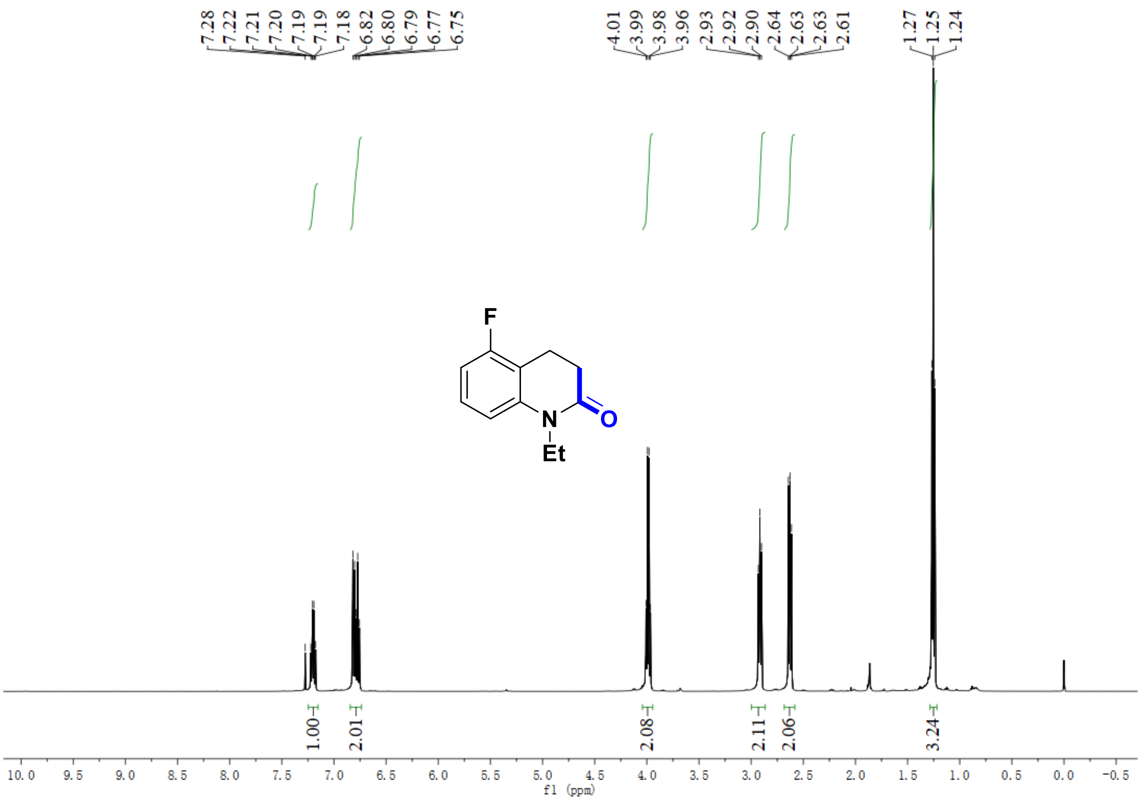


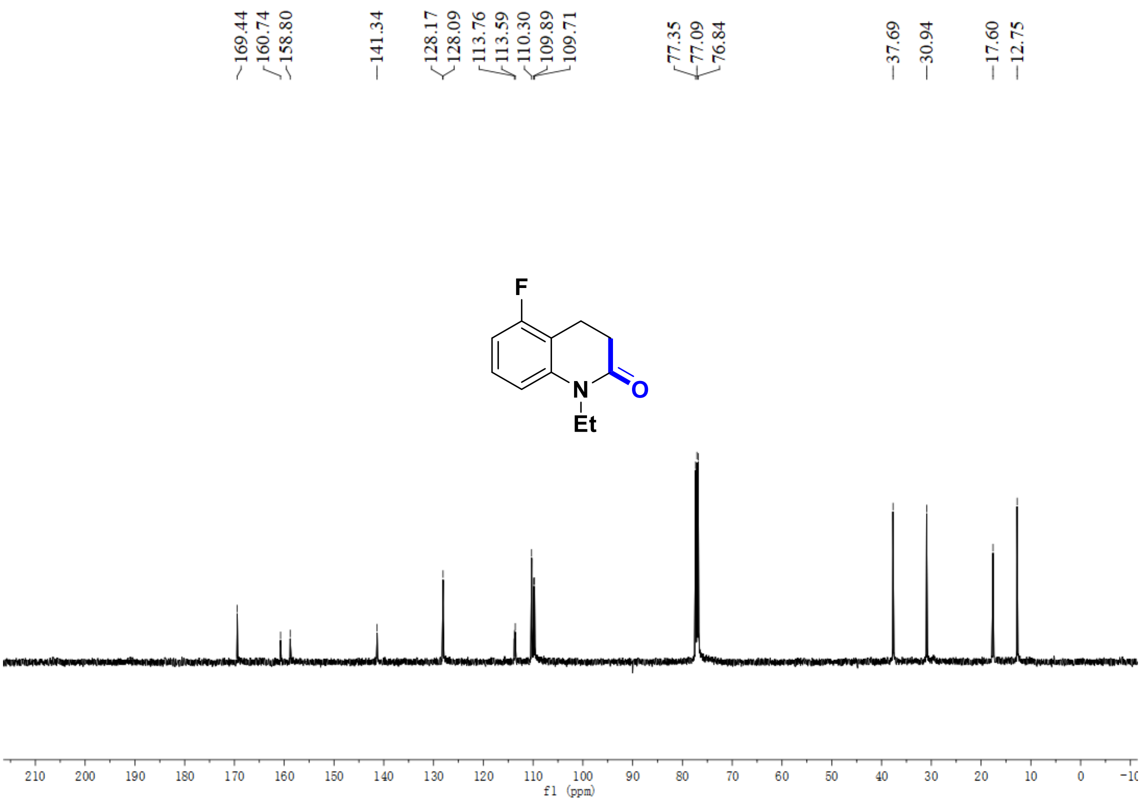
1-ethyl-3,4-dihydroquinolin-2(1H)-one (10a)

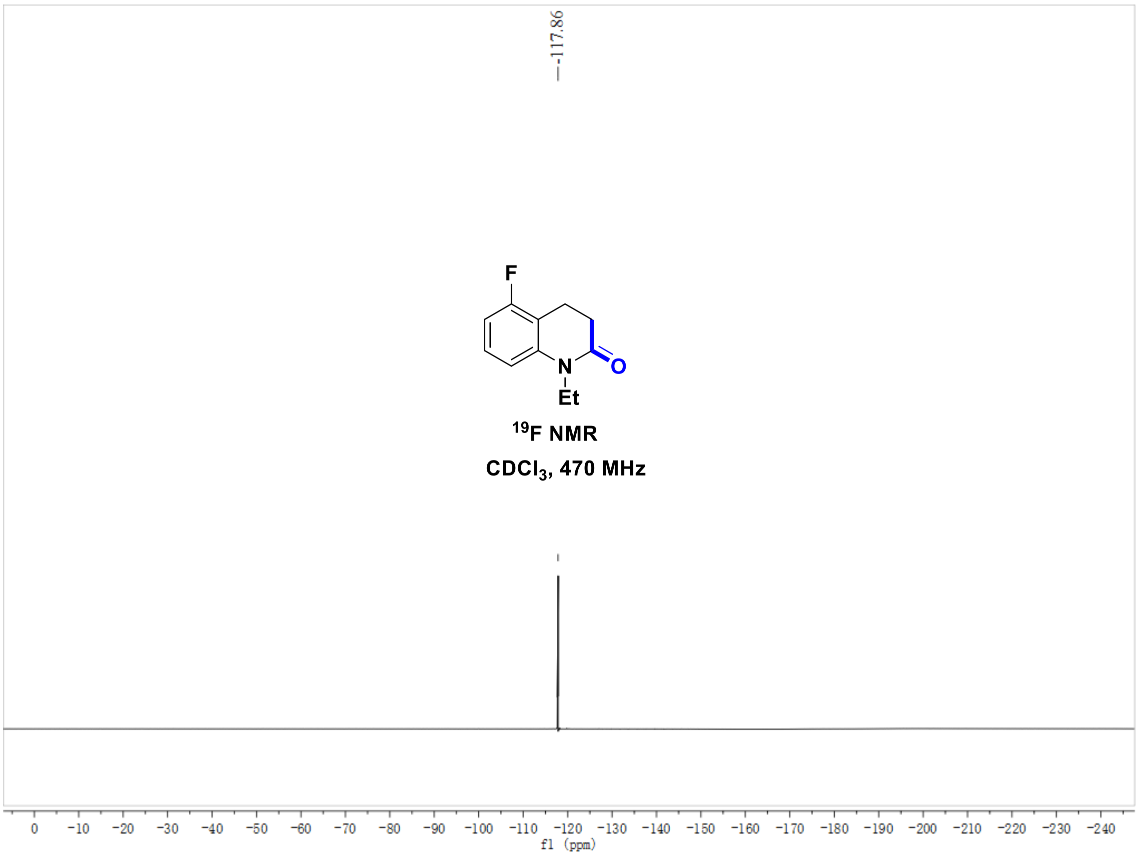




1-ethyl-5-fluoro-3,4-dihydroquinolin-2(1H)-one (10b)







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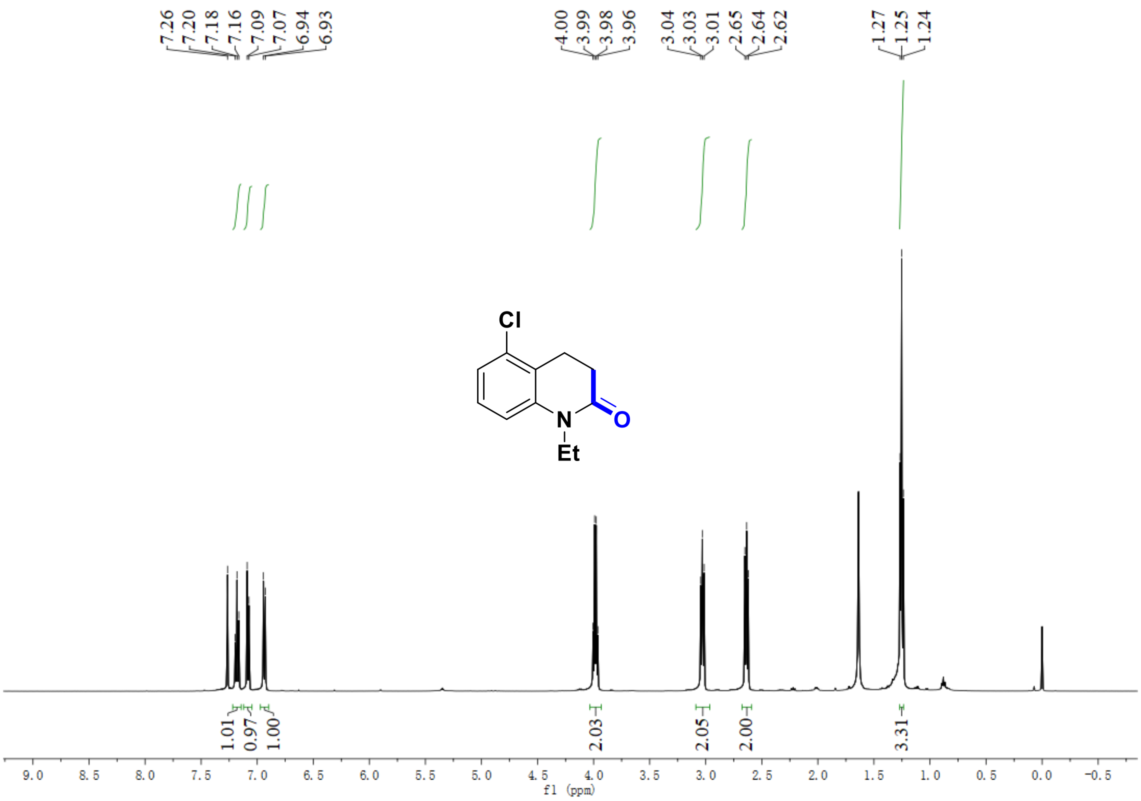
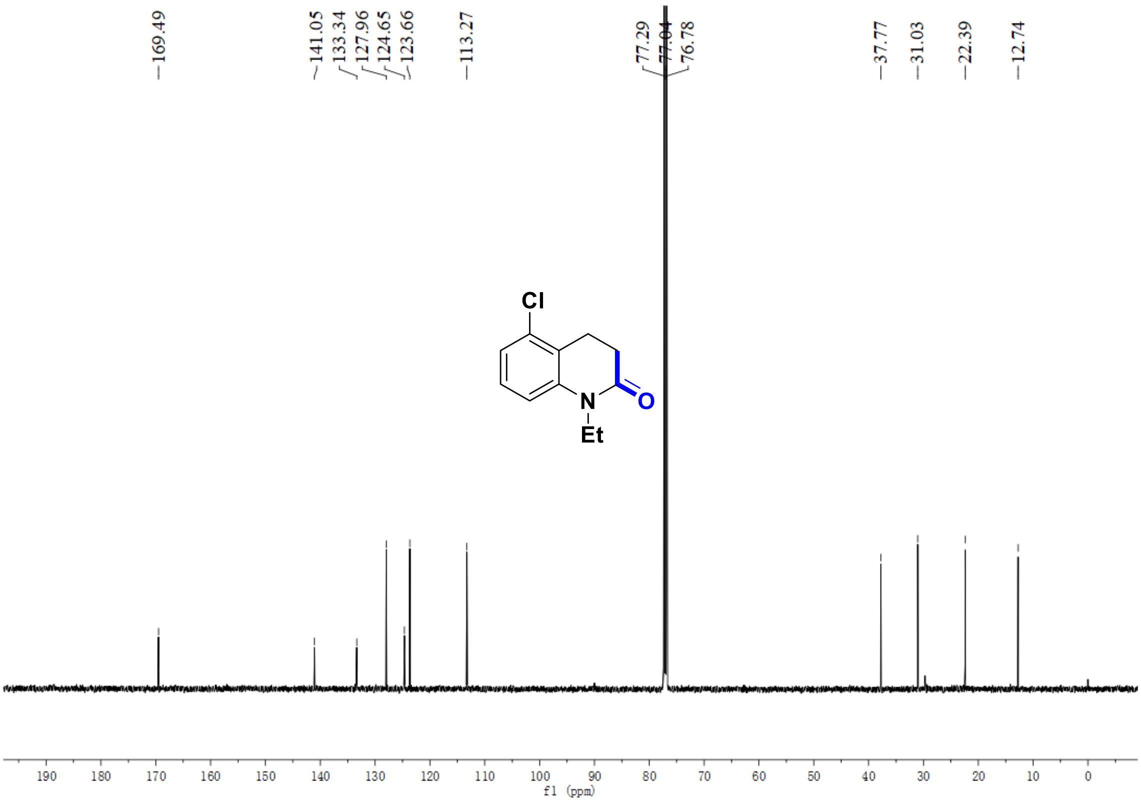
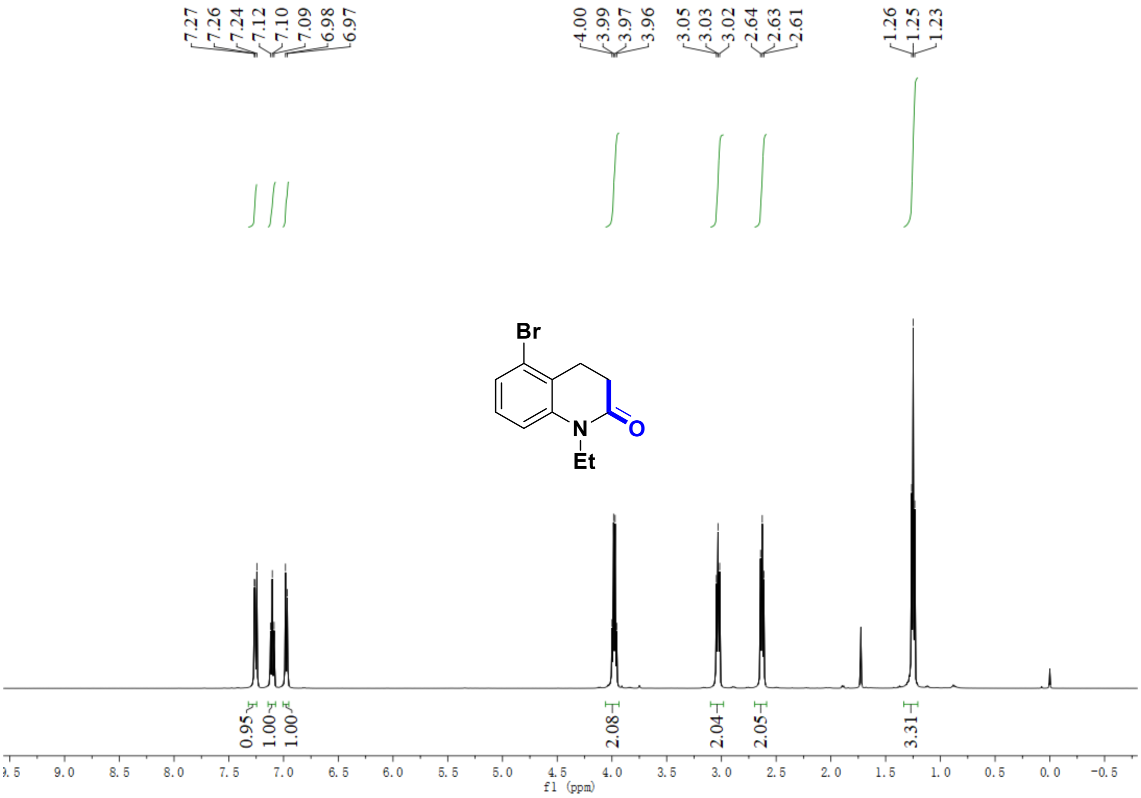
CDCl3, 470 MHz
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

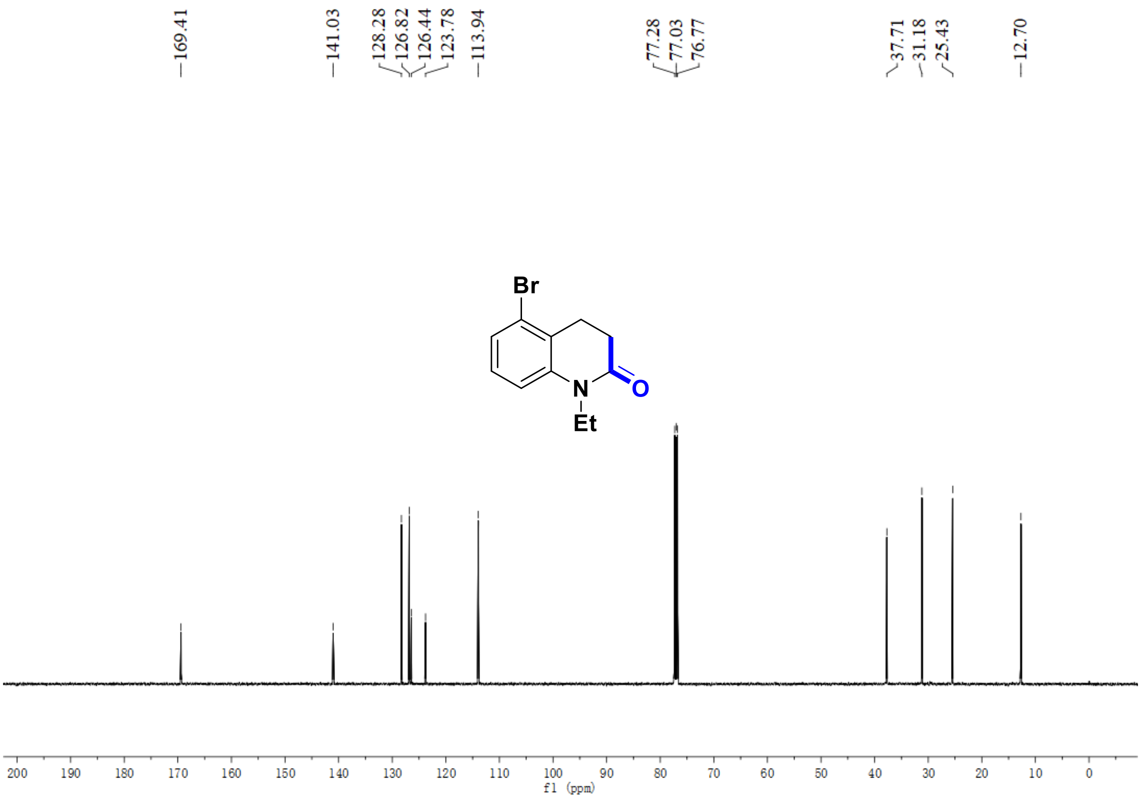
5-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10c)



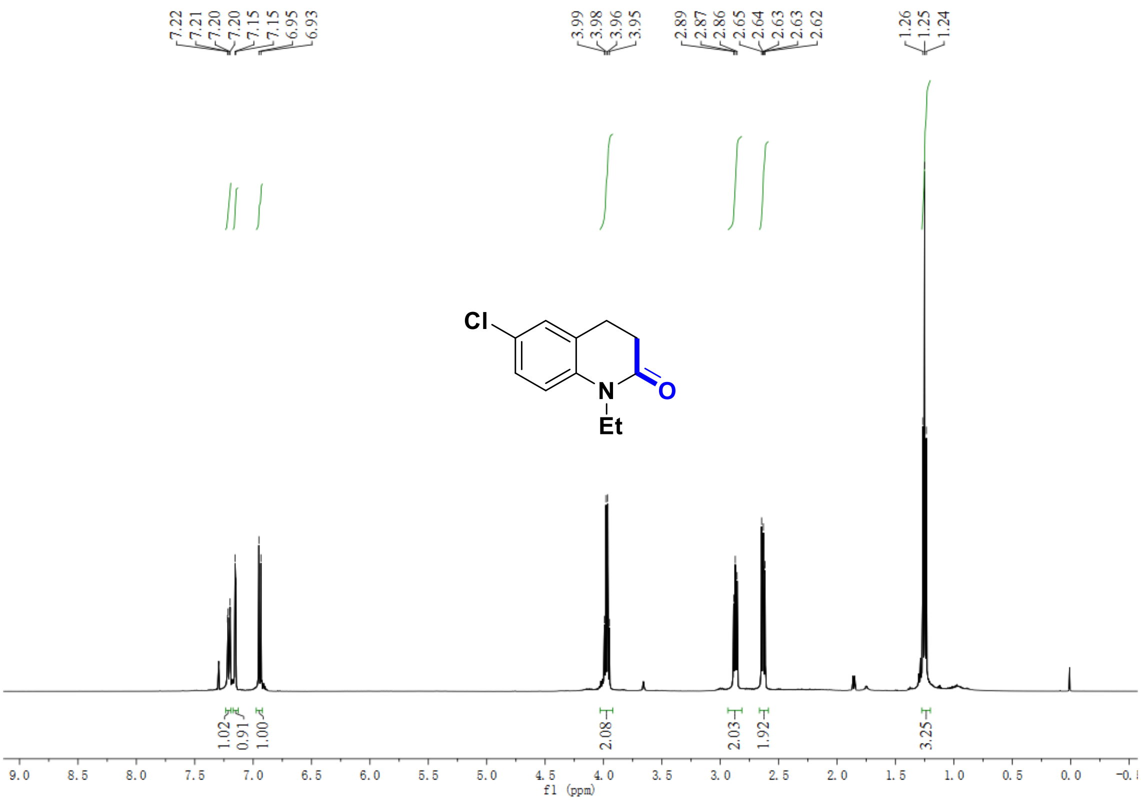


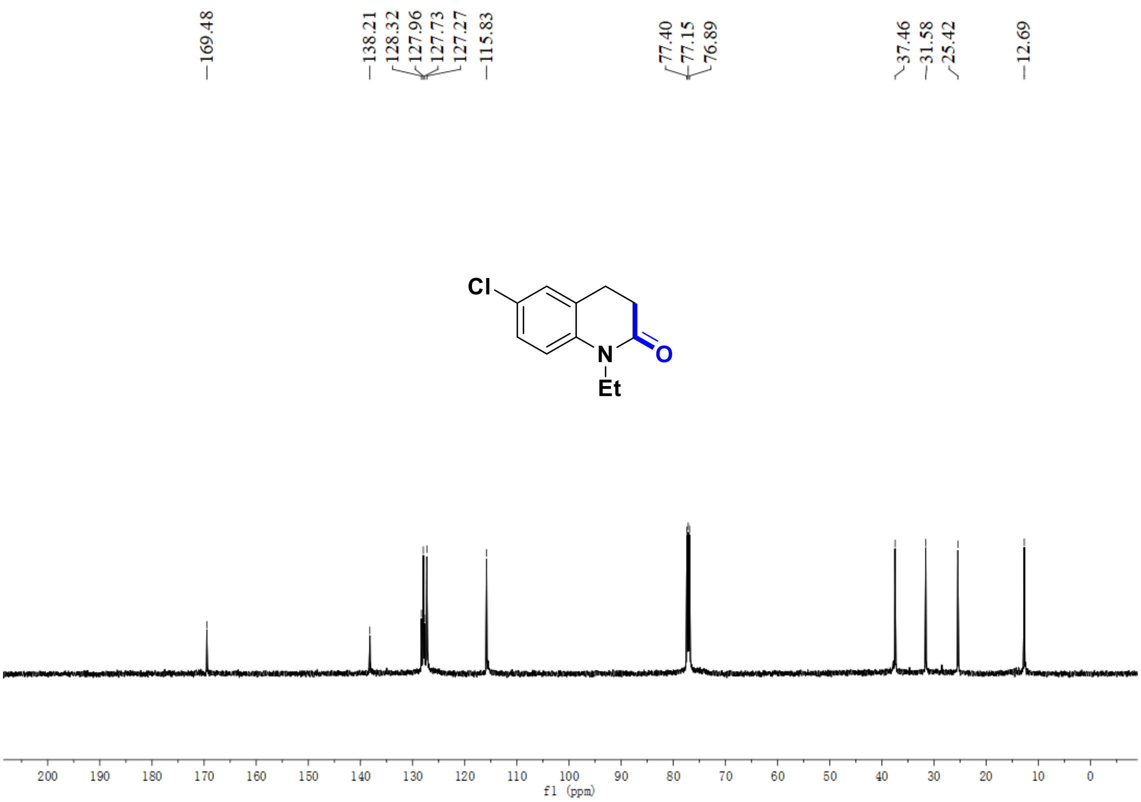
5-bromo-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10d)



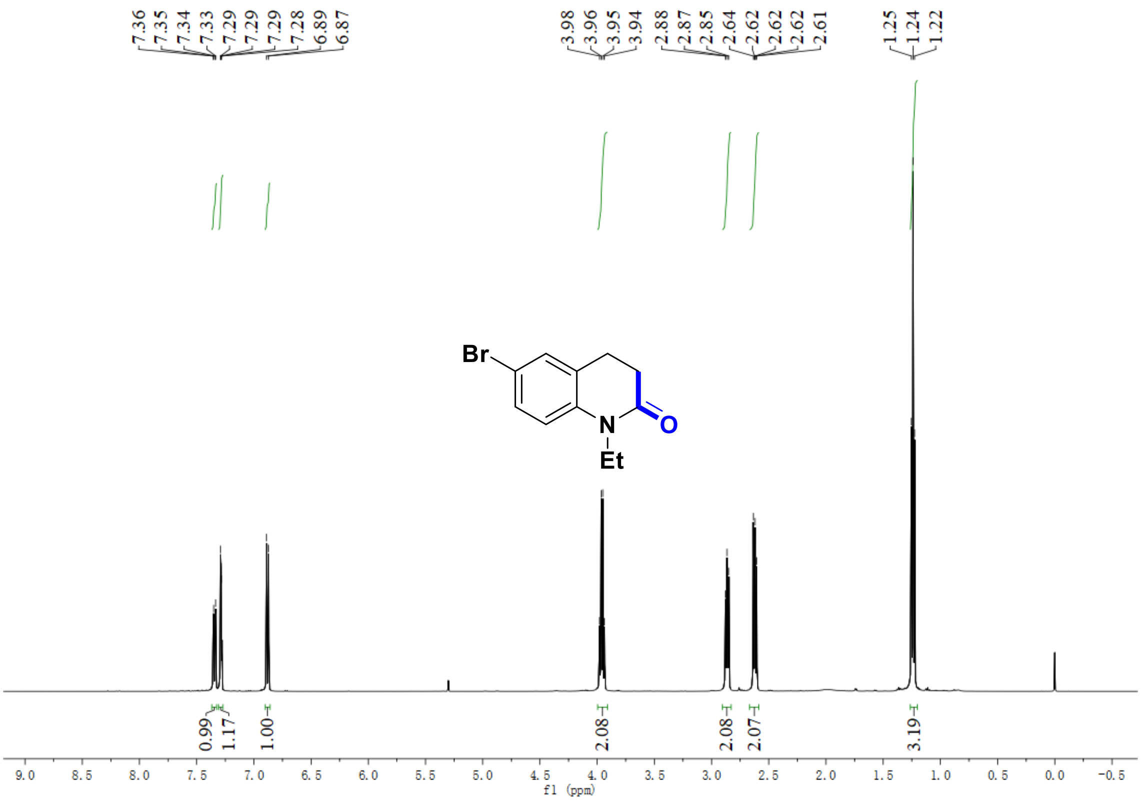


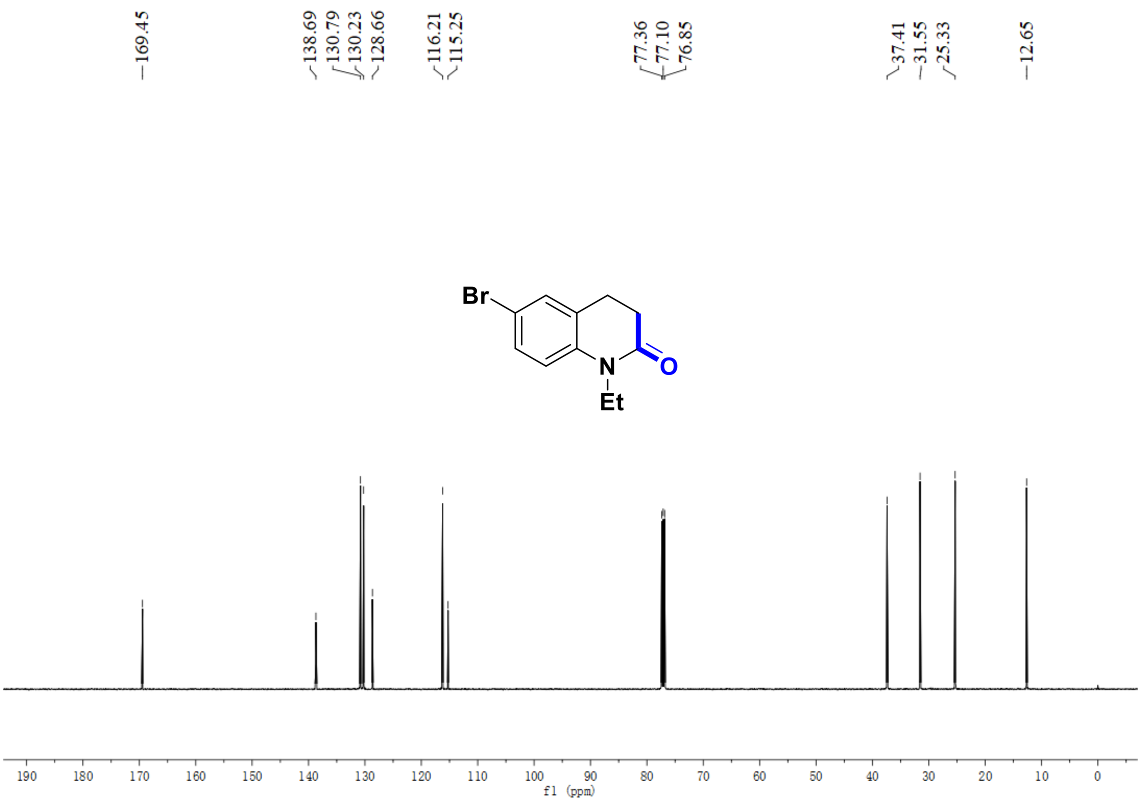
6-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10e)



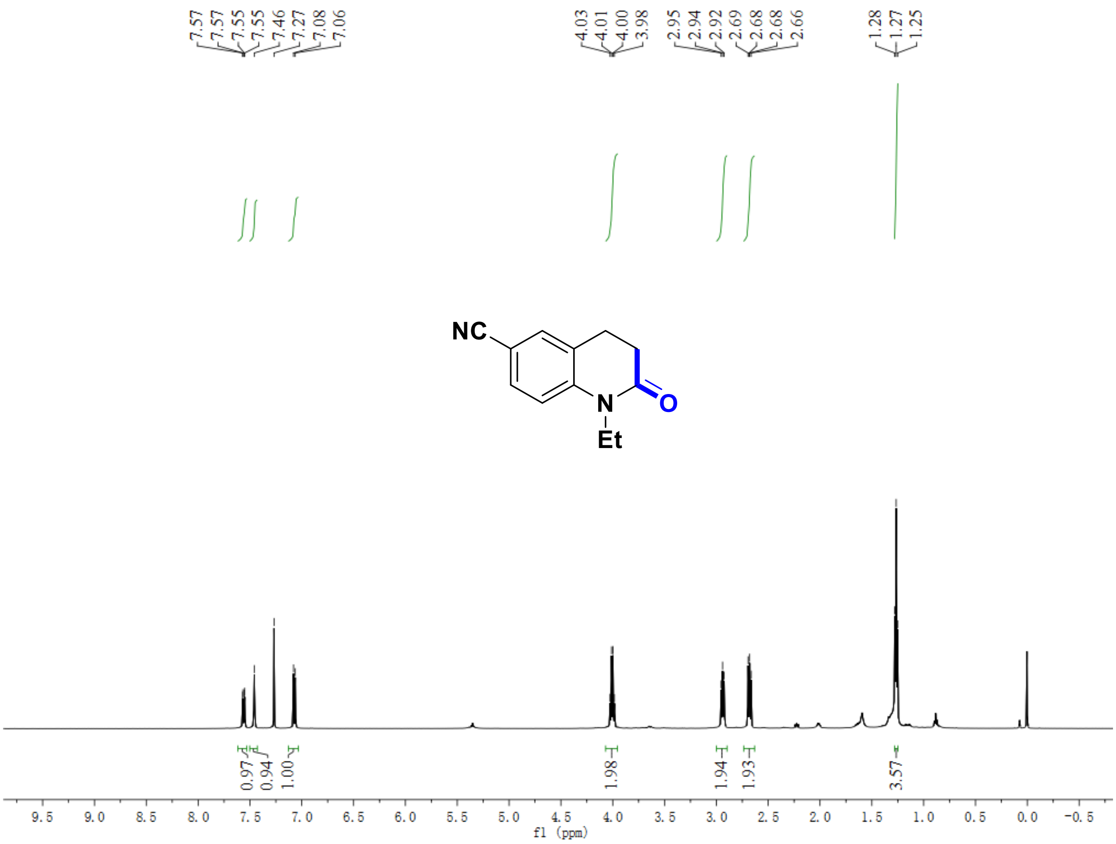


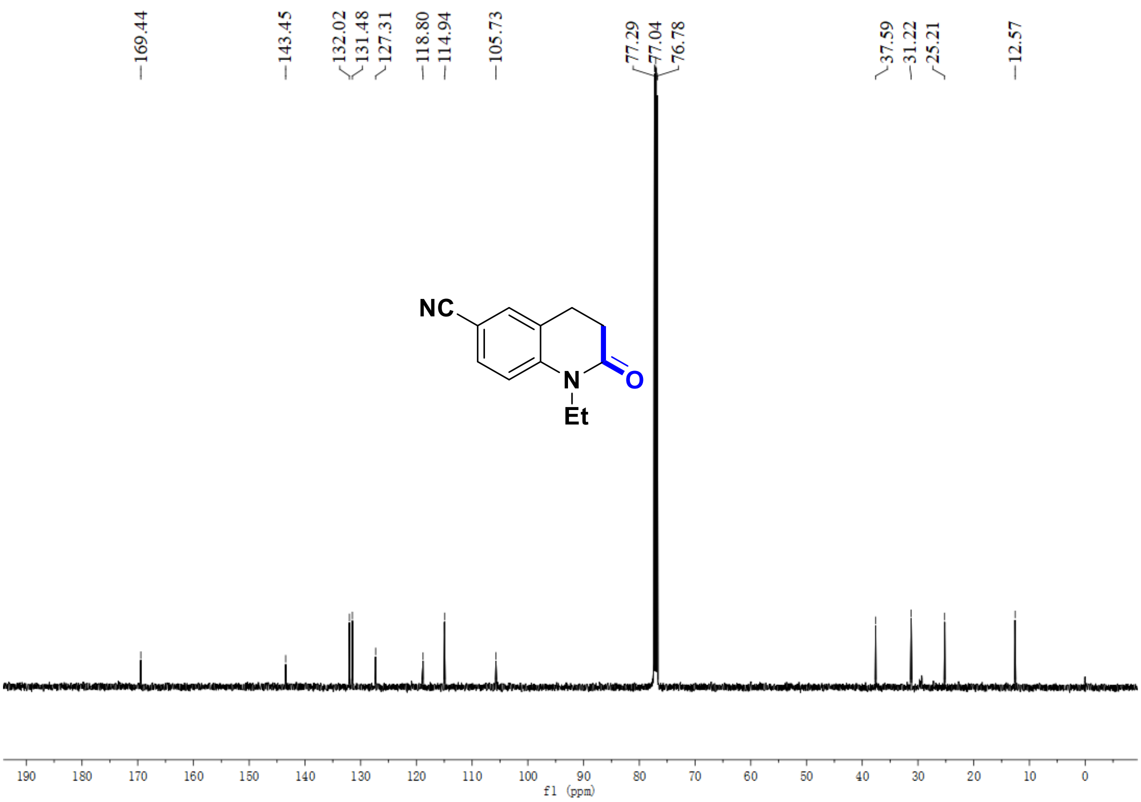
6-bromo-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10f)



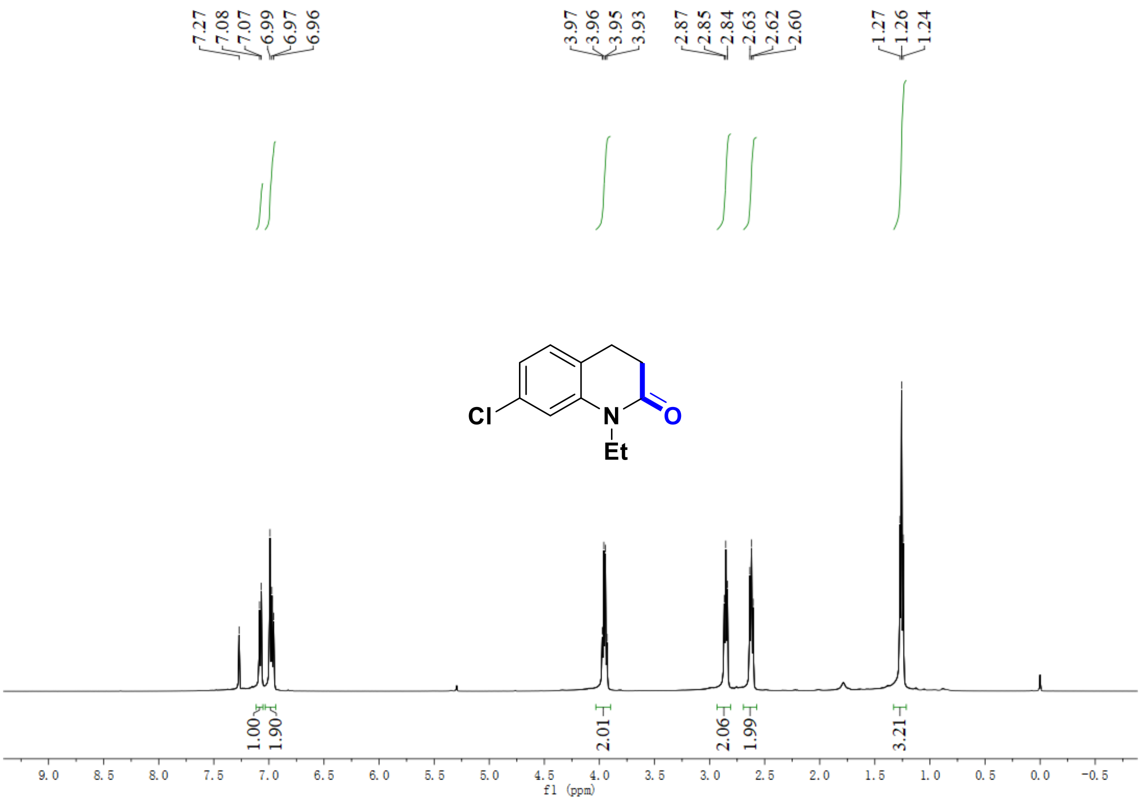


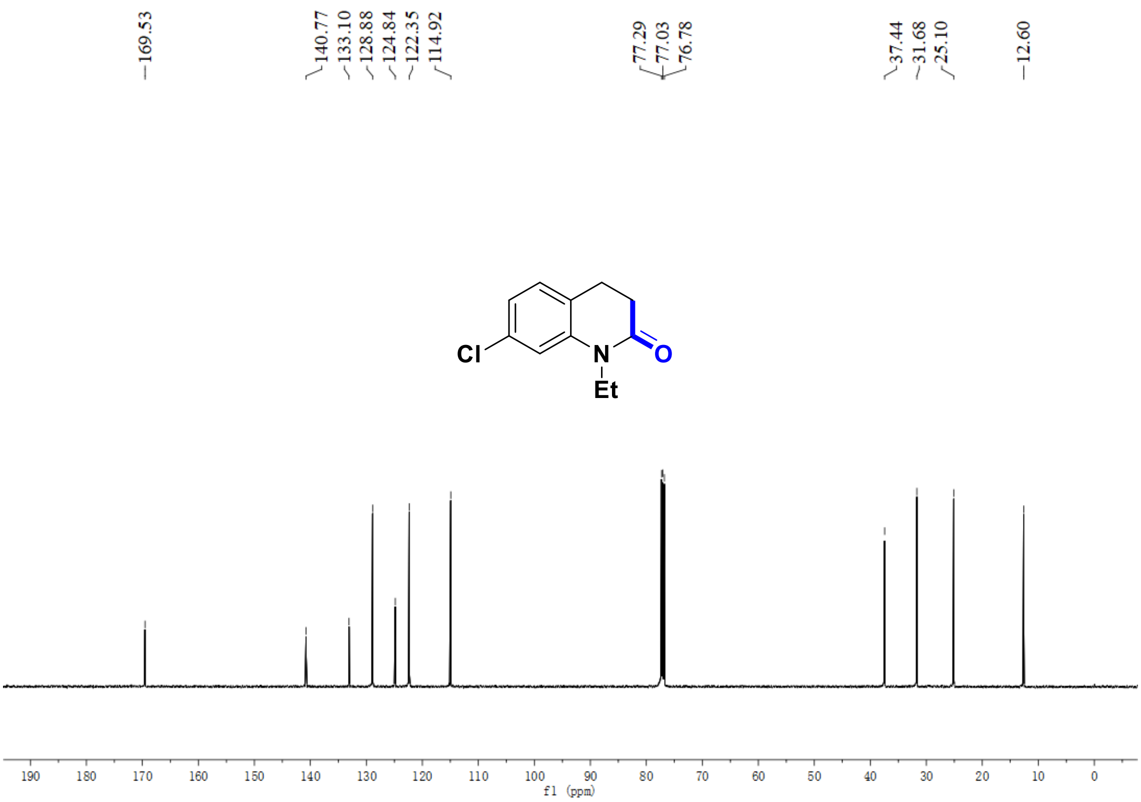
1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carbonitrile (10g)



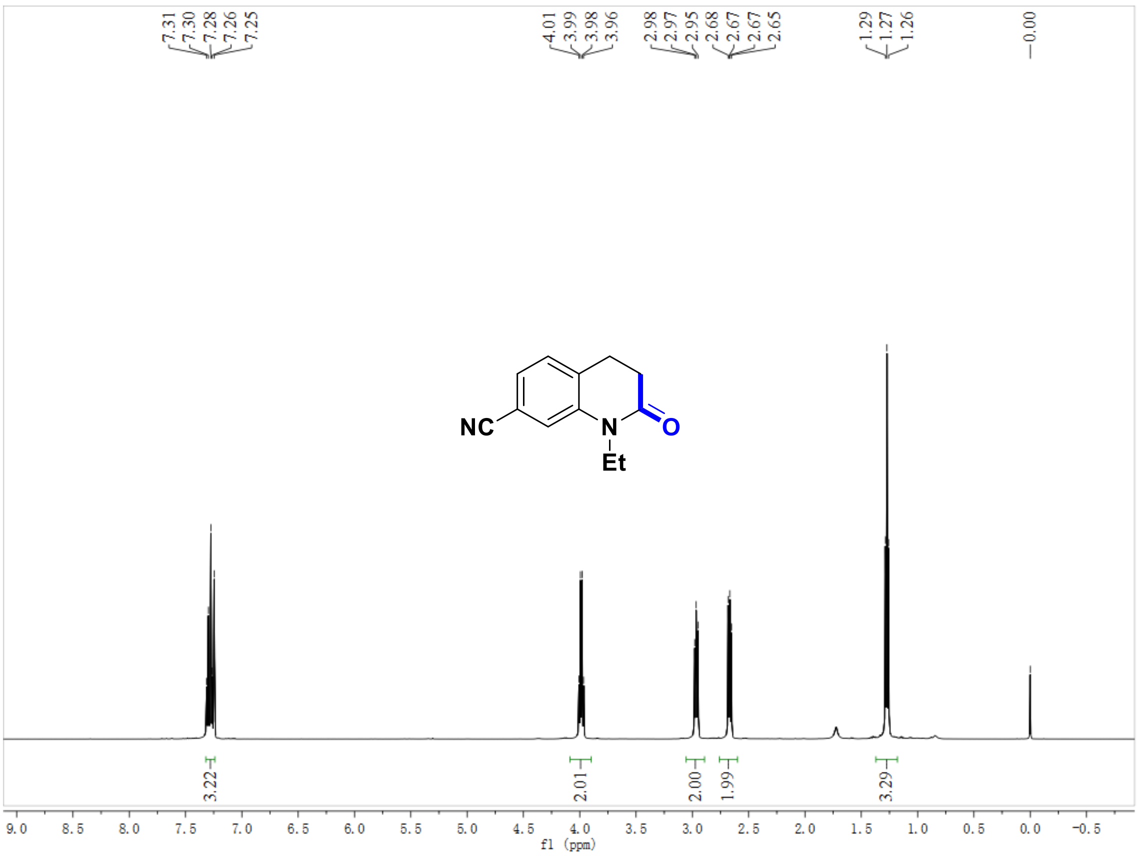


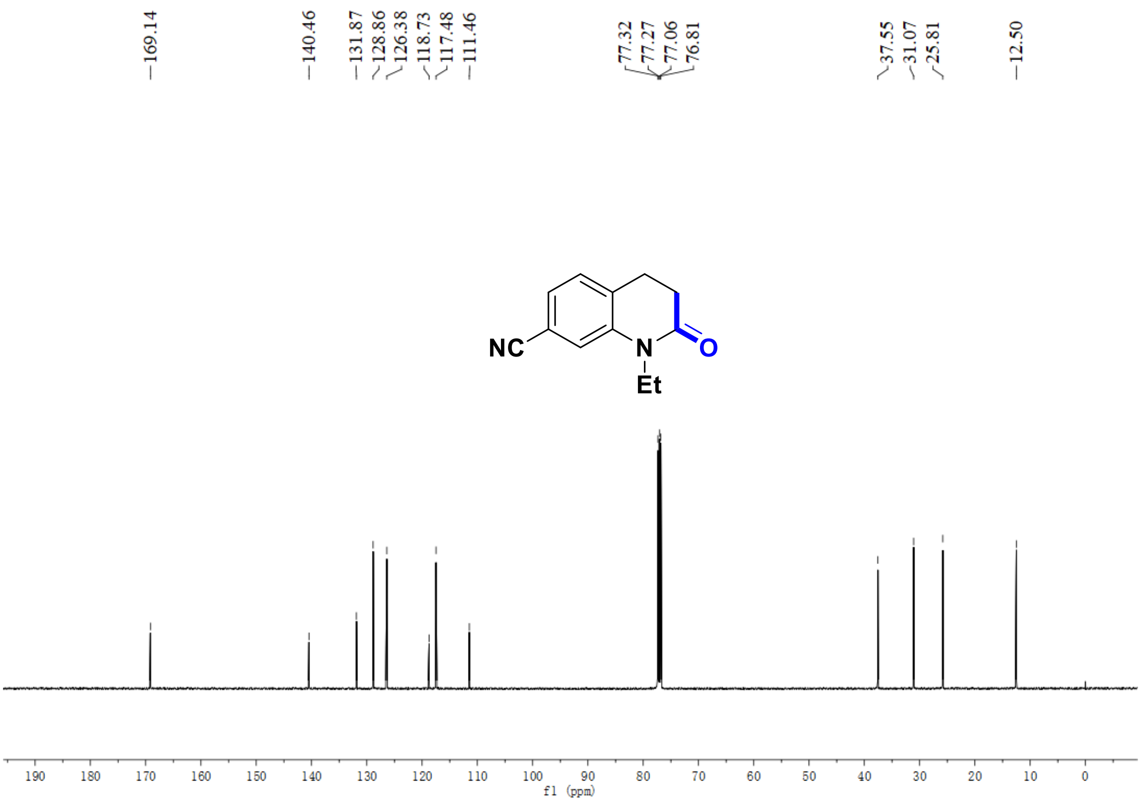
7-chloro-1-ethyl-3,4-dihydroquinolin-2(1H)-one (10h)



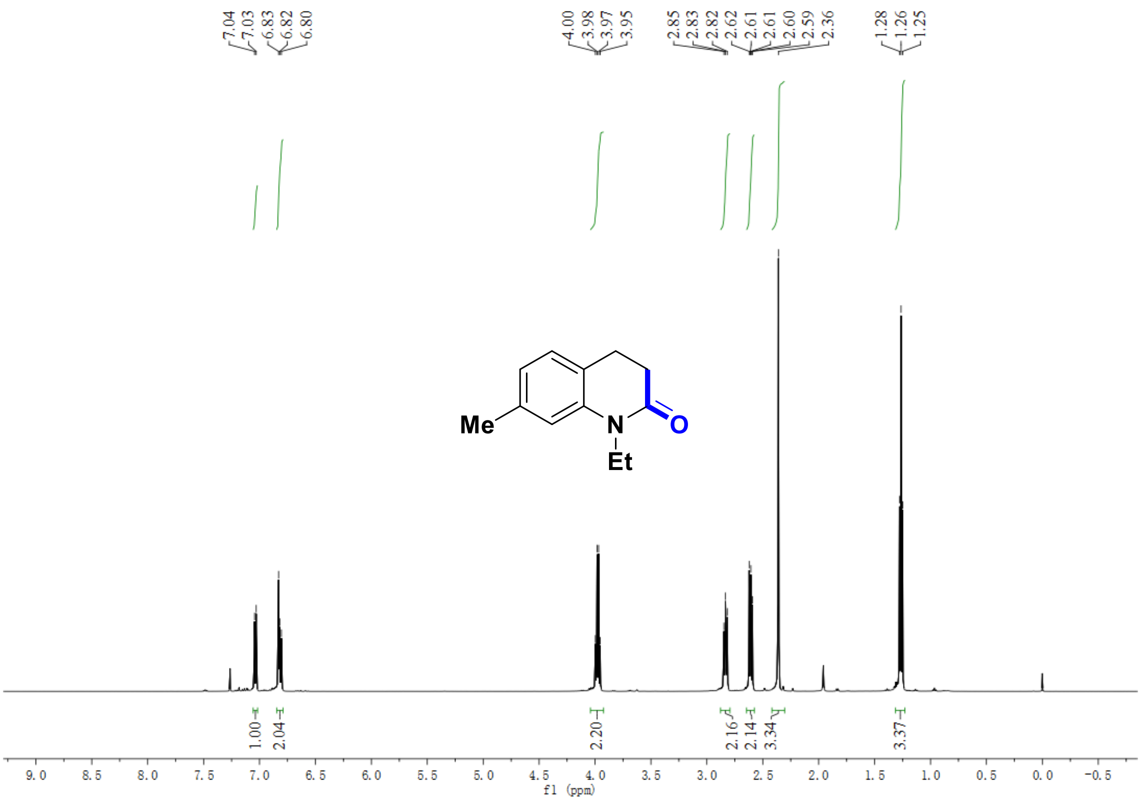


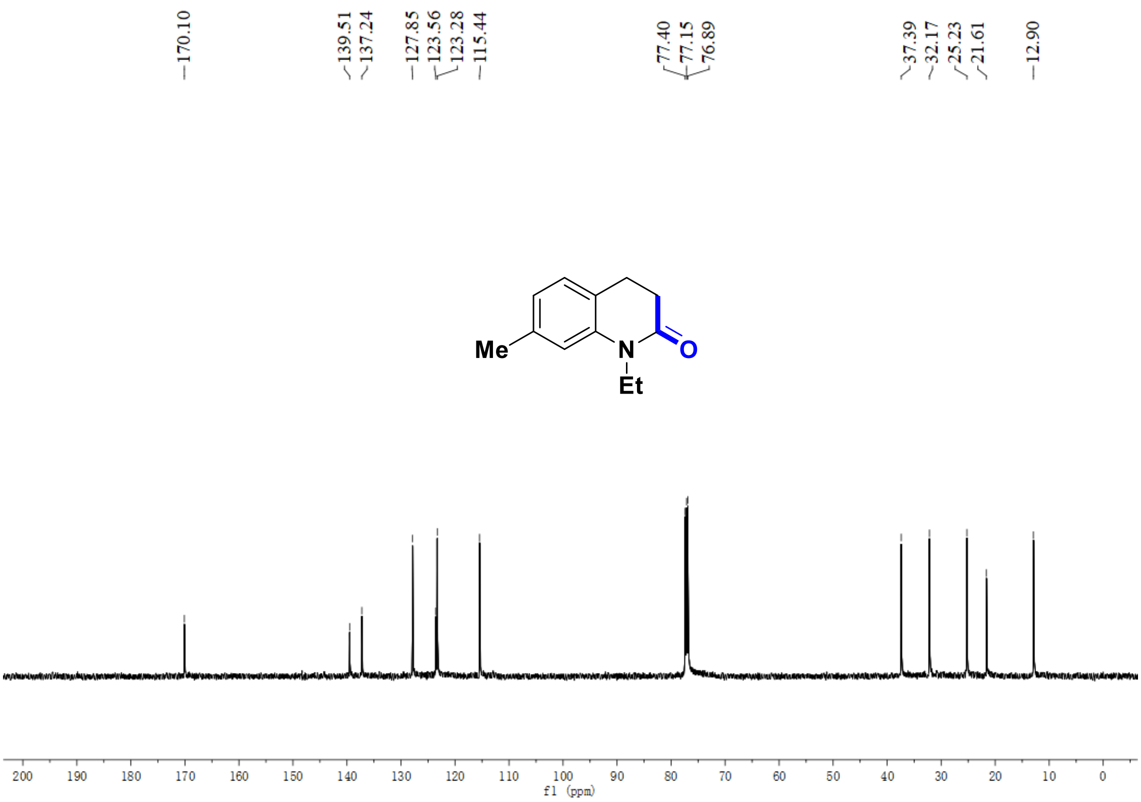
1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-7-carbonitrile (10i)



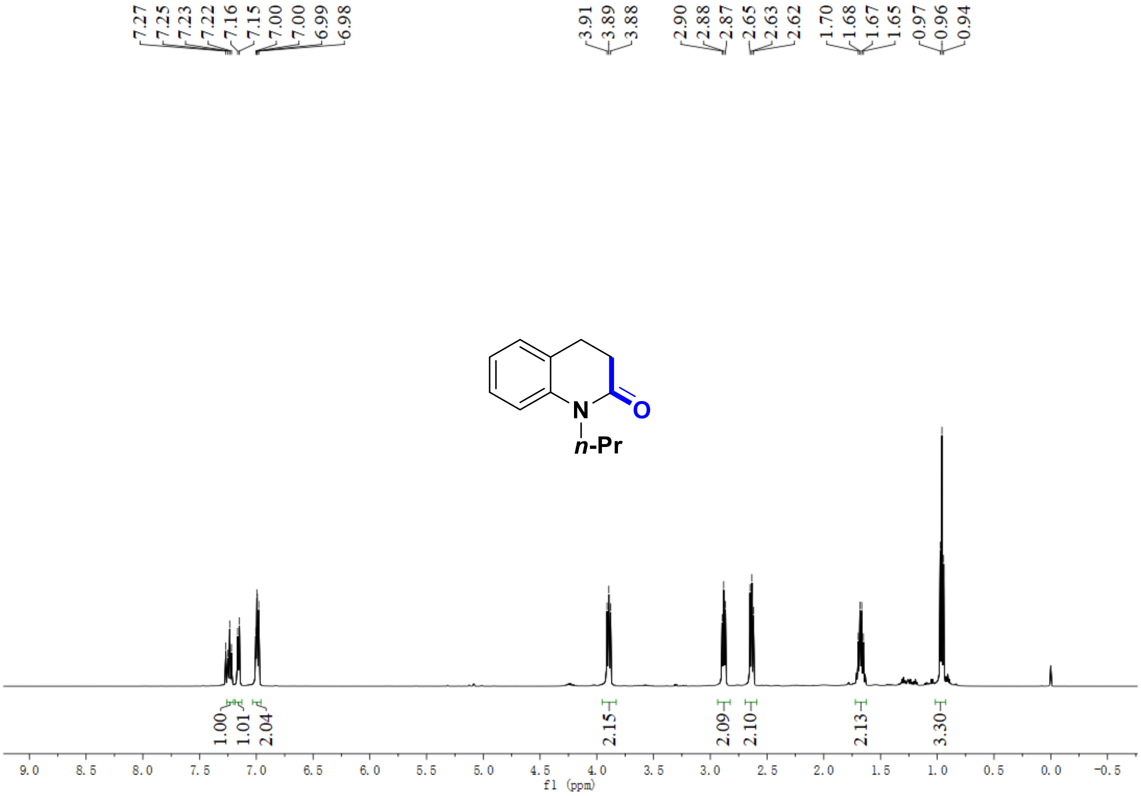


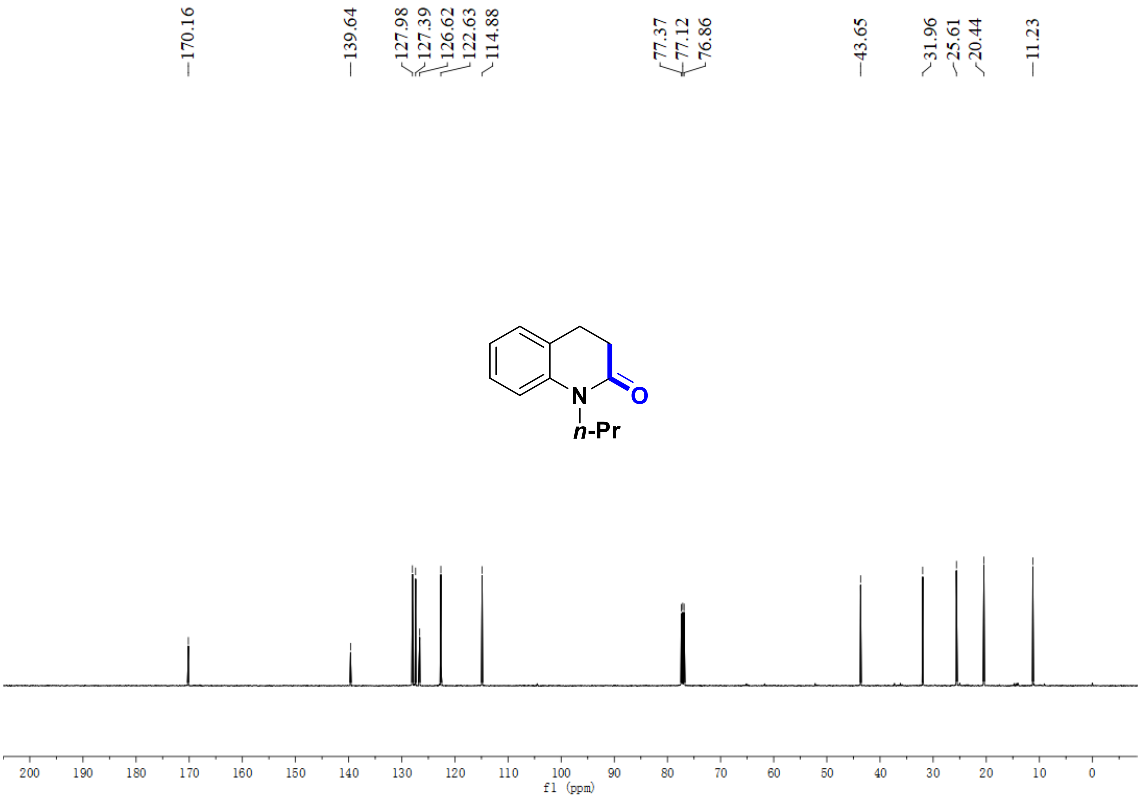
1-ethyl-7-methyl-3,4-dihydroquinolin-2(1H)-one (10j)



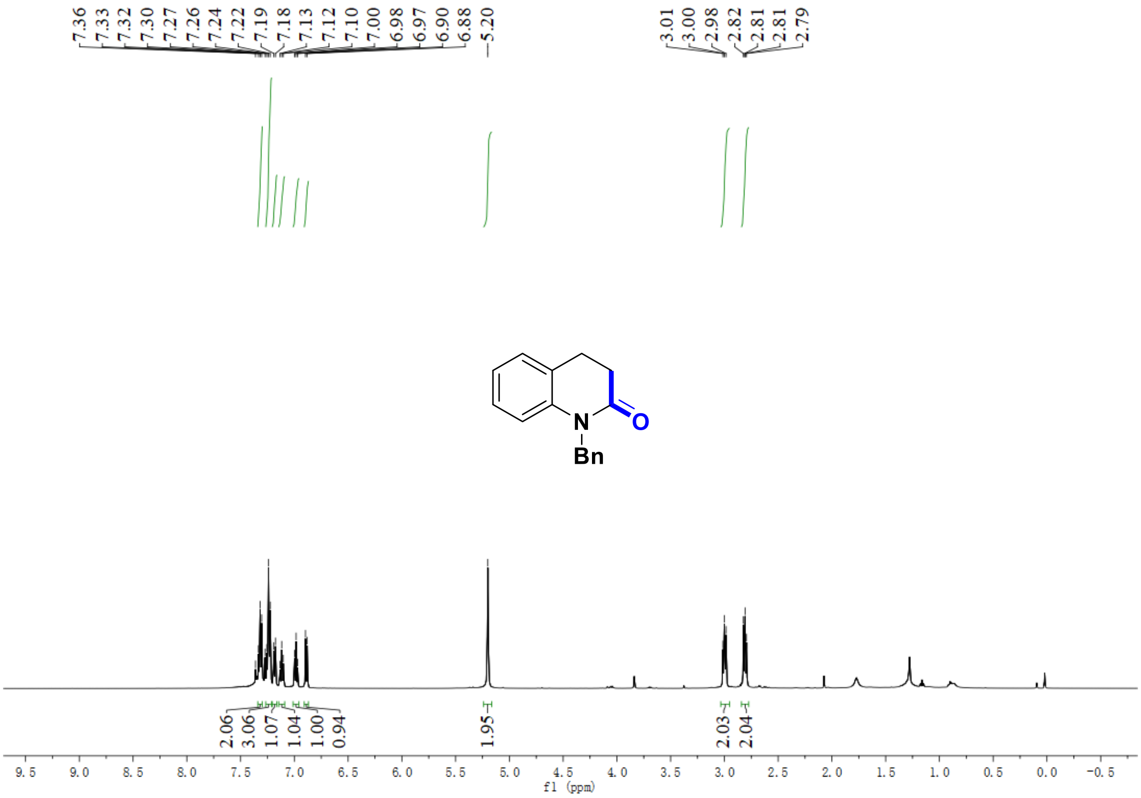


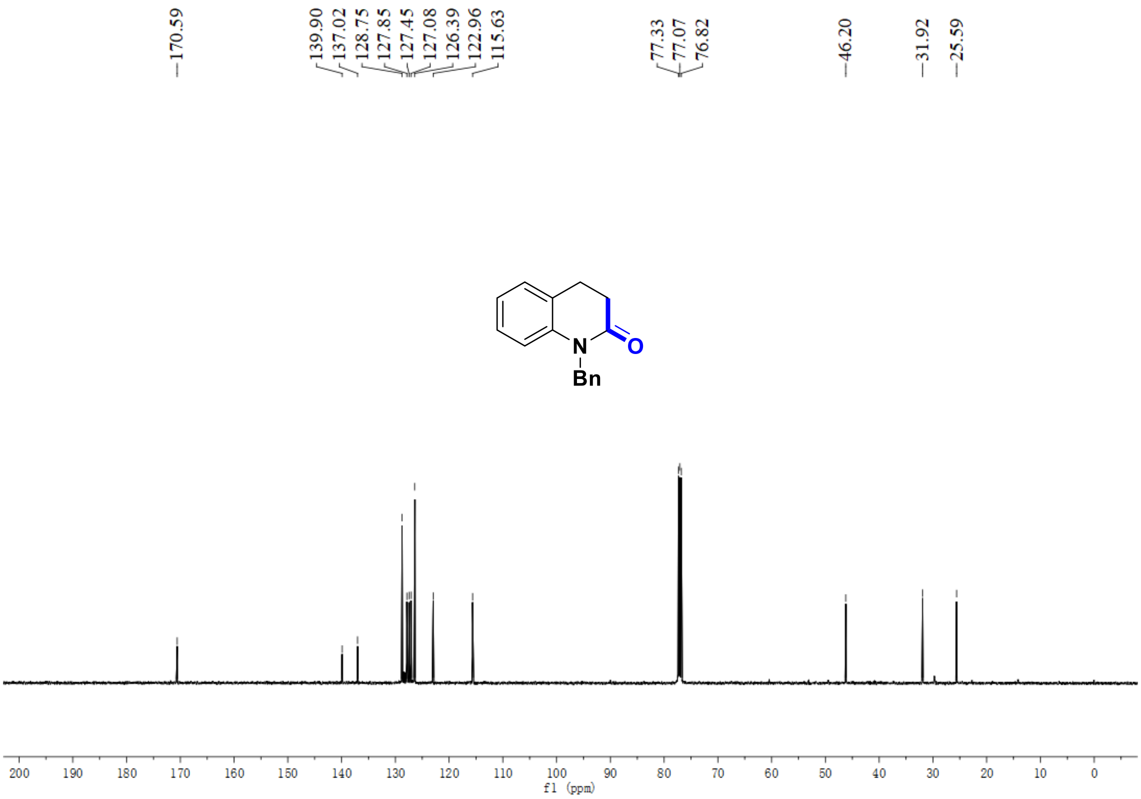
1-propyl-3,4-dihydroquinolin-2(1H)-one (10k)



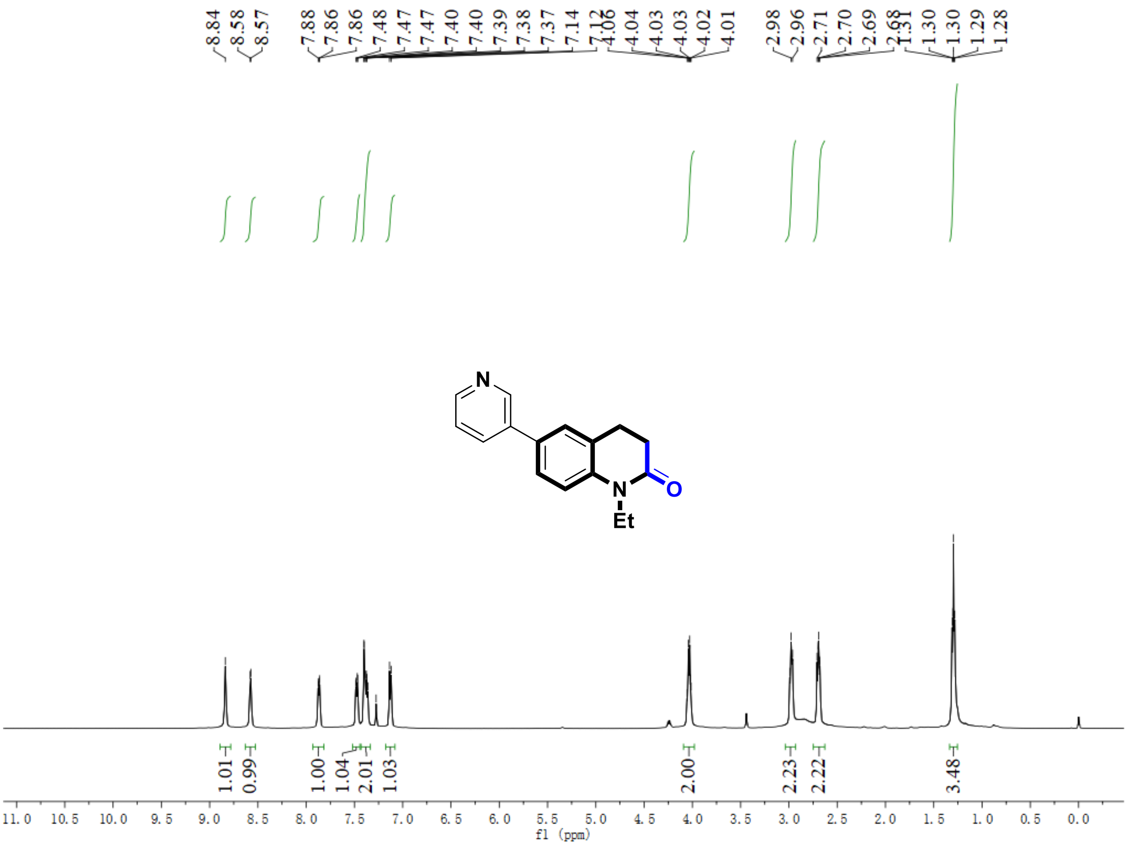


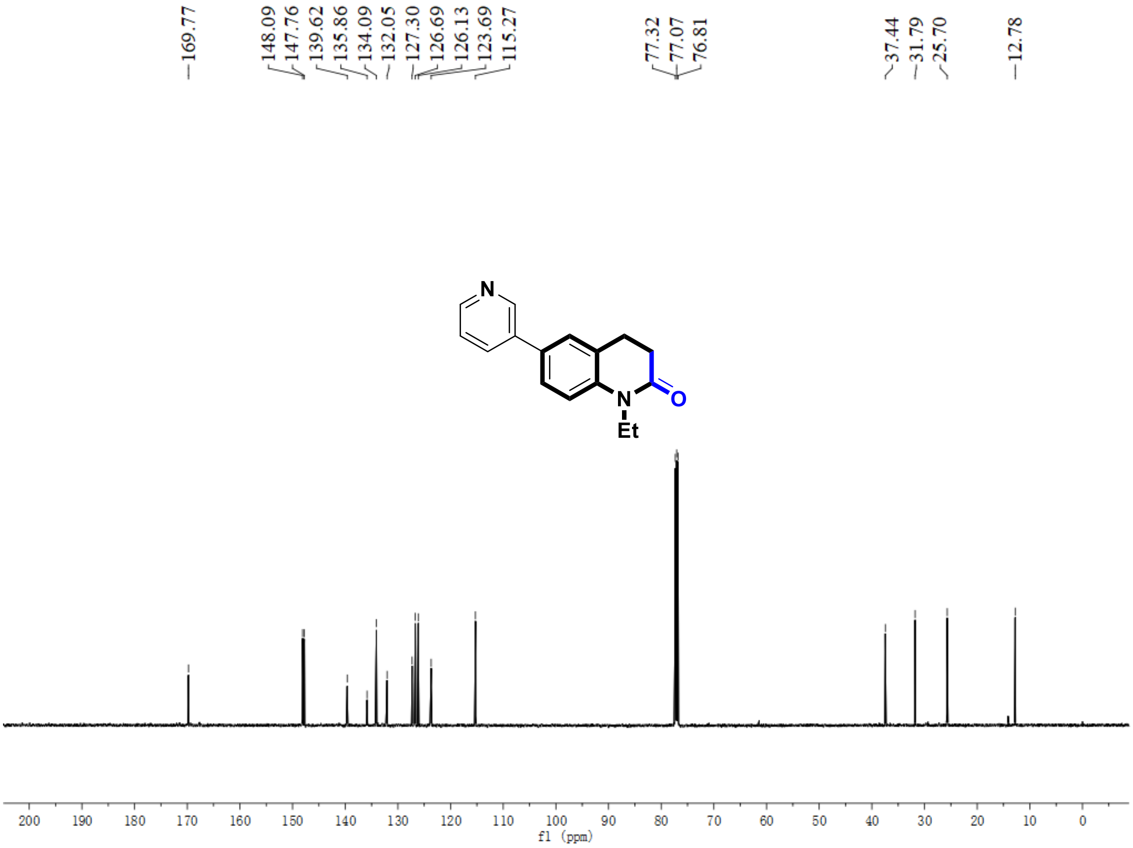
1-benzyl-3,4-dihydroquinolin-2(1H)-one (10l)



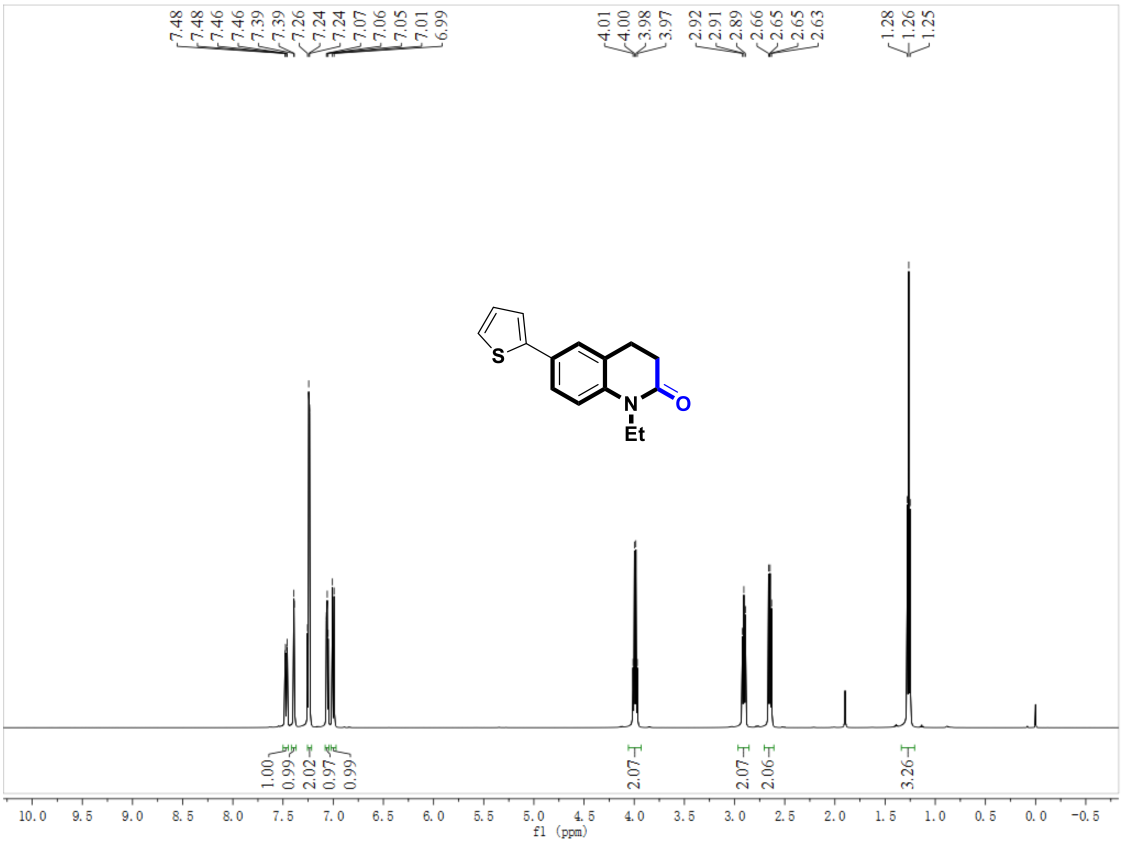


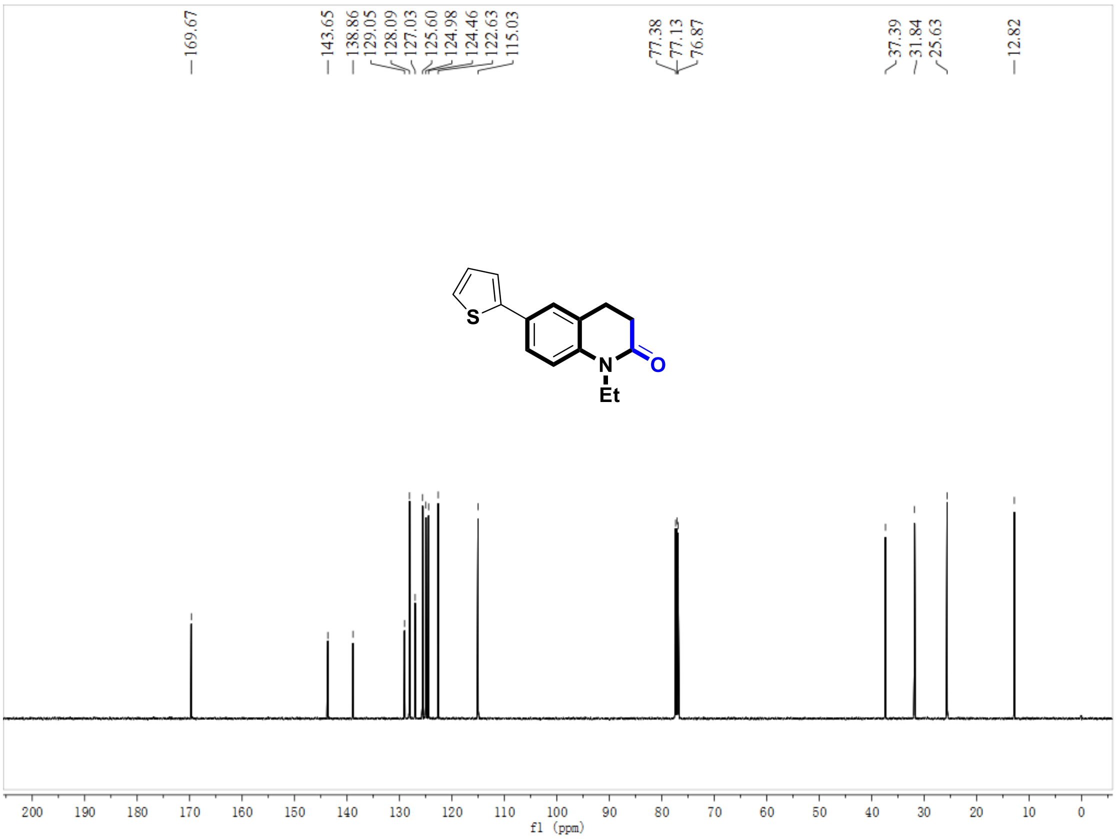
1-ethyl-6-(pyridin-3-yl)-3,4-dihydroquinolin-2(1H)-one (10m)





1-ethyl-6-(thiophen-2-yl)-3,4-dihydroquinolin-2(1H)-one (10n)





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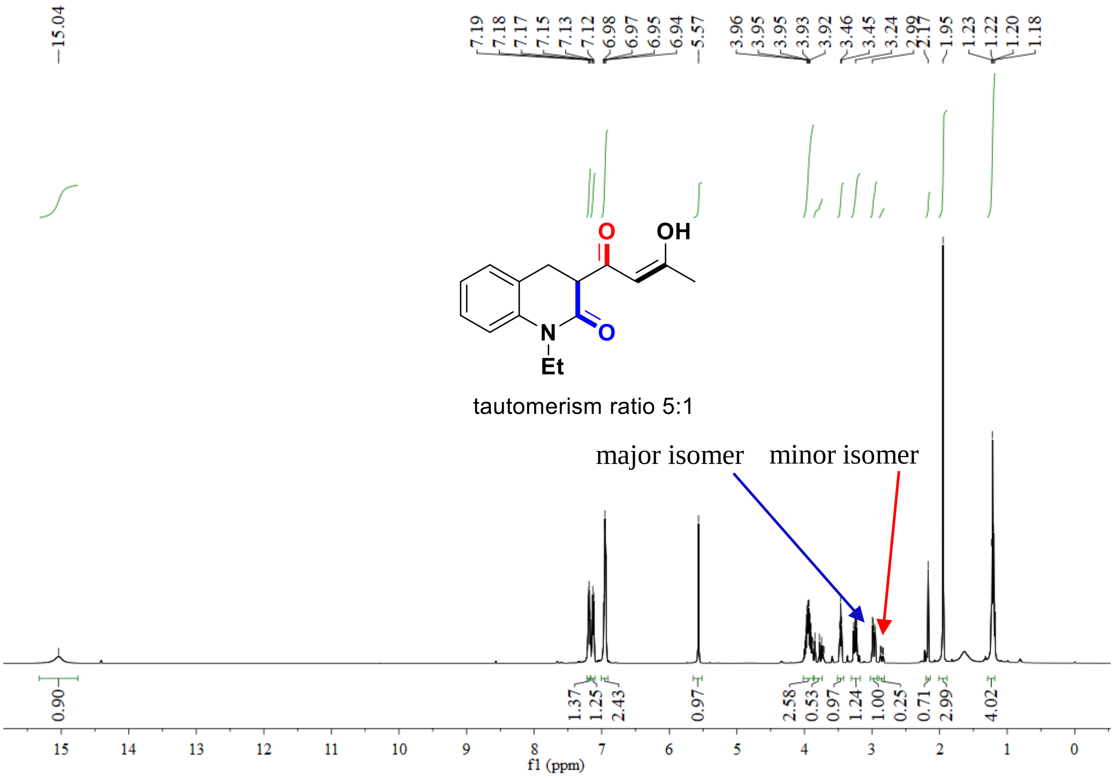
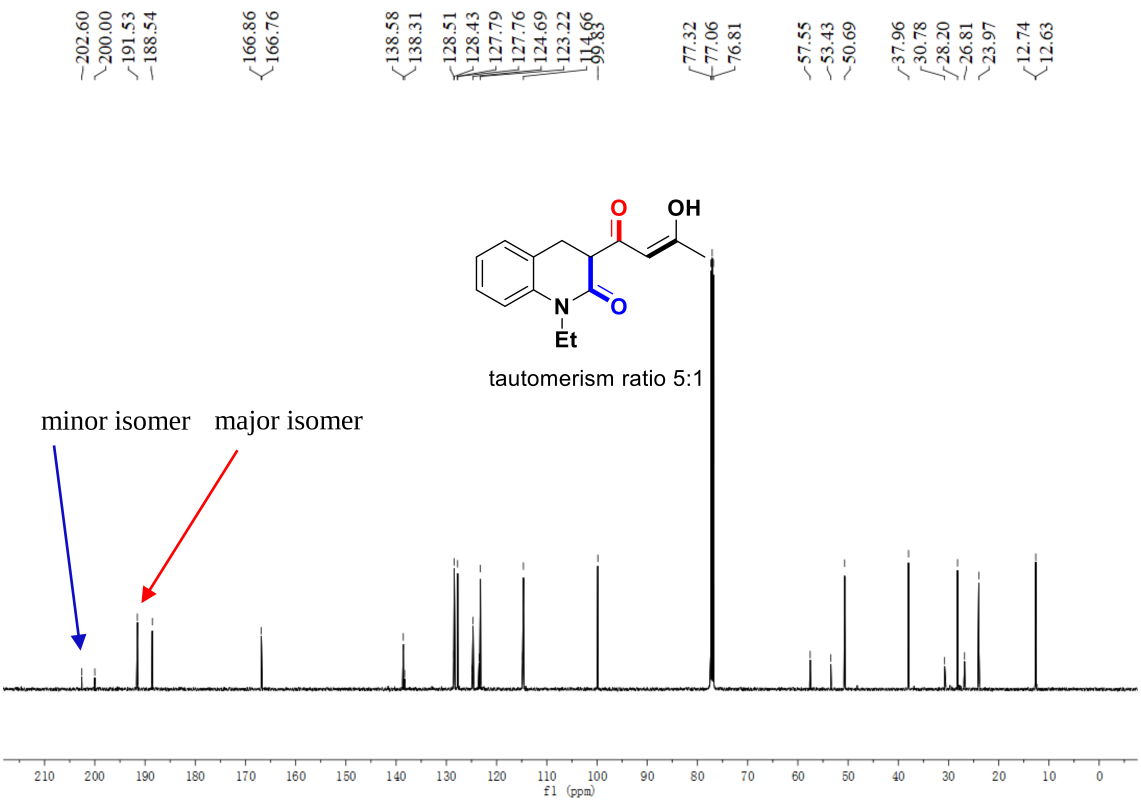
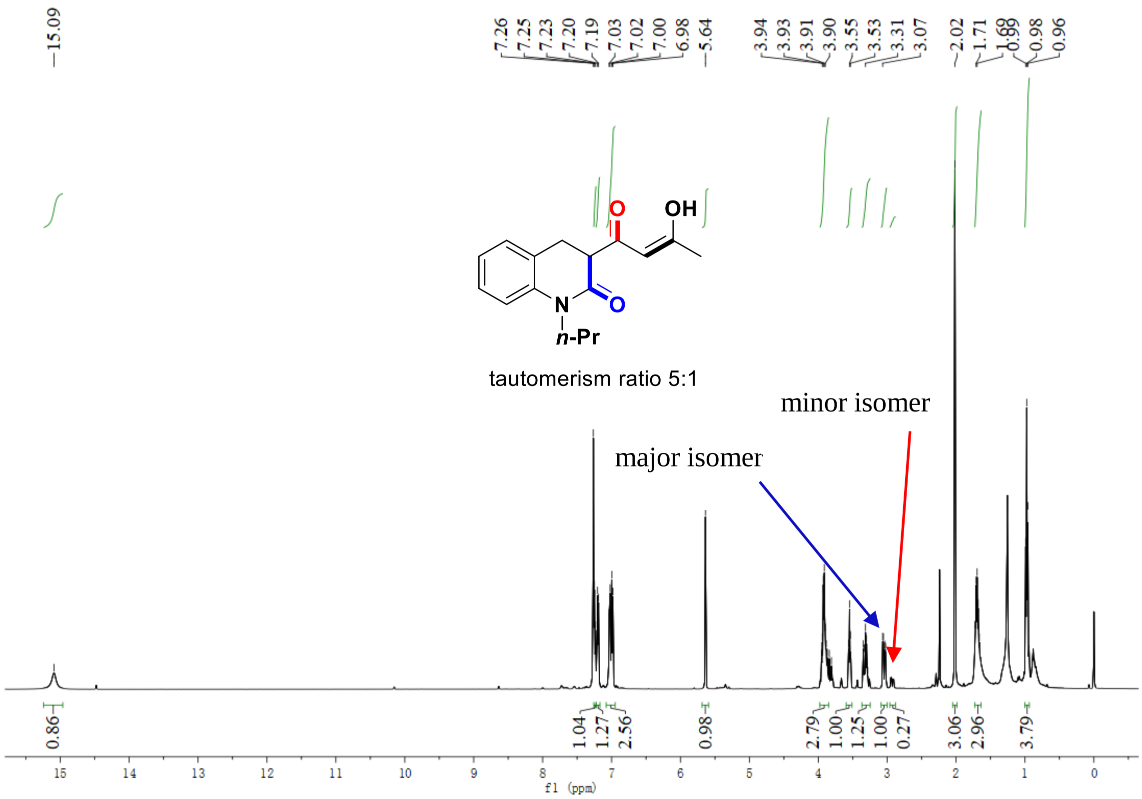
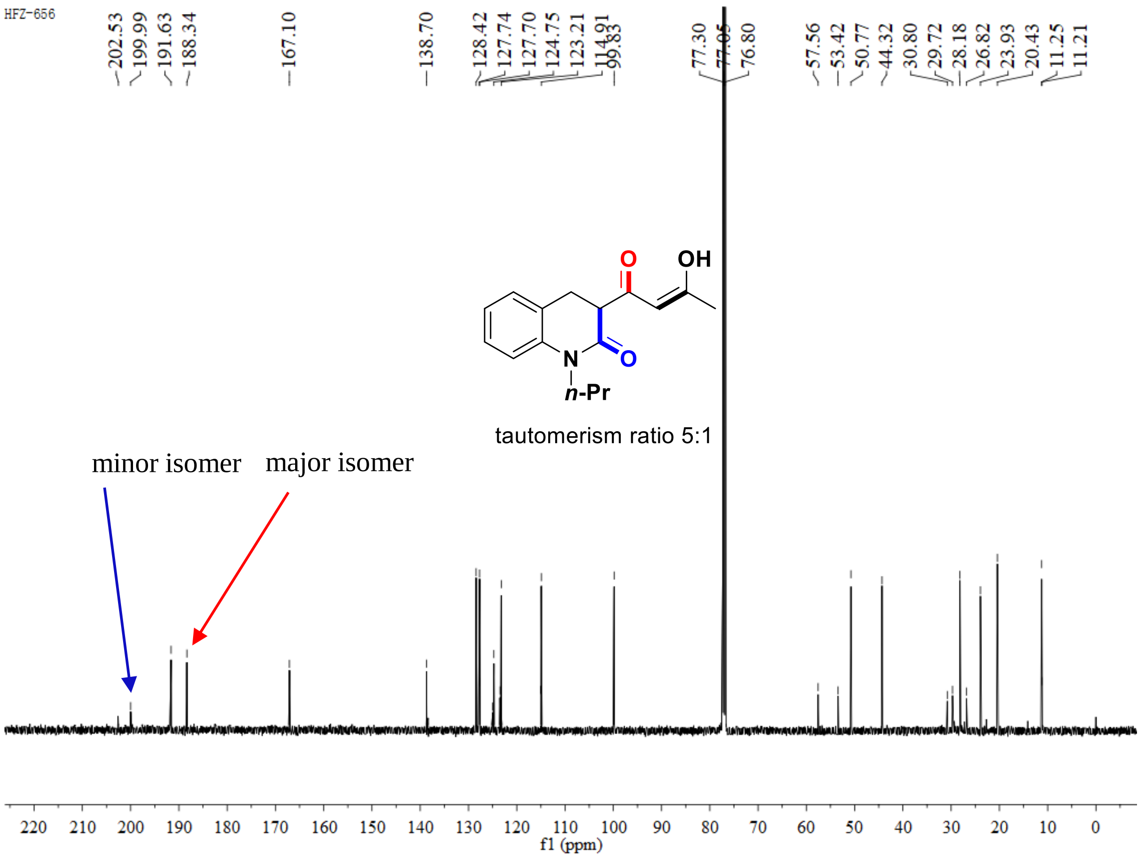


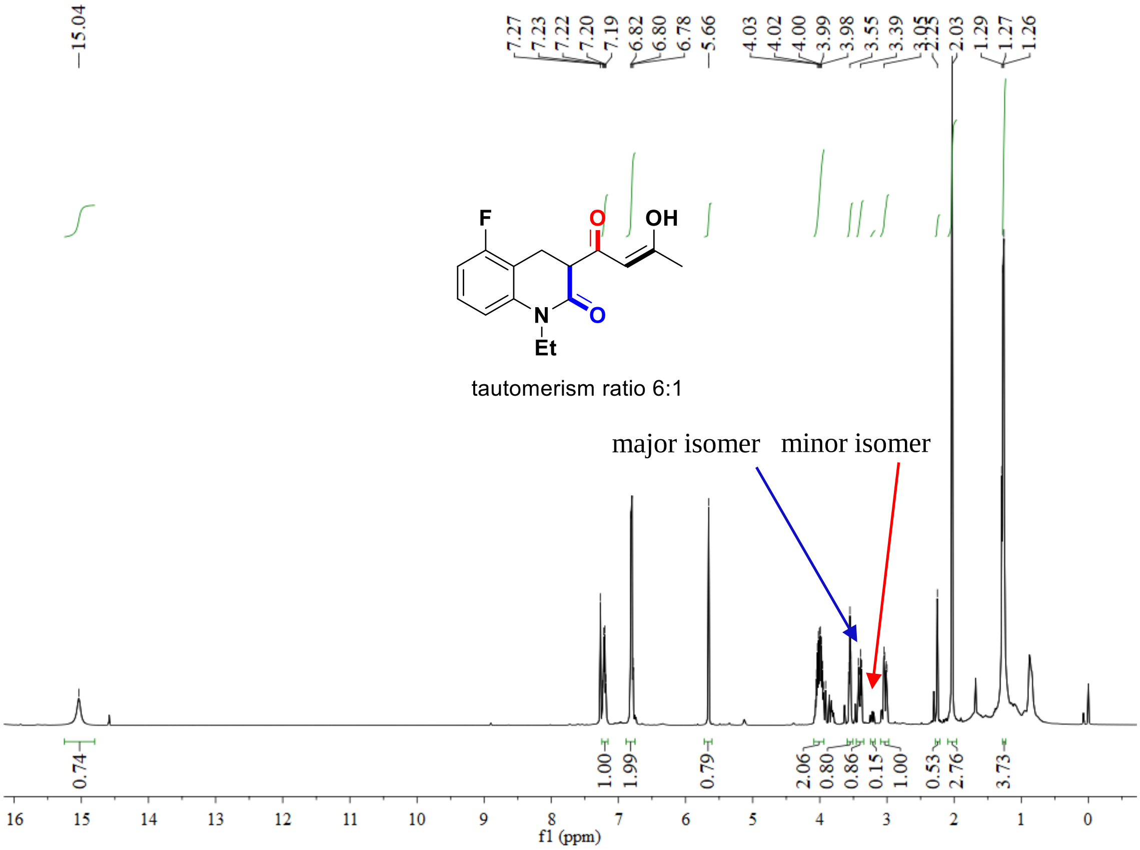


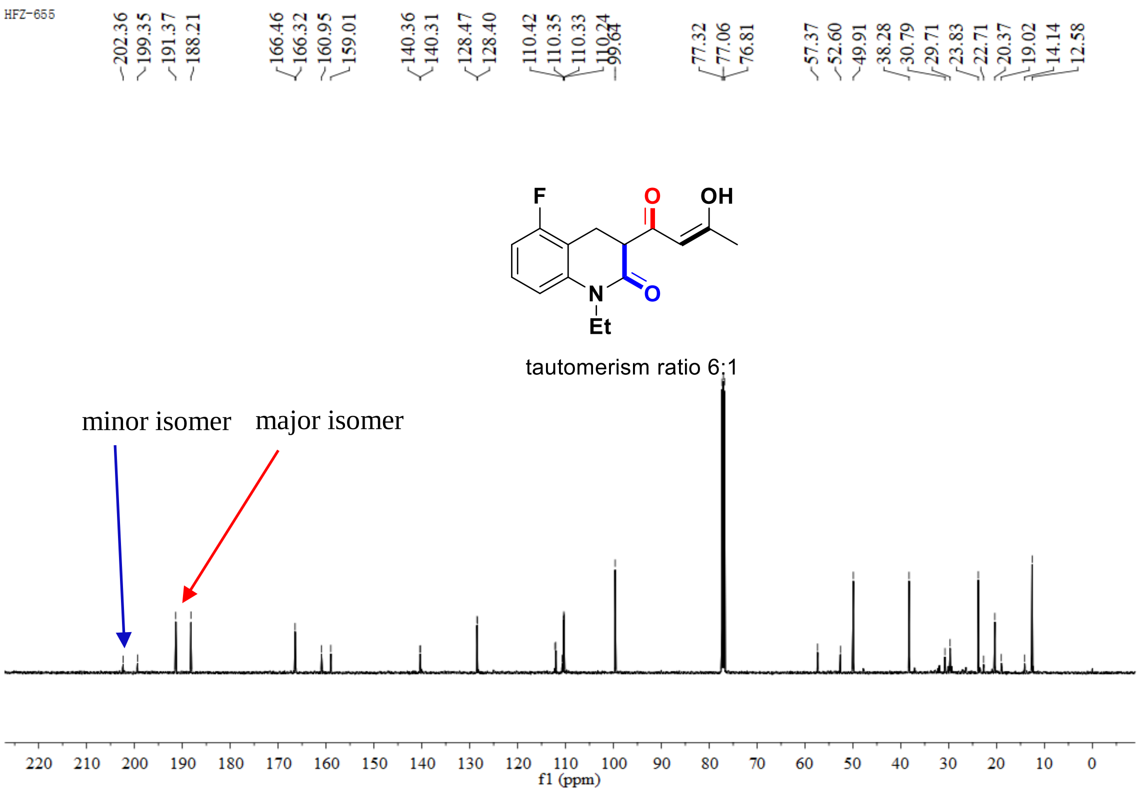
(Z)-3-(3-hydroxybut-2-enoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (11b)

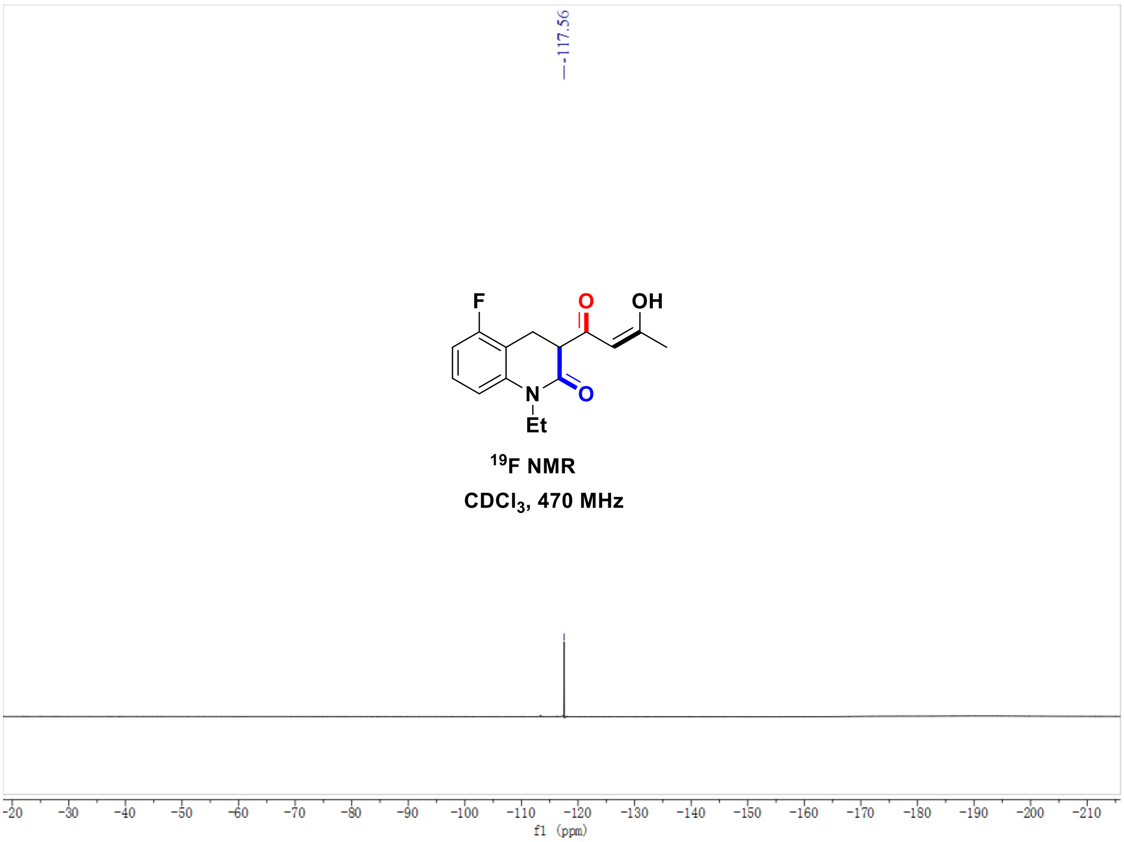




(Z)-3-(3-hydroxybut-2-enoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (11c)







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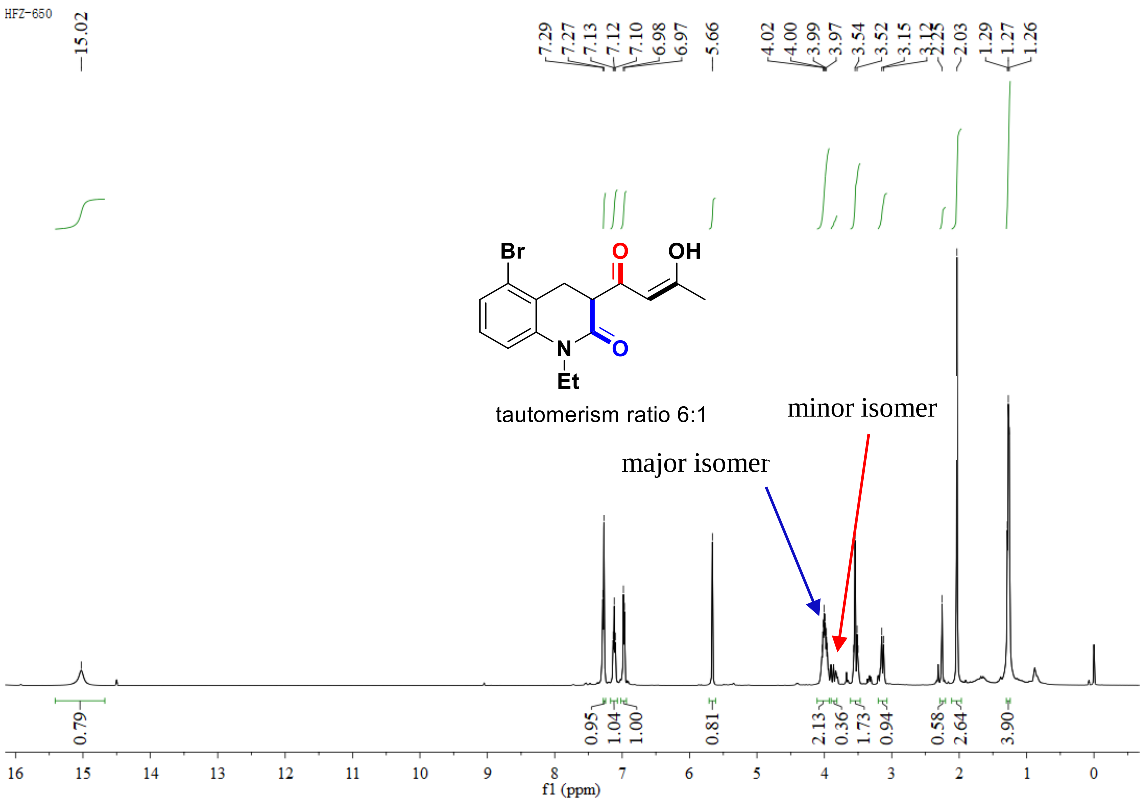
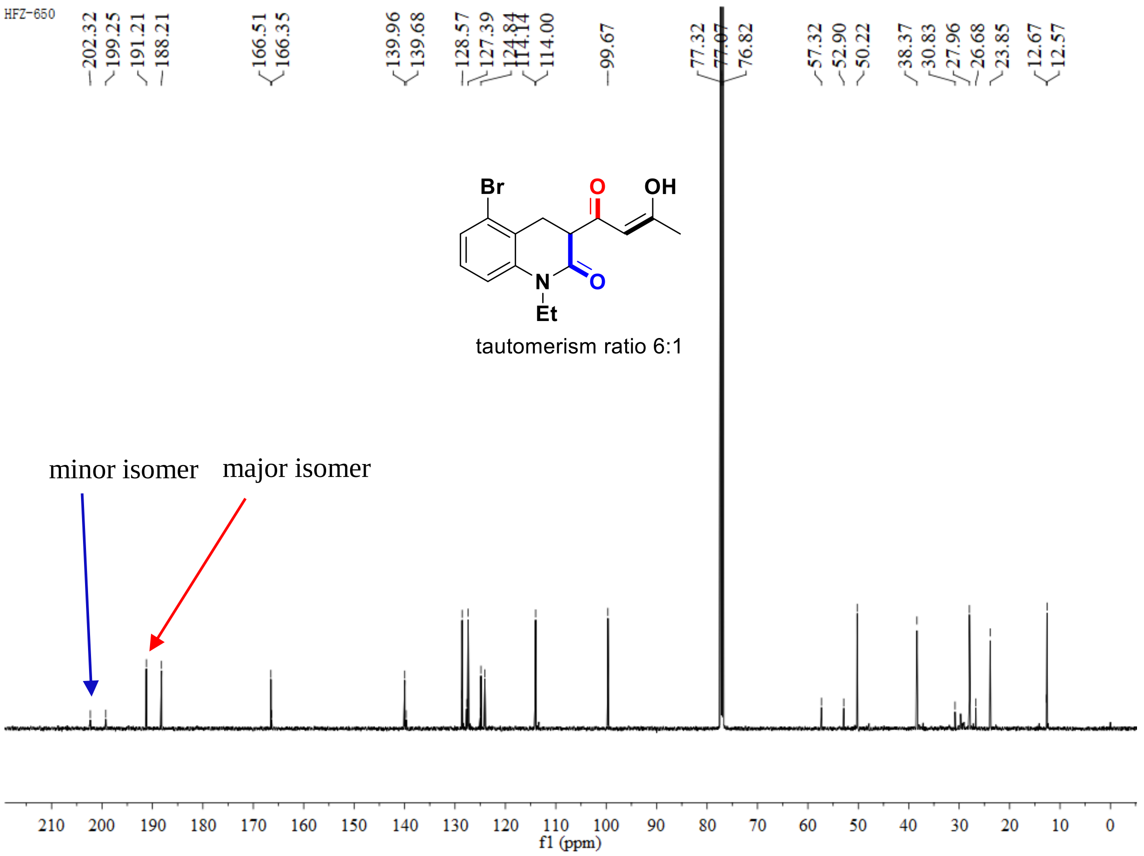
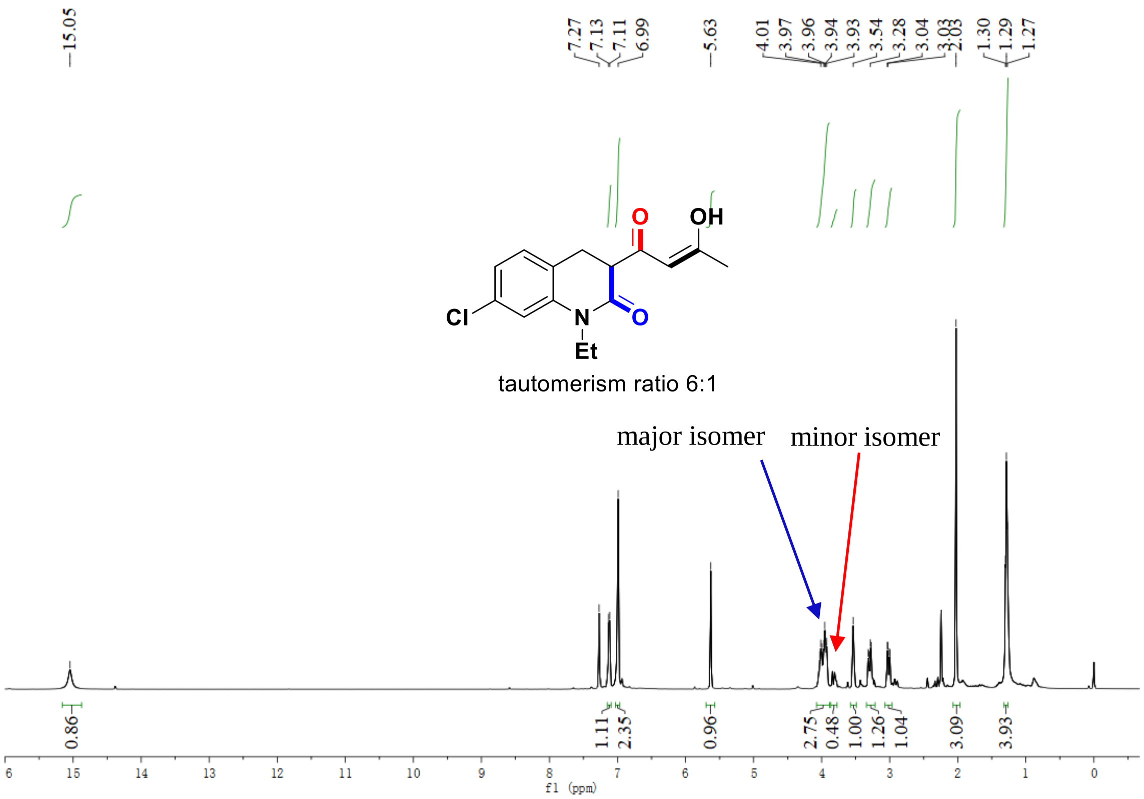
Et
O
19F NMR
CDCl3, 470 MHz
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

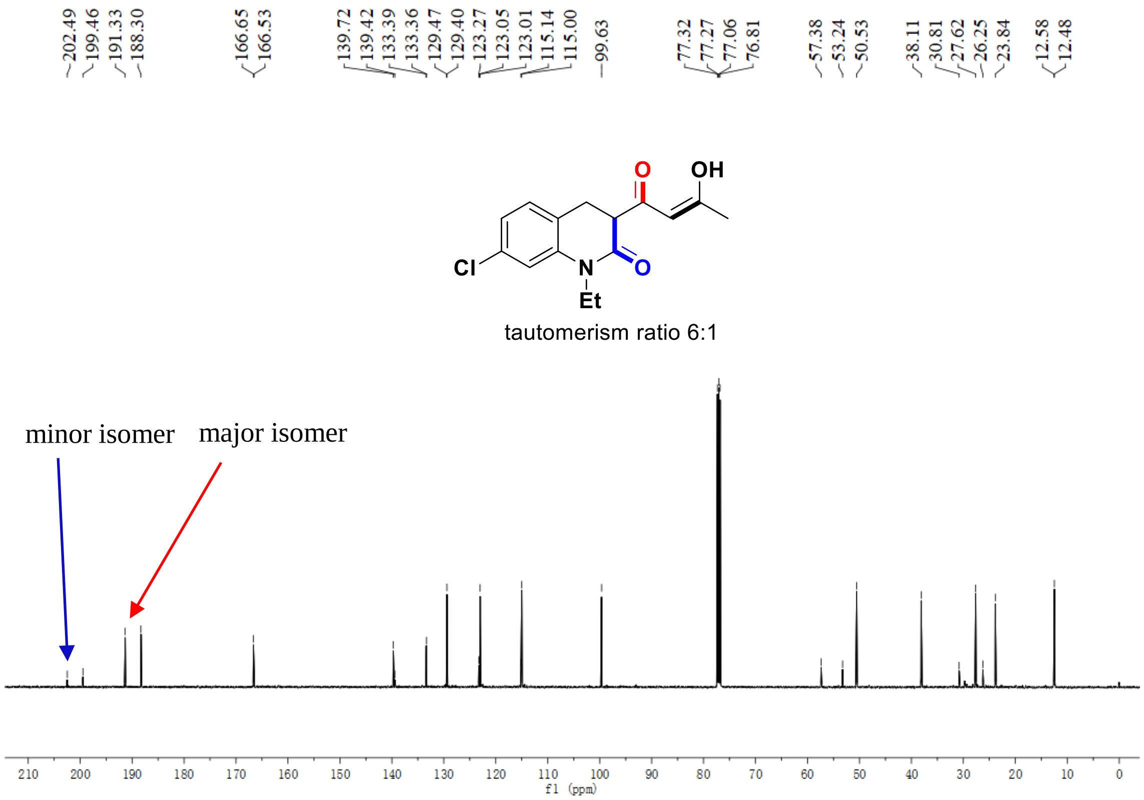
(Z)-5-bromo-1-ethyl-3-(3-hydroxybut-2-enoyl)-3,4-dihydroquinolin-2(1H)-one (11d)



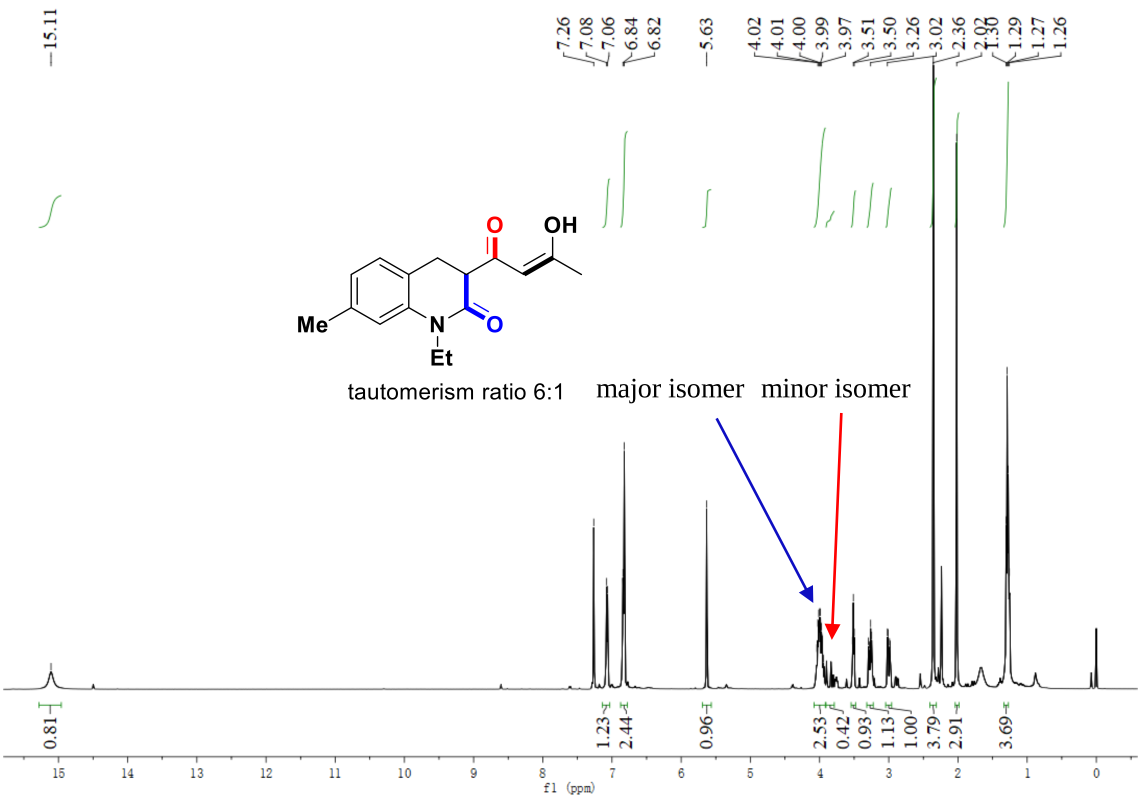


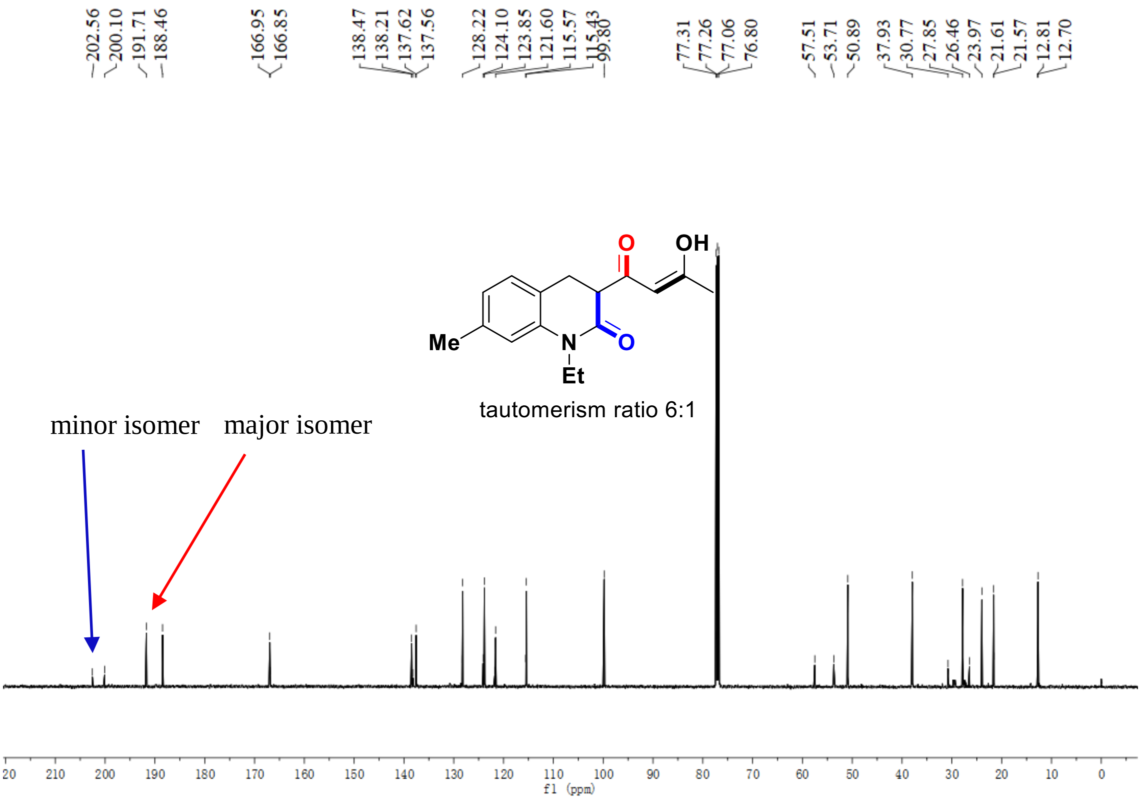
(Z)-7-chloro-1-ethyl-3-(3-hydroxybut-2-enoyl)-3,4-dihydroquinolin-2(1H)-one (11e)



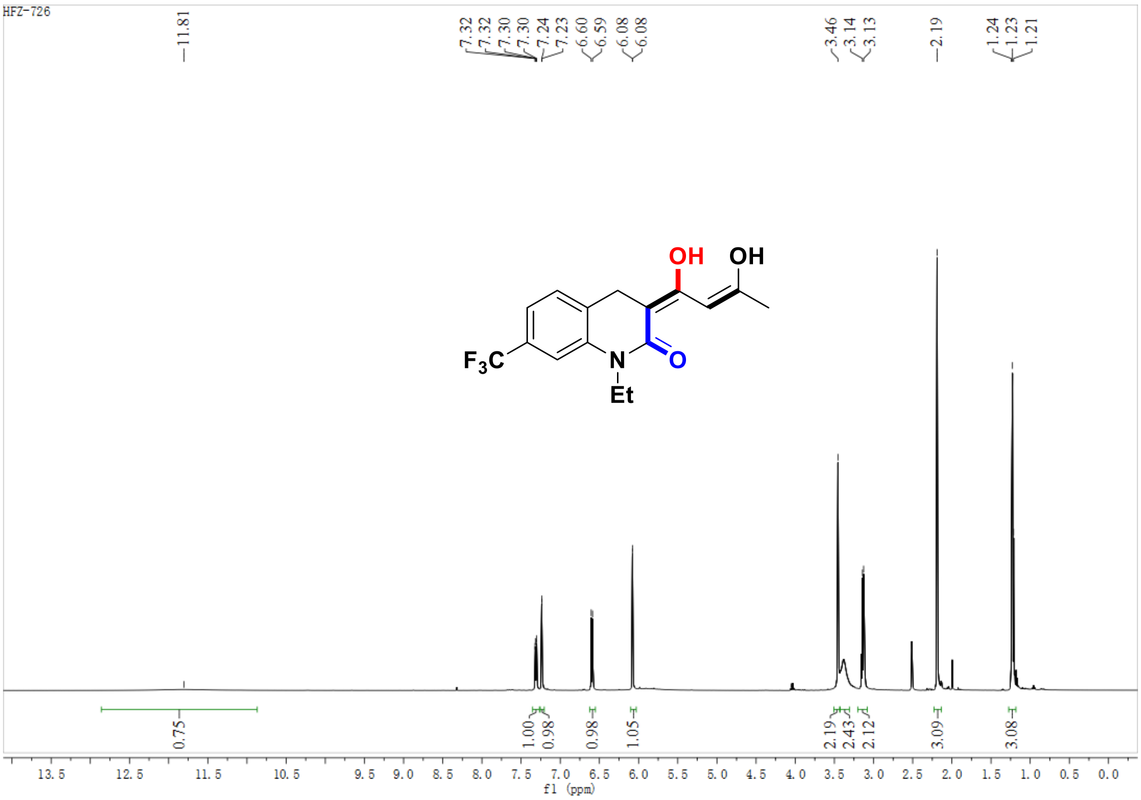


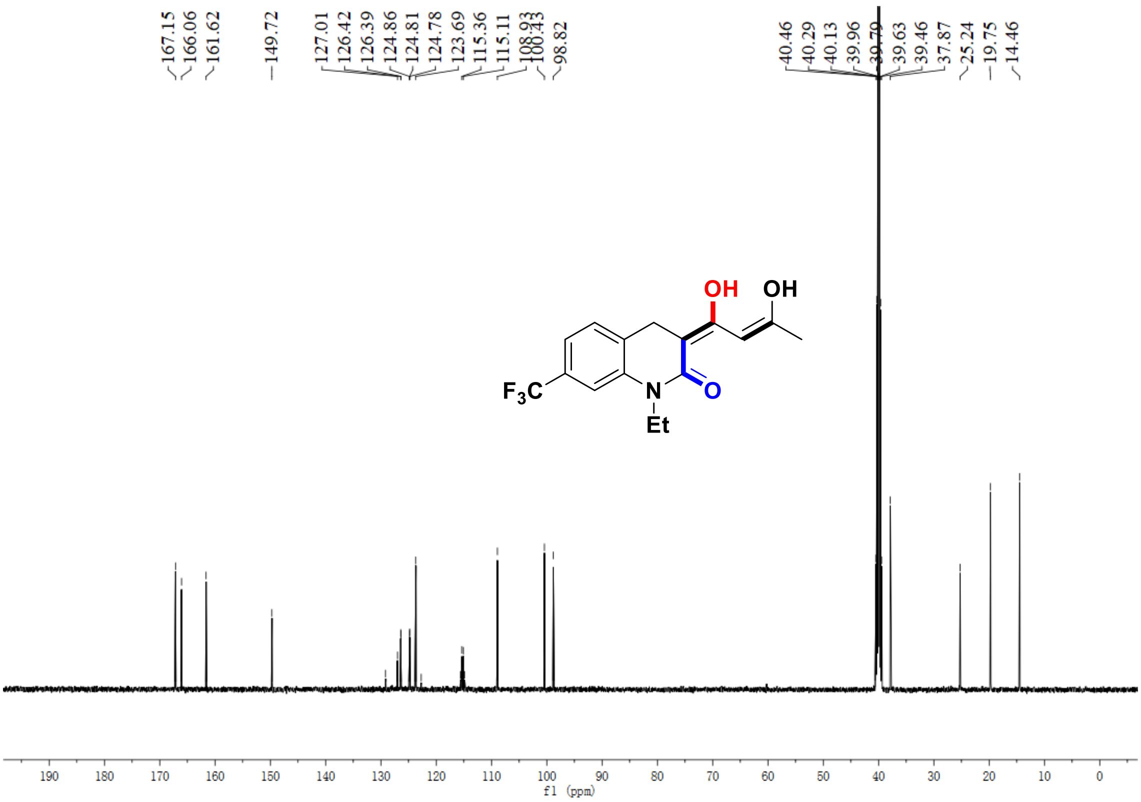
(Z)-1-ethyl-3-(3-hydroxybut-2-enoyl)-7-methyl-3,4-dihydroquinolin-2(1H)-one (11f)

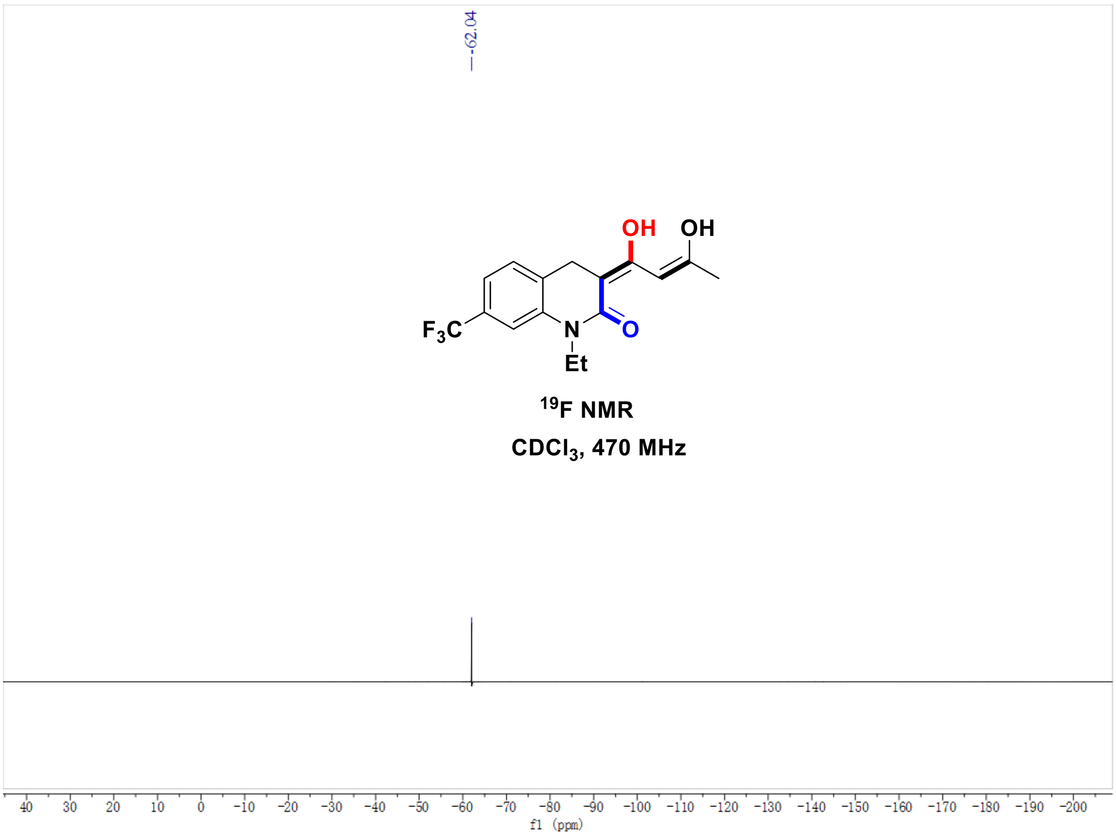




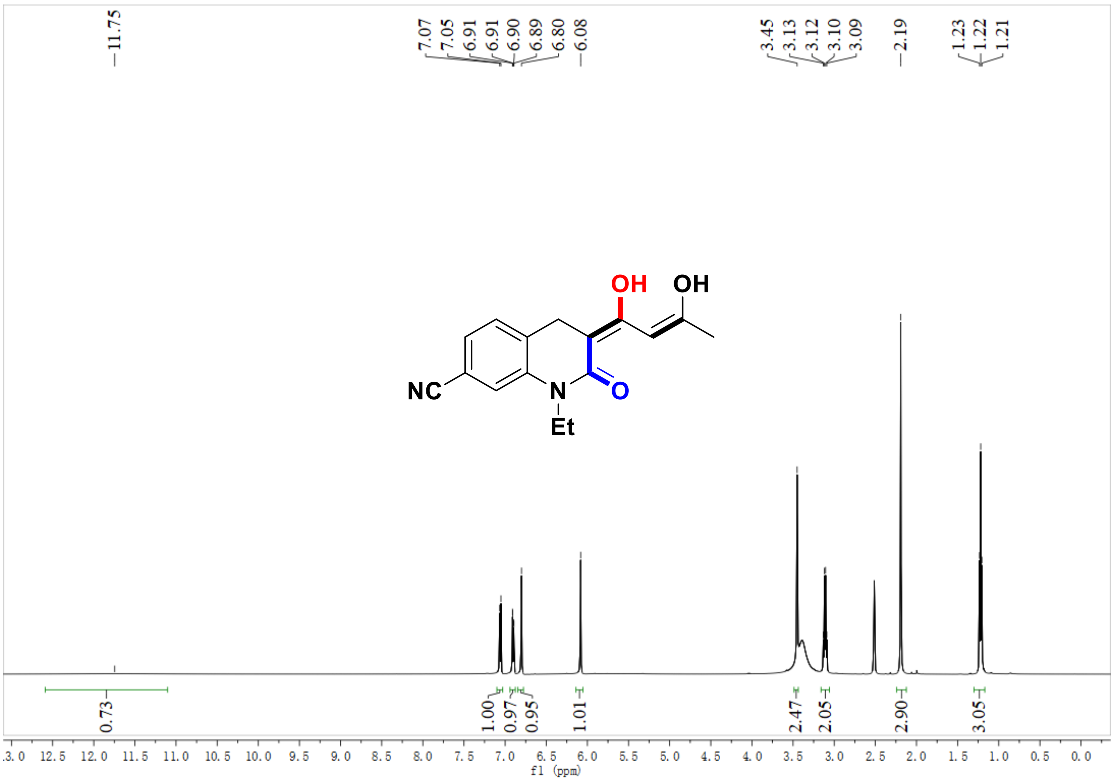
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-7-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (12a)

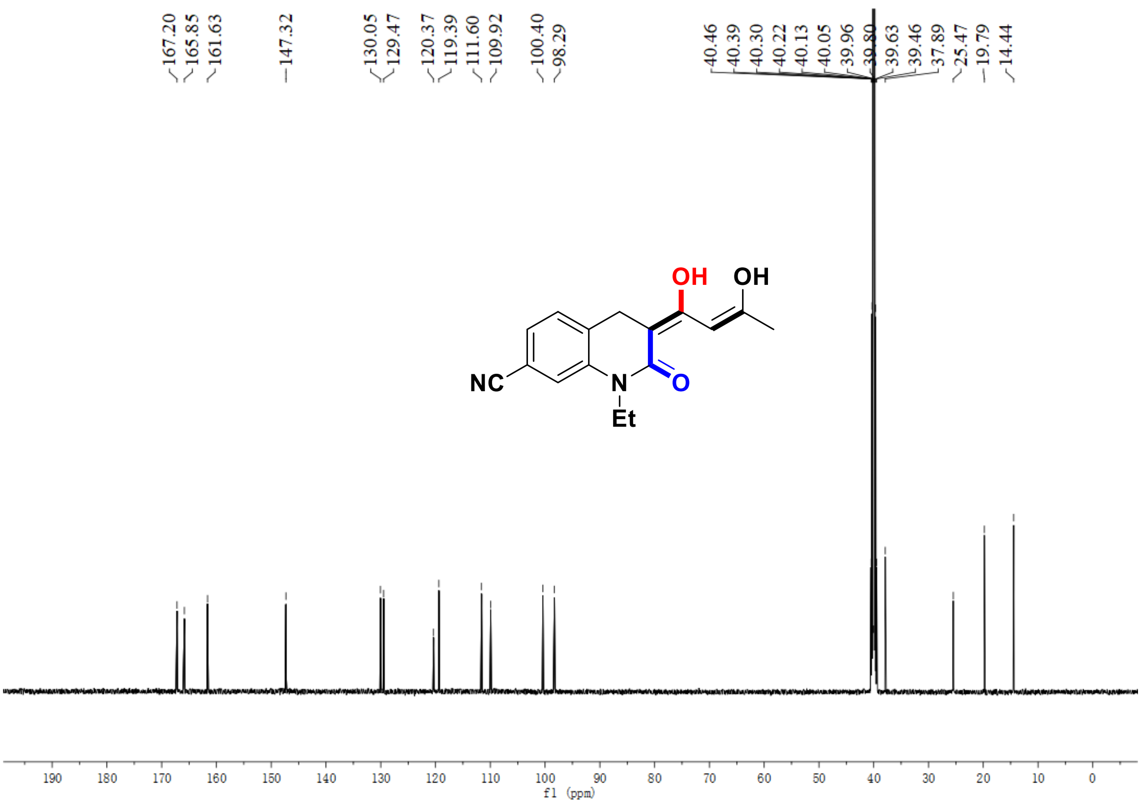




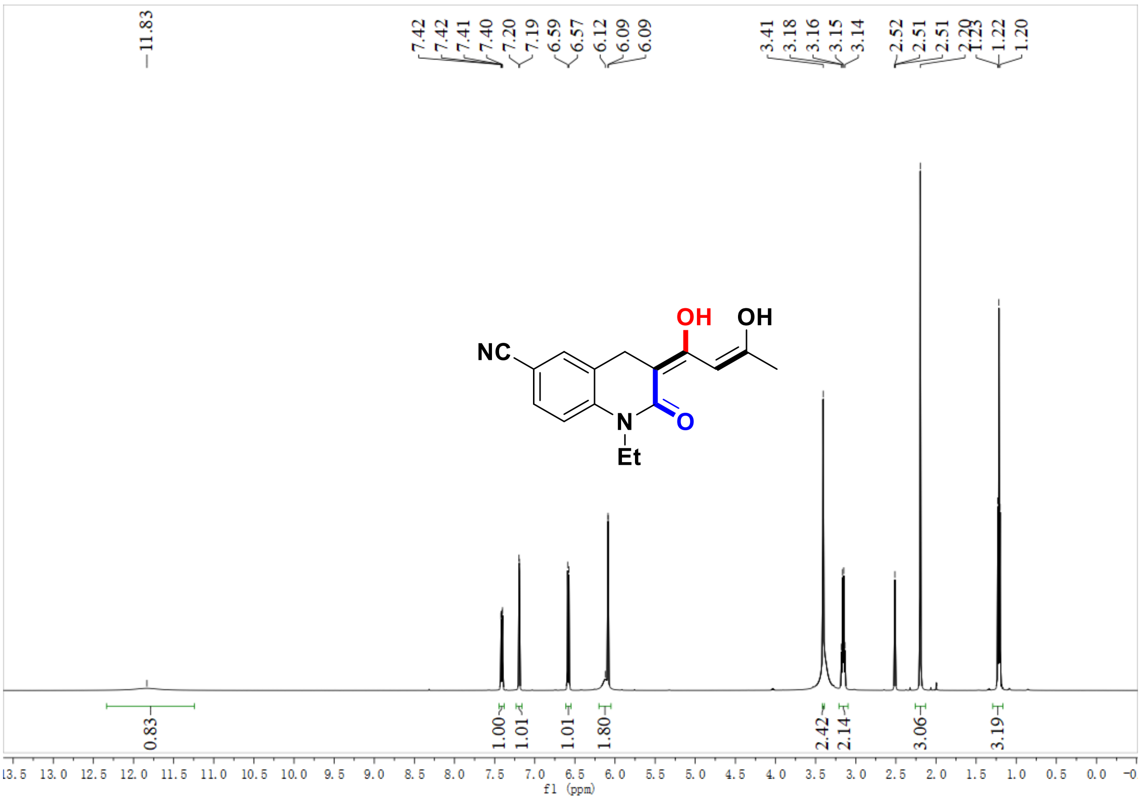

-62.04
OH
OH
F3C
N
O
Et
19F NMR
CDCl3, 470 MHz
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

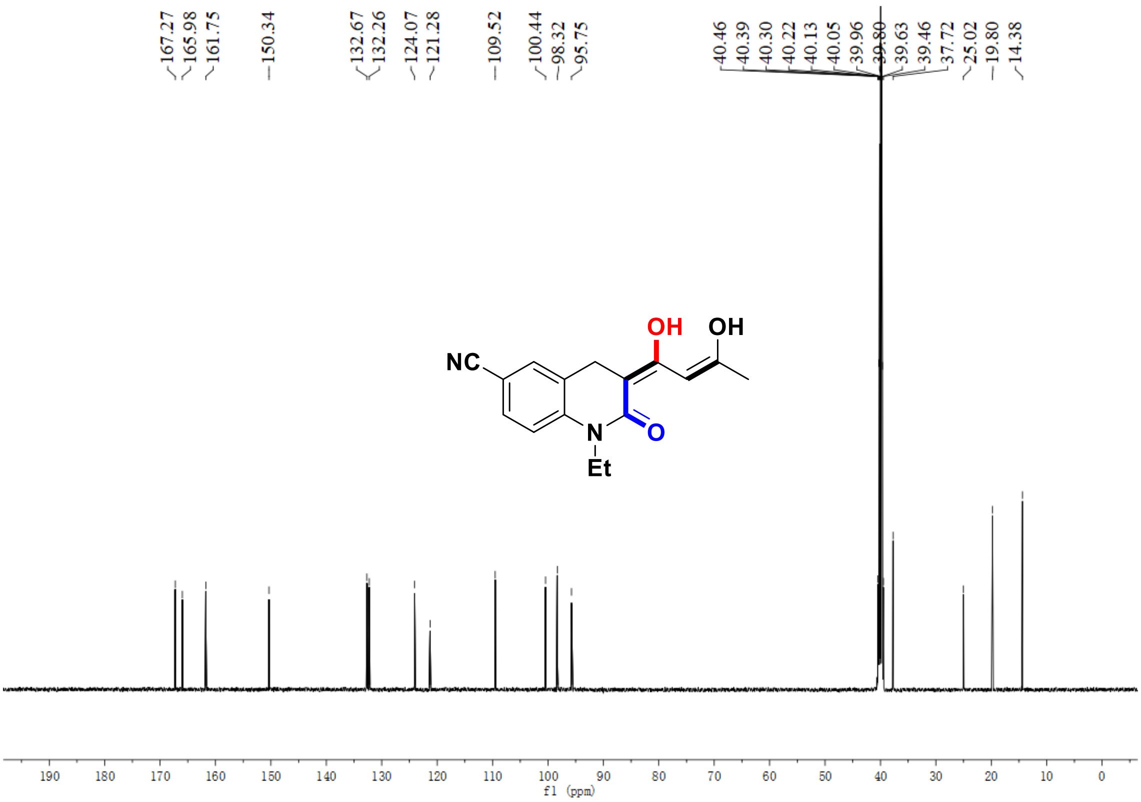
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-7-carbonitrile (12b)



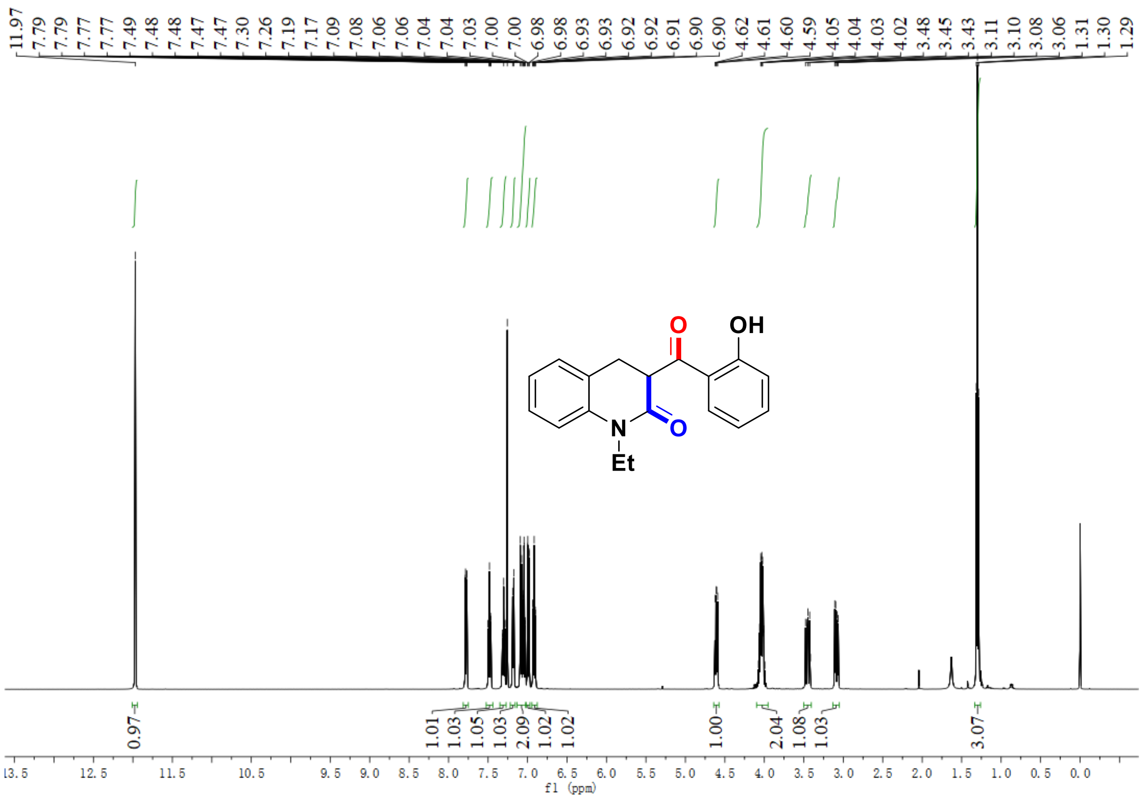


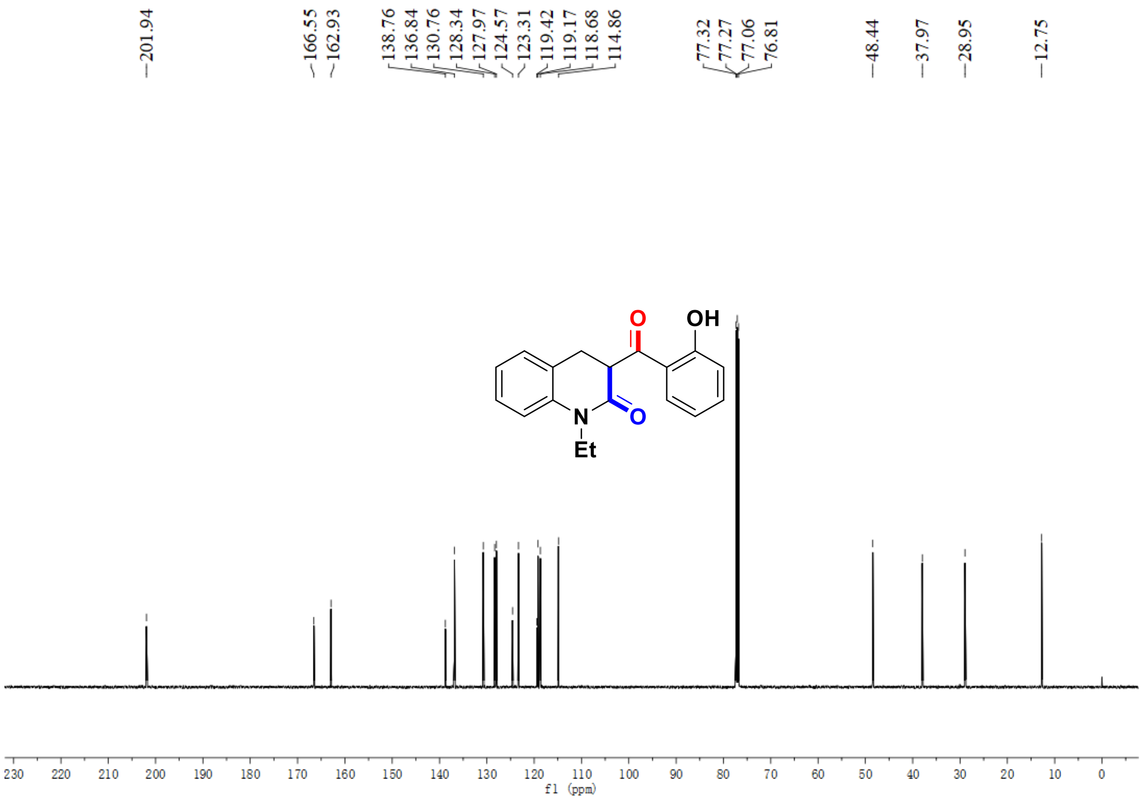
(E)-3-((Z)-1,3-dihydroxybut-2-en-1-ylidene)-1-ethyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carbonitrile (12c)



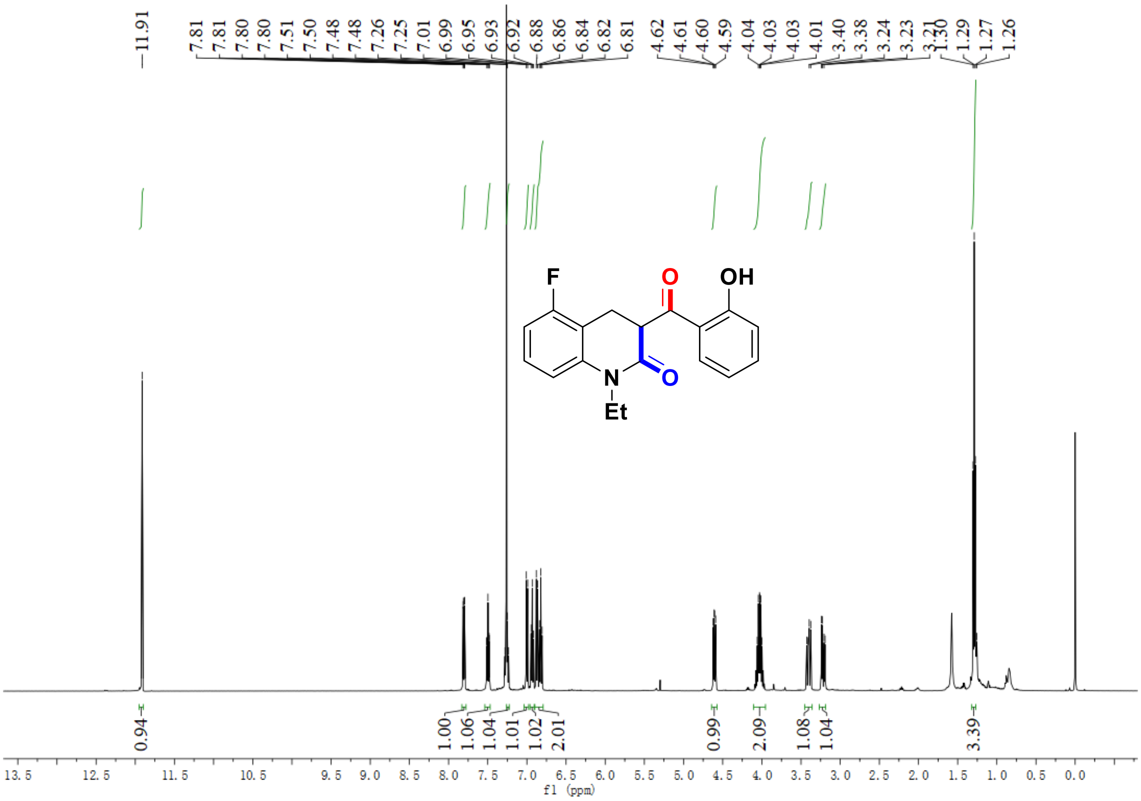


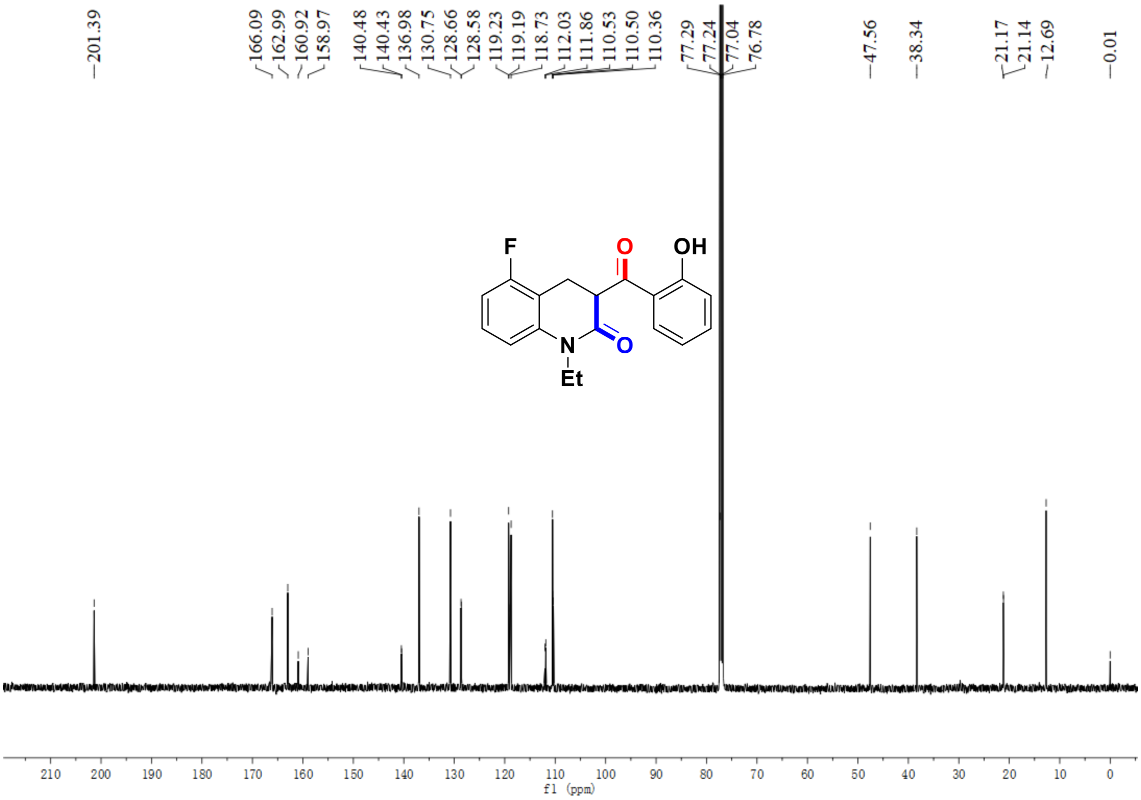
1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13a)

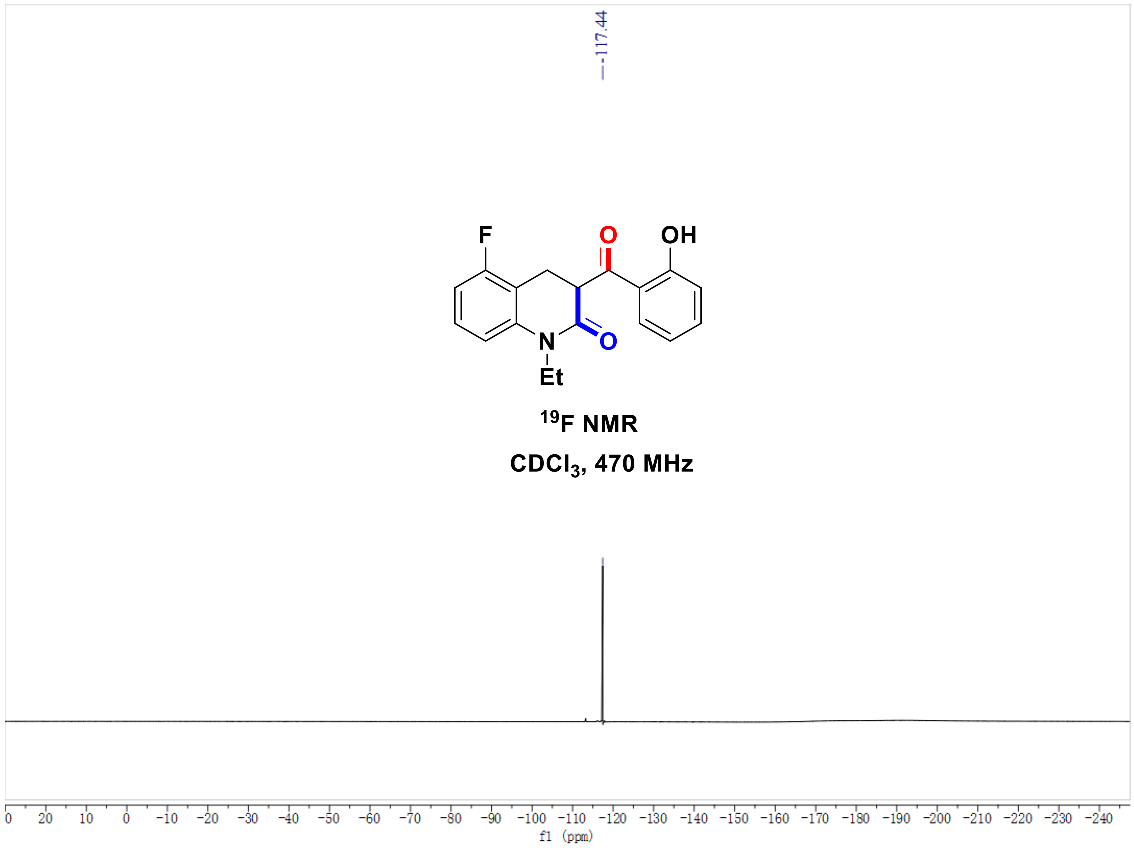




1-ethyl-5-fluoro-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13b)

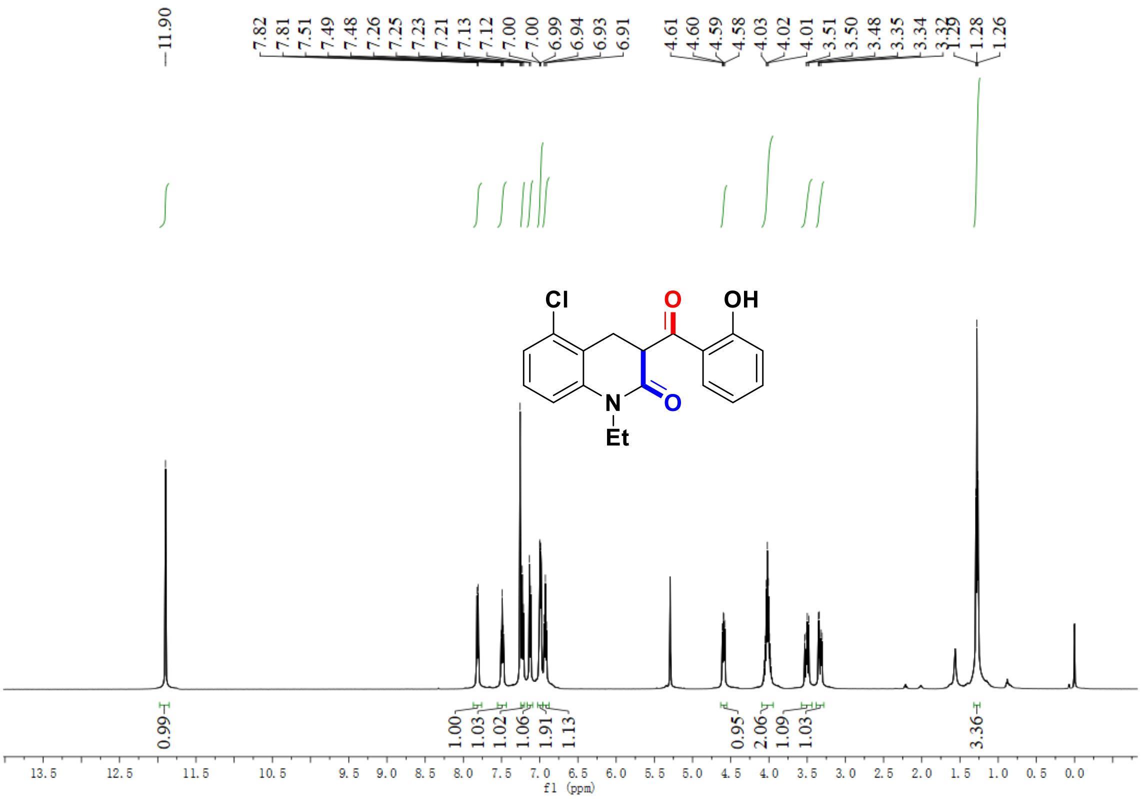


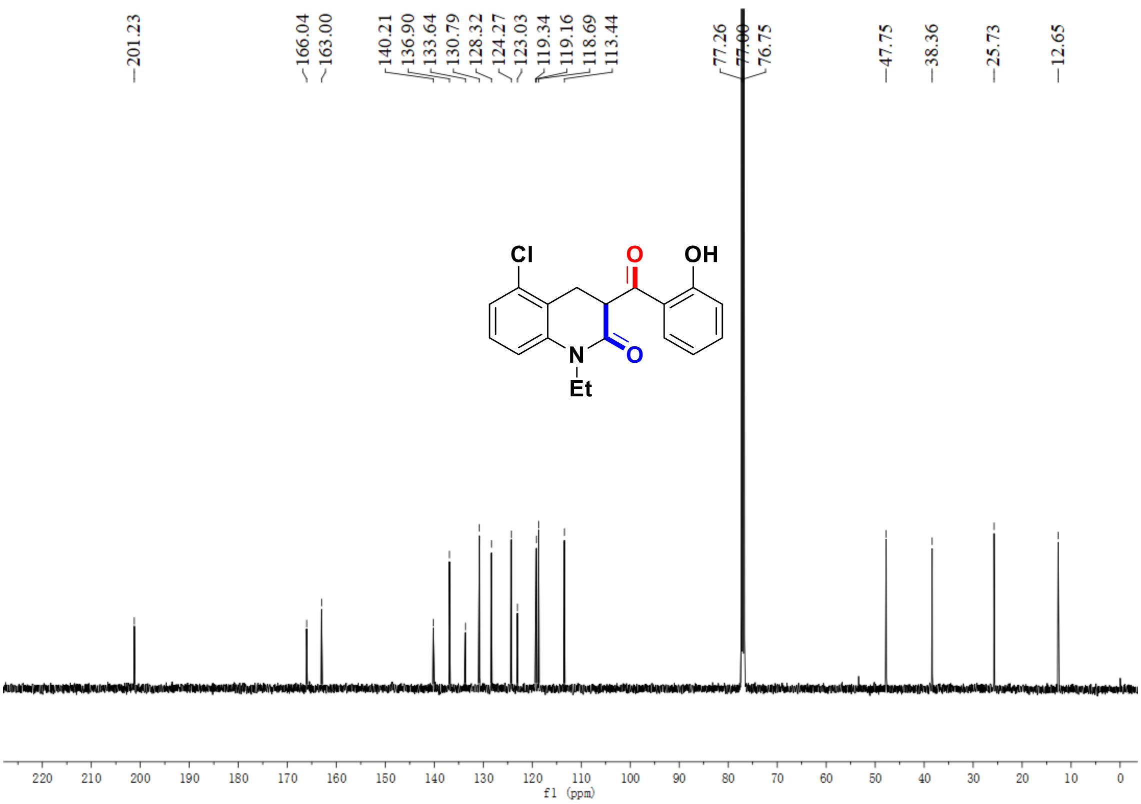




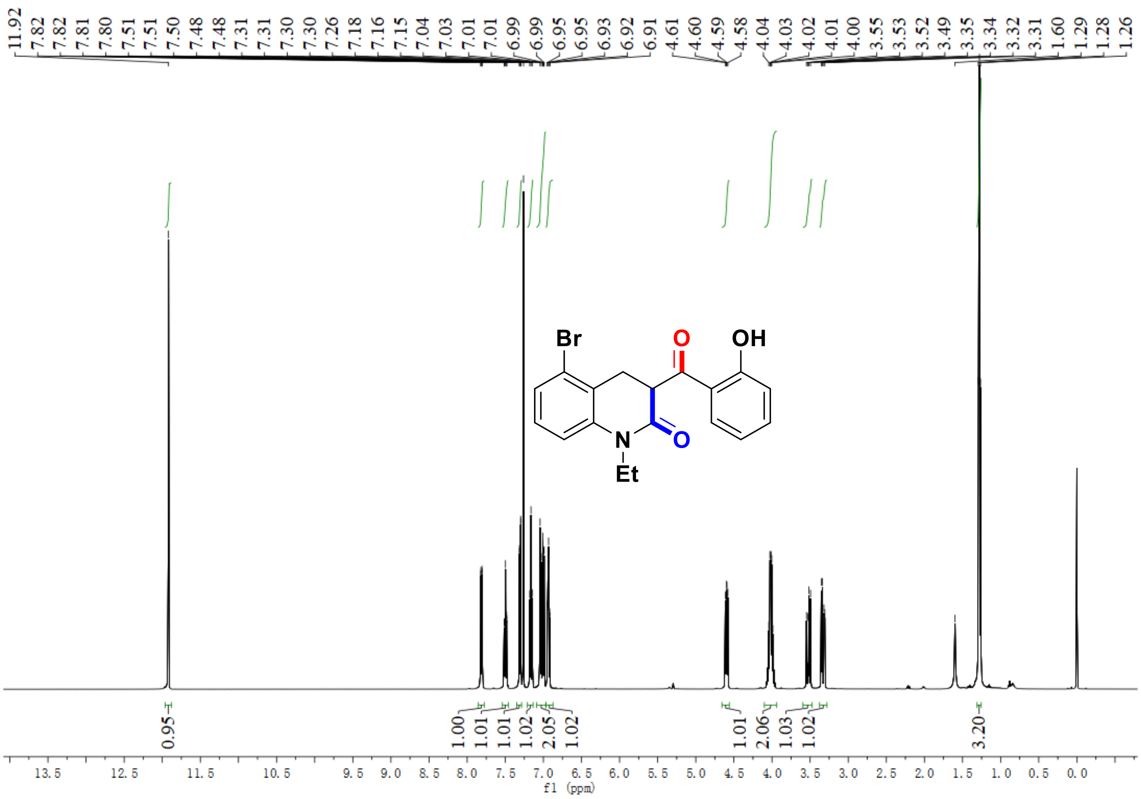
-117.44
F
O
OH
N
O
Et
19F NMR
CDCl3, 470 MHz
f1 (ppm)

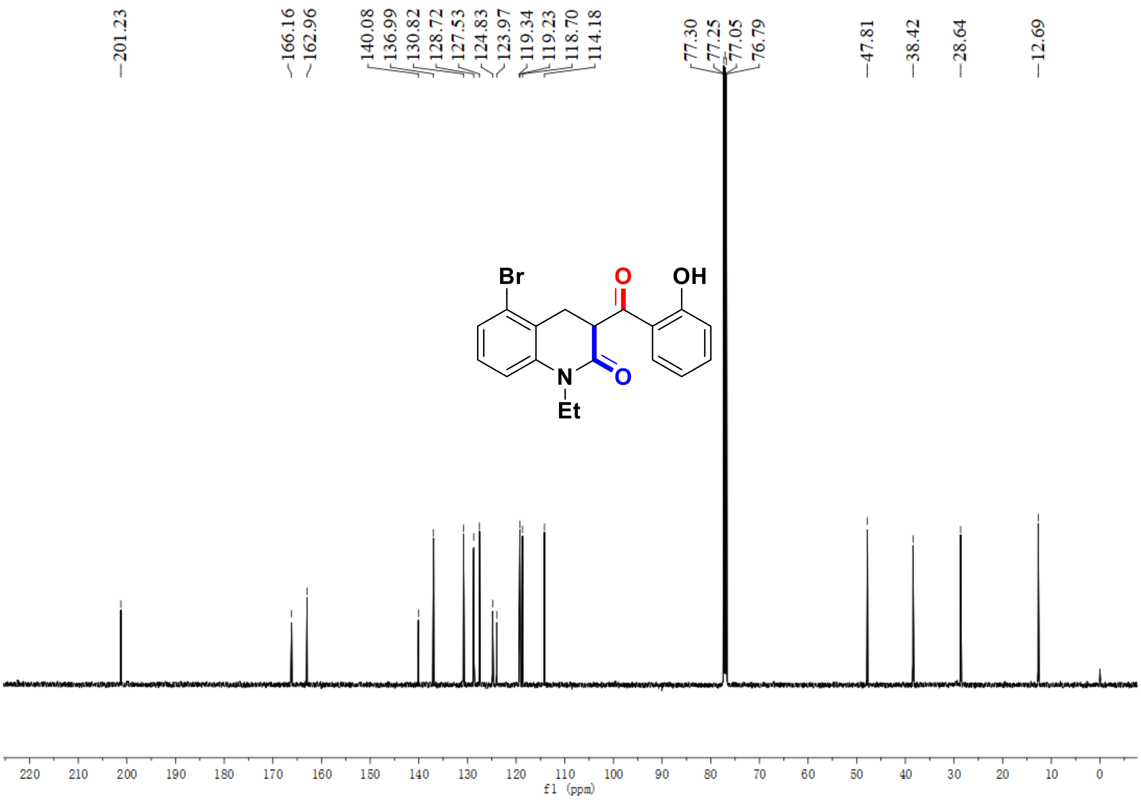
5-chloro-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13c)



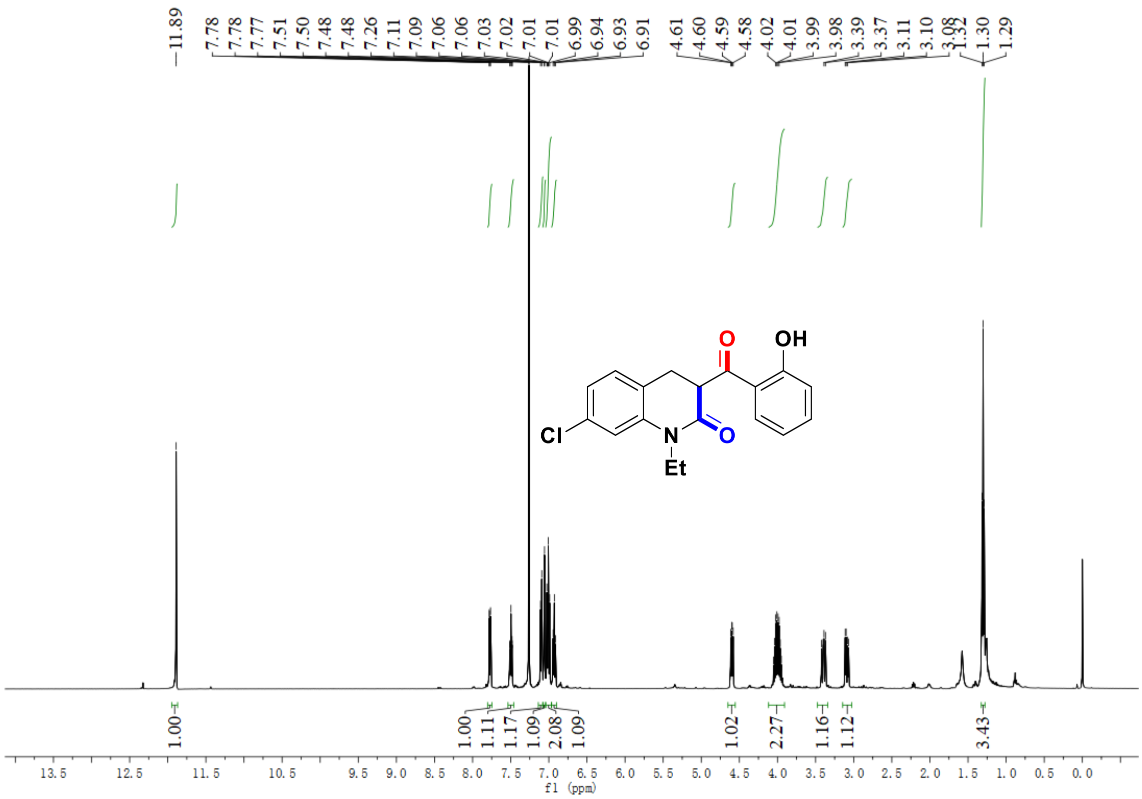


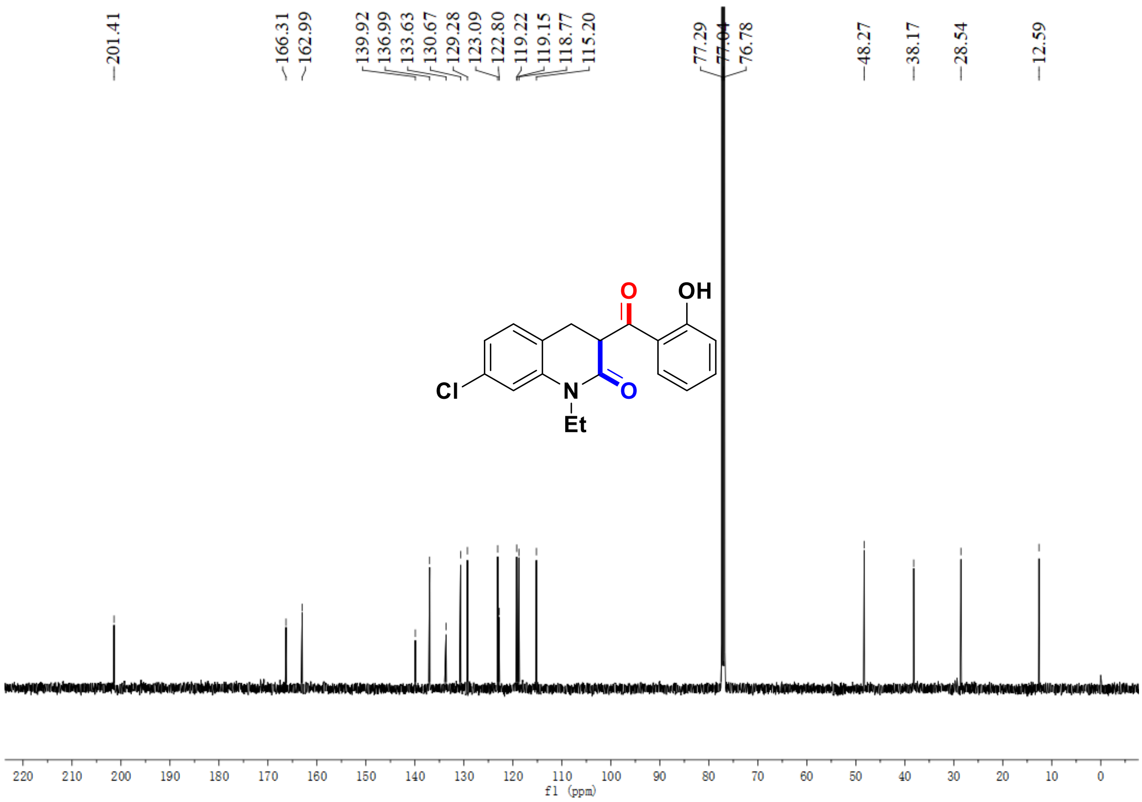
5-bromo-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13d)



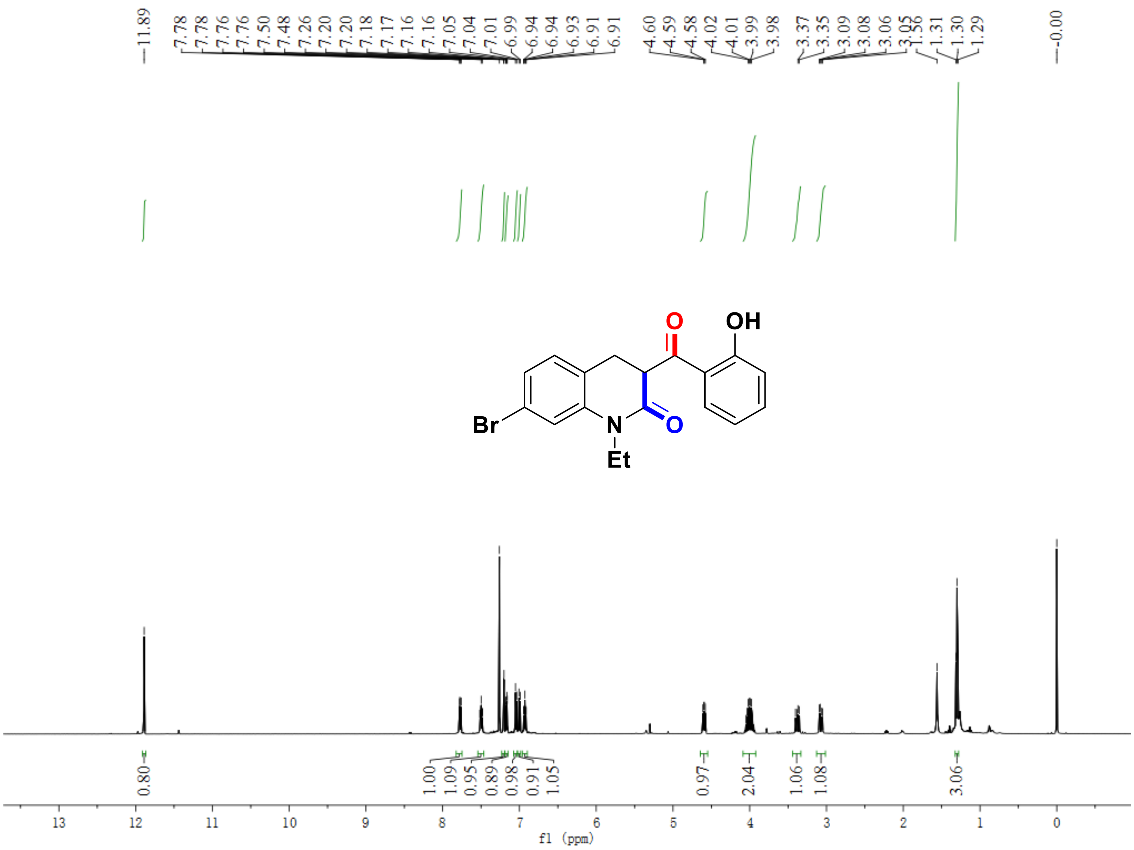


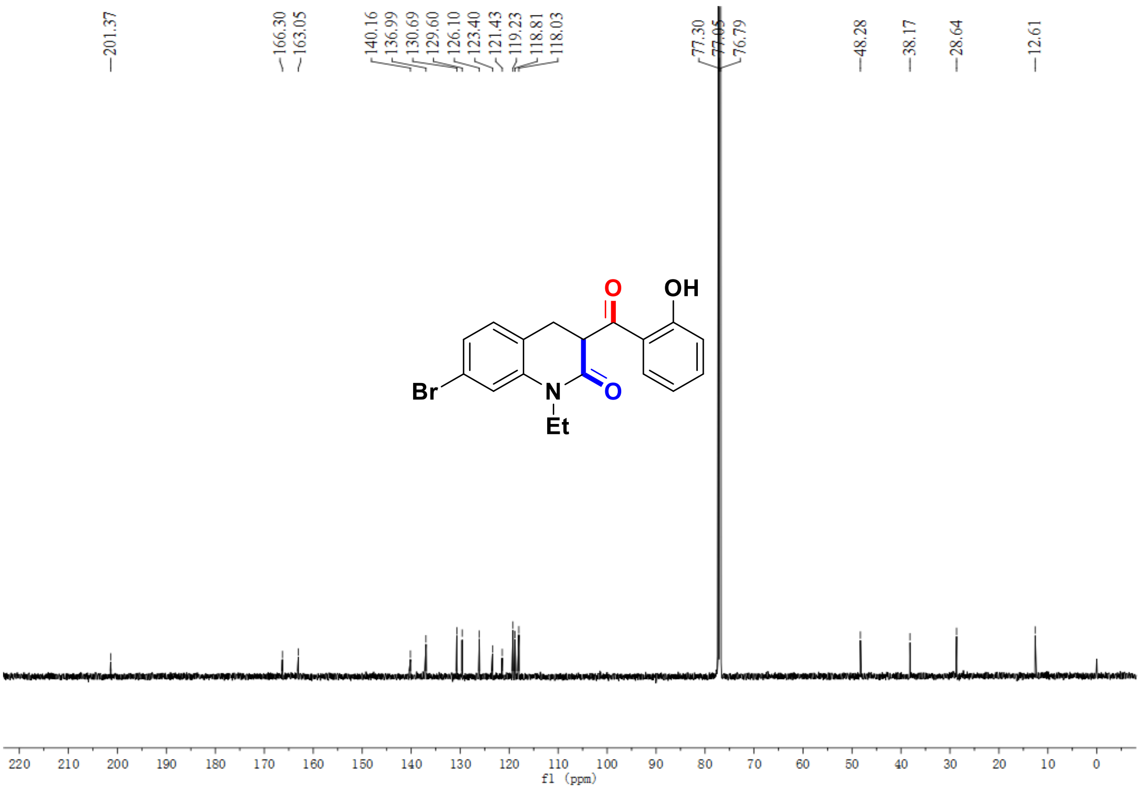
7-chloro-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13e)



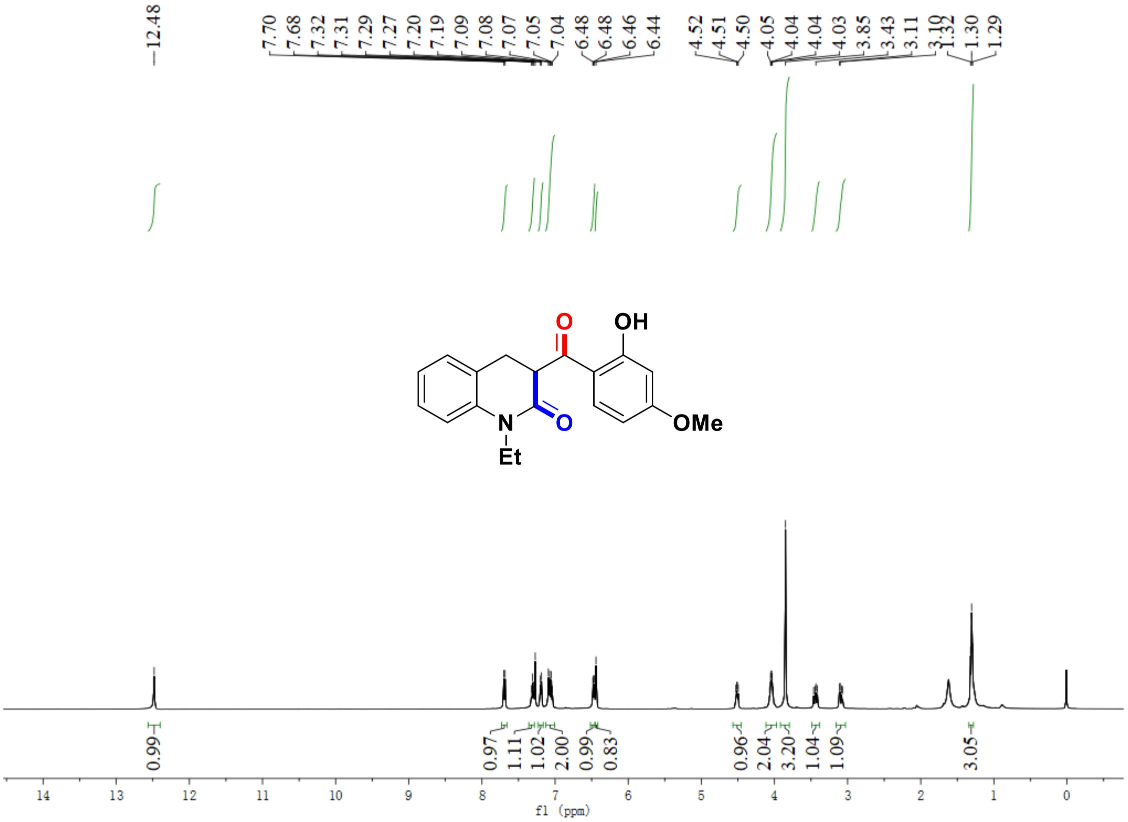


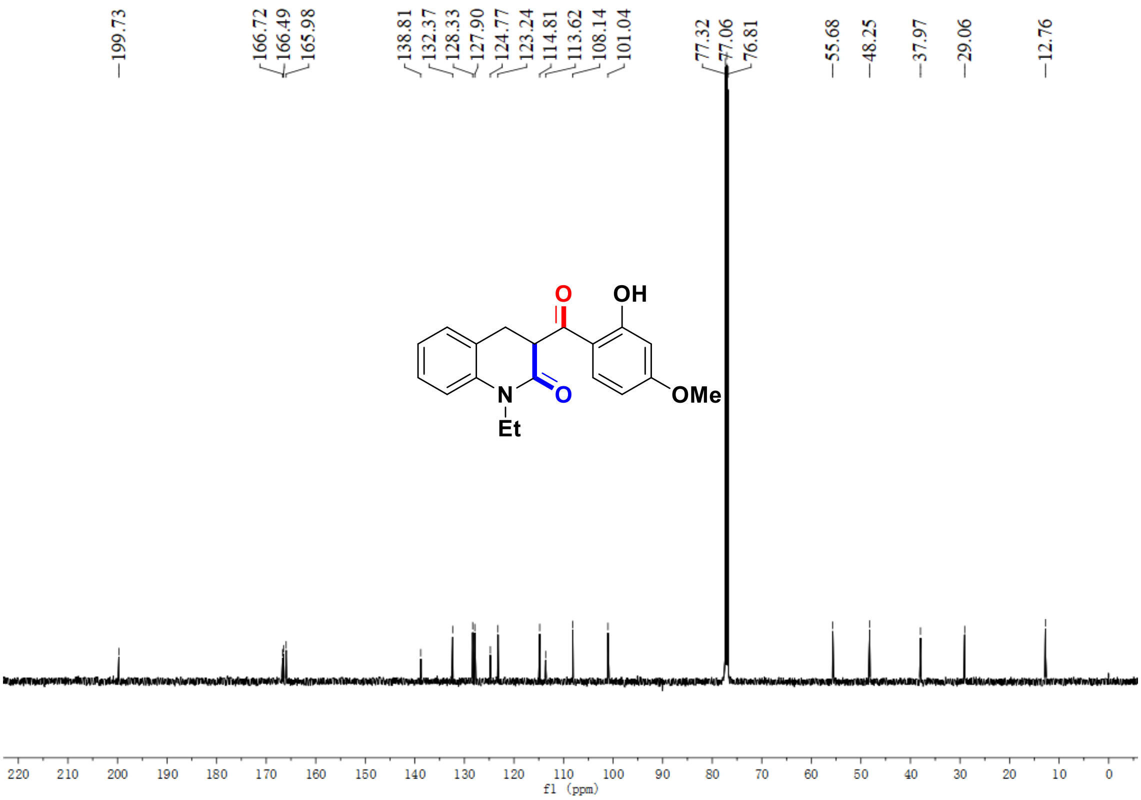
7-bromo-1-ethyl-3-(2-hydroxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13f)



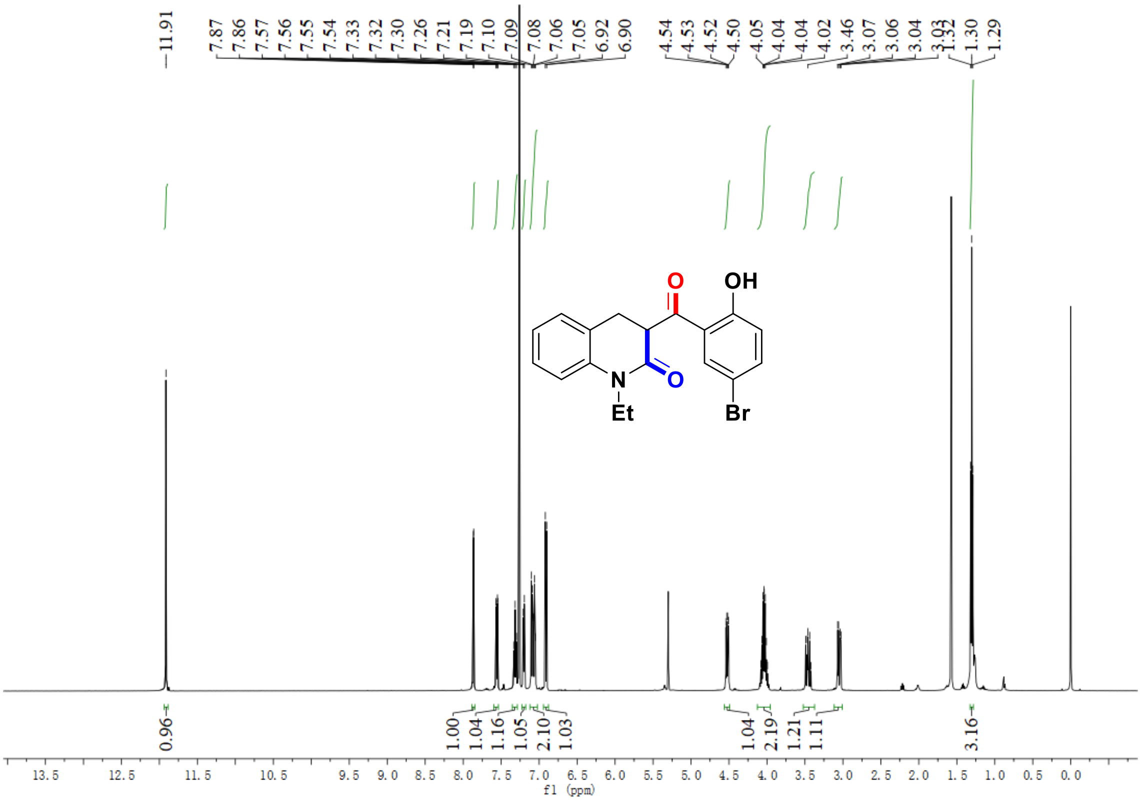


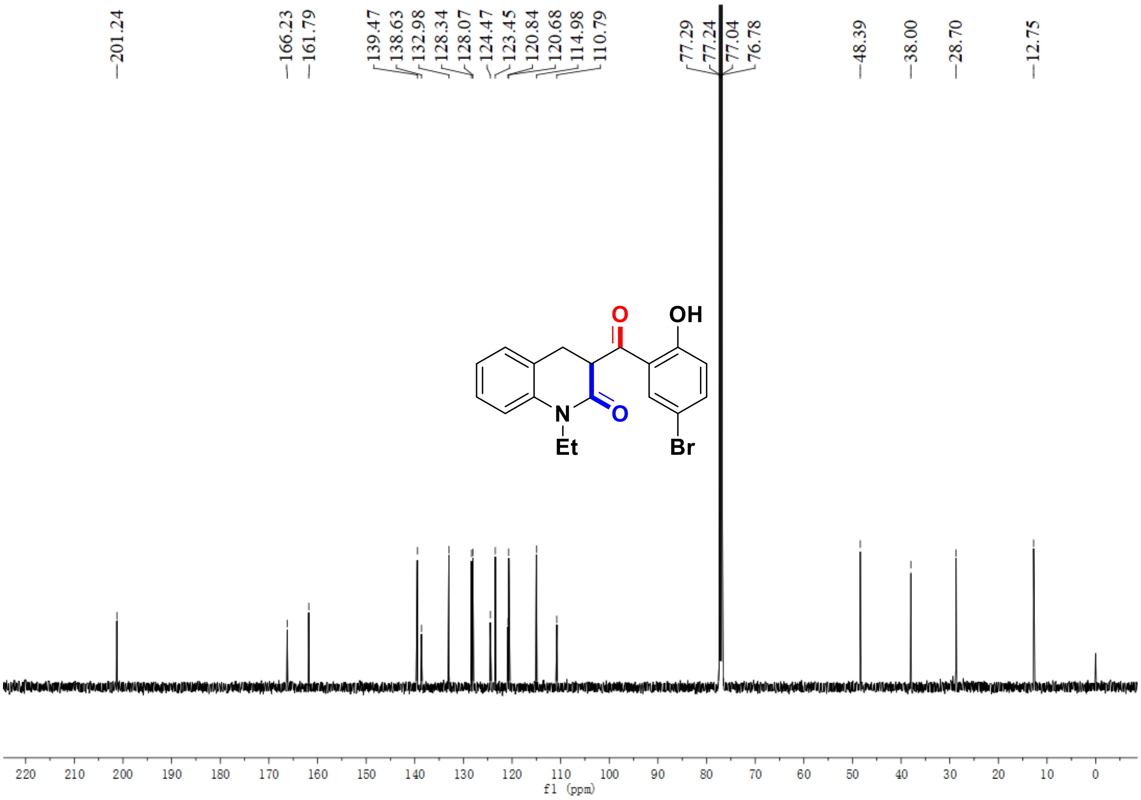
1-ethyl-3-(2-hydroxy-4-methoxybenzoyl)-3,4-dihydroquinolin-2(1H)-one (13g)



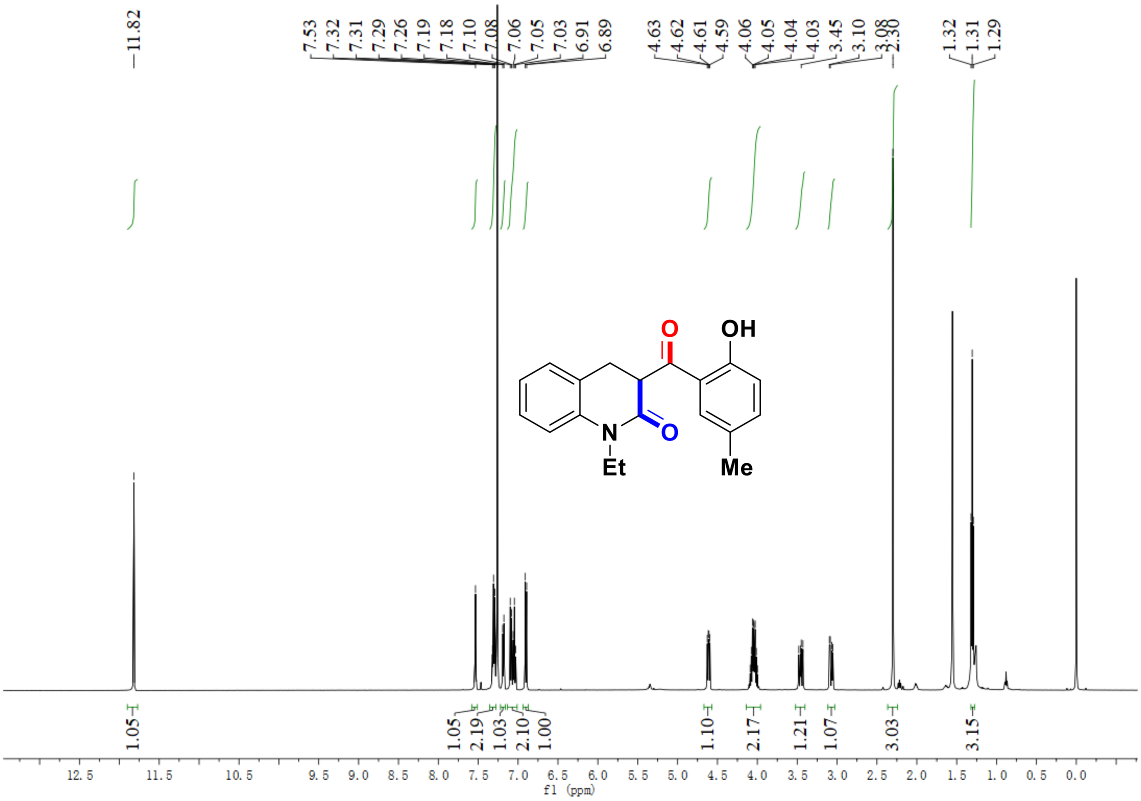


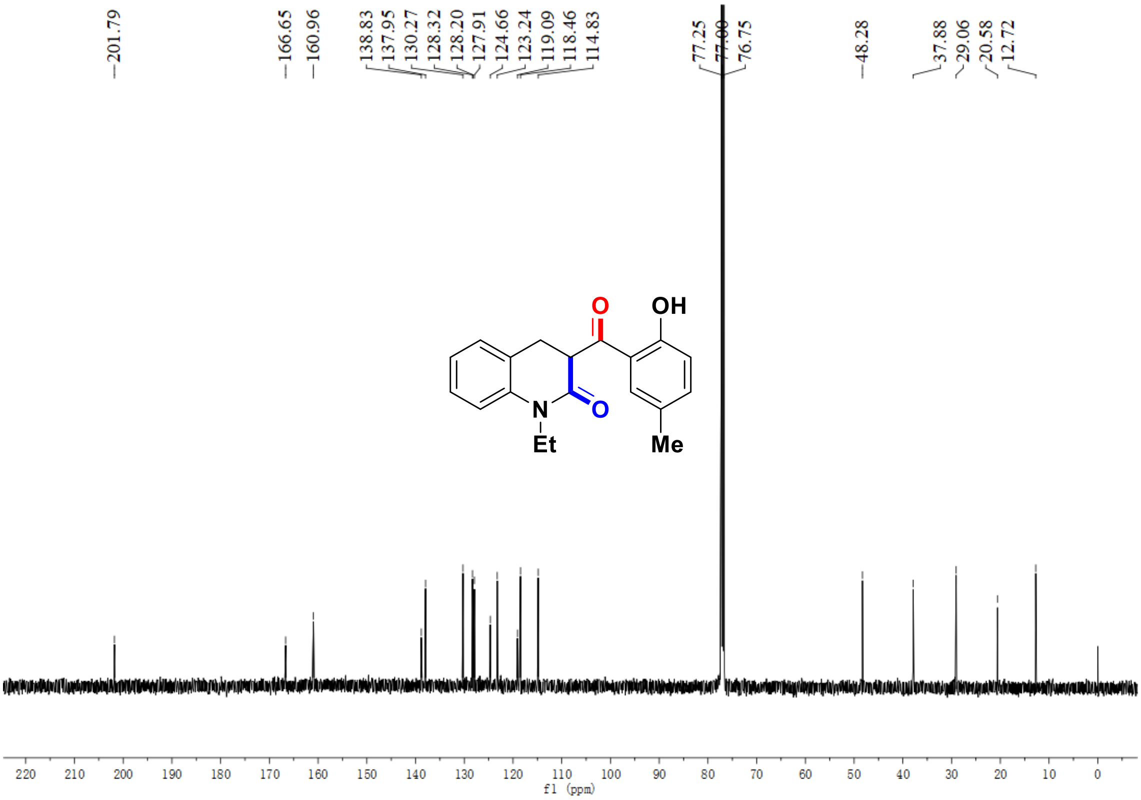
3-(5-bromo-2-hydroxybenzoyl)-1-ethyl-3,4-dihydroquinolin-2(1H)-one (13h)



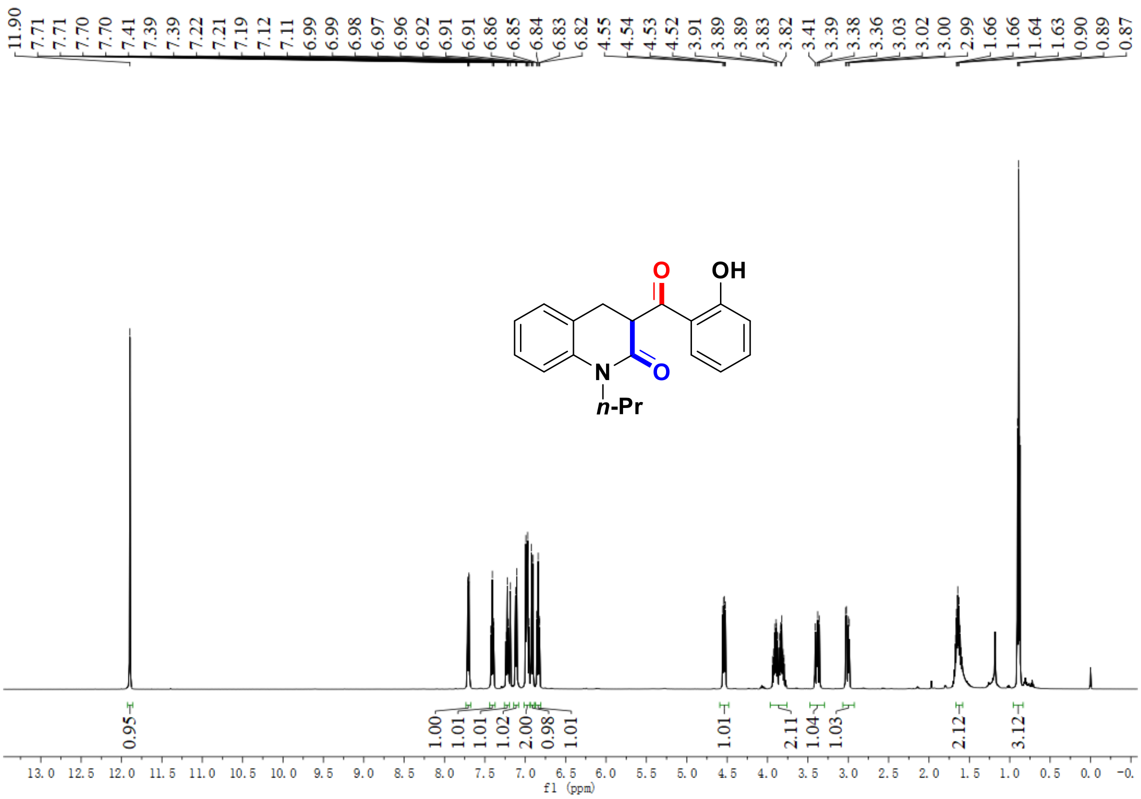


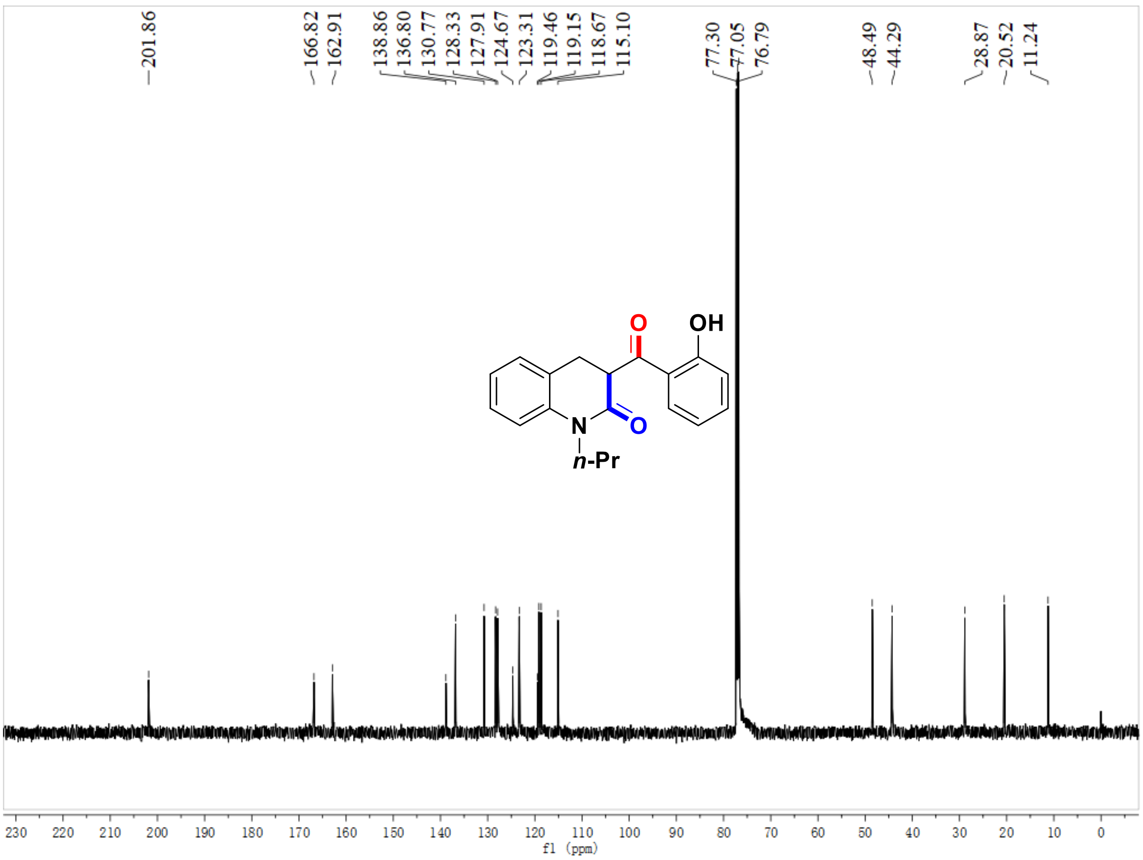
1-ethyl-3-(2-hydroxy-5-methylbenzoyl)-3,4-dihydroquinolin-2(1H)-one (13i)



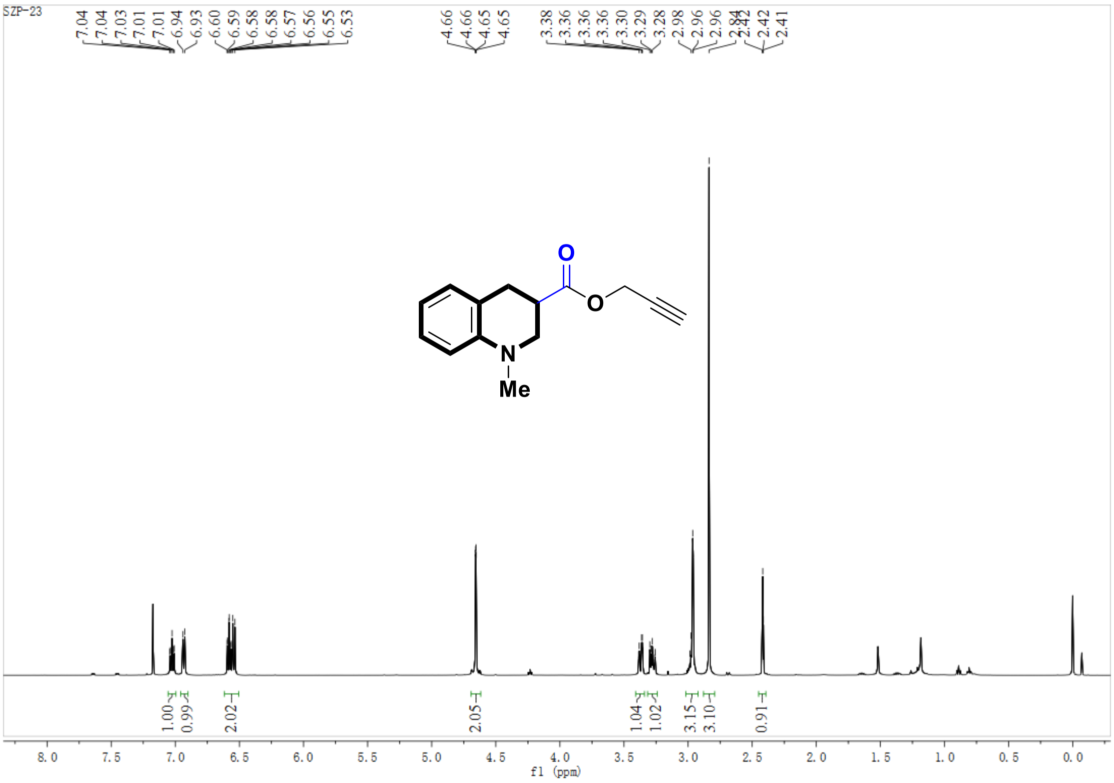


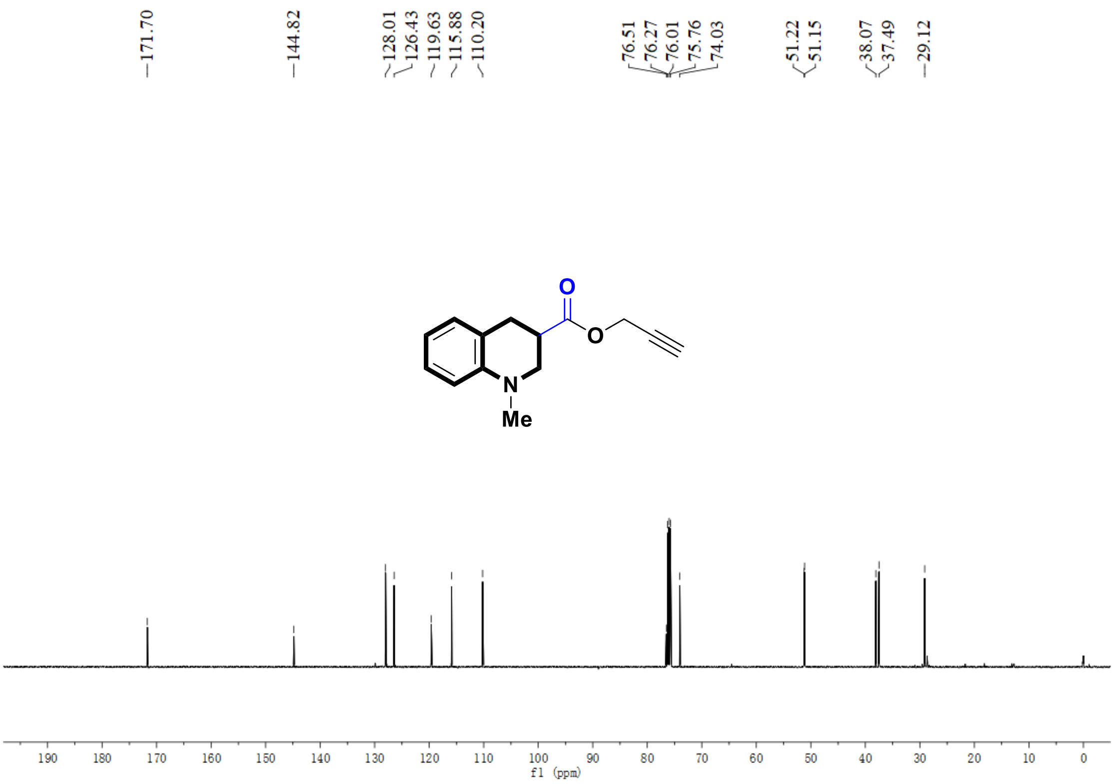
3-(2-hydroxybenzoyl)-1-propyl-3,4-dihydroquinolin-2(1H)-one (13j)



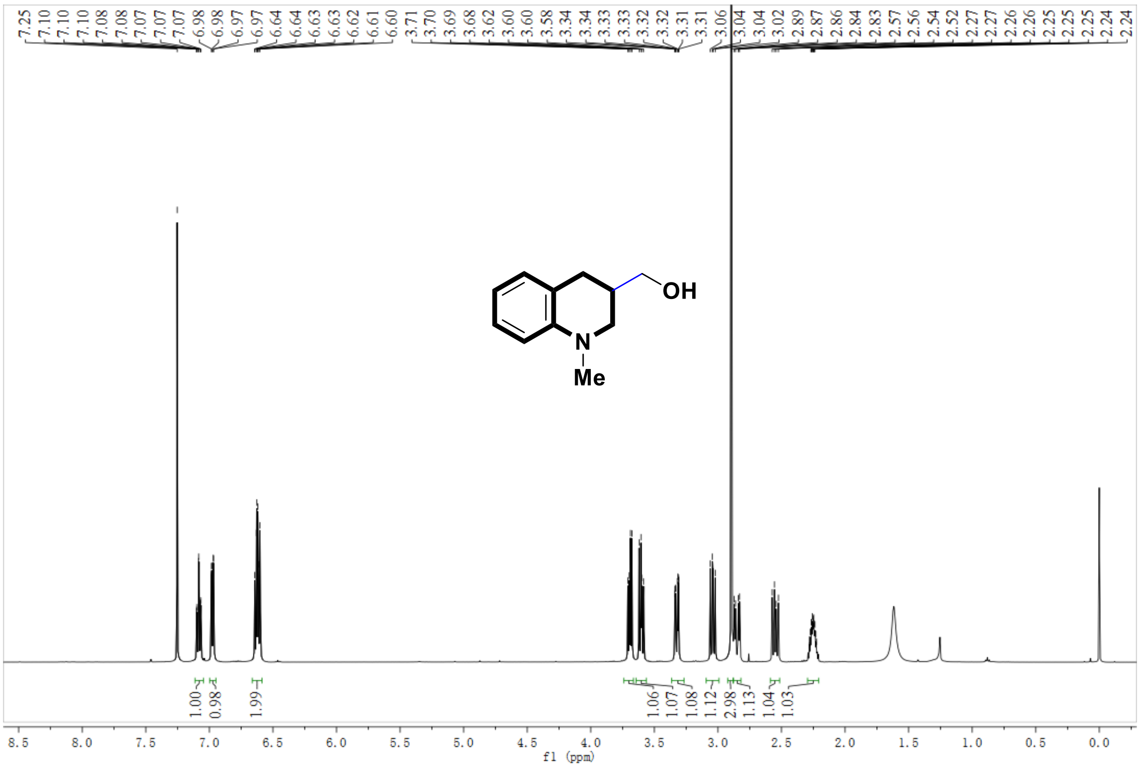


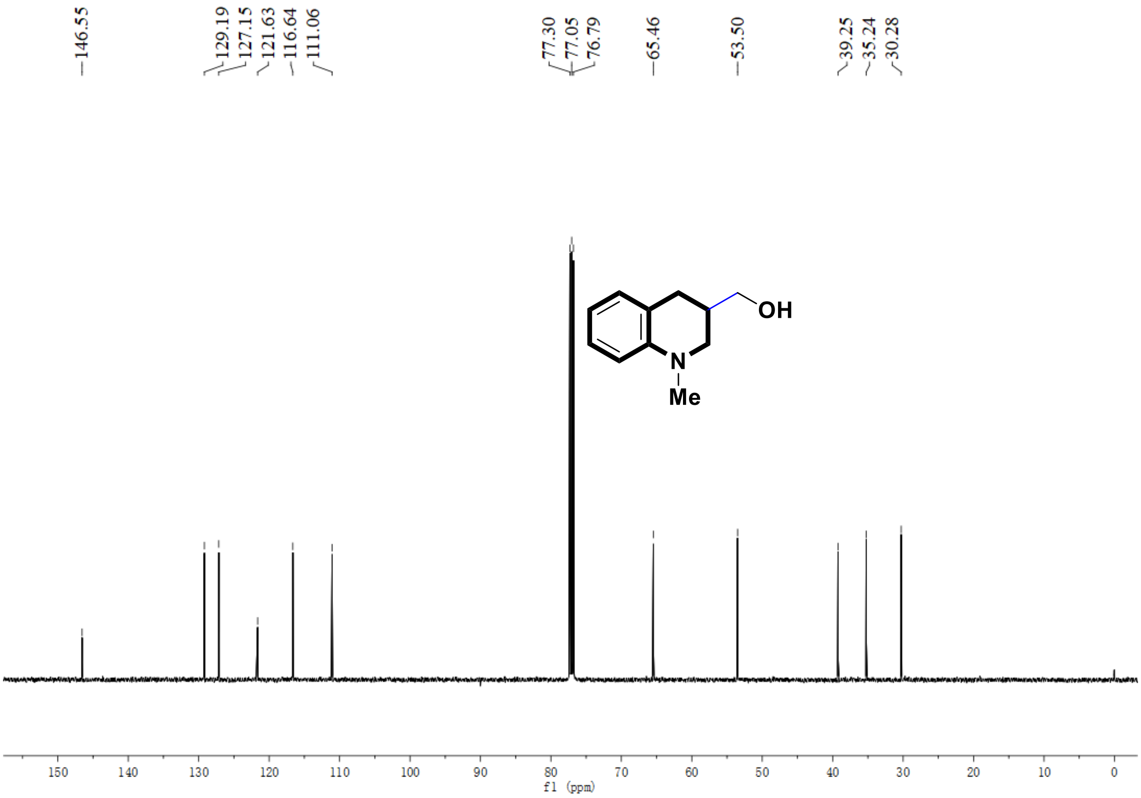
prop-2-yn-1-yl-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (14a)





(1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)methanol (15a)





(1-methyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl acetate (16a)