# Supporting Information

## Substrate-induced Dual Utilization Cascade Reaction of *N*-alkyl Anilines: Highly Site-selective Sustainable Synthesis of Chromeno[4,3-*b*]quinolin-6-ones

Zhou Zhang,[a] Sihan Zhao,[a] Yuanmin Wen,[a] Guiyun Zeng,[a] Minglong Yuan*[a,b] and Chao Huang*[a,b]

[a] Key Laboratory of Biomass Green Chemical Conversion of Yunnan Provincial Education Department, National and Local Joint Engineering Research Center for Green Preparation Technology of Biobased Materials, School of Chemistry & Environment, Yunnan Minzu University, Kunming 650504, PR China.

[b] National and Local Joint Engineering Research Center for Green Preparation Technology of Biobased Materials, School of Chemistry & Environment, Yunnan Minzu University, Kunming 650504, PR China.

E-mail: huangchao@ynu.edu.cn

Table of Contents

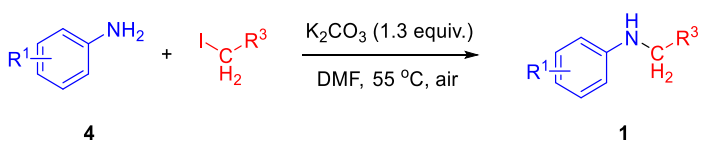
# 1. General Methods

All reagents were obtained from commercial suppliers and used without further purification. All compounds were characterized by full spectroscopic data. The $^{1}H$ and $^{13}C$ nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 400 MHz ($^{1}H$ NMR: 400 MHz, $^{13}C$ NMR: 101 MHz) using $CDCl_3$ and DMSO-$d_6$ as solvent with TMS as internal standard. Chemical shifts are given in ppm ($\delta$) referenced to $CDCl_3$ with 7.26 for $^{1}H$ and 77.00 for $^{13}C$, DMSO-$d_6$ with 2.50 for $^{1}H$ and 39.50 for $^{13}C$. Signals are abbreviated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, and coupling constants are expressed in hertz. HRMS were performed on an Agilent LC/MSD TOF instrument. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF254. Column chromatography was performed with 200−300 mesh silica gel. All yields refer to isolated products after purification. The melting points were determined on Tech X-5 melting point apparatus and are uncorrected.

# 2. Experimental Procedures and Spectral Data of Compounds

## 2.1 General procedure for the synthesis of *N*-alkyl anilines 1

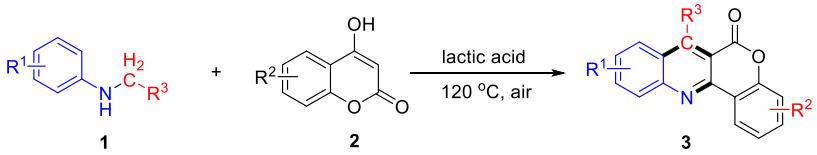
To a solution of anilines (2.0 mmol) in DMF (5.0 mL) at 0 °C, $K_2CO_3$ (2.6 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 15 minutes and R–I (2.0 mmol) was added at same temperature. Then the reaction tube was sealed and reaction mixture was heated to 55 °C in an oil bath for 24 h. After complete consumption of the starting material, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford the products *N*-alkyl anilines **1**.[1]




**4** **1**

### 2.2 General procedure for the synthesis of coumarin-fused quinolinones 3

The mixture of *N*-alkyl anilines **1** (0.60 mmol) and 4-hydroxy coumarins **2** (0.50 mmol) were stirred in lactic acid (0.10 mL) at 120 °C for 24 h, until the completion of the reaction, which was monitored by TLC. After the completion of the reaction, the mixture was cooled to room temperature. The reaction mixture was quenched with ethyl acetate, then concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (mesh 200–300, gradient: petroleum ether/ethyl acetate = 20/1 (v/v)) to afford the desired products **3**.

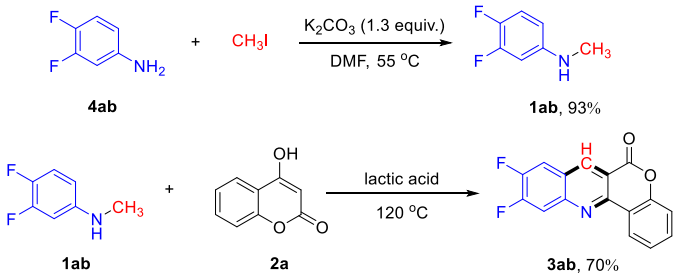



# 3 Details in Control Experiment

### 3.1 Synthesis of anticancer agent

To a solution of 3,4-difluoroaniline (2.0 mmol) in DMF (5.0 mL) at 0 °C, $K_2CO_3$ (2.6 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 15 minutes and $CH_3I$ (2.0 mmol) was added at same temperature. Then the reaction tube was sealed and reaction mixture was heated to 55 °C in an oil bath for 24 h. After complete consumption of the starting material, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford the products 3,4-difluoro-*N*-methylaniline **1ab**.

The mixture of 3,4-difluoro-*N*-methylaniline **1ab** (0.60 mmol) and 4-hydroxy coumarin **2a** (0.50 mmol) were stirred in lactic acid (0.10 mL) at 120 °C for 24 h., until the completion of the reaction, which was monitored by TLC. After the completion of the reaction, the mixture was cooled to room temperature. The reaction mixture was quenched with ethyl acetate, then concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (mesh 200–300, gradient: petroleum ether/ethyl acetate = 20/1 (v/v)) to afford the desired products **3ab**.




## 3.2 General procedure for the synthesis of 3b-*d*

To a solution of 4-toluidine (2.0 mmol) in DMF (5.0 mL) at 0 ℃, $K_2CO_3$ (2.6 mmol) was added slowly. The reaction mixture was stirred at 0 ℃ for 15 minutes and $CD_3I$ (2.0 mmol) was added at same temperature. Then the reaction tube was sealed and reaction mixture was heated to 55 ℃ in an oil bath for 24 h. After complete consumption of the starting material, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford the products deuterated *N*-methyl aniline (**1b-*d*$_3$**).

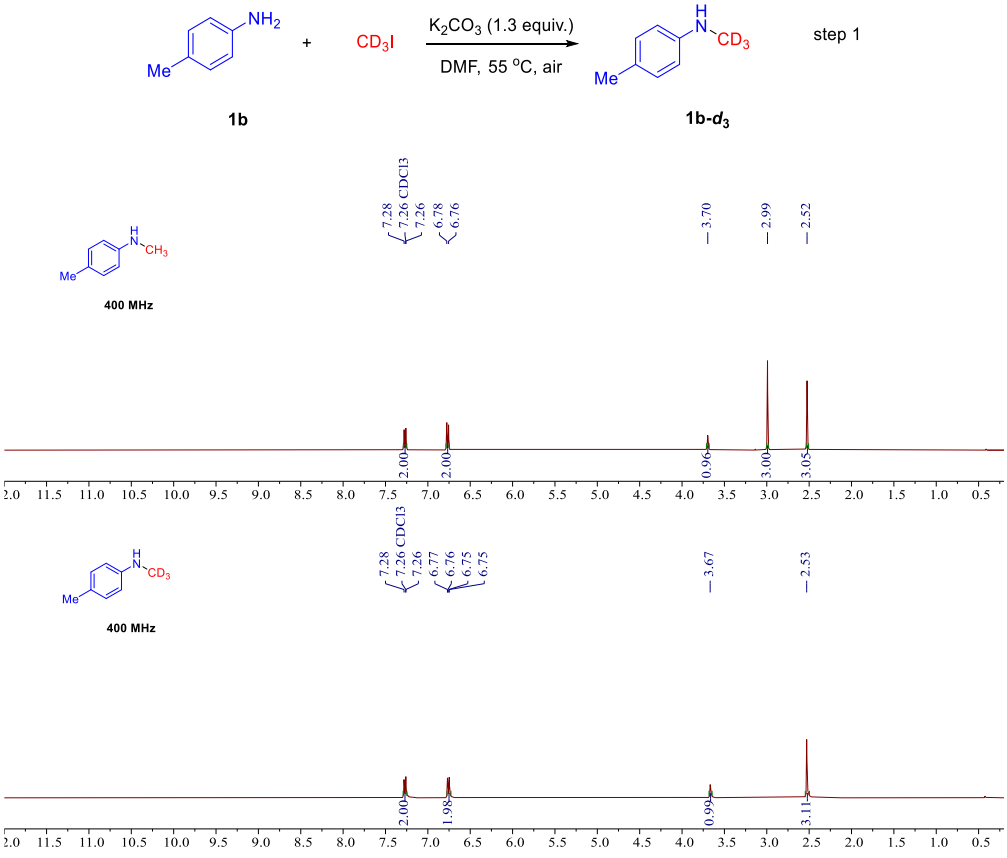



**Figure S1.** $^1$H NMR (400 MHz $CDCl_3$) spectra of compound **1b-*d*$_3$** and **1b**

The mixture of deuterated *N*,4-dimethyl **1b-*d*$_3$** (0.24 mmol) and 4-hydroxy coumarin **1b** (0.20 mmol) was stirred in lactic acid (0.10 mL) at 120 °C for 24 h, until the completion of the reaction, which was monitored by TLC. After the completion of the reaction, the mixture was cooled to room temperature. The reaction mixture was quenched with ethyl acetate, then concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (mesh 200–300, gradient: petroleum ether/ethyl acetate = 20/1 (v/v)) to afford the desired products **3b-*d***.

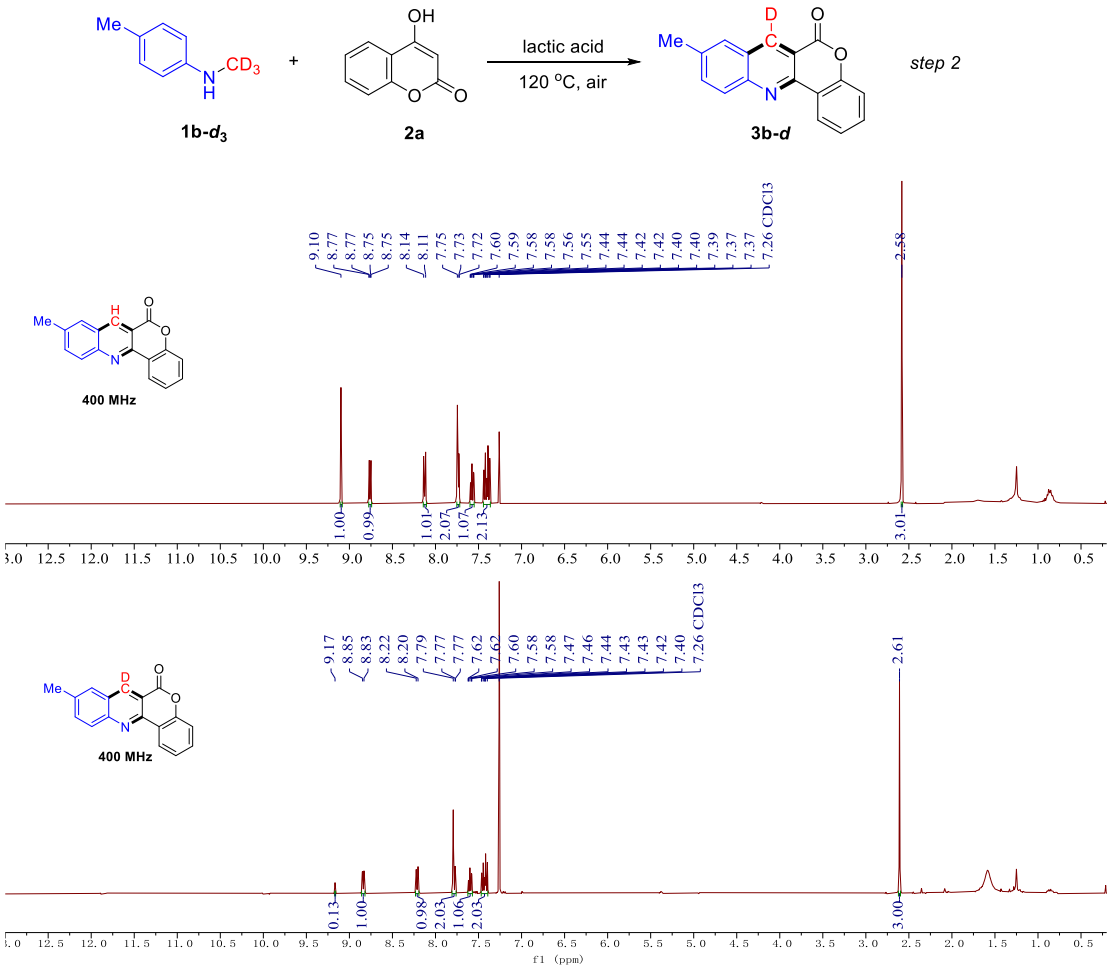



**Figure S2.** $^1$H NMR (400 MHz $CDCl_3$) spectra of compound **3b-*d*** and **3b**

## 3.3 General procedure for the synthesis of 4b-2

The mixture of 4-(*p*-tolylamino)-2*H*-chromen-2-one **4b** (0.50 mmol), $CH_3I$ (0.50 mmol) and $K_2CO_3$ (1.3 mmol) was stirred in DMF (2.0 mL) at 55 °C for 24 h, until the completion of the reaction, which was monitored by TLC. After the completion of the reaction, the mixture was cooled to room temperature. The reaction mixture was quenched with brine and extracted with ethyl acetate.

The combined organic layer was dried over $Na_2SO_4$. After removal of $Na_2SO_4$ through filtration, the solution was concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (mesh 200−300, gradient: petroleum ether/ethyl acetate = 4/1 (v/v)) to afford the desired products **4b-2**.

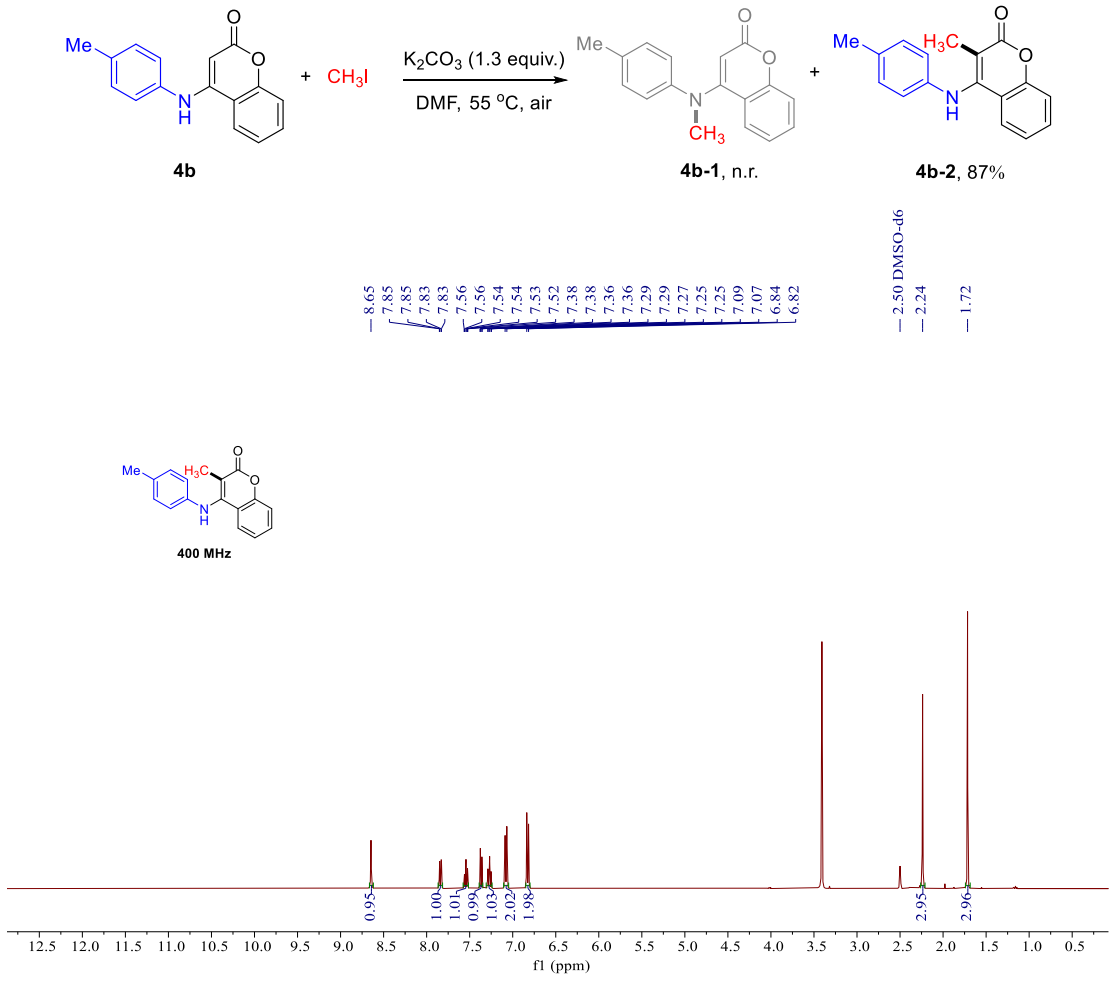



**Figure S3.** $^1$H NMR (400 MHz DMSO-$d_6$) spectra of compound **4b-2**

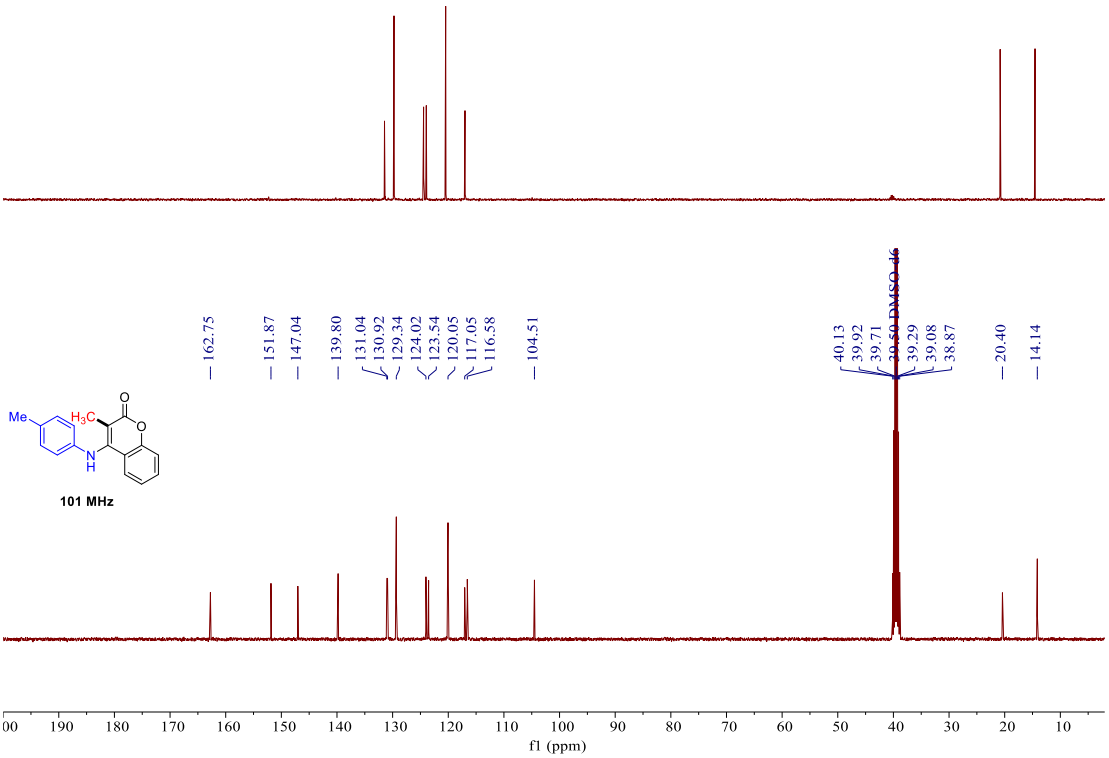



**Figure S4.** $^{13}$C NMR (101 MHz DMSO-$d_6$) spectra of compound **4b-2**

## 3.4 HRMS of intermediate

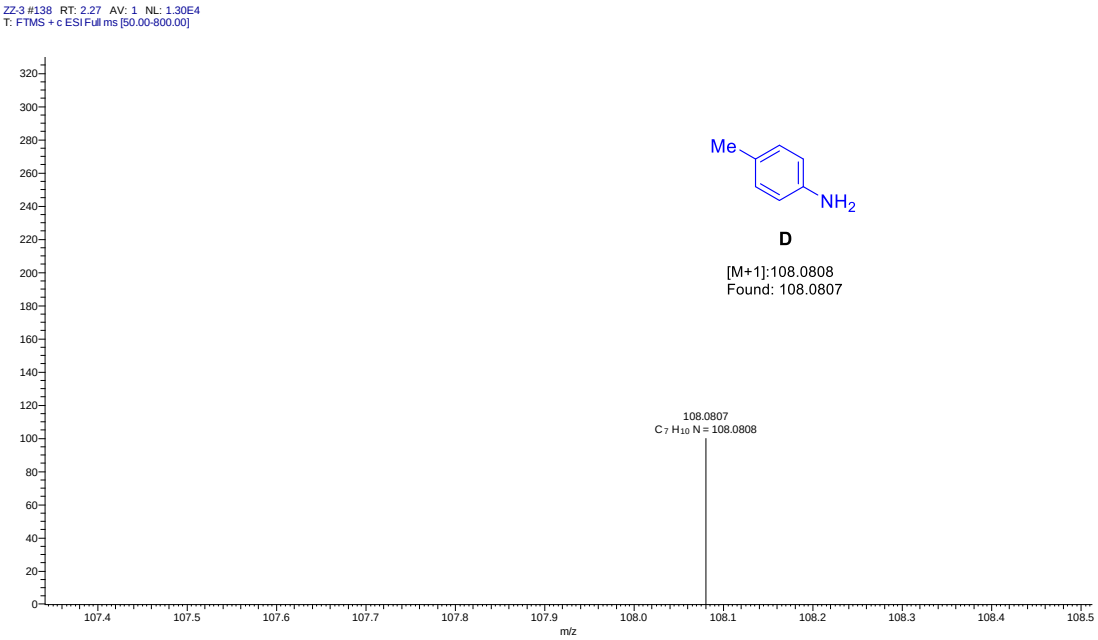



**Figure S5.** HRMS of intermediate **D**

## 3.5 Site-selective synthesis of 3a

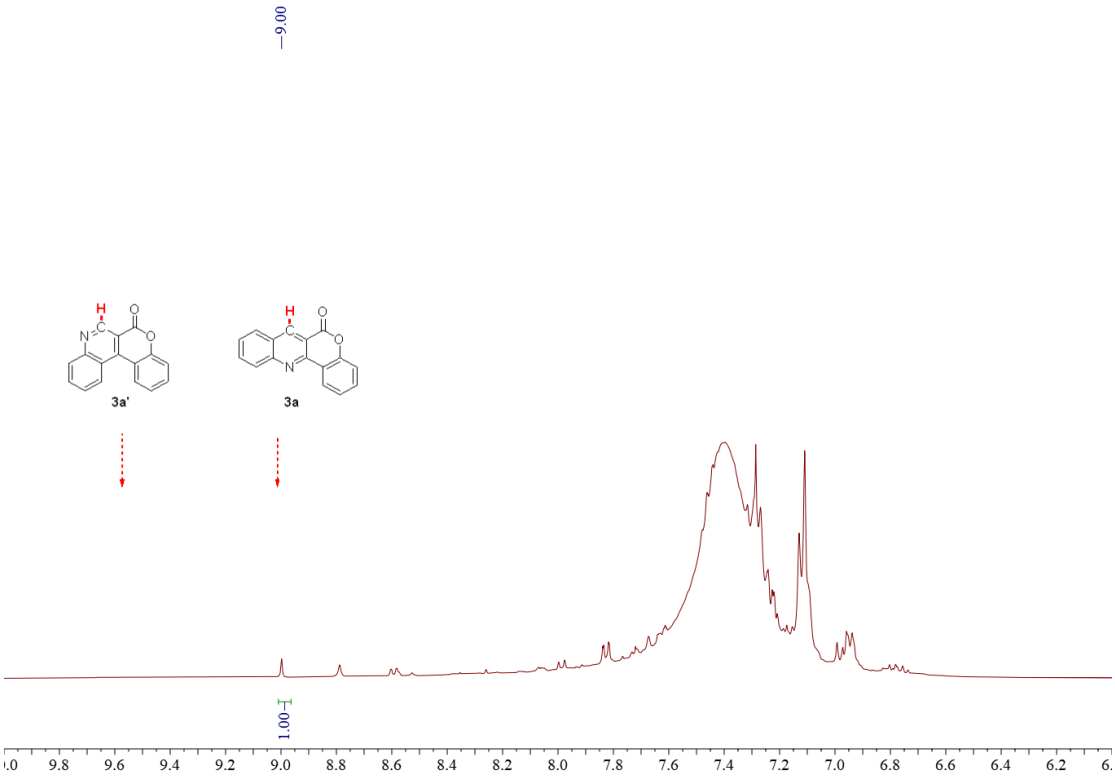
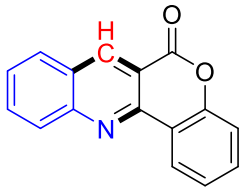



**Figure S6.** Crude $^{1}H$ NMR (400 MHz $CDCl_3$) spectra refer to this literature.[7]

# 4. Spectroscopic Data of Compounds

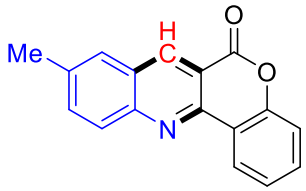
Since it was done in the same laboratory, these compounds data (**3a-3d**, **3f**, **3i-3j**, **3l-3p**) refer to this literature[2].

***6H-Chromeno[4,3-b]quinolin-6-one*** **(3a)**[2]



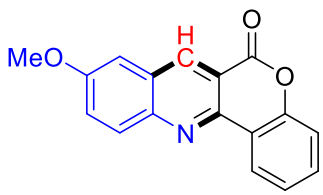

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (96.4 mg, yield 78%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.20 (s, 1H), 8.77 (d, $J$ = 7.9 Hz, 1H), 8.23 (d, $J$ = 8.6 Hz, 1H), 8.01 (d, $J$ = 8.2 Hz, 1H), 7.91 (t, $J$ = 7.7 Hz, 1H), 7.66–7.56 (m, 2H), 7.46–7.36 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.3, 152.7, 151.0, 149.6, 141.1, 133.4, 132.4, 129.5, 129.4, 127.4, 127.3, 125.2, 124.9, 119.6, 117.4, 115.7.

***9-Methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3b)**[2]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (107.0 mg, yield 82%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.09 (s, 1H), 8.75 (d, $J$ = 7.8 Hz, 1H), 8.11 (d, $J$ = 9.1 Hz, 1H), 7.74 (s, 2H), 7.57 (t, $J$ = 7.7 Hz, 1H), 7.45–7.36 (m, 2H), 2.58 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.5, 152.5, 149.7, 148.8, 140.1, 137.6, 135.9, 132.1, 129.1, 127.9, 127.3, 125.1, 124.9, 119.7, 117.3, 115.7, 21.6.

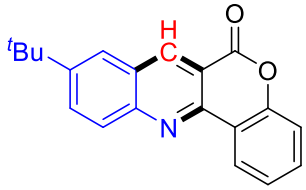
***9-Methoxy-6H-chromeno[4,3-b]quinolin-6-one*** **(3c)**[2]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent

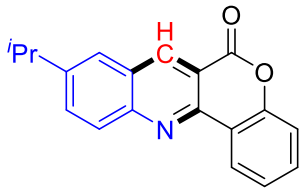
with Rf = 0.2. White solid (110.8 mg, yield 80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.07 (s, 1H), 8.73 (d, $J$ = 7.8 Hz, 1H), 8.12 (d, $J$ = 9.3 Hz, 1H), 7.59–7.54 (m, 2H), 7.44–7.36 (m, 2H), 7.20 (s, 1H), 3.98 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.6, 158.4, 152.3, 147.6, 147. 5, 138.9, 131.7, 130.9, 128.5, 127.1, 124.9, 124.8, 119.8, 117.3, 115.9, 105.5, 55.8.

***9-(Tert-butyl)-6H-chromeno[4,3-b]quinolin-6-one*** **(3d)**[2]



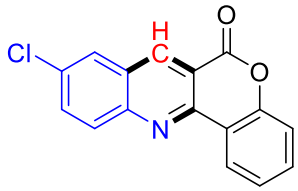

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.25. White solid (128.8 mg, yield 85%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.16 (s, 1H), 8.76 (d, $J$ = 7.8 Hz, 1H), 8.16 (d, $J$ = 9.0 Hz, 1H), 8.01 (d, $J$ = 9.0 Hz, 1H), 7.90 (s, 1H), 7.57 (t, $J$ = 7.7 Hz, 1H), 7.44–7.35 (m, 2H), 1.46 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.5, 152.5, 150.5, 149.8, 149.0, 140.8, 132.7, 132.1, 129.0, 127.1, 125.1, 124.9, 124.1, 119.7, 117.3, 115.6, 35.1, 30.9.

***9-Isopropyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3e)**



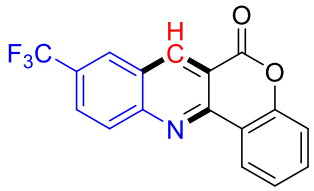

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (119.9 mg, yield 83%). m.p.: 174–175 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.10 (s, 1H), 8.71 (dd, $J$ = 7.9, 1.6 Hz, 1H), 8.11 (d, $J$ = 8.8 Hz, 1H), 7.80 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.74 (d, $J$ = 1.7 Hz, 1H), 7.54 (m, 1H), 7.41–7.32 (m, 2H), 3.13 (m, 1H), 1.38 (d, $J$ = 6.9 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.4, 152.4, 149.9, 148.7, 148.2, 140.4, 133.6, 132.0, 129.3, 127.3, 125.1, 125.1, 124.8, 119.6, 117.2, 115.5, 34.0, 23.6. HRMS (ESI): $m/z$ calcd for $C_{19}H_{16}NO_2^+$ $[M+H]^+$: 290.1181, found: 290.1186.

***9-Chloro-6H-chromeno[4,3-b]quinolin-6-one*** **(3f)**[2]



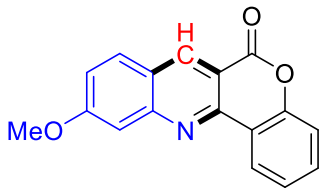

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (105.3 mg, yield 75%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.10 (s, 1H), 8.72 (d, $J$ = 7.9 Hz, 1H), 8.15 (d, $J$ = 9.1 Hz, 1H), 7.96 (s, 1H), 7.82 (d, $J$ = 9.1 Hz, 1H), 7.60 (t, $J$ = 7.7 Hz, 1H), 7.46–7.36 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.9, 152.6, 149.8, 149.4, 139.9, 134.3, 133.3, 132.6, 131.1, 127.7, 125.2, 125.1, 119.3, 117.4, 116.4.

***9-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one*** (**3g**)




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.25. White solid (119.7 mg, yield 76%). m.p.: 215–216 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.26 (s, 1H), 8.73 (dd, $J$ = 7.9, 1.5 Hz, 1H), 8.31 (d, $J$ = 10.0 Hz, 2H), 8.04 (dd, $J$ = 8.9, 1.9 Hz, 1H), 7.65–7.59 (m, 1H), 7.48–7.35 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.6, 152.9, 151.7, 151.5, 142.0, 133.2, 130.8, 129.3, 128.9, 128.7, 128.7, 127.3, 127.2, 126.0, 125.5, 125.2, 124.9, 122.2, 119.0, 117.5, 116.8. $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ -62.7. HRMS (ESI): *m/z* calcd for $C_{17}H_9F_3NO_2^+$ $[M+H]^+$: 316.0585, found: 316.0581.

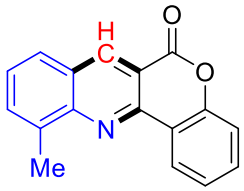
***10-Methoxy-6H-chromeno[4,3-b]quinolin-6-one*** (**3h**)




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (94.2 mg, yield 68%). m.p.: 234–235 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.07 (s, 1H), 8.76 (d, $J$ = 6.9 Hz, 1H), 7.85 (d, $J$ = 9.0 Hz, 1H), 7.59–7.53 (m, 2H), 7.43–7.35 (m, 2H), 7.23 (s, 1H), 4.02 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 164.2, 161.9, 152.8, 149.9, 139.8, 132.4,

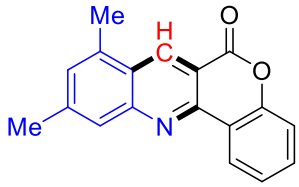
130.6, 125.2, 124.9, 122.9, 121.6, 117.4, 113.6, 106.6, 55.9. HRMS (ESI): *m/z* calcd for $C_{17}H_{12}NO_3^+$ $[M+H]^+$: 278.0817, found: 278.0820.

***11-Methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3i)**[2]



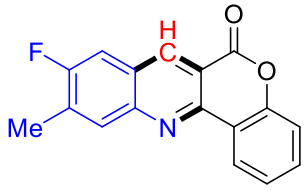

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (94.2 mg, yield 75%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.15 (s, 1H), 8.80 (dd, $J$ = 7.9, 1.6 Hz, 1H), 7.84 (d, $J$ = 8.2 Hz, 1H), 7.75 (d, $J$ = 6.9 Hz, 1H), 7.60–7.55 (m, 1H), 7.54–7.49 (m, 1H), 7.45–7.36 (m, 2H), 2.92 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.6, 152.6, 150.0, 148.3, 141.1, 137.8, 133.2, 132.1, 127.3, 127.2, 125.2, 124.9, 120.0, 117.3, 115.3, 17.9.

***8,10-Dimethyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3j)**[2]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 30:1 as an eluent with Rf = 0.2. White solid (108.7 mg, yield 79%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.11 (s, 1H), 8.67–8.64 (m, 1H), 7.73 (s, 1H), 7.58–7.53 (m, 1H), 7.41–7.31 (m, 2H), 7.15 (s, 1H), 2.64 (s, 3H), 2.51 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.6, 152.5, 151.5, 148.9, 144.2, 136.8, 136.2, 131.9, 130.1, 126.4, 125.0, 124.9, 124.7, 119.5, 117.1, 113.9, 22.2, 18.6.

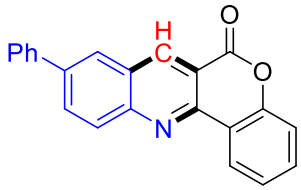
***9-Fluoro-10-methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3k)**




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (97.7 mg, yield 70%). m.p.: 183–184 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.06 (s, 1H), 8.69 (d, $J$ = 7.8 Hz, 1H), 8.04 (d, $J$ = 6.9 Hz, 1H), 7.60–7.55 (m, 1H), 7.52 (d, $J$ = 9.2

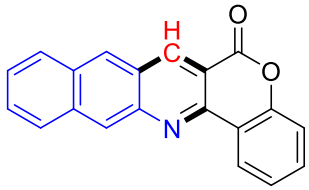
Hz, 1H), 7.40 (d, $J$ = 7.4 Hz, 1H), 7.36 (d, $J$ = 8.2 Hz, 1H), 2.55 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.7, 161.3, 159.2, 152.6, 149.0, 149.0, 148.3, 139.9, 139.9, 135.4, 135.2, 132.4, 131.6, 131.6, 126.7, 126.6, 125.2, 125.1, 119.6, 117.5, 115.7, 111.5, 111.3, 16.2, 16.2. $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ -113.5, -114.7. HRMS (ESI): *m/z* calcd for $C_{17}H_{10}FNO_2^+$ $[M+H]^+$: 280.0768, found: 280.0765.

***9-Phenyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3l)**[2]



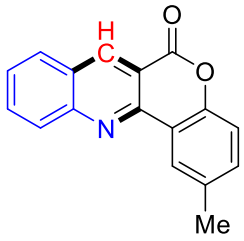

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (90.5 mg, yield 65%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.23 (s, 1H), 8.78 (dd, $J$ = 7.9, 1.6 Hz, 1H), 8.29 (d, $J$ = 8.8 Hz, 1H), 8.20–8.14 (m, 2H), 7.75–7.72 (m, 2H), 7.61–7.56 (m, 1H), 7.53 (t, $J$ = 7.5 Hz, 2H), 7.47–7.41 (m, 2H), 7.40–7.37 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.3, 152.7, 150.4, 149.5, 141.1, 140.2, 139.4, 133.2, 132.3, 129.9, 129.2, 128.3, 127.5, 127.4, 126.6, 125.2, 124.9, 119.7, 117.4, 116.1.

***6H-Benzo[g]chromeno[4,3-b]quinolin-6-one*** **(3m)**[2]



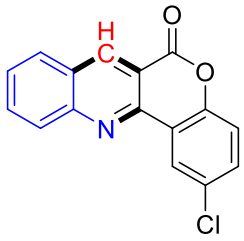

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 30:1 as an eluent with Rf = 0.2. White solid (95.1 mg, yield 64%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.88 (s, 1H), 8.78 (dd, $J$ = 24.0, 8.0 Hz, 2H), 8.18–8.06 (m, 2H), 7.96 (d, $J$ = 7.8 Hz, 1H), 7.75 (m, 2H), 7.61 (t, $J$ = 7.7 Hz, 1H), 7.48–7.40 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.7, 152.7, 152.2, 149.7, 135.3, 134.4, 132.2, 131.5, 129.7, 129.0, 128.4, 128.3, 127.7, 125.2, 125.1, 124.9, 123.2, 119.5, 117.3, 115.1.

***2-Methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3n)**[2]



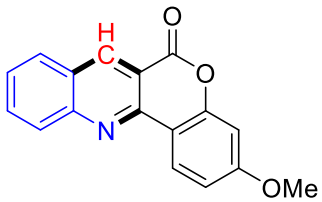

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (105.7 mg, yield 81%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.20 (s, 1H), 8.56–8.53 (m, 1H), 8.23 (d, $J$ = 8.6 Hz, 1H), 8.01 (d, $J$ = 8.2 Hz, 1H), 7.92 (m, 1H), 7.67–7.61 (m, 1H), 7.38 (dd, $J$ = 8.4, 2.0 Hz, 1H), 7.27 (d, $J$ = 8.1 Hz, 1H), 2.51 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.5, 150.9, 150.7, 149.7, 141.2, 134.7, 133.4, 133.3, 129.4, 129.4, 127.3, 127.2, 124.9, 119.0, 117.1, 115.6, 20.9.

***2-Chloro-6H-chromeno[4,3-b]quinolin-6-one*** **(3o)**[3]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (102.6 mg, yield 73%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.24 (s, 1H), 8.77 (d, $J$ = 2.5 Hz, 1H), 8.26 (d, $J$ = 8.6 Hz, 1H), 8.05 (d, $J$ = 8.3 Hz, 1H), 7.96 (t, $J$ = 7.7 Hz, 1H), 7.69 (t, $J$ = 7.3 Hz, 1H), 7.54 (dd, $J$ = 8.7, 2.6 Hz, 1H), 7.35 (d, $J$ = 8.8 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.9, 151.1, 148.5, 141.3, 133.7, 132.2, 130.7, 129.6, 129.5, 127.8, 127.5, 124.9, 120.9, 118.9, 115.6.

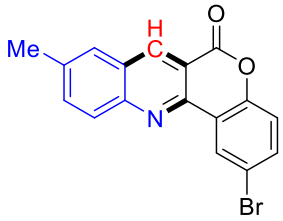
***3-Methoxy-6H-chromeno[4,3-b]quinolin-6-one*** **(3p)**[4]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (96.9 mg, yield 70%). m.p.: 252–253 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$

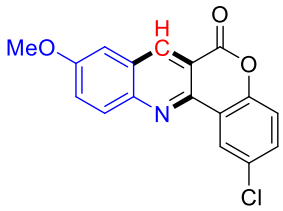
9.18 (s, 1H), 8.68 (d, $J$ = 8.8 Hz, 1H), 8.20 (d, $J$ = 8.5 Hz, 1H), 7.99 (d, $J$ = 8.2 Hz, 1H), 7.90 (t, $J$ = 7.7 Hz, 1H), 7.60 (t, $J$ = 7.5 Hz, 1H), 7.00 (d, $J$ = 8.8 Hz, 1H), 6.87 (s, 1H), 3.92 (s, 3H). HRMS (ESI): *m/z* calcd for $C_{17}H_{12}NO_3^+$ $[M+H]^+$: 278.0817, found: 278.0816.

***2-Bromo-9-methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3q)**[2]



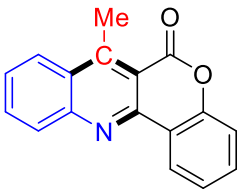

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (122.0 mg, yield 72%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.13 (s, 1H), 8.90 (d, $J$ = 2.4 Hz, 1H), 8.15 (d, $J$ = 9.2 Hz, 1H), 7.81–7.77 (m, 2H), 7.66 (dd, $J$ = 8.7, 2.5 Hz, 1H), 7.28 (d, $J$ = 8.7 Hz, 1H), 2.61 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.9, 151.4, 149.7, 147.6, 140.3, 138.2, 136.3, 134.8, 129.2, 127.9, 127.8, 127.6, 121.4, 119.2, 118.0, 115.5, 21.7.

***2-Chloro-9-methoxy-6H-chromeno[4,3-b]quinolin-6-one*** **(3r)**[2]



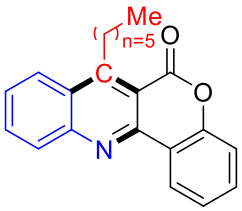

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 20:1 as an eluent with Rf = 0.2. White solid (112.8 mg, yield 75%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.08 (s, 1H), 8.70 (d, $J$ = 2.5 Hz, 1H), 8.13 (d, $J$ = 9.3 Hz, 1H), 7.59 (dd, $J$ = 9.3, 2.8 Hz, 1H), 7.50 (dd, $J$ = 8.7, 2.6 Hz, 1H), 7.33 (d, $J$ = 8.7 Hz, 1H), 7.22 (d, $J$ = 2.7 Hz, 1H), 3.99 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 161.0, 158.7, 150.7, 147.6, 146.3, 138.9, 131.6, 131.0, 130.6, 128.8, 127.4, 124.4, 121.1, 118.8, 115.7, 105.5, 55.8.

***7-Methyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3s)**[4]



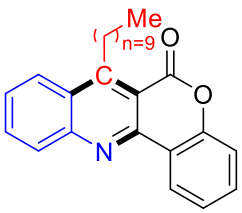

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (84.8 mg, yield 65%). m.p.: 220–221 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.81 (d, $J$ = 7.9 Hz, 1H), 8.29 (d, $J$ = 8.4 Hz, 1H), 8.22 (d, $J$ = 8.5 Hz, 1H), 7.88 (t, $J$ = 7.6 Hz, 1H), 7.63 (t, $J$ = 7.7 Hz, 1H), 7.59–7.54 (m, 1H), 7.40 (t, $J$ = 7.6 Hz, 1H), 7.33 (d, $J$ = 8.2 Hz, 1H), 3.32 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.8, 154.9, 152.3, 149.8, 149.3, 132.7, 132.2, 130.1, 127.8, 127.0, 125.7, 125.4, 124.6, 119.6, 116.7, 114.0, 29.7, 16.9.

***7-Hexyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3t)**



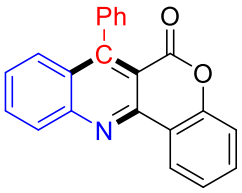

Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 30:1 as an eluent with Rf = 0.2. Yellow oil (94.4 mg, yield 57%). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.80 (d, $J$ = 7.9 Hz, 1H), 8.28 (d, $J$ = 8.6 Hz, 1H), 8.19 (d, $J$ = 8.5 Hz, 1H), 7.87 (t, $J$ = 7.5 Hz, 1H), 7.64 (t, $J$ = 7.7 Hz, 1H), 7.56 (t, $J$ = 7.6 Hz, 1H), 7.42–7.31 (m, 2H), 3.86–3.80 (m, 2H), 1.78–1.73 (m, 2H), 1.63 (dd, $J$ = 14.4, 7.1 Hz, 2H), 1.38 (d, $J$ = 11.6 Hz, 3H), 0.93 (t, $J$ = 6.6 Hz, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.3, 159.1, 152.4, 150.2, 149.9, 132.5, 132.1, 130.4, 127.3, 127.0, 125.7, 125.3, 124.5, 119.9, 116.6, 113.3, 31.6, 30.9, 30.1, 29.6, 22.6, 14.1. HRMS (ESI): *m/z* calcd for $C_{22}H_{22}NO_2^+$ $[M+H]^+$: 332.1645, found: 332.1650.

***7-Decyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3u)**



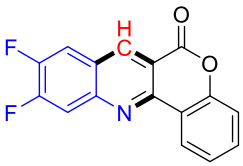
Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 30:1 as an eluent with Rf = 0.2. Yellow oil (83.2 mg, yield 43%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.81 (d, $J$ = 7.9 Hz, 1H), 8.29 (d, $J$ = 8.7 Hz, 1H), 8.21 (d, $J$ = 8.5 Hz, 1H), 7.88 (t, $J$ = 7.6 Hz, 1H), 7.65 (t, $J$ = 7.6 Hz, 1H), 7.56 (t, $J$ = 7.7 Hz, 1H), 7.42–7.32 (m, 2H), 3.87–3.81 (m, 2H), 2.82–2.75 (m, 1H), 1.79–1.73 (m, 2H), 1.65–1.60 (m, 2H), 1.46–1.40 (m, 4H), 1.28 (s, 4H), 0.88 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.3, 159.2, 152.5, 150.6, 149.9, 132.5, 132.1, 130.4, 127.3, 127.0, 125.7, 125.3, 124.5, 119.9, 116.6, 31.9, 31.0, 30.4, 29.6, 29.4, 29.3, 22.7, 14.1. HRMS (ESI): *m/z* calcd for $C_{26}H_{30}NO_2^+$ $[M+H]^+$: 388.2271, found: 388.2268.

***7-Phenyl-6H-chromeno[4,3-b]quinolin-6-one*** **(3v)**[5]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (114.7 mg, yield 71%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.91 (d, $J$ = 7.9 Hz, 1H), 8.30 (d, $J$ = 8.6 Hz, 1H), 7.89 (m, 1H), 7.61–7.53 (m, 5H), 7.46 (m, 2H), 7.34 (d, $J$ = 8.2 Hz, 1H), 7.31–7.28 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 159.4, 155.8, 152.7, 150.2, 150.1, 136.9, 132.9, 132.4, 129.4, 128.3, 128.2, 128.0, 127.9, 127.1, 125.8, 124.6, 119.8, 116.9, 113.2.

***9,10-Difluoro-6H-chromeno[4,3-b]quinolin-6-one*** **(3ab)**[3]




Purified by analytical TLC on silica gel with petroleum ether/ethyl acetate = 25:1 as an eluent with Rf = 0.2. White solid (108.7 mg, yield 79%). m.p.: 176–177 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.13 (s, 1H), 8.70 (d, $J$ = 7.8 Hz, 1H), 7.99–7.92 (m, 1H), 7.74 (t, $J$ = 9.0 Hz, 1H), 7.61 (t, $J$ = 7.7 Hz, 1H), 7.46–7.36 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 160.8, 156.4, 156.3, 153.8, 153.7, 152.7, 152.1, 149.9, 149.4, 148.9, 148.7, 140.1, 140.0, 132.8, 125.2, 125.1, 124.3, 124.2, 119.1, 117.4, 115.9, 115.8, 115.7, 114.4, 114.2. $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ -124.0, -132.4. HRMS (ESI): *m/z* calcd for $C_{16}H_8F_2NO_2^+$ $[M+H]^+$: 284.0518, found: 284.0514.

# 5. Copies of $^{1}H$ and $^{13}C$ Spectra of Compounds

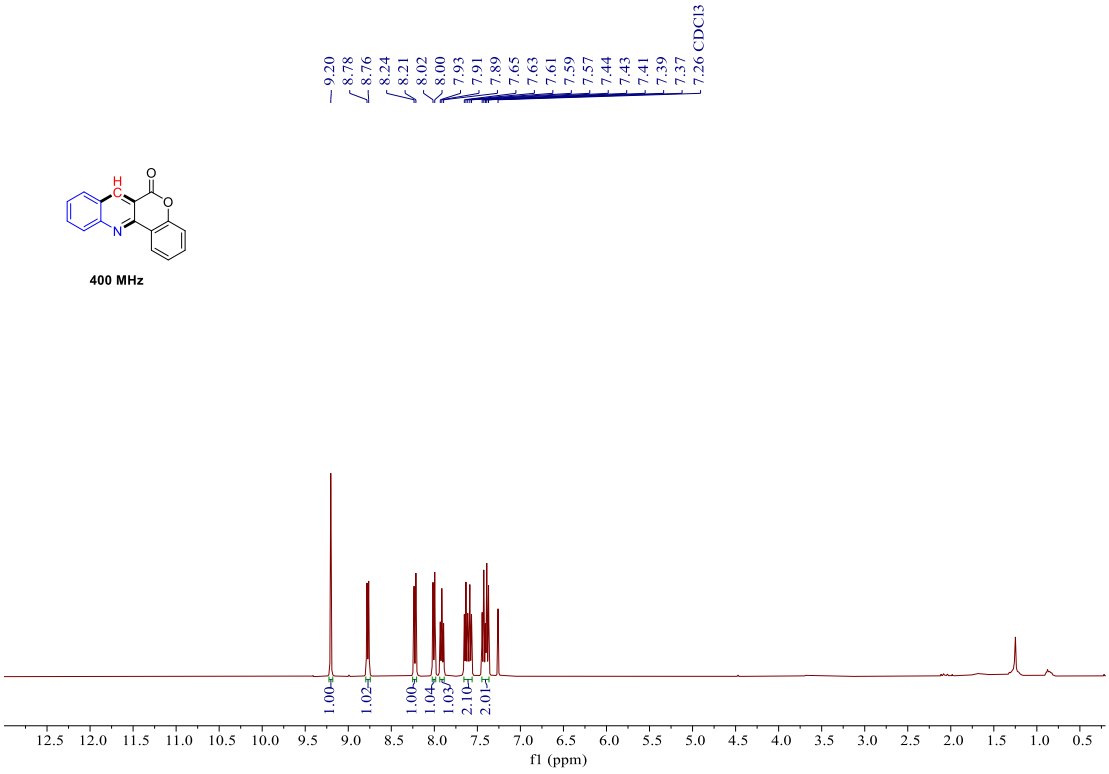



**Figure S7.** $^{1}H$ NMR (400 MHz $CDCl_3$) spectra of compound **3a**

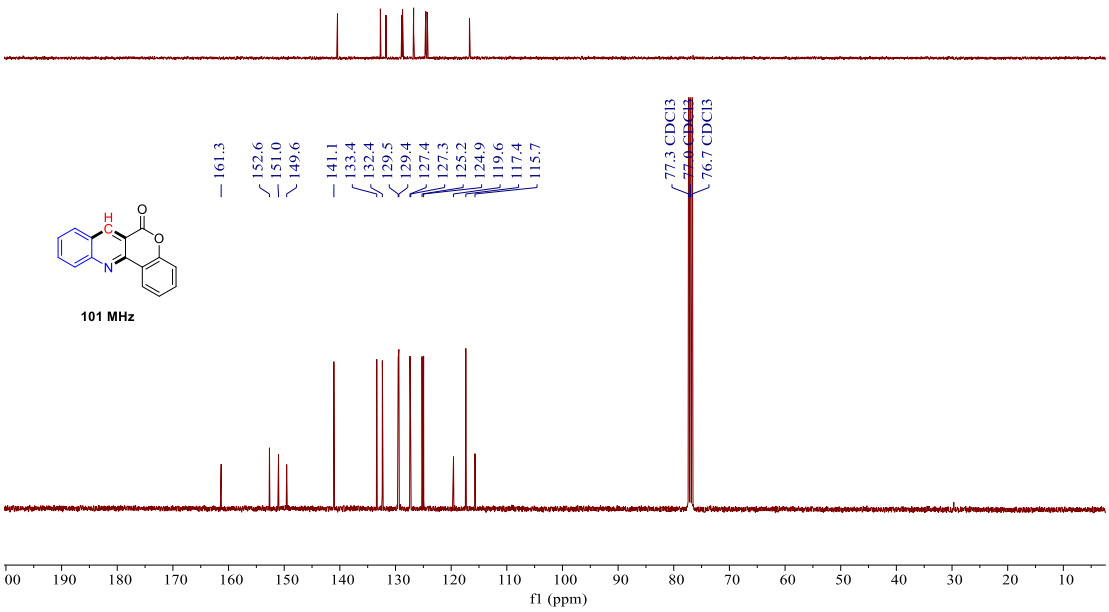



**Figure S8.** $^{13}C$ NMR (101 MHz $CDCl_3$) spectra of compound **3a**

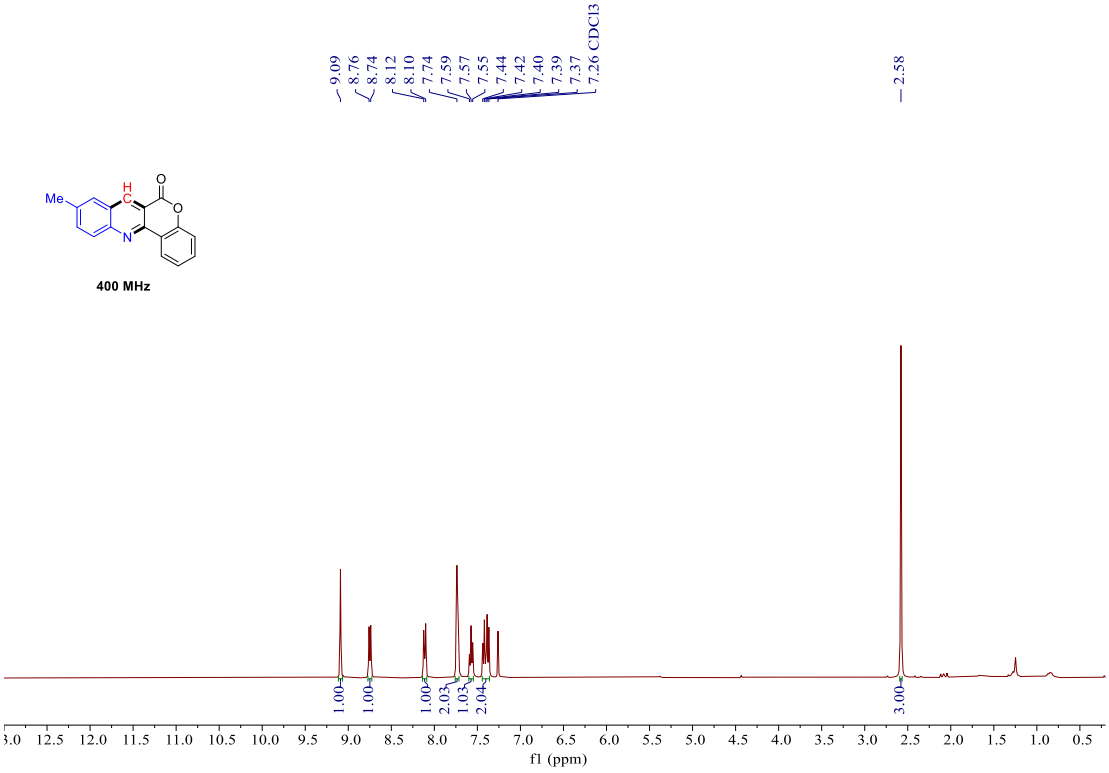



**Figure S9.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3b**

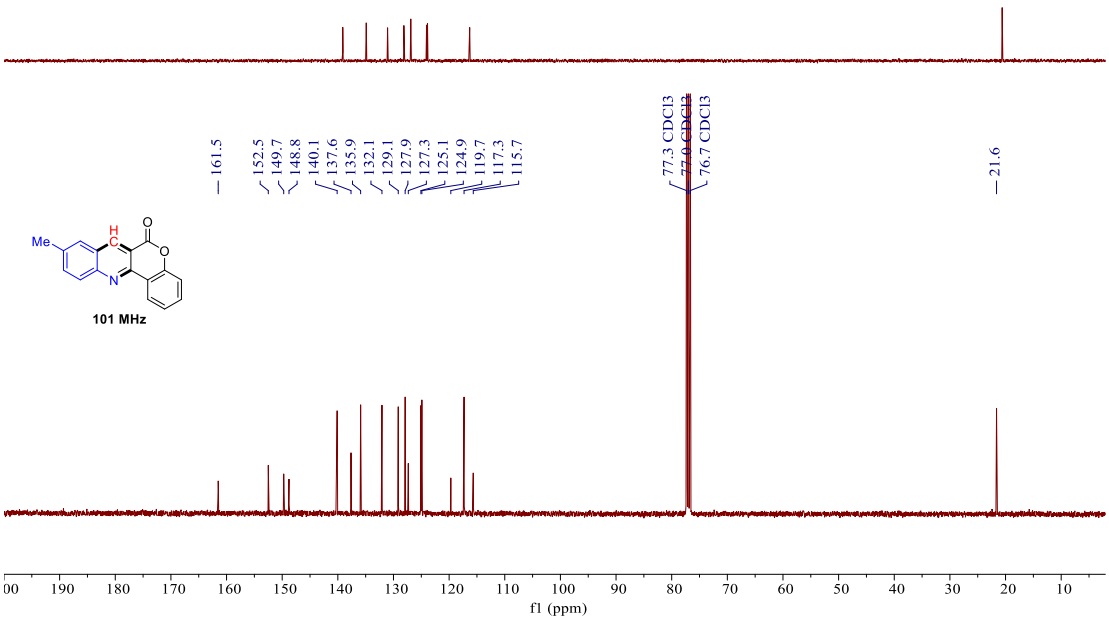



**Figure S10.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3b**

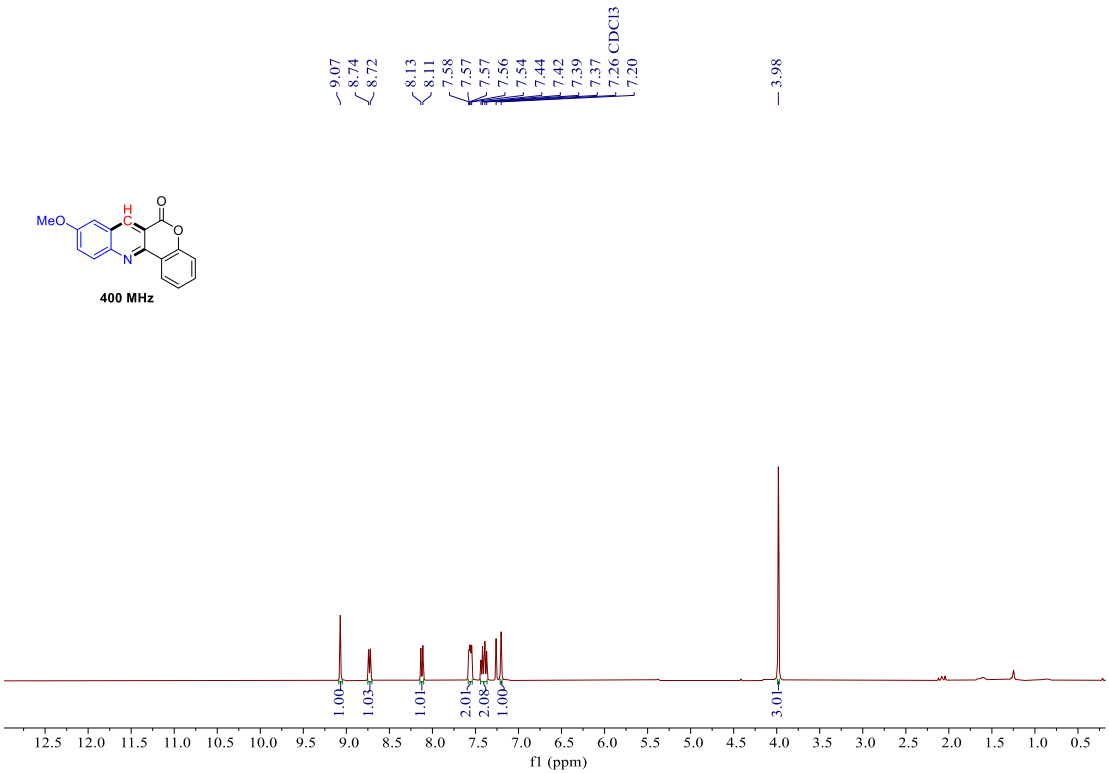



**Figure S11.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3c**

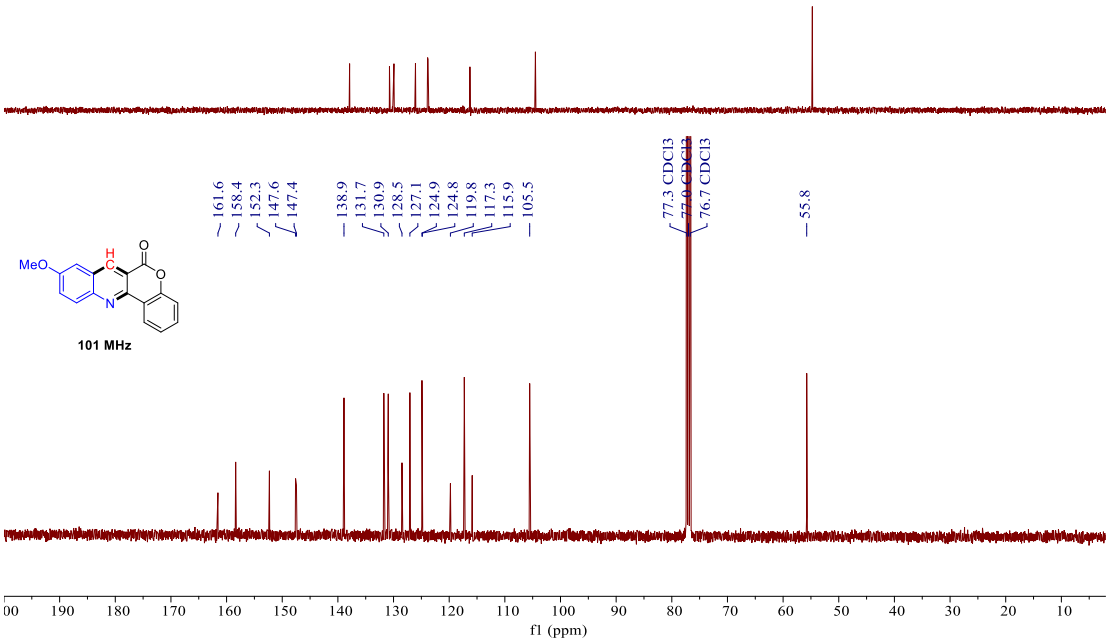



**Figure S12.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3c**

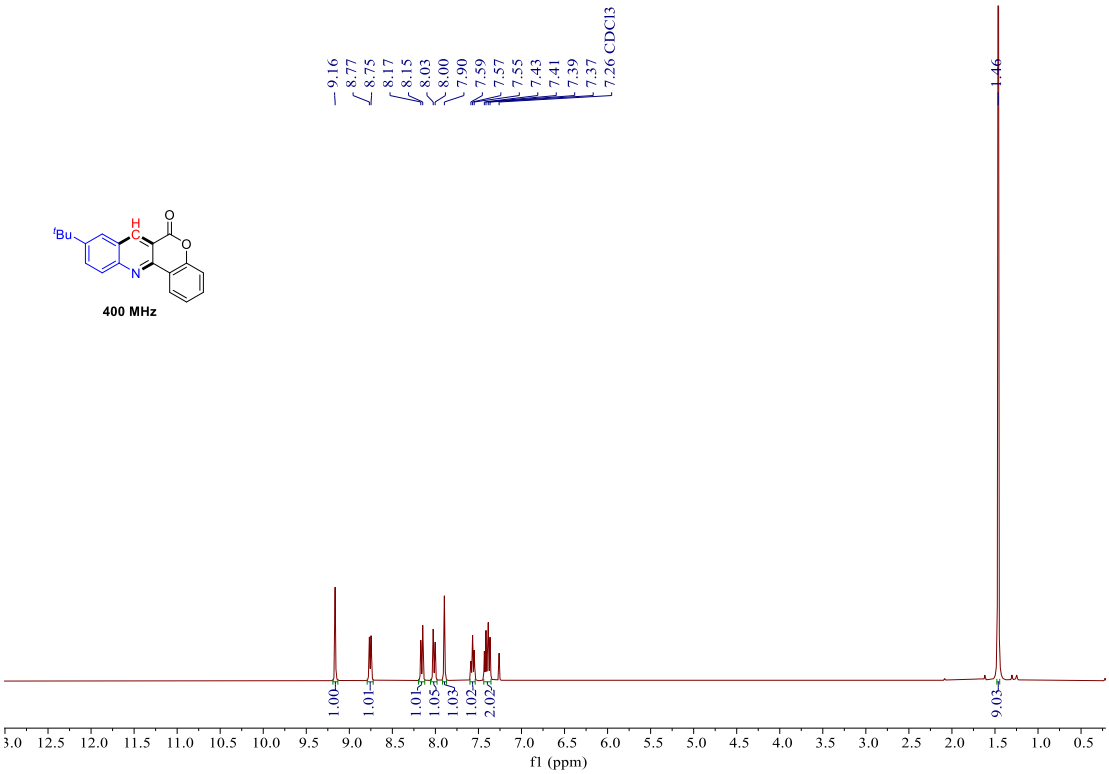



**Figure S13.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3d**

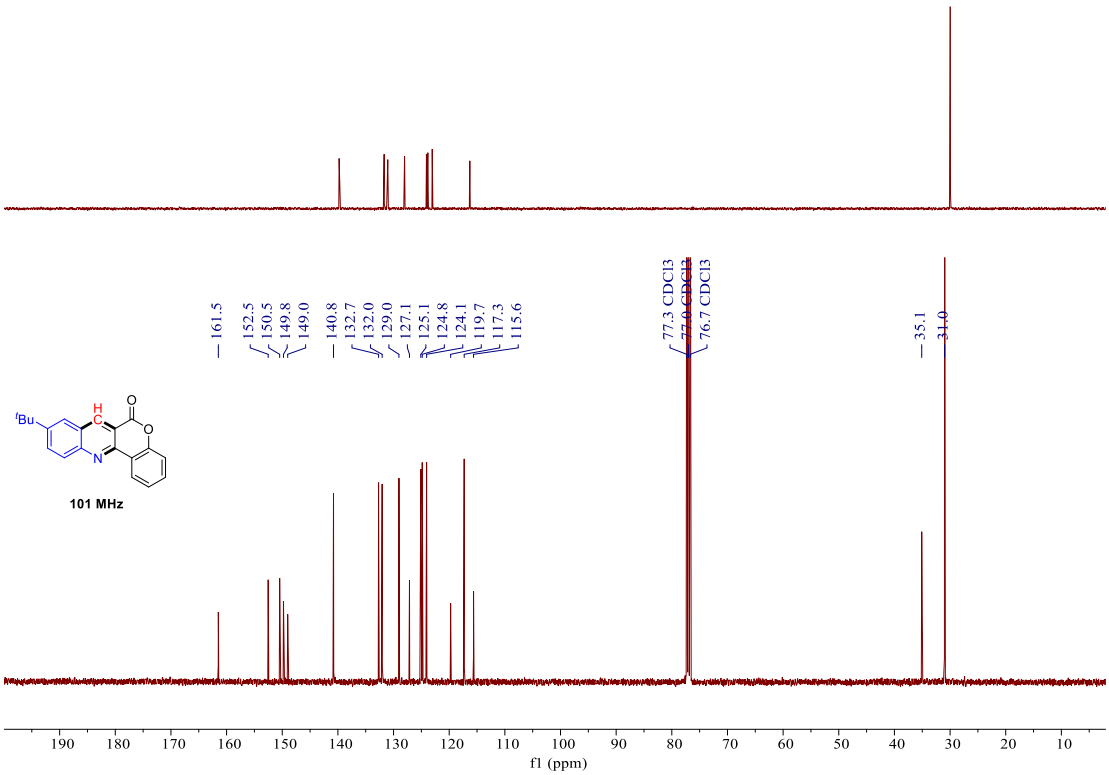



**Figure S14.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3d**

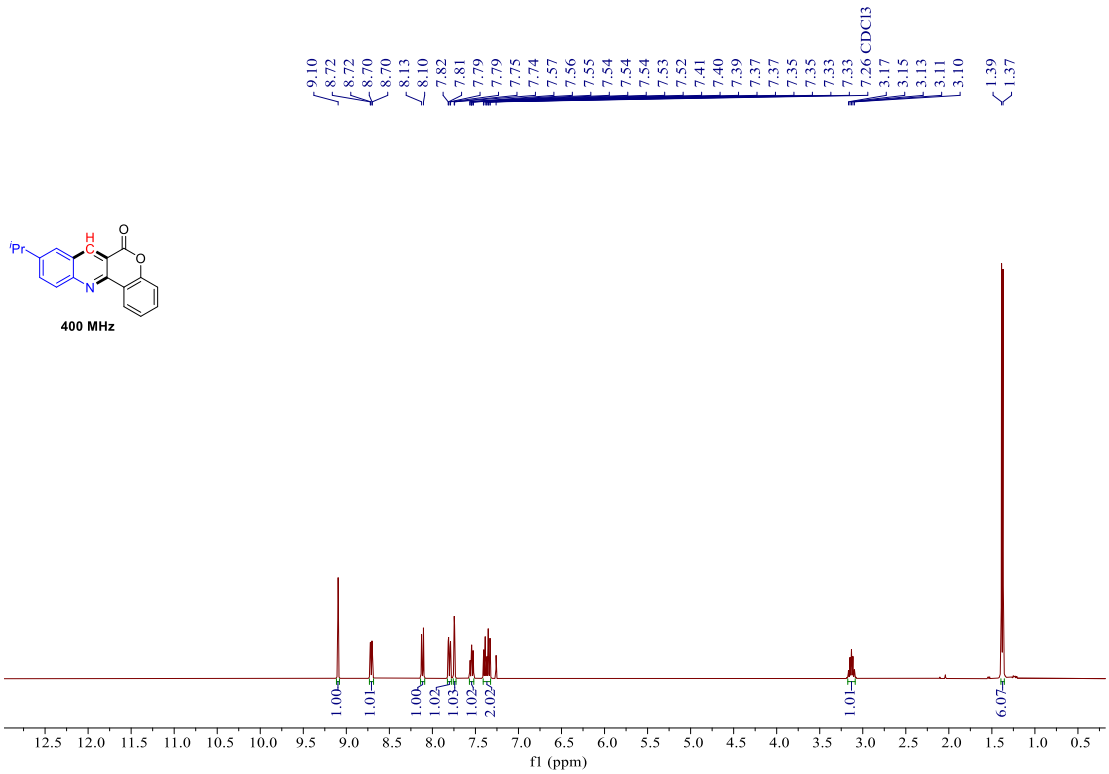



**Figure S15.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3e**

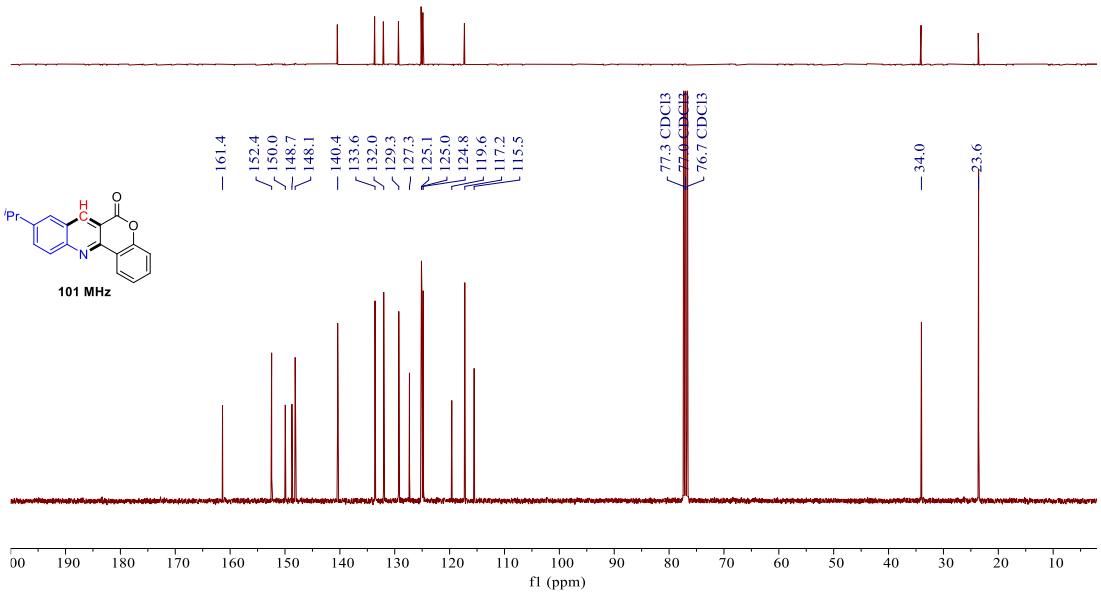



**Figure S16.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3e**

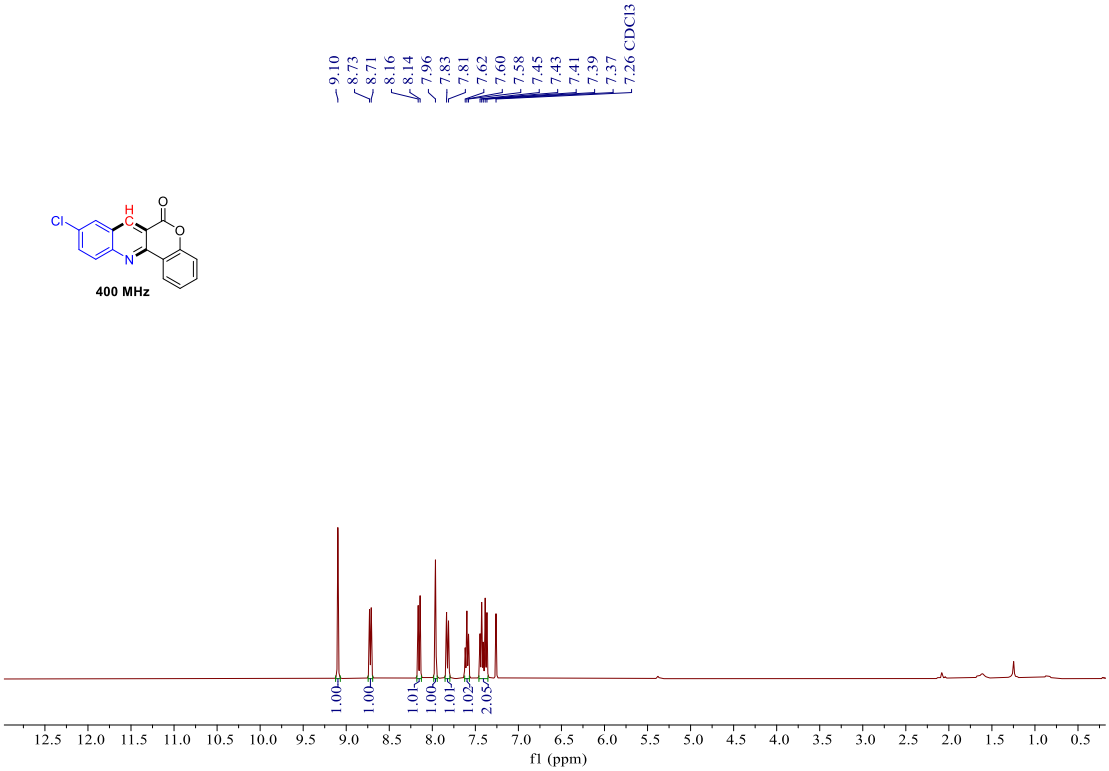



**Figure S17.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3f**

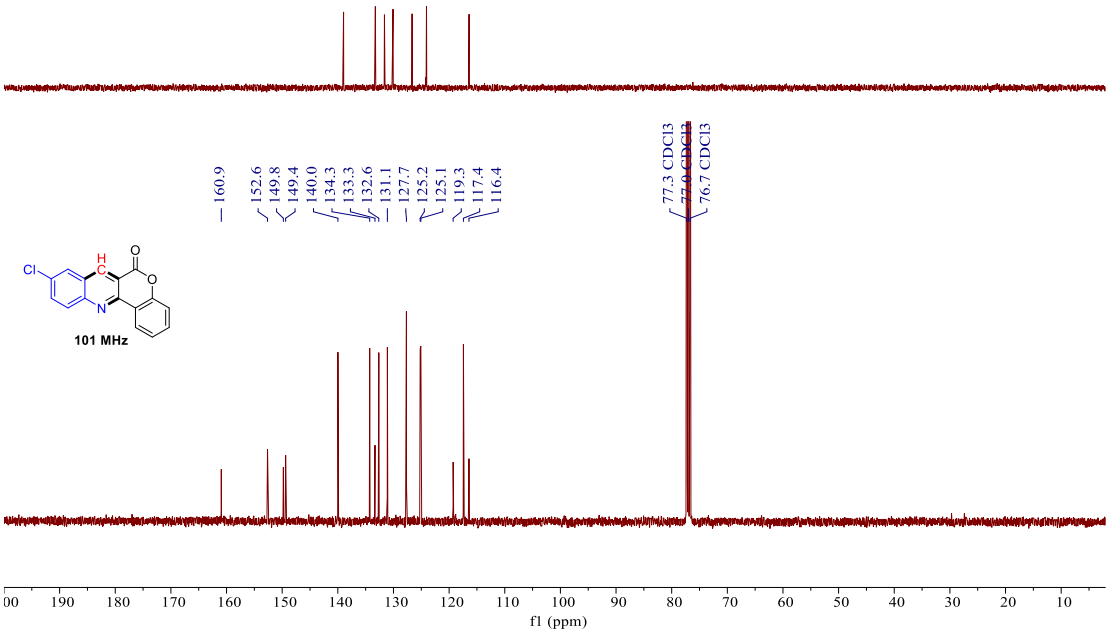



**Figure S18.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3f**

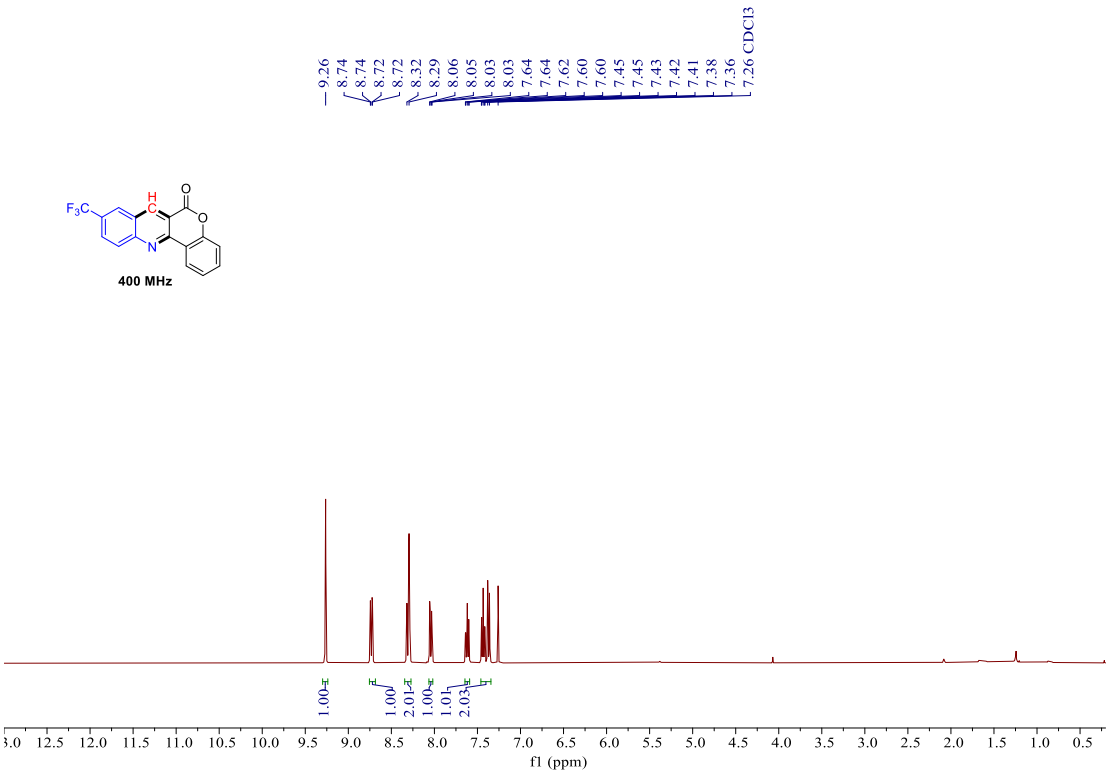



**Figure S19.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3g**

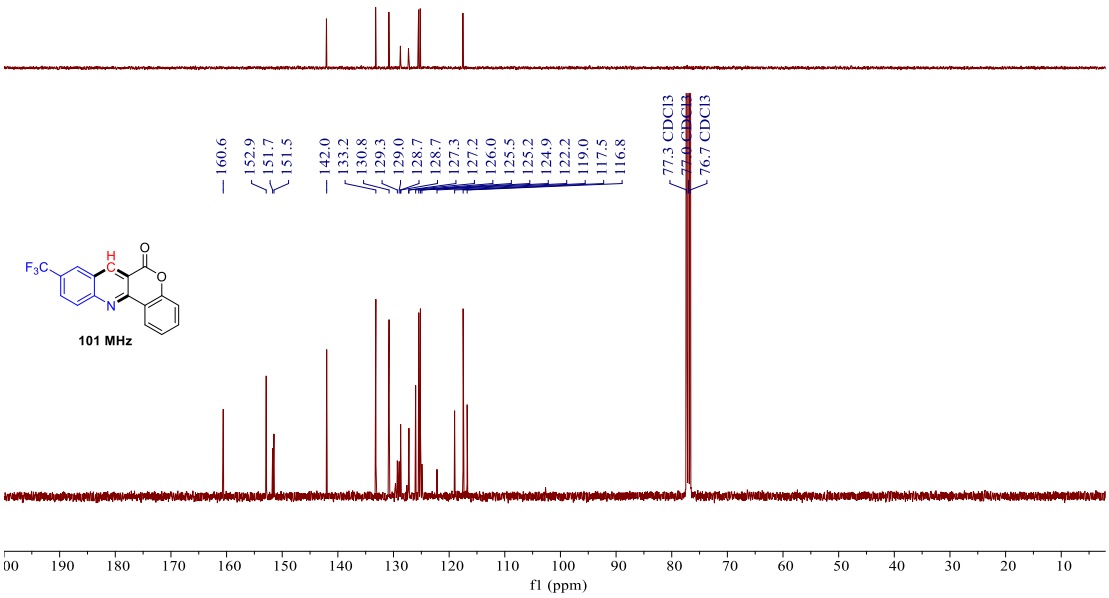



**Figure S20.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3g**

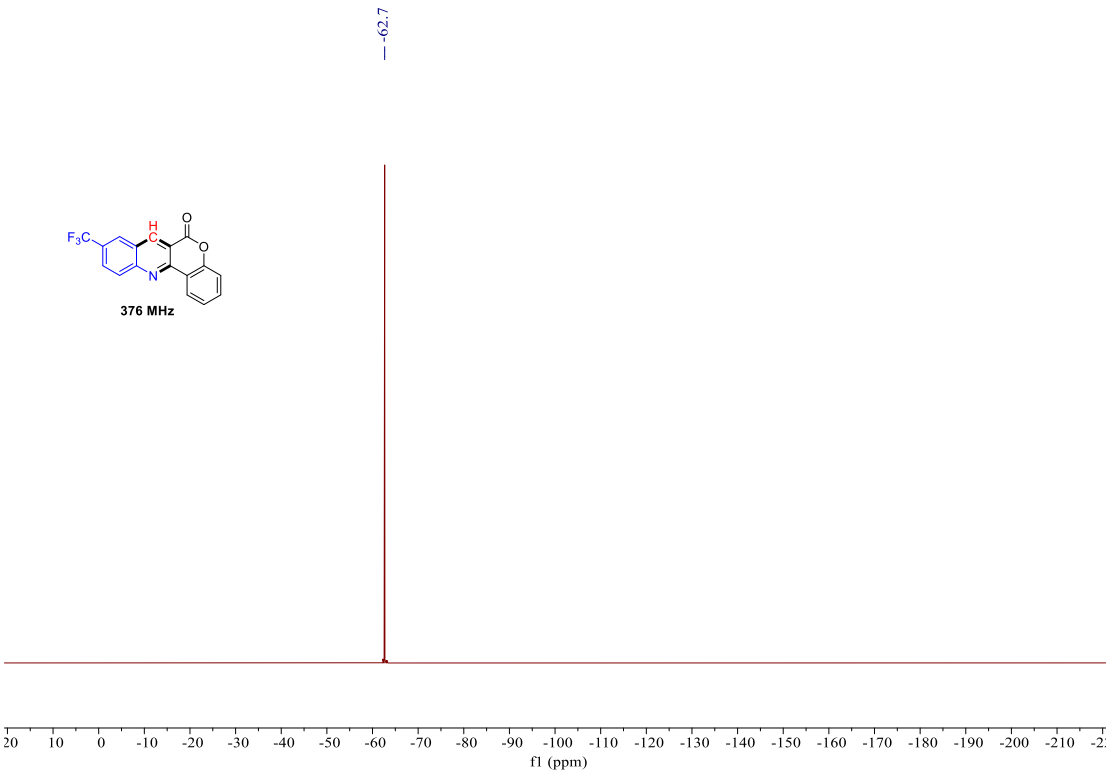



**Figure S21.** $^{19}F$ NMR (376 MHz $CDCl_3$) spectra of compound **3g**

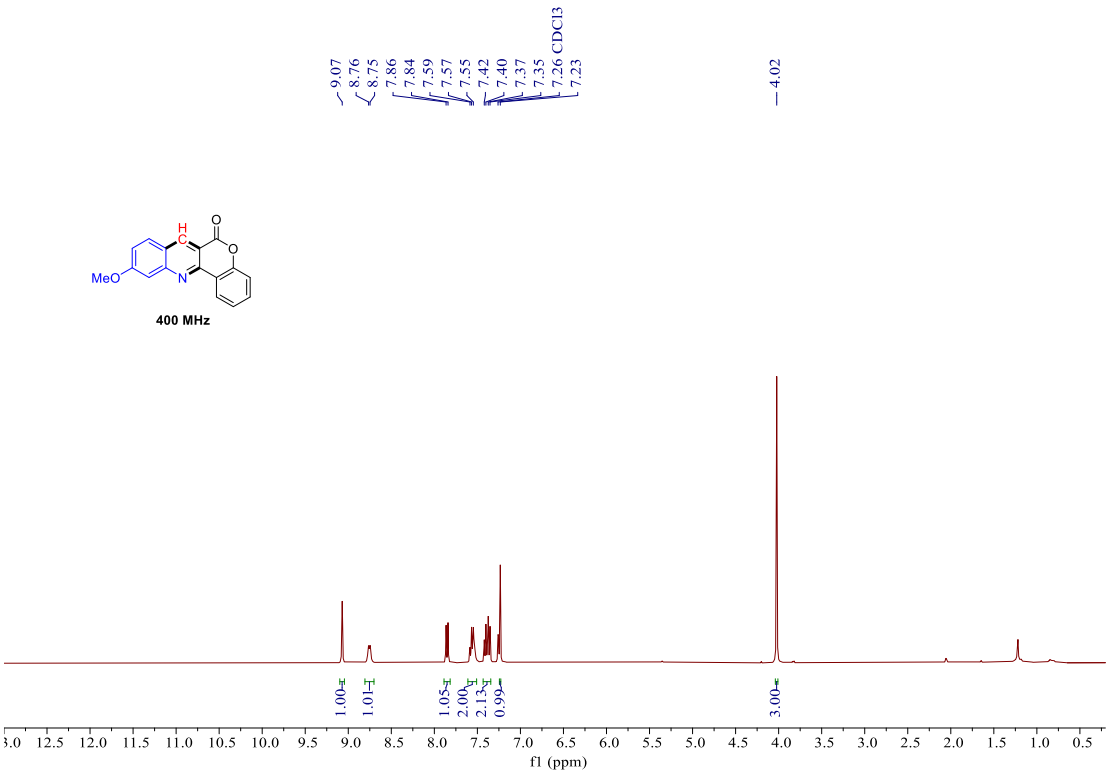



**Figure S22.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3h**

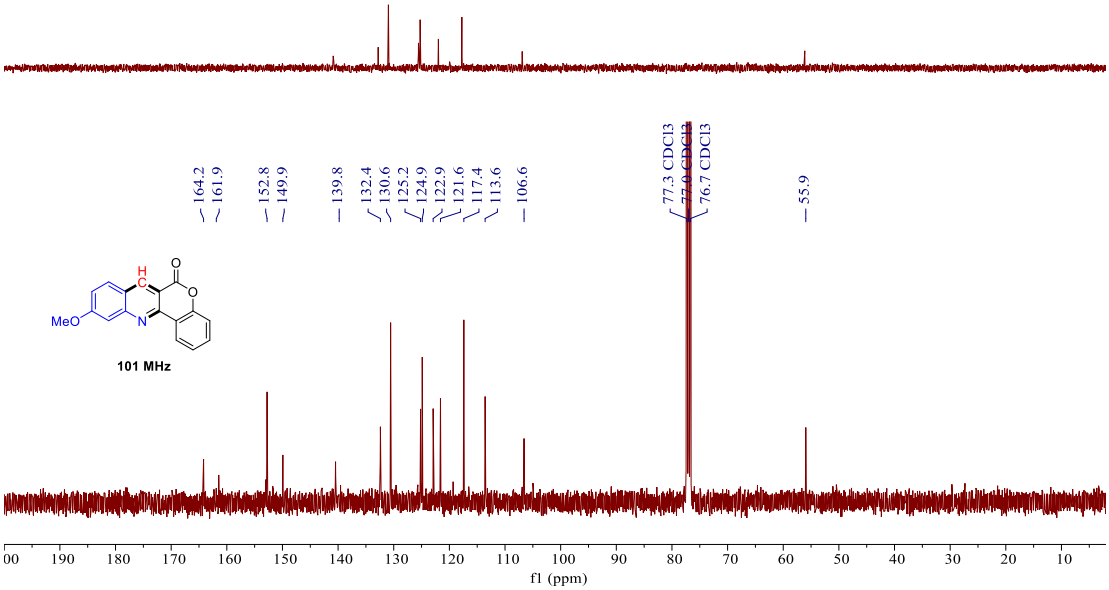



**Figure S23.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3h**

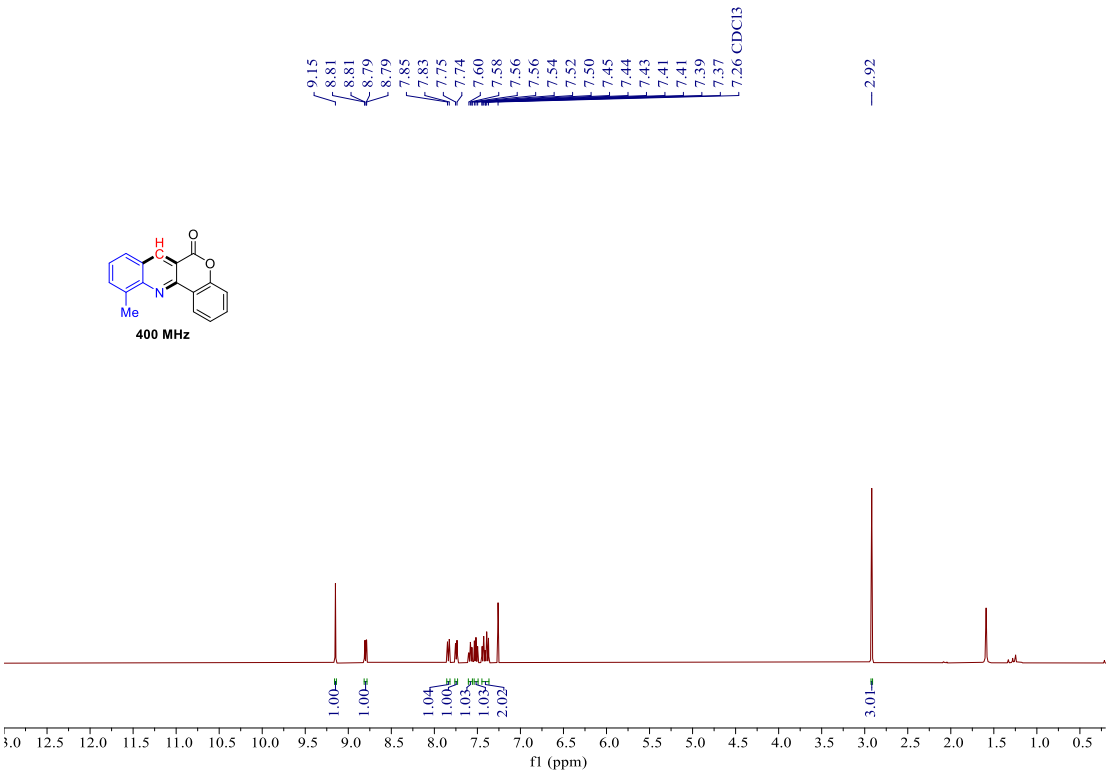



**Figure S24.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3i**

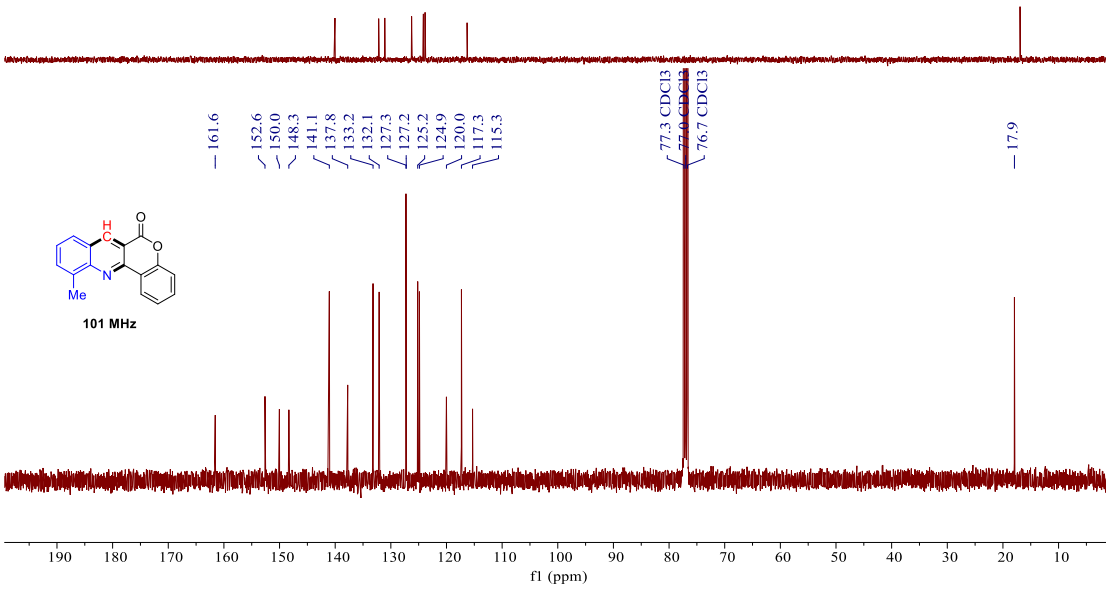



**Figure S25.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3i**

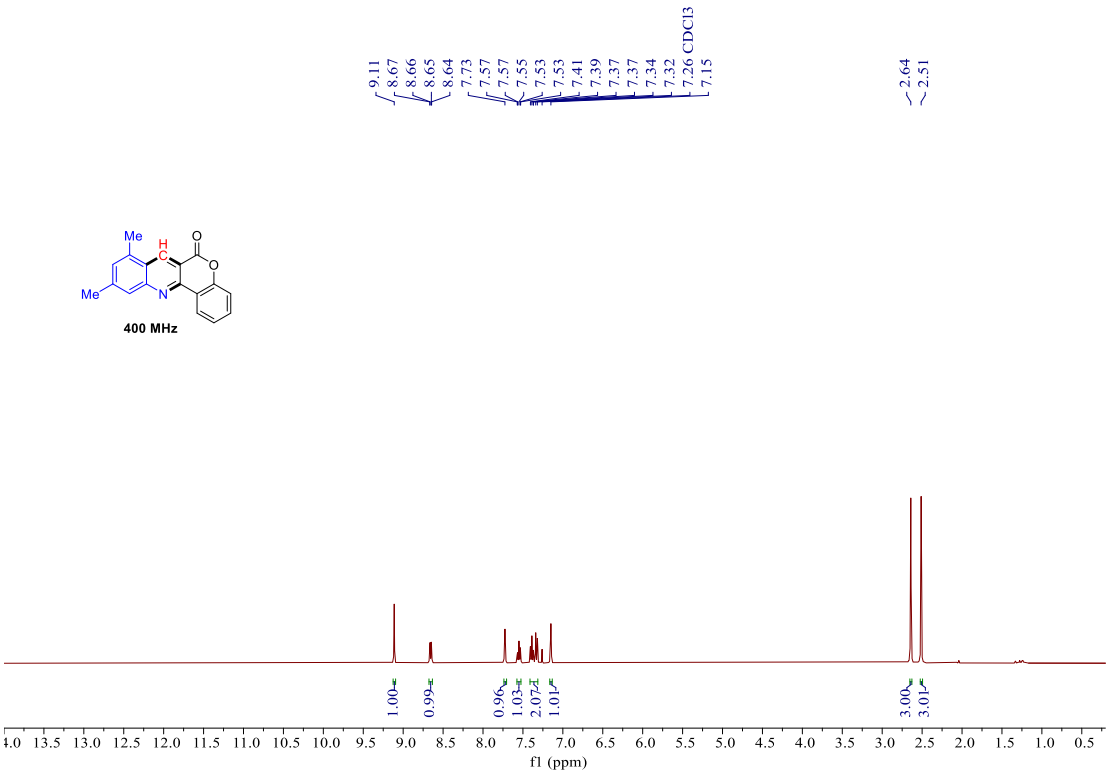



**Figure S26.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3j**

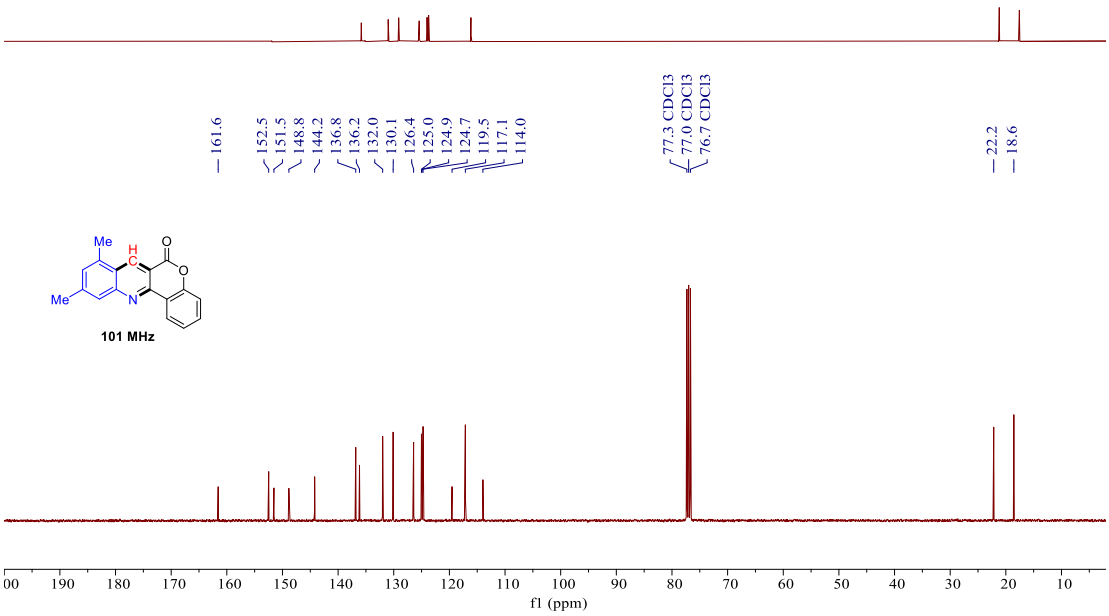



**Figure S27.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3j**

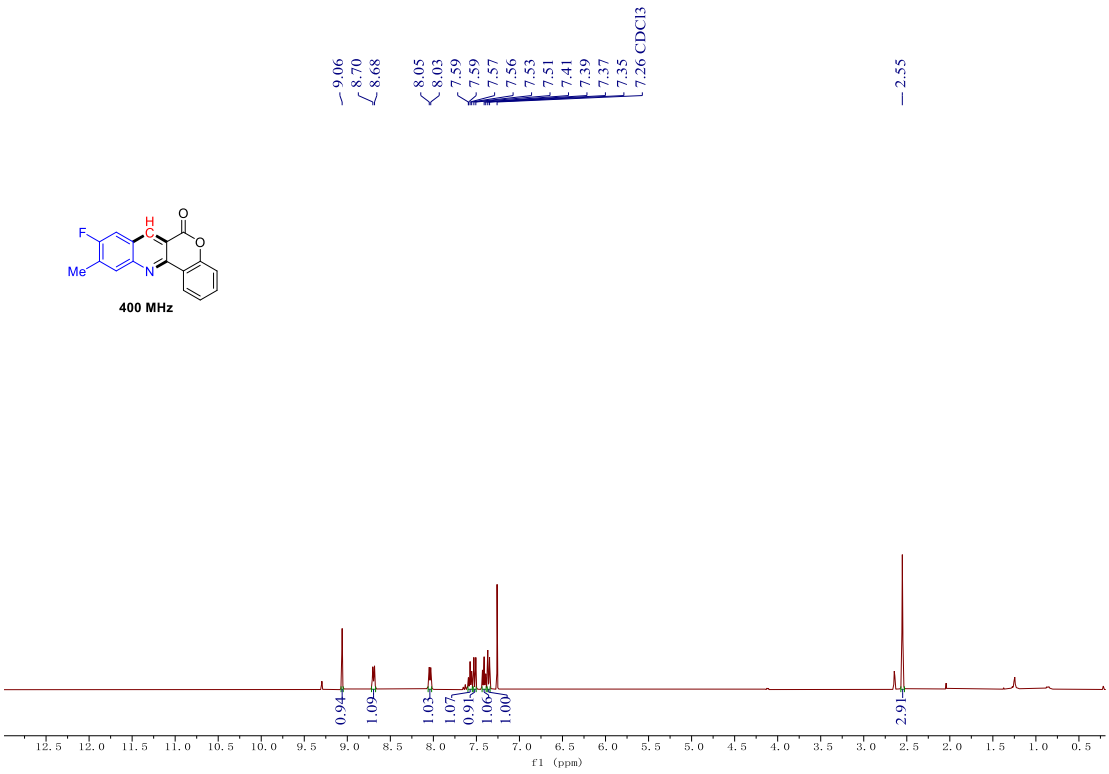



**Figure S28.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3k**

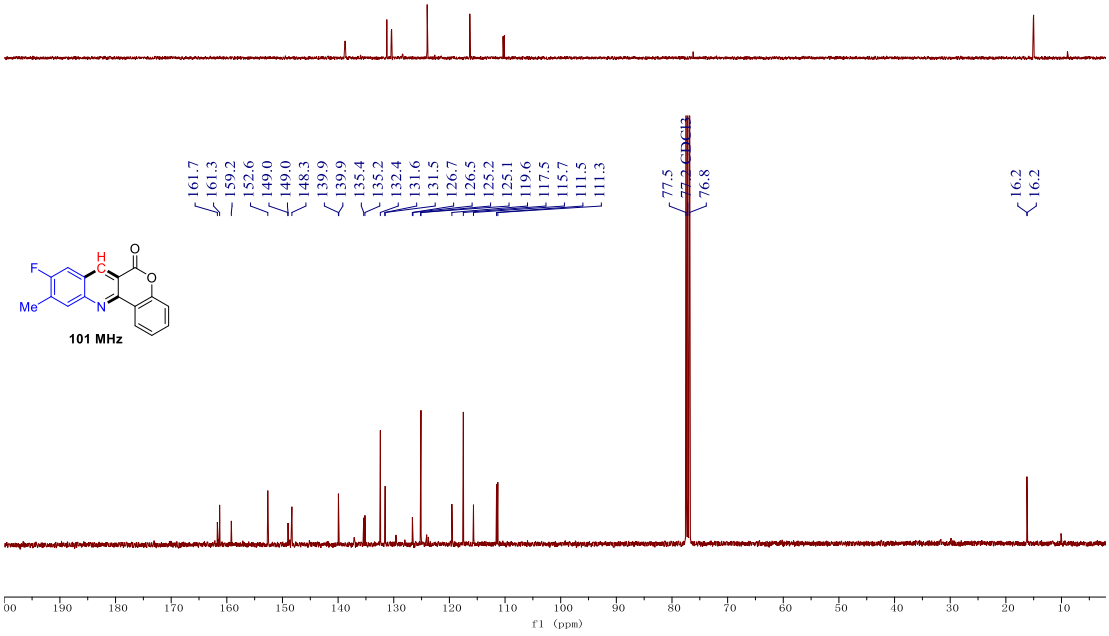



**Figure S29.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3k**

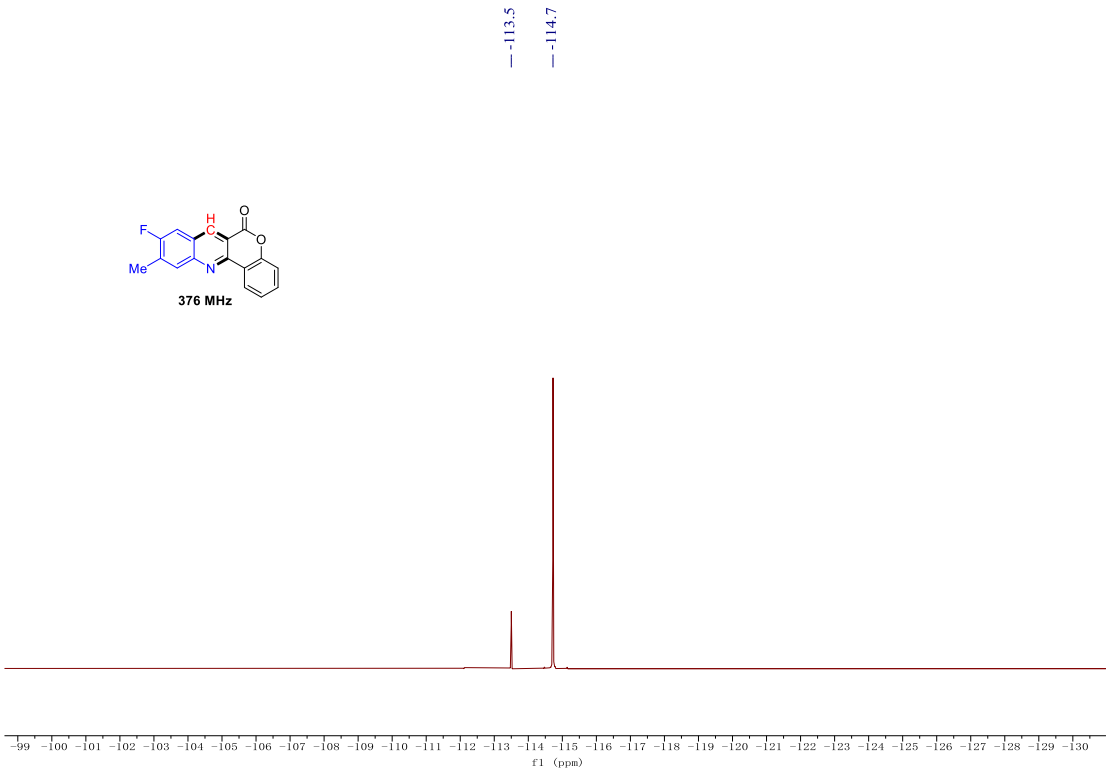



**Figure S30.** $^{19}F$ NMR (376 MHz $CDCl_3$) spectra of compound **3k**

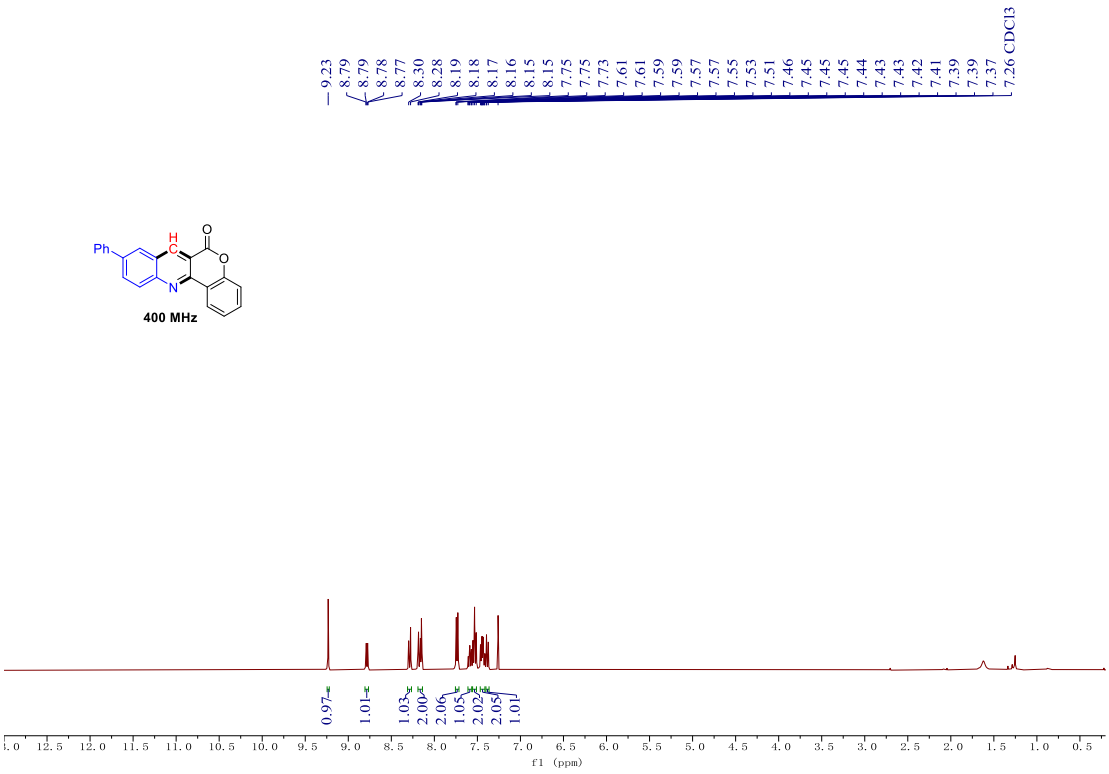



**Figure S31.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3l**

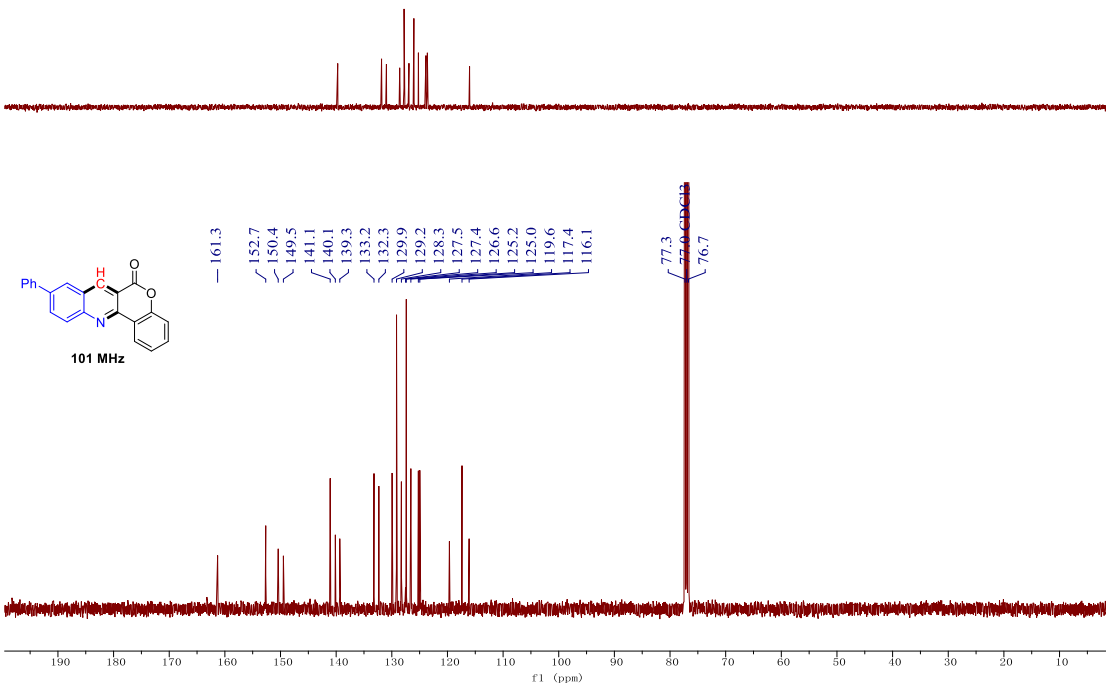



**Figure S32.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3l**

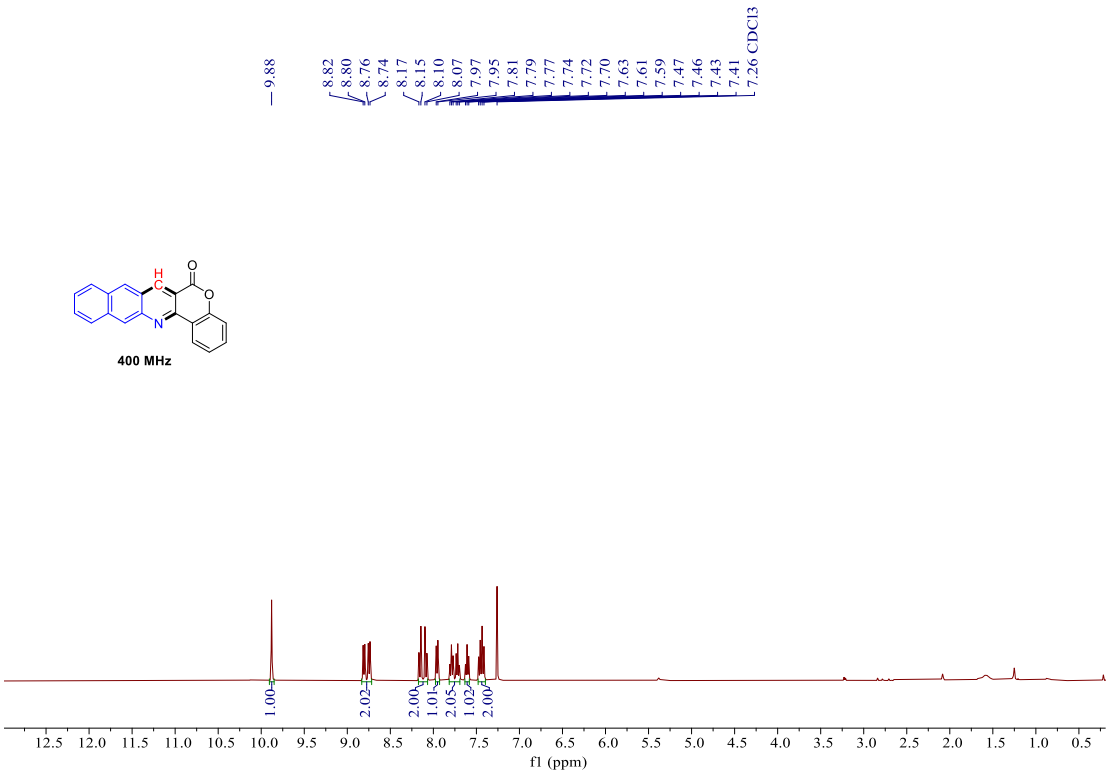



**Figure S33.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3m**

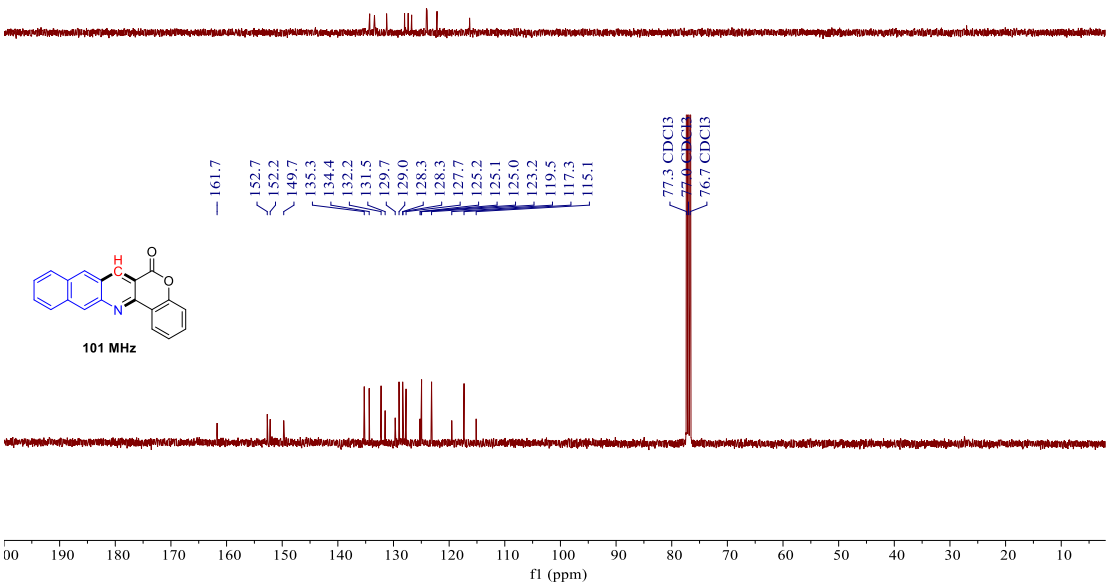



**Figure S34.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3m**

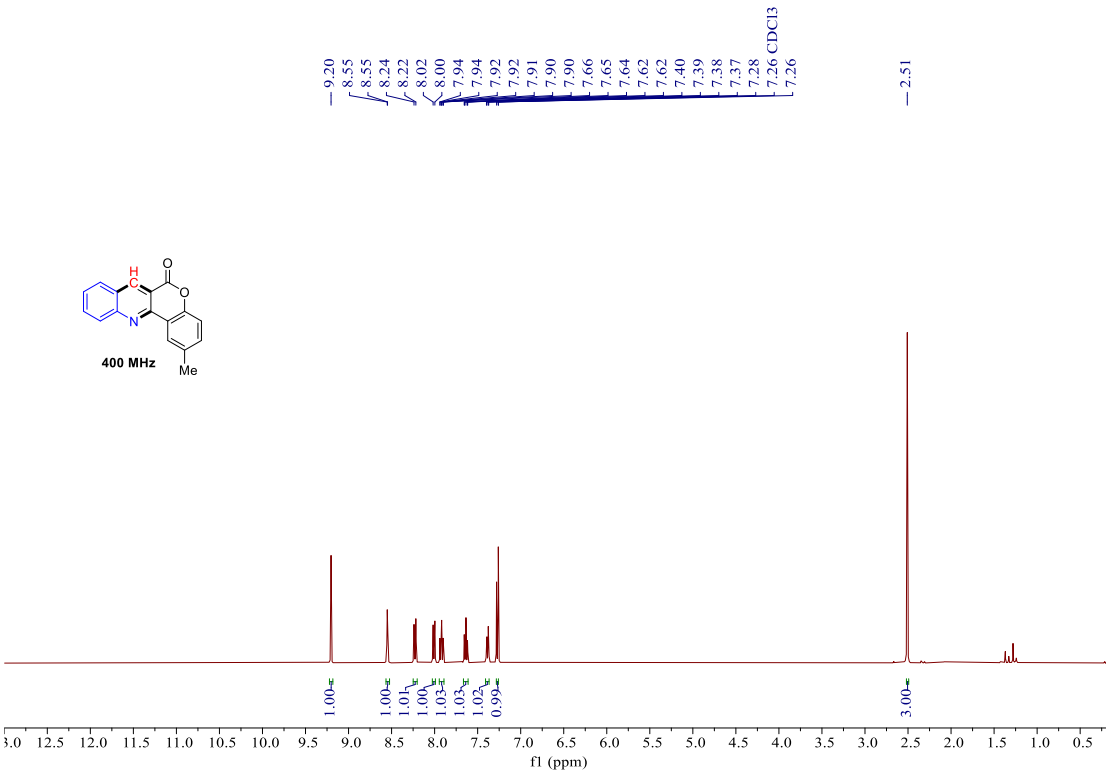



**Figure S35.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3n**

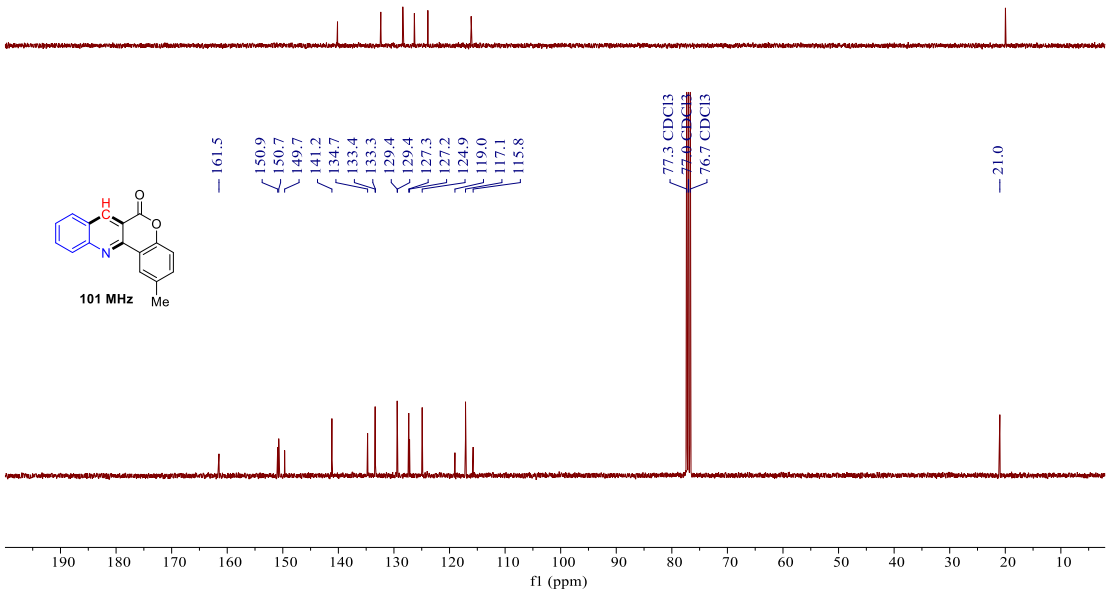



**Figure S36.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3n**

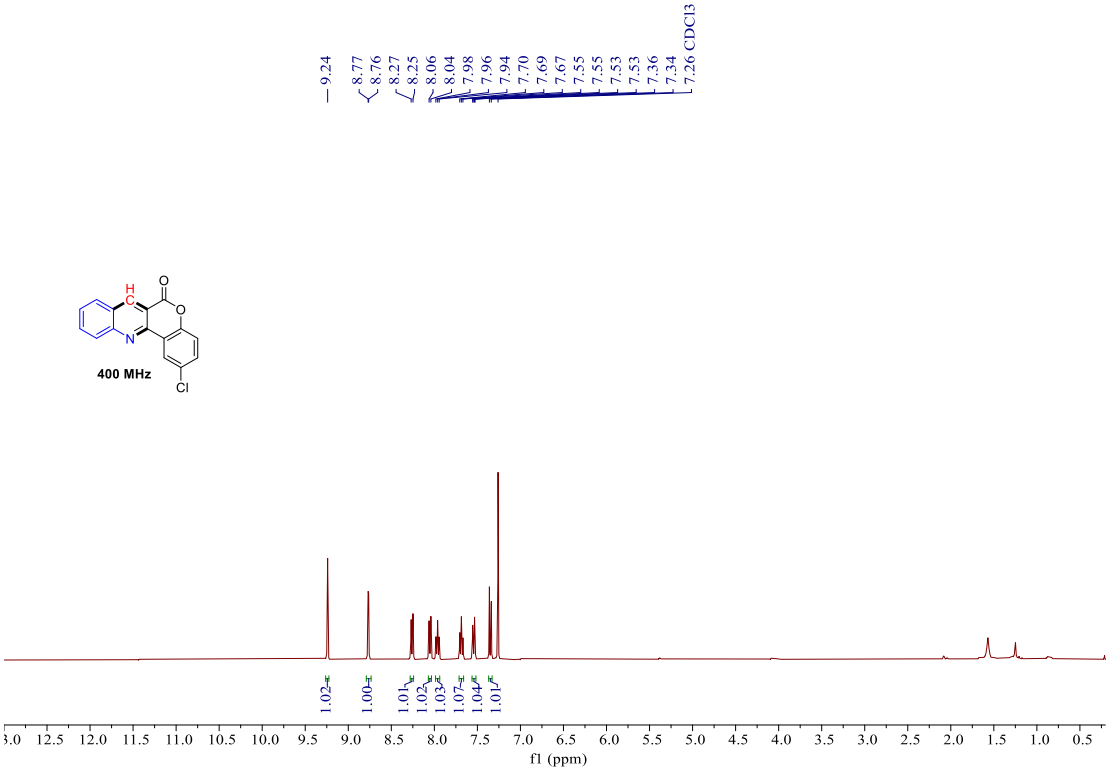



**Figure S37.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3o**

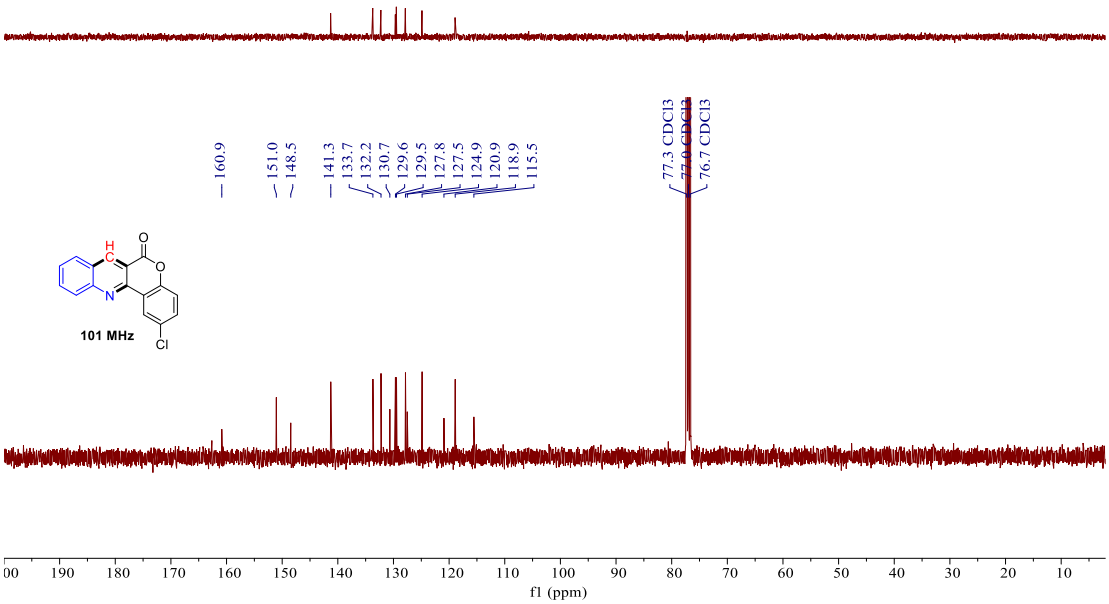



**Figure S38.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3o**

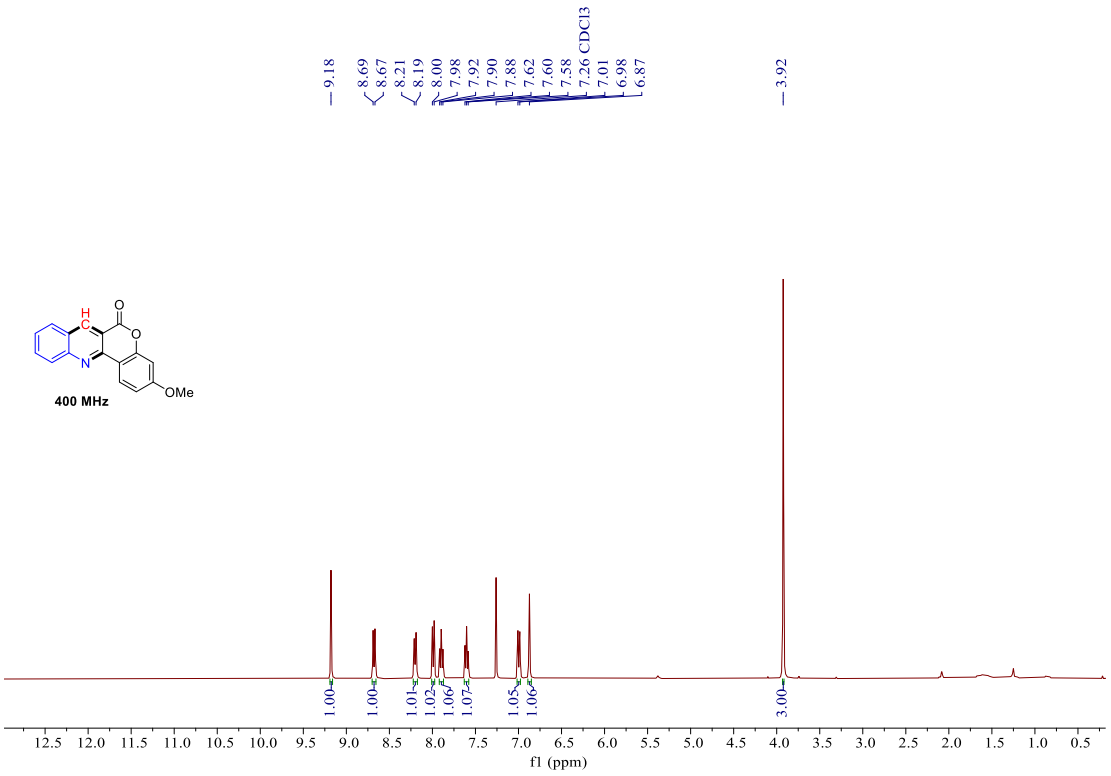



**Figure S39.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3p**

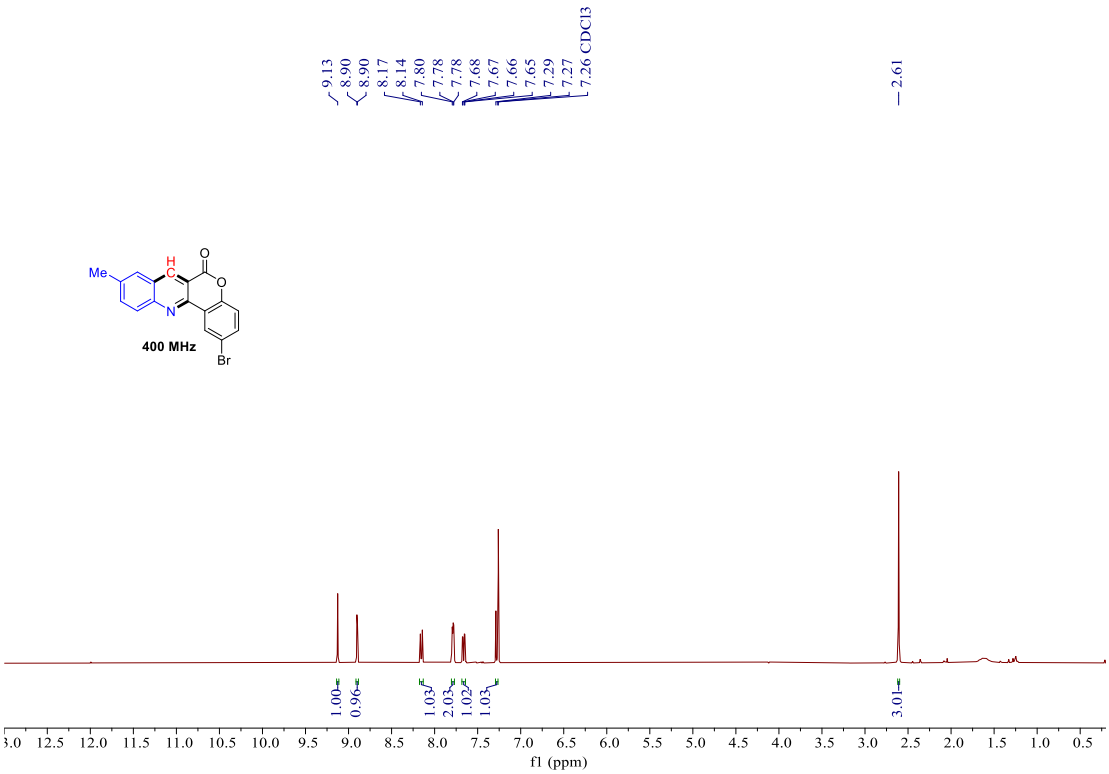



**Figure S40.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3q**

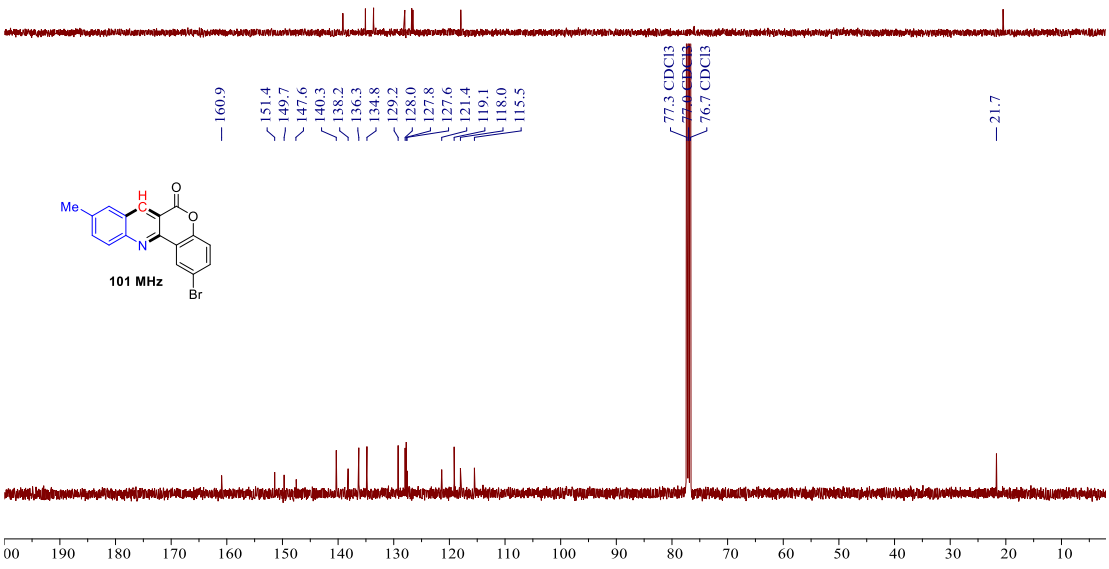



**Figure S41.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3q**

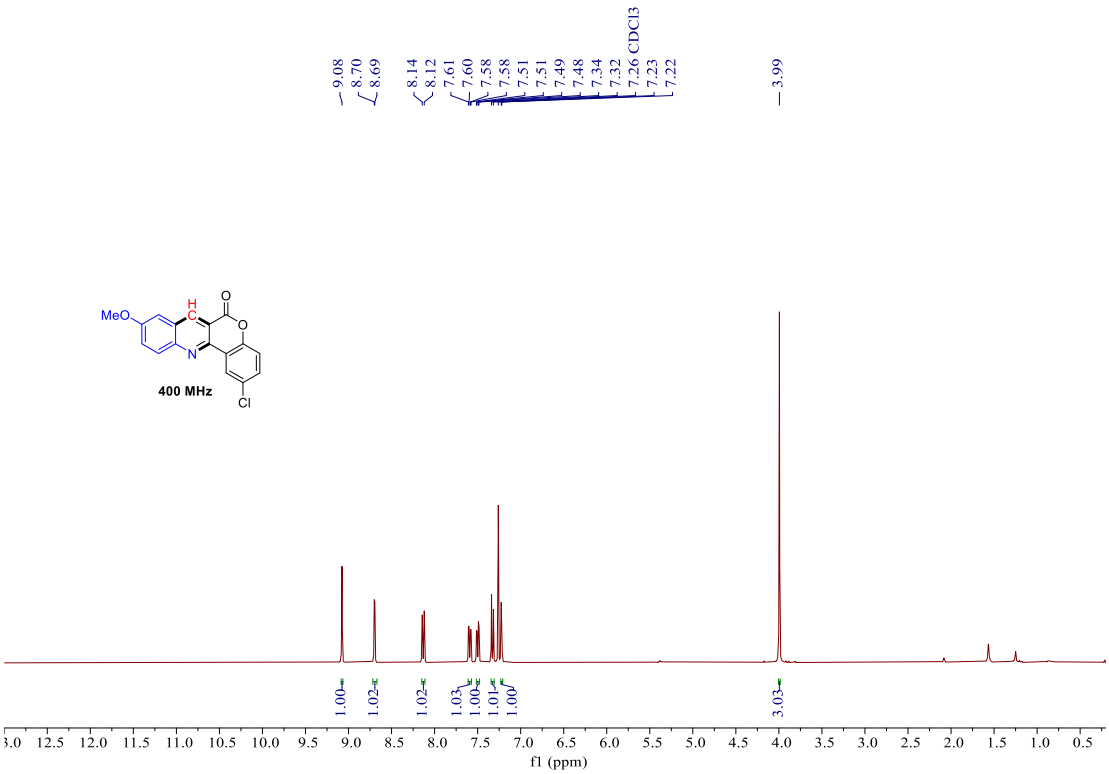



**Figure S42.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3r**

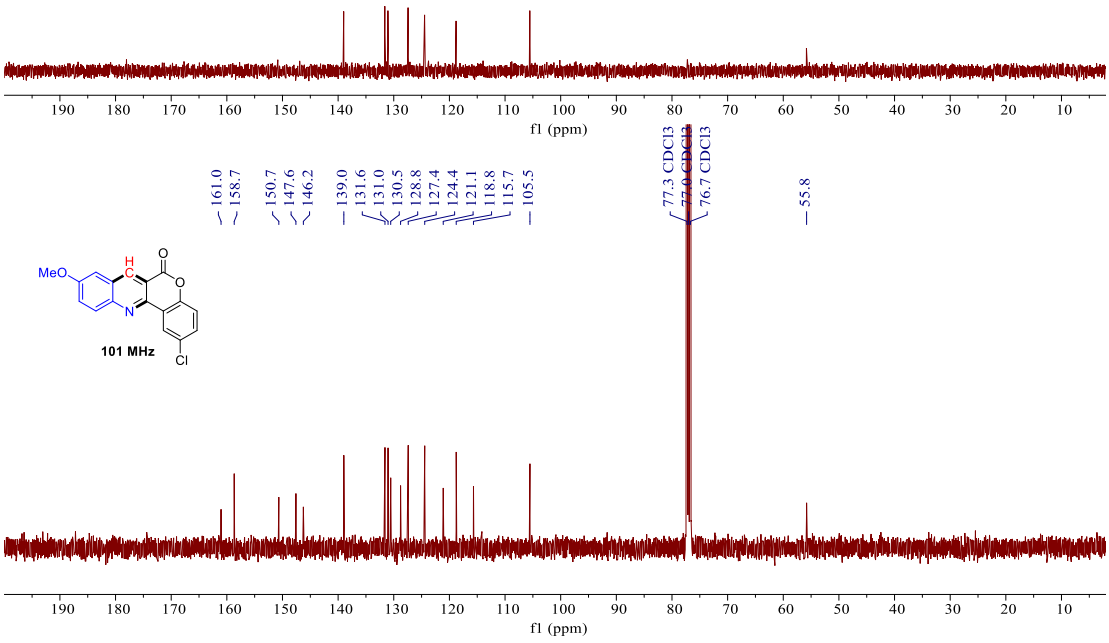



**Figure S43.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3r**

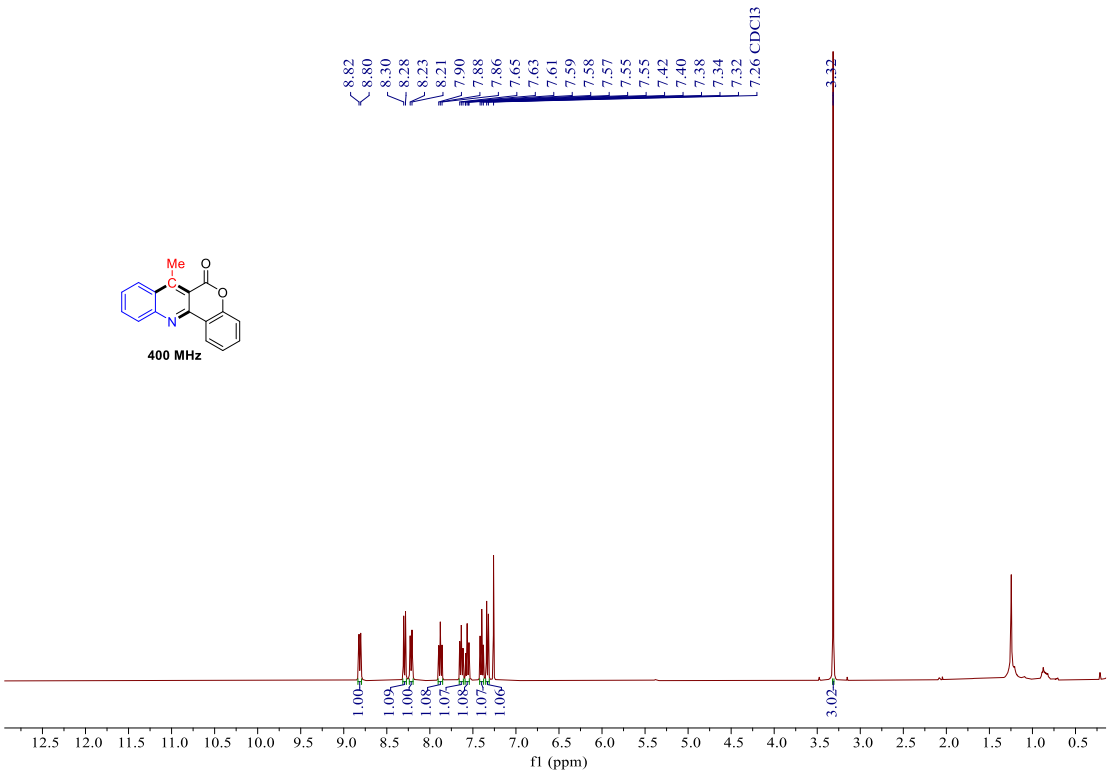



**Figure S44.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3s**

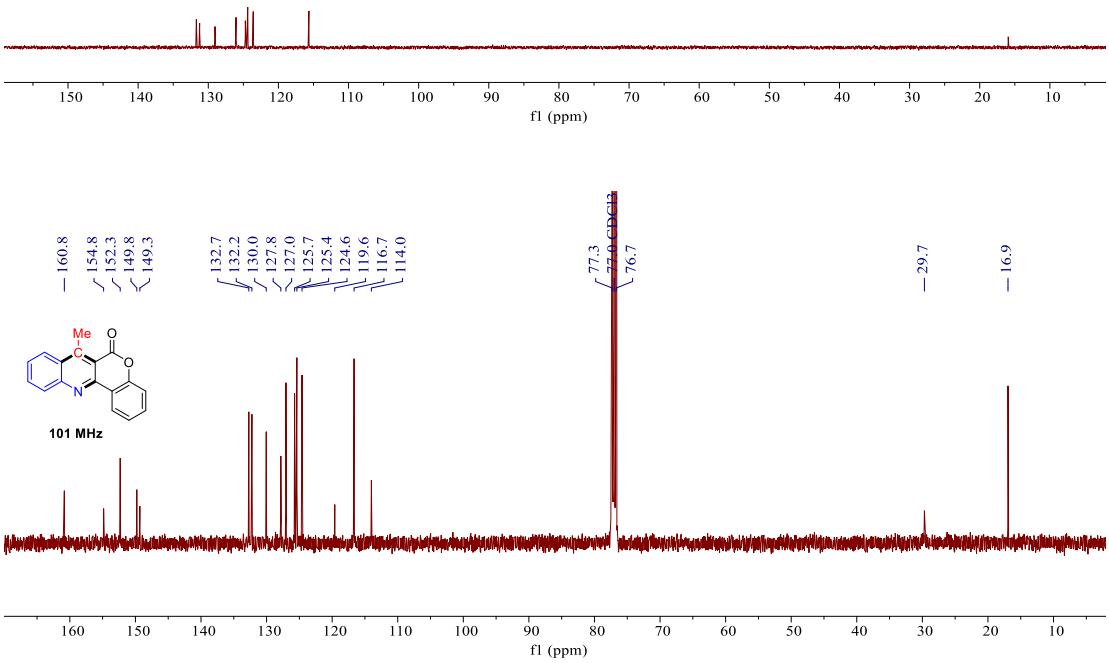



**Figure S45.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3s**

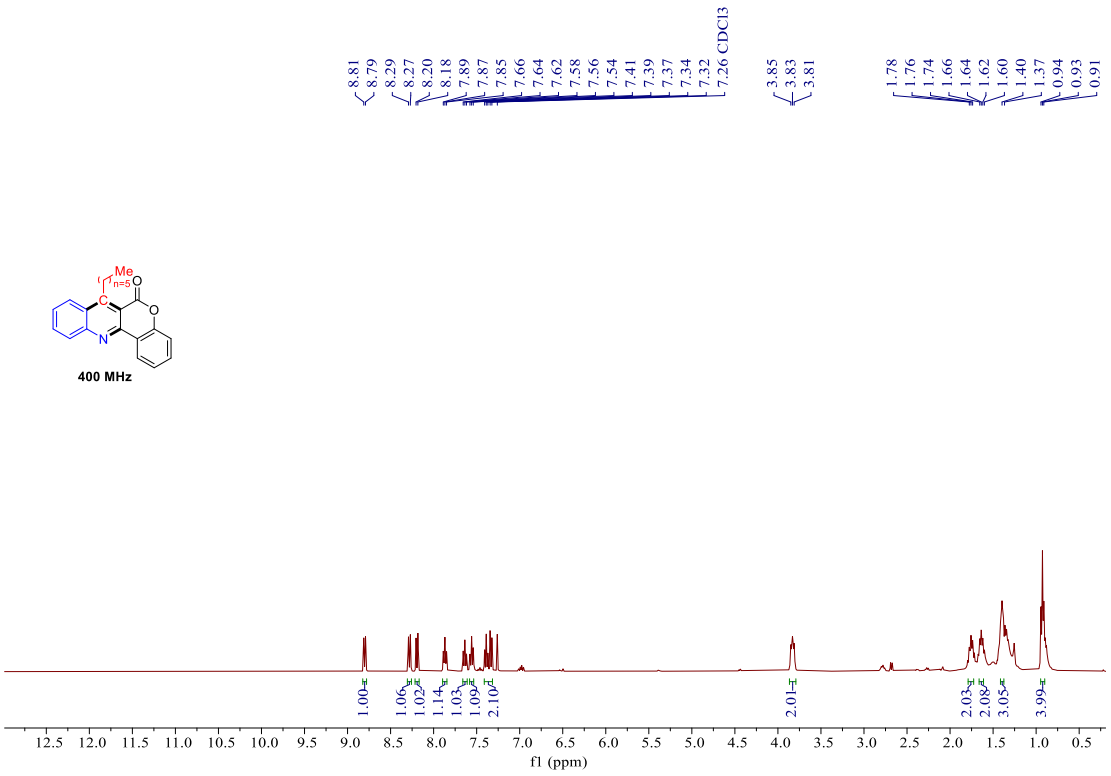



**Figure S46.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3t**

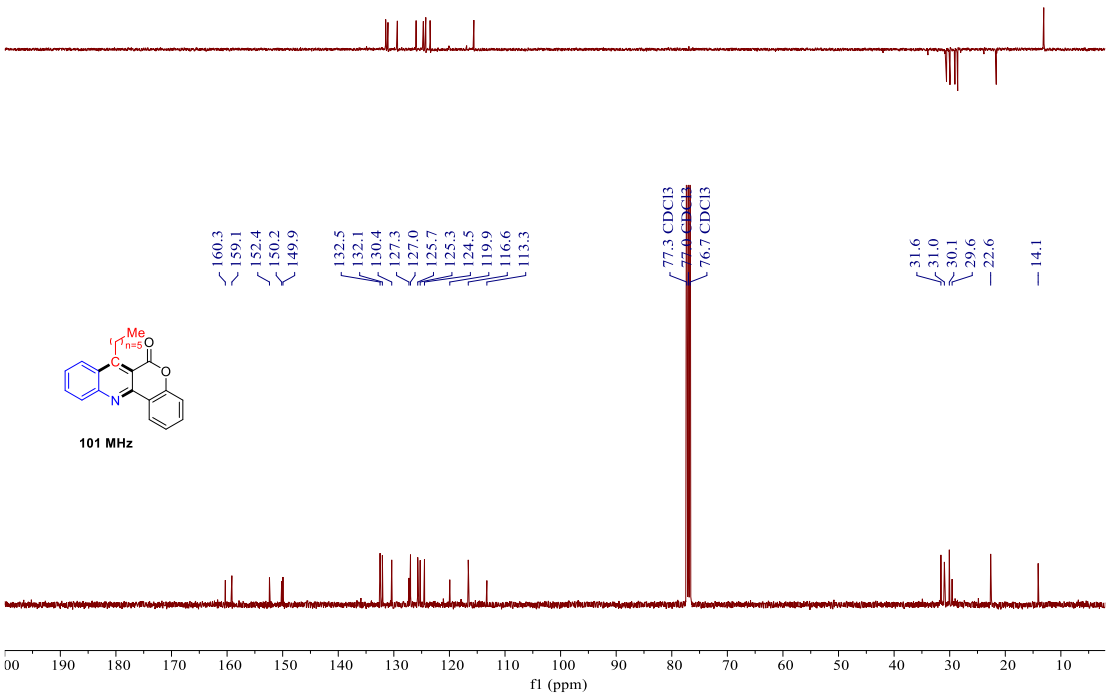



**Figure S47.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3t**

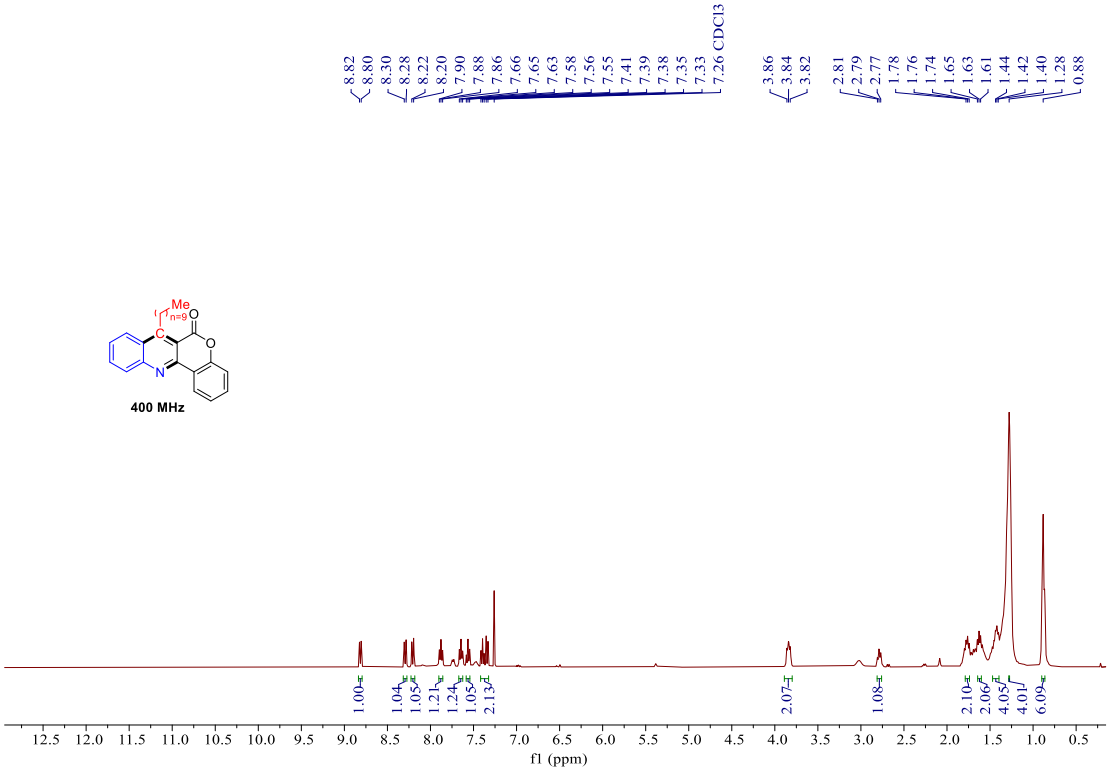



**Figure S48.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3u**

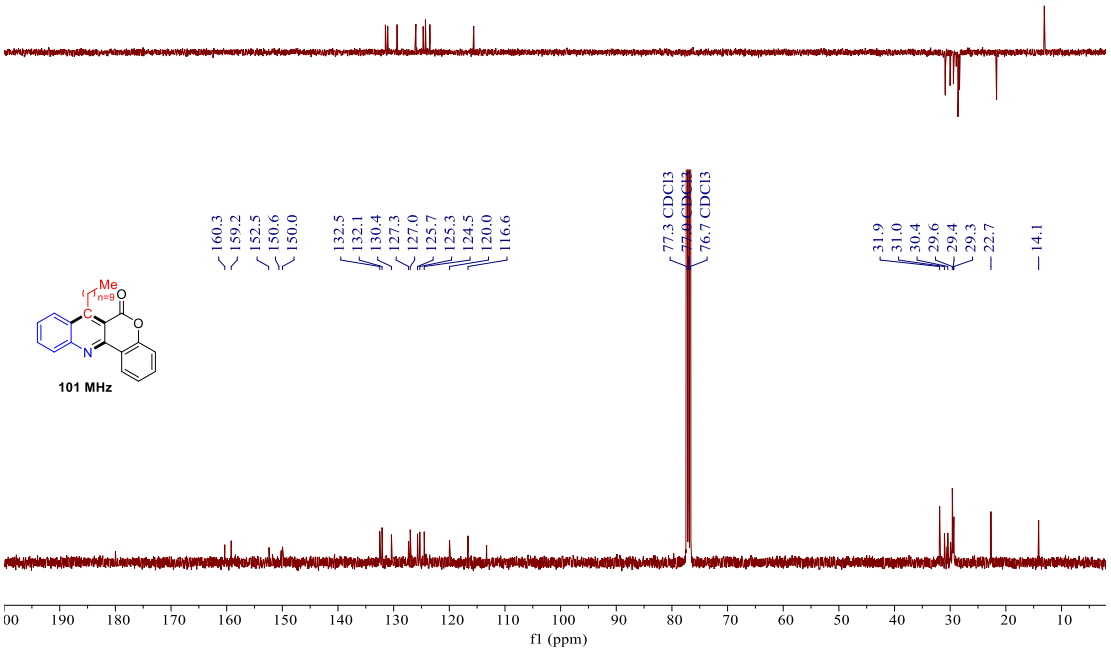



**Figure S49.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3u**

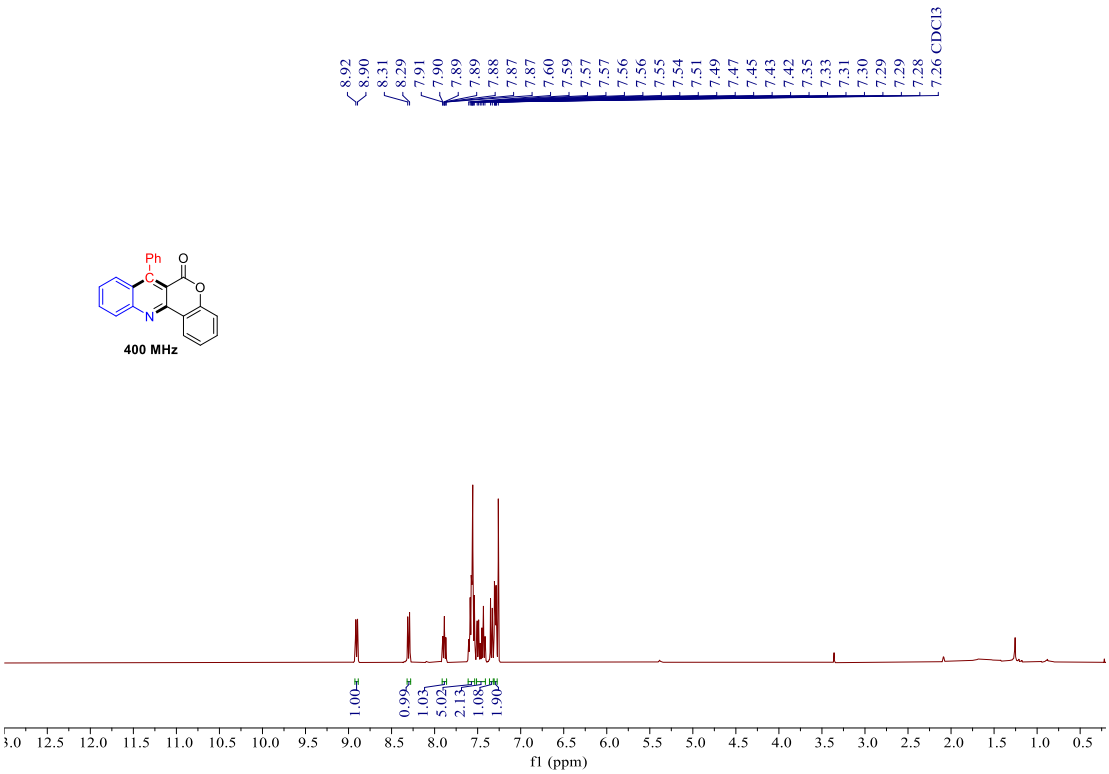



**Figure S50.** $^{1}$H NMR (400 MHz $CDCl_3$) spectra of compound **3v**

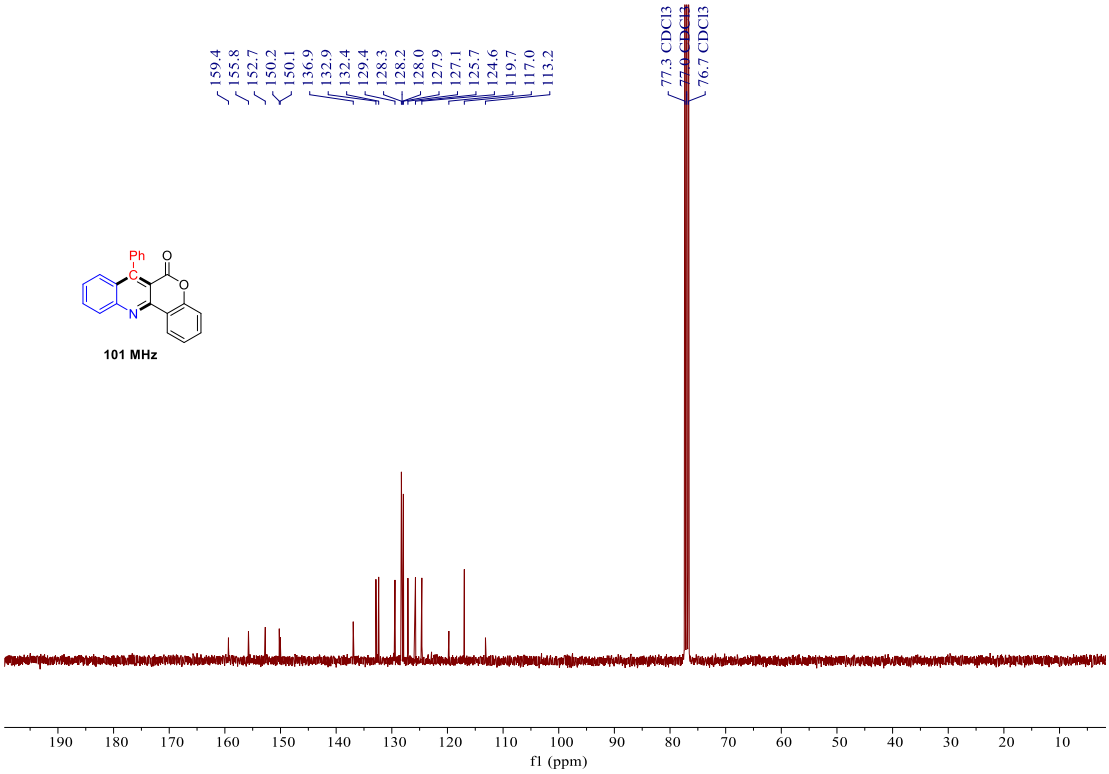



**Figure S51.** $^{13}$C NMR (101 MHz $CDCl_3$) spectra of compound **3v**

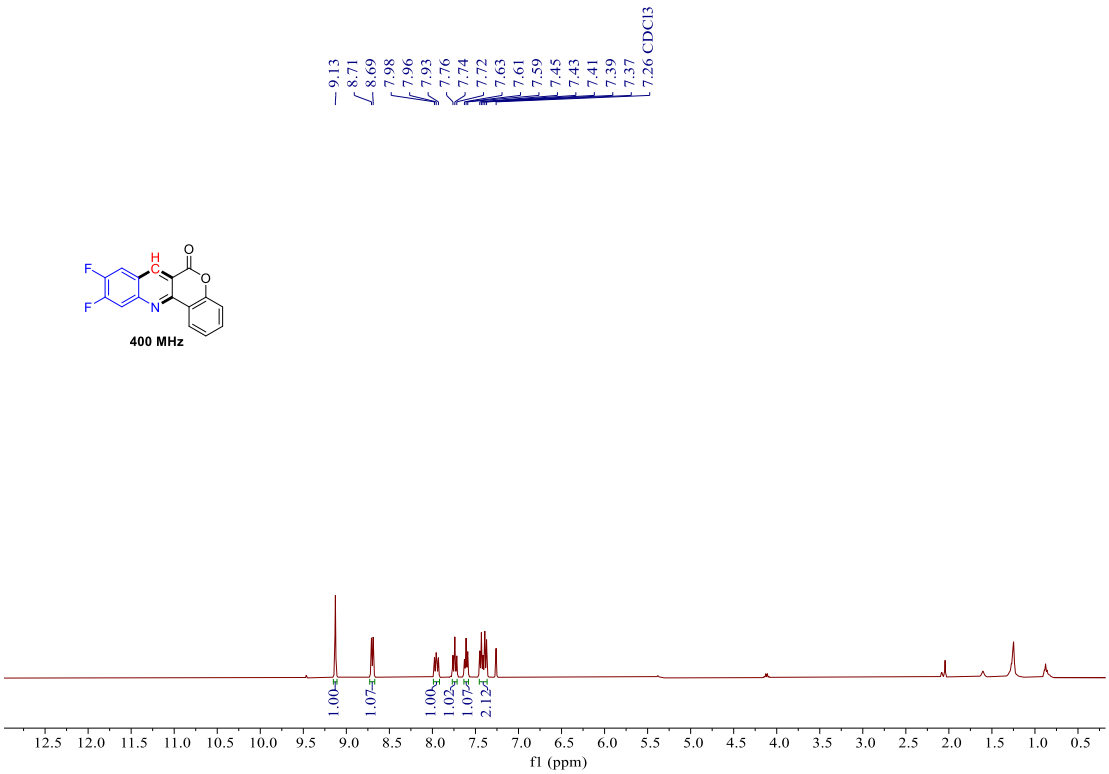



**Figure S52.** $^{1}H$ NMR (400 MHz $CDCl_3$) spectra of compound **3ab**

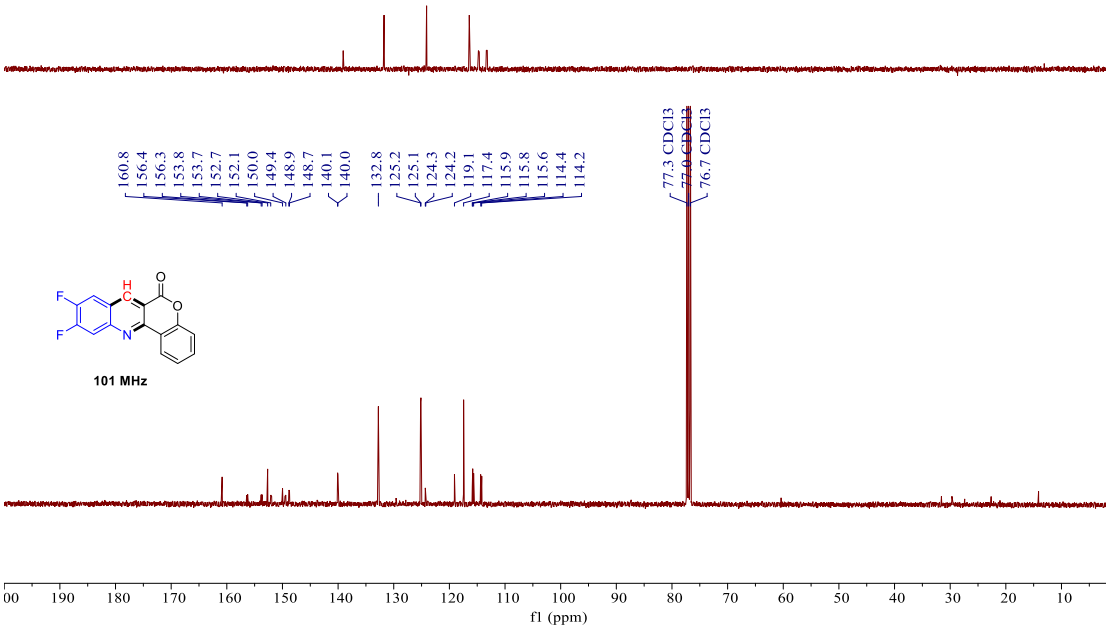



**Figure S48.** $^{13}C$ NMR (101 MHz $CDCl_3$) spectra of compound **3ab**

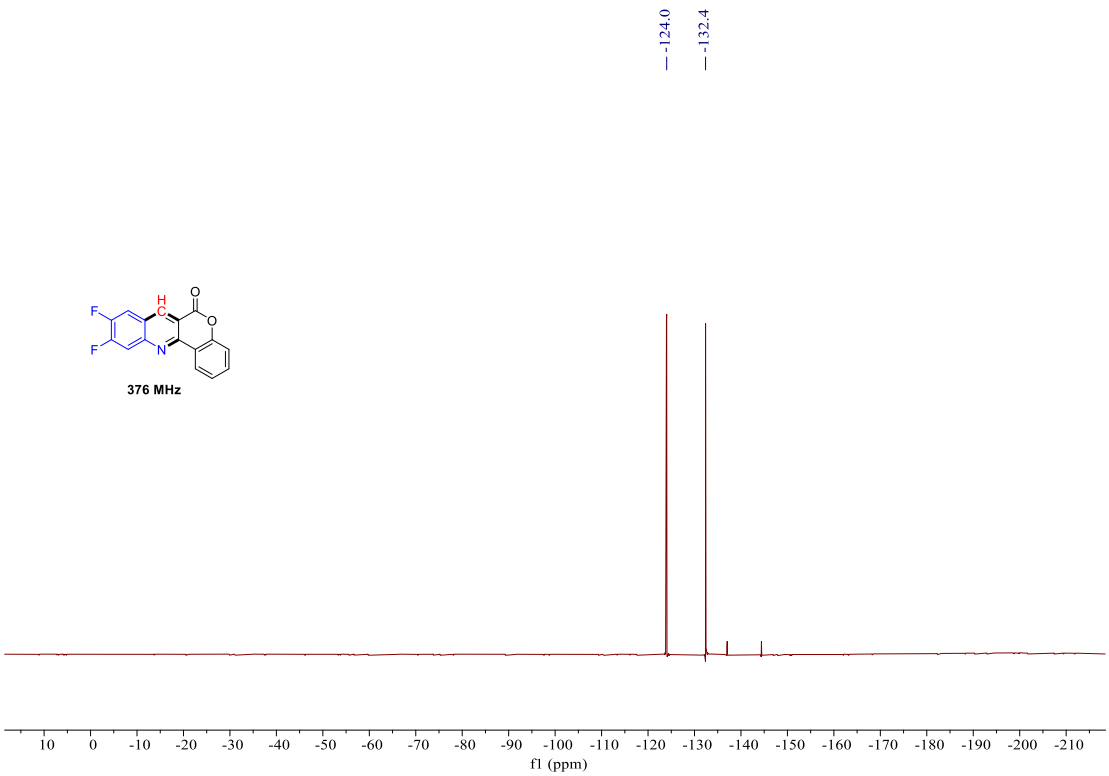



**Figure S49.** $^{19}F$ NMR (376 MHz $CDCl_3$) spectra of compound **3ab**

# 6. Calculation of Green Metrics[6]

**Table S1.** Solvent post-treatment and calculation of green metrics.[a]


| entry | conditions | atom economy (%) | reaction mass efficiency (%)[b] | | E factor[c] | |
|---|---|---|---|---|---|---|
| 1 | DMSO, KI, TBPB, PivOH, 60 °C | 64.7 | 3.0 | 5.8[d] | 32.7 | 16.2[d] |
| 2 | DMSO, $I_2$, $O_2$, 120 °C | 57.6 | 3.1 | 19.5[d] | 31.6 | 4.1[d] |
| 3 | DMF, CuI, $K_2S_2O_8$, 120 °C | 69.8 | 0.7 | 21.2[d] | 146.9 | 3.7[d] |
| 4 | EtOH, $FeCl_3$, $H_2O_2$, r.t. | 79.0 | 9.6 | 37.4[d] | 9.3 | 1.7[d] |
| 5 | $CH_3COOH$, $I_2$, 165 °C | 89.4 | 20.0 | 72.4[d] | 4.0 | 0.4[d] |
| 6 | DMSO, 130 °C | 74.2 | 3.0 | 16.2[d] | 32.5 | 5.2[d] |
| 7 | DMF, $NaHSO_3$, NaOAc, NaI, 95 °C | 79.7 | 1.5 | 38.2[d] | 64.2 | 1.6[d] |
| 8 | Solvent-free, Air, No catalyst, 120 °C | 71.8 | 6.2 | 28.5[d] | 15.0 | 2.5[d] |
| 9 | $CH_3COOH$, $O_2$, 120 °C | 86.7 | 1.8 | 27.2[d] | 52.7 | 2.7[d] |
| 10 | Lactic acid, Air, No catalyst, 120 °C | **91.8** | **36.4** | **66.8[d]** | **1.7** | **0.5[d]** |

[a] For compound **3a** (when considering solvent). [b] Reaction mass efficiency = {Mass of the desired product}/{Total mass of the reagents}*100. [c] E factor = {Total mass of waste}/{Mass of product}. [d] When solvent not considered.

**For compound 3a (when considering solvent):**

Atom Economy = 100*{Molecular weight of the desired product}/(Molecular weight of the starting materials)

Reaction Mass efficiency= {Mass of the desired product}/{Total mass of the reagents}*100

E factor = {Total mass of waste}/{Mass of product}

Amount of solvent taken = 0.10 mL= (1.209*0.10) g = 120.9 mg

Amount of *N*-methyl aniline taken = (0.1070735*0.60) g = 64.2 mg

Amount of 4-hydroxy coumarin taken = (0.1600317*0.50) g = 80.0 mg

Atom economy = 100*(247.0633/269.1052) = 91.8%

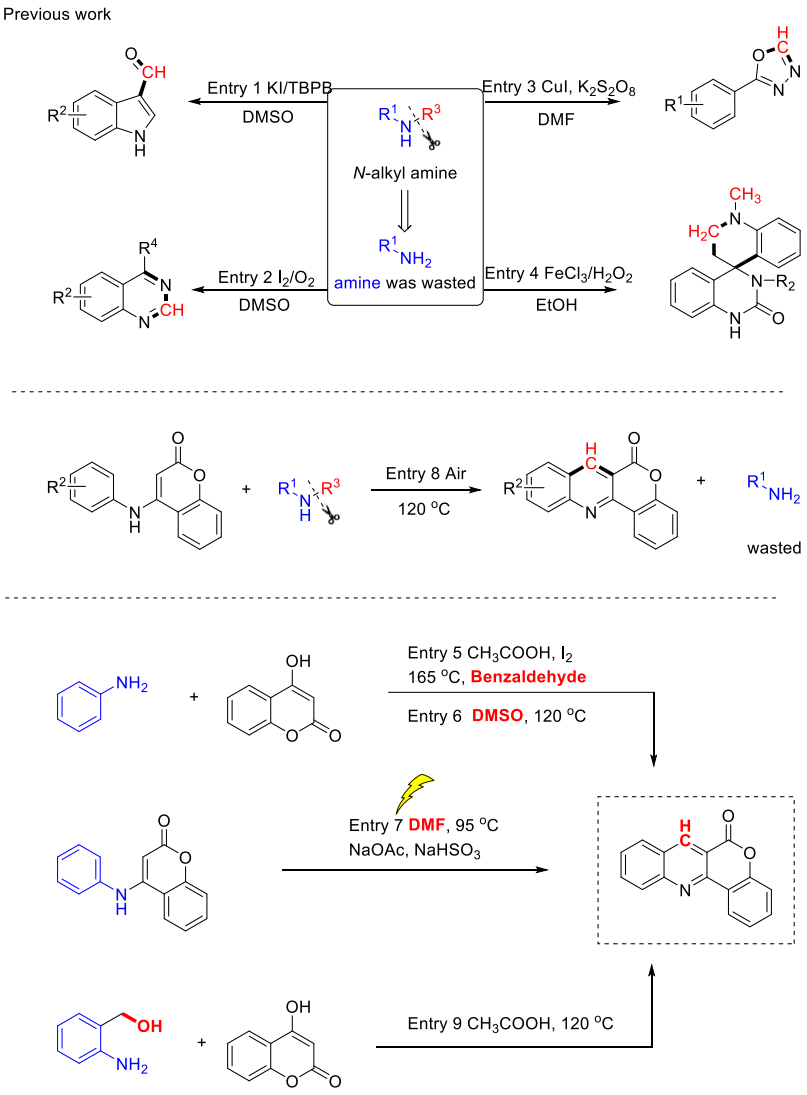
Reaction mass efficiency = 100*((96.4/(120.9+64.2+80.0) = 36.4%

E factor calculation = ((265.16-96.4)/96.4) = 1.75

**When solvent not considered:**

Reaction mass efficiency = 100*((96.4/(64.2+80.0) = 66.8%

E factor calculation = ((64.2+80.0-96.4)/96.4) = 0.50




**Scheme S2**. Cleavage of *N*-alkyl Amines and Strategies of Coumarin-Fused Quinolinone.

# 7. References


(1) J. Jiao, F. T. Xiao, C. Wang, Z. P. Zhang, *J. Org. Chem.* **2022**, *87*, 4965–4970.

(2) Z. Zhang, J. Wan, L. Yin, M. T. Fu, C. Huang, *Adv. Synth. Catal*. **2024**, *366*, 1430–1435.

(3) Y. Y. Weng, H. T. Chen, N. H. Li, L. Yang, L. Ackermann, *Adv. Synth. Catal*. **2021**, *363*, 2773–2777.

(4) N. N. H. Ton, H. V. Dang, N. T. S. Phan, T. T. Nguyen, *RSC Adv*. **2019**, *9*, 16215–16222.

(5) K. V. Sashidhara, G. R. Palnati, L. R. Singh, A. Upadhyay, S. R. Avula, A. Kumara, R. Kant, *Green Chem*. **2015**, *17*, 3766–3770.

(6) C. J.-González, D. J. C. Constable, C. S. Ponder, *Chem. Soc. Rev.* **2012**, *41*, 1485–1498.

(7) T. L. Yao, D. W. Yue, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 9985–9989.