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A Catalyst-Free Approach to 3-Thiocyanato-4H-chromen-4-one

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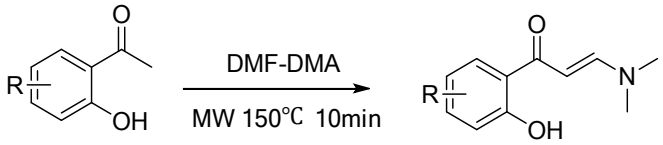
Supporting Information

General information:

NMR spectra were obtained on an Agilent 400-MR DD2 spectrometer. The ^{1}H NMR (400 MHz) chemical shifts were measured relative to $CDCl_3$ as the internal reference ($CDCl_3$: δ=7.26). The ^{13}C NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ=77.16). High-resolution mass spectra (HRMS) were obtained with a Shimadzu LCMS-IT-TOF(ESI). Microwave experiments were conducted in the commercial microwave reactor especially designed for synthetic chemistry: Anton Paar Monowave 300™ is a monomode cavity with a microwave power delivery system ranging from 0 to 850 W allowing pressurized reactions (0 to 30 bars) to be carried out in sealed glass vials (4 to 30 mL) equipped a snap cap and a silicon septum. The temperature (0 to 300 ℃) was monitored via a contact-less infrared sensor and was calibrated with a Ruby Thermometer. Temperature, pressure, and power profiles were edited and monitored through a touch screen control panel.

Procedures for the Synthesis of enaminone:

Starting from 2-hydroxyacetophenones, condensation with N,N-dimethylformamide dimethyl acetal (DMF-DMA) under microwave irradiation.[1]

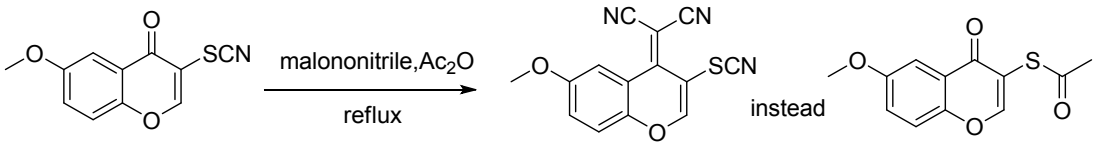


To a 10-20 mL microwave vessel was added 2′-hydroxyacetophenone (1.2 mL, 10mmol) and dimethylformamide dimethylacetal (1.34mL, 10 mmol). The vessel was capped and heated to 150°C for 10 minutes with 30 seconds prestirring. The reactions were allowed to cool to ambient temperature and subsequently crystallized. The crystals were vacuum filtered, washed with Hexanes, and dried under vacuum to afford the enaminone (3.4 g, 89%), which was used without further purification

General procedure for the synthesis of 3-Thiocyanato-4H-chromen-4-one

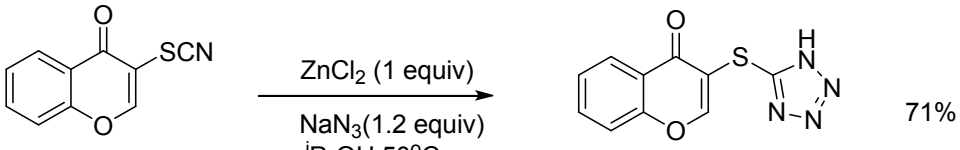
To a reaction tube were added compounds 1 (0.4 mmol，76.5mg), KSCN (3 equiv,116.6mg), $K_2S_2O_8$ (2 equiv, 216mg) and DCE (2 mL). Then the mixture was stirred at room temperature with open flask for 6 hours. Afterward, the reaction mixture was extracted with CH_2Cl_2 and the organic layer was washed with water. After drying with Na_2SO_4, the combined CH_2Cl_2 extracts were concentrated in vacuum. The residue was purified by column chromatography eluting with hexane and ethyl acetate (3:1) to afford the desired product to give **3a** as white solid ; yield : 69mg (85%).

Derivatization of Products 3b and 3a



3b **3bb** no detected **3ba**

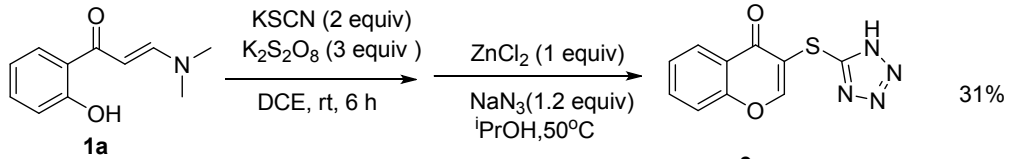
Initially, we want to obtain **3bb** according to the literature.[2] To a reaction tube were added compounds **3b** (2 mmol，1 equiv), malononiyrile (1.2 equiv), acetic anhydride (5 mL). The mixture was refluxed for 14 hours. Then water was added into the solution and refluxed for another 30 minutes. Afterward, the mixture was concentrated under reduced pressure and purified by column chromatography using (petroleum ether: DCM=1:5) as eluent. Interesting, we obtained the prodct **3ba** instead of **3bb** based on the HR-MS, ^{1}H and ^{13}C NMR Spectra. The reaction is still in further research.



3a **3aa**

A 10 mL oven-dried Schlenk-tube was charged with 3a (0.4 mmol, 1.0 equiv), $ZnCl_2$(0.4 mmol, 1.0 equiv) and NaN_3 (0.48 mmol, 1.2 equiv). 2 mL of ^{i}PrOH was then injected into the tube by syringe. The resulting mixture was heated to 50 ^{o}C and stirred vigorously for 1.5 h. After cooling to room temperature, the the solvent was evaporated under reduced pressure. Next, 5%NaOH (5 mL) was added and the mixture was stirred for 20 minutes, until the original precipitate had dissolved and a suspension of $Zn(OH)_2$ had formed. The suspension was filtered, and the solid washed with 5% NaOH (5 mL). The pH of the filtrate was adjusted to 1.0 with concd HCl, which caused the tetrazole product to precipitate. The tetrazole was filtered, washed with 9% HCl (2 × 4 mL) and dried.

One-pot synthesis of 3aa



1a **3aa**

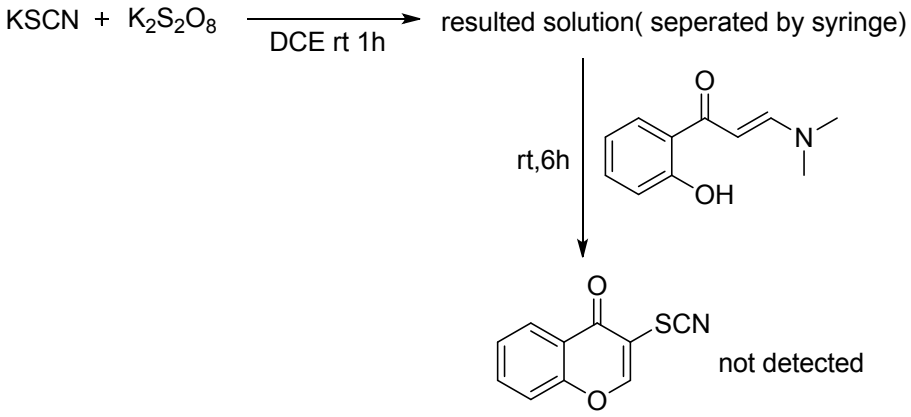
The enaminones **1** (0.4 mmol), KSCN (3 equiv), $K_2S_2O_8$ (2 equiv), and DCE (2 mL) were added into a 10 mL oven-dried tube. Then the resulting mixture was stirred at room temperature for 6 hours under open flask. After the reaction was completed, the solvent was evaporated under reduced pressure in a 25 mL round bottom flask. Then $ZnCl_2$(0.4 mmol, 1.0 equiv) and NaN_3 (0.48 mmol, 1.2 equiv). 2

mL of ^{i}PrOH was added into the resulteded mixture. The resulting mixture was heated to 50 ^{o}C and stirred vigorously for 1.5 h. After cooling to room temperature, the the solvent was evaporated under reduced pressure. Next, 5%NaOH (5 mL) was added and the mixture was stirred for 20 minutes, until the original precipitate had dissolved and a suspension of $Zn(OH)_2$ had formed. The suspension was filtered, and the solid washed with 5% NaOH (5 mL). The pH of the filtrate was adjusted to 1.0 with concd HCl, which caused the tetrazole product to precipitate. The tetrazole was filtered, washed with 9% HCl (2 × 4 mL) and dried. After all, the **3aa** was obtained in 31% yield.

References:
1: Gammill, R. B. *Synthesis-Stuttgart* .**1979**, 901-903.
2: Zhang, X.; Zhang, L.; Liu, Y.; Bao, B.; Zang, Y.; Li, J.; Lu, W. *Tetrahedron* **2015**, 71 (29), 4842-4845.

Supplementary experiments for mechanism

(a) Two-step synthesis of **3a**



The mixture of KSCN (3 equiv, 116.6 mg), $K_2S_2O_8$ (2 equiv, 216 mg) and DCE (2 mL) was stirred at room temperature for 6 h. After removing the remained solids, compound **1a** was added into the resulted solution and stirred for another 6 h. TLC and GC-mass analysis both showed that no product formation was observed. This result indicates that $(SCN)_2$ may not be involved in this transformation.

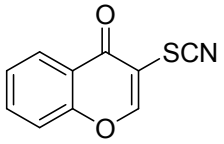
(b) Detection $(SCN)_2$ formation with UV spectrum

KSCN and $K_2S_2O_8$ were stirred in DCE under room temperature for 1 h. and the resulted solution was analyzed with UV spectrum. No obvious peak at 296 nm was found [1].

References:
1. Alguindigue Nimmo, Susan L.; Kelemu Lemma and Michael T. Ashby. *Heteroatom Chemistry* **2007**, 467-471.

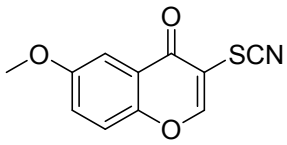
Characterization Data

3-thiocyanato-4H-chromen-4-one (3a)



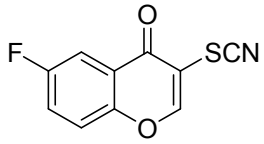
White solid 69 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 15.2, 7.9 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 156.3, 155.4, 135.0, 126.6, 126.1, 122.6, 118.4, 112.5, 108.9. HRMS (ESI) m/z: [M+Na] $^{+}$ Calcd for $C_{10}H_5NNaO_2S^{+}$ 225.9939, Found 225.9936.

6-methoxy-3-thiocyanato-4H-chromen-4-one (3b)



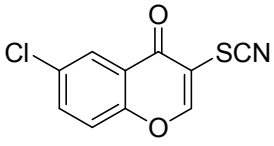
White solid 70.9 mg (76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.58 (s, 1H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.35 (d, *J* = 9.2 Hz, 1H), 3.92 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 157.9, 155.29, 151.2, 125.0, 123.4, 119.8, 111.5, 109.0, 104.9, 56.1. HRMS (ESI) m/z: [M+Na] $^{+}$ Calcd for $C_{11}H_7NNaO_3S^{+}$ 256.0044, Found 256.0023.

6-fluoro-3-thiocyanato-4H-chromen-4-one (3c)



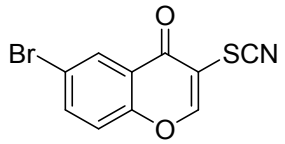
White solid 73.45 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.89 (d, *J* = 7.4 Hz, 1H), 7.64 – 7.55 (m, 1H), 7.52 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4 , 161.4 , 158.9 , 155.6 , 152.6 , 123.6 (dd, *J* = 46.8, 16.6 Hz), 120.7 (d, *J* = 8.2 Hz), 112.1 , 111.1 (d, *J* = 24.1 Hz), 108.7 . HRMS (ESI) m/z: [M+H] $^{+}$ Calcd for $C_{10}H_5FNO_2S^{+}$ 222.0025, Found 222.0026.

6-chloro-3-thiocyanato-4H-chromen-4-one (3d)



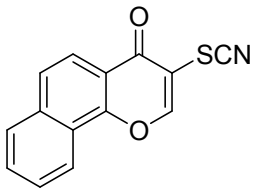
White solid 81.76 mg (86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.21 (s, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.53 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (100 MHz $CDCl_3$) δ 171.9, 155.3, 154.6, 135.3, 132.74, 125.4, 123.5, 120.1, 112.9, 108.6. HRMS (ESI) m/z: [M+H] $^+$ Calcd for $C_{10}H_5ClNO_2S^+$ 237.9730, Found 237.9714.

6-bromo-3-thiocyanato-4H-chromen-4-one (3e)



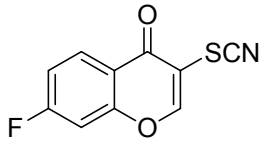
White solid 88.02 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 10.2 Hz, 2H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (100 MHz $CDCl_3$) δ 171.8, 155.3, 155.1, 138.0, 128.61, 123.8, 120.3, 120.2, 112.9, 108.5. HRMS (ESI) m/z: [M+Na] $^+$ Calcd for $C_{10}H_4BrNNaO_2S^+$ 303.9044, Found 303.9031.

3-thiocyanato-4H-benzo[h]chromen-4-one (3f)



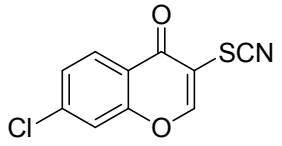
White solid 75.99 mg (75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 2H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.82 – 7.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 154.2, 153.2, 136.2, 130.2, 128.3, 127.9, 126.9, 123.5, 122.2, 120.2, 118.8, 114.8, 108.7. HRMS (ESI) m/z: [M+H] $^+$ Calcd for $C_{14}H_8NO_2S^+$ 254.0276, Found 254.0278.

7-fluoro-3-thiocyanato-4H-chromen-4-one (3g)



White solid 72.57 mg (82%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.28 (s, 1H), 7.23 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1 , 167.5 , 164.9, 157.3 (d, *J* = 8.3 Hz), 155.1, 128.8 (d, *J* = 10.8 Hz), 119.5, 115.6(d, *J* = 22.9 Hz) , 113.2 , 108.62 , 105.2 (d, *J* = 25.7 Hz),. HRMS (ESI) m/z: [M+Na] $^+$ Calcd for $C_{10}H_4FNNaO_2S^+$ 243.9844, Found 243.9842.

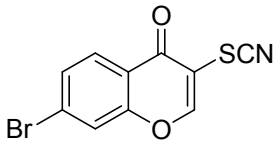
7-chloro-3-thiocyanato-4H-chromen-4-one (3h)



White solid 83.66 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.58 (s,

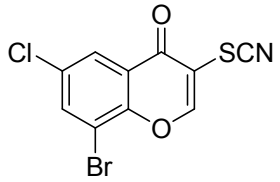
1H), 7.49 (d, J = 8.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 156.3, 155.0, 141.3, 127.6, 127.4, 121.1, 118.5, 113.3, 108.6. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_4ClNNaO_2S^+$ 259.9549, Found 259.9545.

7-bromo-3-thiocyanato-4H-chromen-4-one (3i)



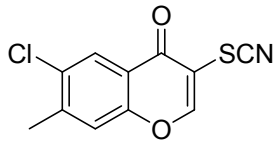
White solid 90.28 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.75 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 156.2, 155.0, 130.3, 129.5, 127.4, 121.5, 121.4, 113.3, 108.6. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_4BrNNaO_2S^+$ 303.9044, Found 303.9030.

8-bromo-6-chloro-3-thiocyanato-4H-chromen-4-one (3j)



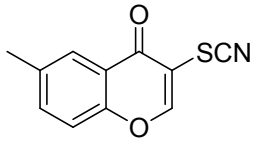
Pink solid 105.1 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.17 (s, 1H), 7.98 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 155.0, 151.7, 138.3, 132.9, 124.8, 124.1, 113.5, 113.1, 108.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_3BrClNNaO_2S^+$ 337.8654, Found 337.8655.

6-chloro-7-methyl-3-thiocyanato-4H-chromen-4-one (3k)



White solid 83.56 mg (83%). ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.44 (s, 1H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 155.2, 154.5, 144.7, 133.4, 125.6, 121.5, 120.1, 112.6, 108.7, 21.0. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_6ClNNaO_2S^+$ 273.9705, Found 273.9706.

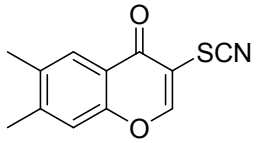
6-methyl-3-thiocyanato-4H-chromen-4-one (3l)



White solid 71.26 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.01 (s, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.6 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 155.4, 154.6, 136.9, 136.2, 125.3, 122.3, 118.1, 112.1, 109.1, 21.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{10}NO_2S^+$

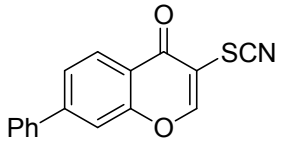
218.0276, Found 218.0267.

6,7-dimethyl-3-thiocyanato-4H-chromen-4-one (**3m**)



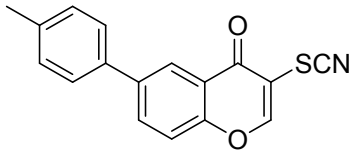
Yellow solid 85.9 mg (93%).^{1}H NMR (400 MHz,$CDCl_3$) δ 8.27 (s, 1H), 7.97 (s, 1H), 7.31 (s, 1H), 2.42 (s, 3H), 2.38 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 172.9, 154.9, 154.9, 145.9, 136.2, 125.5, 120.4, 118.4, 112.1, 109.2, 20.6, 19.4. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9NNaO_2S^+$ 254.0252,Found 254.0237.

7-phenyl-3-thiocyanato-4H-chromen-4-one (**3n**)



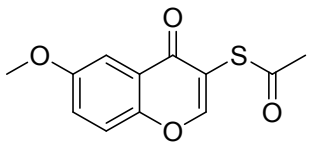
White solid 100.8mg (90%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.30 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.50 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 156.7, 155.3, 148.2, 138.5, 129.2, 129.2, 127.4, 126.5, 125.7, 121.3, 116.2, 112.8, 108.9. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_9NNaO_2S^+$ 302.0252,Found 302.0242.

3-thiocyanato-6-(p-tolyl)-4H-chromen-4-one (3o)



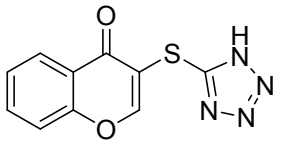
White solid 108.3mg (92%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.34 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 155.5, 155.1, 139.9, 138.3, 135.7, 133.7, 129.8, 127.0, 123.4, 122.8, 118.8, 112.6, 108.9, 21.1.HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{11}NNaO_2S^+$ 316.0408,Found 316.0401

S-(6-methoxy-4-oxo-4H-chromen-3-yl) ethanethioate (3ba)



Gray solid 95mg (19%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.60 (s, 1H), 7.43 (d, *J* = 9.1 Hz, 1H), 7.29 (d, *J* = 8.7 Hz, 1H), 3.90 (s, 3H), 2.48 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 174.2, 159.5, 157.4, 151.1, 124.5, 124.2, 119.6, 113.5, 105.5, 56.0, 30.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{10}NaO_4S^+$ 273.0197,Found 273.0190

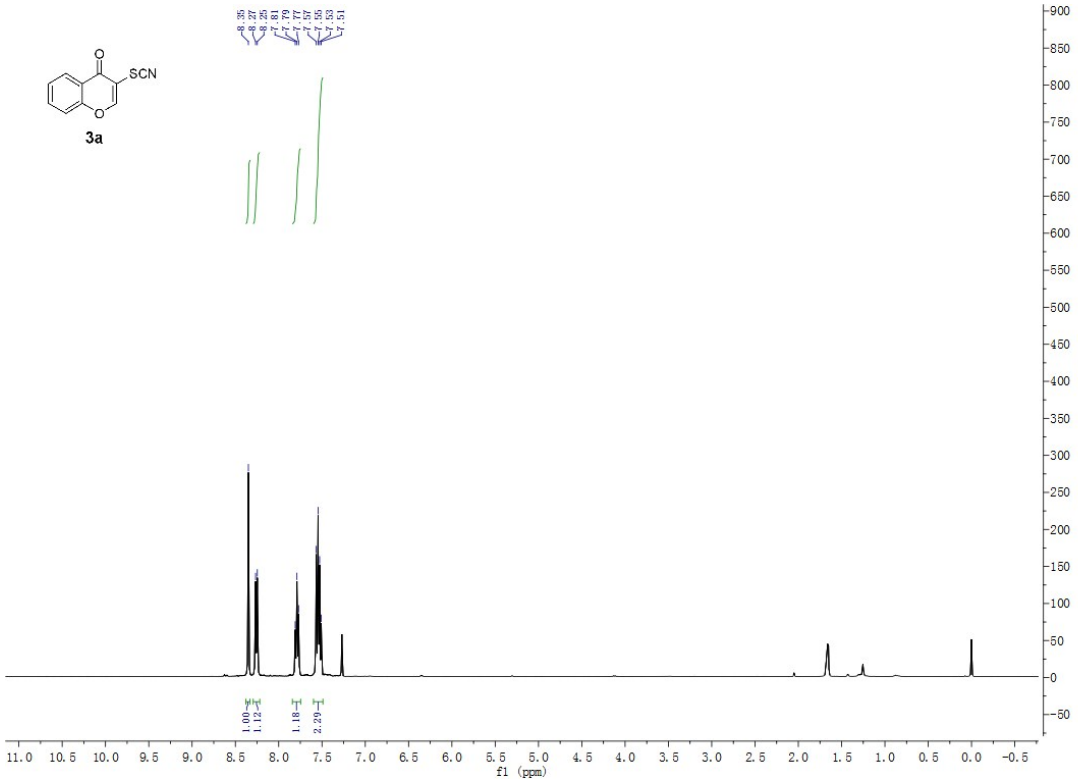
3-((1H-tetrazol-5-yl)thio)-4H-chromen-4-one (3aa)



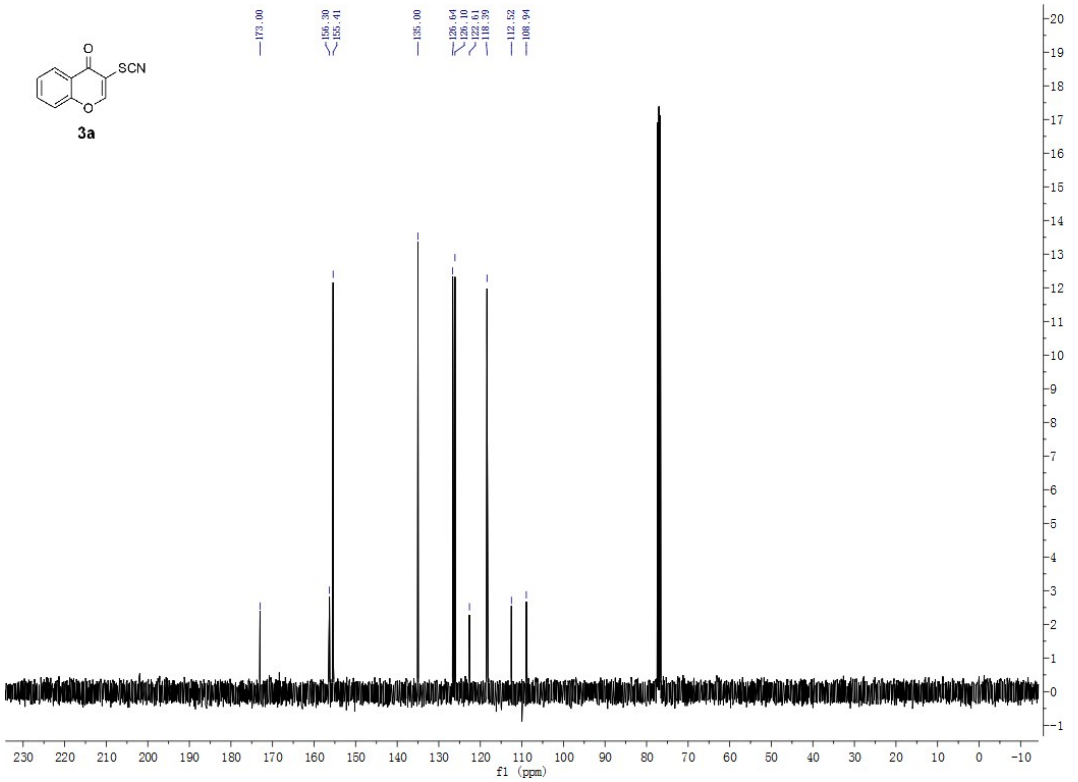
Gray solid 69.9mg (71%).^{1}H NMR (400 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.09 (d, J = 7.9 Hz, 1H), 7.91 (t, J = 7.7 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.9, 162.4, 156.3, 153.6, 135.4, 126.9, 125.9, 123.7, 119.1, 112.4.HRMS (ESI) m/z: $[M-H]^-$ Calcd for $C_{10}H_5N_4O_2S^-$ 245.0133,Found 245.0135.

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

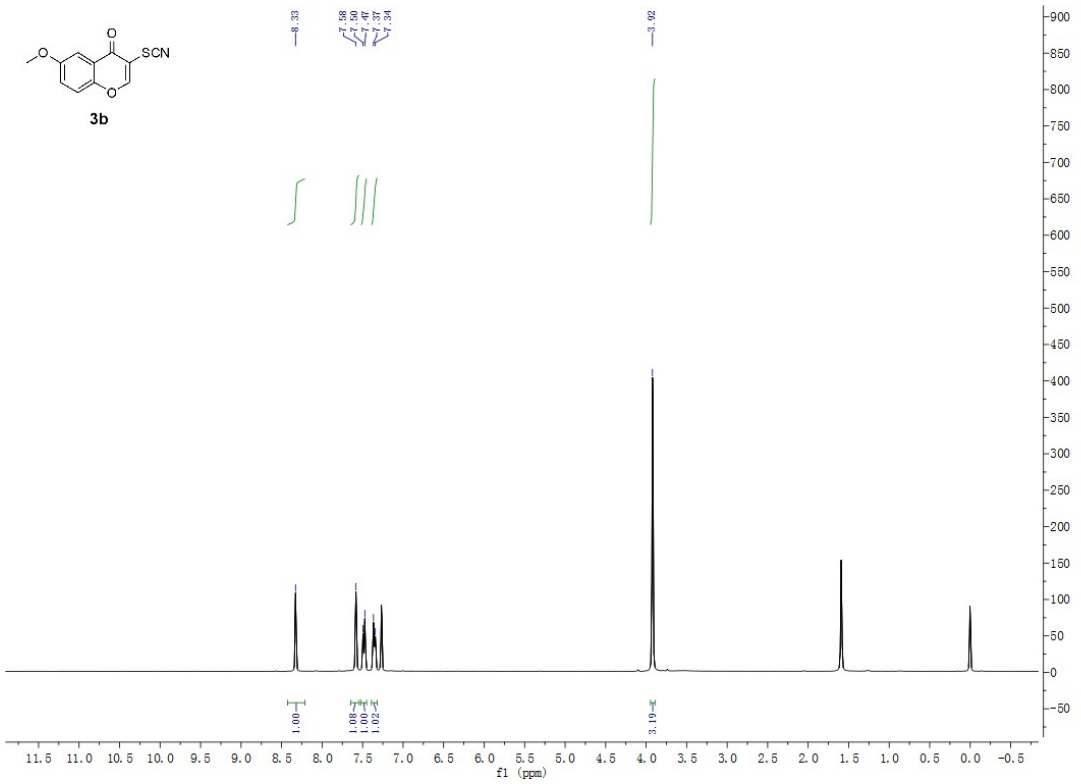
1H NMR of compound 3a



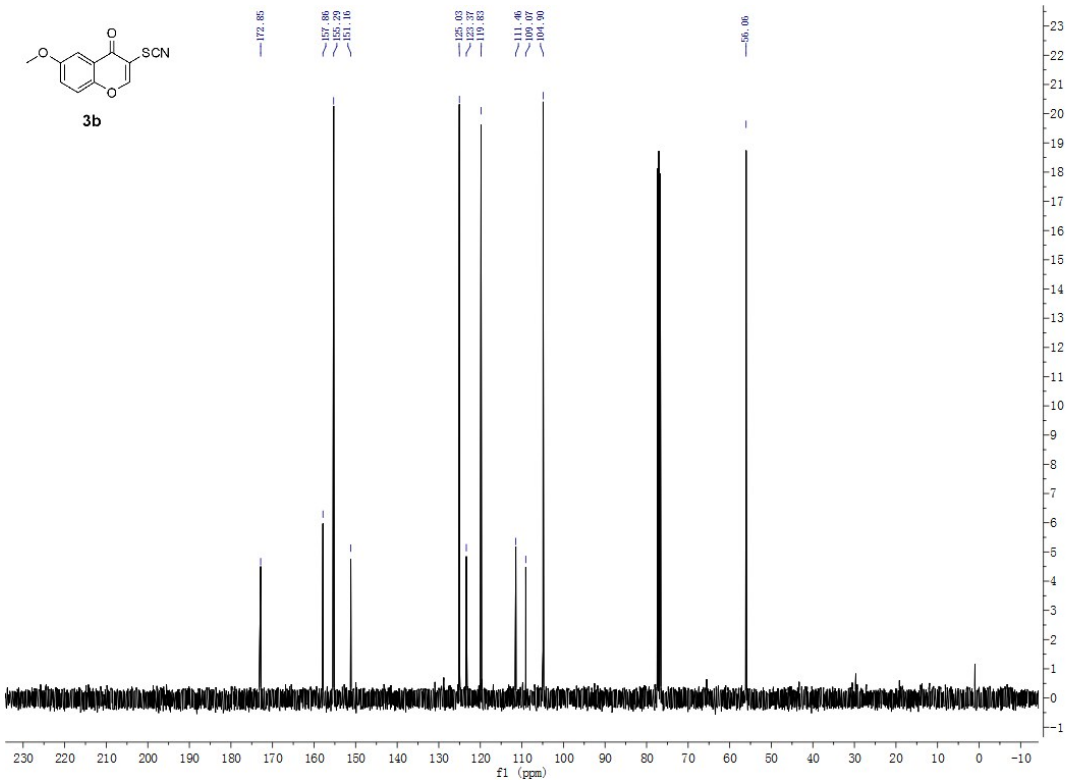
^{13}C NMR of compound **3a**



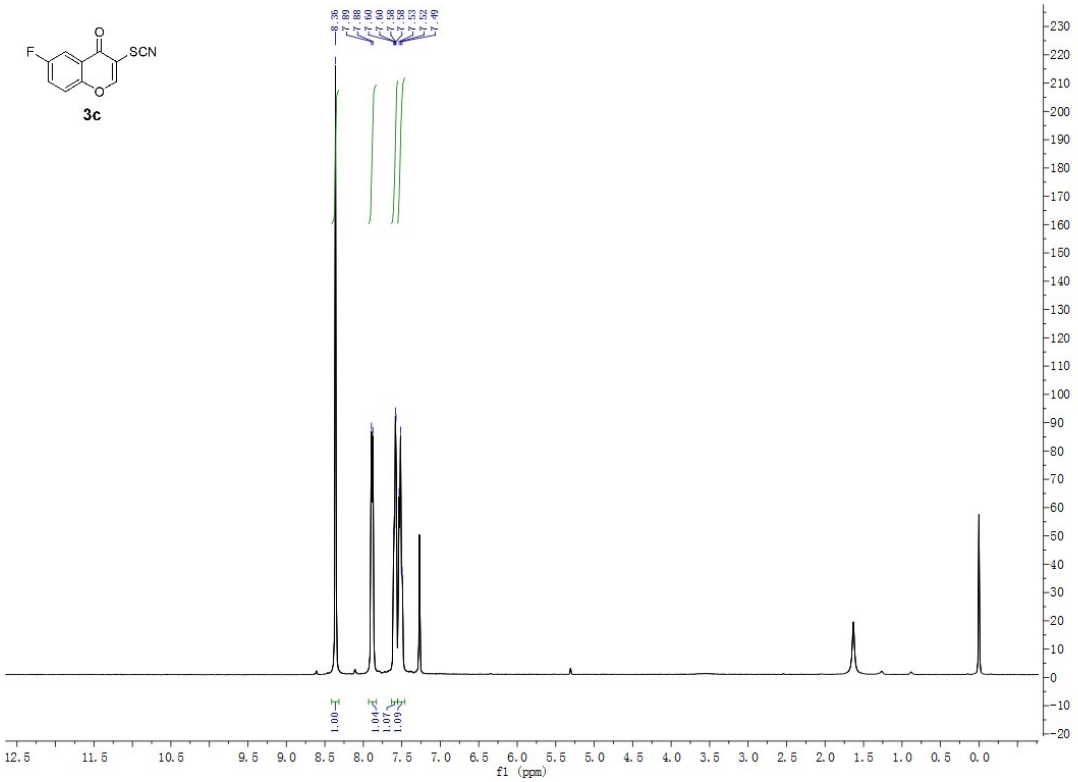
^{1}H NMR of compound **3b**



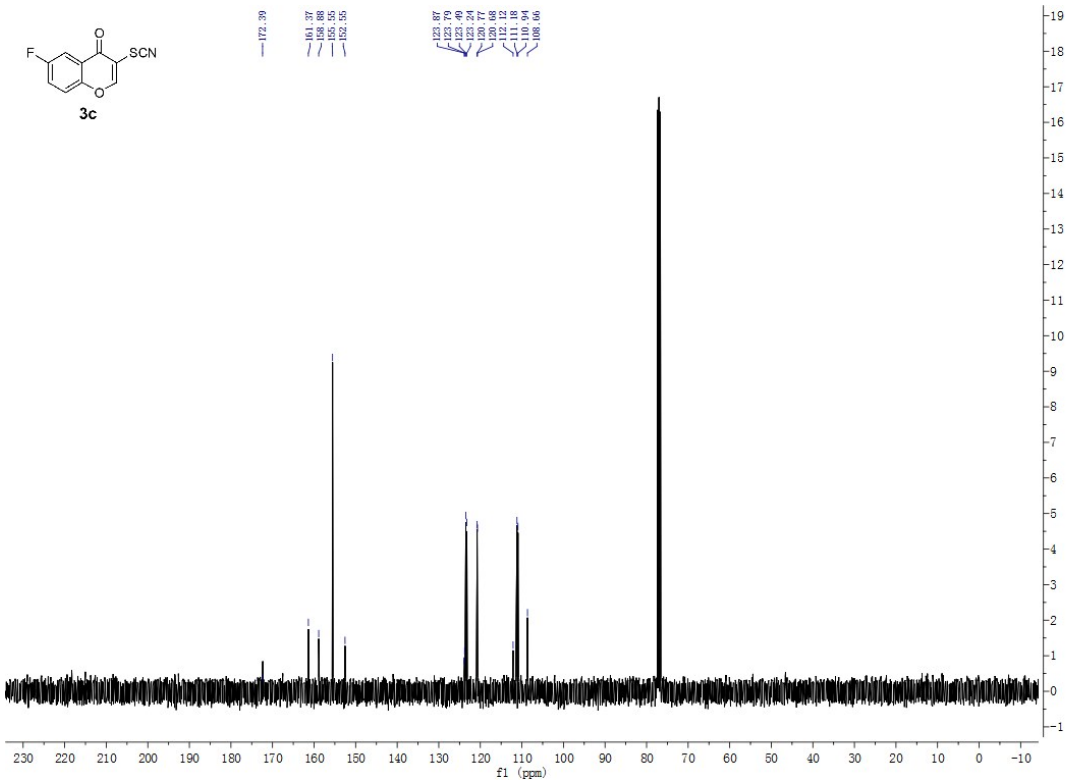
^{13}C NMR of compound **3b**



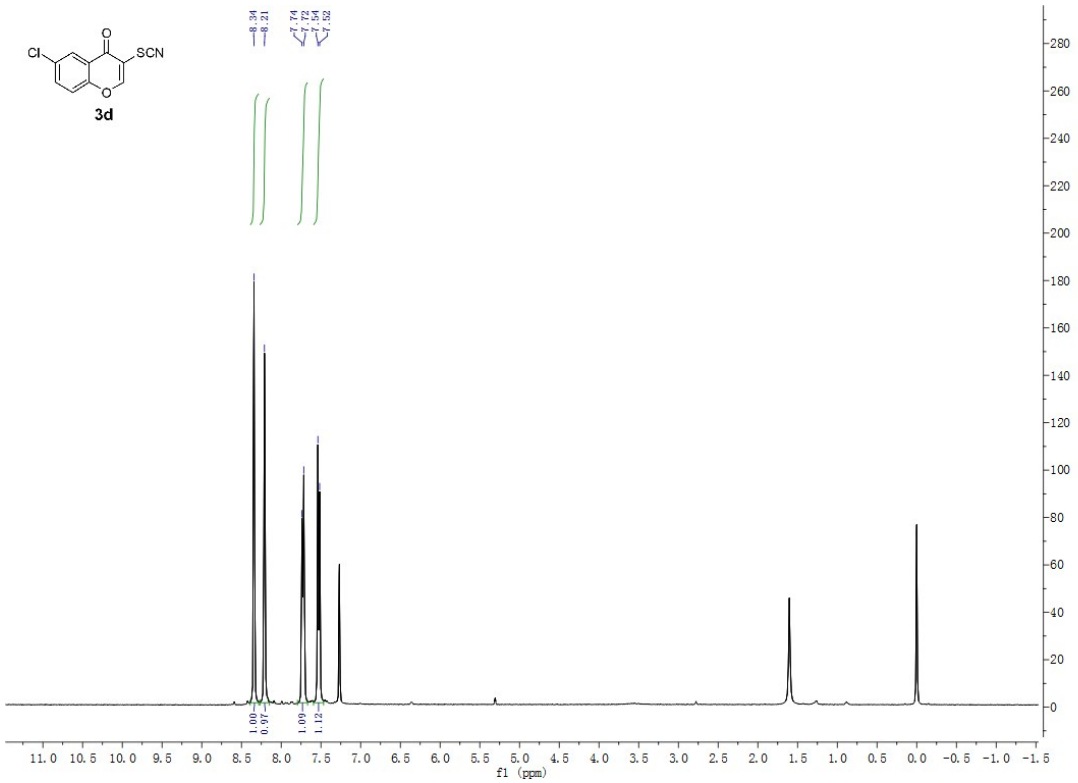
^{1}H NMR of compound **3c**



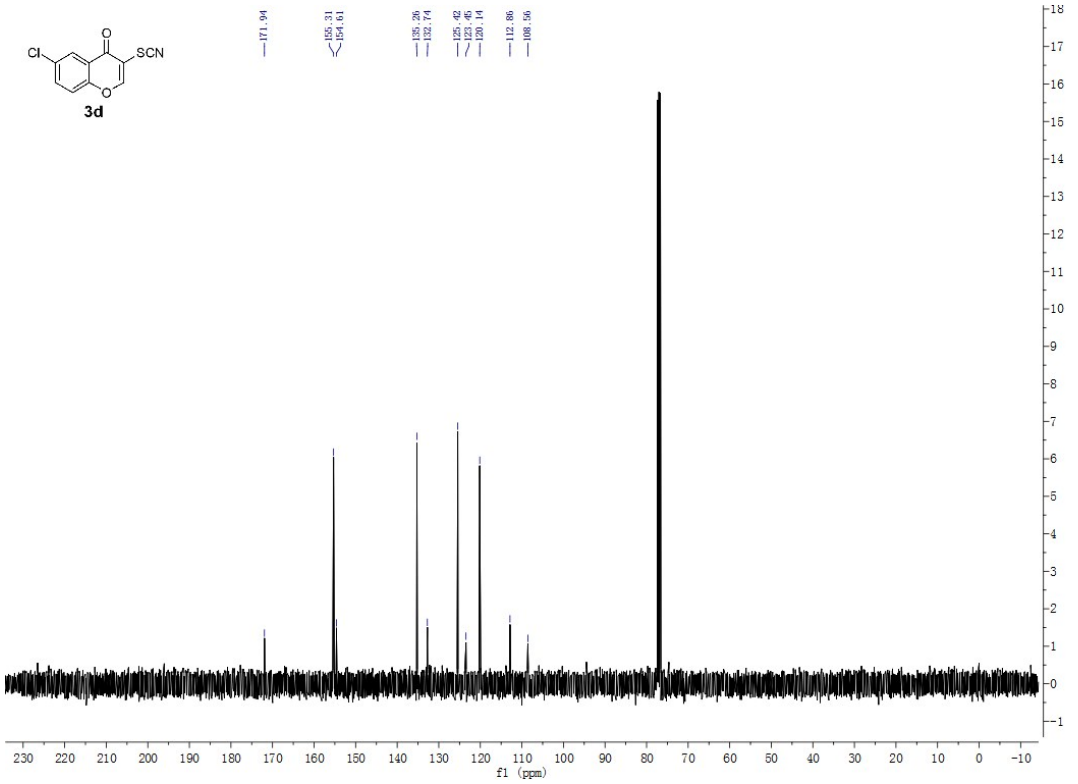
^{13}C NMR of compound **3c**



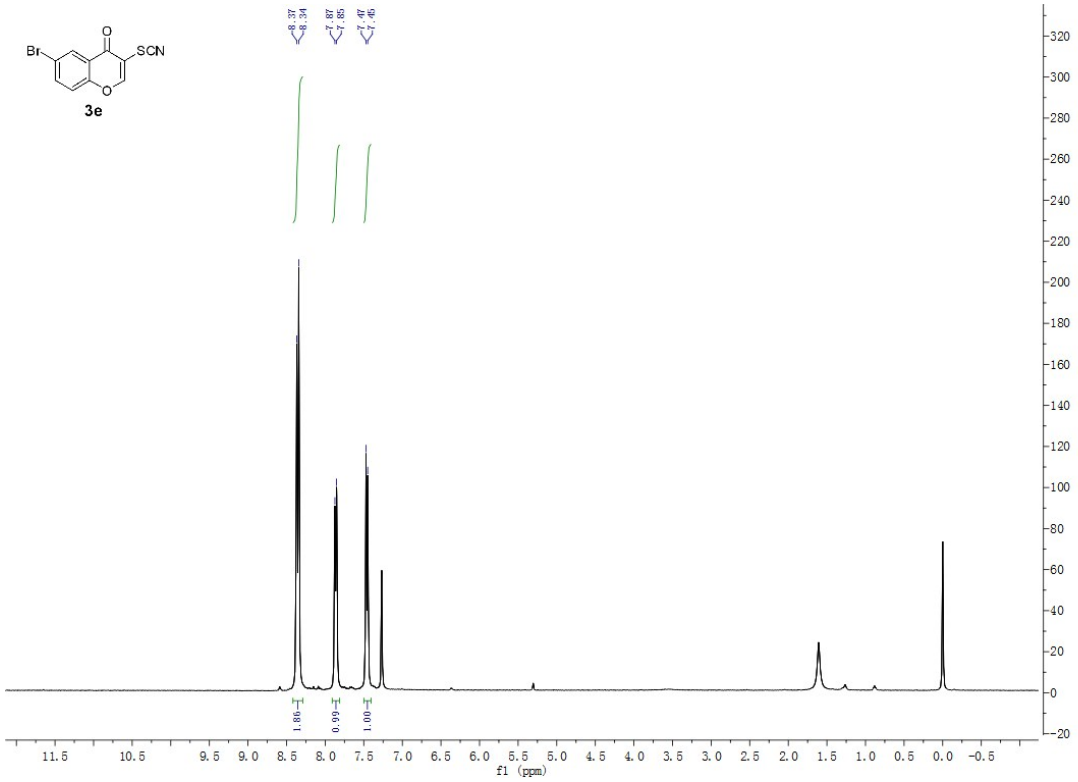
^{1}H NMR of compound **3d**



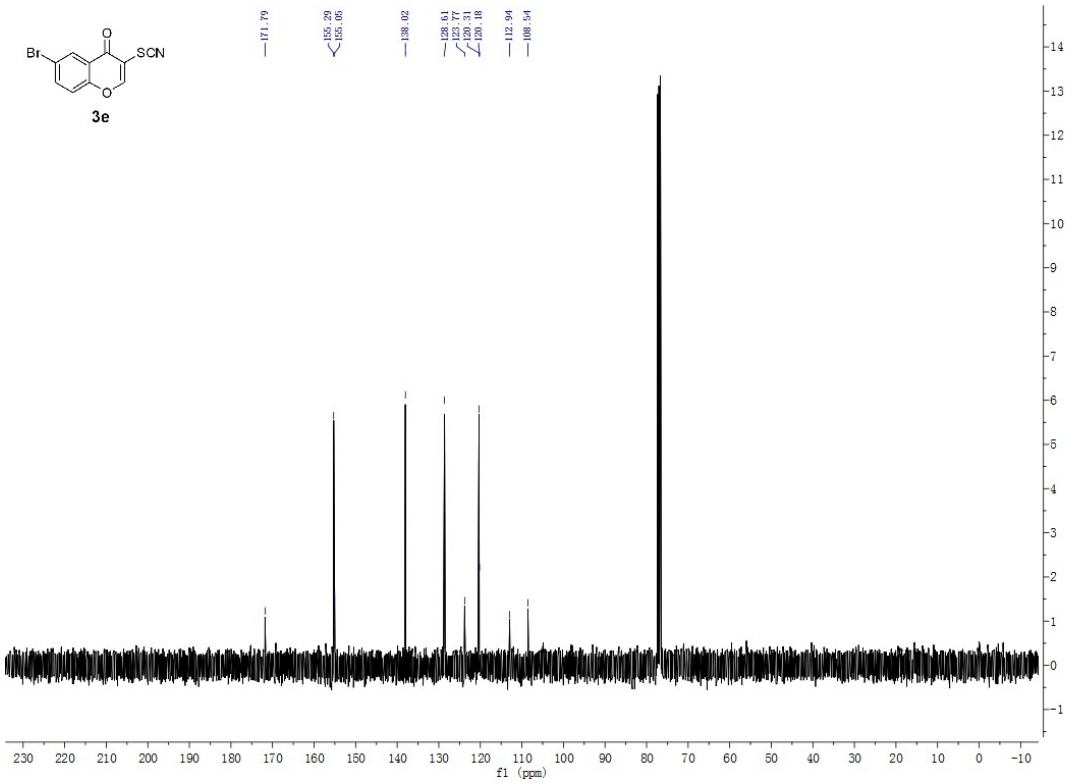
^{13}C NMR of compound **3d**



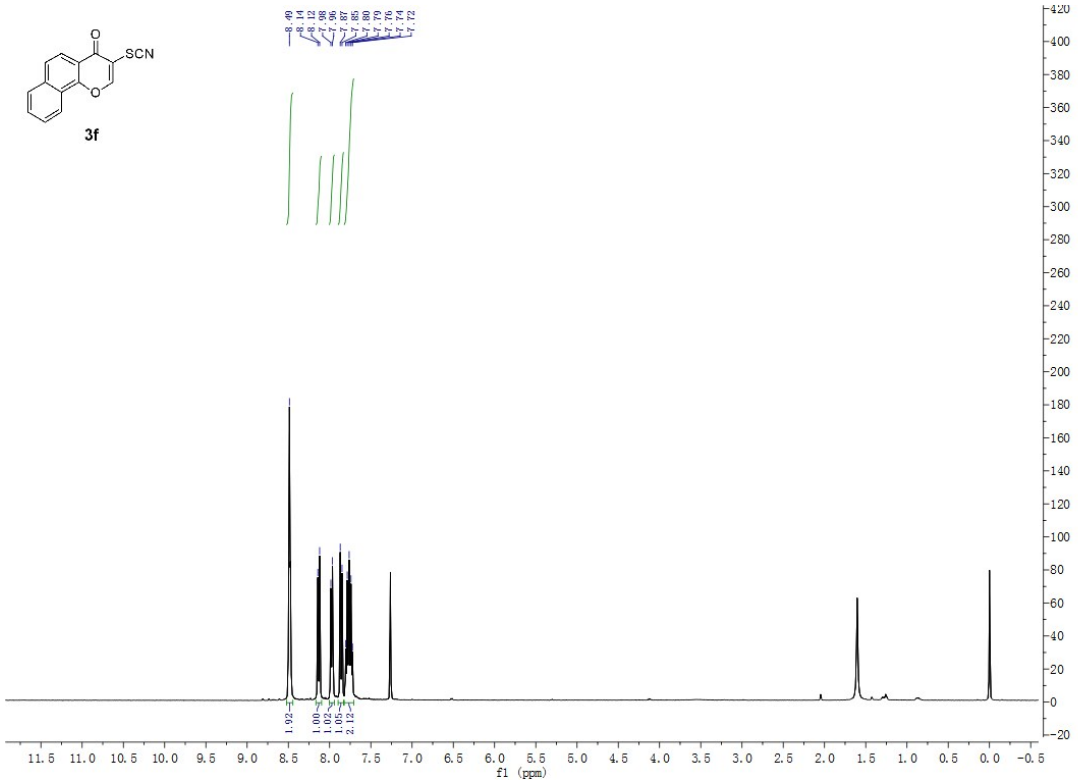
^{1}H NMR of compound **3e**



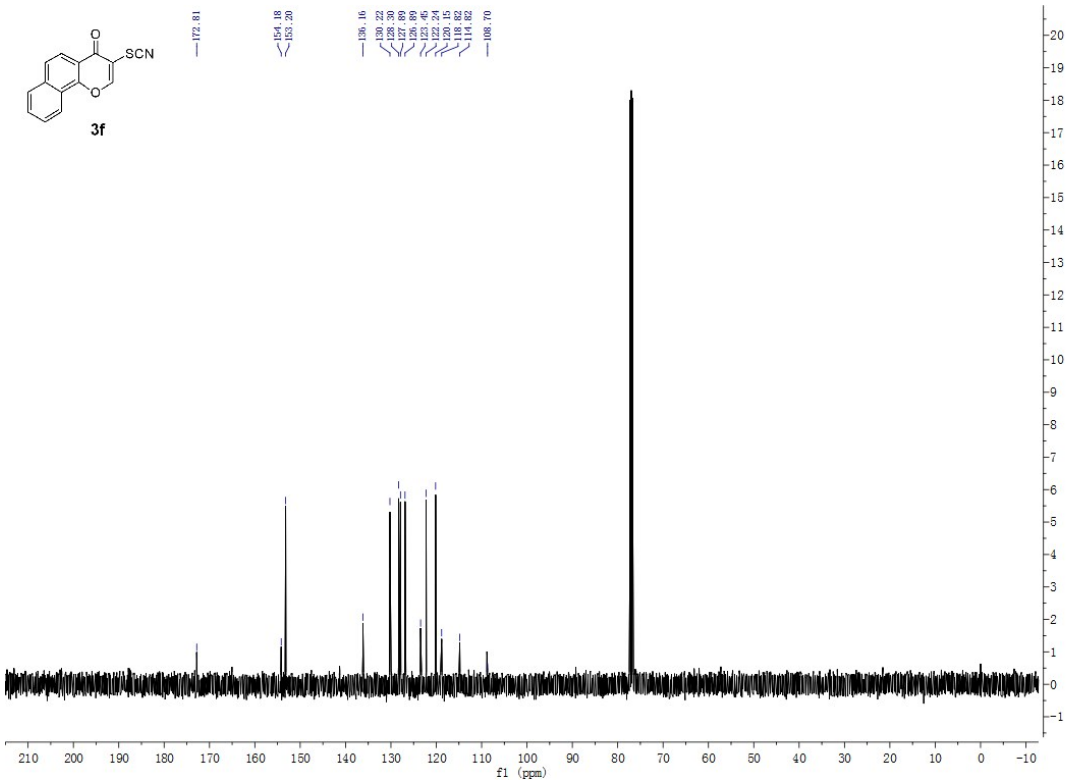
^{13}C NMR of compound **3e**



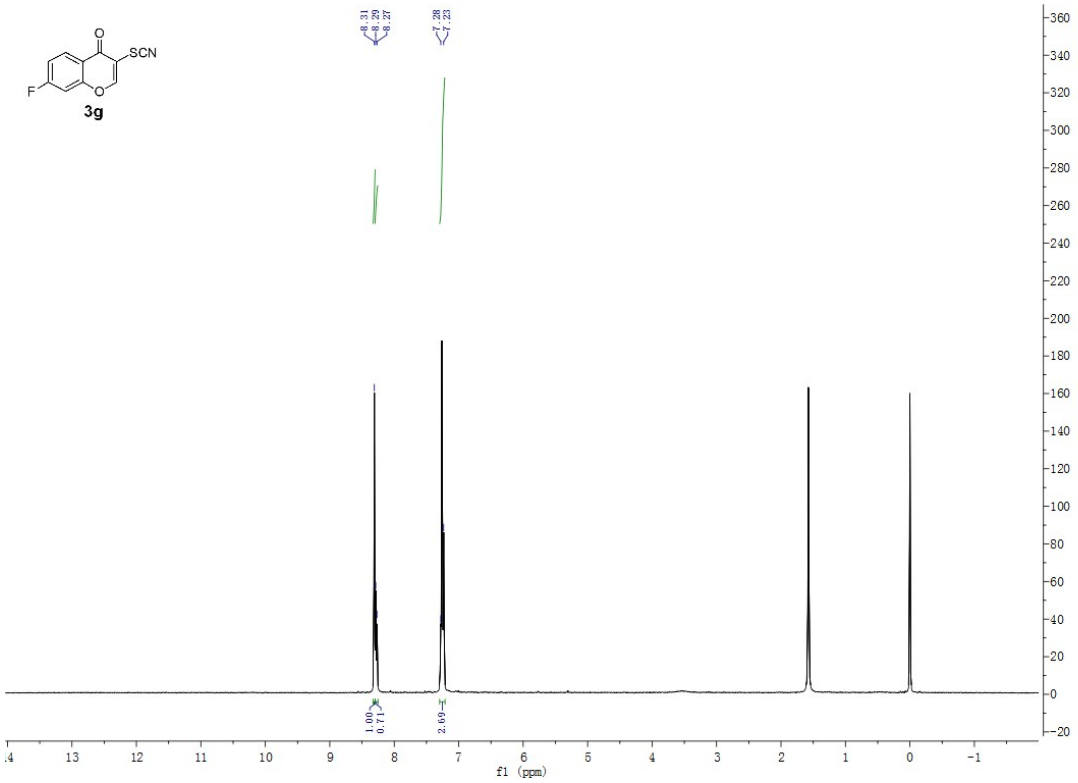
^{1}H NMR of compound **3f**



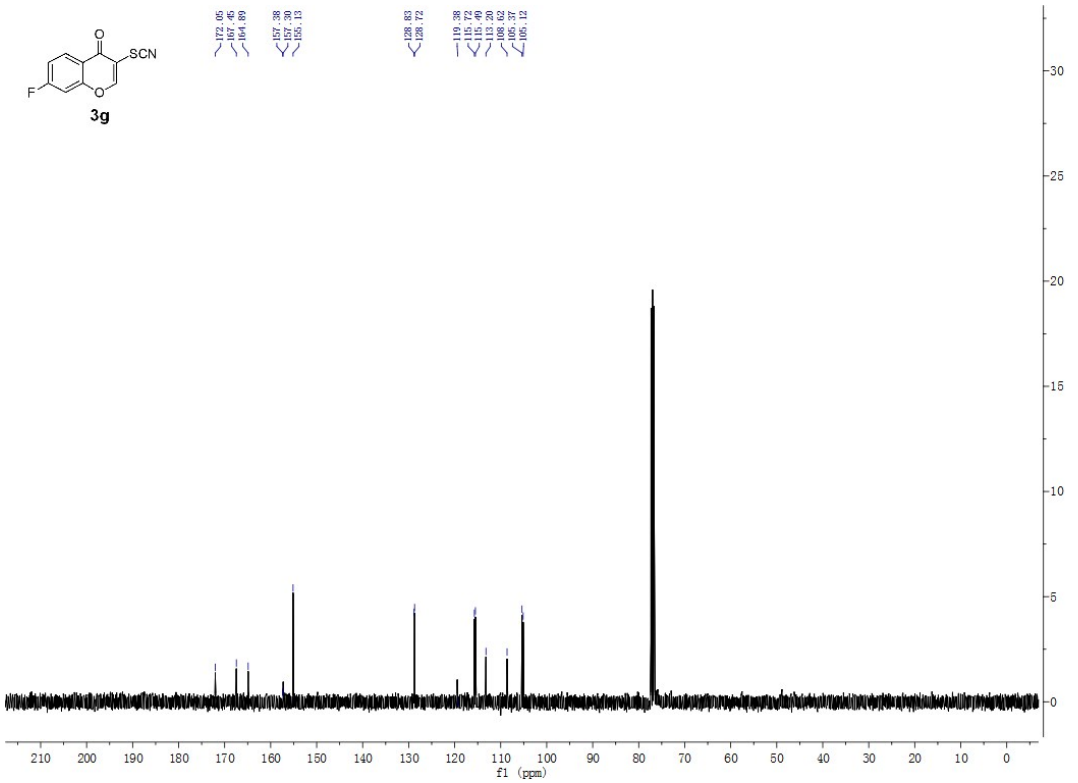
^{13}C NMR of compound **3f**



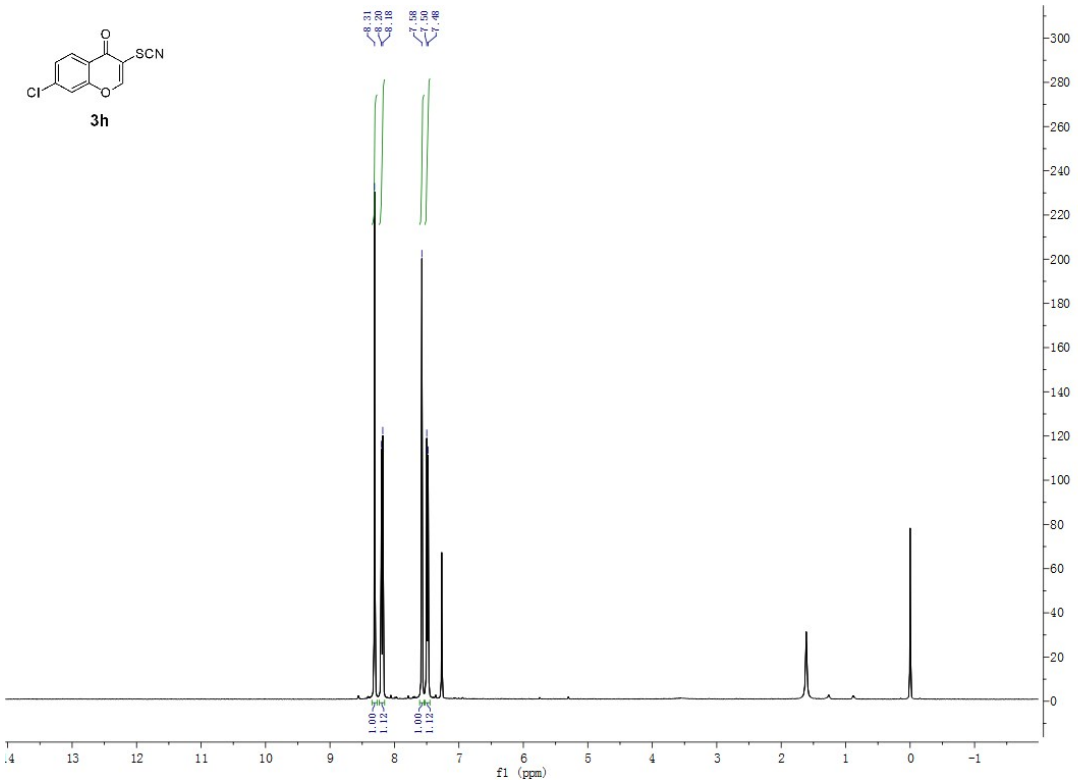
^{1}H NMR of compound **3g**



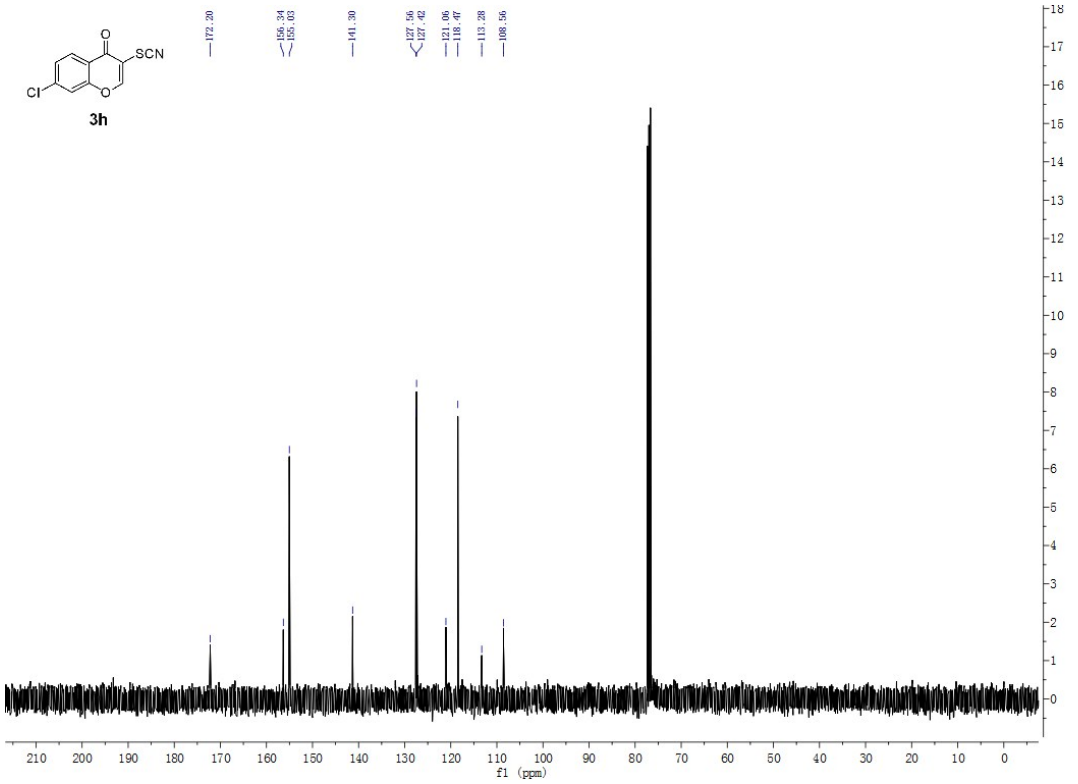
^{13}C NMR of compound **3g**



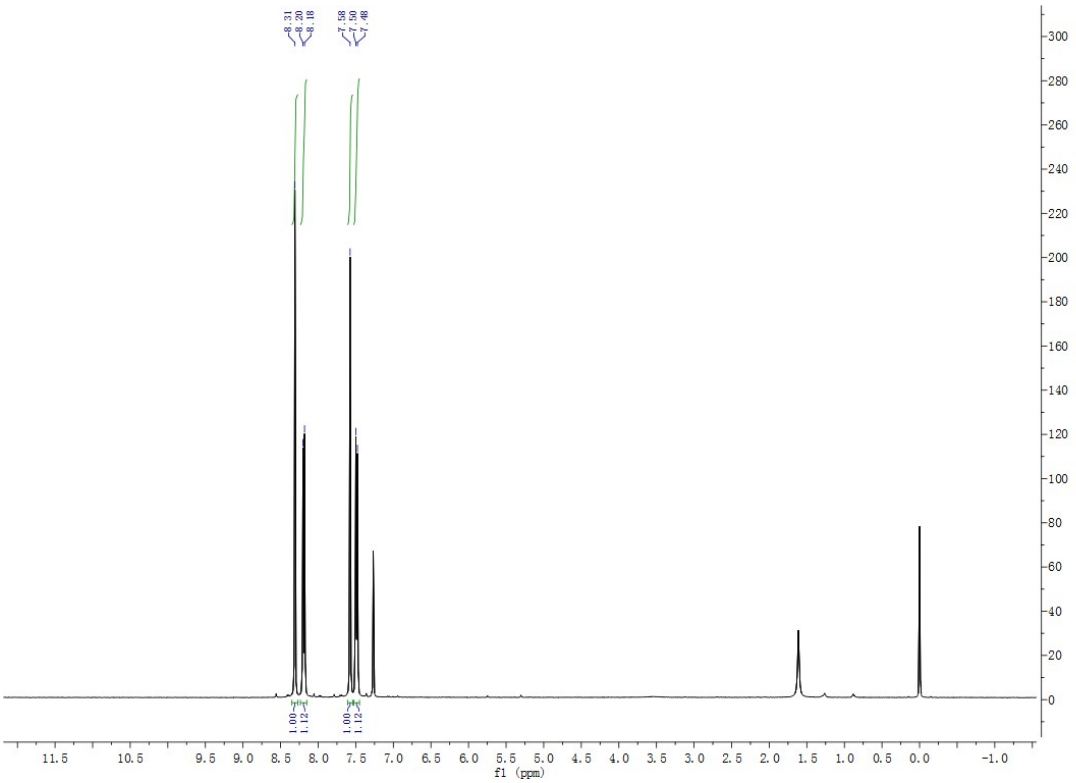
^{1}H NMR of compound **3h**



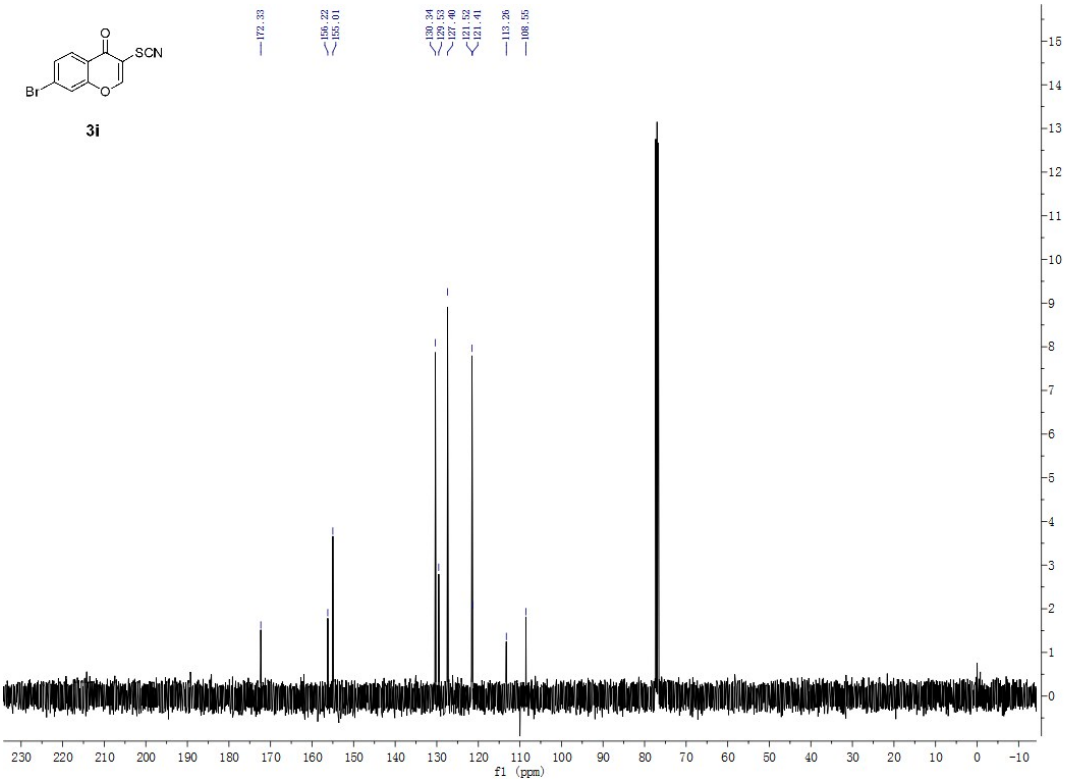
^{13}C NMR of compound **3h**



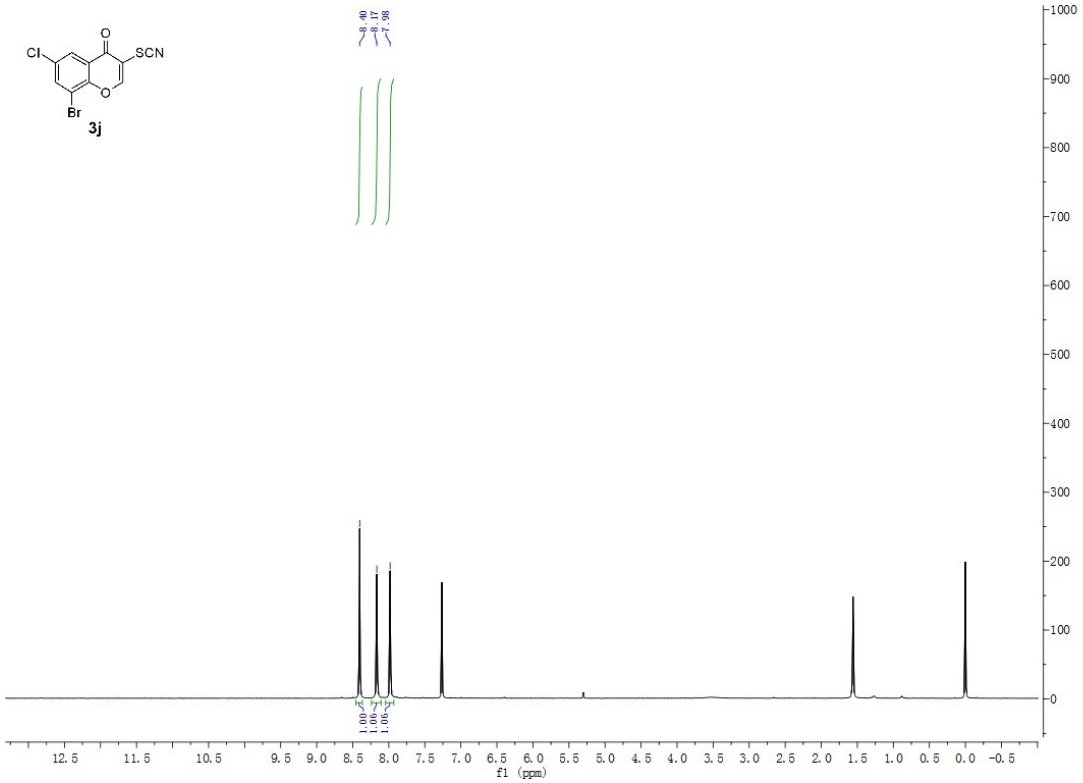
^{1}H NMR of compound **3i**



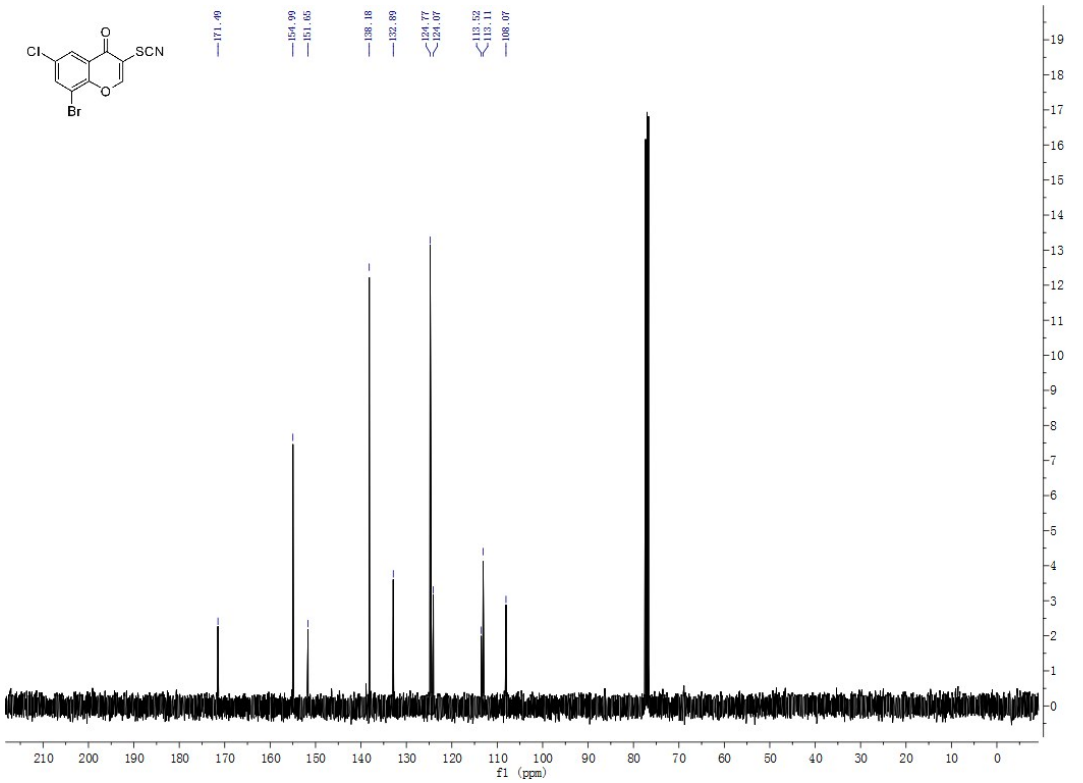
^{13}C NMR of compound **3i**



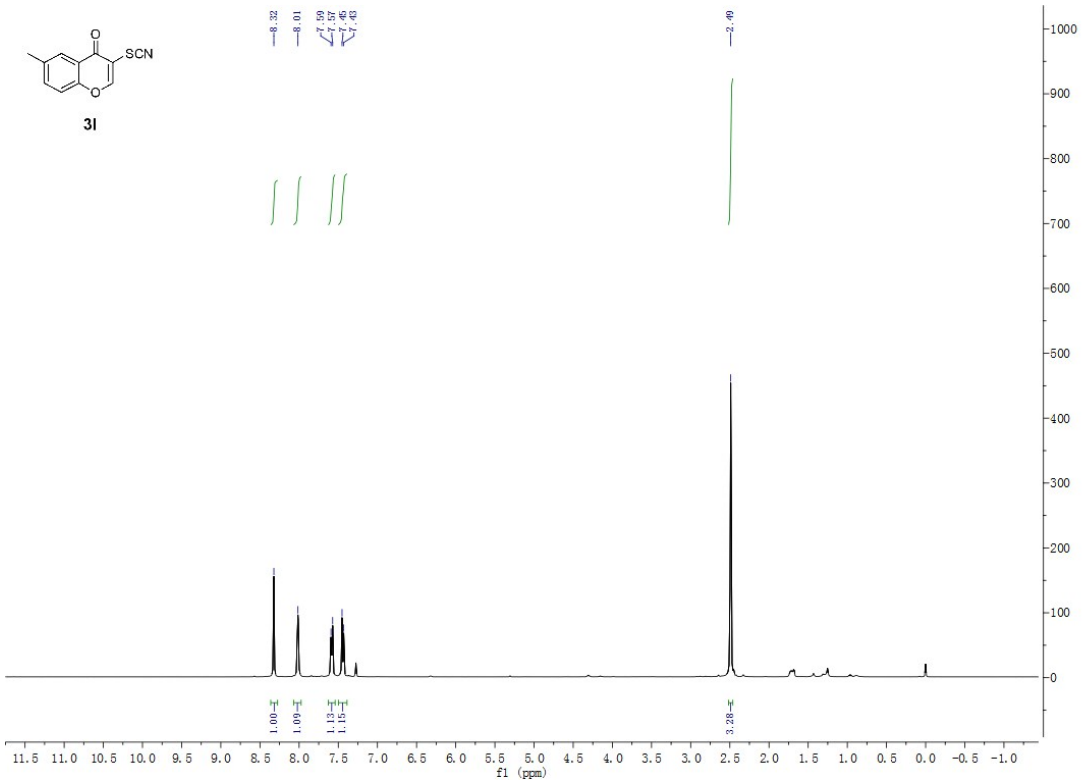
^{1}H NMR of compound **3j**



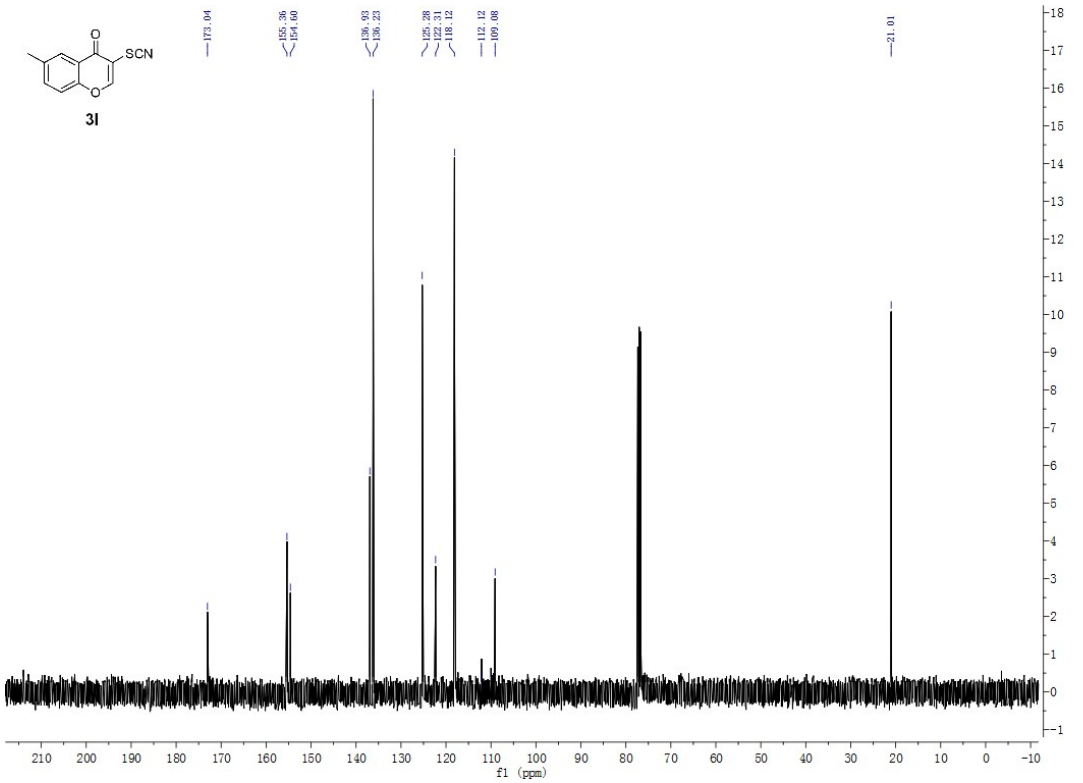
^{13}C NMR of compound **3j**



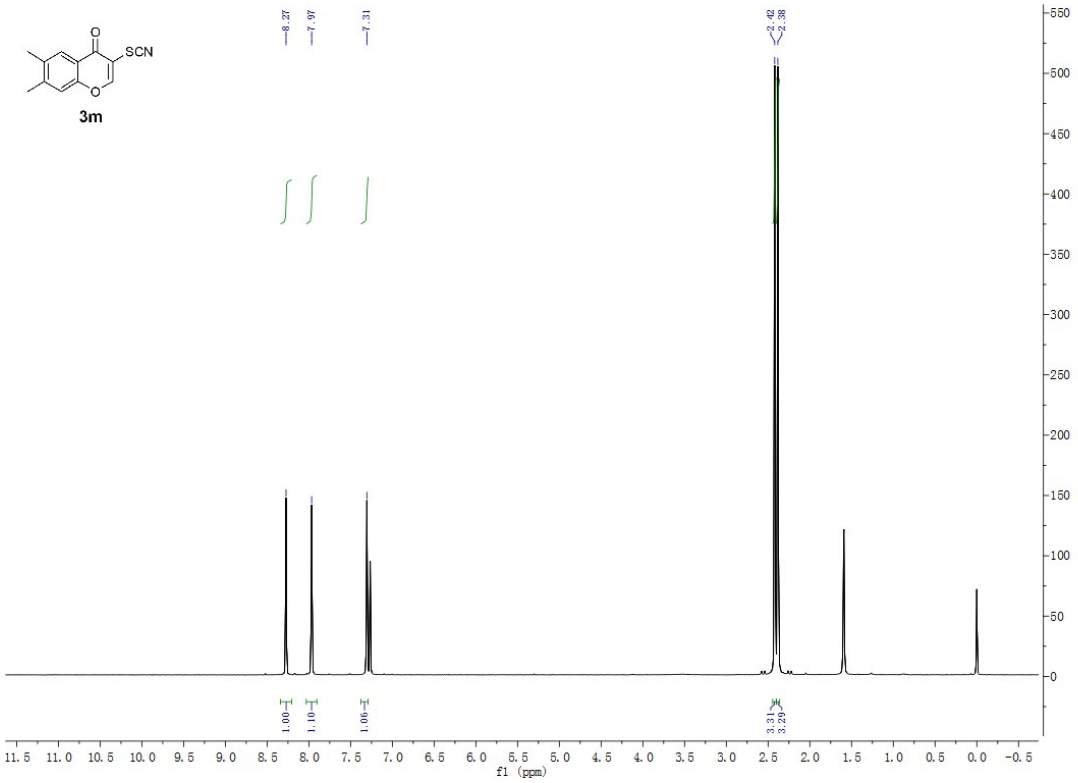
^{1}H NMR of compound **3l**



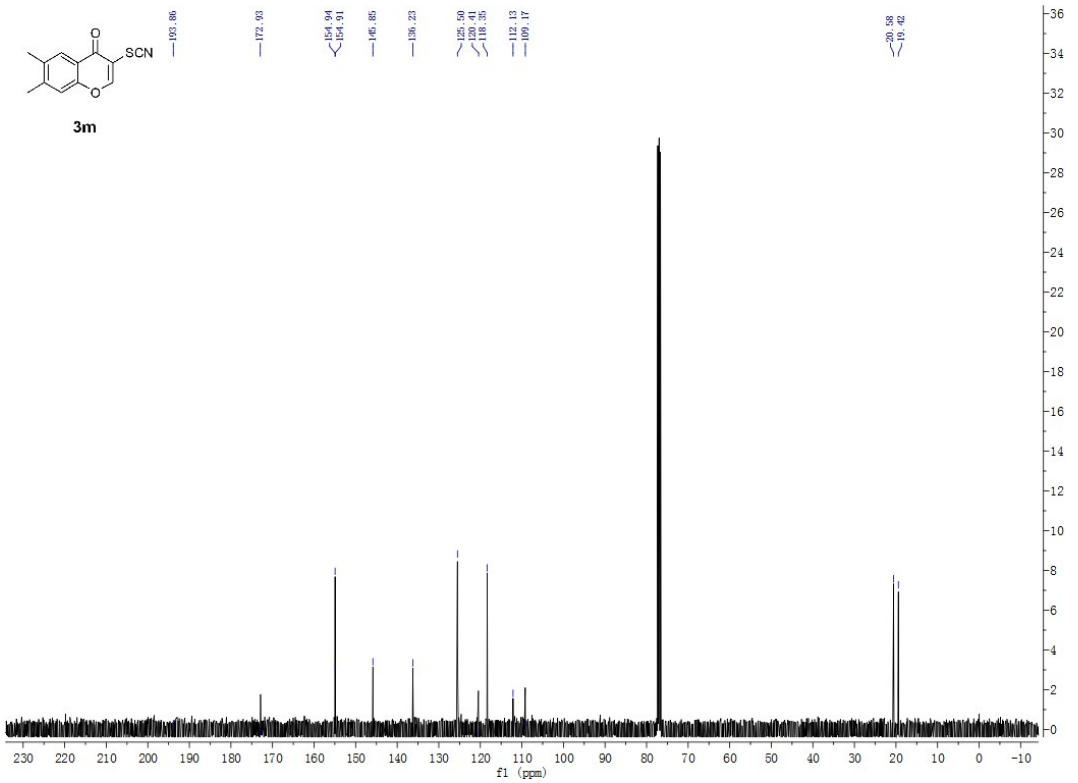
^{13}C NMR of compound **3l**



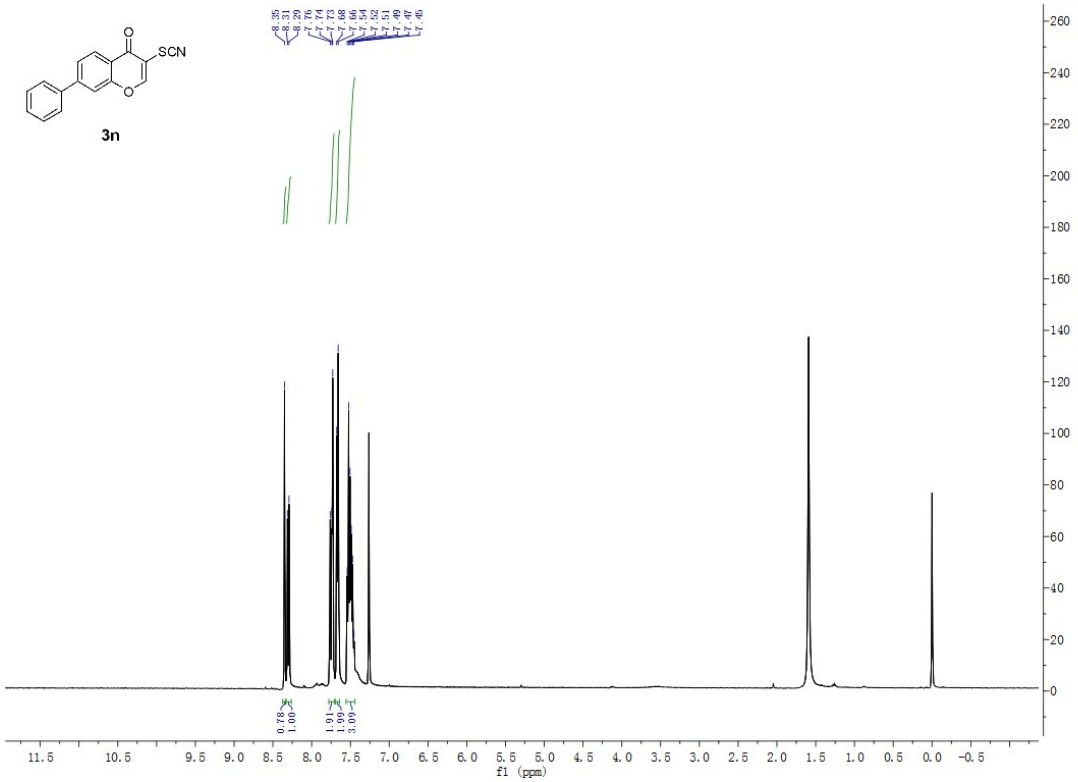
^{1}H NMR of compound **3m**



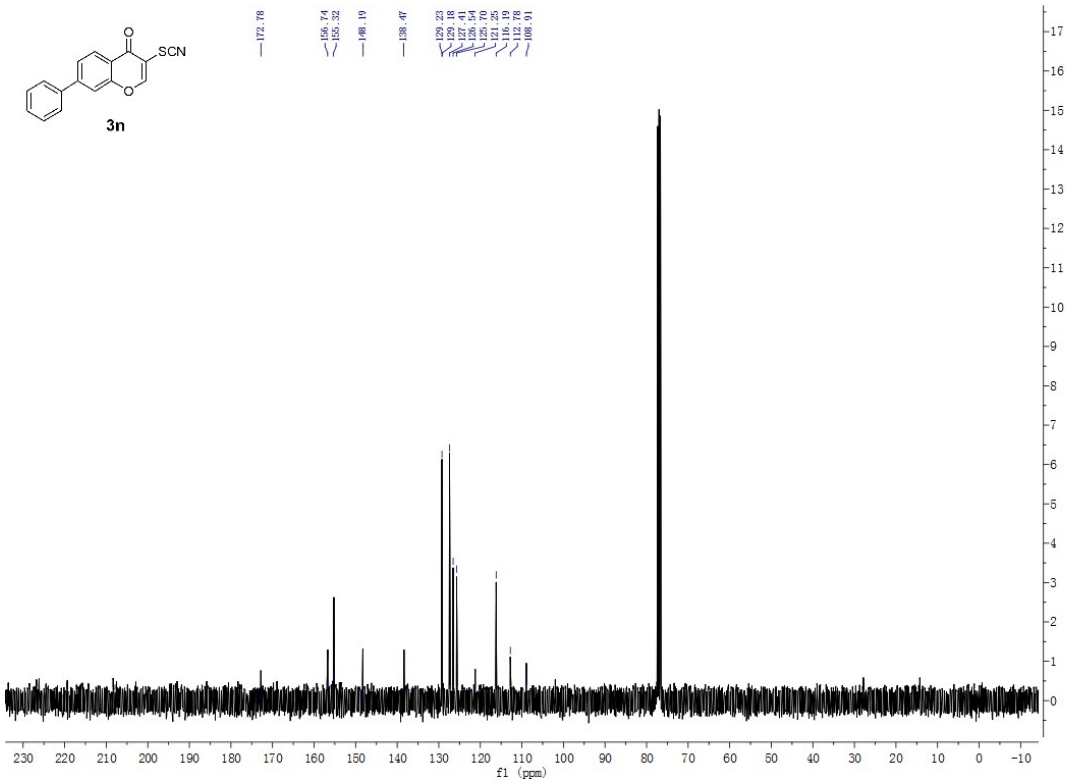
^{13}C NMR of compound **3m**



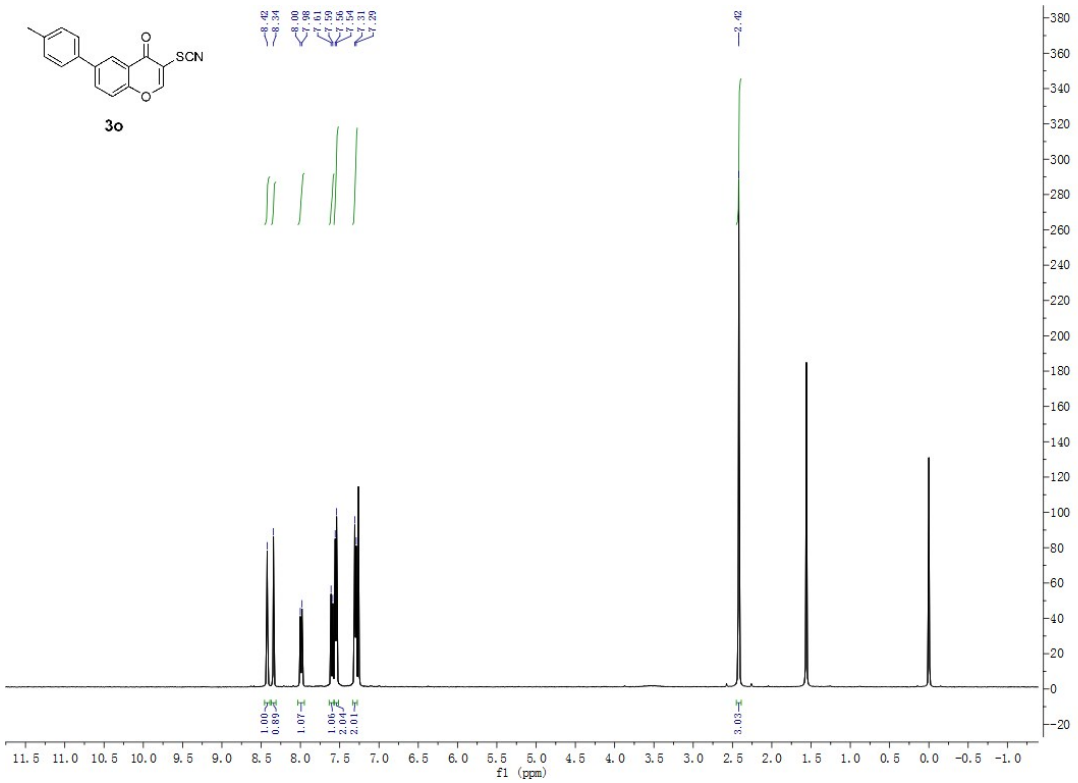
^{1}H NMR of compound **3n**



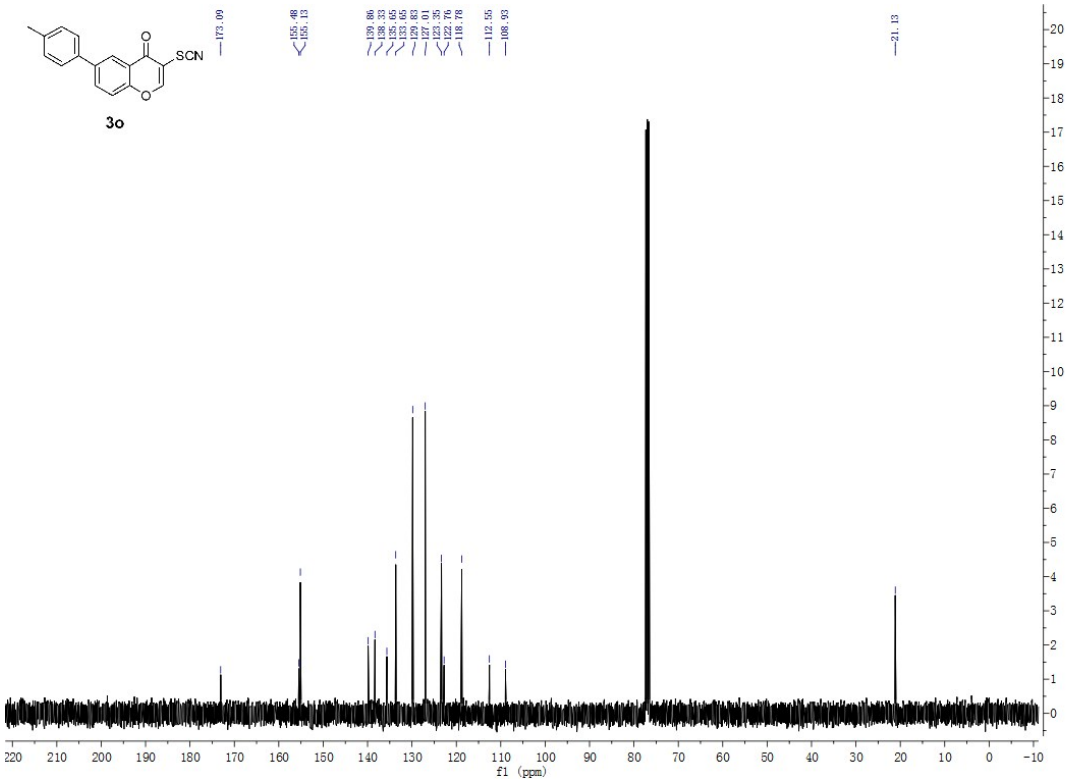
^{13}C NMR of compound **3n**



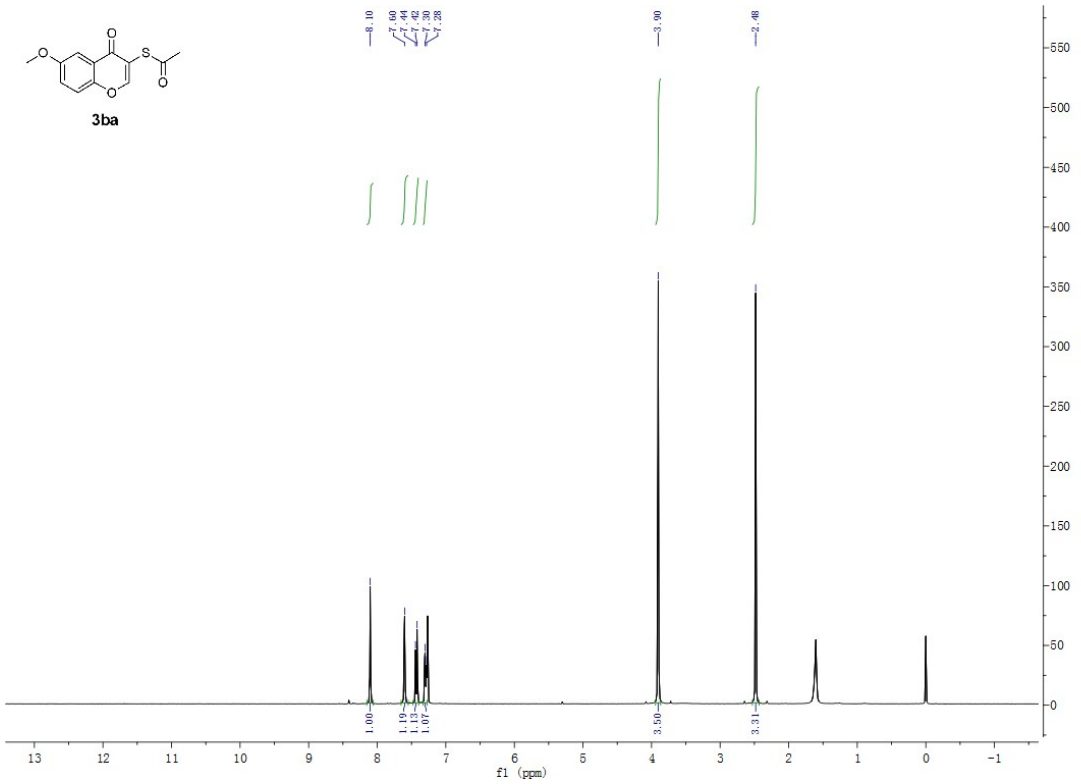
^{1}H NMR of compound **3o**



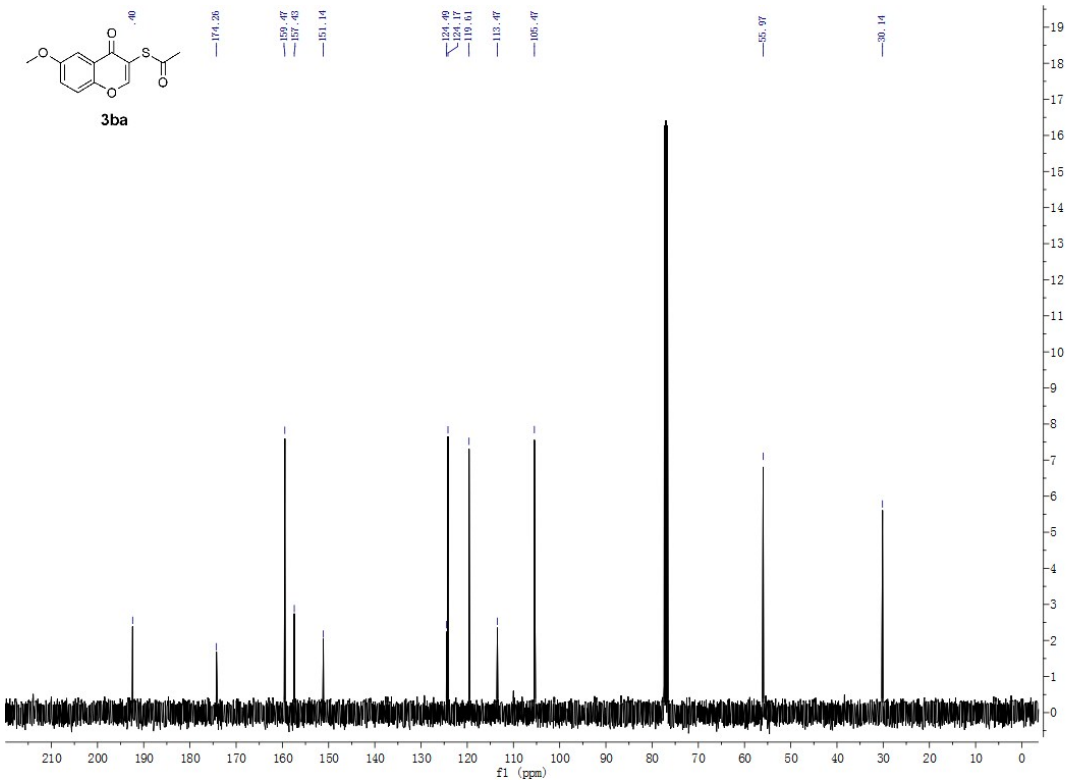
^{13}C NMR of compound **3o**



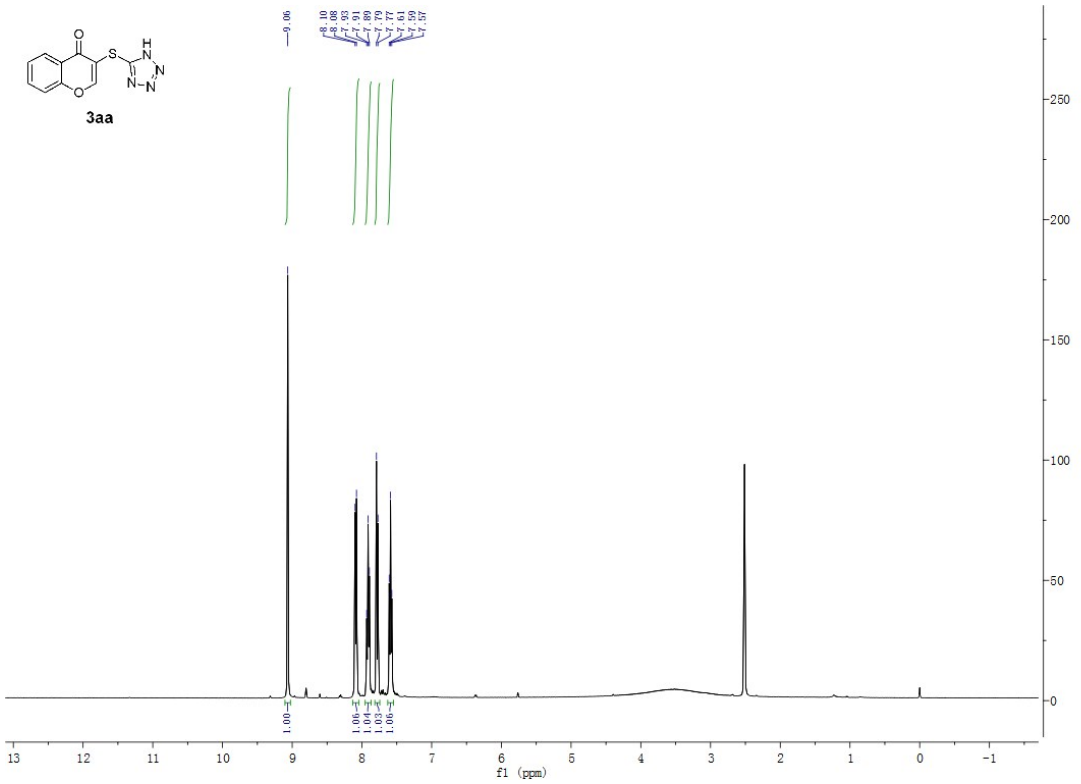
^{1}H NMR of compound **3ba**



^{13}C NMR of compound **3ba**



^{1}H NMR of compound **3aa**



^{13}C NMR of compound **3aa**