Supporting Information

Rhodium-Catalysed Conjugate Addition/Cyclization Cascade for Asymmetric Synthesis of 2-Amino-4*H*-Chromenes

Zhiqian Chang,[a] Huilong Zhu,[a] Changhui Wu,[a] Junhao Xing,[*a] and Xiaowei Dou[*a]

[a]Department of Chemistry, School of Science, China Pharmaceutical University, Nanjing 211198, China
Fax: (+86)-25-8618-5179; e-mail: xjh2017@cpu.edu.cn (J.X.); dxw@cpu.edu.cn (X.D.)

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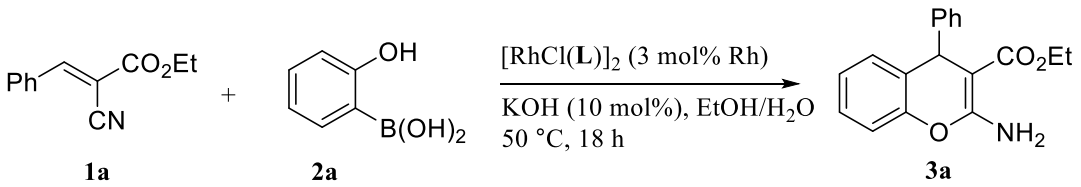
1. General Information

All air-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or argon. NMR spectra were recorded on Bruker AVANCE AV-400 spectrometer (400 MHz for ^{1}H, 101 MHz for ^{13}C) or Bruker AVANCE AV-300 spectrometer (300 MHz for ^{1}H, 75 MHz for ^{13}C). Chemical shifts were reported in δ (ppm) referenced to the residual solvent peak of $CDCl_3$ (δ 7.26) for ^{1}H NMR and $CDCl_3$ (δ 77.00) for ^{13}C NMR, the residual solvent peak of DMSO-d_6 (δ 2.50) for ^{1}H NMR and DMSO-d_6 (δ 39.52) for ^{13}C NMR. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Coupling constants were reported in Hertz (Hz). Specific rotations were measured on an ANTON PAAR MCP 100 automatic polarimeter. High resolution mass spectra (HRMS) were obtained on Thermo Scientific LTQ Orbitrap XL (ESI). For thin layer chromatography (TLC), Yantai pre-coated TLC plates (HSGF 254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with $KMnO_4$ followed by heating. Column chromatography separations were performed on silica gel (300–400 mesh). Enantiomeric excesses (ee) were determined by HPLC analysis on SHIMADZU HPLC system with Daicel chiral columns.

2. Materials

Toluene was distilled over benzophenone ketyl under N_2. EtOH and THF (Extra Dry, with molecular sieves, stabilized with BHT, water ≤50 ppm (by K.F.)) were purchased from commercial supplier and used as received. Rhodium complex $[RhCl(cod)]_2$[1] was purchased from commercial suppliers and used as received. Catalysts $[RhCl(L1)]_2$[2], $[RhCl(L2)]_2$[2], $[RhCl(L3)]_2$[3] and $[RhCl((R,R)\text{-Ph-bod})]_2$[4] were prepared according to the literature procedures. All the organoboronic acids were purchased from commercial suppliers and used as received.

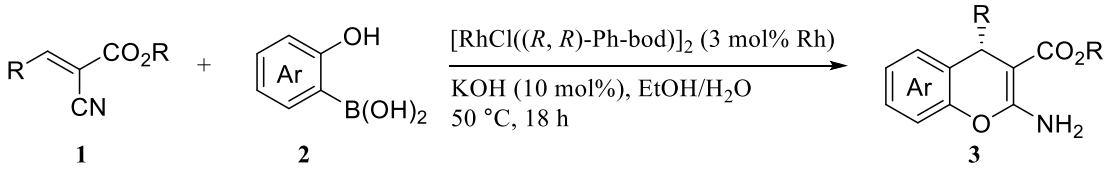
3. A Typical Procedure for Table 1



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

1a (40.2 mg, 0.20 mmol), **2a** (41.4 mg, 0.30 mmol), [RhCl(**L**)]$_2$ (3.0 μmol, 3 mol % Rh), were placed in an oven-dried Schlenk tube under nitrogen. EtOH (1.0 mL) and KOH (10 mol%, in 0.10 mL H_2O) were added, and the reaction was stirred at 50 ℃ for 18 h. Upon completion, the reaction mixture was diluted with water (5.0 mL) and EtOAc (5.0 mL). The layers were separated and the aqueous layer was extracted again with EtOAc for two more times (5.0 mL × 2). The solvent was removed on a rotary evaporator. The residue was dissolved in dichloromethane (5.0 mL), KOH (2 mmol, in 10.0 mL H_2O) were added, and the mixture was stirred at room temperature for 10 min (Note: to remove phenol from protodeboronation of **2a**, phenol shares a very similar polarity with **3a**). The organic layer was separated and dried with Na_2SO_4, and the solvent was removed on a rotary evaporator. The crude product was subjected to silica gel chromatography with petroleum ether/EtOAc (v/v = 15/1) to give **3a** as a white solid.

4. Procedure for Scheme 3

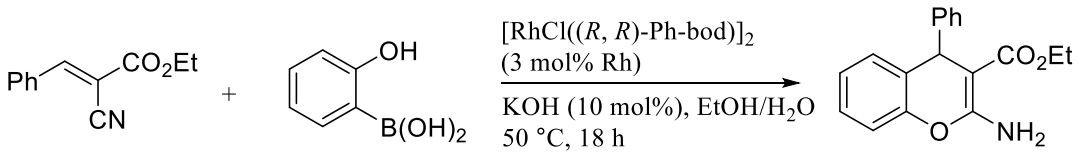


1 **2** **3**

1 (0.20 mmol), **2** (0.30 mmol), and [RhCl((*R*, *R*)-Ph-bod)]$_2$ (2.5 mg, 3 mol % Rh) were placed in an oven-dried Schlenk tube under nitrogen. EtOH (1.0 mL) and KOH (10 mol%, in 0.10 mL H_2O) were added, and the reaction was stirred at 50 ℃ for 18 h. Upon completion, the reaction mixture was diluted with water (5.0 mL) and EtOAc (5.0 mL). The layers were separated and the aqueous layer was extracted again with EtOAc

for two more times (5.0 mL × 2). The solvent was removed on a rotary evaporator. The residue was dissolved in dichloromethane (5.0 mL), KOH (2 mmol, in 10.0 mL H_2O) were added, and the mixture was stirred at room temperature for 10 min (Note: to remove phenols from protodeboronation of **2**). The organic layer was separated and dried over Na_2SO_4, and the solvent was removed on a rotary evaporator. The crude product was subjected to silica gel chromatography with petroleum ether/EtOAc to give **3**.

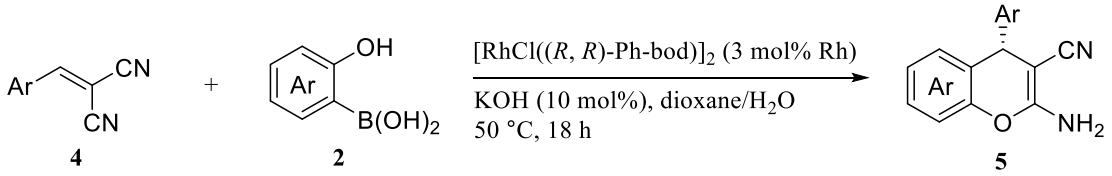
5. Procedure for Scheme 4



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

1a (703.5 mg, 3.50 mmol), **2a** (724.1 mg, 5.25 mmol), [RhCl((*R*, *R*)-Ph-bod)]$_2$ (41.6 mg, 52.5 μmol), were placed in an oven-dried Schlenk tube (100 mL) under nitrogen. EtOH (17.5 mL) and KOH (10 mol%, in 1.75 mL H_2O) were added, and the reaction was stirred at 50 ℃ for 18 h. Upon completion, the reaction mixture was diluted with water (20.0 mL) and EtOAc (20.0 mL). The layers were separated and the aqueous layer was extracted again with EtOAc for two more times (20.0 mL × 2). The solvent was removed on a rotary evaporator. The residue was dissolved in dichloromethane (30.0 mL), KOH (35 mmol, in 30.0 mL H_2O) were added, and the mixture was stirred at room temperature for 20 min (Note: to remove phenol from protodeboronation of **2a**, phenol shares a very similar polarity with **3a**). The organic layer was separated and dried with Na_2SO_4, and the solvent was removed on a rotary evaporator. The crude product was subjected to silica gel chromatography with petroleum ether/EtOAc (v/v = 50/1) to give **3a** (937 mg) as a white solid.

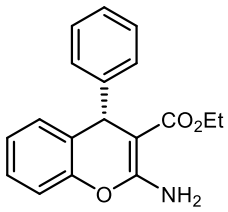
6. Procedure for Scheme 5



4 (0.20 mmol), **2** (0.30 mmol), and [RhCl((*R*, *R*)-Ph-bod)]$_2$ (2.5 mg, 3 mol % Rh) were placed in an oven-dried Schlenk tube under nitrogen. 1,4-Dioxane (1.0 mL) and KOH (10 mol%, in 0.10 mL H_2O) were added, and the reaction was stirred at 50 ℃ for 18 h. Upon completion, the reaction mixture was diluted with water (5.0 mL) and EtOAc (5.0 mL). The layers were separated and the aqueous layer was extracted again with EtOAc for two more times (5.0 mL × 2). The solvent was removed on a rotary evaporator, and the crude product was subjected to silica gel chromatography with petroleum ether/EtOAc/dichloromethane to give **5**.

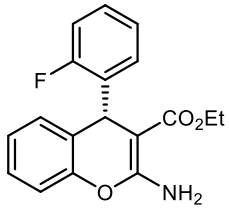
7. Characterization of the Products

Ethyl (*S*)-2-amino-4-phenyl-4*H*-chromene-3-carboxylate (3a)



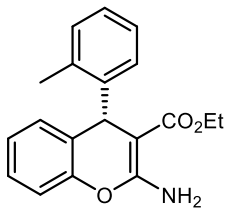
Compound 3a. (98% yield, 91% ee (*S*)). White solid, 57.9 mg at 0.20 mmol scale. The ee of **3a** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 14.9 min (*S*), t_{minor} = 10.2 min (*R*)); $[\alpha]^{20}_D$ +91 (*c* 0.34, CH_2Cl_2) for 91% ee (*S*). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.05 (t, J = 7.0 Hz, 3H), 3.97 (q, J = 7.1 Hz, 2H), 4.94 (s, 1H), 6.99 – 7.13 (m, 3H), 7.15 – 7.30 (m, 6H), 7.68 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 14.7, 40.1, 59.1, 76.6, 116.2, 124.9, 126.4, 126.9, 127.5, 128.1, 128.7, 129.8, 148.5, 149.0, 161.6, 168.7. HRMS (ESI) m/z calcd for $C_{18}H_{17}NNaO_3^+$ $(M+Na)^+$ 318.1101, found 318.1102.

Ethyl (*S*)-2-amino-4-(2-fluorophenyl)-4*H*-chromene-3-carboxylate (3b)



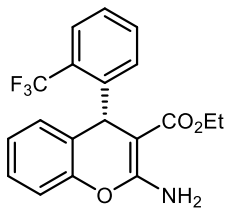
Compound 3b. (93% yield, 89% ee (*S*)). White solid, 58.5 mg at 0.20 mmol scale. The ee of **3b** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 13.9 min (*S*), t_{minor} = 9.0 min (*R*)); $[\alpha]^{20}_D$ +69 (*c* 0.17, CH_2Cl_2) for 89% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.00 (t, J = 7.1 Hz, 3H), 3.84 – 3.96 (m, 2H), 5.23 (s, 1H), 6.98 – 7.11 (m, 4H), 7.11 – 7.25 (m, 4H), 7.72 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.5, 33.9 (d, J = 2.4 Hz), 59.0, 74.8, 115.7 (d, J = 22.0 Hz), 116.2, 124.8 (d, J = 16.2 Hz), 125.0, 125.3, 128.39, 128.45 (d, J = 8.9 Hz), 129.5, 130.0 (d, J = 4.6 Hz), 135.1 (d, J = 13.3 Hz), 149.0, 159.9 (d, J = 242.9 Hz), 161.7, 168.6. HRMS (ESI) m/z calcd for $C_{18}H_{16}FNNaO_3^+$ $[M+Na]^+$ 336.1006, found 336.1008.

Ethyl (*S*)-2-amino-4-(o-tolyl)-4*H*-chromene-3-carboxylate (3c)



Compound 3c. (90% yield, 83% ee (*S*)). White solid, 55.7 mg at 0.20 mmol scale. The ee of **3c** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 98/2, 254 nm, t_{major} = 9.3 min (*S*), t_{minor} = 10.1 min (*R*)); $[\alpha]^{20}_D$ +90 (*c* 0.42, CH_2Cl_2) for 83% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.01 (t, J = 7.1 Hz, 3H), 2.55 (s, 3H), 3.80 – 4.05 (m, 2H), 5.20 (s, 1H), 6.94 – 7.12 (m, 7H), 7.13 –7.23 (m, 1H), 7.67 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.6, 19.9, 35.7, 59.1, 76.9, 116.3, 124.9, 126.1, 126.7, 127.0, 128.0, 128.7, 129.3, 130.5, 134.2, 147.6, 148.7, 161.4, 168.9. HRMS (ESI) m/z calcd for $C_{19}H_{19}NNaO_3^+$ $[M+Na]^+$ 332.1257, found 332.1259.

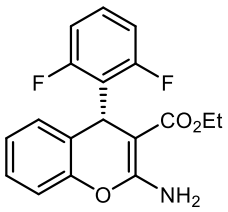
Ethyl (*S*)-2-amino-4-(2-(trifluoromethyl)phenyl)-4*H*-chromene-3-carboxylate (3d)



Compound 3d. (93% yield, 83% ee (*S*)). White solid, 67.7 mg at 0.20 mmol scale. The ee of **3d** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 98/2, 254 nm, t_{major} = 8.1 min (*S*), t_{minor} =9.0 min (*R*)); $[\alpha]^{20}_D$ +69 (*c* 0.48, CH_2Cl_2) for 83% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.88 (t, J = 7.1 Hz, 3H), 3.82 – 3.94 (m, 2H), 5.37 (s, 1H), 6.96 – 7.06 (m, 1H), 7.10 (m, 2H), 7.17 – 7.26 (m, 1H), 7.26 – 7.35 (m, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.60 – 7.68 (m, 1H), 7.84 (s, 2H). ^{13}C

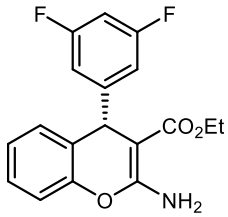
NMR (75 MHz, DMSO-d_6) δ 14.4, 35.6, 58.8, 76.7, 116.7, 125.0, 125.2 (q, J = 273.1 Hz), 125.5, 125.9 (q, J = 29.0 Hz), 126.1 (q, J = 5.8 Hz), 126.9, 128.5, 129.2 (q, J = 3.0 Hz), 130.8, 133.3, 148.2, 148.6, 161.7, 168.6. HRMS (ESI) m/z calcd for $C_{19}H_{16}F_3NNaO_3^+$ $[M+Na]^+$ 386.0974, found 386.0974.

Ethyl (*S*)-2-amino-4-(2,6-difluorophenyl)-4*H*-chromene-3-carboxylate (3e)



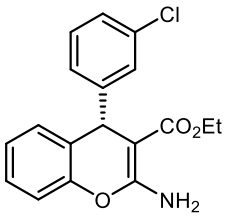
Compound 3e. (98% yield, 82% ee (*S*)). White solid, 65.1 mg at 0.20 mmol scale. The ee of **3e** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/ isopropanol = 95/5, 254 nm, t_{major} = 10.6 min (*S*), t_{minor} = 9.2 min (*R*)); $[\alpha]^{20}_D$ +55 (*c* 0.32, CH_2Cl_2) for 82% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (t, J = 7.1 Hz, 3H), 3.91 – 4.06 (m, 2H), 5.02 (s, 1H), 6.84 – 7.02 (m, 3H), 7.03 – 7.12 (m, 2H), 7.20 – 7.35 (m, 2H), 7.77 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ13.3, 39.2 (t, J = 3.9 Hz), 58.6, 76.7, 100.5 (t, J = 50.8 Hz), 109.4 (q, J = 24.4 Hz), 115.2, 123.7, 123.8, 126.9, 128.3, 147.7, 150.7 (t, J = 15.4 Hz), 159.3, 161.8 (q, J = 258.9 Hz), 168.0. HRMS (ESI) m/z calcd for $C_{18}H_{15}F_2NNaO_3^+$ $[M+Na]^+$ 354.0912, found 354.0918.

Ethyl (*S*)-2-amino-4-(3,5-difluorophenyl)-4*H*-chromene-3-carboxylate (3f)



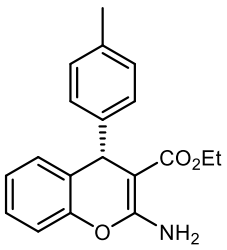
Compound 3f. (96% yield, 92% ee (*S*)). White solid, 63.5 mg at 0.20 mmol scale. The ee of **3f** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/ isopropanol = 95/5, 254 nm, t_{major} = 13.8 min (*S*), t_{minor} = 9.1 min (*R*)); $[\alpha]^{20}_D$ +10 (*c* 0.29, CH_2Cl_2) for 92% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (t, J = 7.1 Hz, 3H), 3.95 – 4.10 (m, 2H), 5.02 (s, 1H), 6.84 – 7.00 (m, 3H), 7.02 – 7.12 (m, 2H), 7.17 – 7.41 (m, 2H), 7.77 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 40.3 (t, J = 4.1 Hz), 59.6, 77.7, 101.6 (t J = 50.7 Hz), 110.4 (q, J = 24.4 Hz), 116.3, 124.75, 124.81, 128.0, 129.3, 148.7, 151.8 (t, J = 15.3 Hz), 160.4, 162.9 (q, J = 259.1 Hz), 169.1. HRMS (ESI) m/z calcd for $C_{18}H_{15}F_2NNaO_3^+$ $[M+Na]^+$ 354.0912, found 354.0918.

Ethyl (*S*)-2-amino-4-(3-chlorophenyl)-4*H*-chromene-3-carboxylate (3g)



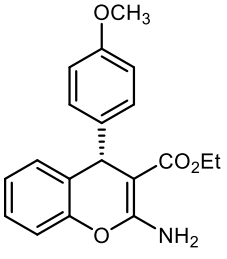
Compound 3g. (88% yield, 89% ee (*S*)). White solid, 57.9 mg at 0.20 mmol scale. The ee of **3g** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/dichloromethane= 95/5, 254 nm, t_{major} = 12.8 min (*S*), t_{minor} = 10.2 min (*R*)); $[\alpha]^{20}_{D}$ +68 (*c* 0.42, CH_2Cl_2) for 89% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.06 (t, J = 7.1 Hz, 3H), 3.90 – 4.06 (m, 2H), 4.97 (s, 1H), 7.02 – 7.19 (m, 4H), 7.19 – 7.30 (m, 4H), 7.72 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 14.7, 39.7, 59.1, 76.0, 116.3, 125.1, 126.0, 126.2, 126.4, 127.4, 128.4, 129.8, 130.7, 133.2, 149.0, 151.0, 161.5, 168.5. HRMS (ESI) m/z calcd for $C_{18}H_{16}ClNNaO_3^+$ $[M+Na]^+$ 352.0711, found 352.0719.

Ethyl (*S*)-2-amino-4-(p-tolyl)-4*H*-chromene-3-carboxylate (3h)



Compound 3h. (92% yield, 88% ee (*S*)). Colorless oil, 56.9 mg at 0.20 mmol scale. The ee of **3h** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 14.9 min (*S*), t_{minor} = 9.5 min (*R*)); $[\alpha]^{20}_{D}$ +85 (*c* 0.38, CH_2Cl_2) for 88% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.08 (t, J = 7.1 Hz, 3H), 2.19 (s, 3H), 3.90 – 4.05 (m, 2H), 4.89 (s, 1H), 6.95 – 7.10 (m, 6H), 7.15 – 7.25 (m, 2H), 7.64 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 21.1, 40.0, 59.5, 79.0, 116.0, 124.6, 126.7, 127.3, 127.5, 129.0, 129.5, 135.6, 145.0, 148.9, 160.4, 169.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}NNaO_3^+$ $[M+Na]^+$ 332.1257, found 332.1257.

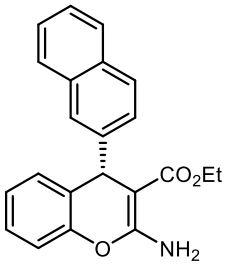
Ethyl (*S*)-2-amino-4-(4-methoxyphenyl)-4*H*-chromene-3-carboxylate (3i)



Compound 3i. (88% yield, 88% ee (*S*)). Colorless oil, 57.3 mg at 0.20 mmol scale. The ee of **3i** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} =14.8 min (*S*), t_{minor} =9.4 min (*R*)); $[\alpha]^{20}_{D}$ +93 (*c* 0.42, CH_2Cl_2) for 88% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.08 (t, J = 7.1 Hz, 3H), 2.19 (s, 3H), 3.91 – 4.03 (m, 2H), 4.89 (s, 1H), 6.96 – 7.10 (m, 6H), 7.16 – 7.23 (m, 2H), 7.64 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.8, 21.0, 39.7, 59.1, 76.7, 116.2, 124.9, 127.1, 127.3, 128.0, 129.2, 129.7, 135.3, 145.6, 149.0, 161.5,

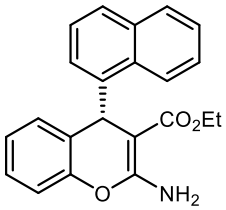
168.8. HRMS (ESI) m/z calcd for $C_{19}H_{19}NNaO_4^+$ $[M+Na]^+$ 348.1206, found 348.1208.

Ethyl (*S*)-2-amino-4-(naphthalen-2-yl)-4H-chromene-3-carboxylate (3j)



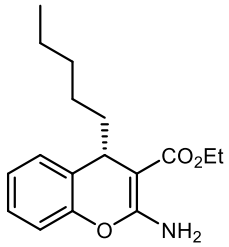
Compound 3j. (96% yield, 87% ee (*S*)). White solid, 66.4 mg at 0.20 mmol scale. The ee of **3j** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 20.6 min (*S*), t_{minor} = 13.3 min (*R*)); $[\alpha]^{20}_D$ +72 (*c* 0.44, CH_2Cl_2) for 87% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, J = 7.1 Hz, 3H), 3.88 – 7.35 (m, 2H), 5.12 (s, 1H), 6.96 – 7.07 (m, 1H), 7.11 (d, J = 8.2Hz, 1H), 7.18 – 7.35 (m, 3H), 7.37 – 7.47 (m, 2H), 7.69 – 7.75 (m, 3H), 7.76 – 7.86 (m, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.7, 40.3, 59.1, 76.4, 116.3, 125.0, 125.4, 125.9, 126.4, 126.5, 126.6, 127.9, 128.0, 128.2, 128.5, 129.9, 132.1, 133.3, 145.9, 149.1, 161.5, 168.8. HRMS (ESI) m/z calcd for $C_{22}H_{19}NNaO_3^+$ $[M+Na]^+$ 368.1257, found 368.1252.

Ethyl (*S*)-2-amino-4-(naphthalen-1-yl)-4H-chromene-3-carboxylate (3k)



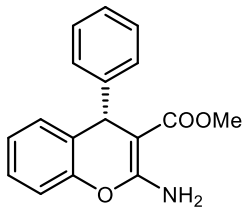
Compound 3k. (98% yield, 73% ee (*S*)). White solid, 67.7 mg at 0.20 mmol scale. The ee of **3k** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 98/2, 254 nm, t_{major} = 11.7 min (*S*), t_{minor} = 13.6 min (*R*)); $[\alpha]^{20}_D$ +1.5×10^2 (*c* 0.24, CH_2Cl_2) for 73% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.67 (t, J = 7.1 Hz, 3H), 3.62 – 3.92 (m, 2H), 5.89 (s, 1H), 6.84 – 6.97 (m, 1H), 7.00 – 7.22 (m, 3H), 7.23 – 7.32 (m, 1H), 7.38 (t, J = 7.7 Hz, 1H), 7.46 – 7.55 (m, 1H), 7.56 – 7.64 (m, 1H), 7.64 – 7.78 (m, 3H), 7.80 – 7.96 (m, 1H), 8.63 (d, J = 8. 6 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.2, 34.5, 58.9, 77.2, 116.4, 124.2, 124.8, 125.9, 126.1, 126.2, 126.4, 126.8, 127.1, 128.1, 128.9, 129.0, 131.0, 133.8, 146.1, 148.6, 161.4, 168.9. HRMS (ESI) m/z calcd for $C_{22}H_{19}NNaO_3^+$ $[M+Na]^+$ 368.1257, found 368.1253.

Ethyl (*S*)-2-amino-4-pentyl-4H-chromene-3-carboxylate (3l)



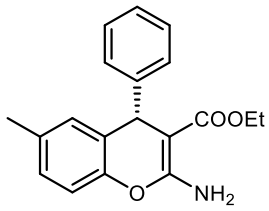
Compound 3l. (83% yield, 60% ee (*S*)). Colorless oil, 47.9 mg at 0.20 mmol scale. The ee of **3l** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 9.0 min (*S*), t_{minor} = 7.1 min (*R*)); $[\alpha]^{20}_D$ +59 (*c* 0.18, CH_2Cl_2) for 60% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.76 (t, J = 6.7 Hz, 3H), 0.88 – 1.03 (m, 1H), 1.07 – 1.19 (m, 5H), 1.23 (t, J = 7.1 Hz, 3H), 1.38 – 1.58 (m, 2H), 3.78 (t, J = 5.3 Hz, 1H), 3.97 – 4.23 (m, 2H), 6.94 – 7.03 (m, 1H), 7.06 – 7.14 (m, 1H), 7.15 – 7.27 (m, 2H), 7.48 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.7, 14.4, 21.9, 24.1, 31.1, 33.1, 38.5, 58.4, 75.2, 115.2, 124.0, 127.0, 127.1, 128.3, 149.8, 161.8, 168.3. HRMS (ESI) m/z calcd for $C_{17}H_{23}NNaO_3^+$ $[M+Na]^+$ 312.1570, found 312.1570.

Methyl (*S*)-2-amino-4-phenyl-4*H*-chromene-3-carboxylate (3m)



Compound 3m. (92% yield, 92% ee (*S*)). White solid, 51.9 mg at 0.20 mmol scale. The ee of **3m** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 20.1 min (*S*), t_{minor} = 11.9 min (*R*)); $[\alpha]^{20}_D$ $+12\times10^2$ (*c* 0.35, CH_2Cl_2) for 92% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.52 (s, 3H), 4.95 (s, 1H), 7.00 – 7.14 (m, 3H), 7.16 – 7.29 (m, 6H), 7.71 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.3, 50.9, 78.7, 116.0, 124.6, 126.2, 126.5, 127.42, 127.44, 128.4, 129.4, 147.7, 148.9, 160.6, 169.8. HRMS (ESI) m/z calcd for $C_{17}H_{15}NNaO_3^+$ $[M+Na]^+$ 304.0944, found 304.0948.

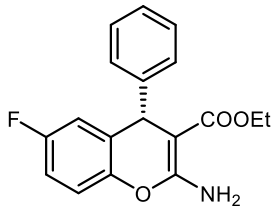
Ethyl (*S*)-2-amino-6-methyl-4-phenyl-4*H*-chromene-3-carboxylate (3n)



Compound 3n. (96% yield, 91% ee (*S*)). White solid, 59.2 mg at 0.20 mmol scale. The ee of **3n** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/isopropanol = 95/5, 254 nm, t_{major} = 10.5 min (*S*), t_{minor} = 9.1 min (*R*)); $[\alpha]^{20}_D$ +46 (*c* 0.38, CH_2Cl_2) for 91% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.06 (t, J = 7.1 Hz, 3H), 2.17 (s, 3H), 3.96 (q, J = 7.1 Hz, 2H), 4.87 (s, 1H), 6.93 – 7.02

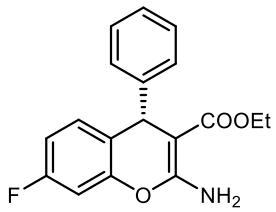
(m, 3H), 7.05 – 7.13 (m, 1H), 7.16 – 7.27 (m, 4H), 7.64 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.7, 20.7, 40.2, 59.0, 76.7, 116.0, 126.4, 126.5, 127.5, 128.6, 128.7, 129.8, 133.9, 147.0, 148.6, 161.7, 168.8. HRMS (ESI) m/z calcd for $C_{19}H_{19}NNaO_3^+$ $[M+Na]^+$ 332.1257, found 332.1259.

Ethyl (*S*)-2-amino-6-fluoro-4-phenyl-4*H*-chromene-3-carboxylate (3o)



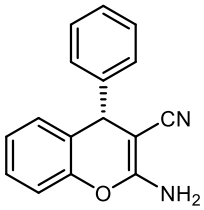
Compound 3o. (74% yield, 83% ee (*S*)). White solid, 46.1 mg at 0.20 mmol scale. The ee of **3o** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/iso-propanol, 254 nm, t_{major} = 13.7 min (*S*), t_{minor} = 9.6 min (*R*)); $[\alpha]^{20}_D$ +85 (*c* 0.31, CH_2Cl_2) for 83% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (t, *J* = 7.1 Hz, 3H), 3.96 (q, *J* = 7.1 Hz, 2H), 4.95 (s, 1H), 6.99 – 7.08 (m, 1H), 7.08 – 7.15 (m, 3H), 7.17 – 7.28 (m, 4H), 7.69 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.7, 59.1, 75.8, 114.8, 115.290 (d, *J* = 69.9 Hz), 115.293 (d, *J* = 22.8 Hz), 117.9 (d, *J* = 8.7 Hz), 126.6, 127.4, 128.8, 128.9 (d, *J* = 8.6 Hz),145.4 (d, *J* = 2.2 Hz), 147.9, 158.8 (d, *J* = 238.9 Hz), 161.6, 168.6. HRMS (ESI) m/z calcd for $C_{18}H_{16}FNNaO_3^+$ $[M+Na]^+$ 336.1006, found 336.1008.

Ethyl (*S*)-2-amino-7-fluoro-4-phenyl-4*H*-chromene-3-carboxylate (3p)



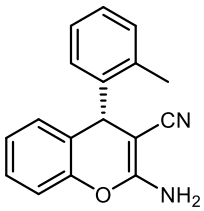
Compound 3p. (68% yield, 83% ee (*S*)). Colorless oil, 42.9 mg at 0.20 mmol scale. The ee of **3p** was determined by HPLC analysis: (Chiralcel IA column, 1.0 mL/min, hexane/iso-propanol, 254 nm, t_{major} = 14.9 min (*S*), t_{minor} = 10.2 min (*R*)); $[\alpha]^{20}_D$ +75 (*c* 0.27, CH_2Cl_2) for 83% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (t, *J* = 7.1 Hz, 3H), 3.96 (q, *J* = 7.1 Hz, 2H), 4.92 (s, 1H), 6.82 – 7.02 (m, 2H), 7.04 – 7.14 (m, 1H), 7.15 – 7.33 (m, 5H), 7.69 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 14.7, 39.5, 59.2, 76.6, 103.7 (d, *J* = 25.3 Hz), 112.1 (d, *J* = 21.1 Hz), 123.2 (d, *J* = 2.8 Hz), 126.5, 127.4, 128.8, 131.2 (d, *J* = 9.8 Hz), 148.4, 149.5 (d, *J* = 12.3 Hz), 161.1, 161.3 (d, *J* = 241.7 Hz), 168.6. HRMS (ESI) m/z calcd for $C_{18}H_{16}FNNaO_3^+$ $[M+Na]^+$ 336.1006, found 336.1008.

(*S*)-2-Amino-4-phenyl-4*H*-chromene-3-carbonitrile (5a)



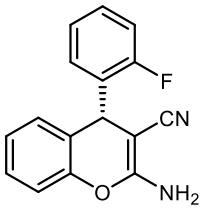
Compound 5a. (89% yield, 91% ee (*S*)). White solid, 44.2 mg at 0.20 mmol scale. A known compound.[5] The ee of **5a** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 9.8 min (*S*), t_{minor} = 12.2 min (*R*)); $[\alpha]^{20}_{D}$ +39 (*c* 0.38, acetone) for 91% ee (*S*), [ref. 5: $[\alpha]^{20}_{D}$ = +36 (*c* 0.40, acetone) for 92% ee (*S*)]. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.78 (s, 1H), 6.99 (d, J = 3.0 Hz, 2H), 7.03 – 7.11 (m, 3H), 7.16 – 7.27 (m, 4H), 7.28 – 7.36 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 40.9, 56.3, 116.5, 121.0, 124.0, 125.1, 127.3, 127.9, 128.6, 129.2, 129.8, 146.4, 148.8, 160.9.

(*S*)-2-Amino-4-(o-tolyl)-4*H*-chromene-3-carbonitrile (5b)



Compound 5b (91% yield, 82% ee (*S*)). Pale yellow solid, 47.7 mg at 0.20 mmol scale. The ee of **5b** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 8.5 min (*S*), t_{minor} = 10.7 min (*R*)); $[\alpha]^{20}_{D}$ –7.1 (*c* 0.24, CH_2Cl_2) for 82% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.35 (s, 3H), 5.06 (s, 1H), 6.84 – 6.93 (m, 3H), 6.95 – 7.02 (m, 1H), 7.01 – 7.09 (m, 2H), 7.09 – 7.19 (m, 3H), 7.19 – 7.28 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 19.6, 37.7, 56.2, 116.4, 120.9, 123.8, 125.1, 127.0, 127.2, 128.7, 129.6, 129.8, 131.2, 135.4, 144.2, 149.0, 160.5. HRMS (ESI) m/z calcd for $C_{17}H_{14}N_2NaO^+$ $[M+Na]^+$ 285.0998, found 285.0998.

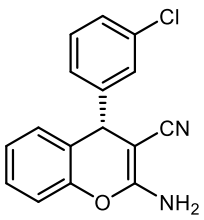
(*S*)-2-Amino-4-(2-fluorophenyl)-4*H*-chromene-3-carbonitrile (5c)



Compound 5c. (84% yield, 82% ee (*S*)). Pale yellow solid, 44.8 mg at 0.20 mmol scale. The ee of **5c** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 8.7 min (*S*), t_{minor} = 10.3 min (*S*)); $[\alpha]^{20}_{D}$ +24 (*c* 0.30, $CHCl_3$) for 82% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.04 (s, 1H), 6.97 – 7.10 (m, 5H), 7.11 – 7.20 (m, 2H), 7.20 – 7.32 (m, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 35.5, 54.7, 116.3 (d, J = 21.3 Hz), 116.5, 120.8, 122.7, 125.2 (d, J = 3.5 Hz), 125.3, 128.9, 129.4, 129.6 (d, J = 8.3 Hz), 130.4 (d, J = 4.2 Hz), 132.7 (d, J = 12.6 Hz), 149.0, 160.4

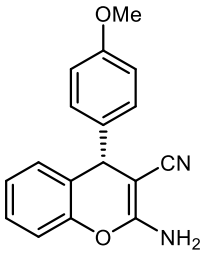
(d, J = 243.9 Hz), 162.0. HRMS (ESI) m/z calcd for $C_{16}H_{11}FN_2NaO^+$ $[M+Na]^+$ 289.0748, found 289.0748.

(*S*)-2-Amino-4-(3-chlorophenyl)-4*H*-chromene-3-carbonitrile (5d)



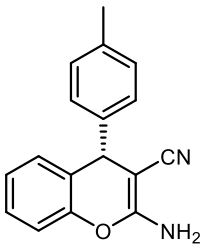
Compound 5d. (72% yield, 83% ee (*S*)). Pale yellow solid, 40.9 mg at 0.20 mmol scale. The ee of **5d** was determined by HPLC analysis: (Chiralcel IF column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 9.7 min (*S*), t_{minor} = 11.2 min (*R*)); $[\alpha]^{20}_D$ +9.3 (*c* 0.26, CH_2Cl_2) for 83% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.85 (s, 1H), 7.08 (d, J = 4.4 Hz, 5H), 7.14 – 7.21 (m, 1H), 7.22 – 7.32 (m, 3H), 7.32 – 7.40 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 40.4, 55.7, 116.7, 120.8, 123.2, 125.3, 126.7, 127.4, 127.6, 128.9, 129.7, 131.2, 133.7, 148.7, 148.8, 161.0. HRMS (ESI) m/z calcd for $C_{16}H_{11}ClN_2NaO^+$ $[M+Na]^+$ 305.0452, found 305.0454.

(*S*)-2-Amino-4-(4-methoxyphenyl)-4*H*-chromene-3-carbonitrile (5e)



Compound 5e. (82% yield, 90% ee (*S*)). Pale yellow solid, 45.8 mg at 0.20 mmol scale. The ee of **5e** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 12.3 min (*S*), t_{minor} = 18.0 min (*R*)); $[\alpha]^{20}_D$ +23 (*c* 0.17, CH_2Cl_2) for 90% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.72 (s, 3H), 4.72 (s, 1H), 6.78 – 6.98 (m, 4H), 7.00 – 7.08 (m, 3H), 7.09 – 7.16 (m, 2H), 7.17 – 7.27 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 40.1, 55.5, 56.6, 114.5, 116.5, 121.1, 124.3, 125.0, 128.5, 129.0, 129.8, 138.5, 148.7, 158.6, 160.7. HRMS (ESI) m/z calcd for $C_{17}H_{14}N_2NaO_2^+$ $[M+Na]^+$ 301.0947, found 301.0947.

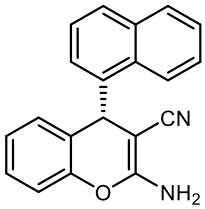
(*S*)-2-Amino-4-(p-tolyl)-4*H*-chromene-3-carbonitrile (5f)



Compound 5f. (81% yield, 88% ee (*S*)). Pale yellow solid, 42.7 mg at 0.20 mmol scale. The ee of **5f** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 9.1 min (*S*), t_{minor} = 11.2 min (*R*)); $[\alpha]^{20}_D$ +21 (*c* 0.30, CH_2Cl_2) for 88% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.25 (s, 3H), 4.72 (s, 1H), 6.94 (s, 2H), 6.99 – 7.07 (m, 3H), 7.07 – 7.16 (m, 4H), 7.18 – 7.27

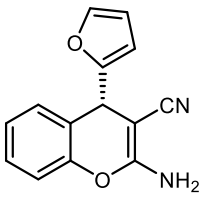
(m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 21.1, 40.5, 56.4, 116.5, 121.0, 124.1, 125.0, 127.8, 128.6, 129.7, 129.8, 136.4, 143.5, 148.7, 160.8. HRMS (ESI) m/z calcd for $C_{17}H_{14}N_2NaO^+$ $[M+Na]^+$ 285.0998, found 285.0999.

(*R*)-2-Amino-4-(naphthalen-1-yl)-4*H*-chromene-3-carbonitrile (5g)



Compound 5g. (43% yield, 71% ee (*R*)). Pale yellow solid, 25.8 mg at 0.20 mmol scale. The ee of **5g** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 11.9 min (*S*), t_{minor} = 20.2 min (*R*)); $[\alpha]^{20}_D$ +31 (*c* 0.17, CH_2Cl_2) for 71% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.69 (s, 1H), 6.84 – 6.98 (m, 2H), 7.06 (s, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.28 (m, 1H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.43 – 7.61 (m, 3H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.91 – 8.01 (m, 1H), 8.17 – 8.45 (m, 1H). ^{13}C NMR (75 MHz, DMSO) δ 160.8, 148.8, 134.3, 131.2, 129.3, 129.1, 128.8, 128.2, 127.7, 126.7, 126.2, 126.2, 125.1, 124.2, 124.0, 121.0, 116.6, 56.8. HRMS (ESI) m/z calcd for $C_{20}H_{14}N_2NaO^+$ $[M+Na]^+$ 321.0998, found 321.0997.

(*S*)-2-Amino-4-(furan-2-yl)-4*H*-chromene-3-carbonitrile (5h)



Compound 5h. (35% yield, 86% ee (*S*)). Yellow solid, 16.7 mg at 0.20 mmol scale. The ee of **5h** was determined by HPLC analysis: (Chiralcel IB column, 1.0 mL/min, hexane/isopropanol = 90/10, 254 nm, t_{major} = 10.0 min (*S*), t_{minor} = 11.1 min (*R*)); $[\alpha]^{20}_D$ +24 (*c* 0.14, CH_2Cl_2) for 86% ee (*S*). ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.91 (s, 1H), 6.19 (d, *J* = 3.2 Hz, 1H), 6.36 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.95 – 7.07 (m, 3H), 7.07 – 7.15 (m, 1H), 7.15 – 7.21 (m, 1H), 7.23 – 7.31 (m, 1H), 7.52 (dd, *J* = 1.9, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 34.2, 53.0, 105.8, 110.3, 116.0, 120.1, 120.8, 124.5, 128.5, 128.9, 142.5, 148.6, 156.4, 161.0. HRMS (ESI) m/z calcd for $C_{14}H_{10}N_2NaO_2^+$ $[M+Na]^+$ 261.0634, found 261.0635.

8. References

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9. X-ray crystal structures of 3a

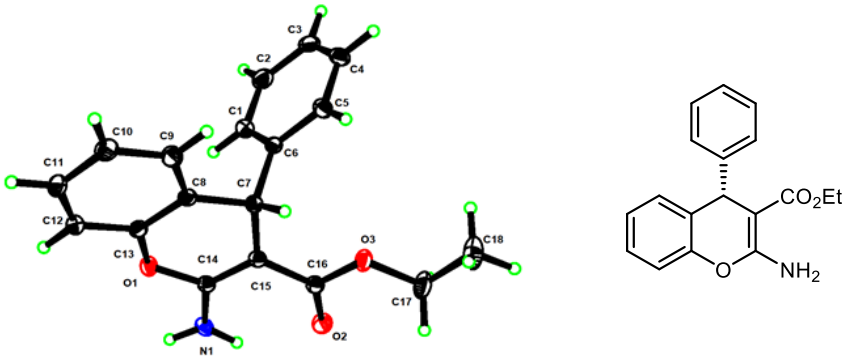
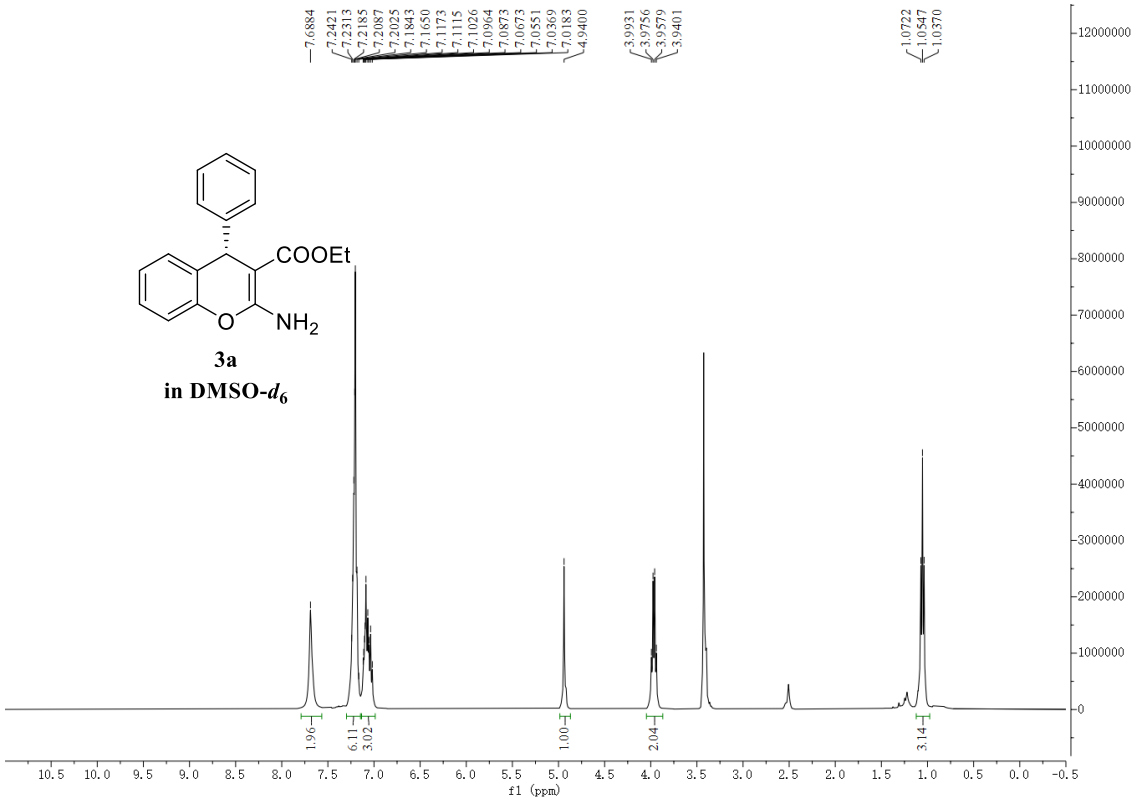


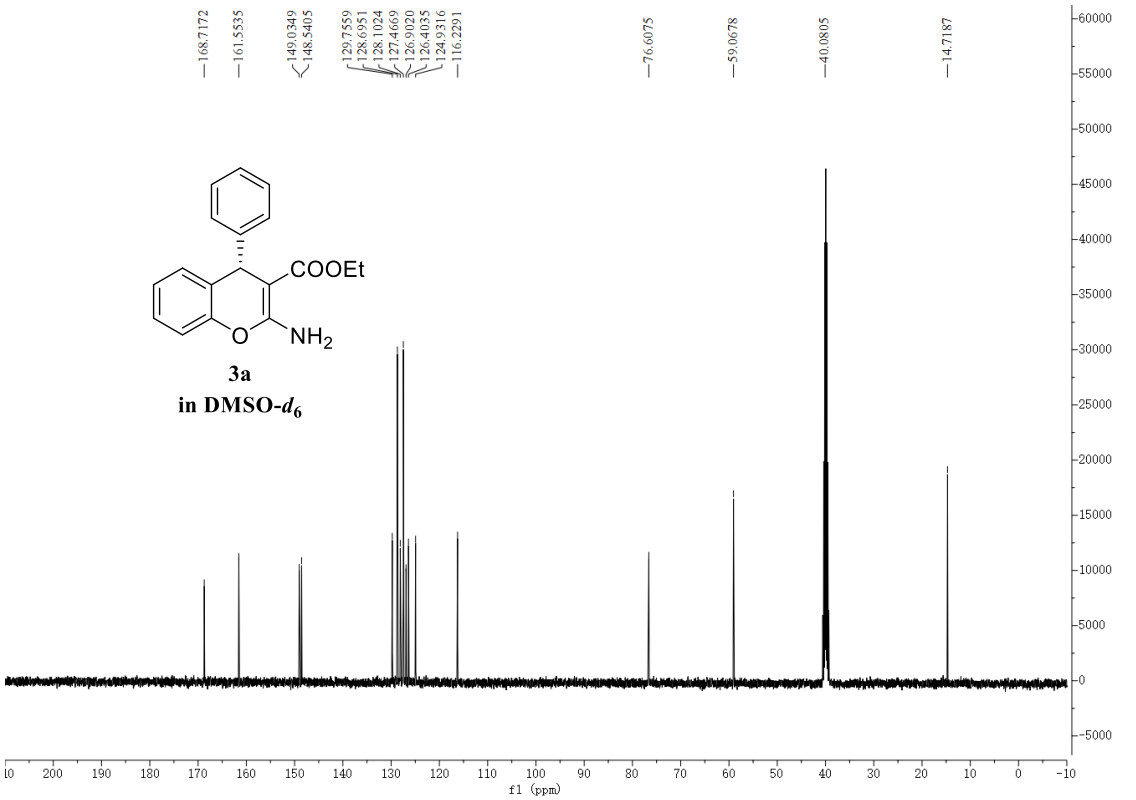
Figure S1. ORTEP illustration of 3a.

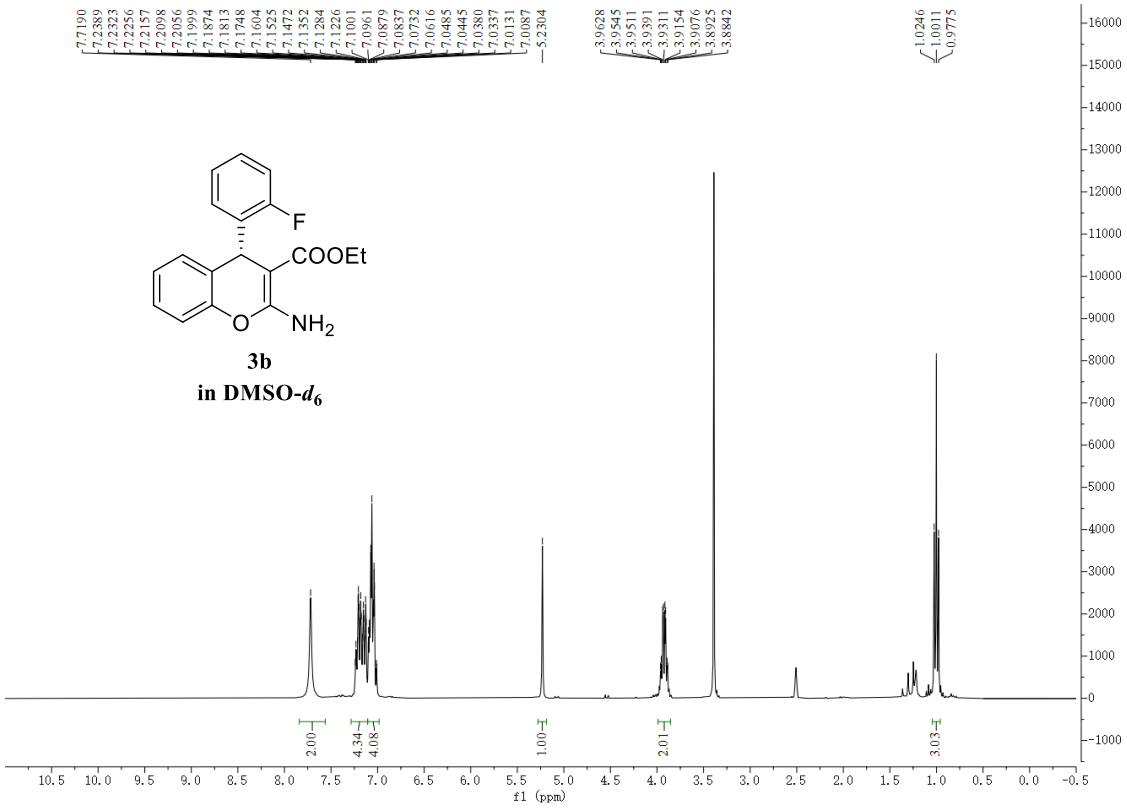
Identification code	1114DXWCZQ01_0m
Empirical formula	$C_{18}H_{17}NO_3$
Formula weight	295.32
Temperature/K	153.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.9919(2)
b/Å	12.2777(2)
c/Å	14.0831(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1554.77(5)
Z	4
ρ_{calc}g/cm^3	1.262
μ/mm^{-1}	0.698
F(000)	624.0
Crystal size/mm^3	0.26 × 0.16 × 0.13

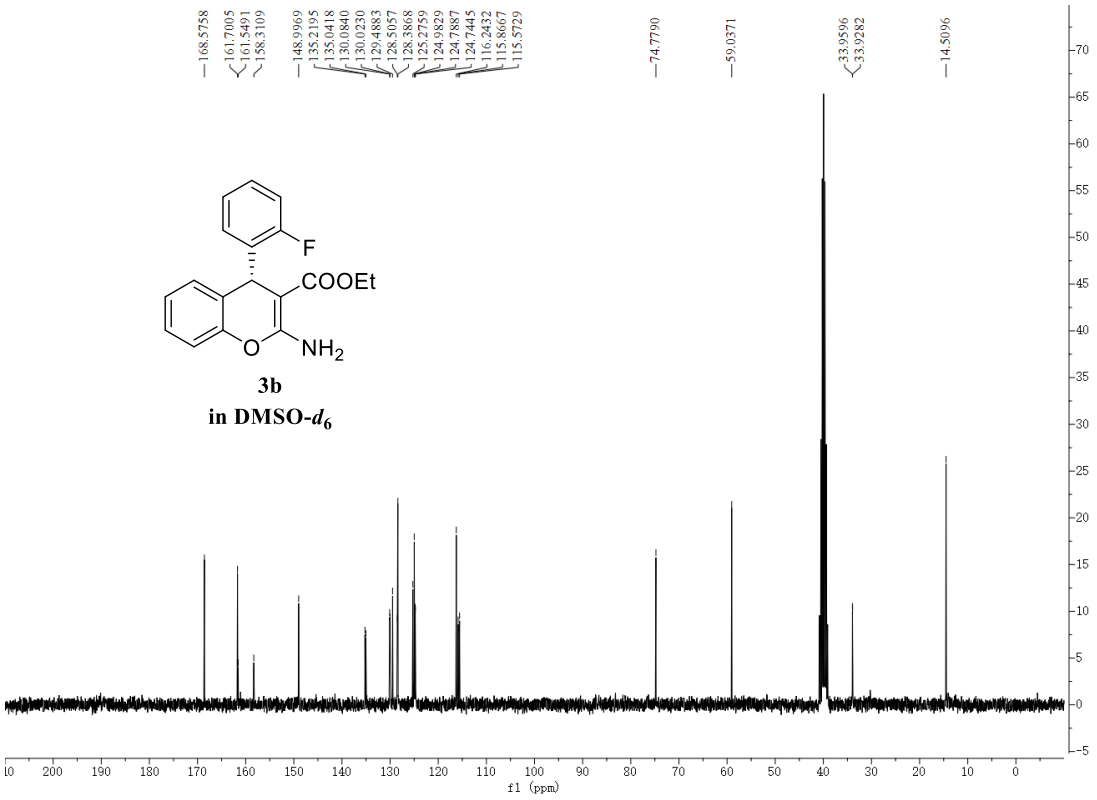
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	11.676 to 148.96
Index ranges	$-11 \leq h \leq 11$, $-14 \leq k \leq 15$, $-17 \leq l \leq 17$
Reflections collected	13884
Independent reflections	3127 [R_{int} = 0.0418, R_{sigma} = 0.0302]
Data/restraints/parameters	3127/0/205
Goodness-of-fit on F^2	1.087
Final R indexes [I>=2σ (I)]	R_1 = 0.0324, wR_2 = 0.0807
Final R indexes [all data]	R_1 = 0.0355, wR_2 = 0.0834
Largest diff. peak/hole / e $Å^{-3}$	0.13/-0.18
Flack parameter	0.00(9)

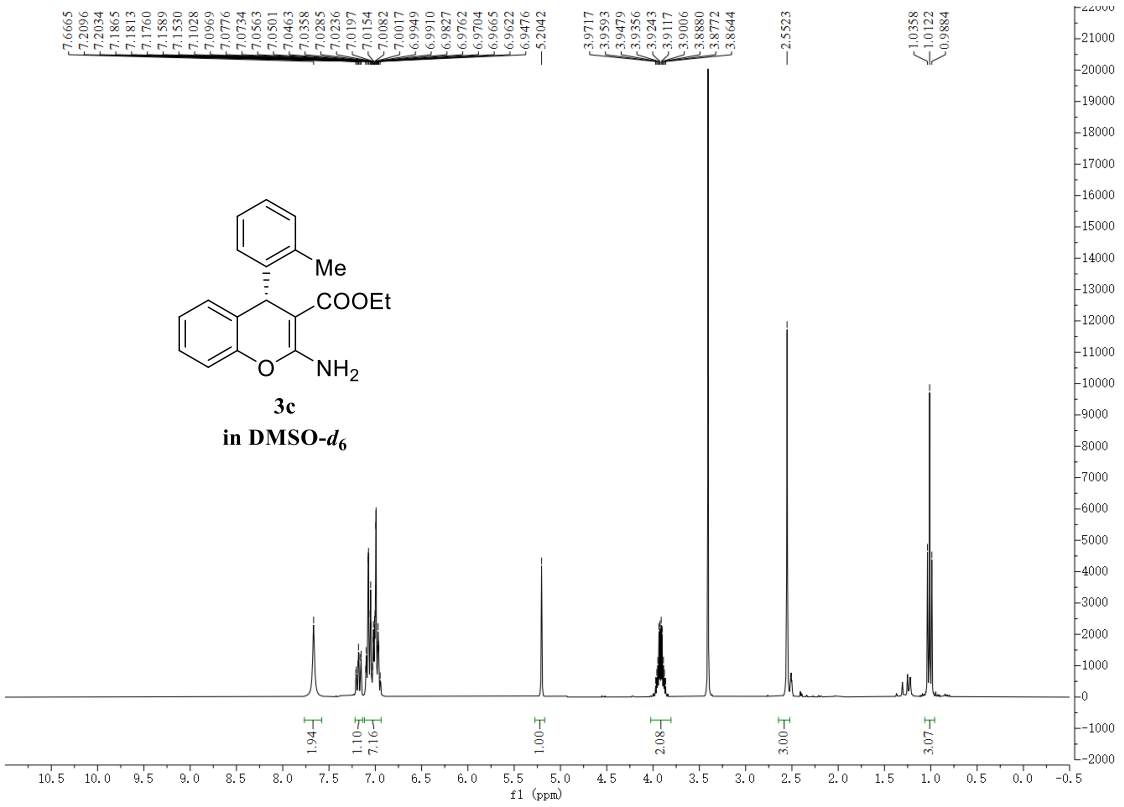
10.NMR Spectra

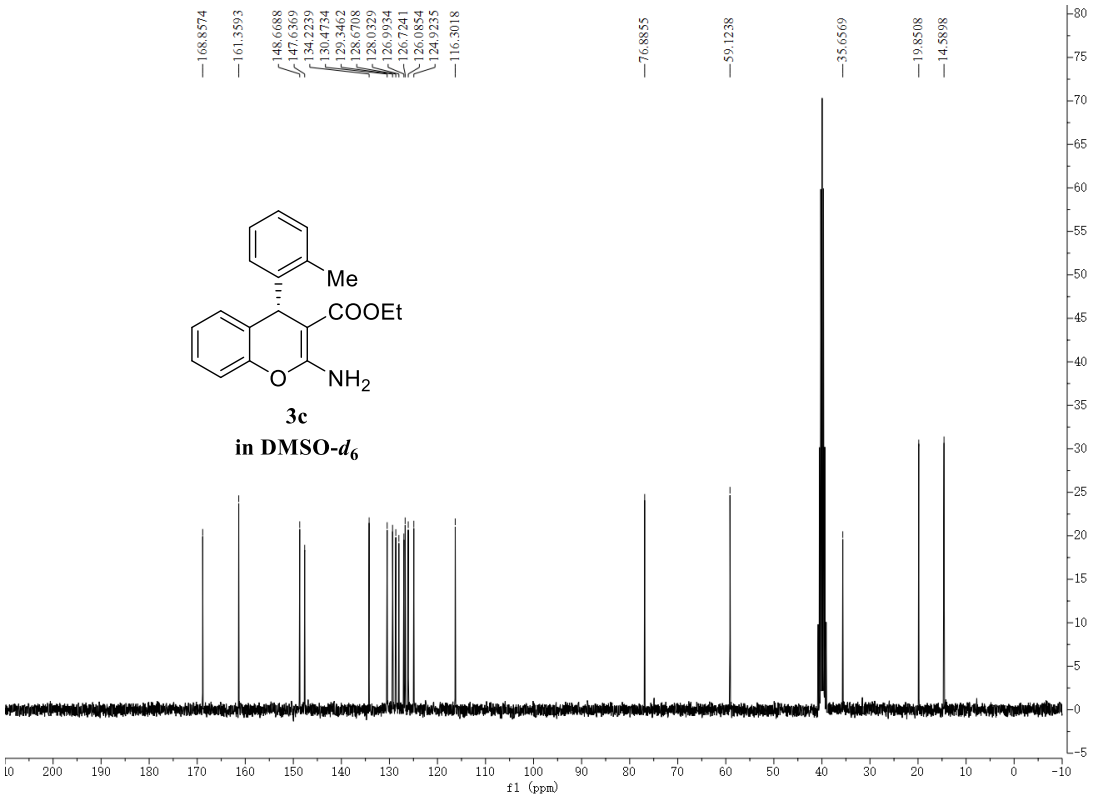


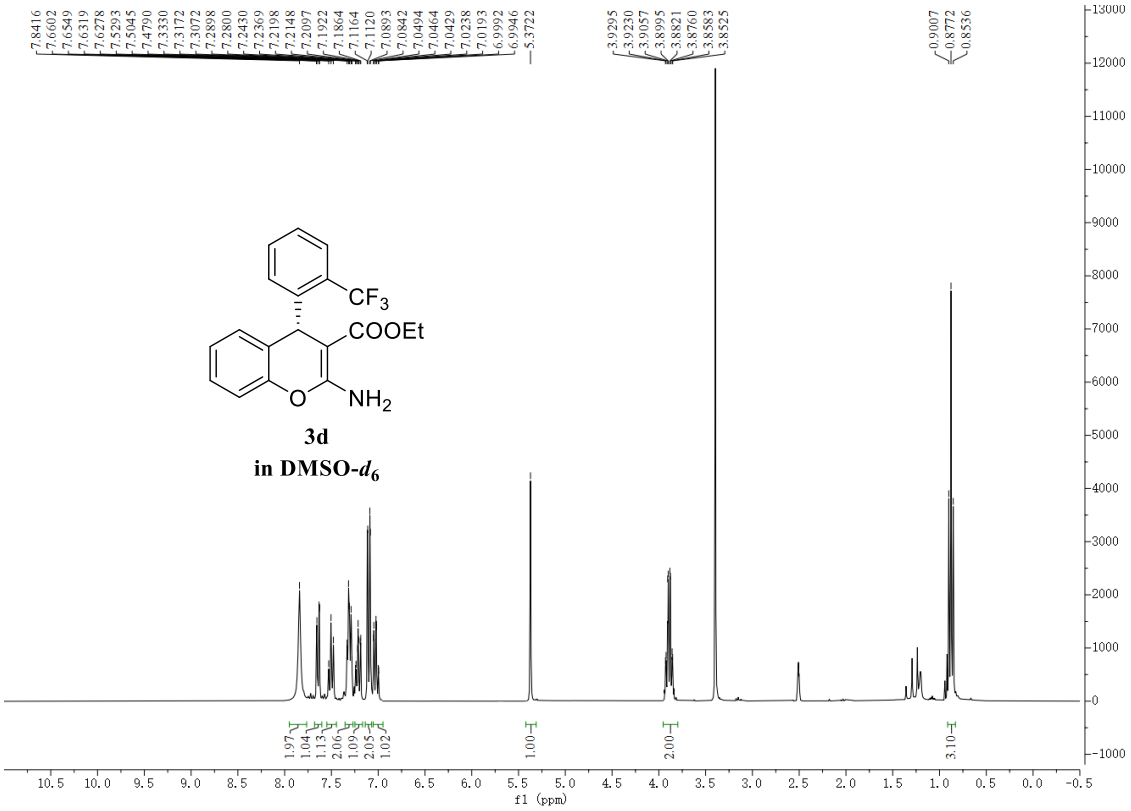


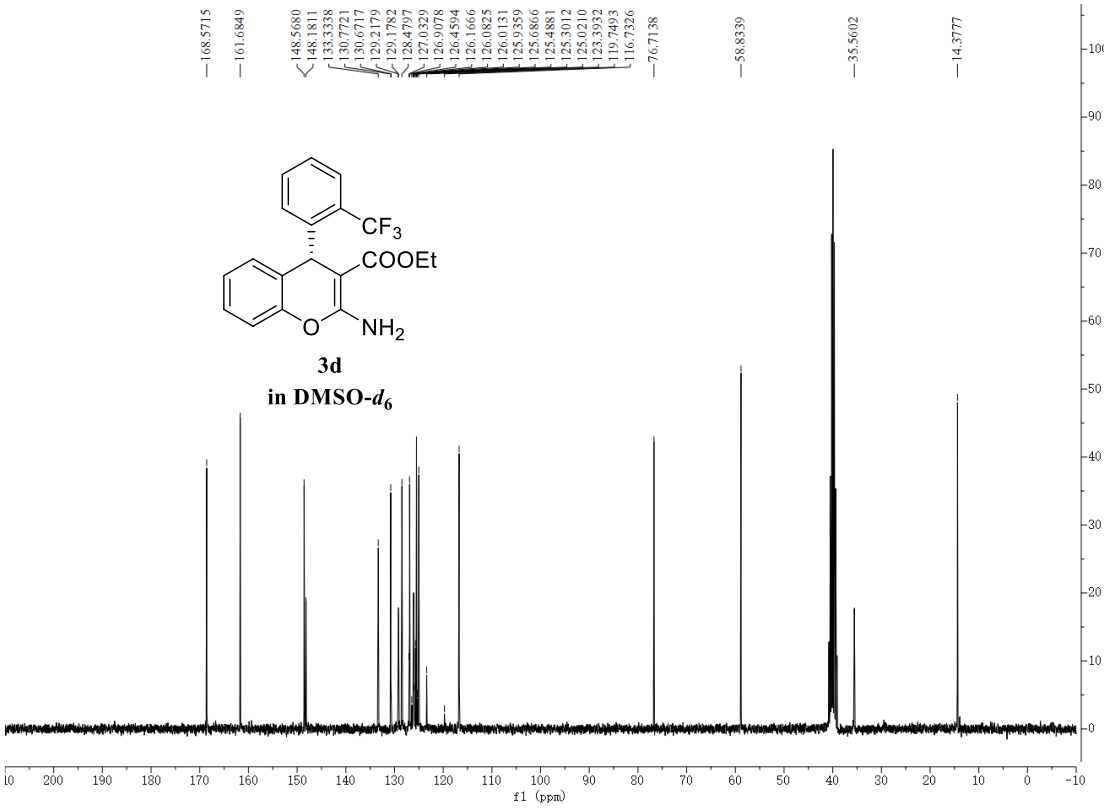

F
COOEt
O
NH2
3b
in DMSO-d6
f1 (ppm)

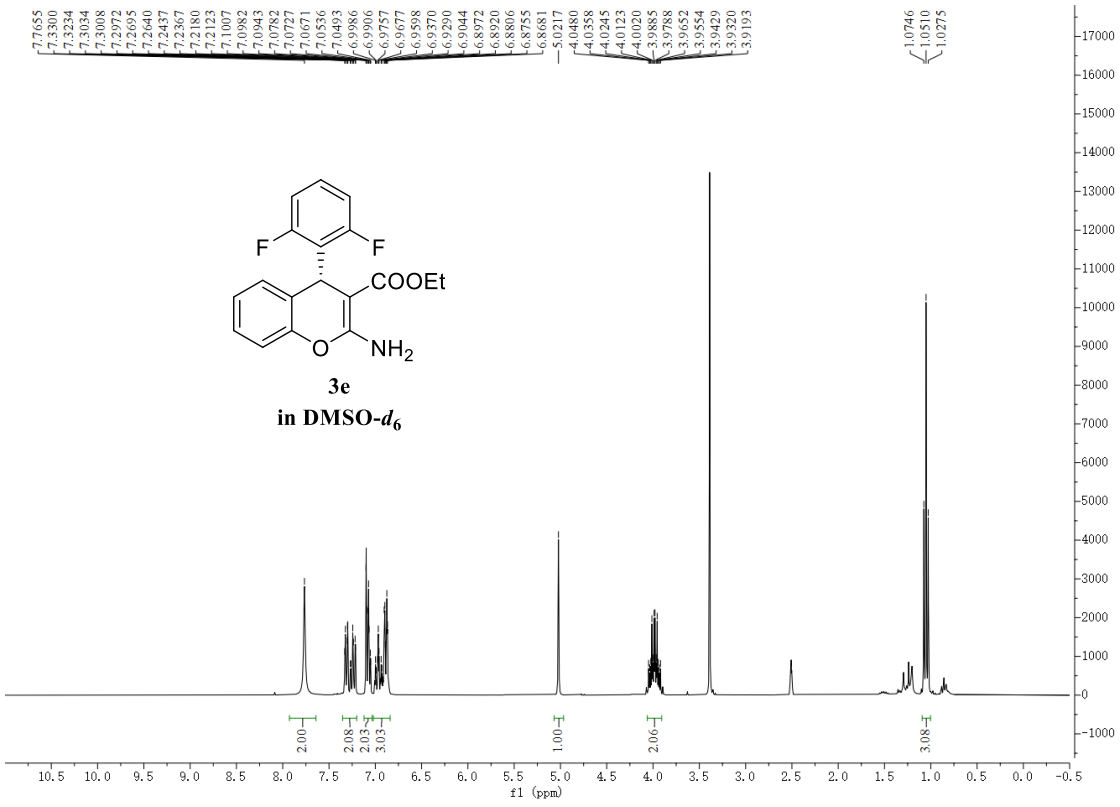

F
COOEt
O
NH2
3b
in DMSO-d6
f1 (ppm)


Me
COOEt
O
NH2
3c
in DMSO-d6
f1 (ppm)

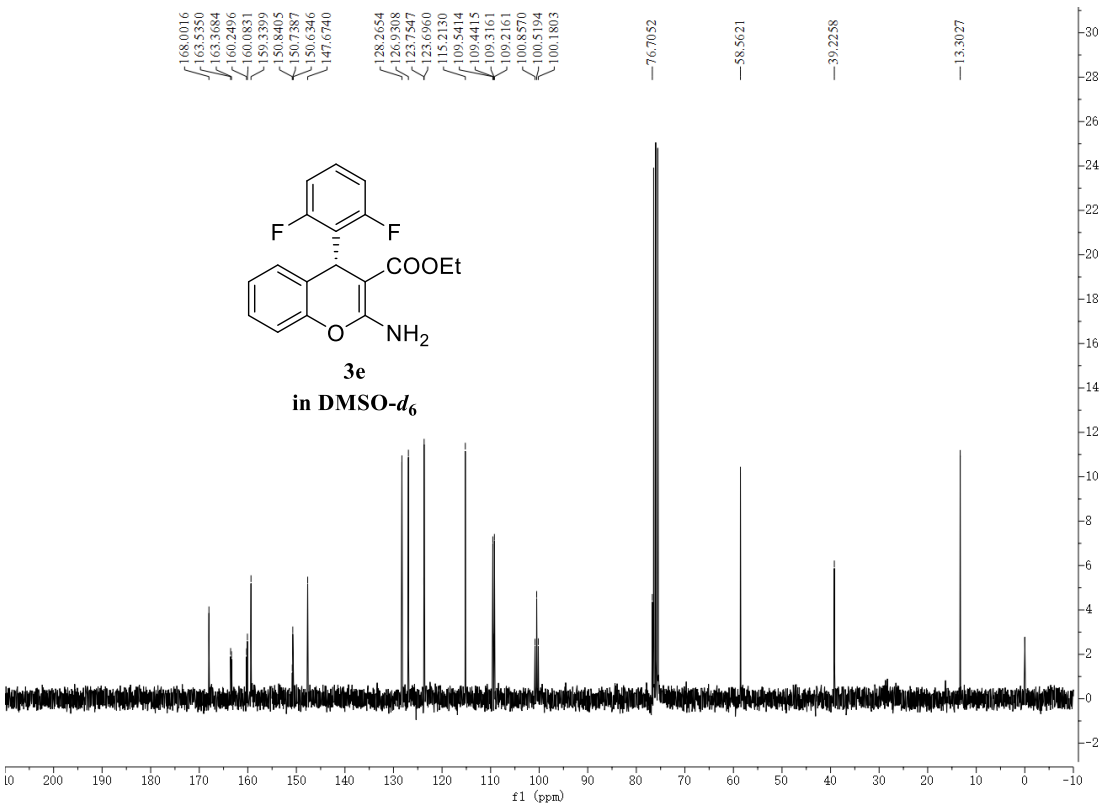

Me
COOEt
O
NH2
3c
in DMSO-d6
f1 (ppm)


CF3
COOEt
O
NH2
3d
in DMSO-d6
f1 (ppm)

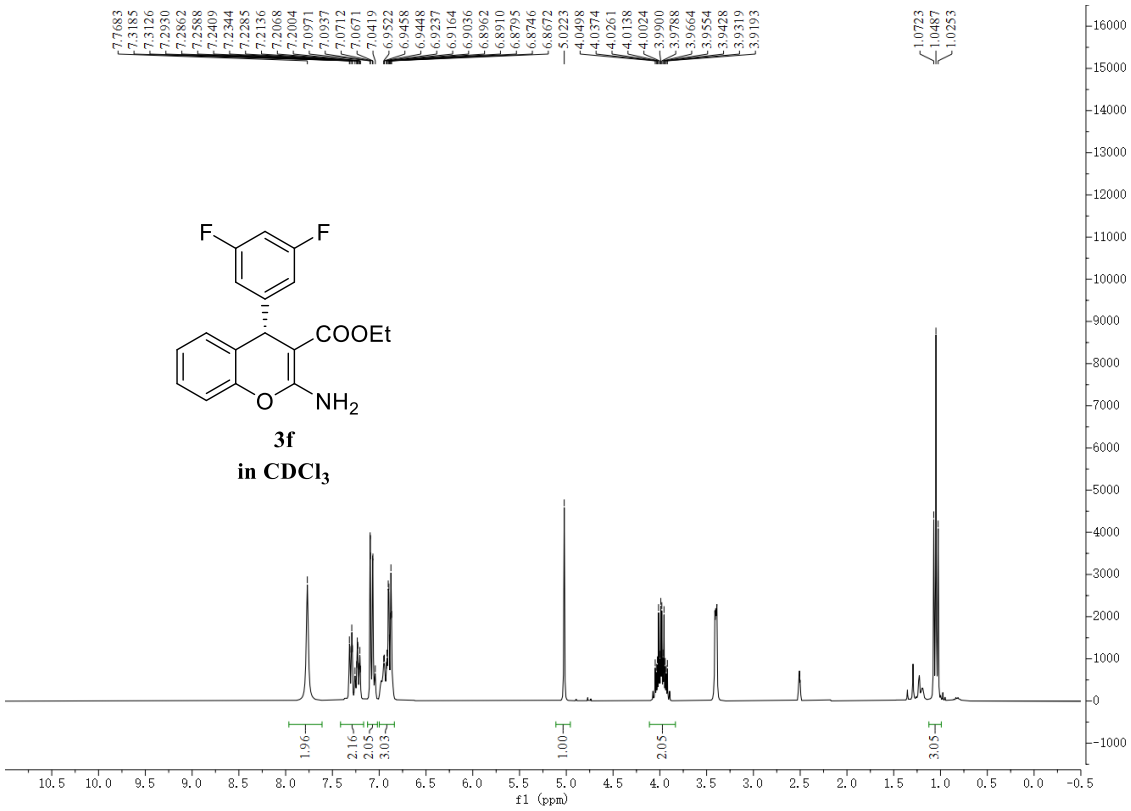

CF3
COOEt
O
NH2
3d
in DMSO-d6
f1 (ppm)



3e
in DMSO-d_6



3e
in DMSO-d_6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7.2409
7.2344
7.2285
7.2136
7.2068
7.2004
7.0971
7.0937
7.0712
7.0671
7.0419
6.9522
6.9458
6.9448
6.9237
6.9164
6.9036
6.8962
6.8910
6.8795
6.8746
6.8672
5.0223
4.0498
4.0374
4.0261
4.0138
4.0024
3.9900
3.9788
3.9664
3.9554
3.9428
3.9319
3.9193
1.0723
1.0487
1.0253
F
F
COOEt
O
NH2
3f
in CDCl3
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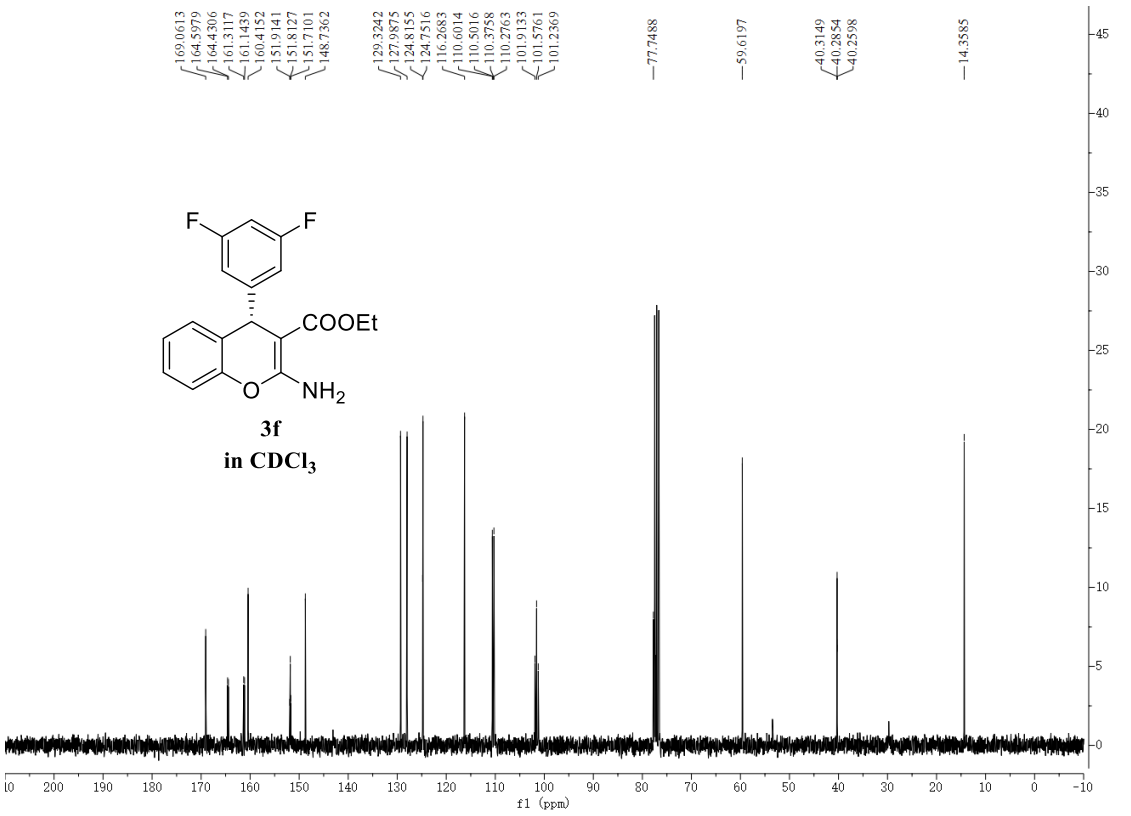
2.16
2.05
3.03
1.00
2.05
3.05
f1 (ppm)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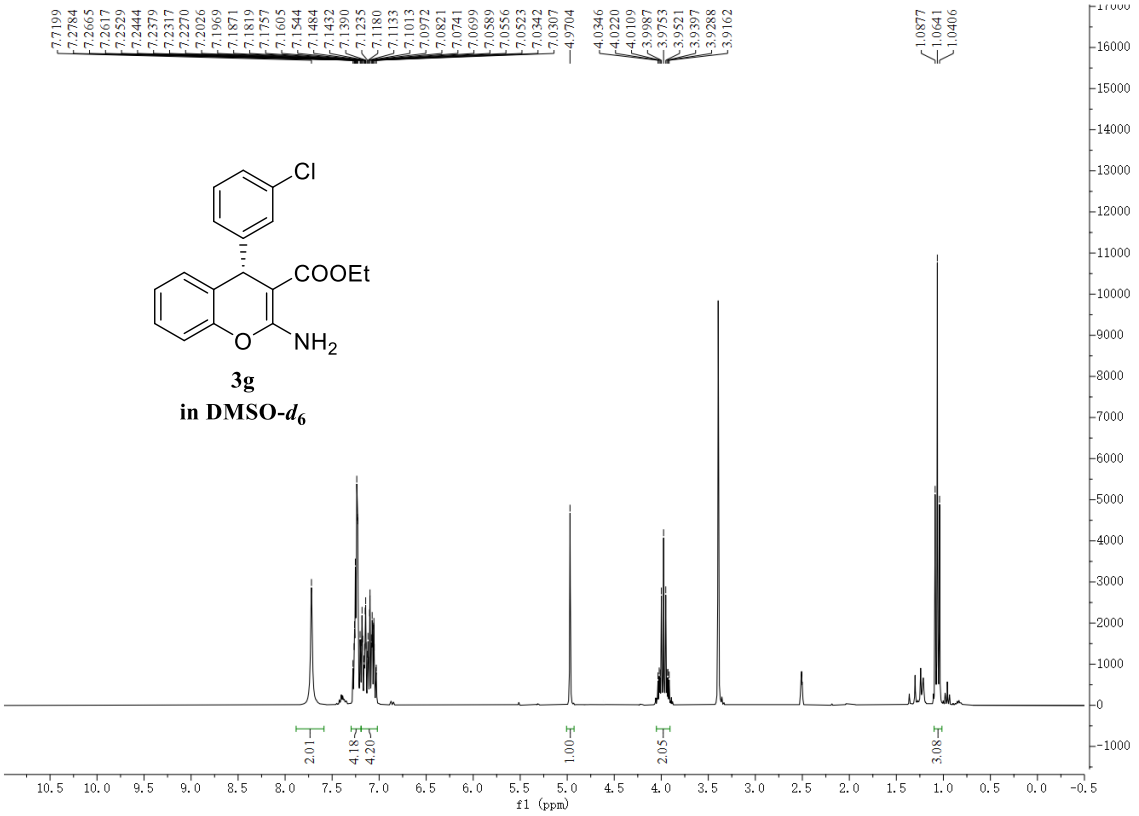
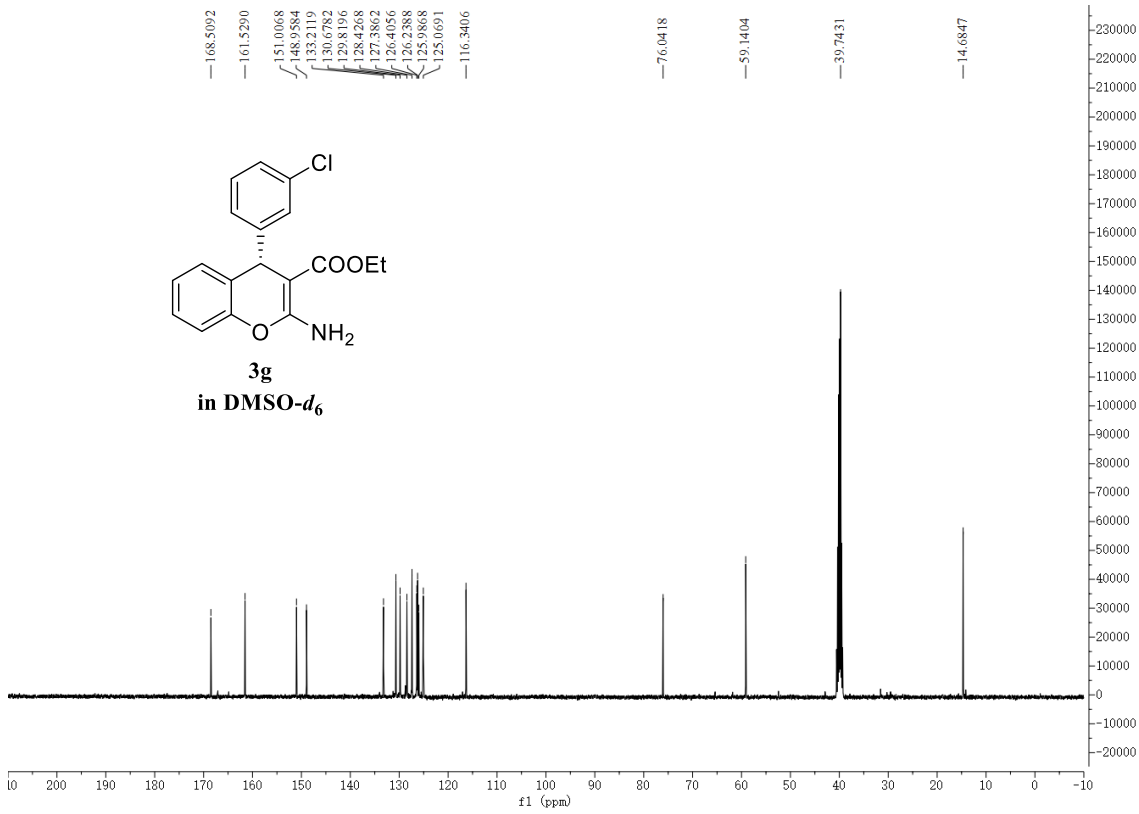
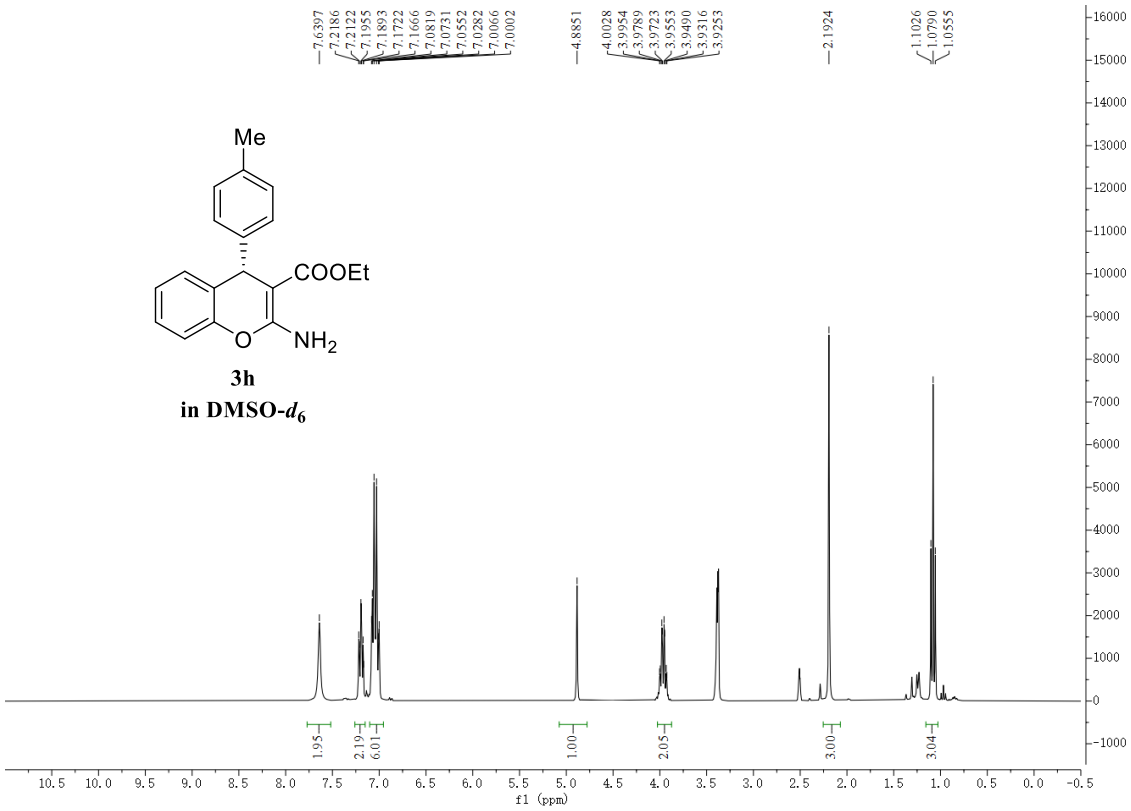
164.4306
161.3117
161.1439
160.4152
151.9141
151.8127
151.7101
148.7362
129.3242
127.9875
124.8155
124.7516
116.2683
110.6014
110.5016
110.3758
110.2763
101.9133
101.5761
101.2369
77.7488
59.6197
40.3149
40.2854
40.2598
14.3585
F
F
COOEt
O
NH2
3f
in CDCl3
f1 (ppm)


Cl
COOEt
O
NH2
3g
in DMSO-d6
f1 (ppm)


Cl
COOEt
O
NH2
3g
in DMSO-d6
f1 (ppm)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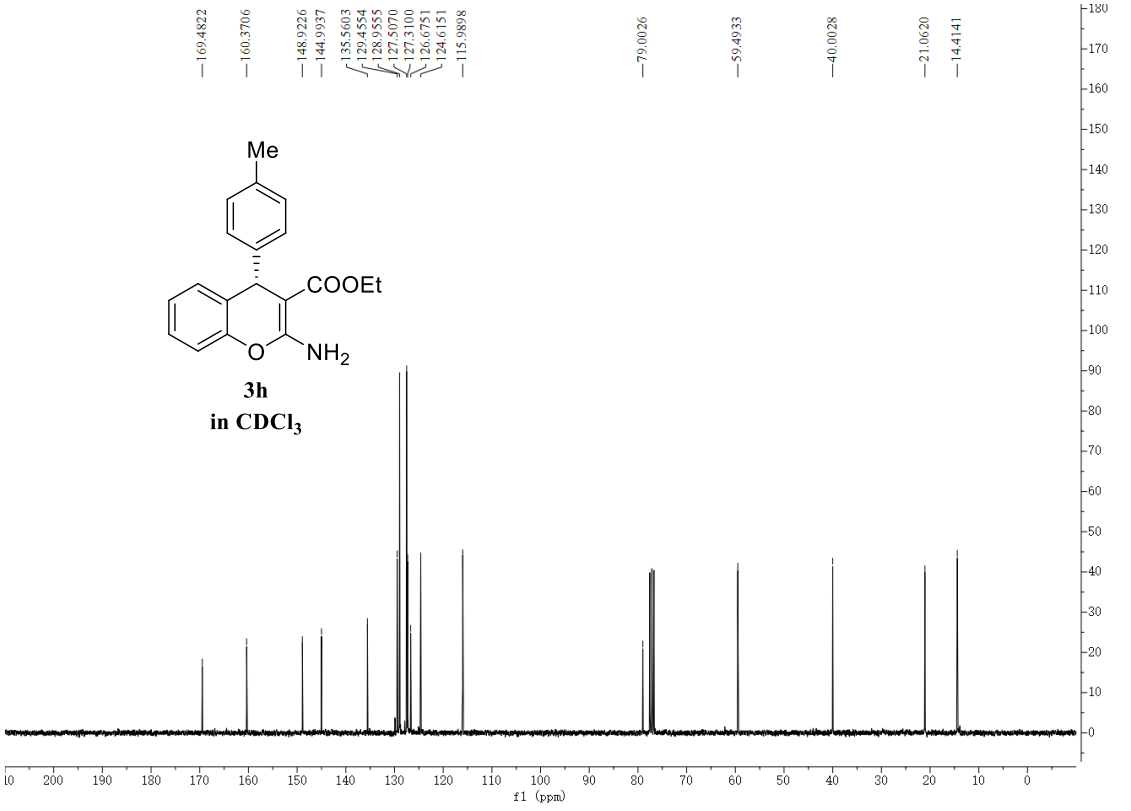
7.0282
7.0066
7.0002
4.8851
4.0028
3.9954
3.9789
3.9723
3.9553
3.9490
3.9316
3.9253
2.1924
1.1026
1.0790
1.0555
Me
COOEt
O
NH2
3h
in DMSO-d6
1.95
2.19
6.01
1.00
2.05
3.00
3.04
f1 (ppm)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144.9937
135.5603
129.4554
128.9555
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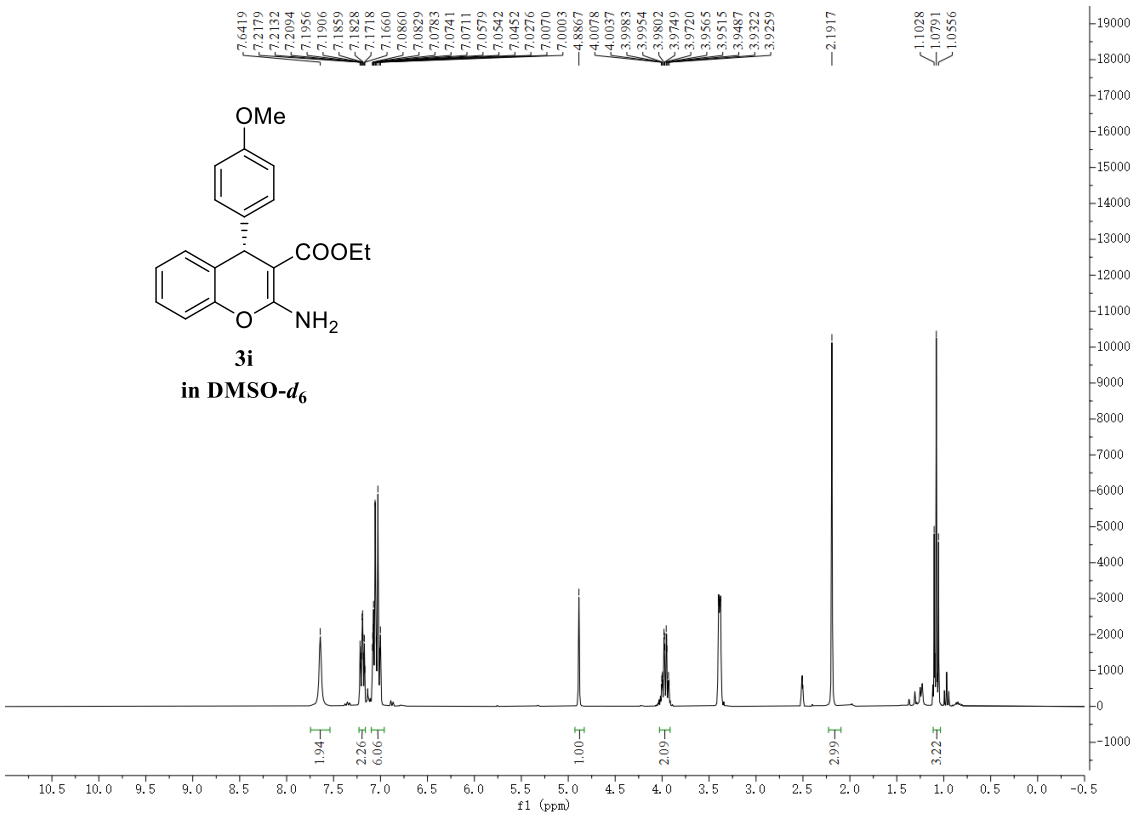
126.6751
124.6151
115.9898
79.0026
59.4933
40.0028
21.0620
14.4141
Me
COOEt
O
NH2
3h
in CDCl3
f1 (ppm)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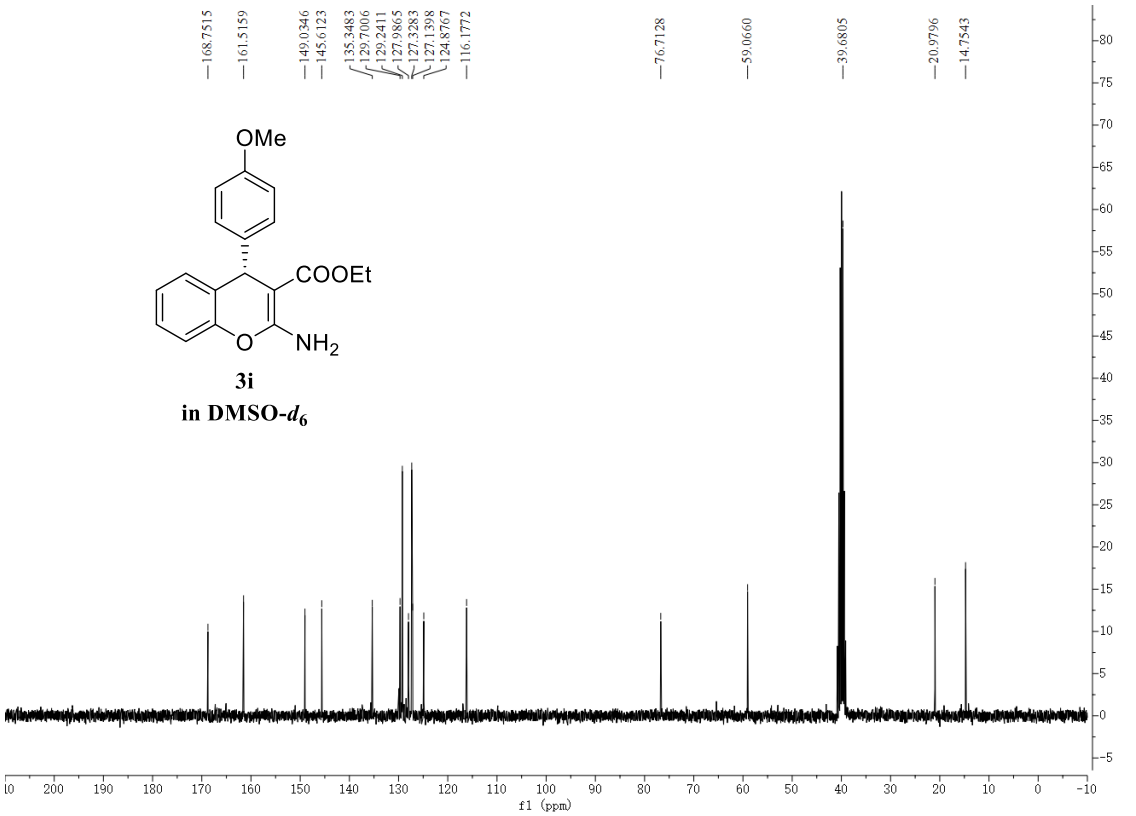
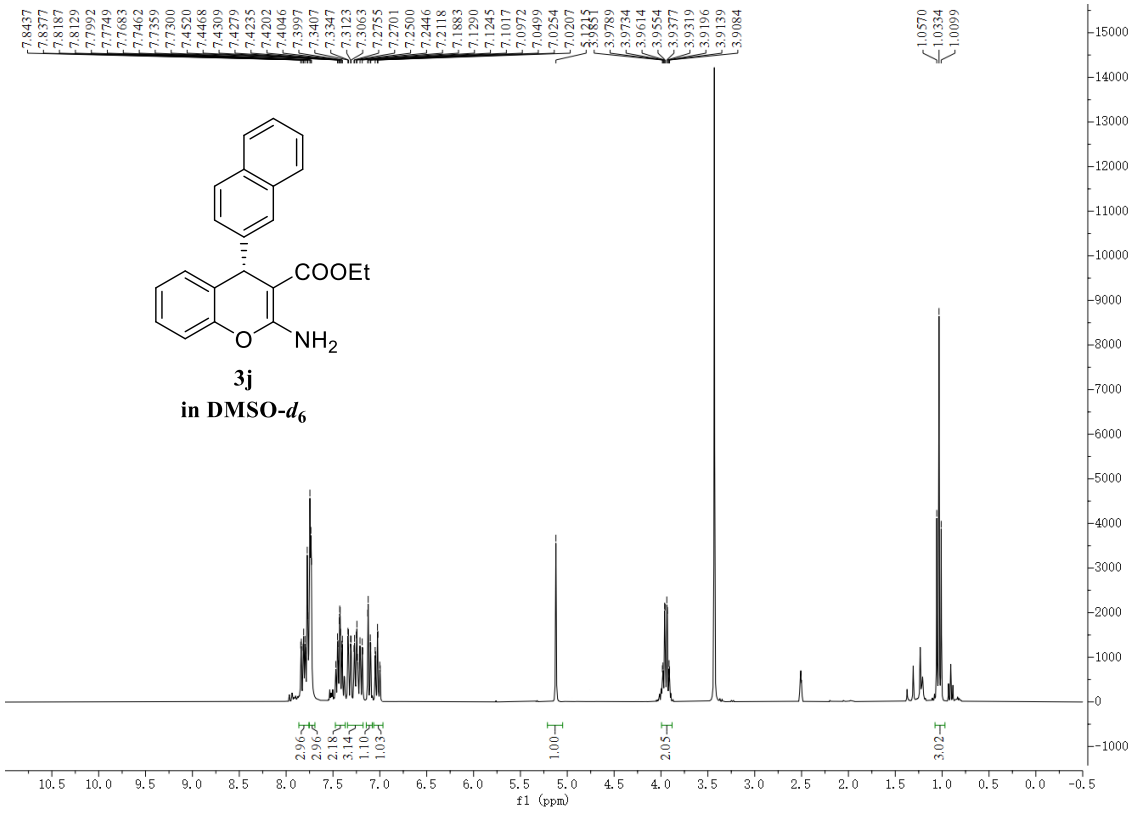
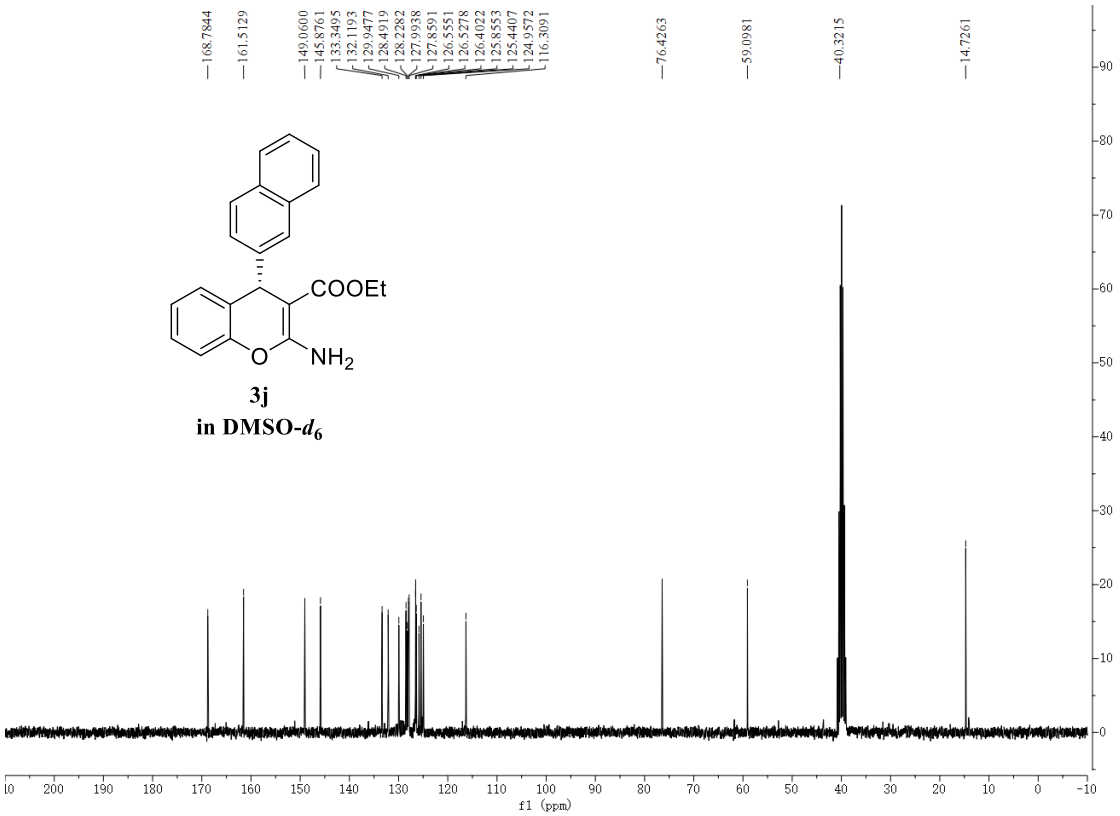
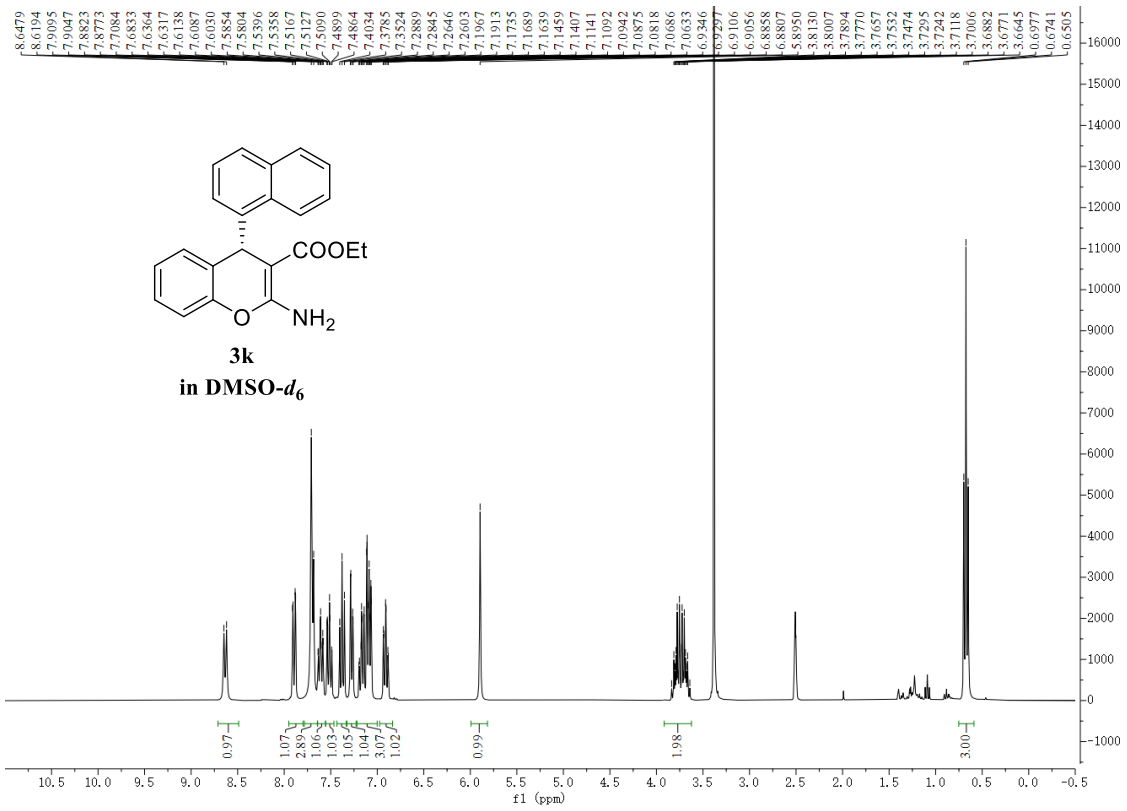
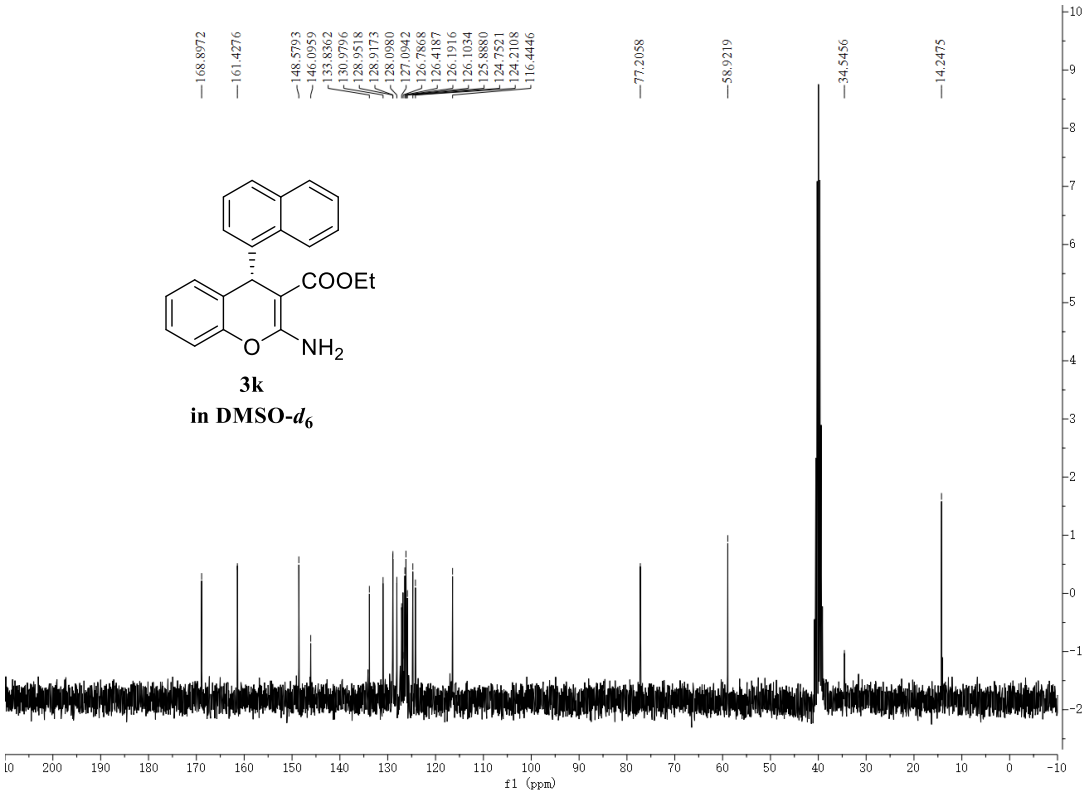
COOEt
O
NH2
3i
in DMSO-d6
f1 (ppm)

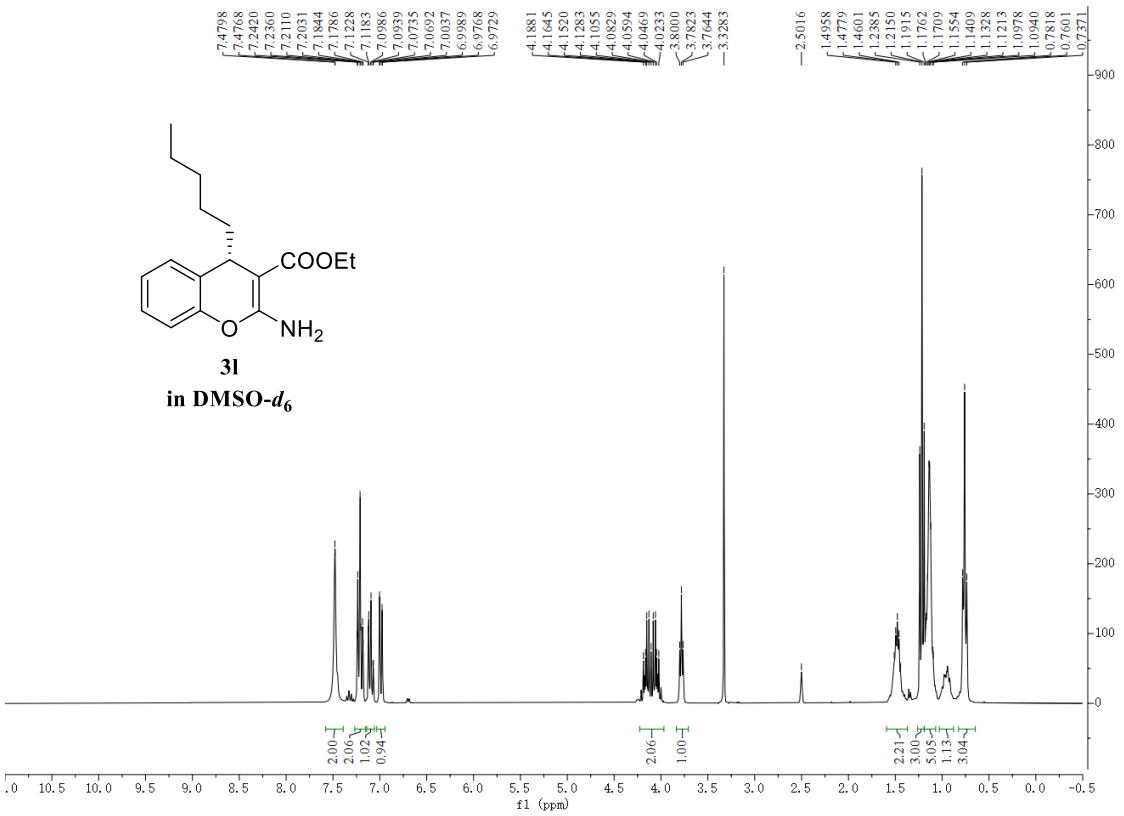

OMe
COOEt
O
NH2
3i
in DMSO-d6
f1 (ppm)


COOEt
NH2
3j
in DMSO-d6
f1 (ppm)


COOEt
NH2
3j
in DMSO-d6
f1 (ppm)

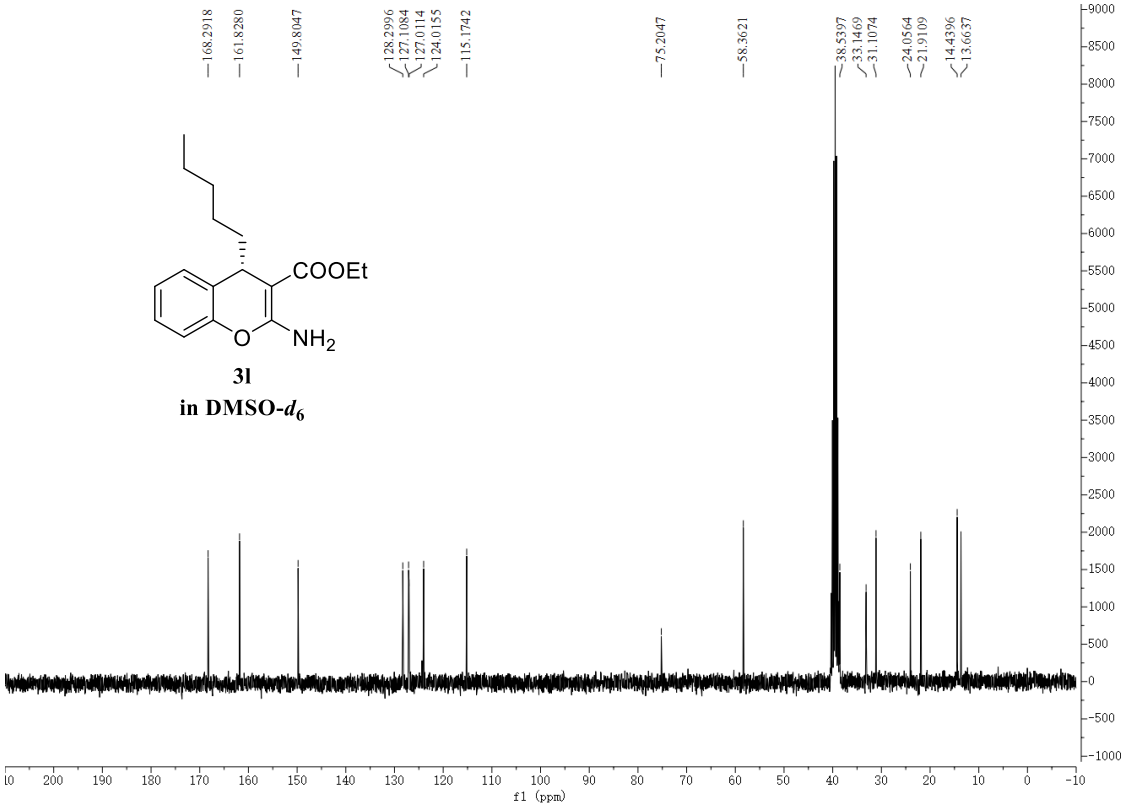

COOEt
O
NH2
3k
in DMSO-d6
f1 (ppm)


COOEt
O
NH2
3k
in DMSO-d6
f1 (ppm)



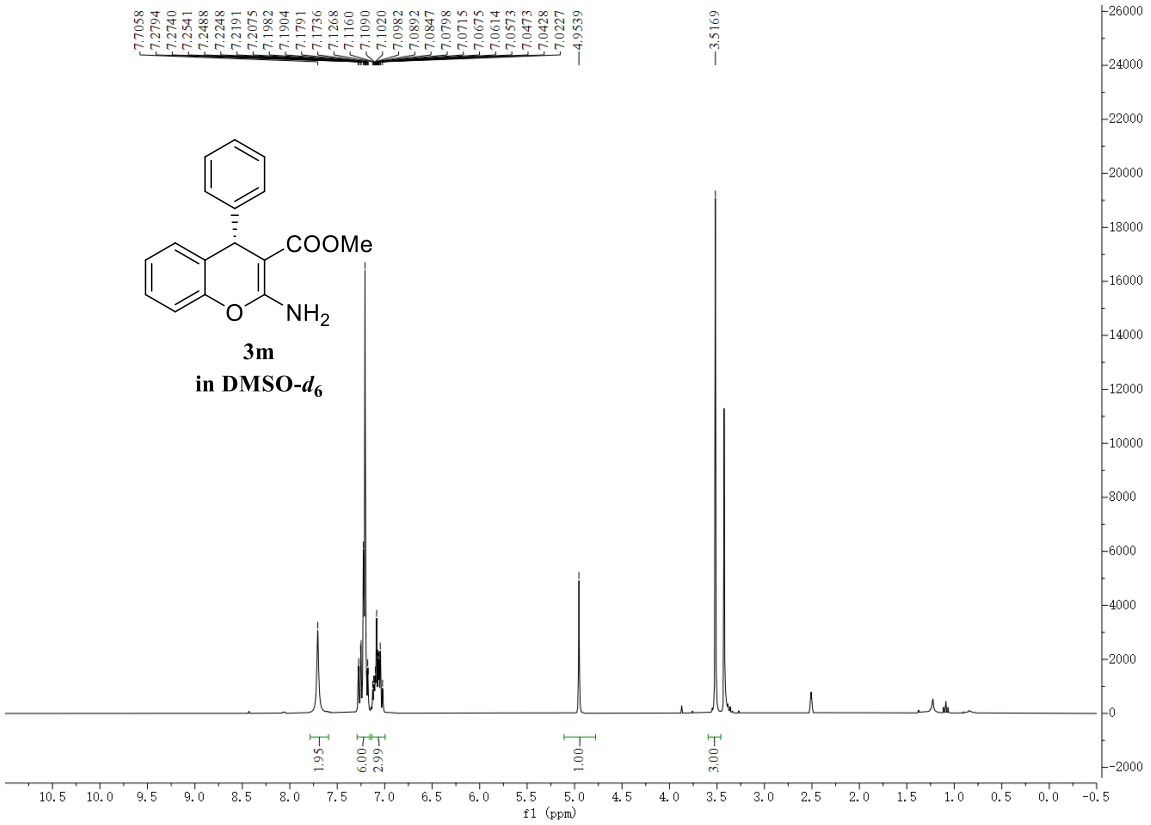
3l

in DMSO-d_6



3l

in DMSO-d_6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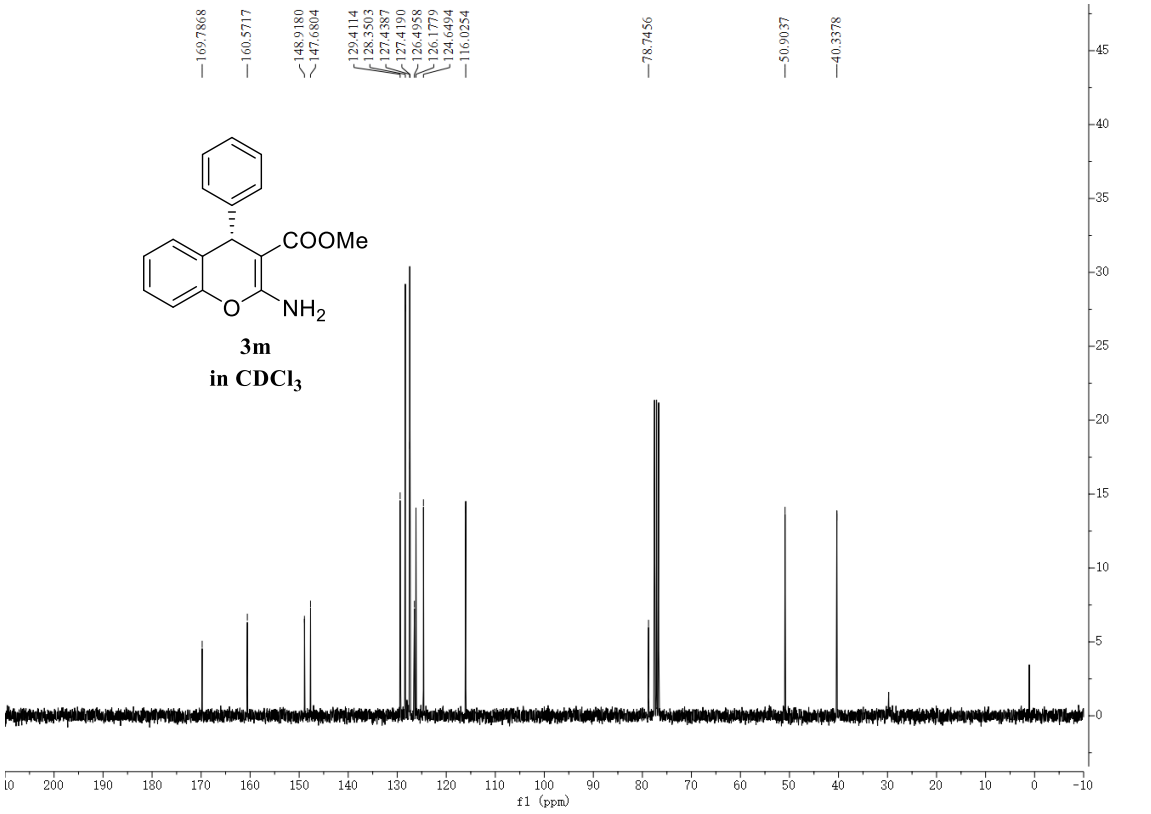
7.2191
7.2075
7.1982
7.1904
7.1791
7.1736
7.1268
7.1160
7.1090
7.1020
7.0982
7.0892
7.0847
7.0798
7.0715
7.0675
7.0614
7.0573
7.0473
7.0428
7.0227
4.9539
3.5169
COOMe
NH2
O
3m
in DMSO-d6
1.95
6.00
2.99
1.00
3.00
f1 (ppm)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127.4190
126.4958
126.1779
124.6494
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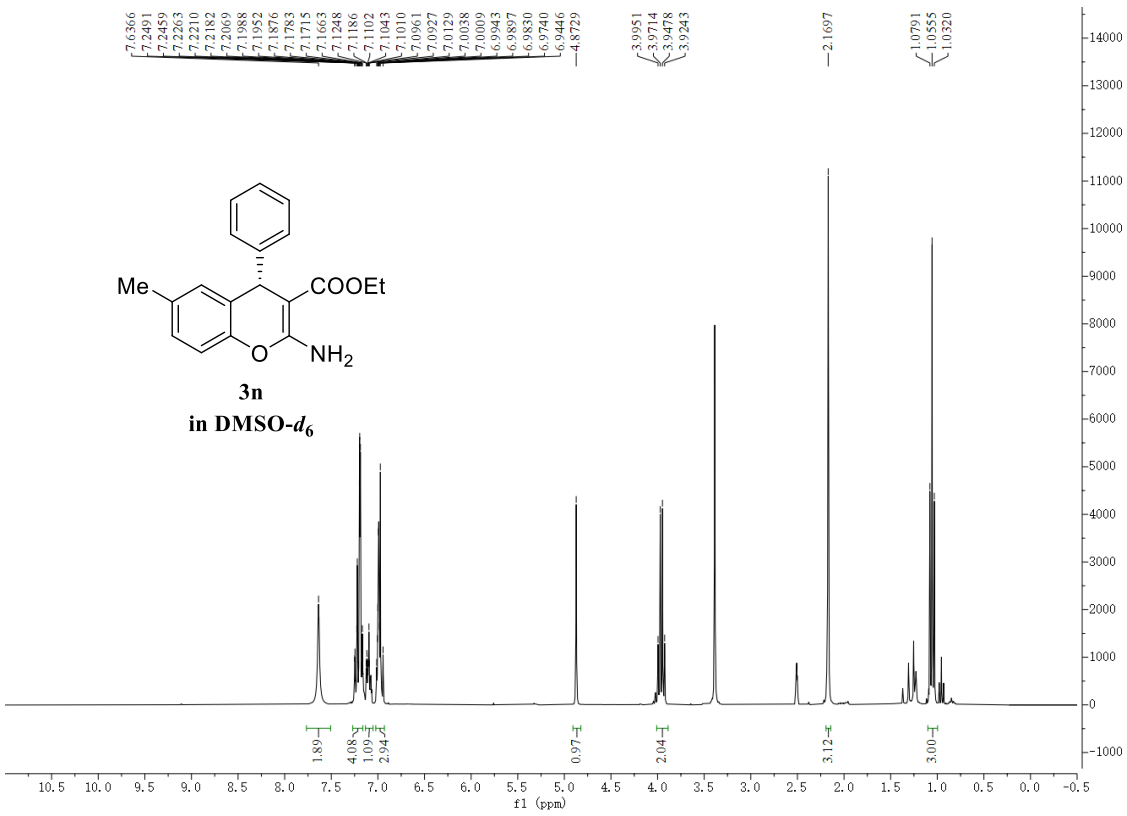
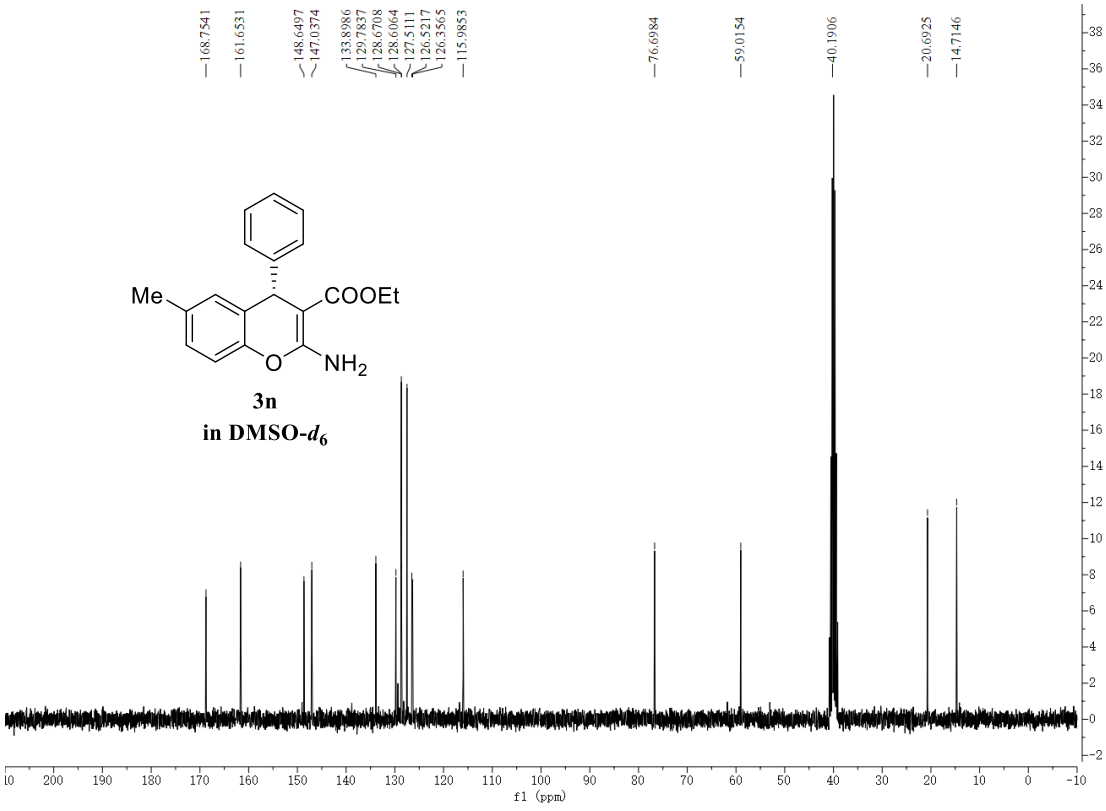
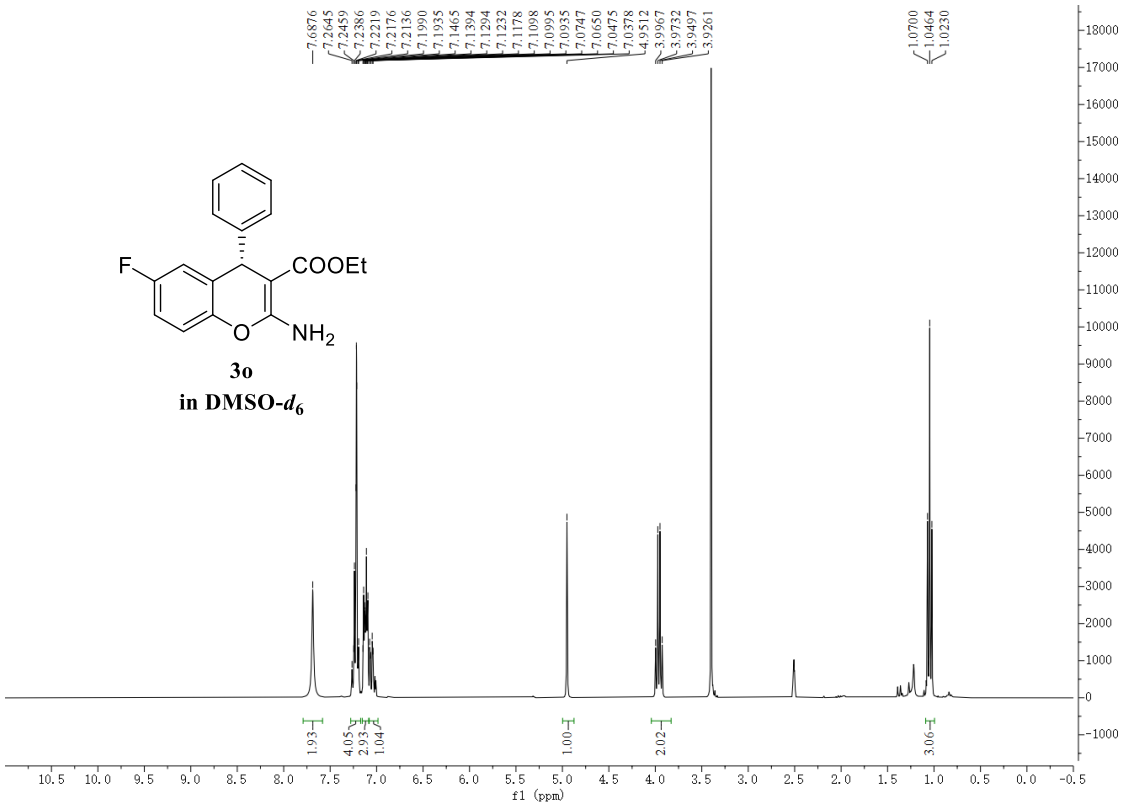
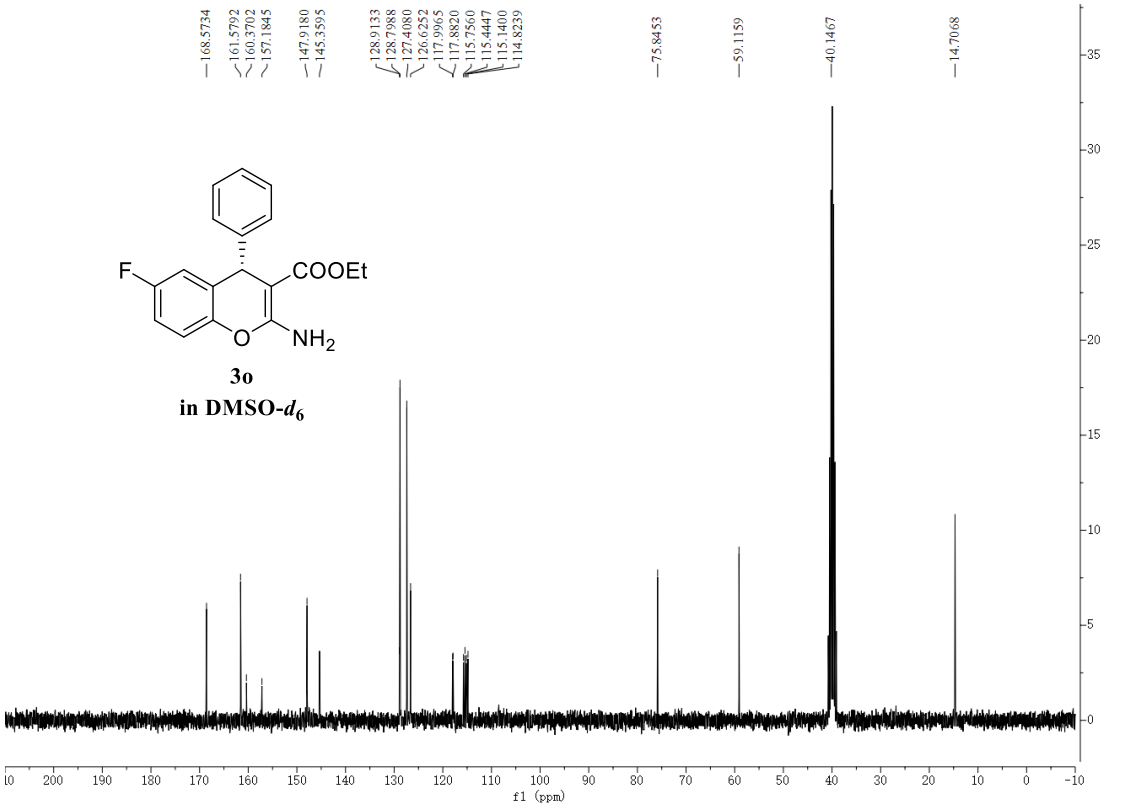
78.7456
50.9037
40.3378
COOMe
NH2
O
3m
in CDCl3
f1 (ppm)


Me
COOEt
O
NH2
3n
in DMSO-d6
f1 (ppm)

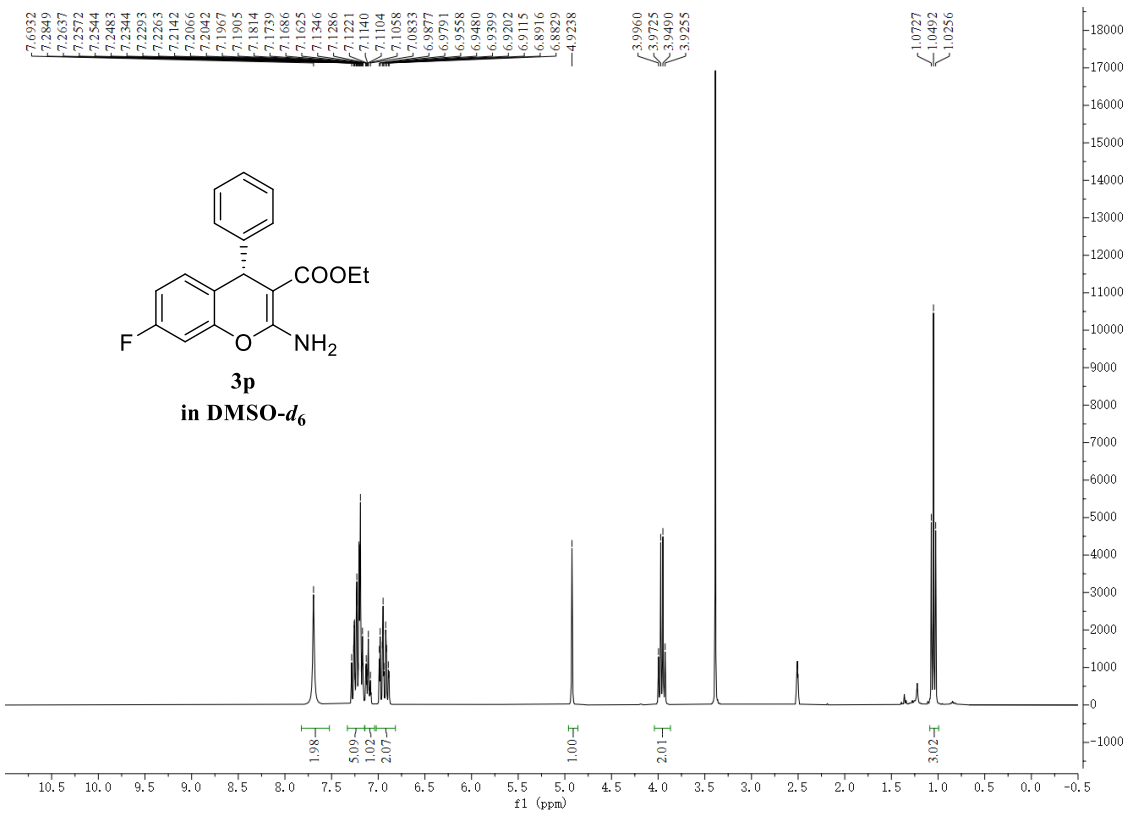

Me
COOEt
O
NH2
3n
in DMSO-d6
f1 (ppm)



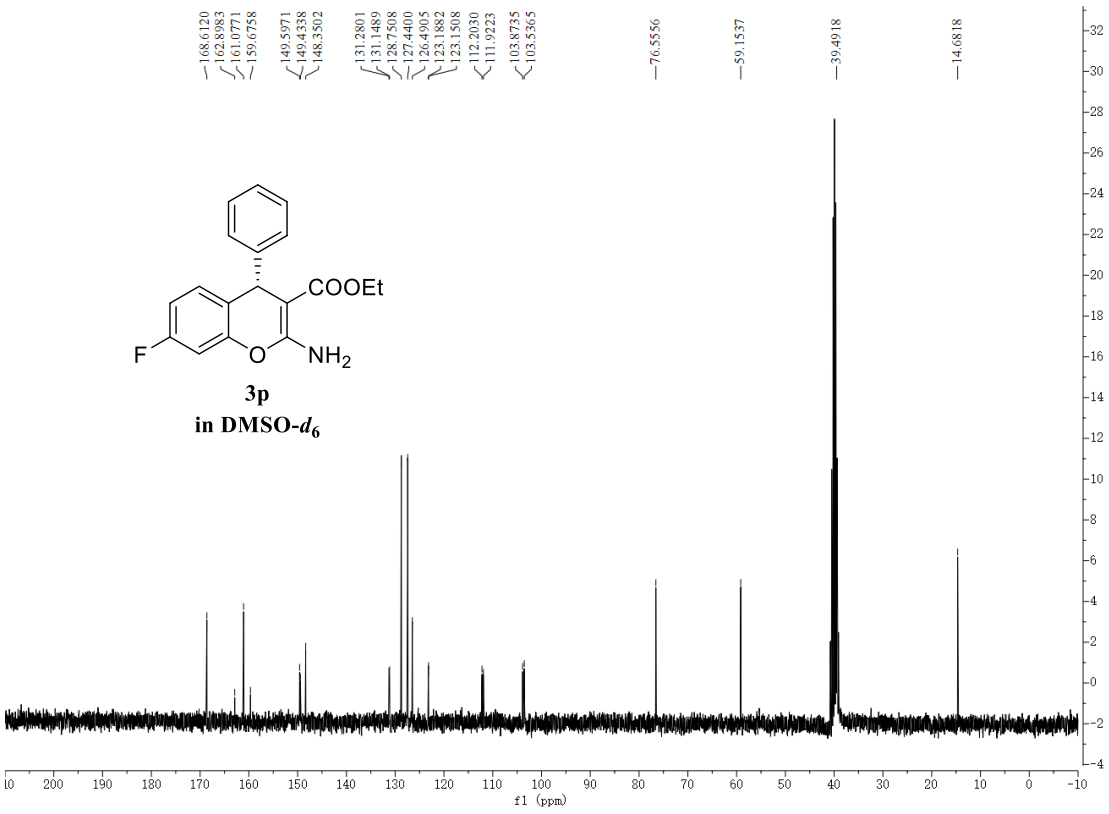
3o
in DMSO-d_6



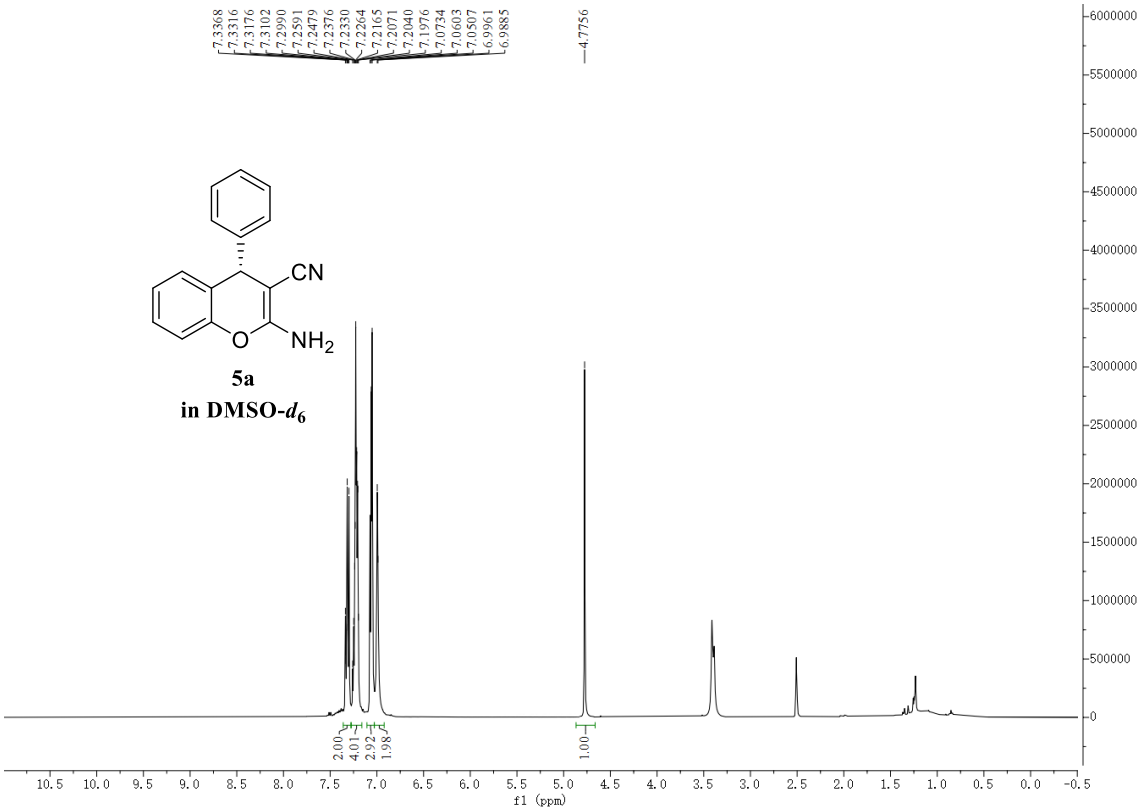
3o
in DMSO-d_6



3p
in DMSO-d_6



3p
in DMSO-d_6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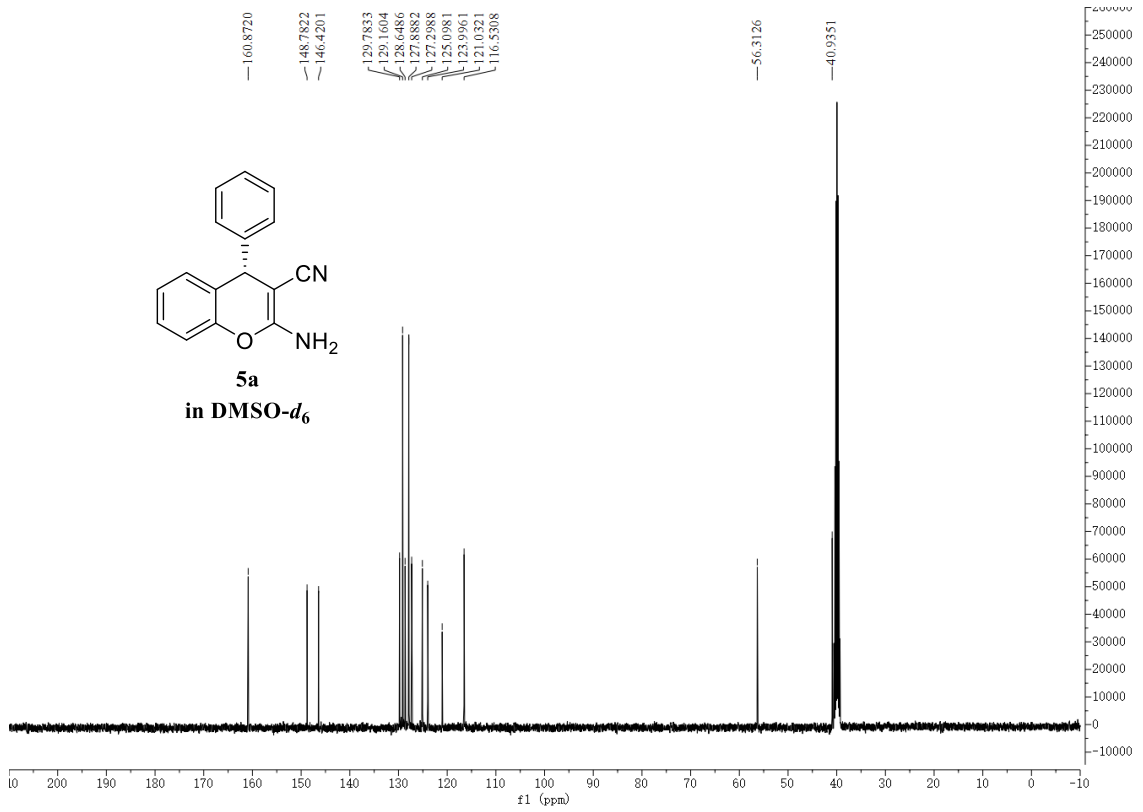
7.2330
7.2264
7.2165
7.2071
7.2040
7.1976
7.0734
7.0603
7.0507
6.9961
6.9885
4.7756
CN
NH2
O
5a
in DMSO-d6
2.00
4.01
2.92
1.98
1.00
f1 (ppm)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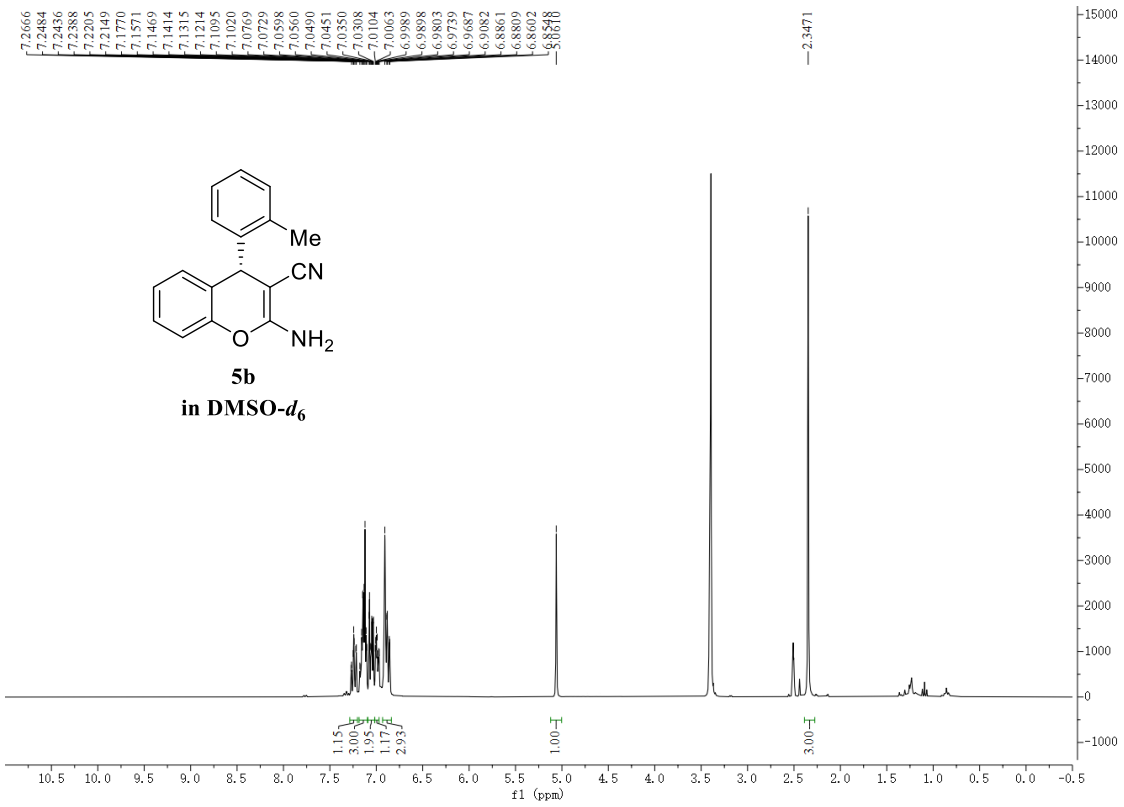
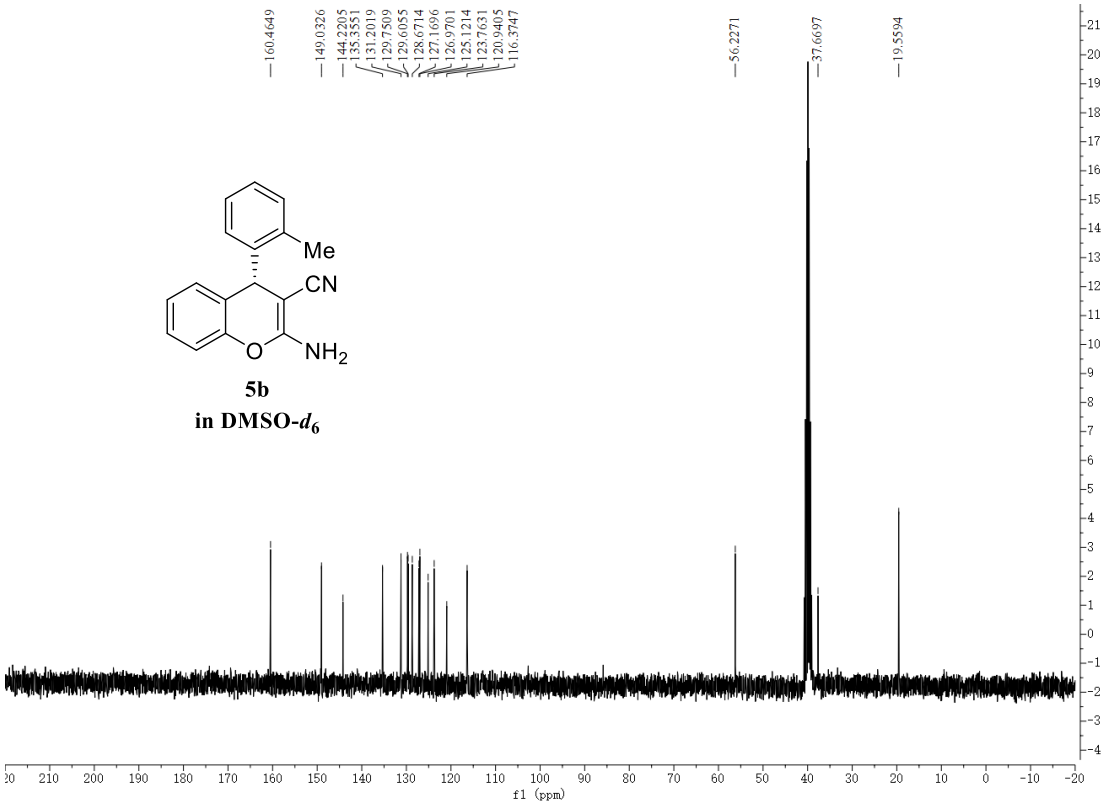
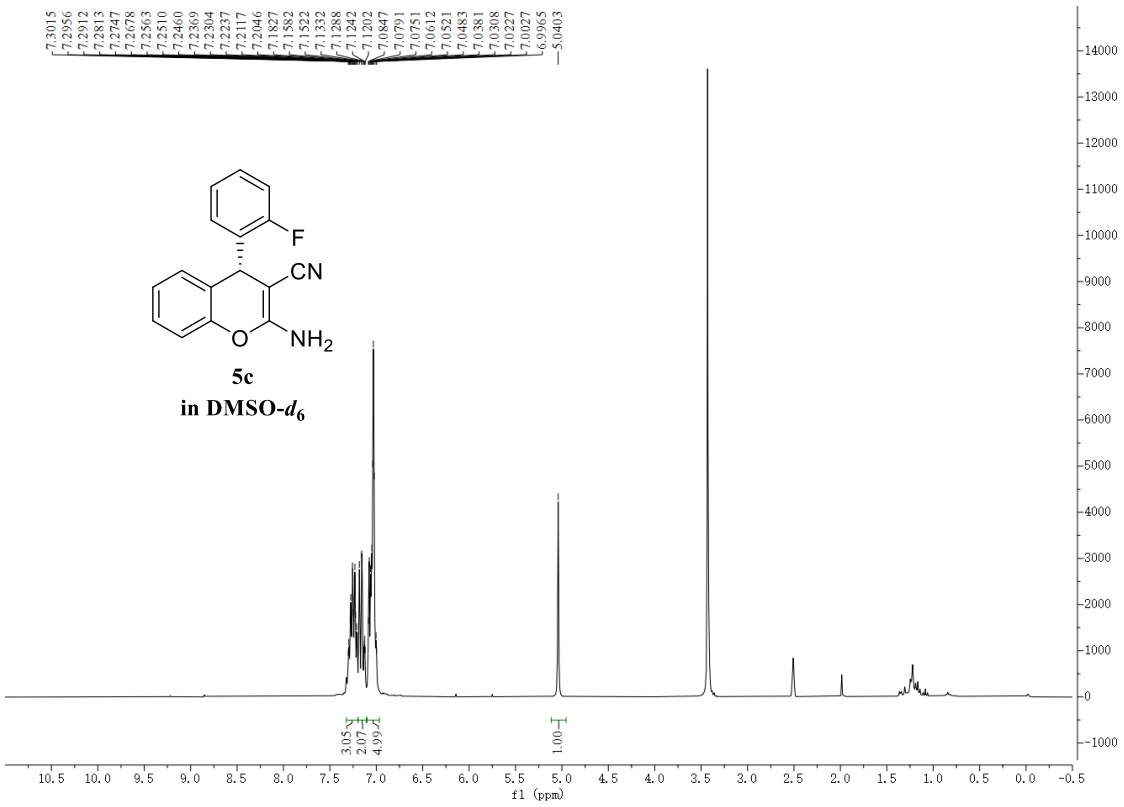
146.4201
129.7833
129.1604
128.6486
127.8882
127.2988
125.0981
123.9961
121.0321
116.5308
56.3126
40.9351
CN
NH2
O
5a
in DMSO-d6
f1 (ppm)


Me
CN
O
NH2
5b
in DMSO-d6
f1 (ppm)


Me
CN
O
NH2
5b
in DMSO-d6
f1 (ppm)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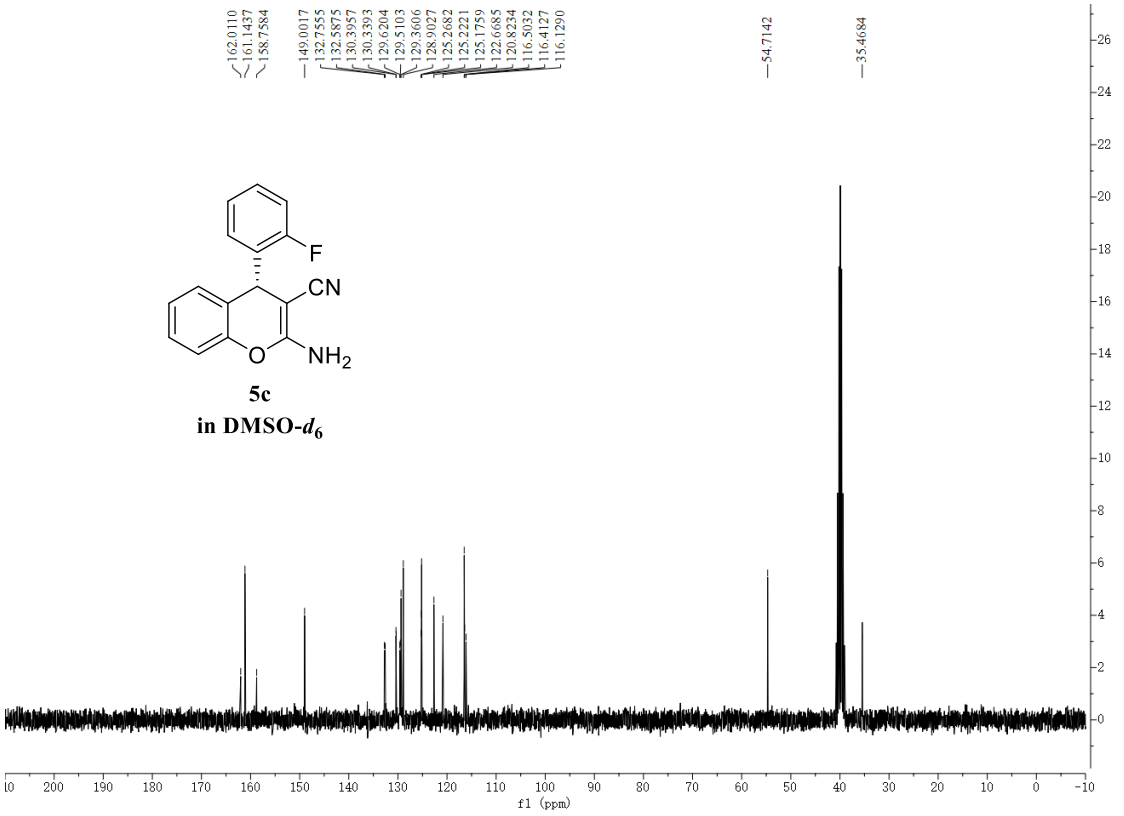
7.2747
7.2678
7.2563
7.2510
7.2460
7.2369
7.2304
7.2237
7.2117
7.2046
7.1827
7.1582
7.1522
7.1332
7.1288
7.1242
7.1202
7.0847
7.0791
7.0751
7.0612
7.0521
7.0483
7.0381
7.0308
7.0227
7.0027
6.9965
5.0403
F
CN
O
NH2
5c
in DMSO-d6
3.05
2.07
4.994
1.00
f1 (ppm)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149.0017
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132.5875
130.3957
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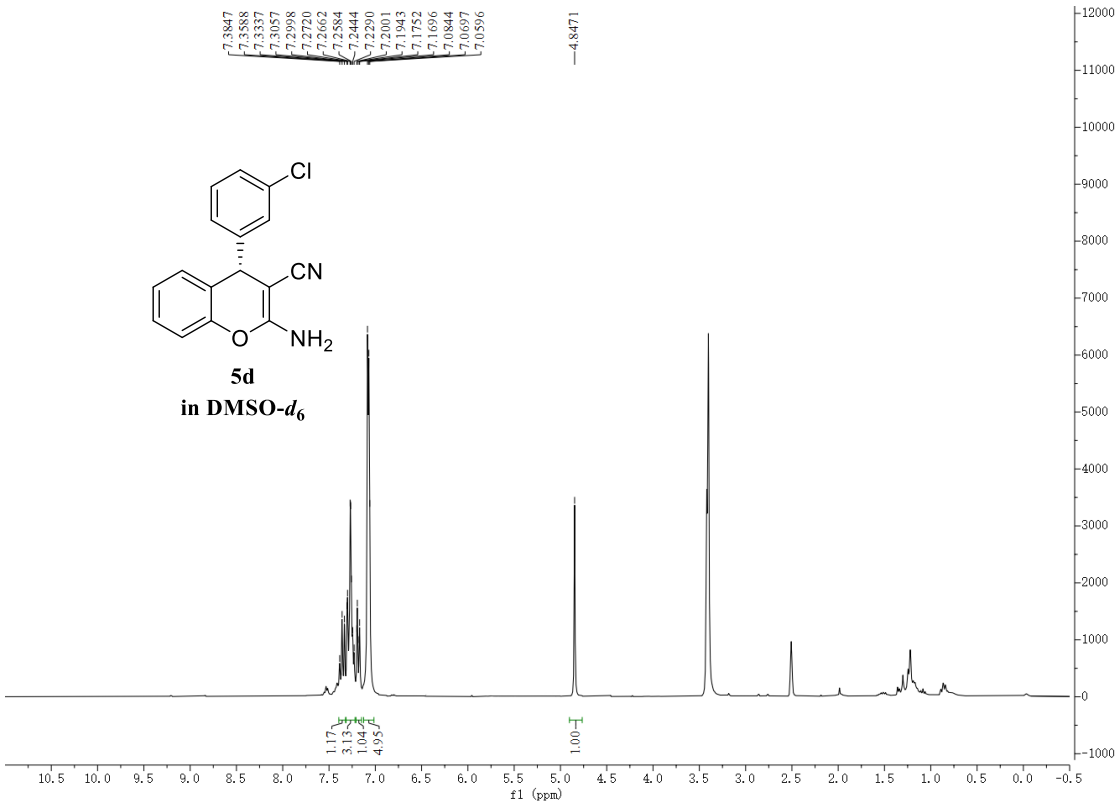
129.6204
129.5103
129.3606
128.9027
125.2682
125.2221
125.1759
122.6685
120.8234
116.5032
116.4127
116.1290
54.7142
35.4684
F
CN
O
NH2
5c
in DMSO-d6
f1 (ppm)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7.1943
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7.0844
7.0697
7.0596
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Cl
CN
O
NH2
5d
in DMSO-d6
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3.13
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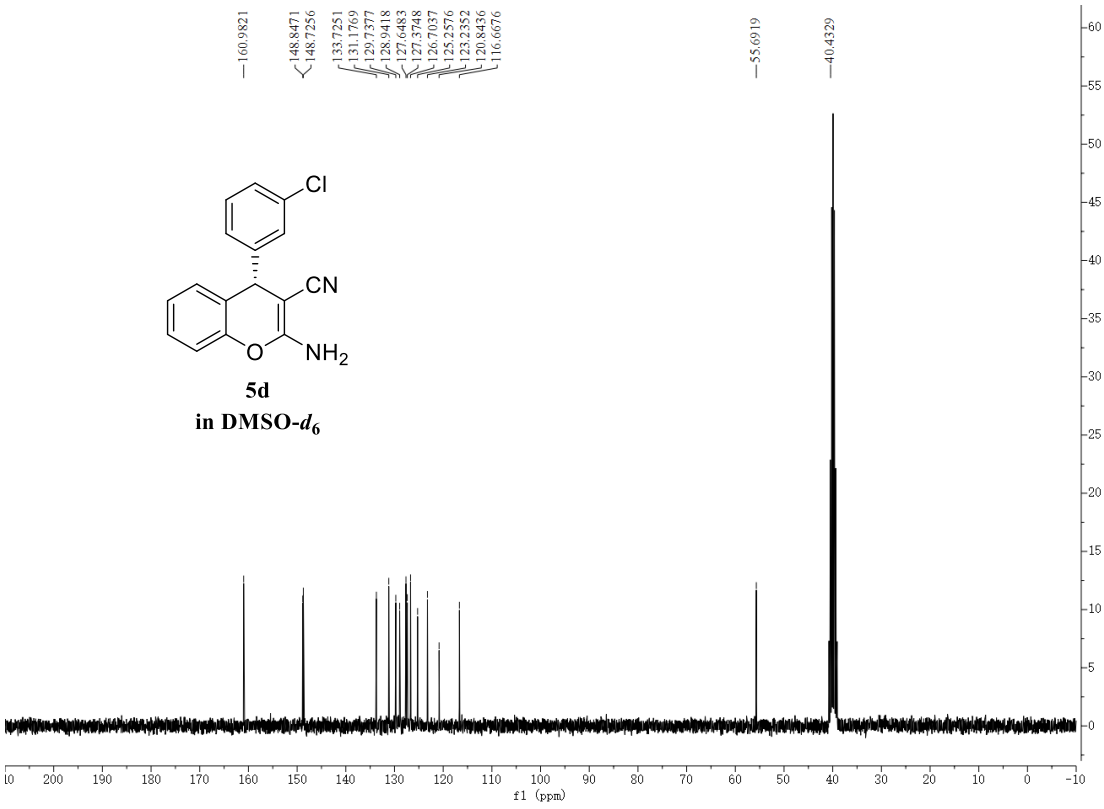
f1 (ppm)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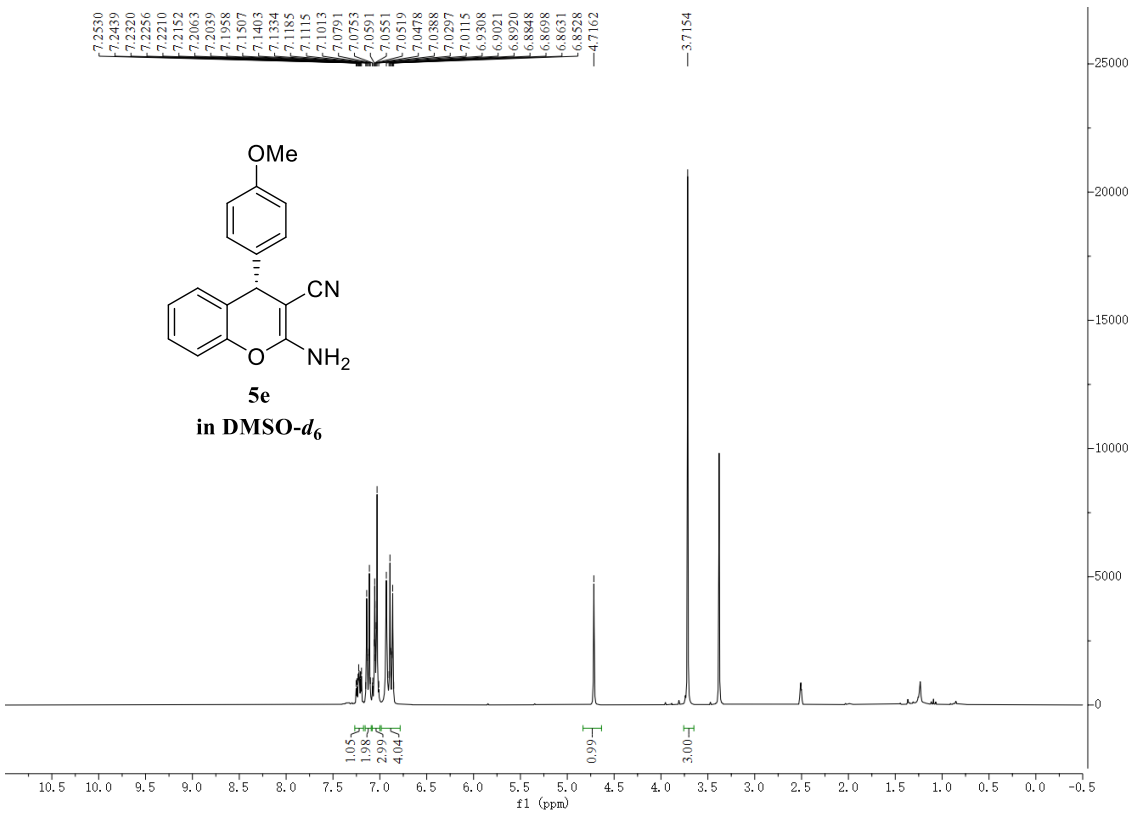
O
NH2
5d
in DMSO-d6
f1 (ppm)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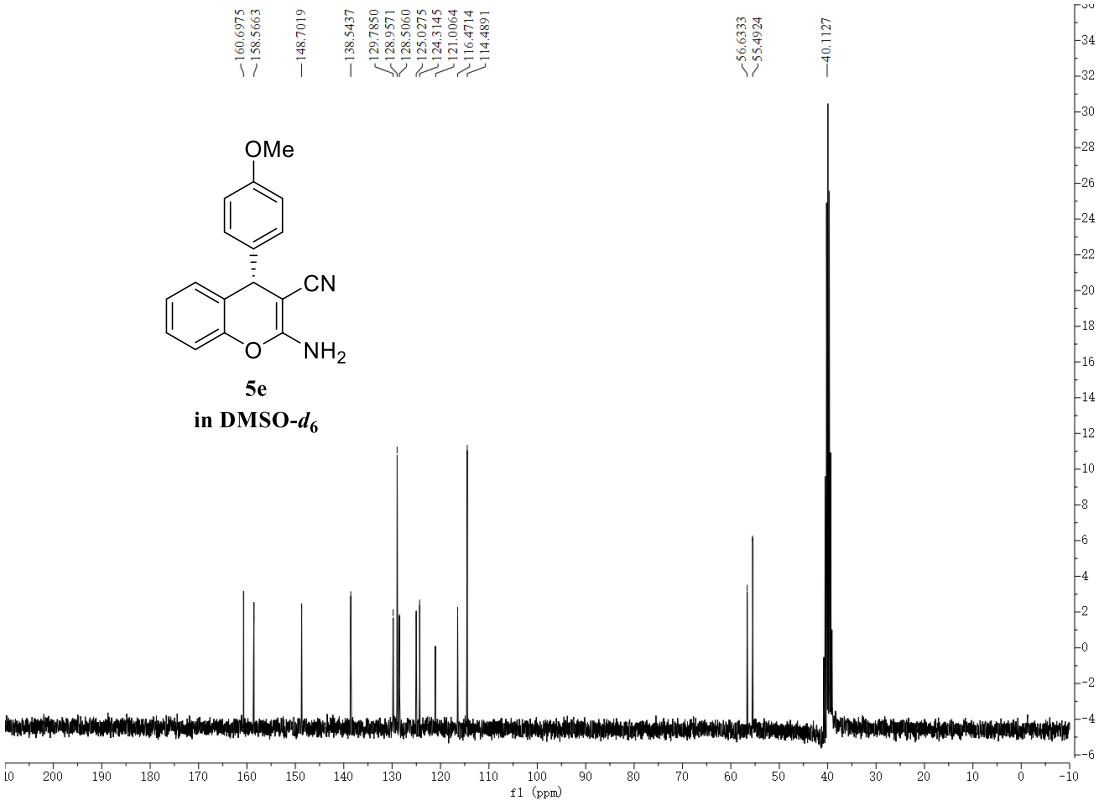
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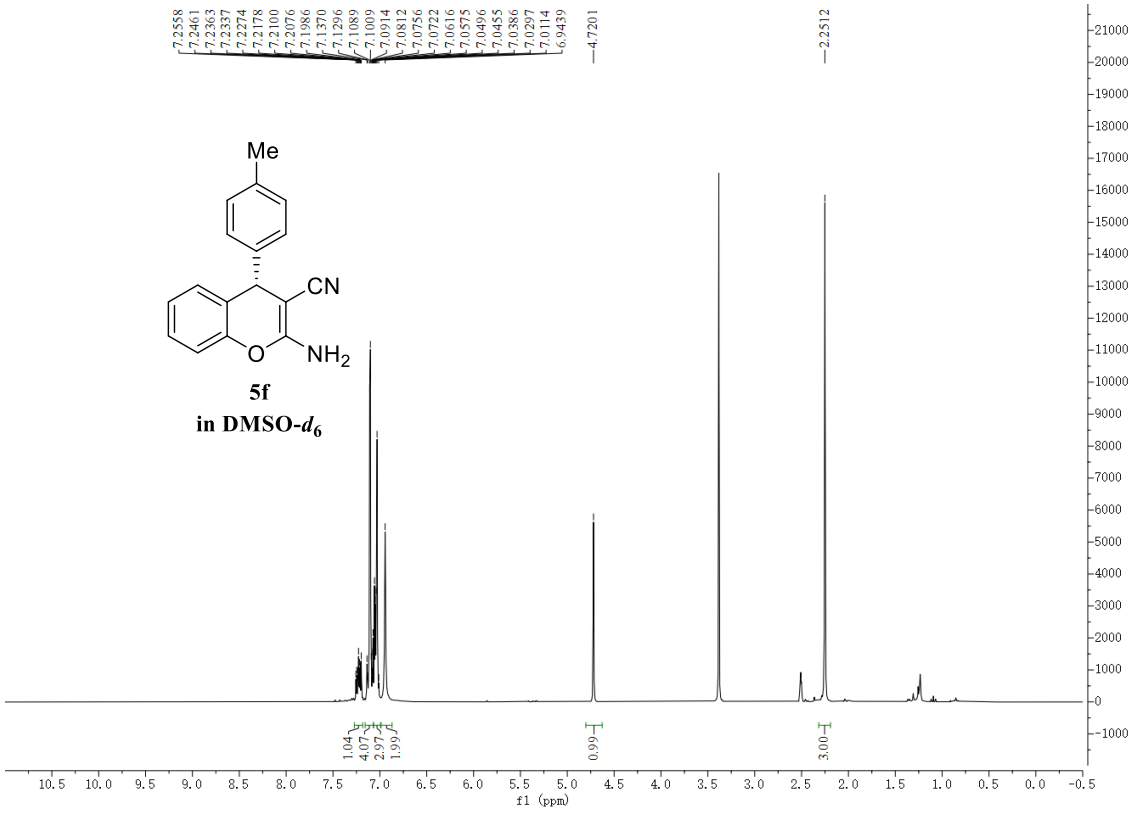
CN
O
NH2
5e
in DMSO-d6
f1 (ppm)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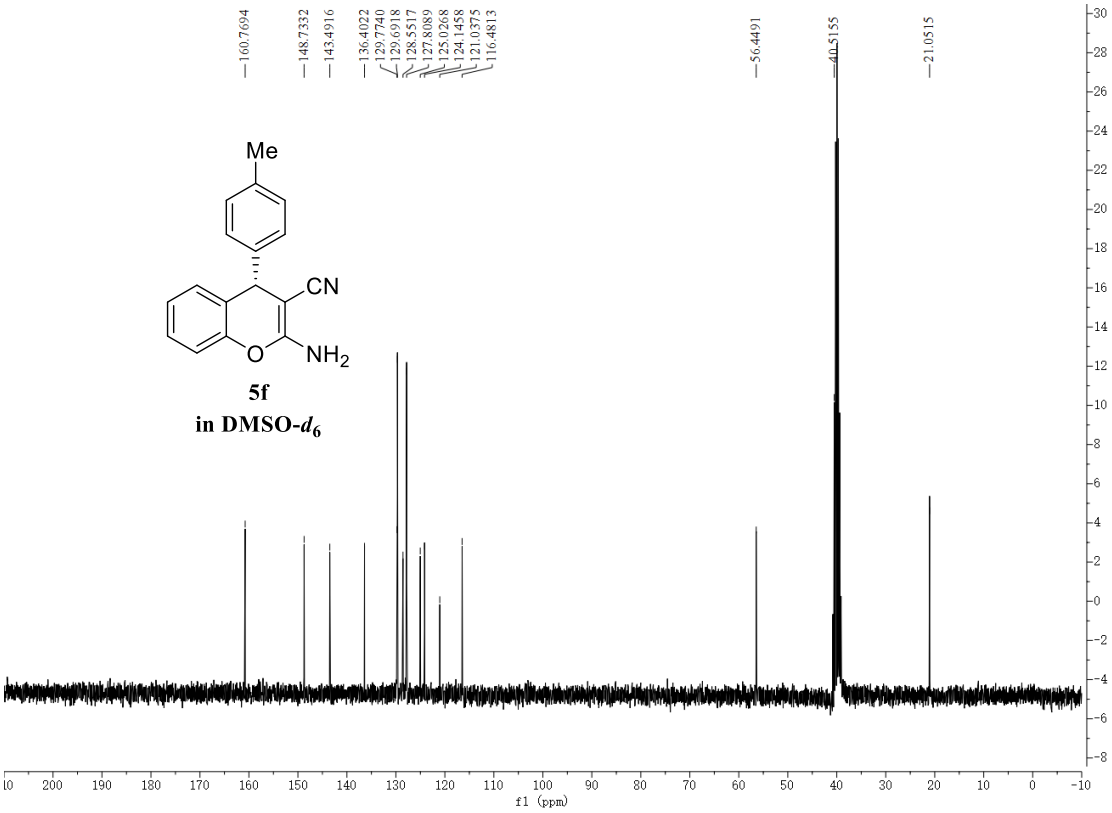
5f
in DMSO-d6
f1 (ppm)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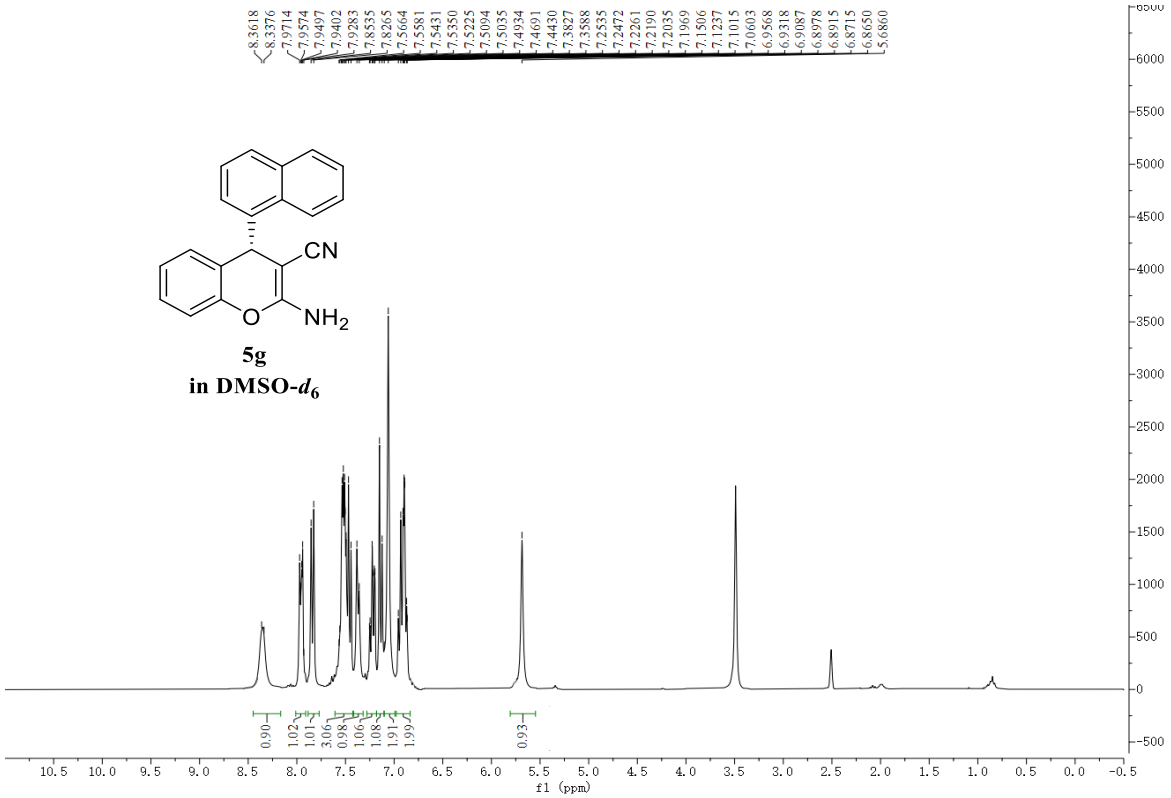
5f
in DMSO-d6
f1 (ppm)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6.8650
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CN
O
NH2
5g
in DMSO-d6
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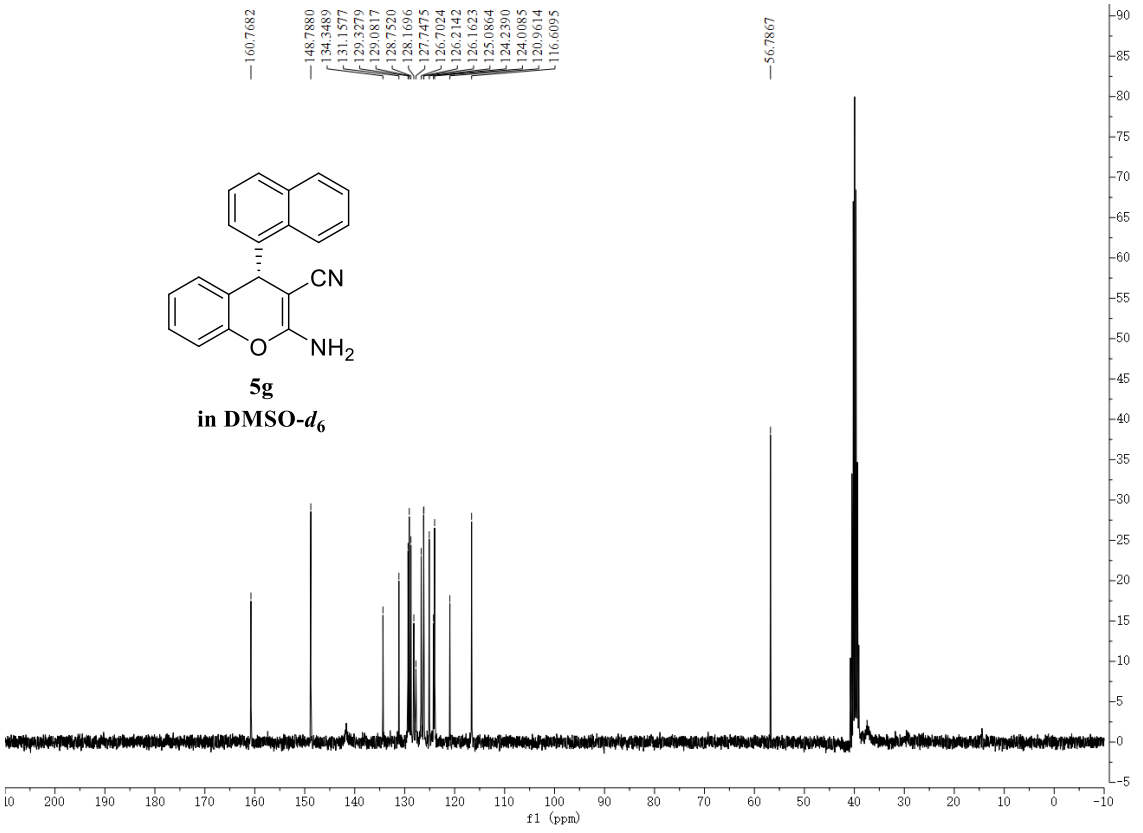
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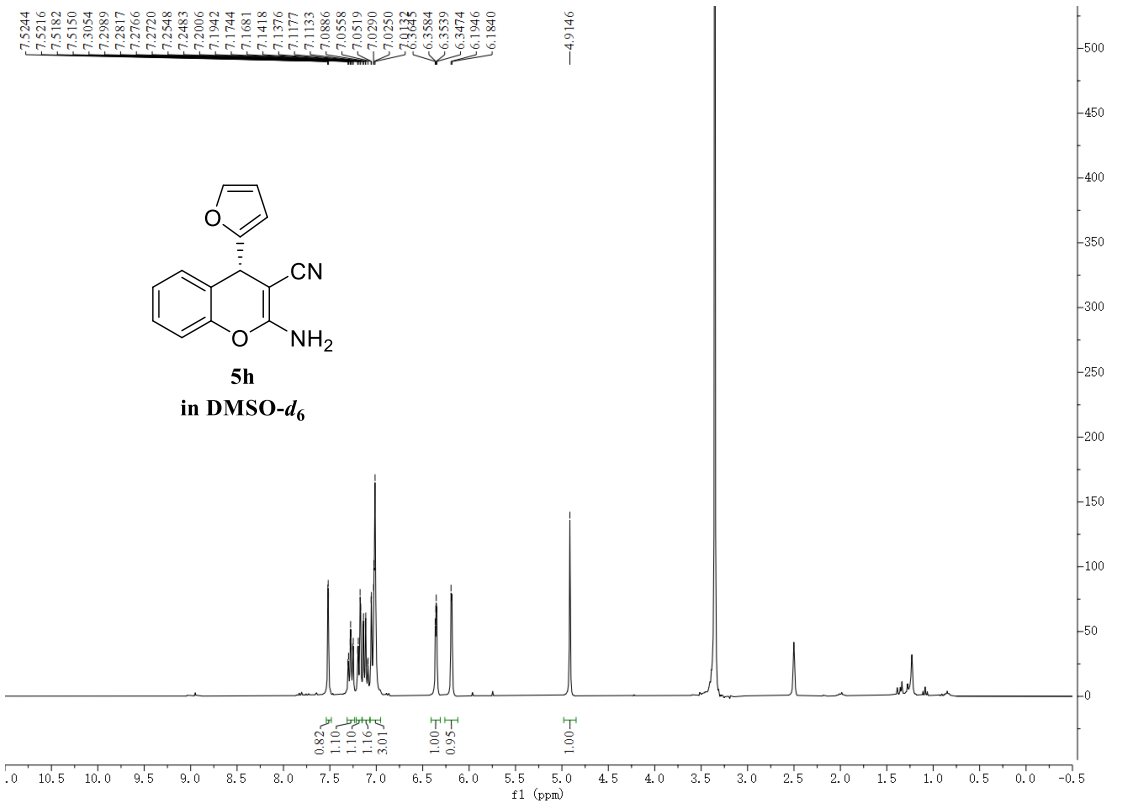
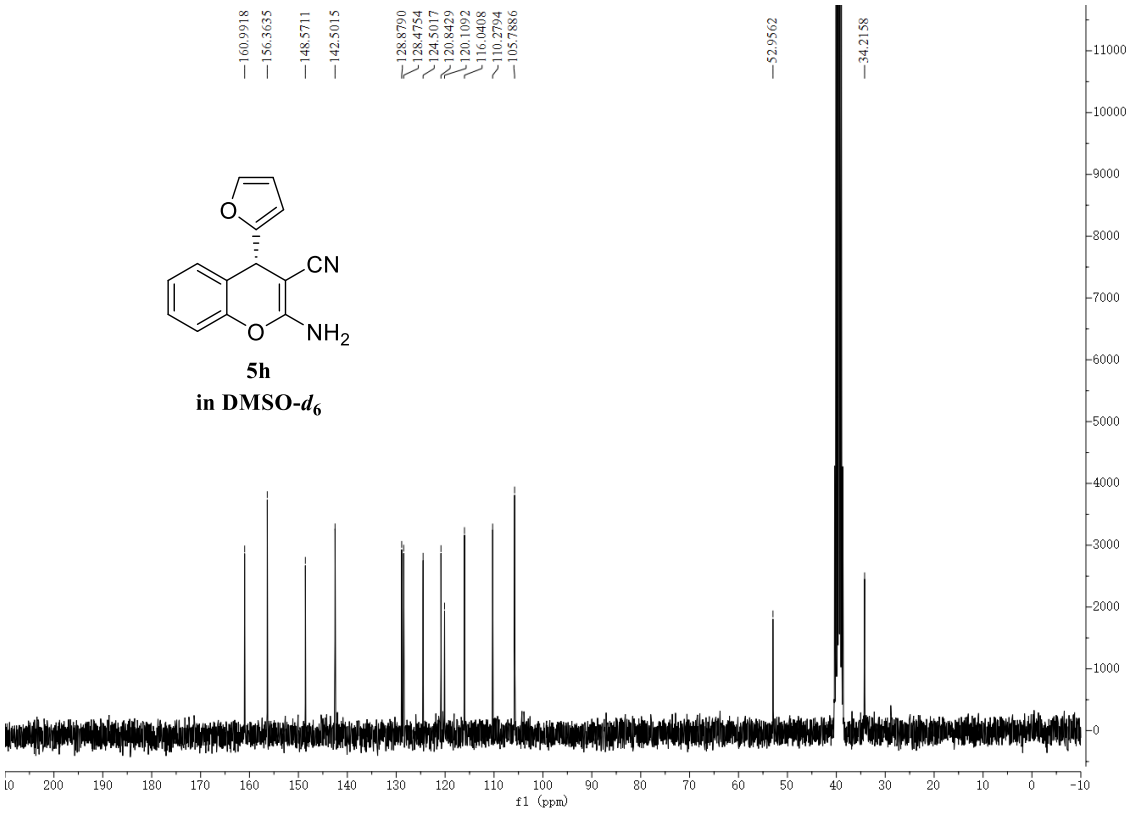
CN
O
NH2
5g
in DMSO-d6
f1 (ppm)

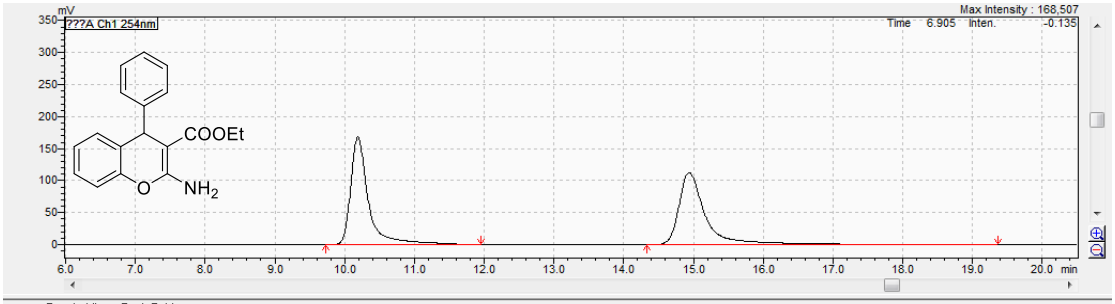


5h
in DMSO-d_6



5h
in DMSO-d_6

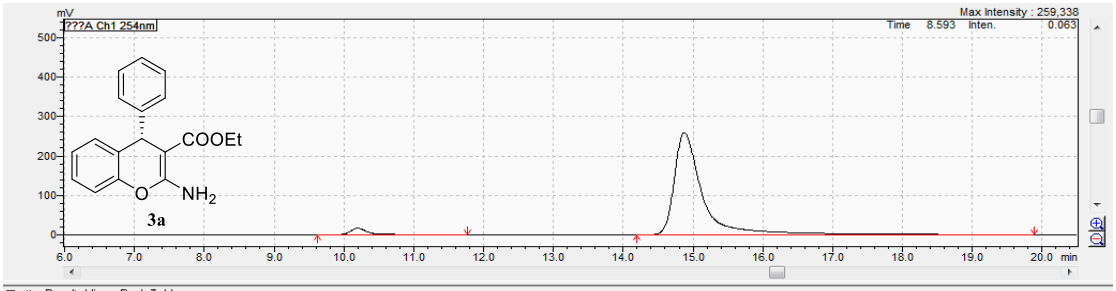
11.HPLC Charts



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

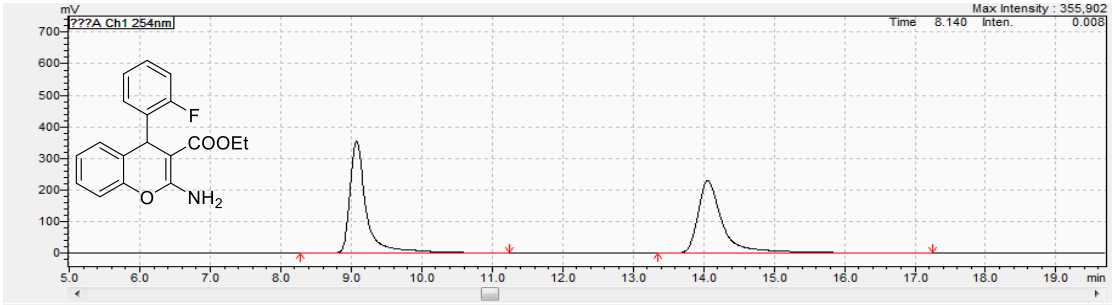
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.190	3054222	168727	49.992	49.992
2	14.940	3055164	112935	50.008	50.008
Total		6109386	281663	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

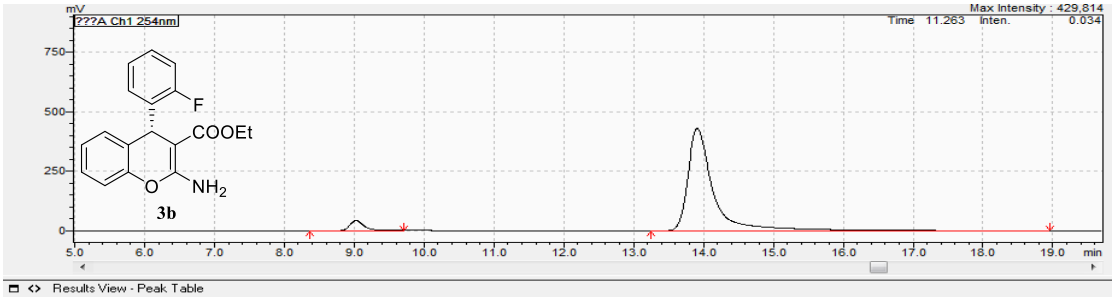
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.198	332568	16997	4.338	4.338
2	14.875	7333216	259221	95.662	95.662
Total		7665784	276219	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

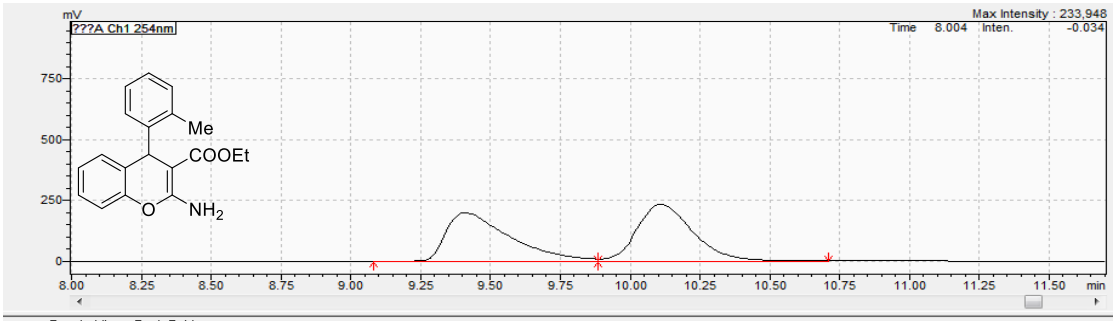
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.075	5932328	355954	50.351	50.351
2	14.060	5849715	231338	49.649	49.649
Total		11782044	587292	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

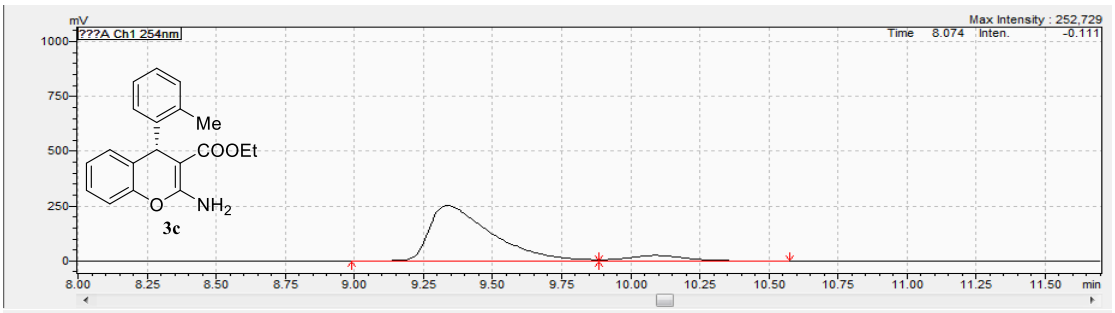
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.027	632451	42443	5.427	5.427
2	13.911	11021844	429923	94.573	94.573
Total		11654295	472366	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

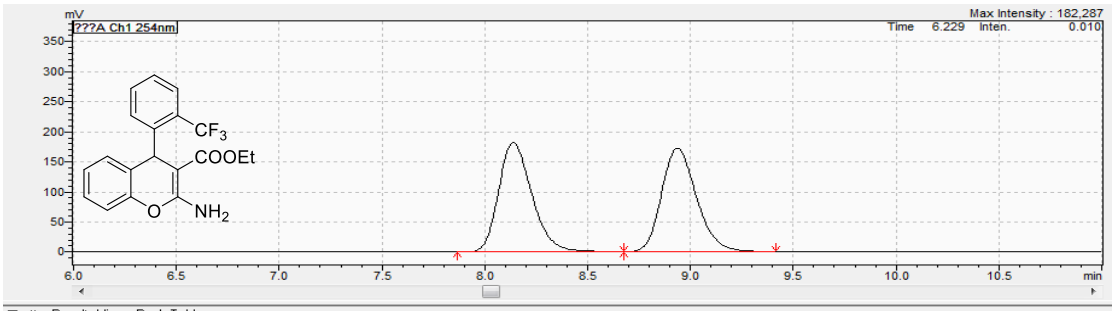
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.408	3143194	199344	49.179	49.179
2	10.110	3248102	233958	50.821	50.821
Total		6391297	433302	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

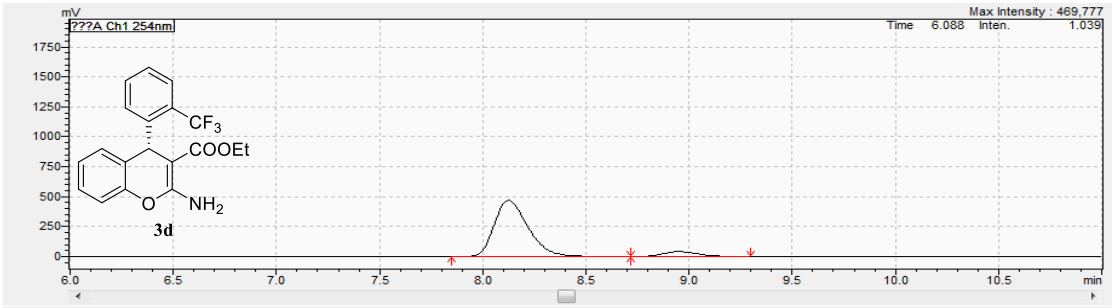
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.336	3952361	252947	91.322	91.322
2	10.091	375567	25441	8.678	8.678
Total		4327928	278389	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

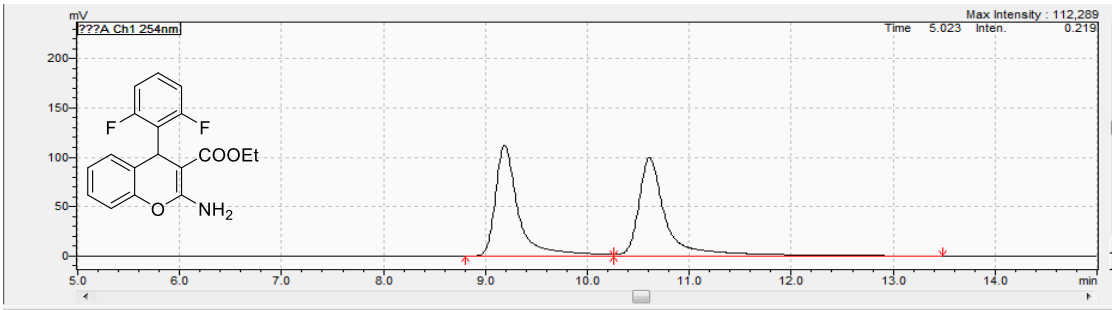
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.138	2057273	182318	50.054	50.054
2	8.936	2052853	172826	49.946	49.946
Total		4110126	355145	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

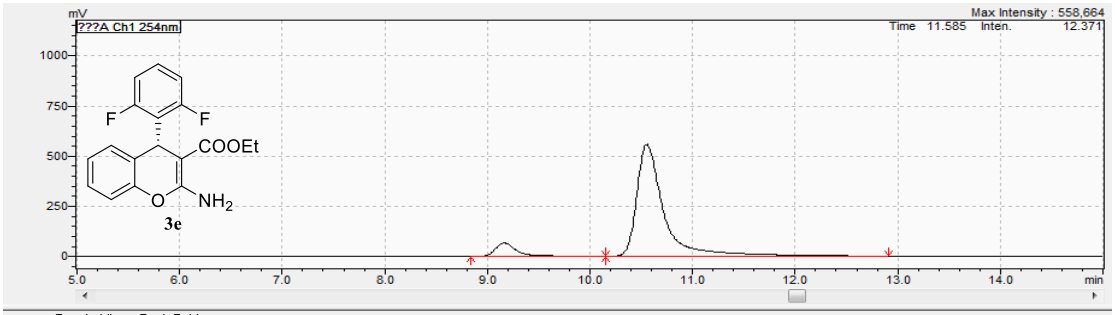
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.125	5361901	469789	91.601	91.601
2	8.951	491613	40671	8.399	8.399
Total		5853515	510460	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

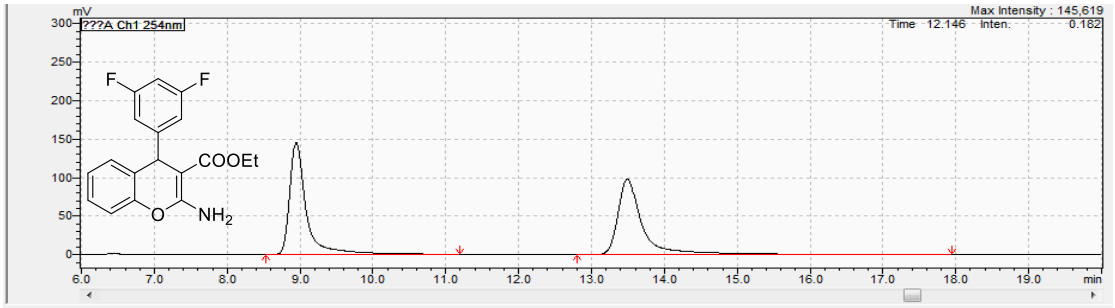
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.188	1749944	112138	48.517	48.517
2	10.609	1856936	99492	51.483	51.483
Total		3606880	211630	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

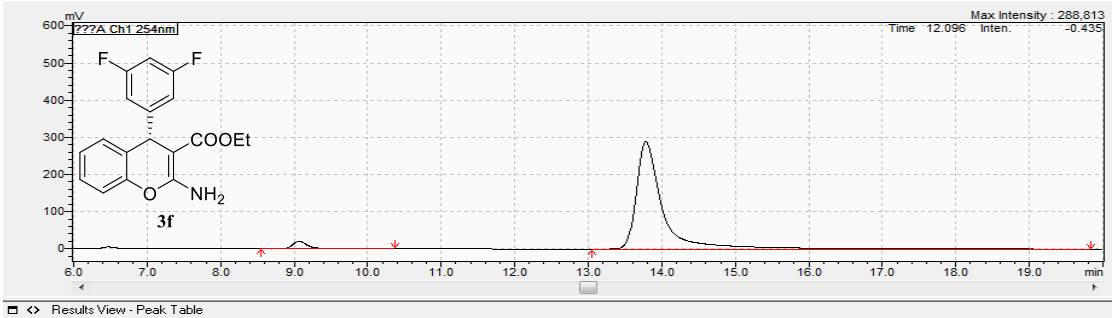
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.163	1045909	66976	9.013	9.013
2	10.555	10559156	558629	90.987	90.987
Total		11605065	625605	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

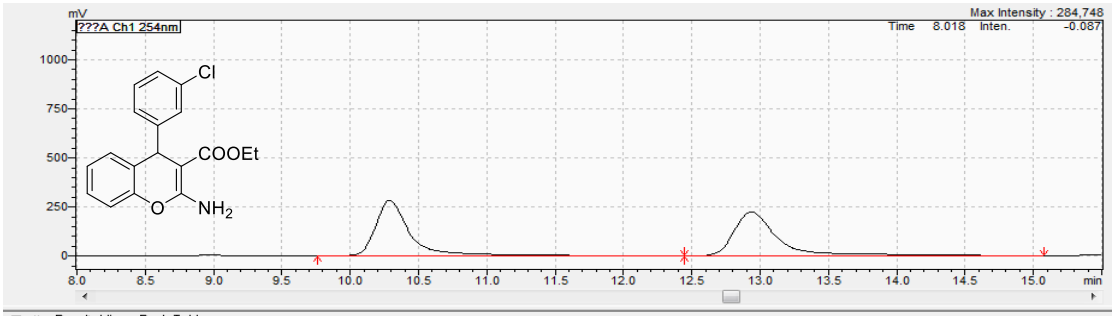
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.948	2287732	145347	49.698	49.698
2	13.494	2315511	98001	50.302	50.302
Total		4603243	243349	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

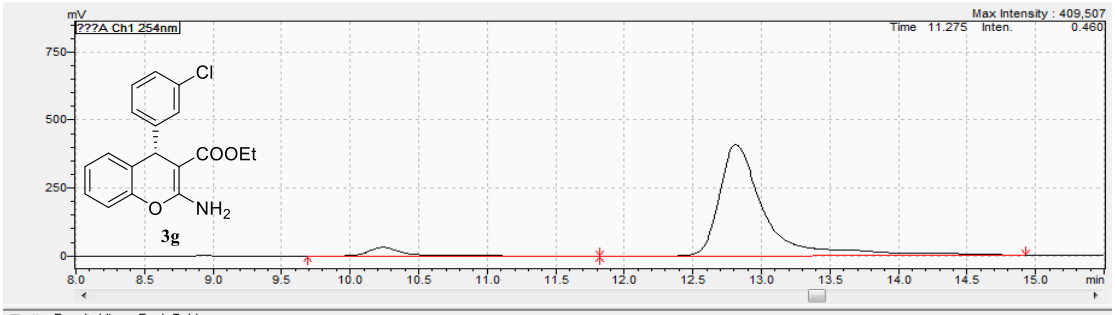
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.064	317212	20685	4.192	4.192
2	13.782	7250588	289403	95.808	95.808
Total		7567800	310087	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

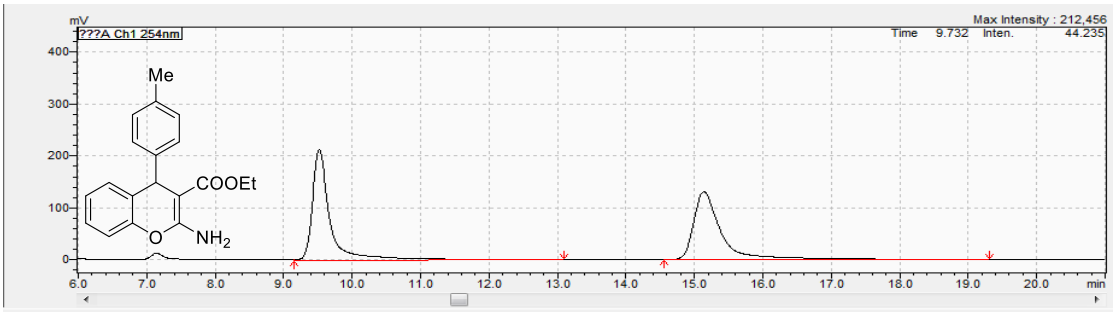
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.289	5257501	284871	49.582	49.582
2	12.935	5346175	226106	50.418	50.418
Total		10603676	510976	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

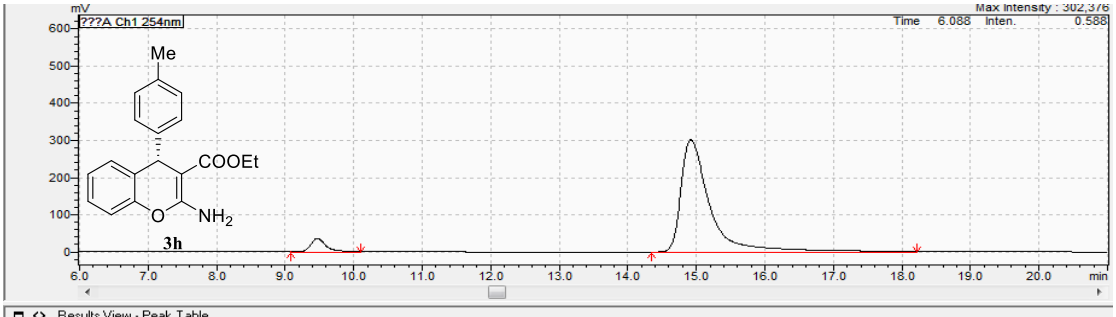
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.238	546787	31572	5.586	5.586
2	12.815	9242257	408195	94.414	94.414
Total		9789044	439768	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

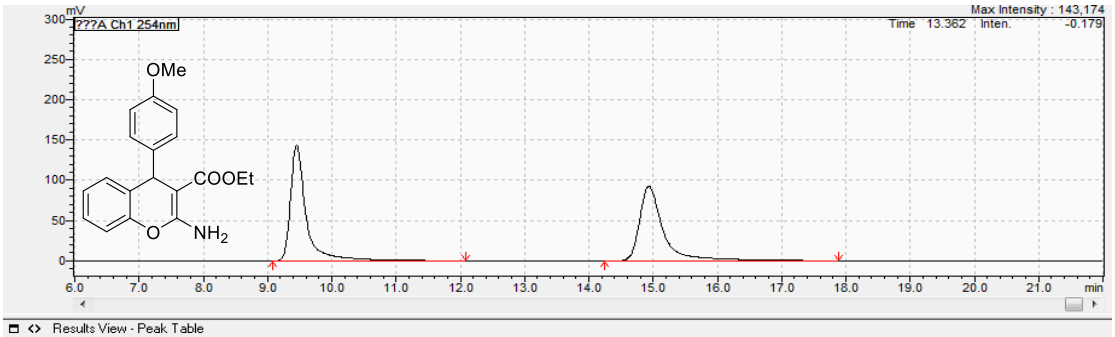
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.520	3929233	212889	50.526	50.526
2	15.138	3847395	130848	49.474	49.474
Total		7776628	343737	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

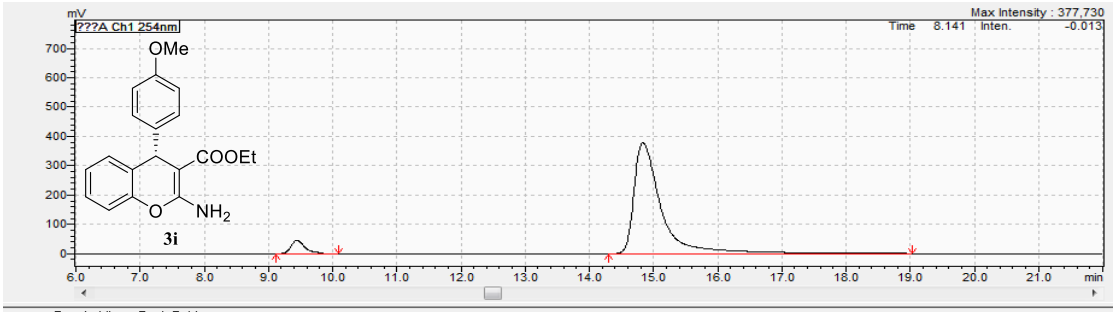
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.470	586354	36343	6.133	6.133
2	14.919	8973682	302482	93.867	93.867
Total		9560037	338825	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

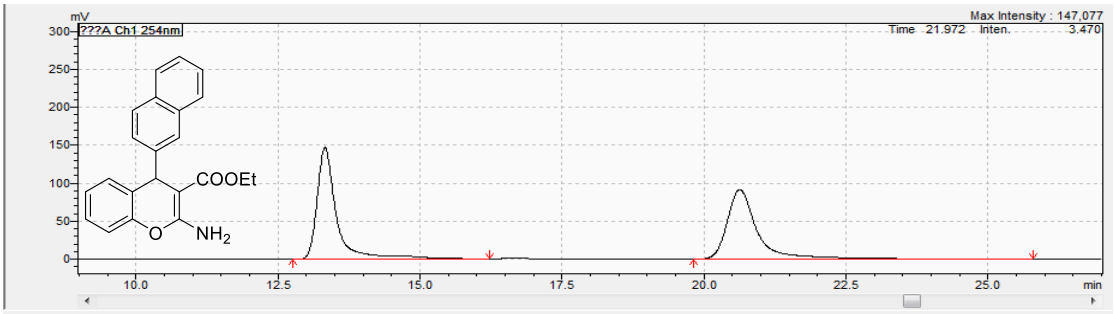
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.454	2455652	143285	50.688	50.688
2	14.935	2388992	92438	49.312	49.312
Total		4844643	235723	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

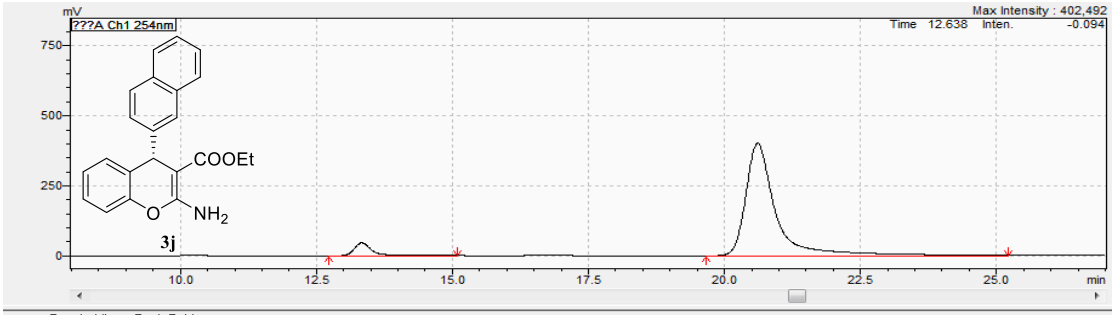
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.447	749266	46252	6.185	6.185
2	14.836	11364619	377868	93.815	93.815
Total		12113885	424121	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

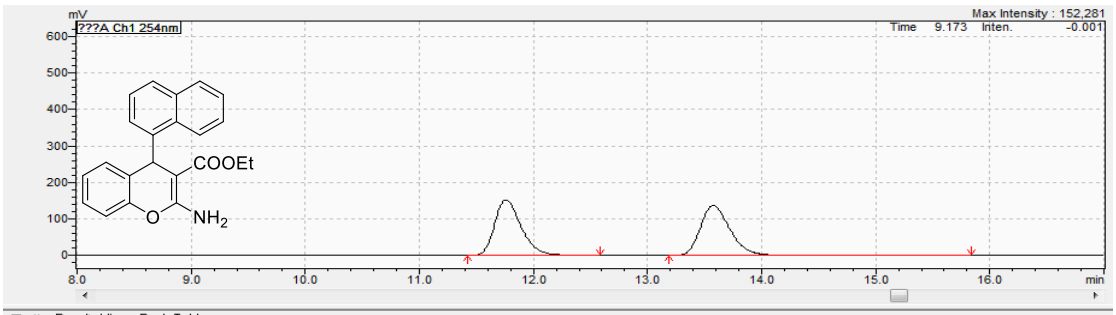
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13.327	3516825	147001	50.207	50.207
2	20.629	3487876	91909	49.793	49.793
Total		7004701	238911	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

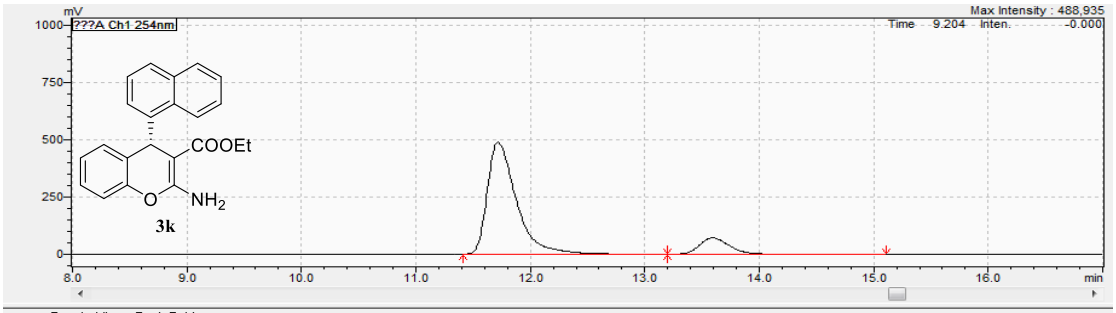
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13.333	1082203	46064	6.485	6.485
2	20.609	15605998	402689	93.515	93.515
Total		16688201	448753	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

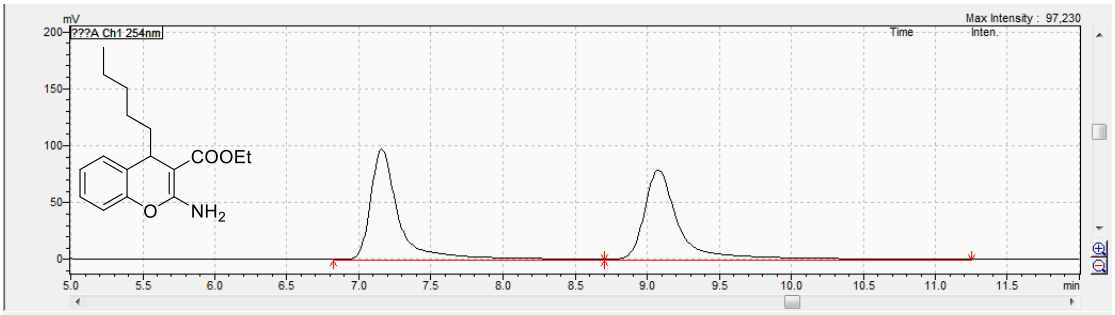
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.759	2487557	152296	49.937	49.937
2	13.577	2493873	137184	50.063	50.063
Total		4981430	289479	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

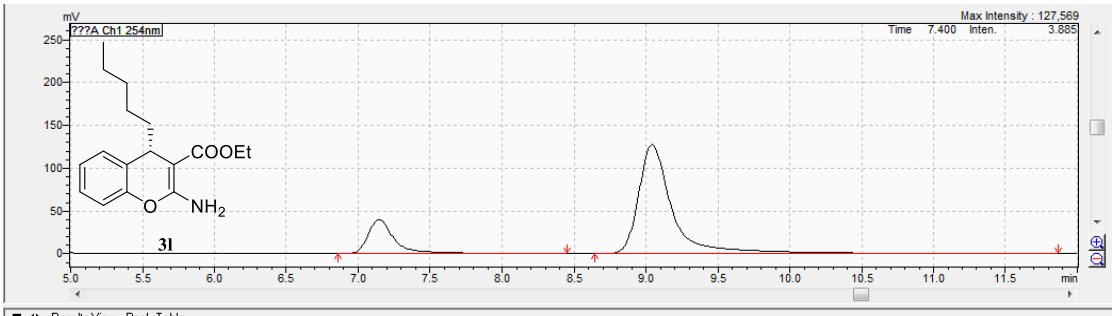
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.719	8697173	489131	86.642	86.642
2	13.593	1340915	71371	13.358	13.358
Total		10038088	560502	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

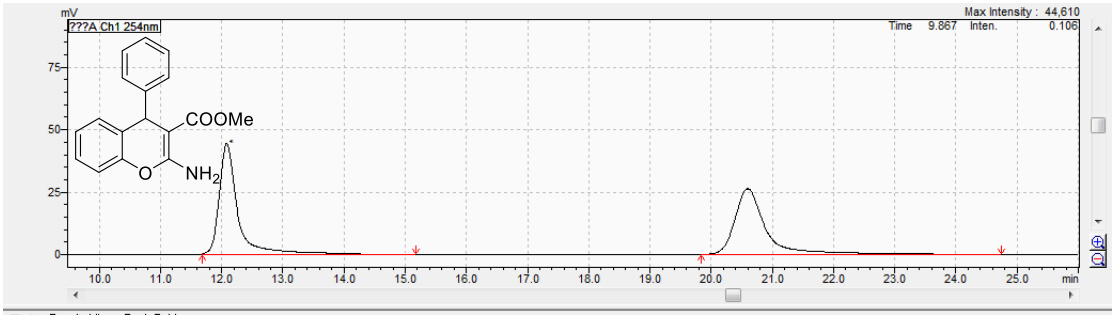
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	7.158	1391910	97876	50.206	50.206
2	9.077	1380465	79214	49.794	49.794
Total		2772375	177090	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

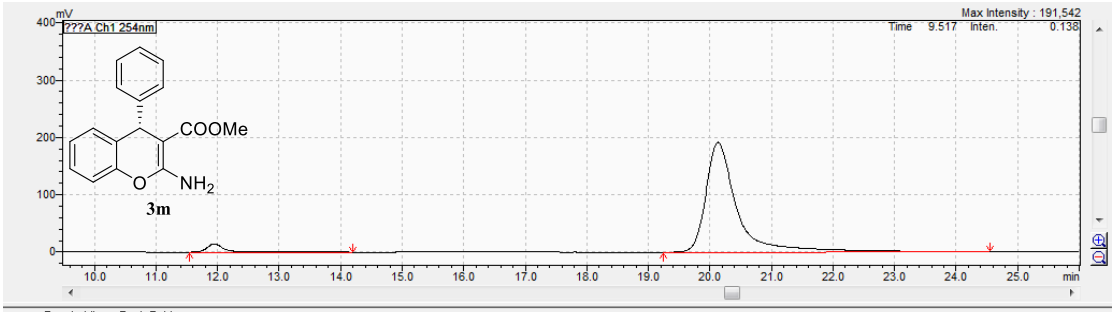
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	7.145	532722	40010	20.098	20.098
2	9.043	2117964	127266	79.902	79.902
Total		2650685	167276	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

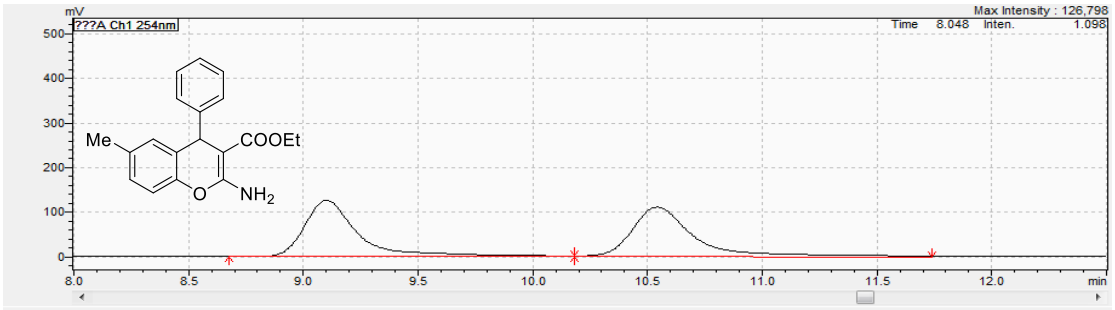
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12.083	965270	44525	50.913	50.913
2	20.598	930640	26281	49.087	49.087
Total		1895910	70806	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

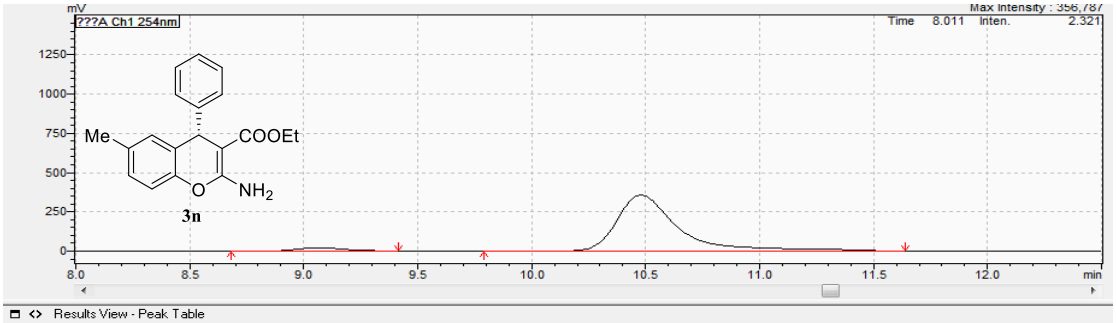
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.946	290493	14346	4.058	4.058
2	20.132	6867425	191621	95.942	95.942
Total		7157919	205968	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

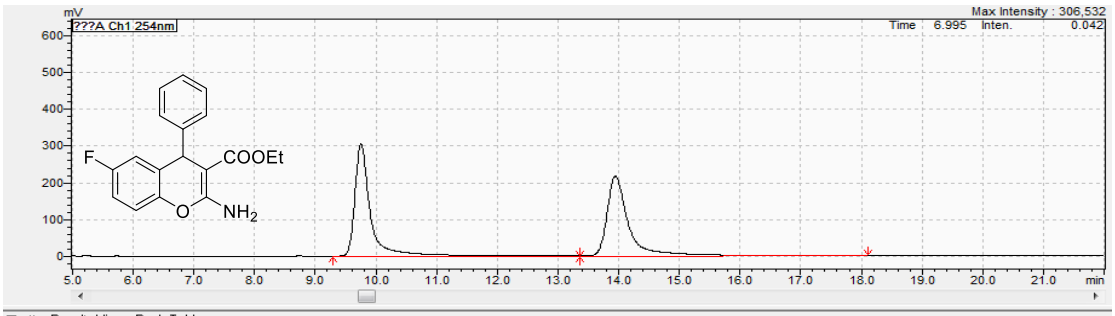
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.100	2086810	126174	49.739	49.739
2	10.542	2108746	110946	50.261	50.261
Total		4195556	237120	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

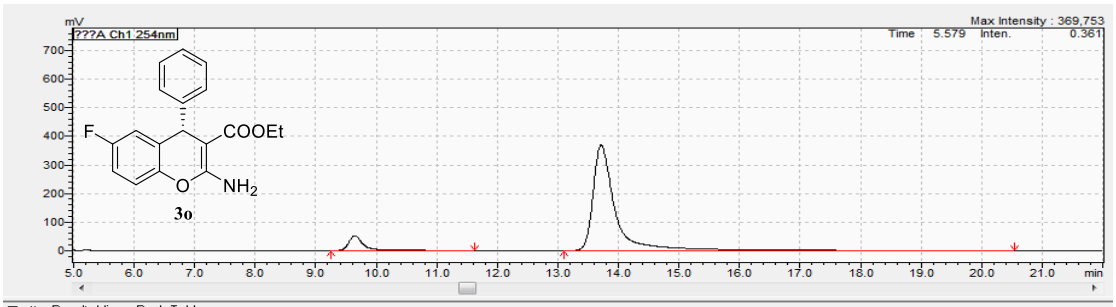
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.067	320577	21736	4.545	4.545
2	10.479	6732891	356648	95.455	95.455
Total		7053468	378384	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

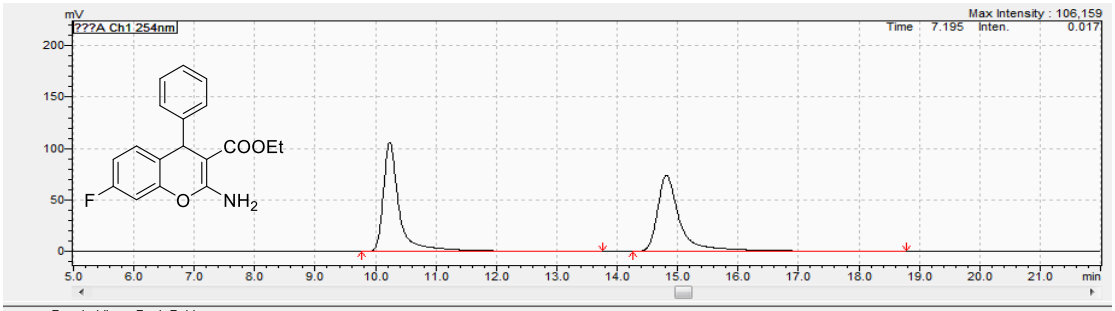
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.753	5544700	306753	50.466	50.466
2	13.946	5442293	217079	49.534	49.534
Total		10986993	523832	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

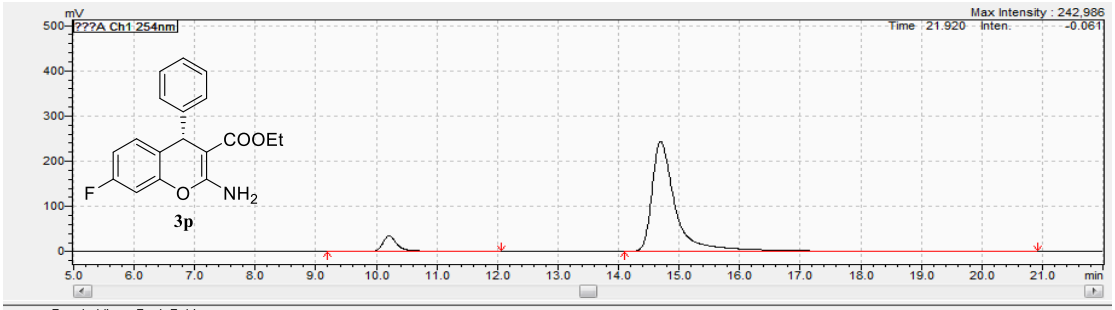
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.644	888612	51824	8.592	8.592
2	13.713	9453614	369776	91.408	91.408
Total		10342226	421600	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

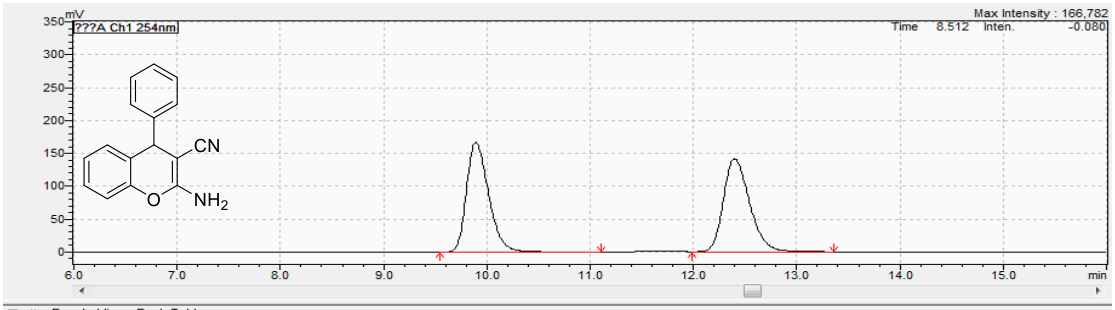
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.235	1985833	106156	50.341	50.341
2	14.815	1958945	74014	49.659	49.659
Total		3944778	180170	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

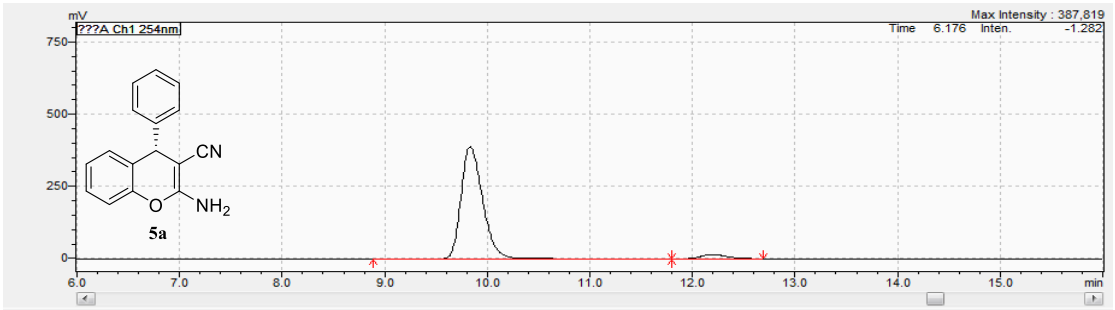
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.209	621639	34813	8.420	8.420
2	14.694	6761556	243028	91.580	91.580
Total		7383196	277842	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

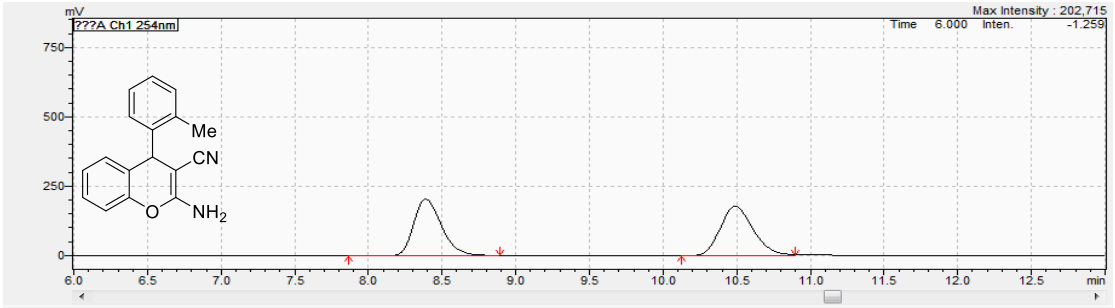
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.893	2490452	166953	49.869	49.869
2	12.399	2503569	141451	50.131	50.131
Total		4994020	308403	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

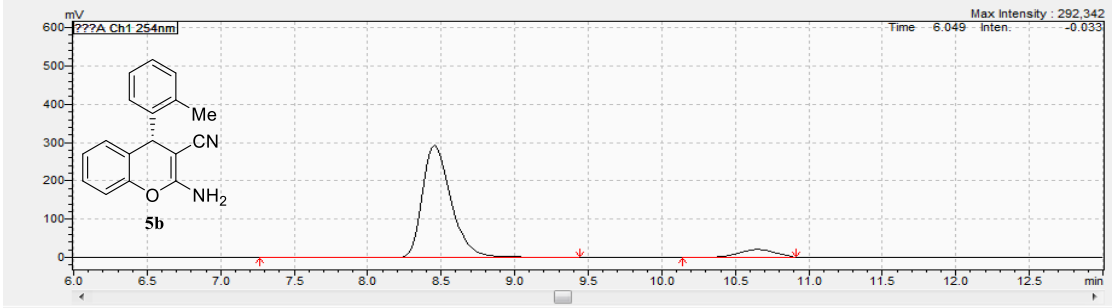
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.834	5701406	389203	95.368	95.368
2	12.193	276907	15254	4.632	4.632
Total		5978313	404457	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

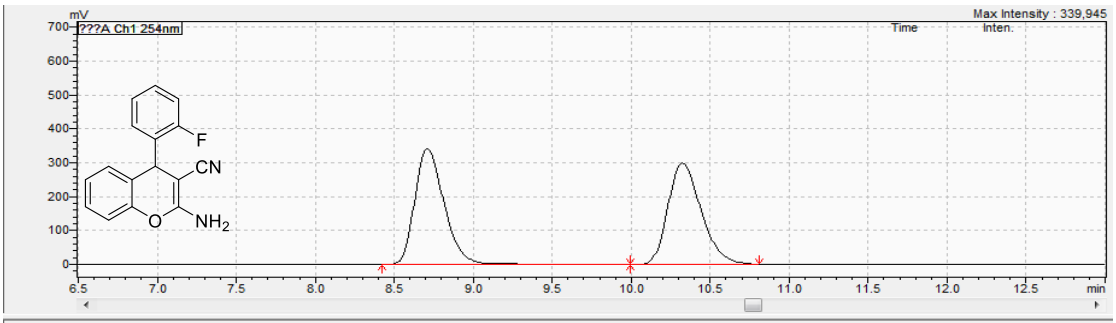
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.391	2709471	203819	49.611	49.611
2	10.487	2751935	178003	50.389	50.389
Total		5461407	381822	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

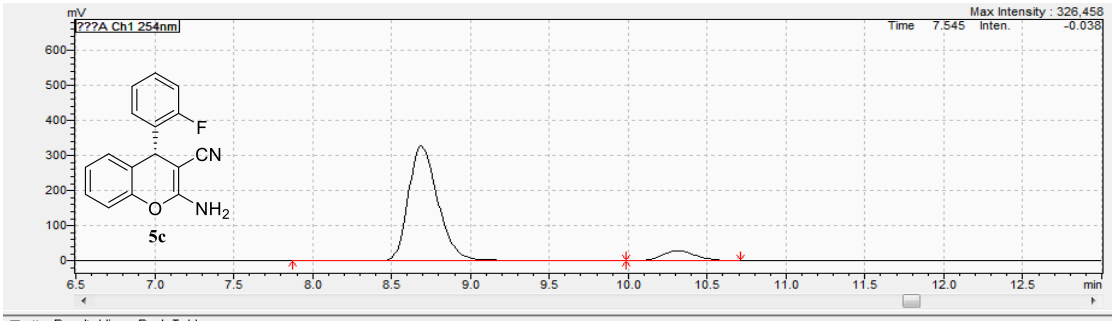
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.455	3962932	292002	91.158	91.158
2	10.651	384380	20948	8.842	8.842
Total		4347312	312950	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

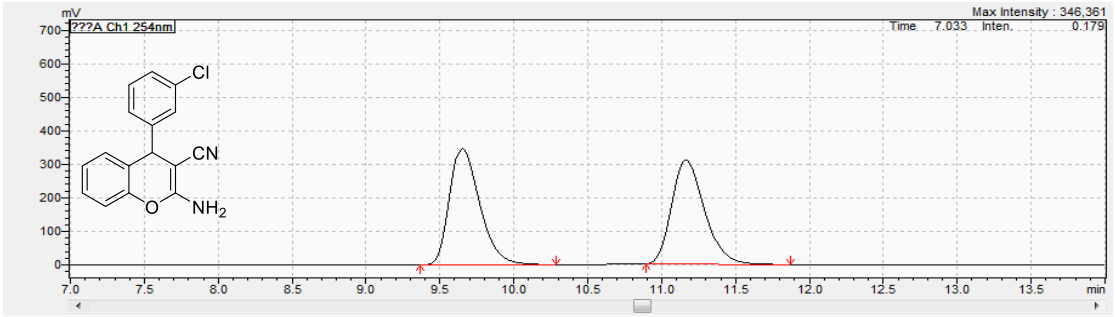
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.710	4435588	340039	50.197	50.197
2	10.324	4400800	299316	49.803	49.803
Total		8836388	639354	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

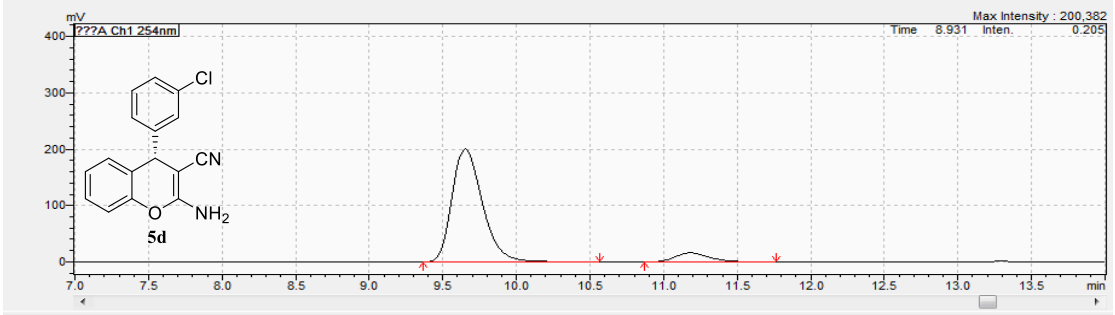
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.687	4261042	326461	91.109	91.109
2	10.313	415831	28589	8.891	8.891
Total		4676874	355049	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

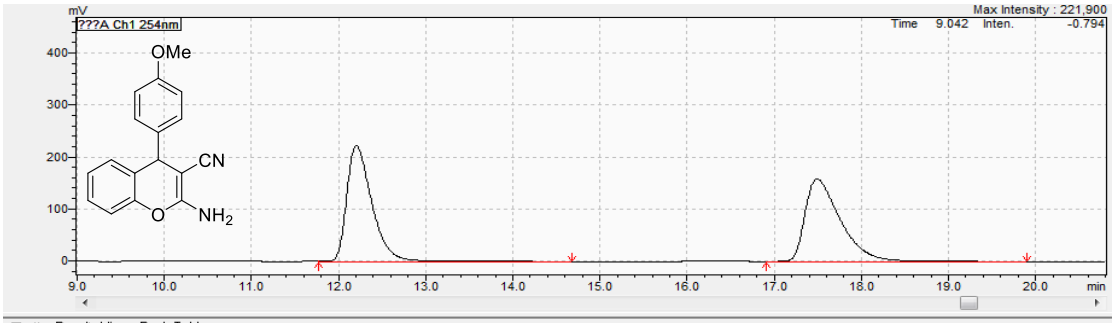
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.649	4864061	345763	50.129	50.129
2	11.166	4838969	310068	49.871	49.871
Total		9703030	655831	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

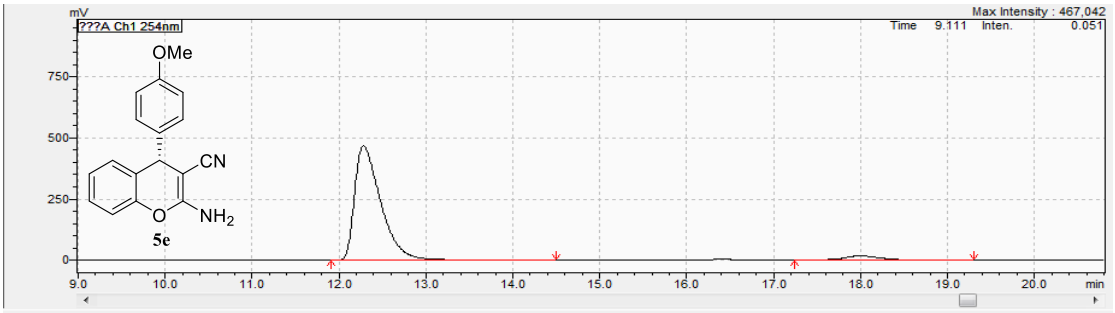
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.651	2844756	200383	91.644	91.644
2	11.183	259398	16155	8.356	8.356
Total		3104154	216538	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

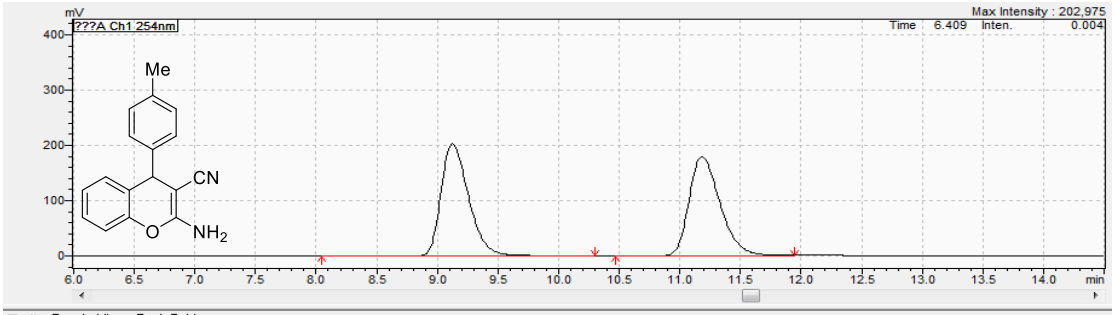
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12.205	4453142	222779	49.866	49.866
2	17.492	4477069	158748	50.134	50.134
Total		8930212	381527	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

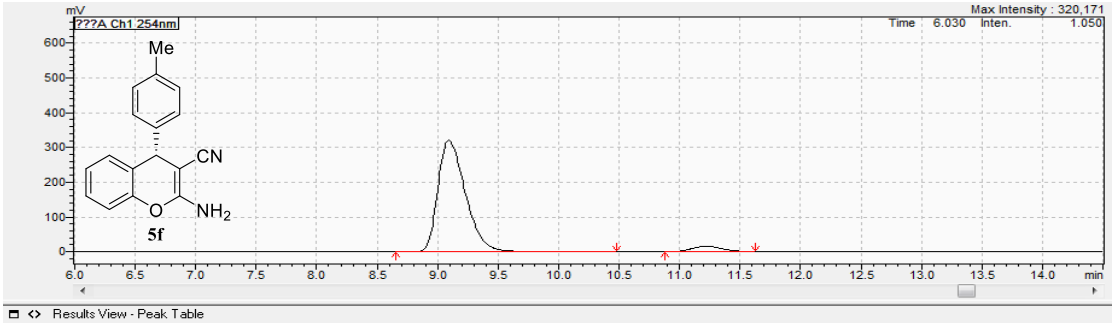
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12.283	9808140	467047	94.750	94.750
2	17.996	543442	17443	5.250	5.250
Total		10351582	484490	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

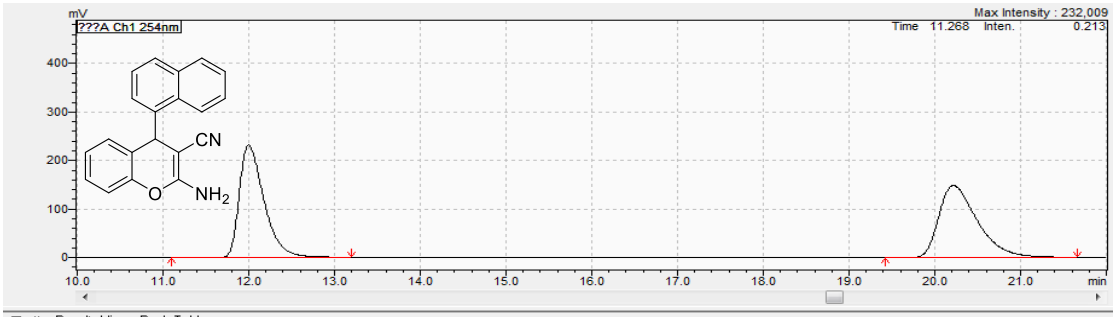
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.124	3199708	202759	49.884	49.884
2	11.183	3214615	179683	50.116	50.116
Total		6414322	382442	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

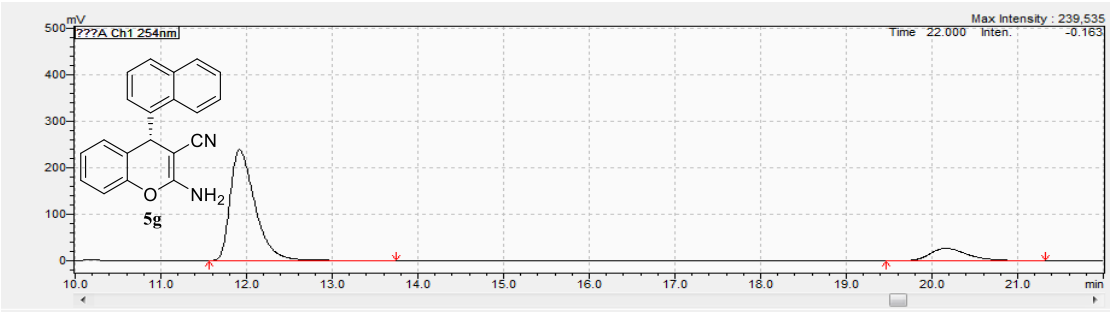
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.093	5068733	319959	94.931	94.931
2	11.218	270645	15574	5.069	5.069
Total		5339378	335532	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

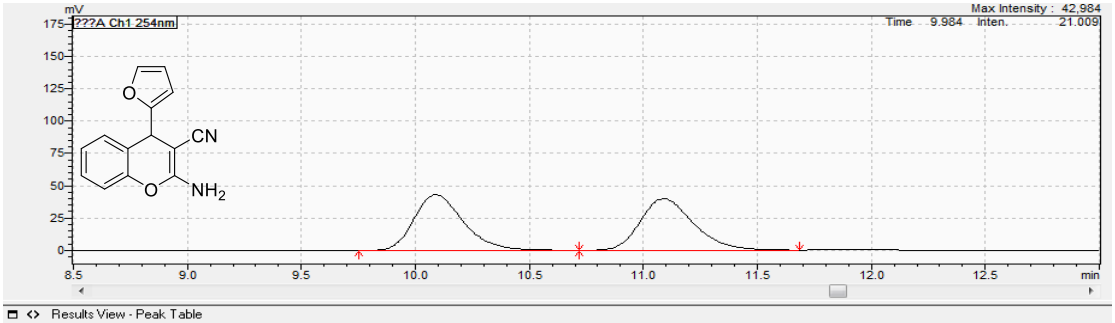
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12.000	4614357	231418	49.665	49.665
2	20.217	4676588	148781	50.335	50.335
Total		9290945	380199	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

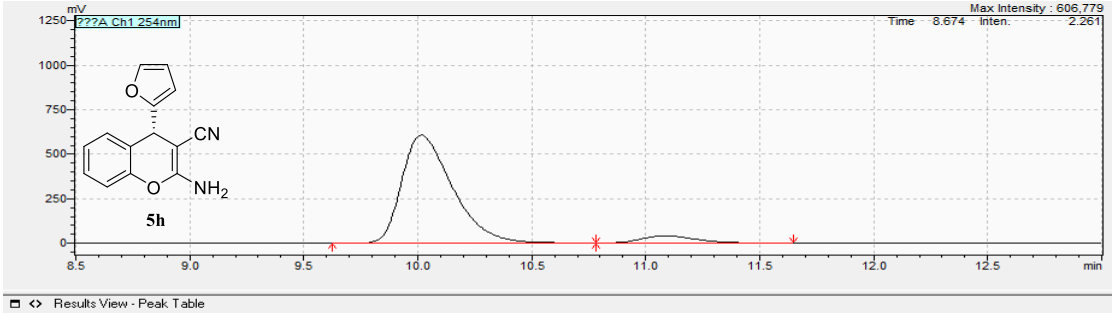
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.919	4831629	239470	85.266	85.266
2	20.162	834888	26918	14.734	14.734
Total		5666517	266388	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.088	652393	43115	49.804	49.804
2	11.089	657536	39923	50.196	50.196
Total		1309929	83037	100.000	100.000



Results View - Peak Table

Peak Table | Compound | Group | Calibration Curve

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.015	9422260	606765	93.087	93.087
2	11.086	699704	40987	6.913	6.913
Total		10121964	647752	100.000	100.000