Cascade synthesis of novel functionalized pyridine-fused coumarins in aqueous medium

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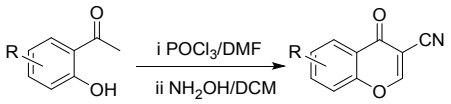
1. Experimental procedures

General information

Unless otherwise noted, all solvents and other reagents are commercially available and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury-300/400/500 and Varian Mercury-400/500 spectrometers. MS and HRMS spectra were performed on a Finnigan MAT 95 spectrometer. Melting points were measured by Büchi 510 melting point apparatus without further corrected.

Typical procedure for synthesis of compound 1[1]

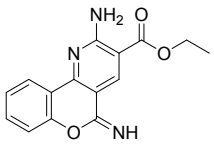


A mixture of dimethylformamide (6.2 mL, 80 mmol) and phosphorus oxychloride (3.7 mL, 40 mmol) was stirred at 0 ℃ for 30 min. To this solution 2-hydroxyacetophenone (1.4 g, 10 mmol) was added dropwise at 0 ℃. The mixture was stirred at room temperature for 4 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with dichloromethane (40 mL). The mixture was cooled to 0 ℃ and hydroxylamine hydrochloride (2.1 g, 30 mol) in DMF (10 mL) was added and the mixture stirred at room temperature for 3 – 4 h. After the reaction was complete, as indicated by TLC, it was diluted with cold water (100 mL) and extracted with DCM (2 × 50 mL). The combined organic phases were washed with water (2 × 50 mL), saturated $NaHCO_3$ solution (10 mL) and finally with water (50 mL). The combined extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residual solid was applied on a silica-gel column give **1a** as yellow solid.

Typical procedure for synthesis of compound 3

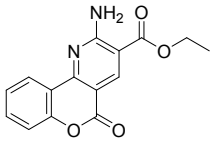
A mixture of **1a** (0.5 mmol), **2a** (0.5 mmol), and NaOAc (2.0 mmol) in DMSO/H_2O (4/1, 5 mL) was heated to 80 ℃ under air atmosphere. After the completion of the reaction as indicated by LC-MS, the reaction was cooled to room temperature, and then diluted by water (40 mL). The mixtures was extracted with EtOAc (3 x 30 mL), washed with water and brine, dried over anhydrous Na_2SO_4 and filtered. The solvent was removed under vacuum. The residue was applied on a silica-gel column.

Characterization of the compounds



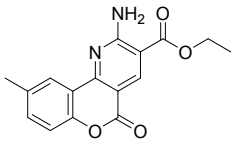
Ethyl 2-amino-5-imino-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (intermediate B)

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.79 (s, 1H), 8.20 (d, J = 7.6 Hz, 1H), 7.85 (br s, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 8.3 Hz, 1H), 4.32 (q, J = 6.9 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H)



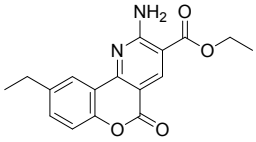
Ethyl 2-amino-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3a)

Yellow solid (85%). Mp 224-225 ℃. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.66 (s, 1H), 8.33 – 8.25 (m, 2H), 8.06 (br s, 1H), 7.65 (td, J = 8.0, 1.3 Hz, 1H), 7.44 – 7.34 (m, 2H), 4.32 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.36 , 162.41 , 160.81 , 155.88 , 154.45 , 143.27 , 134.39 , 125.78 , 125.73 , 119.35 , 118.26 , 108.30 , 107.38 , 62.46 , 15.22 . *m/z* (EI):284 [M^+, 100%], 239 (44%), 212 (56%). Calculated for $C_{15}H_{12}N_2O_4$, 284.0797; found, 284.0801 [M^+].



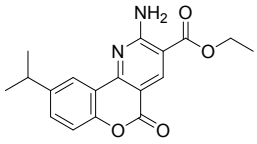
Ethyl 2-amino-9-methyl-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3b)

Yellow solid (87%). Mp 269-270 ℃. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.03 (s, 1H), 8.30 (s, 1H), 8.17 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 5.94 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 165.55 , 161.00 , 160.44 , 155.05 , 151.38 , 142.91 , 133.72 , 133.46 , 124.39 , 117.61 , 116.51 , 107.36 , 107.33 , 61.12 , 20.42 , 13.78 . *m/z* (EI):298 [M $^{+}$, 100%], 253 (28%), 226 (40%). Calculated for $C_{16}H_{14}N_2O_4$, 298.0954; found, 298.0958 [M $^{+}$].



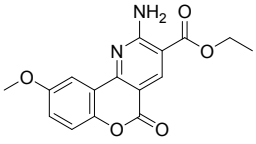
Ethyl 2-amino-9-ethyl-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3c)

Yellow solid (77%). Mp 223-224 ℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.32 (br s, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 8.08 (br s, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.23 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.73 (q, *J* = 7.5 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.71 , 161.74 , 160.27 , 155.31 , 153.87 , 150.62 , 142.59 , 125.01 , 124.93 , 116.38 , 107.25 , 106.31 , 61.71 , 28.62, 15.48 , 14.52 . *m/z* (EI):312 [M $^{+}$, 100%], 267 (24%), 226 (25%). Calculated for $C_{17}H_{16}N_2O_4$, 312.1110; found, 312.1109 [M $^{+}$].



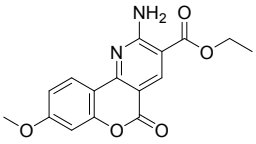
Ethyl 2-amino-9-isopropyl-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3d)

Yellow solid (83%). Mp 158-160 ℃. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.05 (s, 1H), 8.31 (br s, 1H), 8.25 (d, *J* = 2.3 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 6.00 (br s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.03 (hept, *J* = 6.8 Hz, 1H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.32 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.73 , 161.73 , 160.30 , 155.34 , 152.13 , 145.15 , 142.70 , 132.23 , 122.07 , 118.33 , 117.54 , 107.54 , 106.71 , 61.78 , 33.50 , 24.38 , 14.54 . *m/z* (EI):326 [M $^{+}$, 45%], 311(100%), 265 (24%). Calculated for $C_{18}H_{18}N_2O_4$, 326.1267; found, 326.1267 [M $^{+}$].



Ethyl 2-amino-9-methoxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3e)

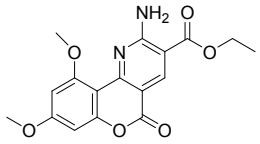
Yellow solid (86%). Mp 226-228 ℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.31 (br s, 1H), 8.03 (br s, 1H), 7.78 – 7.58 (m, 1H), 7.32 – 7.12 (m, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 1.35 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.14 , 161.08 , 159.60 , 155.66 , 154.38 , 147.49 , 142.01 , 120.71 , 118.51 , 118.23 , 107.04 , 106.24 , 106.08 , 61.24 , 55.57 , 13.98 . *m/z* (EI):314 [M $^{+}$, 100%]. Calculated for $C_{16}H_{14}N_2O_5$, 314.0903; found, 314.0900 [M $^{+}$].



Ethyl 2-amino-8-methoxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3f)

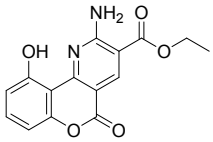
Yellow solid (84%). Mp 238-239 ℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (s, 1H), 8.30 (br s, 1H), 8.21 (d, *J* =

8.7 Hz, 1H), 8.09 (br s, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 6.99 (s, 1H), 4.34 (d, *J* = 7.3 Hz, 2H), 3.89 (s, 3H), 1.36 (q, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.77 , 163.86 , 161.79 , 160.40 , 155.42 , 142.69 , 126.38 , 112.97 , 111.72 , 106.72 , 105.39 , 101.68 , 61.66 , 56.46 , 14.55 . *m/z* (EI):314 [M $^+$, 100%] 269 (22%), 242 (30%). Calculated for $C_{16}H_{14}N_2O_5$, 314.0903; found, 314.0902 [M $^+$].



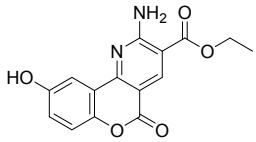
Ethyl 2-amino-8,10-dimethoxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3g)

Yellow solid (63%). Mp 244-246 ℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.65 (s, 1H), 7.97 (s, 2H), 7.89 (s, 1H), 6.57 (s, 1H), 6.53 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 4H), 3.87 (s, 3H), 1.36 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.84 , 163.57 , 161.24 , 160.96 , 160.25 , 156.77 , 156.45 , 142.17 , 105.37 , 104.79 , 102.26 , 96.86 , 94.46 , 61.53 , 56.85 , 56.34 , 14.56 . *m/z* (EI):344 [M $^+$, 100%], 315 (62%), 297 (35%), 269 (64%). Calculated for $C_{17}H_{16}N_2O_6$, 344.1008; found, 344.1000 [M $^+$].



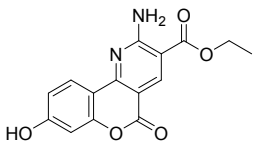
Ethyl 2-amino-10-hydroxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3h)

Yellow solid (67%). Mp 263-264 ℃.67% ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.95 (s, 1H), 8.95 (br s, 1H), 8.65 (s, 1H), 8.26 (br s, 1H), 7.47 (t, *J* = 8.3 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.17 , 159.94 , 159.50 , 159.48 , 157.20 , 154.08 , 142.51 , 134.34 , 112.47 , 107.16 , 106.75 , 105.18 , 103.71 , 61.80 , 14.50 . *m/z* (EI):300 [M $^+$, 100%], 272 (26%), 254 (85%).Calculated for $C_{15}H_{12}N_2O_5$, 300.0746; found, 300.0745 [M $^+$].



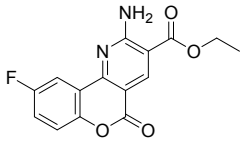
Ethyl 2-amino-9-hydroxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3i)

Yellow solid (57%). Mp 286-287 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.67 (s, 1H), 8.27 (br s, 1H), 8.07 (br s, 1H), 7.66 (s, 1H), 7.23 (d, *J* = 8.9 Hz, 1H), 7.07 (d, *J* = 8.9 Hz, 1H), 4.33 (q, *J* = 7.3 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H).[x131016-2] ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.71 , 161.62 , 160.33 , 155.23 , 154.44 , 146.98 , 142.62 , 121.59 , 119.21 , 118.50 , 109.44 , 107.46 , 106.68 , 61.73 , 14.51 . *m/z* (EI):300 [M $^+$, 100%], 272 (12%), 255(25%), 228 (40%). Calculated for $C_{15}H_{12}N_2O_5$, 300.0746; found, 300.0748 [M $^+$].



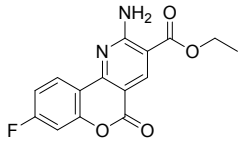
Ethyl 2-amino-8-hydroxy-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3j)

Yellow solid (87%). Mp 298-299 ℃. 1H NMR (300 MHz, DMSO-d_6) δ 10.61 (s, 1H), 8.60 (s, 1H), 8.18 (br s, 1H), 8.10 (d, J = 8.7 Hz, 1H), 8.02 (br s, 1H), 6.82 (dd, J = 8.7, 2.3 Hz, 1H), 6.67 (d, J = 2.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.80 , 162.74 , 161.76 , 160.49 , 155.60 , 155.44 , 142.69 , 126.68 , 113.74 , 110.48 , 106.33 , 105.10 , 103.09 , 61.60 , 14.54 . *m/z* (EI):300 [M $^+$, 100%], 272 (10%), 255(28%), 228 (38%). Calculated for $C_{15}H_{12}N_2O_5$, 300.0746; found, 300.0738 [M $^+$].



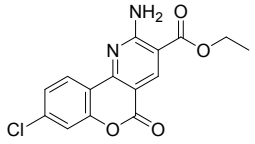
Ethyl 2-amino-9-fluoro-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3k)

Yellow solid (85%). Mp 225-226 ℃. ^{1}H NMR (400 MHz, Chloroform-d) δ 9.03 (s, 1H), 8.34 (br s, 1H), 8.04 (dd, J = 8.6, 2.9 Hz, 1H), 7.46 – 7.16 (m, 2H), 5.99 (br s, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-d) δ 165.38 , 161.00 , 159.93 , 158.66 (d, *J* = 243.9 Hz, FC), 154.16 , 149.34 , 142.88 , 119.81 (d, *J* = 24.7 Hz, FCCH), 119.29 (d, *J* = 8.7 Hz, FCCHC), 118.38 (d, *J* = 8.2 Hz, FCCHCH), 110.31 (d, *J* = 25.1 Hz, FCCH), 108.01 , 107.20 , 61.27 , 13.75 . *m/z* (EI):302 [M $^+$, 100%], 272 (10%), 257 (44%), 230 (52%). Calculated for $C_{15}H_{11}FN_2O_4$, 302.0703; found, 302.0711 [M $^+$].



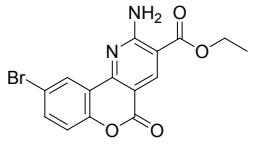
Ethyl 2-amino-8-fluoro-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3l)

Yellow solid (70%). Mp 239-240 ℃. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 8.64 (s, 1H), 8.41 – 8.24 (m, 2H), 8.09 (br s, 1H), 7.41 – 7.19 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-d) δ 165.96 , 165.34 (d, *J* = 253.8 Hz, CF), 161.57 , 160.49 , 154.92 , 154.81 (d, *J* = 14.3 Hz, CCHCF), 143.50 , 127.25 (d, *J* = 10.5 Hz, CHCHCF), 115.19 , 112.61 (d, *J* = 22.4 Hz, CHCF), 107.97 , 106.95 , 104.67 (d, *J* = 25.4 Hz, CHCF), 61.74 , 14.29 . *m/z* (EI):302 [M $^+$, 100%], 272 (10%), 257 (40%), 230 (47%). Calculated for $C_{15}H_{11}FN_2O_4$, 302.0703; found, 302.0701 [M $^+$].



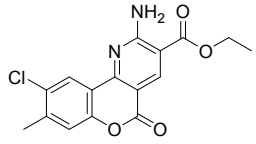
Ethyl 2-amino-8-chloro-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3m)

Yellow solid (82%). Mp 240-242 ℃. ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.67 (s, 1H), 8.40 (br s, 1H), 8.27 (d, J = 8.5 Hz, 1H), 8.13 (br s, 1H), 7.59 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 165.58 , 161.69 , 159.74 , 154.47 , 154.13 , 142.55 , 137.71 , 126.56 , 125.40 , 117.75 , 117.63 , 107.85 , 106.53 , 61.84 , 14.51 . *m/z* (EI):320 [M $^+$,Cl^{37} 32%], 318 [M $^+$, Cl^{35} 100%], 273 (34%), 246 (44%). Calculated for $C_{15}H_{11}ClN_2O_4$, 318.0407; found, 318.0404 [M $^+$].



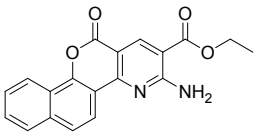
Ethyl 2-amino-9-bromo-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3n)

Yellow solid (82%). Mp 262-264 ℃. ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 8.62 (s, 1H), 8.40 (br s, 1H), 8.35 (d, *J* = 2.5 Hz, 1H), 8.08 (br s, 1H), 7.79 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 165.49 , 161.63 , 159.67 , 153.88 , 152.82 , 142.50 , 135.94 , 127.17 , 120.56 , 120.05 , 116.90 , 108.16 , 106.75 , 61.86 , 14.52 . *m/z* (EI): 364[M$^+$, Br^{81}, 98%], 362 [M$^+$, Br^{79}, 100%], 292 (Br^{81}, 32%), 290 (Br^{79}, 34%). Calculated for $C_{15}H_{11}BrN_2O_4$, 361.9902;found; 361.9902 [M $^+$, Br^{79}].



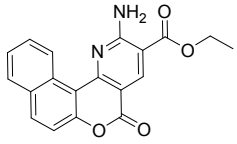
Ethyl 2-amino-9-chloro-8-methyl-5-oxo-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (3o)

Yellow solid (67%). Mp 250-251 ℃. ^{1}H NMR (500 MHz, Chloroform-d) δ 9.02 (s, 1H), 8.32 (s, 2H), 7.21 (s, 1H), 5.99 (br s, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 3H), 1.45 (t, *J* = 7.3 Hz, 4H). ^{13}C NMR (126 MHz, Chloroform-d) δ 165.94 , 161.52 , 160.51 , 154.57 , 151.95 , 143.37 , 141.86 , 130.64 , 124.97 , 119.21 , 117.59 , 108.11 , 107.42 , 61.73 , 20.70 , 14.27 . *m/z* (EI):334 [M $^+$,Cl^{37} 32%], 332 [M $^+$, Cl^{35} 100%], 287 (26%), 260 (44%). Calculated for $C_{16}H_{13}ClN_2O_4$, 332.0564; found, 332.0561 [M $^+$].



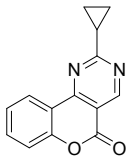
Ethyl 3-amino-12-oxo-12*H*-benzo[7,8]chromeno[4,3-*b*]pyridine-2-carboxylate (3p)

Yellow solid (60%). Mp 288-290 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (s, 1H), 8.46 – 8.26 (m, 3H), 8.14 (br s, 1H), 8.08 – 8.01 (m, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.69 (m, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-d) δ 166.08 , 161.64 , 160.79 , 156.02 , 150.87 , 143.46 , 135.83 , 128.79 , 127.86 , 126.99 , 124.34 , 123.42 , 122.70 , 120.59 , 113.84 , 107.80 , 107.75 , 61.67 , 14.33 . *m/z* (EI):334 [M $^{+}$, 100%], 306 (18%), 262 (30%). Calculated for $C_{19}H_{14}N_2O_4$, 334.0954; found, 334.0961 [M $^{+}$].



Ethyl 2-amino-5-oxo-5*H*-benzo[5,6]chromeno[4,3-*b*]pyridine-3-carboxylate (3q)

Yellow solid (54%). Mp 285-286 ℃. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.57 (d, J = 8.7 Hz, 1H), 8.69 (s, 1H), 8.59 (s, 1H), 8.17 (d, *J* = 8.9 Hz, 1H), 8.10 (s, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.48 (d, *J* = 8.9 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.10 , 160.52 , 159.53 , 157.39 , 154.19 , 142.07 , 134.84 , 130.84 , 130.16 , 128.73 , 128.55 , 127.99 , 125.63 , 117.51 , 110.30 , 106.78 , 105.68 , 61.21 , 14.06 . *m/z* (EI):237 [M $^{+}$, 100%], 306 (14%), 262 (21%). Calculated for $C_{19}H_{14}N_2O_4$, 334.0954; found, 334.0962 [M $^{+}$].



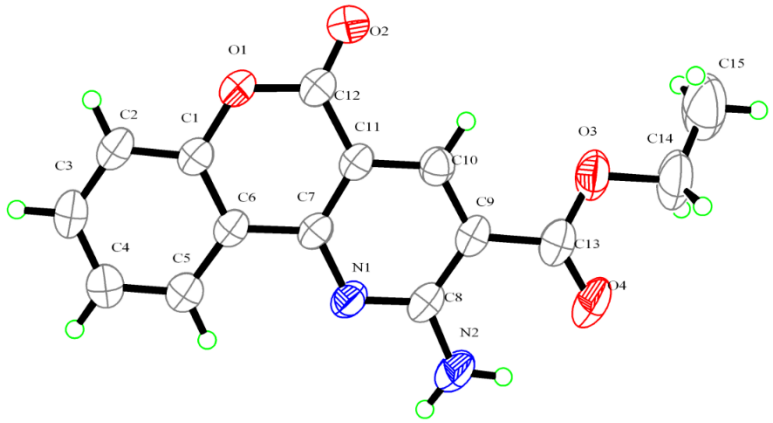
2-Cyclopropyl-5*H*-chromeno[4,3-*d*]pyrimidin-5-one (3r)

Yellow solid (90%). Mp 178-180 ℃. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.38 (s, 1H), 8.53 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.65 (td, *J* = 7.8, 1.7 Hz, 1H), 7.44 – 7.32 (m, 2H), 2.53 – 2.38 (m, 1H), 1.42 – 1.35 (m, 2H), 1.31 – 1.26 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.79 , 160.07 , 159.89 , 157.76 , 154.33 , 134.19 , 125.08 , 124.99 , 117.76 , 117.48 , 111.66 , 19.59 , 13.09 . *m/z* (EI):238 [M $^{+}$, 48%], 237 (100%). Calculated for $C_{14}H_{10}N_2O_2$, 238.0742; found, 238.0736 [M $^{+}$].

References

1. K. S. Levchenko, I. S. Semenova, V. N. Yarovenko, P. S. Shmelin and M. M. Krayushkin, *Tetrahedron Lett*, 2012, **53**, 3630-3632.

2. X-ray crystallography of compound 3a, and 3r.



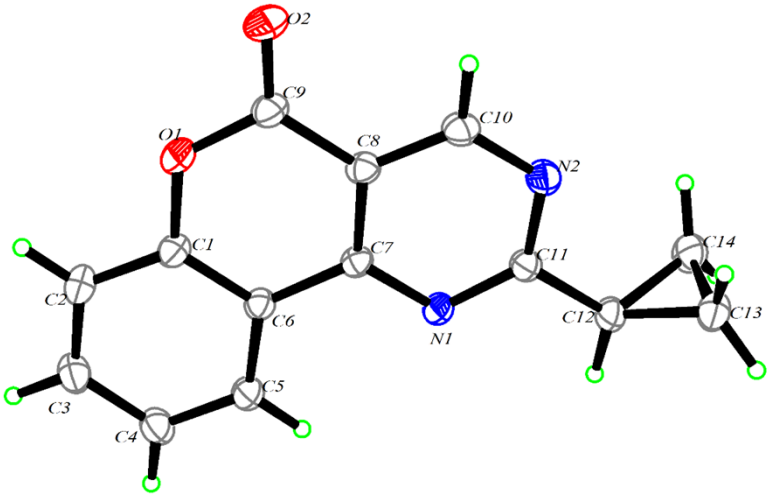
3a

A specimen of $C_{15}H_{12}N_2O_4$, approximate dimensions 0.030 mm x 0.050 mm x 0.200 mm, was used for the X-ray crystallographic analysis.The X-ray intensity data were measured.

The total exposure time was 2.98 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 8943 reflections to a maximum θ angle of 24.99° (0.84 Å resolution), of which 2301 were independent (average redundancy 3.887, completeness = 99.7%, R_{int} = 2.33%, R_{sig} = 2.15%) and 1666 (72.40%) were greater than $2\sigma(F^2)$.The final cell constants of a = 7.9465(5) Å, b = 18.6642(12) Å, c = 8.8245(6) Å, β = 95.265(5)°, volume = 1303.28(15) $Å^3$, are based upon the refinement of the XYZ-centroids of 2179 reflections above 20 σ(I) with 5.123° < 2θ < 47.99°.Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.914. The calculated minimum and maximum transmission coefficients (based on crystal
size) are 0.9790 and 0.9968.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{15}H_{12}N_2O_4$.The final anisotropic full-matrix least-squares refinement on F^2 with 191 variables converged at R1 = 5.25%, for the observed data and wR2 = 13.49% for all data. The goodness-of-fit was 1.025. The largest peak in the final difference electron density synthesis was 0.461 $e^-/Å^3$ and the largest hole was -0.325 $e^-/Å^3$ with an RMS deviation of 0.049 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.438 g/cm^3 and F(000), 584 e^-.

The crystal structure for **3a** has been deposited at the Cambridge Crystallographic Data Center and allocated the reference no. CCDC 974573.



3r

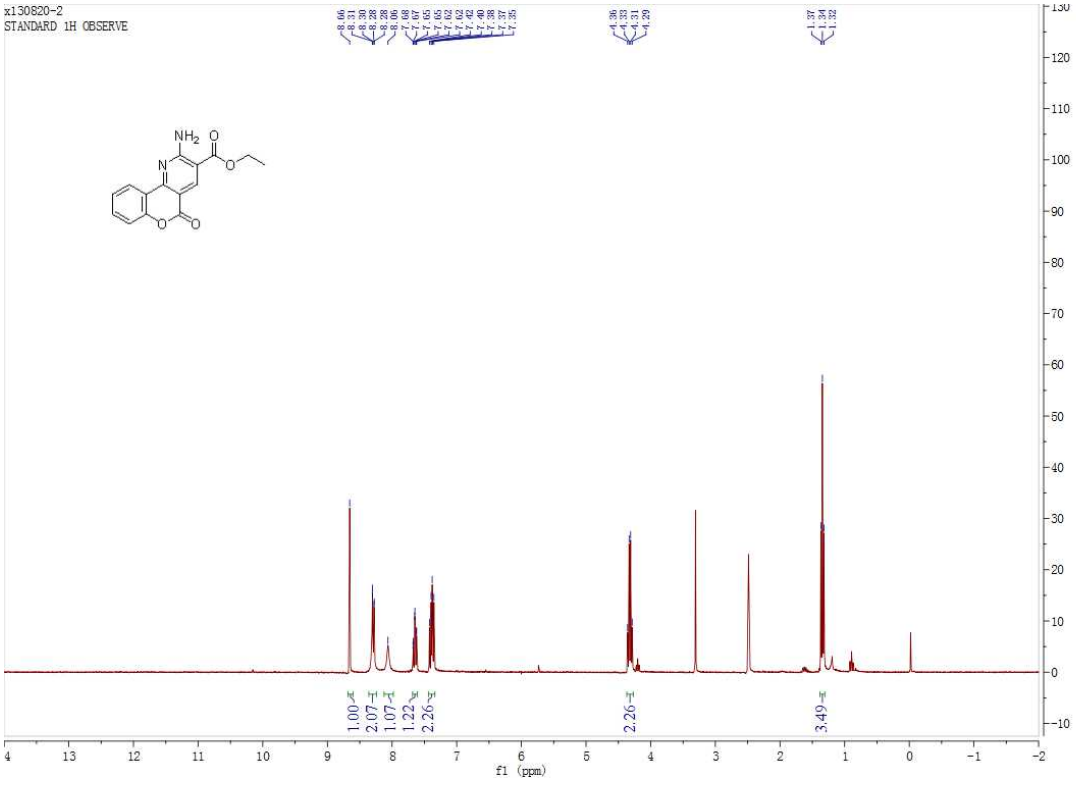
A specimen of $C_{14}H_{10}N_2O_2$, approximate dimensions 0.100 mm x 0.100 mm x 0.700 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

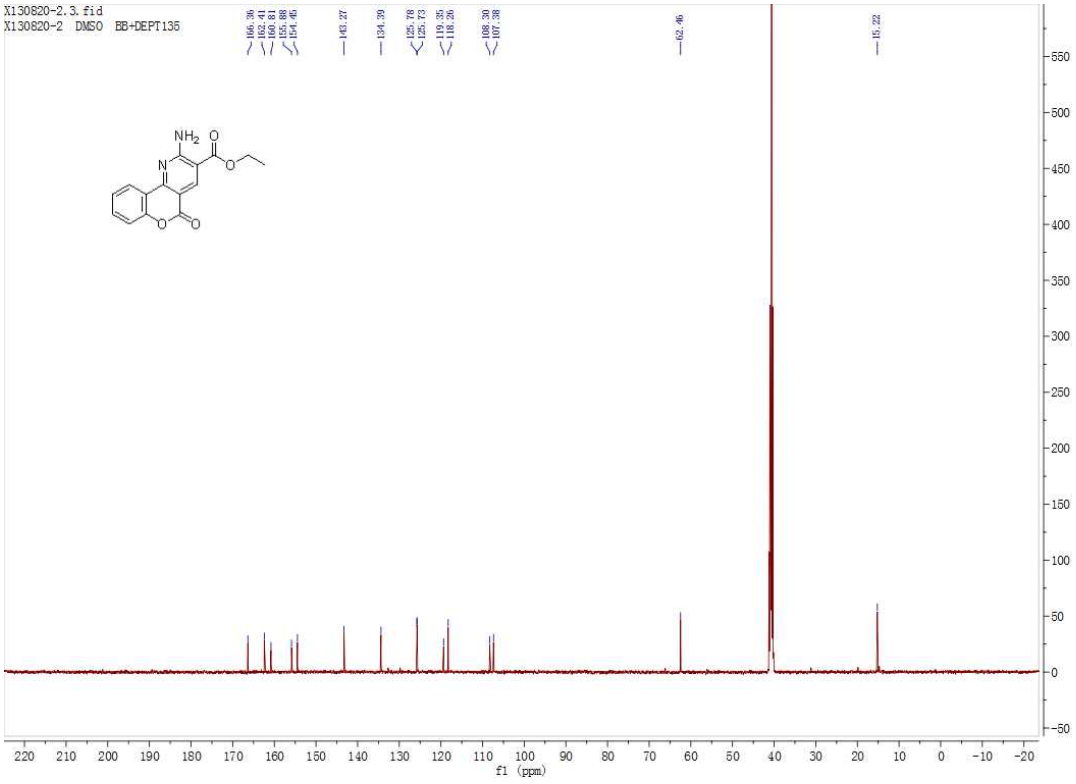
The total exposure time was 3.12 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 5288 reflections to a maximum θ angle of 24.99° (0.84 Å resolution), of which 1878 were independent (average redundancy 2.816, completeness = 95.4%, R_{int} = 2.04%, R_{sig} = 2.33%) and 1475 (78.54%) were greater than $2\sigma(F^2)$. The final cell constants of a = 5.2272(9) Å, b = 8.0305(13) Å, c = 13.945(2) Å, α = 88.537(11)°, β = 82.628(11)°, γ = 74.066(10)°, volume = 558.20(16) $Å^3$, are based upon the refinement of the XYZ-centroids of 2480 reflections above 20 σ(I) with 5.275° < 2θ < 55.33°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.868. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9260 and 0.9889.

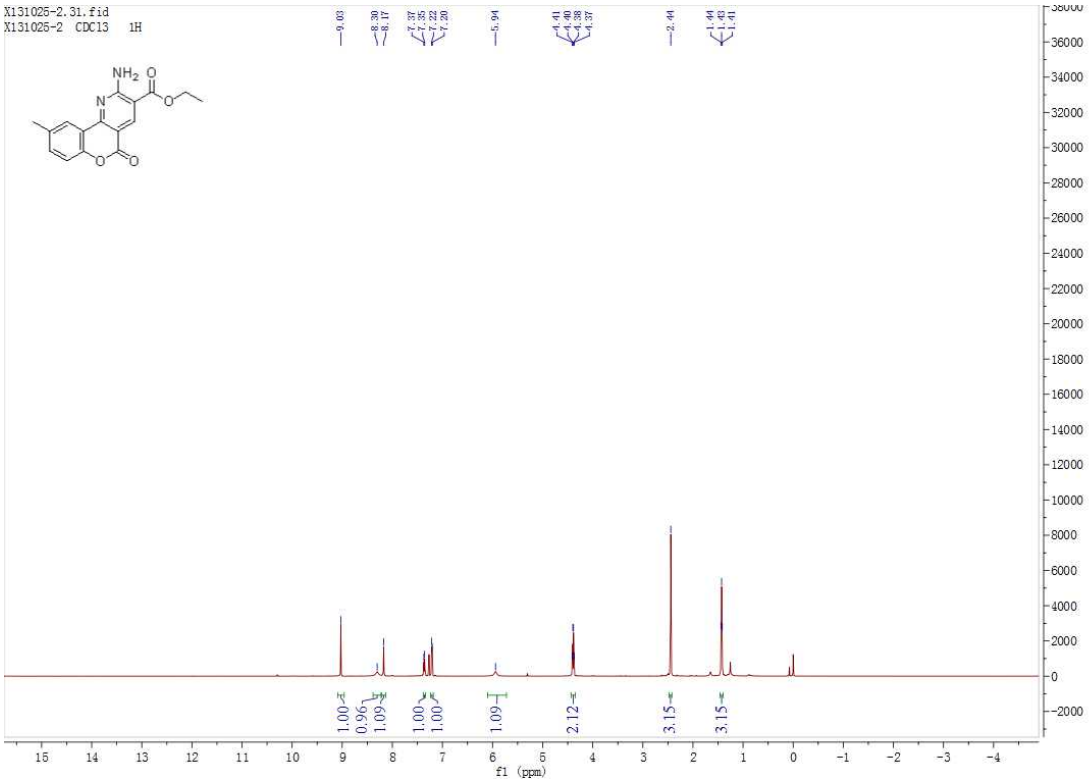
The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P -1, with Z = 2 for the formula unit, $C_{14}H_{10}N_2O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 163 variables converged at R1 = 4.15%, for the observed data and wR2 = 12.42% for all data. The goodness-of-fit was 1.459. The largest peak in the final difference electron density synthesis was 0.145 $e^-/Å^3$ and the largest hole was -0.293 $e^-/Å^3$ with an RMS deviation of 0.067 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.418 g/cm^3 and F(000), 278 e^-.

The crystal structure for **3r** has been deposited at the Cambridge Crystallographic Data Center and allocated the reference no. CCDC 974574.

3. ^{1}H NMR and ^{13}C NMR



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4.41
4.40
4.38
4.37
2.44
1.44
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1.00
1.00
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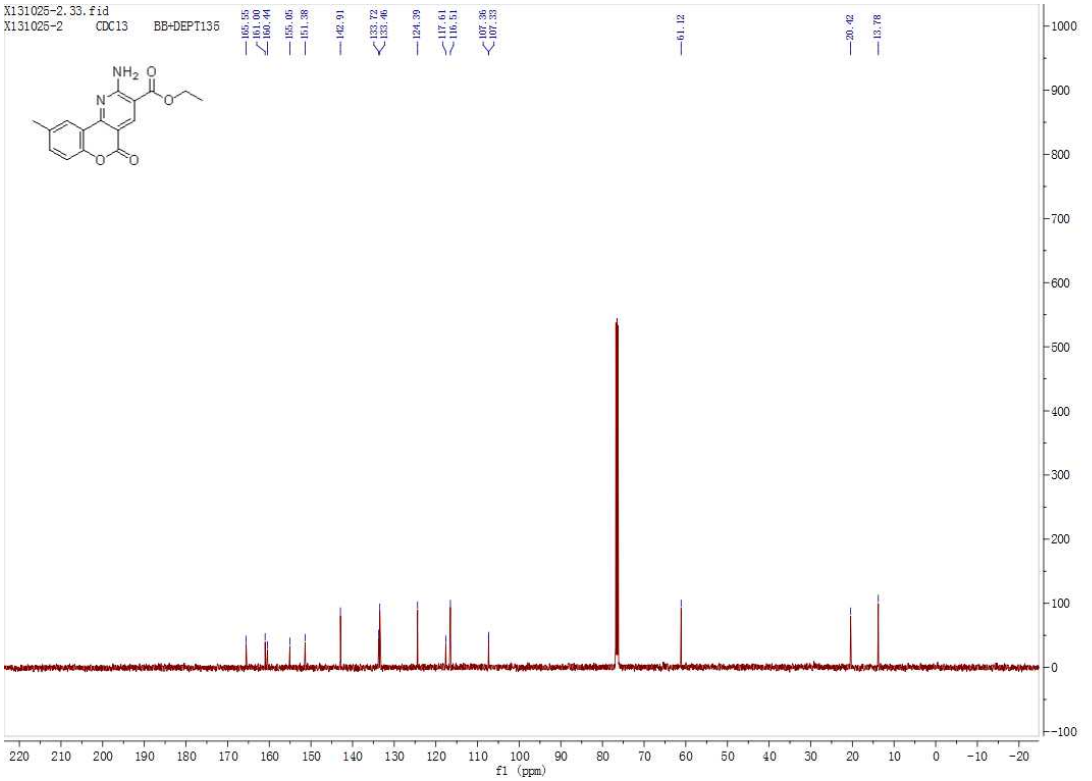
3.15
f1 (ppm)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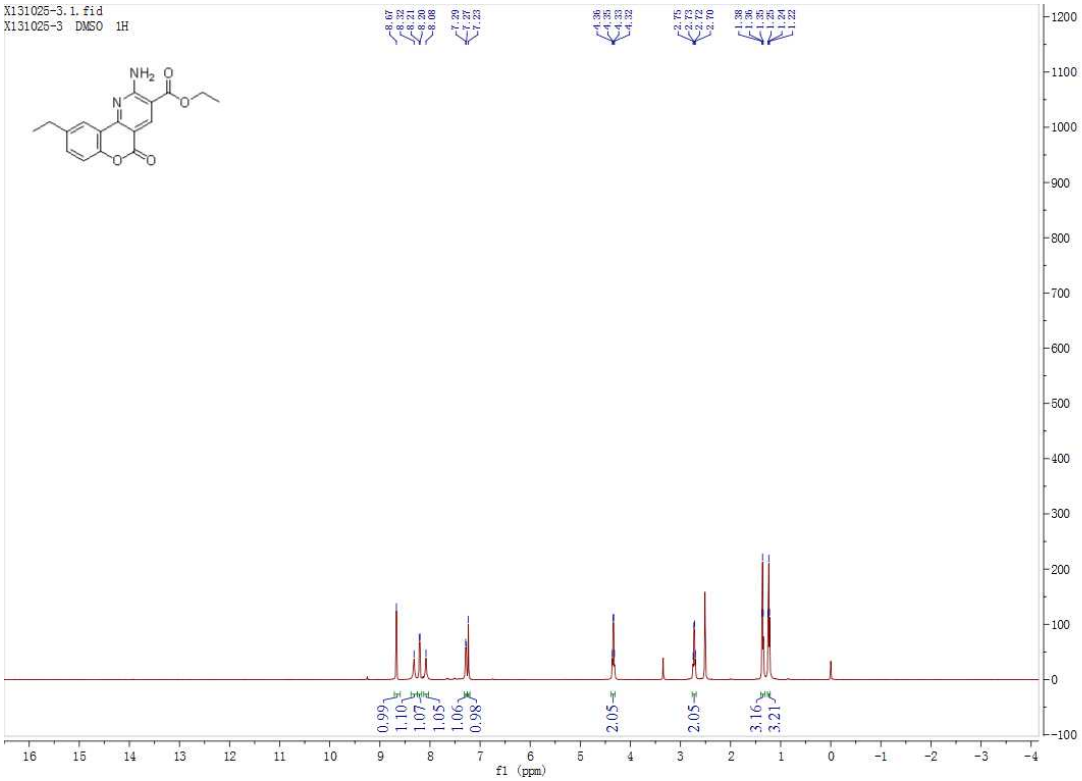
f1 (ppm)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4.32
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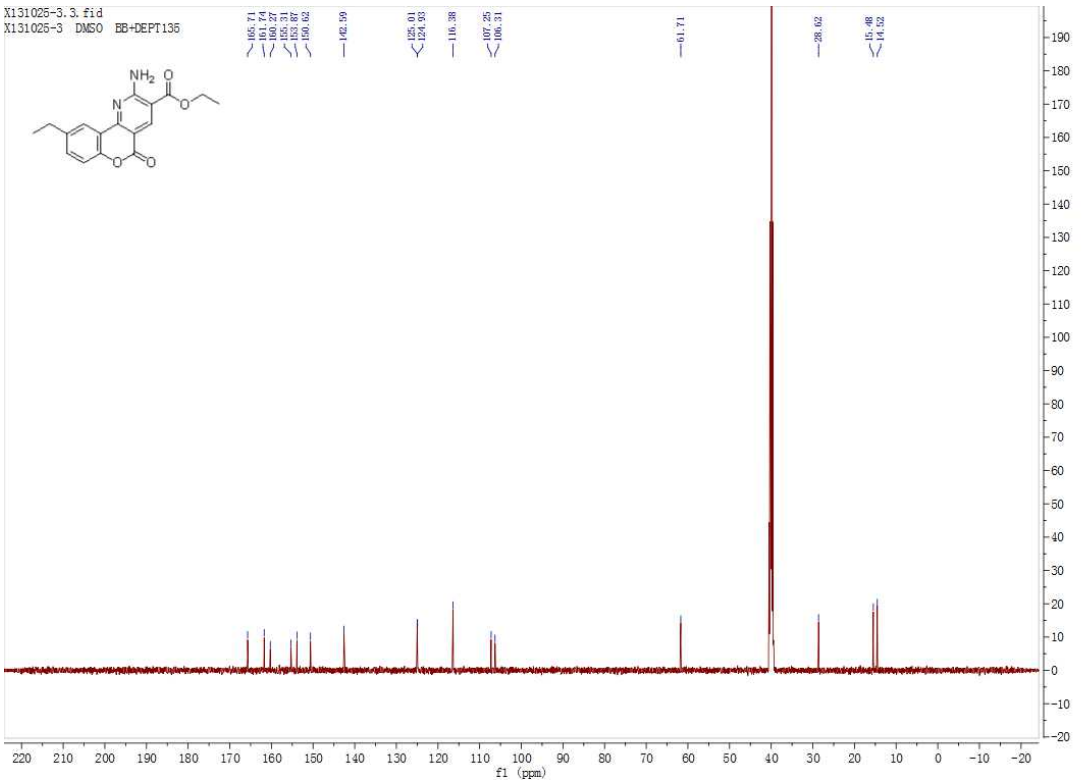
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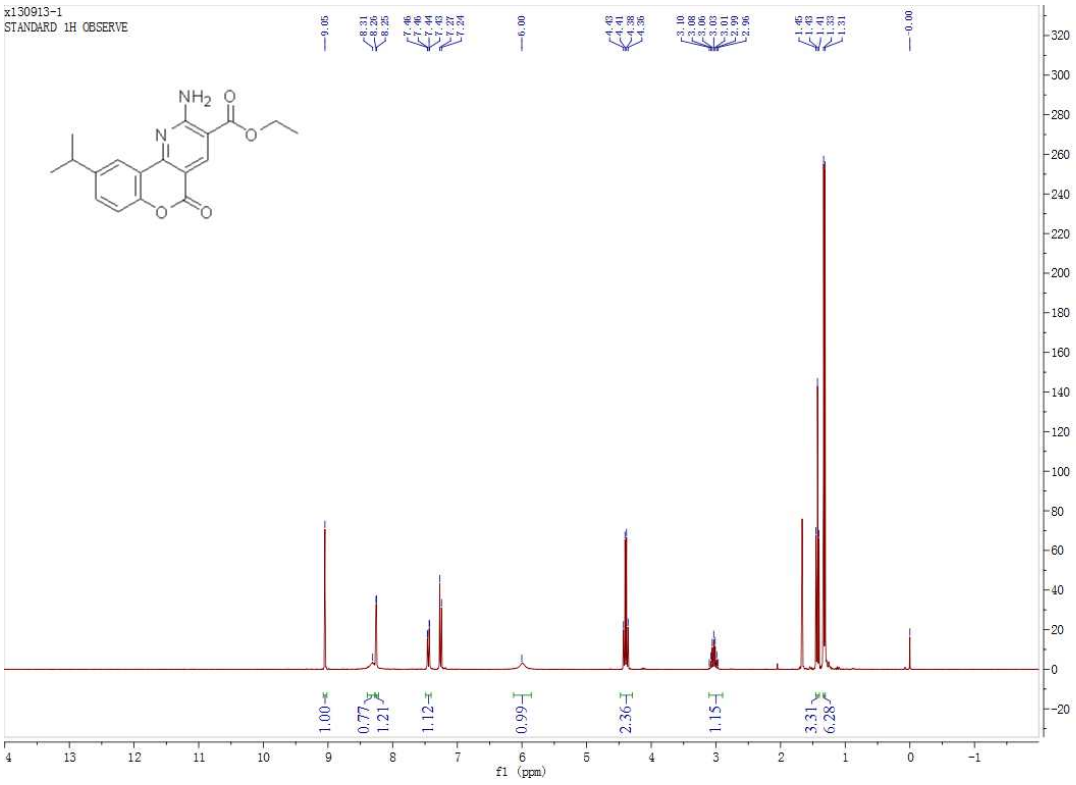
O
f1 (ppm)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4.41
4.38
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3.10
3.08
3.06
3.03
3.01
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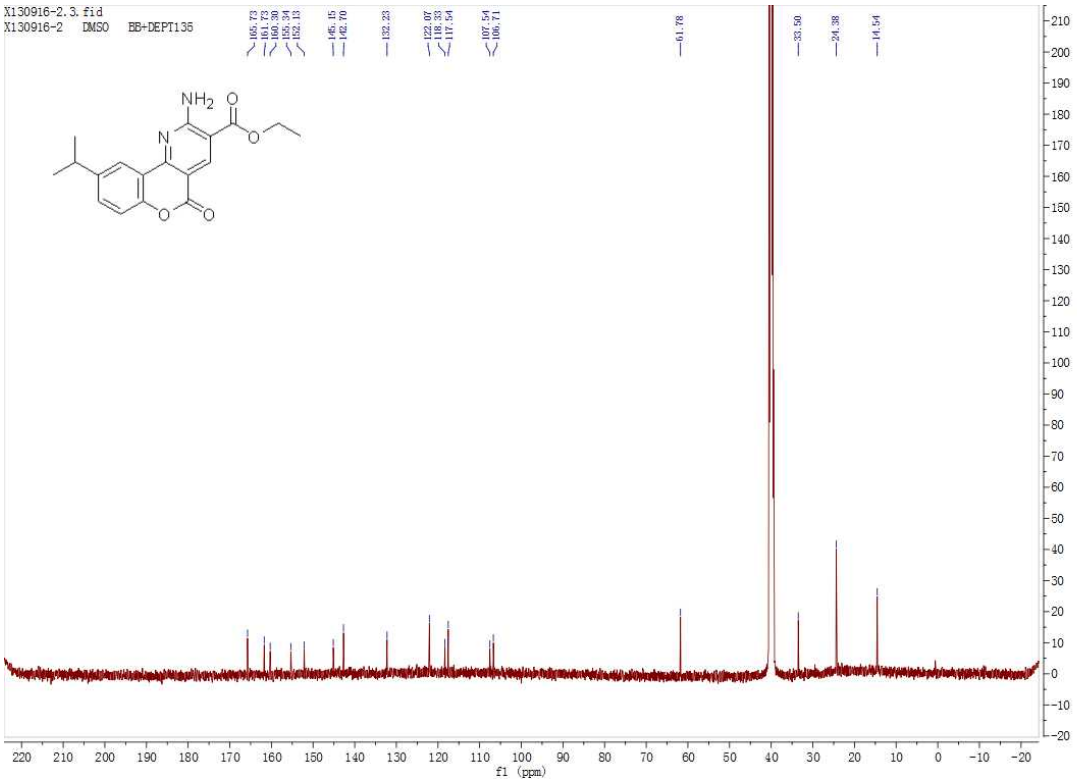
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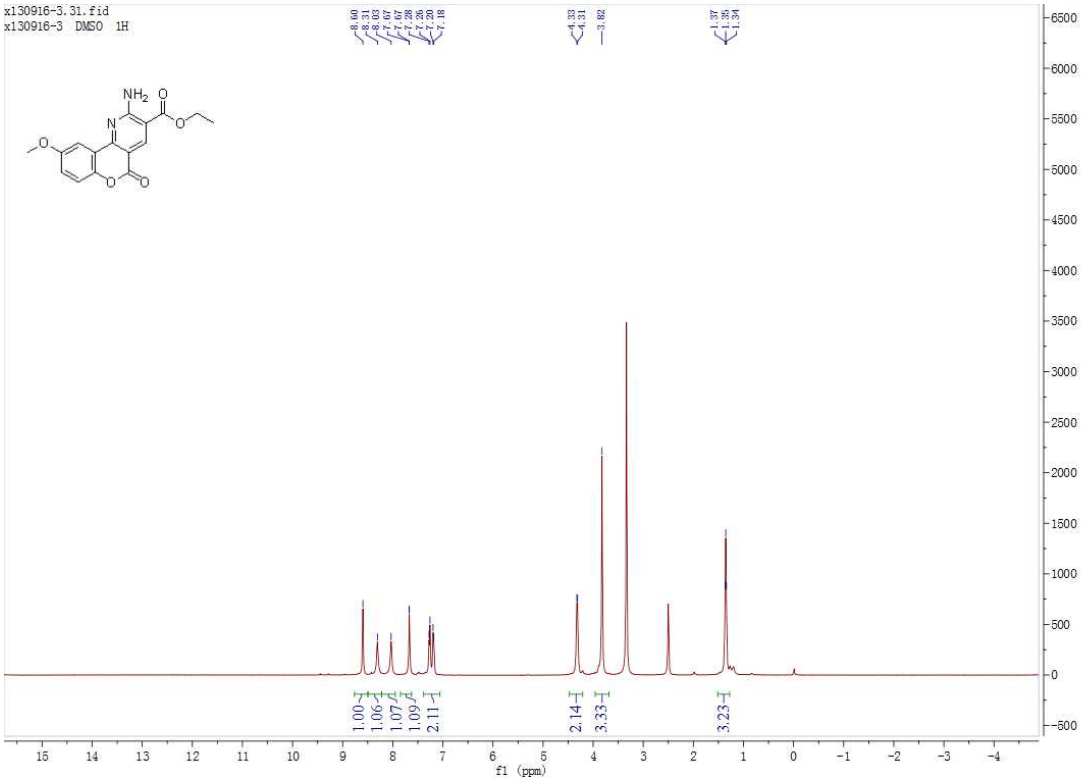
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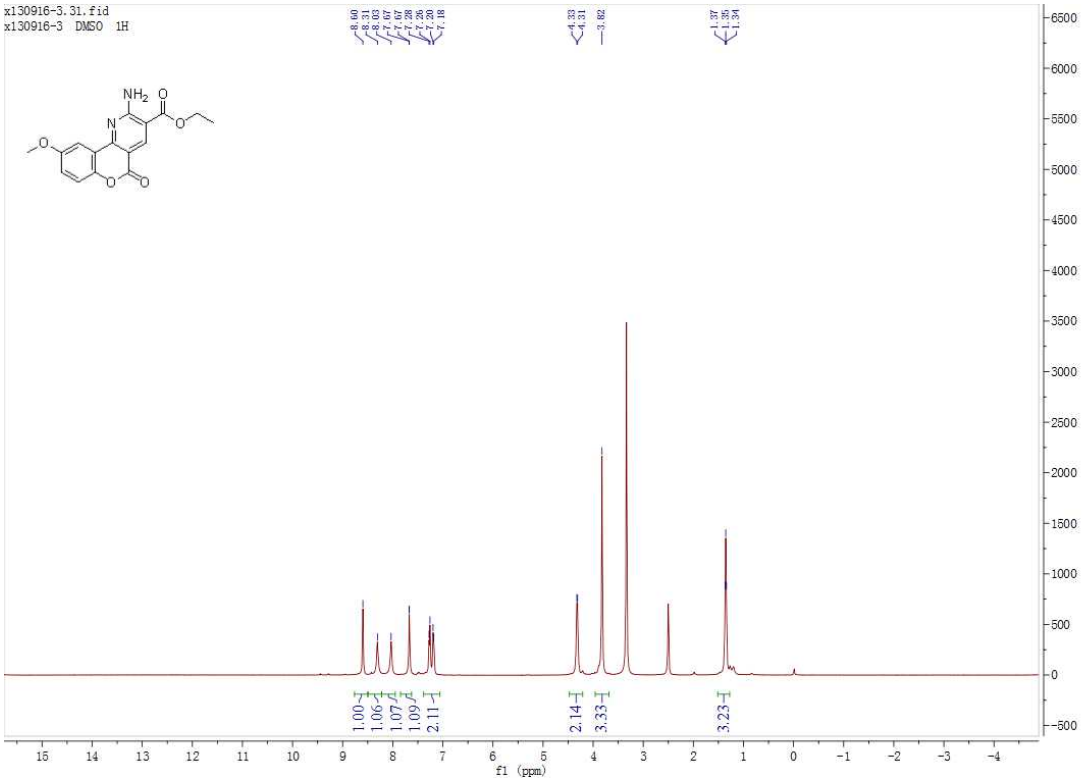
f1 (ppm)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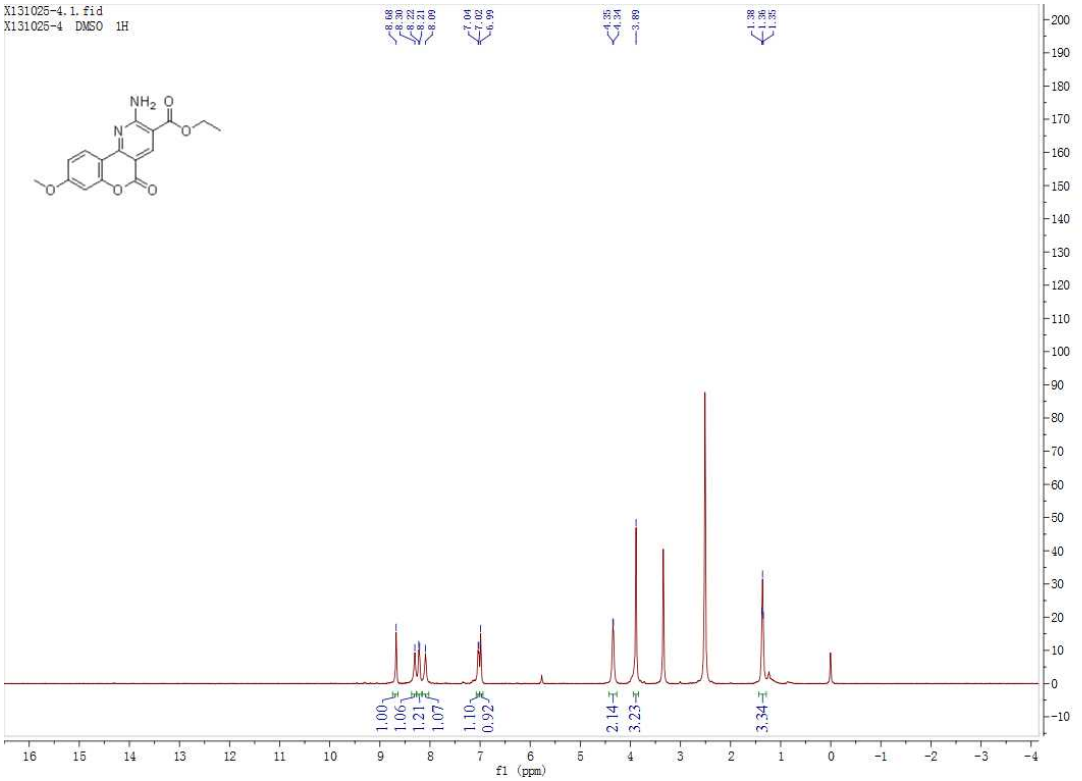
f1 (ppm)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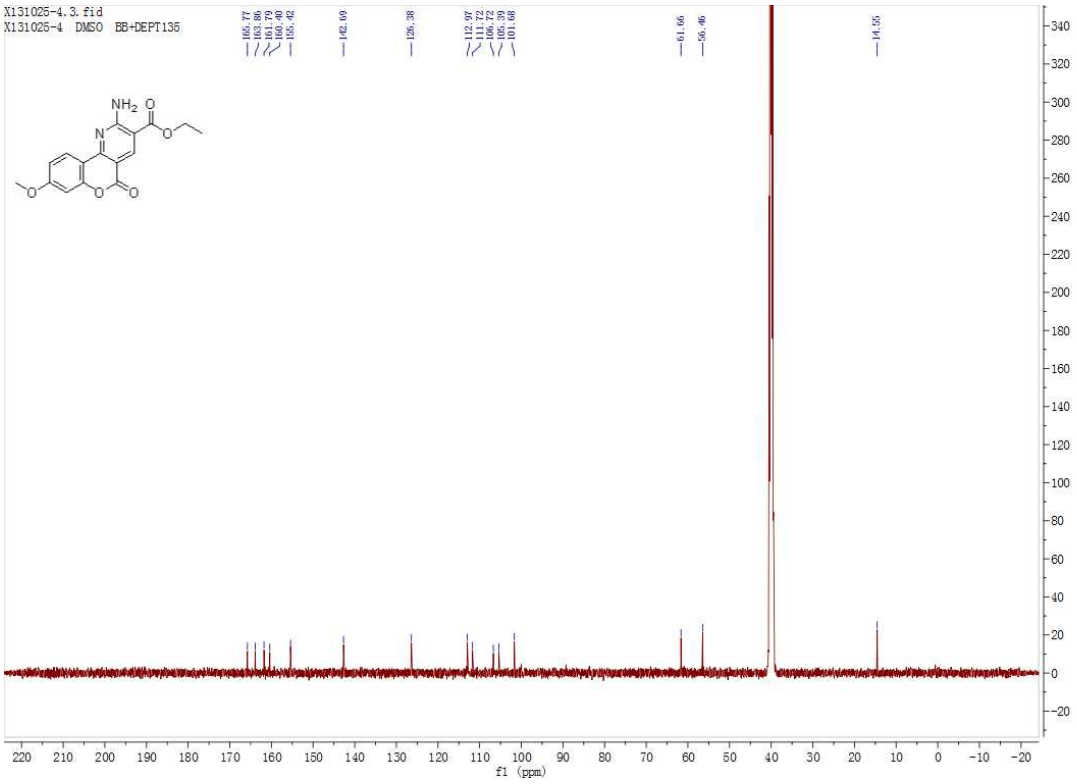
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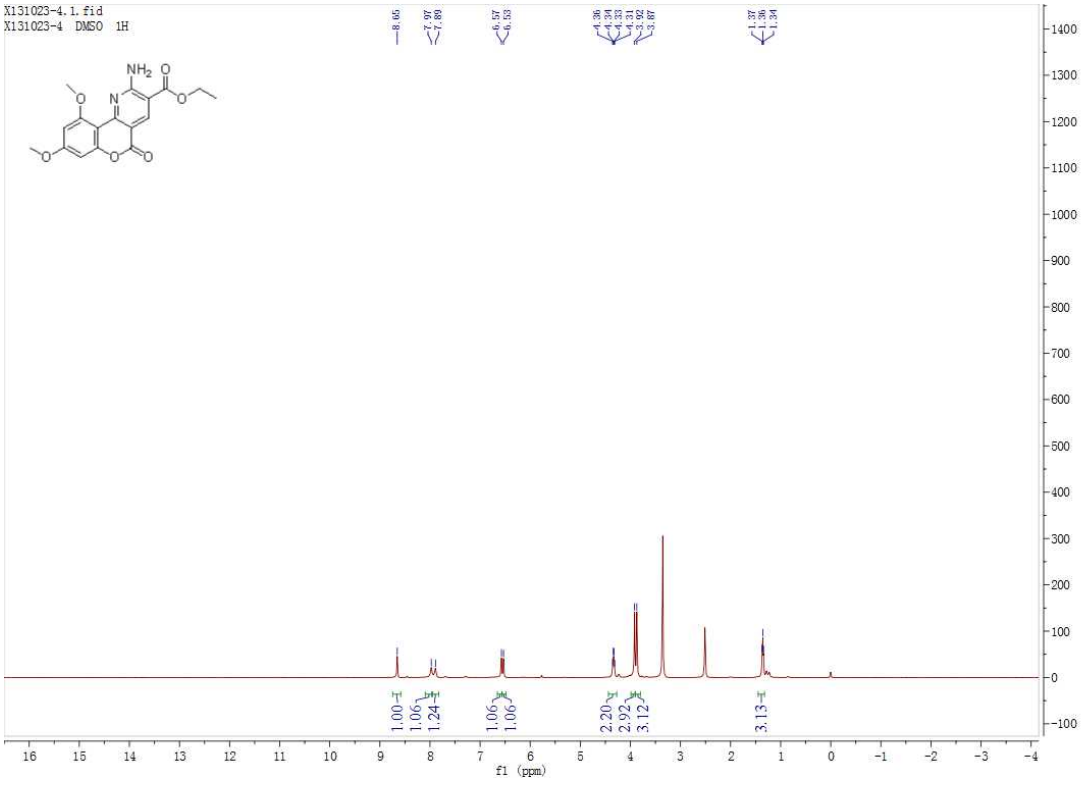
O
O
f1 (ppm)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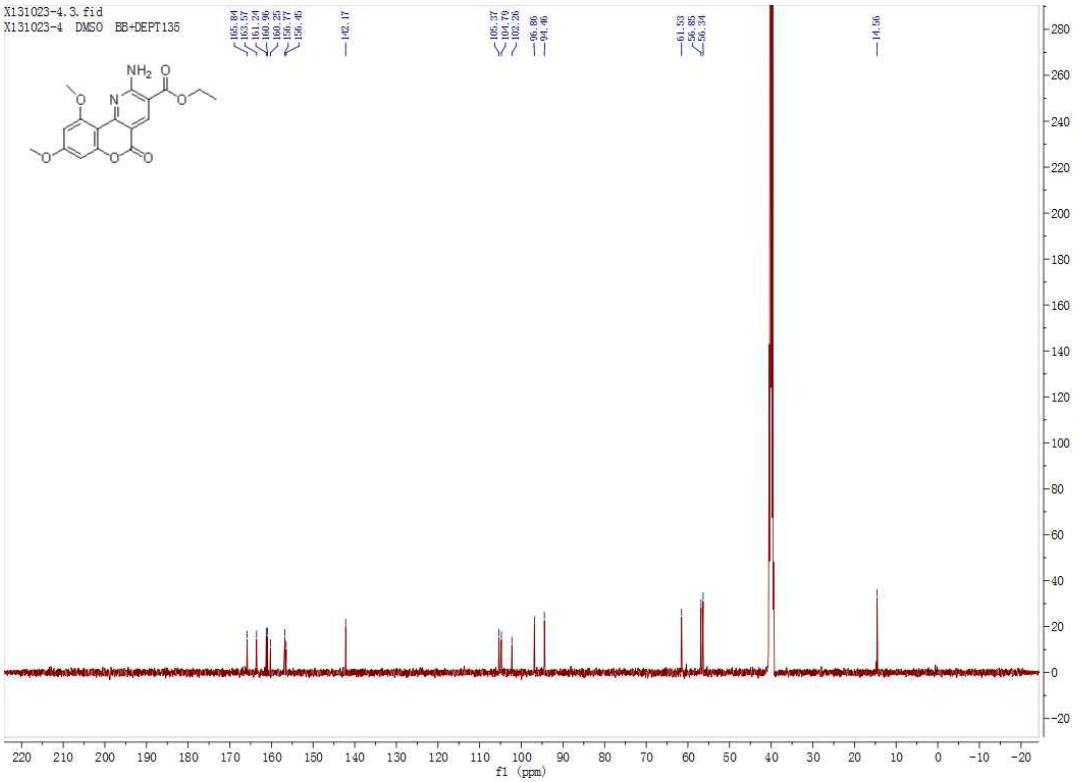
f1 (ppm)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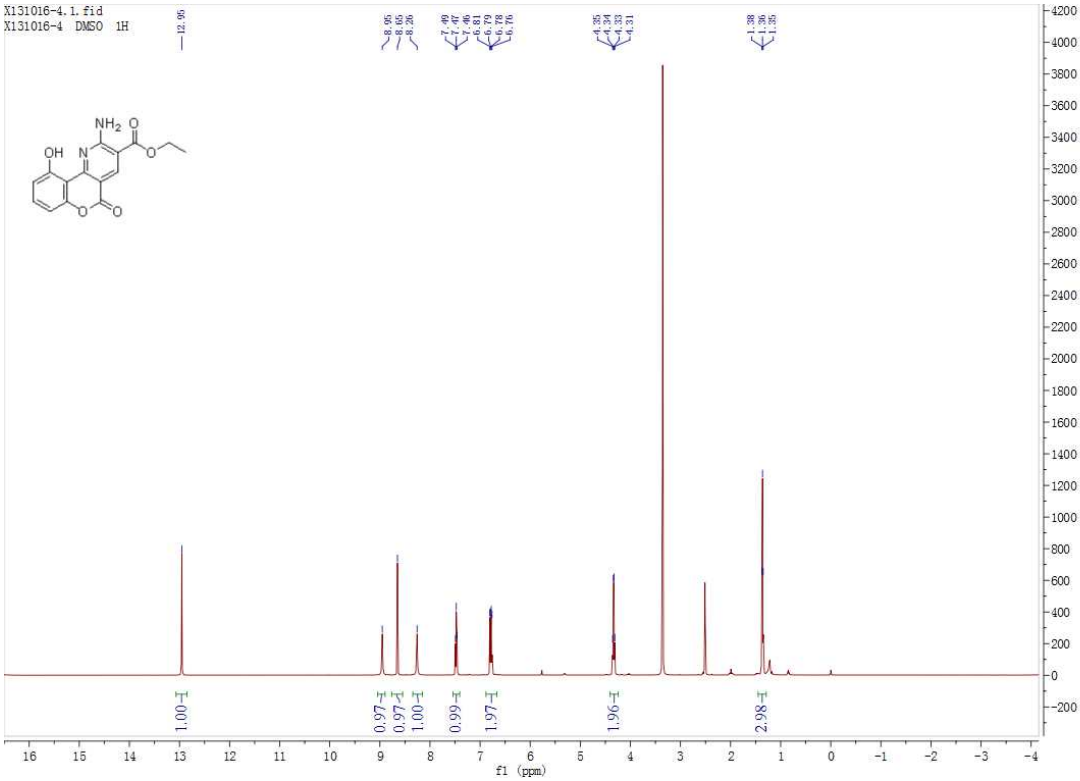
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4.33
4.31
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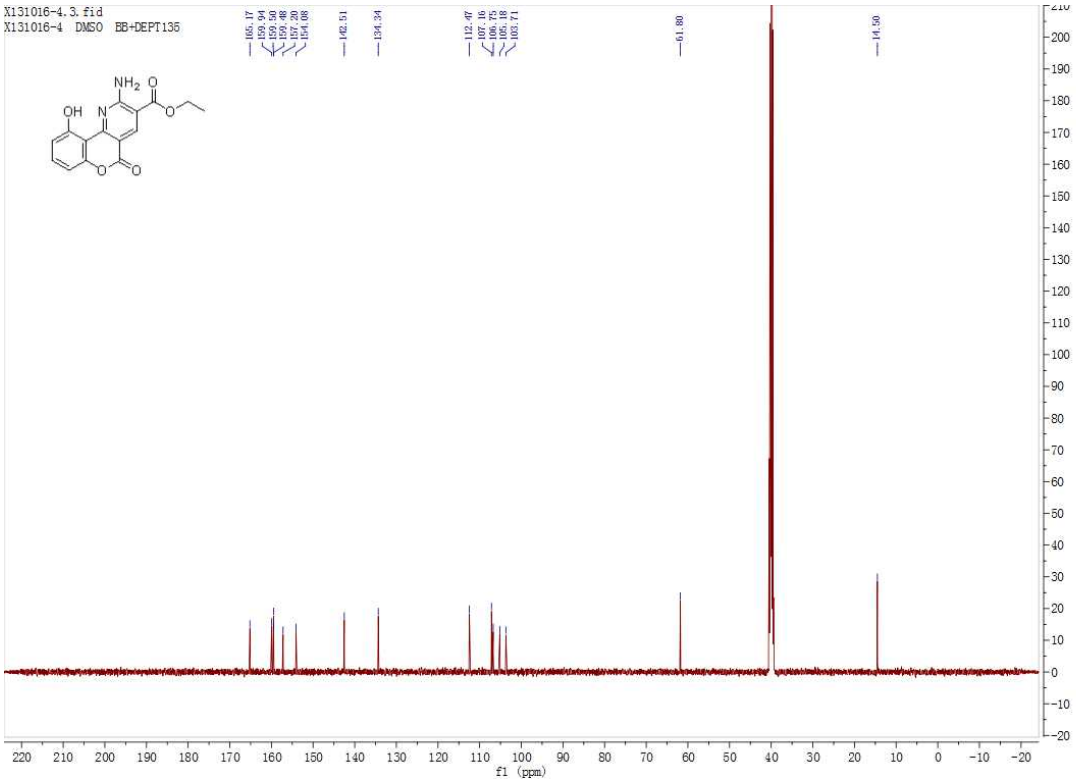
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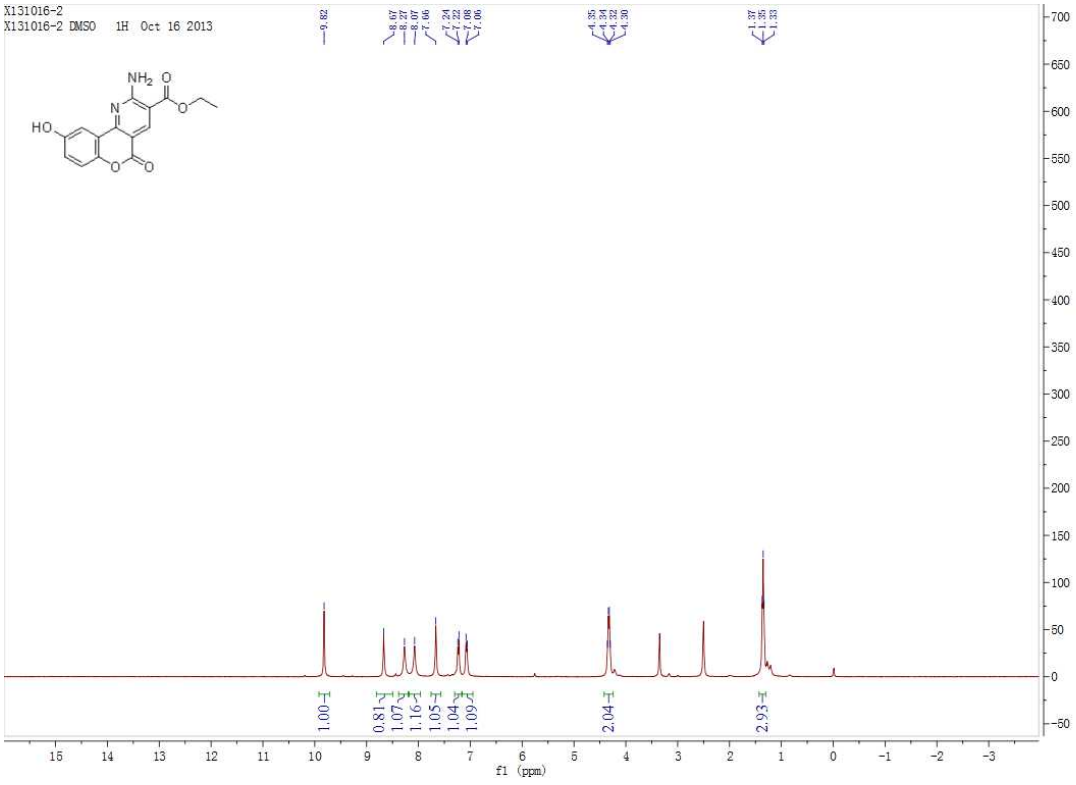
O
f1 (ppm)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X131016-2 DMSO 1H Oct 16 2013
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4.34
4.32
4.30
1.37
1.35
1.33
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O
HO
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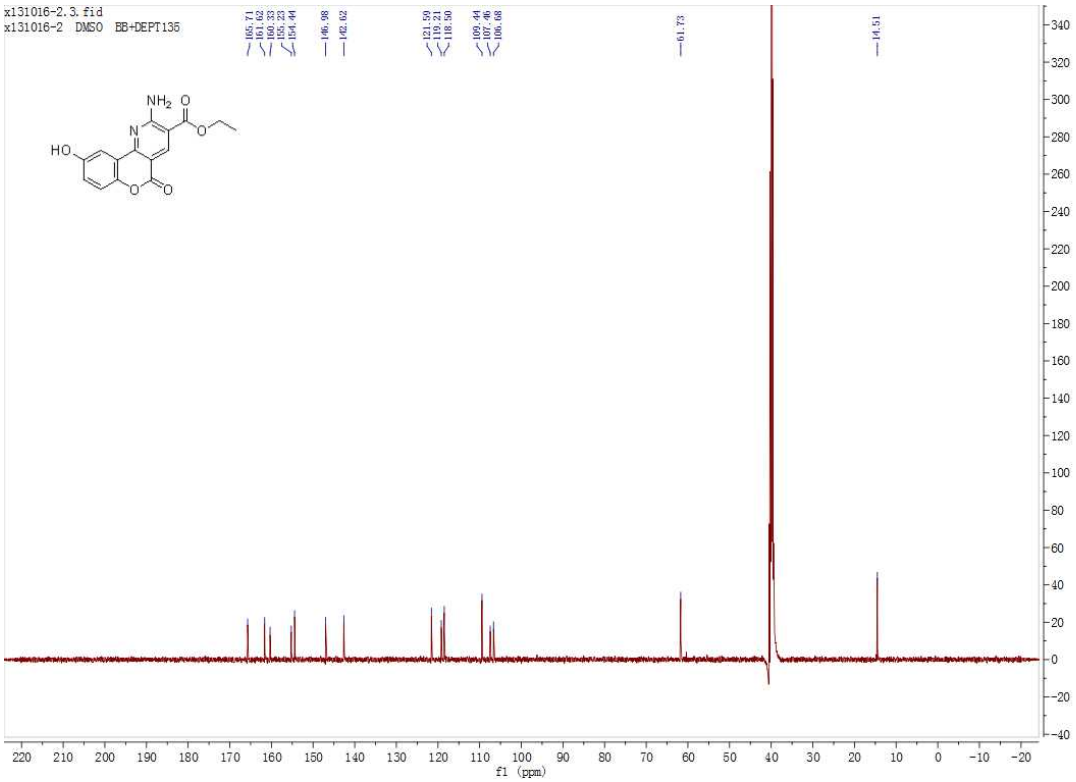
f1 (ppm)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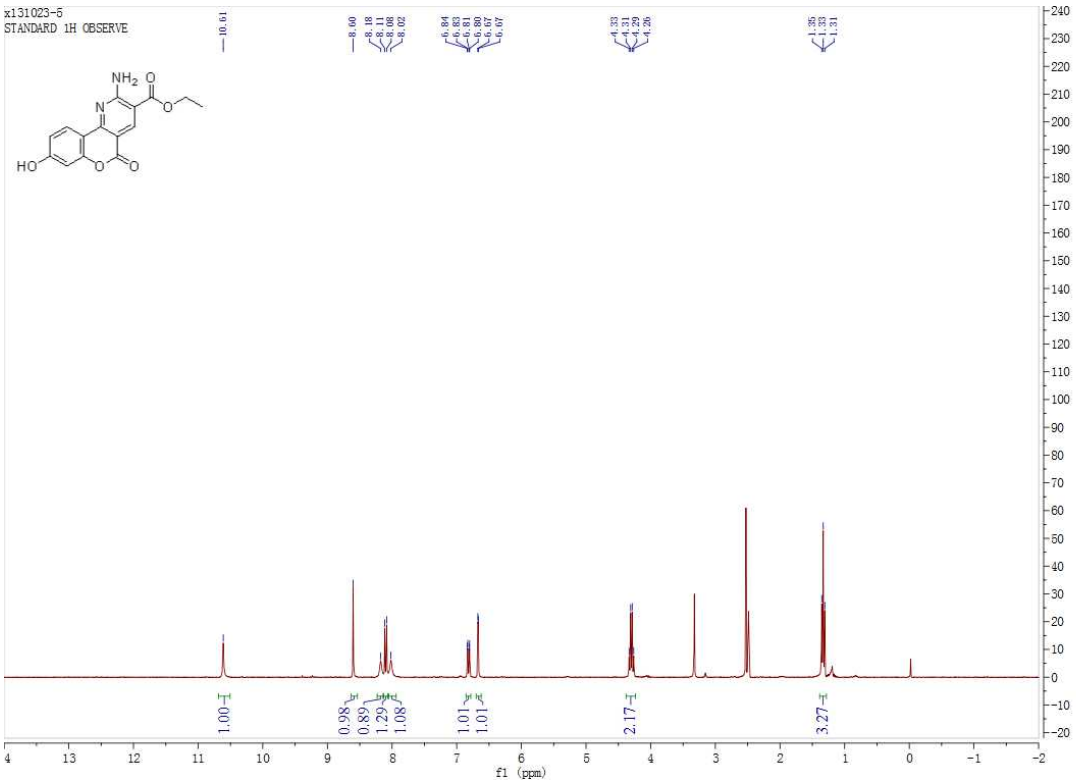
HO
O
O
f1 (ppm)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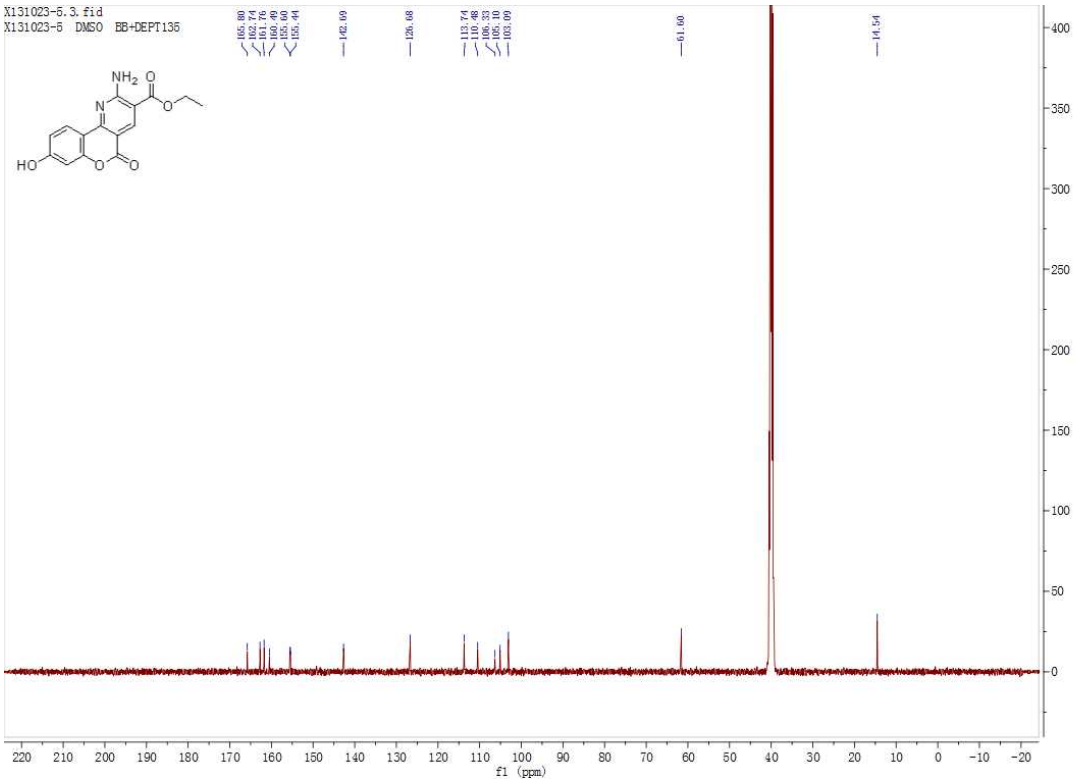
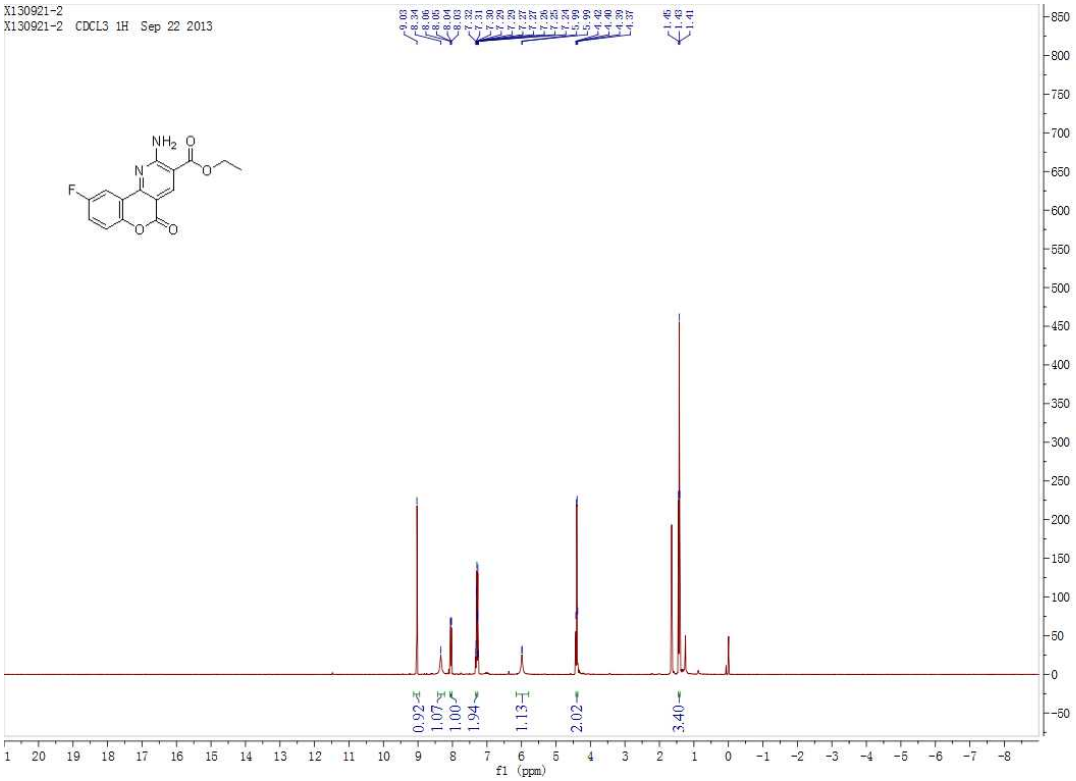
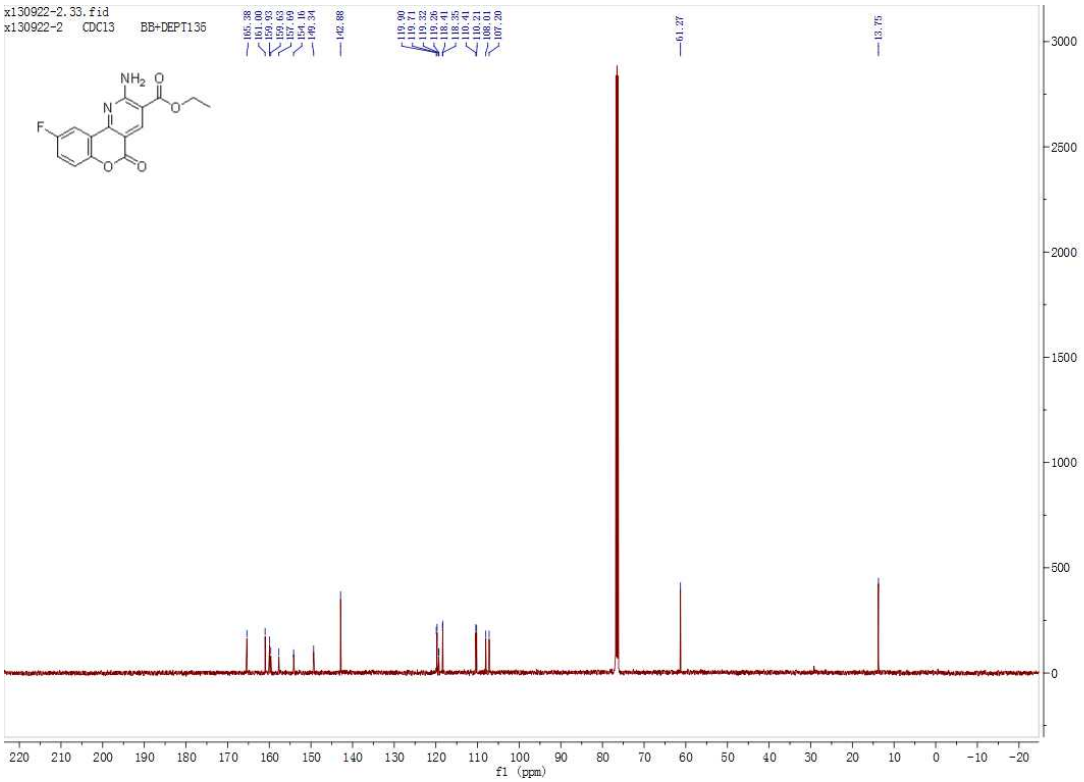
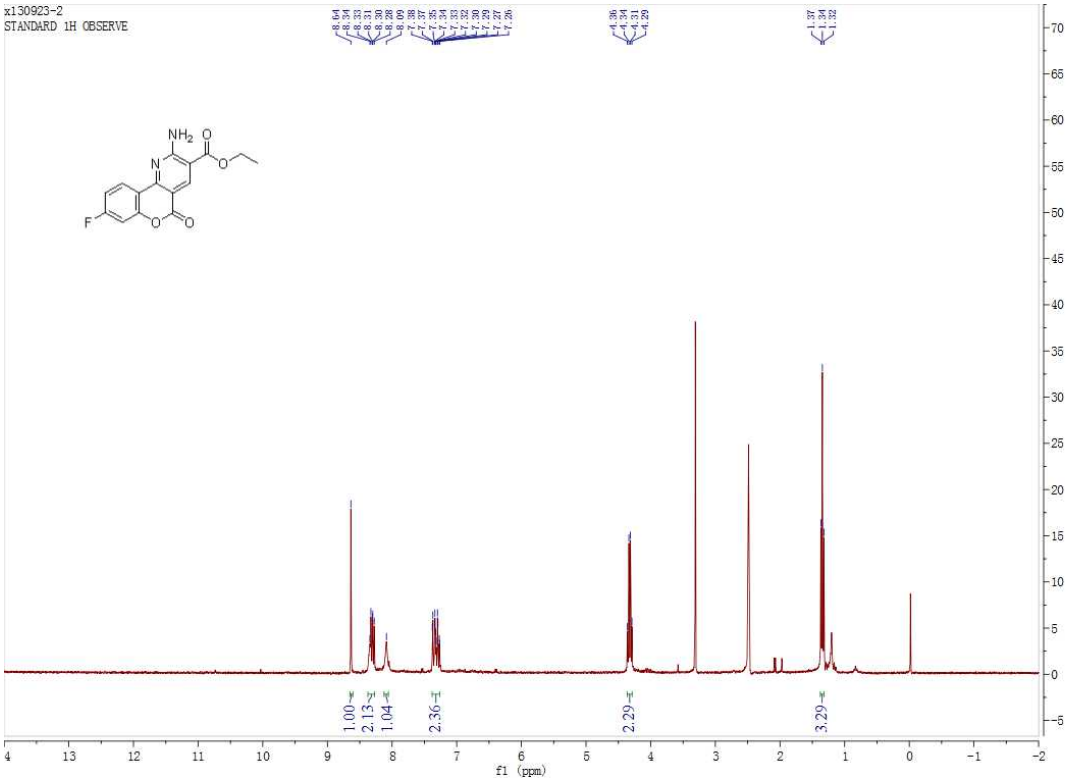
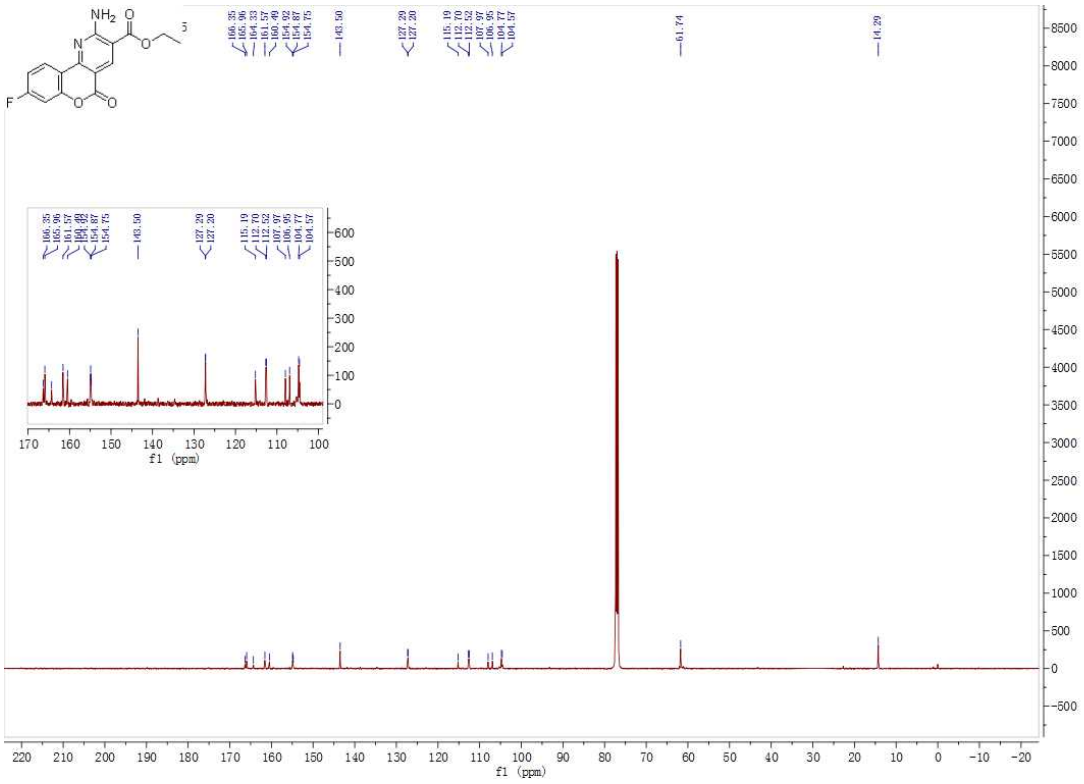
6.67
6.67
4.33
4.31
4.29
4.26
1.35
1.33
1.31
NH2
O
N
HO
O
O
1.00
0.98
0.89
1.29
1.08
1.01
1.01
2.17
3.27
f1 (ppm)

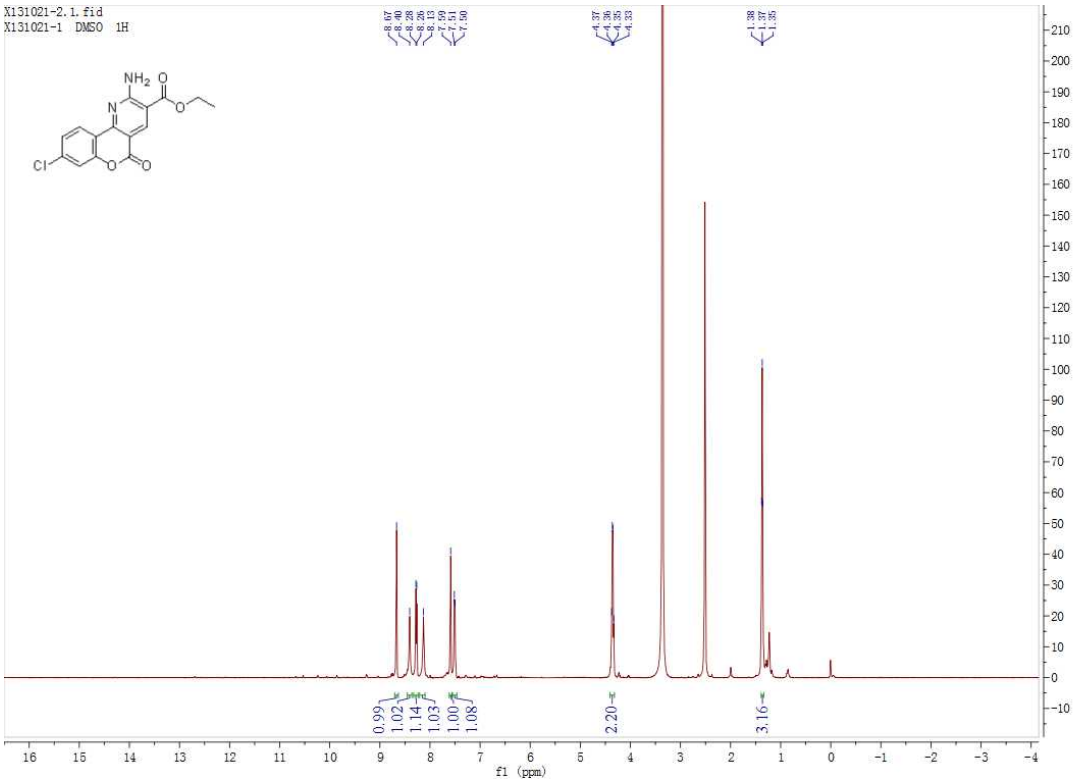

X131023-5.3.fid
X131023-5 DMSO BB+DEPT135
165.89
162.74
161.76
160.49
155.60
155.44
142.69
126.68
113.74
110.48
106.33
105.10
103.09
61.60
14.54
NH2
O
N
O
HO
O
O
f1 (ppm)

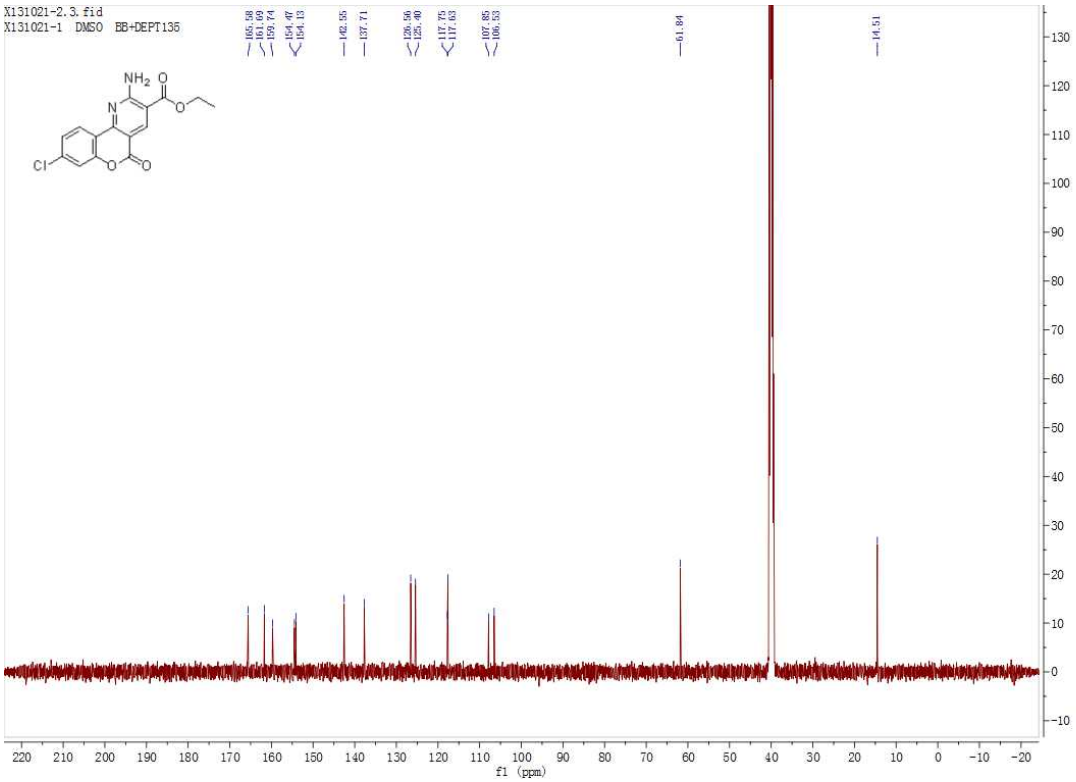

X130921-2
X130921-2 CDCL3 1H Sep 22 2013
9.03
8.34
8.06
8.05
8.04
8.03
7.32
7.31
7.30
7.29
7.29
7.27
7.27
7.26
7.25
7.24
5.99
4.42
4.40
4.39
4.37
1.45
1.43
1.41
NH2
O
N
O
F
O
O
0.92
1.07
1.00
1.94
1.13
2.02
3.40
f1 (ppm)

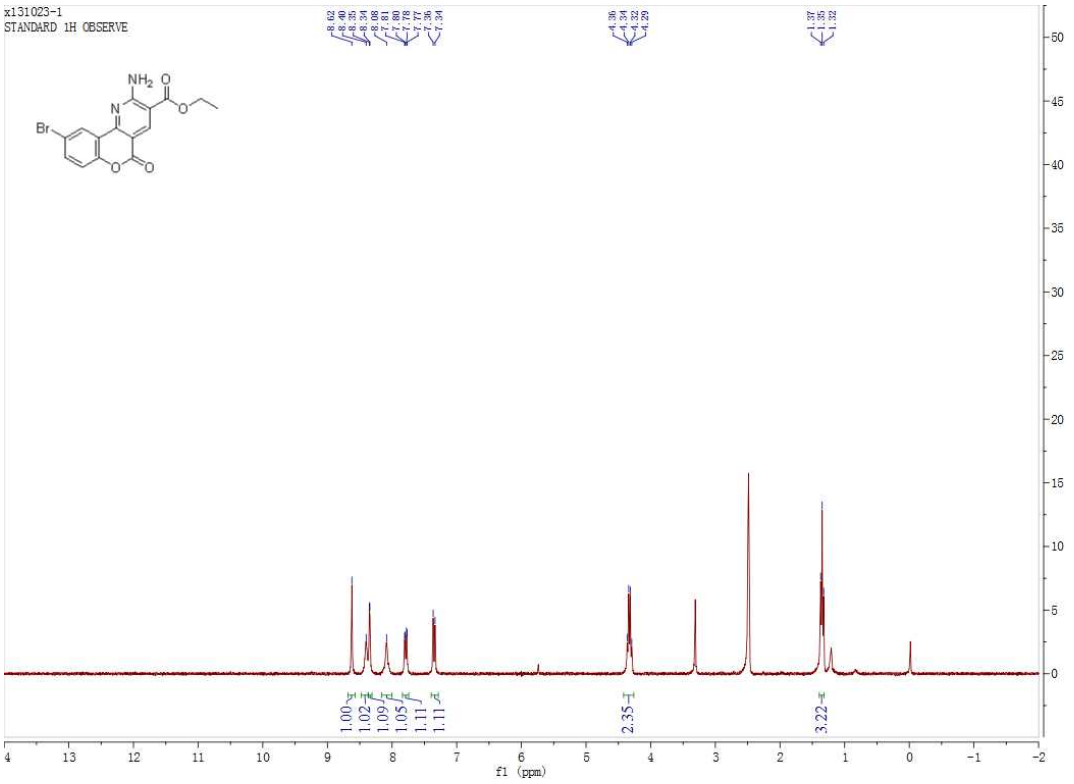

x130922-2.33.fid
x130922-2 CDC13 BB+DEPT135
165.38
161.00
159.83
158.65
157.69
154.16
149.34
142.88
119.90
119.71
119.32
119.26
118.41
118.35
110.41
110.21
108.01
107.20
61.27
13.75
f1 (ppm)

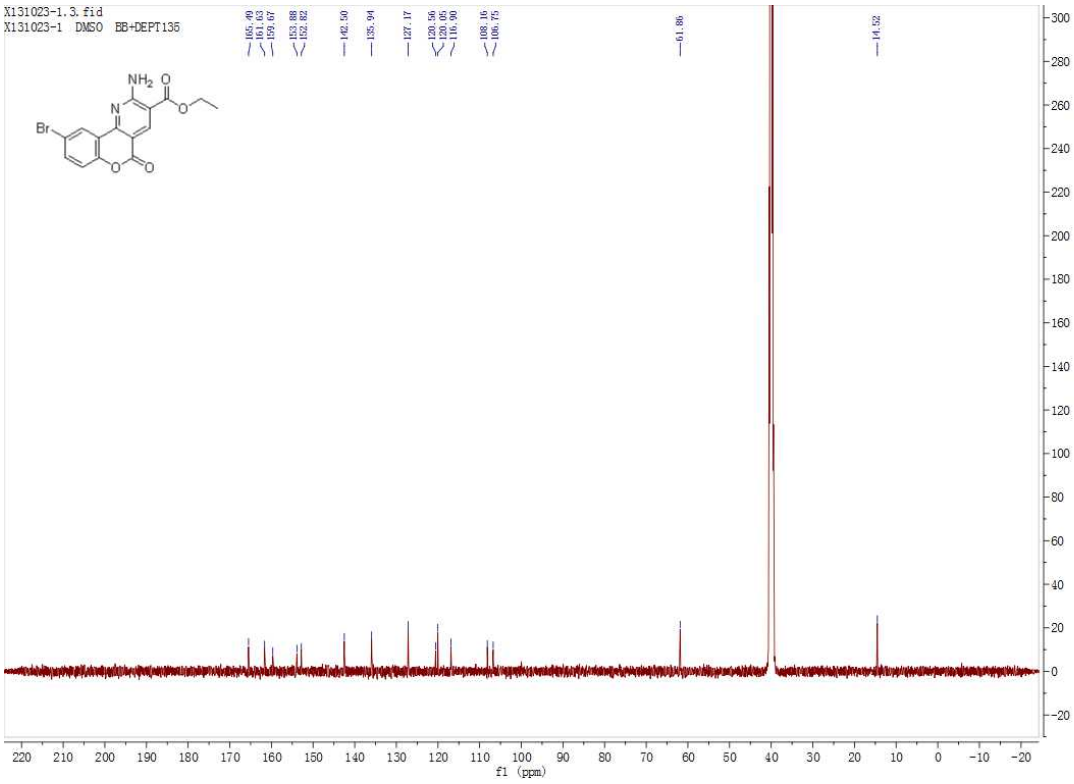

x130923-2
STANDARD 1H OBSERVE
8.64
8.34
8.33
8.31
8.30
8.28
8.09
7.38
7.37
7.35
7.34
7.33
7.32
7.30
7.29
7.27
7.26
4.36
4.34
4.31
4.29
1.37
1.34
1.32
1.00
2.13
1.04
2.36
2.29
3.29
f1 (ppm)

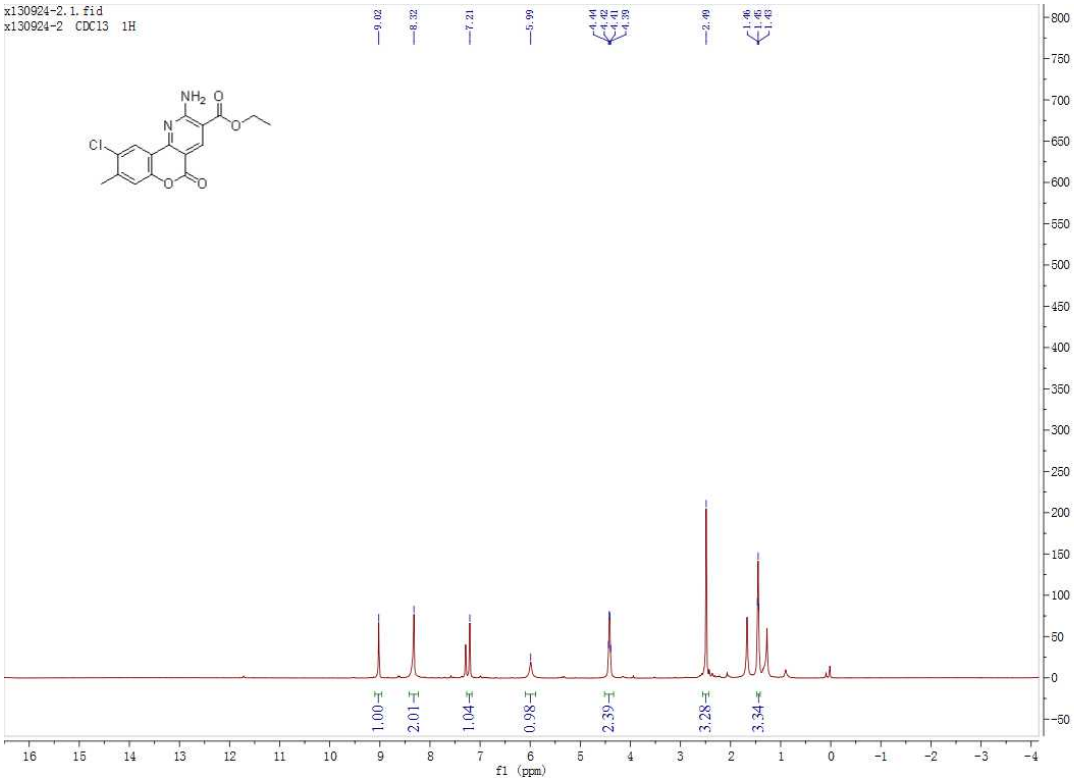

NH2
O
N
O
O
F
O
166.35
165.96
164.33
161.57
160.49
154.92
154.87
154.75
143.50
127.29
127.20
115.19
112.70
112.52
107.97
106.95
104.77
104.57
61.74
14.29
f1 (ppm)

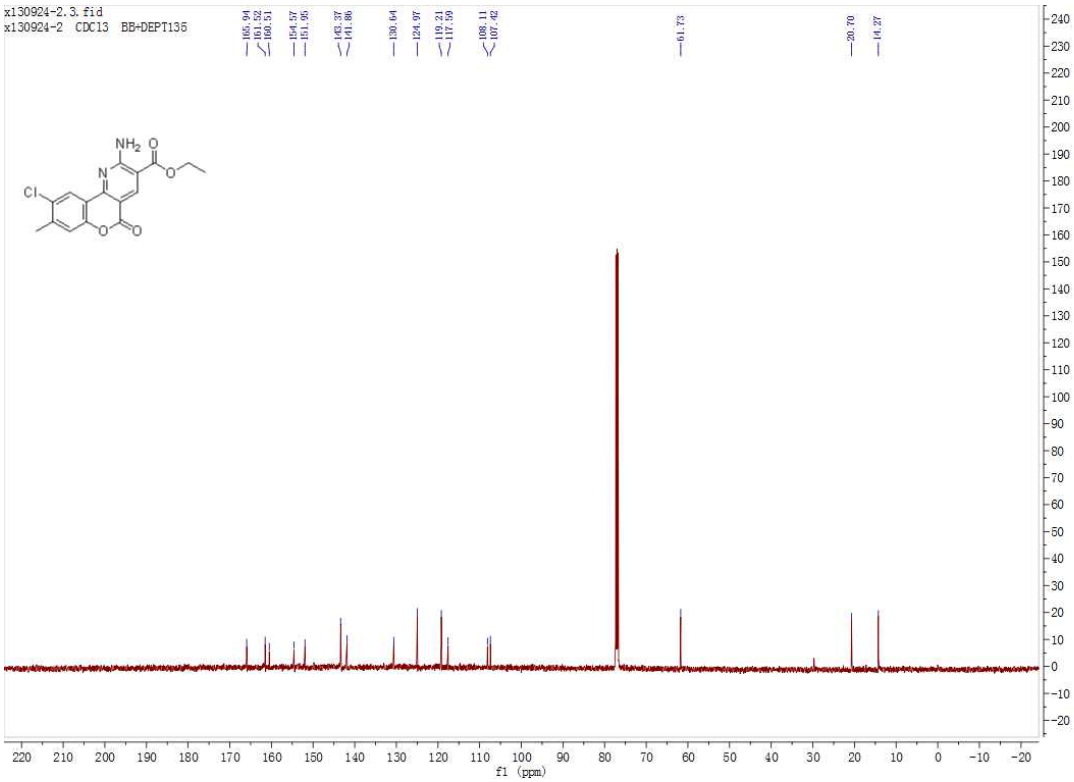

X131021-2.1.fid
X131021-1 DMSO 1H
8.67
8.40
8.28
8.26
8.13
7.59
7.51
7.50
4.37
4.36
4.35
4.33
1.38
1.37
1.35
NH2
O
N
O
Cl
O
0.99
1.02
1.14
1.03
1.00
1.08
2.20
3.16
f1 (ppm)

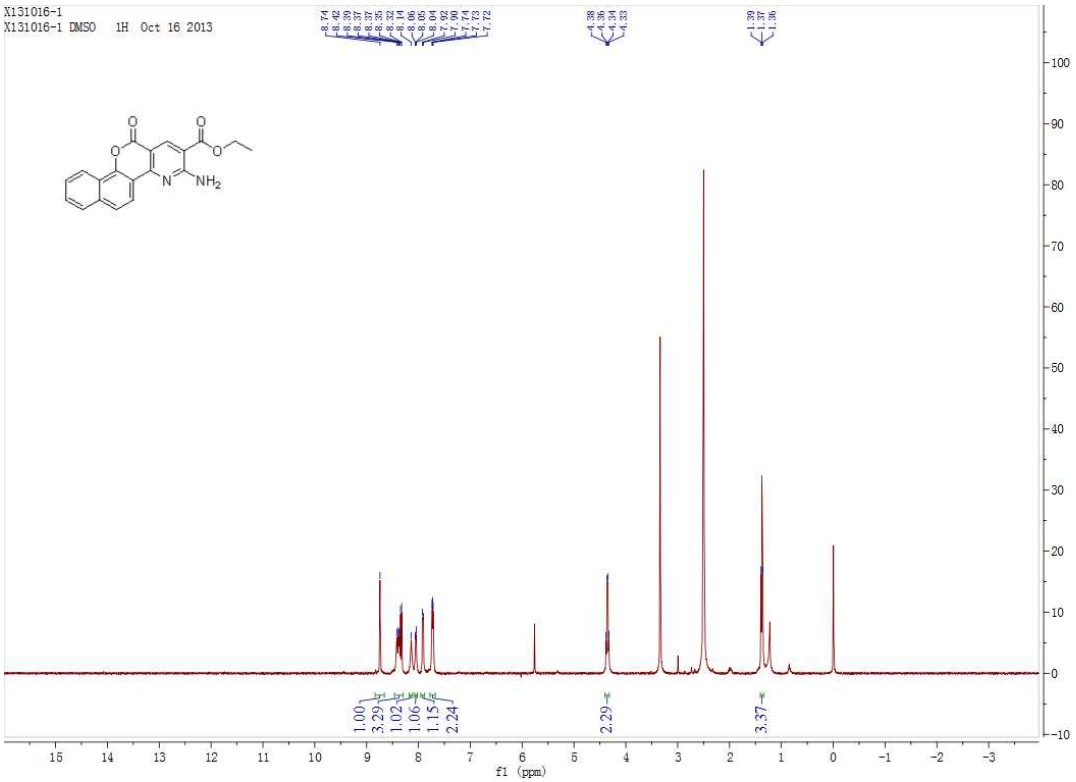

X131021-2.3.fid
X131021-1 DMSO BB+DEPT135
165.58
161.69
159.74
154.47
154.13
142.55
137.71
126.56
125.40
117.75
117.63
107.85
106.53
61.84
14.51
NH2
O
N
O
Cl
O
f1 (ppm)

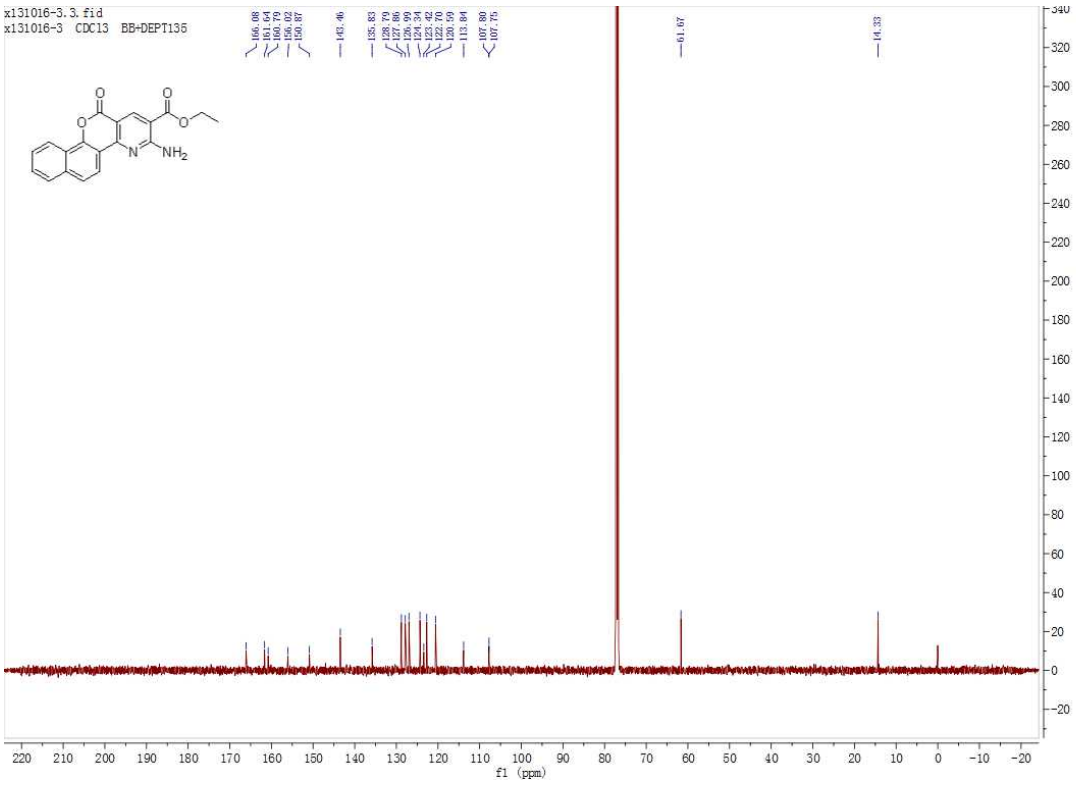

x131023-1
STANDARD 1H OBSERVE
f1 (ppm)

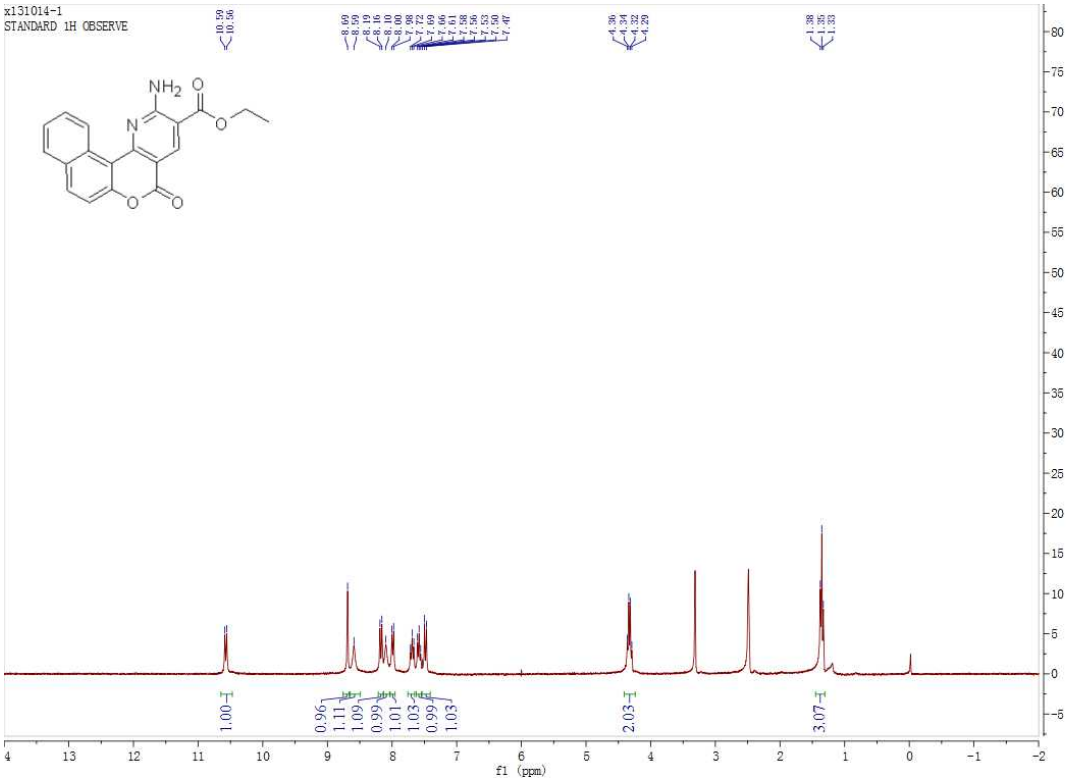

X131023-1.3.fid
X131023-1 DMSO BB+DEPT135
f1 (ppm)

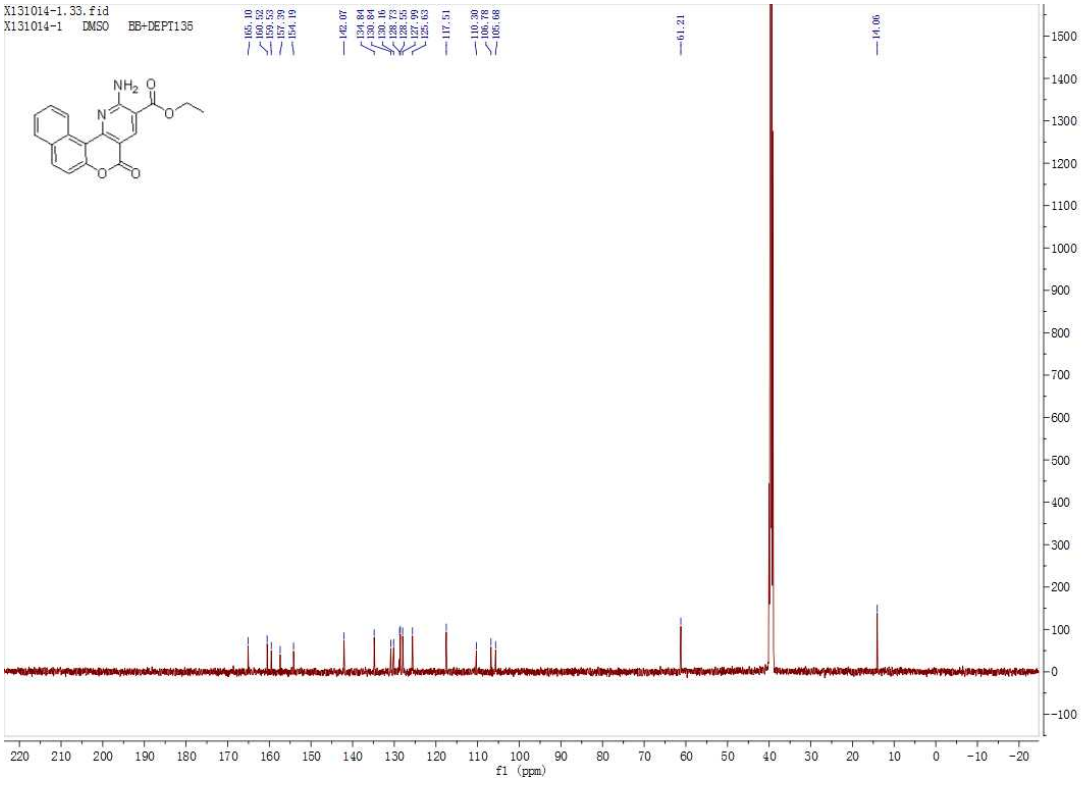

x130924-2.1.fid
x130924-2 CDCl3 1H
9.02
8.32
7.21
5.99
4.44
4.42
4.41
4.39
2.49
1.46
1.45
1.43
NH2
O
N
Cl
O
O
1.00
2.01
1.04
0.98
2.39
3.28
3.34
f1 (ppm)

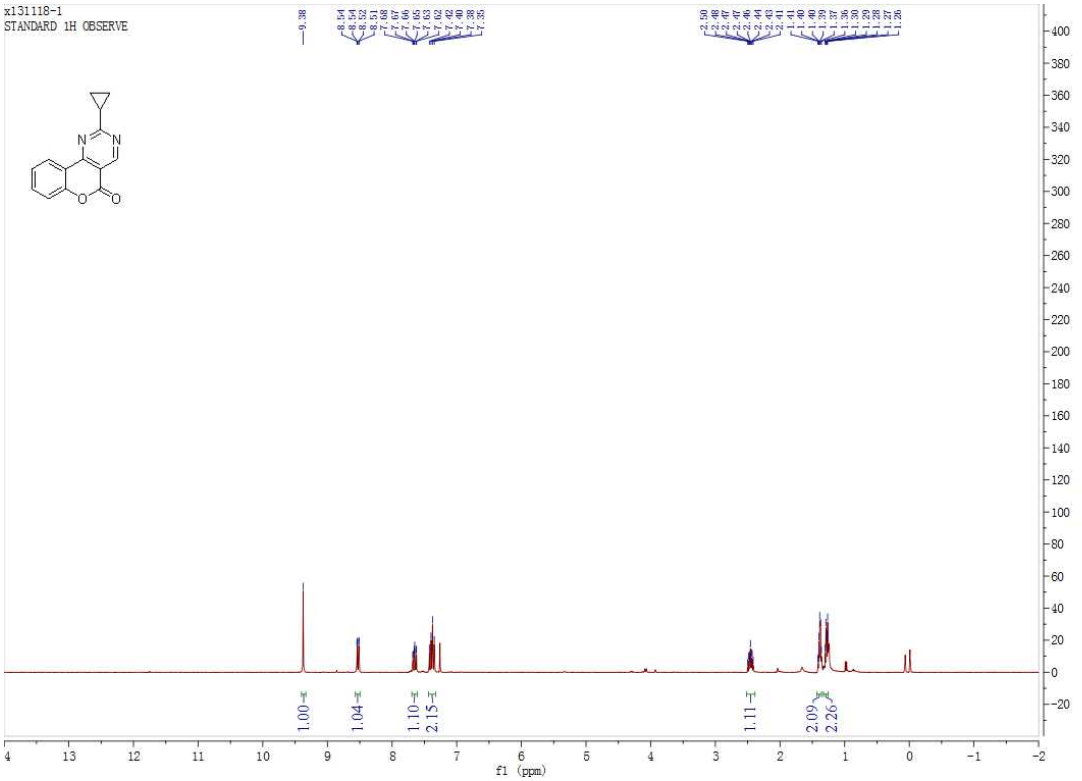

x130924-2.3.fid
x130924-2 CDCl3 BB+DEPT135
165.94
161.52
160.51
154.57
151.95
143.37
141.86
130.64
124.97
119.21
117.09
108.11
107.42
61.73
20.70
14.27
NH2
O
N
Cl
O
O
f1 (ppm)

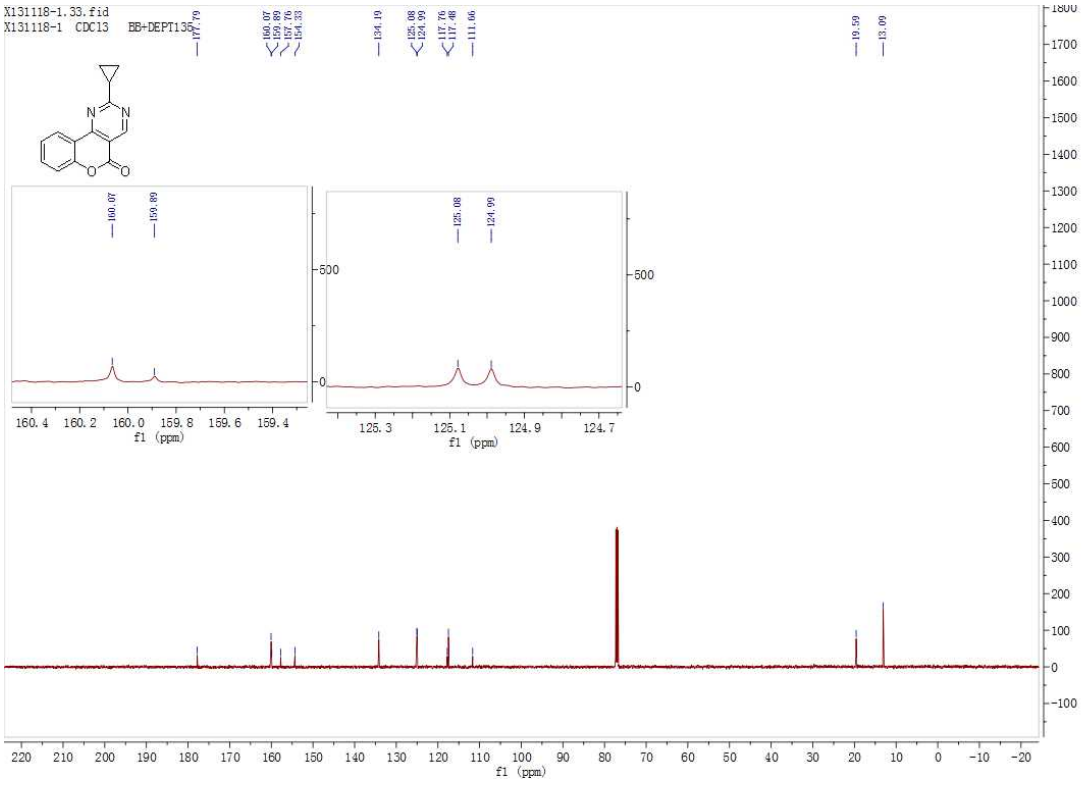

X131016-1
X131016-1 DMSO 1H Oct 16 2013
f1 (ppm)


x131016-3.3.fid
x131016-3 CDCl3 BB+DEPT135
f1 (ppm)


x131014-1
STANDARD 1H OBSERVE
10.59
10.56
8.69
8.59
8.19
8.16
8.10
8.00
7.98
7.72
7.69
7.66
7.61
7.58
7.56
7.53
7.50
7.47
4.36
4.34
4.32
4.29
1.38
1.35
1.33
NH2
O
N
O
O
1.00
0.96
1.11
1.09
0.99
1.01
1.03
0.99
1.03
2.03
3.07
f1 (ppm)


X131014-1.33.fid
X131014-1 DMSO BB+DEPT136
165.10
160.52
159.53
157.39
154.19
142.07
134.84
130.16
128.77
128.55
127.99
125.63
117.51
110.30
106.78
105.68
61.21
14.06
NH2
O
N
O
O
f1 (ppm)


x131118-1
STANDARD 1H OBSERVE
f1 (ppm)


X131118-1.33.fid
X131118-1 CDCl3 BB+DEPT135
f1 (ppm)