Supporting Information

Copper-Catalyzed Intramolecular Cross Dehydrogenative Coupling Approach to Coumestans from 2'-Hydroxyl-3-arylcoumarins

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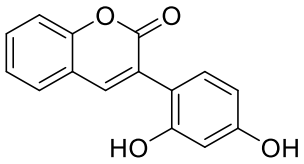
1. General Information

All reagents used in the synthesis were obtained commercially and used without further purification unless otherwise specified. The reactions were monitored by thin-layer chromatography (TLC) on glass-packed precoated silica gel plates and visualized in an iodine chamber or with a UV lamp. The ^{1}H NMR and ^{13}C NMR spectra were recorded using TMS as the internal standard on a Bruker BioSpin GmbH spectrometer at 400 and 100 MHz, respectively, and the coupling constants are reported in hertz. The high-resolution mass spectra (HRMS) were obtained using a Shimadzu LCMS-ITTOF mass spectrometer. Flash column chromatography was performed using silica gel (200-300mesh) purchased from Qingdao Haiyang Chemical Co. Ltd. EPR spectra were recorded on a Bruker A300 spectrometer. X-ray diffraction data were collected at 100 K on an in-house Oxford Diffraction Xcalibur Nova diffractometer (Cu Kα radiation). The data were processed using the program *CrysAlis Pro.*

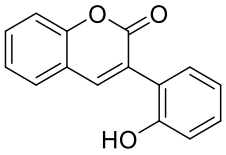
General procedure A for the synthesis of 2'-hydroxyl-3-arylcoumarins (2). A mixture of corresponding 2-hydroxyphenylacetic acid (4, 5 mmol) and ortho-hydroxy-benzaldehyde (3, 5 mmol), acetic anhydride (1.42 mL, 15 mmol), triethylamine (1.38 mL, 10 mmol) were added to a 25 mL round-bottom flask equipped with a condenser. Then raising the temporature to 110 ˚C with stirring for 6 h. After completion of the reaction (monitored by TLC), the hot mixture was poured into ice water（30 mL） and washed thoroughly while stirring. A brown solid was obtained and collected by filtration. The solid was then dissolved in 10% aq NaOH (50 mL), and the resulting aqueous solution was decolored by extracting with ethyl acetate. The aqueous layer was acidified with concd. HCl（17 mL） to pH 3-4. The percipitated crude product was collected by filtration, The crude product was then purified by flash column chromatograph (eluting with 1:4 EtOAc/petroleum ether).

***3-(2,4-dihydroxyphenyl)coumarin* (2a)[9]**



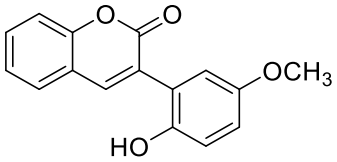
77% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 9.52 (s, 1H), 7.91 (s, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.27 – 7.14 (m, 2H), 6.93 – 6.71 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.23, 159.21, 156.61, 153.26, 141.54, 131.94, 131.51, 128.58, 126.33, 124.85, 119.95, 116.24, 113.68, 106.77, 103.11. HRMS-ESI (m/z): [M - H]$^-$ calculated for $C_{15}H_9O_4$, 253.0506, found 253.0510.

***3-(2-Hydroxyphenyl)coumarin* (2b)[5]**



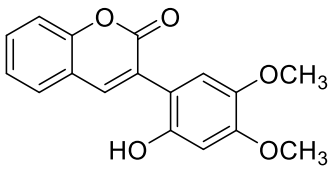
78% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.61 (s, 1H), 8.04 (s, 1H), 7.74 (dd, J = 1.6, 8.0 Hz, 1H), 7.59 – 7.64 (m, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.37 (td, J = 0.8, 7.6 Hz, 1H), 7.27 (dd, J = 1.6, 7.6 Hz, 1H), 7.21-7.25 (m, 1H), 6.91 (dd, J = 0.8, 8.0 Hz, 1H), 6.86 (td, J = 0.8, 7.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.4, 155.1, 153.1, 141.9, 131.5, 130.8, 129.7, 128.4, 126.0, 124.5, 122.2, 119.3, 118.7, 115.9, 115.7. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{15}H_{11}O_4$, 239.0703, found 239.0697.

***3-(2-hydroxy-5-methoxyphenyl)coumarin* (2c)**



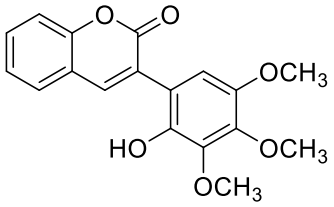
80% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.08 (s, 1H), 8.04 (s, 1H), 7.74 (dd, J = 7.7, 1.4 Hz, 1H), 7.61 (ddd, J = 8.7, 7.4, 1.6 Hz, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.37 (td, J = 7.6, 1.0 Hz, 1H), 6.90 (t, J = 1.7 Hz, 1H), 6.84 (d, J = 1.7 Hz, 2H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.74, 153.56, 152.27, 149.38, 142.55, 131.96, 128.84, 126.28, 124.93, 123.08, 119.75, 116.88, 116.41, 116.36, 115.73, 55.98. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{16}H_{13}O_4$, 269.0808, found 269.0807.

***3-(2-hydroxy-4,5-dimethoxyphenyl)coumarin* (2d)**



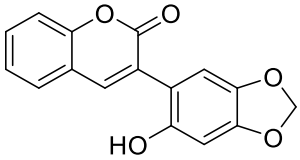
81% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.23 (s, 1H), 8.07 (s, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.65 (dd, *J* = 11.4, 4.2 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 6.98 (s, 1H), 6.61 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H). ^{13}C -NMR (100 MHz, DMSO-*d*$_6$) δ 160.10, 153.36, 150.49, 150.00, 142.13, 141.91, 131.68, 128.67, 125.99, 124.89, 119.90, 116.28, 115.73, 113.24, 101.49, 56.94, 55.95. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{17}H_{15}O_5$, 299.0914, found 299.0912.

***3-(2-hydroxy-3,4,5-trimethoxyphenyl)coumarin* (2e)**



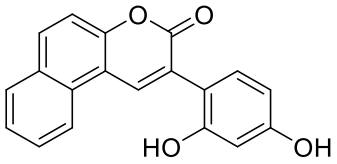
81% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.67 (s, 1H), 8.03 (s, 1H), 7.74 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.65-7.58 (m, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 6.76 (s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 159.80, 153.50, 145.78, 143.39, 143.10, 142.55, 142.05, 131.95, 128.79, 126.04, 124.97, 119.76, 117.56, 116.37, 110.10, 61.30, 60.99, 56.82. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{18}H_{17}O_6$, 329.1020, found 329.1008.

***3-(2-hydroxy-4,5-methylenedioxyphenyl)coumarin* (2f)**



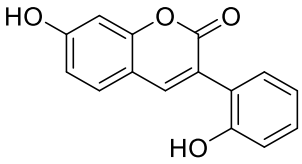
86% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.39 (s, 1H), 7.99 (s, 1H), 7.72 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.63 – 7.56 (m, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.35 (dd, *J* = 13.7, 6.2 Hz, 1H), 6.87 (s, 1H), 6.54 (s, 1H), 5.97 (s, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 160.06, 153.35, 150.73, 148.33, 142.37, 140.07, 131.76, 128.70, 125.92, 124.91, 119.84, 116.30, 113.89, 110.30, 101.46, 98.32. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{16}H_{11}O_5$, 283.0601, found 283.0597.

***2-(2,4-dihydroxyphenyl)-3H-benzo[f]chromen-3-one* (2g)**



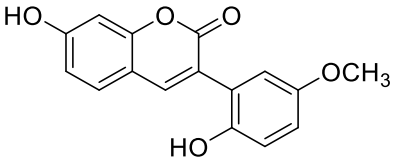
^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.48 (d, *J* = 2.9 Hz, 2H), 8.77 (s, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.67 – 7.52 (m, 2H), 7.20 (d, *J* = 8.3 Hz, 1H), 6.42 (d, *J* = 2.0 Hz, 1H), 6.34 (dd, *J* = 8.3, 2.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 163.34, 163.19, 159.07, 153.51, 139.65, 133.59, 132.52, 132.29, 129.28, 127.44, 127.42, 125.12, 125.11, 124.47, 119.21, 118.91, 112.70, 106.68, 103.61. HRMS-ESI (m/z): [M + H]$^{+}$ calculated for $C_{19}H_{13}O_4$, 305.0808, found 305.0813.

***7-hydroxy-3-(2-hydroxyphenyl)coumarin* (2h)[8]**



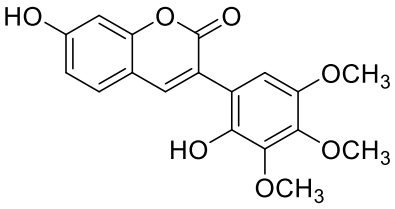
88% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.55 (s, 1H), 9.50 (s, 1H), 7.89 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.27 – 7.16 (m, 2H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.87 – 6.79 (m, 2H), 6.76 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 161.36, 160.28, 155.52, 155.44, 142.84, 131.34, 130.07, 129.76, 123.09, 121.74, 119.17, 116.13, 113.60, 112.25, 102.27. HRMS-ESI (m/z): [M + H]$^{+}$ calculated for $C_{15}H_{12}O_4$, 255.0652, found 255.0657.

***7-hydroxy-3-(2-hydroxy-5-methoxyphenyl)coumarin* (2i)**



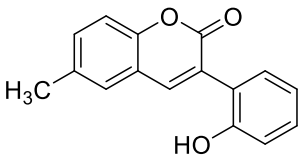
76% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.56 (s, 1H), 9.02 (s, 1H), 7.91 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 6.85 (dd, *J* = 2.3, 1.0 Hz, 1H), 6.84 – 6.78 (m, 3H), 6.76 (d, *J* = 2.2 Hz, 1H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 161.41, 160.19, 155.46, 152.25, 149.35, 143.04, 130.10, 123.49, 121.54, 116.79, 116.52, 115.26, 113.62, 112.21, 102.26, 55.94. HRMS-ESI (m/z): [M + H]$^{+}$ calculated for $C_{16}H_{13}O_5$, 285.0758, found 285.0762.

***7-hydroxy-3-(2-hydroxy-3,4,5-trimethoxyphenyl)coumarin* (2j)**



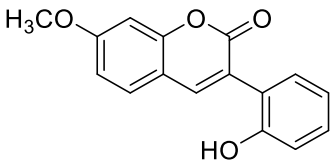
73% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.57 (s, 1H), 8.55 (s, 1H), 7.89 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 6.81 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.76 (t, *J* = 2.4 Hz, 1H), 6.71 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 161.38, 160.25, 155.41, 153.00, 145.73, 143.04, 142.02, 130.04, 121.32, 117.97, 113.63, 112.23, 110.28, 106.54, 102.26, 61.26, 60.97, 56.85. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{18}H_{17}O_7$, 345.0969, found 345.0961.

***3-(2-Hydroxyphenyl)-6-methylcoumarin* (2k)[8]**



80% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 9.57 (s, 1H), 7.96 (s, 1H), 7.52 (s, 1H), 7.42 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.18 (m, 2H), 6.96 – 6.89 (m, 1H), 6.86 (td, *J* = 7.5, 1.0 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 159.98, 155.55, 151.68, 142.31, 134.11, 132.75, 131.28, 130.12, 128.43, 126.35, 122.77, 119.51, 119.16, 116.16, 116.13, 20.75. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{13}O_3$, 253.0859, found 253.0856.

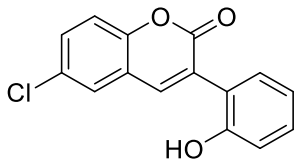
***3-(2-hydroxyphenyl)-7-methoxylcoumarin* (2l)[8]**



78% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.53 (s, 1H), 7.94 (s, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.26 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.96 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 162.61, 160.14, 155.53, 155.35, 142.57, 131.32, 129.89, 129.83, 122.94, 122.77, 119.19, 116.16, 113.32,

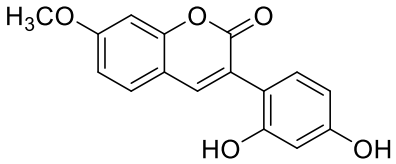
112.78, 100.81, 56.38. 2l HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{13}O_4$, 269.0808, found 269.0816.

6-chloro-3-(2-hydroxyphenyl)coumarin **(2m)**



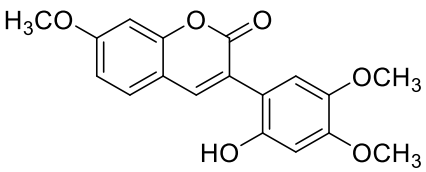
91% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.65 (s, 1H), 8.01 (s, 1H), 7.88 (d, *J* = 2.4 Hz, 1H), 7.65 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.25 (dd, *J* = 14.4, 7.6 Hz, 2H), 6.98 – 6.80 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 159.38, 155.56, 152.15, 141.13, 131.47, 131.20, 130.41, 128.66, 127.83, 127.61, 122.30, 121.18, 119.19, 118.40, 116.21. 2m HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{15}H_8O_3Cl$, 271.0167, found 271.0180.

3-(2,4-dihydroxyphenyl)-7-methoxylcoumarin **(2n)**



79% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.40 (s, 1H), 9.37 (s, 1H), 7.87 (s, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 7.00 (d, *J* = 1.6 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.36 (d, *J* = 1.9 Hz, 1H), 6.27 (d, *J* = 8.3 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 162.28, 160.51, 158.93, 156.52, 155.05, 141.83, 131.92, 129.60, 122.73, 113.90, 113.49, 112.69, 106.69, 103.09, 100.71, 56.34. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{13}O_5$, 285.0758, found 285.0754.

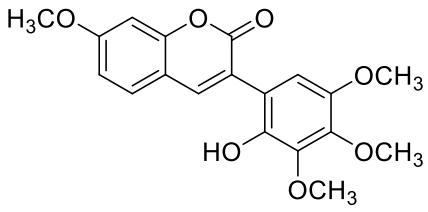
3-(2-hydroxy-4,5-dimethoxyphenyl)-7-methoxylcoumarin **(2o)**



79% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.69 (s, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.04 – 6.85 (m, 2H), 6.76 (s, 1H), 6.64 (s, 1H), 4.07 – 3.71 (m, 9H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 162.42, 160.39, 155.15, 150.19, 149.88, 142.41,

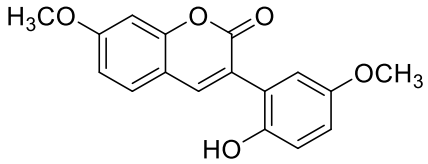
141.83, 129.69, 122.35, 115.69, 113.45, 113.42, 112.76, 101.41, 100.72, 56.87, 56.35, 55.90. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{18}H_{17}O_6$, 329.1020, found 329.1010.

***3-(2-hydroxy-3,4,5-trimethoxyphenyl)-7-methoxylcoumarin* (2p)**



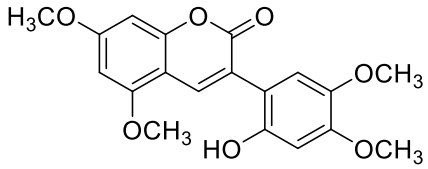
79% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.60 (s, 1H), 7.95 (s, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.73 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 163.59, 159.20, 158.28, 155.93, 155.64, 149.04, 146.62, 144.54, 117.28, 106.17, 106.07, 98.49, 98.32, 95.48, 93.93, 60.50, 59.28, 56.81, 56.40. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{19}H_{19}O_7$, 359.1125, found 359.1116.

***3-(2-hydroxy-5-methoxyphenyl)-7-methoxylcoumarin* (2q)**



88% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.05 (s, 1H), 7.97 (s, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.03 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.87 (d, *J* = 1.5 Hz, 1H), 6.82 (d, *J* = 1.4 Hz, 2H), 3.88 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 162.63, 160.03, 155.37, 152.21, 149.35, 142.79, 129.87, 123.28, 122.56, 116.77, 116.42, 115.39, 113.27, 112.83, 100.80, 56.40, 55.92. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{15}O_5$, 299.0914, found 299.0911.

***3-(2-hydroxy-4,5-dimethoxyphenyl)-5,7-dimethoxylcoumarin* (2r)**

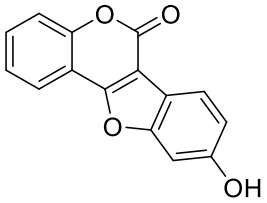


82% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 9.11 (s, 1H), 7.96 (s, 1H), 6.92 (s, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 6.53 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.75 (s,

3H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ163.94, 163.19, 161.50, 154.06, 153.90, 153.58, 141.71, 139.48, 126.79, 116.36, 112.57, 104.65, 100.85, 97.37, 95.04, 61.26, 60.03, 56.83, 56.08. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{19}H_{19}O_7$, 359.1125, found 359.1121.

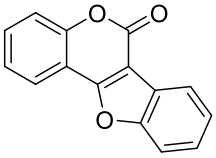
General procedure B for the synthesis coumestans (1). An oven-dried vial was charged with corresponding substrate (2, 1mmol), $Cu(OAc)_2$ (0.2 mmol, 20 mol%), 1,10-phen (0.2 mmol, 20 mol%), DMSO (3 mL) and H_2O (1 mL). The vial was sealed under air and heated to 135 ℃ with stirring for 18 hours. After cooling down, the mixture was diluted with H_2O（20 mL） and extracted with EtOAc (20 mL × 3). The organic layer was dried, filtered and concentrated to give the crude product which was directly applied to a flash column chromatography (EtOAc/petroleum ether) to give the corresponding coumestans (1).

9-hydroxy-6H-benzofuro[3,2-c]chromen-6-one **(1a)[1]**



78% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.03 (dd, J = 7.8, 1.3 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.69 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.59 (dd, J = 8.4, 0.6 Hz, 1H), 7.53 – 7.45 (m, 1H), 7.22 (d, J = 1.9 Hz, 1H), 7.00 (dd, J = 8.5, 2.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.26, 157.68, 157.23, 156.42, 152.53, 131.62, 124.95, 121.34, 121.13, 117.07, 114.44, 114.34, 112.19, 105.39, 98.68. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{15}H_9O_4$, 253.0495, found 253.0494.

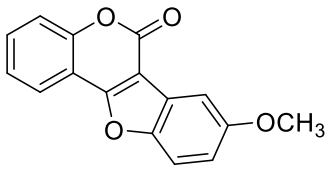
6H-benzofuro[3,2-c]chromen-6-one **(1b)[3]**



70% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (dd, J = 7.8, 1.4 Hz, 1H), 8.03 – 7.97 (m, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.75 (ddd, J = 8.7, 7.4, 1.6 Hz, 1H), 7.64 – 7.50 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.12, 157.64, 155.40, 153.65, 133.03, 127.56, 125.97, 125.57, 123.33, 122.39, 121.35, 117.73, 112.76, 112.46,

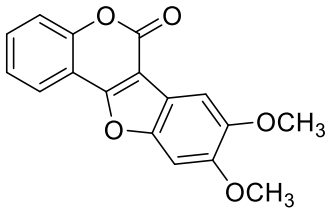
105.60. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{15}H_9O_3$, 237.0546, found 237.0539.

8-methoxy-6H-benzofuro[3,2-c]chromen-6-one **(1c)**



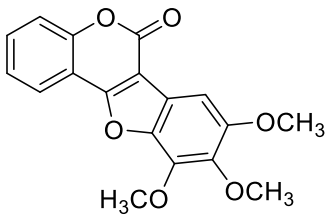
83% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (dd, J = 7.8, 1.4 Hz, 1H), 7.86 (d, J = 9.1 Hz, 1H), 7.80 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.18 (dd, J = 9.1, 2.7 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.53, 157.75, 157.66, 153.52, 150.07, 132.92, 125.54, 124.15, 122.26, 117.71, 115.84, 113.46, 112.52, 105.67, 103.39, 56.23. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{11}O_4$, 267.0652, found 267.0652.

8,9-dimethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1d)[1]**



71% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (d, J = 7.7 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.60 – 7.51 (m, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.30 (s, 1H), 3.86 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.82, 158.41, 152.95, 150.31, 149.52, 148.09, 131.06, 124.59, 121.23, 117.37, 115.31, 112.90, 106.25, 102.16, 95.42, 56.50, 56.37. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{13}O_5$, 297.0758, found 297.0756.

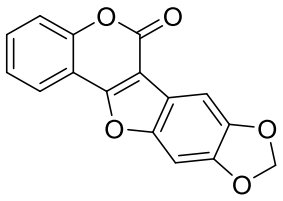
8,9,10-trimethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1e)**



66% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (dd, J = 7.7, 1.4 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.13

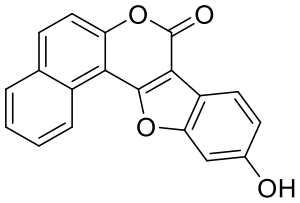
(d, *J* = 6.5 Hz, 1H), 4.21 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 159.76, 157.69, 153.24, 152.82, 141.80, 140.55, 139.54, 132.69, 125.52, 122.20, 119.40, 117.62, 112.48, 105.78, 96.67, 61.53, 56.71. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{18}H_{15}O_6$, 327.0863, found 327.0854.

8,9-methylenedioxy-6H-benzofuro[3,2-c]chromen-6-one **(1f)**



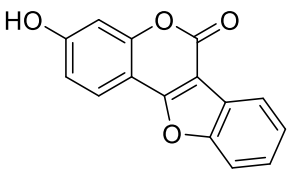
39% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.01 (d, *J* = 7.5 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 10.7 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.33 (s, 1H), 6.18 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.24, 158.25, 152.98, 151.03, 147.97, 146.34, 131.19, 124.65, 121.31, 117.46, 116.97, 112.90, 106.52, 102.11, 100.33, 94.07. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{16}H_9O_5$, 281.0444, found 281.0444.

11-hydroxy-8H-benzo[f]benzofuro[3,2-c]chromen-8-one **(1g)**



70% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.22 (s, 1H), 9.12 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 9.0 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.85 (dd, *J* = 15.4, 8.0 Hz, 2H), 7.70 (dd, *J* = 15.3, 8.2 Hz, 2H), 7.35 (s, 1H), 7.04 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 160.09, 158.22, 157.69, 156.96, 153.10, 133.08, 130.54, 129.45, 129.35, 127.10, 126.87, 125.45, 121.57, 117.73, 115.13, 114.26, 107.10, 106.20, 99.23. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{19}H_{11}O_4$, 303.0652, found 303.0645.

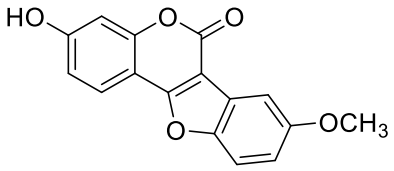
3-hydroxy-6H-benzofuro[3,2-c]chromen-6-one **(1h)**



81% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.78 (s, 1H), 7.88 –

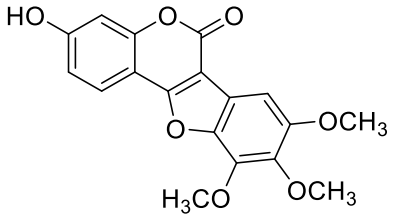
7.79 (m, 2H), 7.78 – 7.71 (m, 1H), 7.49 – 7.35 (m, 2H), 6.94 – 6.81 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.41, 161.11, 157.93, 155.75, 154.96, 126.68, 125.72, 123.74, 123.60, 120.82, 114.35, 112.43, 104.26, 103.54, 102.17, 40.57, 40.37, 40.16, 39.95, 39.74, 39.53, 39.32. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{15}H_9O_4$, 253.0495, found 253.0493.

3-hydroxy-8-methoxy-6H-benzofuro[3,2-c]chromen-6-one **(1i)**



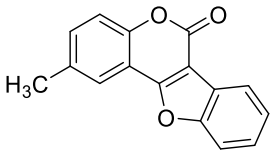
58% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.09 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.04 – 6.91 (m, 2H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.33, 161.61, 157.97, 157.64, 155.64, 149.62, 124.46, 123.65, 114.65, 114.34, 113.09, 104.38, 103.55, 103.28, 102.35, 56.18. HRMS $[M+H]^+$ calculated 283.0601, found 283.0595.

3-hydroxy-8,9,10-trimethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1j)**



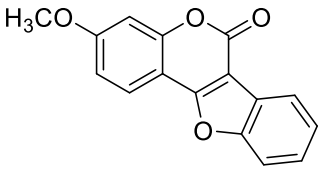
53% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.77 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.13 (s, 1H), 6.95 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 4.19 (s, 3H), 3.90 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.10, 160.85, 158.01, 155.35, 152.61, 141.19, 139.92, 139.46, 123.56, 119.69, 114.28, 104.41, 103.50, 102.45, 96.54, 61.50, 61.47, 56.68. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{18}H_{15}O_7$, 343.0812, found 343.0803.

2-methyl-6H-benzofuro[3,2-c]chromen-6-one **(1k)[4]**



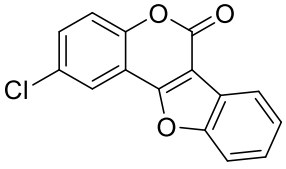
58% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.96 (d, *J* = 7.3 Hz, 1H), 7.90 – 7.79 (m, 2H), 7.59 – 7.44 (m, 4H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.00, 158.20, 155.48, 151.90, 134.54, 132.98, 126.62, 125.14, 123.55, 121.82, 121.48, 117.18, 112.26, 111.66, 105.75, 20.93. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{11}O_3$, 251.0703, found 251.0701.

3-methoxy-6H-benzofuro[3,2-c]chromen-6-one **(1l)[13]**



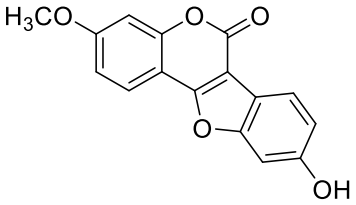
76% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.00 (d, *J* = 8.7 Hz, 1H), 7.97 – 7.91 (m, 1H), 7.87 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.11 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.18, 165.54, 162.61, 160.43, 159.86, 131.70, 130.59, 128.26, 125.71, 118.45, 117.31, 110.28, 107.69, 106.85, 61.34. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{11}O_4$, 267.0652, found 267.0650.

2-chloro-6H-benzofuro[3,2-c]chromen-6-one **(1m)[6]**



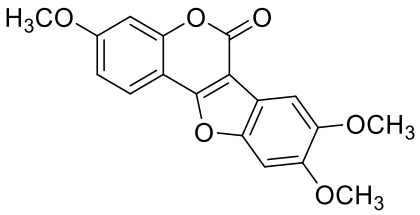
40% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.11 (m, 1H), 8.02 (d, *J* = 2.3 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.58 – 7.43 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.61, 157.42, 155.66, 151.95, 131.86, 130.27, 127.25, 125.46, 123.18, 122.01, 121.35, 118.95, 113.72, 111.86, 106.61. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{15}H_8ClO_3$, 271.0156, found 271.0156.

9-hydroxy-3-methoxy-6H-benzofuro[3,2-c]chromen-6-one **(1n)[12]**



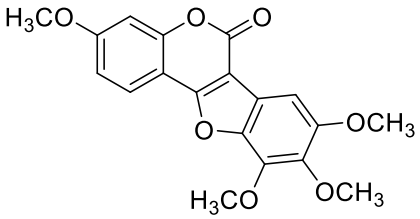
79% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.07 (s, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.14 (m, 2H), 7.10 (d, *J* = 8.7 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 162.81, 159.58, 157.98, 157.70, 156.57, 155.03, 122.99, 121.24, 114.97, 114.64, 113.55, 105.89, 103.26, 102.10, 99.20, 56.53. HRMS [M+H]$^+$ calculated 283.0601, found 283.0598.

3,8,9-trimethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1o)**[5]



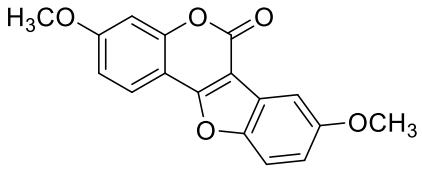
69% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.58 (s, 1H), 7.35 (s, 1H), 7.21 (s, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 3.89 (d, *J* = 10.3 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.45, 159.76, 158.76, 154.92, 150.00, 149.08, 148.04, 122.29, 115.60, 113.04, 106.33, 103.89, 102.32, 101.47, 95.62, 56.55, 56.42, 55.83. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{18}H_{15}O_6$, 327.0863, found 327.0861.

3,8,9,10-tetramethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1p)**



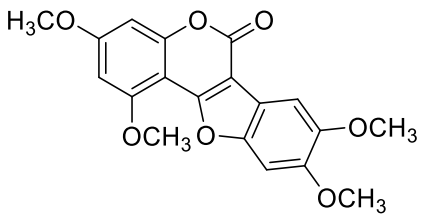
67% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.90 (d, *J* = 8.7 Hz, 1H), 7.09 (s, 1H), 7.02 (d, *J* = 10.0 Hz, 2H), 4.19 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 163.07, 160.30, 157.76, 155.12, 152.60, 141.26, 140.01, 139.40, 123.15, 119.47, 113.46, 105.49, 103.04, 101.91, 96.43, 61.46, 61.41, 56.60, 56.48. HRMS-ESI (m/z): [M + H]$^+$ calculated for $C_{19}H_{17}O_7$, 357.0969, found 357.0964.

3,8-dimethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1q)**



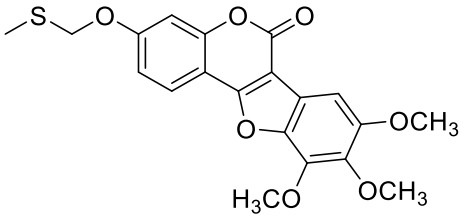
77% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.99 (d, *J* = 8.7 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.39 (s, 1H), 7.23 (s, 1H), 7.12 (dd, *J* = 12.5, 5.6 Hz, 2H), 3.96 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.98, 161.18, 158.55, 157.63, 155.49, 149.99, 124.42, 122.80, 115.18, 113.09, 112.15, 106.06, 103.42, 101.47, 100.00, 56.06, 55.85. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{13}O_5$, 297.0758, found 297.0756.

1,3,8,9-tetramethoxy-6H-benzofuro[3,2-c]chromen-6-one **(1r)**[5]



37% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.51 (s, 1H), 7.31 (s, 1H), 6.76 (s, 1H), 6.64 (s, 1H), 4.00 (s, 3H), 3.88 (d, *J* = 6.3 Hz, 9H). ^{13}C NMR (100MHz, DMSO-*d*$_6$) δ 162.61, 160.08, 155.33, 145.72, 143.15, 143.05, 142.78, 142.02, 129.81, 122.35, 117.81, 113.28, 112.85, 110.17, 100.80, 61.28, 60.98, 56.81, 56.40. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{19}H_{17}O_7$, 357.0969, found 357.0965.

8,9,10-trimethoxy-3-((methylthio)methoxy)-6H-benzofuro[3,2-c]chromen-6-one **(1jj)**



31% yield, pale yellow solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.03 (d, *J* = 8.7 Hz, 1H), 7.29 (d, *J* = 2.3 Hz, 1H), 7.16 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.13 (s, 1H), 5.46 (s, 2H), 4.20 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 160.56, 160.36, 157.90, 154.88, 152.72, 141.43, 140.16, 139.52, 123.28, 119.57,

114.86, 106.29, 104.19, 103.52, 96.58, 72.91, 61.53, 56.71, 14.40. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{20}H_{19}O_7S$, 403.0846, found 403.0853.

Synthesis of 1s(coumestrol), 1t(9-methoxy-coumestrol) and the detailed synthetic procedures for compounds 7, 5s, 4s, 5t, 5s, 4t, 2s, 2t.

2-bromo-4-hydroxymandelic acid (**7**). 3-Bromophenol (**8**, 8.65 g, 50.0 mmol) was added to a three-necked, round-bottom flask equipped with a condenser and a mechanical stirrer. When the reaction temperature was raised to 40 ^oC, a 50 % aqueous solution of glyoxylic acid (50.0 mmol) and an 8% aqueous NaOH (75.0 mmol) solution were added simultaneously through two constant-pressure funnels over 1 h. The mixture was stirred for 8 h. After completion (as monitored by TLC), the mixture was cooled to room temperature and acidified to pH 1−2 with 2 M HCl. (50 mL) The aqueous solution was washed with toluene (2 × 50 mL), and the product was extracted with EtOAc (2 × 50 mL). The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a yellow oil (11.36 g, 92.0% yield): ^1H NMR (DMSO-d_6, 400 MHz) δ 12.36 (s, 1H), 9.90 (s, 1H), 7.27 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 6.79 (dd, J = 8.4, 2.4 Hz, 1H), 5.86 (s, 1H), 5.20 (s, 1H).-^{13}C NMR (100 MHz, DMSO-*d_6*) δ 173.96, 158.23, 130.39, 129.94, 123.39, 119.09, 115.51, 71.58. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_8H_6O_4Br$, 244.9455, found 244.9463.

2-bromo-4-hydroxyphenylacetic acid **(5s)**. 2-Bromo-4-hydroxymandelic acid (**7**) (9.9 g, 40.0 mmol), $SnCl_2·2H_2O$ (10.2 g, 45.0 mmol), and concentrated HCl (20 mL) were added into a round-bottom flask equipped with a condenser, the mixture was stirred at 80 °C for 3 h. After completion of the reaction as indicated by TLC, H_2O (40 mL) was added and the mixture was heated to reflux until a clear solution was obtained. The resulting mixture was cooled to room temperature, whereupon compound **5s** recrystallized to afford a white solid (7.39 g, 80.0% yield): mp 176−178 °C; ^1H NMR

(400 MHz, DMSO-d_6,) δ 12.35 (s, 1H), 9.80 (s, 1H), 7.15 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 6.72 (dd, 8.4 Hz, 2.4 Hz, 1H), 3.57 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 157.6, 133.0, 125.6, 124.9, 119.2, 115.2, 40.6. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_8H_6O_3Br$, 228.9506, found 228.9502.

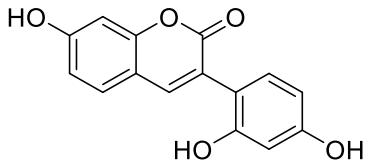
2,4-dihydroxyphenylacetic acid (**4s**). *2-(2-bromo-4-hydroxyphenyl)acetic acid* (**5s**), 10.0 mmol), Oxine-copper complex (1.0 mmol), NaOH (100.0 mmol) and H_2O (40 mL) were added into a round-bottom flask equipped with a condenser. The mixture was stirred at 110 °C for 10 h. After completion of the reaction as indicated by TLC. The resulting mixture was cooled to room temperature. The solid was filtrated off and the aqueous solution was acidified to pH 1−2 with 2 M HCl (60 mL). The product was extracted with EtOAc (2 × 50 mL). The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give *2,4-Dihydroxyphenylacetic acid* (**4s**). yellow solid, 1.39 g, 83.0% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 9.20 (s, 1H), 9.03 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.26 (d, J = 2.3 Hz, 1H), 6.14 (dd, J = 8.1, 2.3 Hz, 1H), 3.32 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.7, 157.6, 156.5, 131.7, 112.9, 106.3, 102.7, 35.1. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_8H_6O_4$, 167.0350, found 167.0345.

methyl 2-(2-bromo-4-methoxyphenyl)acetate (**5t**). 2-bromo-4-hydroxyphenylacetic acid (**5s**, 4.62 g, 20.0 mmol) was added to a solution of predissolved K_2CO_3 (13.8 g, 100 mmol) in H_2O (100 mL) and acetone (100 mL). To this solution was added Me_2SO_4 (5.04 g, 40.0 mmol) in acetone (20 mL) over 2 h, and the mixture was stirred for an additional 30 min. After removal of acetone, the reaction mixture was extracted with EtOAc (2 × 100 mL), and the combined organic extracts were washed with water (2 × 100 mL) and brine (2 × 100 mL) and finally dried over Na_2SO_4. The extracts were filtered and concentrated under vacuum, and the residue was purified by flash chromatography on silica gel (elution with EtOAc/petroleum ether = 1/5) to afford white solid **5t** 4.46 g, 86.0% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.5 Hz, 1H), 7.15 (d, J = 2.5 Hz, 1H), 6.86 (dd, J = 8.5, 2.5 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 2H),

3.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.37, 159.30, 131.80, 126.18, 125.16, 118.04, 113.67, 55.53, 52.13, 40.55.

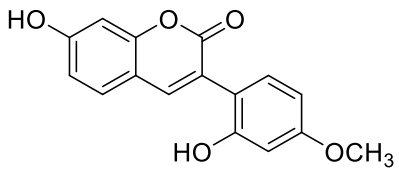
2-(2-hydroxy-4-methoxyphenyl)acetic acid (**4t**). The experimental procedure to synthesize **4t** is the same as that of **4s**. yellow solid, 1.60g, 88.0% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H), 9.53 (s, 1H), 6.99 (d, J = 8.2 Hz, 1H), 6.38 (d, J = 1.4 Hz, 1H), 6.33 (d, J = 8.3 Hz, 1H), 3.68 (s, 3H), 3.39 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 159.6 , 156.6 , 131.8, 114.7, 104.4, 101.4, 55.3, 35.1. 4t HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_9H_9O_4$, 181.0506, found 181.0512.

3-(2,4-dihydroxyphenyl)-7-hydroxy-2H-chromen-2-one **(2s)**.



The experimental procedure to synthesize 2s is the same as that of 2'-hydroxyl-3-arylcoumarins (2). **2s** was obtained from **4s** and **3b** following general procedure A. 1.23 g, 91% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 9.37 (s, 1H), 9.33 (s, 1H), 7.81 (s, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.4, 1H), 6.79 (dd, J = 2.0, 8.4 Hz, 1H), 6.73 (d, J = 2.0, 1H), 6.36 (d, J = 2.0, 1H), 6.27 (dd, J = 2.0, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.6, 160.2, 158.4, 156.1, 154.7, 141.7, 131.5, 129.4, 121.3, 113.6, 113.0, 112.0, 106.2, 102.6, 101.7. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{15}H_9O_5$, 271.0601, found 271.0603.

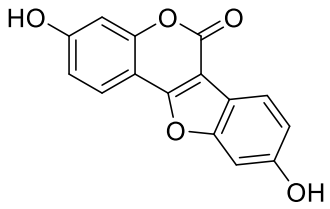
7-hydroxy-3-(2-hydroxy-4-methoxyphenyl) cou-marin (**2t**).[3m]



2t was obtained from **4t** and **3b** following general procedure A. 1.27 g, 89.0% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.51 (s, 1H), 9.58 (s, 1H), 7.84 (s, 1H),

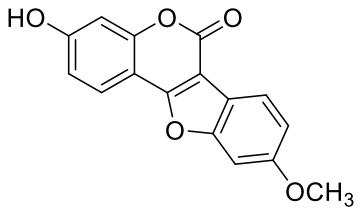
7.53 (d, J = 8.5 Hz, 1H), 7.17 (d, J = 8.1 Hz, 1H), 6.79 (dd, J = 8.5, 2.3 Hz, 1H), 6.74 (d, J = 2.2 Hz, 1H), 6.45 (q, J = 2.3 Hz, 2H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 163.9, 163.2, 161.2, 156.0, 142.9, 133.5, 130.5, 125.9, 114.4, 112.1, 109.9, 103.2, 102.8, 101.5, 56.0. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{13}O_5$, 285.0758, found 285.0762.

3,9-dihydroxy-6H-benzofuro[3,2-c]chromen-6-one (**coumestrol**, **1s**).[5c]



1s was obtained from **2s** following general procedure B. 128.7 mg, 48.0% yield, white solid. M.p. 361-364 ºC. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 10.04 (s, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 1.7 Hz, 1H), 7.01 – 6.86 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.8, 159.9, 158.1, 157.5, 156.4, 155.1, 123.2, 121.1, 115.1, 114.5, 114.3, 104.6, 103.5, 102.5, 99.2. HRMS-ESI: m/z $[M + H]^+$ calculated for $C_{15}H_9O_5$ 269.0444, found 269.0446.

3-hydroxy-9-methoxy-6H-benzofuro[3,2-c]chromen -6-one **(9-methoxy-coumestrol, 1t)**.[5]



1t was obtained from **2t** following general procedure B. 177.8 mg, 63.0% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (s, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 2.1 Hz, 1H), 7.10 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.02 – 6.88 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 160.5, 159.3, 158.0,

156.4, 155.3, 123.3, 121.0, 116.4, 114.3, 113.97, 104.6, 103.6, 102.4, 97.8, 56.4. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_{11}O_5$, 283.0601, found 283.0602.

Synthesis of 1u(8,9-dimethoxy-coumestrol), 1v(medicagol), 1w(flemichapparin C) and the detailed synthetic procedures for compounds 5u, 5v, 4u, 4v, 2u, 2v, 2w.

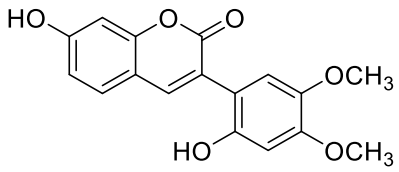
2-(2-bromo-4,5-dimethoxyphenyl)acetic acid (**5u**). To a solution of 2-(3,4-dimethoxyphenyl)acetic acid (**6u**) (9.8 g, 50.0 mmol) in acetic acid (100 mL) was added Br_2 (8.8 g, 55.0 mmol) dropwise at room temperature. The resulting solution was stirred at room temperature for 18 h. The reaction was quenched by slow addition of a 10% $Na_2S_2O_3$ (40 mL) solution until the red color disappeared. The mixture was poured into ice water (600 mL). A white solid was obtained and collected by filtration and recrystallized from EtOAc/petroleum ether to afford the product *2-Bromo-4,5-dimethoxyphenylacetic acid* (**5u**). white solid, 11.28 g, 82.0% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 1H), 6.79 (s, 1H), 3.86 (s, 3H), 3.86 (s, 3H), 3.76 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 149.0, 148.5, 125.4, 115.6, 115.1, 114.0, 56.2, 56.1, 40.8. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{10}H_{10}O_4Br$, 272.9768, found 272.9778.

2-bromo-4,5-methylenedioxyphenylacetic acid (**5v**). The experimental procedure to synthesize **5v** is the same as that of **5u.**white solid, 11.5 g, 89.0% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (s, 1H), 7.19 (s, 1H), 7.00 (s, 1H), 6.05 (s, 2H), 3.62 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.0, 147.7, 147.4, 128.5, 115.3, 112.5, 112.1, 102.3, 41.3. HRMS-ESI (m/z): [M - H]- calculated for C9H6O4Br, 256.9455, found 256.9450.

2-(2-hydroxy-4,5-dimethoxyphenyl)acetic acid (**4u**). The experimental procedure to synthesize **4u** is the same as that of **4s.** yellow solid, 1.97 g,93.0% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ6.63 (s, 1H), 6.53 (s, 1H), 3.82 (s, 6H), 3.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 149.6, 148.7, 143.3, 114.3, 110.7, 102.4, 56.6, 56.0, 36.6. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{10}H_{11}O_5$, 211.0612, found 211.0622.

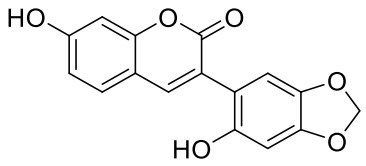
2-hydroxy-4,5-methylenedioxyphenylacetic acid (**4v**). The experimental procedure to synthesize **4v** is the same as that of **4s.** white solid, 1.80 g, 92.0% yield. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 12.04 (s, 1H), 9.14 (s, 1H), 6.68 (s, 1H), 6.42 (s, 1H), 5.88 (s, 2H), 3.37 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ 173.4, 150.3, 146.6, 139.8, 113.8, 110.9, 100.9, 97.8, 35.4. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_9H_7O_5$, 195.0299, found 195.0300.

7-hydroxy-3-(2-hydroxy-4,5-dimethoxyphenyl) coumarin (**2u**).[10]



2u was obtained from **4u** and **3b** following general procedure A. 1.11 g, 71.0% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 10.48 (s, 1H), 9.04 (s, 1H), 7.88 (s, 1H), 7.54 (d, J = 8.5 Hz, 1H), 6.88 (s, 1H), 6.80 (dd, J = 8.5, 2.3 Hz, 1H), 6.74 (d, J = 2.2 Hz, 1H), 6.53 (s, 1H), 3.75 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ 161.2, 160.5, 155.3, 150.1, 149.9, 142.7, 141.9, 129.9, 121.4, 115.9, 113.7, 113.6, 112.4, 102.2, 101.5, 56.9, 55.9. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{15}O_6$, 315.0863, found 315.0852.

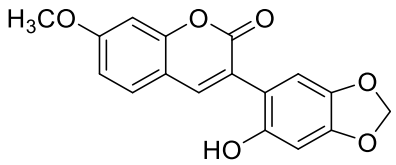
7-hydroxy-3-(2-hydroxy-4,5-methylenedioxyphenyl) coumarin (**2v**).[11]



2v was obtained from **4v** and **3b** following general procedure A. 1.16 g, 78.0% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 10.51 (s, 1H), 9.25 (s, 1H), 7.86 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 6.82 (s, 1H), 6.79 (dd, J = 8.5, 2.2 Hz, 1H), 6.74 (d, J = 2.1 Hz, 1H), 6.52 (s, 1H), 5.95 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ 161.2, 160.5,

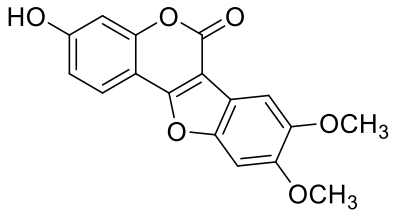
155.3, 150.6, 147.9, 142.9, 140.0, 129.9, 121.3, 114.4, 113.6, 112.3, 110.4, 102.2, 101.4, 98.3. HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{17}H_{11}O_6$, 297.0405, found 297.0415.

7-methoxy-3-(2-hydroxy-4,5-methylenedioxy-phenyl)coumarin (**2w**).



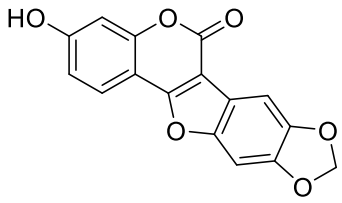
2w was obtained from **4v** and **3c** following general procedure A. 1.09 g, 70.0% yield, yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.92 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.02 (d, J = 2.3 Hz, 1H), 6.96 (dd, J = 8.6, 2.4 Hz, 1H), 6.84 (s, 1H), 6.53 (s, 1H), 5.96 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 160.4, 155.2, 150.6, 148.1, 142.6, 140.0, 129.7, 122.3, 114.2, 113.4, 112.8, 110.4, 101.4, 100.7, 98.3, 56.4. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_9O_6$, 313.0707, found 313.0706.

3-hydroxy-8,9-dimethoxy-6H-benzofuro[3,2-c] chromen-6-one (**8,9-dimethoxy-coumestrol**, **1u**).[3]



1u was obtained from **2u** following general procedure B. 190.5 mg, 61.0% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.55 (s, 1H), 7.33 (s, 1H), 7.05 – 6.83 (m, 2H), 3.87 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.65, 159.99, 158.17, 155.02, 149.81, 149.30, 148.23, 123.06, 115.16, 114.30, 104.76, 103.57, 102.75, 101.97, 97.21, 56.64, 56.45. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{13}O_6$, 313.0707, found 313.0704.

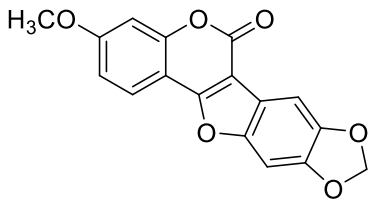
3-hydroxy-8,9-methylenedioxy -6H-benzofuro[3,2-c]chromen-6-one (**medicagol**, **1v**).[2]



1v was obtained from **2v** following general procedure B.106.6 mg, 36.0% yield, white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.73 (s, 1H), 7.83 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.56 (d, *J* = 3.3 Hz, 1H), 7.28 (d, *J* = 3.5 Hz, 1H), 6.92 (dd, *J* = 11.0, 5.1 Hz, 2H), 6.16 (s, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 161.2, 159.8, 157.5, 154.5, 149.8, 146.9, 145.8, 122.6, 116.3, 113.8, 104.1, 103.0, 102.4, 102.1, 98.7, 94.7. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{16}H_9O_6$, 297.0394, found 297.0391.

3-methoxy*-8,9-methylenedioxy-*6H-benzofuro[3,2-c]chromen-6-one

(**flemichapparin C**, **1w**).[3]



1w was obtained from **2w** following general procedure B. 152.0 mg, 49.0% yield, pale yellow solid. M.p. 270-272 ºC. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.92 (d, *J* = 8.5 Hz, 1H), 7.58 (s, 1H), 7.30 (s, 1H), 7.20 (s, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.16 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 163.2, 160.6, 156.1, 155.9, 150.5, 147.9, 140.0, 137.7, 119.5, 114.4, 110.4, 103.7, 101.4, 98.3, 97.7, 92.5, 56.15. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{11}O_6$, 311.0550, found 311.0550.

4. The Single Crystal X-ray Diffraction Study of 1e

To ascertain the structural correctness of these products, a crystallizing form of **1e** was obtained and the structure was undisputedly confirmed by single crystal X-ray analysis. The abtained crystallographic data of **1e** ($C_{18}H_{14}O_6$) have been deposited at the Cambridge Crystallographic Data Centre (**CCDC**) with the reference number **1552229**.

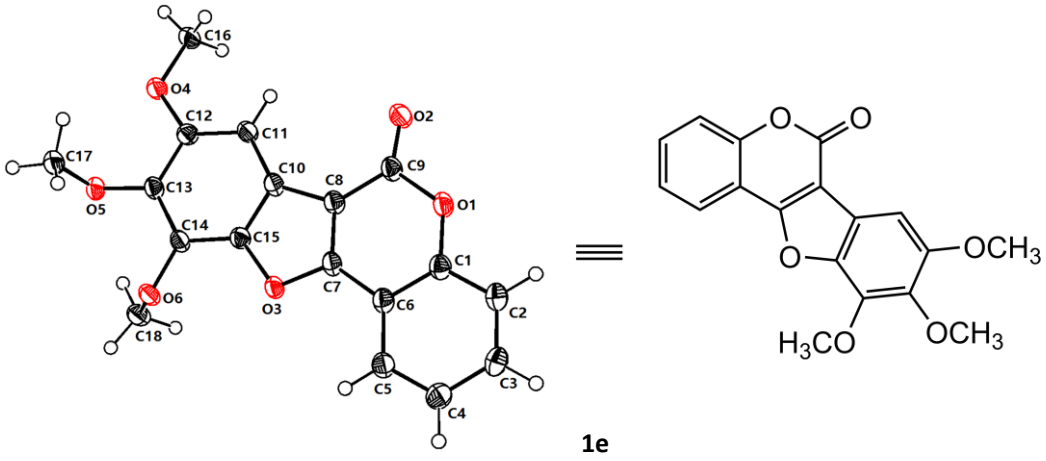


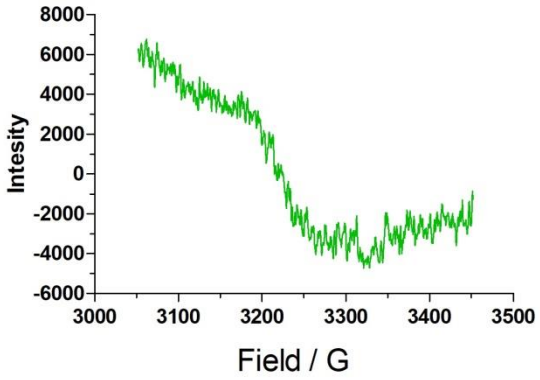
Fig. S1 X-ray single crystal structure of **1e**

Empirical formula	$C_{18}H_{14}O_6$
Formula weight	326.31
Temperature/K	100
Crystal system	triclinic
Space group	P-1
a/Å	9.1056(6)
b/Å	11.7060(8)
c/Å	14.8314(8)
α/°	78.547(5)
β/°	77.009(5)
γ/°	73.528(6)
Volume/Å^3	1461.74(17)
Z	4
ρ_{calc}g/cm^3	1.4826
μ/mm^{-1}	0.944
F(000)	682.6
Crystal size/mm^3	0.4 × 0.2 × 0.2
Radiation	Cu Kα (λ = 1.54184)

2Θ range for data collection/°	6.18 to 134.16
Index ranges	$-10 \leq h \leq 11$, $-13 \leq k \leq 14$, $-11 \leq l \leq 18$
Reflections collected	11521
Independent reflections	5184 [R_{int} = 0.0611, R_{sigma} = 0.0586]
Data/restraints/parameters	5184/0/439
Goodness-of-fit on F^2	1.018
Final R indexes [I>=2σ (I)]	R_1 = 0.0641, wR_2 = 0.1851
Final R indexes [all data]	R_1 = 0.0764, wR_2 = 0.2124
Largest diff. peak/hole / e $Å^{-3}$	0.44/-0.40

5. EPR experiment

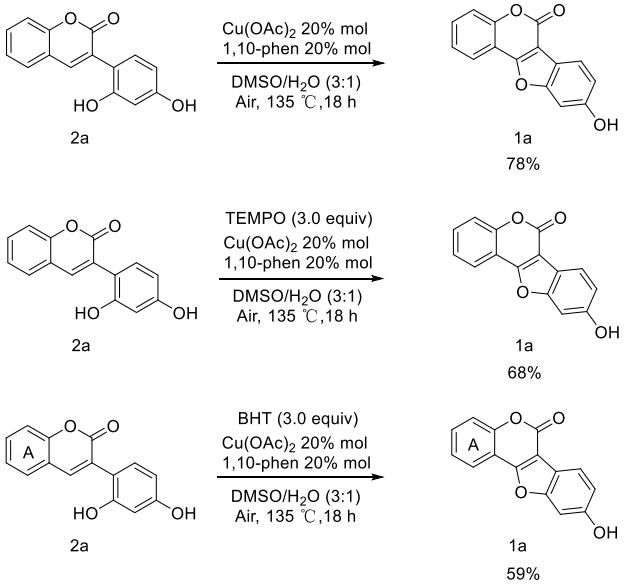
To further explore the reaction mechanism, the electron paramagnetic resonance (EPR) experiment was carried out using **2a** as the substrate under the standard conditions. Results showed that no obvious EPR signals were observed in the reaction mixture (Scheme S1).



Scheme S1 EPR experiment

6. Radical trapping experiment

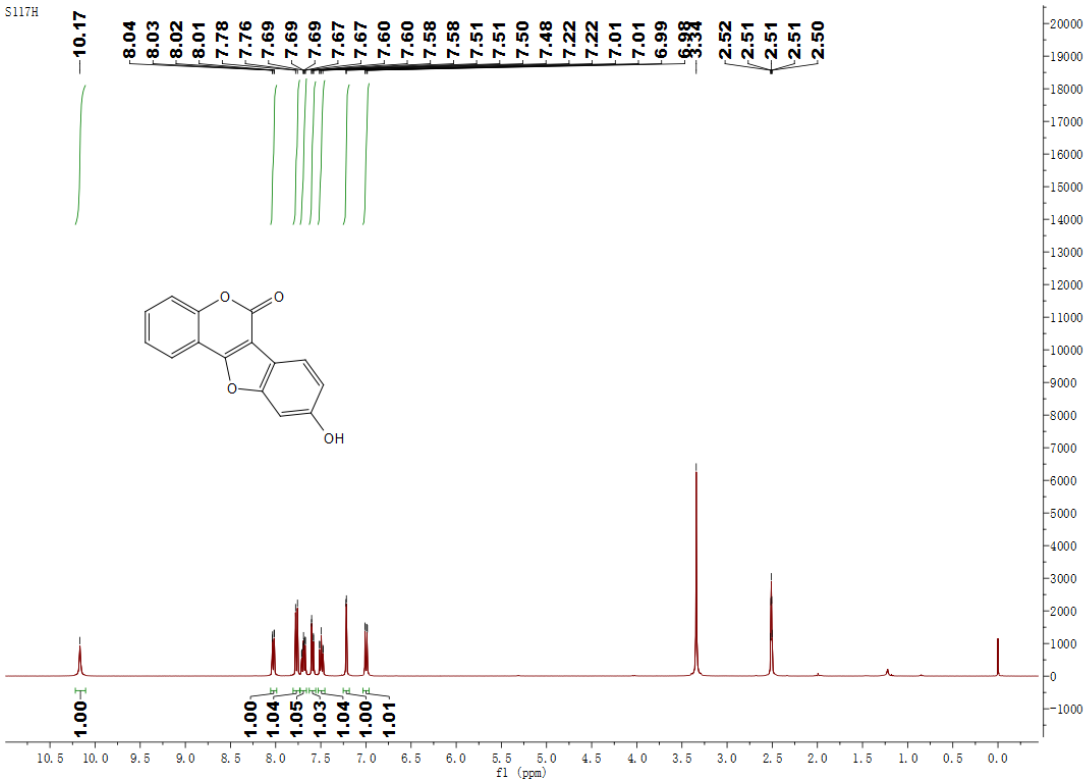
The addition of the typical radical scavengers including TEMPO and BHT (3.0 equiv) to the reaction solution of **2a** did not significantly reduce the yields of this reaction, the desired product (1a) was obtained in 68% and 59% yield, respectively.

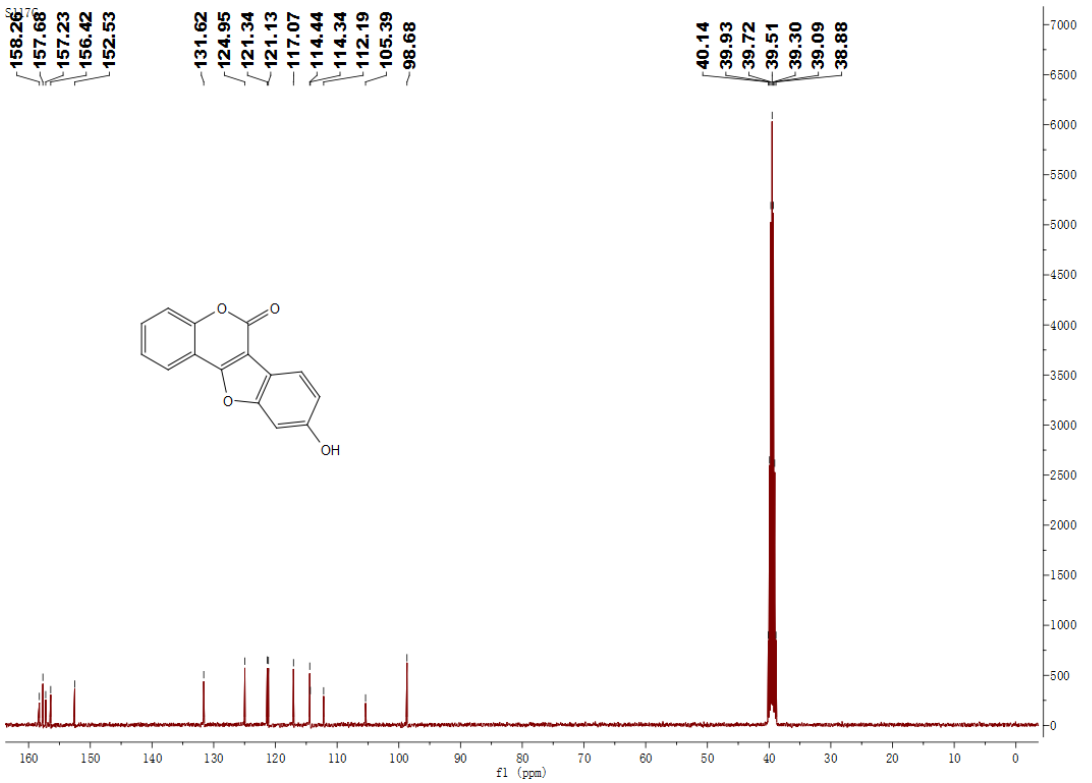


Scheme S2 Radical trapping experiment

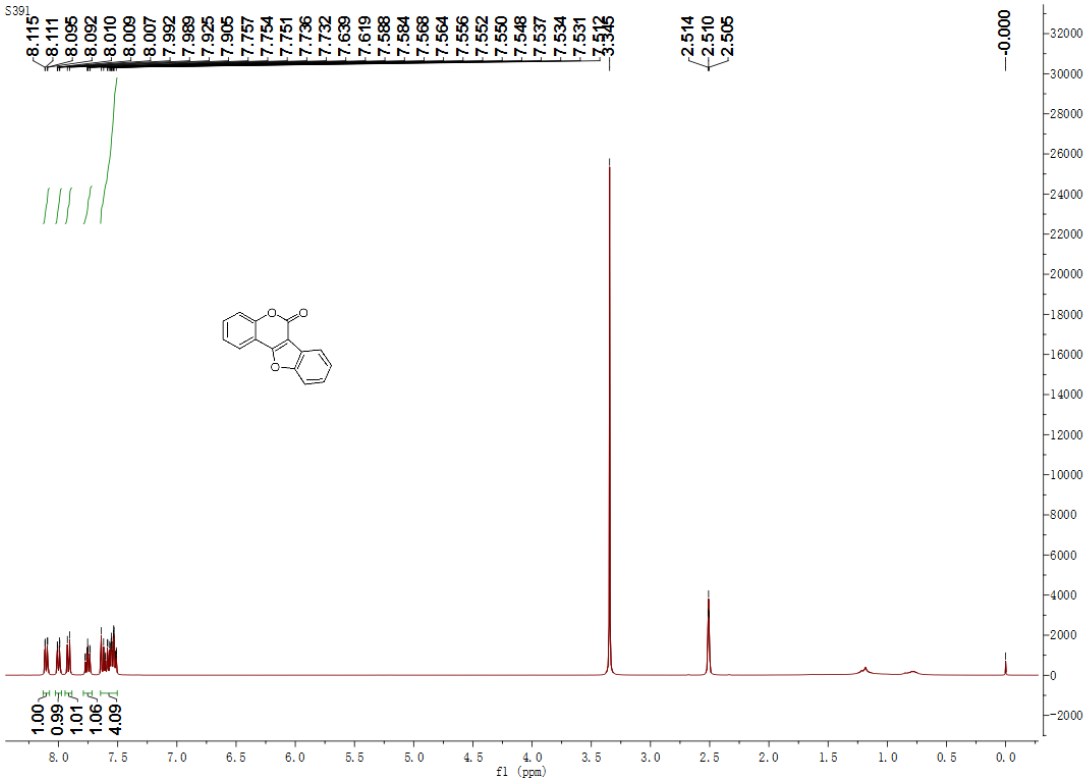
7. Copies of ^{1}H- and ^{13}C-NMR

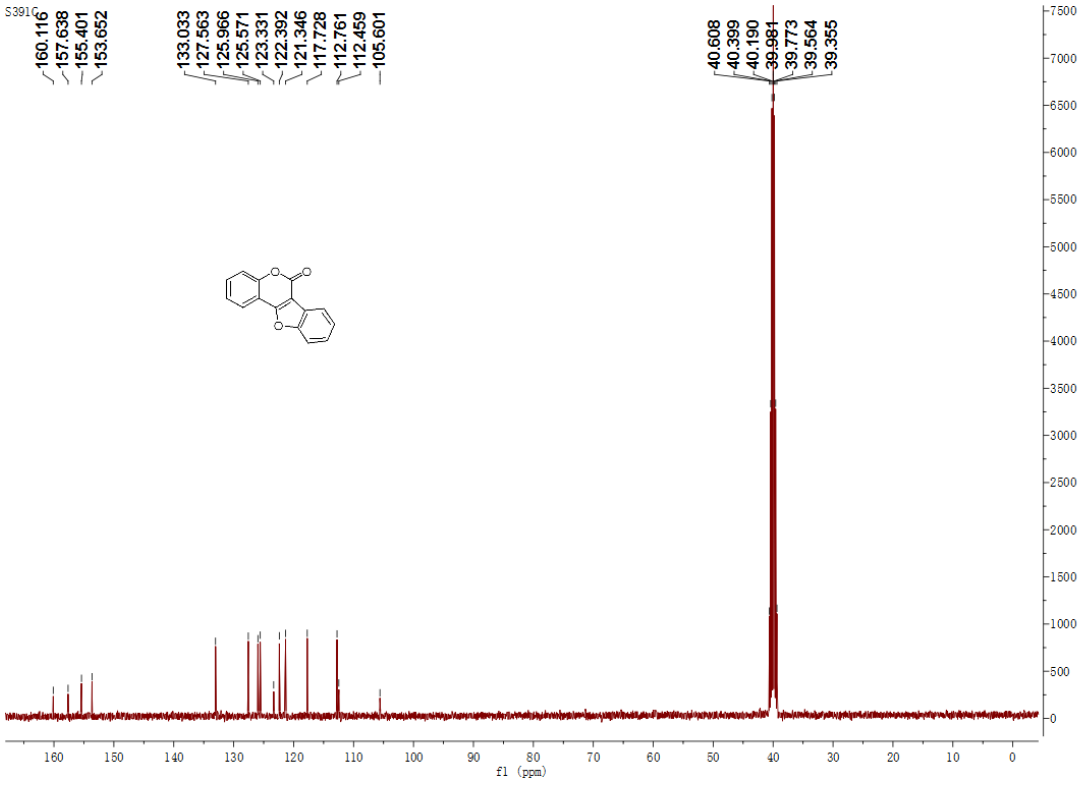
^{1}H- and ^{13}C-NMR spectra of 1a



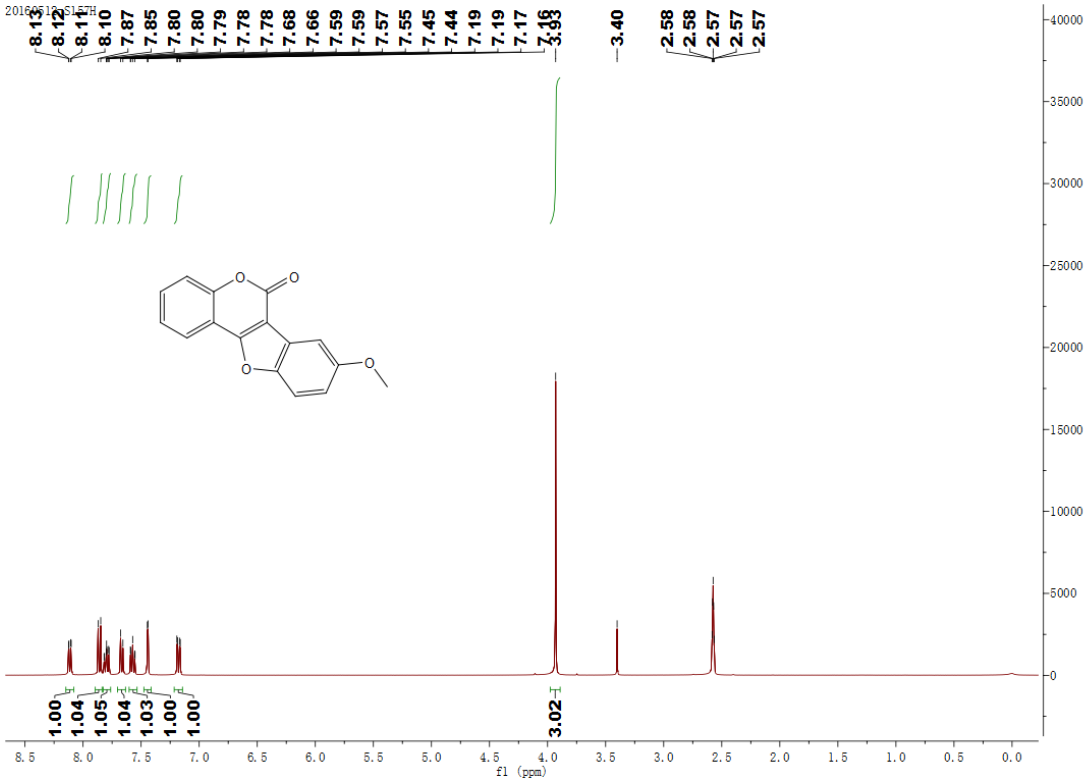


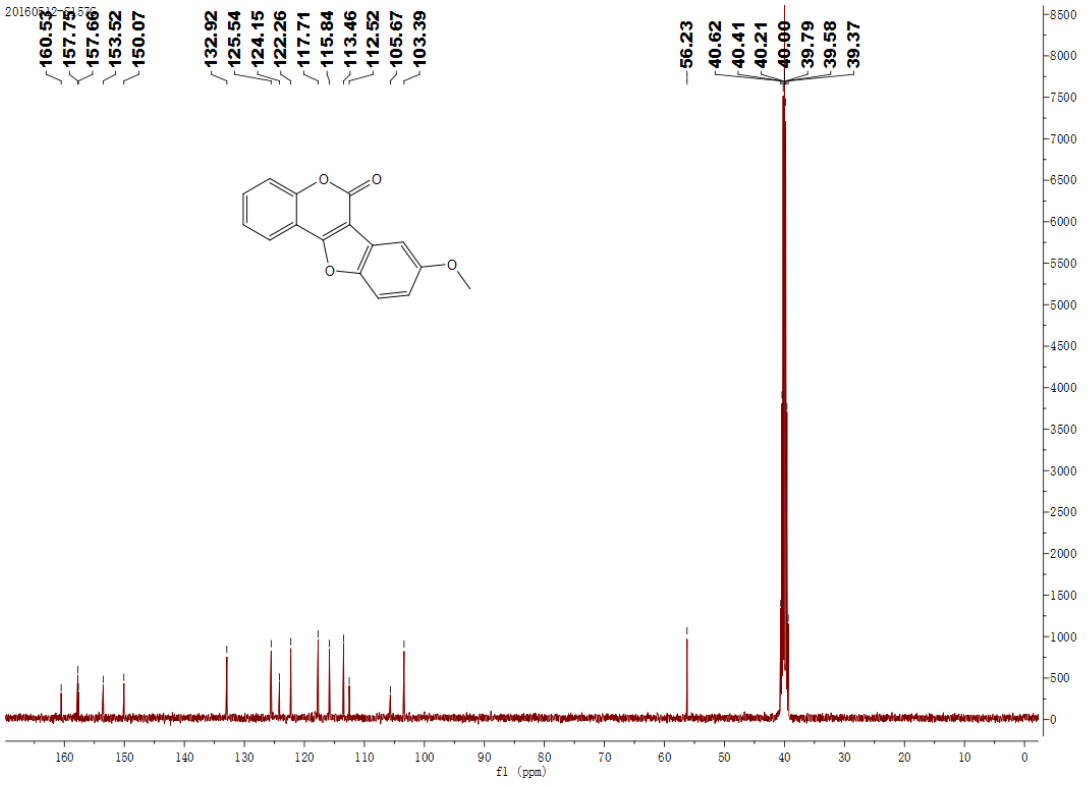
^{1}H- and ^{13}C-NMR spectra of 1b



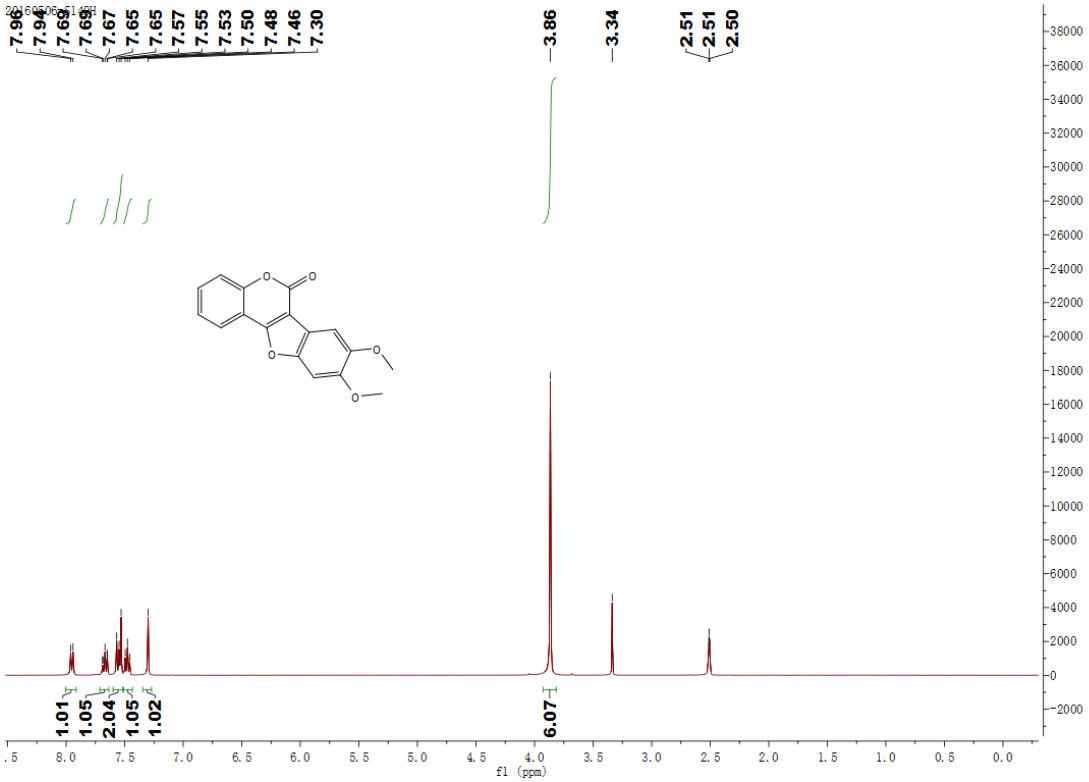


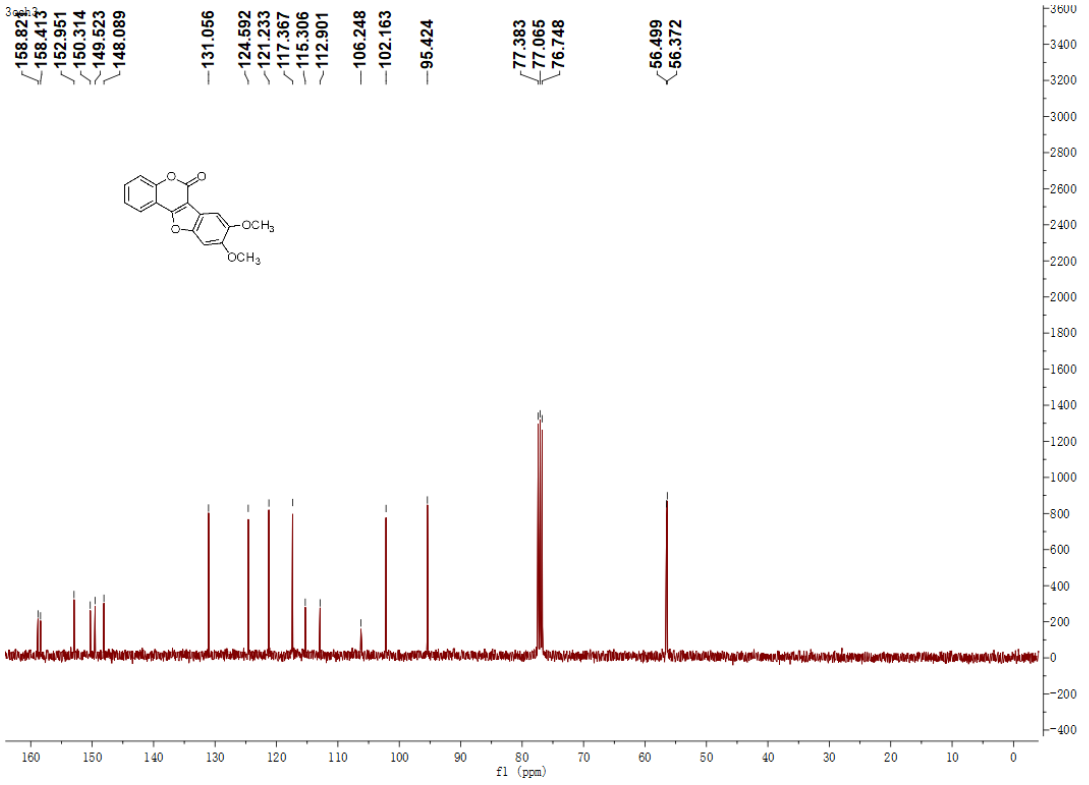
^{1}H- and ^{13}C-NMR spectra of 1c



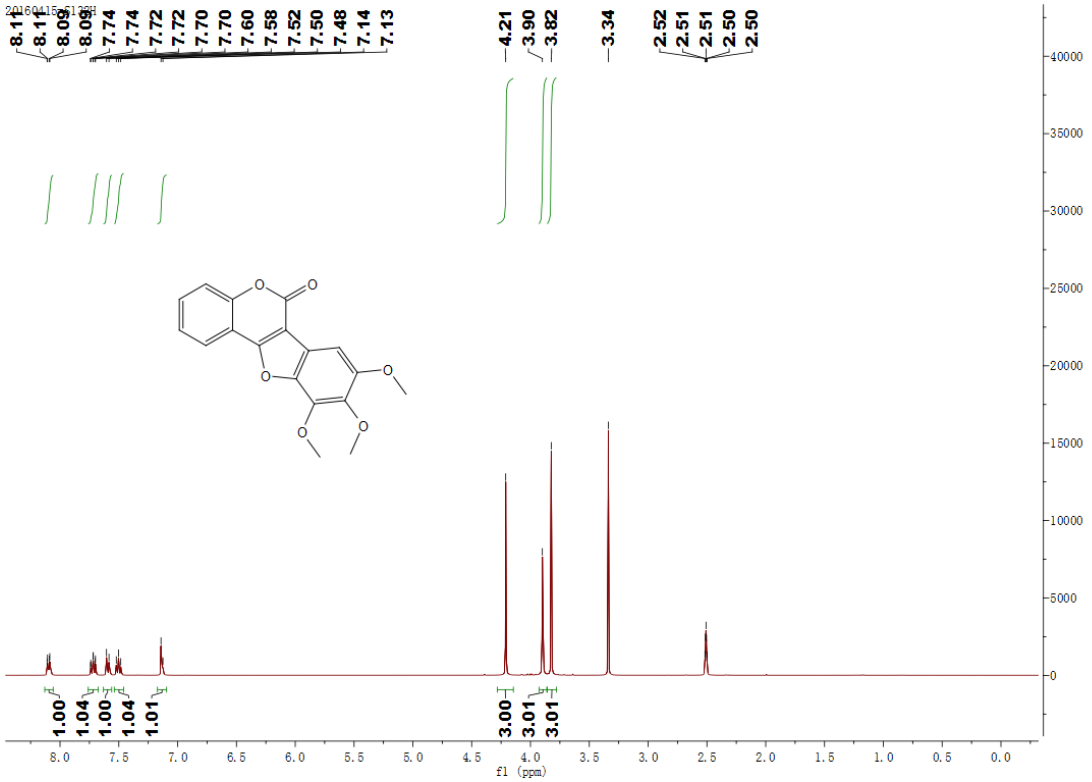


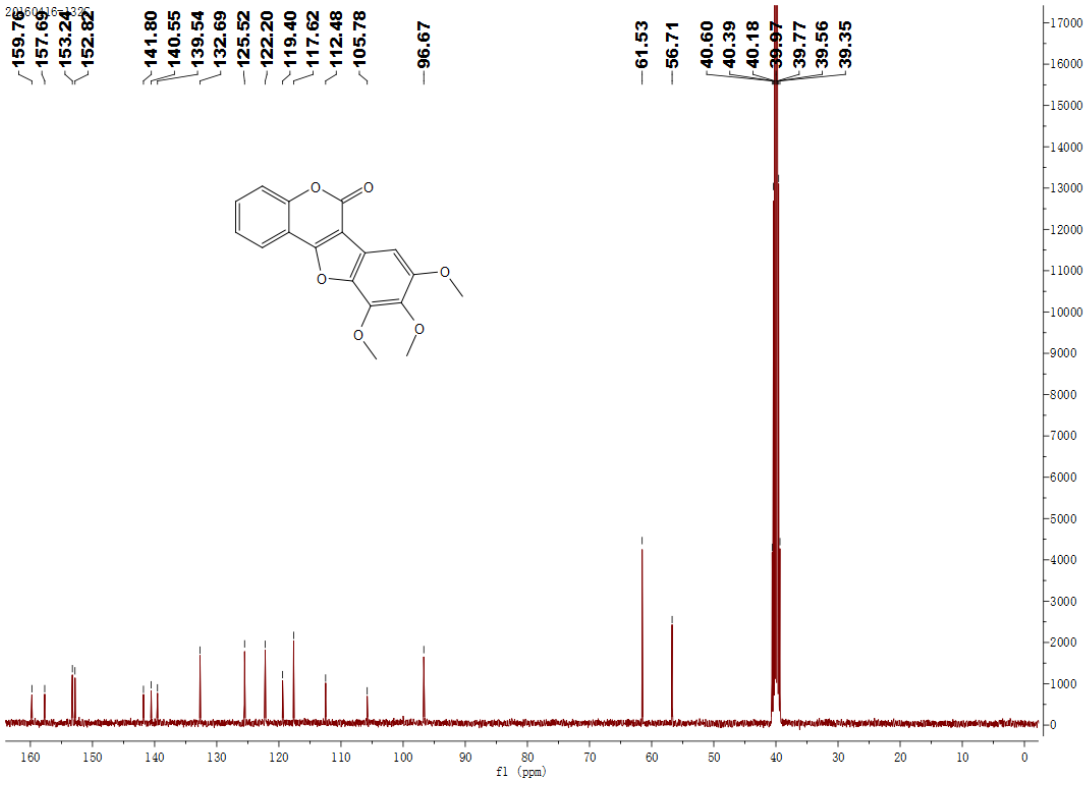
^{1}H- and ^{13}C-NMR spectra of 1d



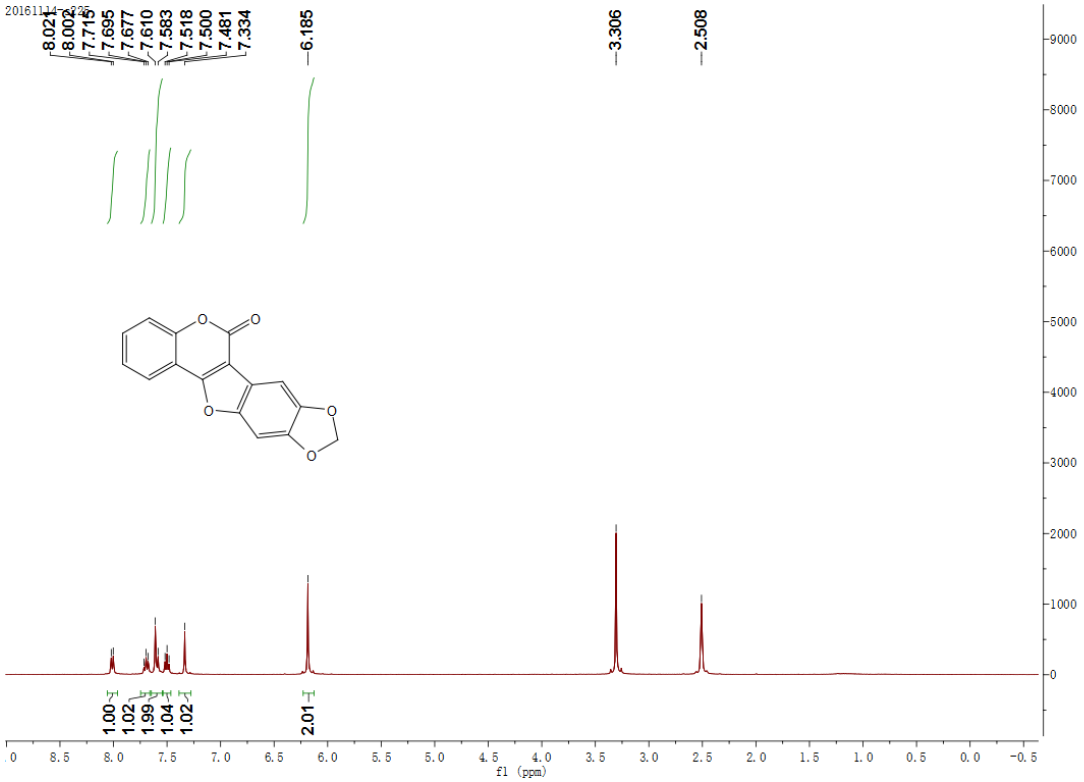


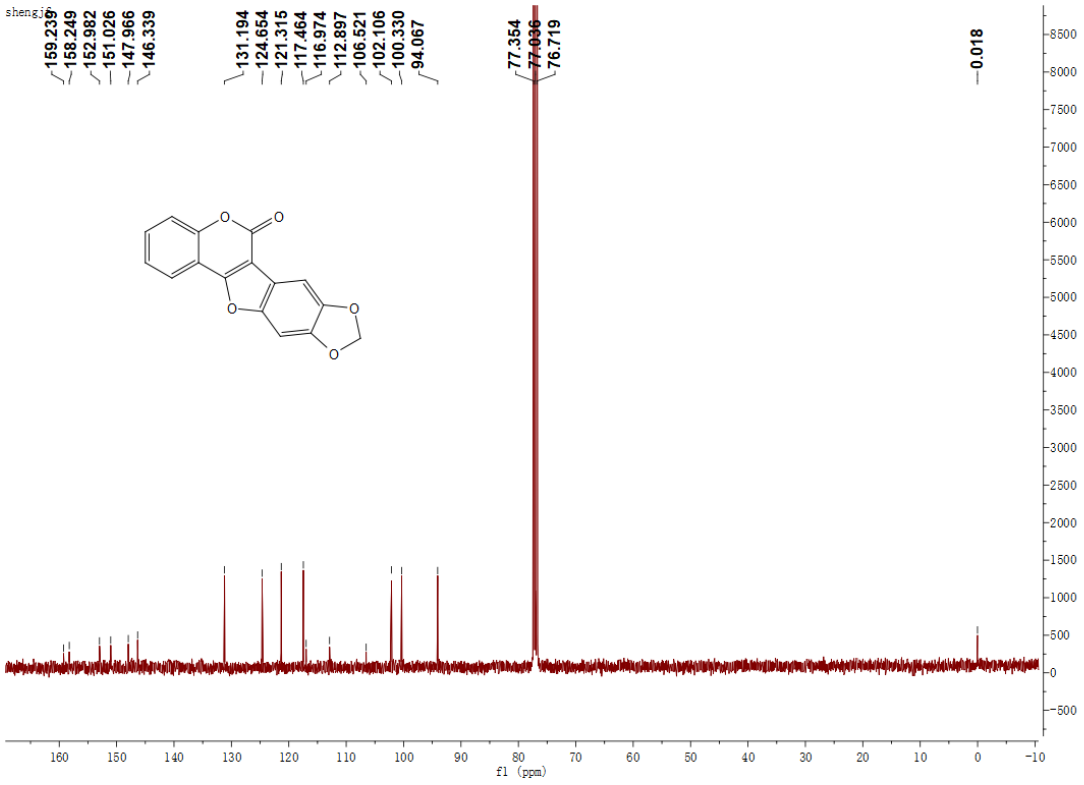
^{1}H- and ^{13}C-NMR spectra of 1e



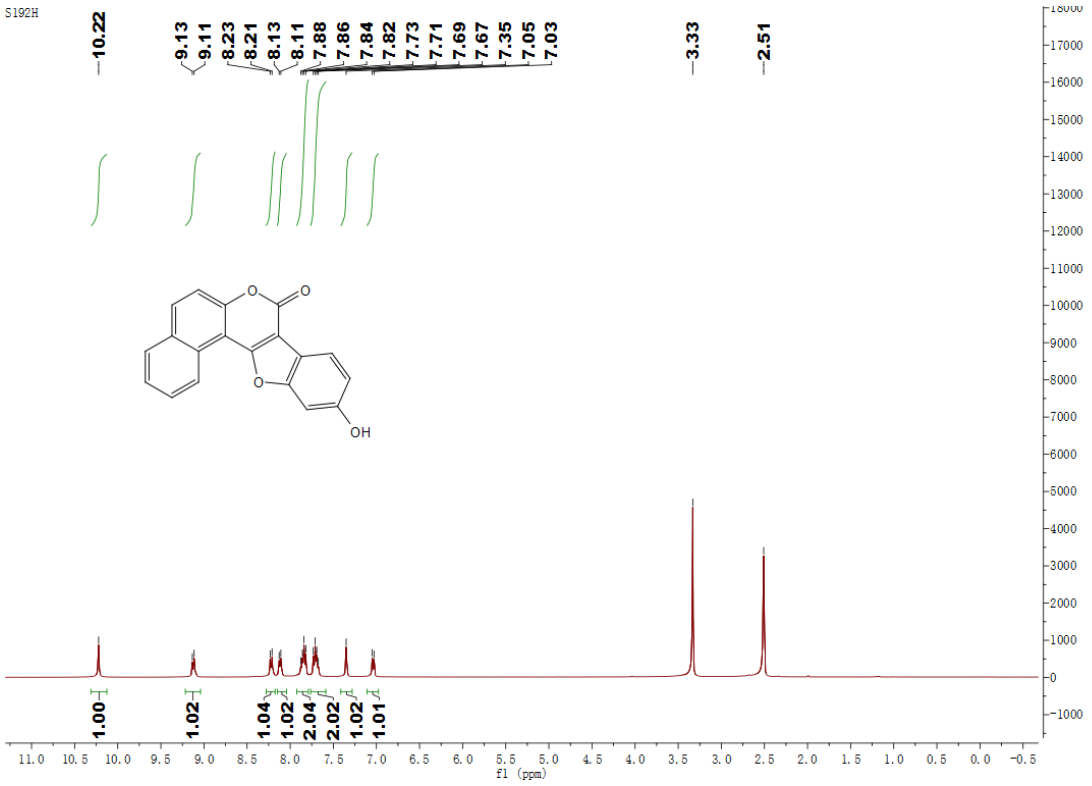


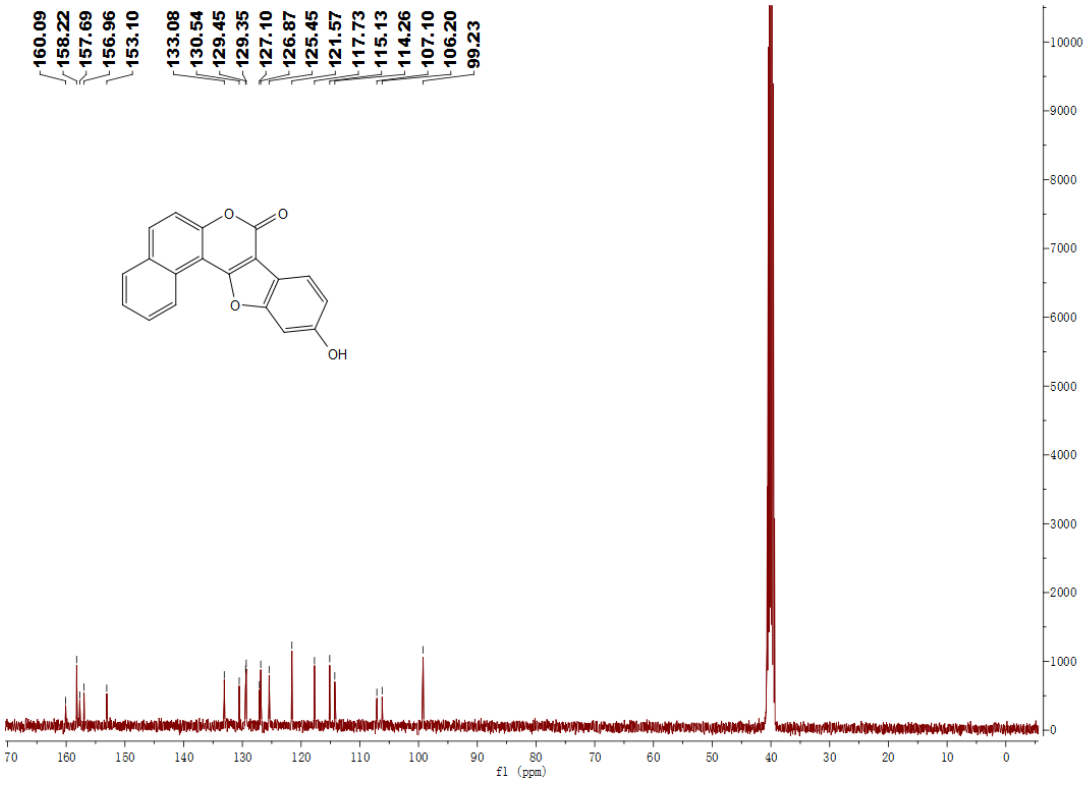
^{1}H- and ^{13}C-NMR spectra of 1f



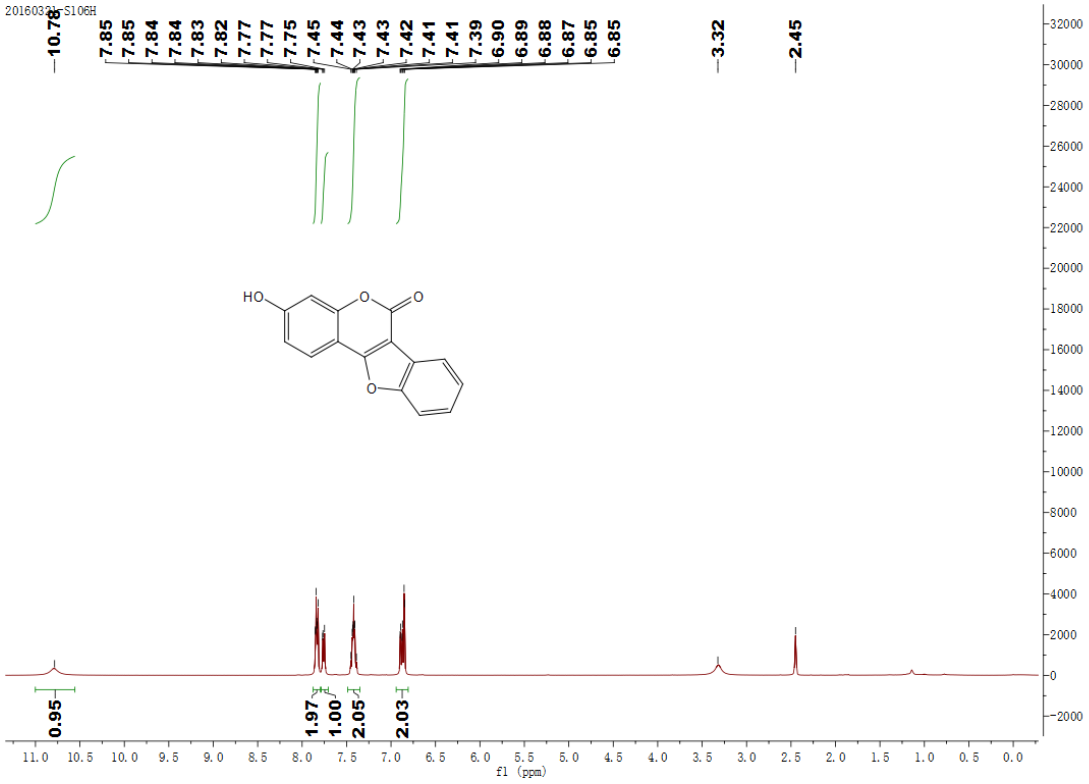


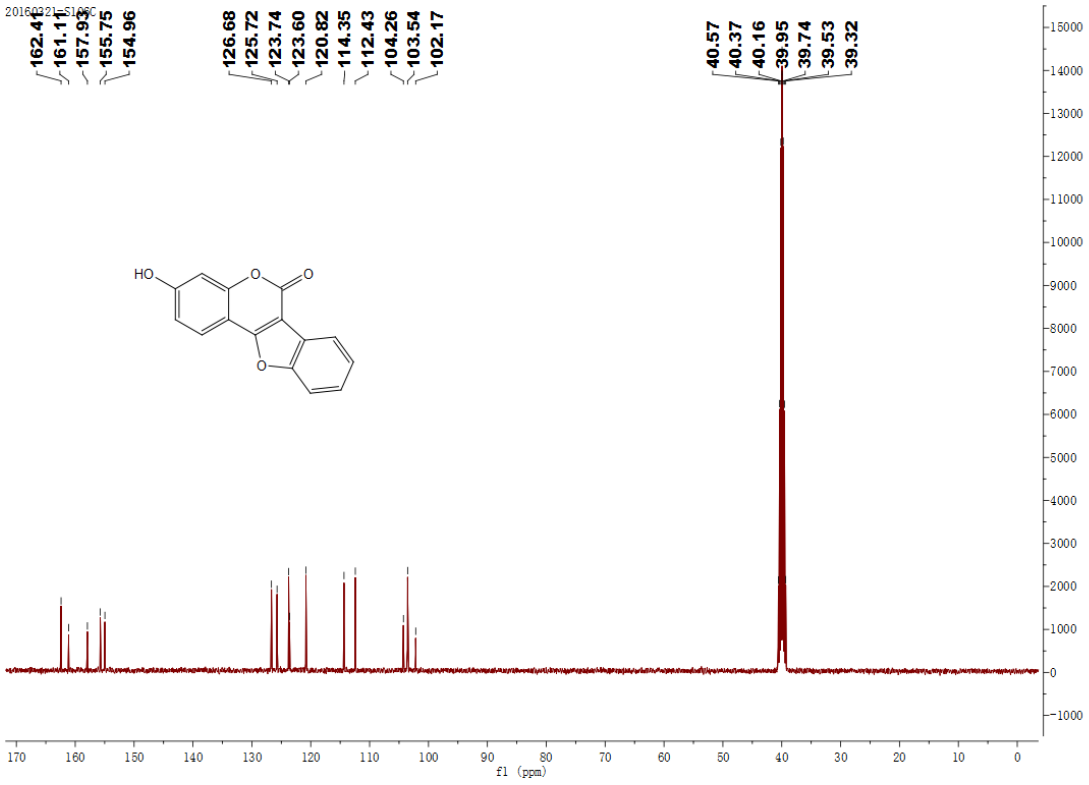
^{1}H- and ^{13}C-NMR spectra of 1g



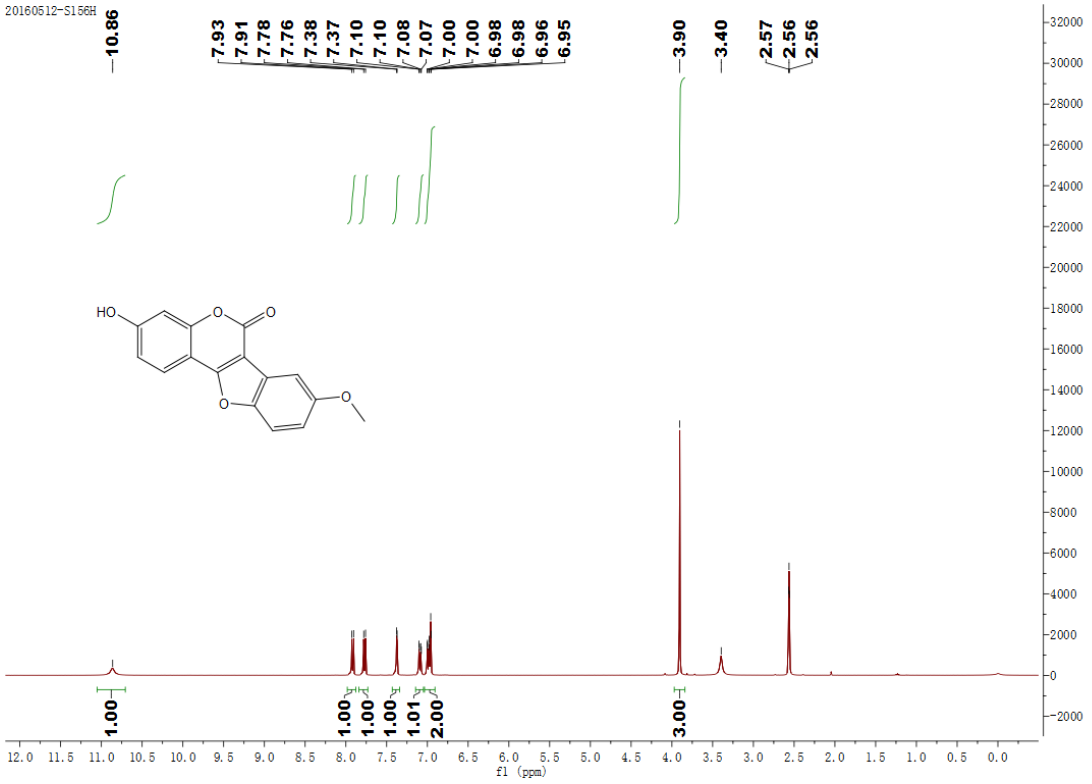


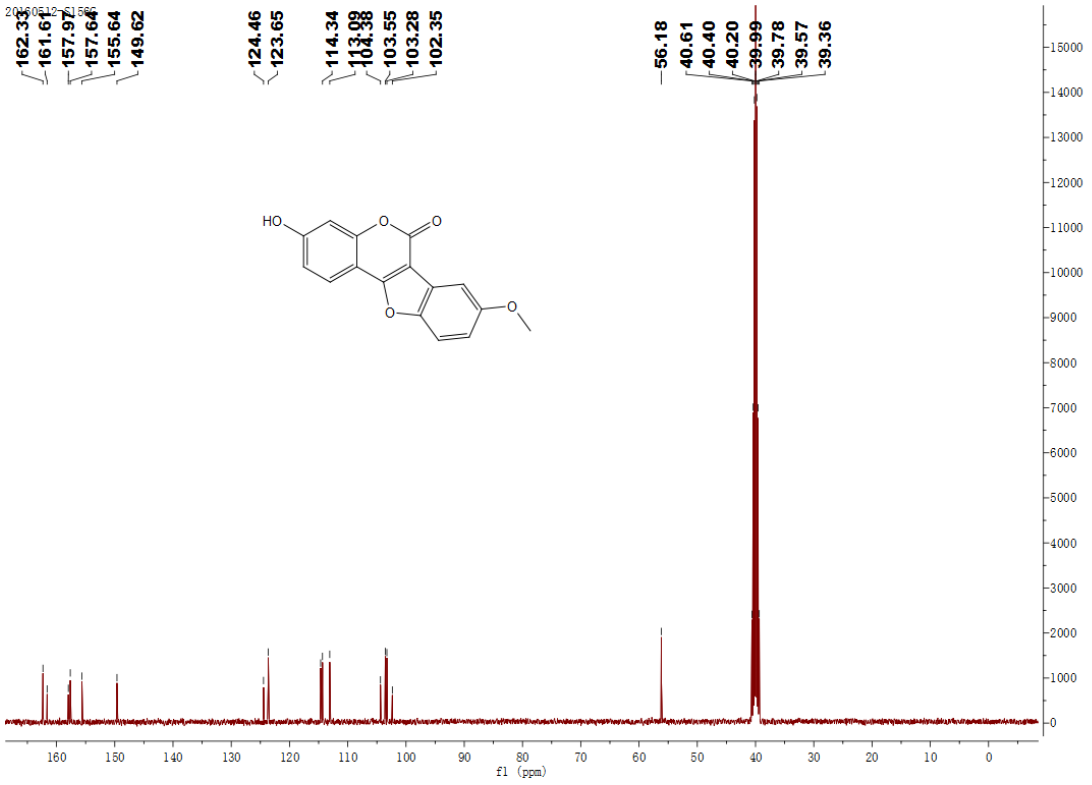
^{1}H- and ^{13}C-NMR spectra of 1h



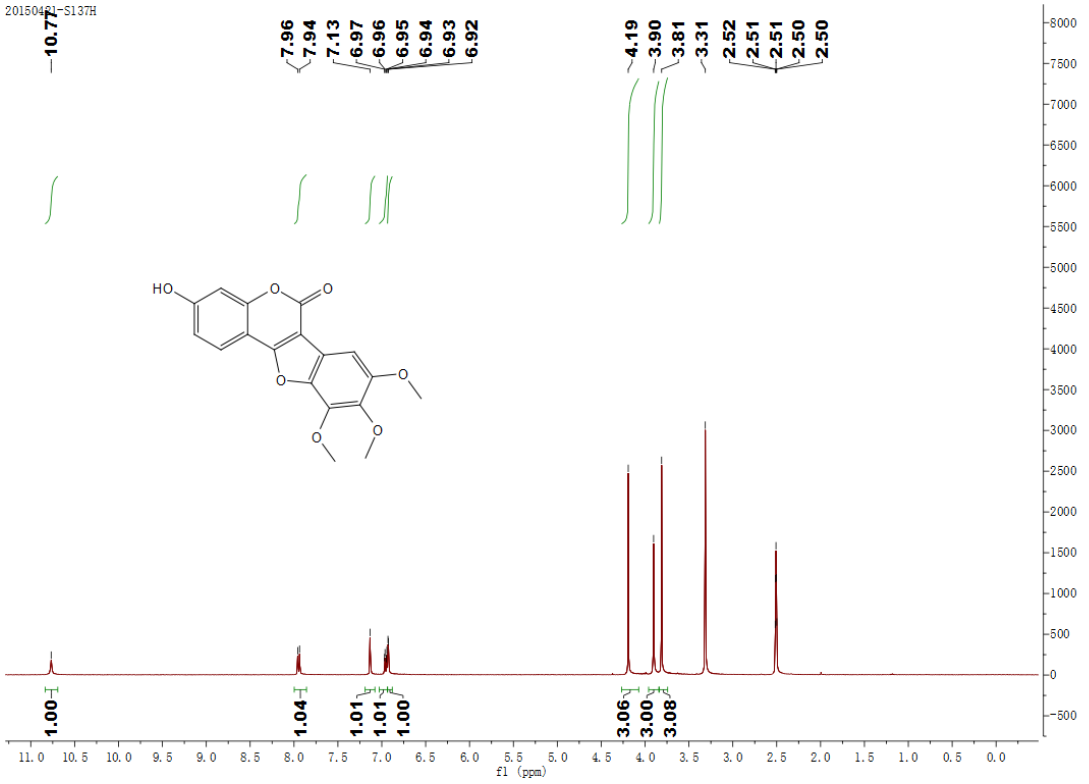


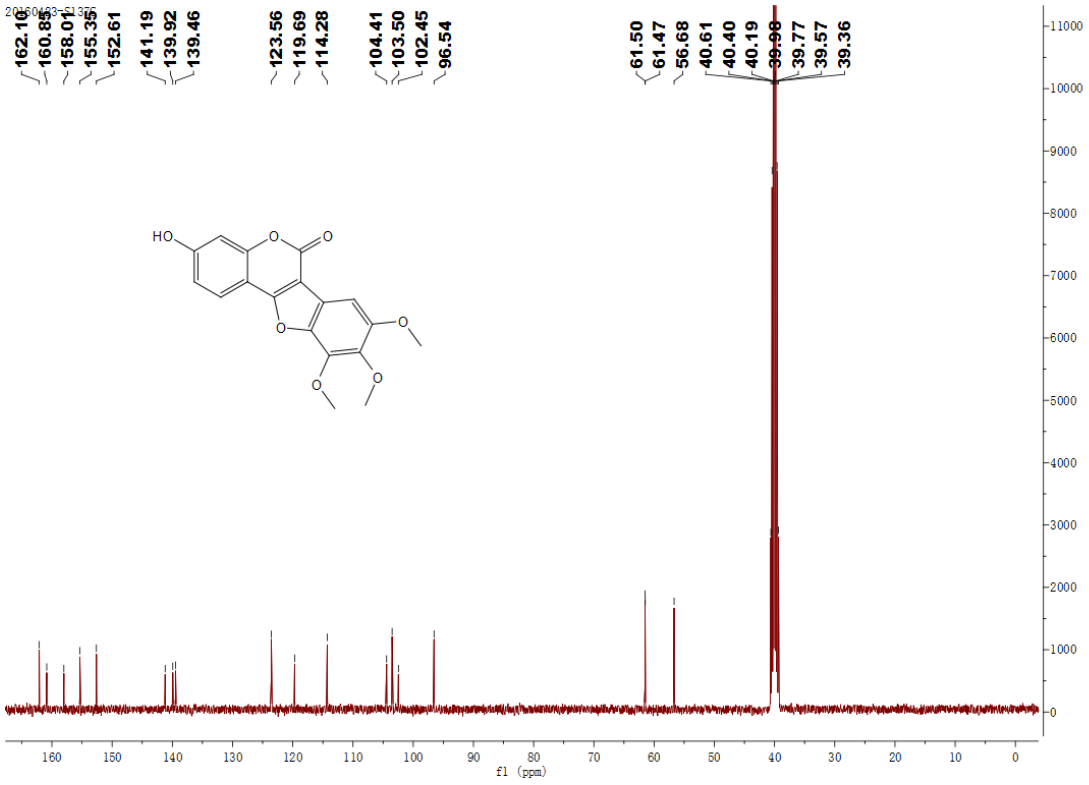
^{1}H- and ^{13}C-NMR spectra of 1i



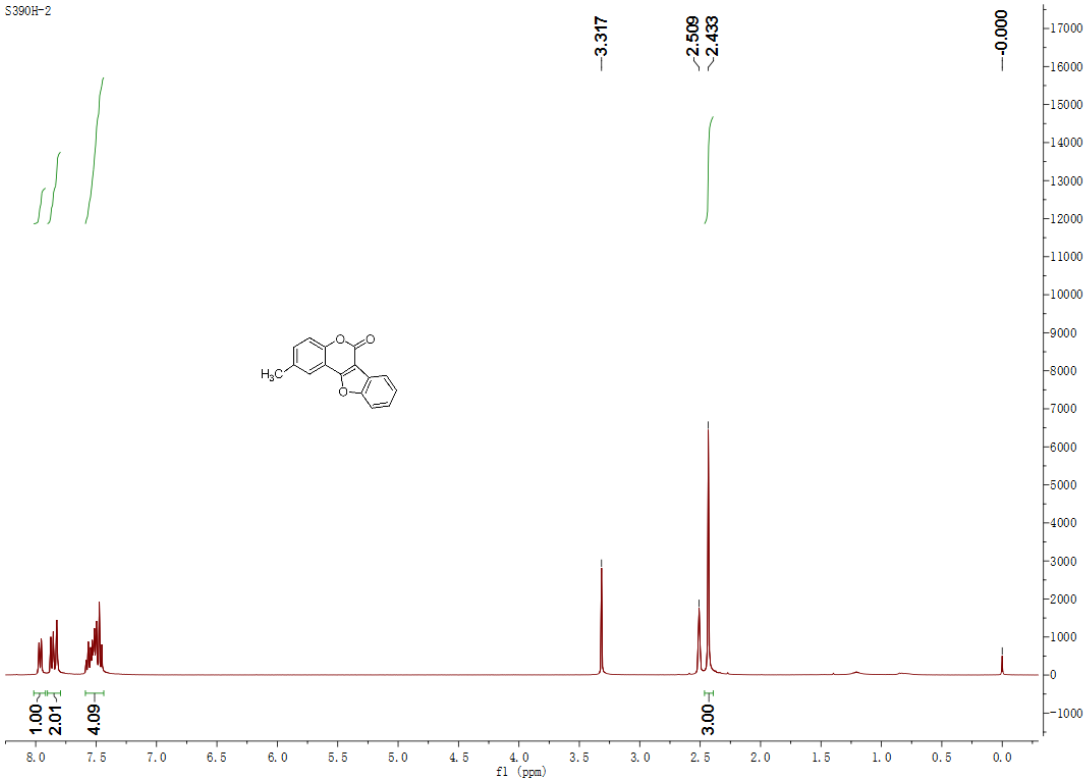


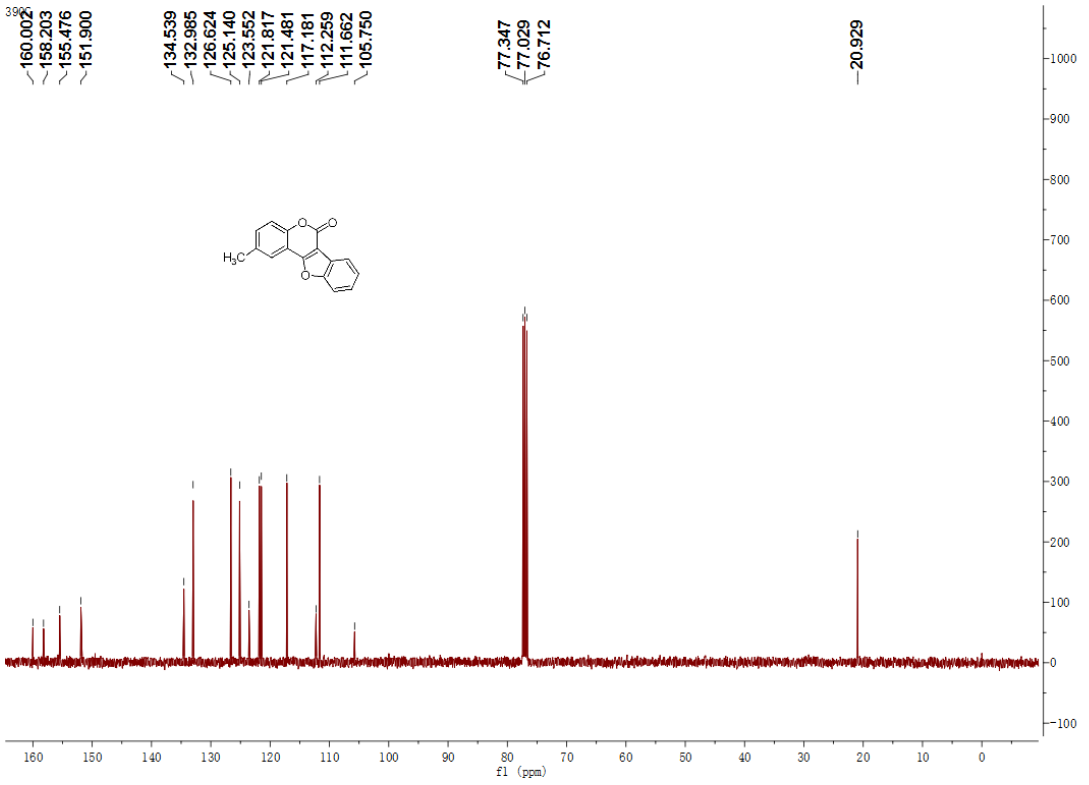
^{1}H- and ^{13}C-NMR spectra of 1j



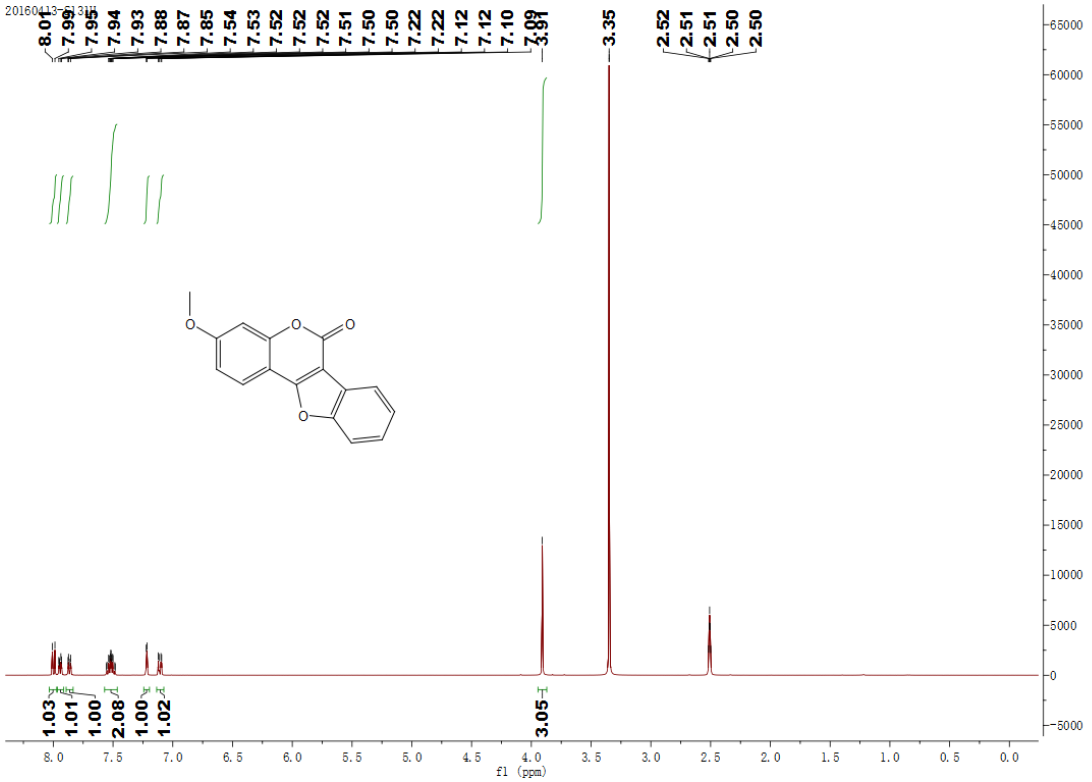


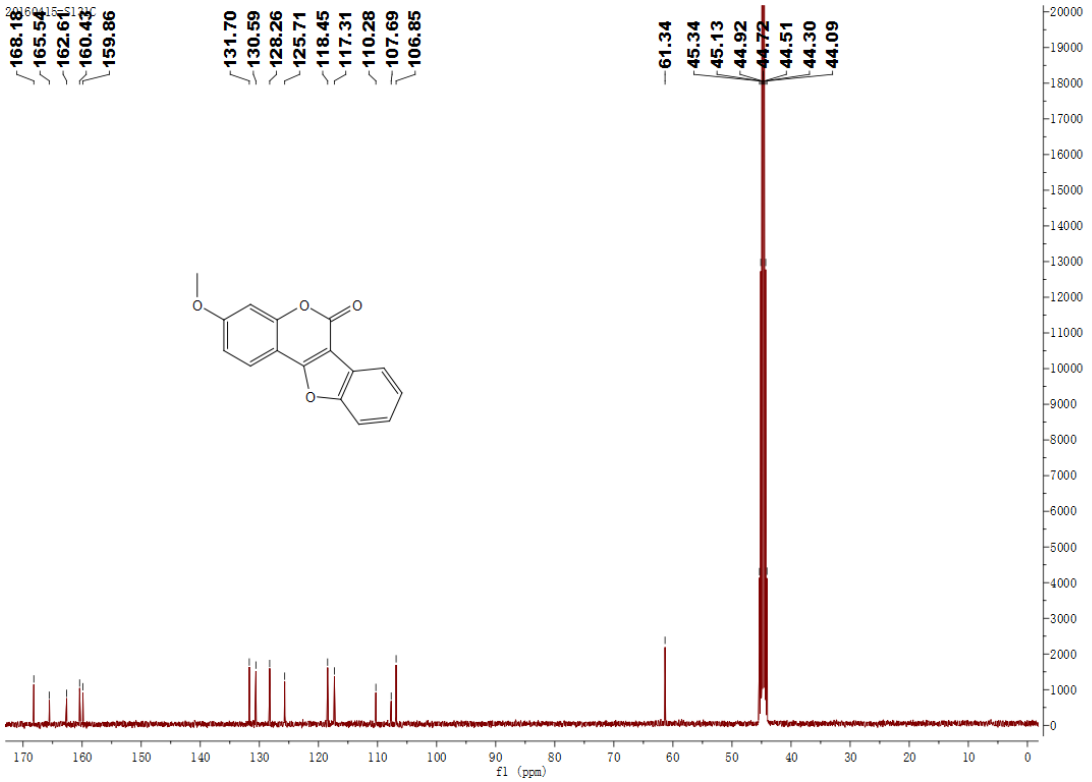
^{1}H- and ^{13}C-NMR spectra of 1k



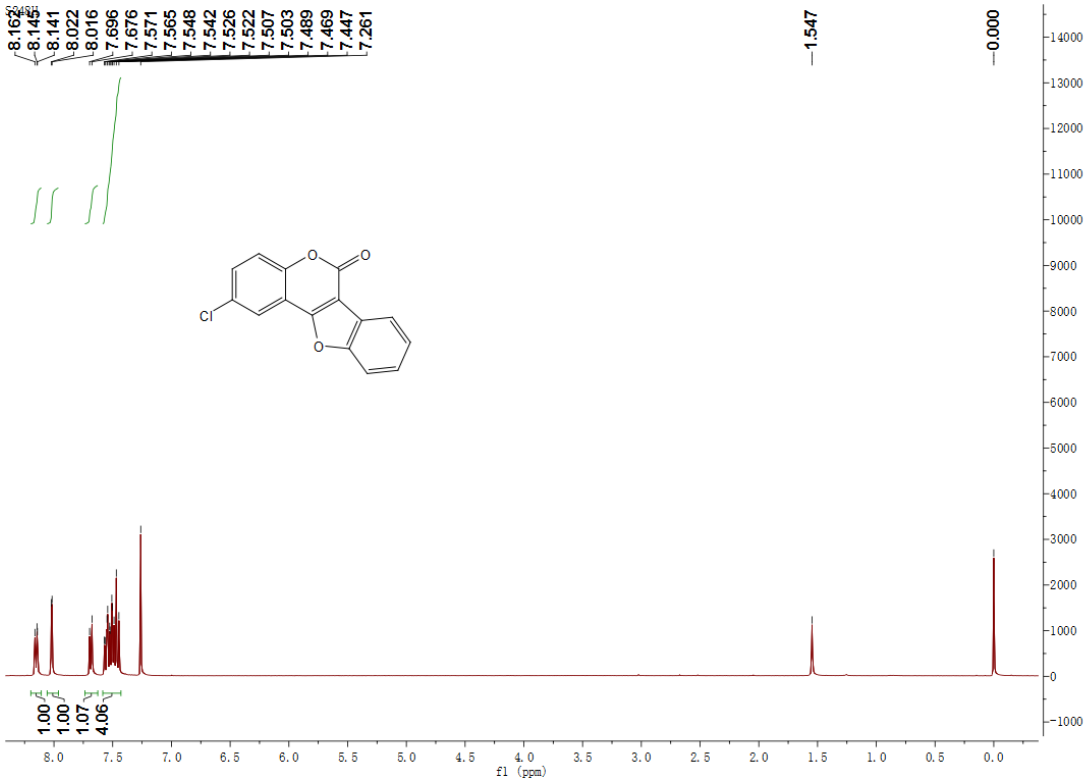


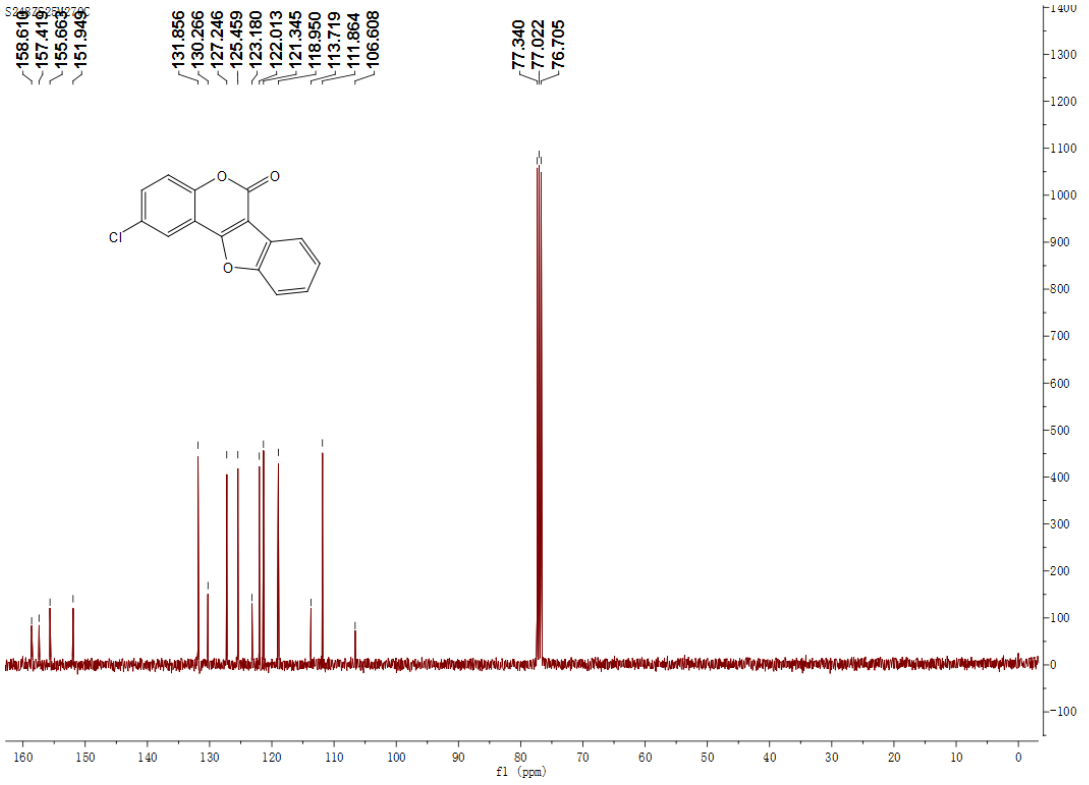
^{1}H- and ^{13}C-NMR spectra of 1l



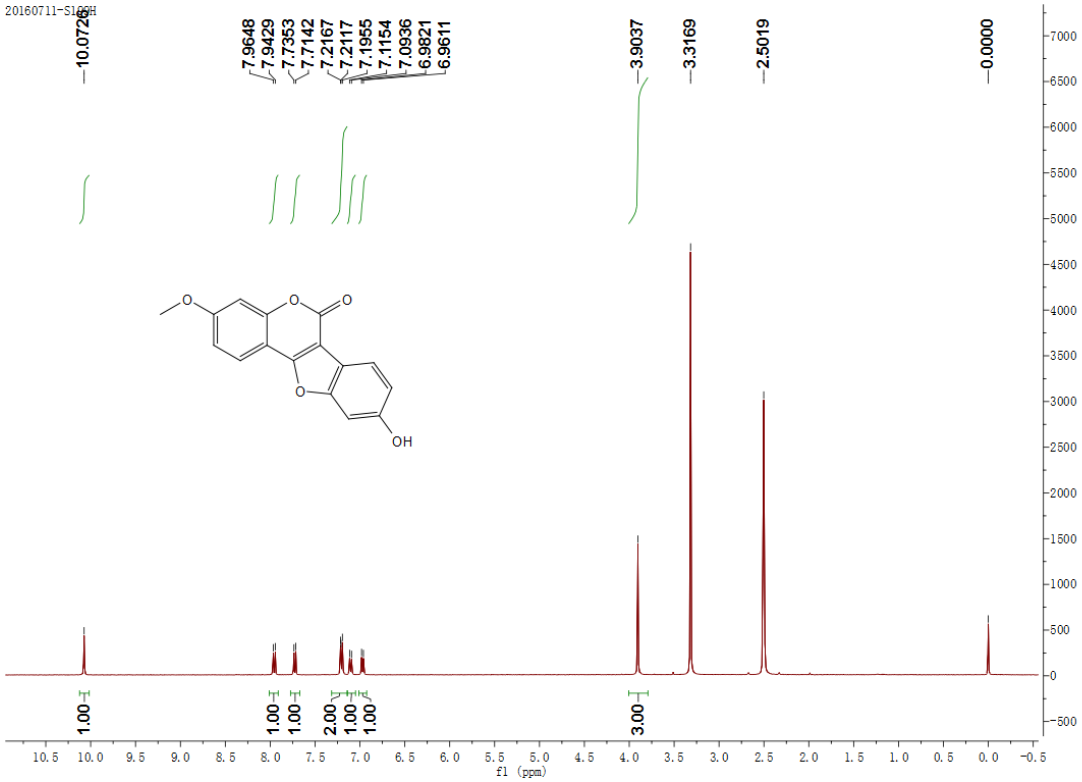


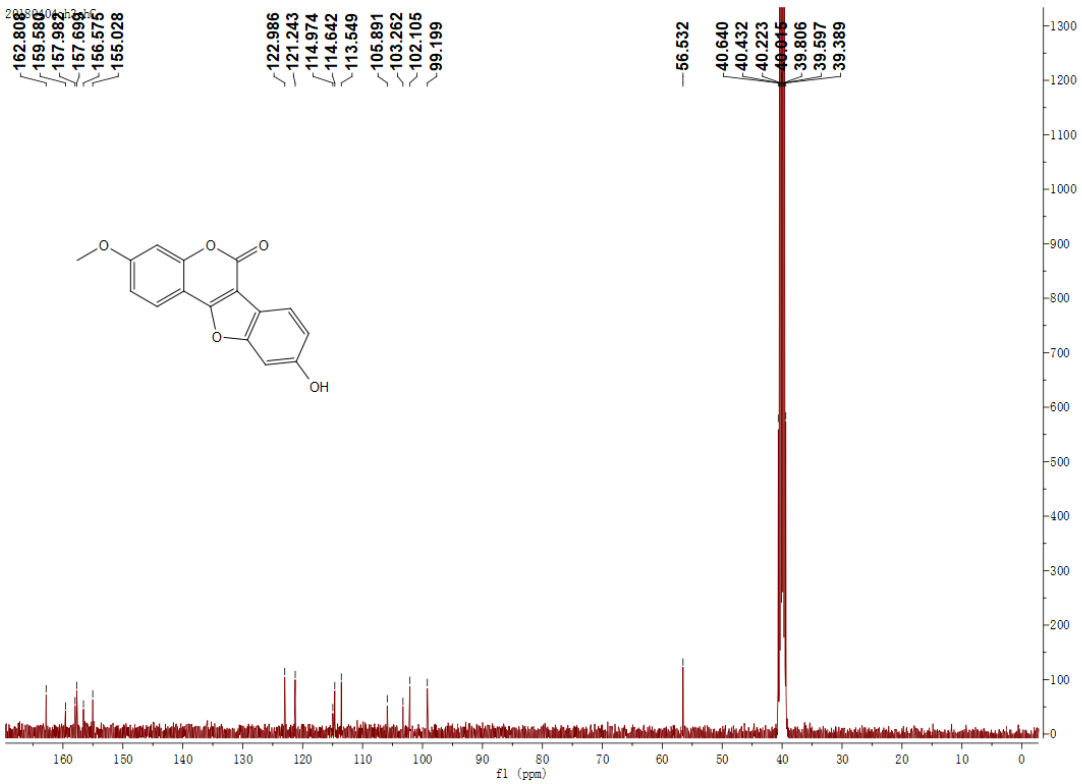
^{1}H- and ^{13}C-NMR spectra of 1m



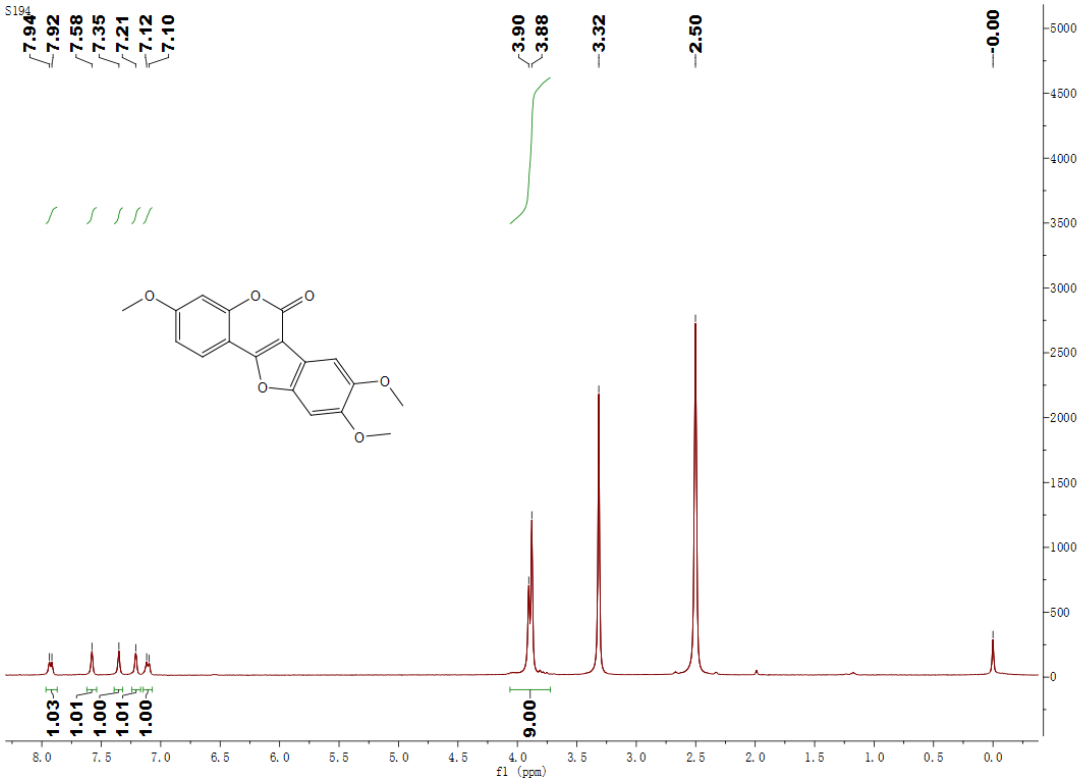


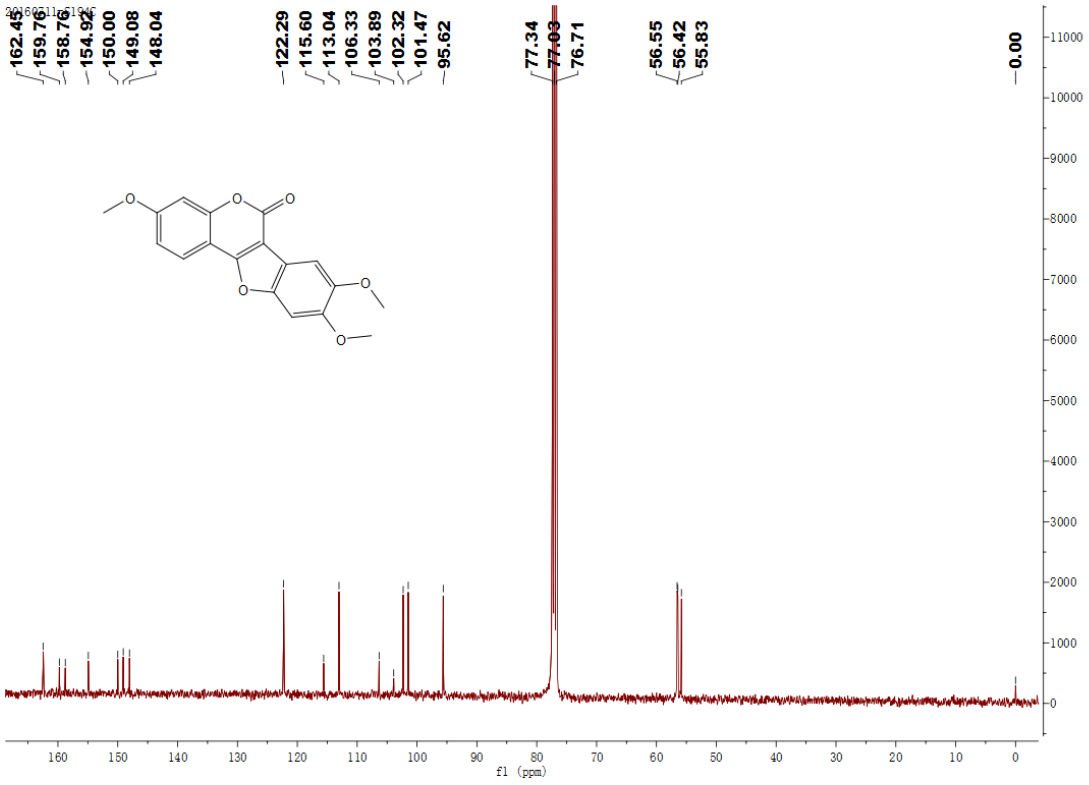
^{1}H- and ^{13}C-NMR spectra of 1n



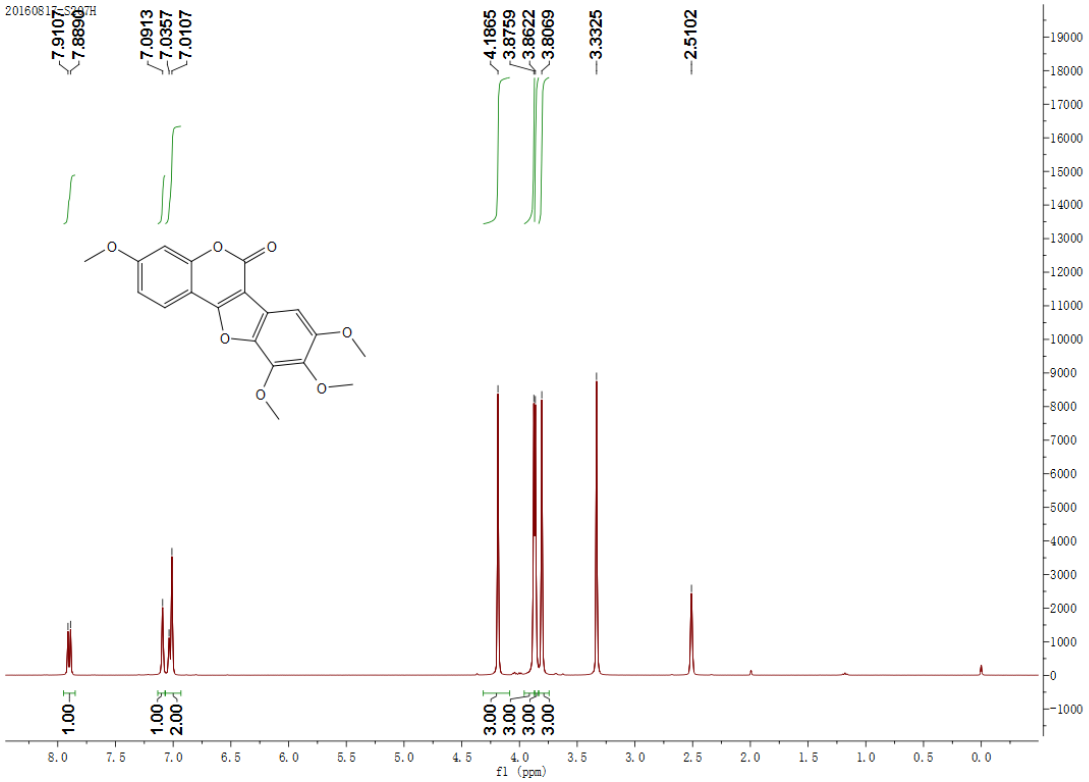


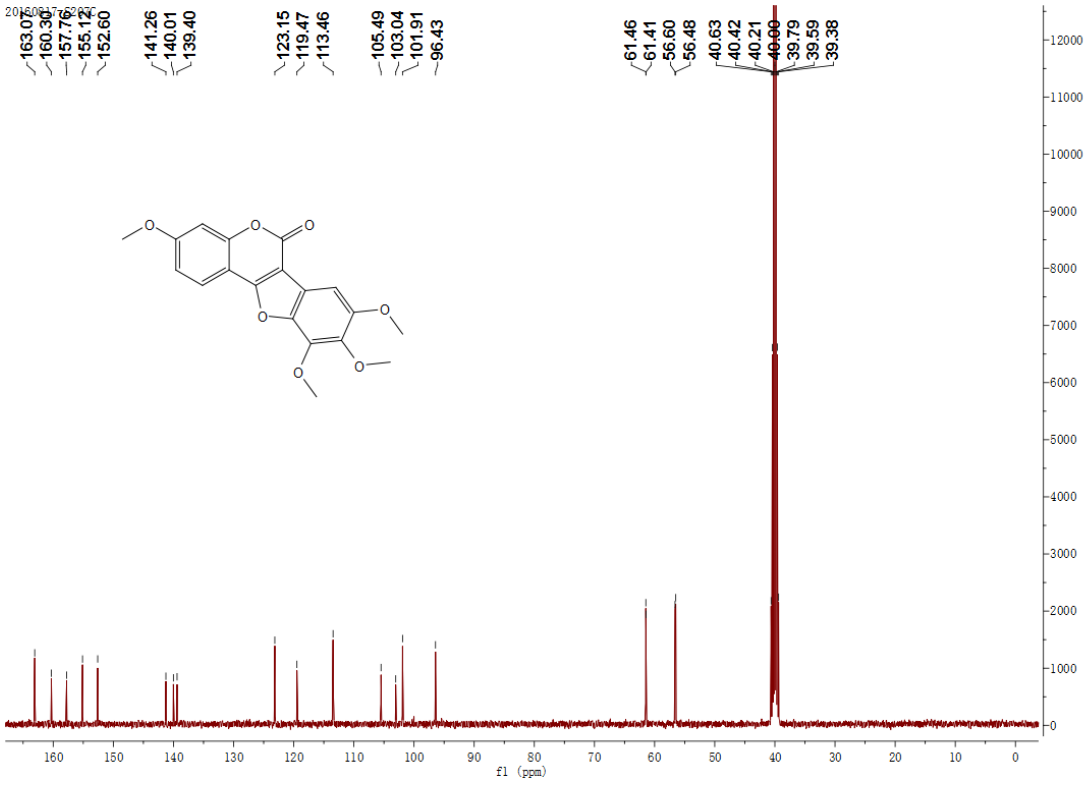
^{1}H- and ^{13}C-NMR spectra of 1o



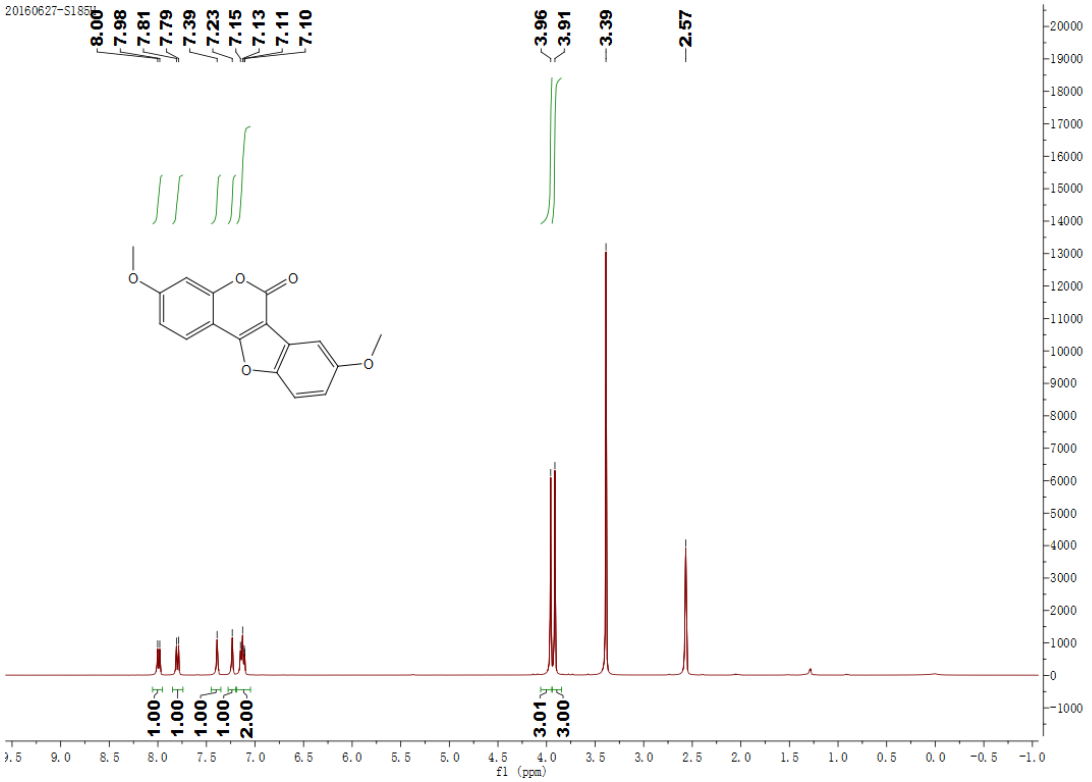


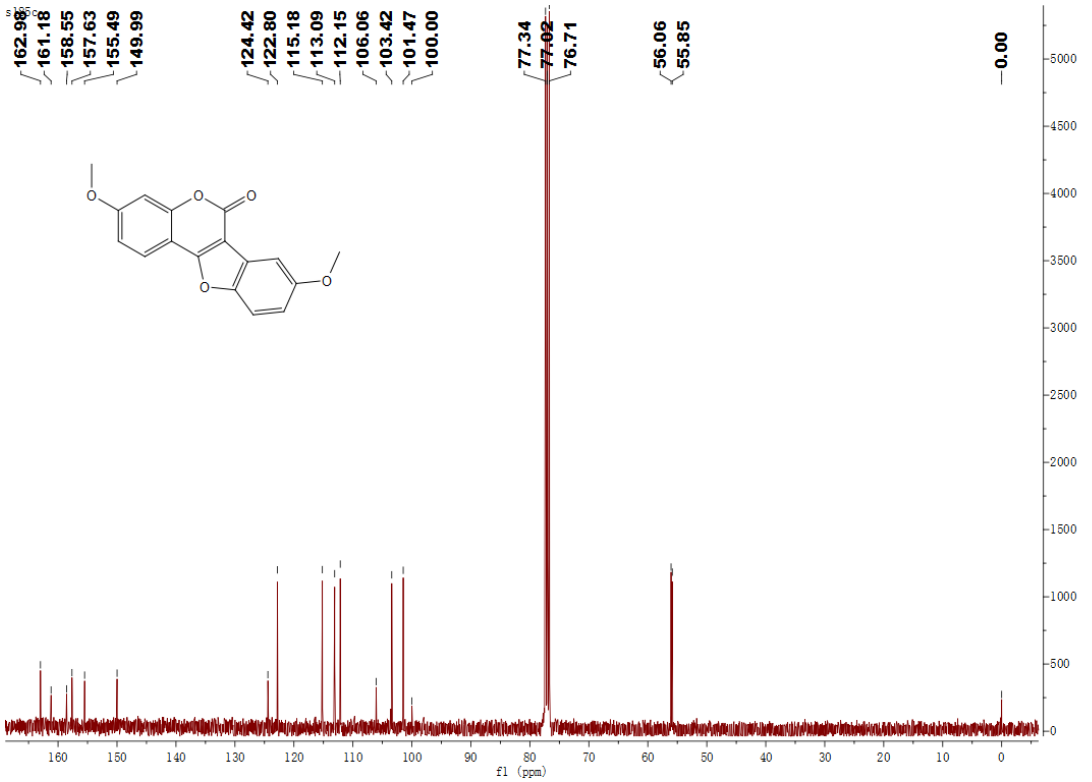
^{1}H- and ^{13}C-NMR spectra of 1p



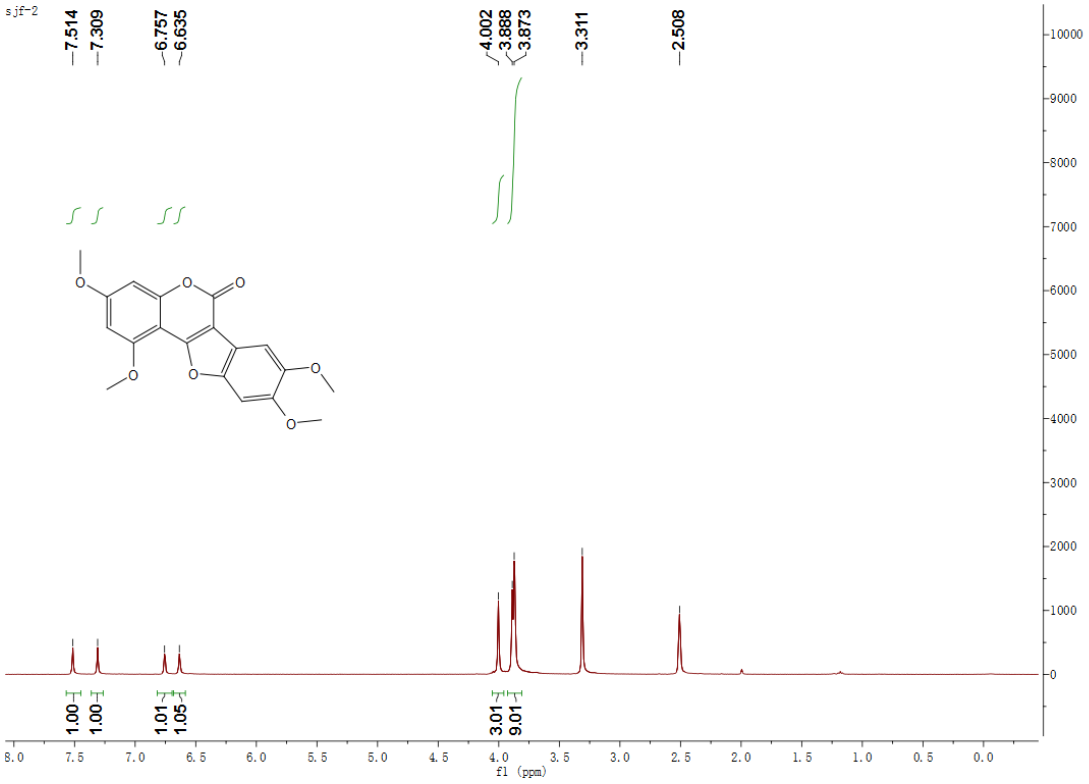


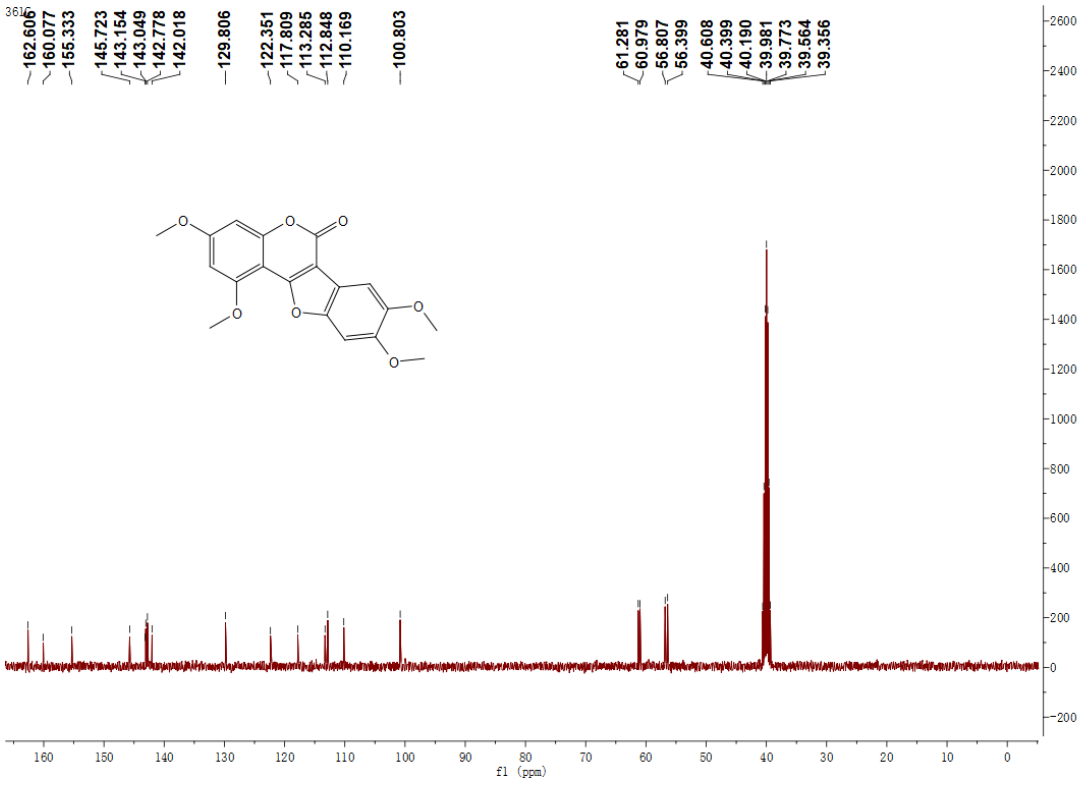
^{1}H- and ^{13}C-NMR spectra of 1q



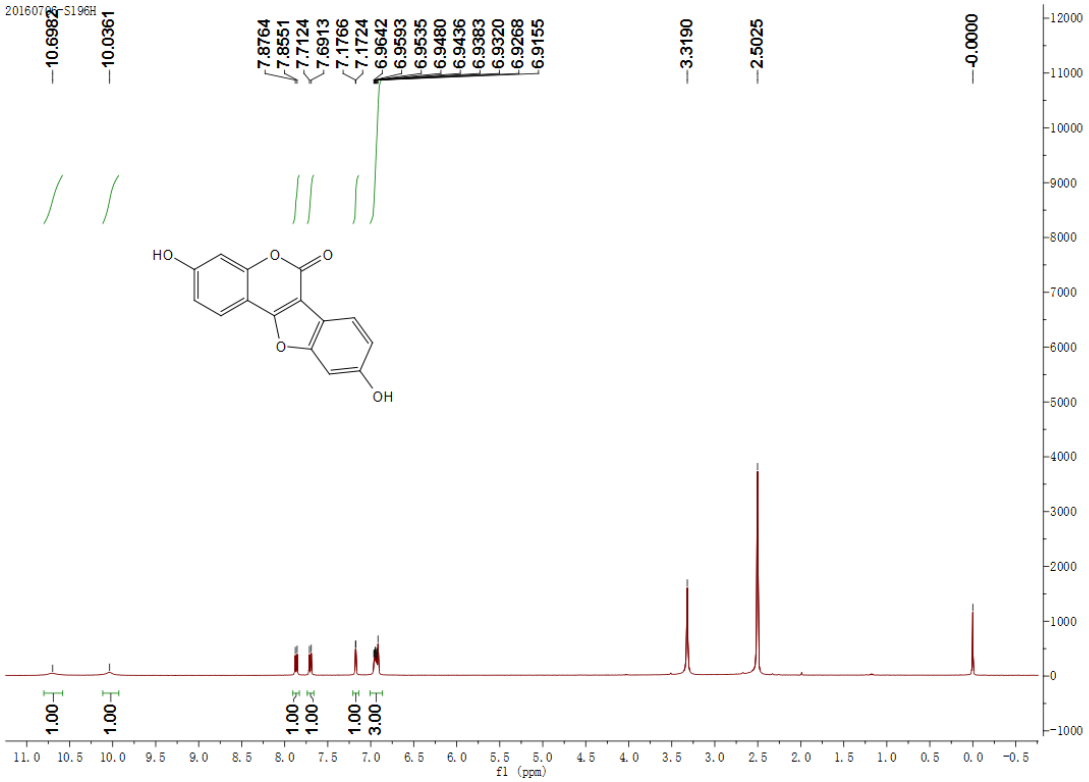


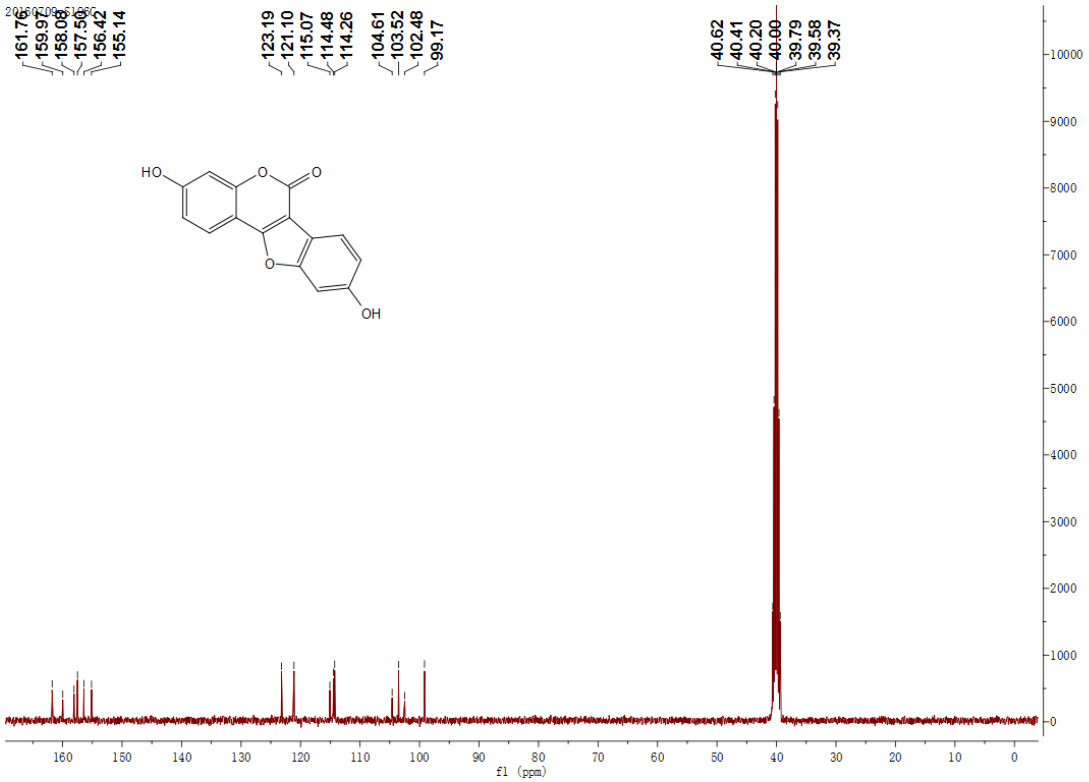
^{1}H- and ^{13}C-NMR spectra of 1r



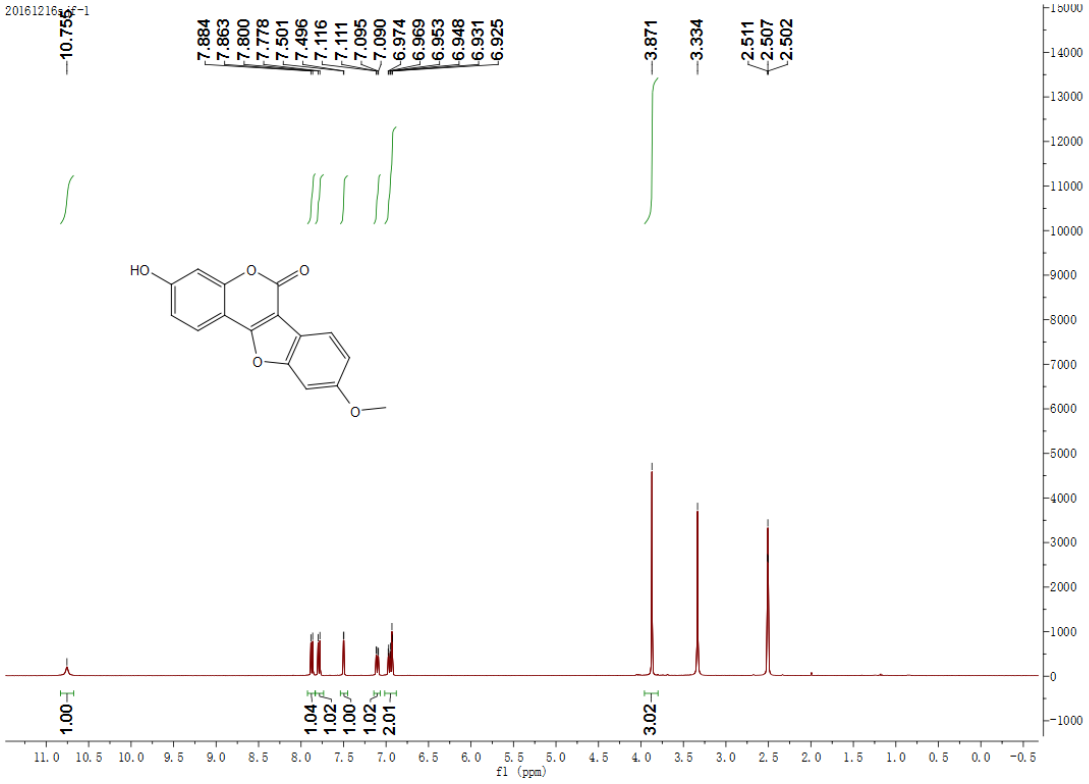


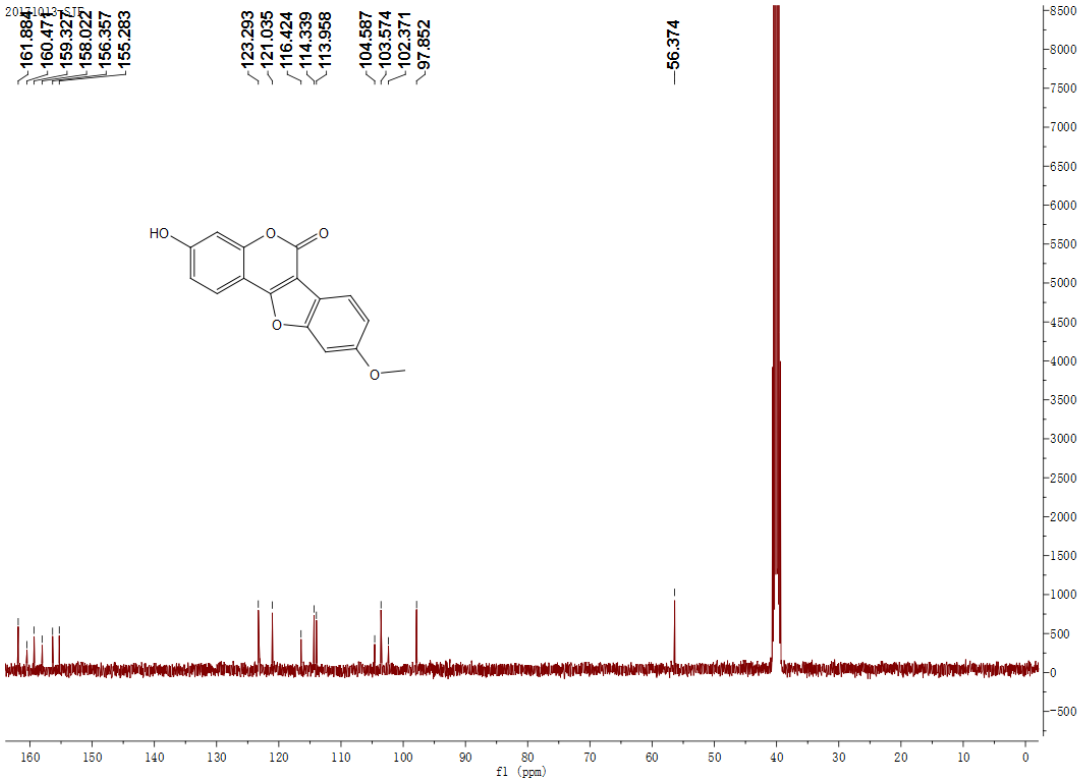
^{1}H- and ^{13}C-NMR spectra of 1s



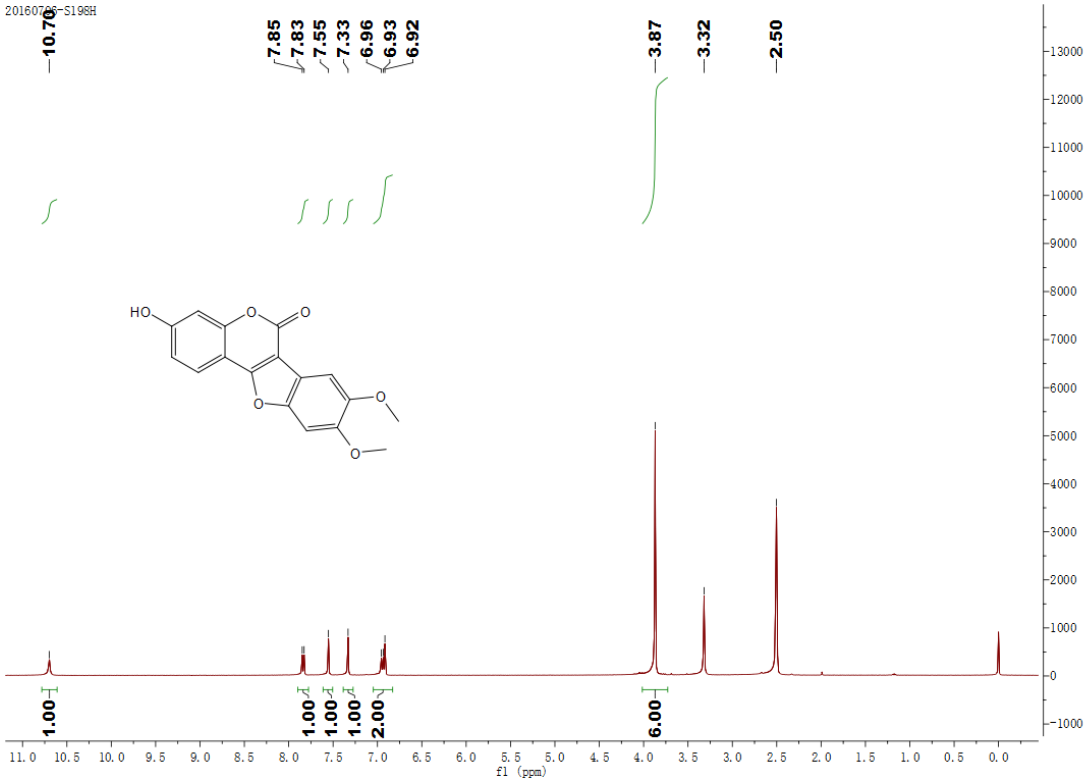


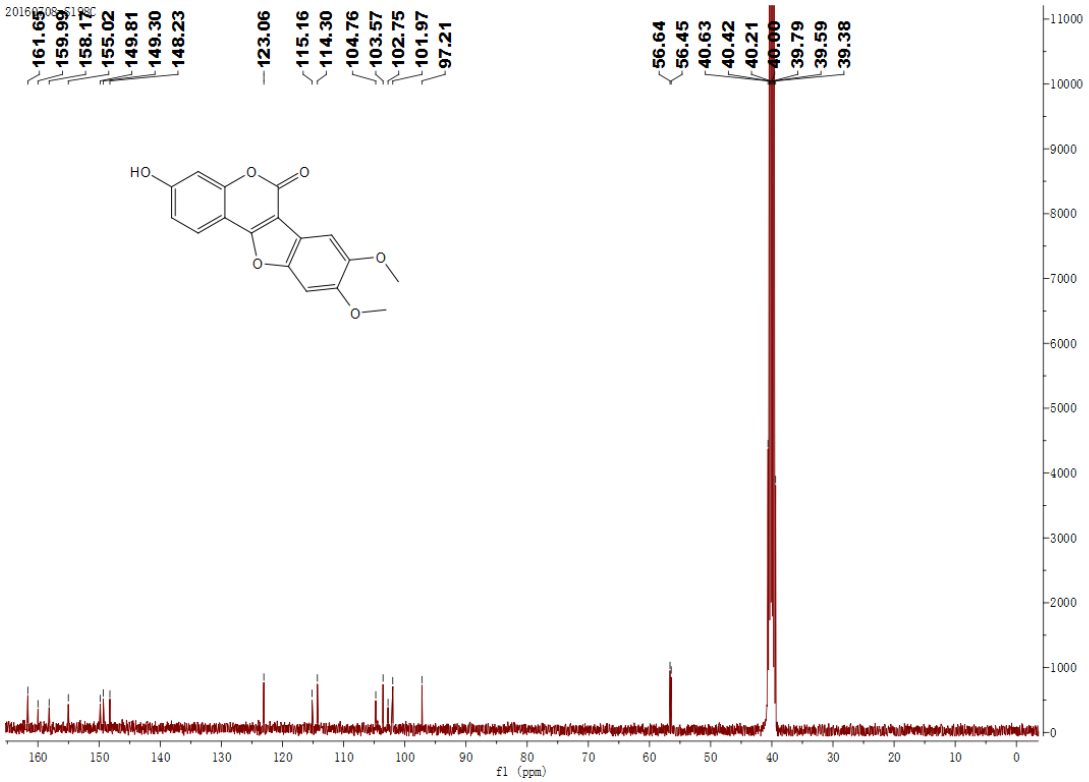
^{1}H- and ^{13}C-NMR spectra of 1t



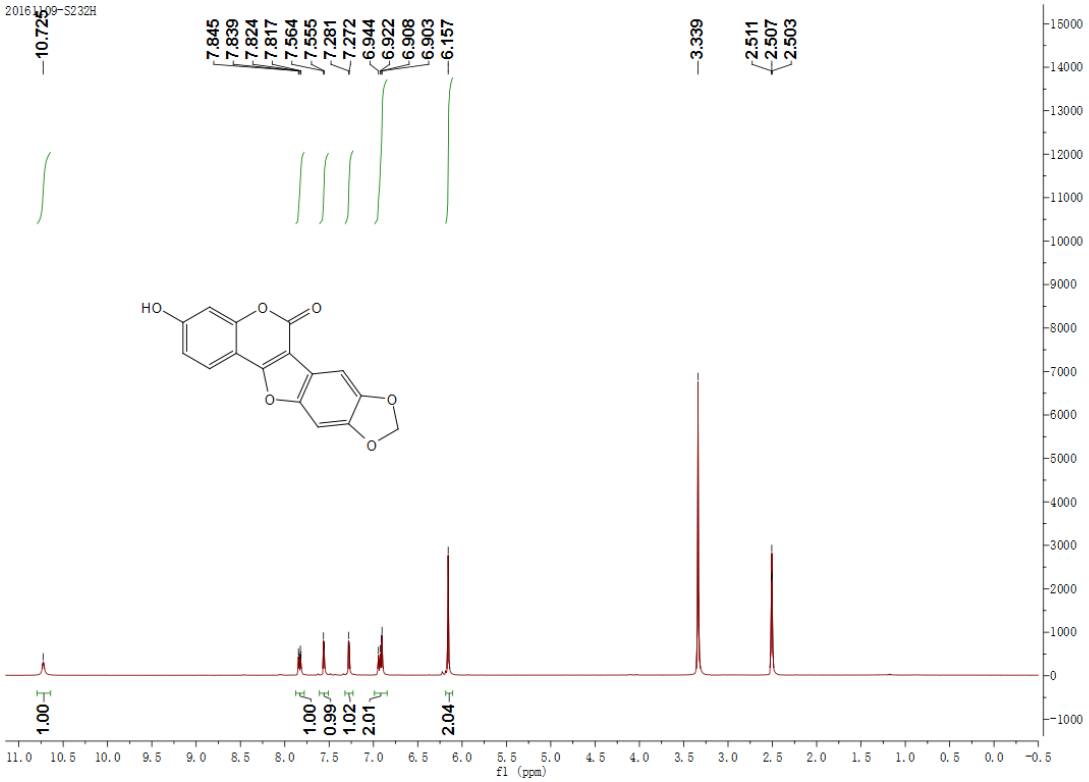


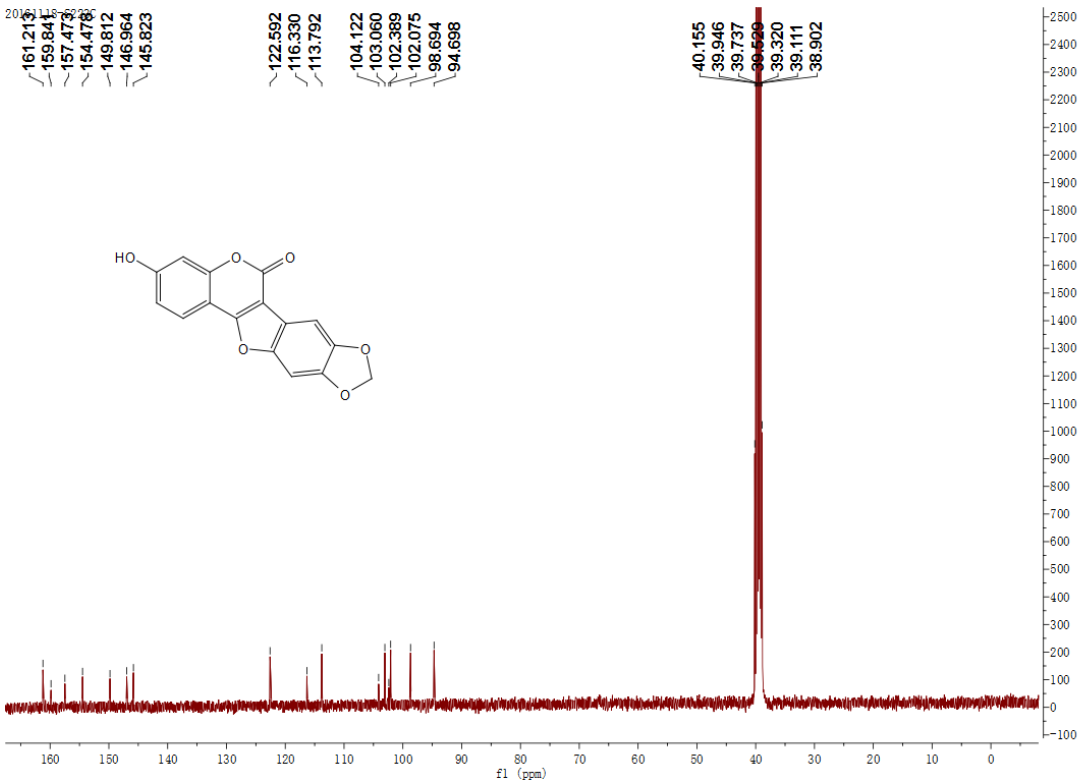
^{1}H- and ^{13}C-NMR spectra of 1u



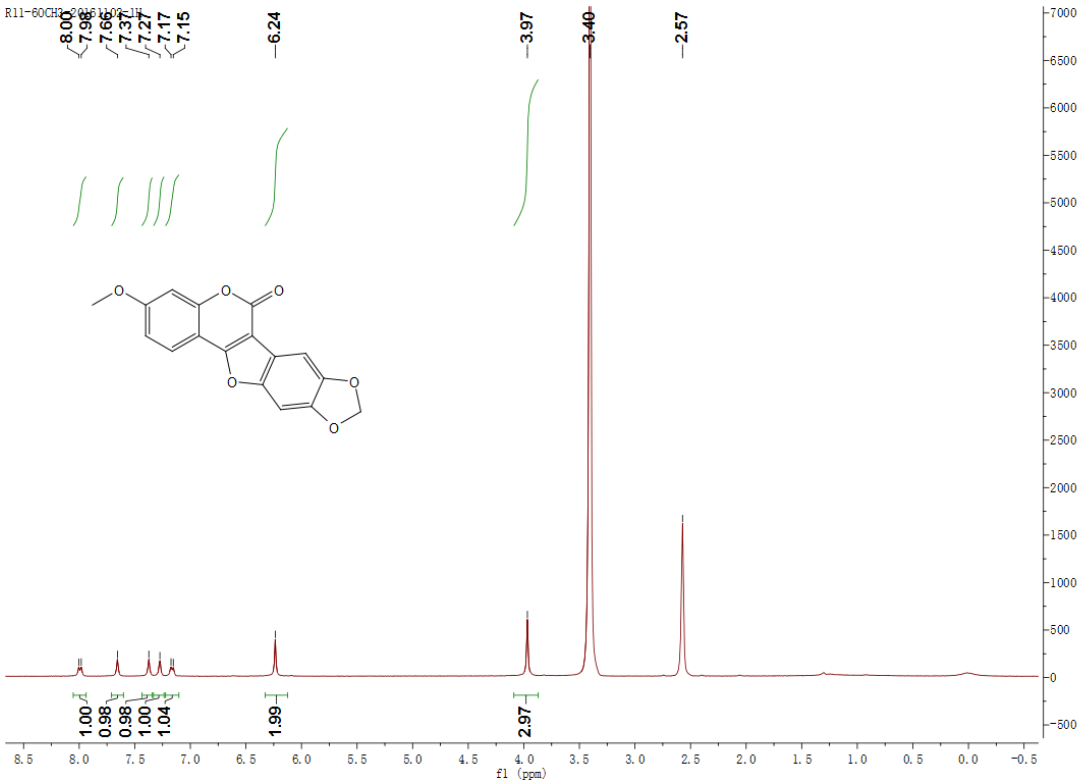


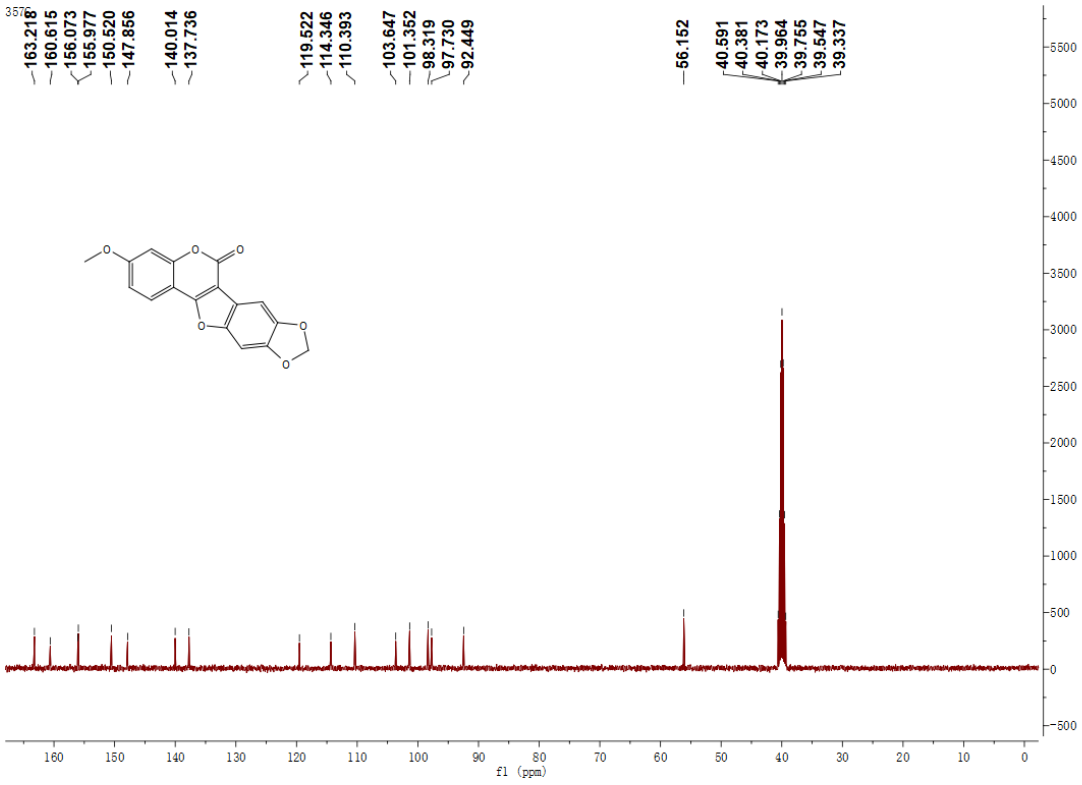
^{1}H- and ^{13}C-NMR spectra of 1v



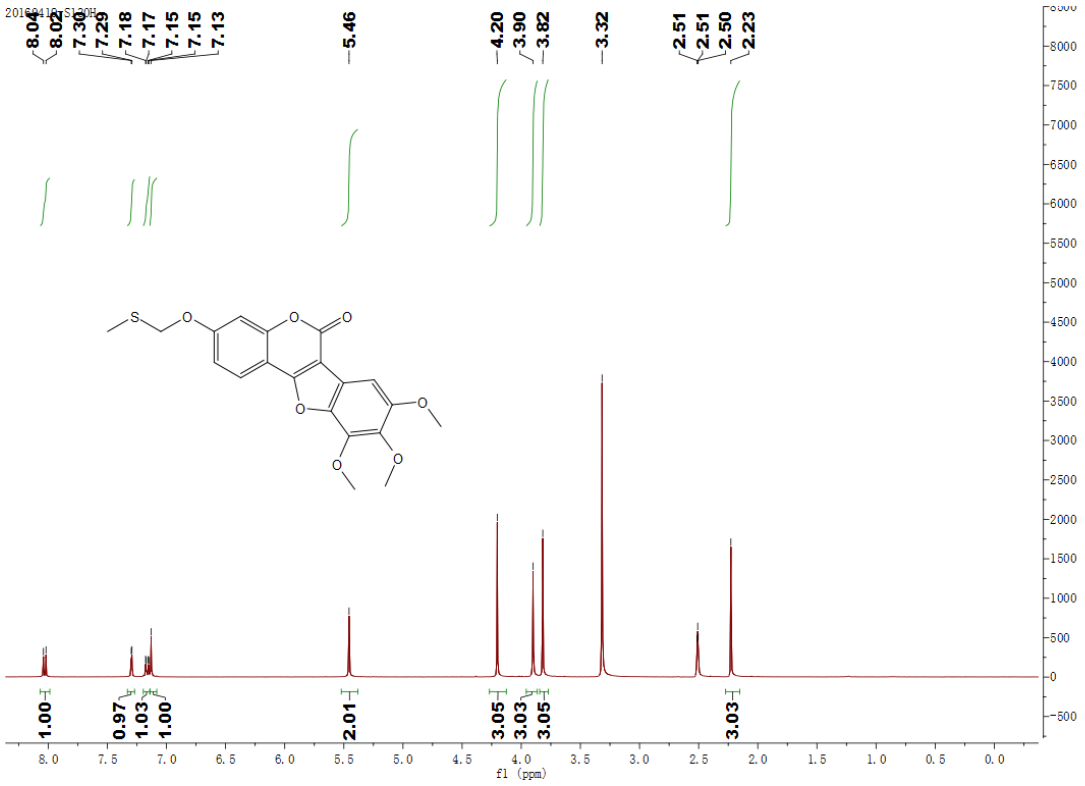


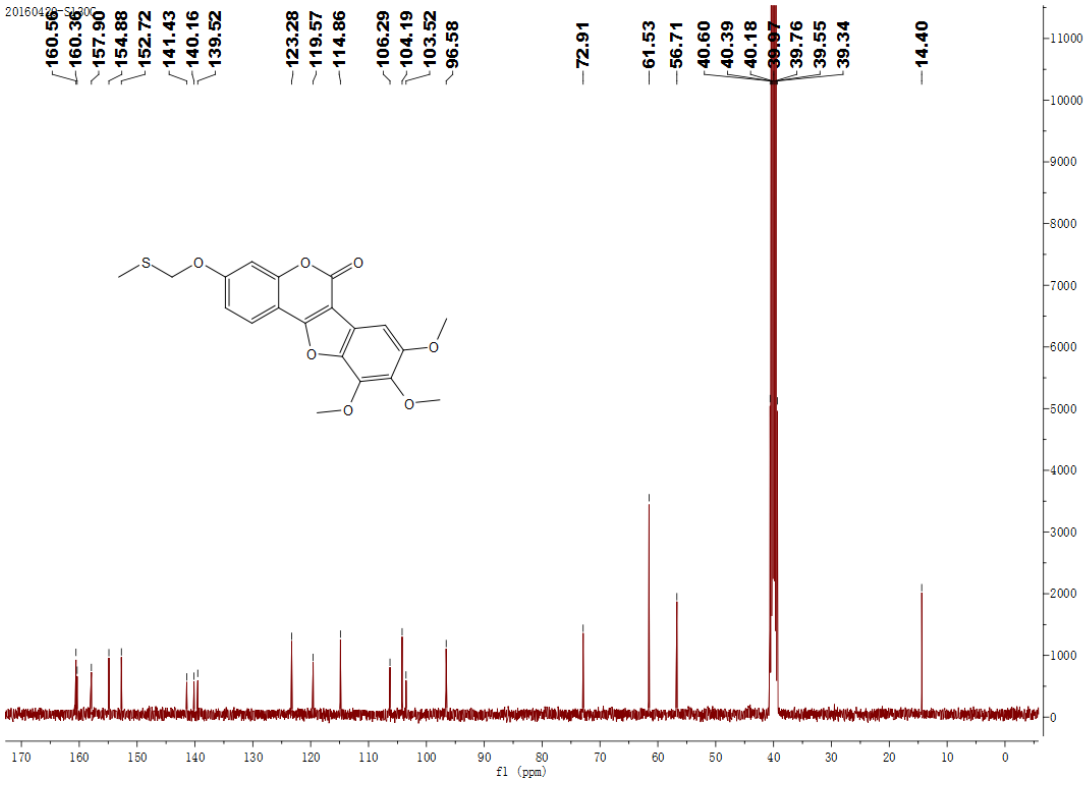
^{1}H- and ^{13}C-NMR spectra of 1w





^{1}H- and ^{13}C-NMR spectra of 1jj





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