Electronic Supplementary Material (ESI) for RSC Advances.

Design, Synthesis and Bioactivity of Myricetin Derivatives for Control of Fungal Disease and Tobacco Mosaic virus Disease

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Contents

1. Abbreviation

	Abbreviation	Full-name
1	^{1}H NMR	^{1}H nuclear magnetic resonance
2	^{13}C NMR	^{13}C nuclear magnetic resonance
3	^{19}F NMR	^{19}F nuclear magnetic resonance
4	HRMS	High-resolution mass spectroscopy
5	*Rs*	*Rhizoctonia solani*
6	*Bc*	*Botrytis cinerea*
7	*Pc*[1]	*Phytophthora capsici*
8	*Ss*	*Sclerotinia sclerotiorum*
9	*Fg*	*Fusarium graminearum*
10	*Psp*	*Phomopsis sp*
11	*Cc*	*Colletotrichum capsici*
12	*Bd*	*Botryosphaeria dothidea*
13	*Cg*	*Colletotrichum gloeosporioides*
14	*Pc*[2]	*Plectosphaerella cucumerina*
15	*Fe*	*Fusarium equiseti*
16	*Fd*	*Fusarium dimerum*
17	DMSO	Dimethylsulfoxide
18	DMF	*N*,*N*-dimethylformamide
19	NCS	*N*-Chlorosuccinimide
20	TLC	Thin Layer Chromatography
21	m.p.	Melting point
22	EC_{50}	Median effective concentration
23	PDA	Potato dextrose agar
24	PDB	Potato Dextrose Broth
25	Azo	Azoxystrobin
26	Krm	Kresoxim-methyl
27	MST	Microscale thermophoresis

2. Chemical synthesis

2.1 General Procedures for Preparing Intermediates 1-4

First, various substituted aldehydes (5 mmol), $NH_2OH·HCl$ (5 mmol), EtOH (10 mL) and distilled water (10 mL) were added to a 50 mL round bottom flask, mixed well, adjusted the pH to neutral with 5% NaOH solution, stirred for at room temperature 3 h, extracted with DCM, dried the solvent to obtain **intermediate 1**; Secondly, the **intermediate 1** (5 mmol), DMF (10 mL) were mixed evenly, added NCS (5.5 mmol) in batches, reacted for 4h at room temperature, extracted with ethyl acetate, dried the solvent to obtain **intermediate 2**. Then, saturated sodium bicarbonate solution (6 mL) was added to a mixture containing **intermediate 2** (3 mmol), 3-bromopropyne (7.5 mmol) and DCM (20 mL), reacted at room temperature for 24 h, the organic layer was washed with water, and the solvent was dried to obtain **intermediate 3**. Finally, myricitrin (30 mmol), crystalline K_2CO_3 (390 mmol), DMF (240 mL) were stirred at room temperature for 5 min, CH_3I (30 mL) was added, and the reaction was continued for 48 h before filtration. After drying the solvent, absolute ethanol (300 mL) was added for reflux for 2 h, followed by concentrated hydrochloric acid (30 mL) for another 3 h. After cooling, filtration is carried out to obtain **intermediate 4**.

2.2 General Procedures for Preparing Target Compounds Y1-Y28

Intermediate 4 (0.9 mmol), **intermediate 3** (1.35 mmol), anhydrous K_2CO_3 (1.8 mmol) and DMF (10 mL) were stirred at 60 °C. The reaction was monitored by TLC. After the reaction stopped, the target compounds **Y1**-**Y28** were obtained by DCM extraction and recrystallization of methanol.

3. Biological activities tests

3.1 In Vitro Antifungal Assay

Firstly, the tested fungi were cultured in potato glucose agar(PDA) to form new mycelia. The target compounds **Y1-Y28** dissolved with dimethyl sulfoxide(DMSO) were added to the PDA solution and the final mixture was concentrated at 100 μg/mL. The fungus cake with a diameter of 5 mm was placed in the center of PDA and cultured at 28 ℃. DMSO was used as the blank control and azoxystrobin and Kresoxim-methyl were used as positive controls. Repeat three times for each sample. The cross-sectional method was used to measure the diameter of fungal mycelia, and the formula of *in vitro* inhibition rate of fungi was as follows:

$$I\ (\%) = [(C - T)/(C - 5)] \times 100\%$$

C represents the mycelium diameter of the blank control group

T represents the mycelium diameter of the drug group,

I represents the inhibition rate.

3.2 In vivo Antiviral activity

There are 3 modes of anti-TMV activity *in vivo*, namely curative, protective and inactivating activity. 2 mg of each target compound was dissolved in 30 μL DMSO and then 4mL of 1% Tween 80 was added for a final concentration of approximately 500 μg/mL. The 1% Tween 80 solution

containing DMSO was used as the blank control, and the commercial antiviral agent ningnanmycin was used as the positive control.

Curative activity

Select the heart leaf tobacco with consistent growth, discard the top and retain 3-5 leaves. Rub the TMV on the leaves sprinkled with emery with a brush, and rinse it after 30min. After being dried, the right half of the leaves were coated with a solution containing medicine with a brush, and the left half of the leaves were coated with a blank control solution. Then they were cultured in a greenhouse at 28 ℃. Record the number of the spot after the withered spot is complete.

Protective activity

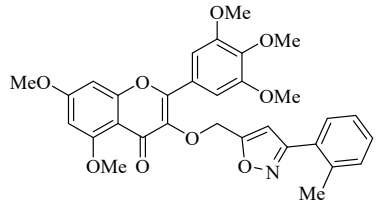
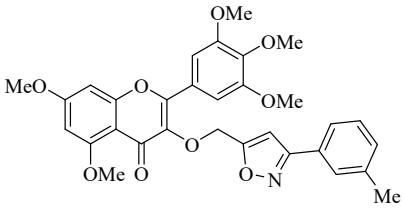
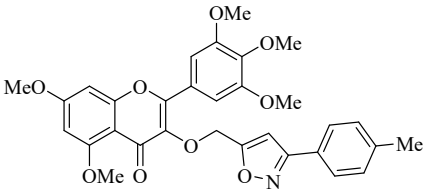
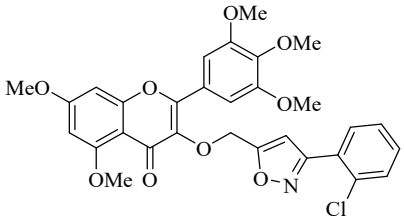
Select the heart leaf tobacco with consistent growth, discard the top and retain 3-5 leaves. The right half of the leaf is applied with a brush to the solution containing medicine, and the left half of the leaf is applied with blank control solution. After 12 hours, rub the TMV on the leaves sprinkled with carborundum with a pen, rinse it after 30 minutes, and then cultivate it in a greenhouse at 28 ℃. Record the number of dead spots after the spots are completely formed.

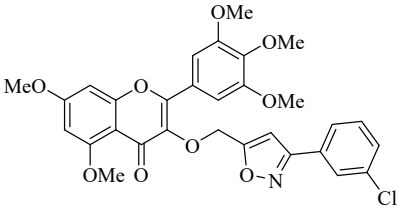
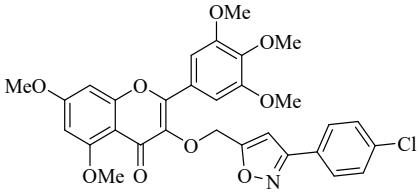
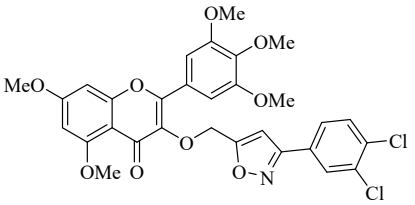
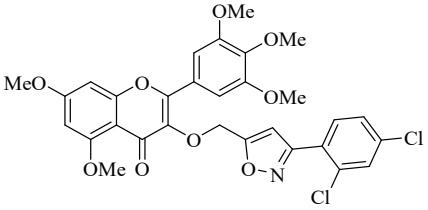
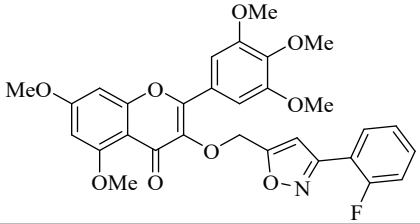
Inactivating activity

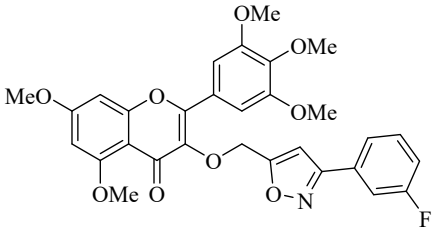
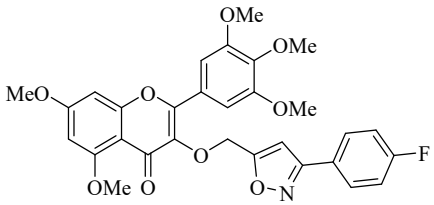
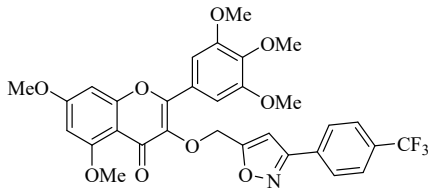
Select the heart leaf tobacco with consistent growth, discard the top and retain 3-5 leaves. Mix the medicine and TMV solution with the same volume for inactivation for 30 min, rub the mixture on the right half leaf sprinkled with emery with a brush, and rub the mixture of ningnanmycin and TMV with the same volume on the left half leaf sprinkled with emery. After 30min, wash it clean, and then cultivate it in the greenhouse at 28 ℃. Record the number of the spot after the withered spot is complete.

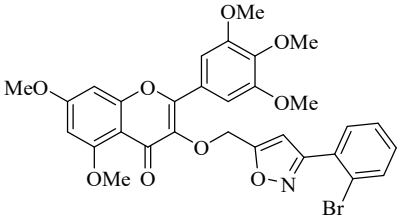
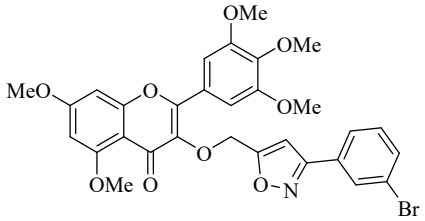
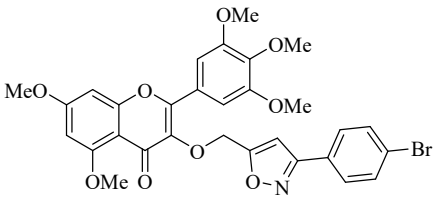
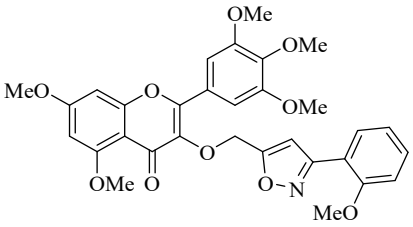
4. Spectral data of compounds Y1-Y28

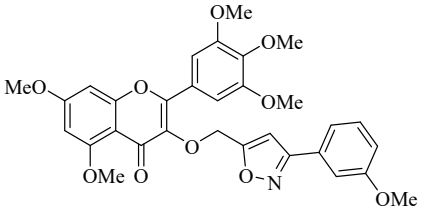
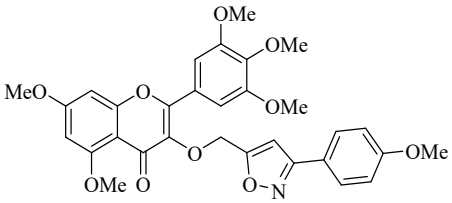
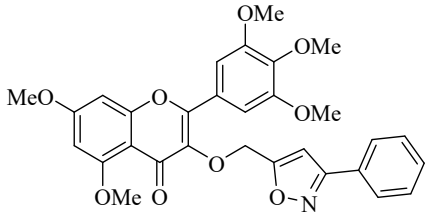
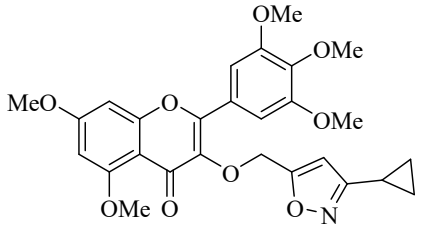
4.1 ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectrum of the target compounds

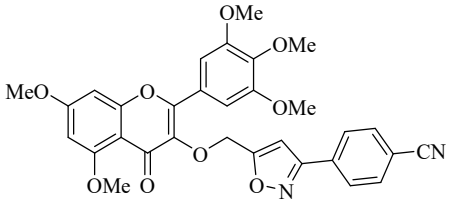
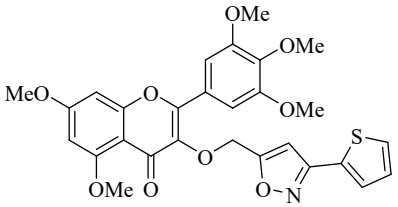
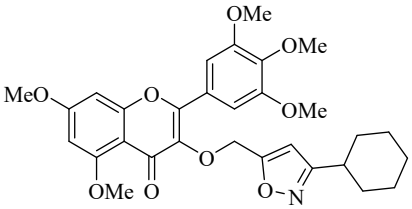
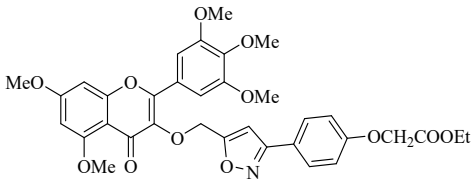
	Physical and chemical data
 5,7-dimethoxy-3-((3-(o-tolyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y1**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.37 (dd, J = 7.6, 1.5 Hz, 1H, Ph-H), 7.32 (s, 2H, Ph-H), 7.30 – 7.22 (m, 3H, Ph-H), 6.52 (d, J = 2.2 Hz, 1H, Ph-H), 6.43 (s, 1H, Ph-H, Isoxazole-H), 6.39 (d, J = 2.2 Hz, 1H), 5.35 (s, 2H, -O-CH2-), 3.99 (s, 3H, Ph-OCH3), 3.92 (d, J = 3.2 Hz, 9H, Ph-OCH3), 3.89 (s, 3H, Ph-OCH3), 2.37 (s, 3H, Ph-CH3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.70, 167.34, 164.25, 162.95, 161.03, 158.83, 153.42, 152.98, 140.17, 139.14, 136.80, 131.04, 129.53, 129.36, 128.46, 125.99, 125.46, 109.24, 106.01, 105.18, 96.08, 92.53, 63.35, 60.96, 56.49, 56.33, 55.90, 20.97. **HRMS (ESI)** calcd for $C_{31}H_{29}NO_9$ [M+H]+: 560.19151, found 560.19116. White solid, m.p. 111.2-112.7 °C, yield 85%.
 5,7-dimethoxy-3-((3-(m-tolyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y2**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.54 (s, 1H, Ph-H), 7.48 (d, *J* = 7.6 Hz, 1H, Ph-H), 7.32 (t, *J* = 7.6 Hz, 1H, Ph-H), 7.26 (s, 2H, Ph-H), 7.24 (d, *J* = 7.5 Hz, 1H, Ph-H), 6.53 (s, 1H, Isoxazole-H), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.32 (s, 2H -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.88 (s, 9H, Ph-OCH_3), 2.40 (s, 3H, Ph-CH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.72, 168.20, 164.26, 162.46, 161.04, 158.87, 153.64, 152.97, 140.12, 139.08, 138.69, 130.83, 128.81, 128.62, 127.34, 125.49, 123.87, 109.27, 106.03, 102.65, 96.09, 92.55, 63.45, 60.94, 56.50, 56.29, 55.90, 21.37. **HRMS** (ESI) calcd for $C_{31}H_{29}NO_9$ [M+H]$^{+}$: 560.19151, found 560.19092. White solid, m.p. 101.3-102.9 °C, yield 95%.
 5,7-dimethoxy-3-((3-(p-tolyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y3**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.60 (s, 1H, Ph-H), 7.58 (s, 1H, Ph-H), 7.27 (s, 2H, Ph-H), 7.24 (s, 1H, Ph-H), 7.22 (s, 1H, Ph-H), 6.52 – 6.50 (m, 2H, Ph-H ; Isoxazole-H), 6.38 (d, *J* = 2.2 Hz, 1H Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 3.99 (s, 3H, Ph-OCH_3), 3.91 (s, 3H, Ph-OCH_3), 3.88 (d, *J* = 2.6 Hz, 9H, Ph-OCH_3), 2.39 (s, 3H, Ph-CH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.71, 168.14, 164.24, 162.30, 161.03, 158.85, 153.58, 152.97, 140.21, 140.11, 139.11, 129.60, 126.69, 126.62, 125.91, 125.51, 109.26, 106.02, 102.50, 99.84, 96.08, 92.54, 63.46, 60.96, 56.67, 56.49, 56.30, 55.89, 21.44. **HRMS** (ESI) calcd for $C_{31}H_{29}NO_9$ [M+H]$^{+}$: 560.19151, found 560.19110. White solid, m.p. 168.7-170.4 °C, yield 93%.
 3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y4**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.63 (dd, J = 7.4, 2.1 Hz, 1H, Ph-H), 7.45 (dd, J = 7.6, 1.7 Hz, 1H, Ph-H), 7.39 – 7.33 (m, 2H, Ph-H), 7.30 (s, 2H, Ph-H), 6.71 (s, 1H, Isoxazole-H), 6.52 (d, J = 2.2 Hz, 1H, Ph-H), 6.39 (d, J = 2.3 Hz, 1H, Ph-H), 5.37 (s, 2H, -O-CH2-), 3.99 (s, 3H, Ph-OMe), 3.92 (s, 3H, Ph-OMe), 3.90 (d, J = 3.3 Hz, 9H, Ph-OMe); **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.68, 167.47, 164.24, 161.03, 160.93, 158.84, 153.49, 152.95, 140.15, 139.07, 132.83, 130.93, 130.89, 130.38, 128.04, 127.10, 125.42, 109.25, 106.02, 105.85, 96.07, 92.51, 63.34, 60.97, 56.49, 56.32, 55.89; **HRMS** (ESI) calcd for $C_{30}H_{26}ClNO_9$ [M+H]+: 580.13689, found 580.13654. White solid, m.p. 163.4-165.3 °C, yield 87%.

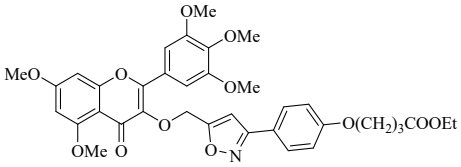
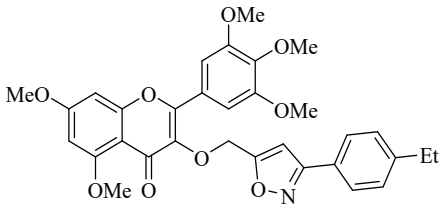
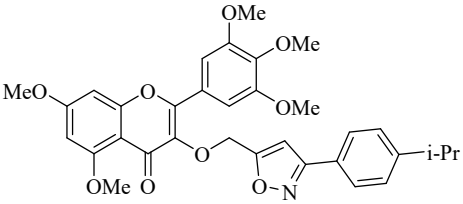
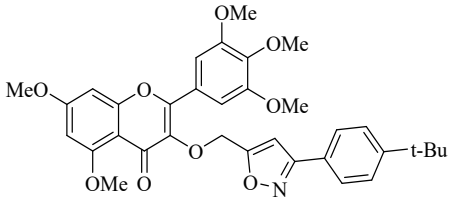
 3-((3-(3-chlorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y5**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.71 (t, *J* = 1.8 Hz, 1H, Ph-H), 7.59 (dt, *J* = 7.2, 1.6 Hz, 1H, Ph-H), 7.43 – 7.37 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 6.54 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.40 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.32 (s, 2H,-O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H Ph-OCH_3), 3.89 (s, 9H Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.64, 168.78, 164.27, 161.23, 161.03, 158.86, 153.64, 152.96, 140.14, 139.01, 134.92, 130.50, 130.22, 130.07, 126.80, 125.42, 124.85, 109.24, 106.00, 102.46, 96.10, 92.54, 63.36, 60.95, 56.49, 56.28, 55.88. **HRMS** (ESI) calcd for $C_{30}H_{26}ClNO_9$ $[M+H]^+$: 580.13689, found 580.13660. White solid, m.p. 196.2-197.4 °C, yield 52%.
 3-((3-(4-chlorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y6**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.67 – 7.63 (m, 2H, Ph-H), 7.43 – 7.40 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 6.54 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.31 (s, 2H,-O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-H, Ph-OCH_3), 3.89 (d, *J* = 4.2 Hz, 9H, Ph-H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.75, 168.77, 164.36, 161.47, 161.11, 158.94, 153.70, 153.06, 140.22, 139.15, 136.16, 129.28, 128.08, 127.33, 125.53, 109.32, 106.09, 102.49, 96.19, 92.63, 63.50, 61.05, 56.59, 56.38, 55.98. **HRMS** (ESI) calcd for $C_{30}H_{26}ClNO_9$ $[M+H]^+$: 580.13689, found 580.13684. White solid, m.p. 195.7-197.2 °C, yield 80%.
 3-((3-(3,4-dichlorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y7**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.82 (d, *J* = 1.8 Hz, 1H, Ph-H), 7.57 – 7.50 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 6.55 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.40 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.31 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.90 (d, *J* = 3.1 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.64, 169.12, 164.31, 161.04, 160.49, 158.87, 153.61, 153.00, 140.19, 139.06, 134.24, 133.31, 131.00, 128.75, 128.57, 125.89, 125.42, 109.24, 106.02, 102.36, 96.13, 92.57, 63.40, 60.98, 56.52, 56.31, 55.91. **HRMS** (ESI) calcd for $C_{30}H_{25}Cl_2NO_9$ $[M+H]^+$: 614.09791, found 614.09772. White solid, m.p. 176.8-178.3 °C, yield 93%.
 3-((3-(2,4-dichlorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4H-chromen-4-one (**Y8**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.56 (d, *J* = 8.4 Hz, 1H, Ph-H), 7.45 (d, *J* = 2.1 Hz, 1H, Ph-H), 7.30 (dd, *J* = 8.3, 2.1 Hz, 1H, Ph-H), 7.27(s, 2H, Ph-H), 6.69(s, 1H, 1H, Isoxazole-H), 6.49 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.36 (d, *J* = 2.2 Hz,1H, Ph-H), 5.32(s, 2H, -O-$\underline{CH_2}$-), 3.97 (s, 3H, Ph-OCH_3), 3.90 (s, 3H, Ph-OCH_3), 3.88 (d, *J* = 1.7 Hz, 9H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.75, 167.89, 164.34, 161.08, 160.17, 158.90, 153.58, 153.01, 140.16, 139.12, 136.44, 133.60, 131.72, 130.32, 127.64, 126.65, 125.46, 109.27, 106.02, 105.71, 96.16, 92.57, 63.38, 61.07, 56.57, 56.38, 55.99. **HRMS** (ESI) calcd for $C_{30}H_{25}Cl_2NO_9$ $[M+H]^+$: 614.09791, found 614.09729. White solid, m.p. 194.0-195.1 °C, yield 94%.
	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.87 (td, *J* = 7.6, 1.8 Hz,1H, Ph-H), 7.42 – 7.37 (m,1H, Ph-H), 7.24(s, 2H, Ph-H), 7.20 (td, *J* = 7.6, 1.1 Hz, 1H, Ph-H), 7.16 – 7.10 (m, 1H, Ph-H), 6.65 (d, *J* = 3.5 Hz,1H, Isoxazole-H), 6.50 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.37 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 3.98(s, 3H, Ph-OCH_3), 3.90(s, 3H, Ph-OCH_3), 3.86(s, 6H, Ph-OCH_3), 3.84(s,3H, Ph-OCH_3).

3-((3-(2-fluorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y9**)	**^{13}C NMR (126 MHz, Chloroform-d)** δ 173.74, 168.23, 164.30, 161.23, 161.11, 159.23, 158.94, 157.76, 153.69, 153.00, 140.09, 139.16, 131.84, 131.77, 129.09, 129.07, 125.54, 124.69, 124.66, 116.92, 116.83, 116.52, 116.35, 109.34, 106.00, 105.07, 105.00, 96.15, 92.59, 63.47, 60.99, 56.58, 56.33, 55.97. **^{19}F NMR (471 MHz, Chloroform-d)** δ -114.15. **HRMS** (ESI) calcd for $C_{30}H_{26}FNO_9$ [M+H]$^+$: 564.16644, found 564.16663. White solid, m.p. 178.7-180.3 °C, yield 89%.
 3-((3-(3-fluorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y10**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.48 (dt, *J* = 7.7, 1.3 Hz, 1H, Ph-H), 7.45 – 7.39 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 7.13 (tdd, *J* = 8.4, 2.6, 1.1 Hz, 1H, Ph-H), 6.54 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (d, *J* = 0.8 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.65, 168.79, 164.28, 164.18, 161.73, 161.42, 161.39, 161.04, 158.86, 153.61, 152.99, 140.15, 139.05, 130.89, 130.80, 130.64, 130.56, 125.46, 122.51, 122.48, 117.11, 116.90, 113.82, 113.59, 109.25, 106.01, 102.51, 96.11, 92.55, 63.39, 60.95, 56.51, 56.29, 55.90. **^{19}F NMR (471 MHz, Chloroform-d)** δ -111.92. **HRMS** (ESI) calcd for $C_{30}H_{26}FNO_9$ [M+H]$^+$: 564.16644, found 564.16632. White solid, m.p. 192.4-194.1 °C, yield 94%.
 3-((3-(4-fluorophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y11**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.72 – 7.68 (m, 2H, Ph-H), 7.27 (s, 2H, Ph-H), 7.13 (t, *J* = 8.7 Hz, 2H, Ph-H), 6.52 (d, *J* = 2.7 Hz, 2H, Ph-H), 6.39 (d, *J* = 2.3 Hz, Isoxazole-H), 5.31 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (d, *J* = 3.0 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.67, 168.57, 165.06, 164.28, 162.57, 161.44, 161.04, 158.86, 153.60, 152.99, 140.14, 139.09, 128.71, 128.63, 125.48, 125.02, 124.99, 116.16, 115.94, 109.25, 106.03, 102.41, 96.11, 92.55, 63.43, 60.96, 56.51, 56.30, 55.90. **^{19}F NMR (376 MHz, Chloroform-d)** δ -110.45. **HRMS** (ESI) calcd for $C_{30}H_{26}FNO_9$ [M+H]$^+$: 564.16644, found 564.16626. White solid, m.p. 162.9-164.0 °C, yield 92%
 5,7-dimethoxy-3-((3-(4-(trifluoromethyl)phenyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y12**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.84 (d, *J* = 8.0 Hz, 2H, Ph-H), 7.70 (d, *J* = 7.9 Hz, 2H, Ph-H), 7.27 (s, 2H, Ph-H), 6.62 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.40 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.33 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (d, *J* = 4.3 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.65, 169.08, 164.32, 161.23, 161.03, 158.86, 153.60, 153.00, 140.18, 139.07, 132.23, 132.03, 131.70, 127.10, 127.07, 125.99, 125.95, 125.91, 125.87, 125.43, 125.18, 122.48, 109.22, 106.02, 102.55, 96.13, 92.56, 63.42, 60.96, 56.51, 56.29, 55.90. **^{19}F NMR (376 MHz, Chloroform-d)** δ -62.86. **HRMS** (ESI) calcd for $C_{31}H_{26}F_3NO_9$ [M+H]$^+$: 614.16324, found 614.16293. White solid, m.p. 172.3-173.9 °C, yield 94%.

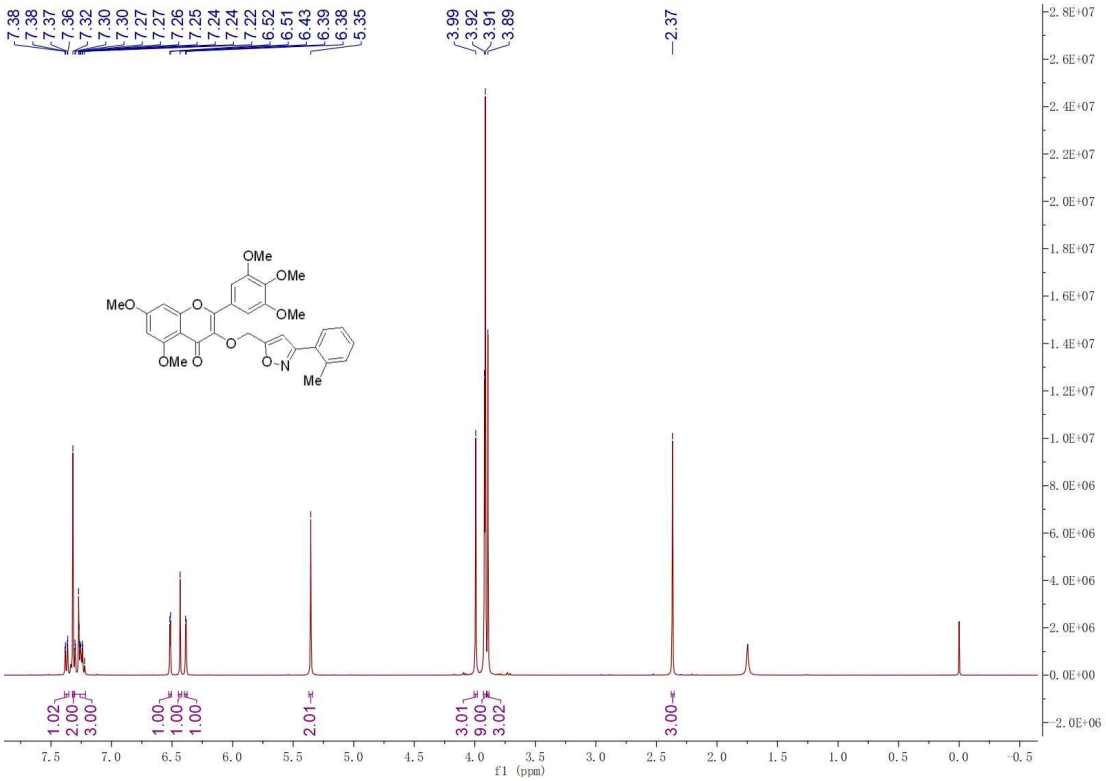
 3-((3-(2-bromophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y13**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.62 (dd, *J* = 8.2, 1.3 Hz, 1H, Ph-H), 7.50 (dd, *J* = 7.6, 1.7 Hz, 1H, Ph-H), 7.35 (td, *J* = 7.5, 1.2 Hz, 1H, Ph-H), 7.29(s, 2H, Ph-H), 7.25(d, 2H, Ph-H), 6.66 (s, 1H, Isoxazole-H), 6.49 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.37 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.36(s, 2H, -O-$\underline{CH_2}$-), 3.97(s, 3H, Ph-OCH_3), 3.90(s, 3H, Ph-OCH_3), 3.89(s, 6H, Ph-OCH_3), 3.88(s, 3H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.76, 167.31, 164.31, 162.38, 161.11, 158.91, 153.56, 153.02, 140.21, 139.07, 133.64, 131.34, 131.12, 130.25, 127.69, 125.50, 122.25, 109.33, 106.09, 96.14, 92.56, 63.31, 61.07, 56.57, 56.42, 55.97. **HRMS** (ESI) calcd for $C_{30}H_{26}BrNO_9$ $[M+H]^+$: 624.08637, found 624.08691. White solid, m.p. 164.5-166.1 °C, yield 93%.
 3-((3-(3-bromophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y14**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.87 (t, *J* = 1.8 Hz, 1H, Ph-H), 7.65 – 7.61 (m, 1H, Ph-H), 7.56 (ddd, *J* = 8.0, 2.0, 1.1 Hz, 1H, Ph-H), 7.31 (t, *J* = 7.9 Hz, 1H, Ph-H), 7.25 (s, 2H, Ph-H), 6.54 (s, 1H, Isoxazole-H), 6.52 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.31 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (s, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.66, 168.79, 164.29, 161.13, 161.03, 158.87, 153.68, 152.98, 140.15, 139.02, 133.02, 130.75, 130.49, 129.69, 125.43, 125.32, 123.00, 109.25, 106.01, 102.48, 96.12, 92.57, 63.38, 60.98, 56.51, 56.31, 55.90. **HRMS** (ESI) calcd for $C_{30}H_{26}BrNO_9$ $[M+H]^+$: 624.08637, found 624.08618. White solid, m.p. 188.6-190.0 °C, yield 91%.
 3-((3-(4-bromophenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y15**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.45 (dt, *J* = 7.6, 1.3 Hz, 1H, Ph-H), 7.42 – 7.37 (m, 2H, Ph-H), 7.23 (s, 2H, Ph-H), 7.13 – 7.09 (m, 1H, Ph-H), 6.51(s, 1H, Isoxazole-H), 6.49 (d, *J* = 2.1 Hz, 1H, Ph-H), 6.37 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.29 (s, 2H, -O-$\underline{CH_2}$-), 3.98(s, 3H, Ph-OCH_3), 3.90(s, 3H, Ph-OCH_3), 3.86(s, 9H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.74, 168.83, 164.35, 164.00, 162.03, 161.47, 161.09, 158.94, 153.72, 153.04, 140.15, 139.10, 130.92, 130.85, 130.72, 130.65, 125.53, 122.58, 122.55, 117.18, 117.01, 113.86, 113.68, 109.31, 106.02, 102.61, 96.19, 92.61, 63.45, 61.03, 56.59, 56.35, 55.98. **HRMS** (ESI) calcd for $C_{30}H_{26}BrNO_9$ $[M+H]^+$: 624.08637, found 624.08600. White solid, m.p. 184.0-185.5 °C, yield 95%.
 5,7-dimethoxy-3-((3-(2-methoxyphenyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y16**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.79 (dd, *J* = 7.7, 1.8 Hz, 1H, Ph-H), 7.40 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H, Ph-H), 7.30 (s, 2H, Ph-H), 7.03 – 6.96 (m, 2H, Ph-H), 6.78 (s, 1H, Isoxazole-H), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.38 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.35 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (d, *J* = 1.3 Hz, 9H, Ph-OCH_3), 3.85 (s, 3H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.76, 166.83, 164.18, 161.04, 159.97, 158.83, 157.15, 153.40, 152.94, 140.09, 139.16, 131.26, 129.36, 125.51, 120.86, 117.68, 111.33, 109.29, 106.23, 105.99, 96.03, 92.50, 63.37, 60.95, 56.49, 56.30, 55.89, 55.46. **HRMS** (ESI) calcd for $C_{31}H_{29}NO_{10}$ $[M+H]^+$: 576.18642, found 576.18628. White solid, m.p. 177.6-178.0 °C, yield 81%.

 5,7-dimethoxy-3-((3-(3-methoxyphenyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one（**Y17**）	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.32 (td, *J* = 8.0, 1.2 Hz, 1H, Ph-H), 7.26 (dt, *J* = 2.6, 1.3 Hz, 1H, Ph-H), 7.24 (d, *J* = 1.1 Hz, 2H, Ph-H), 6.95 (ddd, *J* = 8.3, 2.7, 1.3 Hz, 1H, Ph-H), 6.52(s, 1H, Isoxazole-H), 6.49 (t, *J* = 2.0 Hz, 1H, Ph-H), 6.37 (t, *J* = 2.2 Hz, 1H, Ph-H), 5.30(s, 2H, -O-$\underline{CH_2}$-), 3.98 (d, *J* = 2.0 Hz, 3H, Ph-OCH_3), 3.90 (d, *J* = 1.5 Hz, 3H, Ph-OCH_3), 3.86 (t, *J* = 1.7 Hz, 6H, Ph-OCH_3), 3.83 (d, *J* = 1.3 Hz, 3H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.75, 168.40, 164.31, 162.34, 161.11, 160.00, 158.94, 153.68, 153.04, 140.17, 139.12, 130.08, 130.04, 125.56, 119.31, 116.34, 111.56, 109.35, 106.06, 102.79, 96.17, 92.61, 63.46, 61.02, 56.59, 56.36, 55.97, 55.48. **HRMS** (ESI) calcd for $C_{31}H_{29}NO_{10}$ [M+H]$^+$: 576.18642, found 576.18640. White solid, m.p. 149.5-151.2 °C, yield 80%.
 5,7-dimethoxy-3-((3-(4-methoxyphenyl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one（**Y18**）	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.32 (t, *J* = 7.9 Hz, 1H, Ph-H), 7.26 (t, *J* = 2.0 Hz, 1H, Ph-H), 7.24(s, 2H, Ph-H), 7.23 – 7.21 (m, 1H, Ph-H), 6.95 (dd, *J* = 8.0, 2.6 Hz, 1H, Ph-H), 6.52(s, 1H, Isoxazole-H), 6.49 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.37 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.30(s, 2H, -O-$\underline{CH_2}$-), 3.98(s, 3H, Ph-OCH_3), 3.90(s, 3H, Ph-OCH_3), 3.86 (d, *J* = 2.3 Hz, 6H, Ph-OCH_3), 3.83(s, 3H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.77, 168.39, 164.31, 162.34, 161.09, 159.98, 158.93, 153.71, 153.03, 140.12, 139.11, 130.05, 125.55, 119.31, 116.34, 111.54, 109.33, 106.02, 102.81, 96.17, 92.60, 63.45, 61.03, 56.59, 56.35, 55.98, 55.48. **HRMS** (ESI) calcd for $C_{31}H_{29}NO_{10}$ [M+H]$^+$: 576.18642, found 576.18652. White solid, m.p. 189.7-191.4 °C, yield 80%.
 5,7-dimethoxy-3-((3-phenylisoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y19**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.72 – 7.69 (m, 2H, Ph-H), 7.44 – 7.42 (m, 3H, Ph-H), 7.26 (s, 2H, Ph-H), 6.54 (s, 1H, Isoxazole-H), 6.51 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.88 (d, *J* = 1.1 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.70, 168.33, 164.26, 162.34, 161.03, 158.86, 153.65, 152.97, 140.12, 139.07, 130.08, 130.04, 128.93, 128.75, 126.80, 126.73, 125.50, 109.26, 106.03, 102.57, 96.10, 92.55, 63.43, 60.95, 56.50, 56.30, 55.90. **HRMS** (ESI) calcd for $C_{30}H_{27}NO_9$ [M+H]$^+$: 546.17586, found 546.17603. White solid, m.p. 155.9-157.7 °C, yield 77%.
 3-((3-cyclopropylisoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y20**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.28 (s, 2H, Ph-H), 6.51 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.38 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.91 (s, 1H, Isoxazole-H), 5.20 (s, 2H, -O-$\underline{CH_2}$-), 3.98 (s, 3H, Ph-OCH_3), 3.93 (s, 3H, Ph-OCH_3), 3.92 (s, 9H, Ph-OCH_3), 1.98 – 1.87 (m, 1H, -$\underline{CH}$CH2CH2-), 1.04 – 0.93 (m, 2H, -CH$\underline{CH_2}CH_2$-), 0.70 (dd, *J* = 4.8, 2.0 Hz, 2H, -CHC$H_2\underline{CH_2}$-). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.65, 167.46, 166.45, 164.22, 161.01, 158.81, 153.28, 152.96, 140.12, 139.26, 125.49, 109.24, 105.97, 101.61, 96.04, 92.51, 63.49, 60.99, 56.47, 56.33, 55.88, 8.01, 7.26. **HRMS** (ESI) calcd for $C_{27}H_{27}NO_9$ [M+H]$^+$: 510.17586, found 510.17645. White solid, m.p. 94.5-96.2 °C, yield 73%.

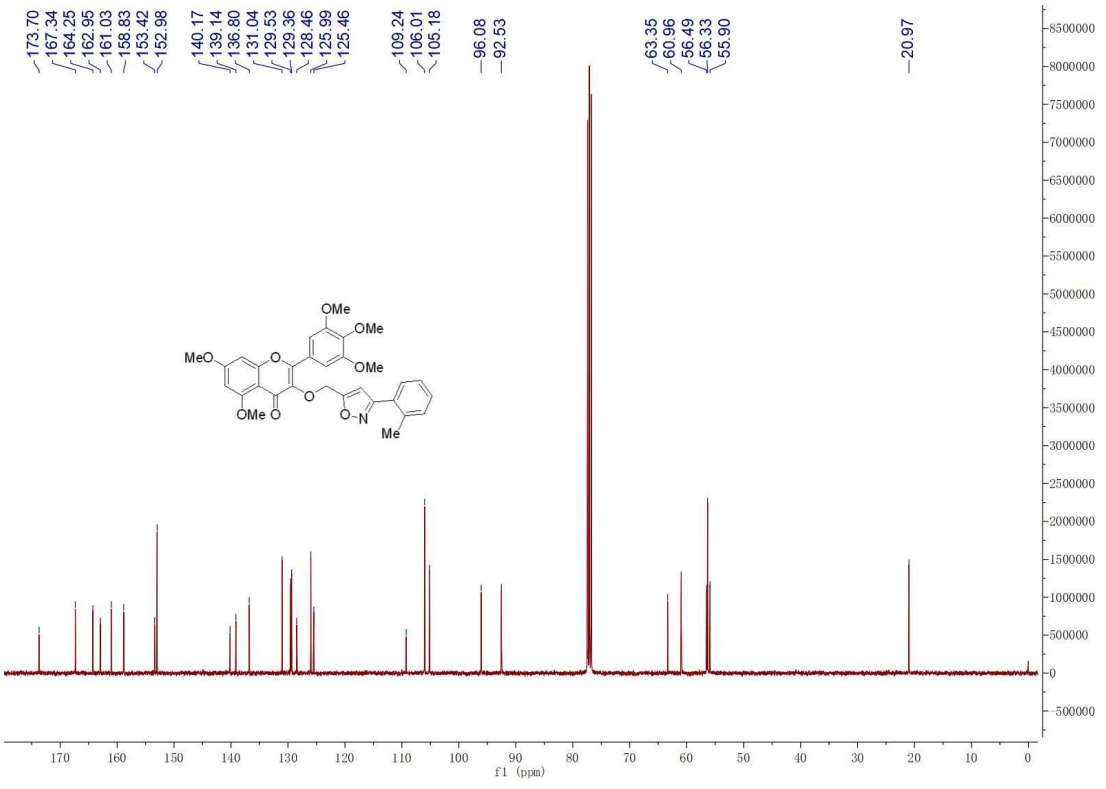
 4-(5-(((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)oxy)methyl)isoxazol-3-yl)benzonitrile (**Y21**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.81 (d, *J* = 8.5 Hz, 2H, Ph-H), 7.72 (d, *J* = 8.5 Hz, 2H, Ph-H), 7.24(s, 2H, Ph-H), 6.60 (s, 1H, Isoxazole-H), 6.50 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.37 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.29 (s, 2H, -O-$\underline{CH_2}$-), 3.98 (s, 3H, Ph-OCH_3), 3.90 (s, 3H, Ph-OCH_3), 3.87 (s, 3H, Ph-OCH_3), 3.86 (s, 6H, Ph-OCH_3). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.70, 169.49, 164.40, 161.09, 160.96, 158.94, 153.67, 153.07, 140.20, 139.14, 133.16, 132.84, 128.19, 127.39, 125.50, 118.43, 113.68, 109.28, 106.04, 102.56, 96.22, 92.63, 63.48, 61.06, 56.61, 56.37, 56.00. **HRMS** (ESI) calcd for $C_{31}H_{26}N_2O_9$ $[M+H]^+$: 571.17111, found 571.16992. White solid, m.p. 220.0-221.7 °C, yield 88%.
 5,7-dimethoxy-3-((3-(thiophen-2-yl)isoxazol-5-yl)methoxy)-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y22**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.40 (dd, *J* = 5.0, 1.2 Hz, 1H, Thiophene-H), 7.36 (dd, *J* = 3.7, 1.2 Hz, 1H, Thiophene-H), 7.25 (s, 2H, Ph-H), 7.09 (dd, *J* = 5.1, 3.7 Hz, 1H Thiophene-H), 6.52 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.48 (s, 1H, Isoxazole-H), 6.39 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.30 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.89 (d, *J* = 3.2 Hz, 9H, Ph-OCH_3). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.65, 168.36, 164.26, 161.04, 158.87, 157.55, 153.66, 152.99, 140.14, 139.02, 130.48, 127.68, 127.65, 127.51, 126.85, 125.45, 109.27, 106.02, 102.57, 101.99, 96.11, 92.56, 63.30, 60.97, 56.51, 56.31, 55.90. **HRMS** (ESI) calcd for $C_{28}H_{25}NO_9S$ $[M+H]^+$: 552.13228, found 552.13214. White solid, m.p. 194.4-195.9 °C, yield 78%.
 3-((3-cyclohexylisoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y23**)	**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.31 (s, 2H, Ph-H), 6.52 (d, J = 2.3 Hz, 1H, Ph-H), 6.38 (d, J = 2.2 Hz, 1H Ph-H), 6.13 (s, 1H, Isoxazole-H), 5 .23 (s, 2H, -O-$\underline{CH_2}$-), 3.99 (s, 3H, Ph-OCH_3), 3.92 (d, J = 1.2 Hz, 6H, Ph-O CH_3), 3.91 (s, 6H, Ph-OCH_3), 2.66 (qt, J = 7.4, 3.0 Hz, 1H, -CHCH2CH2C H2CH2CH2-), 1.90 – 1.68 (m, 6H, -CHCH2CH2CH2CH2CH2-), 1.35 – 1.2 3 (m, 4H,-CHCH2CH2CH2CH2CH2-). **^{13}C NMR (101 MHz, Chloroform-d)** δ 173.67, 168.38, 167.19, 164.21, 161.04, 158.81, 153.18, 152.96, 140.12, 139.34, 125.50, 109.27, 105.95, 102.62, 96.03, 92.51, 63.60, 60.97, 56.49, 56.32, 55.88, 35.76, 31.99, 25.91, 25.82. **HRMS** (ESI) calcd for $C_{30}H_{33}NO_9$ $[M+H]^+$: 552.22281, found 552.22302. White solid, m.p. 89.6-91.4 °C, yield 85%.
 ethyl 2-(4-(5-(((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)methyl)isoxazol-3-yl)phenoxy)acetate (**Y24**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.64 – 7.61 (m, 2H, Ph-H), 7.24(s, 2H, Ph-H), 6.94 – 6.92 (m, 2H, Ph-H), 6.49 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.46(s, 1H, Isoxazole-H), 6.36 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.28(s, 2H, -O-$\underline{CH_2}$-), 4.64(s, 2H, -O$\underline{CH_2}$$COOCH_2CH_3$), 4.26 (q, *J* = 7.2 Hz, 2H -$OCH_2COO\underline{CH_2}CH_3$), 3.97(s, 3H, Ph-$OCH_3$), 3.89(s, 3H, Ph-$OCH_3$), 3.86 (d, *J* = 4.4 Hz, 9H, Ph-OCH_3), 1.29 (t, *J* = 7.2 Hz, 3H, -$OCH_2COOCH_2\underline{CH_3}$). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.77, 168.67, 168.24, 164.30, 161.82, 161.08, 159.20, 158.92, 153.65, 153.03, 140.11, 139.13, 128.30, 125.57, 122.42, 115.04, 109.32, 106.02, 102.45, 96.16, 92.59, 65.35, 63.47, 61.65, 61.04, 56.58, 56.36, 55.97, 14.27. **HRMS** (ESI) calcd for $C_{34}H_{33}NO_{12}$ $[M+H]^+$: 648.20755, found 648.20721. White solid, m.p. 181.2-182.7 °C, yield 93%

 ethyl 4-(4-(5-(((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)oxy)methyl)isoxazol-3-yl)phenoxy)butanoate (**Y25**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.62 – 7.59 (m, 2H, Ph-H), 7.24(s, 2H, Ph-H), 6.92 – 6.89 (m, 2H, Ph-H), 6.49 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.47(s, 1H, Isoxazole-H), 6.37 (d, *J* = 2.2 Hz, 1H, Ph-H), 5.28 (d, *J* = 2.4 Hz, 2 H, -O-$\underline{CH_2}$-), 4.13 (q, *J* = 7.1 Hz, 2H, -O$\underline{CH_2}$$CH_2CH_2COOCH_2CH_3$), 4.02 (t, *J* = 6.2 Hz, 2H, -$OCH_2CH_2CH_2COO\underline{CH_2}CH_3$), 3.97(s, 3H, Ph-$OCH_3$), 3.90(s , 3H, Ph-$OCH_3$), 3.86 (d, *J* = 3.0 Hz, 9H, Ph-OCH_3), 2.51 (t, *J* = 7.2 Hz, 2H , -$OCH_2CH_2\underline{CH_2}COOCH_2CH_3$), 2.12 (q, *J* = 6.2 Hz, 2H, -$OCH_2\underline{CH_2}CH_2COOCH_2CH_3$), 1.24 (t, *J* = 7.2 Hz, 2H, -$OCH_2CH_2CH_2COOCH_2\underline{CH_2}$). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.78, 173.28, 168.12, 164.29, 162.00, 161.09, 160.34, 158.92, 153.62, 153.03, 140.11, 139.18, 128.20, 125.59, 121.36, 114.85, 109.33, 106.02, 102.42, 96.15, 92.59, 66.88, 63.51, 61.05, 60.62, 56.59, 56.37, 55.98, 53.57, 30.81, 24.61, 14.34. **HRMS** (ESI) calcd for $C_{36}H_{37}NO_{12}$ $[M+H]^+$: 676.23885, found 676.23840. White solid, m.p. 158.3-160.2 °C, yield 95%.
 3-((3-(4-ethylphenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y26**)	**^{1}H NMR (500 MHz, Chloroform-d)** δ 7.62 – 7.59 (m, 2H, Ph-H), 7.25 (s, 4H, Ph-H), 6.50 (s, Isoxazole-H;), 6.49 (d, J = 2.3 Hz, 1H, Ph-H), 6.37 (d, J = 2.3 Hz, 1H, Ph-H), 5.30(s, 2H, -O-$\underline{CH_2}$-), 3.98(s, 3H, Ph-OCH_3), 3.90(s, 3H, Ph-OCH_3), 3.86(s, 9H, Ph-OCH_3), 2.69 – 2.64 (m, 2H, Ph-$\underline{CH_2}CH_3$), 1.23 (t, J = 7.6 Hz, 3H, Ph-$CH_2\underline{CH_3}$). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.76, 168.20, 164.30, 162.37, 161.11, 158.92, 153.63, 153.04, 146.58, 140.20, 139.16, 128.49, 126.79, 126.22, 125.57, 109.35, 106.12, 102.58, 96.15, 92.61, 63.51, 61.01, 56.56, 56.37, 55.95, 28.85, 15.52. **HRMS** (ESI) calcd for $C_{32}H_{31}NO_9$ $[M+H]^+$: 574.20716, found 574.20532. White solid, m.p. 156.3-157.7 °C, yield 91%.
 3-((3-(4-isopropylphenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y27**)	**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.65 – 7.61 (m, 2H, Ph-H), 7.31 – 7.28 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 6.54 – 6.50 (m, 2H, Ph-H; Isoxazole-H), 6.39 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.87 (s, 9H, Ph-OCH_3), 2.94 (p, *J* = 6.8 Hz, 1H, -$\underline{CH}(CH_3)_2$), 1.27 (d, *J* = 6.9 Hz, 6H, -$CH(\underline{CH_3})_2$). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.76, 168.16, 164.31, 162.34, 161.09, 158.91, 153.66, 153.03, 151.19, 140.19, 139.14, 127.07, 126.81, 126.34, 125.56, 109.32, 106.11, 102.59, 96.15, 92.62, 63.50, 60.99, 56.54, 56.36, 55.95, 34.13, 23.91. **HRMS** (ESI) calcd for $C_{33}H_{33}NO_9$ $[M+H]^+$: 588.22281, found 588.22083. White solid, m.p. 161.1-162.4 °C, yield 87%.
 3-((3-(4-(tert-butyl)phenyl)isoxazol-5-yl)methoxy)-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (**Y28**)	**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.66 – 7.62 (m, 2H, Ph-H), 7.47 – 7.44 (m, 2H, Ph-H), 7.26 (s, 2H, Ph-H), 6.53 (s, 1H, Isoxazole-H), 6.51 (d, *J* = 2.3 Hz, 1H, Ph-H), 6.39 (d, *J* = 2.3 Hz, 1H, Ph-H), 5.32 (s, 2H, -O-$\underline{CH_2}$-), 4.00 (s, 3H, Ph-OCH_3), 3.92 (s, 3H, Ph-OCH_3), 3.88 (s, 9H, Ph-OCH_3), 1.34 (s, 9H, Ph-t-Bu). **^{13}C NMR (126 MHz, Chloroform-d)** δ 173.75, 168.17, 164.29, 162.27, 161.11, 158.92, 153.62, 153.42, 153.04, 140.20, 139.15, 126.54, 125.99, 125.92, 125.57, 109.35, 106.11, 102.60, 96.14, 92.61, 63.49, 60.99, 56.56, 56.37, 55.95, 34.91, 31.28. **HRMS** (ESI) calcd for $C_{34}H_{35}NO_9$ $[M+H]^+$: 602.23846, found 602.23730. White solid, m.p. 183.2-184.4 °C, yield 83%.

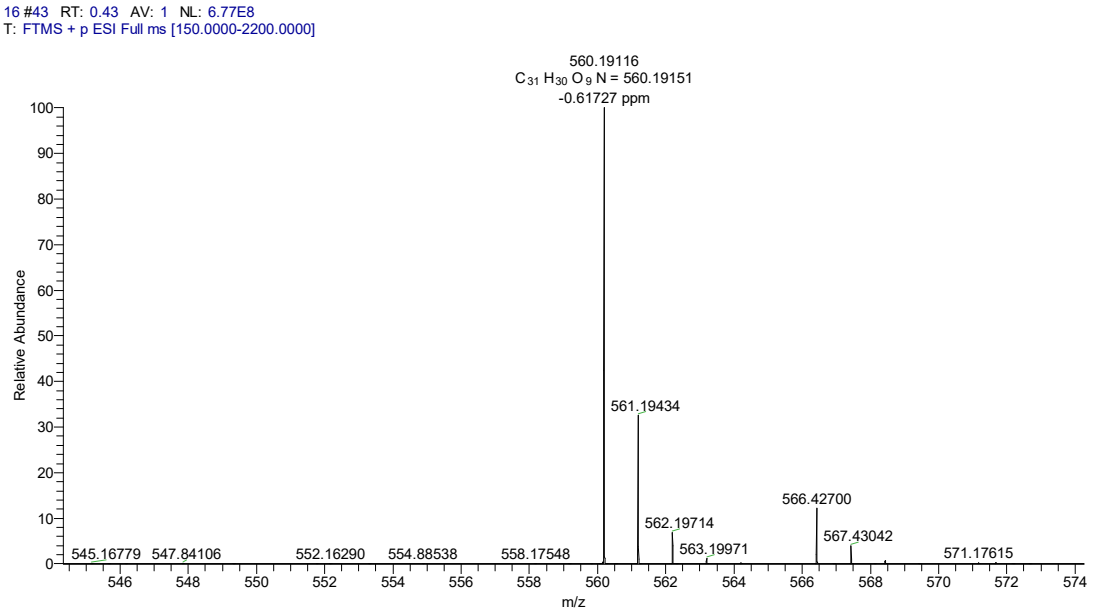
4.2 Spectrum of compounds Y1-Y28



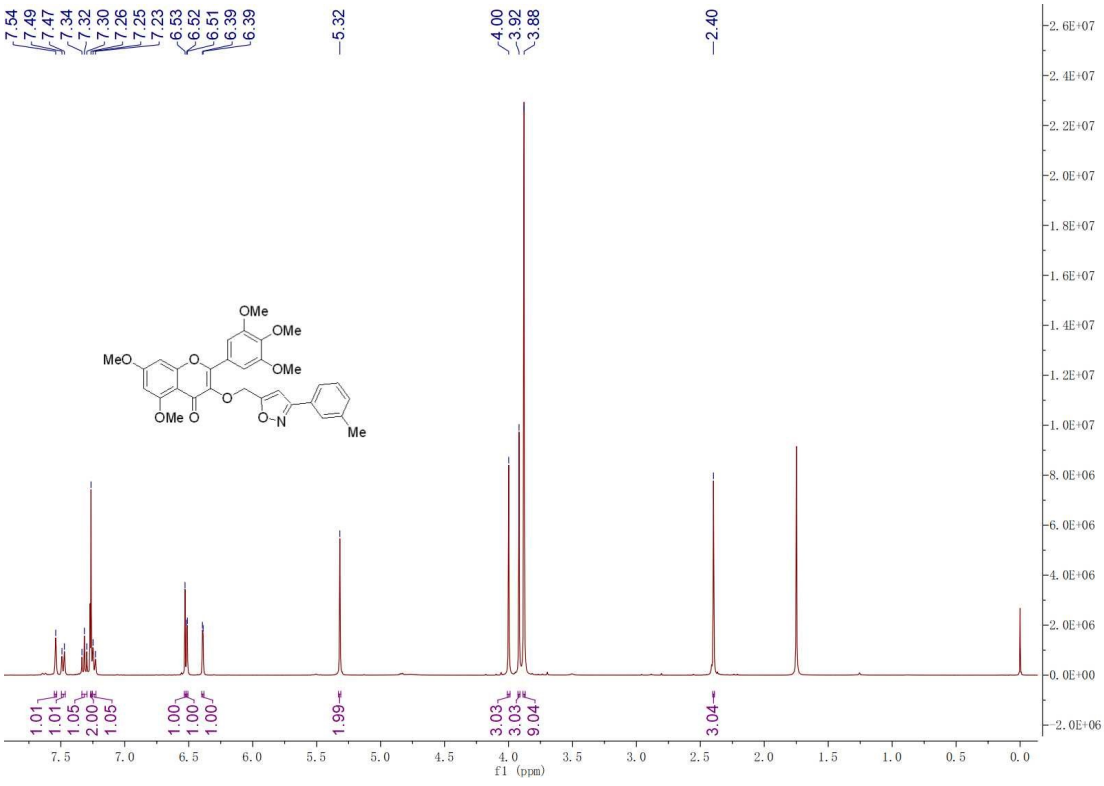
^{1}H NMR spectra of compound **Y1**



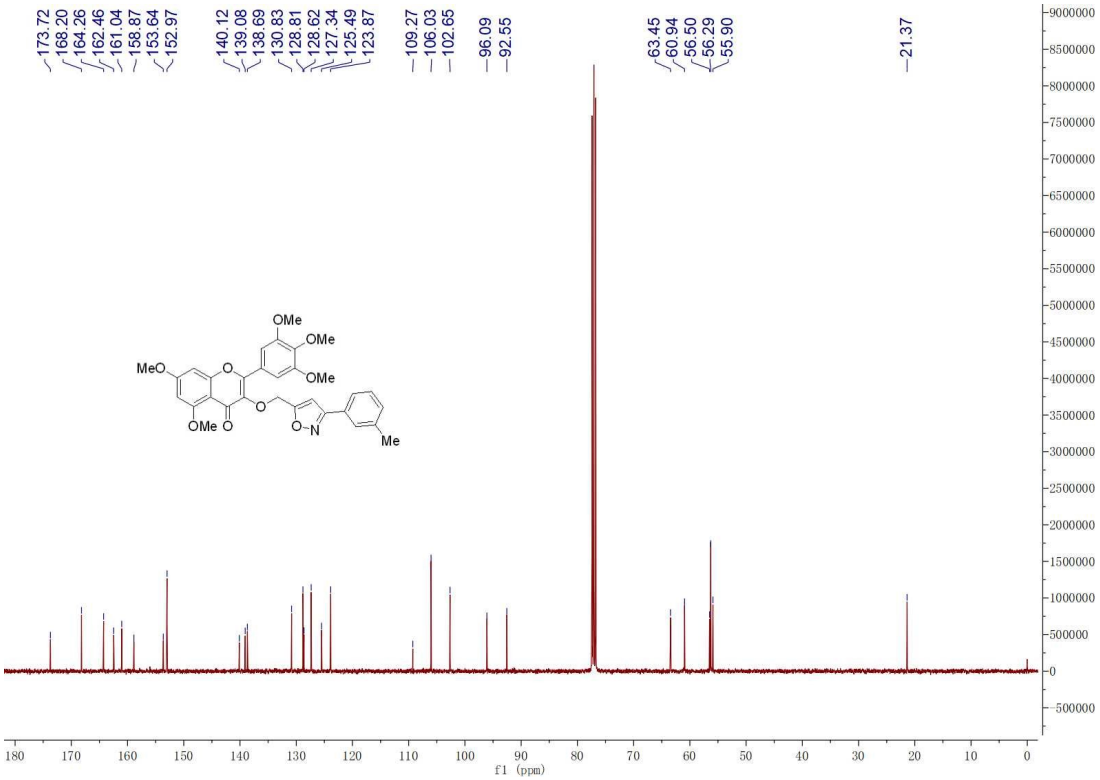
^{13}C NMR spectra of compound **Y1**



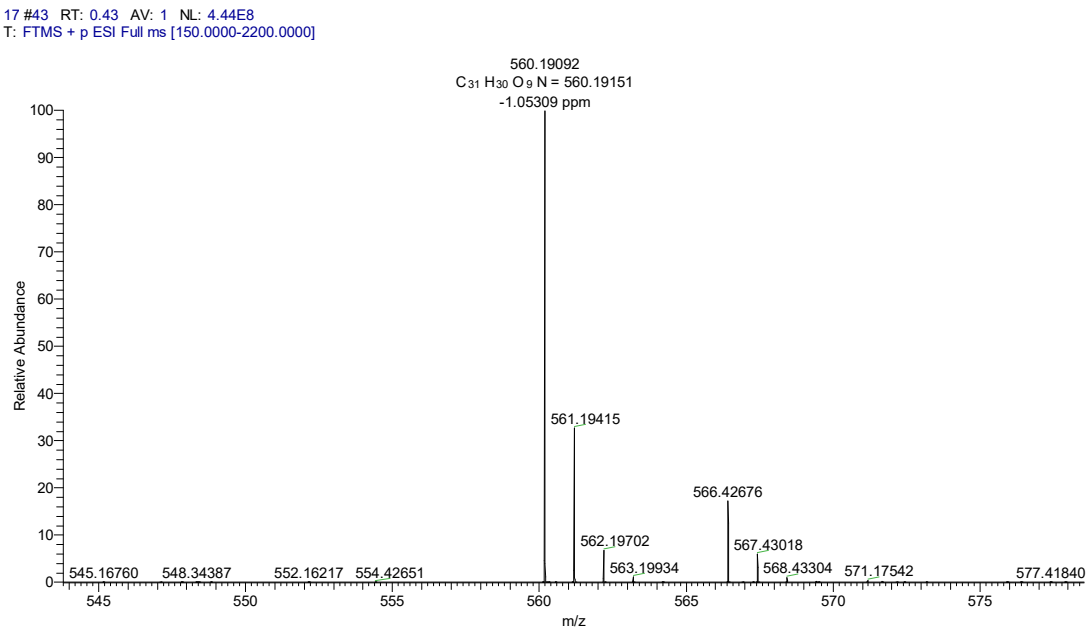
HRMS spectra of compound **Y1**



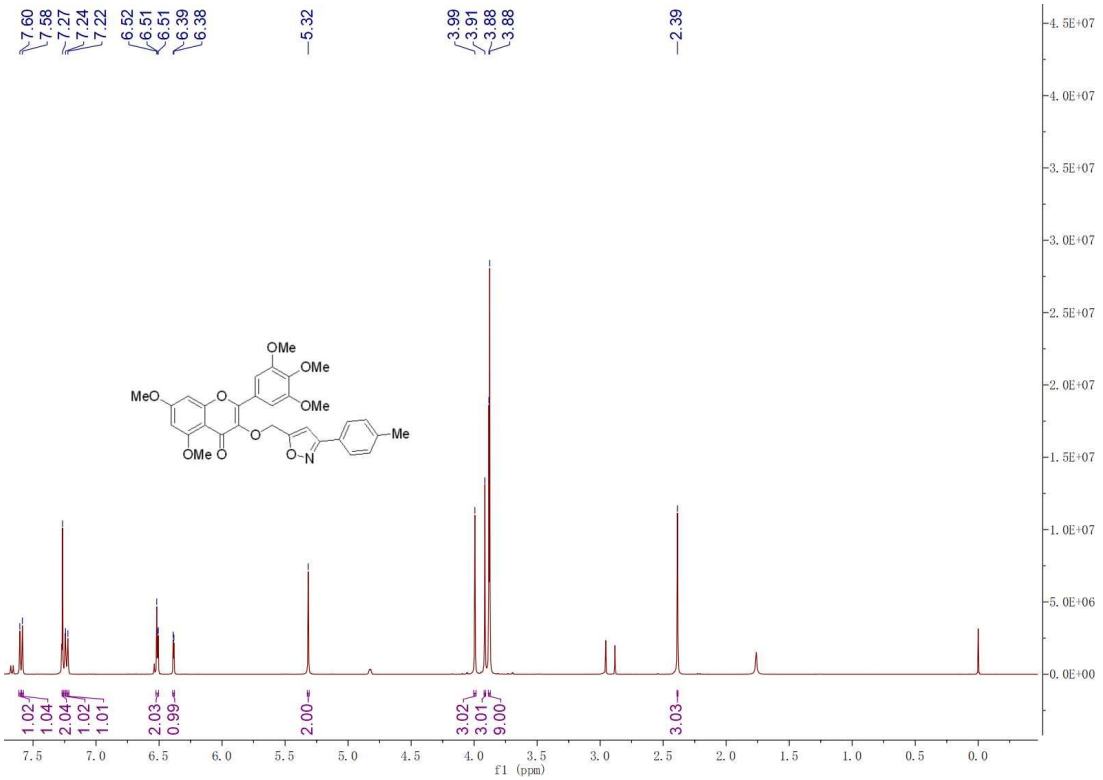
^{1}H NMR spectra of compound **Y2**



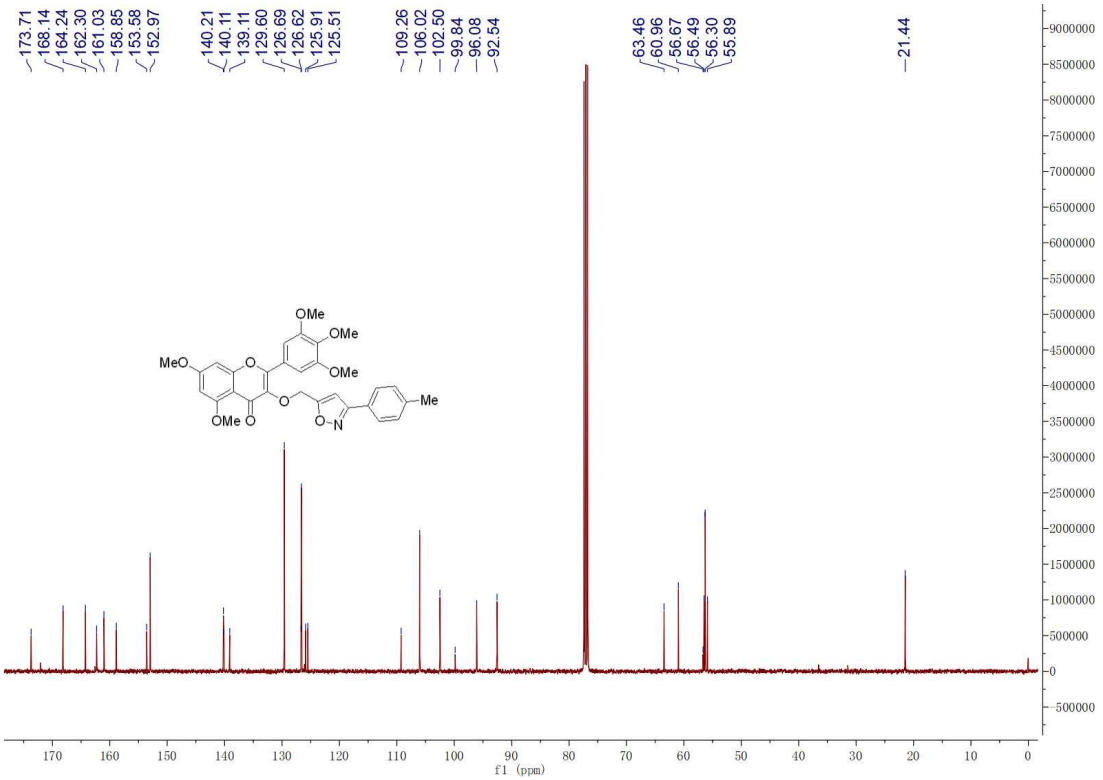
^{13}C NMR spectra of compound **Y2**



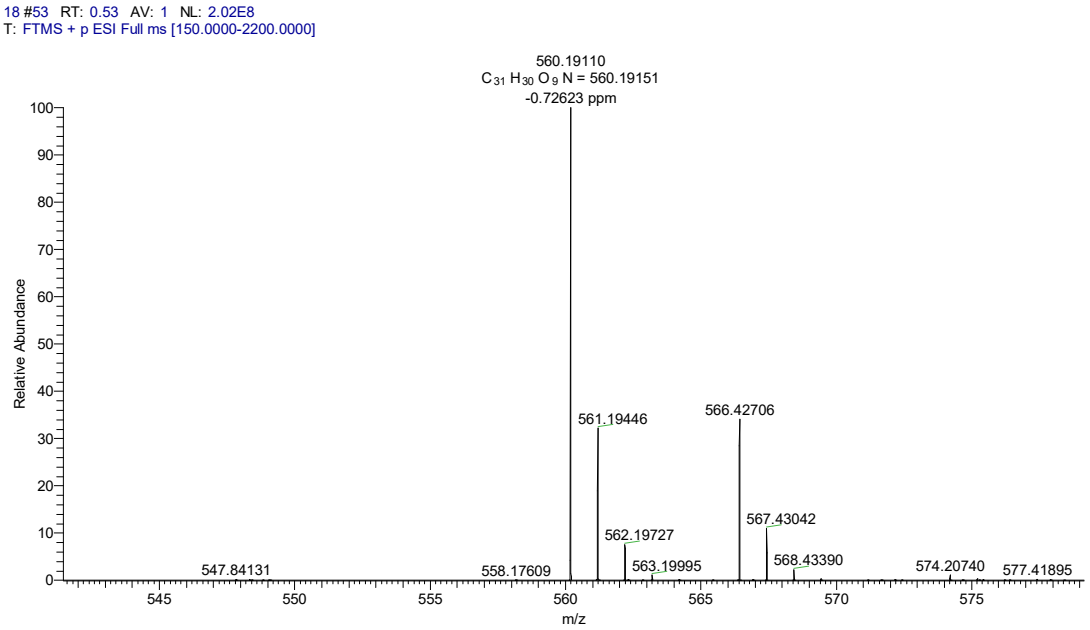
HRMS spectra of compound **Y2**



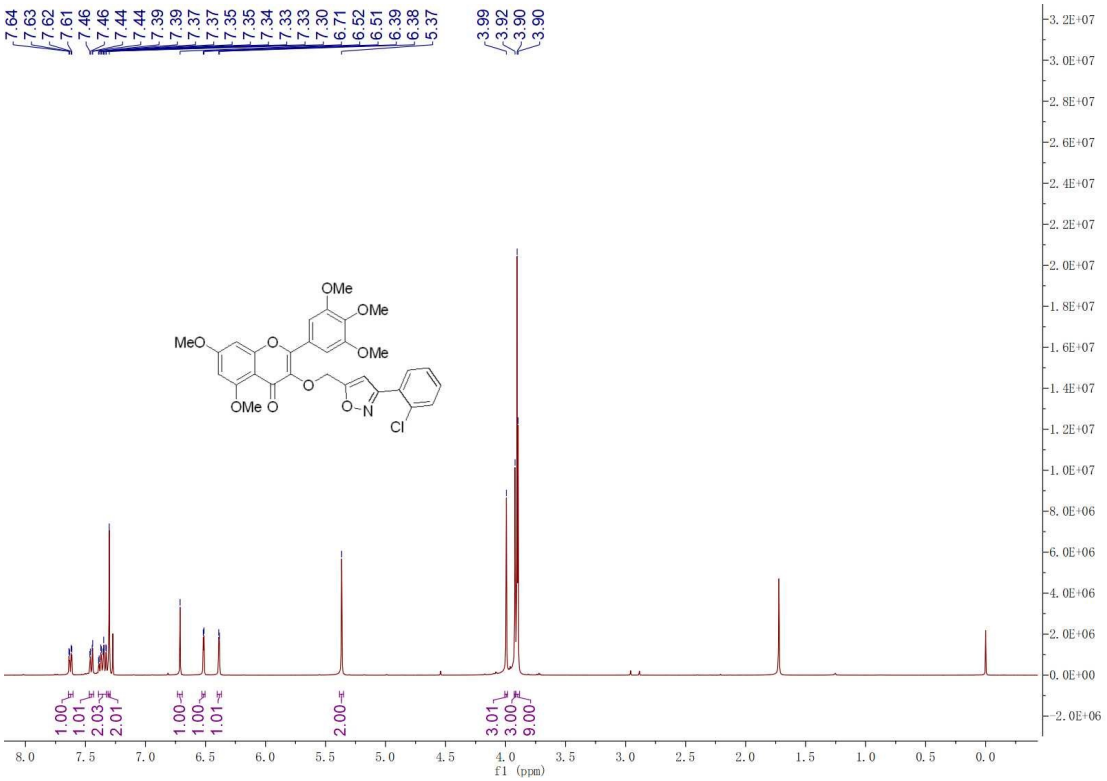
^{1}H NMR spectra of compound **Y3**



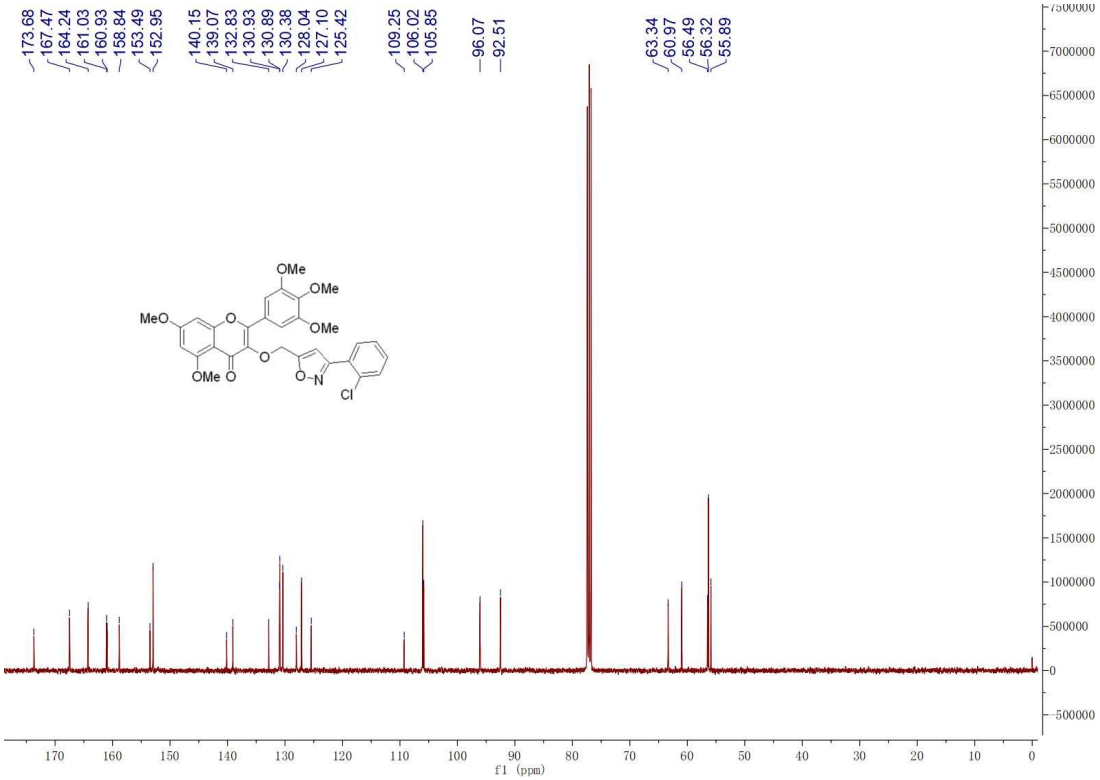
^{13}C NMR spectra of compound **Y3**



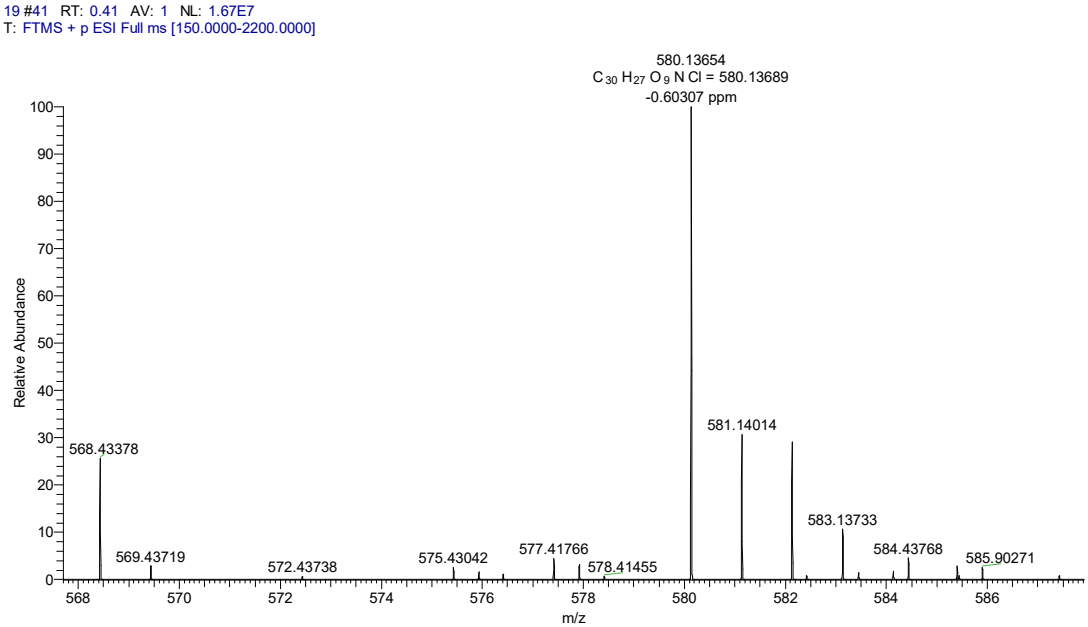
HRMS spectra of compound **Y3**



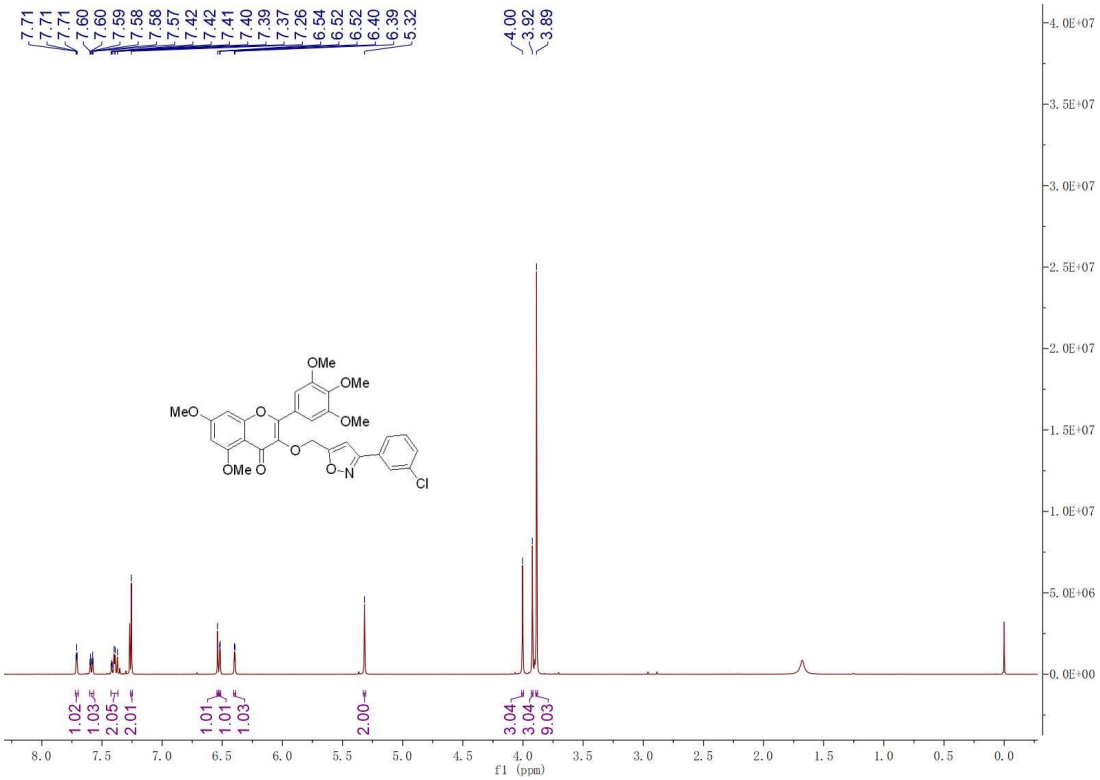
^{1}H NMR spectra of compound **Y4**



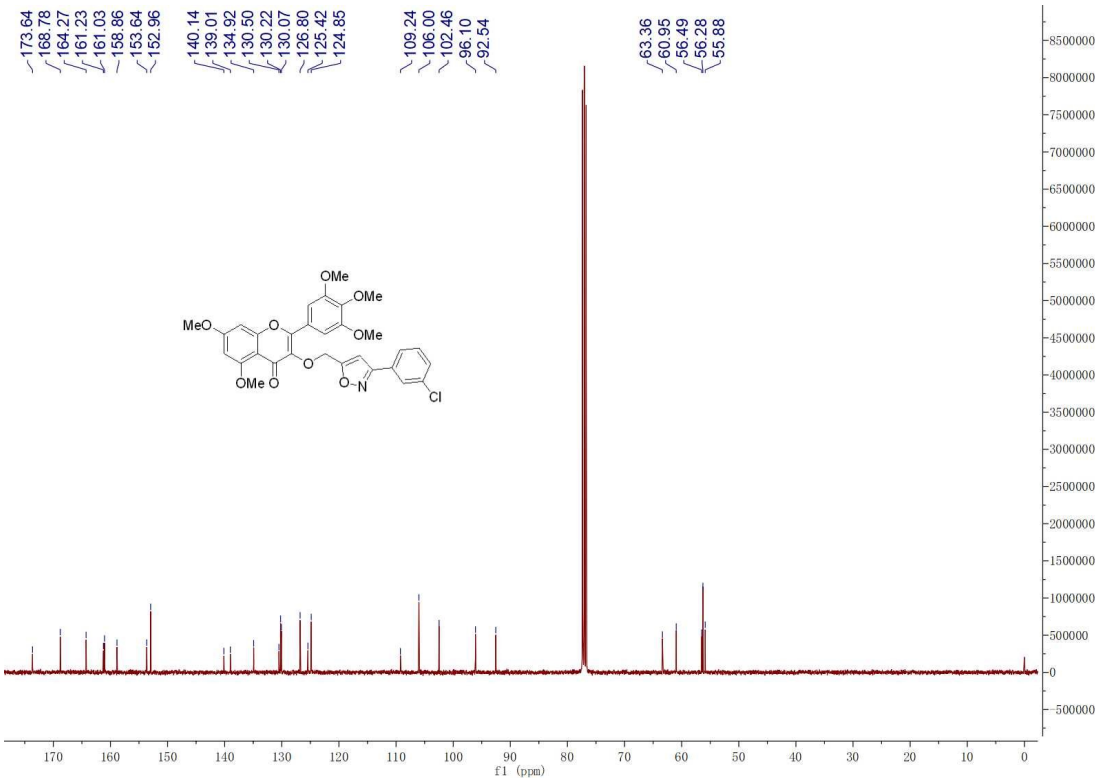
^{13}C NMR spectra of compound **Y4**



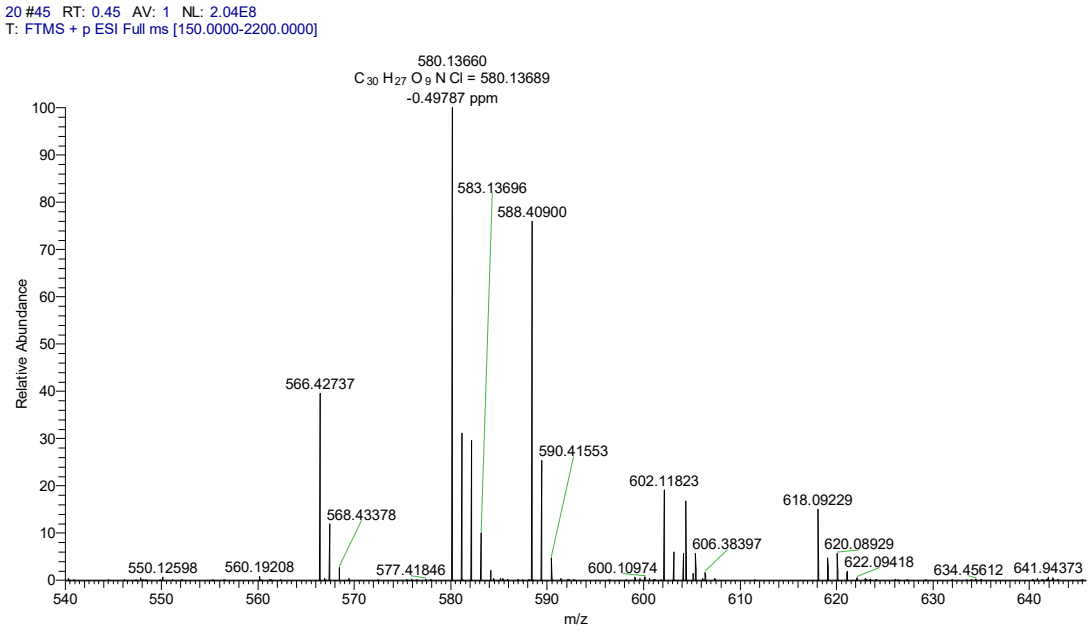
HRMS spectra of compound **Y4**



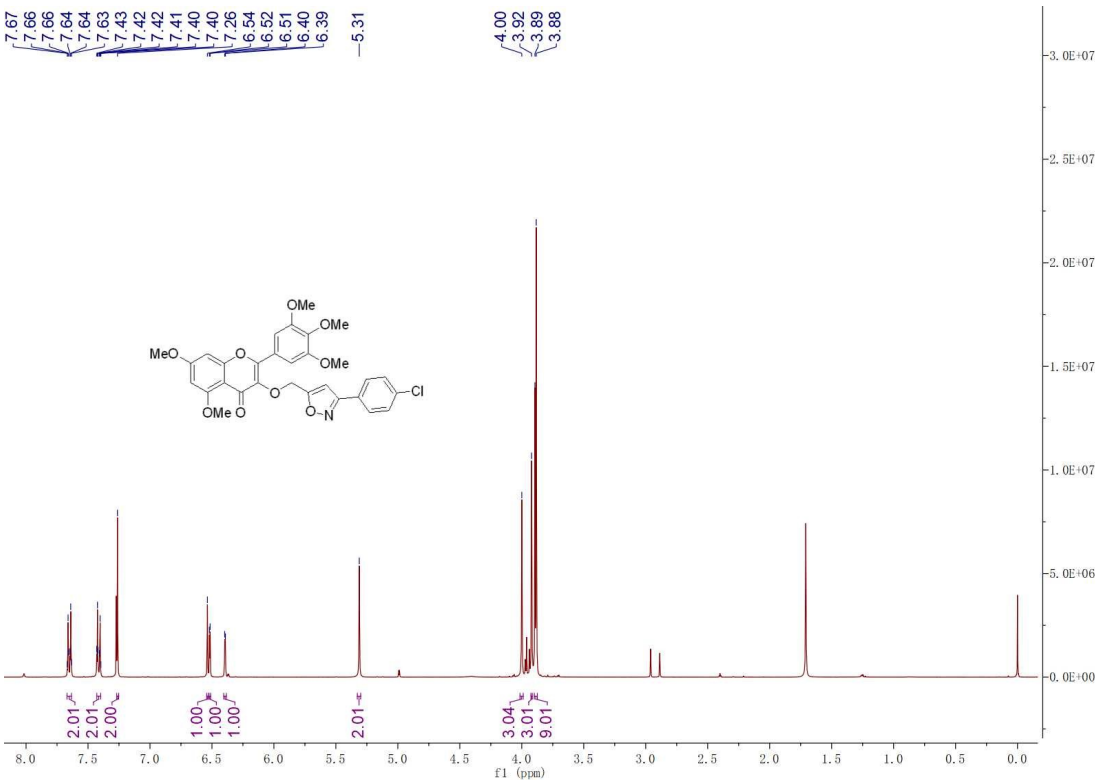
^{1}H NMR spectra of compound **Y5**



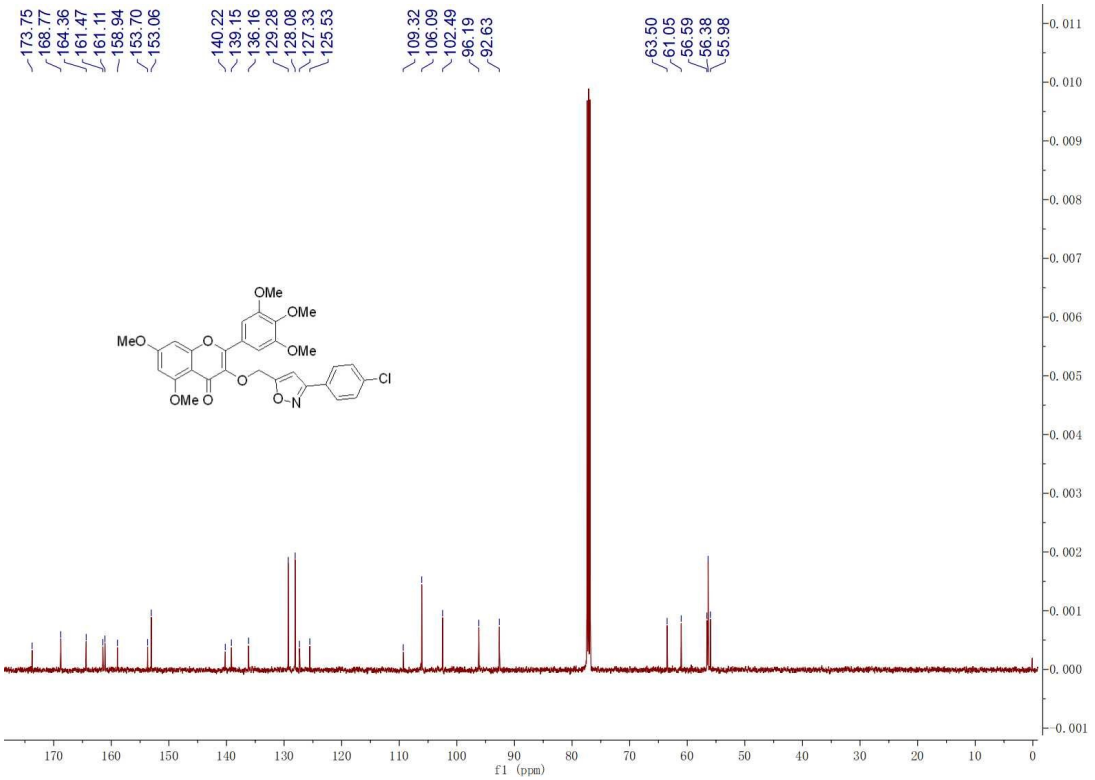
^{13}C NMR spectra of compound **Y5**



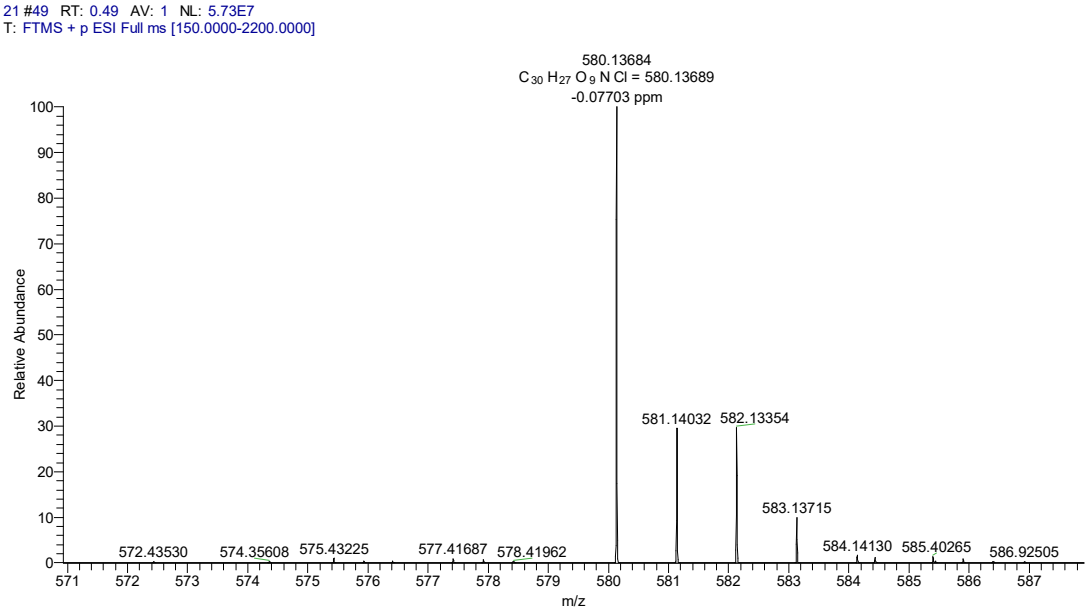
HRMS spectra of compound **Y5**



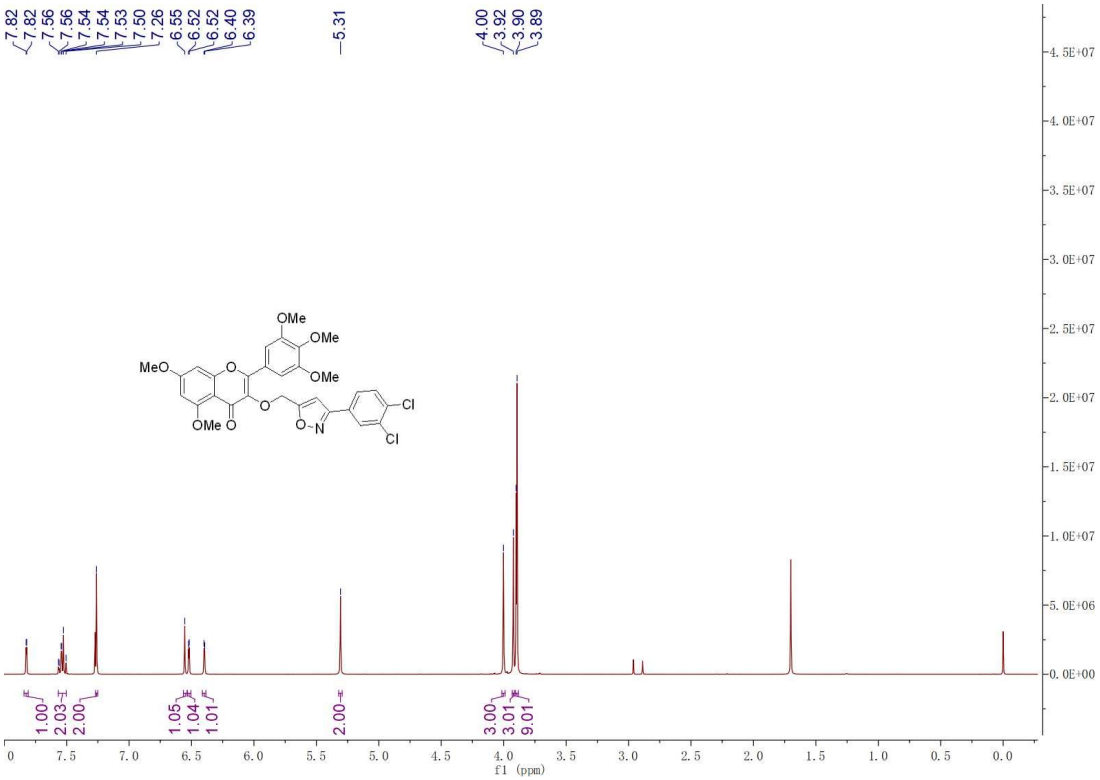
^{1}H NMR spectra of compound **Y6**



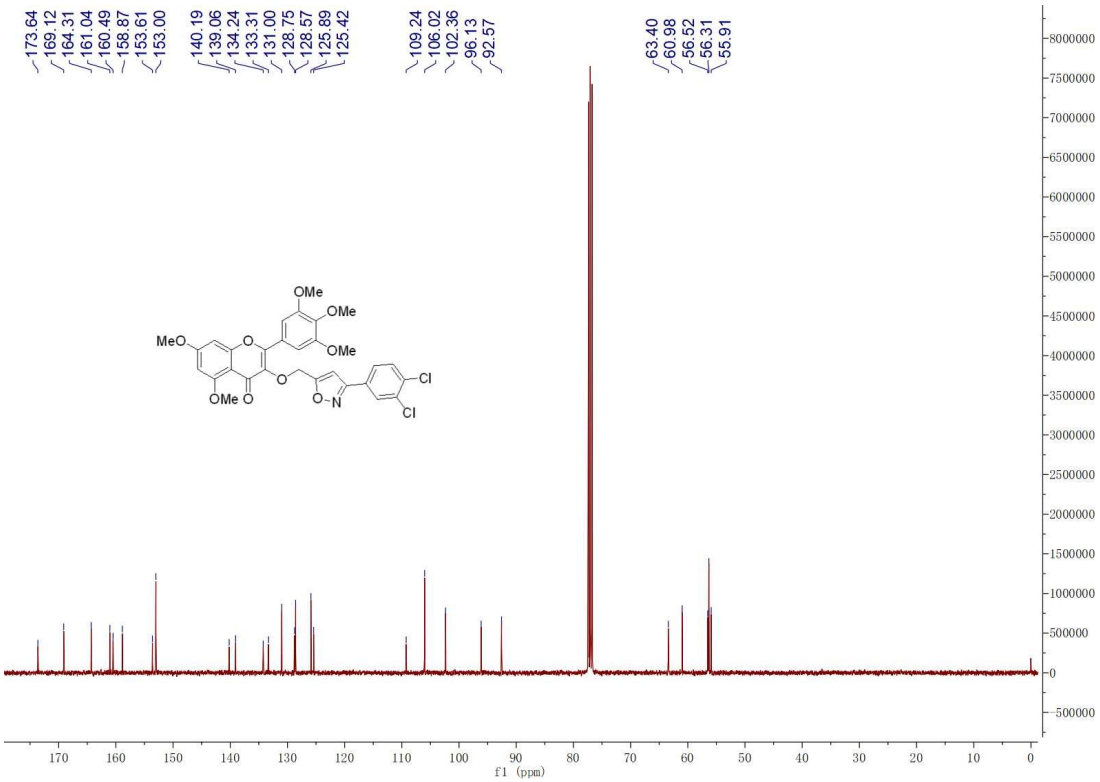
^{13}C NMR spectra of compound **Y6**



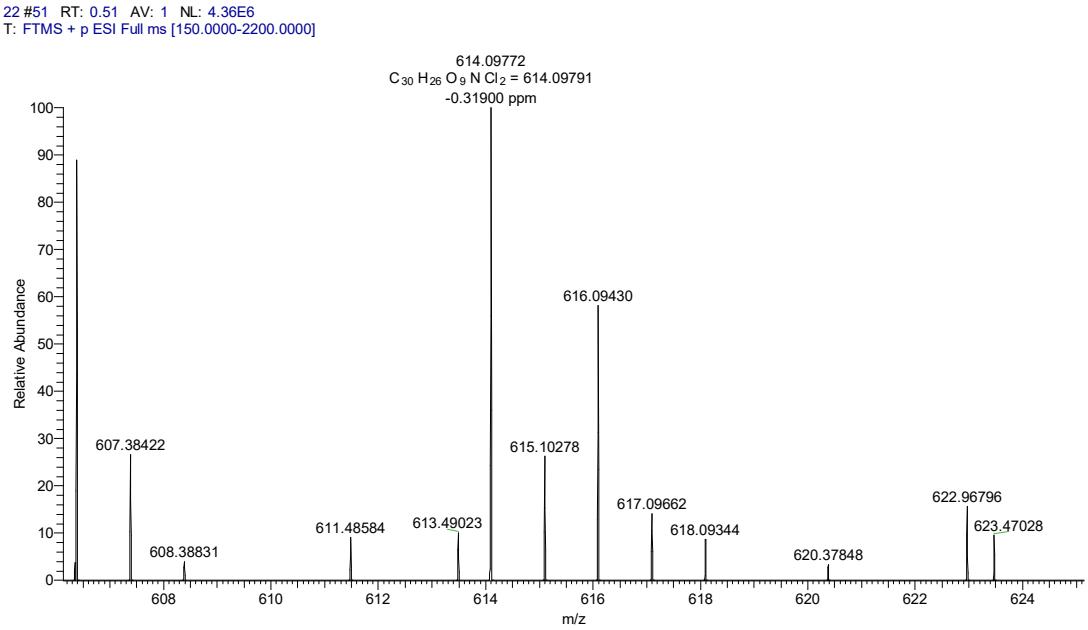
HRMS spectra of compound **Y6**



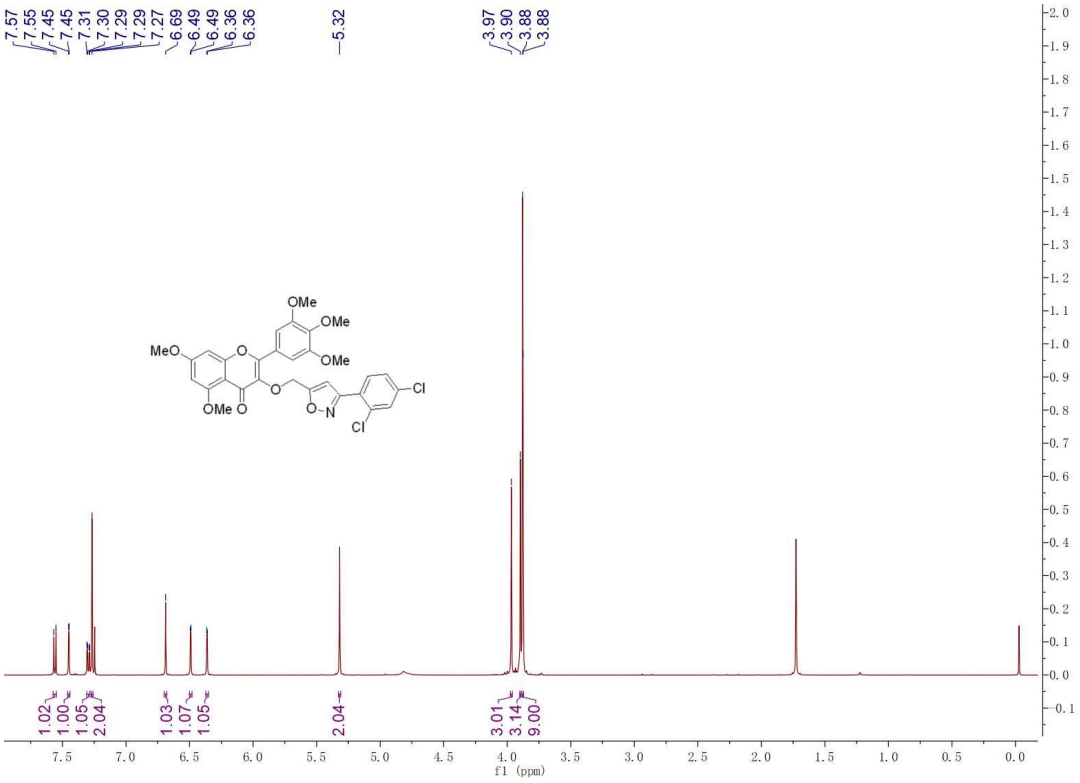
^{1}H NMR spectra of compound **Y7**



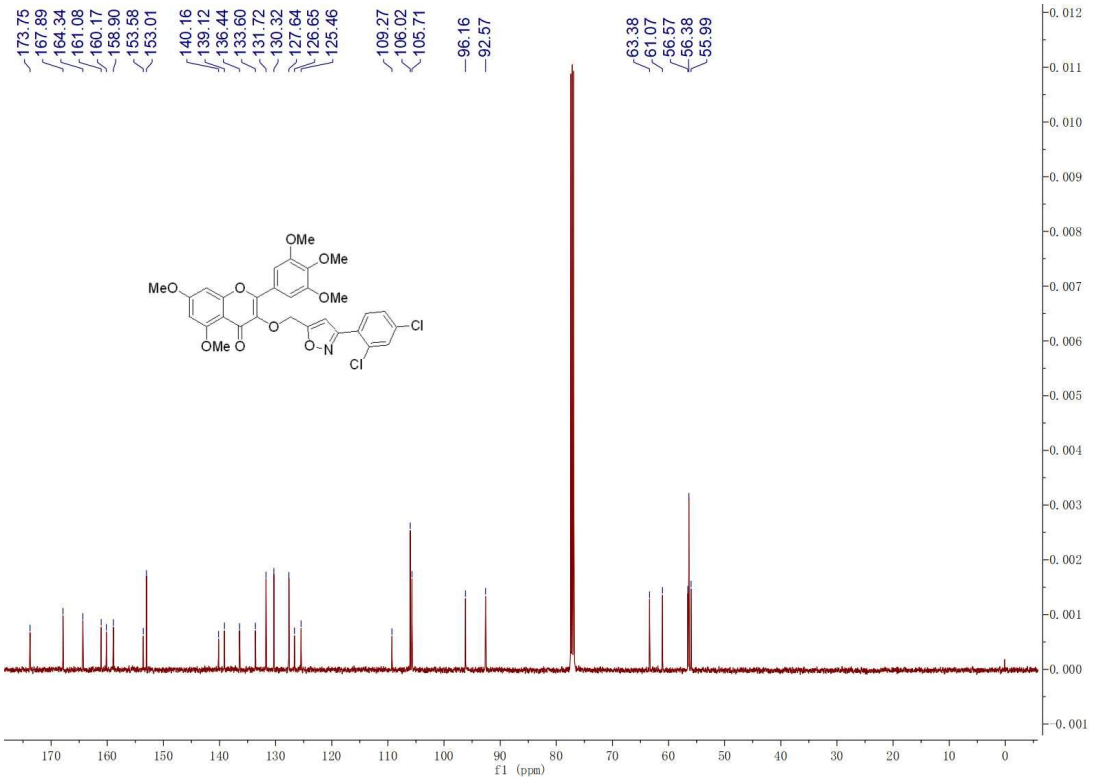
^{13}C NMR spectra of compound **Y7**



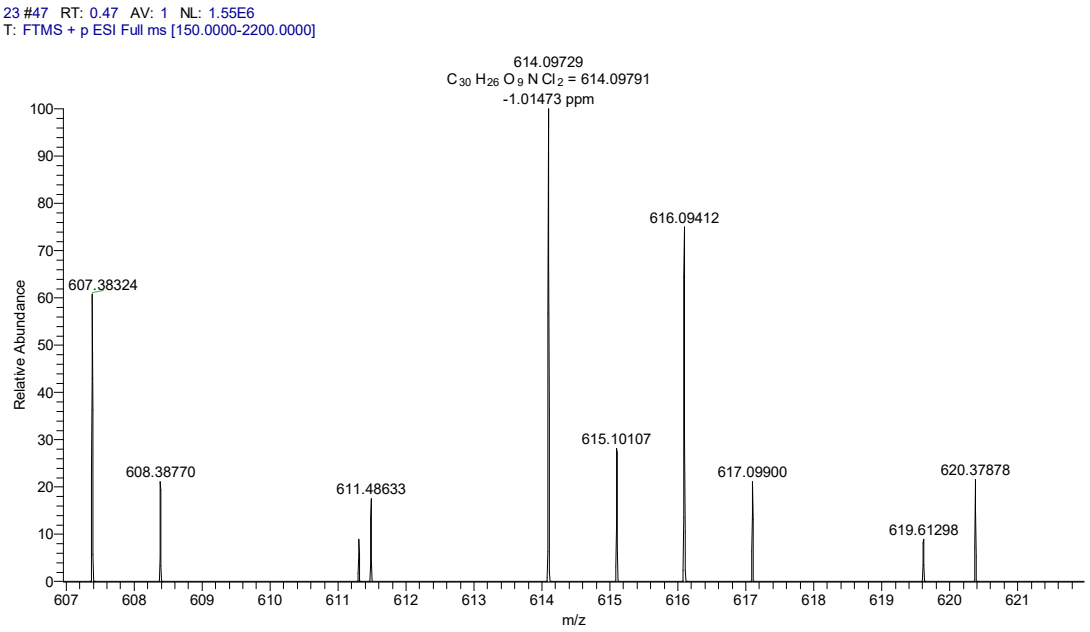
HRMS spectra of compound **Y7**



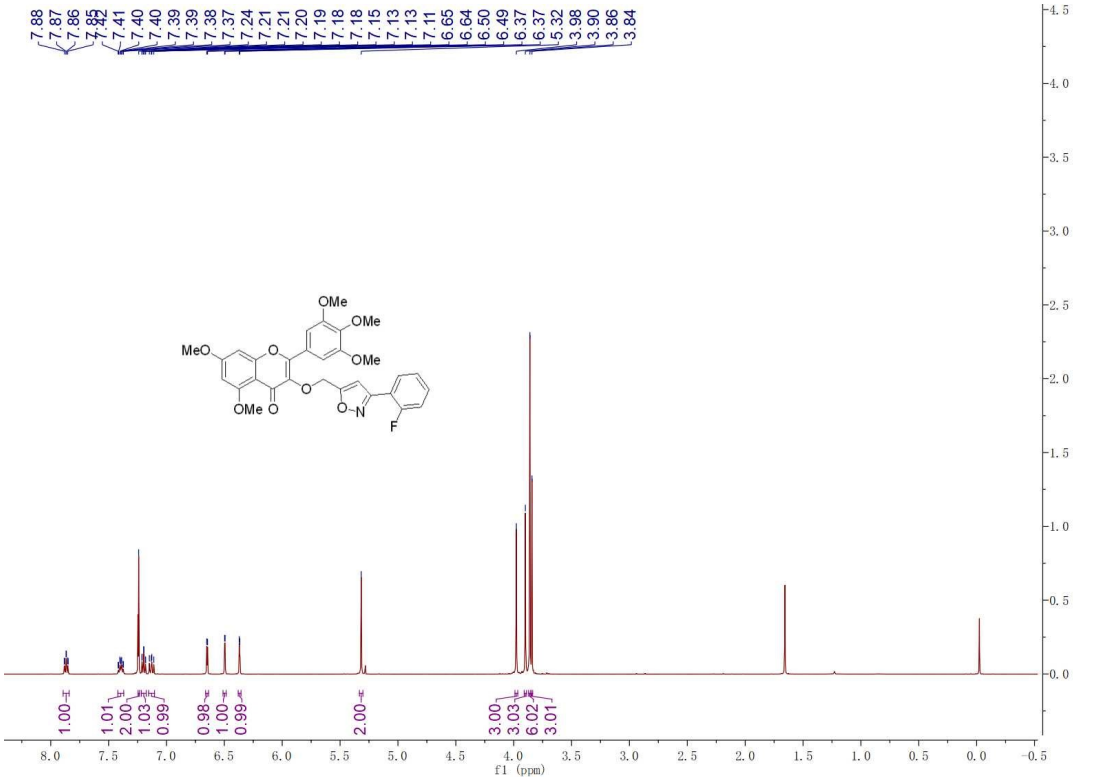
^{1}H NMR spectra of compound **Y8**



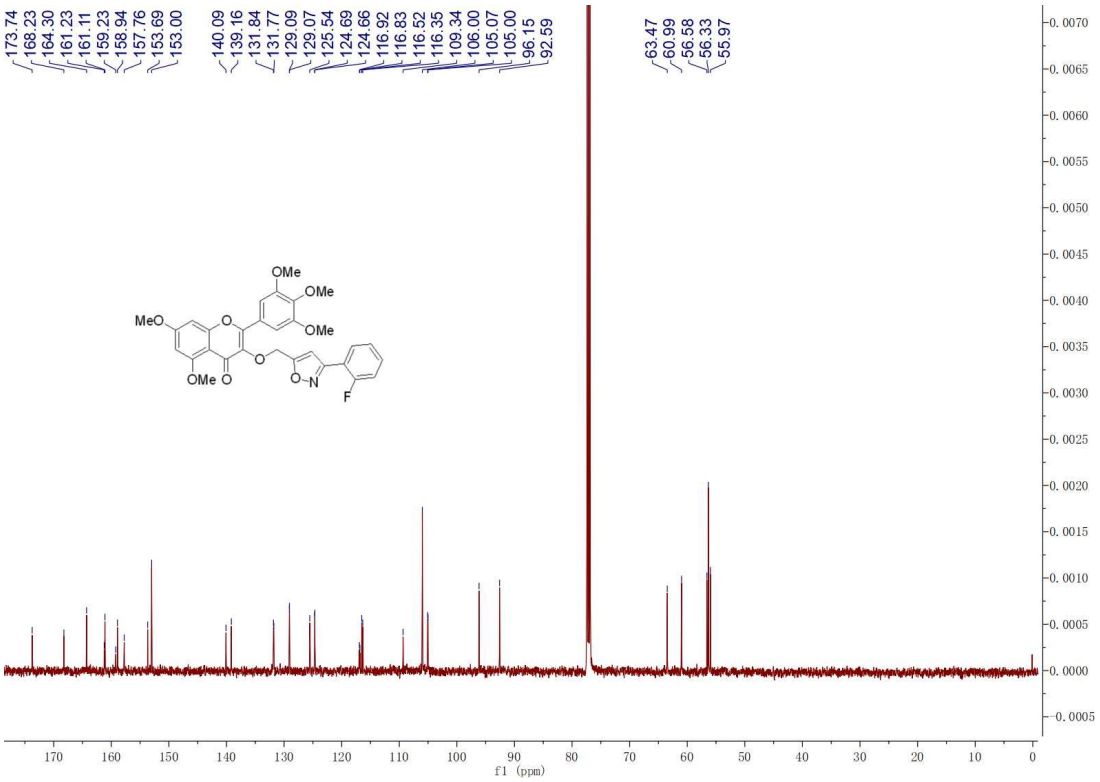
^{13}C NMR spectra of compound **Y8**



HRMS spectra of compound **Y8**

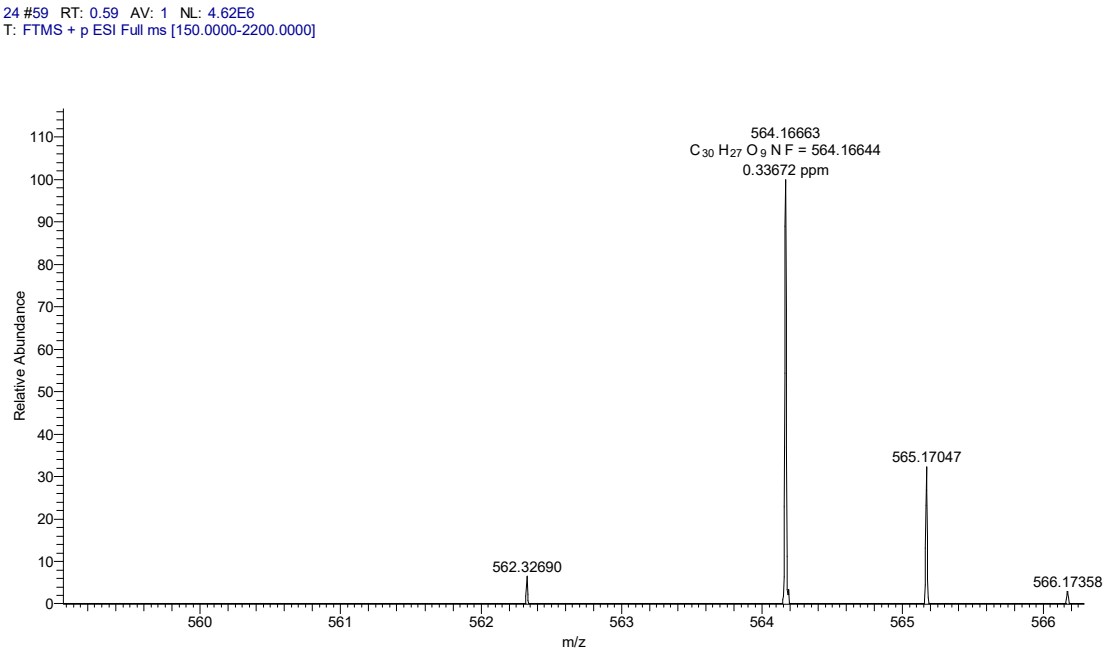


^{1}H NMR spectra of compound **Y9**

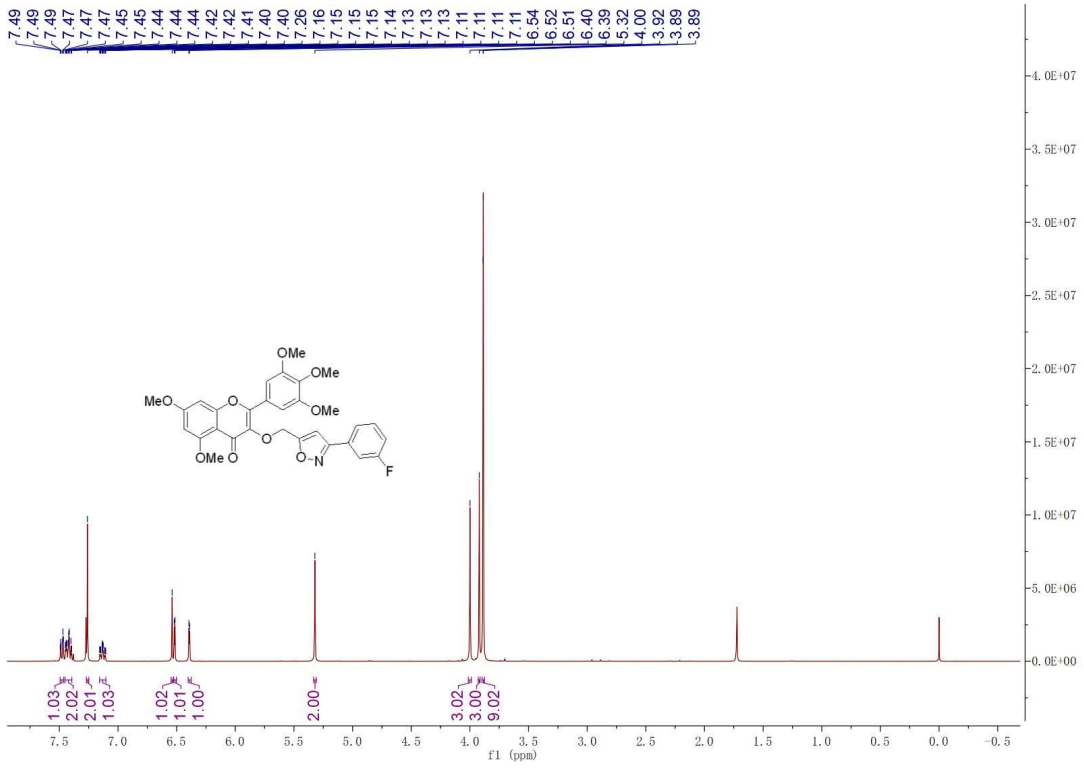


^{13}C NMR spectra of compound **Y9**

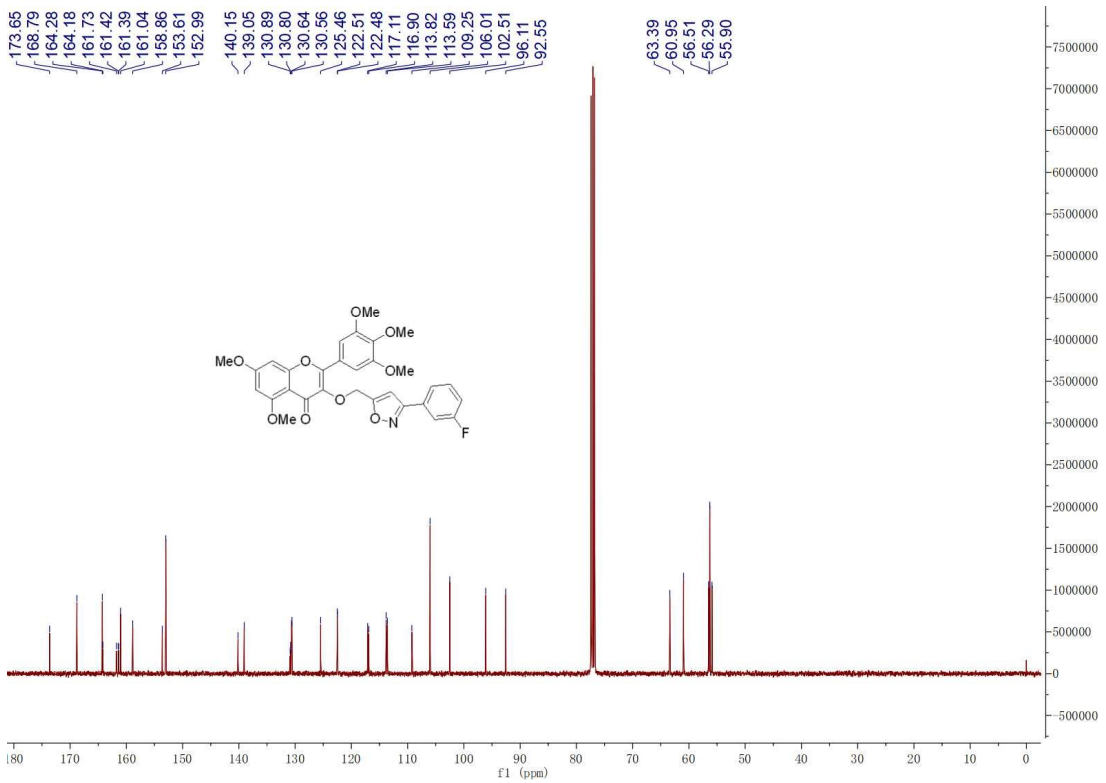
^{19}NMR spectra of compound **Y9**



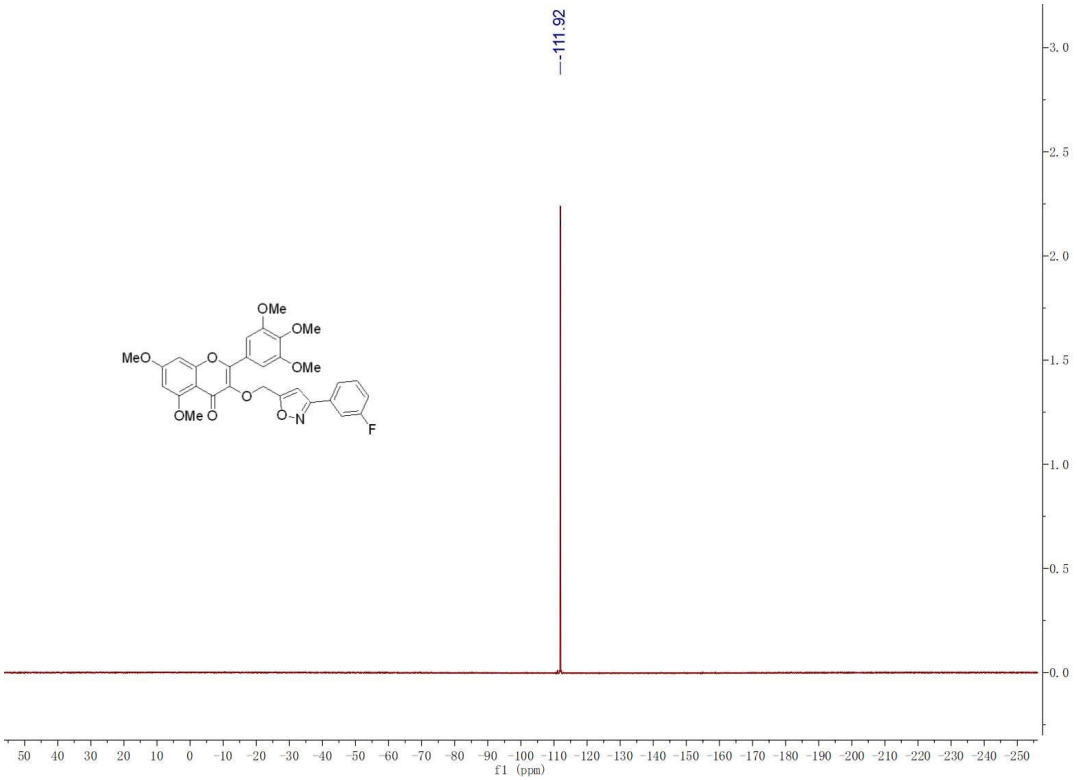
HRMS spectra of compound **Y9**



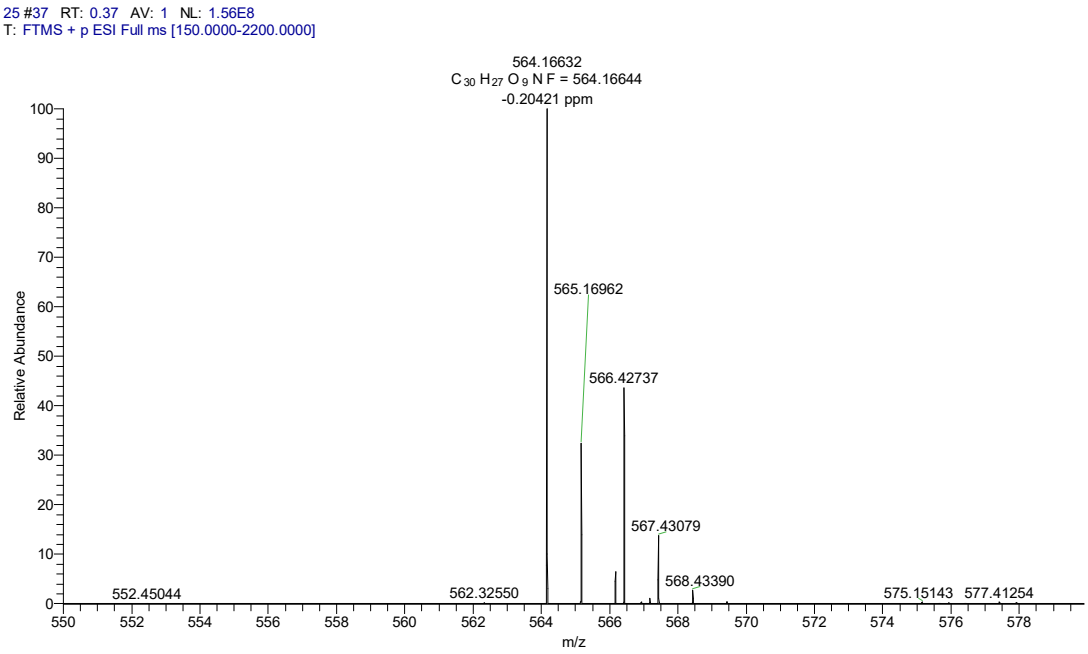
^{1}H NMR spectra of compound **Y10**



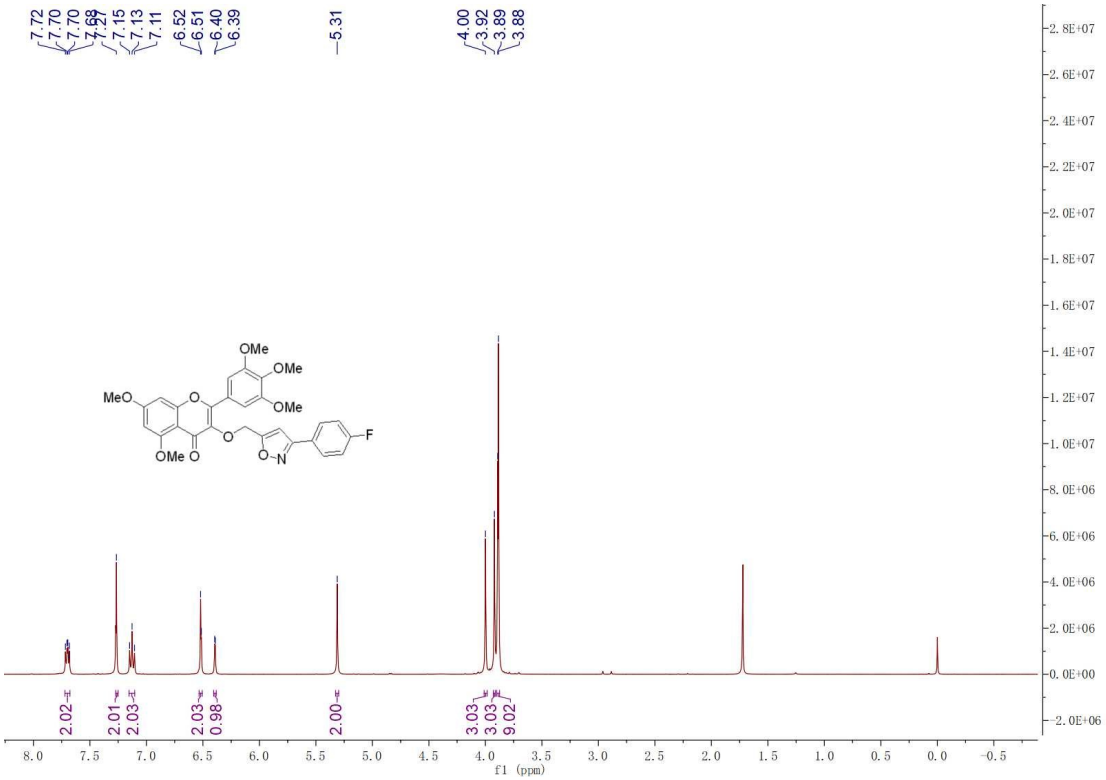
^{13}C NMR spectra of compound **Y10**



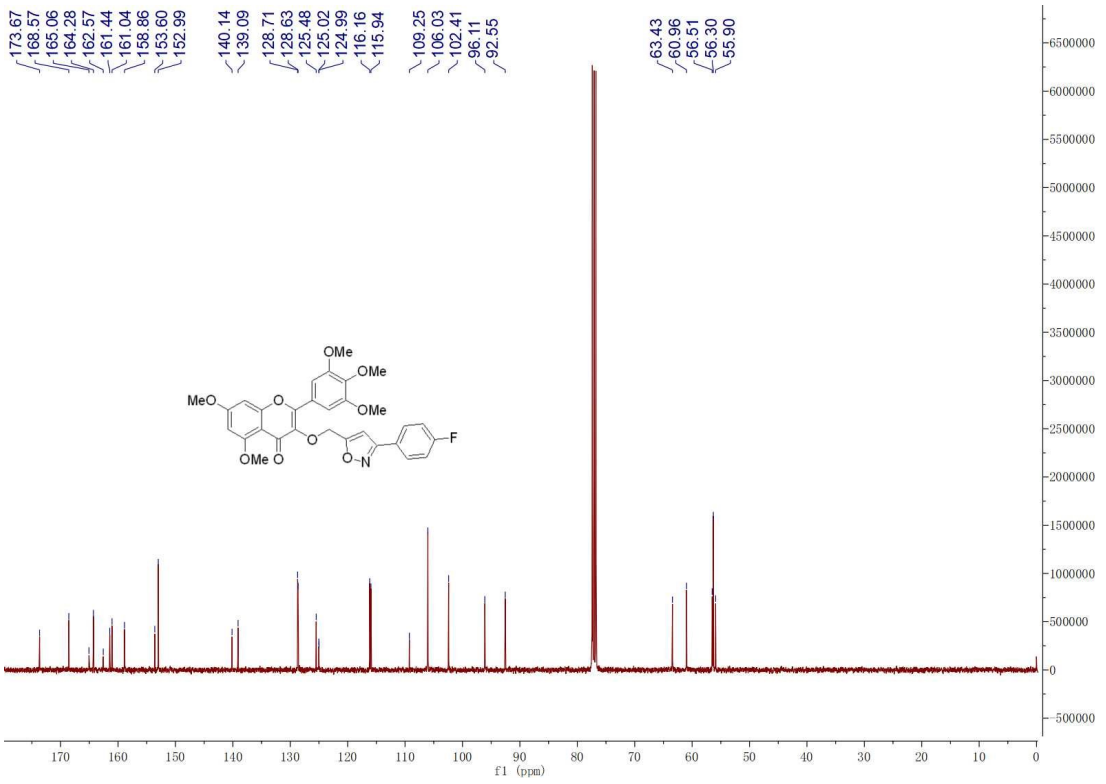
^{19}F NMR spectra of compound **Y10**



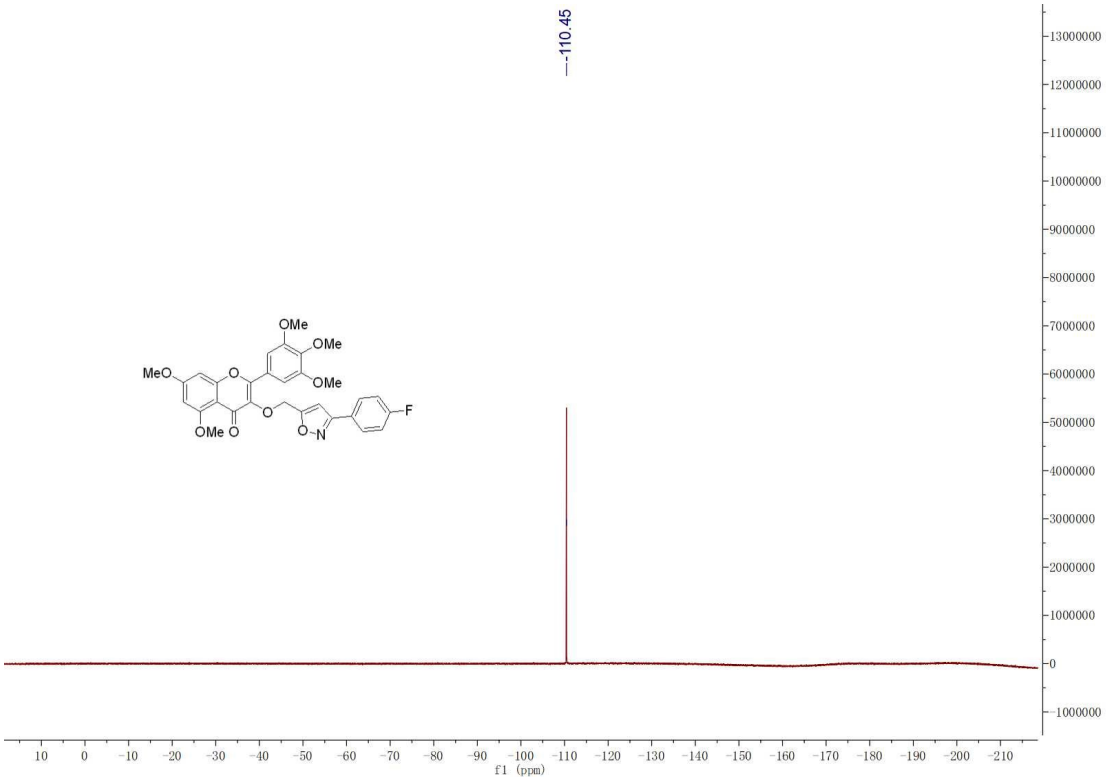
HRMS spectra of compound **Y10**



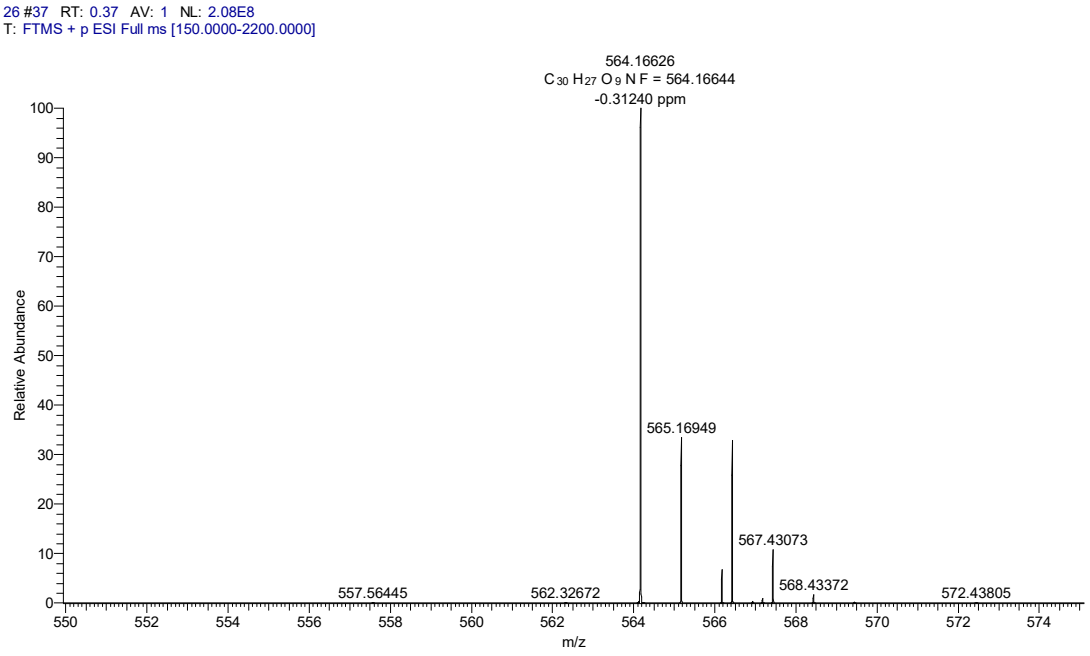
^{1}H NMR spectra of compound **Y11**



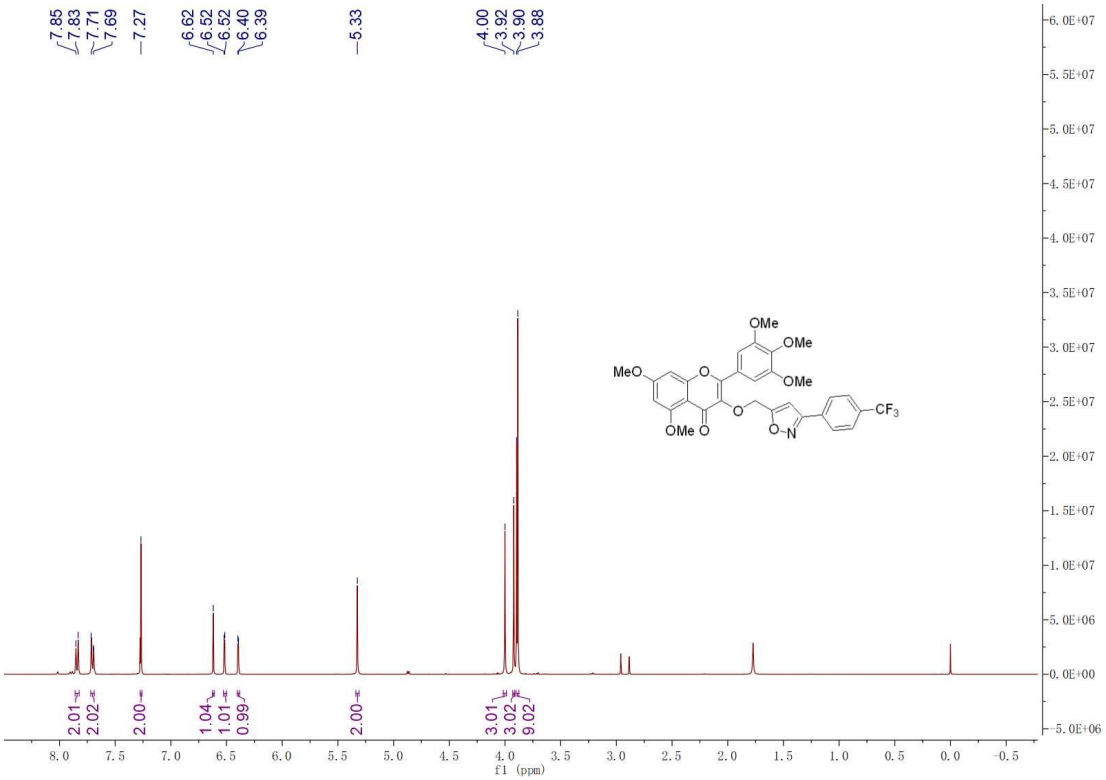
^{13}C NMR spectra of compound **Y11**



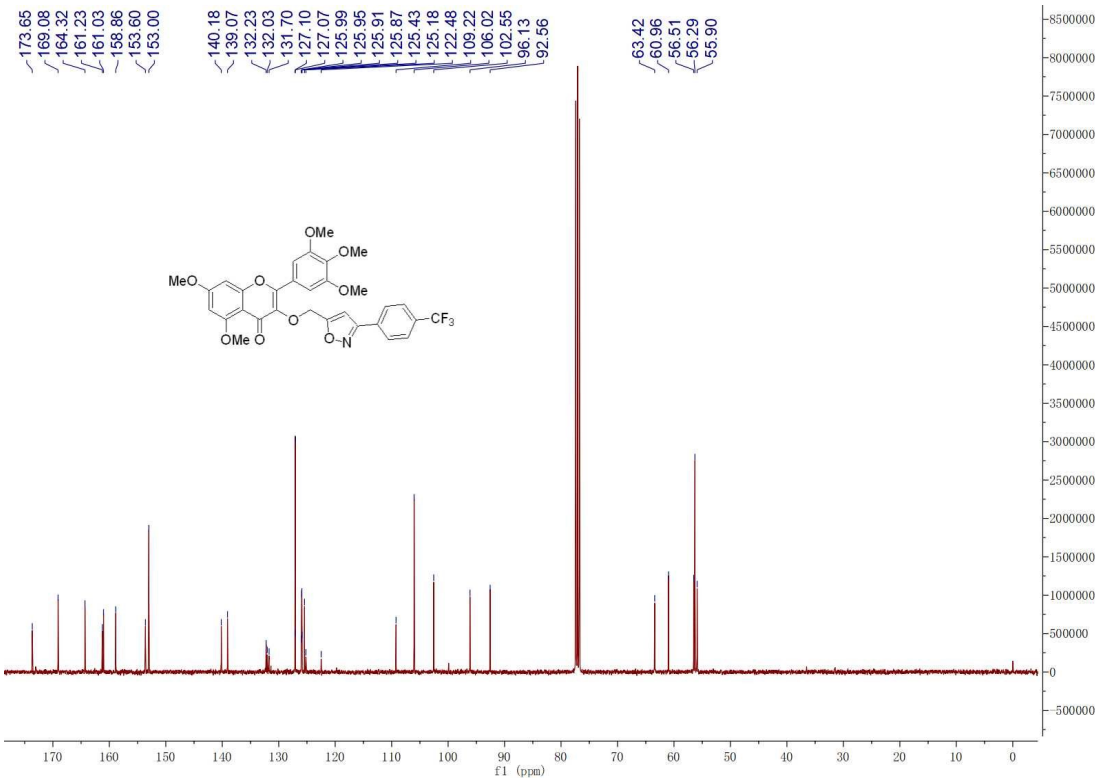
^{19}F NMR spectra of compound **Y11**



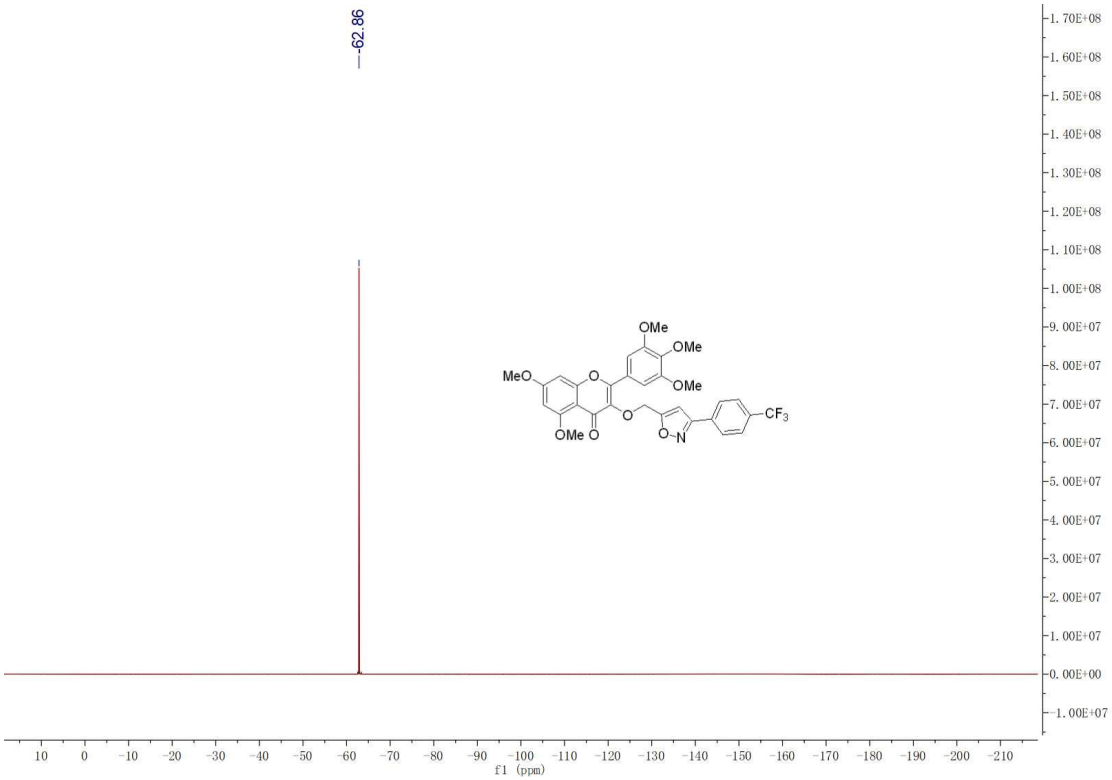
HRMS spectra of compound **Y11**



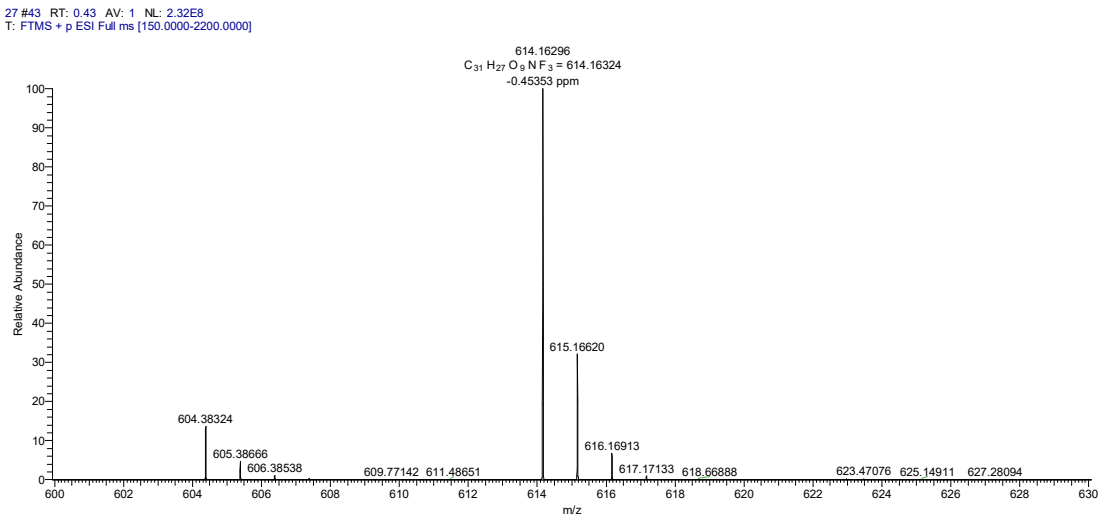
^{1}H NMR spectra of compound **Y12**



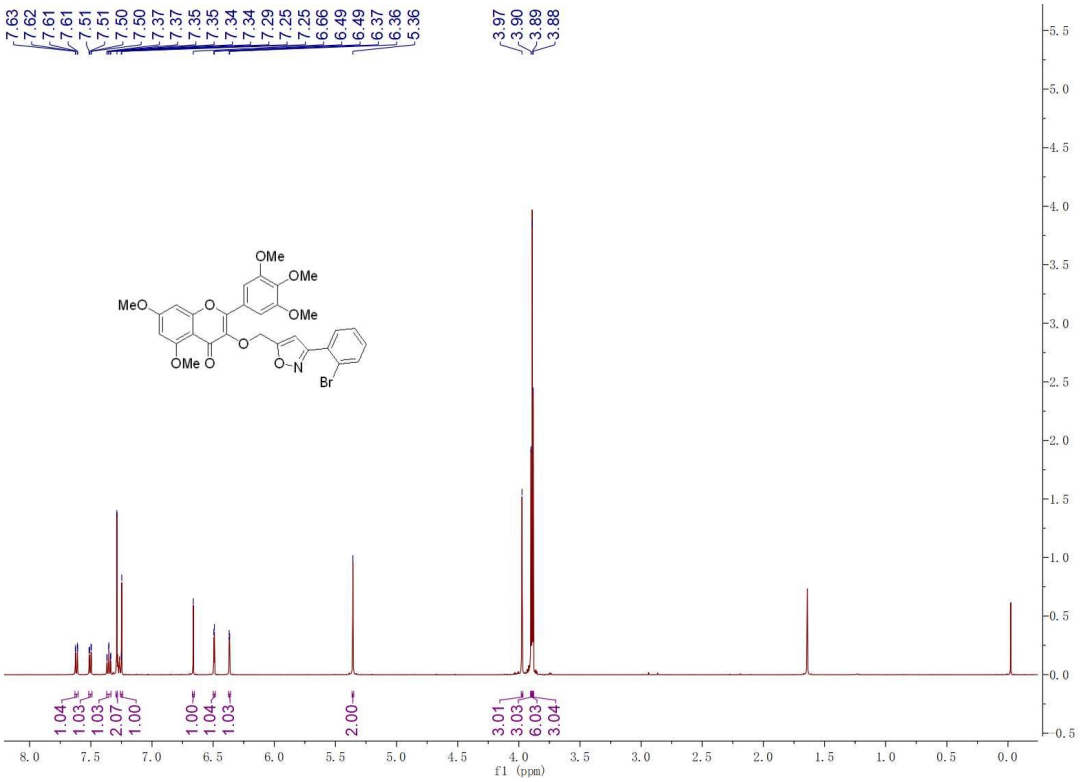
^{13}C NMR spectra of compound **Y12**



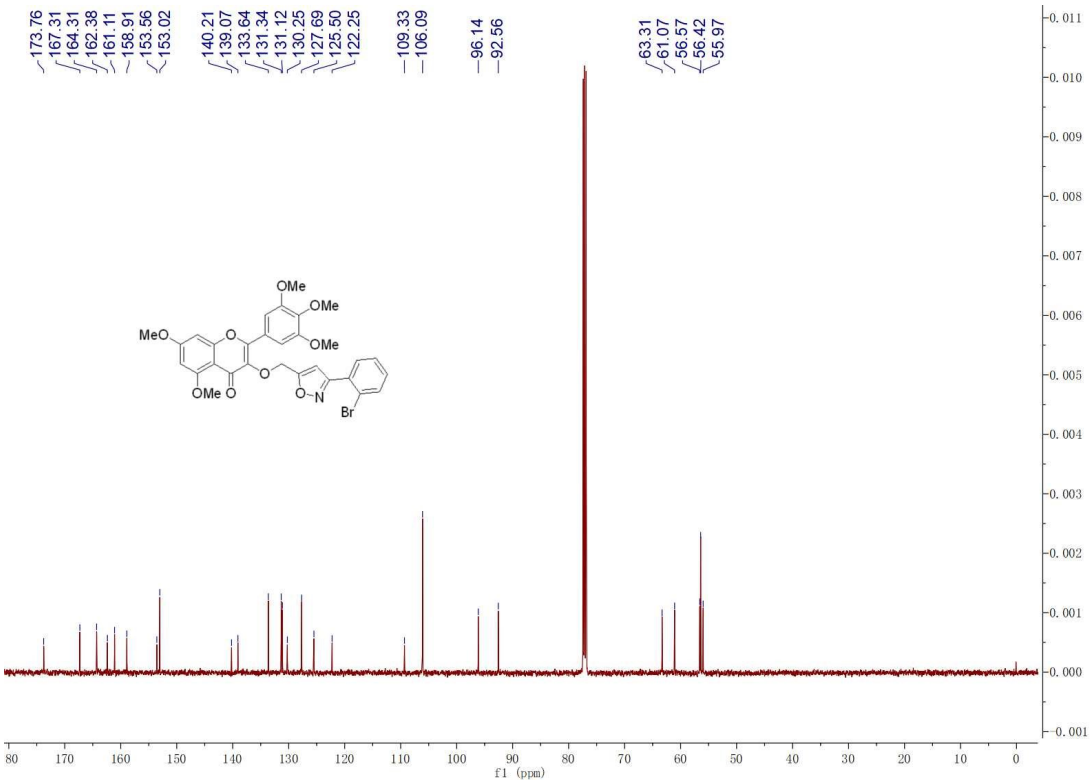
^{19}F NMR spectra of compound **Y12**



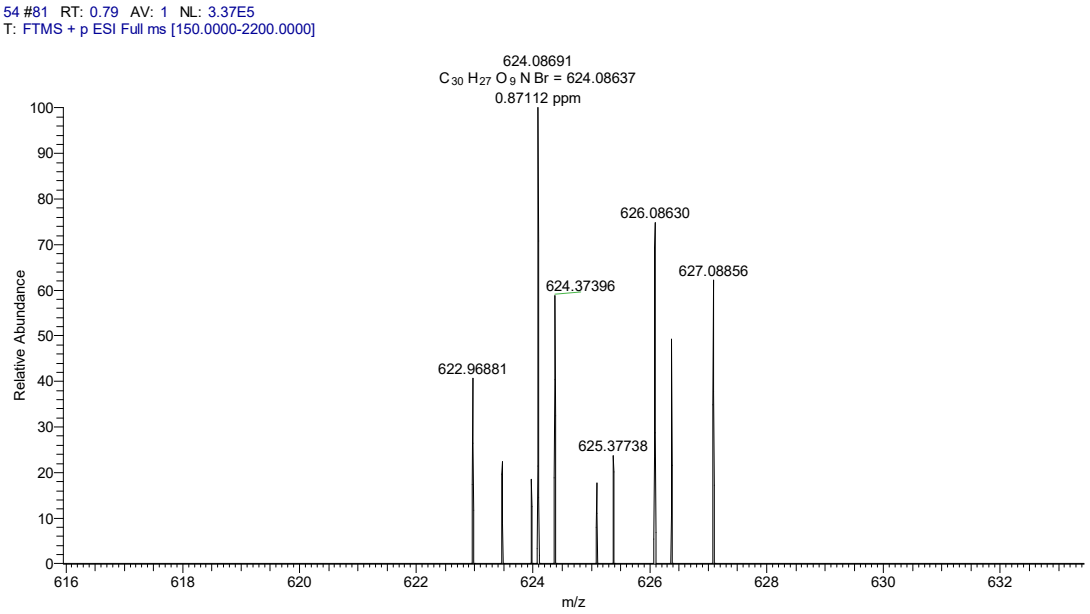
HRMS spectra of compound **Y12**



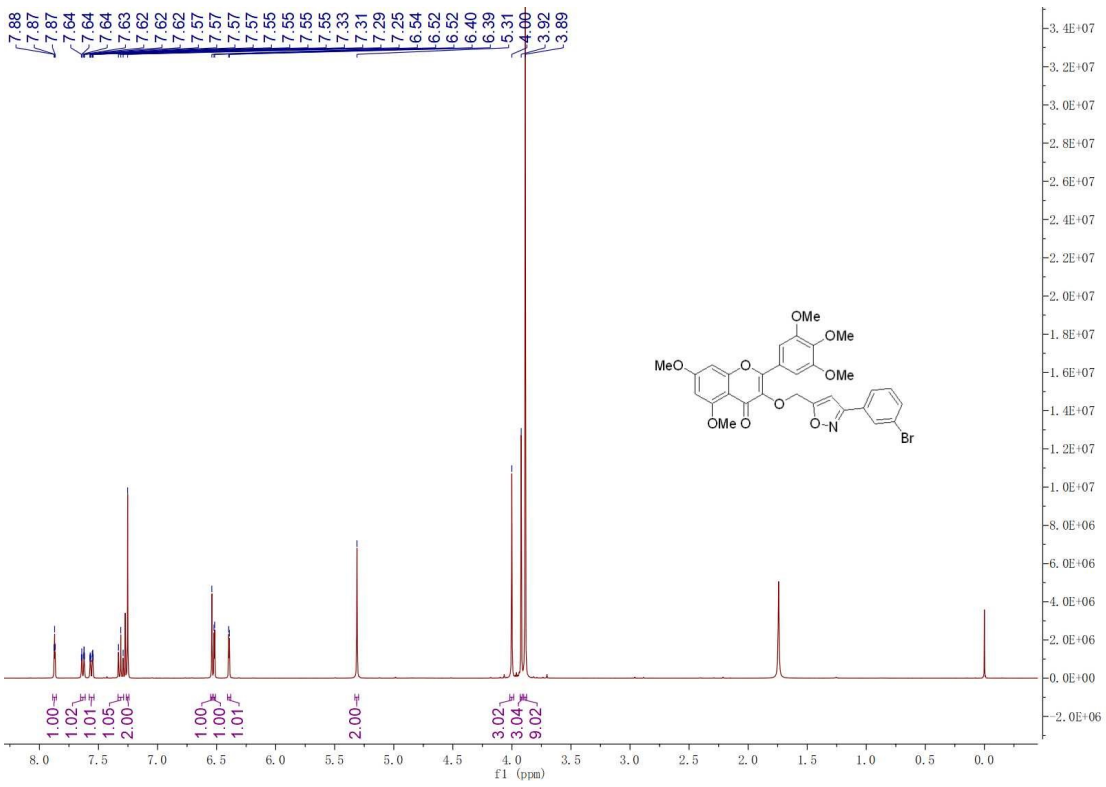
^{1}H NMR spectra of compound **Y13**



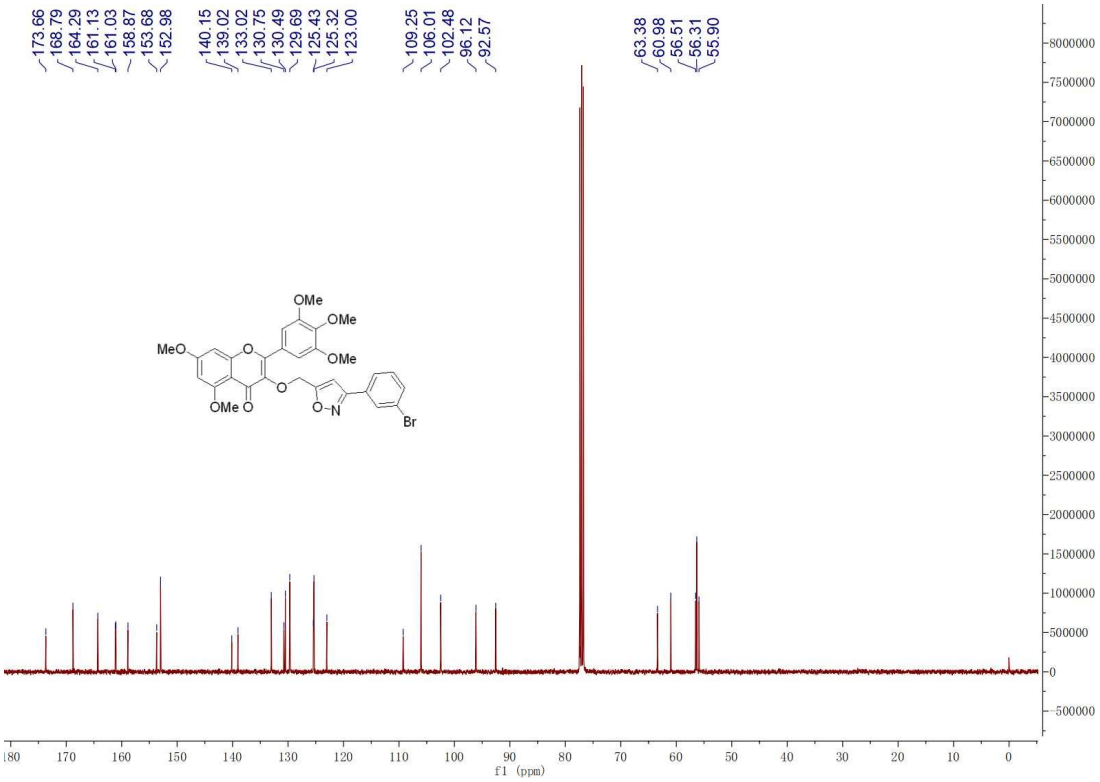
^{13}C NMR spectra of compound **Y13**



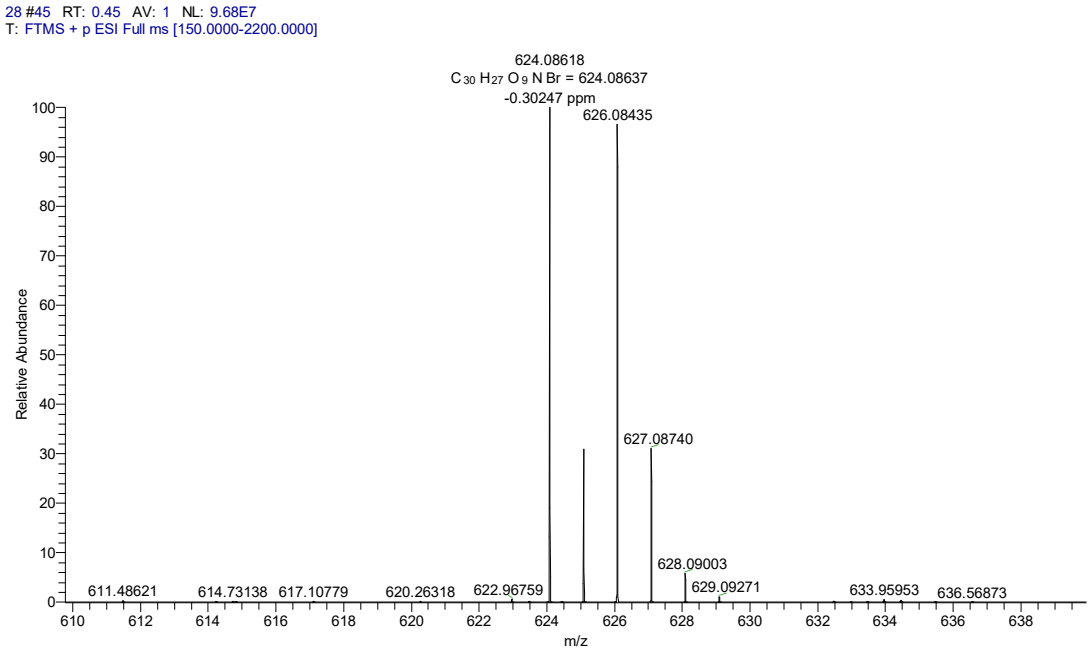
HRMS spectra of compound **Y13**



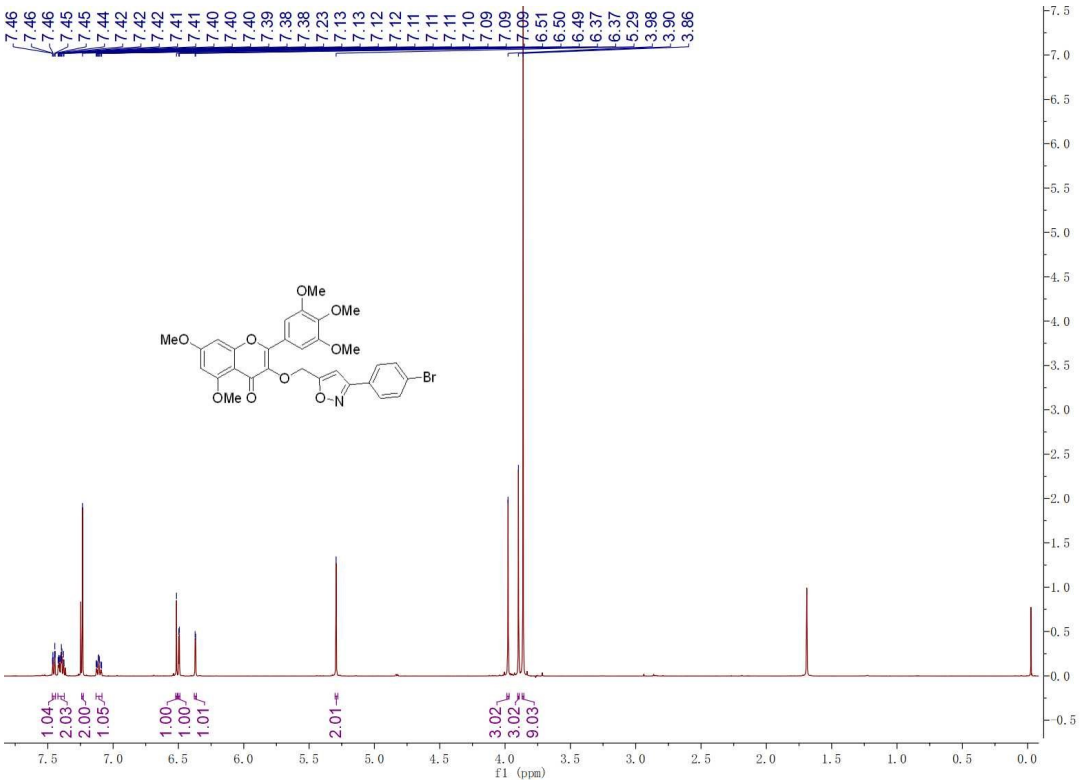
^{1}H NMR spectra of compound **Y14**



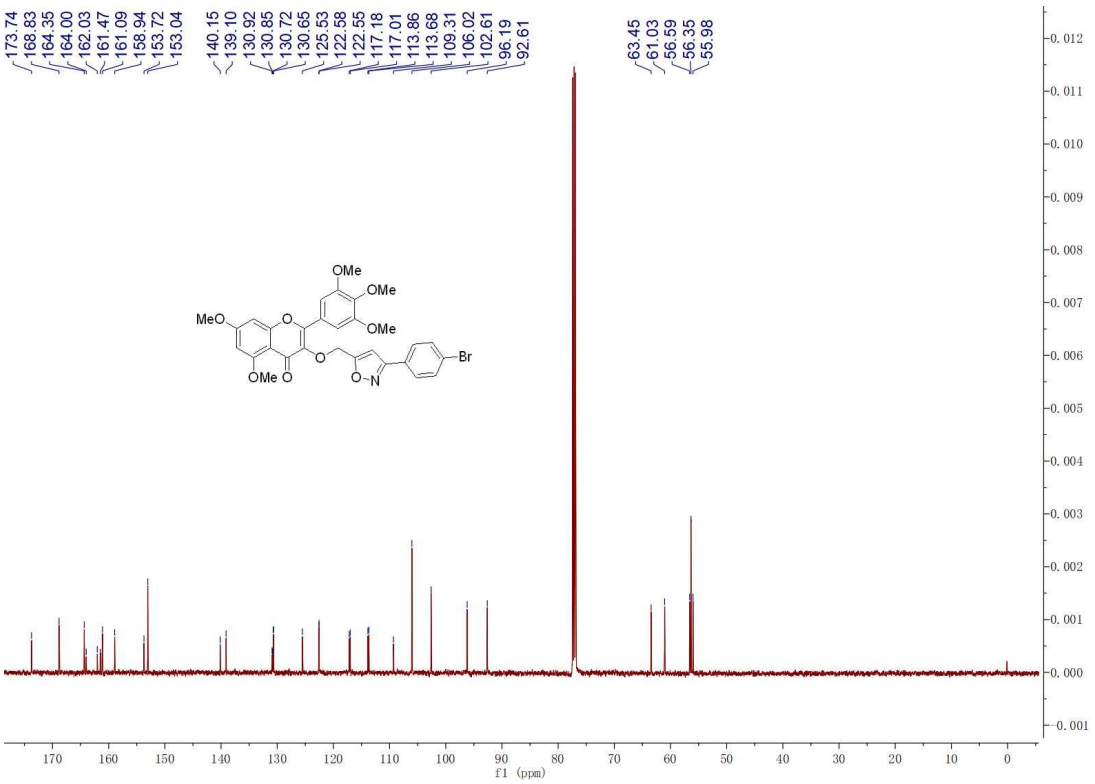
^{13}C NMR spectra of compound **Y14**



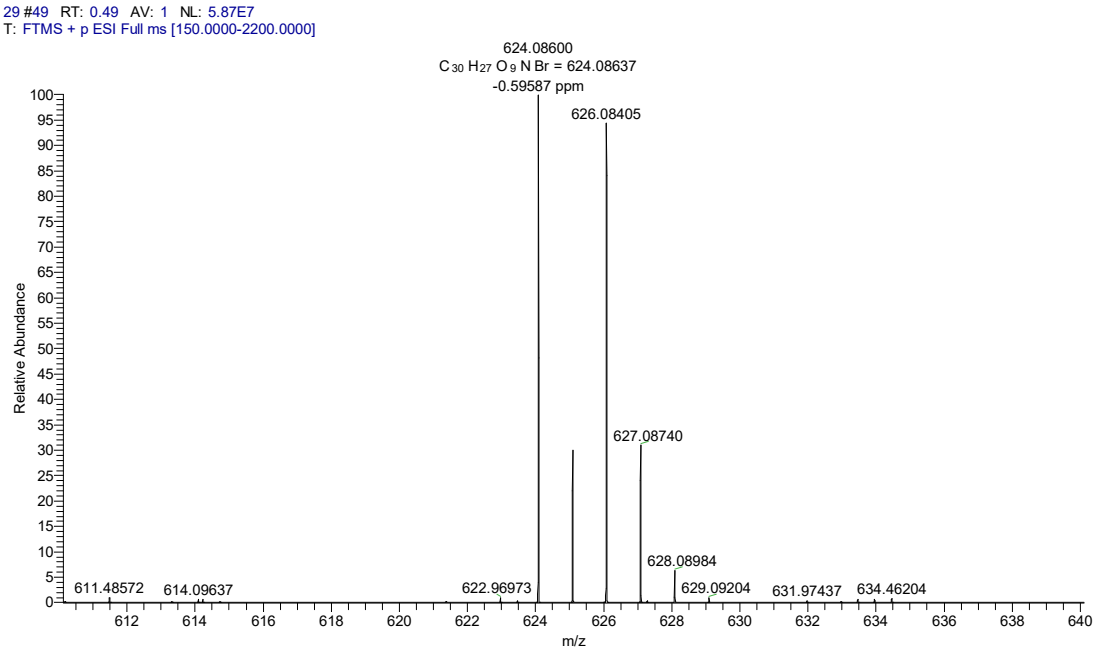
HRMS spectra of compound **Y14**



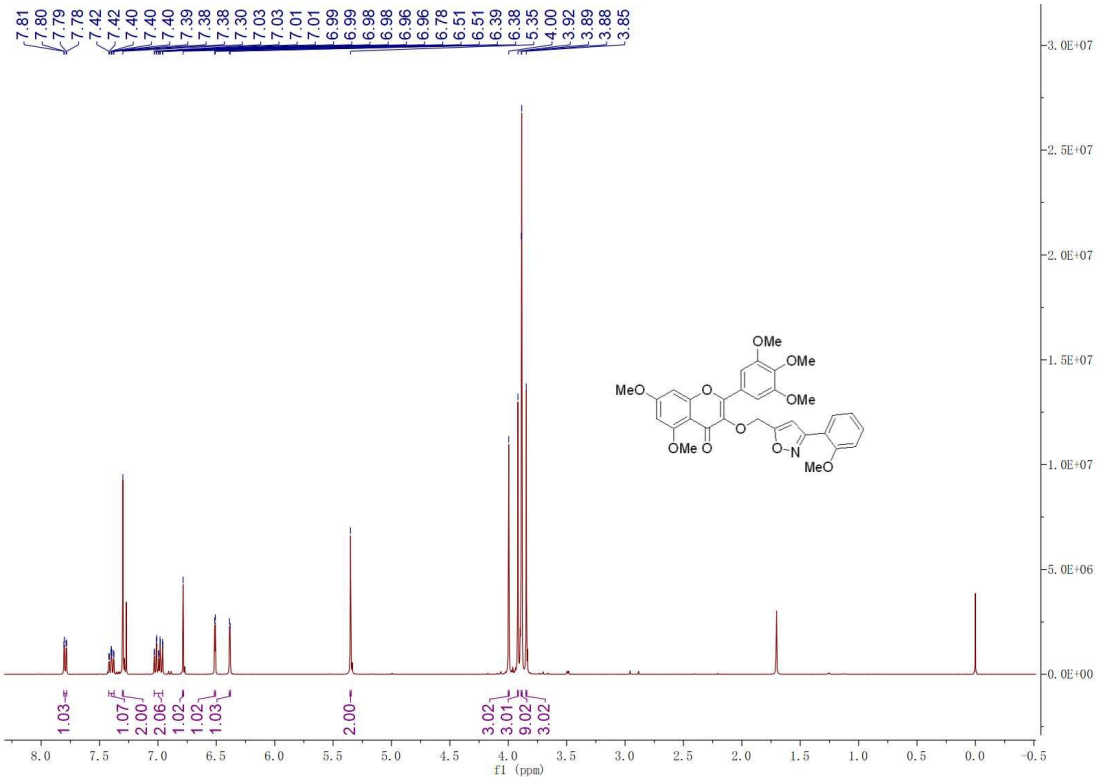
^{1}H NMR spectra of compound **Y15**



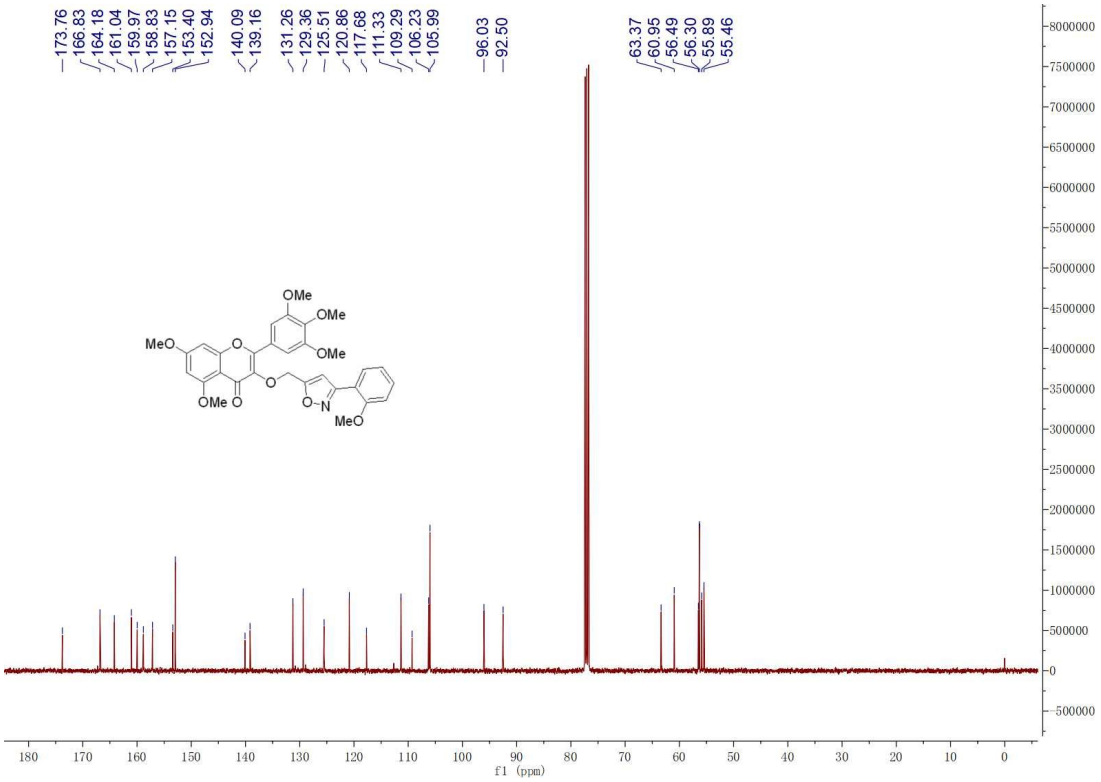
^{13}C NMR spectra of compound **Y15**



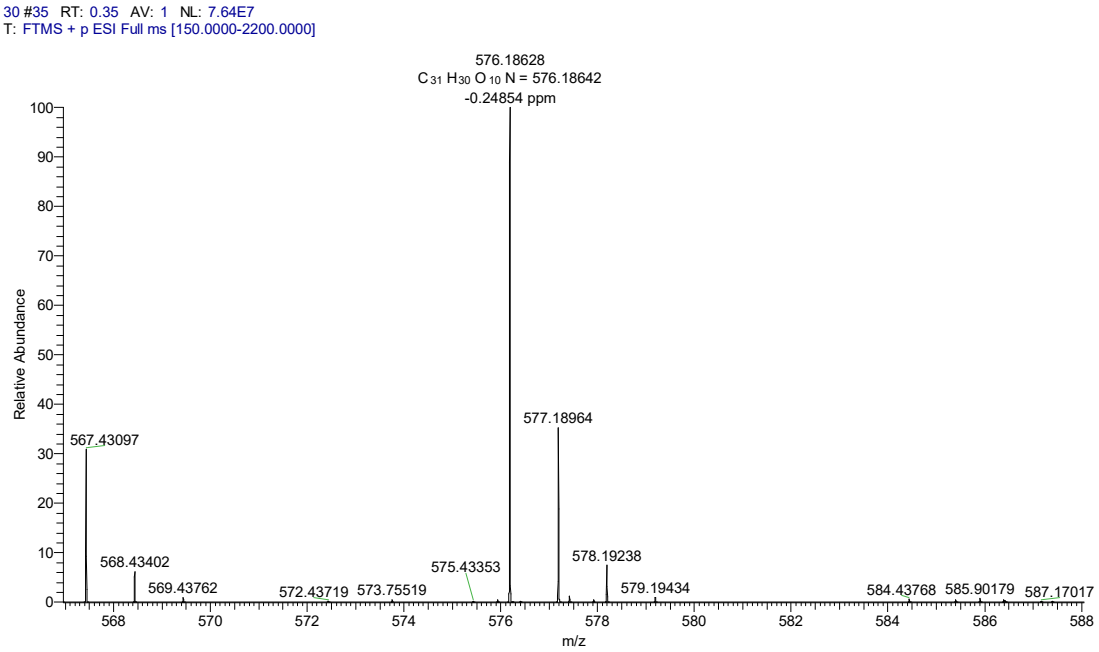
HRMS spectra of compound **Y15**



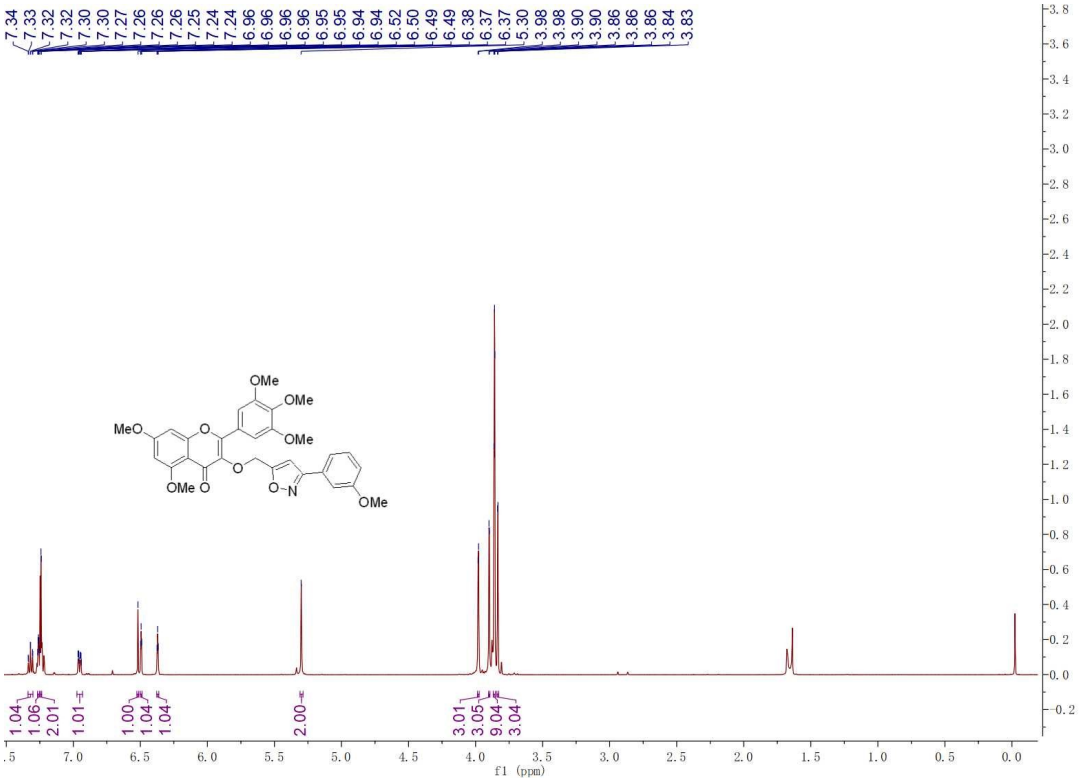
^{1}H NMR spectra of compound **Y16**



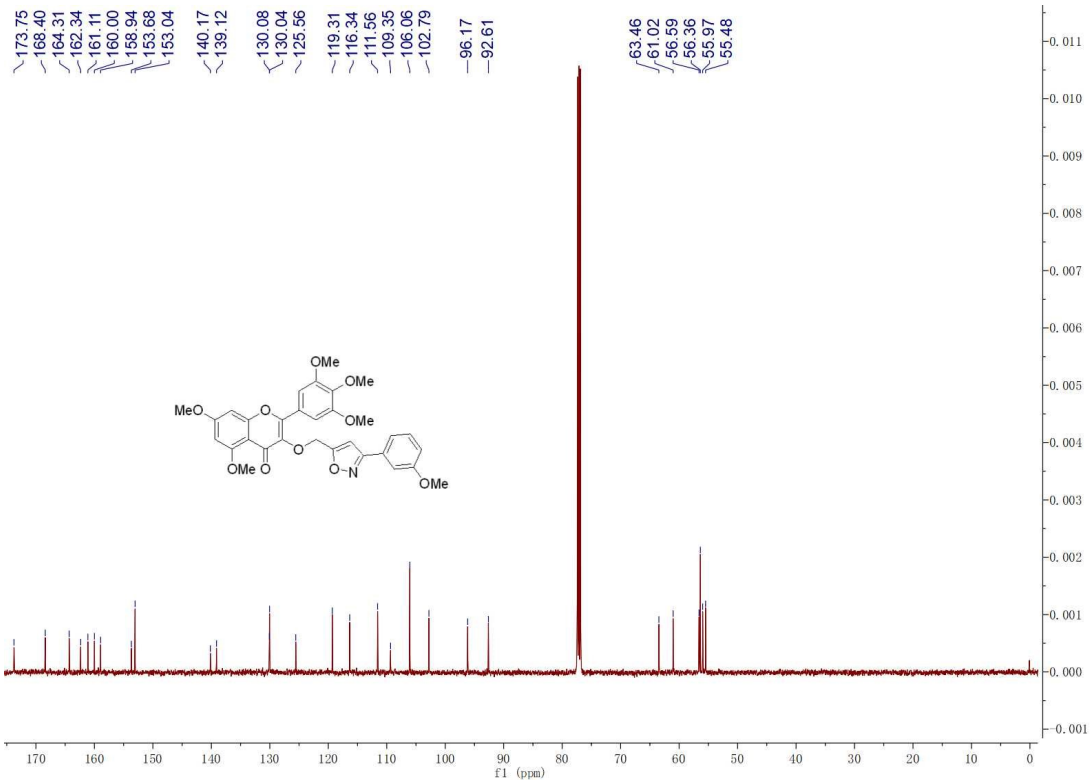
^{13}C NMR spectra of compound **Y16**



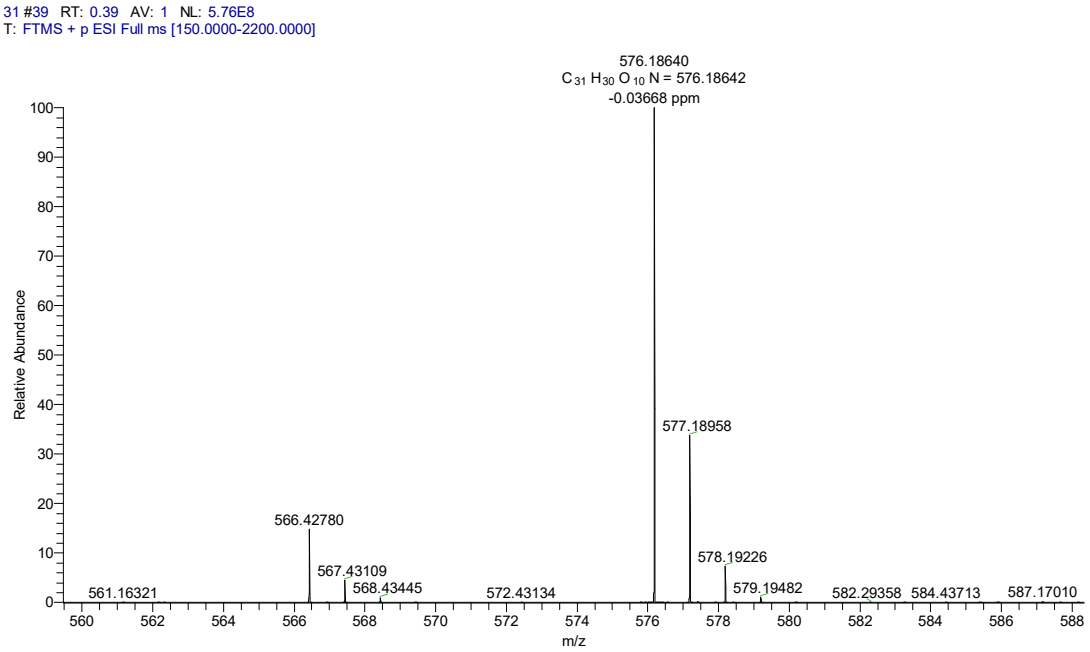
HRMS spectra of compound **Y16**



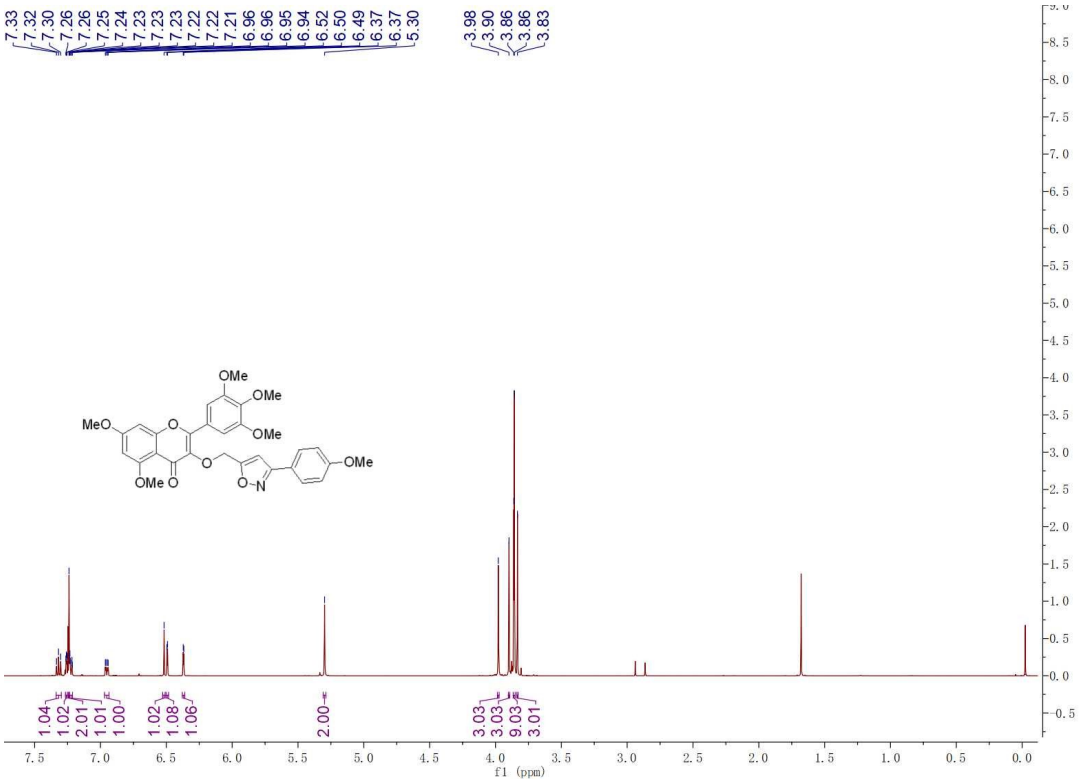
^{1}H NMR spectra of compound **Y17**



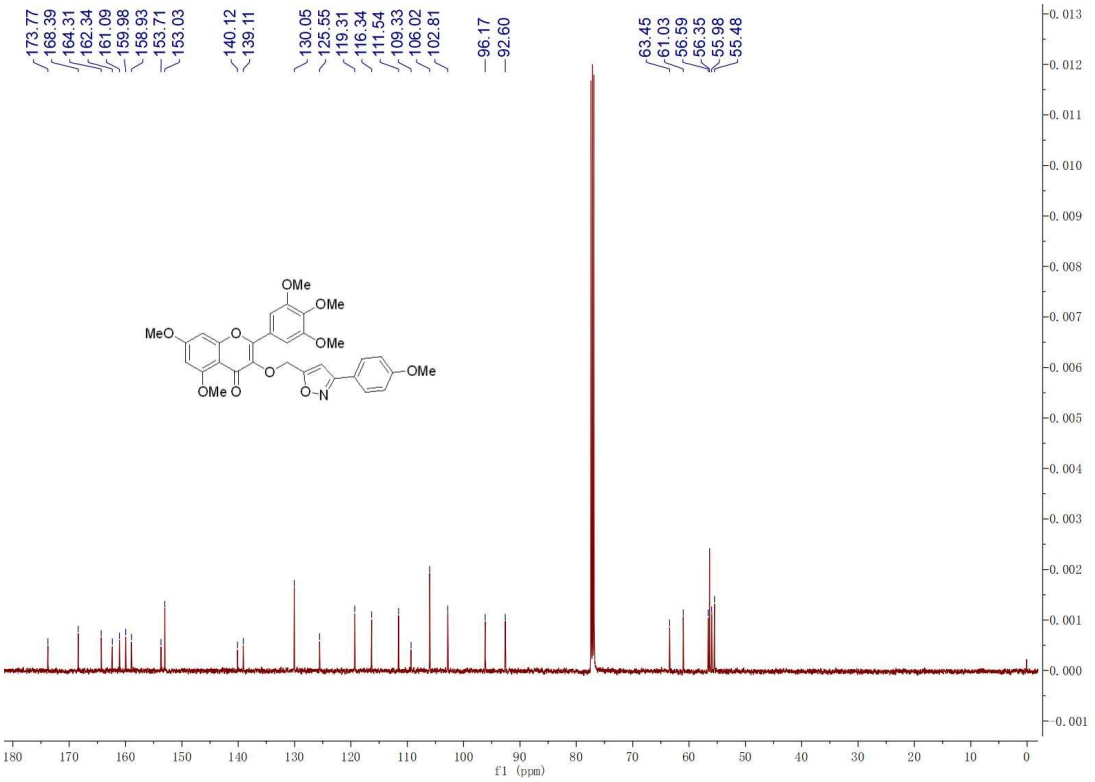
^{13}C NMR spectra of compound **Y17**



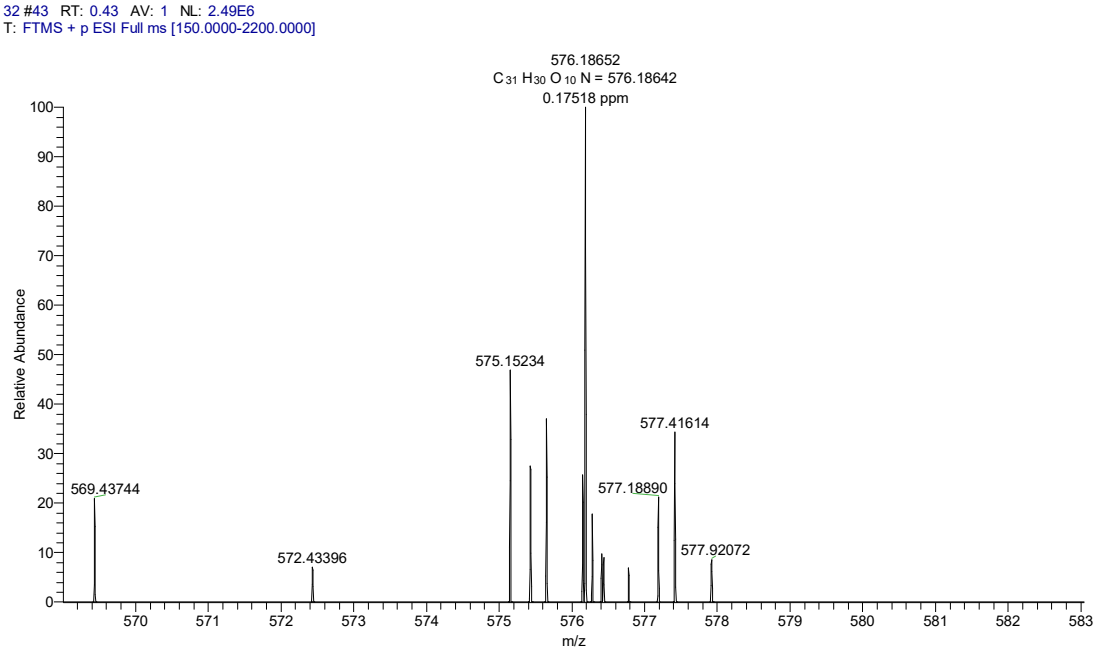
HRMS spectra of compound **Y17**



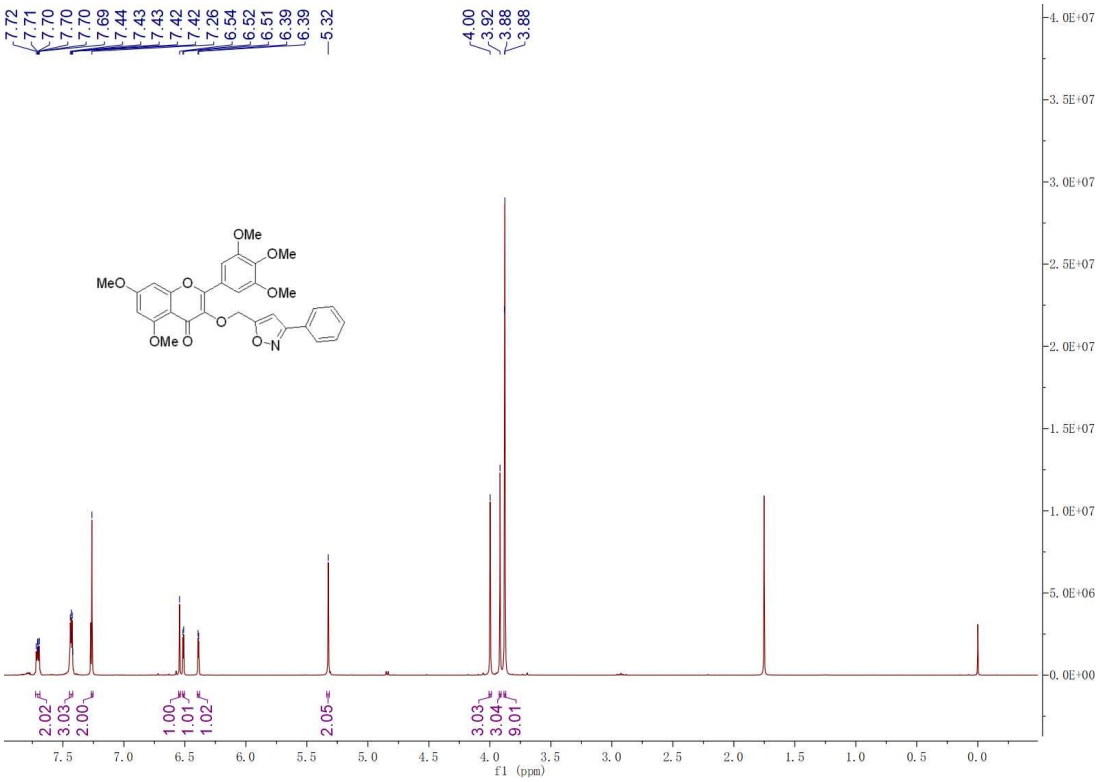
^{1}H NMR spectra of compound **Y18**



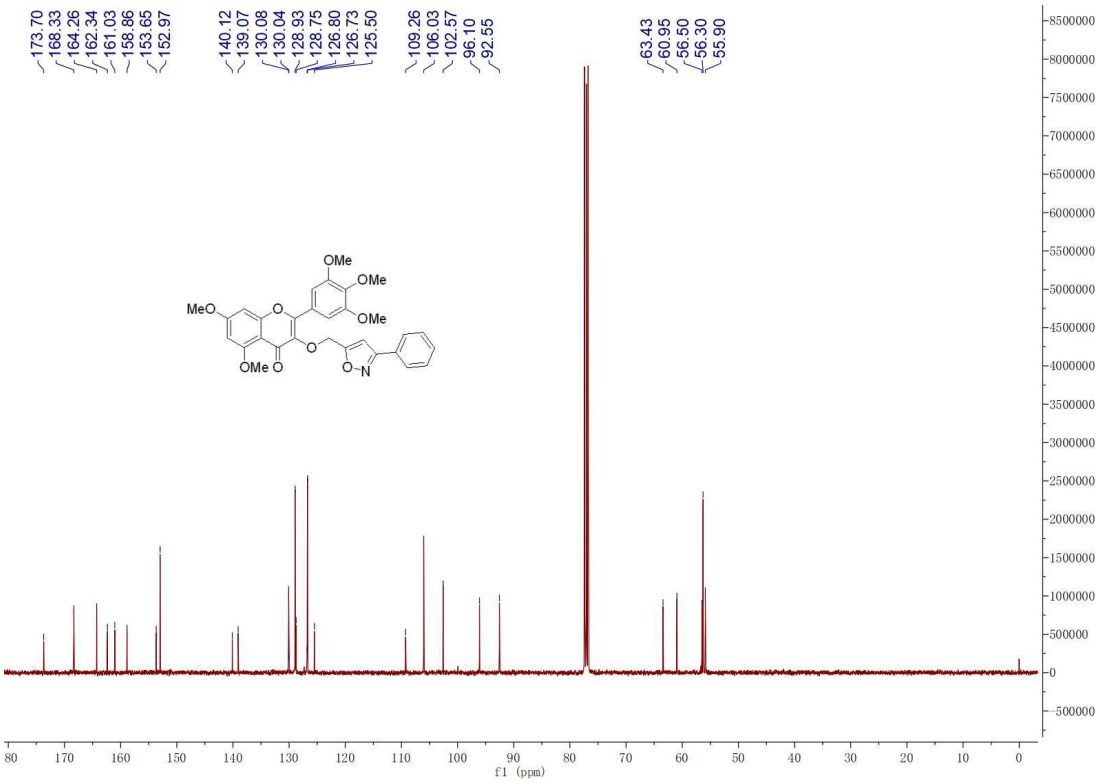
^{13}C NMR spectra of compound **Y18**



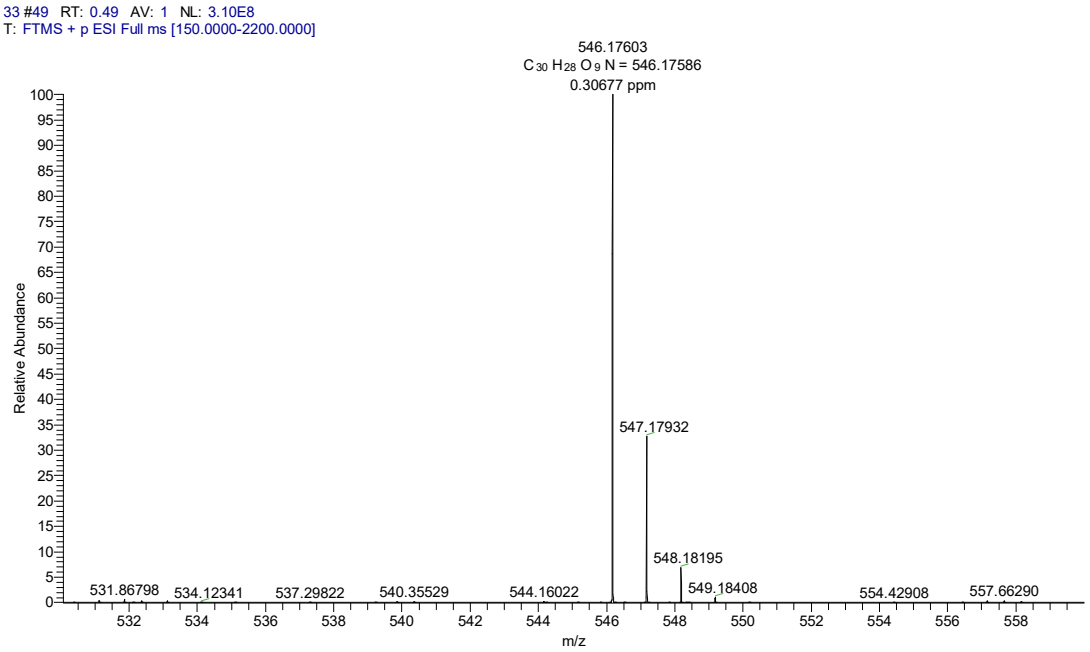
HRMS spectra of compound **Y18**



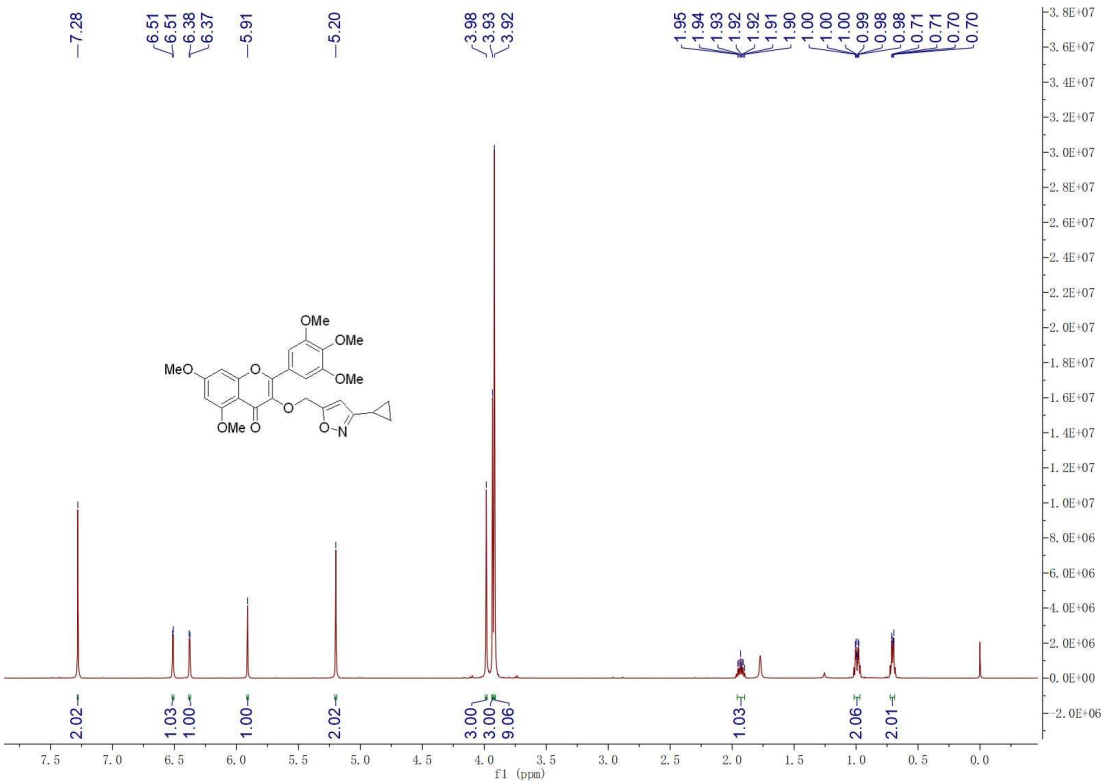
^{1}H NMR spectra of compound **Y19**



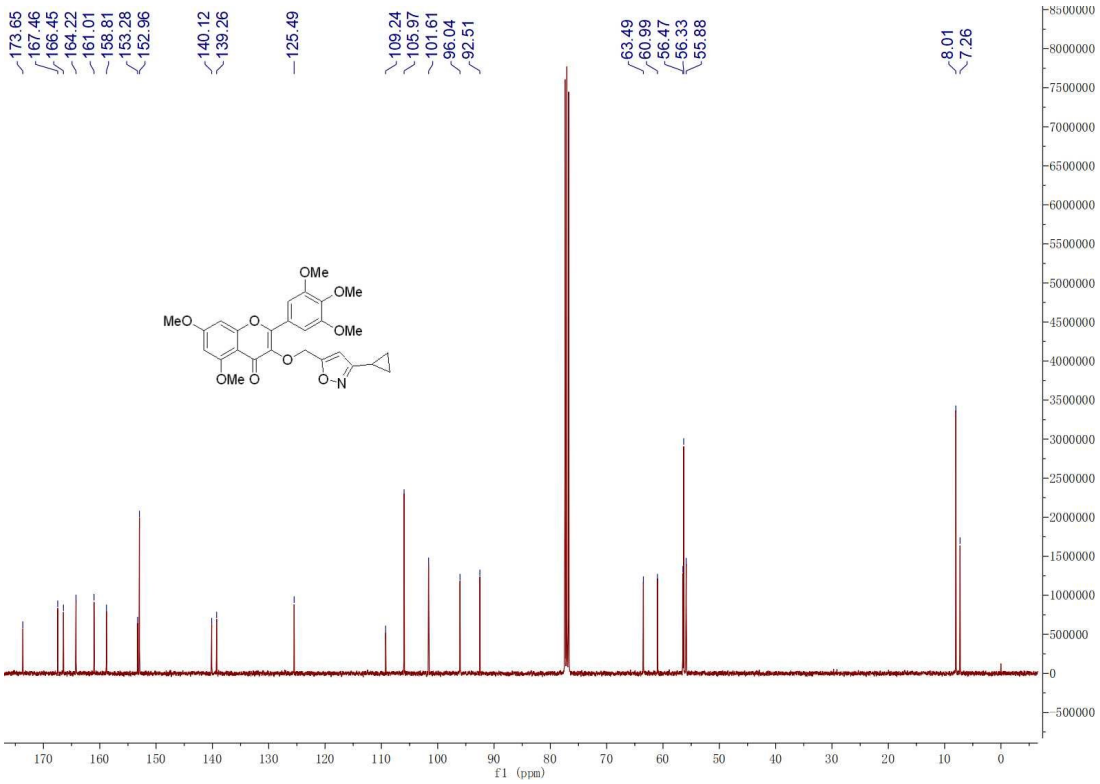
^{13}C NMR spectra of compound **Y19**



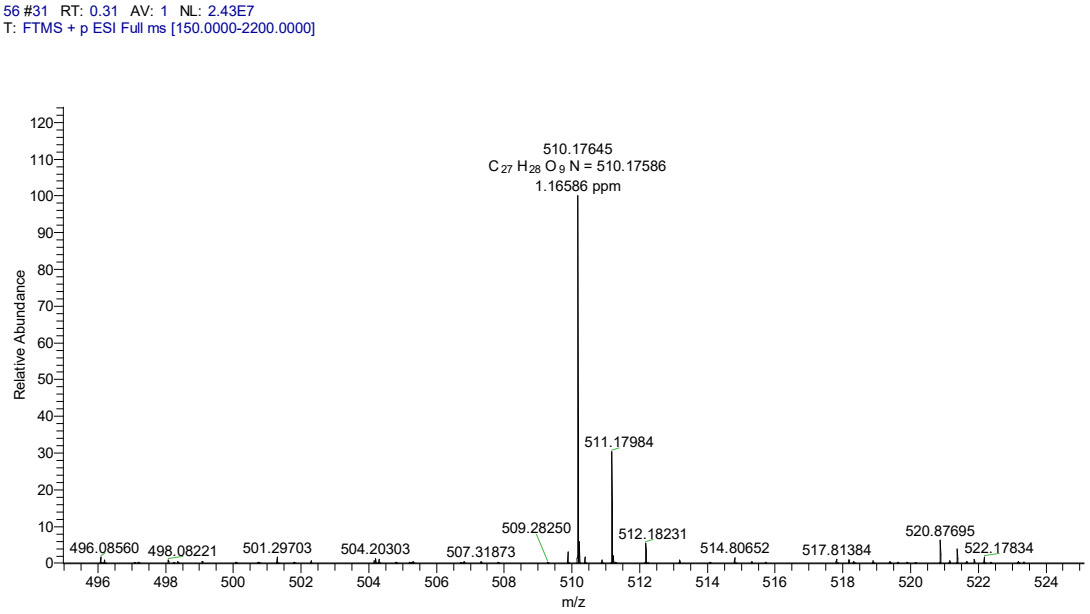
HRMS spectra of compound **Y19**



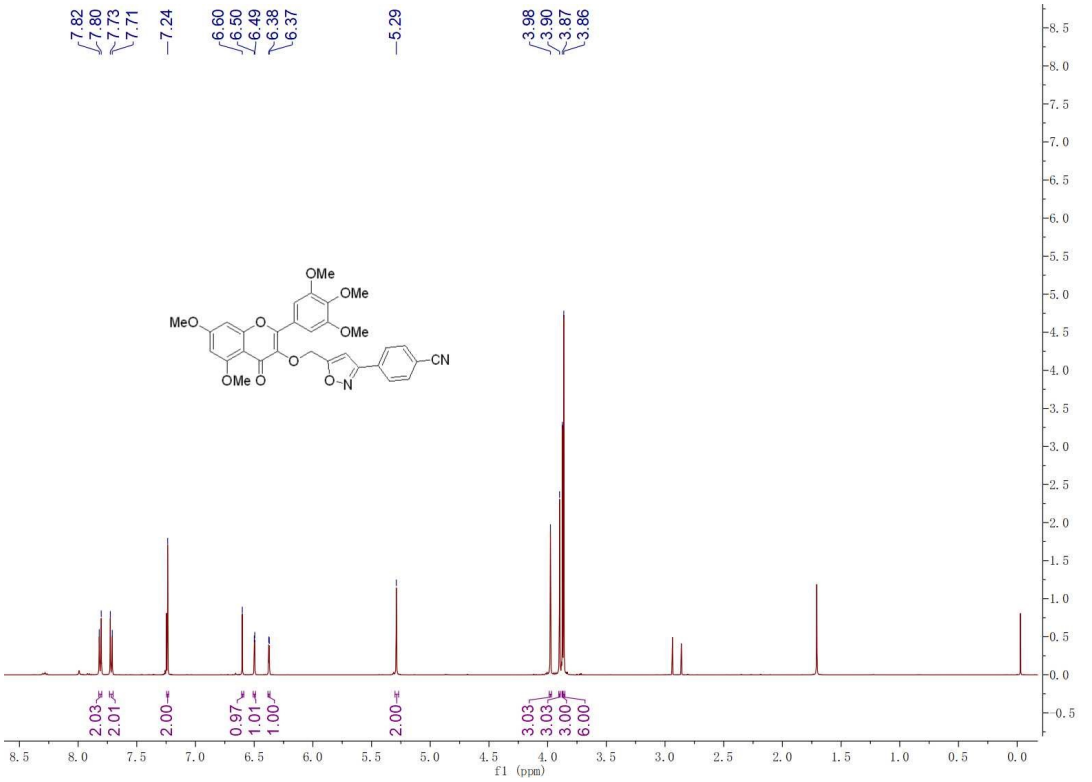
^{1}H NMR spectra of compound **Y20**



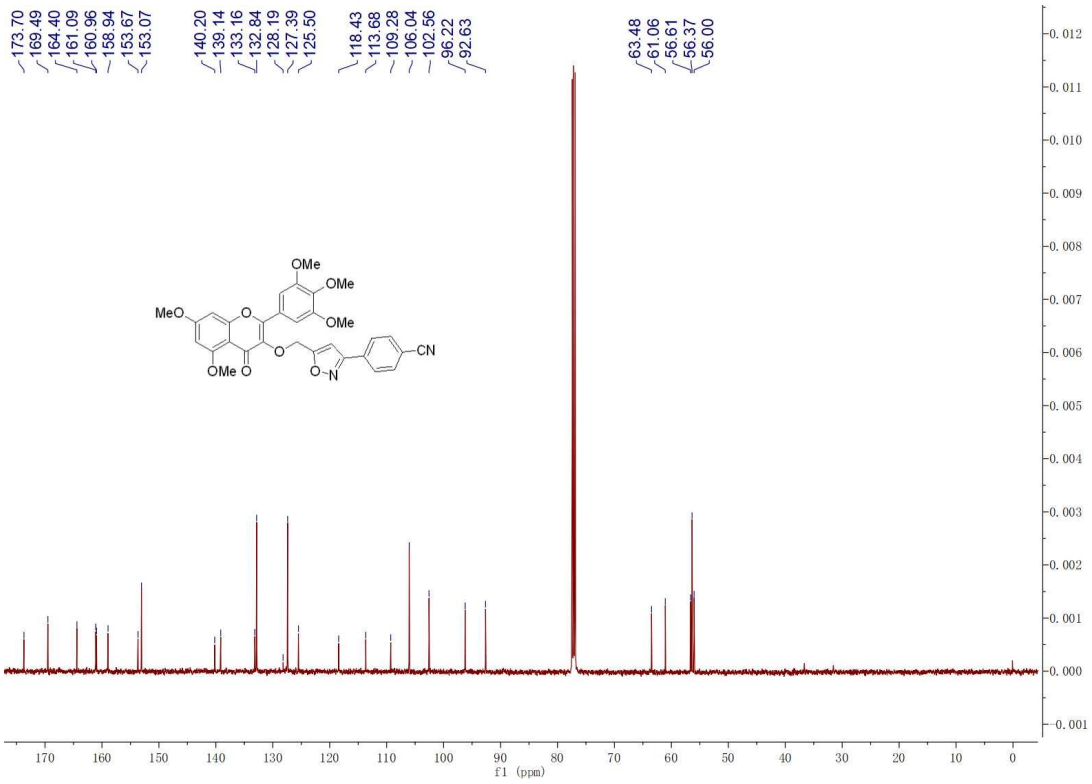
^{13}C NMR spectra of compound **Y20**



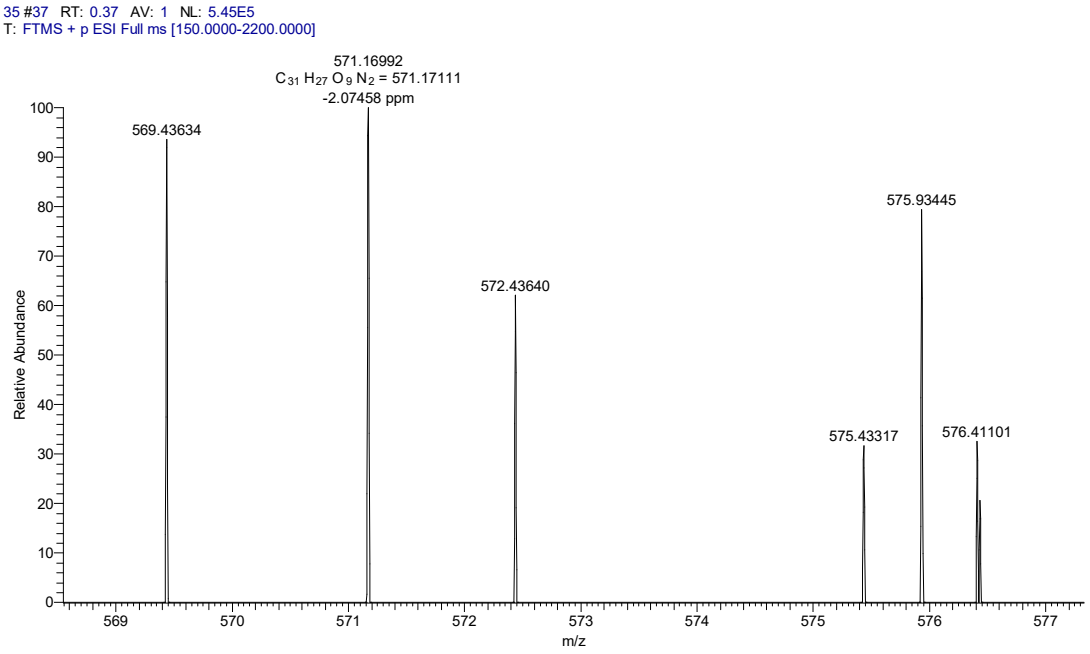
HRMS spectra of compound **Y20**



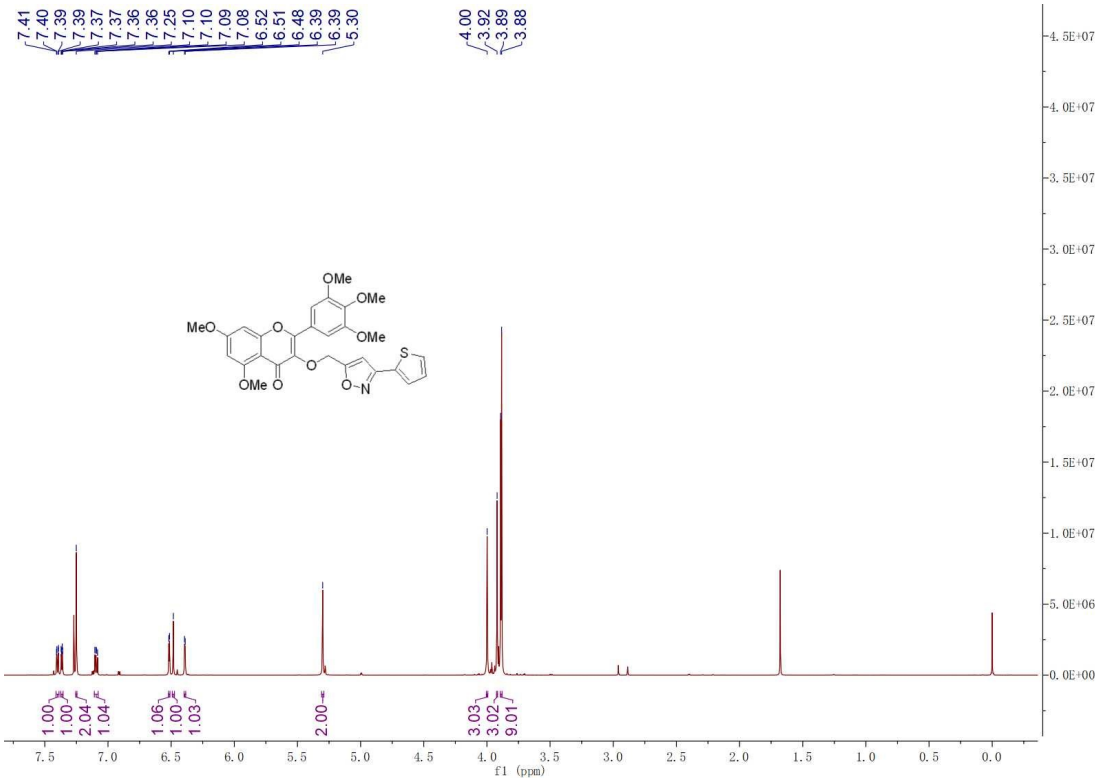
^{1}H NMR spectra of compound **Y21**



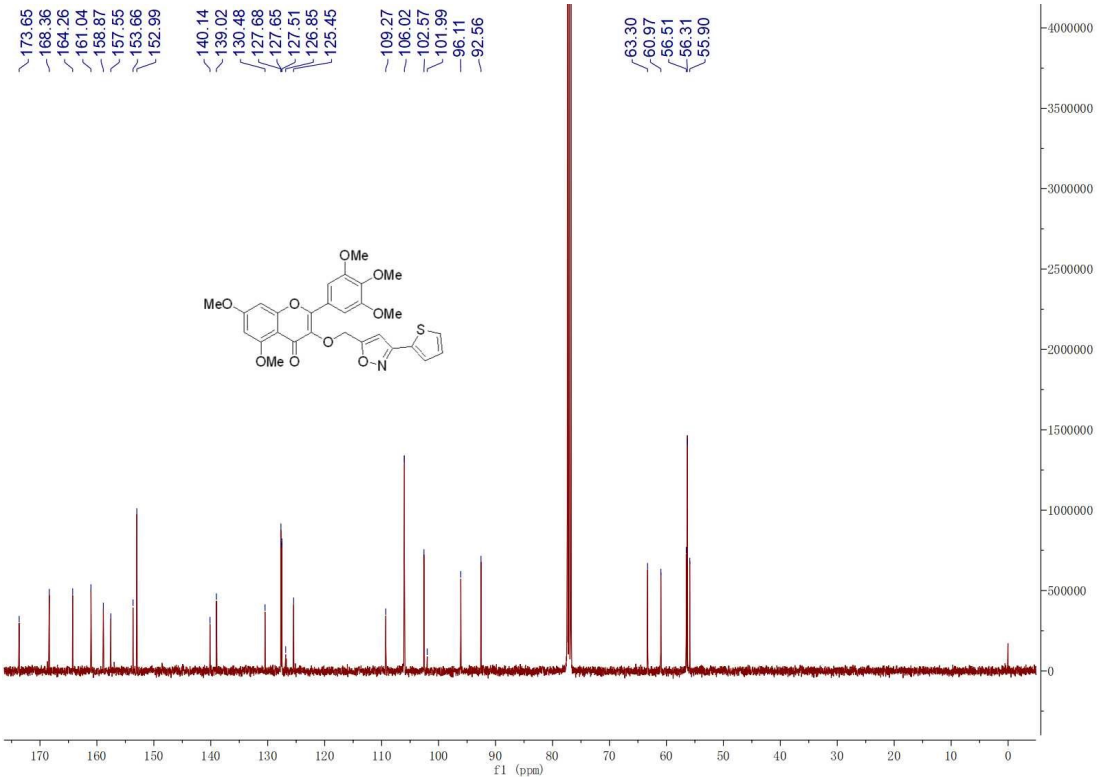
^{13}C NMR spectra of compound **Y21**



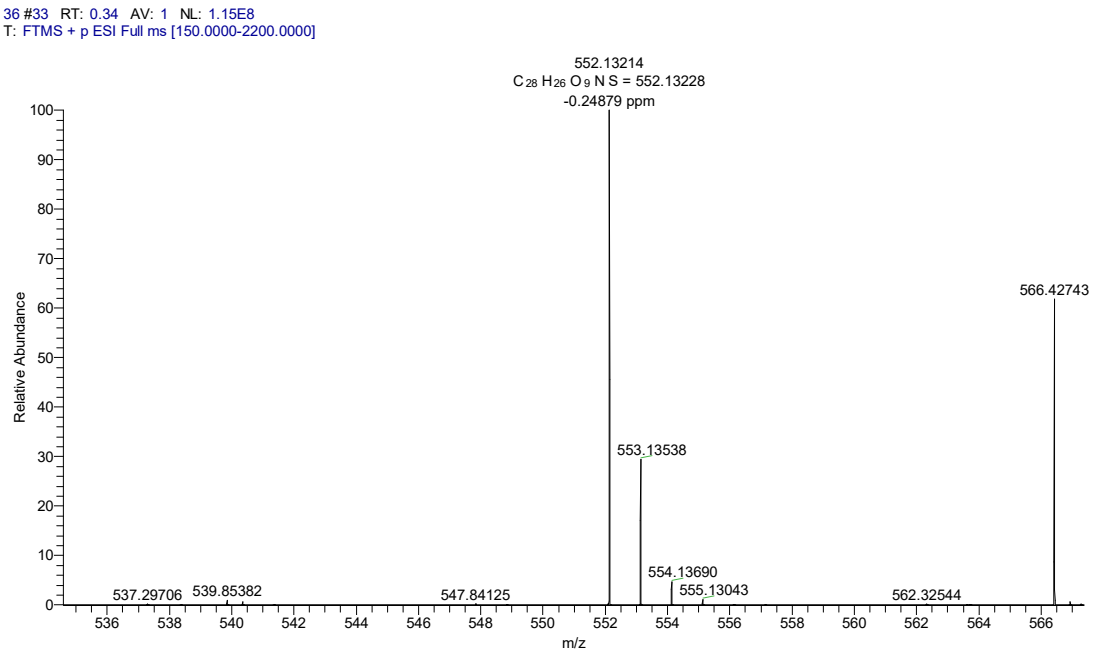
HRMS spectra of compound **Y21**



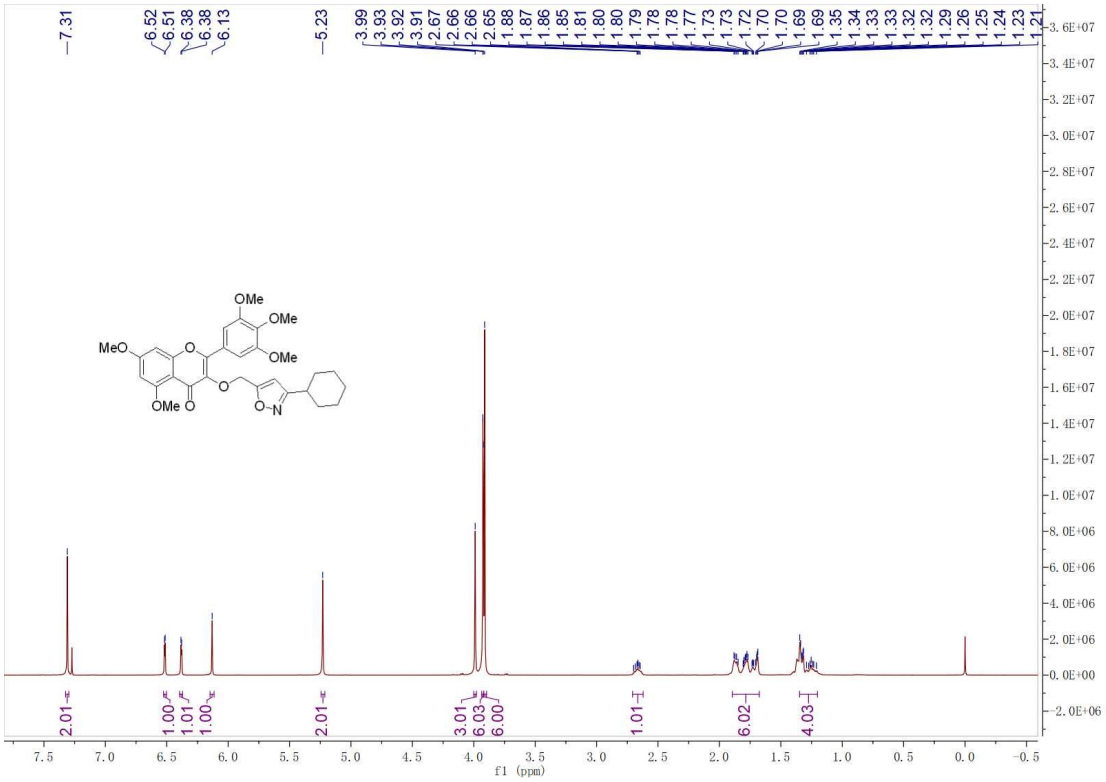
^{1}H NMR spectra of compound **Y22**



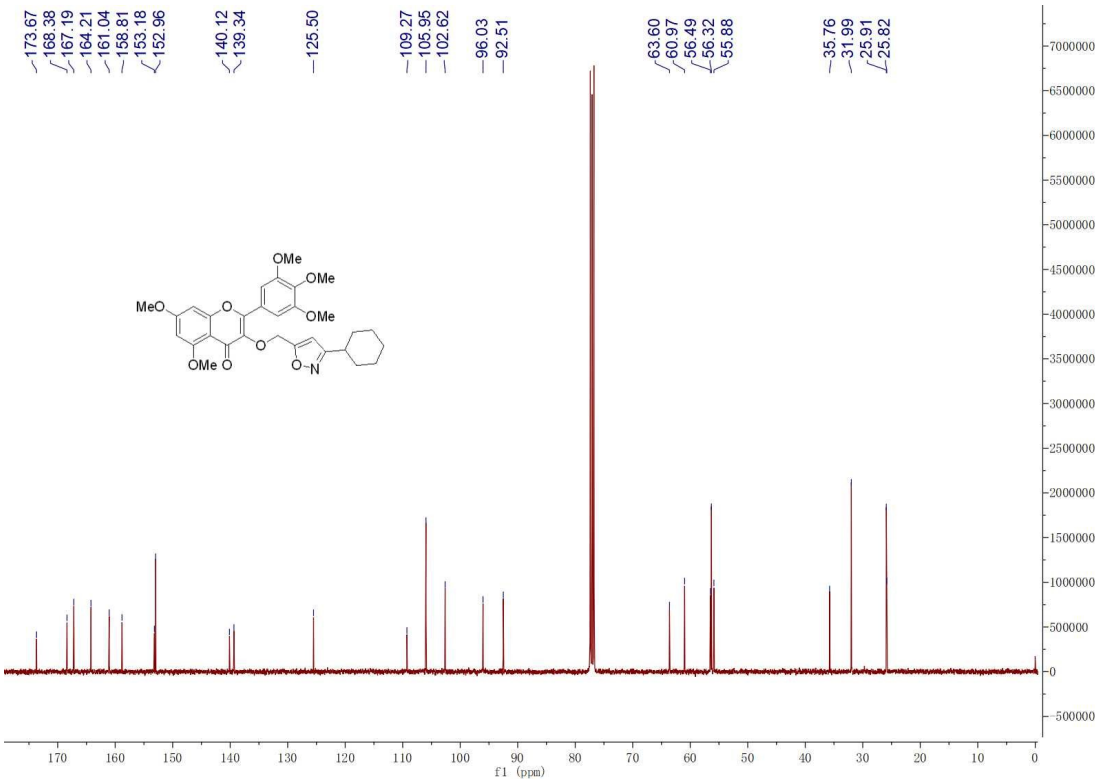
^{13}C NMR spectra of compound **Y22**



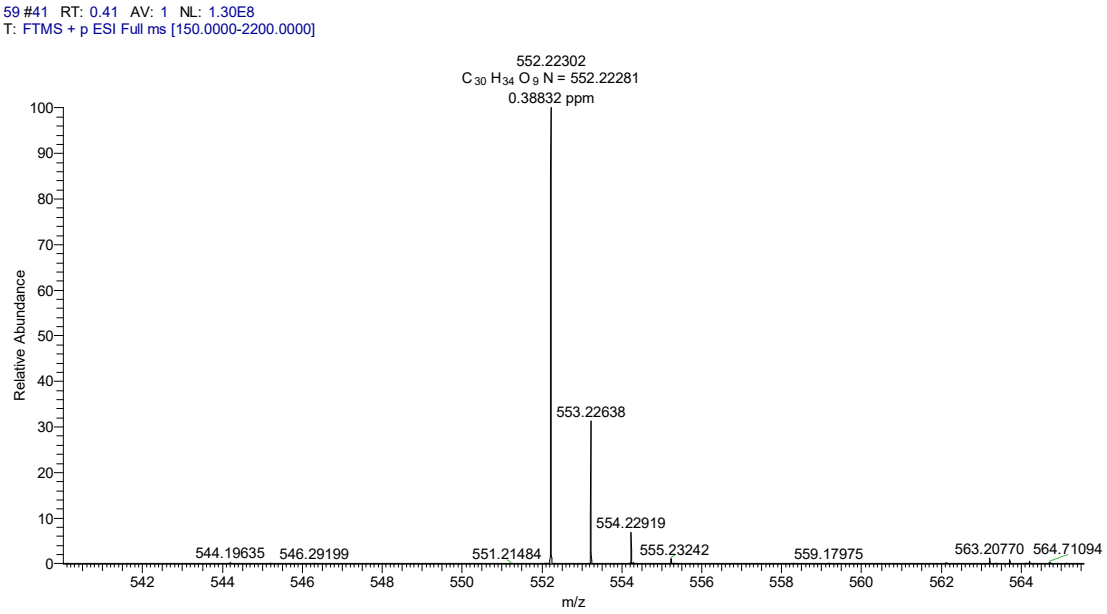
HRMS spectra of compound **Y22**



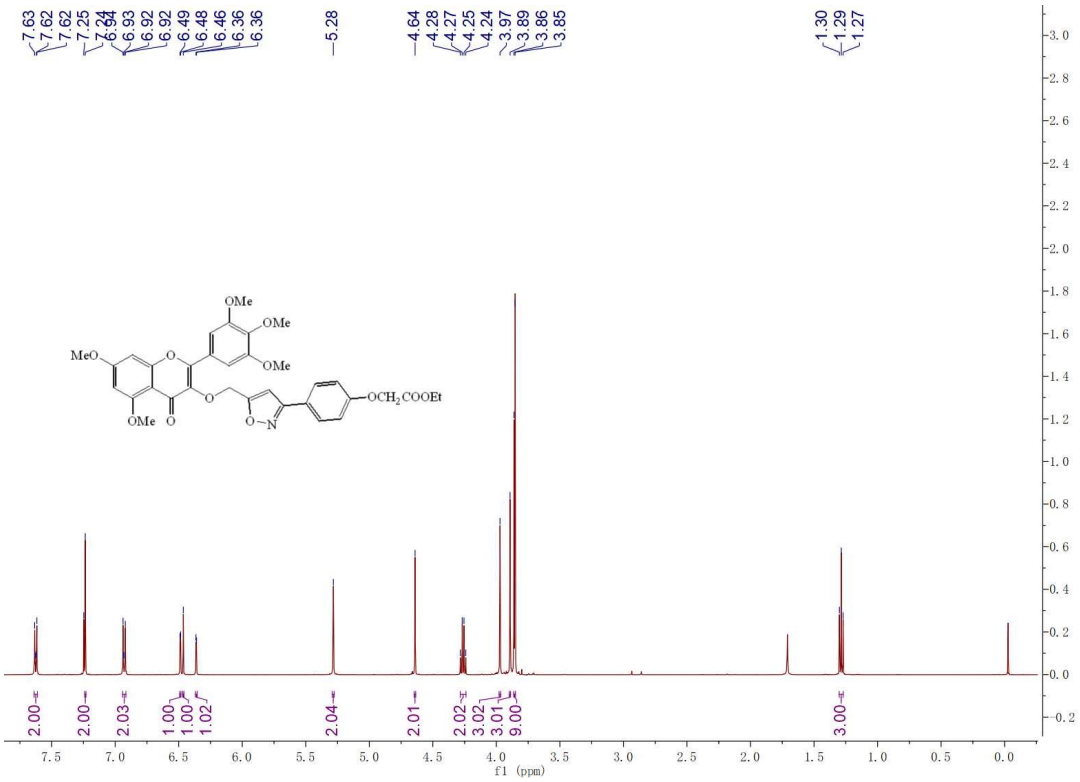
^{1}H NMR spectra of compound **Y23**



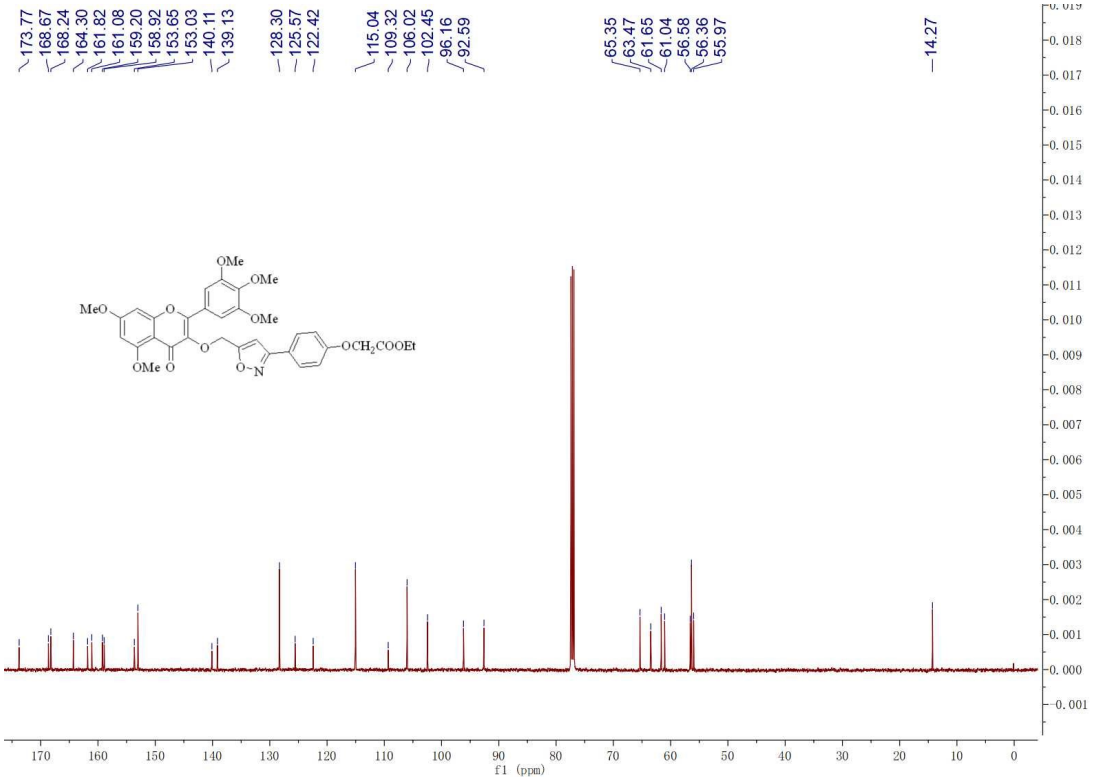
^{13}C NMR spectra of compound **Y23**



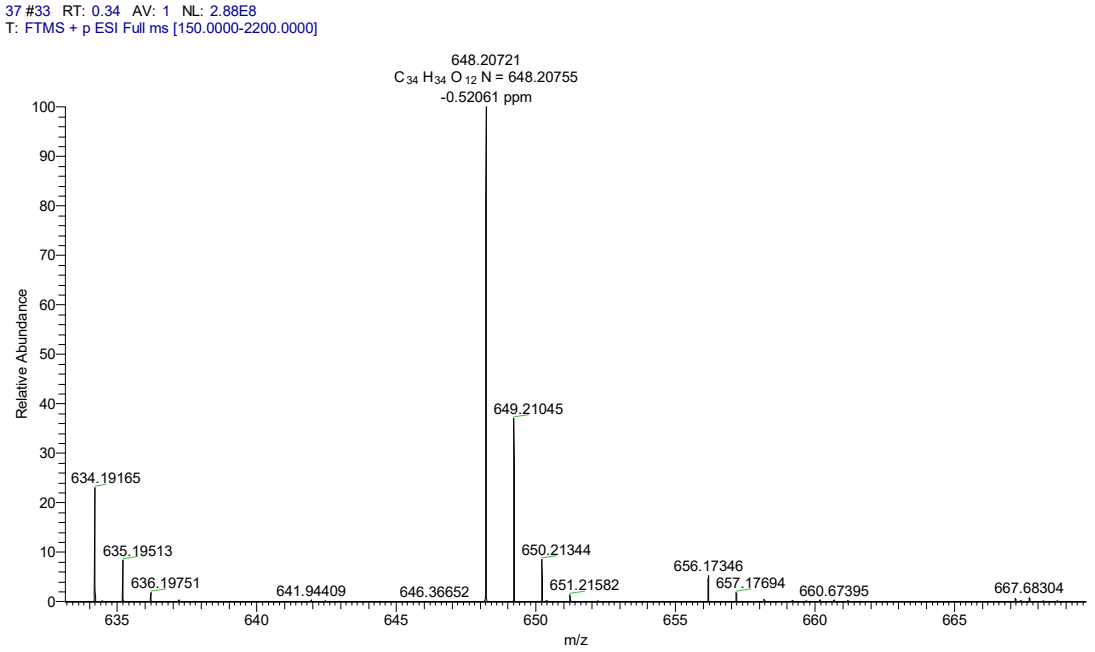
HRMS spectra of compound **Y23**



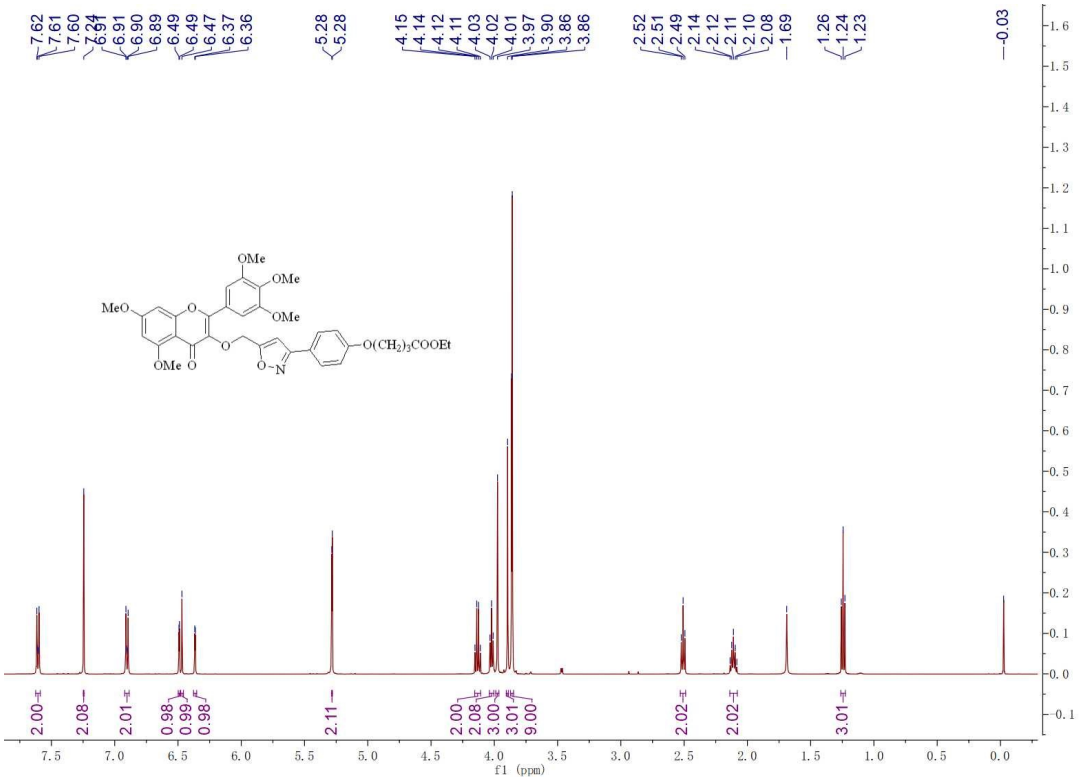
^{1}H NMR spectra of compound **Y24**



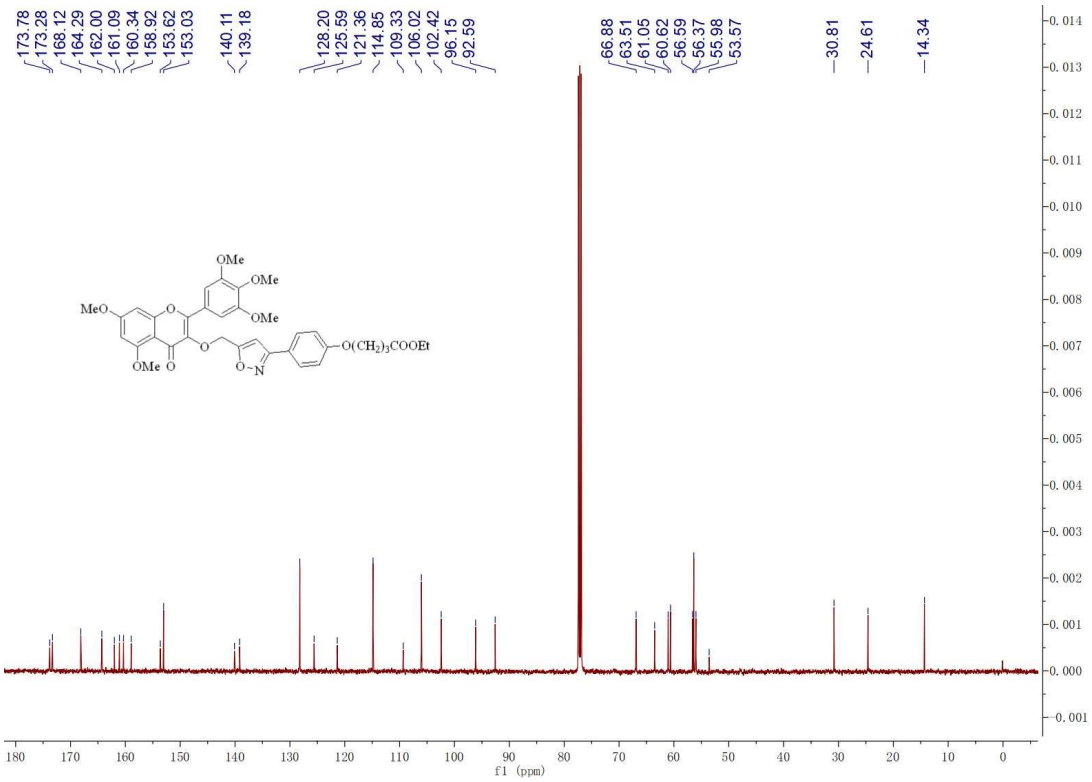
^{13}C NMR spectra of compound **Y24**



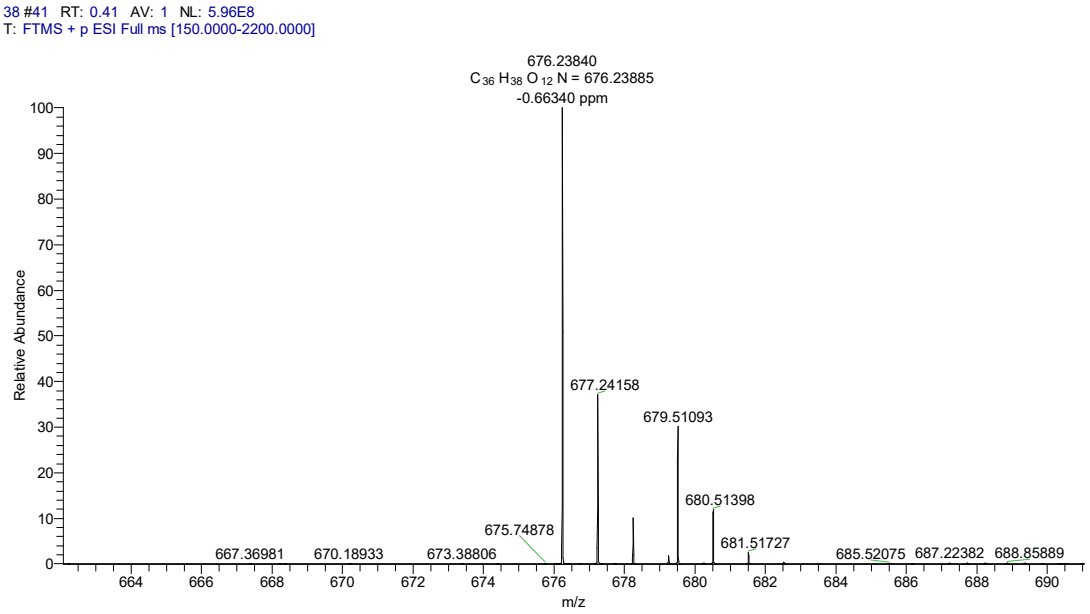
HRMS spectra of compound **Y24**



^{1}H NMR spectra of compound **Y25**



^{13}C NMR spectra of compound **Y25**



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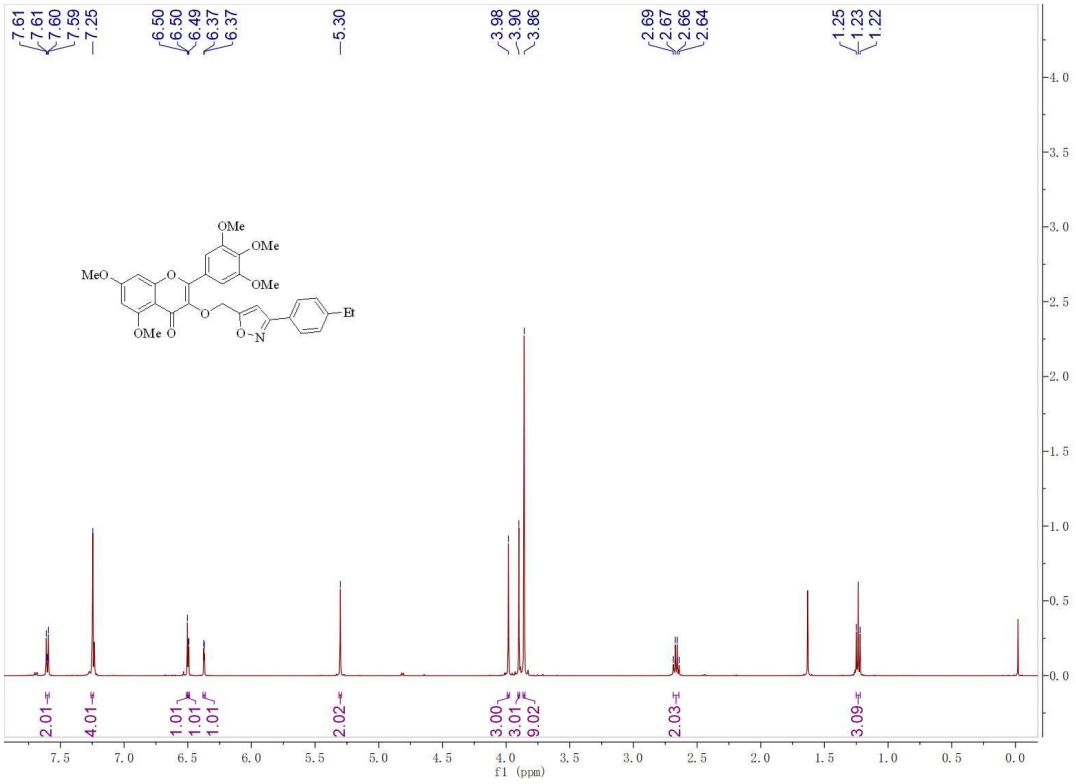
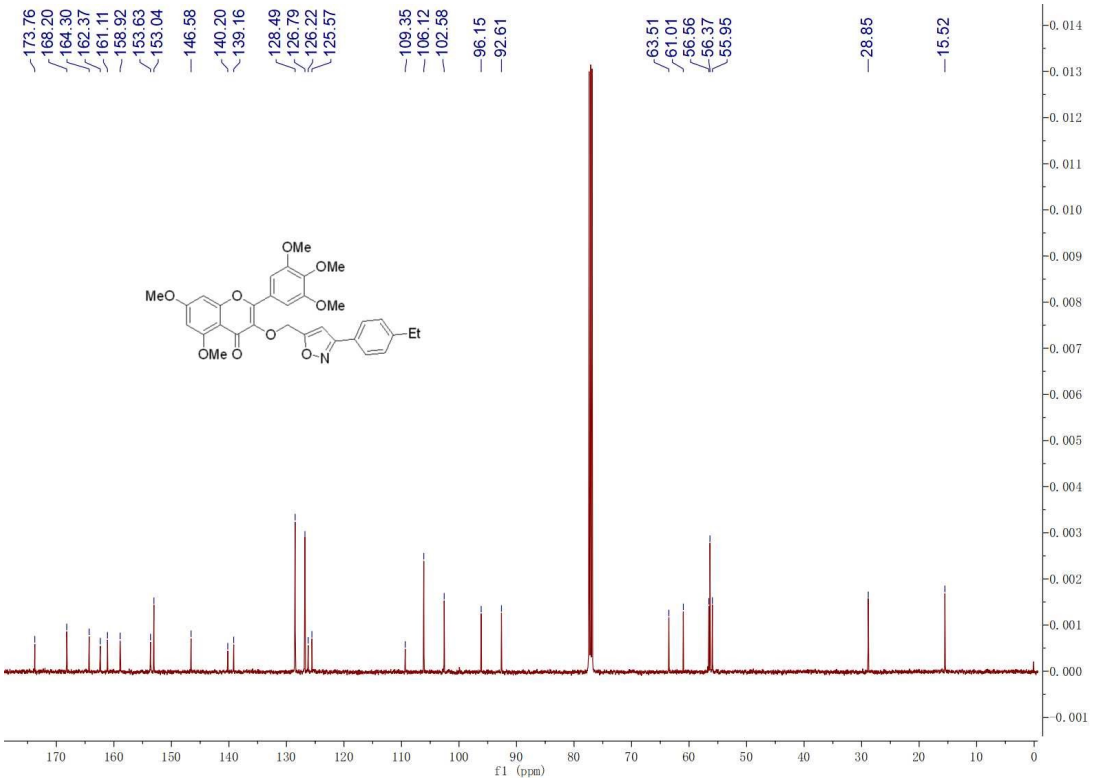
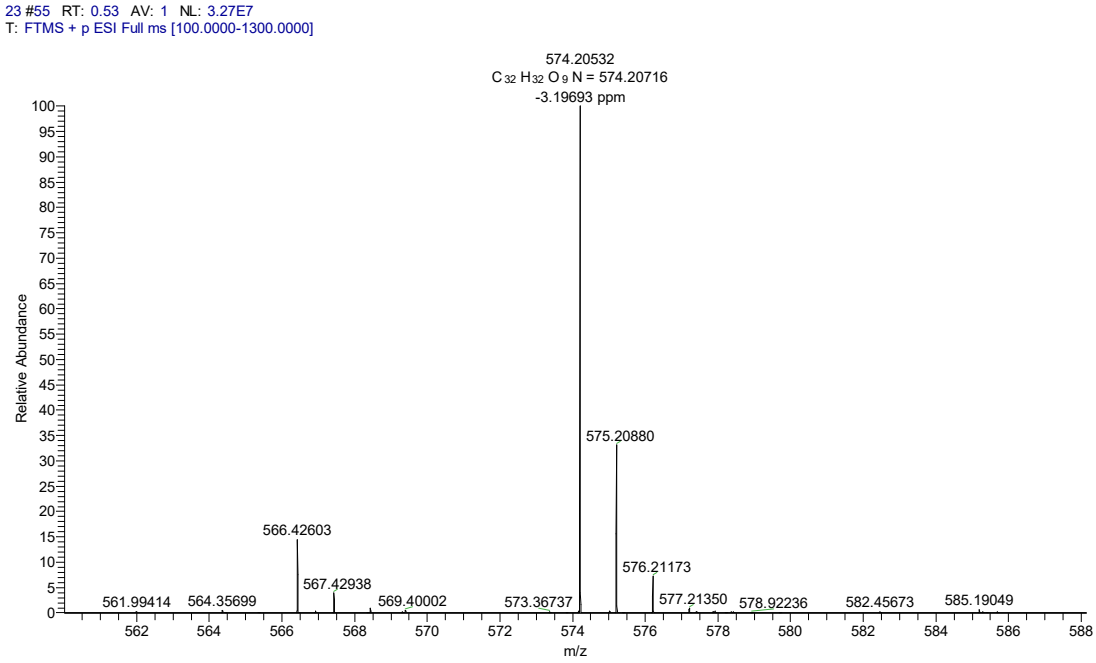


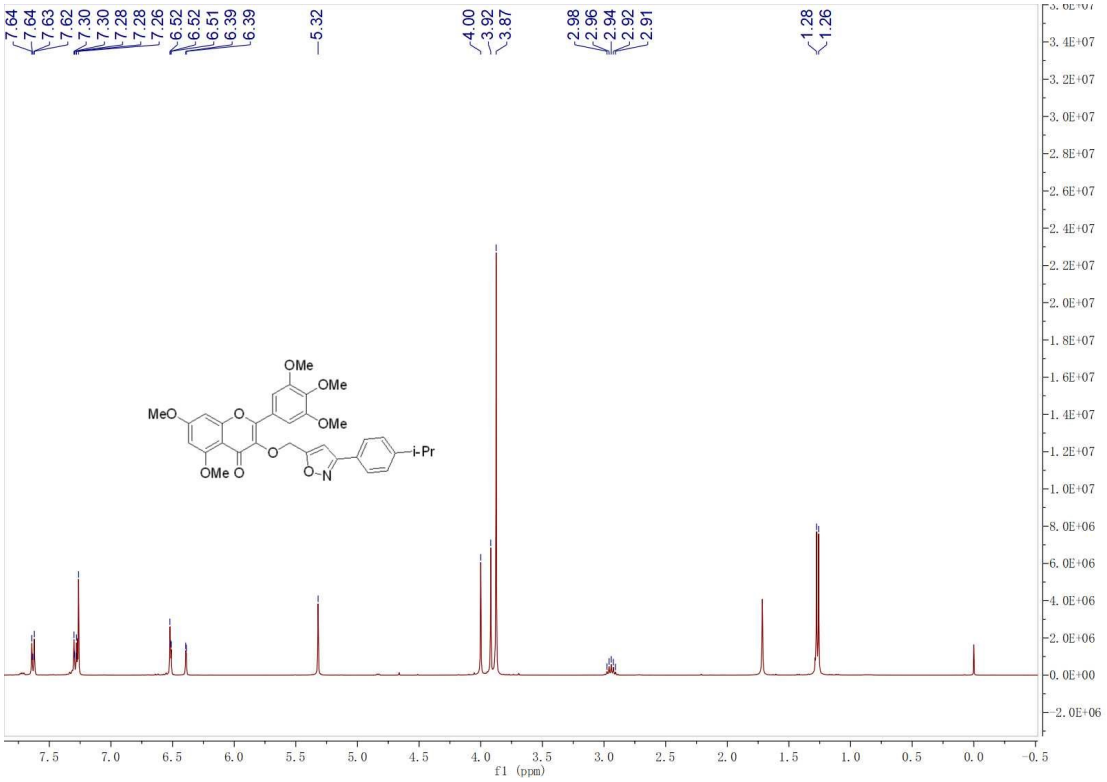
^{1}H NMR spectra of compound **Y26**



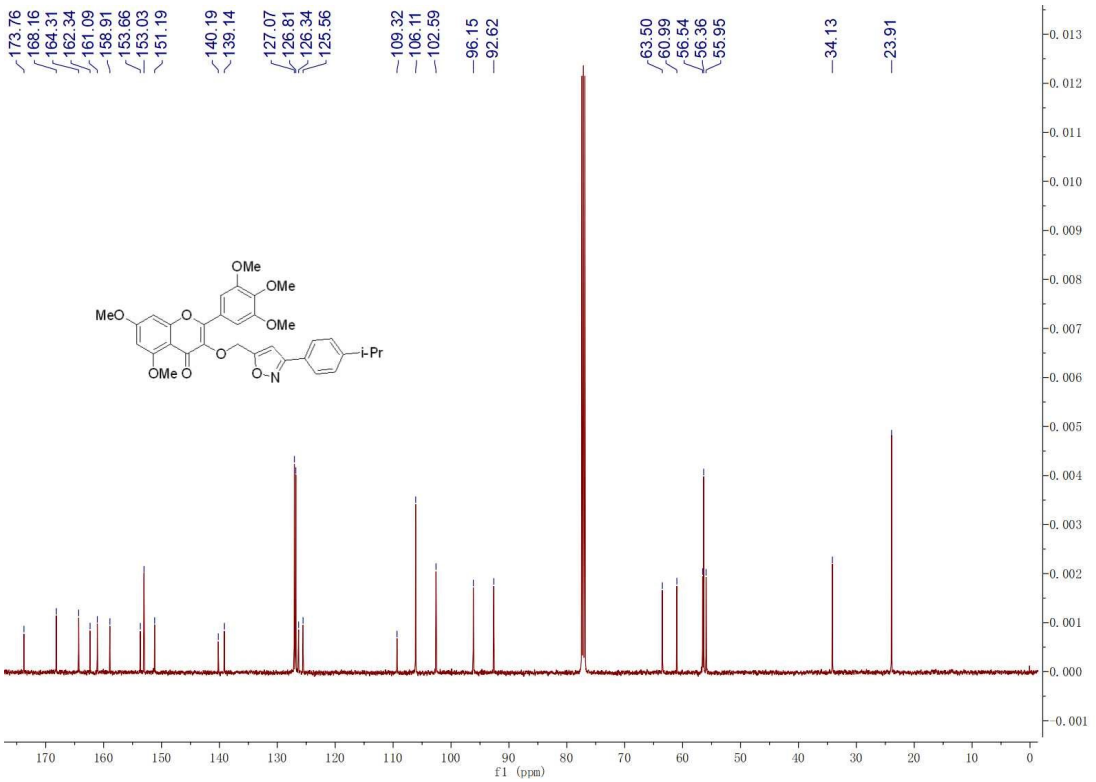
^{13}C NMR spectra of compound **Y26**



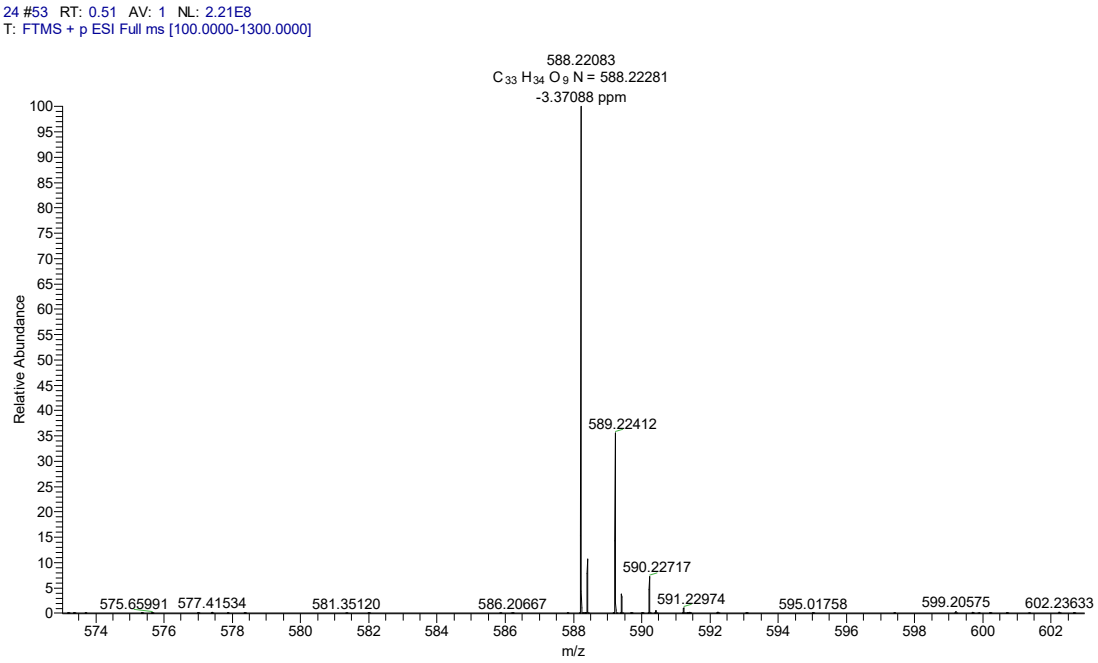
HRMS spectra of compound **Y26**



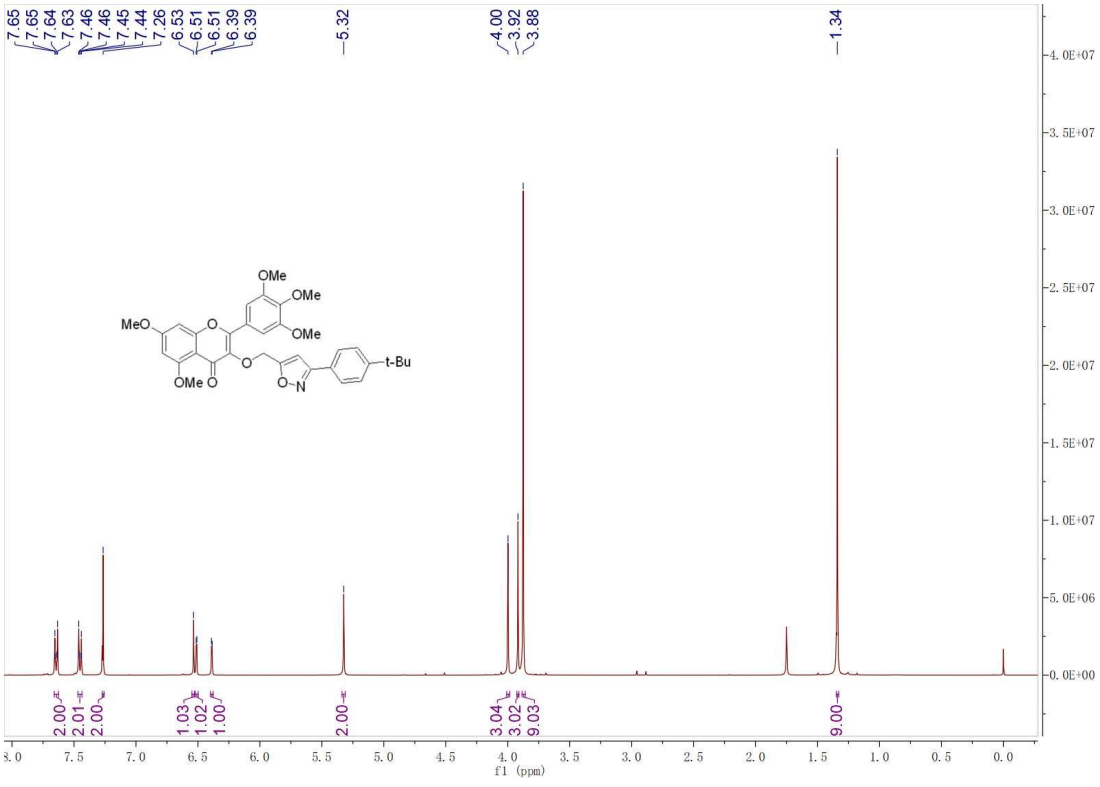
^{1}H NMR spectra of compound **Y27**



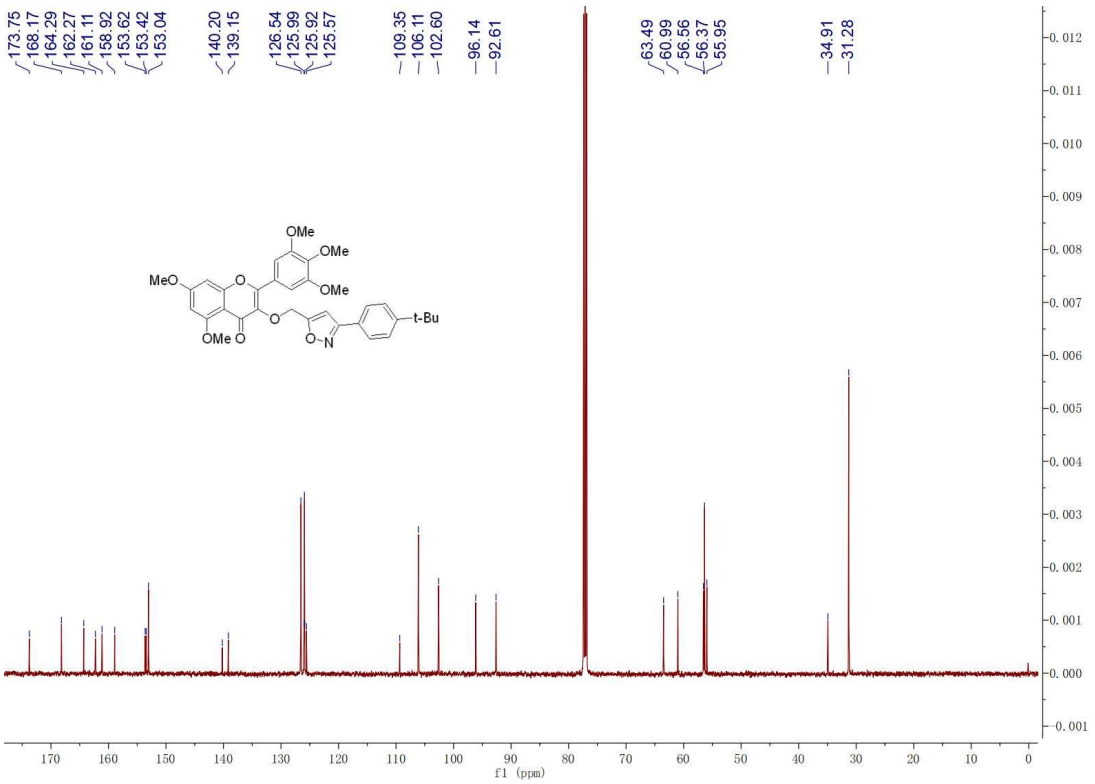
^{13}C NMR spectra of compound **Y27**



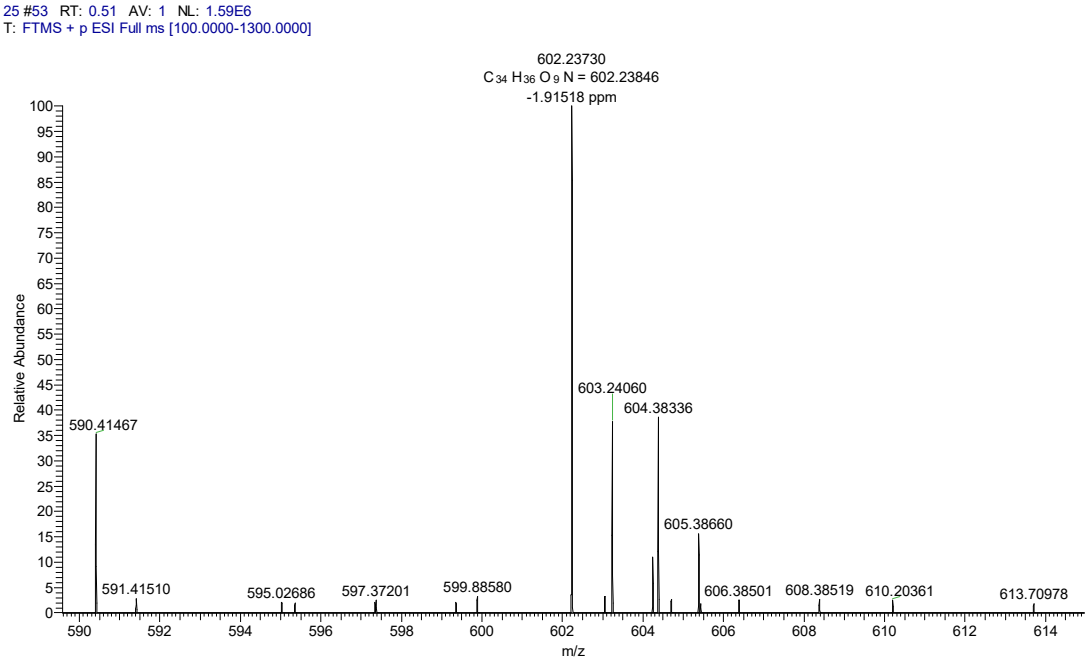
HRMS spectra of compound **Y27**



^{1}H NMR spectra of compound **Y28**



^{13}C NMR spectra of compound **Y28**



HRMS spectra of compound **Y28**

5. High performance liquid chromatography of target compound Y1

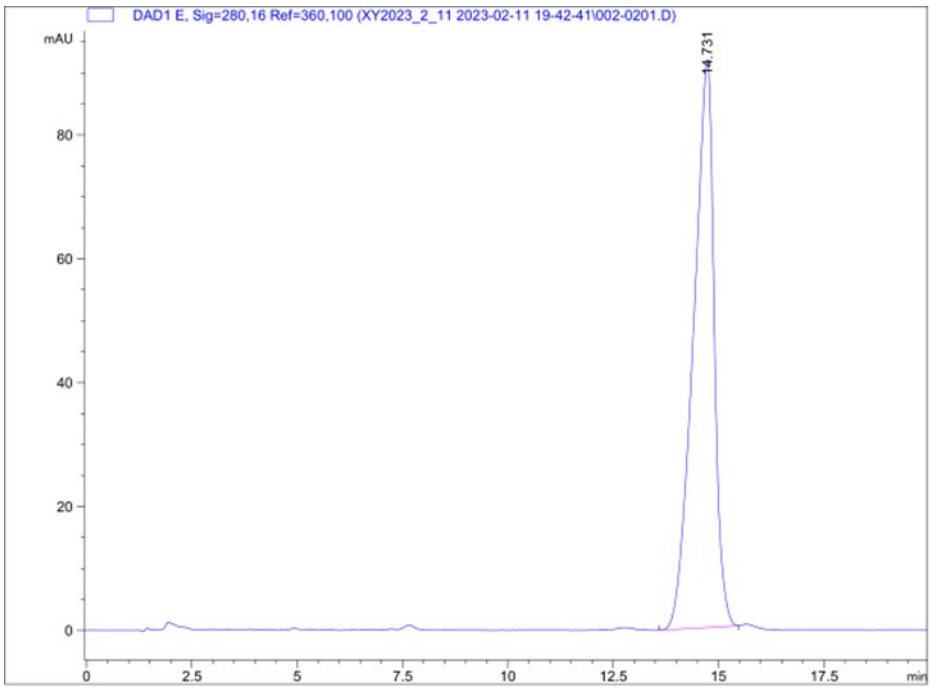


Fig.S1 High performance liquid chromatography of **Y1**

6. Microstructure and appearance state diagram of target compound Y1

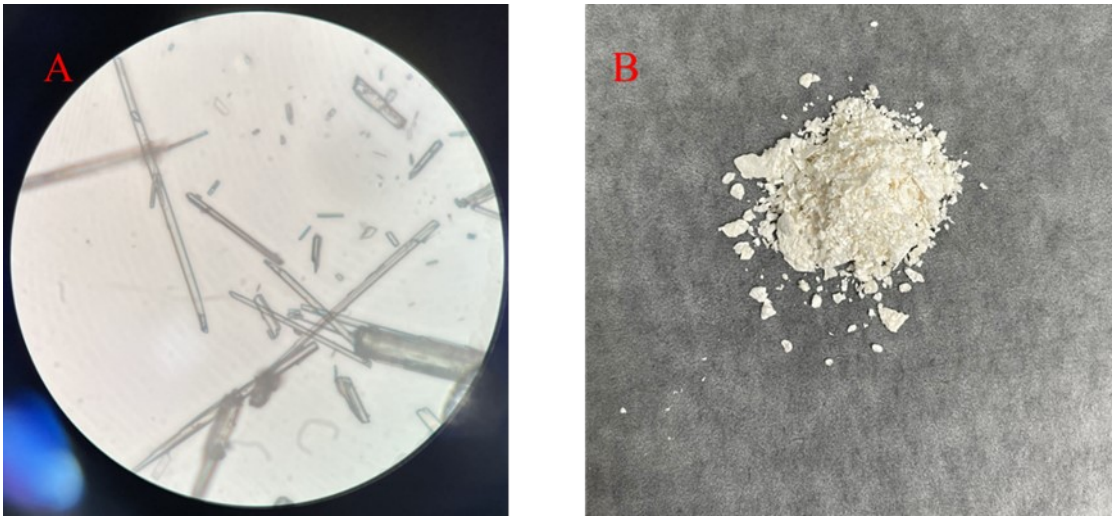


Fig. S2 Microstructure and appearance state diagram of **Y1**
(A: Microstructure diagram; B: Appearance state diagram)

7.Table S1. *In vitro* antifungal activity of target compounds Y1-Y28 at 100 μg/mL

Table S1. *In vitro* antifungal activity of target compounds **Y1**-**Y28** at 100 μg/mL [a]

Compd.	inhibition rate (%)											
	Rs	*Bc*	*Pc*[1]	*Ss*	*Fg*	*Ps*	*Cc*	*Bd*	*Cg*	*Pc*[2]	*Fe*	*Fd*
Y1	30.6±1.1	32.0±2.7	38.0±2.8	43.6±9.9	14.1±4.9	9.9±3.5	16.9±1.8	-	23.0±3.5	16.1±2.6	13.8±6.4	8.8±1.3
Y2	40.4±1.8	33.6±3.1	34.9±4.7	14.4±5.4	8.1±1.4	13.3±4.0	17.3±3.7	28.3±9.1	27.9±3.0	14.0±1.1	38.3±6.8	5.3±1.0
Y3	44.1±1.6	75.8±1.6	67.7±1.9	81.1±2.1	22.6±3.3	30.5±4.8	25.4±1.6	16.4±4.4	28.3±4.6	15.7±5.2	39.2±8.2	3.1±1.9
Y4	43.7±1.4	38.1±4.7	36.7±5.9	54.5±7.7	26.6±4.9	5.6±9.1	10.9±5.4	29.9±9.7	35.3±2.2	28.1±4.6	38.8±5.8	8.4±1.9
Y5	31.4±2.0	23.4±3.8	22.7±3.8	33.7±3.5	12.5±4.0	7.7±0.9	23.0±0.9	-	19.3±2.0	11.6±1.1	27.9±7.1	4.0±1.2
Y6	23.3±1.8	26.6±1.6	29.7±1.7	32.2±2.4	16.5±4.3	7.7±4.9	23.0±3.2	-	28.6±5.7	14.9±2.7	40.4±5.1	6.6±1.9
Y7	40.8±0.9	35.2±3.3	31.0±5.4	59.1±5.2	20.6±3.2	7.3±2.0	27.8±5.2	-	18.2±1.6	12.4±1.1	23.8±3.4	5.3±1.8
Y8	39.6±1.1	30.7±4.0	24.5±4.5	53.0±2.8	12.1±4.2	8.6±3.5	25.8±2.6	-	18.6±1.1	12.4±1.8	34.6±6.8	6.6±1.2
Y9	38.8±2.4	34.0±0.9	17.5±6.0	23.1±6.6	16.9±5.4	11.6±4.5	17.3±2.9	-	25.3±4.0	19.4±4.1	36.3±5.4	4.8±1.5
Y10	33.5±1.6	38.9±2.6	32.8±6.3	51.1±4.0	25.8±2.2	17.6±1.4	28.6±1.2	-	21.2±1.0	14.0±3.3	39.6±4.1	6.2±1.3
Y11	42.4±1.2	54.1±1.8	45.4±3.7	35.6±2.8	20.2±7.6	16.7±1.9	11.3±1.8	-	23.4±2.1	8.3±2.0	30.8±4.6	3.1±2.8
Y12	33.9±3.4	37.3±4.3	33.6±7.8	45.8±2.4	16.5±3.3	15.0±2.5	9.3±7.6	-	23.4±1.6	12.4±3.0	32.1±9.0	2.2±2.1
Y13	42.0±1.8	36.1±2.0	27.1±2.7	47.0±9.4	12.9±2.7	24.0±4.3	16.9±2.9	15.6±2.7	25.3±1.7	15.7±2.0	30.8±1.1	6.2±1.3
Y14	30.2±2.3	39.3±5.7	45.4±4.5	44.3±2.8	12.1±2.6	13.7±3.1	14.9±0.9	1.2±6.7	27.9±3.0	16.1±2.6	33.3±3.0	2.2±1.5
Y15	31.0±1.6	32.8±7.2	36.7±4.0	20.5±2.6	9.7±4.7	3.9±2.8	10.9±2.1	-	22.7±2.7	15.3±1.7	44.6±2.2	4.8±1.5
Y16	35.9±2.1	33.6±3.9	40.2±7.1	53.8±6.4	26.2±3.5	23.2±3.4	15.7±7.5	24.2±7.8	26.8±0.8	19.4±2.7	34.2±4.8	10.1±4.2

Table S1. *In vitro* antifungal activity of target compounds **Y1**-**Y28** at 100 μg/mL (continued Table)

Compd.	inhibition rate (%)											
	Rs	*Bc*	*Pc*[1]	*Ss*	*Fg*	*Ps*	*Cc*	*Bd*	*Cg*	*Pc*[2]	*Fe*	*Fd*
Y17	27.3±1.1	38.9±1.6	48.9±3.2	55.7±1.1	25.0±2.6	7.7±2.7	3.6±0.9	17.6±4.9	26.8±3.0	9.9±2.3	48.3±2.7	3.1±3.5
Y18	30.6±1.1	42.6±2.3	39.7±1.5	31.1±3.1	16.1±8.3	3.4±4.0	1.2±2.1	-	24.9±3.7	27.3±4.6	32.1±4.7	11.5±2.0
Y19	36.3±1.4	49.2±1.8	43.2±2.4	48.1±5.2	23.0±5.2	20.6±1.7	17.7±2.4	-	23.0±1.7	17.4±9.0	38.8±3.9	15.0±1.8
Y20	30.6±1.1	39.3±4.1	40.6±1.2	33.7±4.7	19.4±2.2	15.0±4.6	16.9±2.2	13.5±5.6	23.0±2.5	14.5±2.7	33.8±5.8	7.9±2.3
Y21	33.5±3.2	31.1±2.0	45.0±1.5	54.9±2.4	16.9±5.4	14.2±1.9	8.5±2.5	39.3±1.8	16.7±1.0	19.4±4.6	42.5±6.1	3.1±1.9
Y22	38.0±1.8	38.1±2.6	54.1±3.2	40.2±4.4	17.7±11	12.0±2.7	33.1±4.0	11.1±2.6	31.6±2.7	26.8±4.4	35.4±6.7	4.8±1.5
Y23	42.0±2.3	28.7±2.0	39.7±2.5	50.8±8.1	25.0±4.5	21.9±2.4	34.3±3.2	13.1±3.3	33.8±3.7	19.8±6.0	42.9±2.6	8.8±3.5
Y24	39.6±2.3	21.3±3.1	54.1±5.8	32.2±2.4	8.9±3.8	7.3±2.9	21.8±5.9	-	20.8±1.1	12.8±5.5	40.4±4.7	8.4±4.1
Y25	42.0±1.1	34.0±2.6	28.8±2.7	36.0±5.4	15.7±2.5	5.2±1.7	3.6±2.1	-	18.6±1.1	5.4±3.8	41.3±10	5.7±1.2
Y26	49.4±1.8	48.4±2.1	19.6±3.9	22.6±1.2	5.9±3.9	7.4±4.0	14.7±3.8	8.5±1.7	27.1±2.7	12.0±2.7	52.9±5.0	11.5±2.0
Y27	51.0±2.0	28.7±8.4	52.2±2.2	34.1±7.8	5.5±1.3	14.7±3.0	18.1±3.9	53.9±2.6	24.9±2.4	24.8±1.8	20.8±5.4	23.3±5.3
Y28	47.8±3.6	47.6±2.8	23.9±1.1	42.0±7.5	10.5±3.9	27.0±2.6	19.7±2.1	-	23.0±2.8	20.2±7.9	48.8±3.1	5.7±1.2
Myr.[b]	31.0±2.1	36.5±2.9	41.0±3.2	38.3±2.4	19.4±1.8	16.7±2.4	16.1±2.6	-	20.8±3.5	6.6±1.8	25.0±5.3	2.6±1.8
Krm[b]	70.2±3.5	69.3±2.3	61.6±5.6	62.8±3.2	48.0±4.3	49.4±5.3	63.3±1.6	52.0±4.1	62.8±1.0	69.8±3.8	72.5±3.7	31.3±4.9
Azo[b]	93.9±1.7	96.3±3.0	63.6±2.1	70.3±1.2	43.3±1.3	50.6±2.7	50.8±2.9	66.0±1.7	44.0±2.0	76.3±2.6	60.0±5.3	53.8±3.9

[a]: The average of three trials; [b]: the lead compound myricetin (Myr); commercial antifungal agents kresoxim-methyl (Krm) and azoxystrobin (Azo).