Supporting Information

Synthesis and Antiviral Activity of Novel Myricetin Derivatives Containing a Ferulic Acid Amide Scaffolds

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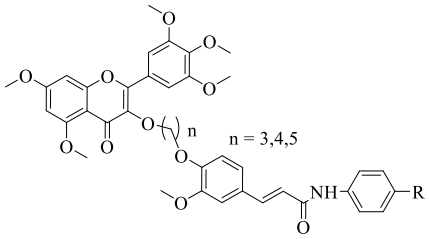
Content

The physical properties of compounds 4a-4v



Compounds **4a-4v**

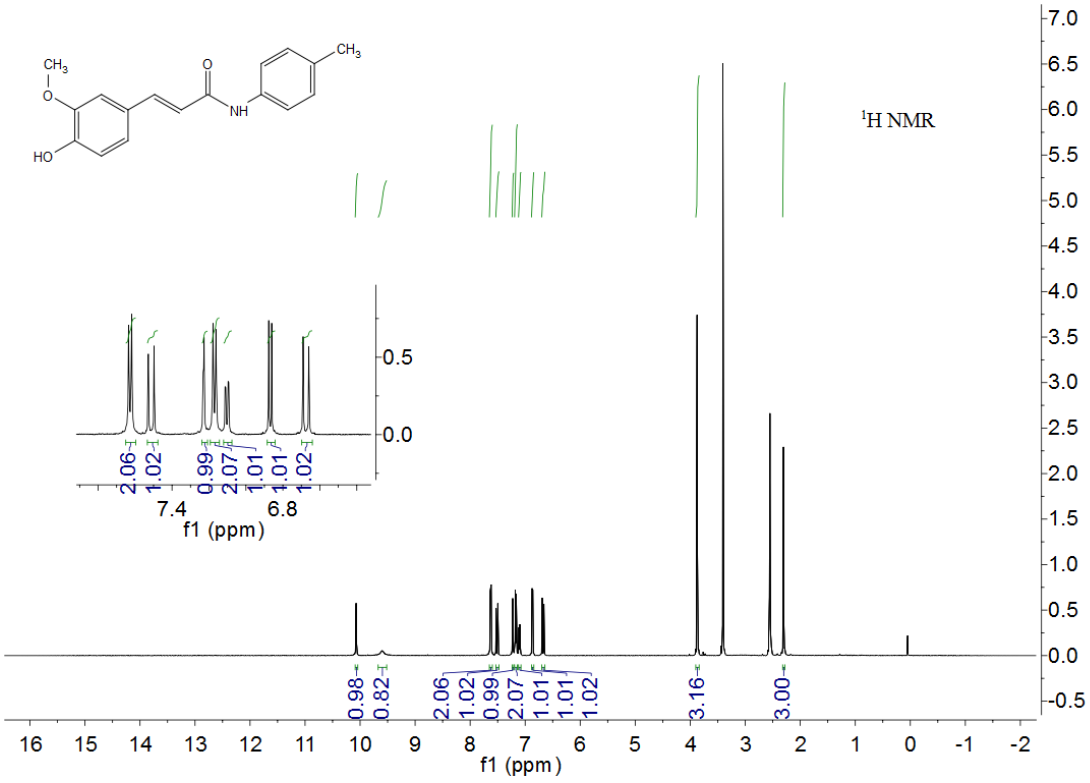
Table 1 The physical properties of compounds **4a**-**4v**

Compounds	R_2	n	Appearance	Yield /%	m.p./°C
4a	4-CH_3	3	Gray solid	215.4-215.5	58.6
4b	4-OCH_3	3	Gray solid	190.3-190.5	39.1
4c	4-CH_3	4	Gray solid	100.1-101.9	51.4
4d	4-OCH_3	4	Gray solid	108.6-109.8	63.6
4e	3-Cl	3	Yellow solid	187.2-187.5	49.6
4f	3-Cl	4	Gray solid	104.1-104.9	55.5
4g	4-Cl	4	Gray solid	103.3-104.8	62.0
4h	H	4	Yellow solid	116.4-116.7	60.3
4i	H	3	Yellow solid	242.5-242.9	49.7
4j	3,4-di-CH_3	3	Gray solid	202.5-202.9	83.9
4k	3,4-di-CH_3	4	Gray solid	107.3-108.1	48.3
4l	3,4-di-OCH_3	3	Green solid	118.0-118.7	65.33
4m	3,4-di-OCH_3	4	Green solid	95.3-96.1	59.6
4n	4-Br	3	Gray solid	208.4-209.6	67.9
4o	4-Br	4	Gray solid	180.3-181.6	58.2
4p	3,4-di-Cl	3	Yellow solid	118.6-119.3	65.5
4q	3,4-di-Cl	4	Gray solid	102.3-103.4	51.7
4r	4-Cl	5	Gray solid	112.3-112.9	58.2
4s	3-Cl	5	Gray solid	153.5-154.1	62.8
4t	4-OCH_3	5	Gray solid	123.6-124.7	64.7
4u	2-F	3	Gray solid	117.6-118.3	54.8
4v	2-F	4	Gray solid	162.3-163.6	66.7

Characterization of intermediate compounds 2a-2j

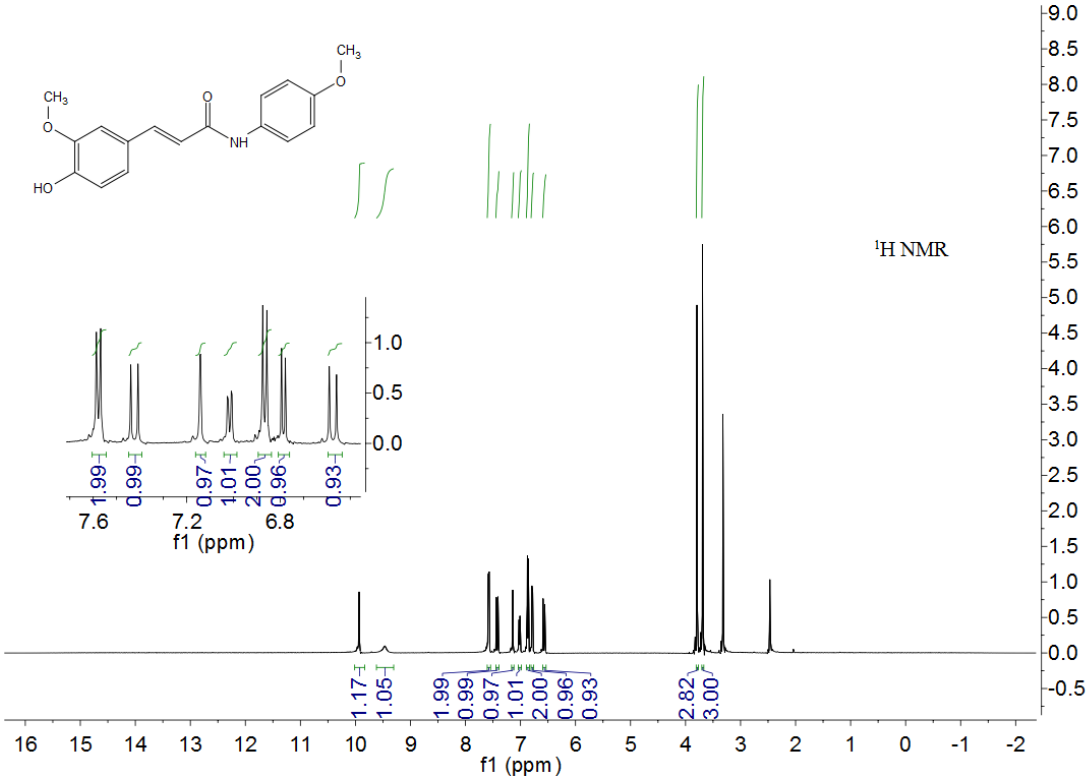
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(4-methylphenyl)acrylamide (**2a**): Yellow solid, yield : 62.14 %, m.p. 137.7 – 138.3, ^{1}H NMR (500 MHz, DMSO) δ 10.07 (s, 1H, OH), 9.60 (s, 1H, NH), 7.63 (d, J = 8.4 Hz, 2H, Ph-2H), 7.51 (d, J = 15.6 Hz, 1H, CO-C=CH), 7.22 (t, J = 5.0 Hz, 1H, CO-CH=), 7.17 (d, J = 8.3 Hz, 2H, Ph-2H), 7.10 (dt, J = 5.9, 2.9 Hz, 1H, Ph-H), 6.86 (t, J = 7.7 Hz, 1H, Ph-H), 6.67 (d, J = 15.6 Hz, 1H, Ph-H), 3.87 (s, 3H, OCH_3), 2.29 (d, J = 11.3 Hz, 3H, CH_3).

Figure S1. ^{1}H NMR spectrum of intermediate **2a**



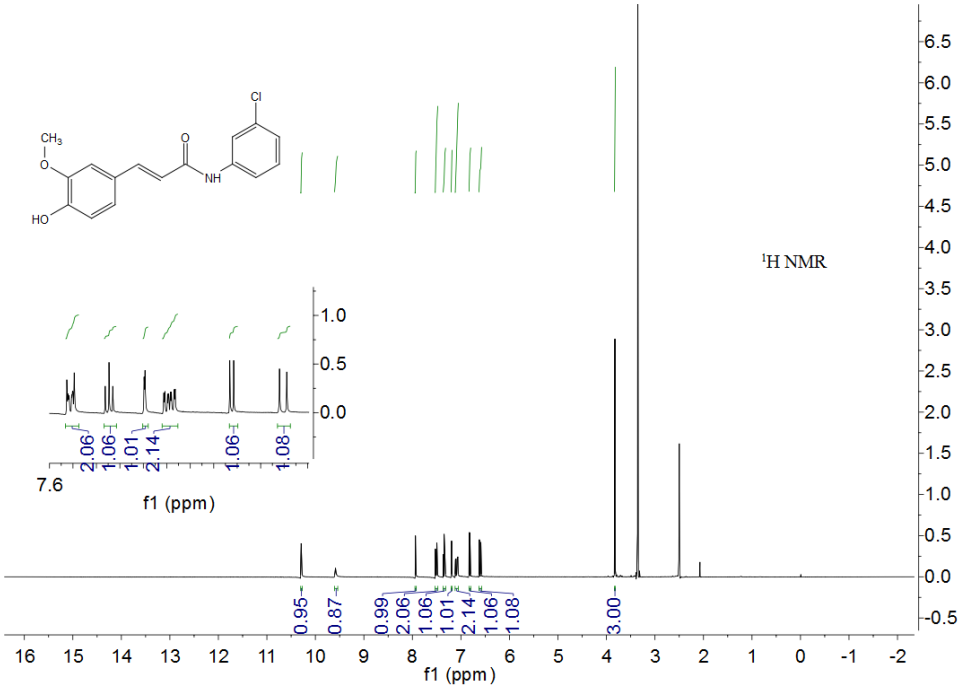
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(4-methoxyphenyl)acrylamide (**2b**): Gray solid, yield : 57.23 %, m.p. 163.1 – 163.7, ^{1}H NMR (500 MHz, DMSO) δ 10.01 – 9.83 (m, 1H, OH), 9.46 (s, 1H, NH), 7.60 – 7.54 (m, 2H, Ph-2H), 7.42 (d, J = 15.6 Hz, 1H, CO-CH=CH), 7.14 (d, J = 1.6 Hz, 1H, Ph-H), 7.01 (dt, J = 11.8, 5.9 Hz, 1H, CO-CH=), 6.89 – 6.84 (m, 2H, Ph-2H), 6.79 (d, J = 8.1 Hz, 1H, Ph-H), 6.57 (d, J = 15.6 Hz, 1H, Ph-H), 3.79 (s, 3H, OCH_3), 3.68 (d, J = 10.1 Hz, 3H, OCH_3).

Figure S2. ^{1}H NMR spectrum of intermediate **2b**



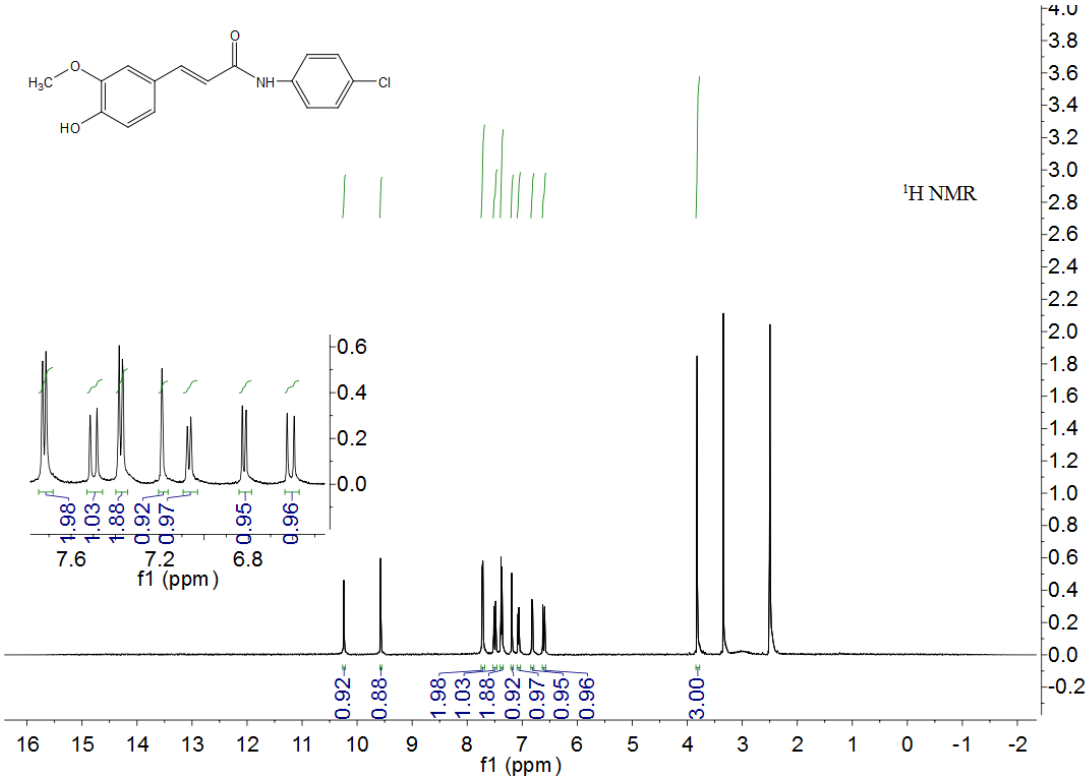
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(3-chlorophenyl)acrylamide (**2c**) : Yellow solid, yield : 60.63 %, m.p. 172.3 – 173.2, ^{1}H NMR (500 MHz, DMSO) δ 10.29 (s, 1H, OH), 9.59 (s, 1H, NH), 7.94 (t, J = 2.0 Hz, 1H, Ph-H), 7.53 – 7.47 (m, 2H, Ph-2H), 7.35 (t, J = 8.1 Hz, 1H, CO-CH=CH), 7.19 (d, J = 1.9 Hz, 1H, CO-CH=), 7.12 – 7.05 (m, 2H, Ph-2H), 6.82 (d, J = 8.1 Hz, 1H, Ph-H), 6.60 (d, J = 15.6 Hz, 1H, Ph-2H), 3.82 (s, 3H, OCH_3).

Figure S3. ^{1}H NMR spectrum of intermediate **2c**



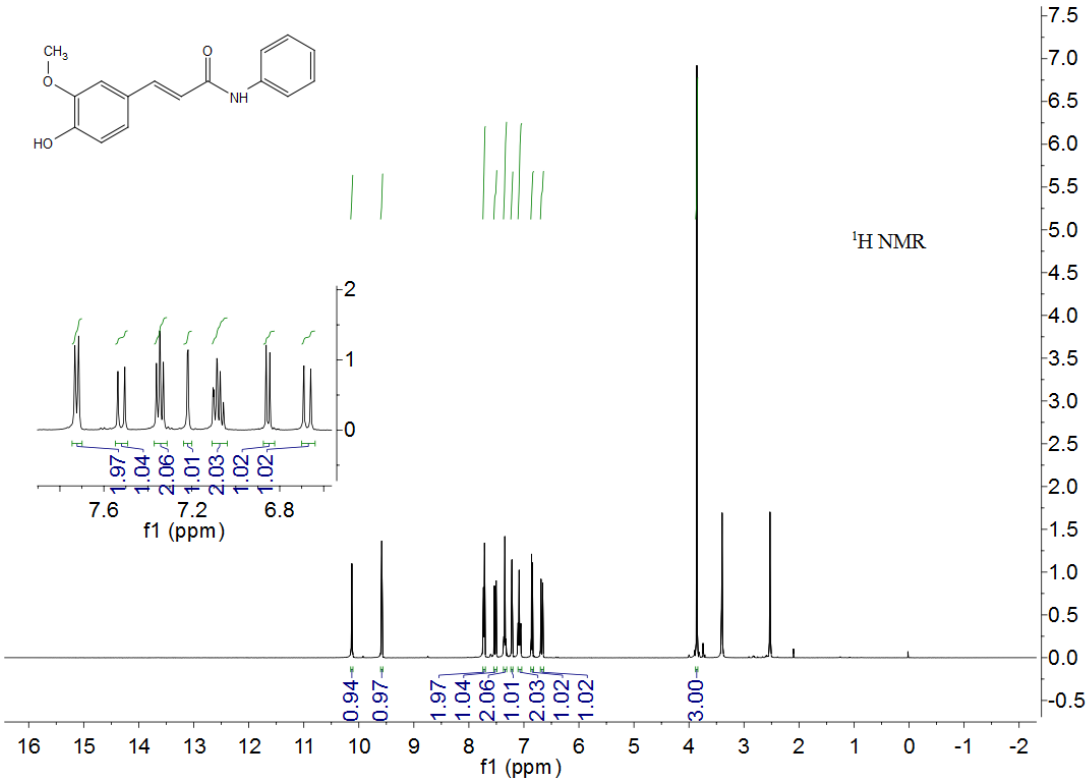
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(4-chlorophenyl)acrylamide (**2d**) : Gray solid, yield : 56.92 %, m.p. 234.7 – 235.2, ^{1}H NMR (500 MHz, DMSO) δ 10.24 (s, 1H, OH), 9.57 (s, 1H, NH), 7.75 – 7.68 (m, 2H, Ph-2H), 7.50 (d, J = 15.4 Hz, 1H, CO-CH=CH), 7.40 – 7.34 (m, 2H, Ph-2H), 7.19 (s, 1H, Ph-H), 7.06 (t, J = 11.3 Hz, 1H, CO-CH=), 6.82 (dd, J = 8.1, 1.0 Hz, 1H, Ph-H), 6.64 – 6.57 (m, 1H, Ph-H), 3.81 (t, J = 7.8 Hz, 3H, OCH_3).

Figure S4. ^{1}H NMR spectrum of intermediate **2d**



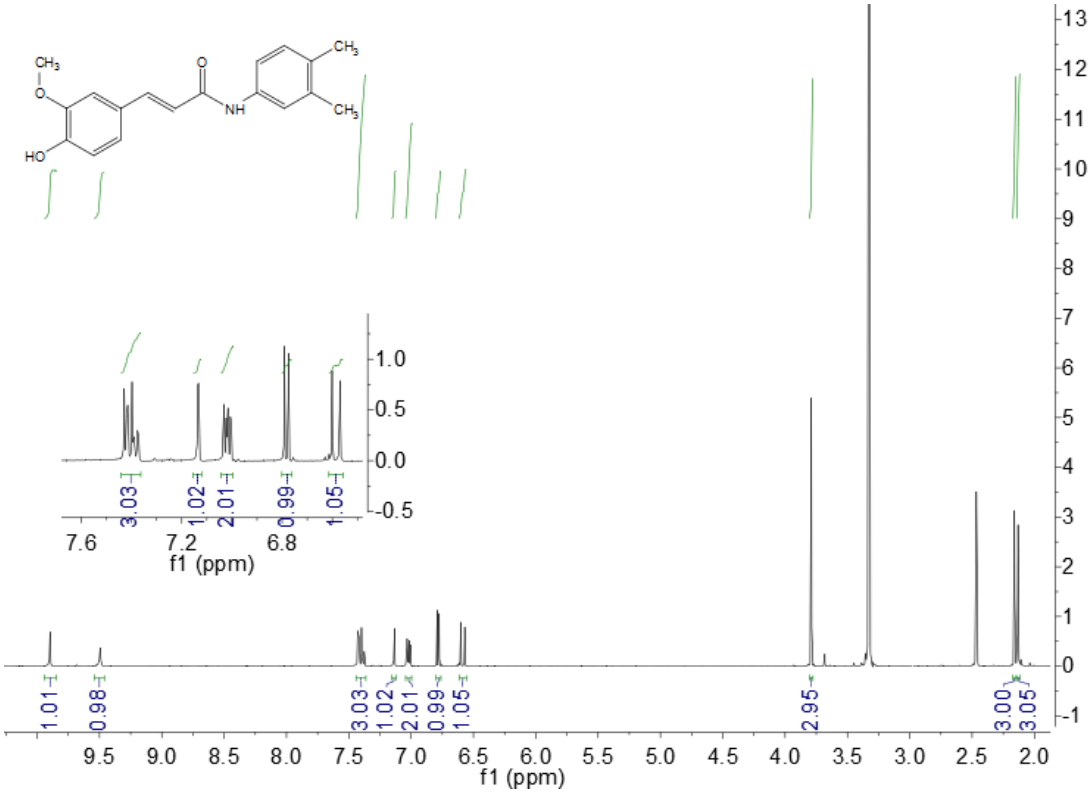
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-phenylacrylamide (**2e**) : Yellow solid, yield : 63.74 %, m.p. 120.3 – 121.1, ^{1}H NMR (500 MHz, DMSO) δ 10.13 (s, 1H, OH), 9.58 (s, 1H, NH), 7.74 – 7.70 (m, 2H, Ph-2H), 7.52 (d, J = 15.6 Hz, 1H, CO-CH=CH), 7.34 (dd, J = 16.1, 8.0 Hz, 2H, Ph-2H), 7.22 (d, J = 1.8 Hz, 1H, CO-CH=), 7.11 – 7.04 (m, 2H, Ph-2H), 6.85 (dd, J = 11.1, 6.1 Hz, 1H, Ph-H), 6.67 (d, J = 15.6 Hz, 1H, Ph-H), 3.86 (s, 3H, OCH_3).

Figure S5. ^{1}H NMR spectrum of intermediate **2e**



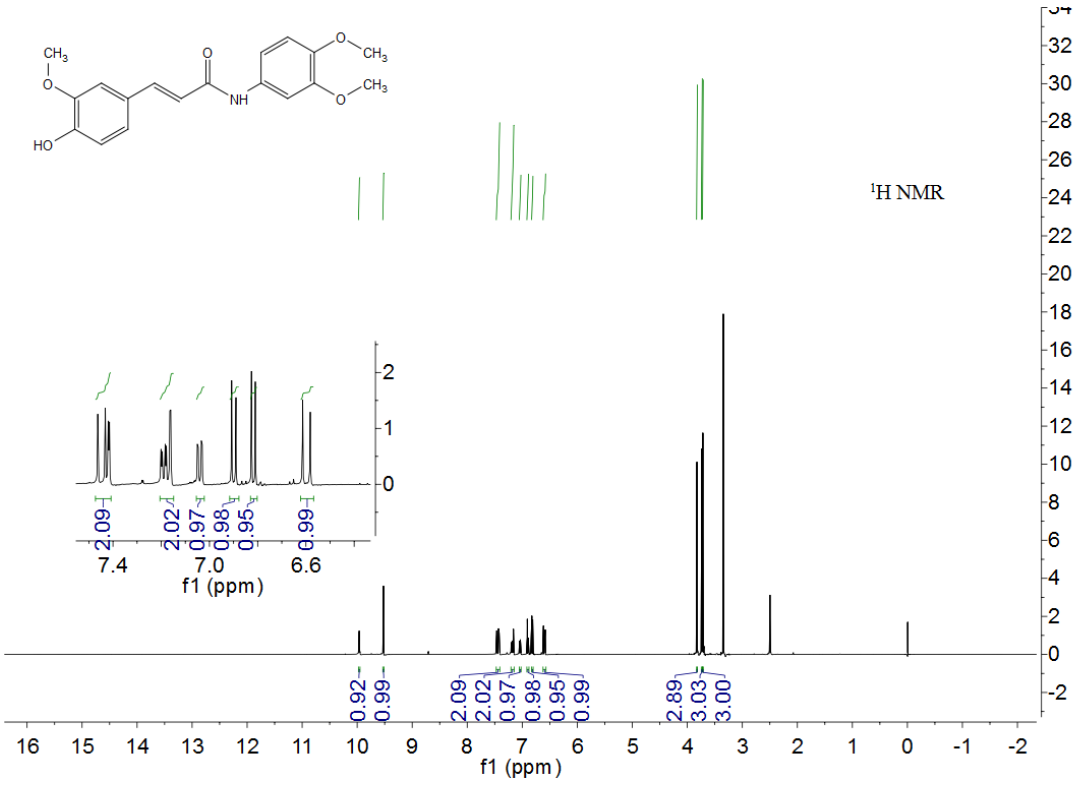
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(3,4-dimethylphenyl)acrylamide (**2f**) : Gray solid, yield : 67.38 %, m.p. 182.4 – 183.6, ^{1}HNMR (500 MHz, DMSO) δ 9.90 (s, 1H), 9.49 (s, 1H), 7.40 (ddd, J = 10.2, 7.5, 3.6 Hz, 3H), 7.13 (d, J = 1.9 Hz, 1H), 7.04 – 7.00 (m, 2H), 6.80 – 6.76 (m, 1H), 6.59 (dd, J = 16.0, 5.4 Hz, 1H), 3.79 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H).

Figure S6. ^{1}H NMR spectrum of intermediate **2f**



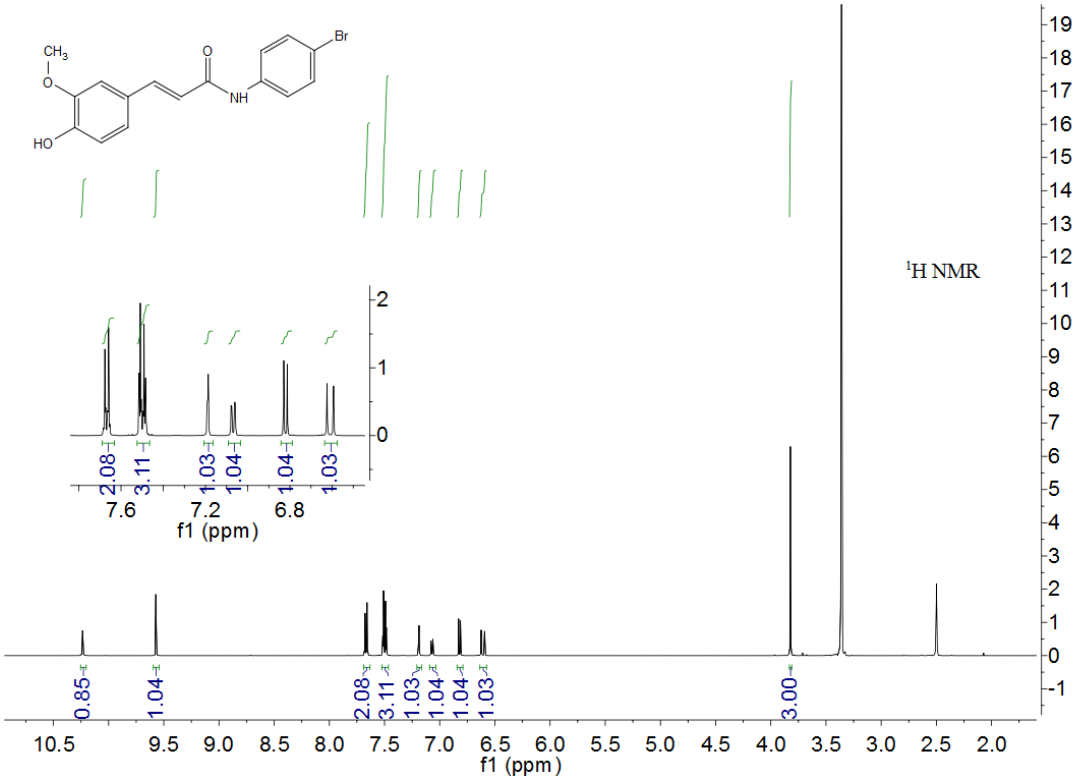
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(3,4-dimethoxyphenyl)acrylamide (**2g**) : Purple solid, yield : 72.85 %, m.p. 91.2 – 91.7, ^{1}H NMR (500 MHz, DMSO) δ 9.96 (s, 1H, OH), 9.52 (s, 1H, NH), 7.43 (dd, J = 15.2, 9.0 Hz, 2H, Ph-2H), 7.21 – 7.15 (m, 2H, Ph-2H), 7.04 (dd, J = 8.2, 1.9 Hz, 1H, CO-CH=CH), 6.90 (d, J = 8.8 Hz, 1H, Ph-H), 6.83 – 6.80 (m, 1H, CO-CH=), 6.60 (d, J = 15.6 Hz, 1H, Ph-H), 3.82 (s, 3H, OCH3), 3.74 (s, 3H, OCH3), 3.72 (s, 3H, OCH3).

Figure S7. ^{1}H NMR spectrum of intermediate **2g**



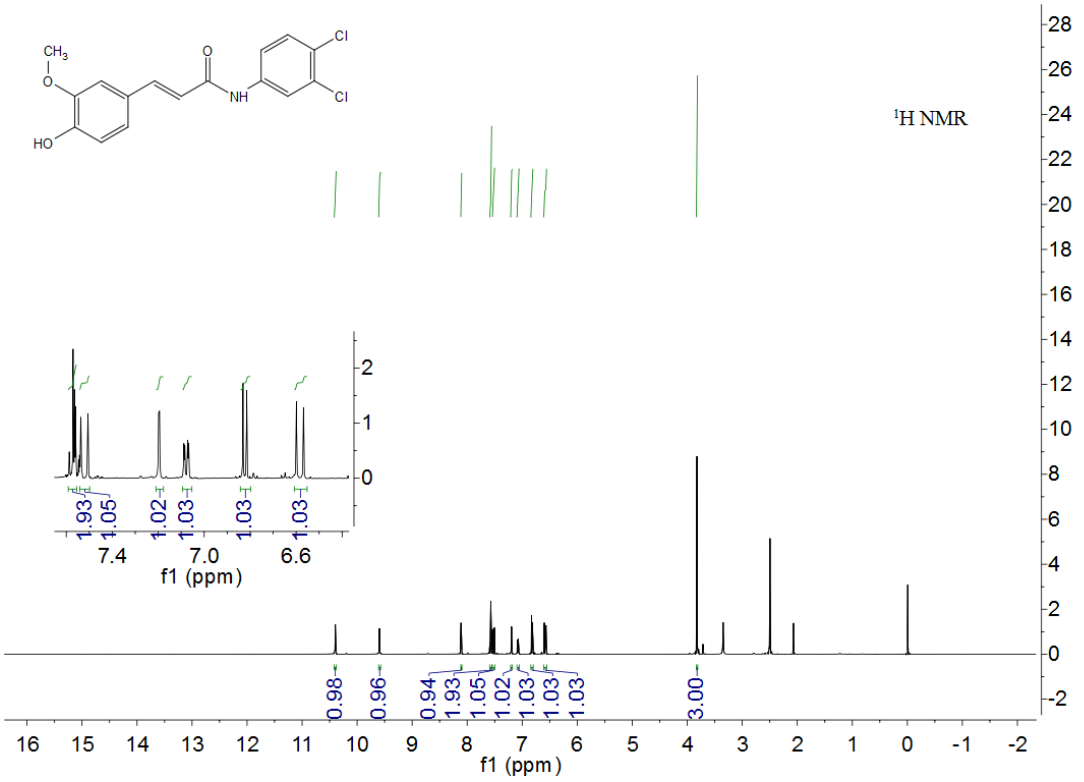
(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(4-bromophenyl)acrylamide (**2h**) : Gray solid, yield : 54.73 %, m.p. 205.3 – 206.7, ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (s, 1H, OH), 9.57 (s, 1H, NH), 7.69 – 7.63 (m, 2H, Ph-2H), 7.52 – 7.46 (m, 3H, Ph-3H), 7.19 (d, *J* = 1.9 Hz, 1H, CO-CH=CH), 7.07 (dd, *J* = 8.2, 1.9 Hz, 1H, CO-CH=), 6.84 – 6.79 (m, 1H, Ph-H), 6.61 (d, *J* = 15.6 Hz, 1H, Ph-H), 3.82 (s, 3H, OCH_3).

Figure S8. ^{1}H NMR spectrum of intermediate **2h**



(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(3,4-dichlorophenyl)acrylamide (**2i**) : Yellow solid, yield : 54.33 %, m.p. 224.4 – 224.9, ^{1}H NMR (500 MHz, DMSO) δ 10.40 (s, 1H, OH), 9.59 (s, 1H, NH), 8.11 (d, *J* = 2.1 Hz, 1H, Ph-H), 7.59 – 7.55 (m, 2H, Ph-2H), 7.52 (d, *J* = 15.6 Hz, 1H, CO-CH=CH), 7.20 (d, *J* = 1.9 Hz, 1H, Ph-H), 7.07 (dt, *J* = 6.8, 3.4 Hz, 1H, CO-CH=), 6.82 (t, *J* = 7.6 Hz, 1H, Ph-H), 6.58 (d, *J* = 15.6 Hz, 1H, Ph-H), 3.82 (s, 3H, OCH_3).

Figure S9. ^{1}H NMR spectrum of intermediate **2i**



(*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-(2-fluorophenyl)acrylamide (**2j**), Yellow solid, yield : 73.34 %, m.p. 190.2 - 190. ^{1}H NMR (400 MHz, DMSO) δ 9.78 (s, 1H), 9.54 (s, 1H), 8.12 (td, *J* = 8.0, 1.6 Hz, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.27 (ddd, *J* = 11.2, 7.9, 1.6 Hz, 1H), 7.22 – 7.11 (m, 3H), 7.07 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.89 (d, *J* = 15.6 Hz, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), ^{19}F NMR (376 MHz, DMSO) δ -125.57 (s).

Figure S10. ^{1}H NMR spectrum of intermediate **2j**

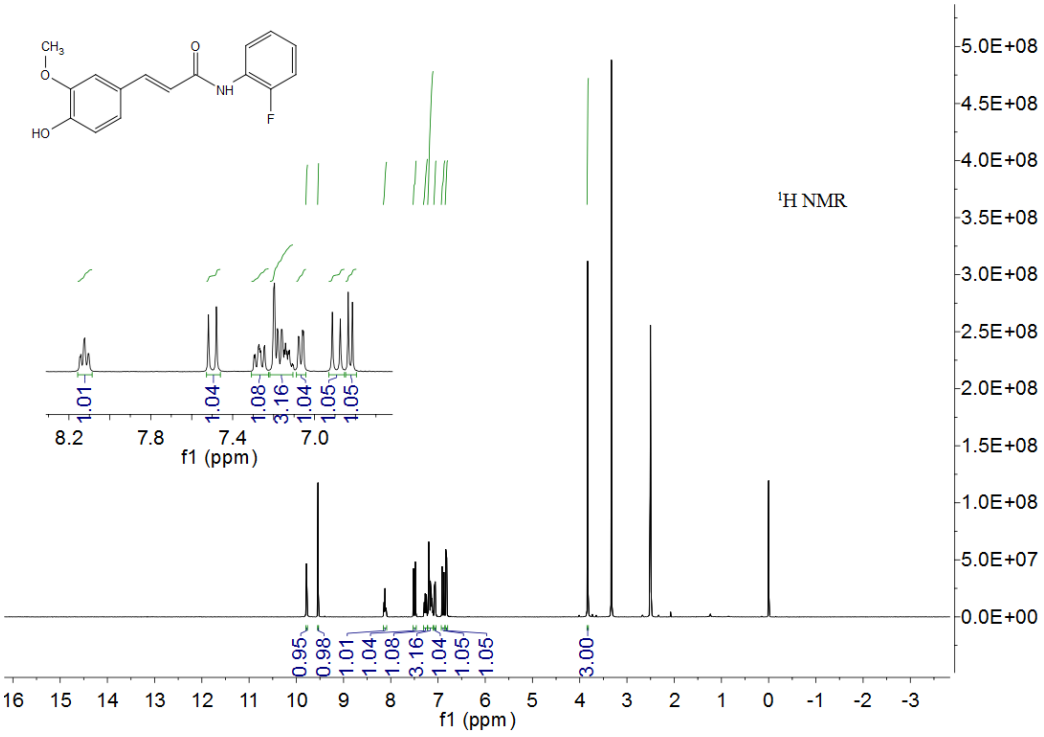
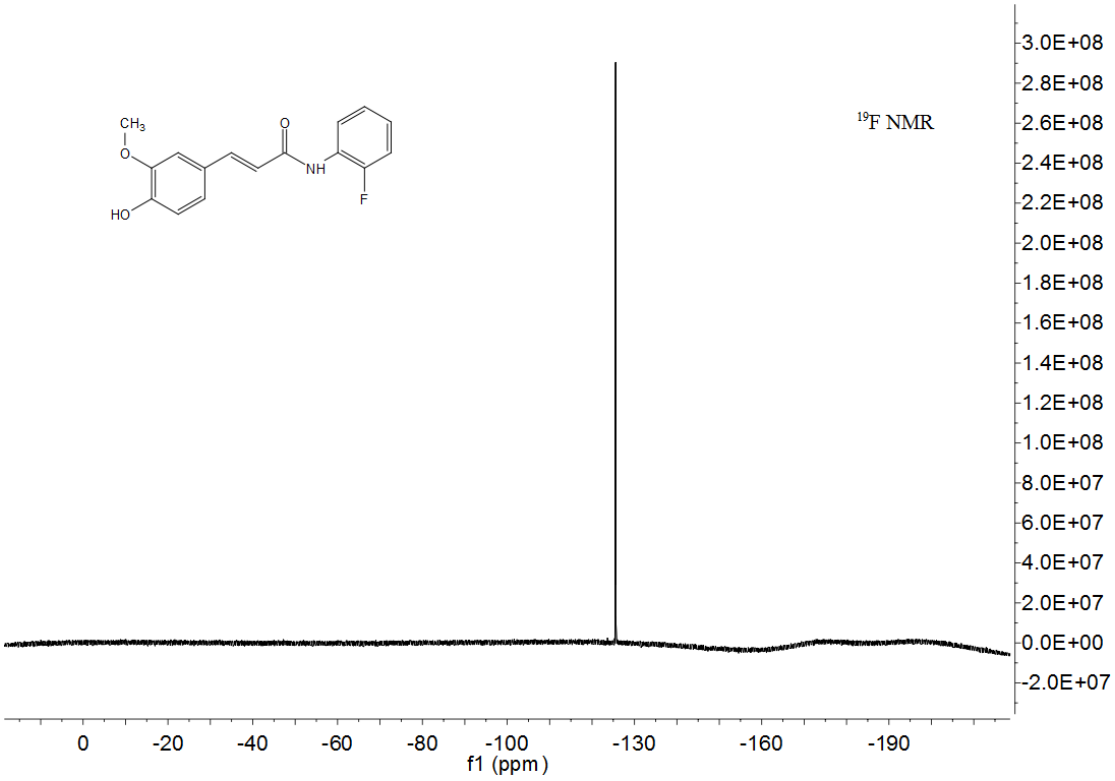


Figure S11. ^{19}F NMR spectrum of intermediate **2j**



Characterization of title compounds 4a-4v

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-(p-tolyl)acrylamide (**4a**) : gray solid, m.p. 215.4-215.5, yield : 58.68 %, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H, NH), 7.63 (t, *J* = 11.8 Hz, 1H, Ph-H), 7.57 (d, *J* = 7.1 Hz, 2H, Ph-2H), 7.32 (s, 2H, Ph-2H), 7.13 (d, *J* = 8.2 Hz, 2H, Ph-2H), 7.00 (d, *J* = 8.3 Hz, 1H, CO-CH=CH), 6.95 (s, 1H, Ph-H), 6.74 (d, *J* = 8.3 Hz, 1H, Ph-H), 6.51 (d, *J* = 2.1 Hz, 1H, Ph-H), 6.47 (s, 1H, CO-CH=), 6.36 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.23 (t, *J* = 5.9 Hz, 2H, CH_2), 4.18 (t, *J* = 6.7 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 3.92 (d, *J* = 3.4 Hz, 6H, 2×OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.77 (s, 3H, OCH_3), 2.31 (d, *J* = 9.9 Hz, 3H, CH_3), 2.25 (dd, *J* = 12.6, 6.3 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.07, 164.12, 163.82, 160.99, 158.83, 153.02, 152.77, 150.00, 149.22, 141.68, 140.56, 140.00, 129.51, 127.77, 125.94, 121.78, 119.88, 112.61, 110.41, 109.35, 105.91, 95.89, 92.49, 69.26, 66.00, 61.01, 56.38, 56.30, 55.86, 55.77, 30.13, 20.91, HRMS calcd for $C_{40}H_{41}NO_{11}[M+H]^+$: 712.2753, found 712.2752.

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-(4-methoxyphenyl)acrylamide (**4b**) : gray solid, m.p. 190.3-190.5, yield : 39.19 %, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H, Ph-H), 7.67 (d, *J* = 5.0 Hz, 1H, Ph-H), 7.66 – 7.61 (m, 2H, Ph-2H), 7.35 (s, 2H, Ph-2H), 7.01 (d, *J* = 8.3 Hz, 1H, CO-CH=CH), 6.96 (s, 1H, Ph-H), 6.89 (d, *J* = 8.8 Hz, 2H, Ph-2H), 6.76 (d, *J* = 8.3 Hz, 1H, CO-CH=), 6.56 – 6.48 (m, 2H, Ph-2H), 6.38 (d, *J* = 2.0 Hz, 1H, Ph-H), 4.25 (t, *J* = 5.9 Hz, 2H, CH_2), 4.19 (t, *J* = 6.6 Hz, 2H, CH_2), 3.97 – 3.92 (m, 9H, 3×OCH_3), 3.90 (s, 6H, 2×OCH_3), 3.81 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 2.34 – 2.20 (m, 2H, CH_2), ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.07, 164.36, 164.13, 160.97, 158.83, 156.20, 153.02, 152.79, 149.94, 149.20, 141.40, 140.56, 140.00, 131.82, 127.83, 125.93, 121.68, 121.52, 119.15, 114.14, 112.61, 110.44, 109.33, 105.90, 95.90, 92.50, 77.39, 77.07, 76.76, 69.27, 65.99, 61.01, 56.36, 56.30, 55.86, 55.75, 55.48, 30.14, HRMS calcd for $C_{40}H_{41}NO_{12}[M+H]^+$: 728.2701, found 712.2691.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-(p-tolyl)acrylamide (**4c**) : gray solid, m. p.100.1-101.9, yield : 51.49 %, ^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H, NH), 7.59 (d, J = 8.4 Hz, 2H, Ph-2H), 7.50 (d, J = 15.5 Hz, 1H, CO-CH=CH), 7.40 (s, 2H, Ph-2H), 7.20 (d, J = 1.8 Hz, 1H, Ph-H), 7.14 (dd, J = 8.5, 3.7 Hz, 2H, Ph-2H), 7.12 (s, 1H, CO-CH=), 6.98 (d, J = 8.4 Hz, 1H, Ph-H),

6.85 (d, J = 2.2 Hz, 1H, Ph-H), 6.68 (d, J = 15.6 Hz, 1H, Ph-H), 6.50 (d, J = 2.3 Hz, 1H, Ph-H), 4.05 – 3.96 (m, 4H, 2×CH2), 3.90 (s, 3H, OCH_3), 3.87 (s, 6H, 2×OCH_3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.26 (s, 3H, CH_3), 1.84 (s, 4H, 2×CH_2), 13C NMR (126 MHz, DMSO) δ 172.74, 164.29, 164.17, 160.80, 158.70, 153.23, 152.11, 150.16, 149.56, 140.54, 140.45, 139.88, 137.49, 132.60, 129.70, 127.97, 126.15, 122.21, 120.40, 119.58, 113.18, 110.59, 108.97, 106.16, 93.62, 71.77, 68.26, 60.71, 56.61, 56.56, 55.89, 26.84, 25.91, 21.02, HRMS calcd for $C_{41}H_{43}NO_{11}[M+H]^+$: 726.2908, found 712.2904.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-(4-methoxyphenyl)acrylamide (**4d**) : gray solid, m. p.108.6-109.8, yield : 63.54 %, ^{1}H NMR (400 MHz, DMSO) δ 10.01 (s, 1H, NH), 7.62 (d, J = 9.1 Hz, 2H, Ph-2H), 7.52 – 7.45 (m, 1H, CO-CH=CH), 7.40 (s, 2H, Ph-2H), 7.21 – 7.18 (m, 1H, Ph-H), 7.14 (dd, J = 8.4, 1.7 Hz, 1H, CO-CH=), 6.98 (d, J = 8.4 Hz, 1H, Ph-H), 6.93 – 6.87 (m, 2H, Ph-2H), 6.84 (t, J = 4.0 Hz, 1H, Ph-H), 6.67 (d, J = 15.6 Hz, 1H, Ph-H), 6.50 (d, J = 2.3 Hz, 1H, Ph-H), 4.01 (dd, J = 6.0, 3.2 Hz, 4H, 2×CH_2), 3.90 (s, 3H, OCH_3), 3.87 (s, 6H, 2×OCH_3), 3.84 (d, J = 3.1 Hz, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.74 (d, J = 5.6 Hz, 6H, 2×OCH_3), 1.84 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.23, 163.86, 160.75, 158.64, 155.62, 153.17, 152.05, 150.06, 149.51, 140.39, 140.22, 139.84, 133.13, 127.97, 126.09, 122.09, 120.97, 120.40, 114.38, 113.16, 110.53, 108.92, 106.12, 96.39, 93.57, 71.72, 68.21, 60.65, 56.51, 55.84, 55.62, 26.78, 25.85, HRMS calcd for $C_{41}H_{43}NO_{12}[M+H]^+$: 742.2858, found 712.2840.

(*E*)-*N*-(3-chlorophenyl)-3-(3-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-4-methoxyphenyl)acrylamide (**4e**) : yellow solid, m.p. 187.2-187.5, yield : 49.65 %, ^{1}H NMR (400 MHz, DMSO) δ 10.34 (s, 1H, NH), 7.97 (t, J = 2.0 Hz, 1H, Ph-H), 7.59 – 7.51 (m, 2H, Ph-2H), 7.40 – 7.34 (m, 3H, Ph-3H), 7.21 (t, J = 5.4 Hz, 1H, CO-CH=CH), 7.19 – 7.10 (m, 2H, Ph-2H), 6.90 (d, J = 8.4 Hz, 1H, CO-CH=), 6.84 (d, J = 2.2 Hz, 1H, Ph-H), 6.68 (d, J = 15.6 Hz, 1H, Ph-H), 6.50 (d, J = 2.3 Hz, 1H, Ph-H), 4.16 – 4.12 (m, 2H, CH_2), 4.09 (t, J = 6.4 Hz, 2H, CH_2), 3.91 (s, 3H, OCH_3), 3.86 (d, J = 1.7 Hz, 9H, 3×OCH_3), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.13 (p, J = 6.2 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.66, 164.61, 164.23, 160.74, 158.64, 153.17, 152.07, 150.15, 149.50, 141.36, 140.37, 139.85, 133.58, 130.95, 127.85, 126.01, 123.31, 122.29, 119.81, 118.99, 117.95,

113.08, 110.72, 108.90, 106.18, 96.38, 93.55, 69.25, 65.71, 60.64, 56.54, 56.48, 55.85, 49.07, 30.11, HRMS calcd for $C_{39}H_{38}ClNO_{11}[M+H]^+$: 732.2206, found 732.2187.

(*E*)-*N*-(3-chlorophenyl)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)acrylamide (**4f**) : gray solid, m. p.104.1-104.9, yield : 55.55 %, ^{1}H NMR (400 MHz, DMSO) δ 10.33 (s, 1H, NH), 7.95 (t, J = 2.0 Hz, 1H, Ph-H), 7.54 (ddd, J = 6.7, 5.8, 4.2 Hz, 2H, Ph-2H), 7.40 (s, 2H, Ph-2H), 7.36 (t, J = 8.1 Hz, 1H, CO-CH=CH), 7.22 (d, J = 1.8 Hz, 1H, CO-CH=), 7.19 – 7.09 (m, 2H, Ph-2H), 6.99 (d, J = 8.4 Hz, 1H, Ph-H), 6.84 (d, J = 2.2 Hz, 1H, Ph-H), 6.67 (d, J = 15.6 Hz, 1H, Ph-H), 6.49 (d, J = 2.3 Hz, 1H, Ph-H), 4.06 – 3.96 (m, 4H, 2×CH_2), 3.90 (s, 3H, OCH_3), 3.87 (d, J = 5.8 Hz, 6H, 2×OCH_3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 1.84 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.67, 164.63, 164.21, 160.74, 158.63, 153.17, 152.02, 150.32, 149.52, 141.43, 141.37, 140.39, 139.85, 133.58, 130.95, 127.68, 126.09, 123.30, 122.42, 119.71, 118.98, 117.94, 113.12, 110.62, 108.92, 106.12, 96.37, 93.55, 71.70, 68.22, 60.64, 56.53, 56.50, 55.86, 26.78, 25.85, HRMS calcd for $C_{40}H_{40}ClNO_{11}[M+H]^+$: 746.2362, found 746.2345.
(*E*)-*N*-(4-chlorophenyl)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)acrylamide (**4g**) : gray solid, m. p.103.3-104.8, yield : 62.00 %, ^{1}H NMR (500 MHz, DMSO) δ 10.29 (s, 1H, NH), 7.74 (d, *J* = 7.7 Hz, 2H, Ph-2H), 7.54 (d, *J* = 15.5 Hz, 1H, Ph-H), 7.41 (d, *J* = 1.2 Hz, 3H, Ph-3H), 7.39 (s, 1H, CO-CH=CH), 7.23 – 7.15 (m, 2H, Ph-2H), 7.00 (d, *J* = 7.9 Hz, 1H, CO-CH=), 6.87 (s, 1H, Ph-H), 6.68 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.51 (s, 1H, Ph-H), 4.05 – 3.98 (m, 4H, 2×CH_2), 3.91 (d, *J* = 1.0 Hz, 3H, OCH_3), 3.87 (d, *J* = 1.1 Hz, 6H, 2×OCH_3), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.75 (d, *J* = 1.3 Hz, 3H, OCH_3), 1.84 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.43, 164.24, 160.75, 158.65, 153.18, 152.06, 150.25, 149.51, 141.16, 140.39, 139.83, 138.88, 129.17, 127.74, 127.14, 126.09, 122.35, 121.06, 119.86, 113.13, 110.59, 108.91, 106.12, 96.41, 93.58, 71.72, 68.21, 60.66, 56.52, 55.85, 26.77, 25.84, HRMS calcd for $C_{40}H_{40}ClNO_{11}[M+H]^+$: 746.2362, found 746.2351.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-phenylacrylamide (**4h**) : yellow solid, m.p.116.4-116.7, yield : 60.30 %, ^{1}H NMR (400 MHz, DMSO) δ 10.13 (s, 1H, NH), 7.71 (d, *J* = 7.6 Hz, 2H, Ph-2H), 7.53 (d, *J* = 15.6 Hz, 1H, CO-CH=CH), 7.41 (s, 2H, Ph-2H), 7.36 – 7.30 (m, 2H, Ph-2H), 7.22

(d, *J* = 1.8 Hz, 1H, CO-CH=), 7.16 (dd, *J* = 8.4, 1.8 Hz, 1H, Ph-H), 7.06 (t, *J* = 7.4 Hz, 1H, Ph-H), 6.99 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.86 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.71 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.07 – 3.96 (m, 4H, 2×CH_2), 3.91 (s, 3H, OCH_3), 3.87 (d, *J* = 7.5 Hz, 9H, 3×OCH_3), 3.82 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 1.85 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) *δ* 172.68, 164.32, 164.24, 160.76, 158.65, 153.18, 152.07, 150.17, 149.53, 140.76, 140.39, 139.92, 139.88, 129.25, 127.88, 126.09, 123.63, 122.23, 120.25, 119.56, 113.19, 110.61, 108.93, 106.16, 96.40, 93.59, 71.74, 68.24, 60.66, 56.53, 55.87, 26.78, 25.85, HRMS calcd for $C_{40}H_{41}NO_{11}[M+H]^+$: 712.2752, found 712.2743.

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-phenylacrylamide (**4i**) : yellow solid, m.p. 242.5-242.9, yield : 49.79 %, ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.99 (d, *J* = 22.6 Hz, 1H, Ph-H), 7.70 – 7.62 (m, 3H, Ph-3H), 7.36 – 7.29 (m, 4H, Ph-4H)), 7.10 (t, *J* = 7.4 Hz, 1H, CO-CH=CH)), 7.01 (d, *J* = 8.3 Hz, 1H, CO-CH=), 6.95 (s, 1H, Ph-H), 6.75 (d, *J* = 8.3 Hz, 1H, Ph-H), 6.54 – 6.43 (m, 2H, Ph-2H), 6.35 (t, *J* = 4.8 Hz, 1H, Ph-H), 4.23 (t, *J* = 5.9 Hz, 2H, CH_2), 4.17 (t, *J* = 6.6 Hz, 2H, CH_2), 3.93 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.77 (s, 3H, OCH_3), 2.25 (p, *J* = 6.2 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 174.09, 164.19, 161.09, 158.90, 153.11, 152.81, 150.20, 149.38, 142.05, 140.64, 140.17, 138.56, 129.07, 127.80, 126.01, 124.17, 121.91, 119.98, 112.80, 110.60, 109.45, 106.08, 95.95, 92.58, 69.33, 66.12, 61.05, 56.43, 56.39, 55.89, 30.22, HRMS calcd for $C_{39}H_{39}NO_{11}[M+H]^+$: 696.2439, found 696.2459.

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-(3,4-dimethylphenyl)acrylamide (**4j**) : gray solid, m. p. 202.5-202.9, yield : 83.97 %, ^{1}H NMR (400 MHz, DMSO) *δ* 9.99 (s, 1H, NH), 7.50 (d, *J* = 15.4 Hz, 2H, Ph-2H), 7.47 – 7.42 (m, 1H, Ph-H), 7.38 (s, 2H, Ph-2H), 7.20 (d, *J* = 1.9 Hz, 1H, Ph-H), 7.14 (dd, *J* = 8.4, 1.8 Hz, 1H, CO-CH=CH), 7.09 (d, *J* = 8.3 Hz, 1H, Ph-H), 6.89 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.86 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.70 (d, *J* = 15.6 Hz, 1H, CO-CH=), 6.53 (d, *J* = 2.3 Hz, 1H, Ph-H), 4.11 (dt, *J* = 19.7, 6.4 Hz, 4H, 2×CH_2), 3.92 (s, 3H, OCH_3), 3.89 – 3.84 (m, 9H, 3×OCH_3), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.21 (d, *J* = 11.8 Hz, 6H, 2×CH_3), 2.12 (dd, *J* = 12.5, 6.3 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 174.07, 164.11, 160.97, 158.82, 153.02, 152.76, 149.94, 149.18, 141.54, 140.56, 139.94, 137.18, 129.97, 127.80,

125.95, 121.77, 121.20, 117.36, 112.54, 110.33, 109.33, 105.85, 95.89, 92.47, 77.40, 77.08, 76.77, 69.25, 65.98, 61.02, 56.39, 56.29, 55.87, 55.74, 30.13, 19.96, 19.24, HRMS calcd for $C_{41}H_{43}NO_{11}$[M+H]$^+$:726.2908, found 726.2902.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-(3,4-dimethylphenyl)acrylamide (**4k**) : gray solid, m. p. 107.3.-108.1, yield : 48.39 %, ^{1}H NMR (400 MHz, DMSO) δ 9.97 (s, 1H, NH), 7.49 (d, *J* = 15.6 Hz, 2H, Ph-2H), 7.43 (dd, *J* = 7.7, 5.9 Hz, 1H, CO-CH=CH), 7.41 (s, 2H, Ph-2H), 7.20 (d, *J* = 1.8 Hz, 1H, Ph-H), 7.14 (dd, *J* = 8.4, 1.7 Hz, 1H, Ph-H), 7.08 (d, *J* = 8.3 Hz, 1H, CO-CH=), 6.99 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.85 (d, *J* = 2.0 Hz, 1H, Ph-H), 6.69 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.50 (d, *J* = 2.1 Hz, 1H, Ph-H), 4.03 (t, *J* = 9.7 Hz, 4H, 2×CH_2), 3.91 (s, 3H, OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.85 (d, *J* = 7.1 Hz, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.76 (d, *J* = 4.7 Hz, 3H, OCH_3), 2.21 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 1.85 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.22, 164.05, 160.75, 158.63, 153.17, 152.03, 150.09, 149.52, 140.39, 140.35, 139.86, 137.68, 136.77, 131.37, 130.08, 127.96, 126.09, 122.09, 120.74, 120.47, 117.10, 113.17, 110.60, 108.92, 106.13, 96.38, 93.56, 71.72, 68.22, 60.65, 56.54, 56.51, 55.85, 26.79, 25.86, 20.16, 19.28, 0.56, HRMS calcd for $C_{42}H_{45}NO_{11}$[M+H]$^+$:740.3065, found 740.3060.

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-(3,4-dimethoxyphenyl)acrylamide (**4l**) : green solid, m. p. 118.0.-118.7, yield : 65.33 %, ^{1}H NMR (400 MHz, DMSO) δ 10.03 (s, 1H, NH), 7.47 (dd, *J* = 21.3, 8.8 Hz, 2H, Ph-2H), 7.36 (d, *J* = 14.3 Hz, 2H, Ph-2H), 7.26 – 7.16 (m, 2H, Ph-2H), 7.13 (d, *J* = 8.3 Hz, 1H, CO-CH=CH), 6.97 – 6.77 (m, 3H, Ph-2H, CO-CH=), 6.68 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.51 (d, *J* = 2.1 Hz, 1H, Ph-H), 4.11 (dt, *J* = 19.2, 6.1 Hz, 4H, 2×CH_2), 3.91 (d, *J* = 7.0 Hz, 3H, OCH_3), 3.85 (t, *J* = 7.1 Hz, 9H, 3×OCH_3), 3.81 (s, 3H, OCH_3), 3.79 – 3.70 (m, 9H, 3×OCH_3), 2.12 (dd, *J* = 12.5, 6.3 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.67, 164.24, 163.90, 160.76, 158.65, 153.17, 152.09, 149.92, 149.52, 149.02, 145.29, 140.37, 140.21, 139.88, 133.57, 128.13, 126.01, 121.99, 120.52, 113.17, 112.61, 111.48, 110.65, 108.91, 106.21, 104.69, 96.39, 93.57, 69.28, 65.73, 60.65, 56.50, 56.19, 55.85, 55.80, 30.12, HRMS calcd for $C_{41}H_{43}NO_{13}$[M+H]$^+$:756.2650, found 756.2675.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-(3,4-dimethoxyphenyl)acrylamide (**4m**) : green solid, m. p.

95.3-96.1, yield : 59.67 %, ^{1}H NMR (400 MHz, DMSO) δ 10.01 (s, 1H, NH), 7.49 (d, *J* = 15.5 Hz, 1H, CO-CH=CH), 7.43 (t, *J* = 3.9 Hz, 1H, Ph-H), 7.41 (s, 2H, Ph-2H), 7.24 – 7.18 (m, 2H, Ph-2H), 7.14 (dd, *J* = 8.4, 1.7 Hz, 1H, CO-CH=), 6.99 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.92 (d, *J* = 8.9 Hz, 1H, Ph-H), 6.85 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.67 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.50 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.02 (dd, *J* = 6.0, 3.1 Hz, 4H, 2×CH_2), 3.91 (s, 3H, OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.86 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.76 (s, 6H, 2×OCH_3), 3.74 (s, 3H), 1.85 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.22, 163.91, 160.75, 158.64, 153.17, 152.04, 150.09, 149.53, 149.01, 145.27, 140.39, 140.24, 139.85, 133.58, 127.96, 126.09, 122.11, 120.43, 113.18, 112.59, 111.45, 110.54, 108.92, 106.14, 104.67, 96.38, 93.57, 71.72, 68.23, 60.65, 56.54, 56.51, 56.18, 55.85, 55.79, 26.78, 25.85, HRMS calcd for $C_{42}H_{45}NO_{13}$[M+H]$^{+}$:772.2963, found 772.2972.

(*E*)-N-(4-bromophenyl)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)acrylamide (**4n**) : gray solid, m. p. 208.4-209.6, yield : 67.92 %,^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 19.4, 12.0 Hz, 3H, Ph-3H), 7.42 (d, *J* = 8.7 Hz, 2H, Ph-2H), 7.32 (s, 2H, Ph-2H), 7.03 – 6.88 (m, 2H, Ph-2H), 6.73 (d, *J* = 8.3 Hz, 1H, CO-CH=CH), 6.50 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.46 (d, *J* = 15.5 Hz, 1H, CO-CH=), 6.35 (d, *J* = 2.1 Hz, 1H, Ph-H), 4.19 (dt, *J* = 13.2, 6.2 Hz, 4H, 2×CH_2), 3.92 (t, *J* = 5.5 Hz, 9H, 3×OCH_3), 3.87 (s, 6H, 2×OCH_3), 3.75 (s, 3H, OCH_3), 2.33 – 2.17 (m, 2H, CH_2), ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.08, 164.51, 164.18, 160.99, 158.85, 153.06, 152.85, 150.21, 149.30, 142.30, 140.56, 140.14, 137.73, 131.92, 127.63, 125.91, 121.82, 121.39, 116.53, 112.71, 110.63, 109.35, 106.02, 95.93, 92.55, 69.29, 66.03, 60.99, 56.33, 55.84, 55.80, 30.16, HRMS calcd for $C_{39}H_{38}BrNO_{11}$[M+H]$^{+}$:776.1701, found 776.1682.

(*E*)-*N*-(4-bromophenyl)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)acrylamide (**4o**) : yellow solid, m. p. 180.3-181.6, yield : 58.25 %, ^{1}H NMR (400 MHz, DMSO) δ 10.30 (s, 1H, NH), 7.72 (d, *J* = 8.9 Hz, 2H, Ph-2H), 7.56 (t, *J* = 7.7 Hz, 2H, Ph-2H), 7.53 (s, 1H, CO-CH=CH), 7.43 (s, 2H , Ph-2H), 7.22 (dd, *J* = 19.9, 5.0 Hz, 2H, Ph-2H), 7.02 (d, *J* = 8.3 Hz, 1H, CO-CH=), 6.88 (t, *J* = 2.1 Hz, 1H, Ph-H), 6.71 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.53 (d, *J* = 1.9 Hz, 1H, Ph-H), 4.08 – 4.01 (m, 4H, 2×CH_2), 3.94 (s, 3H, OCH_3), 3.90 (s, 6H, 2×OCH_3), 3.88 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 1.87 (s, 4H, 2× CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68,

164.46, 164.23, 160.75, 158.64, 153.17, 152.04, 150.27, 149.52, 141.19, 140.39, 139.86, 139.28, 132.06, 127.75, 126.09, 122.34, 121.46, 119.87, 115.18, 113.15, 110.63, 108.92, 106.14, 96.39, 93.57, 71.72, 68.23, 60.65, 56.51, 55.86, 26.78, 25.84, HRMS calcd for $C_{40}H_{40}BrNO_{11}$ $[M+H]^+$:790.1857, found 790.1853.

(*E*)-*N*-(3,4-dichlorophenyl)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)acrylamide (**4p**) : yellow solid, m. p. 118.6-119.3, yield : 65.55 %, ^{1}H NMR (400 MHz, DMSO) δ 10.45 (s, 1H, NH), 8.13 (d, *J* = 1.9 Hz, 1H, Ph-H), 7.60 – 7.57 (m, 2H, Ph-2H), 7.57 – 7.53 (m, 1H, CO-CH=CH), 7.37 (d, *J* = 2.7 Hz, 2H, Ph-H), 7.23 – 7.13 (m, 2H, Ph-2H), 6.87 (dd, *J* = 18.4, 5.3 Hz, 2H, Ph-2H), 6.65 (d, *J* = 15.6 Hz, 1H, CO-CH=), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.16 – 4.03 (m, 4H, 2×CH_2), 3.91 (s, 3H, OCH_3), 3.88 – 3.83 (m, 9H, 3×OCH_3), 3.79 (s, 3H, OCH_3), 3.74 (d, *J* = 2.5 Hz, 3H, OCH_3), 2.18 – 2.05 (m, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.66, 164.70, 164.25, 160.76, 158.66, 153.18, 152.11, 150.23, 149.51, 141.70, 140.37, 140.00, 139.87, 131.48, 131.21, 126.01, 125.00, 122.37, 120.69, 119.53, 113.11, 110.78, 108.91, 106.21, 96.42, 93.59, 69.27, 65.72, 60.65, 56.50, 55.87, 30.10, HRMS calcd for $C_{39}H_{37}Cl_2NO_{11}[M+H]^+$:766.1816, found 766.1801.

(*E*)-*N*-(3,4-dichlorophenyl)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)acrylamide (**4q**) : grey solid, m. p. 102.3-103.4, yield : 51.70 %, ^{1}H NMR (400 MHz, DMSO) δ 10.42 (s, 1H, NH), 8.13 (s, 1H, Ph-H), 7.59 (s, 2H, Ph-2H), 7.55 (s, 1H, CO-CH=CH), 7.41 (s, 2H, Ph-2H), 7.24 – 7.14 (m, 2H, Ph-2H), 7.00 (d, *J* = 8.4 Hz, 1H, CO-CH=), 6.84 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.65 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.50 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.06 – 3.99 (m, 4H, 2×CH_2), 3.92 (s, 3H, OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.86 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 1.85 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.71, 164.22, 160.77, 158.63, 153.18, 152.02, 150.43, 149.57, 141.71, 140.39, 140.00, 139.94, 131.48, 131.15, 127.65, 126.09, 125.00, 122.47, 120.71, 119.61, 119.47, 113.21, 110.78, 108.95, 106.22, 96.37, 93.58, 71.73, 68.29, 60.65, 56.54, 56.49, 55.91, 26.79, 25.86, HRMS calcd for $C_{40}H_{39}Cl_2NO_{11}$ $[M+H]^+$:780.1972, found 780.1976.

(*E*)-*N*-(4-chlorophenyl)-3-(4-((5-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)pentyl)oxy)-3-methoxyphenyl)acrylamide (**4r**) : grey solid, m. p.

112.3-112.9, yield : 58.23 %, ^{1}H NMR (400 MHz, DMSO) δ 10.28 (s, 1H, NH), 7.75 (d, *J* = 8.6 Hz, 2H, Ph-2H), 7.55 (d, *J* = 15.6 Hz, 1H, Ph-H), 7.41 (s, 3H, Ph-3H), 7.39 (s, 1H, CO-CH=CH), 7.23 (s, 1H, Ph-H), 7.18 (d, *J* = 8.5 Hz, 1H, Ph-H), 7.00 (d, *J* = 8.3 Hz, 1H, Ph-H), 6.85 (s, 1H, Ph-H), 6.69 (d, *J* = 15.6 Hz, 1H, CO-CH=), 6.51 (s, 1H, Ph-H), 3.98 (t, *J* = 6.2 Hz, 4H, 2×CH_2), 3.92 (s, 3H, OCH_3), 3.87 (d, *J* = 6.0 Hz, 9H, 3×OCH_3), 3.83 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 1.75 (dd, *J* = 13.6, 6.7 Hz, 4H, 2×CH_2), 1.59 – 1.48 (m, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.44, 164.21, 160.76, 158.63, 153.15, 152.01, 150.32, 149.52, 141.15, 140.46, 139.86, 138.88, 129.15, 127.75, 127.14, 126.12, 122.37, 121.07, 119.88, 113.12, 110.61, 108.94, 106.20, 96.38, 93.56, 71.94, 68.54, 60.65, 56.52, 55.88, 29.86, 28.83, 22.66, HRMS calcd for $C_{41}H_{42}ClNO_{11}$[M+H]$^+$:760.2519, found 760.2507.

(*E*)-*N*-(3-chlorophenyl)-3-(4-((5-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)pentyl)oxy)-3-methoxyphenyl)acrylamide (**4s**) : grey solid, m. p. 153.5-154.1, yield : 62.87 %, ^{1}H NMR (400 MHz, DMSO) δ 10.31 (s, 1H, NH), 7.95 (d, *J* = 1.5 Hz, 1H, Ph-H), 7.53 (dd, *J* = 11.1, 8.8 Hz, 2H, Ph-2H), 7.39 (d, *J* = 1.8 Hz, 2H, Ph-H), 7.34 (dd, *J* = 8.1, 1.6 Hz, 1H, Ph-H), 7.21 (s, 1H, Ph-H), 7.17 (d, *J* = 8.2 Hz, 1H, CO-CH=CH), 7.11 (d, *J* = 7.9 Hz, 1H, Ph-H), 6.99 (d, *J* = 7.1 Hz, 1H, Ph-H), 6.83 (s, 1H, Ph-H), 6.67 (d, *J* = 15.6 Hz, 1H, CO-CH=), 6.49 (s, 1H, Ph-H), 3.96 (t, *J* = 5.6 Hz, 4H, 2×CH_2), 3.90 (d, *J* = 1.5 Hz, 3H, OCH_3), 3.88 – 3.83 (m, 9H, 3×OCH_3), 3.81 (d, *J* = 1.5 Hz, 3H, OCH_3), 3.75 (d, *J* = 1.9 Hz, 3H, OCH_3), 1.73 (d, *J* = 6.3 Hz, 4H, 2×CH_2), 1.52 (d, *J* = 6.8 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.69, 164.63, 164.20, 160.76, 158.63, 153.15, 152.00, 150.39, 149.53, 141.43, 141.37, 140.46, 139.87, 133.58, 130.94, 127.68, 126.12, 123.30, 122.45, 119.72, 118.99, 117.95, 113.12, 110.64, 108.95, 106.21, 96.37, 93.56, 71.94, 68.55, 60.65, 56.53, 56.49, 55.89, 40.61, 40.40, 40.19, 39.98, 39.77, 39.57, 39.36, 29.86, 28.83, 22.66, HRMS calcd for $C_{41}H_{42}ClNO_{11}$ [M+H]$^+$:760.2519, found 760.2507.

(*E*)-3-(4-((5-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)pentyl)oxy)-3-methoxyphenyl)-*N*-(4-methoxyphenyl)acrylamide (**4t**) : grey solid, m. p. 123.6-124.7, yield : 64.75 %, ^{1}H NMR (400 MHz, DMSO) δ 9.99 (s, 1H, NH), 7.61 (d, *J* = 9.0 Hz, 2H, Ph-2H), 7.48 (d, *J* = 15.6 Hz, 1H, CO-CH=CH), 7.38 (s, 2H, Ph-2H), 7.19 (d, *J* = 1.6 Hz, 1H, Ph-H), 7.14 (dd, *J* = 8.3, 1.6 Hz, 1H, Ph-H), 6.97 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.90 (d, *J* = 9.1 Hz, 2H, Ph-2H), 6.83 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.66 (d, *J* = 15.6 Hz, 1H, CO-CH=),

6.48 (d, *J* = 2.2 Hz, 1H, Ph-H), 3.95 (dt, *J* = 12.4, 6.2 Hz, 4H, 2×CH_2), 3.89 (s, 3H, OCH_3), 3.87 – 3.82 (m, 9H, 3×OCH_3), 3.80 (s, 3H, OCH_3), 3.73 (d, *J* = 5.1 Hz, 6H, 2×OCH_3), 1.73 (dq, *J* = 12.8, 6.3 Hz, 4H, 2×CH_2), 1.56 – 1.46 (m, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.69, 164.21, 163.87, 160.76, 158.63, 155.63, 153.15, 152.01, 150.13, 149.52, 140.46, 140.22, 139.86, 133.13, 127.97, 126.12, 122.12, 120.99, 120.41, 114.39, 113.15, 110.55, 108.94, 106.20, 96.37, 93.56, 71.94, 68.54, 60.65, 56.52, 56.50, 55.87, 55.62, 29.86, 28.84, 22.66, HRMS calcd for $C_{42}H_{45}NO_{12}[M+H]^+$:756.3014, found 756.2999.

(*E*)-3-(4-(3-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)propoxy)-3-methoxyphenyl)-*N*-(2-fluorophenyl)acrylamide (**4u**) : grey solid, m. p. 117.6-118.3, yield : 54.83 %, ^1H NMR (400 MHz, DMSO) δ 9.85 (s, 1H, NH), 8.18 – 8.10 (m, 1H, Ph-H), 7.54 (d, *J* = 15.6 Hz, 1H, CO-CH=CH), 7.37 (s, 2H, Ph-2H), 7.29 (ddd, *J* = 11.1, 7.9, 1.6 Hz, 1H, Ph-2H), 7.20 (dd, *J* = 5.5, 1.6 Hz, 2H, Ph-2H), 7.19 – 7.11 (m, 3H, Ph-3H), 6.97 (d, *J* = 15.6 Hz, 1H, Ph-H), 6.89 (d, *J* = 8.4 Hz, 1H, Ph-H), 6.85 (d, *J* = 2.2 Hz, 1H, CO-CH=), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.10 (dt, *J* = 17.9, 6.2 Hz, 4H, 2×CH_2), 3.91 (s, 3H, OCH_3), 3.86 (d, *J* = 3.9 Hz, 9H, 3×OCH_3), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.12 (p, *J* = 6.1 Hz, 2H, CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.66, 164.69, 164.25, 160.76, 158.66, 153.18, 152.11, 150.08, 149.49, 141.25, 140.37, 139.87, 128.04, 126.02, 124.88, 123.89, 122.23, 119.92, 115.96, 115.77, 113.12, 110.71, 108.91, 106.21, 96.42, 93.58, 69.28, 65.71, 60.65, 56.58, 56.50, 55.84, 30.11, ^{19}F NMR (376 MHz, DMSO) δ -125.55 (s), HRMS calcd for $C_{39}H_{38}FNO_{11}[M+H]^+$:716.2501, found 716.2494.

(*E*)-3-(4-(4-((5,7-dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl)oxy)butoxy)-3-methoxyphenyl)-*N*-(2-fluorophenyl)acrylamide (**4v**): grey solid, m. p. 162.3-163.6, yield : 66.77 %,^1H NMR (400 MHz, DMSO) δ 9.86 (s, 1H, NH), 8.19 – 8.12 (m, 1H, Ph-H), 7.55 (d, *J* = 15.6 Hz, 1H, CO-CH=CH), 7.42 (s, 2H, Ph-2H), 7.33 – 7.25 (m, 1H, Ph-H), 7.25 – 7.13 (m, 4H, Ph-4H), 6.99 (t, *J* = 11.5 Hz, 2H, Ph-2H), 6.86 (d, *J* = 2.2 Hz, 1H, CO-CH=), 6.51 (d, *J* = 2.2 Hz, 1H, Ph-H), 4.07 – 3.98 (m, 4H, 2×CH_2), 3.92 (s, 3H, OCH_3), 3.89 (s, 6H, 2×OCH_3), 3.87 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 1.86 (s, 4H, 2×CH_2), ^{13}C NMR (101 MHz, DMSO) δ 172.68, 164.71, 164.23, 160.74, 158.64, 154.84, 153.17, 152.42, 152.05, 150.24, 149.49, 141.29, 140.39, 139.84, 127.86, 127.13, 127.01, 126.09, 124.84, 123.85, 122.35, 119.82, 115.95, 115.76, 113.12, 110.59, 108.91, 106.12, 96.39, 93.56,

71.71, 68.21, 60.65, 56.54, 56.51, 55.82, 49.07, 26.78, 25.84, ^{19}F NMR (376 MHz, DMSO) δ -125.58 (s), HRMS calcd for $C_{40}H_{40}FNO_{11}[M+H]^+$: 730.2658, found 730.2653.

^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectrum of the title compounds4a-4v

Figure S12. ^{1}H NMR spectrum of compound **4a**

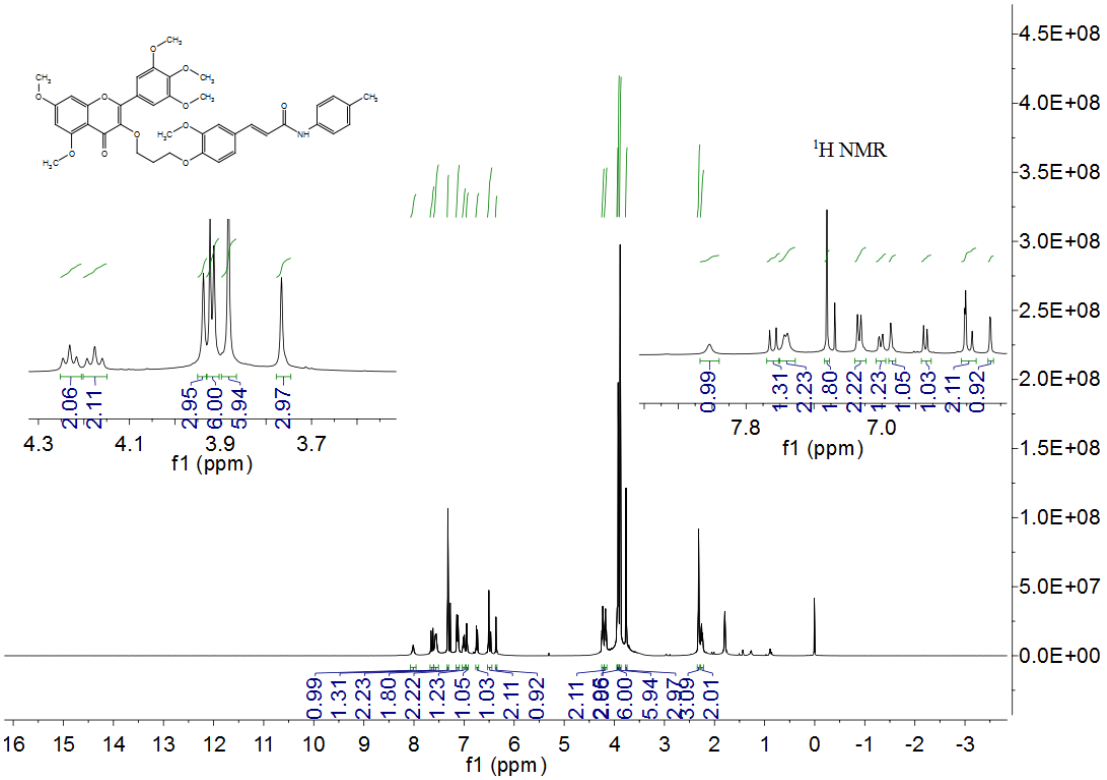


Figure S13. ^{13}C NMR spectrum of compound **4a**

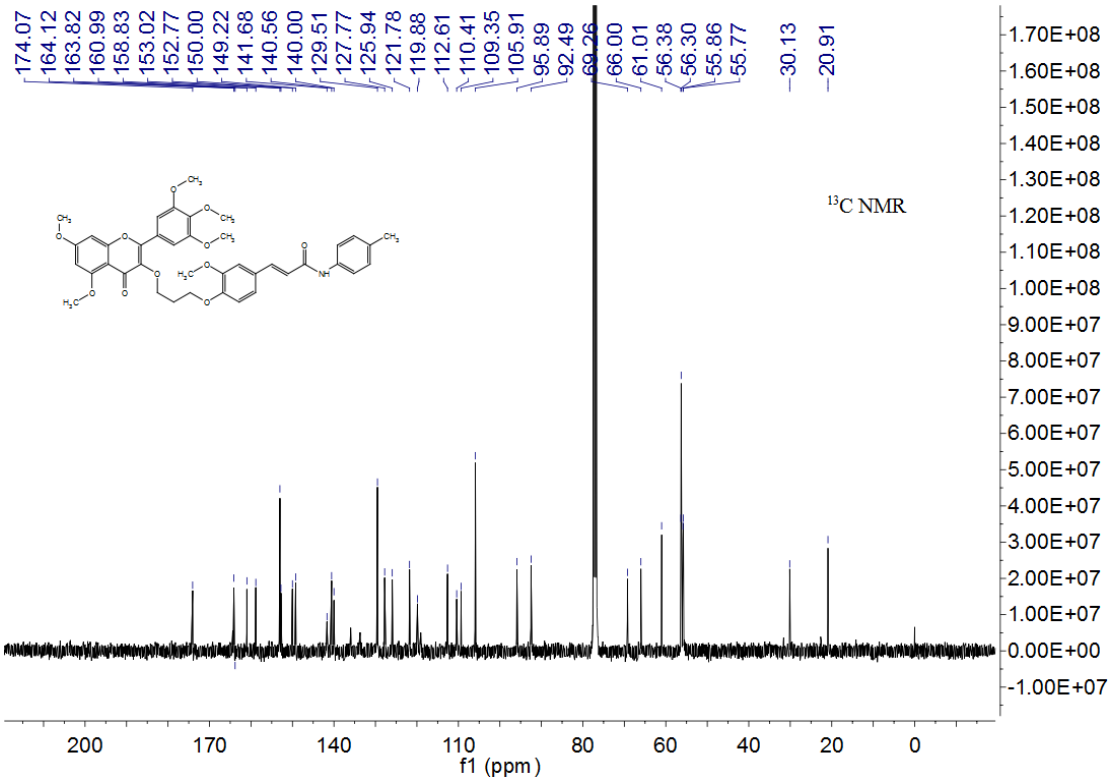


Figure S14. HRMS spectrum of compound **4a**

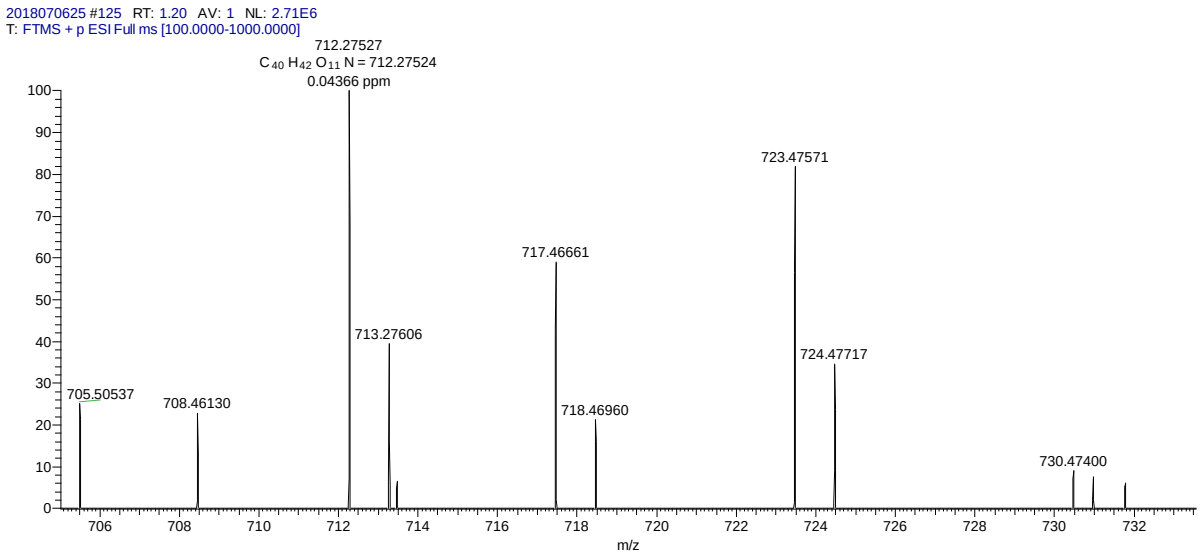


Figure S15. ^{1}H NMR spectrum of compound **4b**

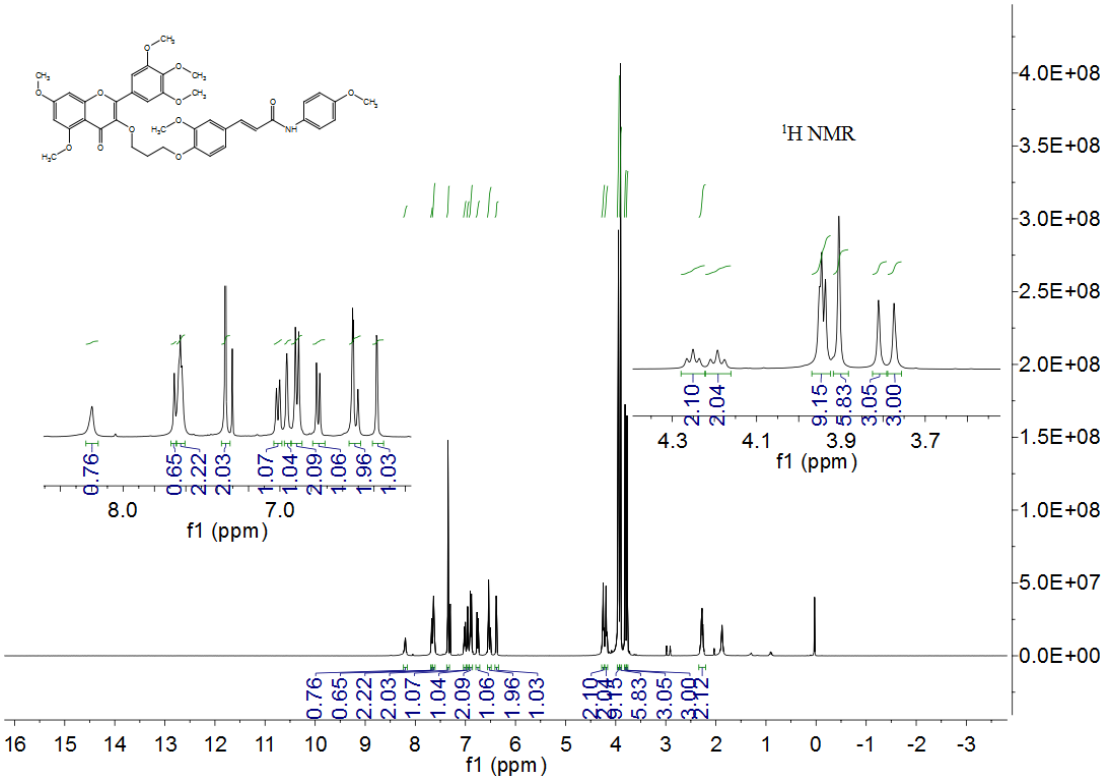


Figure S16. ^{13}C NMR spectrum of compound **4b**

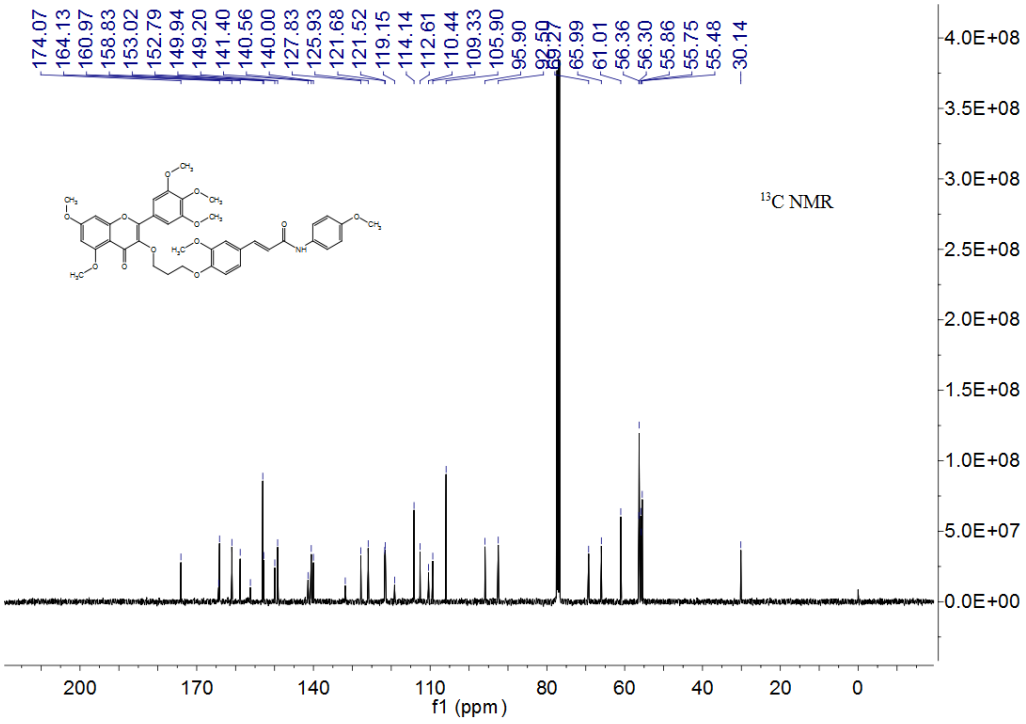


Figure S17. HRMS spectrum of compound **4b**

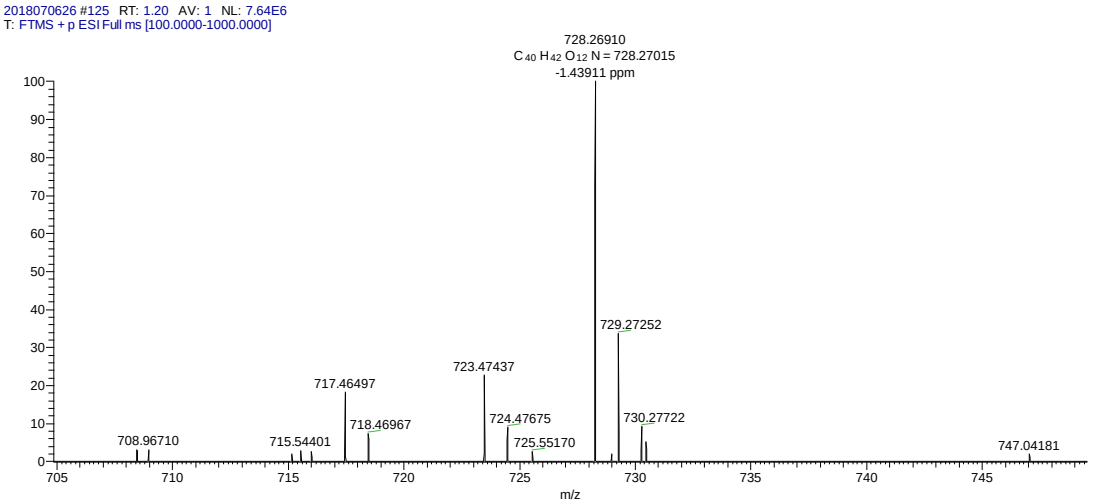


Figure S18. ^{1}H NMR spectrum of compound **4c**

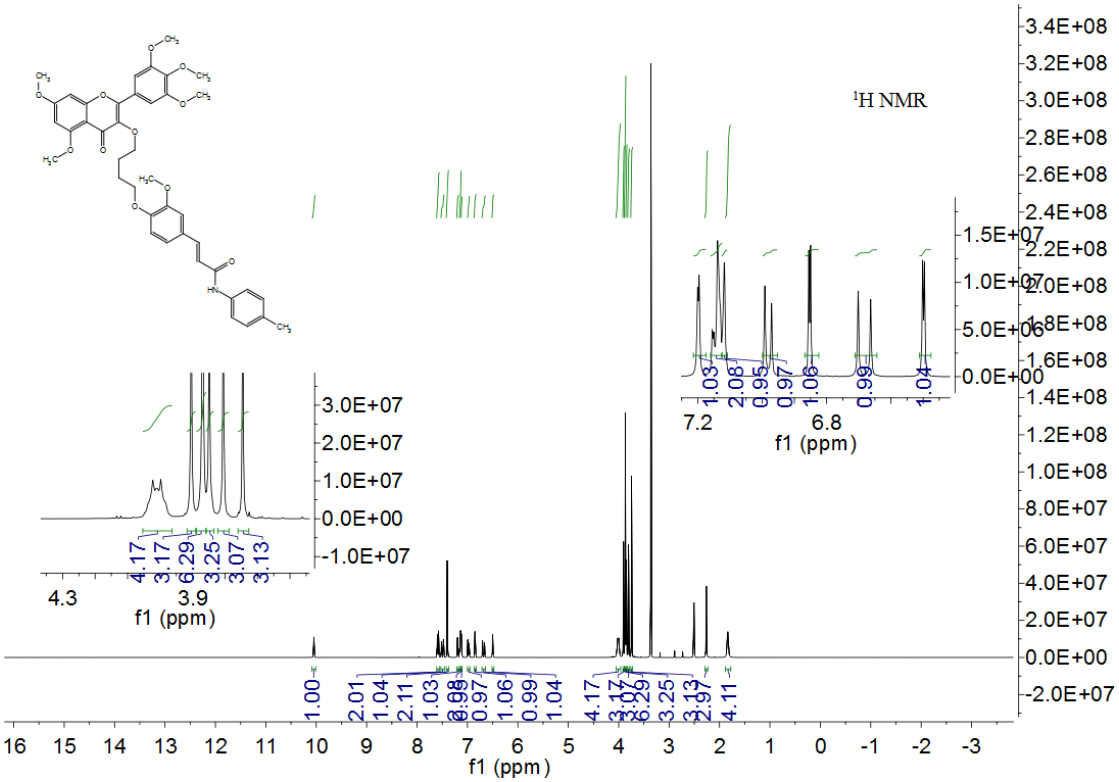


Figure S19. ^{13}C NMR spectrum of compound **4c**

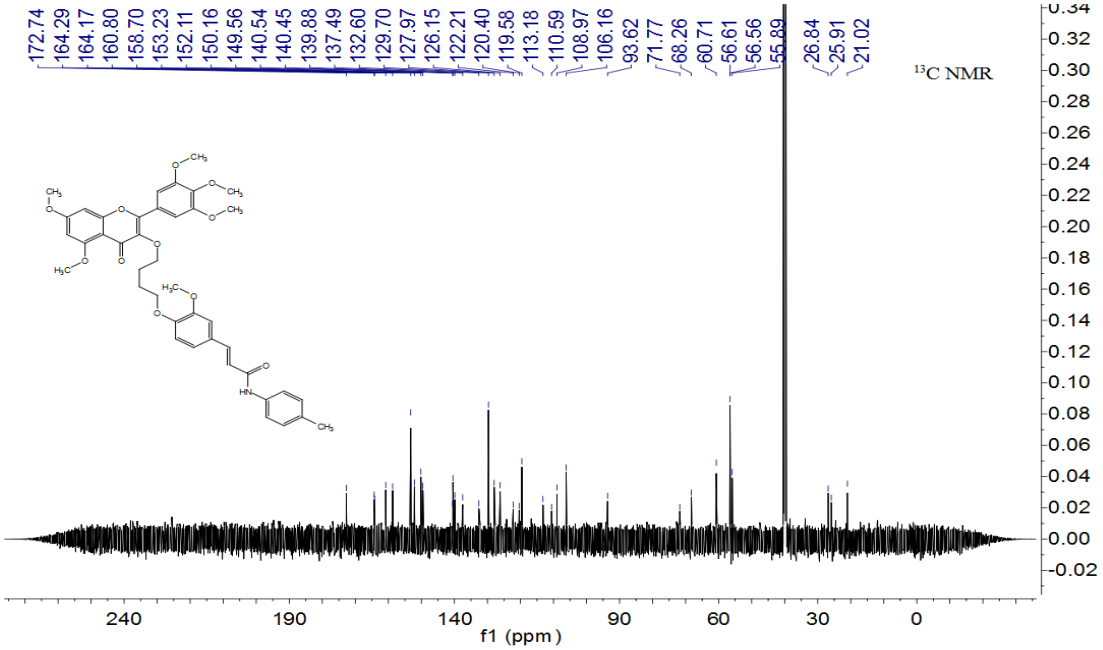


Figure S20. MS spectrum of compound **4c**

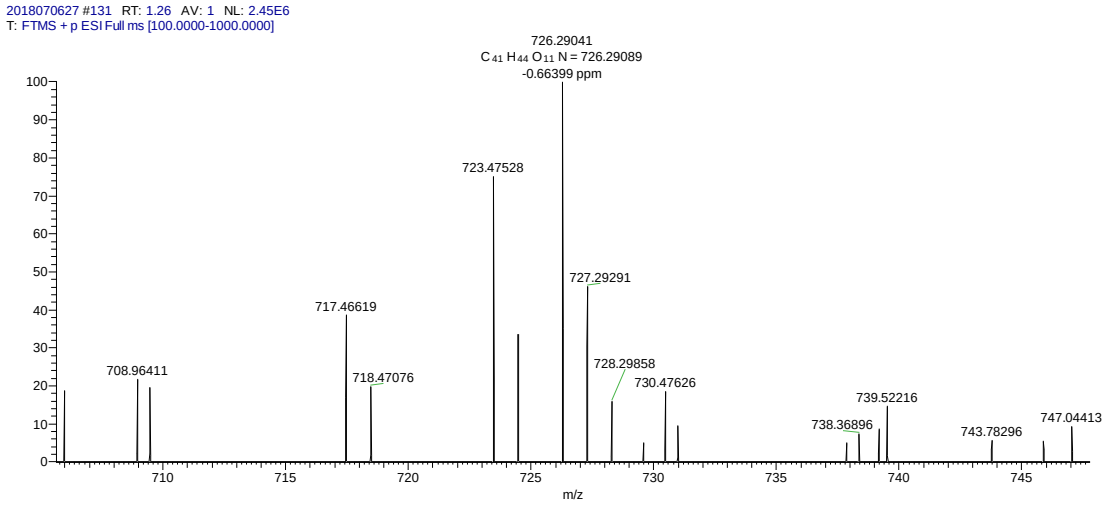


Figure S21. ^{1}H spectrum of compound **4d**

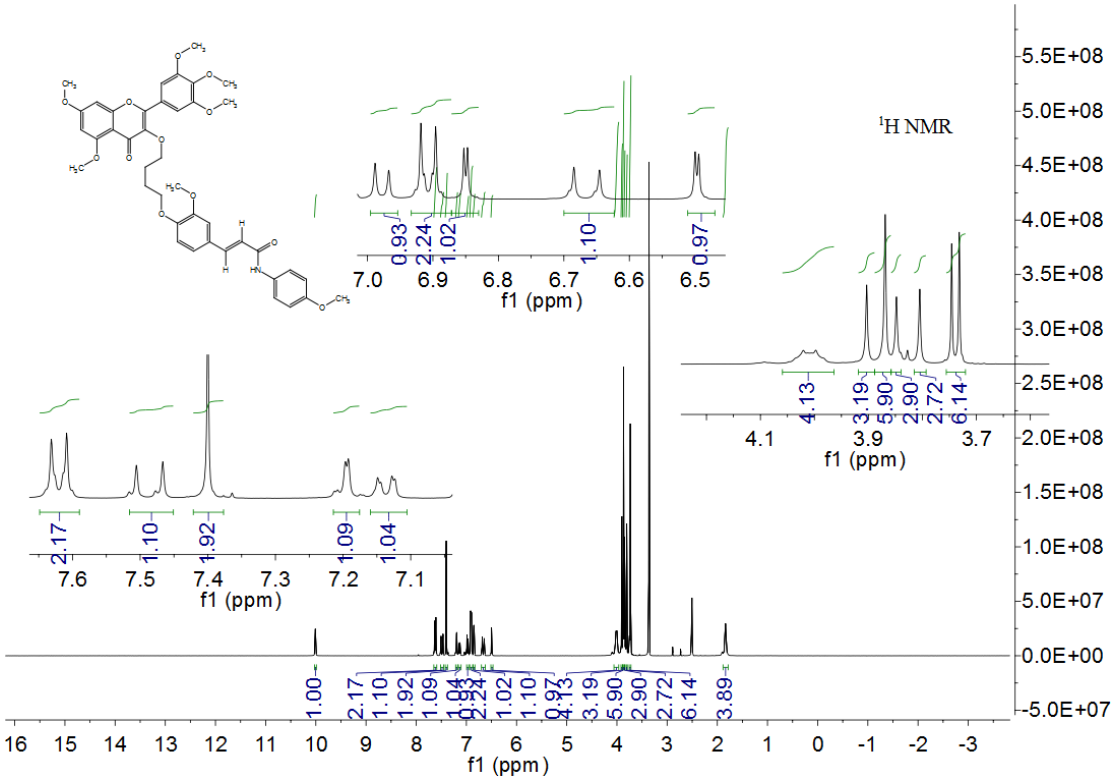


Figure S22. ^{13}C NMR spectrum of compound **4d**

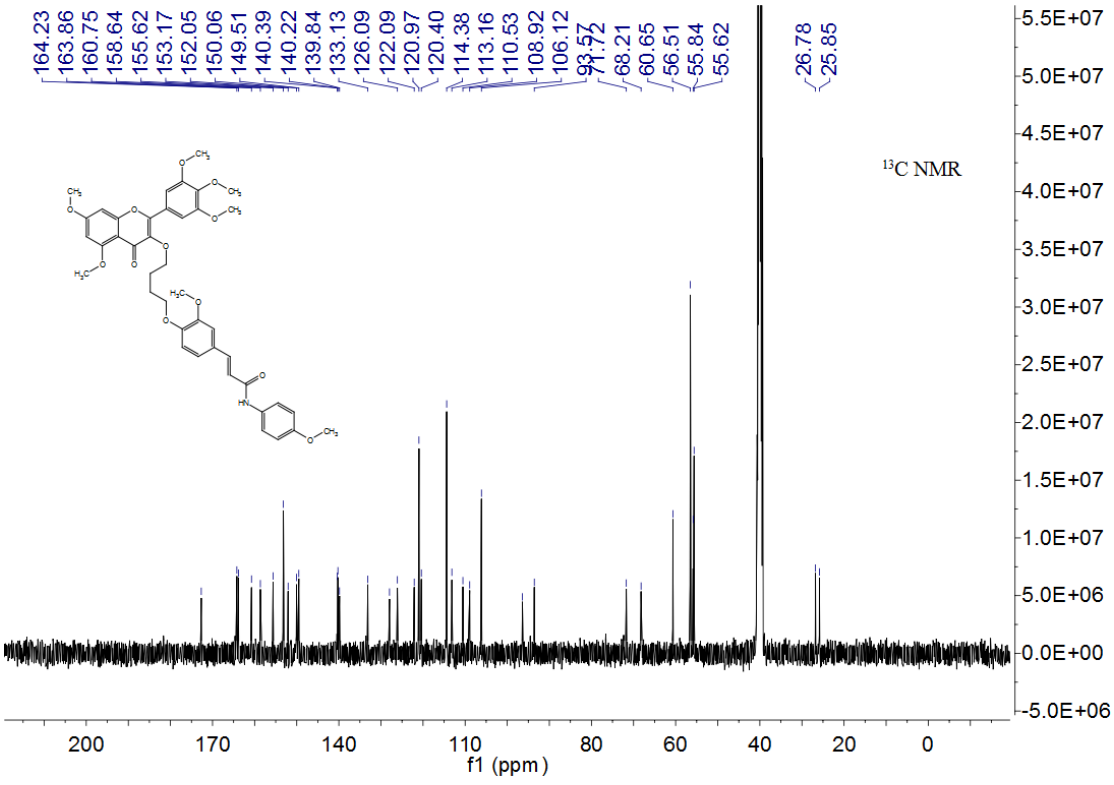


Figure S23. HRMS spectrum of compound **4d**

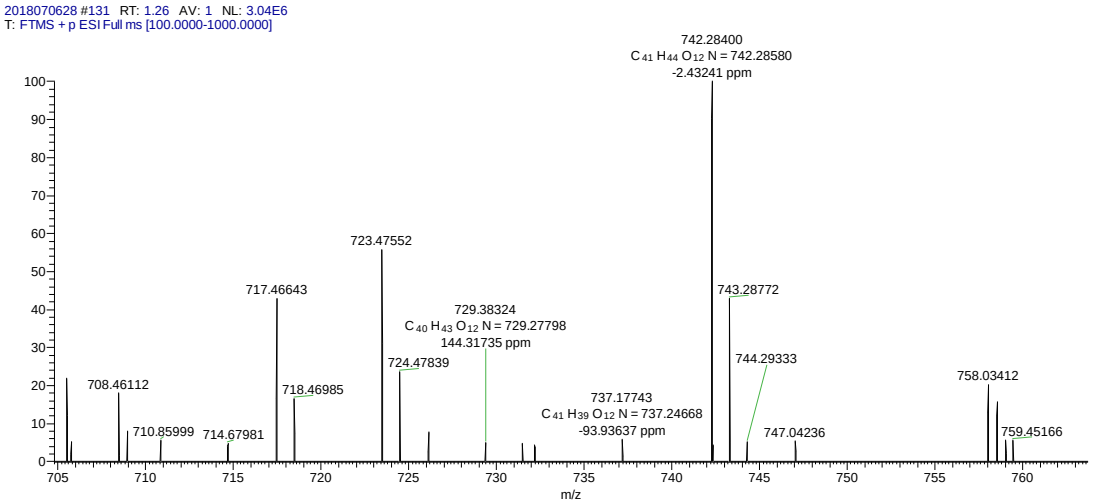


Figure S24. ^{1}HNMR spectrum of compound **4e**

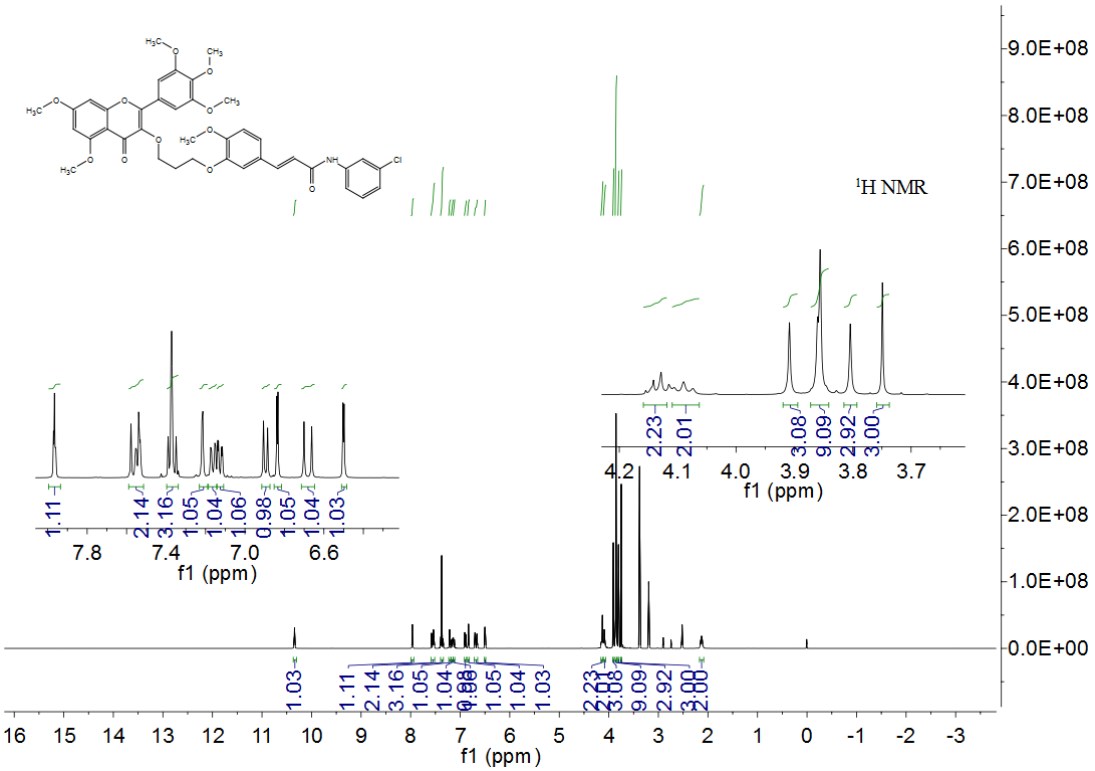


Figure S25.[13]C NMR spectrum of compound **4e**

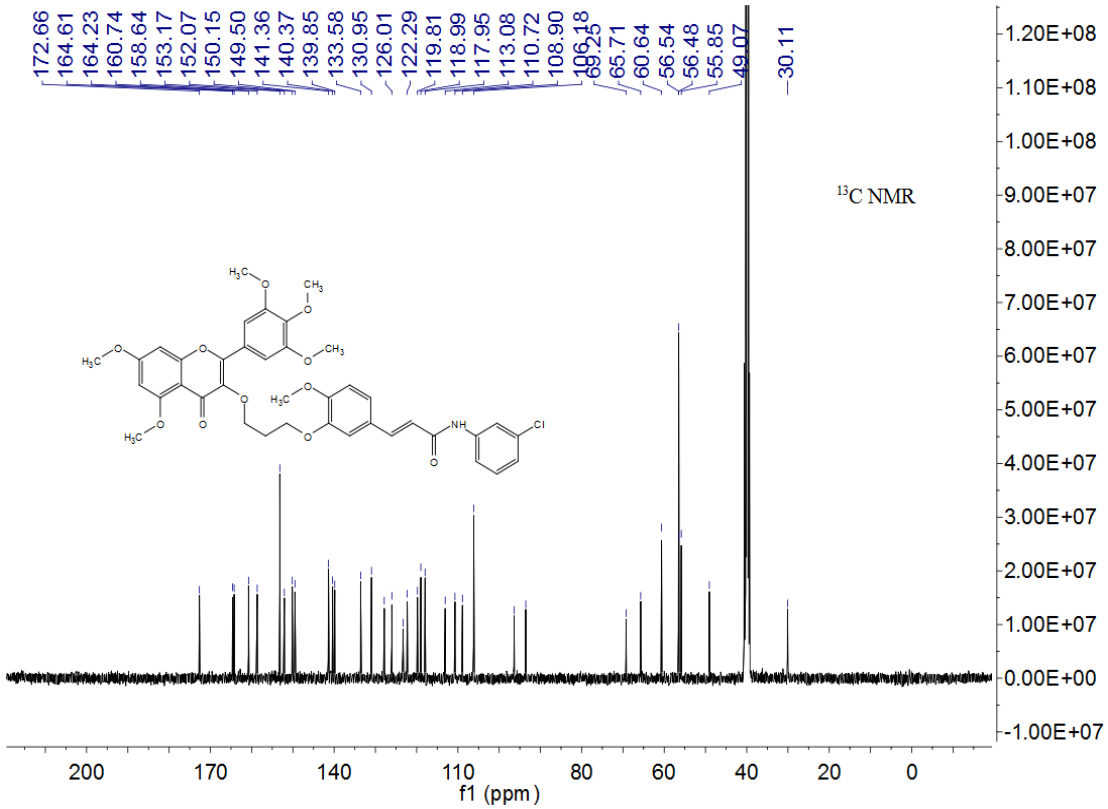


Figure S26. HRMS spectrum of compound **4e**

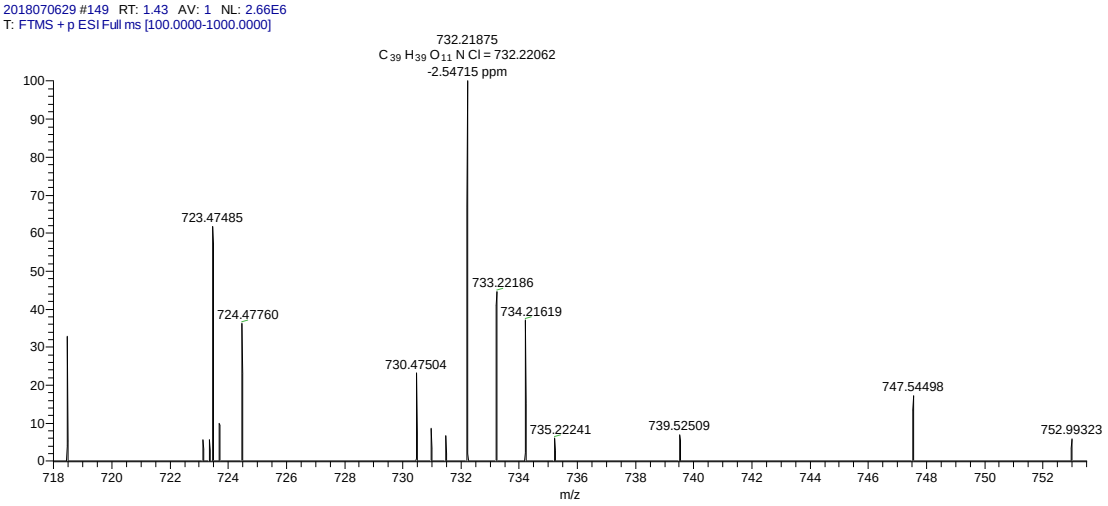


Figure S27. ^{1}H NMR spectrum of compound **4f**

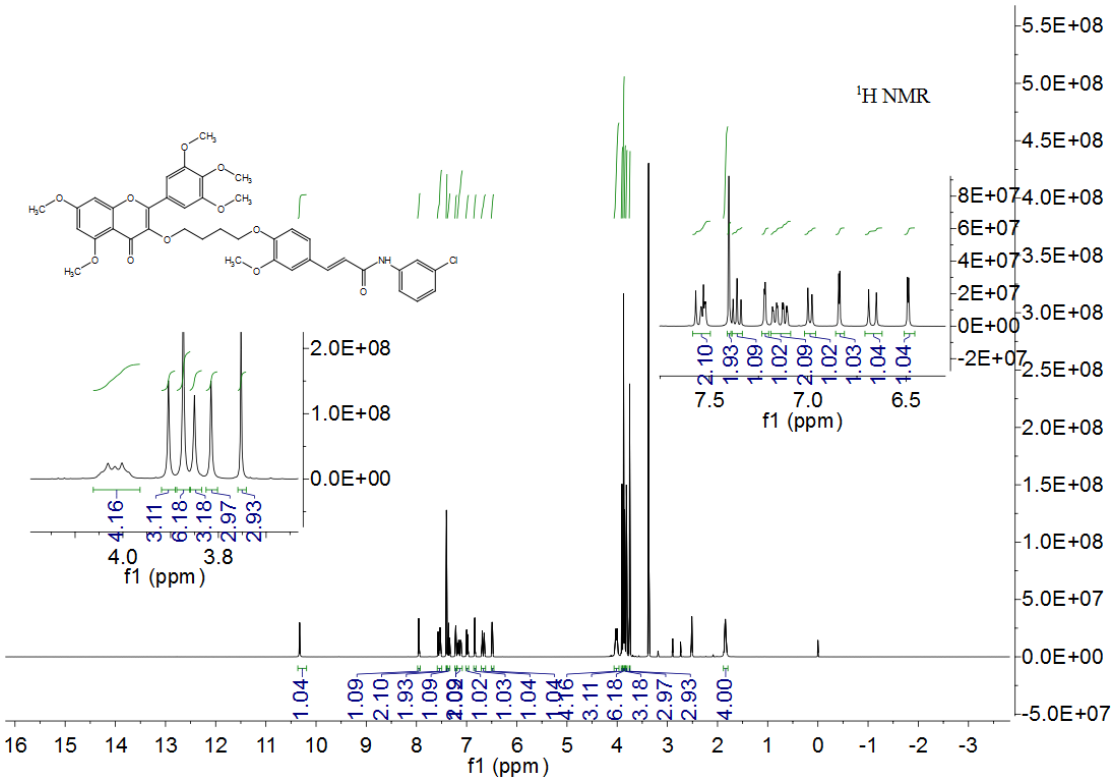


Figure S28. ^{13}C NMR spectrum of compound **4f**

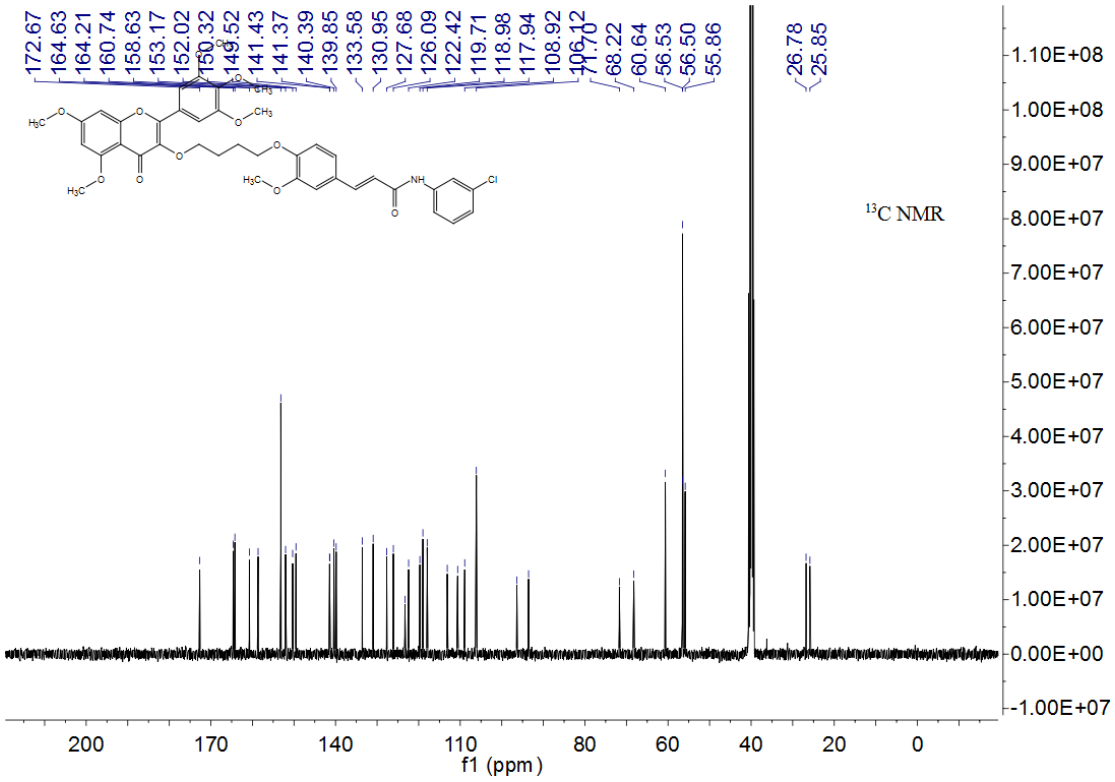


Figure S29.HRMS spectrum of compound **4f**

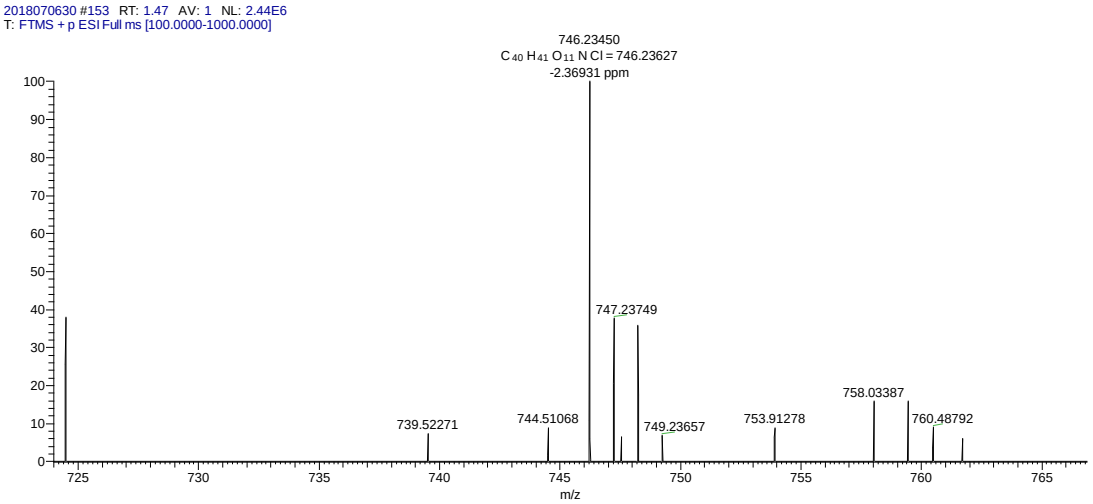


Figure S30 ^{1}H NMR spectrum of compound **4g**

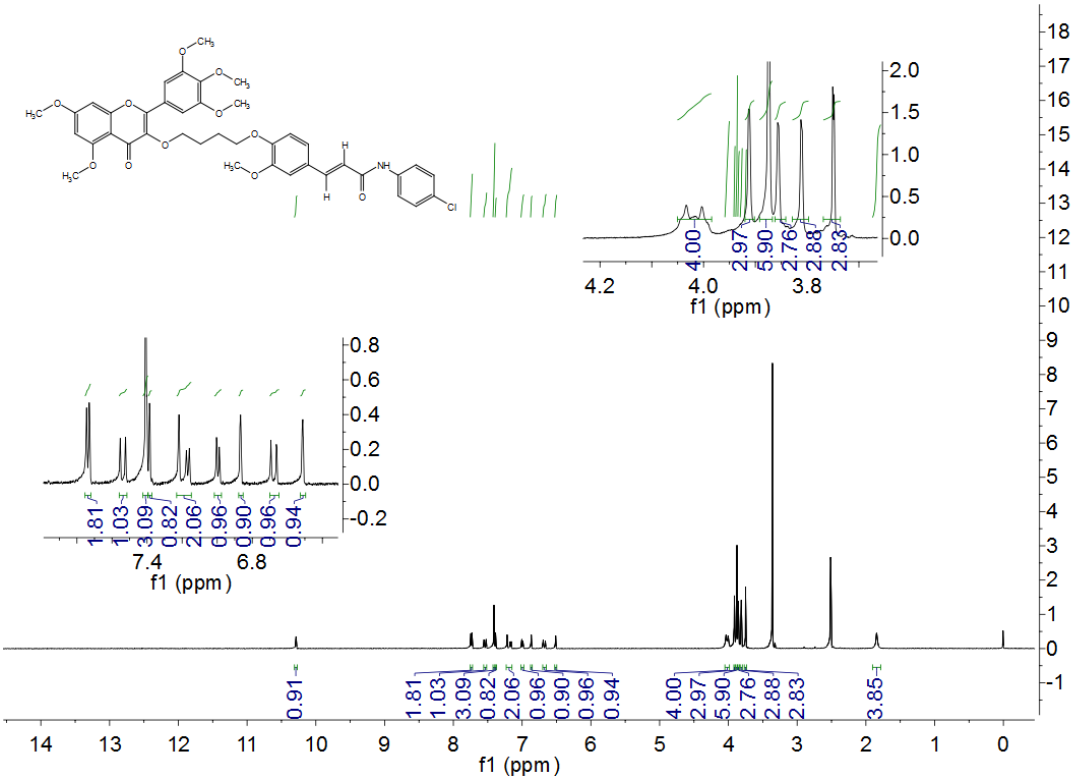


Figure S31.[13]C NMR spectrum of compound **4g**

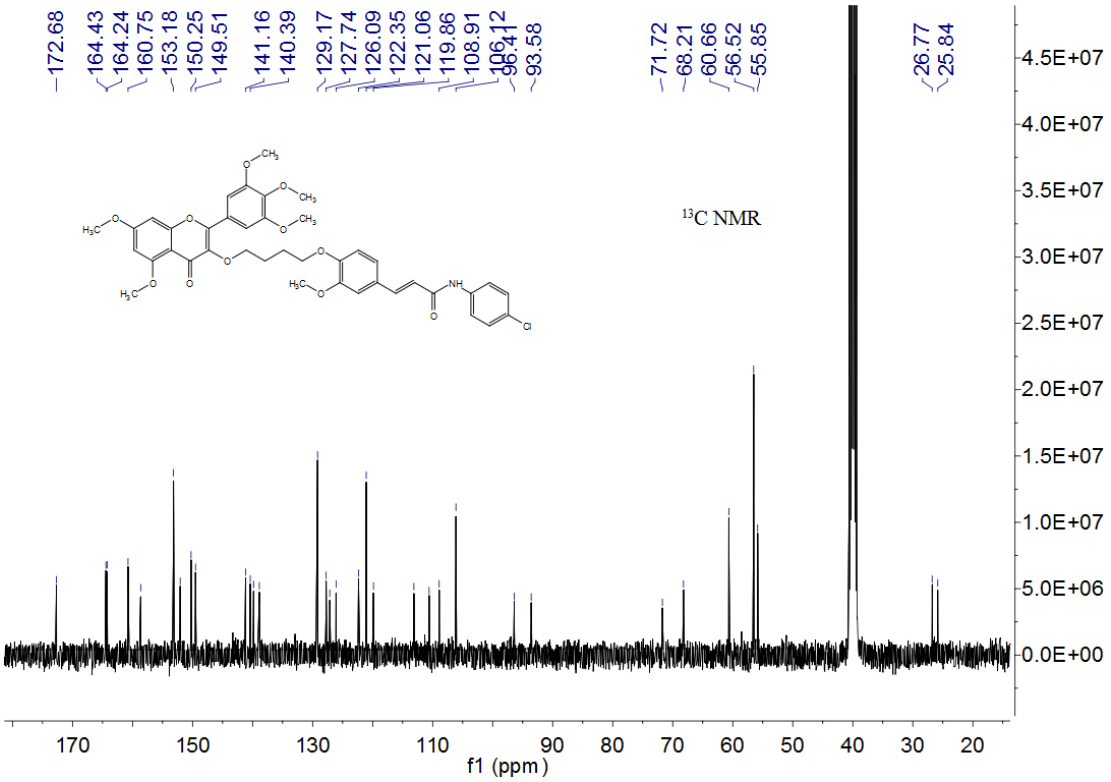


Figure S32.HRMS spectrum of compound **4g**

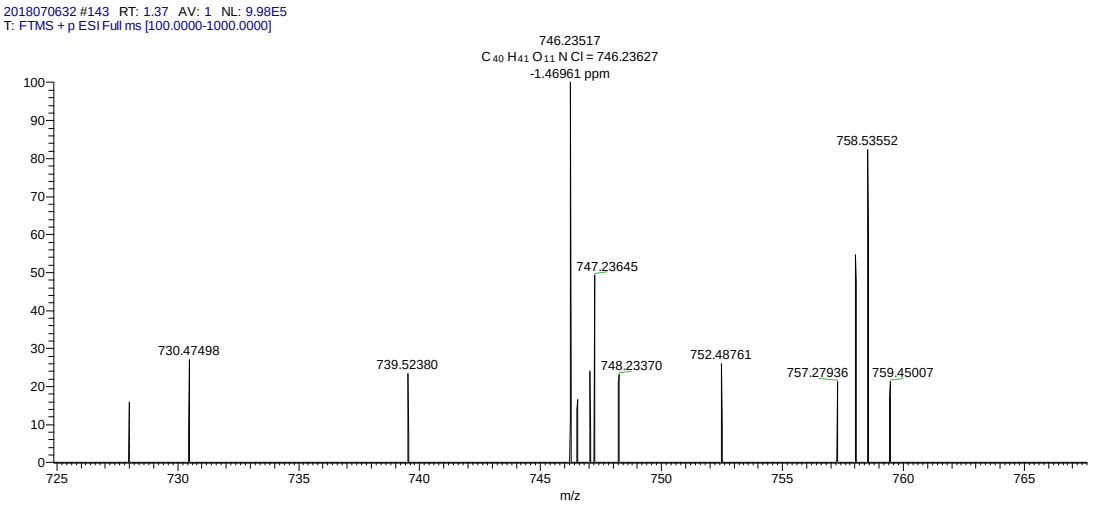


Figure S33. ^{1}H NMR spectrum of compound **4h**

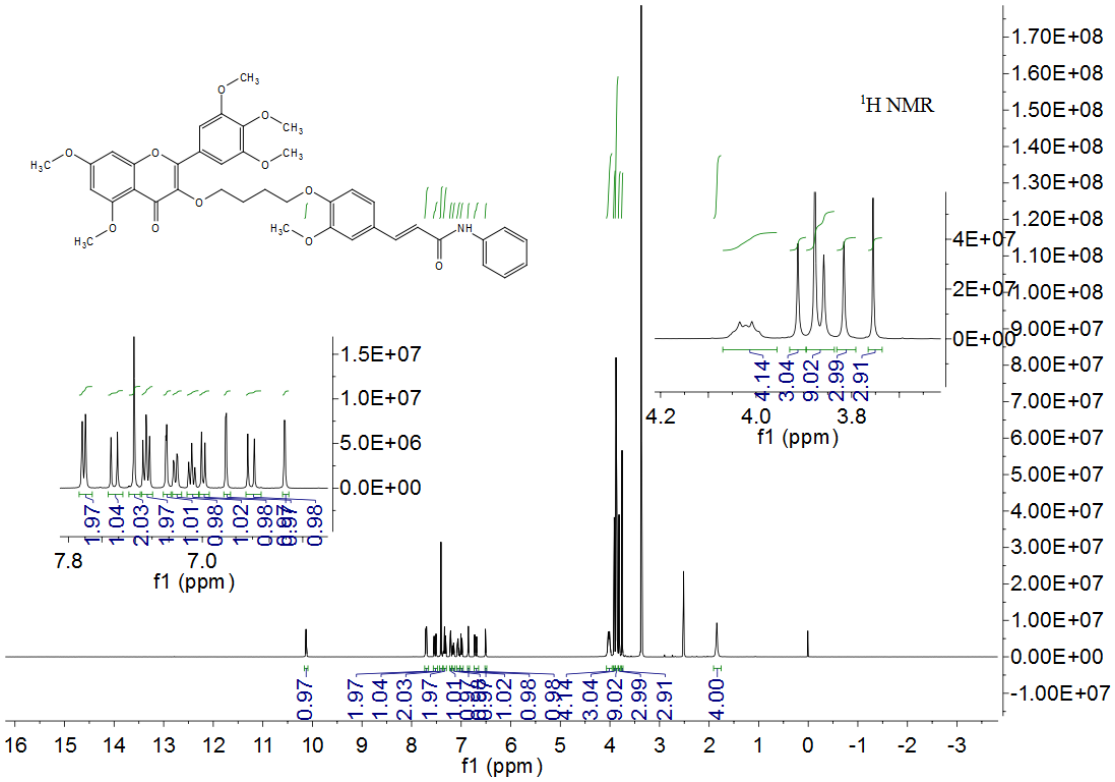


Figure S34. ^{13}C NMR spectrum of compound **4h**

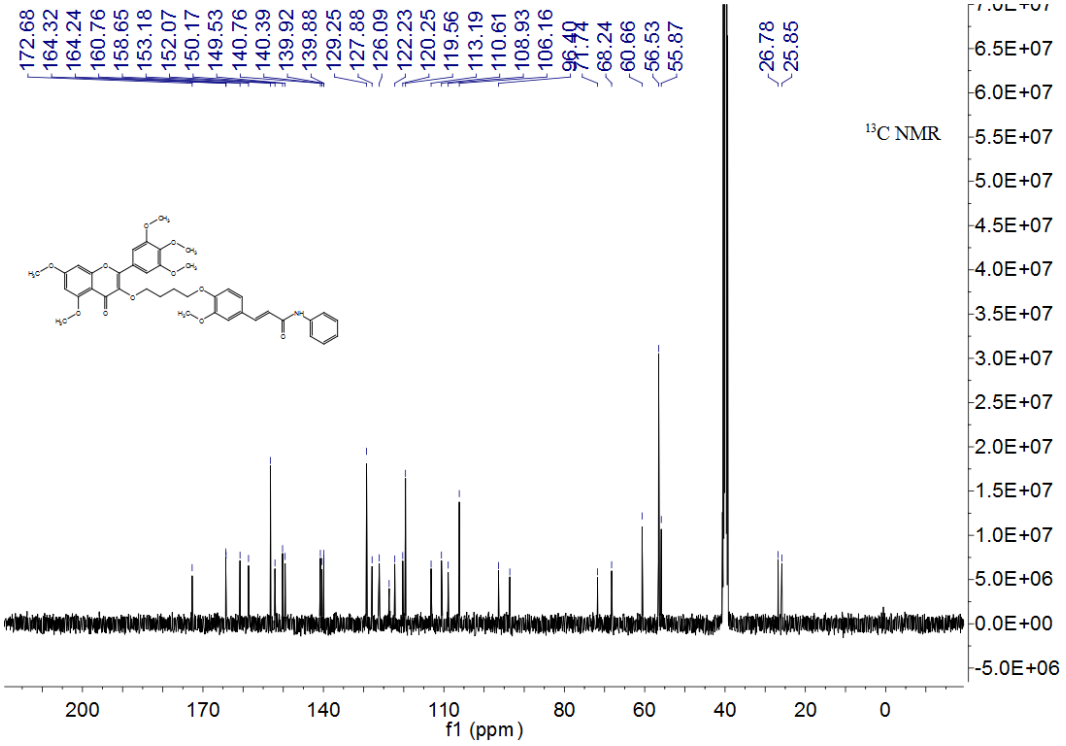


Figure S35. HRMS spectrum of compound **4h**

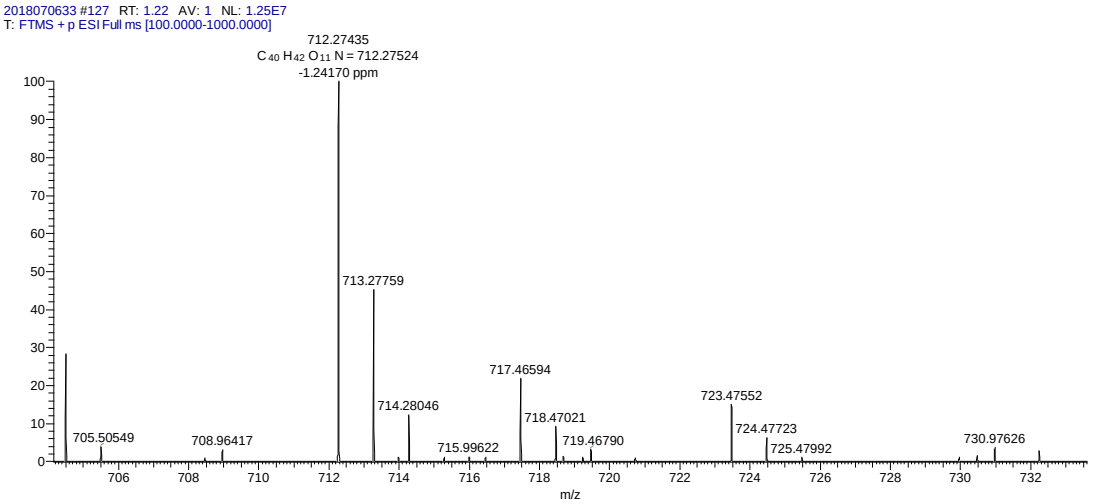


Figure S36.[1]H NMR spectrum of compound **4i**

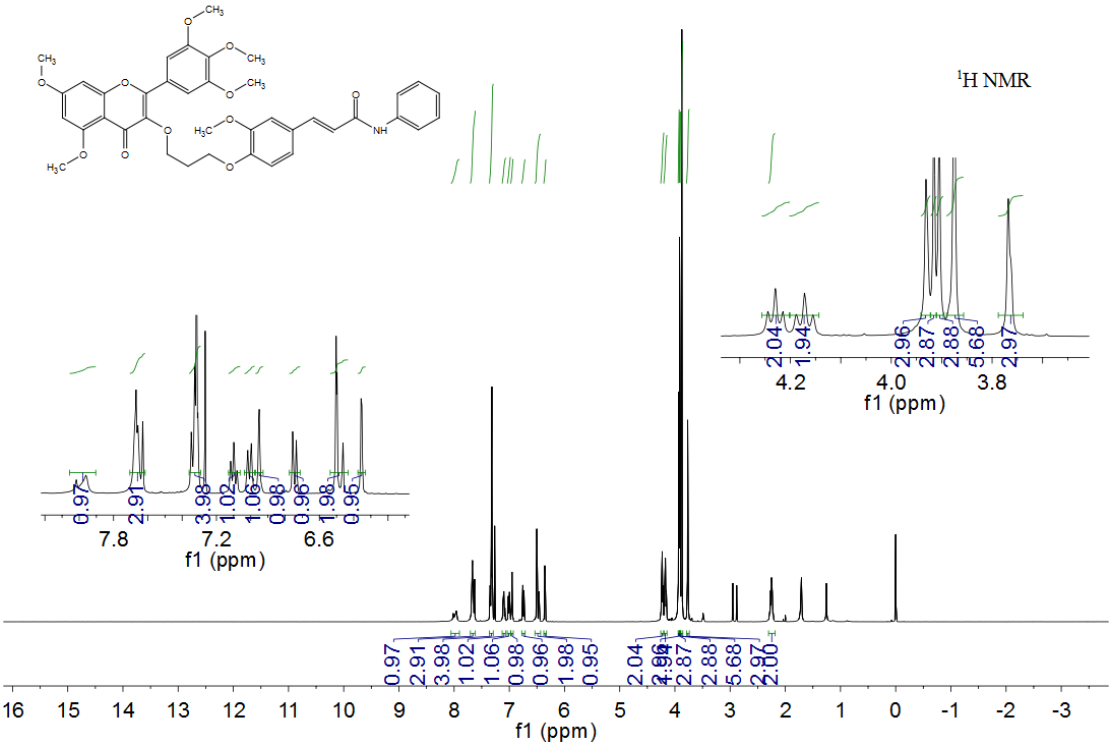


Figure S37.^{13}C NMR spectrum of compound **4i**

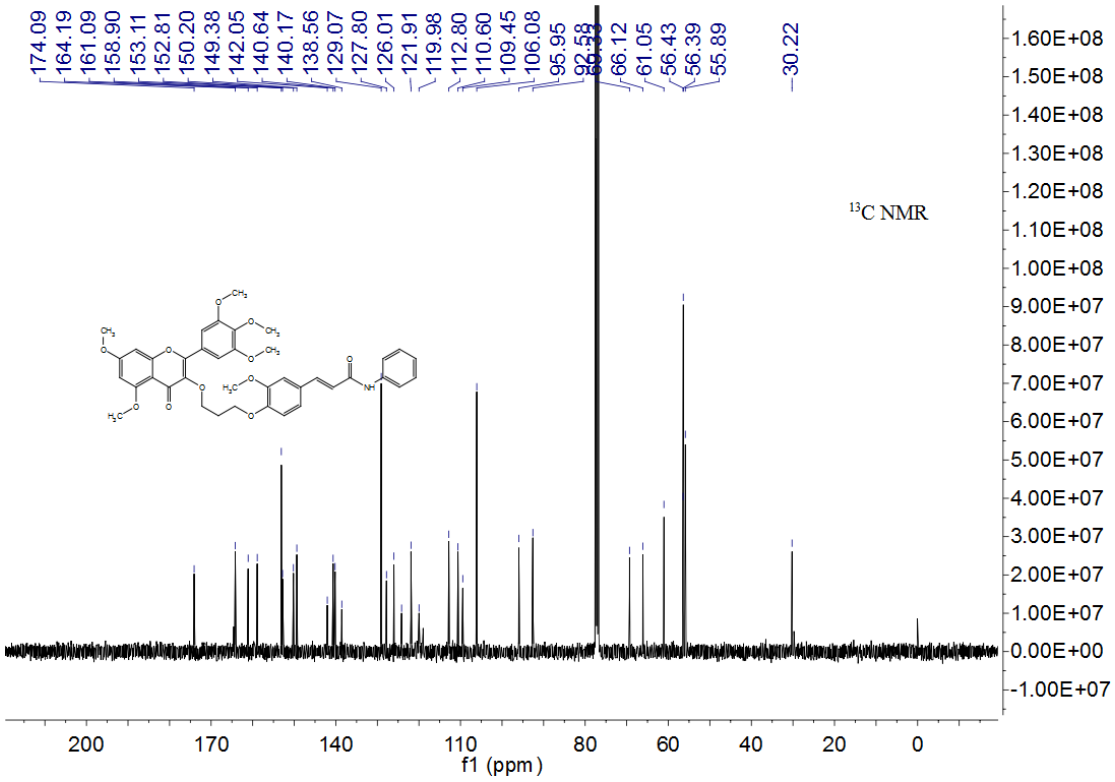


Figure S38. HRMS spectrum of compound **4i**

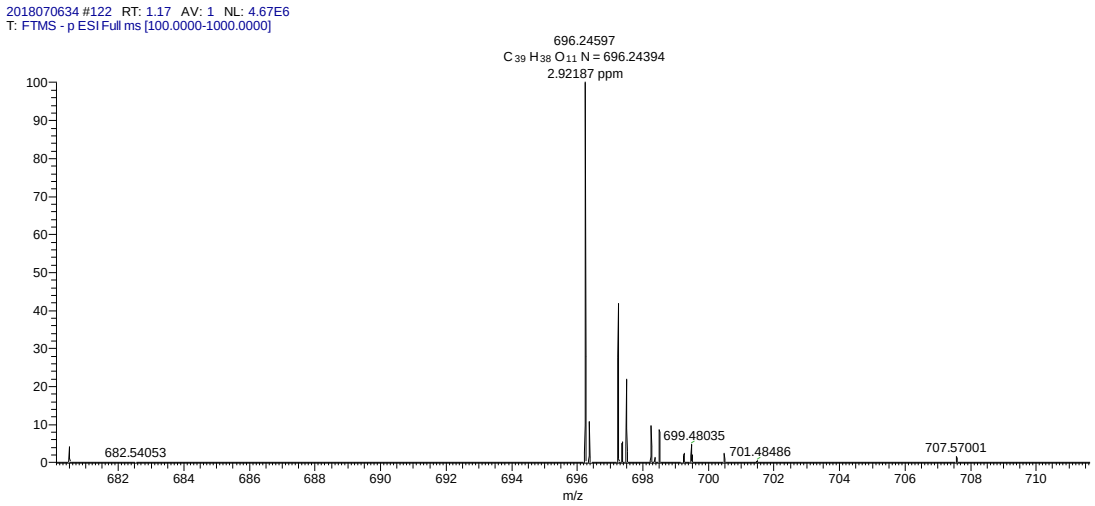


Figure S39. ^{1}H NMR spectrum of compound **4j**

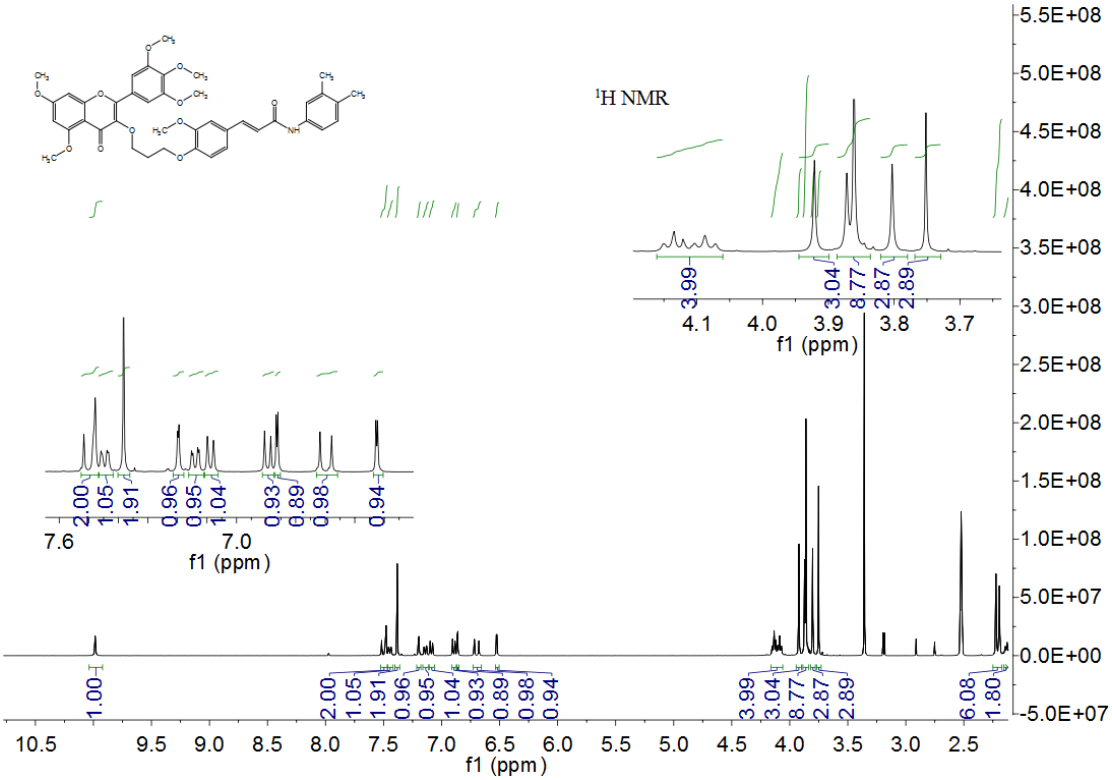


Figure S40. ^{13}C NMR spectrum of compound **4j**

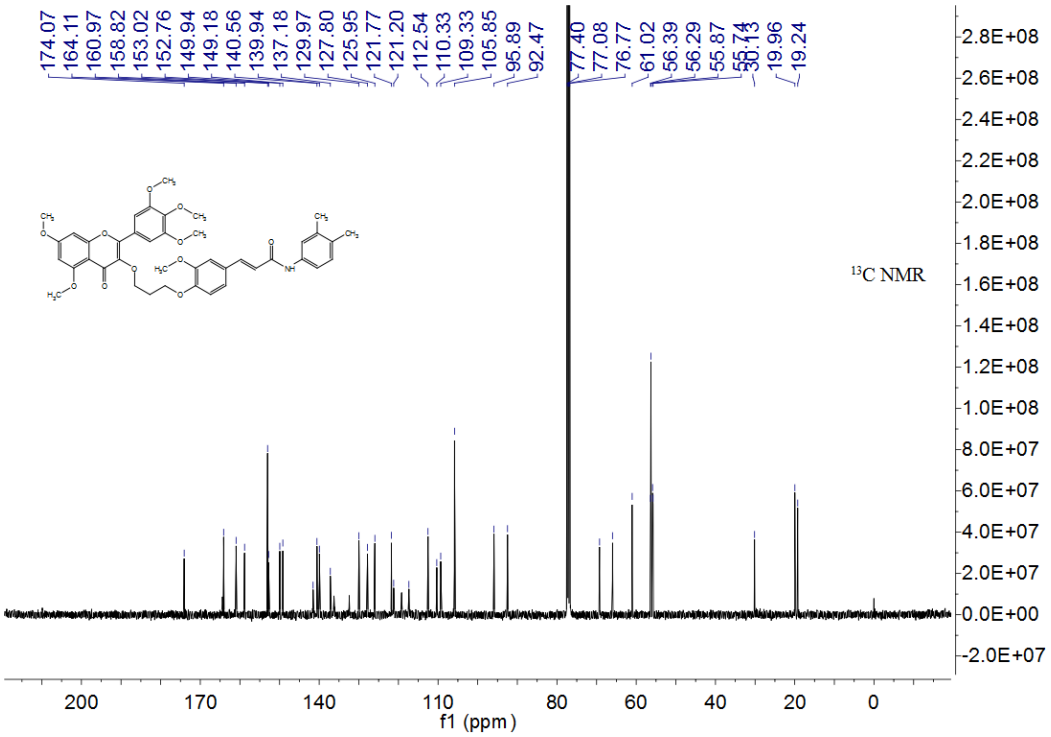


Figure S41. HRMS spectrum of compound **4j**

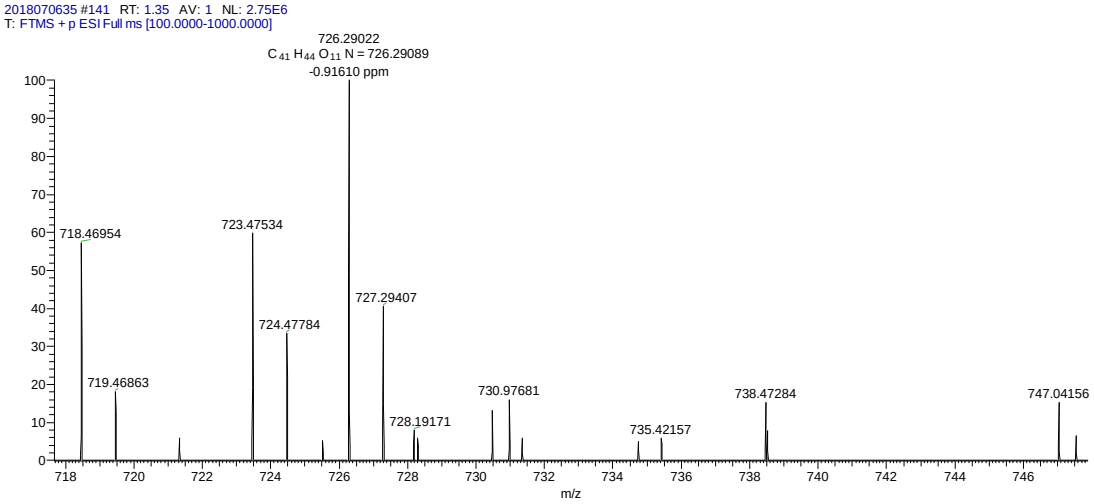


Figure S42. ^{1}H NMR spectrum of compound **4k**

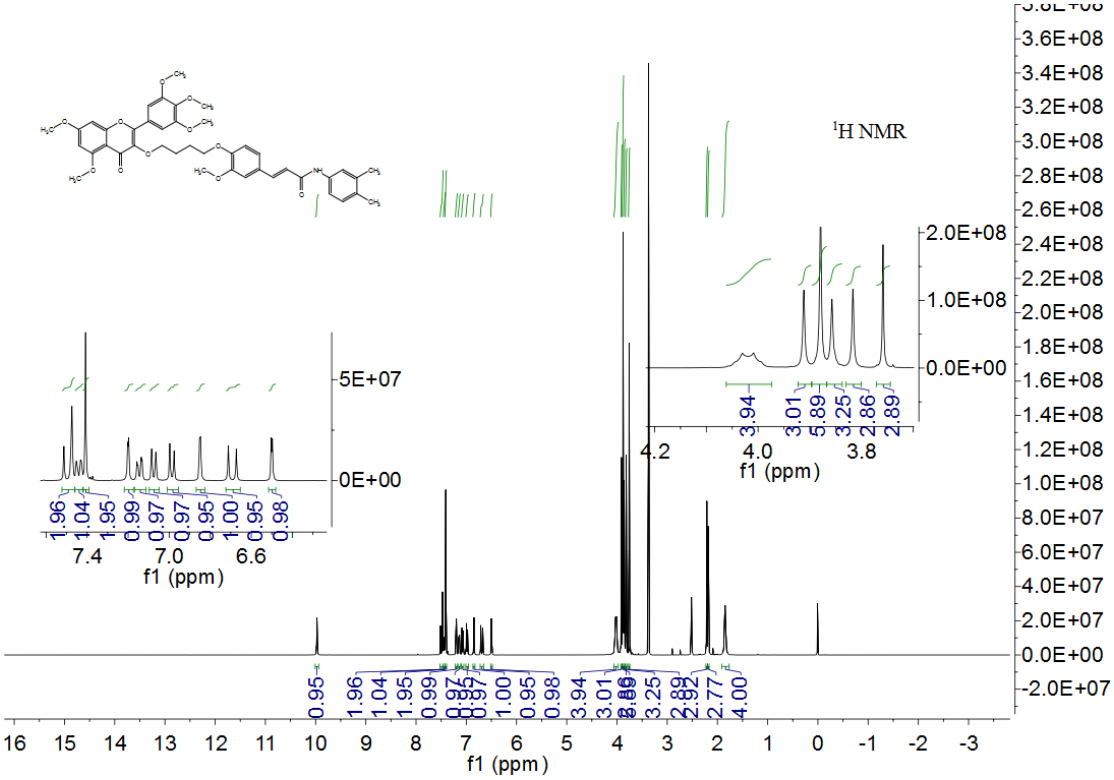


Figure S43. ^{13}C NMR spectrum of compound **4k**

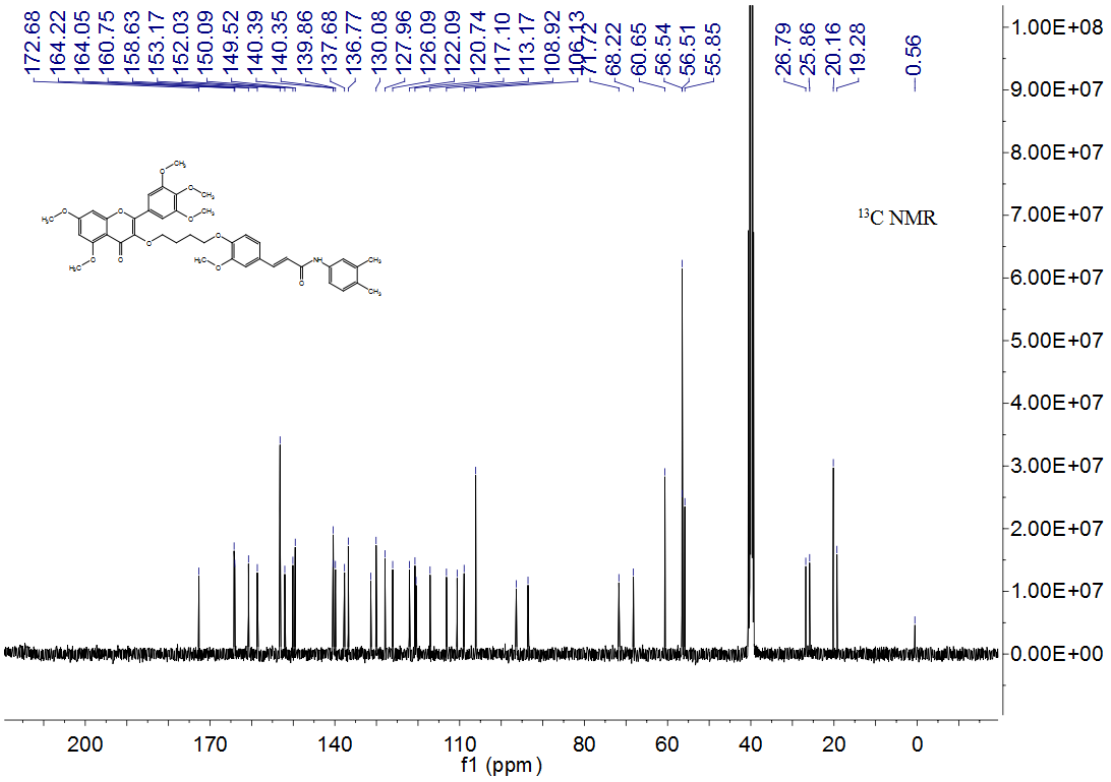


Figure S44. HRMS spectrum of compound **4k**

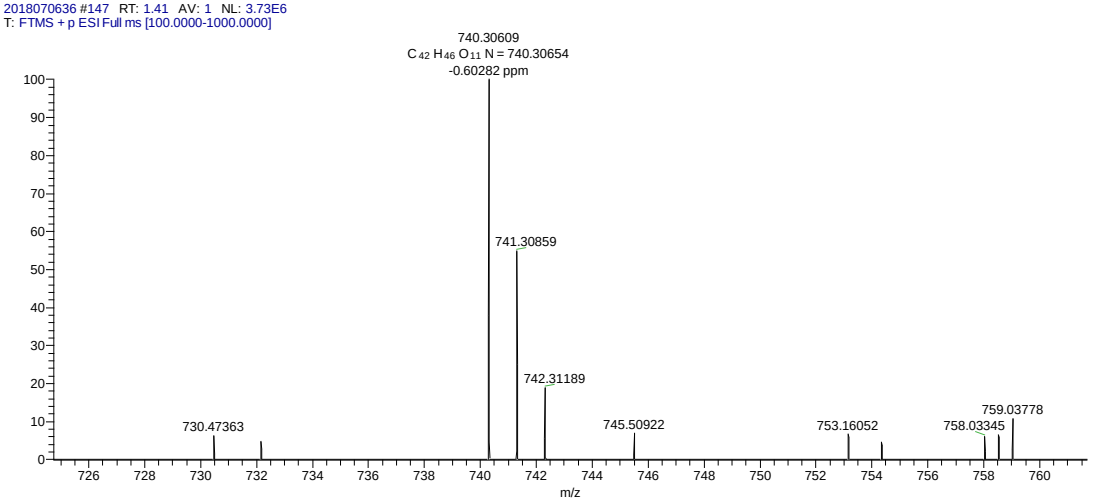


Figure S45. ^{1}H NMR spectrum of compound **41**

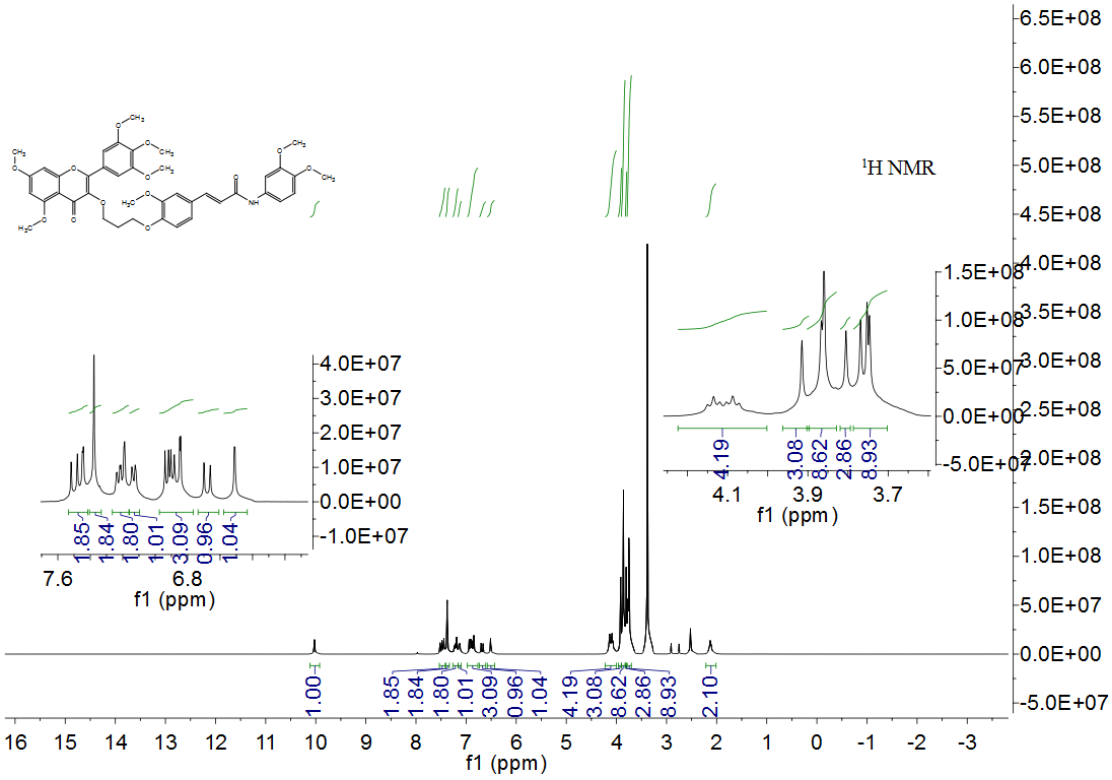


Figure S46. ^{13}C NMR spectrum of compound **41**

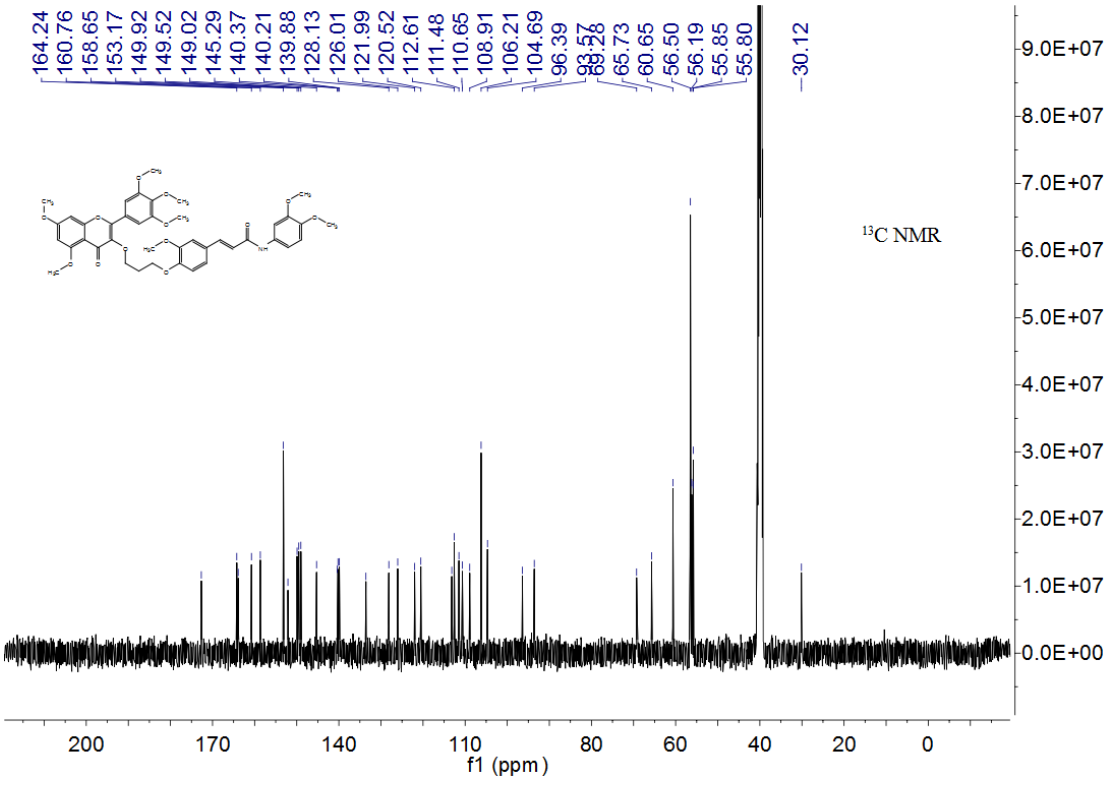


Figure S47. HRMS spectrum of compound **4l**

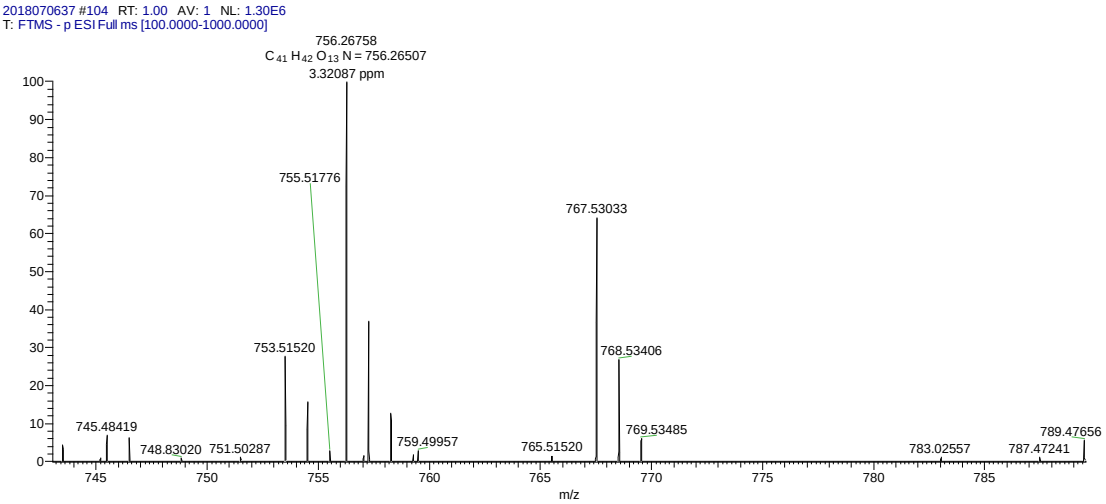


Figure S48. ^{1}H NMR spectrum of compound **4m**

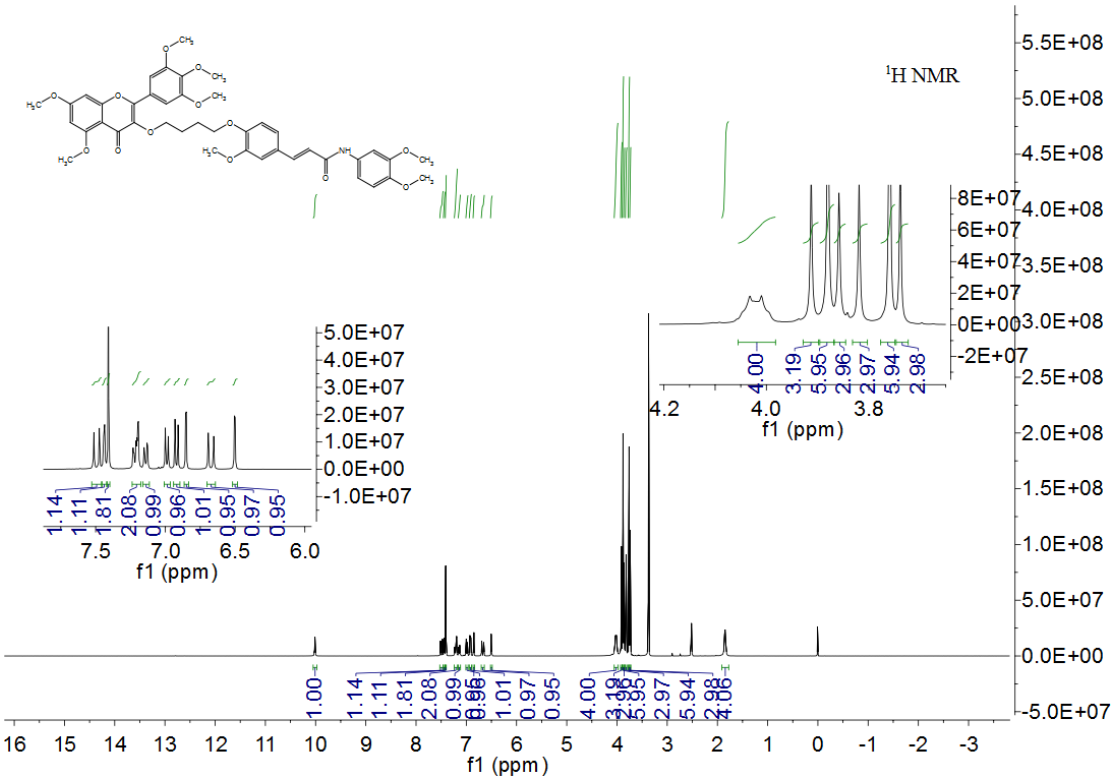


Figure S49. ^{13}C NMR spectrum of compound **4m**

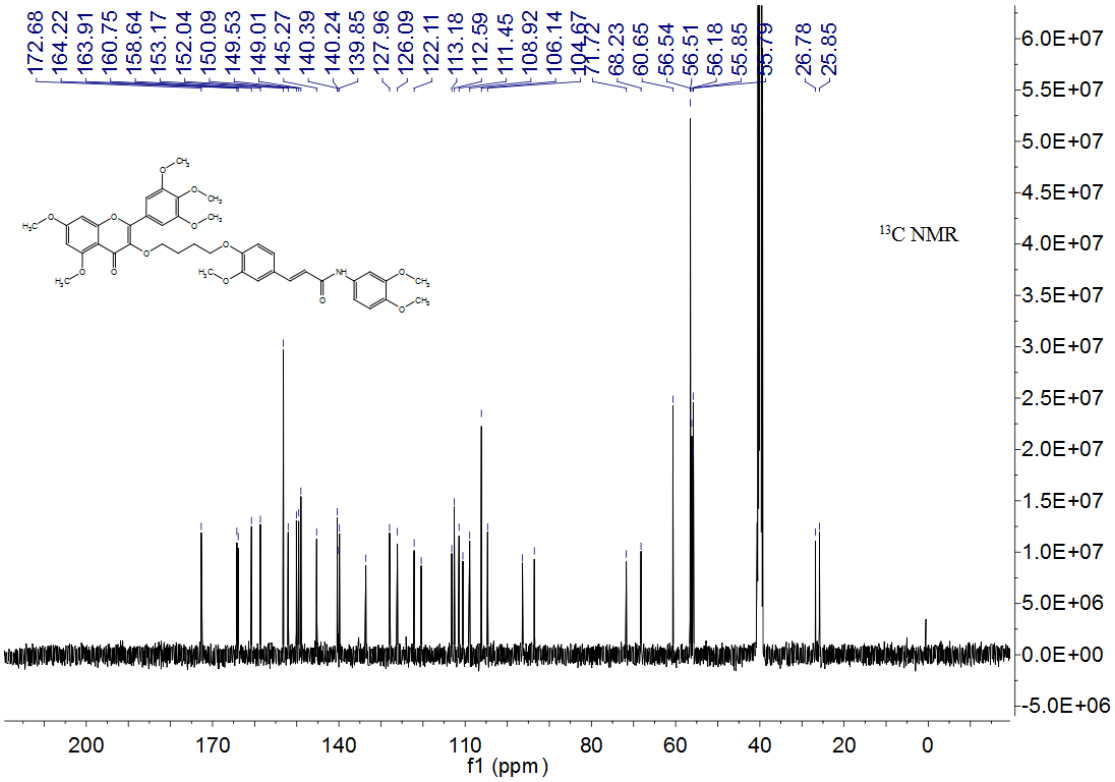


Figure S50. HRMS spectrum of compound **4m**

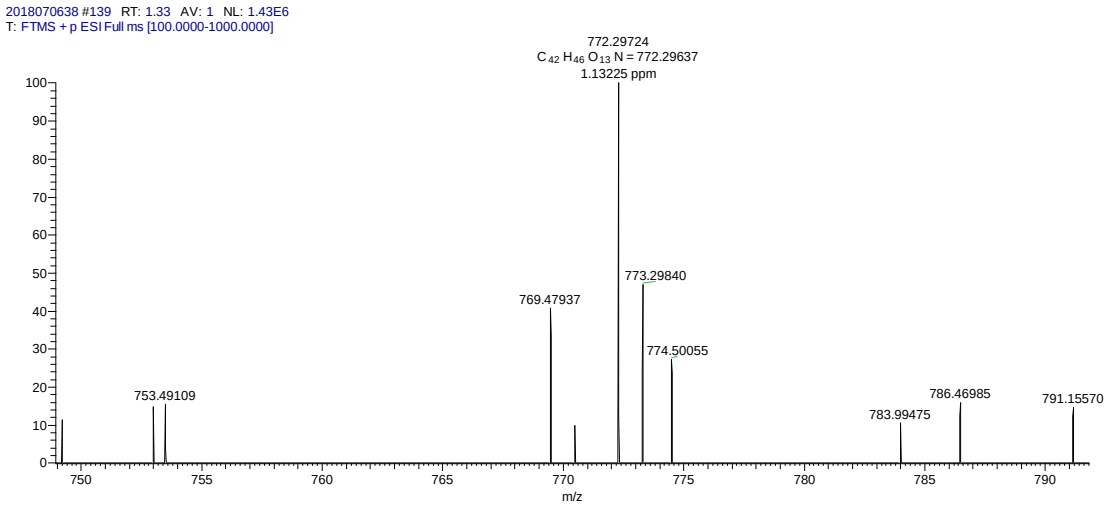


Figure S51. ^{1}H NMR spectrum of compound **4n**

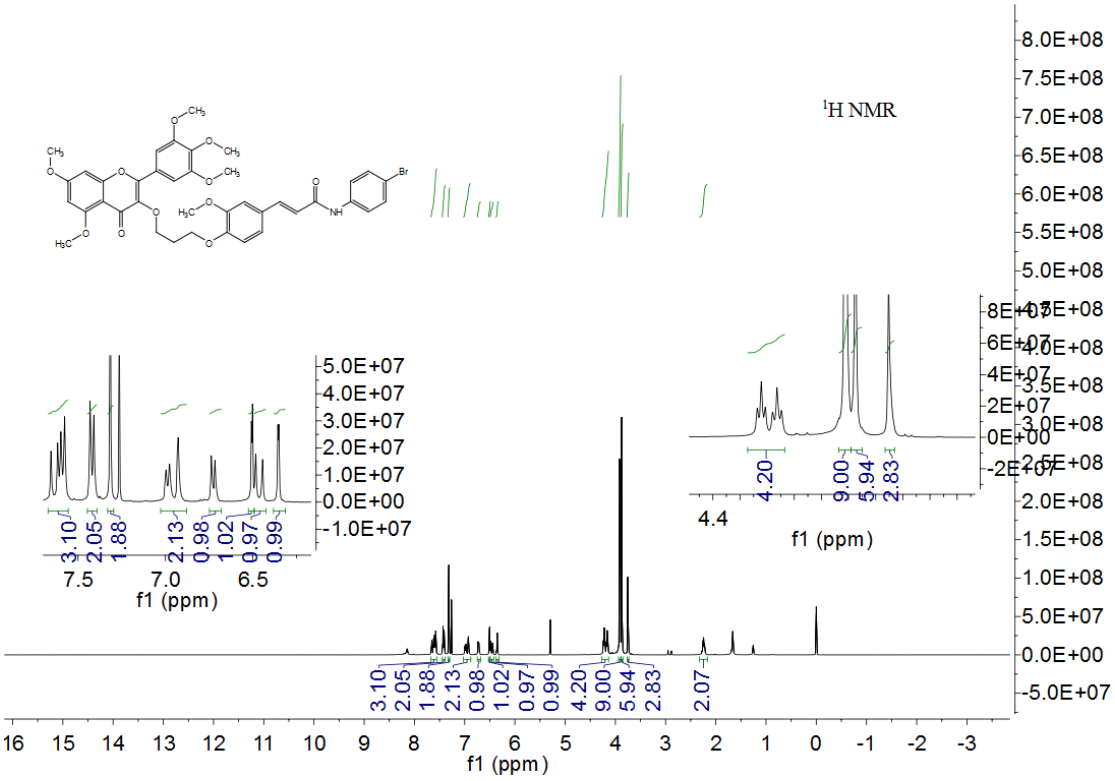


Figure S52. ^{13}C NMR spectrum of compound **4n**

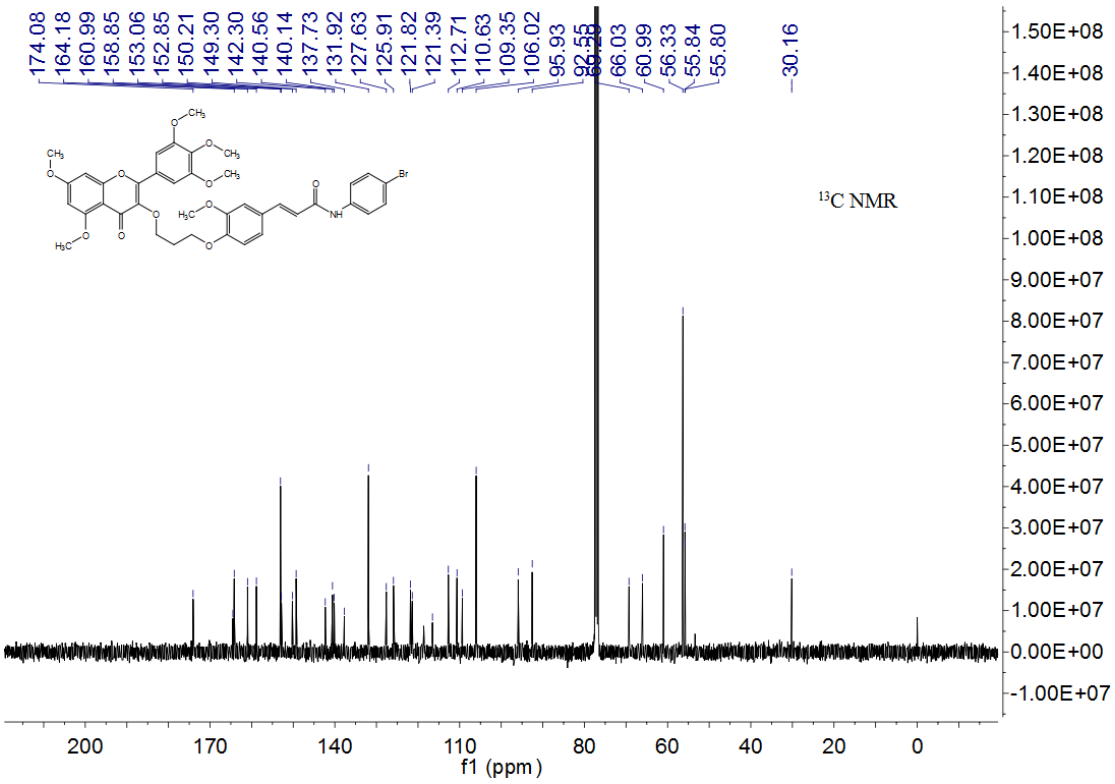


Figure S53. HRMS spectrum of compound **4n**

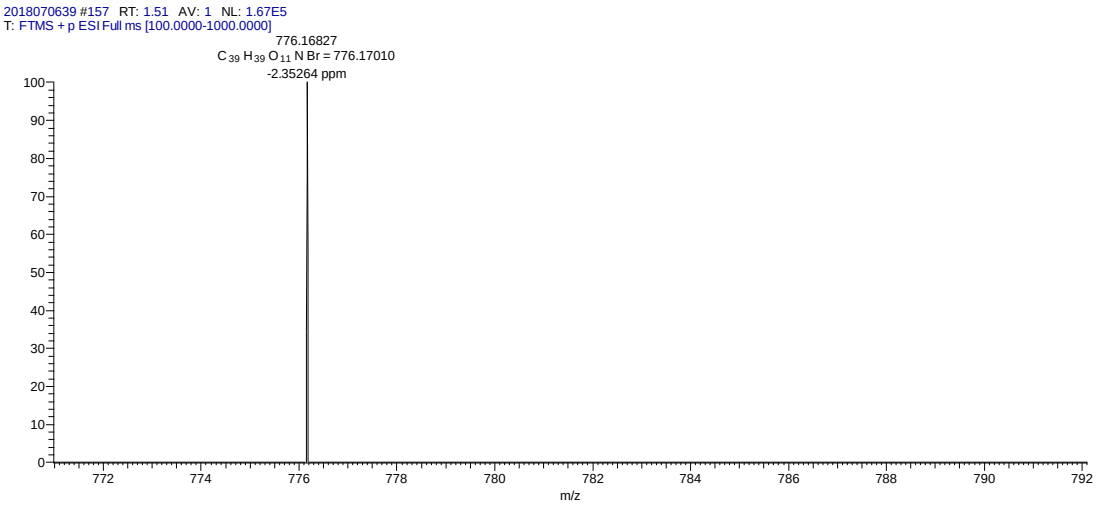


Figure S54. ^{1}H NMR spectrum of compound **4o**

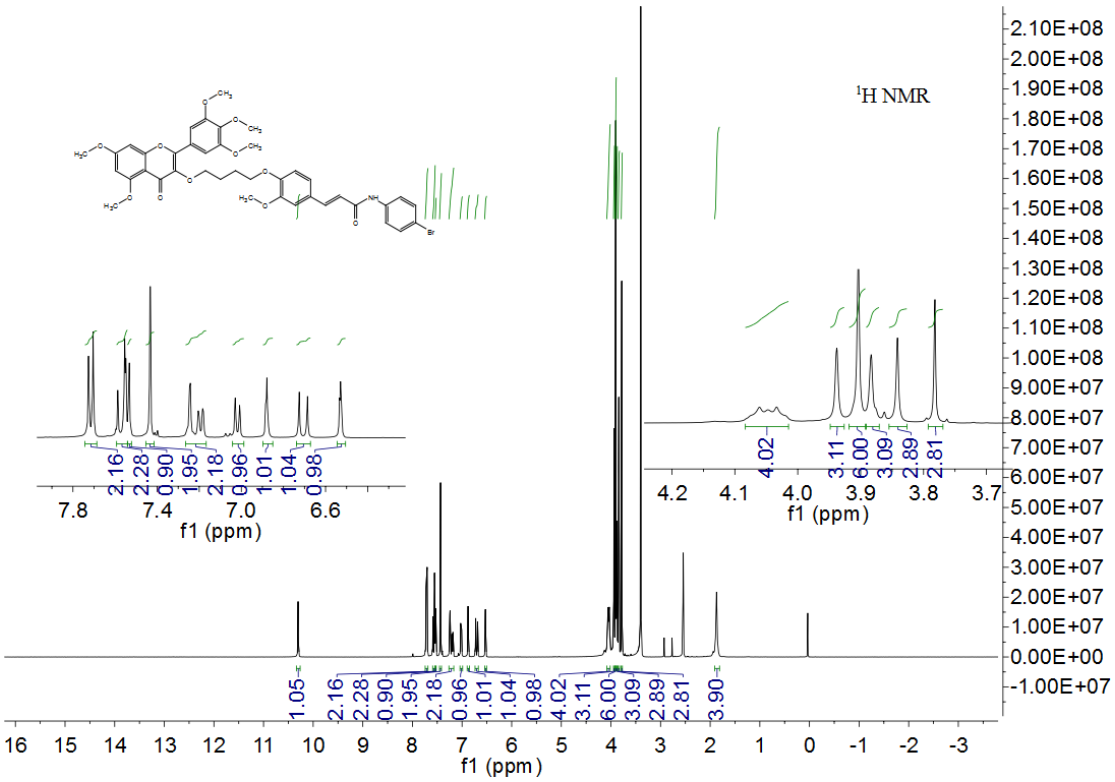


Figure S55. ^{13}C NMR spectrum of compound **4o**

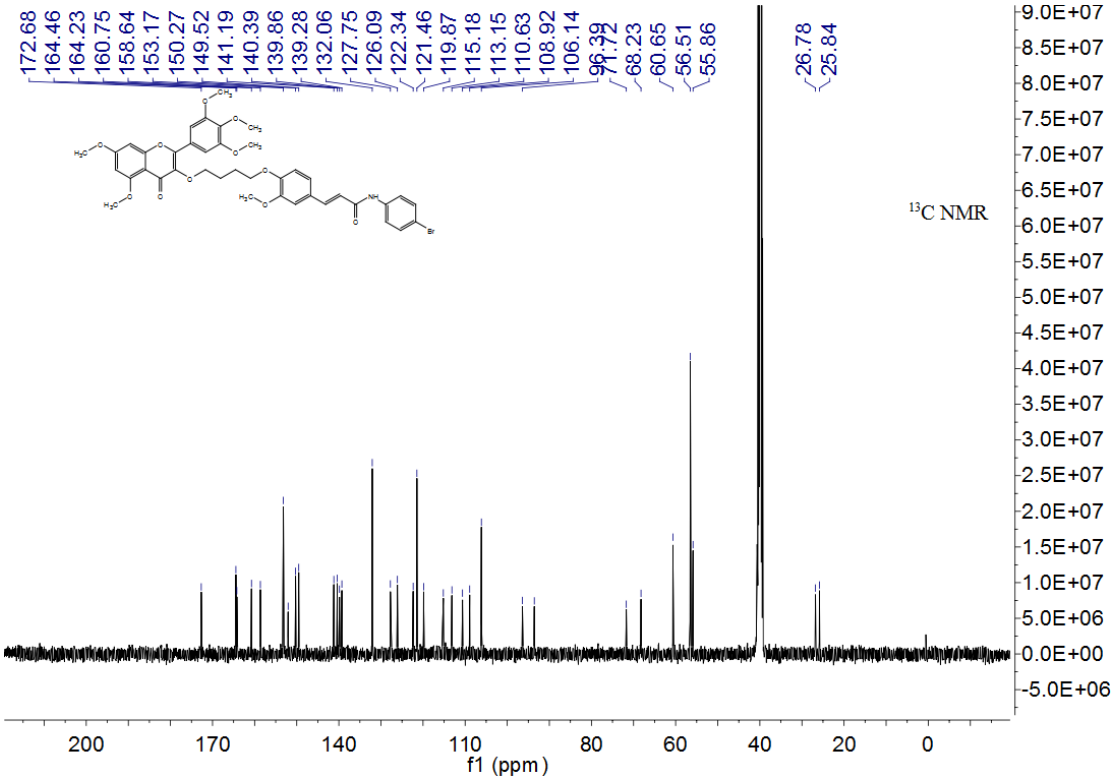


Figure S56. HRMS spectrum of compound **4o**

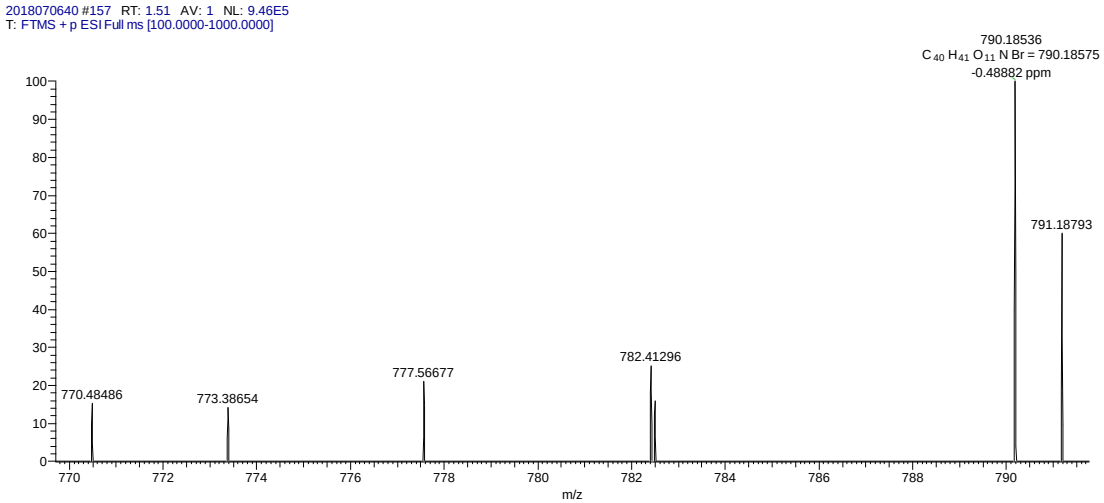


Figure S57. ^{1}H NMR spectrum of compound **4p**

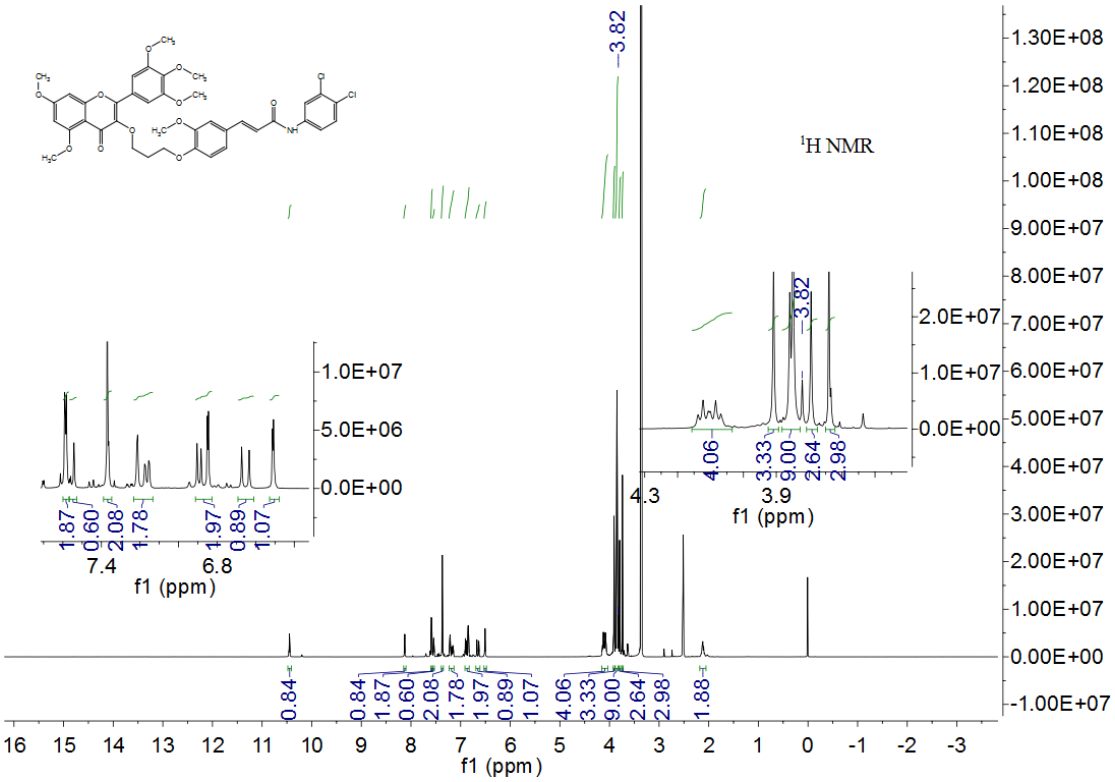


Figure S58. ^{13}C NMR spectrum of compound **4p**

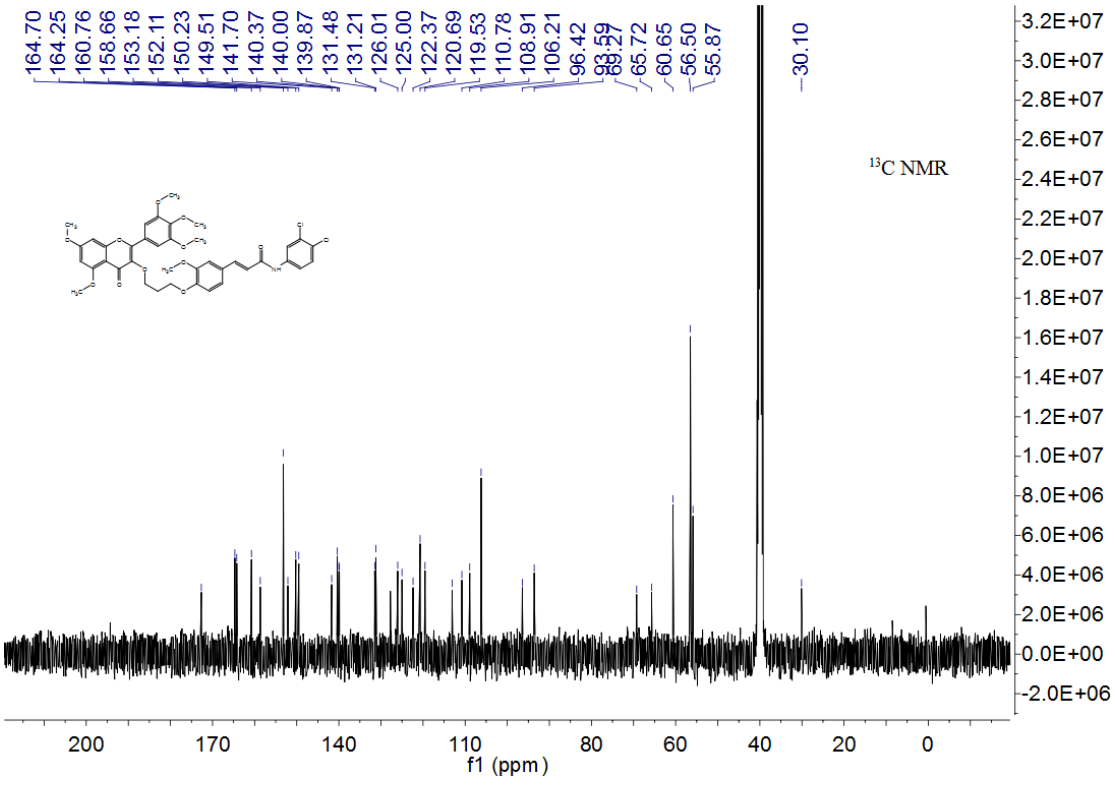


Figure S59. HRMS spectrum of compound **4p**

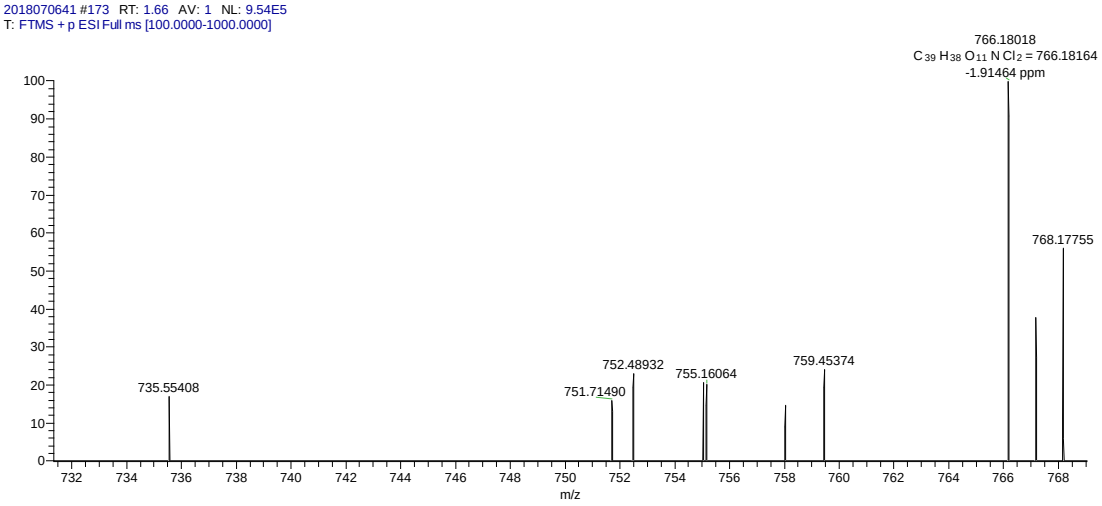


Figure S60. ^{1}H NMR spectrum of compound **4q**

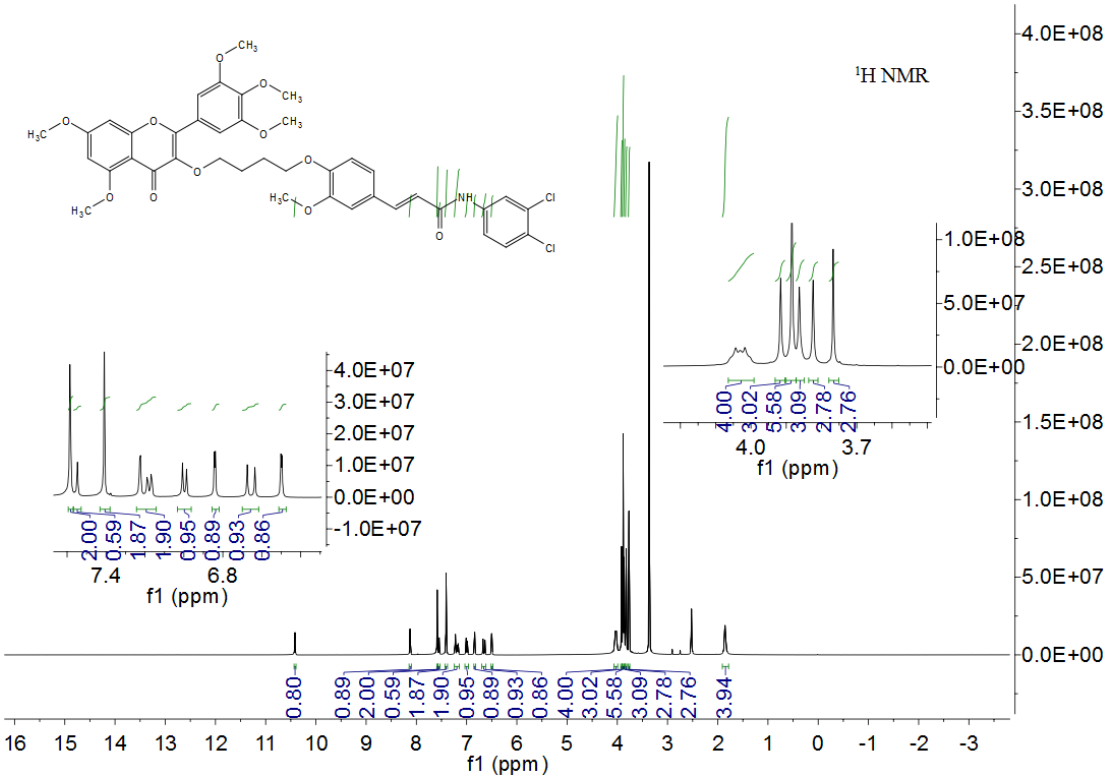


Figure S61. ^{13}C NMR spectrum of compound **4q**

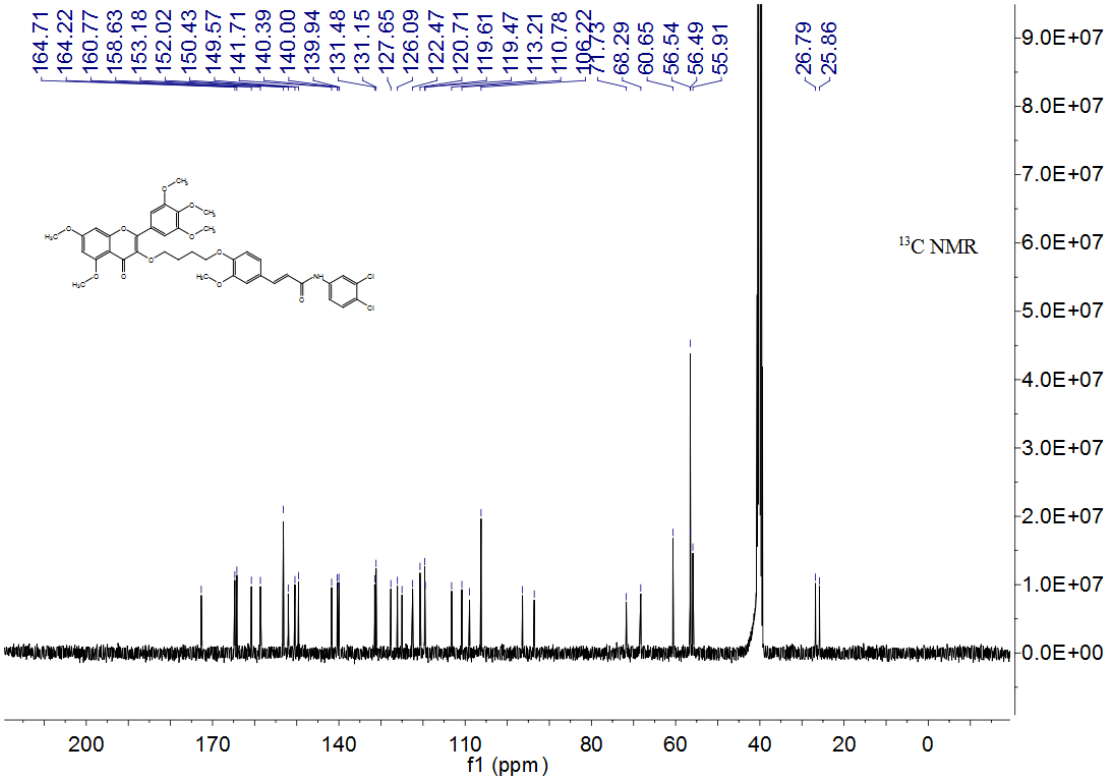


Figure S62. HRMS spectrum of compound **4q**

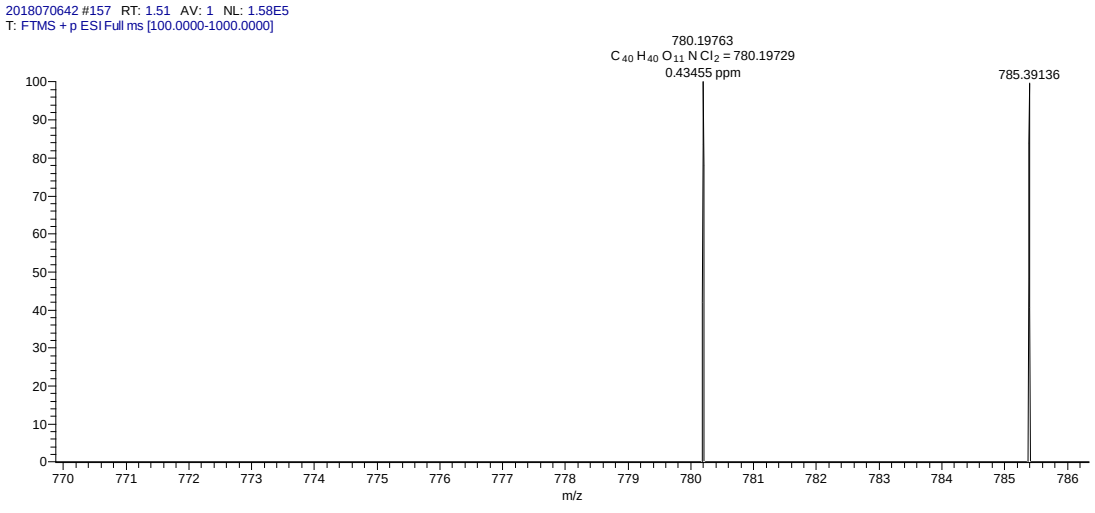


Figure S63. ^{1}H NMR spectrum of compound **4r**

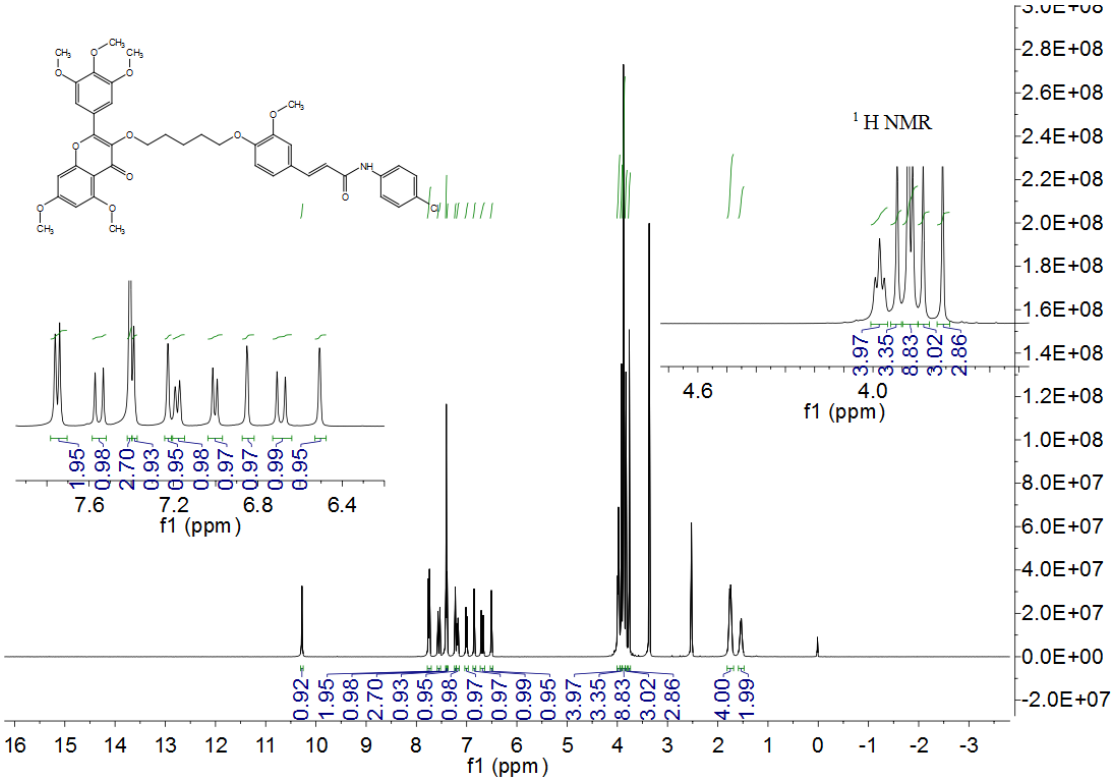


Figure S64. ^{13}C NMR spectrum of compound **4r**

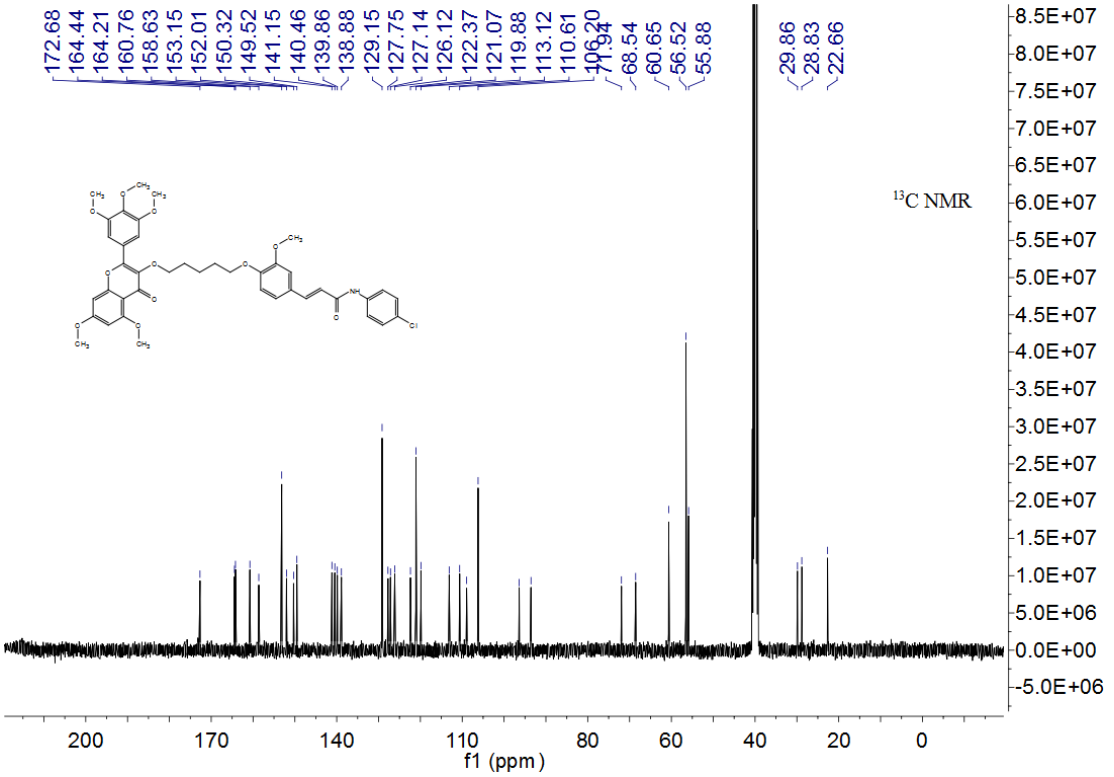


Figure S65. HRMS spectrum of compound **4r**

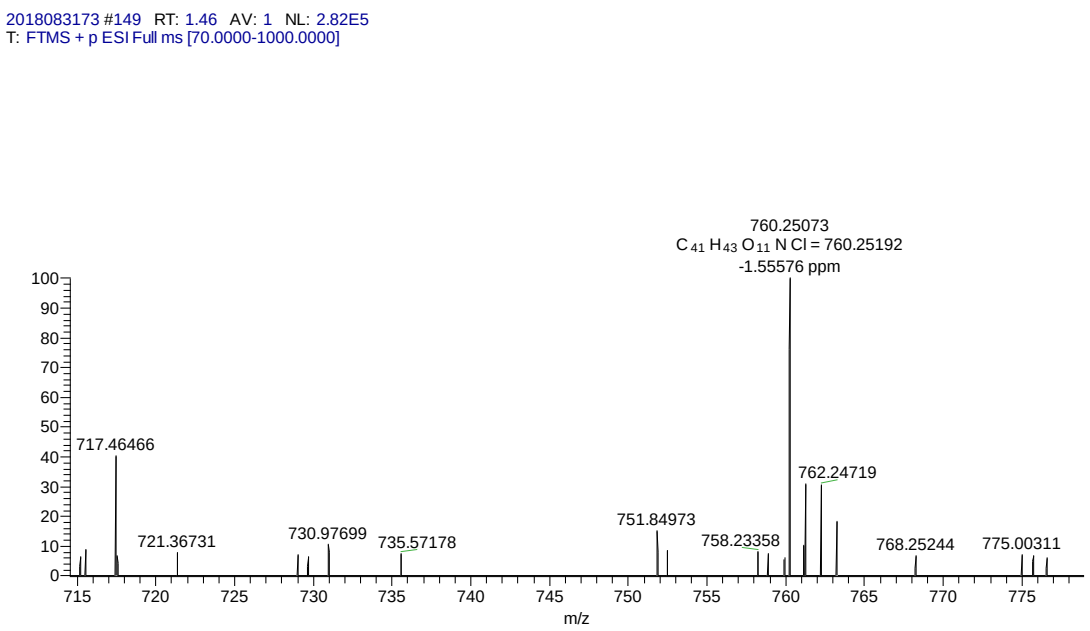


Figure S66. ^{1}H NMR spectrum of compound **4s**

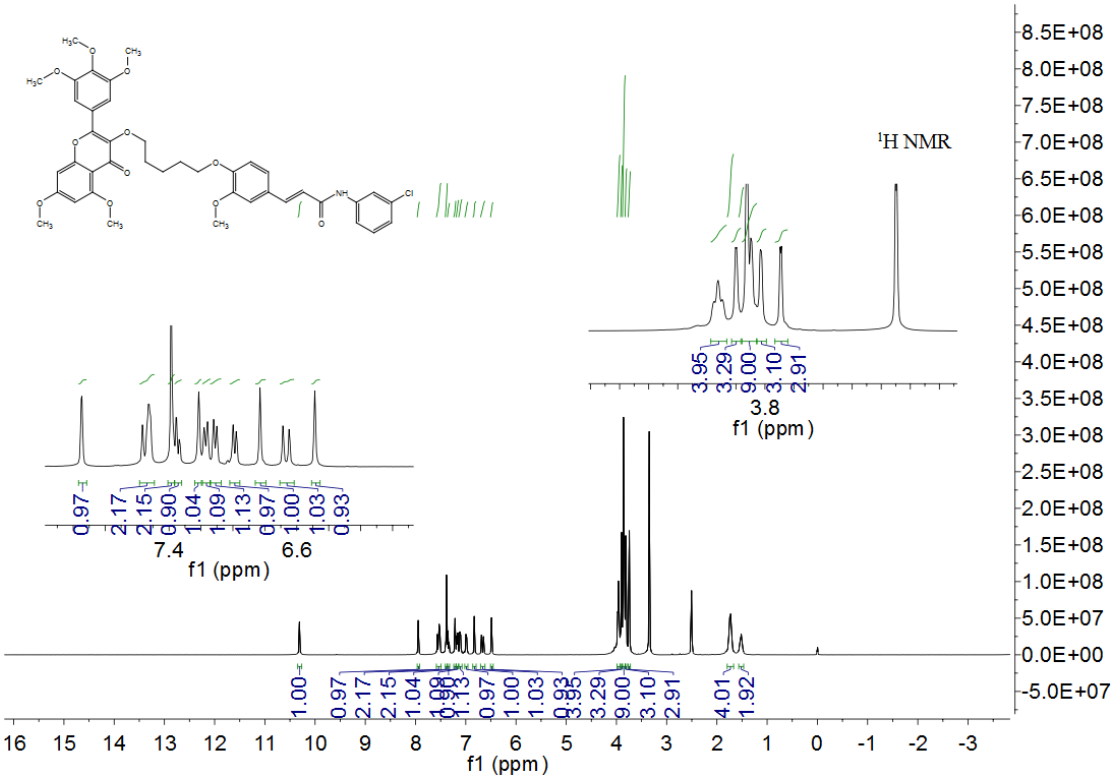


Figure S67. ^{13}C NMR spectrum of compound **4s**

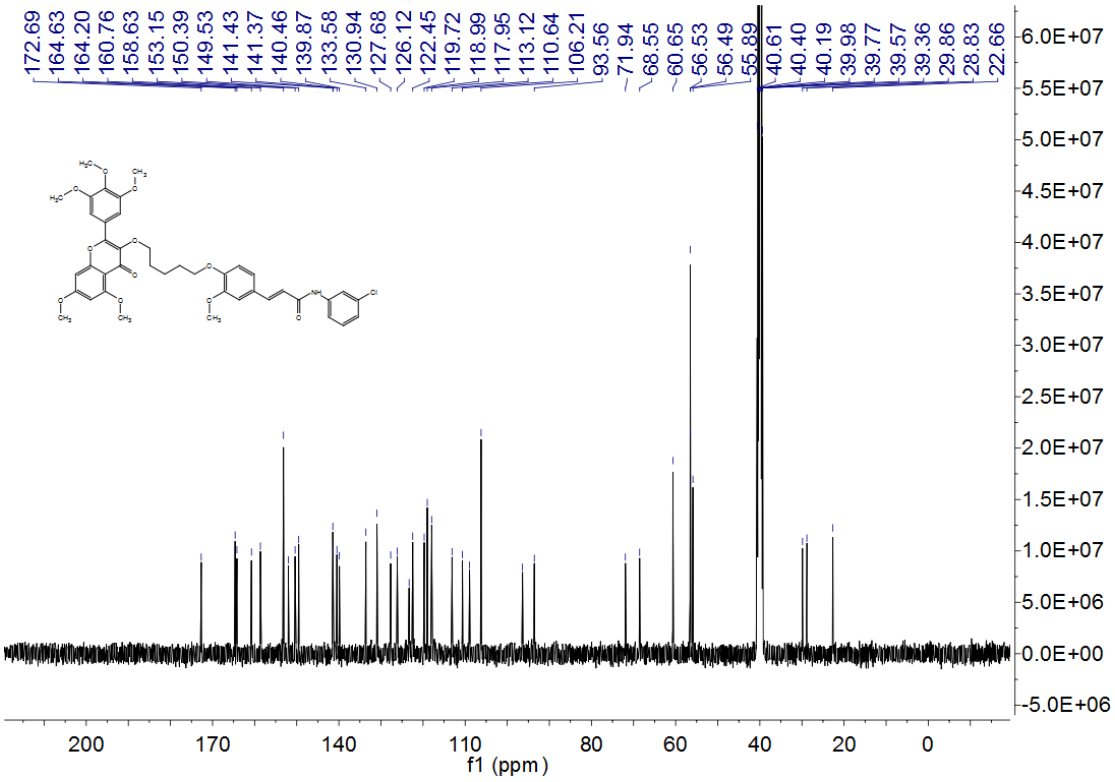


Figure S68. HRMS spectrum of compound **4s**

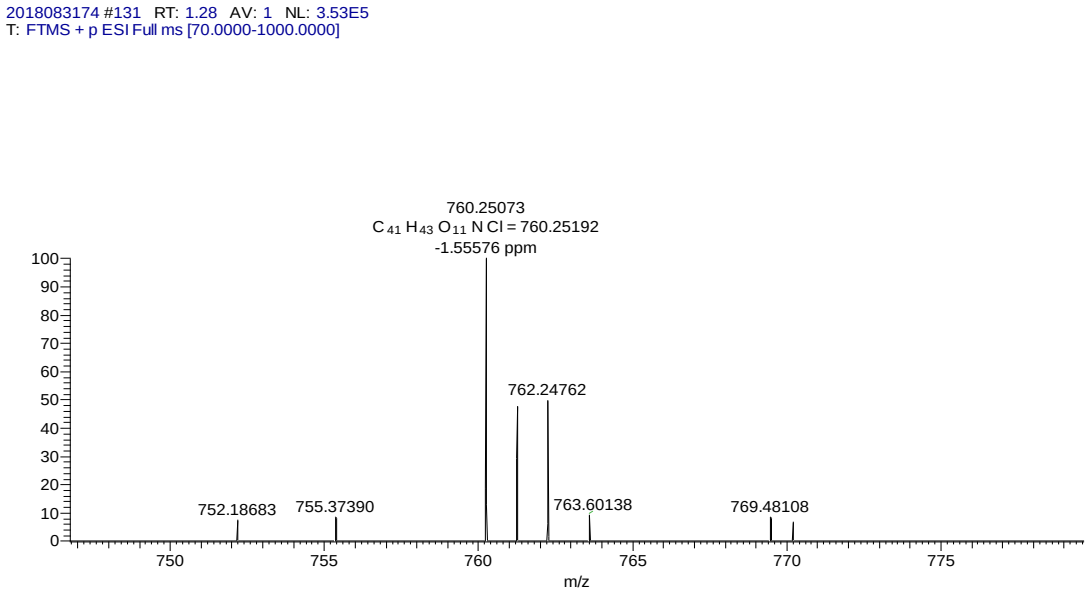


Figure S69. ^{1}H NMR spectrum of compound **4t**

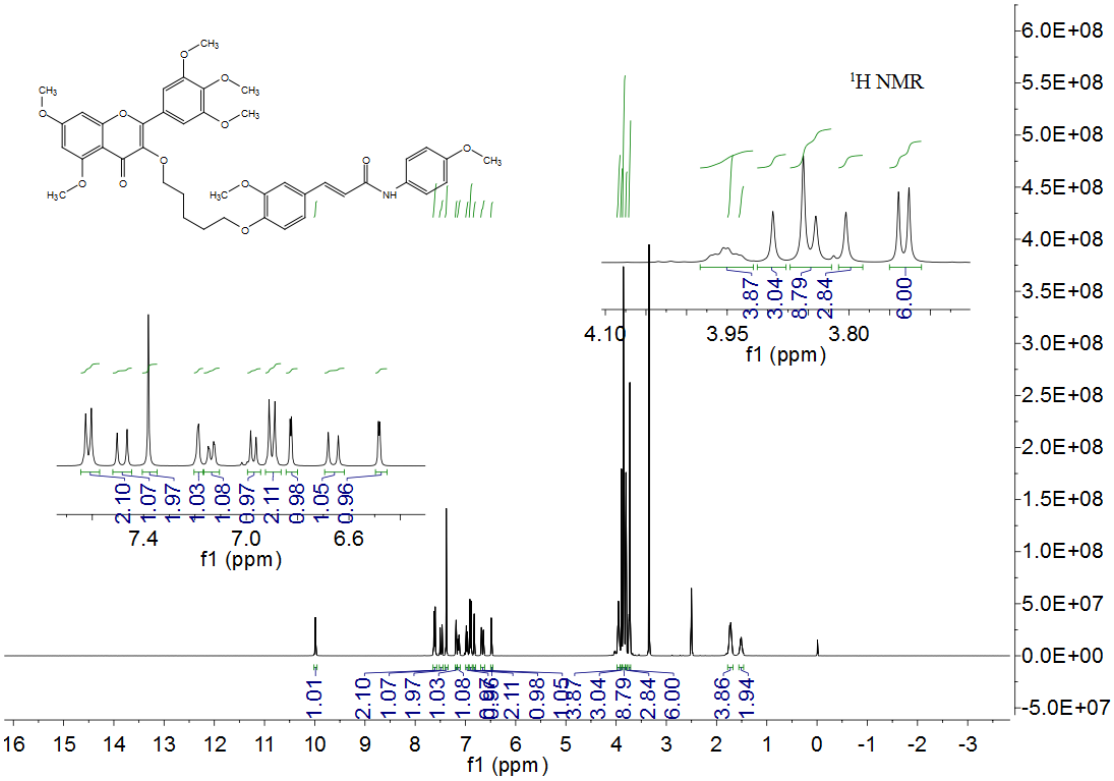


Figure S70. ^{13}C NMR spectrum of compound **4t**

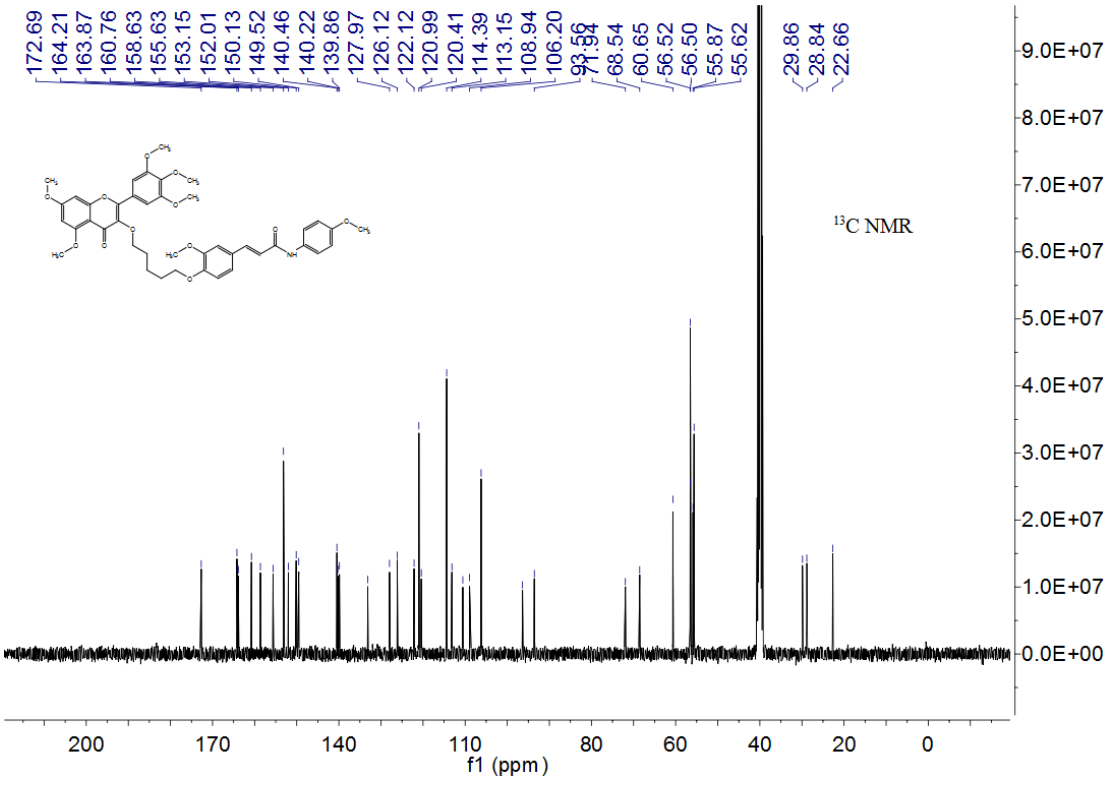


Figure S71. HRMS spectrum of compound **4t**

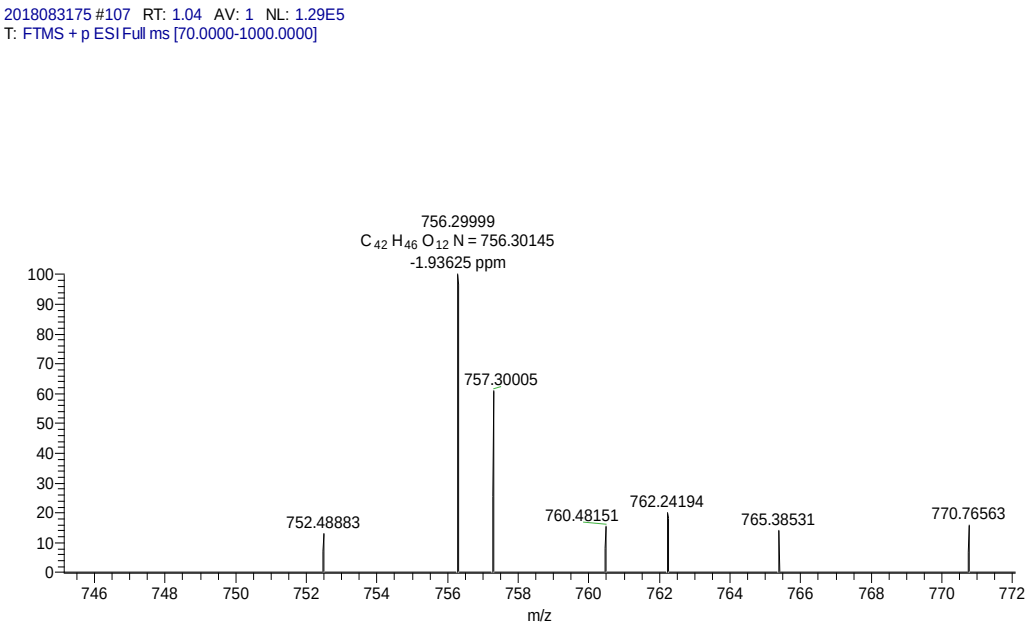


Figure S72. ^{1}H NMR spectrum of compound **4u**

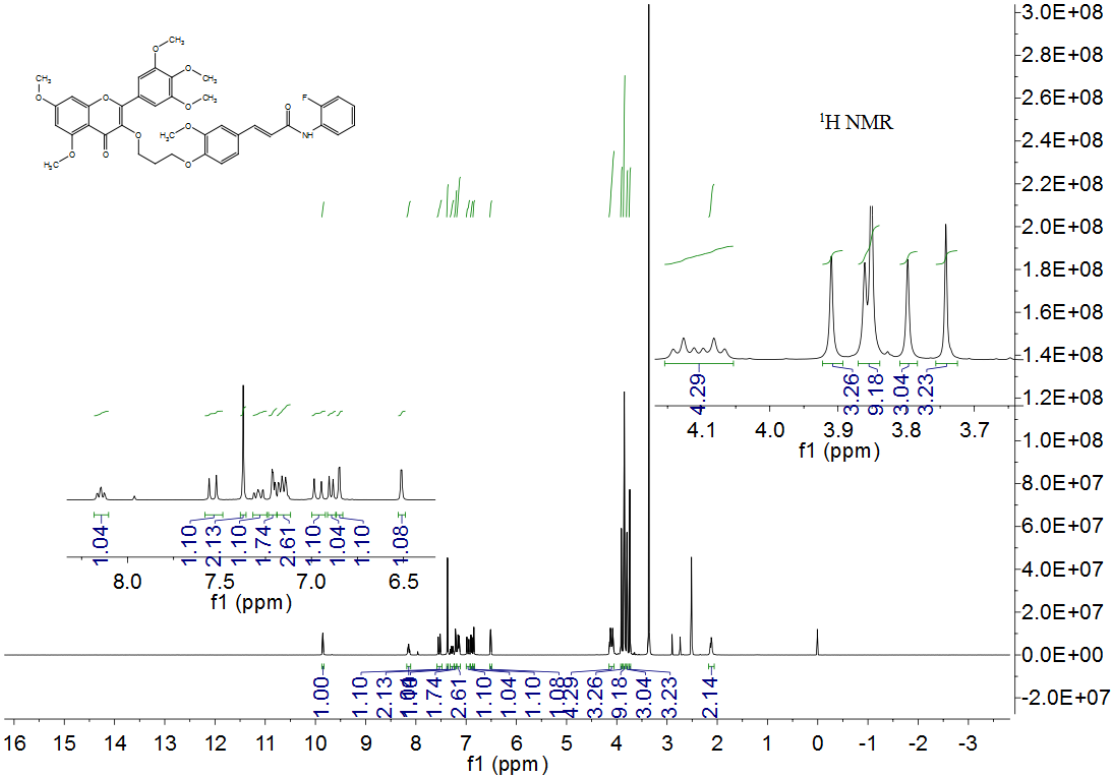


Figure S73. ^{13}C NMR spectrum of compound **4u**

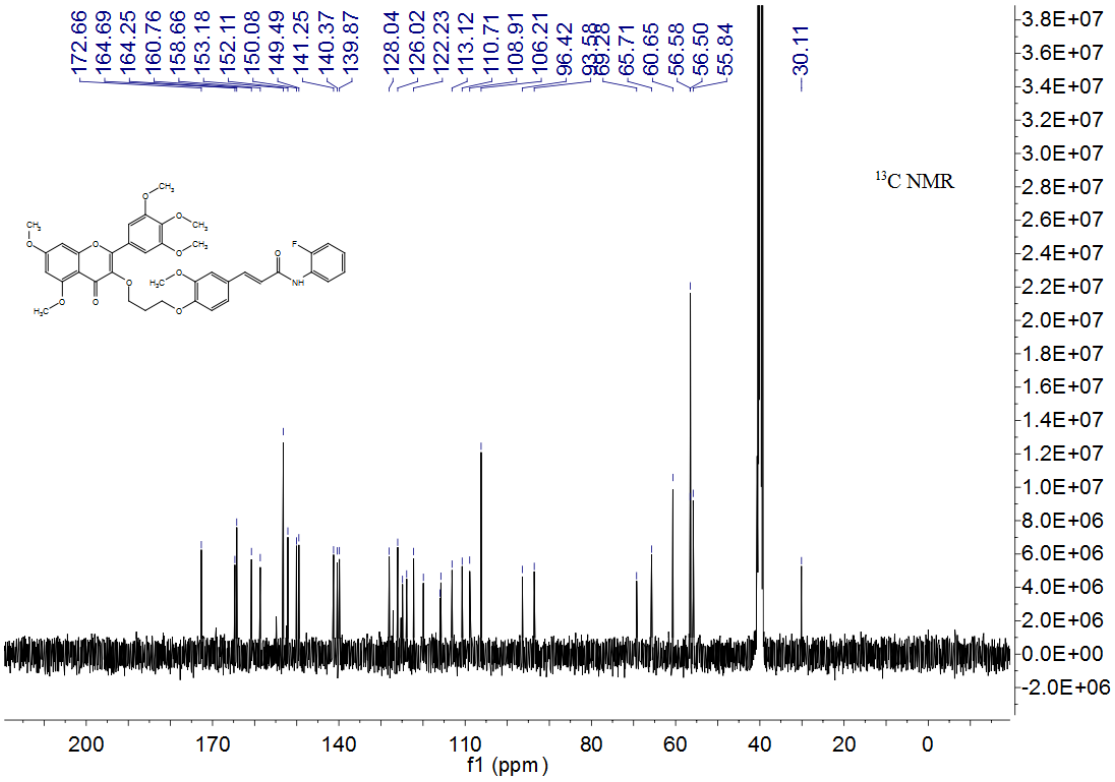


Figure S74. ^{19}F NMR spectrum of compound **4u**

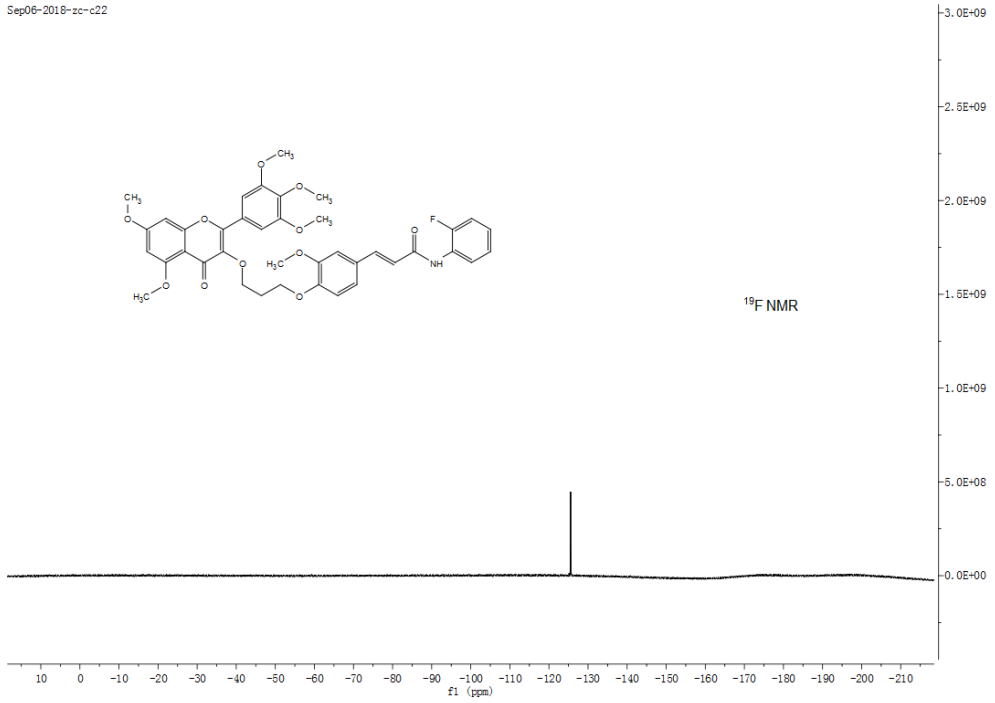


Figure S75. HRMS spectrum of compound **4u**

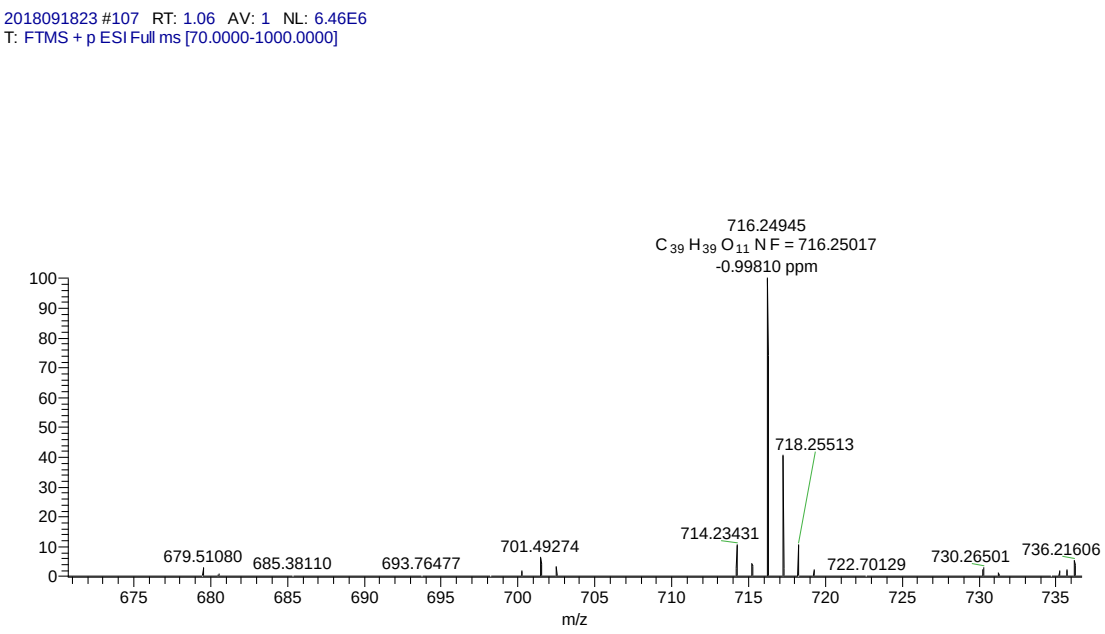


Figure S76. ^{1}H NMR spectrum of compound **4v**

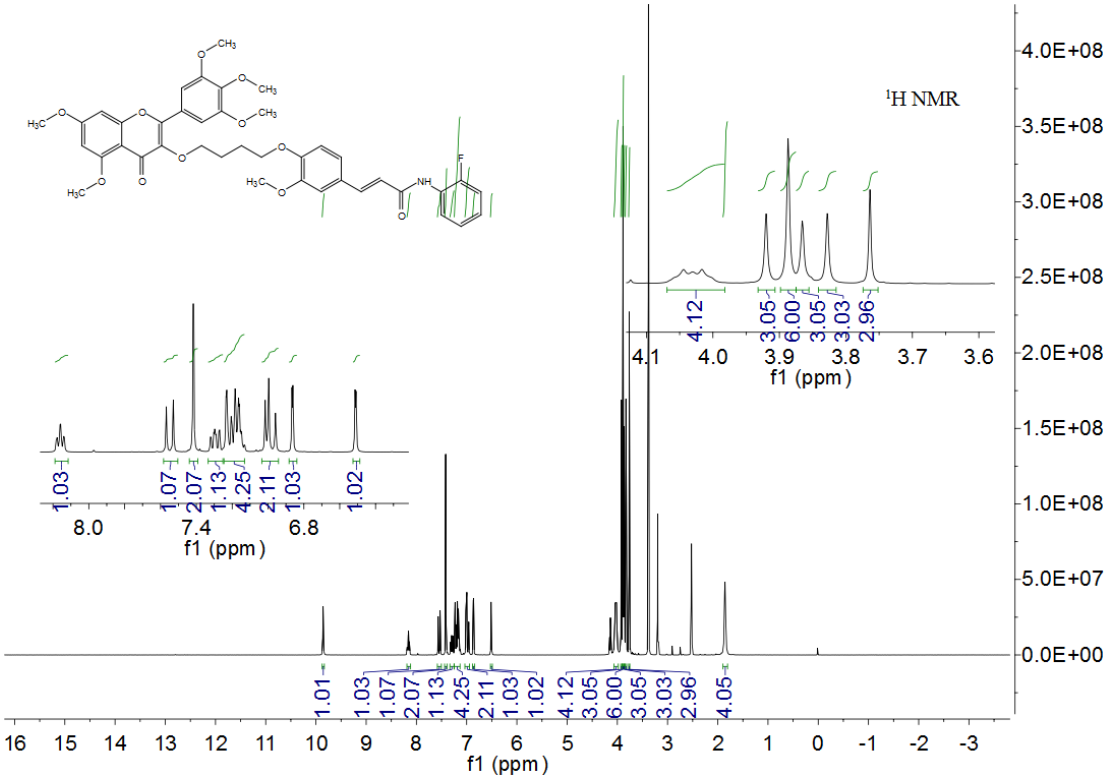


Figure S77. ^{13}C NMR spectrum of compound **4v**

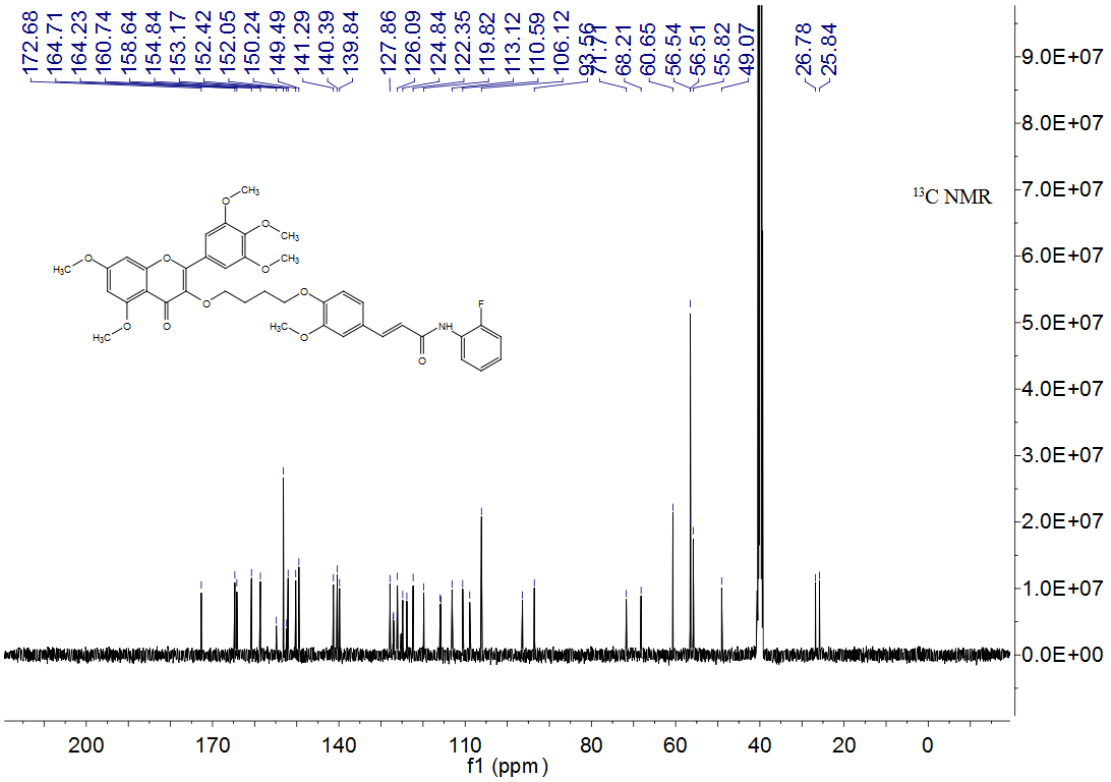


Figure S78. ^{19}F NMR spectrum of compound **4v**

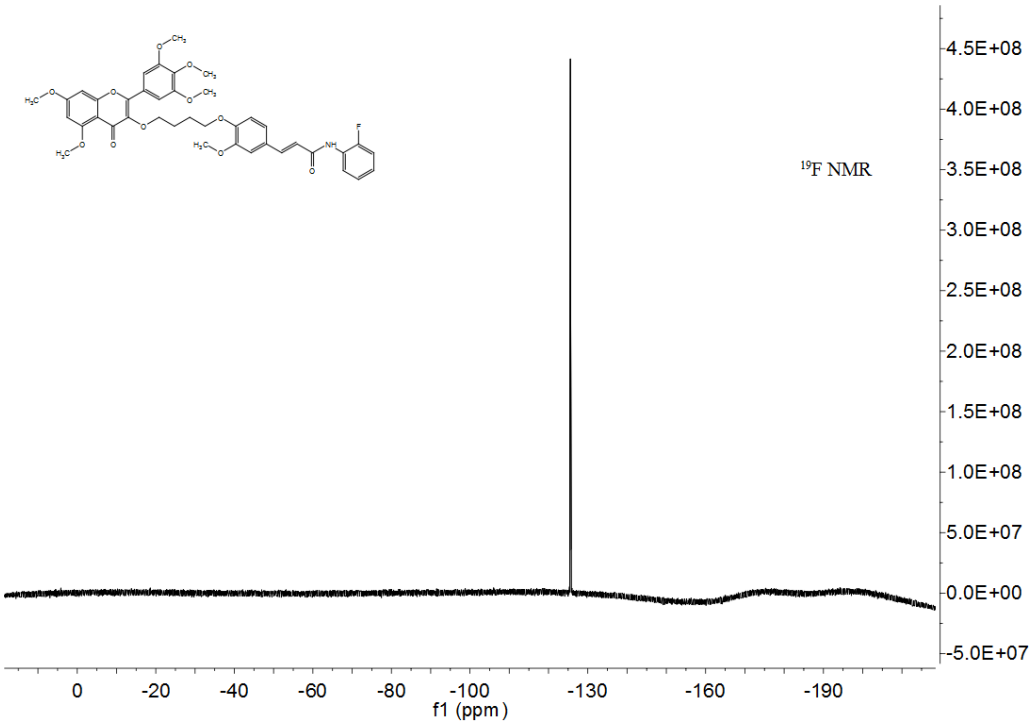


Figure S79. HRMS spectrum of compound **4v**