Supporting information

Ru(II)-Catalyzed Site-Selective Hydroxylation of Flavone and Chromone Derivatives: The Importance of the 5-Hydroxyl Motif for the Inhibition of Aurora Kinases

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General Methods and Materials

Commercial grade reagents and solvents were used without further purification except as indicated below. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F^{254} plates and visualization on TLC was achieved by UV light (254 nm) and ninhydrin solution, and heat as developing agents. Flash column chromatography was undertaken on silica gel (400-630 mesh). ^{1}H NMR was recorded on 400 MHz and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 2.50 ppm for DMSO-d_6. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, h = hexet, m = multiplet, dd = doublet of doublet, td = doublet of triplet, ddd = doublet of doublet of doublet. Coupling constants, *J*, were reported in hertz unit (Hz). ^{13}C NMR was recorded on 100 MHz and was fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 39.5 ppm of DMSO-d_6. Melting points were determined using an electronthermal IA9000 series melting point apparatus. Mass spectral data were obtained from the KAIST Basic Science Institute by using ESI method.

Experimental procedure and data

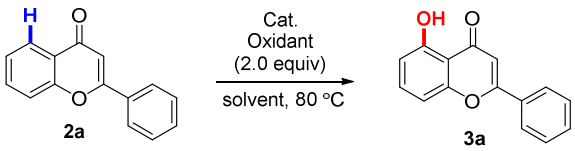
General procedure I (GP I) for preparation of flavone derivatives

The general procedure I was modified from literature (Wheeler, T. S. *Org. synth.* **1952**, *32*, 72-75).

The mixture of 2'-Hydroxyacetophenone derivative (2.0 mmol), aryl chloride (1.5 equiv) was added to 100 mL round bottom flask. After N_2 purging, anhydrous pyridine (6 mL) was added to the mixture. The reaction mixture was stirred at 50 ^{o}C for 0.5-1 h. The reaction mixture was cooled to room temperature and diluted with EtOAc. After the mixture was acidified by 1N HCl (aq), the combined organic layer was extracted and dried over $MgSO_4$. The residue was concentrated under vacuum. The crude mixture and pyridine (5.0 mL) were added to 50 mL round bottom flask. KOH (1.5 equiv) was added in the mixture and the mixture was stirred at 50 ^{o}C for 2 h. The reaction mixture was cooled to room temperature and acidified with 10% AcOH (aq). Precipitate was filtered off and dried under vacuum. The dried solid was added in AcOH to 100 mL two-neck round bottom flask. H_2SO_4 (cat.) was drop-wised and the mixture was stirred under reflux for 2 h. H_2O was added at 0 ^{o}C and

precipitate was filtered off using H_2O as eluent. The filtered solid was dried under vacuum and recrystallized from EtOH to give the desired product.

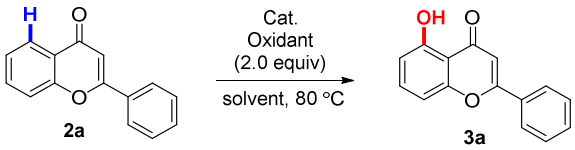
Catalyst screening



entry[a]	cat. (mol%)	solvent	Oxidant	yield (%)[b]
1	$Pd(OAc)_2$ (10 mol%)	TFA/TFAA (9:1)	$PhI(CF_3CO_2)_2$	-
2	$Pd(OAc)_2$ (10 mol%)	DCE	$PhI(CF_3CO_2)_2$	7%
3	$Pd(OAc)_2$ (10 mol%)	TFA/TFAA (1:1)	$PhI(CF_3CO_2)_2$	-
4	$Pd(OPiv)_2$ (10 mol%)	DCE/DME (1:1)	$PhI(CF_3CO_2)_2$	9%
5	$Pd(acac)_2$ (10 mol%)	DCE/DME (1:1)	$PhI(CF_3CO_2)_2$	8%
6	$Pd(TFA)_2$ (10 mol%)	DCE/DME (1:1)	$PhI(CF_3CO_2)_2$	8%
7	$PdCl_2(PPh_3)_2$ (10 mol%)	DCE/DME (1:1)	$PhI(CF_3CO_2)_2$	6%
8	RuCl3-xH_2O (10 mol%)	TFA/TFAA (1:65)	$PhI(CF_3CO_2)_2$	-
9	$RuCl_2(BPY)_3$-6H_2O (10 mol%)	TFA/TFAA (1:65)	$PhI(CF_3CO_2)_2$	-
10	$[Cp^*RhCl_2]_2$ (10 mol%)	TFA/TFAA (1:65)	$PhI(CF_3CO_2)_2$	-
11	$[Cp^*RhCl_2]_2$ (10 mol%) AgSbF6 (40 mol%)	TFA/TFAA (1:65)	$PhI(CF_3CO_2)_2$	-

[a] Reaction conditions: Flavone (**1**, 0.10 mmol, 1.0 equiv), catalyst (5 mol% as indicated), $PhI(CF_3CO_2)_2$ (0.20 mmol, 2.0 equiv), solvent, 80 °C for 12 h. [b] 1H NMR yield using caffeine as internal standard.

Solvent screening

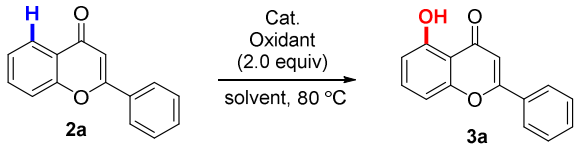


entry[a]	cat. (5 mol%)	solvent	Oxidant	yield (%)[b]

1	$[RuCl_2(p\text{-cymene})]_2$	TFA (1.2 eq)/TFAA (1:65)	$PhI(CF_3CO_2)_2$	53
2	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (5 eq/ 3 eq) in DCE	$PhI(CF_3CO_2)_2$	45
3	$[RuCl_2(p\text{-cymene})]_2$	TFA only	$PhI(CF_3CO_2)_2$	0
3	$[RuCl_2(p\text{-cymene})]_2$	DCE	$PhI(CF_3CO_2)_2$	trace
4	$[RuCl_2(p\text{-cymene})]_2$	PivOH (3 eq) in DCE	$PhI(CF_3CO_2)_2$	trace
5	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (9:1)	$PhI(CF_3CO_2)_2$	13
5	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (7:3)	$PhI(CF_3CO_2)_2$	14
6	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:1)	$PhI(CF_3CO_2)_2$	17
7	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (3:7)	$PhI(CF_3CO_2)_2$	17
8	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:9)	$PhI(CF_3CO_2)_2$	33
9	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:19)	$PhI(CF_3CO_2)_2$	40
10	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:29)	$PhI(CF_3CO_2)_2$	46
11	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:39)	$PhI(CF_3CO_2)_2$	49
12	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:49)	$PhI(CF_3CO_2)_2$	54
13	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:65)	$PhI(CF_3CO_2)_2$	63
14	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA (1:99)	$PhI(CF_3CO_2)_2$	52

[a] Reaction conditions: Flavone (**1**, 0.10 mmol, 1.0 equiv), catalyst (5 mol% as indicated), $PhI(CF_3CO_2)_2$ (0.20 mmol, 2.0 equiv), solvent, 80 °C for 12 h. [b] 1H NMR yield using caffeine as internal standard.

Oxidant screening

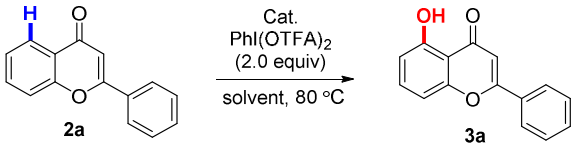


entry[a]	cat. (5 mol%)	TFA/TFAA	oxidant (2 equiv)	yield (%)[b]
1	$[RuCl_2(p\text{-cymene})]_2$	1:65	$PhI(CH_3CO_2)_2$	48
2	$[RuCl_2(p\text{-cymene})]_2$	1:65	$PhI(CF_3CO_2)_2$	63
3	$[RuCl_2(p\text{-cymene})]_2$	1:65	$K_2S_2O_8$	0
4	$[RuCl_2(p\text{-cymene})]_2$	1:65	$Cu(OAc)_2$	0
5	$[RuCl_2(p\text{-cymene})]_2$	1:65	Ag_2O	0

6	$[RuCl_2(p\text{-cymene})]_2$	1:65	TBHP	0
7	$[RuCl_2(p\text{-cymene})]_2$	1:65	NFSI	0

[a] Reaction conditions: Flavone (**1**, 0.10 mmol, 1.0 equiv), catalyst (mol% as indicated), oxdiant (0.20 mmol, 2.0 equiv), TFA/TFAA, 80 °C for 12 h. [b] 1H NMR yield using caffeine as internal standard

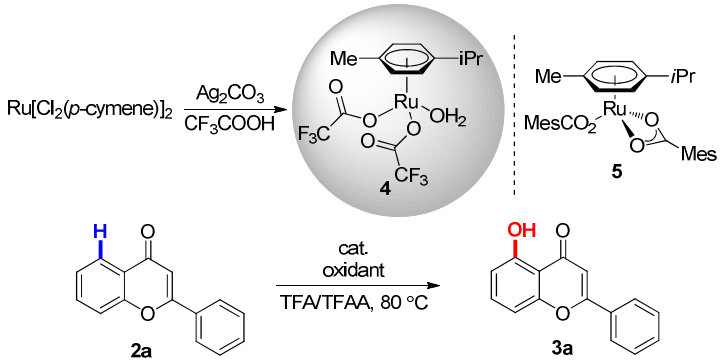
Silver screening



entry[a]	cat. (5 mol%)	TFA/TFAA	additive (1 equiv)	yield (%)[b]
1	$[RuCl_2(p\text{-cymene})]_2$	1:65	$AgNO_3$	-
2	$[RuCl_2(p\text{-cymene})]_2$	1:65	Ag_2O	71
3	$[RuCl_2(p\text{-cymene})]_2$	1:65	AgOTf	36
4	$[RuCl_2(p\text{-cymene})]_2$	1:65	AgOAc	67
5	$[RuCl_2(p\text{-cymene})]_2$	1:65	Ag_2CO_3/NaOAc	8
6	$[RuCl_2(p\text{-cymene})]_2$	1:65	Ag_2CO_3	76
7	$[RuCl_2(p\text{-cymene})]_2$	1:65	AgTFA	74

[a] Reaction conditions: Flavone (**1**, 0.10 mmol, 1.0 equiv), catalyst (mol% as indicated), oxdiant (0.20 mmol, 2.0 equiv), TFA/TFAA, 80 °C for 12 h. [b] 1H NMR yield using caffeine as internal standard

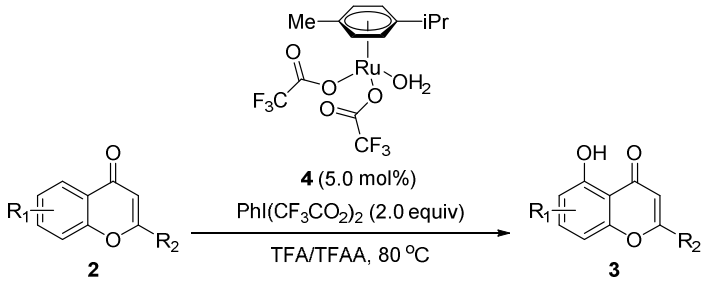
Optimization of reaction conditions with Ru-carboxylate catalyst(4)



entry[a]	cat. (5 mol%)	oxidant (2 equiv)	TFA/TFAA	yield (%)
1	**4**	$PhI(CF_3CO_2)_2$	1:65	87
2	**4**	$PhI(CF_3CO_2)_2$	1:45	78
3	**4**	$PhI(CF_3CO_2)_2$	9:1	0
4	**4**	$PhI(OAc)_2$	1:65	67
5	**4**	$K_2S_2O_8$	1:65	0
6	**5**	$PhI(CF_3CO_2)_2$	1:65	84
7[b]	**4**	$PhI(CF_3CO_2)_2$	1:65	71
8[c]	**4**	$PhI(CF_3CO_2)_2$	-	0
9[d]	**4**	$PhI(CF_3CO_2)_2$	-	trace

[a] Reaction conditions: Flavone (**1**, 0.15 mmol, 1.0 equiv), catalyst (mol% as indicated), $PhI(CF_3CO_2)_2$ (0.30 mmol, 2.0 equiv), TFA/TFAA, 80 °C for 20 h: Yield of isolated product. [b] The reaction was conducted at 100 °C for 8.5 h. [c]1,2-dichloroethane was used as solvent and the reaction was conducted for 12 h. [d] Toluene was used as solvent.

General procedure II (GP II) for hydroxylation of flavone/chromone derivatives



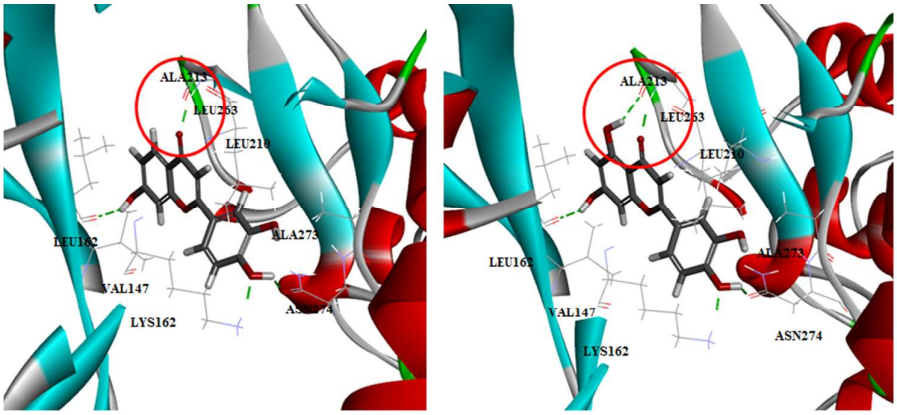
The mixture of substrate (**2**, 0.15 mmol), $Ru(CF_3CO_2)_2$(*p*-cymene)(H_2O) (**4**, 5.0 mol%), $PhI(CF_3CO_2)_2$ (2.0 equiv) and TFAA (2.24 mL) to a screw-capped tube. TFA (3.0 equiv) was added to the reaction mixture and stirred at 80 °C for 12-20 h. The reaction mixture was cooled to room temperature and diluted with DCM. $NaHCO_3$ was added slowly at 0 °C for quenching TFAA and stirred for 30 min at room temperature. The mixture was acidified by 1N HCl (aq) at 0 °C and stirred for 10 min at room temperature. The combined organic layer was extracted and dried over $MgSO_4$. The residue was concentrated under reduced pressure and purified by flash chromatography on silica gel (Hexane/EtOAc or DCM/MeOH as eluent).

Procedure for preparation of Ruthenium catalyst 4

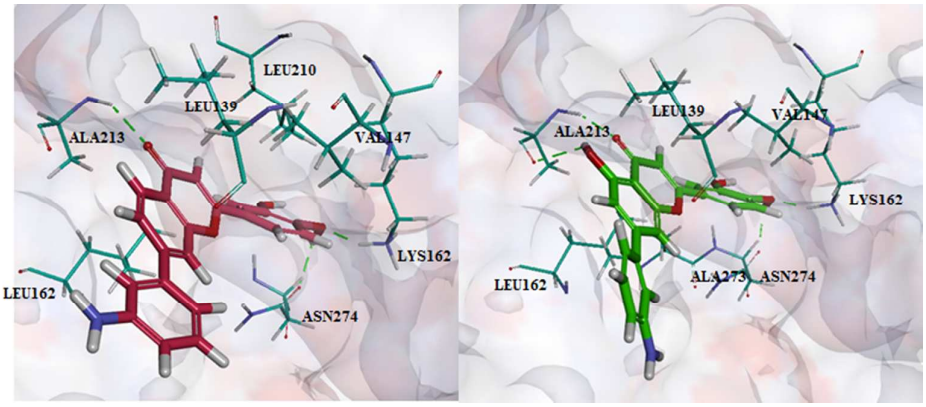
A flame-dried 250-mL round-bottomed flask equipped with a magnetic stir bar was charged with $[RuCl_2(p\text{-cymene})]_2$ (1.00 g, 1.63 mmol, 1.00 equiv) and dry benzene (100 mL) under an atmosphere of nitrogen. To this homogeneous mixture was added silver trifluoroacetate (1.44 g, 6.53 mmol, 4.00 equiv) in one portion. After being stirred at ambient temperature for 5 h, the reaction mixture was filtered through a small pad of Celite® to remove silver chloride. The filtrate was concentrated using a rotary evaporator and the resultant residue was further dried *in vacuo* overnight. The semi-solid thus obtained was dissolved in minimum amount of chloroform. Upon addition of the resultant solution into a pre-cooled 250-mL round-bottomed flask containing hexanes (approximately 100 mL) at –78 ^{o}C, orange red crystals were immediately formed at the bottom of the flask. The crystals were collected in a sintered glass filter, washed with cold hexanes (2×5 mL) and dried under reduced pressure to afford the desired Ru(II) complex as a yellow solid (1.31 g, 84%). (Lo, V. K. -Y.; Guo, Z.; Choi, M. -W.; Yu, W. -Y.; Huang, J. -S.; Che, C. -M. *J. Am. Chem. Soc*. **2012**, *134*, 7588)

Binding mode of Aurora A inhibitors (PDB code 1OL6)

Predicted binding modes of 5-Deoxy Luteolin (left) & Luteolin (right) in ATP binding pocket of Aurora kinase



Predicted binding modes of 5-Deoxy **12a** (left) & **12a** (right)

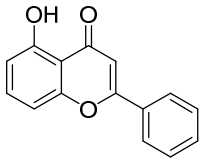


Aurora A Assay.

The effects of compounds on the kinase activity of aurora A were analyzed the Reaction Biology Corp. (Malvern, PA, USA) using radiometric kinase assays ([γ-^{33}P]-ATP). Reactions contained 20 μM of aurora A peptide substrate, [H-LRRASLG], in freshly prepared Base Reaction Buffer (20 mM HEPES (pH 7.5), 10 mM $MgCl_2$, 1 mM EGTA, 0.02% BRIJ-35, 0.02 mg/ml BSA, 0.1 mM Na_3VO_4, 2 mM DTT, 1% DMSO). Testing compounds were dissolved in 100% DMSO to specific concentration. The serial dilution was conducted by epMotion 5070 in DMSO. Reaction procedure: 20 μM of aurora A peptide substrate in freshly prepared Reaction Buffer was prepared and 4 nM of aurora A (Invitrogen) was added into the substrate solution and gently mixed. Testing compounds in 100% DMSO were delivered into the kinase reaction mixture until final 1 μM by Acoustic technology (Echo550; nanoliter range), and the reaction mixture was incubated for 20 min at room temp. 33P-ATP (Specific activity 10 μCi/μl) was delivered into the reaction mixture (1 μM ATP at final) to initiate the reaction and the reaction mixture was incubated for 2 hours at room temperature. Radioactivity was then detected by filter-binding method. Kinase activity data were expressed as the percent remaining kinase activity in test samples compared to vehicle (dimethyl sulfoxide) reactions. IC50 values and curve fits were obtained using Prism (GraphPad Software).

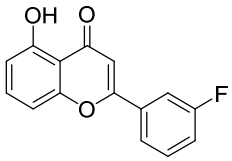
Characterization of hydroxylation products

5-hydroxy-2-phenyl-4H-chromen-4-one (3a)



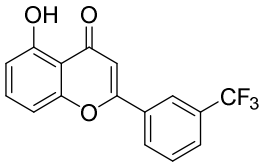
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 87% (31.1 mg). mp 155-156 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.58 (s, 1H), 7.98 – 7.87 (m, 2H), 7.70 – 7.44 (m, 4H), 7.01 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.82 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.75 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.6, 164.6, 160.8, 156.5, 135.4, 132.0, 131.2, 129.1, 126.4, 111.4, 110.9, 107.0, 106.1. HRMS (ESI^+) m/z calcd. $C_{15}H_{10}NaO_3^+$ $[M+Na]^+$: 261.0522, found: 261.0527.

2-(3-fluorophenyl)-5-hydroxy-4H-chromen-4-one (3b)



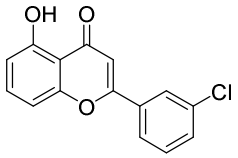
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 84% (32.3 mg). mp 168-169 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.46 (s, 1H), 7.72 – 7.65 (m, 1H), 7.64 – 7.44 (m, 3H), 7.32 – 7.18 (m, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.70 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.4, 163.0 (d, *J* = 247.8 Hz), 162.9 (d, *J* = 2.8 Hz), 160.8, 156.2, 135.6, 133.3 (d, *J* = 8.0 Hz), 130.8 (d, *J* = 8.2 Hz), 122.0 (d, *J* = 3.1 Hz), 118.9 (d, *J* = 21.3 Hz), 113.4 (d, *J* = 24.0 Hz), 111.6, 110.8, 107.0, 106.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.98. HRMS (ESI^+) m/z calcd. $C_{15}H_9FNaO_3^+$ $[M+Na]^+$: 279.0428, found: 279.0435.

5-hydroxy-2-(3-(trifluoromethyl)phenyl)-4H-chromen-4-one (3c)



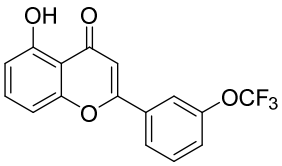
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 85% (39.0 mg). mp 152-153 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.42 (s, 1H), 8.15 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 8.3 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.76 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 162.6, 160.8, 156.2, 135.7, 132.1, 131.8 (q, *J* = 33.0 Hz), 129.8, 129.5, 128.4 (q, *J* = 3.6 Hz), 123.5 (q, *J* = 272.6 Hz), 123.2 (q, *J* = 3.9 Hz), 111.8, 110.8, 107.1, 106.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.87. HRMS (ESI^+) m/z calcd. $C_{16}H_9F_3NaO_3^+$ $[M+Na]^+$: 329.0396, found: 329.0405

2-(3-chlorophenyl)-5-hydroxy-4H-chromen-4-one (3d)



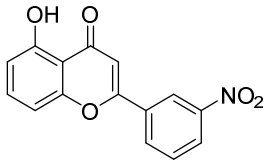
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 86% (35.1 mg). mp 173-174 ^{o}C. Light Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.45 (s, 1H), 7.88 (s, 1H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.39 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.70 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 162.8, 160.7, 156.2, 135.6, 135.3, 132.9, 131.9, 130.4, 126.4, 124.4, 111.6, 110.8, 107.0, 106.6. HRMS (ESI^+) m/z calcd. $C_{15}H_9ClNaO_3^+$ $[M+Na]^+$: 295.0132, found: 295.0134.

5-hydroxy-2-(3-(trifluoromethoxy)phenyl)-4H-chromen-4-one (3e)



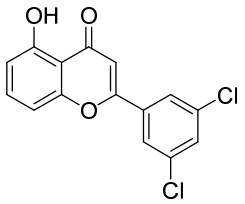
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 84% (40.5 mg). mp 113-115 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.43 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.75 (s, 1H), 7.65 – 7.49(m, 2H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.72 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 162.6, 160.8, 156.2, 149.8 (d, *J* = 1.9 Hz), 135.7, 133.3, 130.7, 124.6, 124.1, 120.4 (d, *J* = 258.5 Hz), 118.9, 111.7, 110.8, 107.0, 106.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.82. HRMS (ESI^+) m/z calcd. $C_{16}H_9F_3NaO_4^+$ $[M+Na]^+$: 345.0345, found: 345.0360

5-hydroxy-2-(3-nitrophenyl)-4H-chromen-4-one (3f)



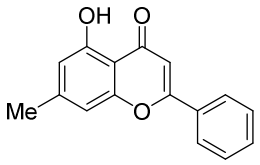
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 80% (34.2 mg). mp 219-221 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 12.38 (s, 1H), 8.78 (s, 1H), 8.39 (d, *J* = 7.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 8.1 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.82-6.80 (m, 2H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 183.7, 162.2, 161.2, 156.7, 149.2, 136.3, 133.4, 132.4, 130.8, 126.6, 121.7, 112.0, 111.2, 107.7, 107.6. HRMS (ESI^+) m/z calcd. $C_{15}H_9NNaO_5^+$ $[M+Na]^+$: 306.0373, found: 306.0371.

2-(3,5-dichlorophenyl)-5-hydroxy-4H-chromen-4-one (3g)



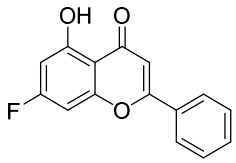
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 77% (35.6 mg). mp 225-226 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 12.37 (s, 1H), 7.82 (d, *J* = 1.8 Hz, 2H), 7.63 – 7.50 (m, 2H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.69 (s, 1H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 183.6, 161.9, 161.1, 156.7, 136.2, 136.2, 134.6, 131.9, 125.2, 112.0, 111.2, 107.6, 107.5. HRMS (ESI^+) m/z calcd. $C_{15}H_8Cl_2NaO_3^+$ $[M+Na]^+$: 328.9743, found: 328.9738.

5-hydroxy-7-methyl-2-phenyl-4H-chromen-4-one (3h)



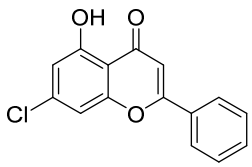
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 78% (29.6 mg). mp 141-142 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.44 (br s, 1H), 7.93 – 7.84 (m, 2H), 7.57 – 7.49 (m, 3H), 6.81 (s, 1H), 6.68 (s, 1H), 6.62 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1, 164.2, 160.4, 156.3, 147.2, 131.8, 131.3, 129.0, 126.3, 112.2, 108.8, 107.4, 105.9, 22.4. HRMS (ESI^+) m/z calcd. $C_{16}H_{12}NaO_3^+$ $[M+Na]^+$: 275.0679, found: 275.0680.

7-fluoro-5-hydroxy-2-phenyl-4H-chromen-4-one (3i)



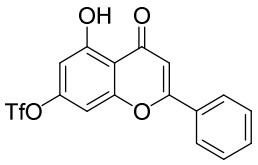
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 67% (25.8 mg). mp 134-135 ^{o}C. Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.88 (s, 1H), 7.88 – 7.88 – 7.86 (m, 2H), 7.59 – 7.50 (m, 3H), 6.71 – 6.68 (m, 2H), 6.53 (dd, J = 10.6, 2.3 Hz, 1H ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.6, 166.8 (d, J = 253.3 Hz), 164.6 (d, J = 1.3 Hz), 162.8 (d, J = 16.3 Hz), 157.3 (d, J = 16.9 Hz), 132.2, 130.8, 129.1, 126.3, 108.0 (d, J = 1.9 Hz), 106.0, 99.9 (d, J = 25.2 Hz), 95.0 (d, J = 26.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.63. HRMS (ESI^+) m/z calcd. $C_{15}H_9FNaO_3^+$ $[M+Na]^+$: 279.0428, found: 279.0432.

7-chloro-5-hydroxy-2-phenyl-4H-chromen-4-one (3j)



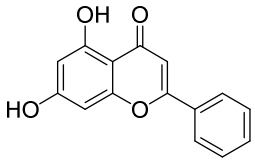
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 51% (20.6 mg). mp 167-168 ^{o}C. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.70 (s, 1H), 7.92 – 7.83 (m, 2H), 7.62 – 7.47 (m, 3H), 7.03 (d, *J* = 1.8 Hz, 1H), 6.82 (d, *J* = 1.8 Hz, 1H), 6.72 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.8, 164.6, 161.4, 156.4, 141.2, 132.3, 130.8, 129.2, 126.4, 112.3, 109.4, 107.7, 106.2. HRMS (ESI^+) m/z calcd. $C_{15}H_9ClNaO_3^+$ $[M+Na]^+$: 295.0132, found: 295.0123.

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl trifluoromethanesulfonate (3k)



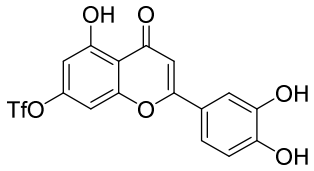
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 64% (37.3 mg). mp 129-131 ^{o}C. Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.93 (s, 1H), 7.95 – 7.84 (m, 2H), 7.64 – 7.47 (m, 3H), 6.98 (d, *J* = 2.3 Hz, 1H), 6.78 (s, 1H), 6.74 (d, *J* = 2.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.6 , 165.3 , 162.6 , 156.6 , 153.2 , 132.6 , 130.4 , 129.3 , 126.5 , 118.6 (q, *J* = 320.9 Hz), 110.4 , 106.4 , 105.1 , 100.8 . ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.63. HRMS (ESI^+) m/z calcd. $C_{16}H_9F_3NaO_6S^+$ $[M+Na]^+$: 408.9964, found: 408.9982.

5,7-dihydroxy-2-phenyl-4H-chromen-4-one (3l)



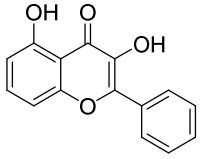
Followed from general procedure II. (reaction time : 20 h, DCM/MeOH as eluent for flash chromatography). Yield 70% (26.7 mg). mp 283-284 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.83 (s, 1H), 10.92 (br s, 1H), 8.09 – 8.02 (m, 2H), 7.66 – 7.50 (m,3H), 6.96 (s, 1H), 6.52 (d, J = 2.1 Hz, 1H), 6.22 (d, J = 2.1 Hz, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 181.9, 164.4, 163.1, 161.4, 157.4, 132.0, 130.7, 129.1, 126.4, 105.2, 104.0, 99.0, 94.1. HRMS (ESI^+) m/z calcd. $C_{15}H_10NaO_4^+$ $[M+Na]^+$: 277.0471, found: 277.0484.

2-(3,4-dihydroxyphenyl)-5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3m)



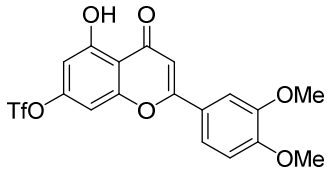
Followed from general procedure II. (reaction time : 15 h, DCM/MeOH/1% AcOH as eluent for flash chromatography). Yield 49% (20.6 mg). Dark yellow solid. mp 244-245 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.30 (s, 1H), 10.13 (br s, 1H), 9.42 (br s, 1H), 7.64 – 7.34 (m, 3H), 7.00 (d, J = 2.1 Hz, 1H), 6.92-6.91 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.0, 165.4, 161.4, 156.1, 152.4, 150.4, 145.8, 120.8, 119.7, 118.2 (q, J = 320.9 Hz), 116.0, 113.9, 109.9, 104.6, 103.8, 101.4. ^{19}F NMR (376 MHz, DMSO-d_6) δ -72.56. HRMS (ESI$^+$) m/z calcd. $C_{16}H_{10}F_3O_8S^+$ $[M+H]^+$: 419.0043, found: 419.0061.

3,5-dihydroxy-2-phenyl-4H-chromen-4-one (3n)



Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 53 (20.6 mg). mp 144-146 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 8.27 – 8.18 (m, 2H), 7.63 – 7.45 (m, 4H), 7.03 (dd, J = 8.5, 1.1 Hz, 1H), 6.81 (dd, J = 8.1, 1.1 Hz, 1H), 6.74 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 159.6, 155.5, 146.1, 137.0, 135.5, 130.6, 130.5, 128.6, 127.8, 109.9, 109.0, 107.6. HRMS (ESI$^+$) m/z calcd. $C_{15}H_{10}NaO_4^+$ $[M+Na]^+$: 277.0471 , found: 277.0471.

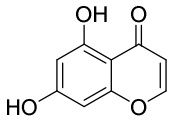
2-(3,4-dimethoxyphenyl)-5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3o)



Followed from general procedure II. (reaction time :20, Hexane/EtOAc as eluent for flash chromatography). Yield 44% (19.2 mg). mp 163-165 ^{o}C. Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.04 (s, 1H), 7.55 (dd,

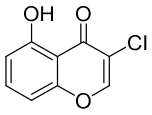
J = 8.5, 2.2 Hz, 1H), 7.34 (d, *J* = 2.2 Hz, 1H), 7.07 – 6.92 (m, 2H), 6.78 – 6.66 (m, 2H), 4.00 (s, 3H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.4, 165.3, 162.6, 156.6, 153.1, 149.5, 122.8, 120.6, 118.6 (q, *J* = 321.1 Hz), 116.3, 111.3, 110.3, 108.8, 105.2, 105.0, 100.8, 56.2, 56.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.63. HRMS (ESI^+) m/z calcd. $C_{18}H_{14}F_3O_8S^+$ $[M+H]^+$: 447.0356, found: 447.0374.

5,7-dihydroxy-4H-chromen-4-one (3p)



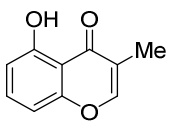
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 80% (21.5 mg). mp 277-279 °C. Light yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.69 (s, 1H), 10.93 (br s, 1H), 8.18 (d, *J* = 5.9 Hz, 1H), 6.36 (d, *J* = 2.1 Hz, 1H), 6.27 (d, *J* = 5.9 Hz, 1H), 6.20 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.2, 164.4, 161.6, 157.8, 157.4, 110.4, 104.8, 99.0, 94.0. HRMS (ESI^+) m/z calcd. $C_9H_7O_4^+$ $[M+H]^+$: 179.0339, found: 179.0348.

3-chloro-5-hydroxy-4H-chromen-4-one (3q)



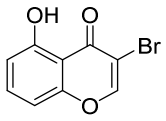
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 76% (22.4 mg). mp 154-155 °C. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.98 (s, 1H), 8.11 (s, 1H), 7.57 (t, *J* = 8.4 Hz, 1H), 6.93 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.86 (dd, *J* = 8.4, 0.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 160.6, 156.2, 153.0, 136.0, 118.9, 112.0, 110.8, 107.3. HRMS (ESI^+) m/z calcd. $C_9H_6ClO_3^+$ $[M+H]^+$: 197.0000, found: 197.0014.

5-hydroxy-3-methyl-4H-chromen-4-one (3r)



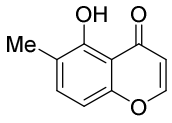
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 46% (12.2 mg). mp 98-99 ^{o}C. Ivory solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.58 (s, 1H), 7.77 (q, *J* = 1.2 Hz, 1H), 7.50 (t, *J* = 8.3 Hz, 1H), 6.86 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.78 (dd, *J* = 8.3, 0.9 Hz, 1H), 2.02 (d, *J* = 1.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.4, 160.8, 157.0, 152.7, 135.1, 119.5, 110.8, 110.8, 107.0, 10.4. HRMS (ESI^+) m/z calcd. $C_{10}H_9O_3^+$ $[M+H]^+$: 177.0546, found: 177.0560.

3-bromo-5-hydroxy-4H-chromen-4-one (3s)



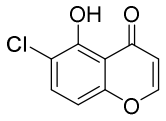
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 71% (25.8 mg). mp 169-171 ^{o}C. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.01 (s, 1H), 8.18 (s, 1H), 7.57 (t, *J* = 8.4 Hz, 1H), 6.93 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.87 (dd, *J* = 8.4, 0.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 160.4, 156.3, 154.7, 136.0, 112.1, 110.6, 108.2, 107.2. HRMS (ESI^+) m/z calcd. $C_9H_5BrNaO_3^+$ $[M+Na]^+$: 262.9314, found: 262.9316.

5-hydroxy-6-methyl-4H-chromen-4-one (3t)



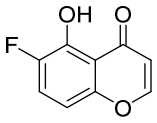
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 84% (22.3 mg). mp 96-98 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.62 (s, 1H), 7.80 (d, *J* = 5.9 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 1H), 6.25 (d, *J* = 5.9 Hz, 1H), 2.26 (s, 3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.2, 158.2, 156.1, 154.9, 136.6, 120.5, 111.3, 111.2, 106.2, 14.7. HRMS (ESI^+) m/z calcd. $C_{10}H_9O_3^+$ $[M+H]^+$: 177.0546, found: 177.0558.

6-chloro-5-hydroxy-4H-chromen-4-one (3u)



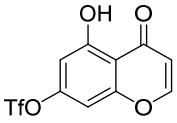
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 78% (22.9 mg). mp 160-162 C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.03 (s, 1H), 7.86 (d, *J* = 6.0 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.32 (d, *J* = 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.5, 156.6, 156.0, 155.0, 135.6, 115.5, 112.3, 111.5, 107.9. HRMS (ESI^+) m/z calcd. $C_9H_5ClNaO_3^+$ $[M+Na]^+$: 218.9819, found: 218.9826.

6-fluoro-5-hydroxy-4H-chromen-4-one (3v)



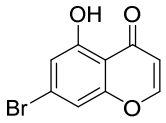
Followed from general procedure II. (reaction time : 20 h, Hexane/EtOAc as eluent for flash chromatography). Yield 56% (15.1 mg). mp 133-135 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.44 (s, 1H), 7.86 (d, *J* = 6.0 Hz, 1H), 7.41 (dd, *J* = 10.5, 9.2 Hz, 1H), 6.88 (dd, *J* = 9.2, 3.3 Hz, 1H), 6.29 (d, *J* = 6.0 Hz, 1H) ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.20 (d, *J* = 2.8 Hz), 156.8, 152.2 (d, *J* = 2.1 Hz), 147.7 (d, *J* = 13.5 Hz), 146.1 (d, *J* = 243.6 Hz), 122.5 (d, *J* = 20.3 Hz), 113.1 (d, *J* = 4.3 Hz), 110.9 , 106.8 (d, *J* = 6.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.35. HRMS (ESI^+) m/z calcd. $C_9H_5FNaO_3^+$ $[M+Na]^+$: 203.0115, found: 203.0116.

5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3w)



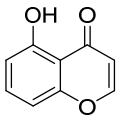
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 72% (33.4 mg). mp 76-78 ^{o}C. Light brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.73 (s, 1H), 7.88 (d, *J* = 6.0 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 6.73 (d, *J* = 2.2 Hz, 1H), 6.36 (d, *J* = 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.0, 162.6, 156.9, 156.7, 153.3, 118.6 (q, *J* = 321.0 Hz), 112.2, 111.4, 105.2, 100.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.66. HRMS (ESI^+) m/z calcd. $C_{10}H_6F_3O_6S^+$ $[M+H]^+$: 310.9832, found: 310.9843.

7-bromo-5-hydroxy-4H-chromen-4-one (3x)



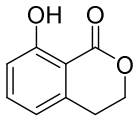
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 74% (26.6 mg). mp 124-125 ^{o}C. Ivory solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.49 (s, 1H), 7.81 (d, *J* = 6.0 Hz, 1H), 7.09 (d, *J* = 1.4 Hz, 1H), 6.98 (d, *J* = 1.4 Hz, 1H), 6.29 (d, *J* = 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.4, 161.2, 156.5, 156.1, 129.4, 115.2, 111.9, 110.8, 110.7. HRMS (ESI^+) m/z calcd. $C_9H_6BrO_3^+$ $[M+H]^+$: 240.9495, found: 240.9494.

5-hydroxy-4H-chromen-4-one (3y)



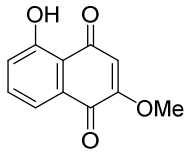
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 86% (21.0 mg). mp 128-130 ^{o}C. Ivory solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.40 (s, 1H), 7.83 (d, *J* = 6.0 Hz, 1H), 7.52 (t, *J* = 8.4 Hz, 1H), 6.89 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.80 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.28 (d, *J* = 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.99, 160.84, 156.71, 156.25, 135.46, 111.87, 111.60, 111.47, 107.15. HRMS (ESI^+) m/z calcd. $C_9H_7O_3^+$ $[M+H]^+$: 163.0390, found: 163.0401.

8-hydroxyisochroman-1-one (3z)



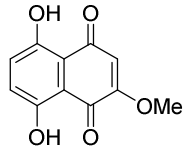
Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 94% (23.1 mg). mp 55-57 ^{o}C. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.97 (s, 1H), 7.42 (dd, *J* = 8.5, 7.4 Hz, 1H), 6.90 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.72 (dd, *J* = 7.4, 1.0 Hz, 1H), 4.59 – 4.56 (m, 2H), 3.07 – 3.04 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 162.3, 139.7, 136.2, 117.8, 116.3, 108.6, 68.0, 27.5. HRMS (ESI^+) m/z calcd. $C_9H_8NaO_3^+$ $[M+Na]^+$: 187.0366, found: 187.0377.

5-hydroxy-2-methoxynaphthalene-1,4-dione (7)



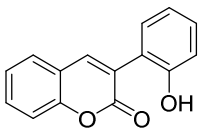
Followed from general procedure II. (reaction time : 12 h, Hexane/EtOAc as eluent for flash chromatography). Yield 83% (25.3 ,g). mp 164-166 ^{o}C. Orange solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 12.20 (s, 1H), 7.66 – 7.50 (m, 2H), 7.23 (dd, J = 7.6, 1.8 Hz, 1H), 6.08 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 191.3, 179.5, 161.6, 161.3, 135.8, 131.5, 125.2, 119.5, 114.6, 109.8, 57.1. HRMS (ESI^+) m/z calcd. $C_{11}H_8NaO_4^+$ $[M+Na]^+$: 227.0315, found: 227.0319.

5,8-dihydroxy-2-methoxynaphthalene-1,4-dione (7')



Followed from general procedure II. (reaction time : 12 h, DCM/MeOH as eluent for flash chromatography). Yield 9% (3.0 mg). mp 187-188 ^{o}C. Pupple solid. 1H NMR (400 MHz, CD_2Cl_2) δ 12.62 (s, 1H), 12.13 (s, 1H), 7.29 – 7.13 (m, 2H), 6.16 (s, 1H), 3.90 (s, 1H).^{13}C NMR (101 MHz, CD_2Cl_2) δ 188.9, 183.1, 161.5, 158.6, 157.2, 130.9, 128.4, 112.1, 111.3, 110.7, 57.2. HRMS (ESI^+) m/z calcd. $C_{11}H_8NaO_5^+$ $[M+Na]^+$: 243.0264, found: 243.0253.

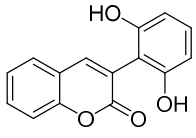
3-(2-hydroxyphenyl)-2H-chromen-2-one (9)



Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 71% (25.4 mg). mp 210-212 ^{o}C. Ivory solid1H NMR (400 MHz, DMSO-d_6) δ 9.59 (s, 1H), 8.03 (s, 1H), 7.74 (dd, J = 7.8, 1.6 Hz, 1H), 7.61 (ddd, J = 8.3, 7.8, 1.6 Hz, 1H), 7.43 (dd, J = 8.3, 1.2 Hz, 1H), 7.36 (td, J = 7.8, 1.2 Hz, 1H), 7.28 (dd, J = 7.6, 1.8 Hz, 1H), 7.23 (ddd, J = 8.0, 7.6, 1.8 Hz, 1H), 6.92 (dd, J = 8.0, 1.2, 1H),

6.86 (td, J = 7.6, 1.2 Hz, 1H).[13]C NMR (101 MHz, DMSO-d_6) δ 159.3, 155.1, 153.0, 141.9, 131.4, 130.8, 129.7, 128.3, 126.0, 124.4, 122.2, 119.3, 118.7, 115.9, 115.7. HRMS (ESI$^+$) m/z calcd. $C_{15}H_{10}NaO_3^+$ $[M+Na]^+$: 261.0522, found: 261.0551.

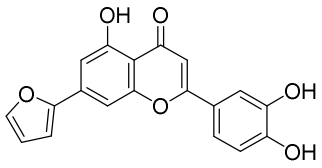
3-(2,6-dihydroxyphenyl)-2H-chromen-2-one (9')



Followed from general procedure II. (reaction time : 16 h, Hexane/EtOAc as eluent for flash chromatography). Yield 25% (9.5 mg). mp 220-222 ^{o}C. Brown solid. [1]H NMR (400 MHz, DMSO-d_6) δ 9.27 (s, 2H), 7.85 (s, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 6.99 (t, J = 8.1 Hz, 1H), 6.37 (d, J = 8.1 Hz, 2H). [13]C NMR (101 MHz, DMSO-d_6) δ 159.3, 156.2, 153.1, 143.1, 131.2, 129.2, 128.0, 124.3, 123.2, 119.4, 115.8, 110.1, 106.3. HRMS (ESI$^+$) m/z calcd. $C_{15}H_{10}NaO_4^+$ $[M+Na]^+$: 277.0471, found: 277.0487.

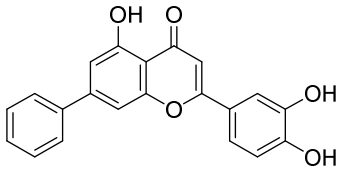
Luteolin derivatives were synthesized via Suzuki cross-coupling from **3m** or **3y**.

2-(3,4-dihydroxyphenyl)-7-(furan-2-yl)-5-hydroxy-4H-chromen-4-one (10b)



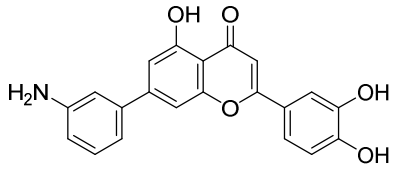
Yield 71% (8.1 mg). mp 307-309 ^{o}C. Yellow solid. [1]H NMR (400 MHz, DMSO-d_6) δ 12.91 (s, 1H), 10.04 (br s, 1H), 9.40 (br s, 1H), 7.89 (s, 1H), 7.51 – 7.45 (m, 3H), 7.31 (d, J = 3.5 Hz, 1H), 7.12 (s, 1H), 6.91 (d, J = 8.2 Hz, 1H), 6.82 (s, 1H), 6.70 – 6.69 (m, 1H). [13]C NMR (101 MHz, DMSO-d_6) δ 182.2, 164.9, 160.3, 156.3, 151.3, 150.0, 145.8, 144.8, 136.4, 121.3, 119.3, 116.0, 113.7, 112.7, 110.0, 108.8, 105.2, 103.5, 101.7. HRMS (ESI$^+$) m/z calcd. $C_{19}H_{12}NaO_6^+$ $[M+Na]^+$: 359.0526, found: 359.0523.

2-(3,4-dihydroxyphenyl)-5-hydroxy-7-phenyl-4H-chromen-4-one (11b)



Yield 73% (10.1 mg) mp 288-290 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.85 (br s, 1H), 10.04 (br s, 1H), 9.40 (br s, 1H), 7.84 – 7.76 (m, 2H), 7.61 – 7.38 (m, 6H), 7.11 (s, 1H), 6.92 (d, J = 8.2 Hz, 1H), 6.85 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.4, 165.0, 160.1, 156.1, 150.1, 147.2, 145.8, 138.2, 129.1, 129.0, 127.2, 121.4, 119.4, 116.0, 113.7, 108.9, 105.4, 103.5. HRMS (ESI$^+$) m/z calcd. $C_{21}H_{14}NaO_5^+$ $[M+Na]^+$: 369.0733, found: 369.0738.

7-(3-aminophenyl)-2-(3,4-dihydroxyphenyl)-5-hydroxy-4H-chromen-4-one (12b)



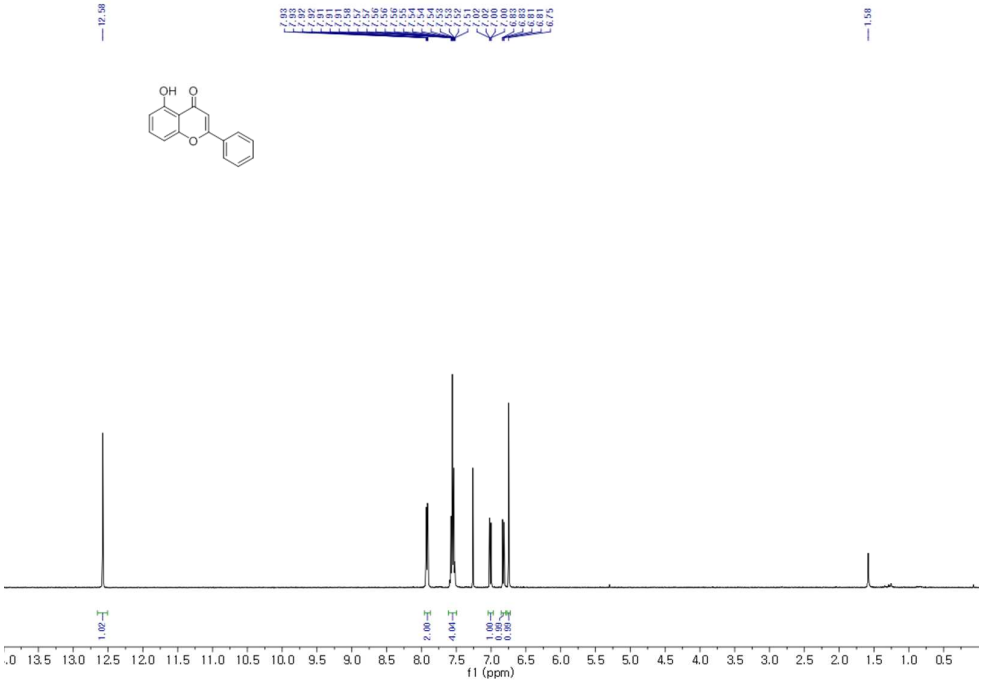
Yield 47% (7.9 mg). mp 265-267 ^{o}C. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (s, 1H), 9.93 (br s, 1H), 9.50 (br s, 1H), 7.57 – 7.43 (m, 2H), 7.32 (s, 1H), 7.15 (t, J = 7.7 Hz, 1H), 7.00 – 6.88 (m, 4H), 6.84 (s, 1H), 6.65 (d, J = 8.1 Hz, 1H), 5.25 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.4, 164.9, 159.9, 156.0, 150.1, 149.3, 148.2, 145.8, 138.9, 129.6, 121.3, 119.3, 116.0, 114.6, 114.6, 113.6, 112.3, 108.8, 108.6, 105.0, 103.4. HRMS (ESI$^+$) m/z calcd. $C_{21}H_{16}NO_5^+$ $[M+H]^+$: 362.1023, found: 362.1037.

Appendix Ⅰ

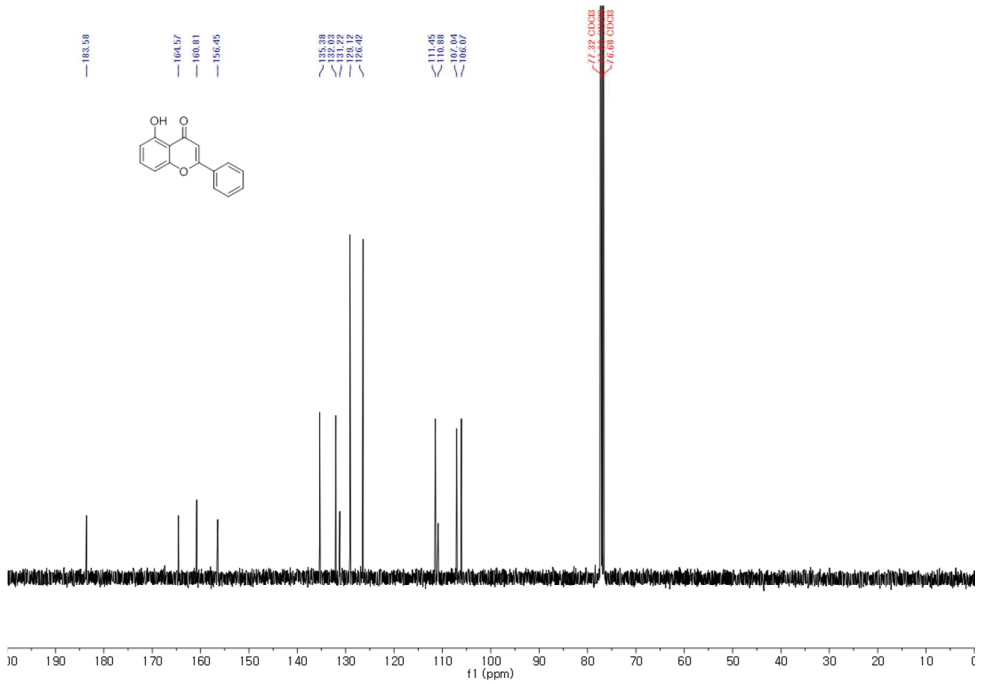
Spectral Copies of ^{1}H and ^{13}C NMR Data

Obtained in this Study

5-hydroxy-2-phenyl-4H-chromen-4-one (3a)

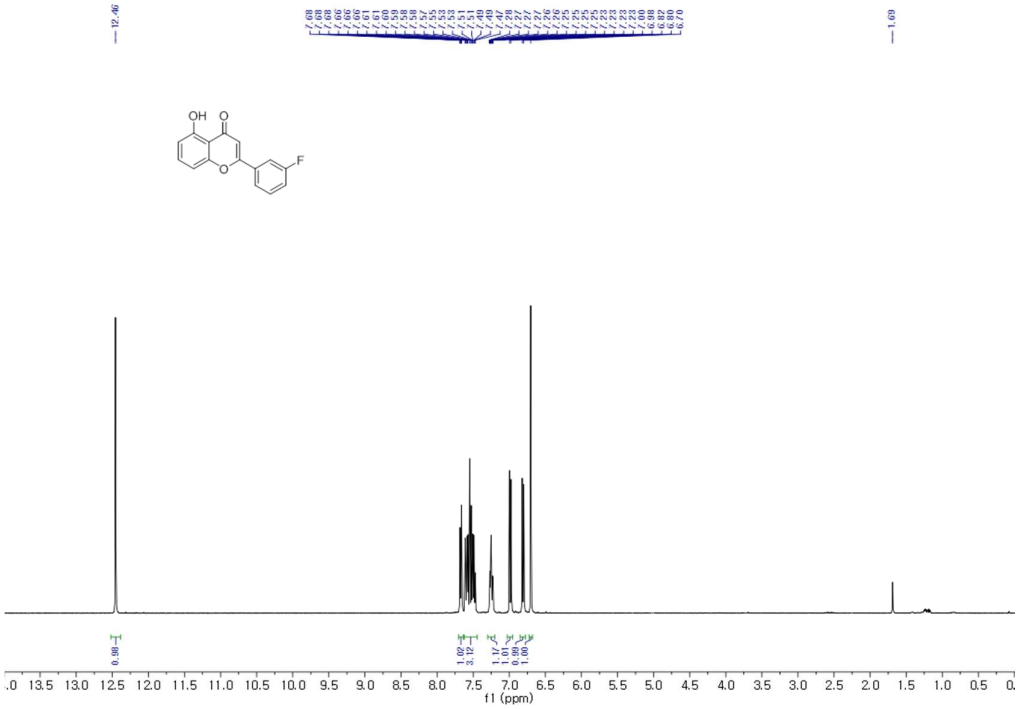


400 MHz, ^{1}H NMR in $CDCl_3$

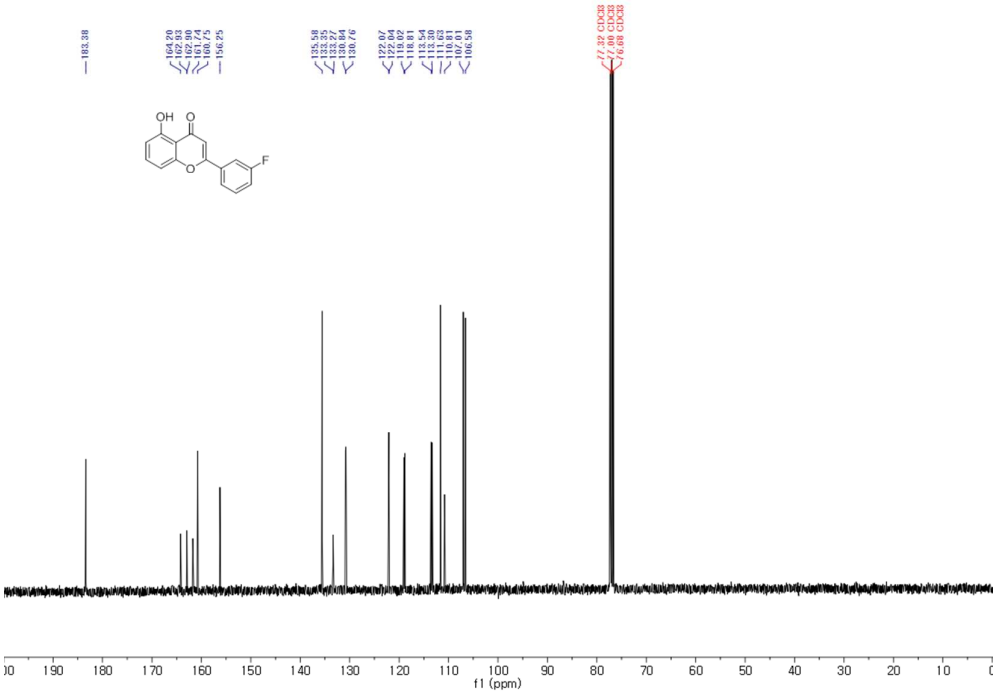


100 MHz, ^{13}C NMR in $CDCl_3$

2-(3-fluorophenyl)-5-hydroxy-4H-chromen-4-one (3b)

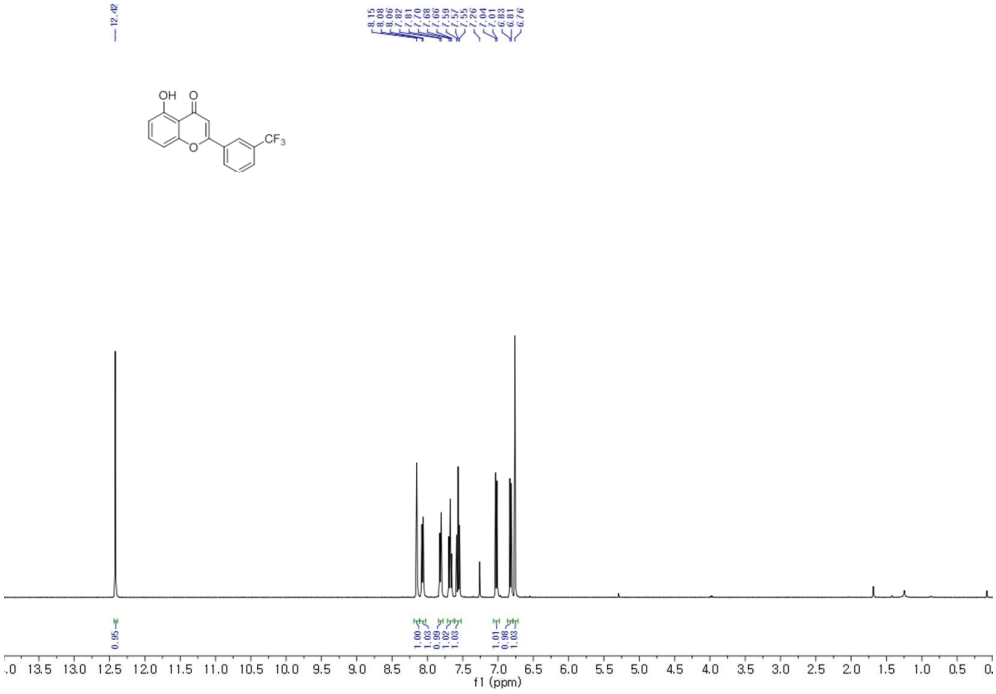


400 MHz, ^{1}H NMR in $CDCl_3$

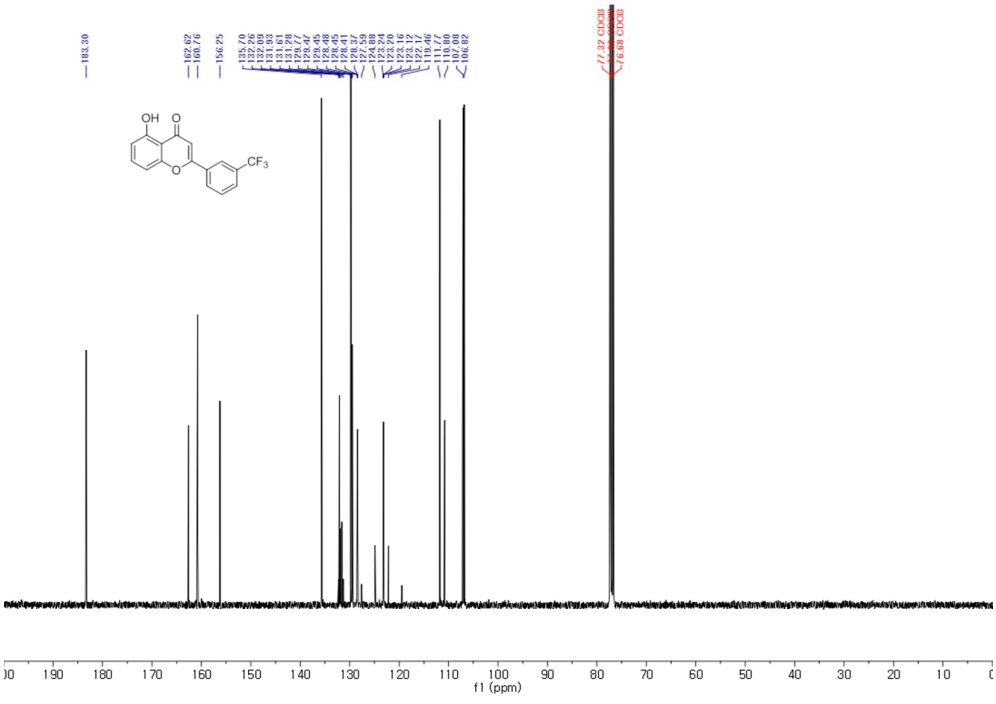


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-2-(3-(trifluoromethyl)phenyl)-4H-chromen-4-one (3c)

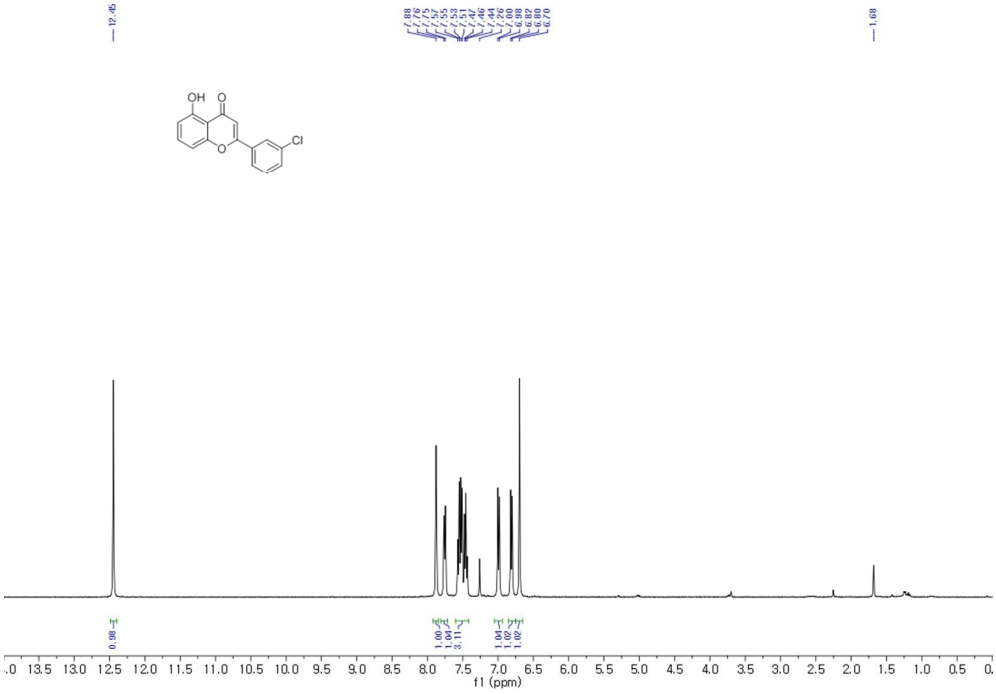


400 MHz, ^{1}H NMR in $CDCl_3$

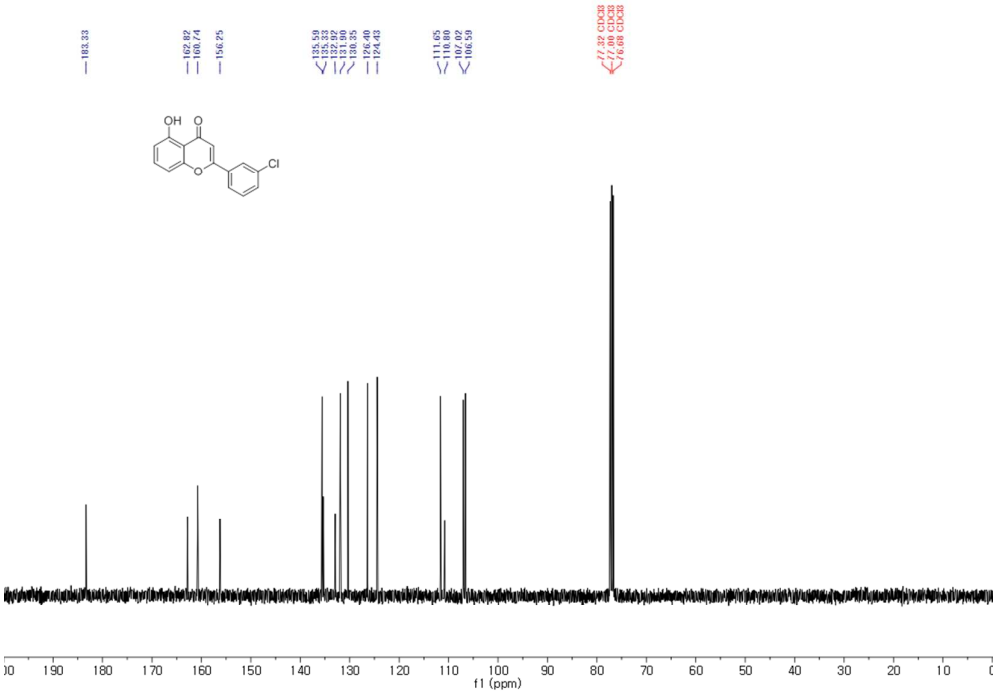


100 MHz, ^{13}C NMR in $CDCl_3$

2-(3-chlorophenyl)-5-hydroxy-4H-chromen-4-one (3d)

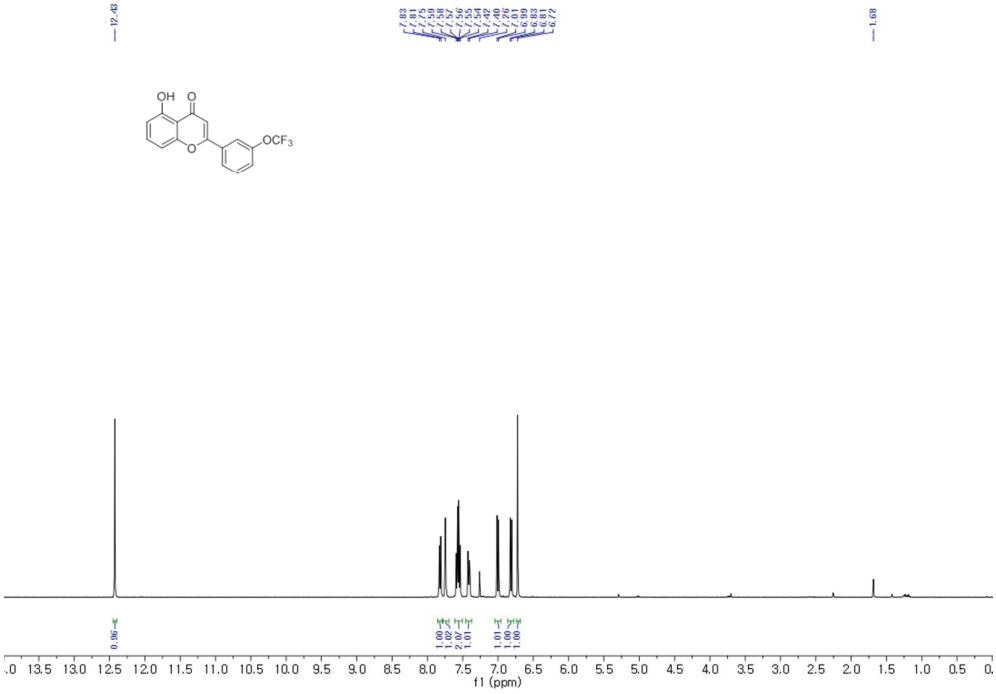


400 MHz, ^{1}H NMR in $CDCl_3$

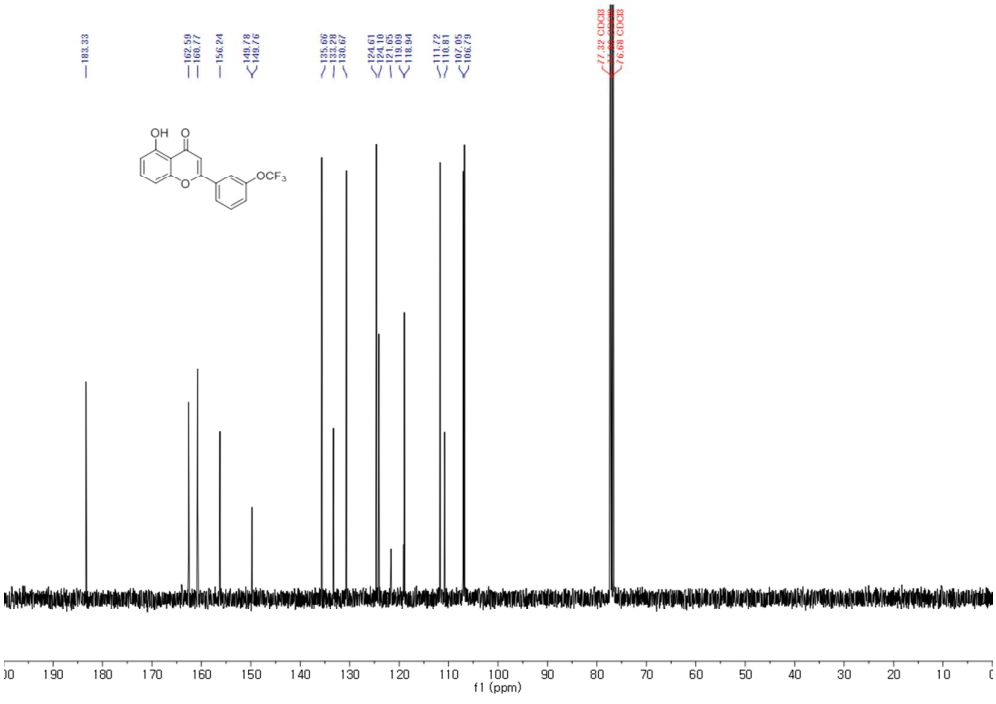


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-2-(3-(trifluoromethoxy)phenyl)-4H-chromen-4-one (3e)

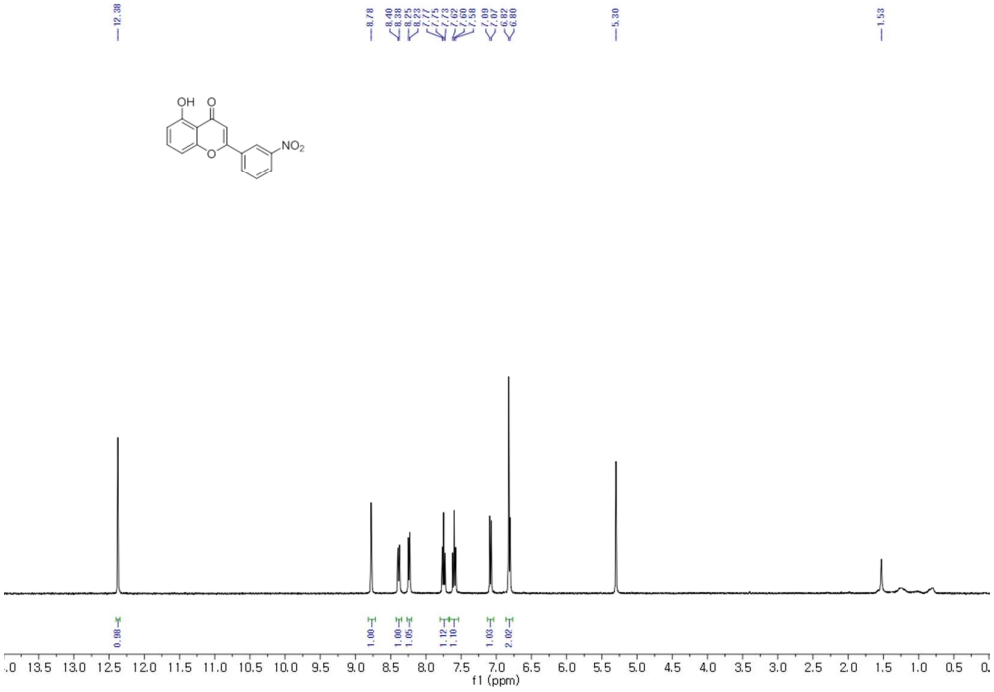


400 MHz, ^{1}H NMR in $CDCl_3$

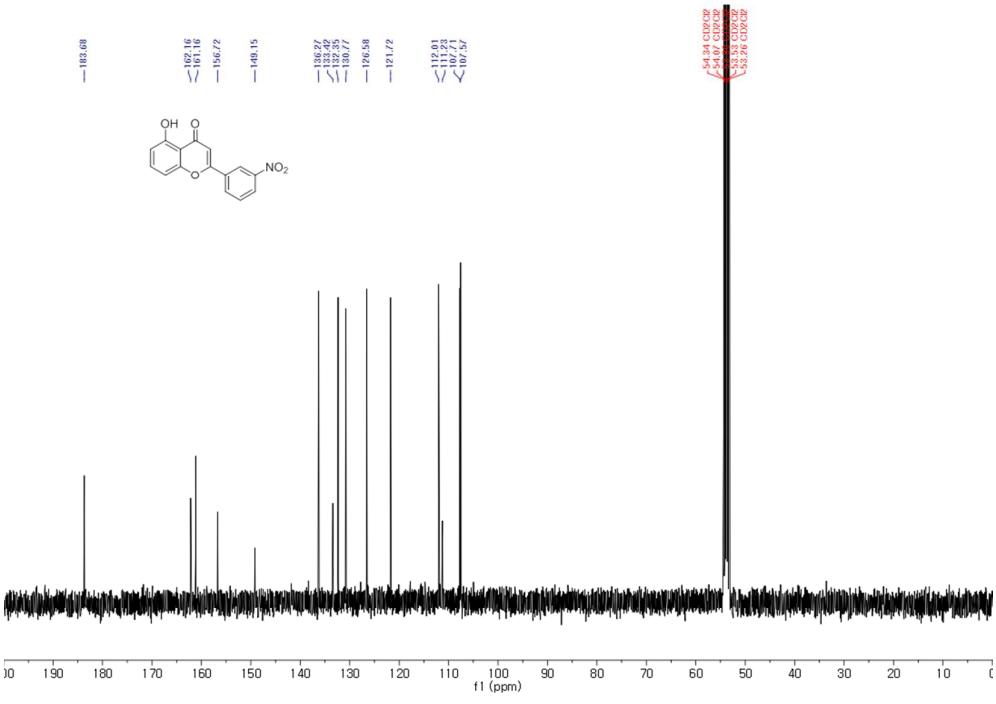


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-2-(3-nitrophenyl)-4H-chromen-4-one (3f)

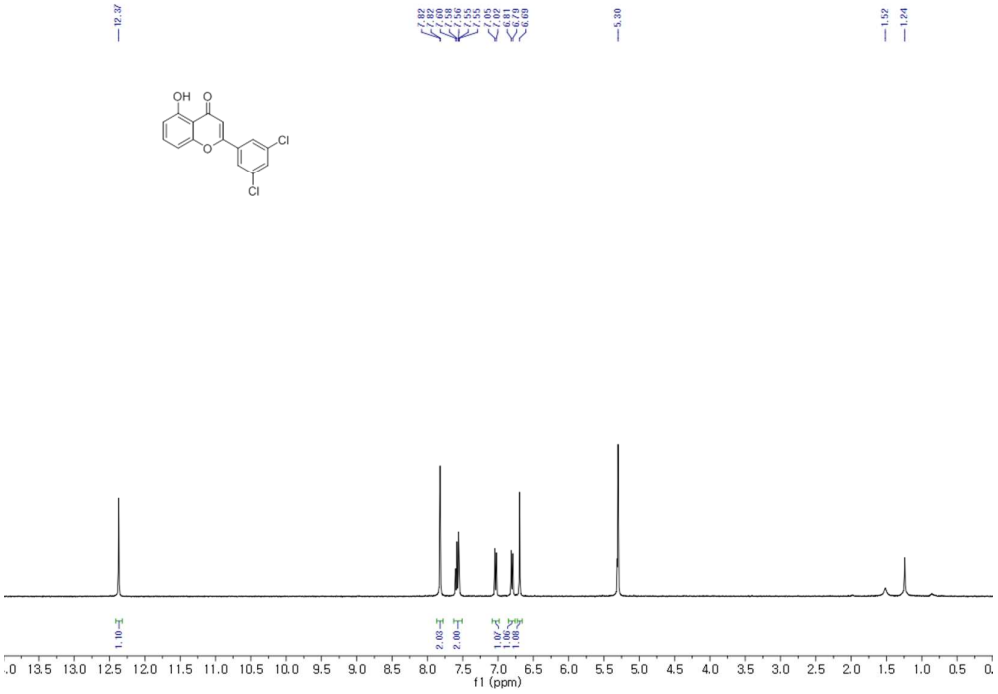


400 MHz, ^{1}H NMR in CD_2Cl_2

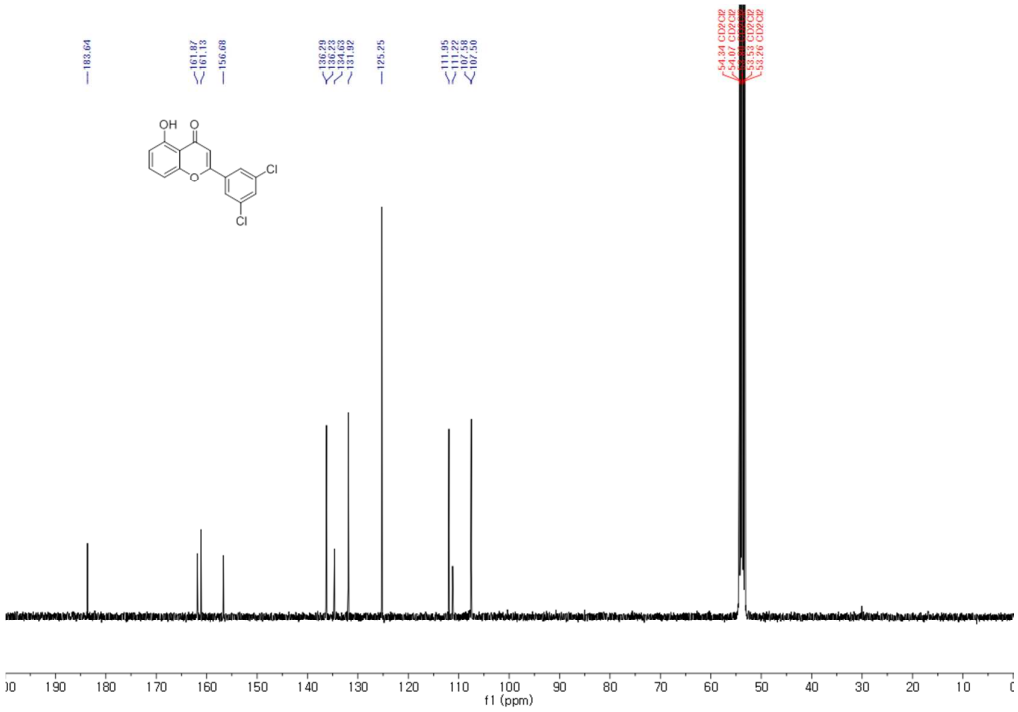


100 MHz, ^{13}C NMR in CD_2Cl_2

2-(3,5-dichlorophenyl)-5-hydroxy-4H-chromen-4-one (3g)

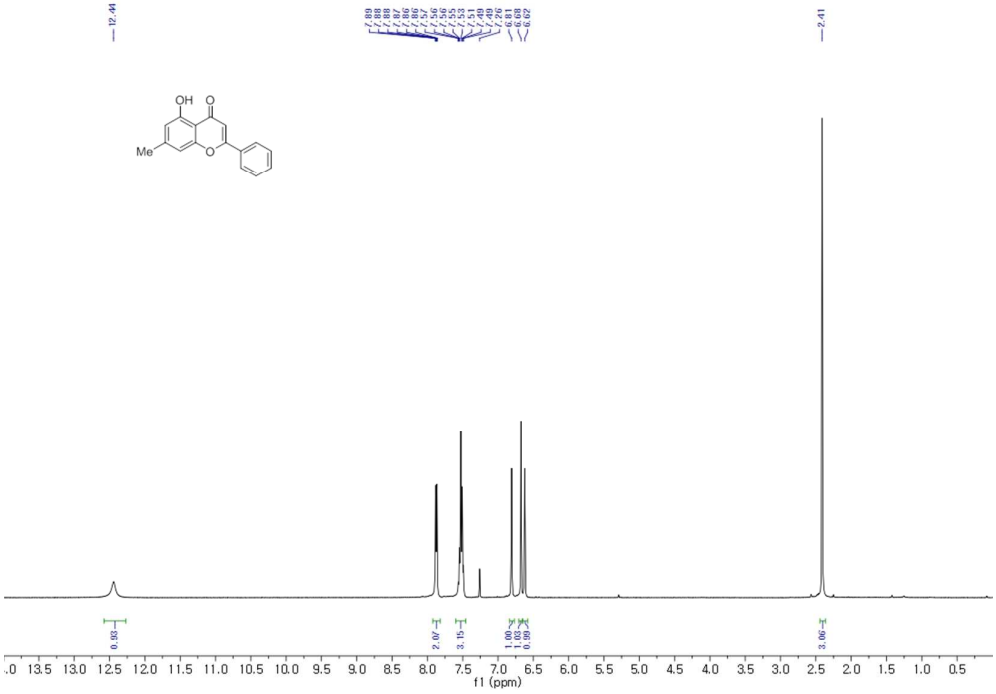


400 MHz, ^{1}H NMR in CD_2Cl_2

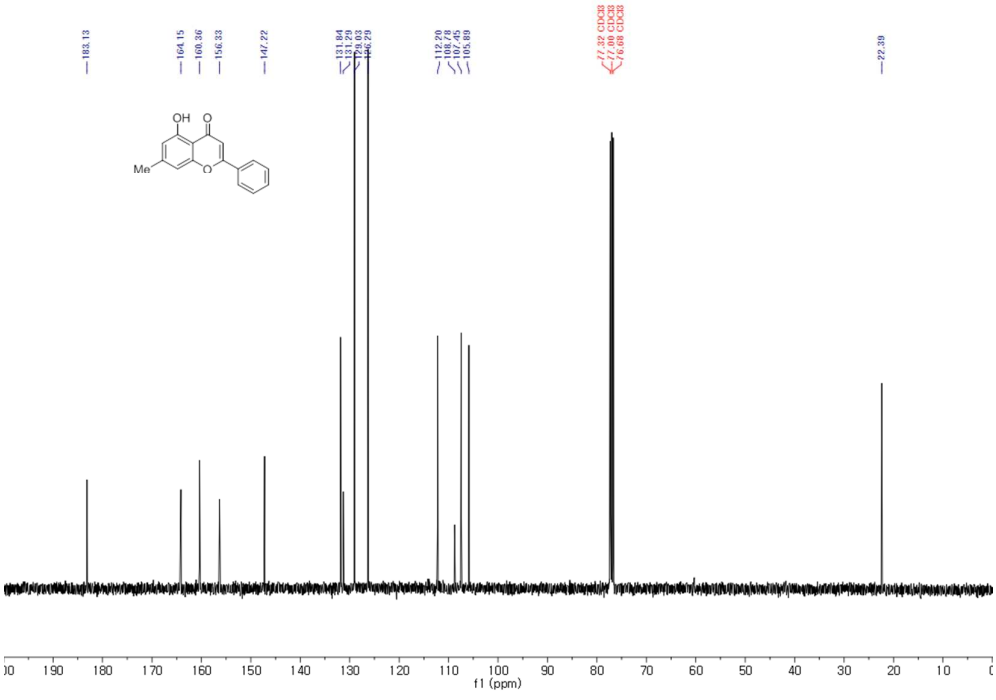


100 MHz, ^{13}C NMR in CD_2Cl_2

5-hydroxy-7-methyl-2-phenyl-4H-chromen-4-one (3h)

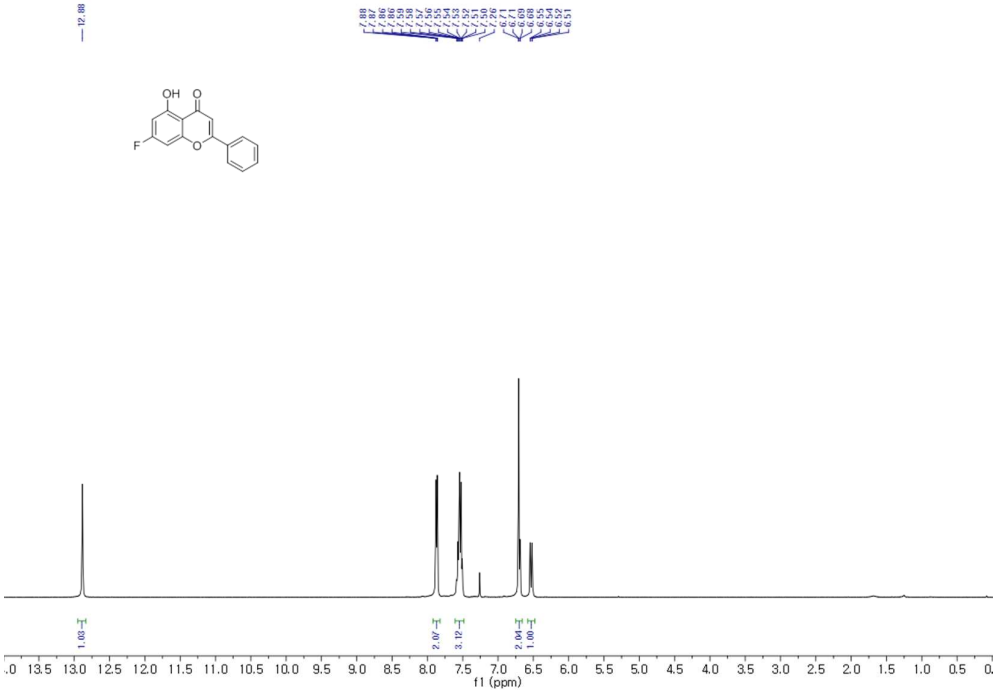


400 MHz, ^{1}H NMR in $CDCl_3$

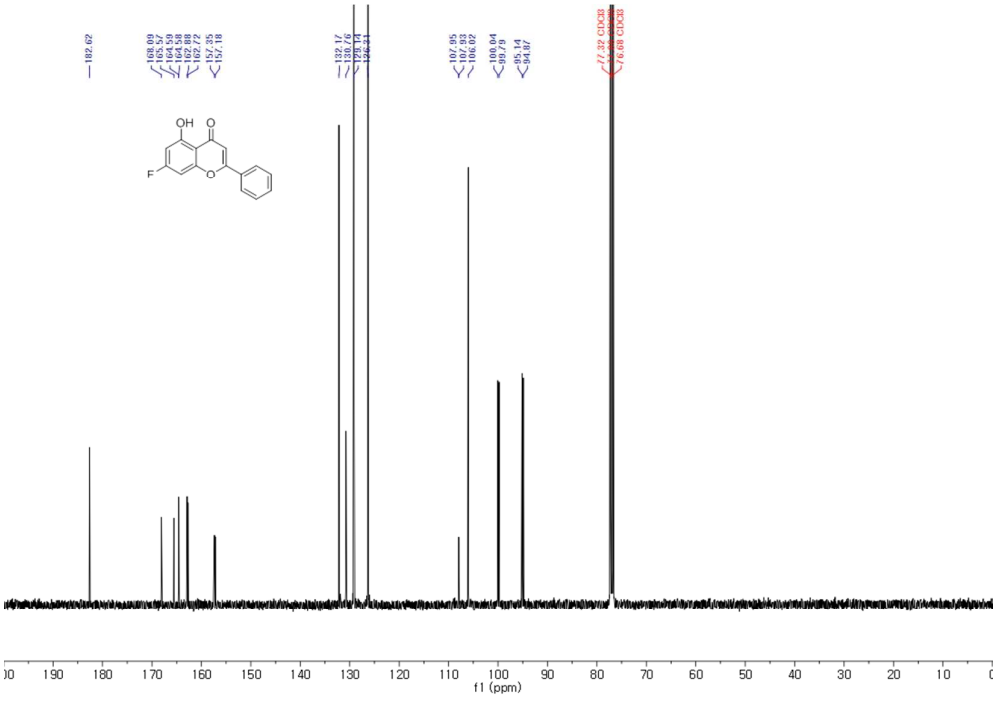


100 MHz, ^{13}C NMR in $CDCl_3$

7-fluoro-5-hydroxy-2-phenyl-4H-chromen-4-one (3i)

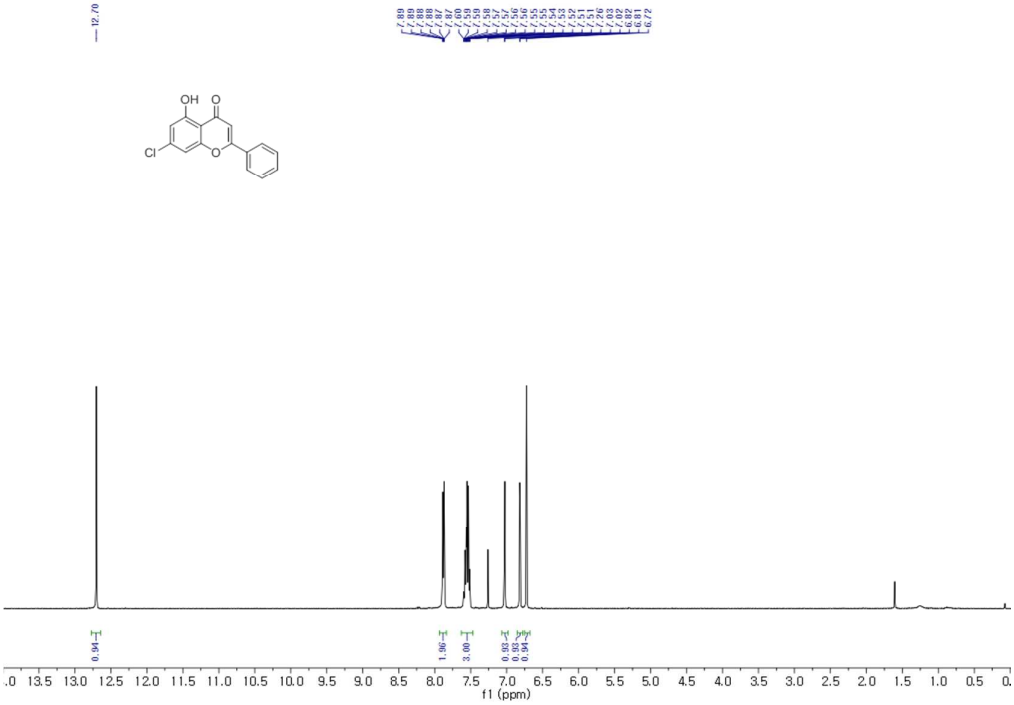


400 MHz, ^{1}H NMR in $CDCl_3$

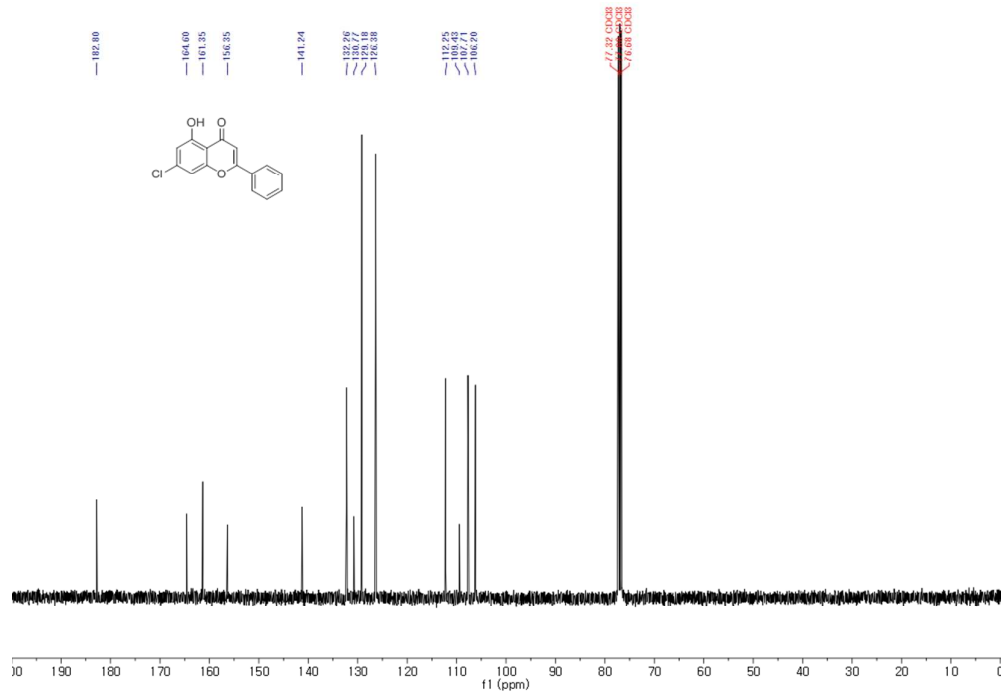


100 MHz, ^{13}C NMR in $CDCl_3$

7-chloro-5-hydroxy-2-phenyl-4H-chromen-4-one (3j)

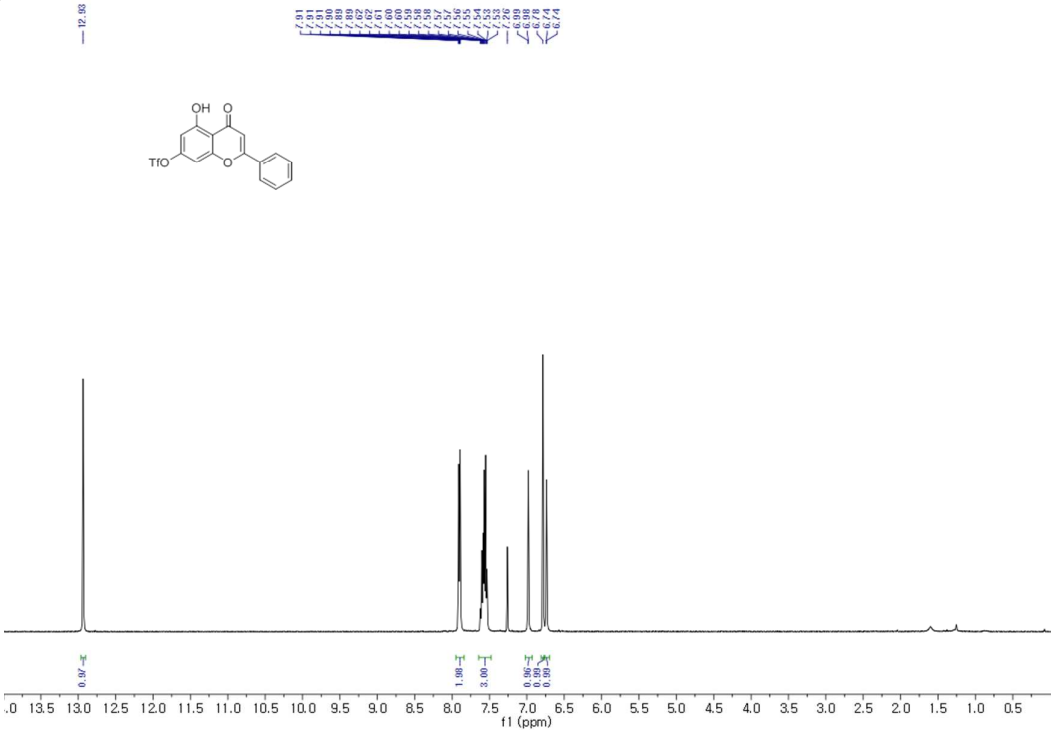


400 MHz, ^{1}H NMR in $CDCl_3$

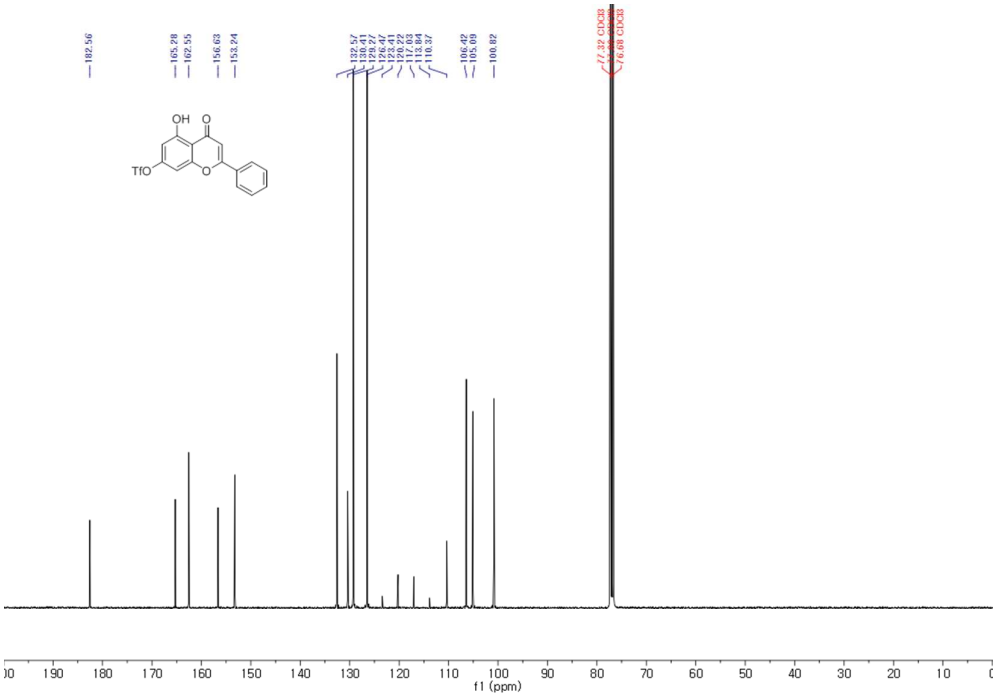


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl trifluoromethanesulfonate (3k)

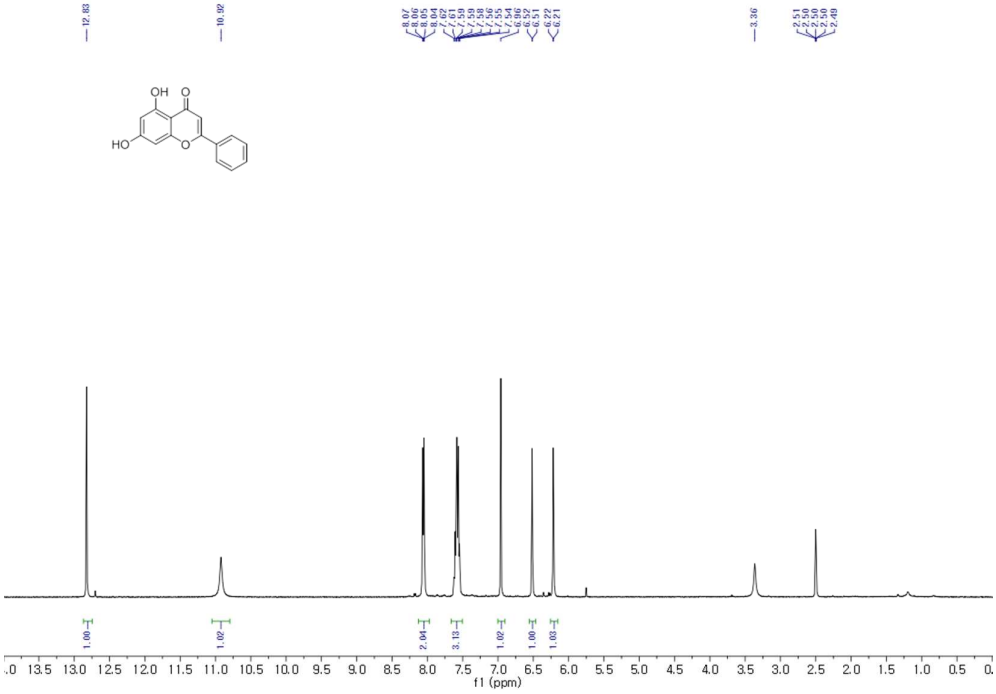


400 MHz, ^{1}H NMR in $CDCl_3$

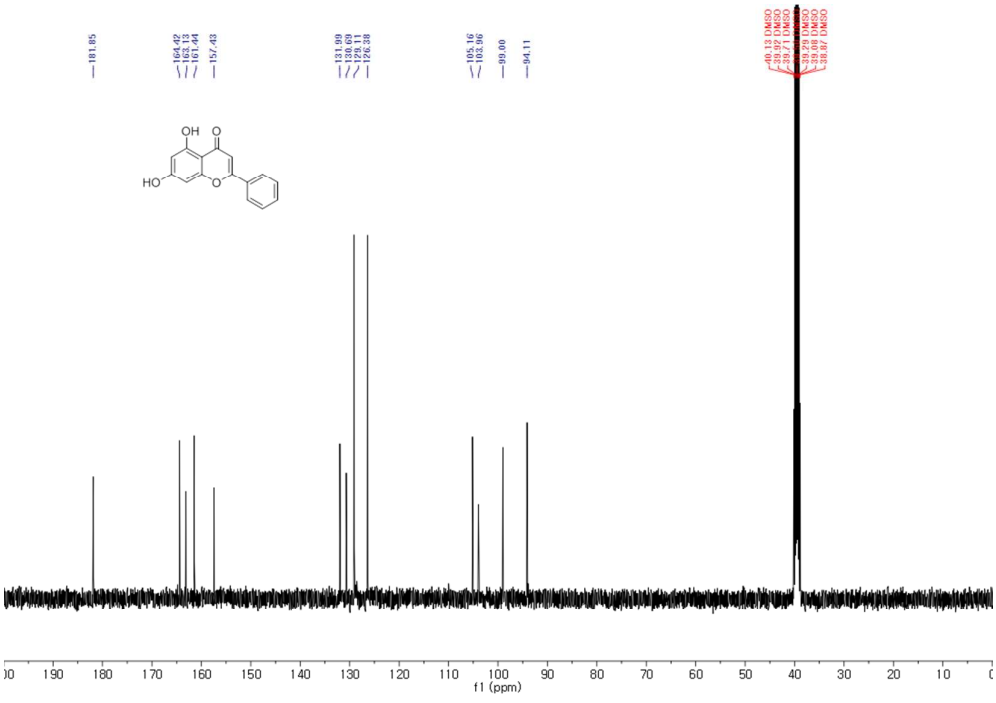


100 MHz, ^{13}C NMR in $CDCl_3$

5,7-dihydroxy-2-phenyl-4H-chromen-4-one (3l)

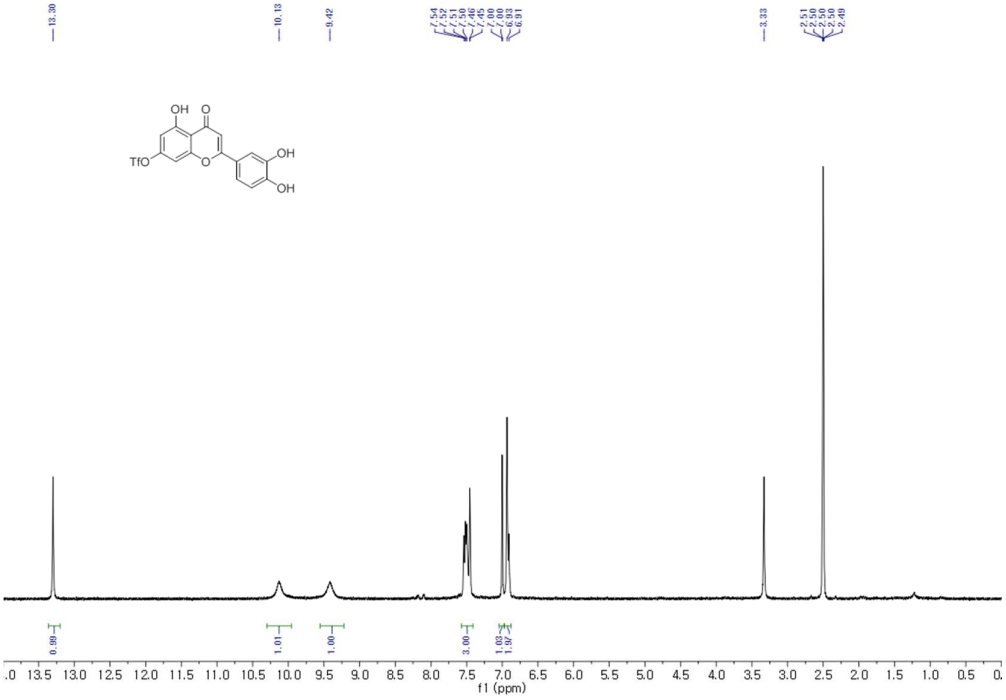


400 MHz, ^{1}H NMR in DMSO-d_6

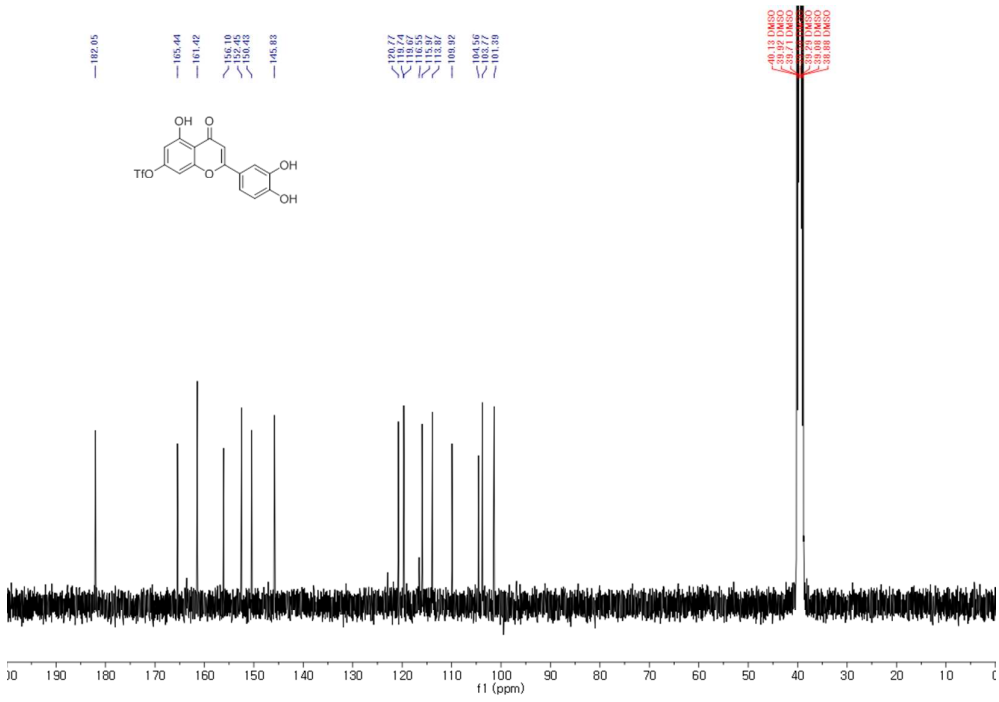


100 MHz, ^{13}C NMR in DMSO-d_6

2-(3,4-dihydroxyphenyl)-5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3m)

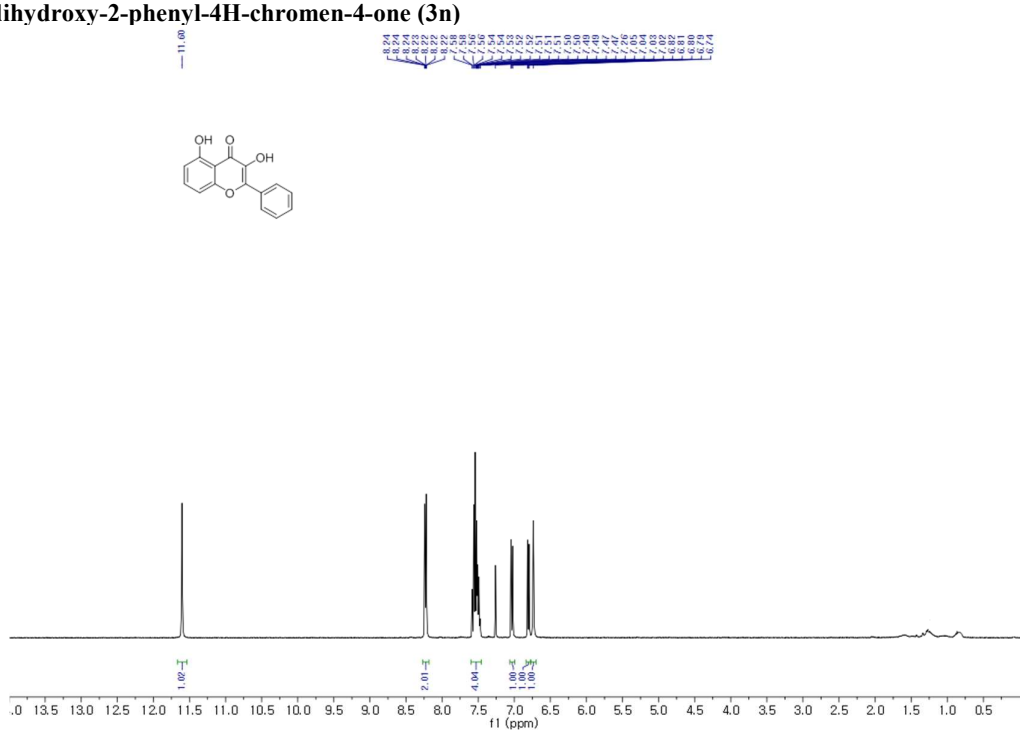


400 MHz, ^{1}H NMR in DMSO-d_6

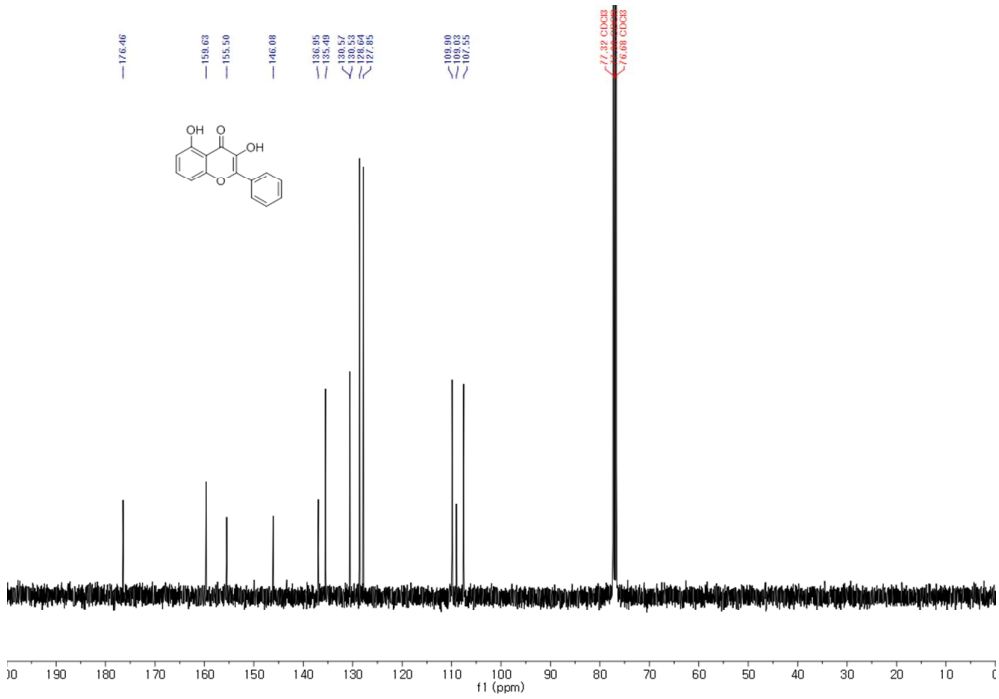


100 MHz, ^{13}C NMR in DMSO-d_6

3,5-dihydroxy-2-phenyl-4H-chromen-4-one (3n)

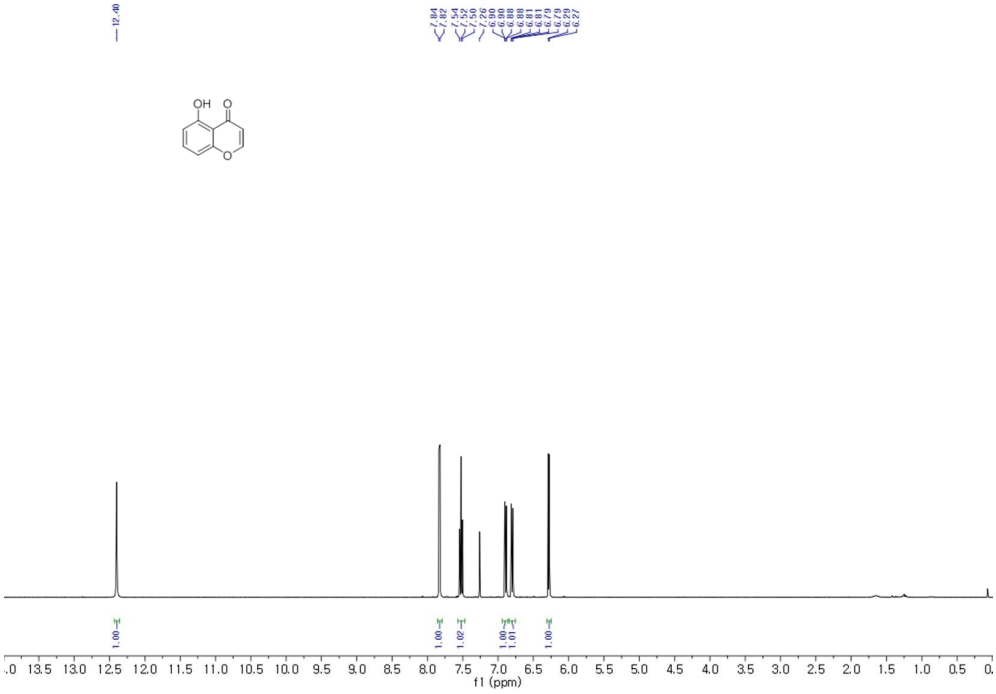


400 MHz, ^{1}H NMR in $CDCl_3$

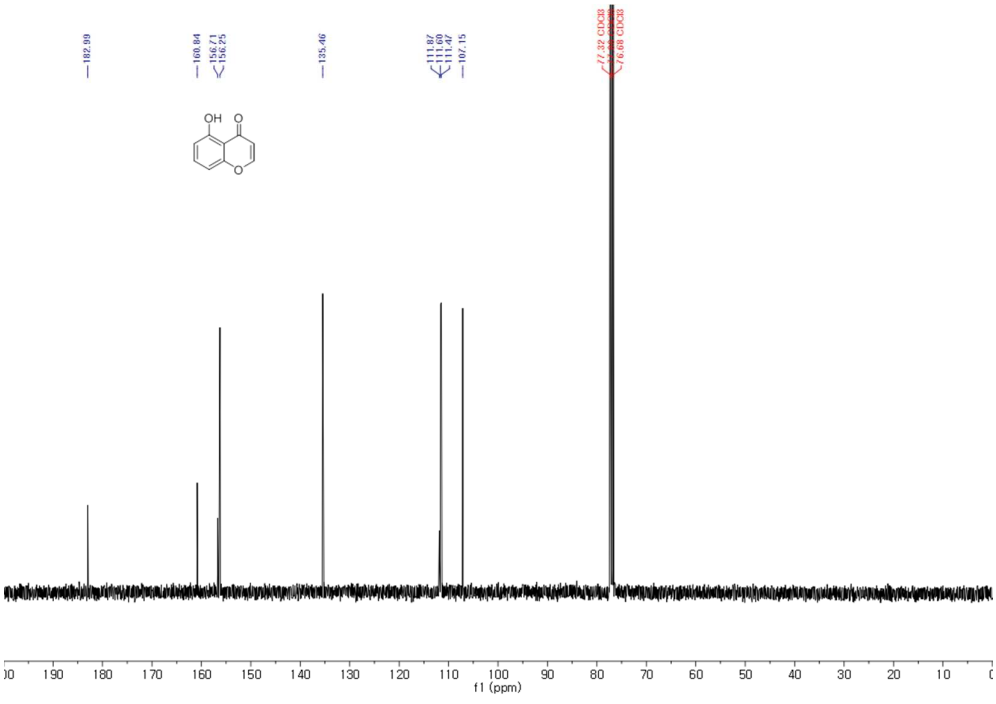


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-4H-chromen-4-one (3o)

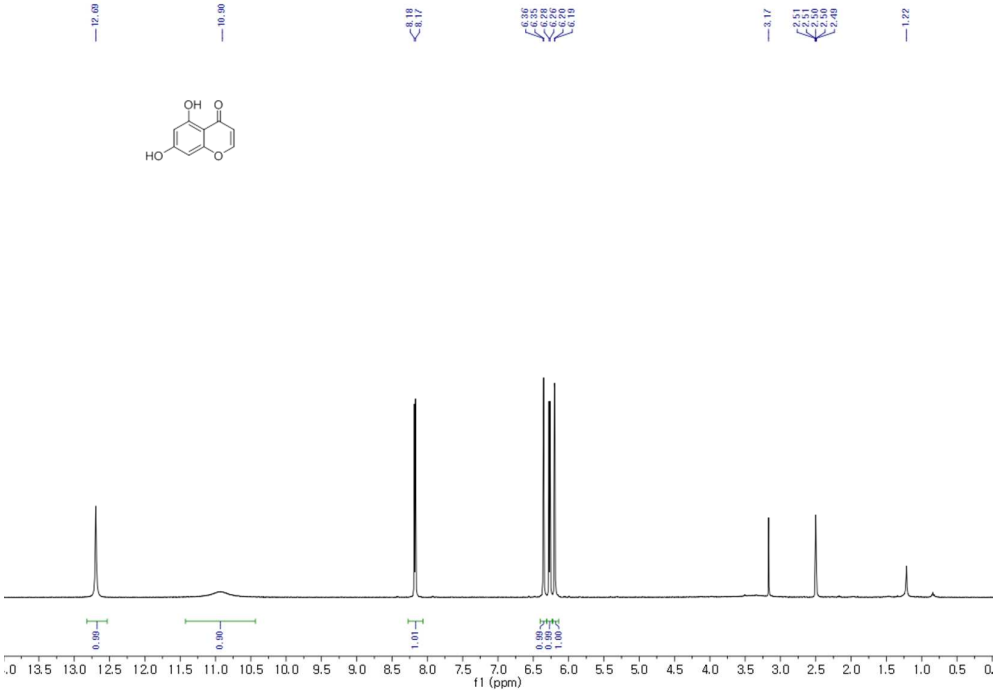


400 MHz, ^{1}H NMR in $CDCl_3$

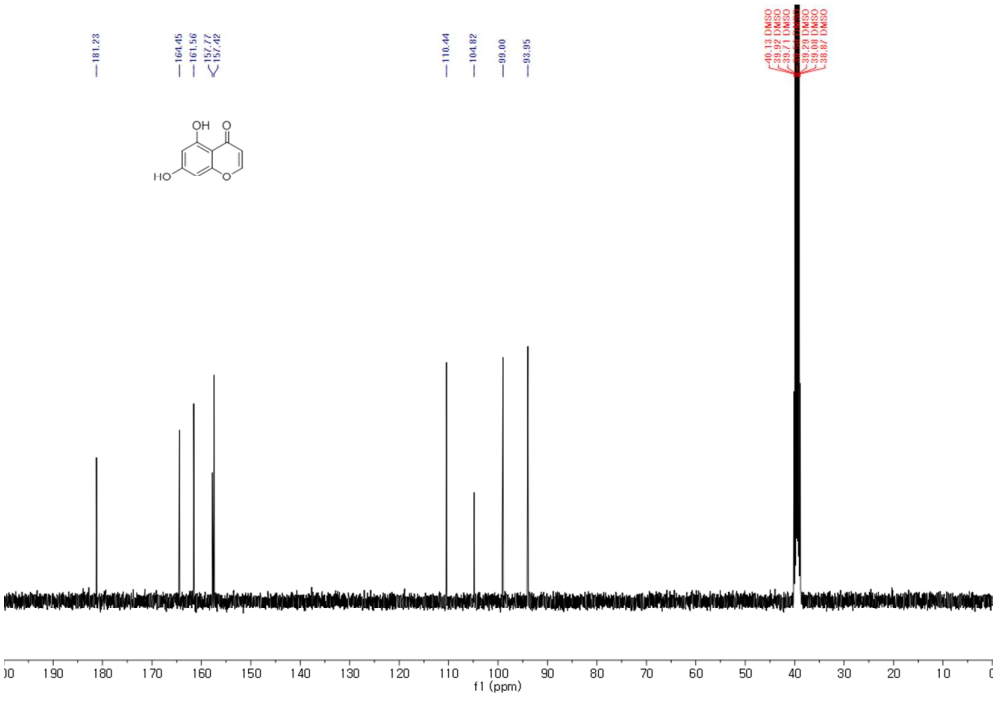


100 MHz, ^{13}C NMR in $CDCl_3$

5,7-dihydroxy-4H-chromen-4-one (3p)

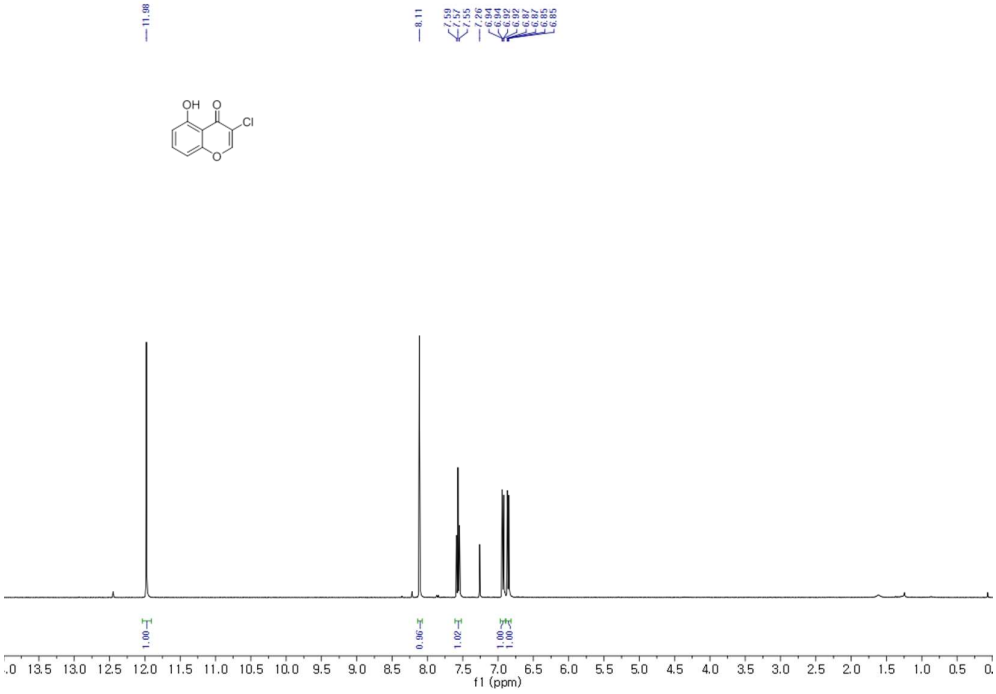


400 MHz, ^{1}H NMR in DMSO-d_6

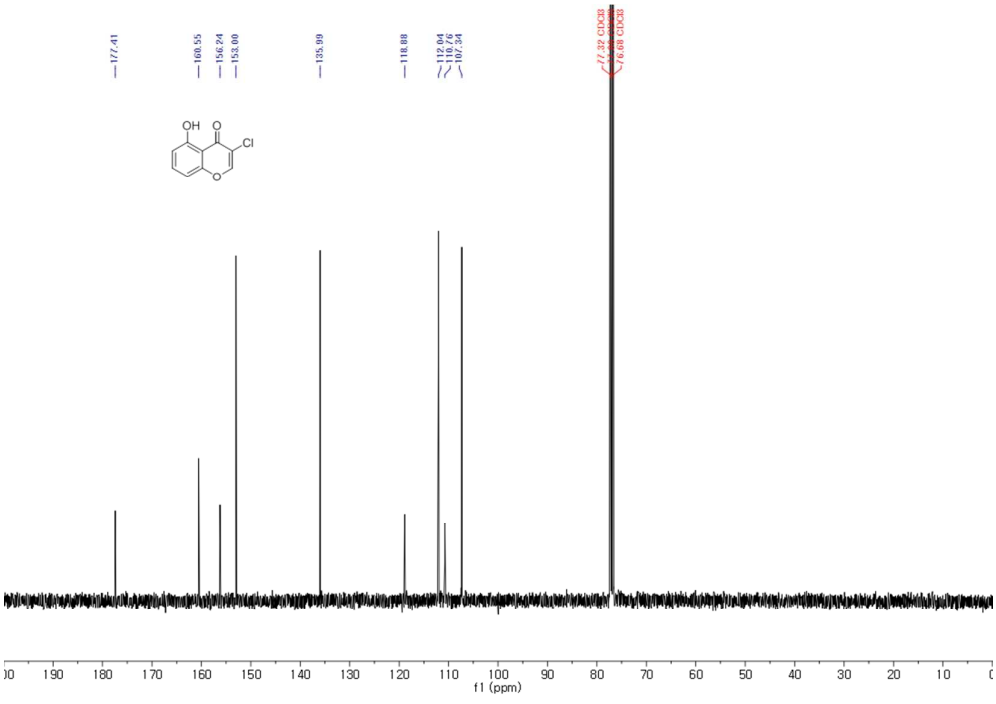


100 MHz, ^{13}C NMR in DMSO-d_6

3-chloro-5-hydroxy-4H-chromen-4-one (3q)

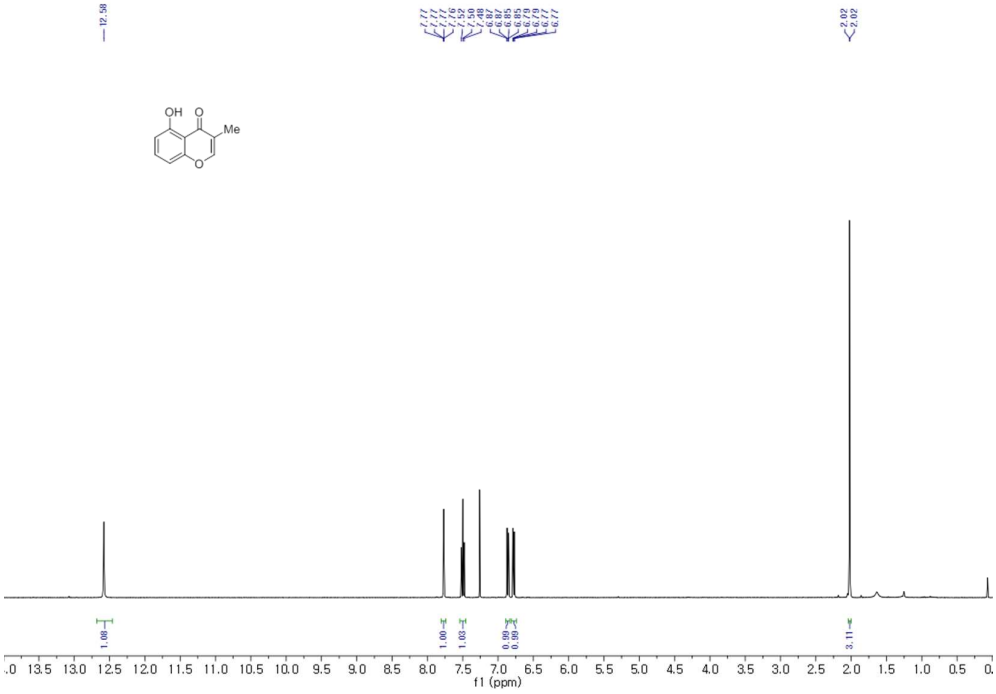


400 MHz, ^{1}H NMR in $CDCl_3$

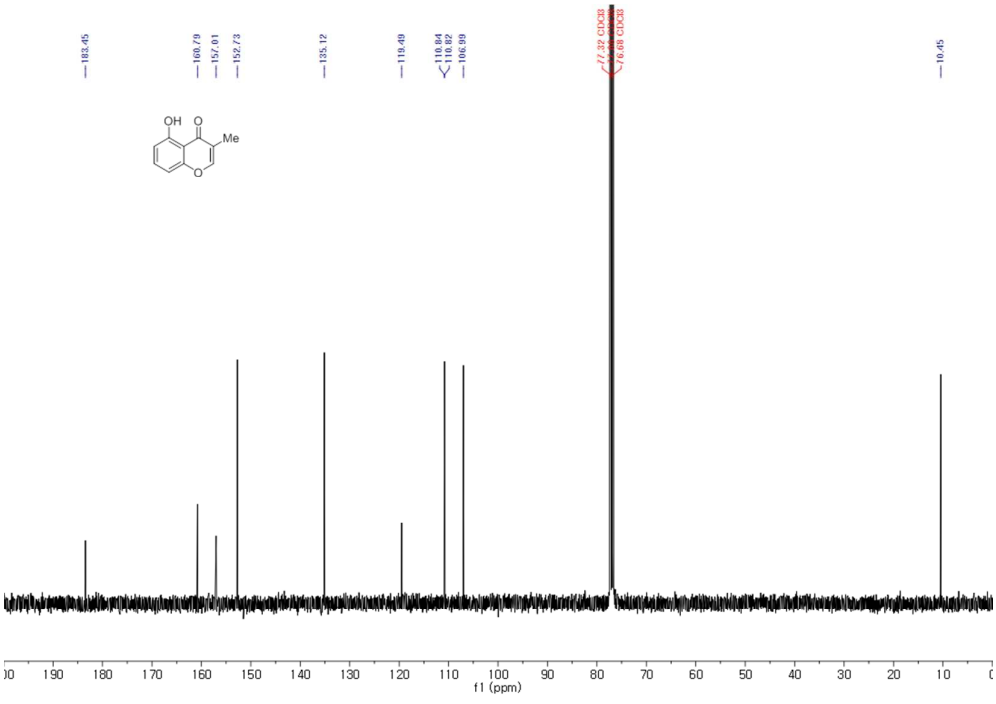


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-3-methyl-4H-chromen-4-one (3r)

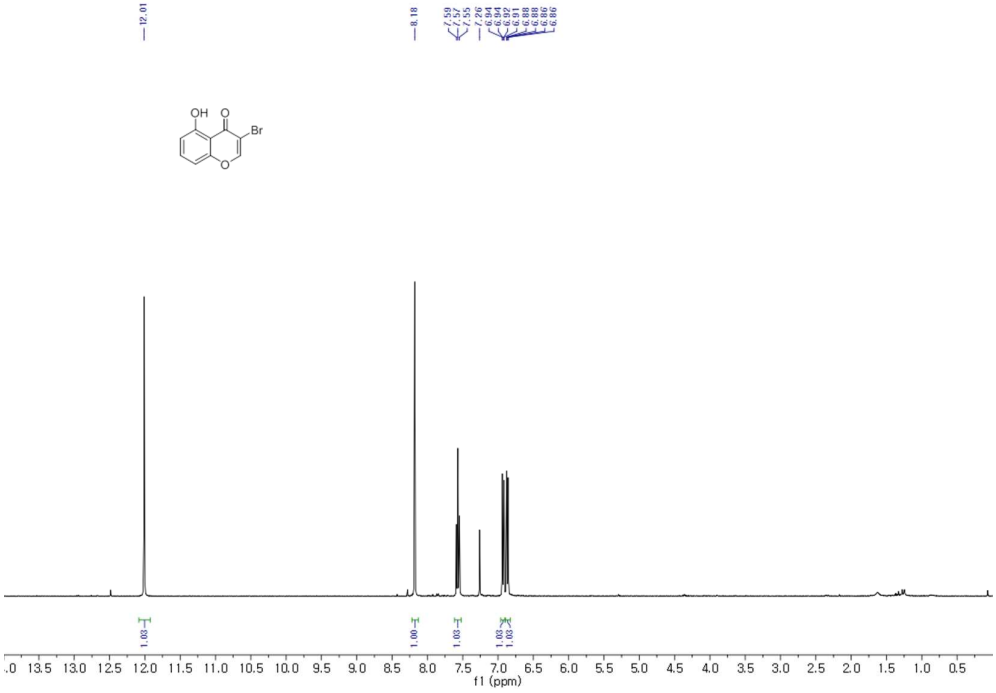


400 MHz, ^{1}H NMR in $CDCl_3$

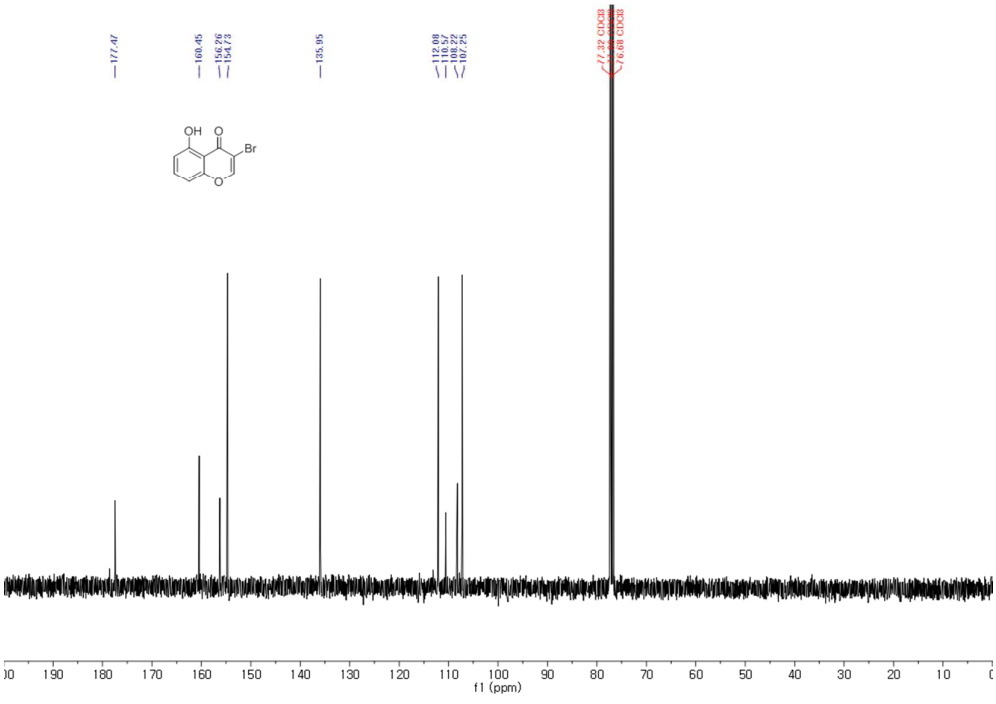


100 MHz, ^{13}C NMR in $CDCl_3$

3-bromo-5-hydroxy-4H-chromen-4-one (3s)

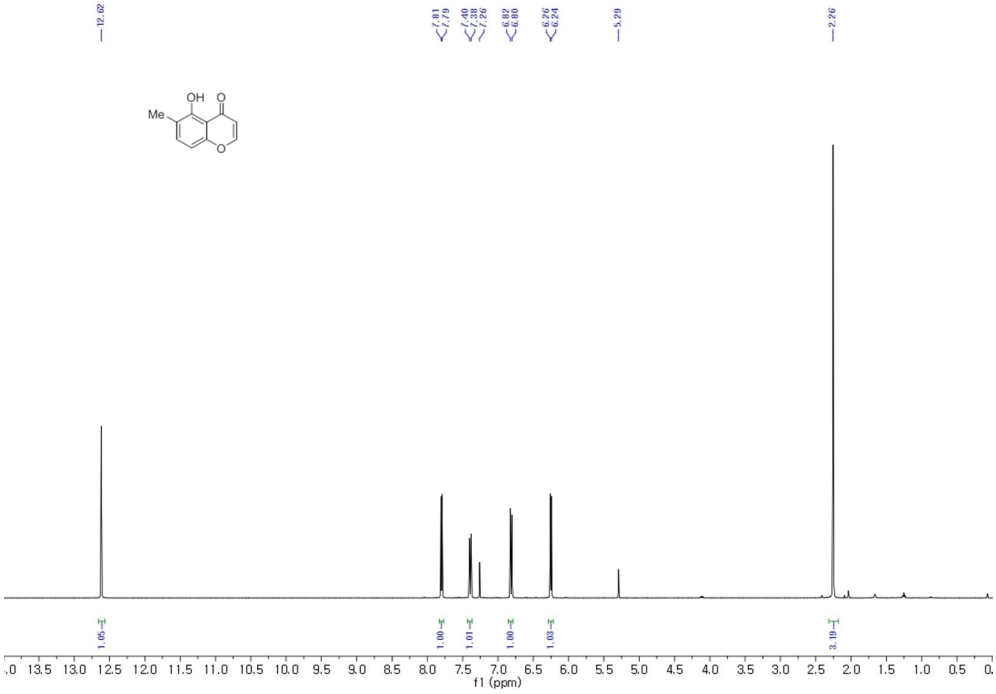


400 MHz, ^{1}H NMR in $CDCl_3$

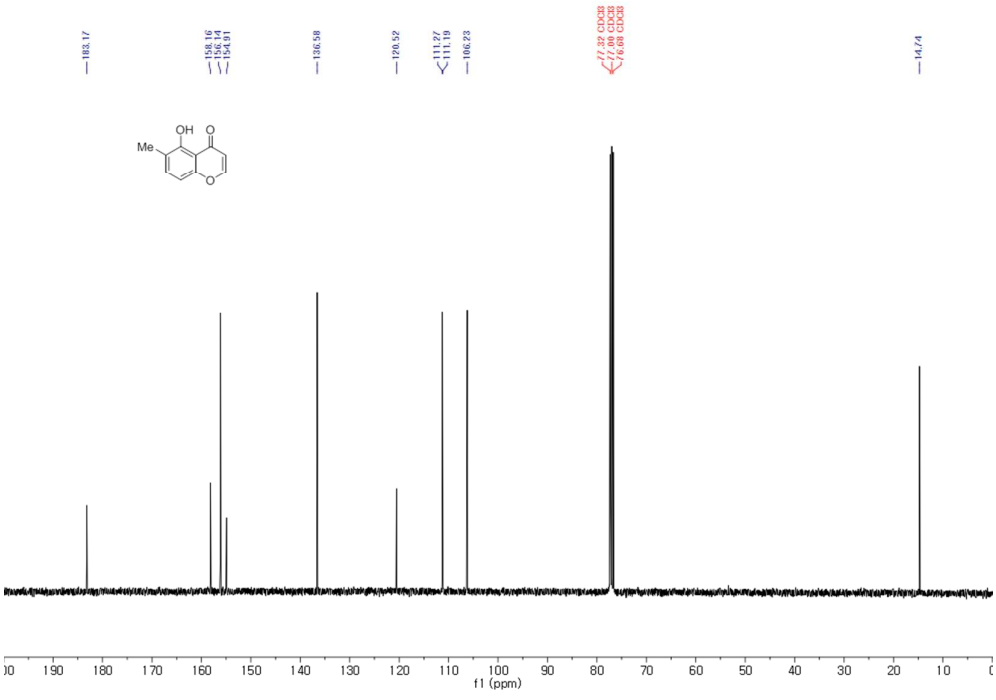


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-6-methyl-4H-chromen-4-one (3t)

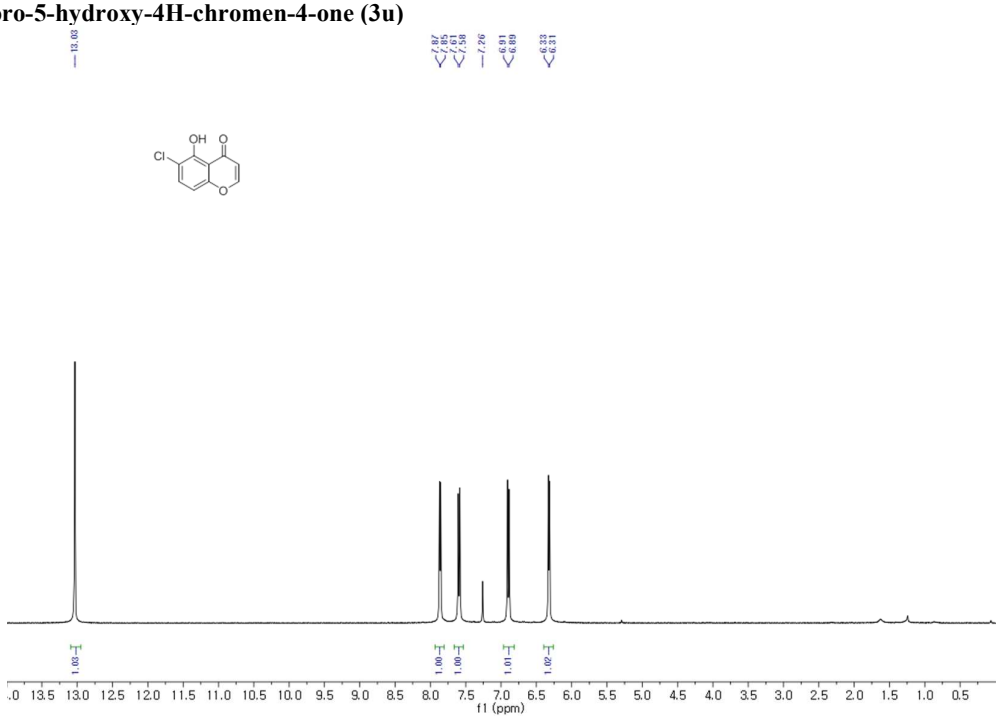


400 MHz, ^{1}H NMR in $CDCl_3$

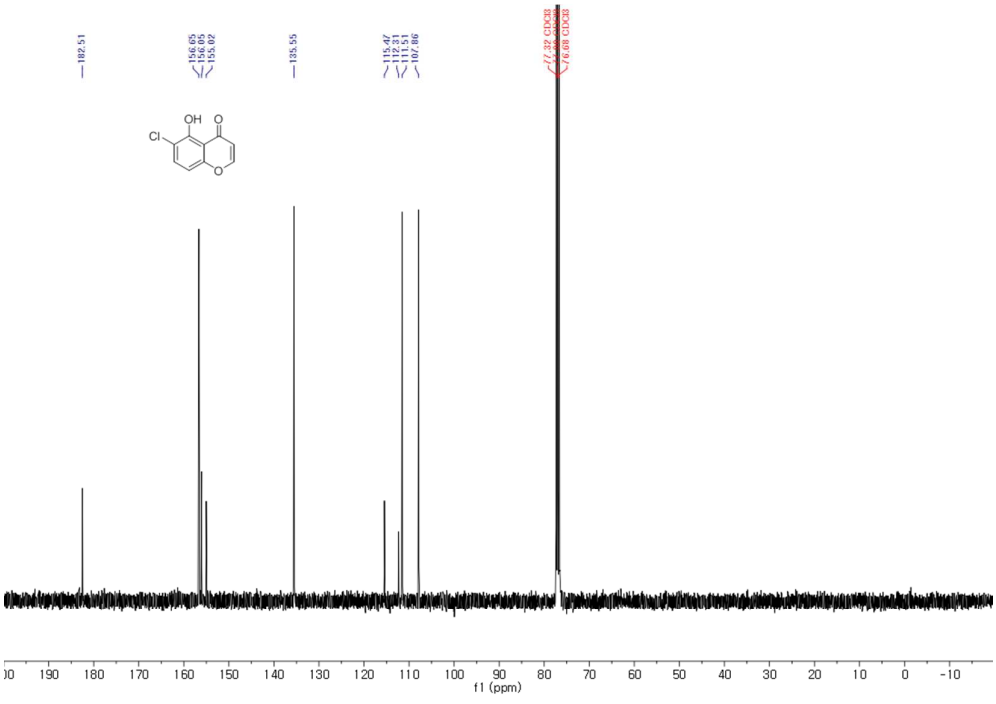


100 MHz, ^{13}C NMR in $CDCl_3$

6-chloro-5-hydroxy-4H-chromen-4-one (3u)

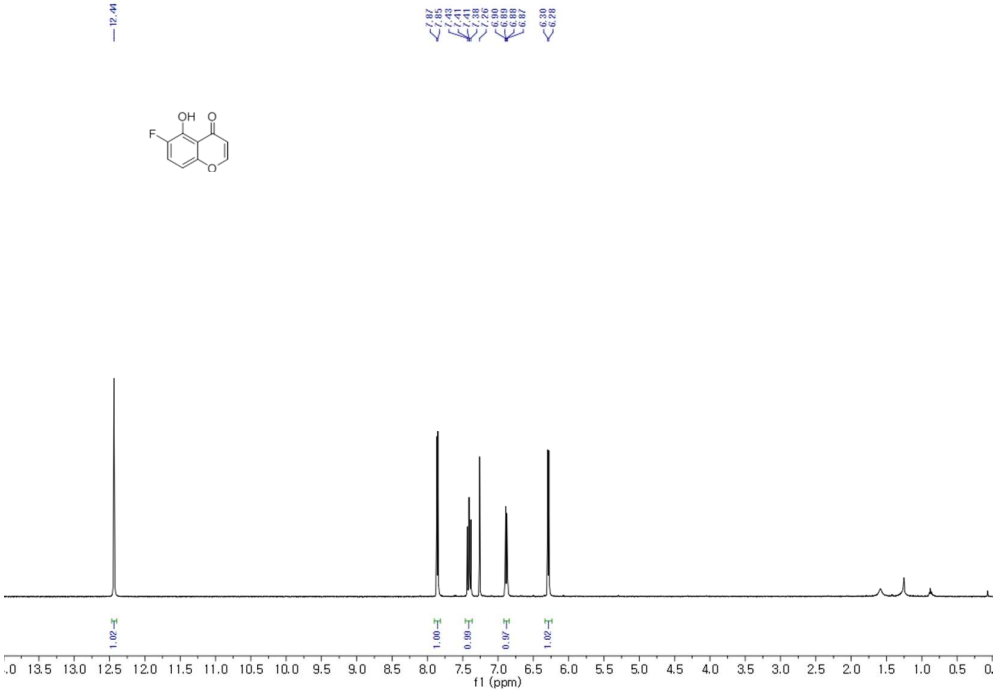


400 MHz, ^{1}H NMR in $CDCl_3$

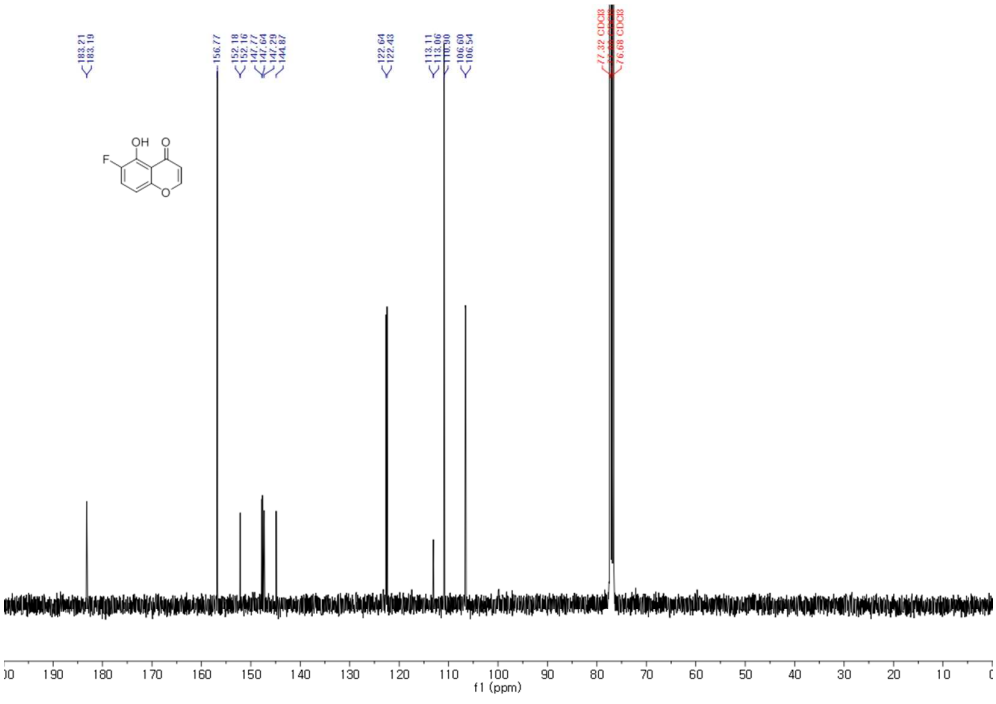


100 MHz, ^{13}C NMR in $CDCl_3$

6-fluoro-5-hydroxy-4H-chromen-4-one (3v)

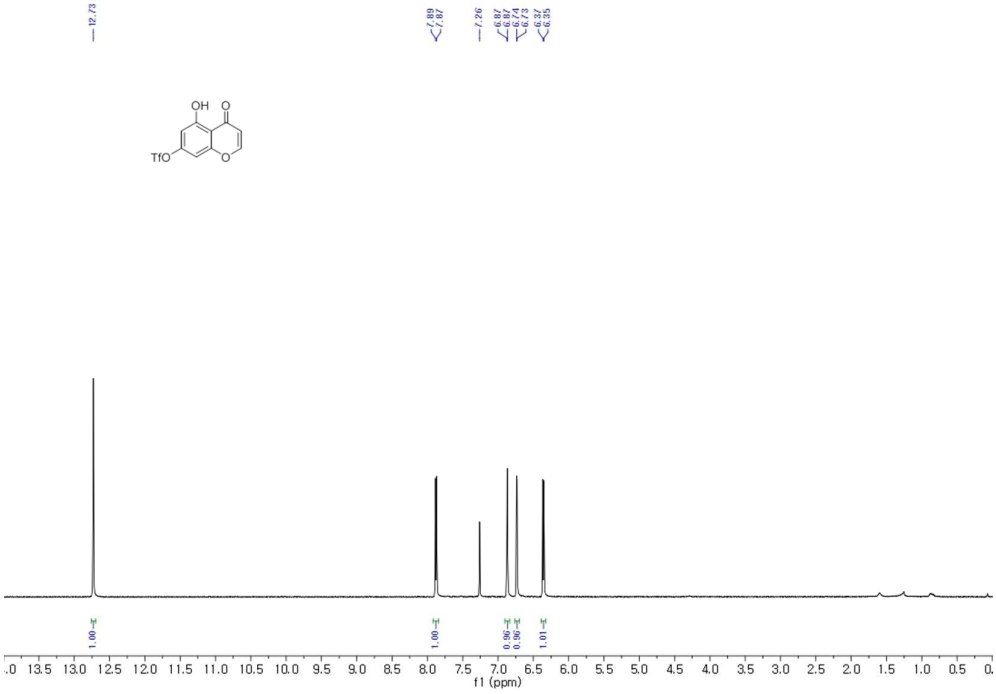


400 MHz, ^{1}H NMR in $CDCl_3$

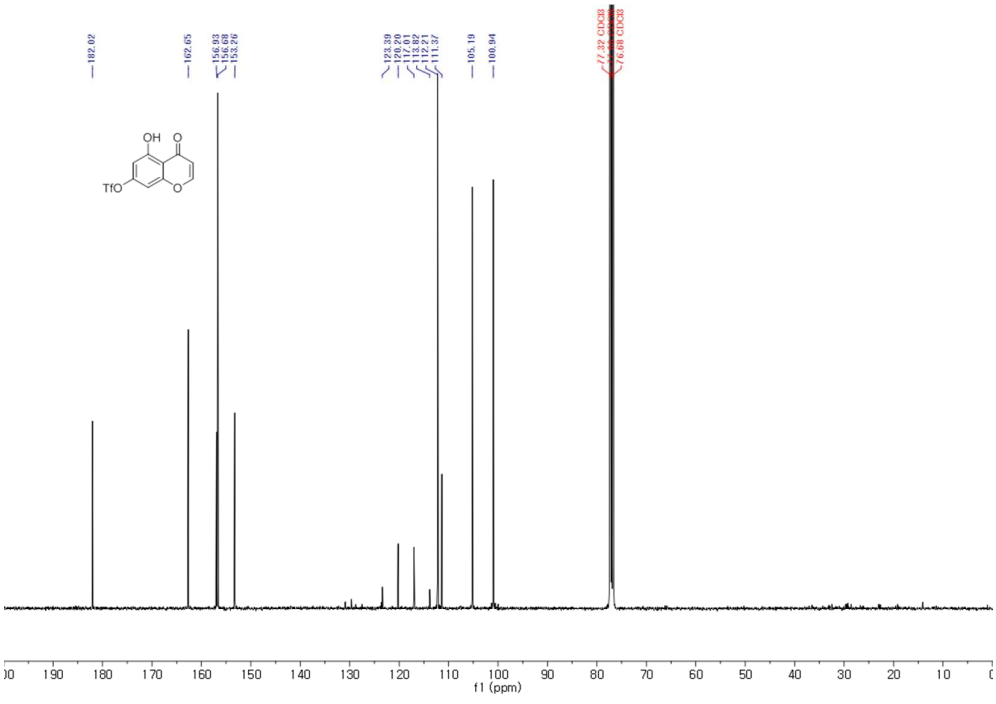


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3w)

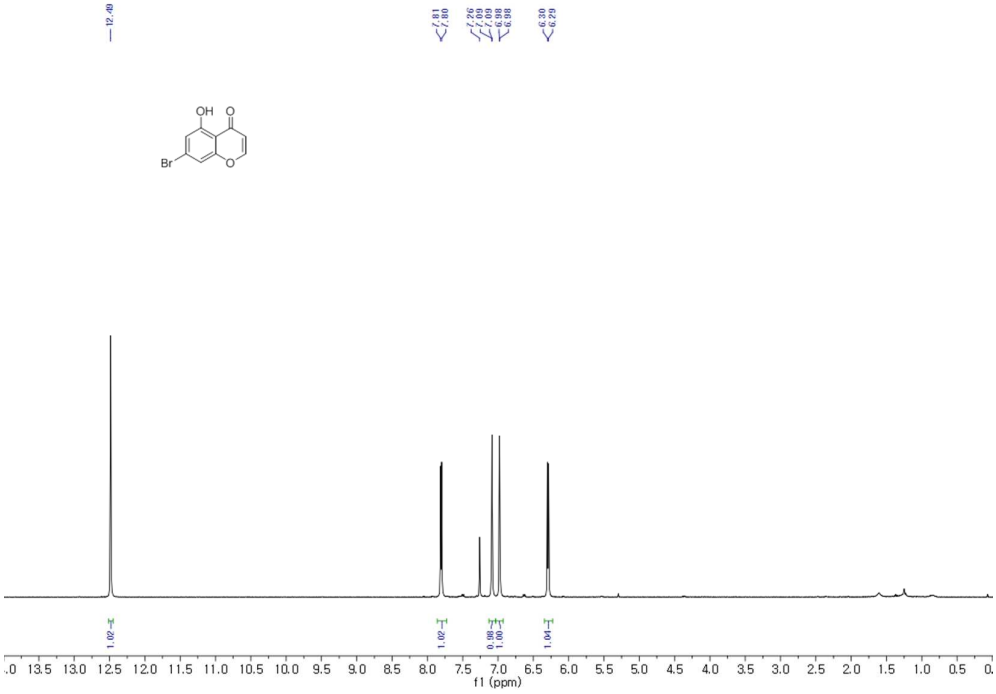


400 MHz, ^{1}H NMR in $CDCl_3$

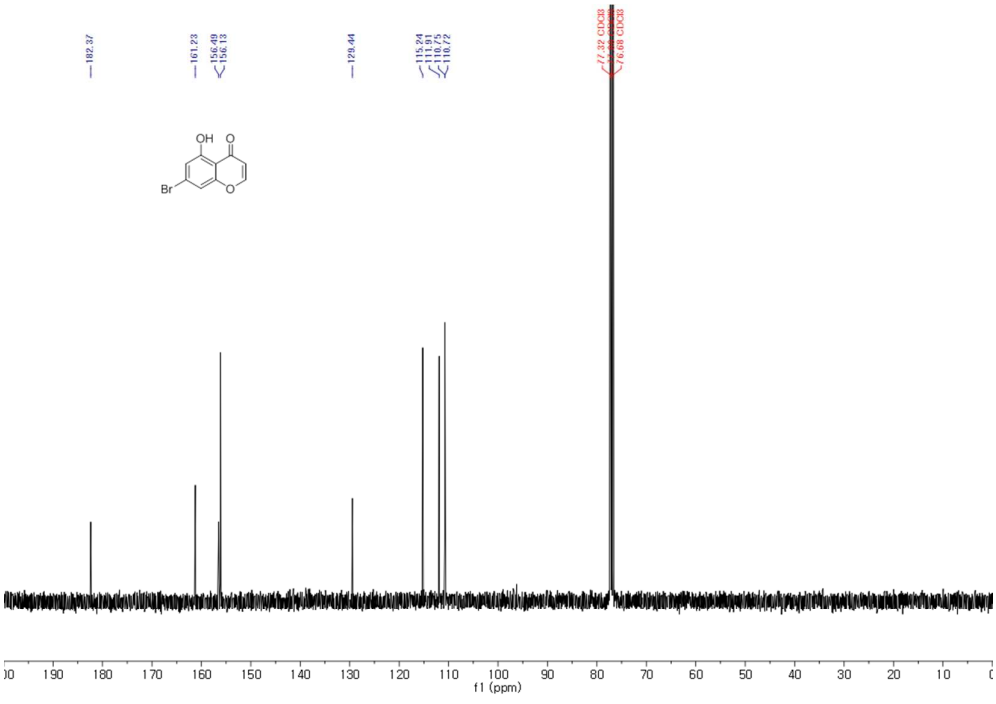


100 MHz, ^{13}C NMR in $CDCl_3$

7-bromo-5-hydroxy-4H-chromen-4-one (3x)

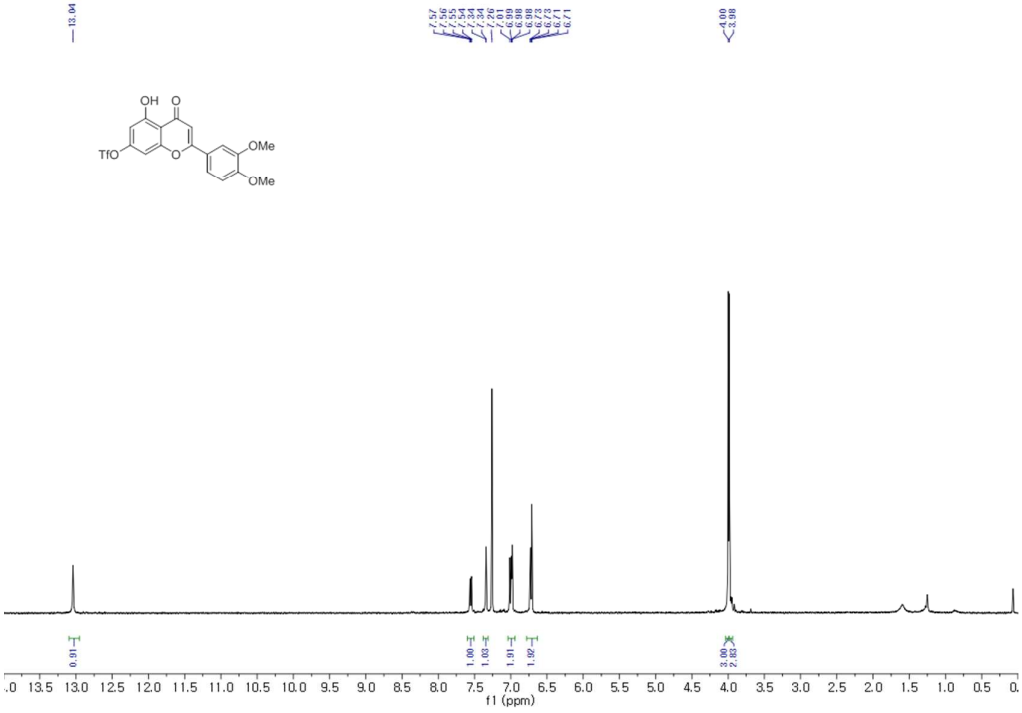


400 MHz, ^{1}H NMR in $CDCl_3$

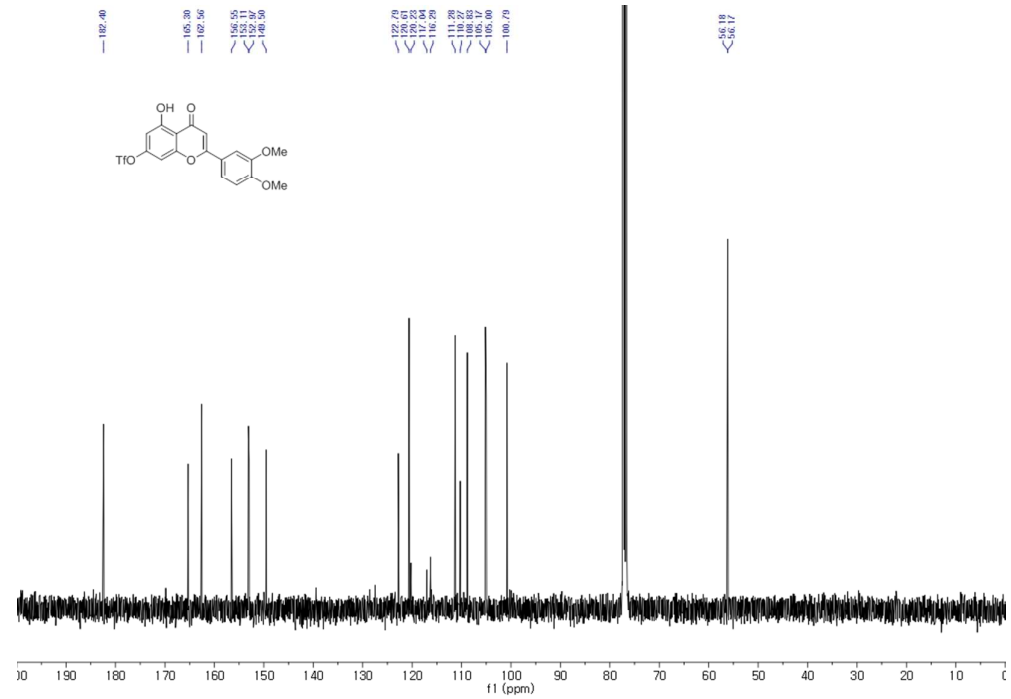


100 MHz, ^{13}C NMR in $CDCl_3$

2-(3,4-dimethoxyphenyl)-5-hydroxy-4-oxo-4H-chromen-7-yl trifluoromethanesulfonate (3y)

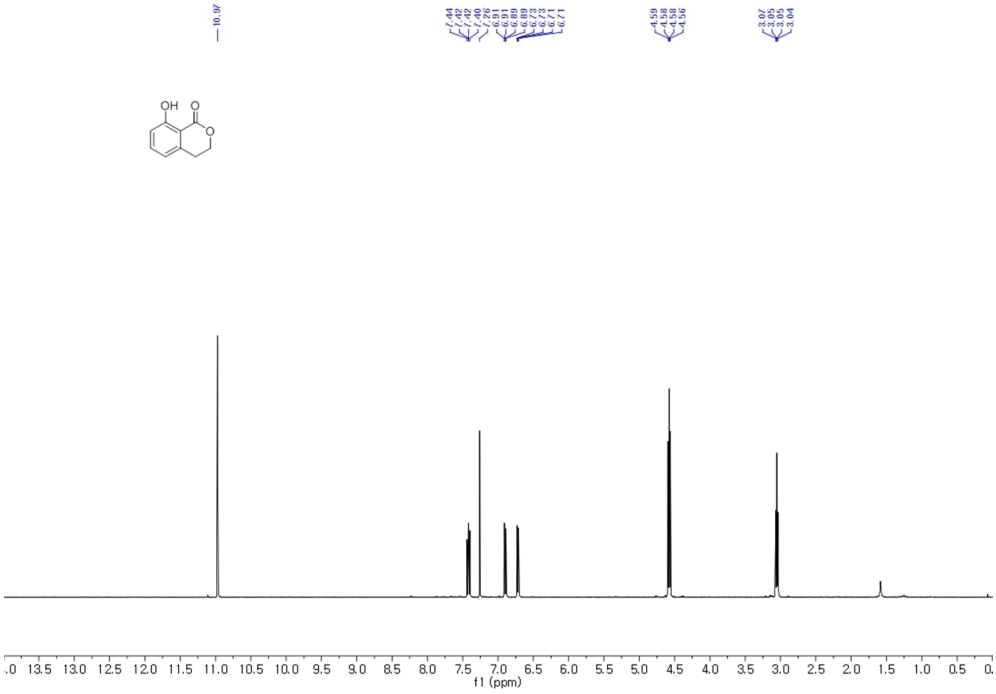


400 MHz, ^{1}H NMR in $CDCl_3$

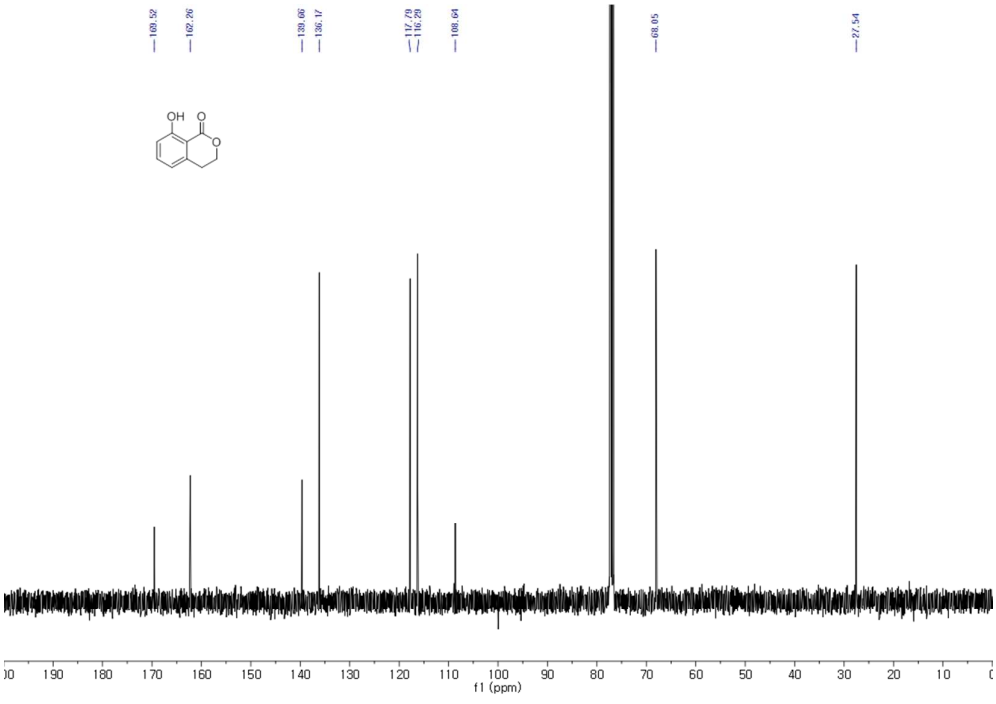


100 MHz, ^{13}C NMR in $CDCl_3$

8-hydroxyisochroman-1-one (3z)

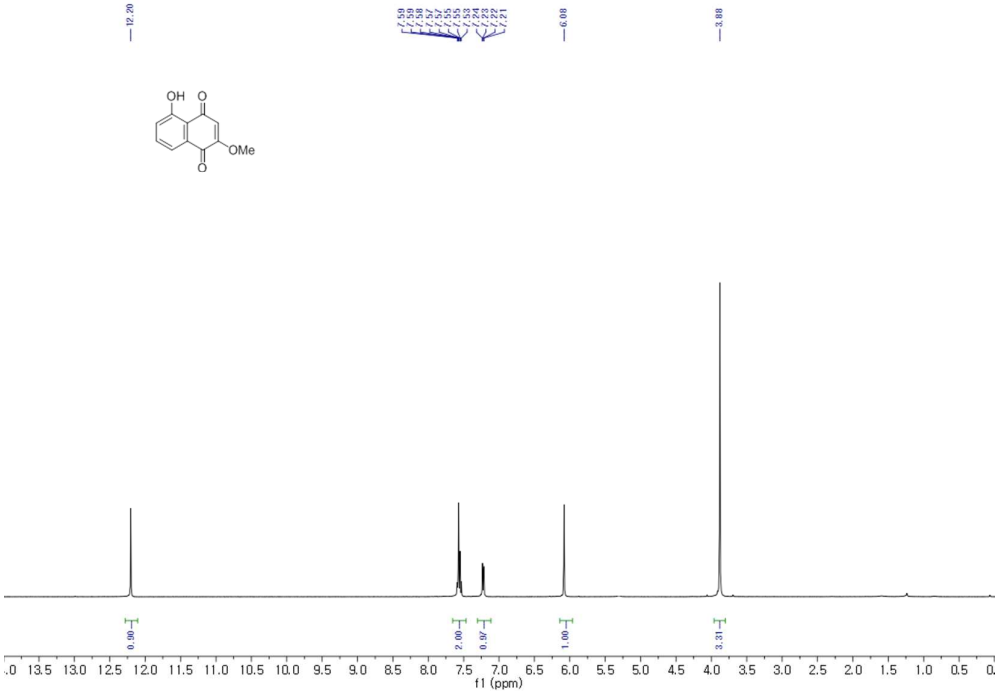


400 MHz, ^{1}H NMR in $CDCl_3$

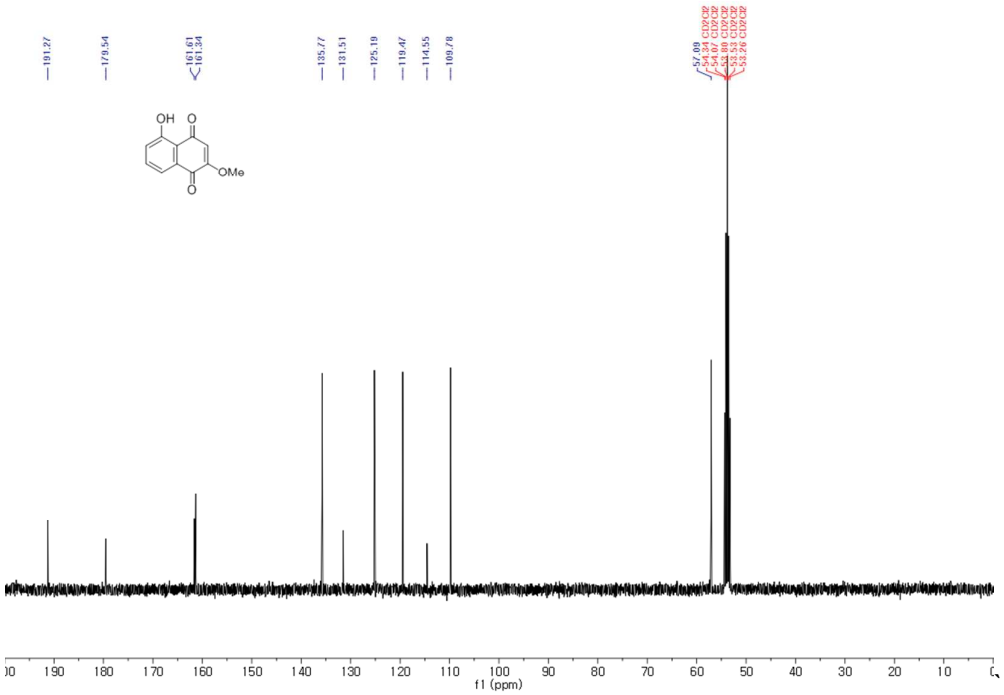


100 MHz, ^{13}C NMR in $CDCl_3$

5-hydroxy-2-methoxynaphthalene-1,4-dione (7)

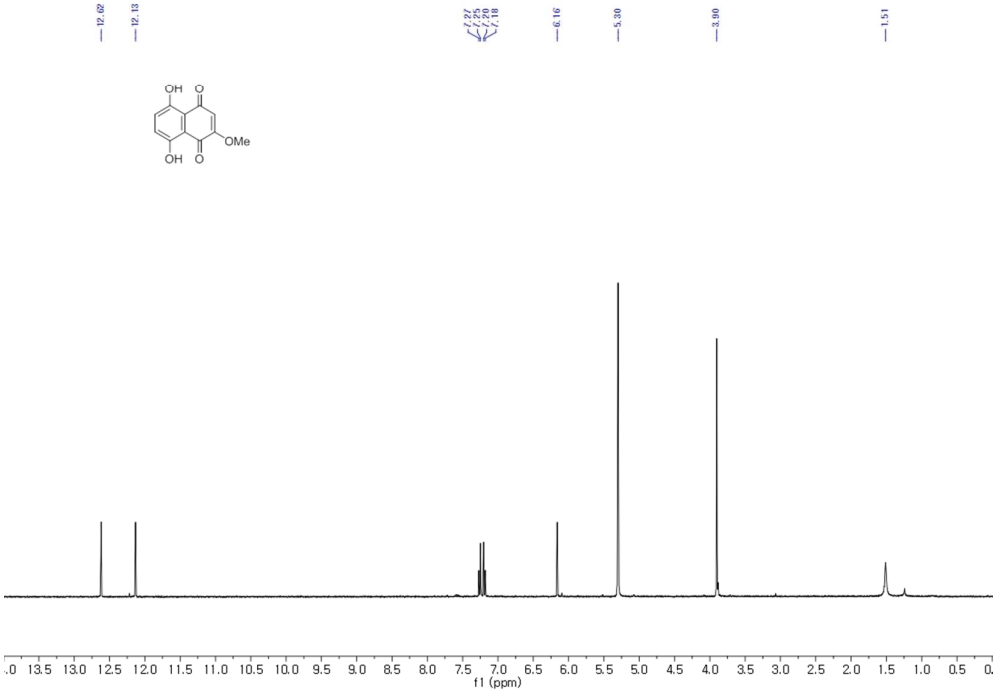


400 MHz, ^{1}H NMR in CD_2Cl_2

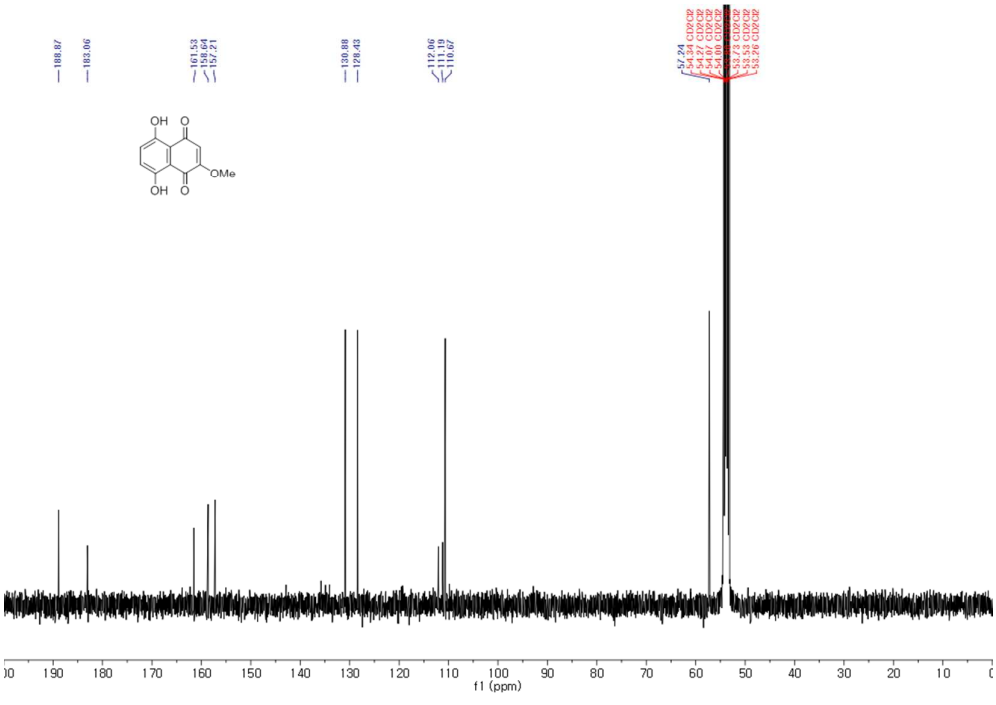


100 MHz, ^{13}C NMR in CD_2Cl_2

5,8-dihydroxy-2-methoxynaphthalene-1,4-dione (7')

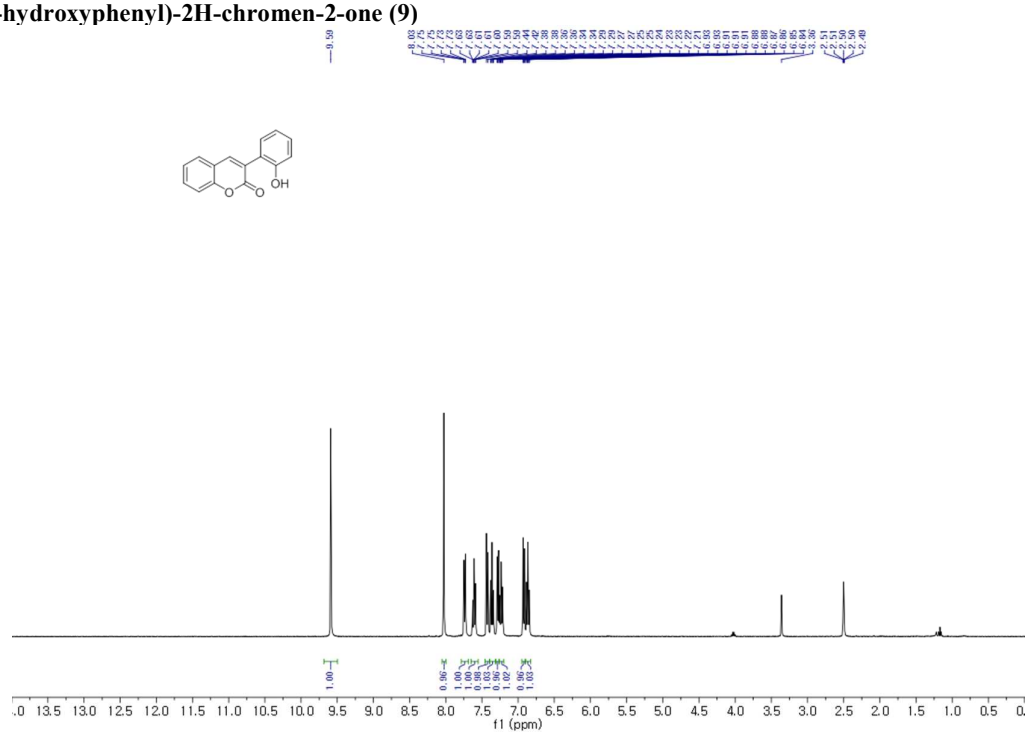


400 MHz, ^{1}H NMR in CD_2Cl_2

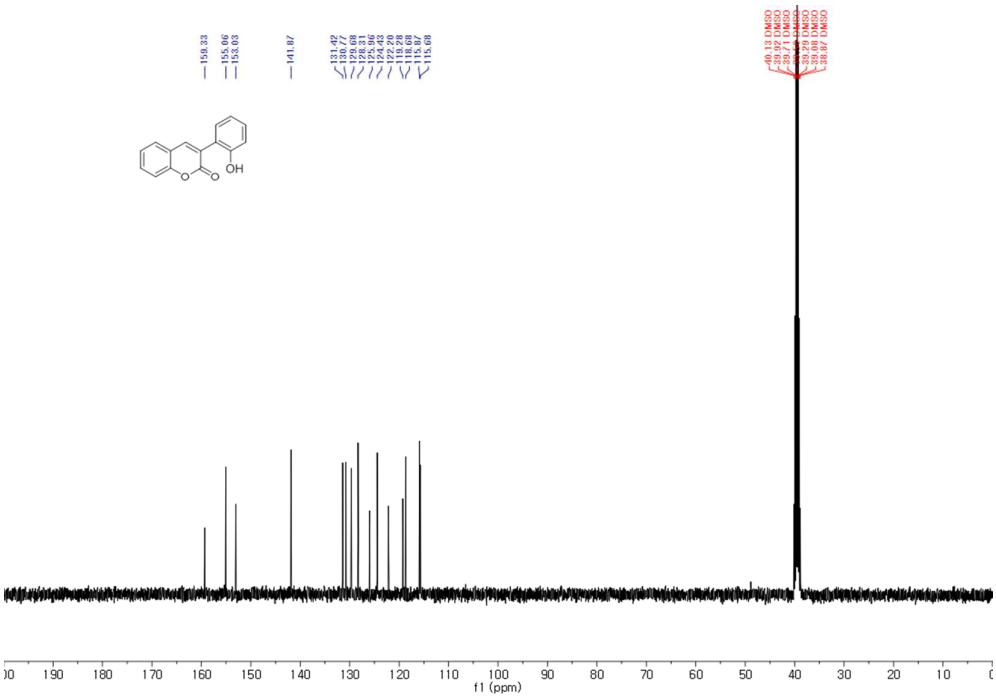


100 MHz, ^{13}C NMR in CD_2Cl_2

3-(2-hydroxyphenyl)-2H-chromen-2-one (9)

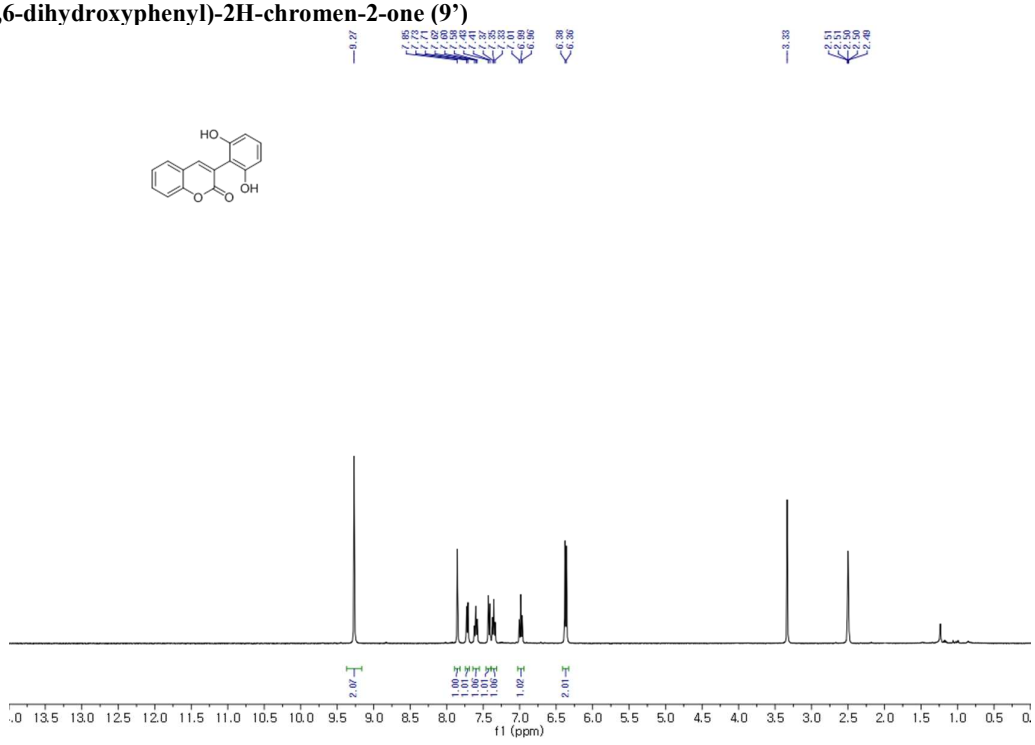


400 MHz, ^{1}H NMR in DMSO-d_6

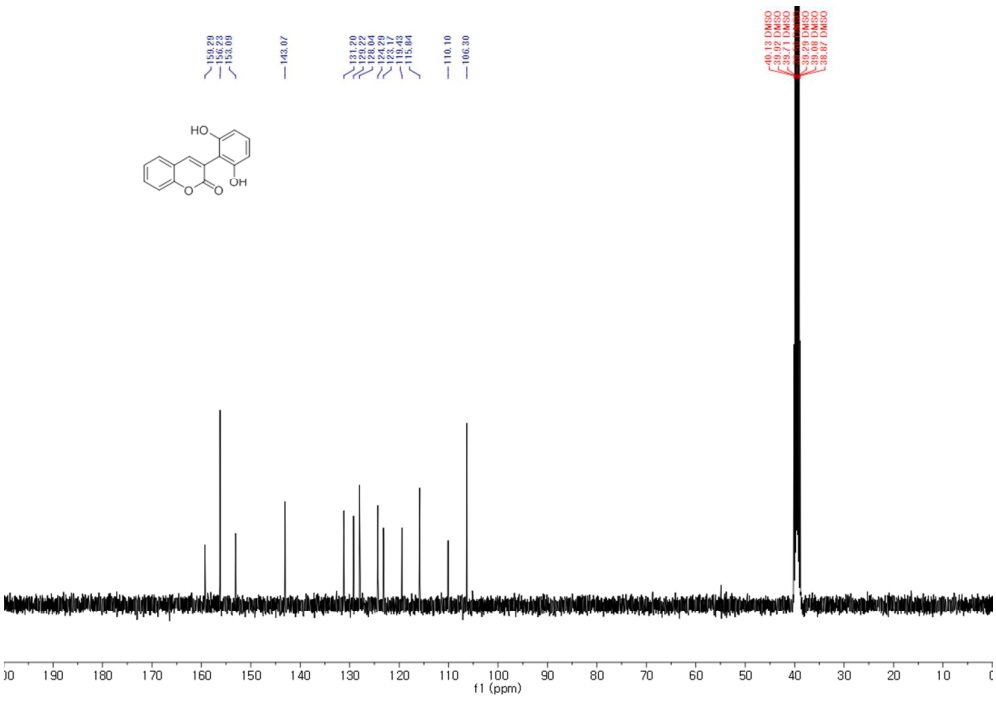


100 MHz, ^{13}C NMR in DMSO-d_6

3-(2,6-dihydroxyphenyl)-2H-chromen-2-one (9')

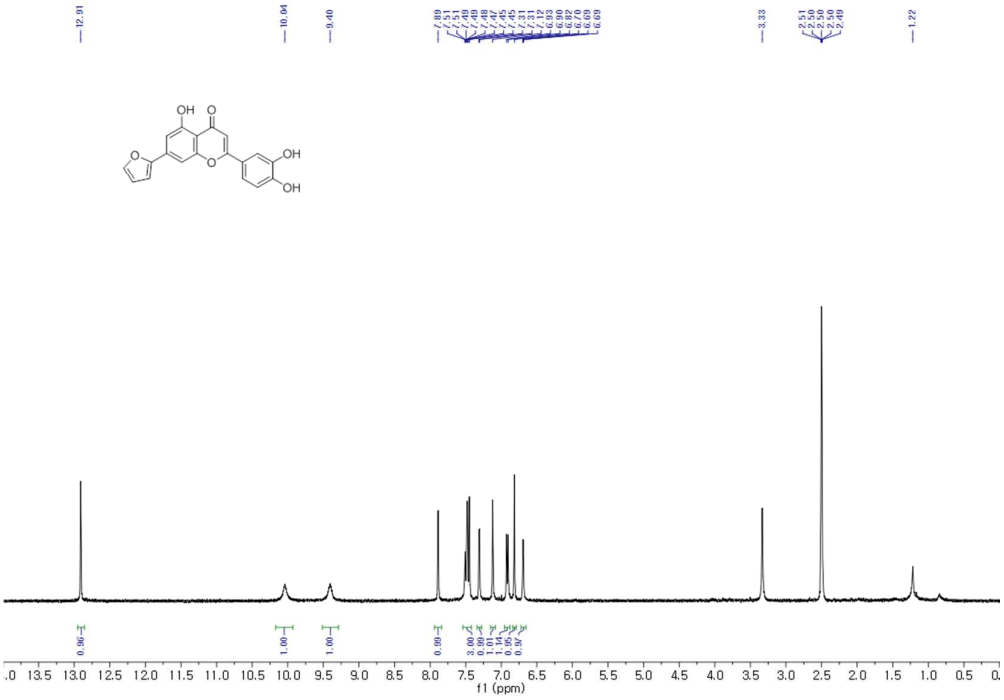


400 MHz, ^{1}H NMR in DMSO-d_6

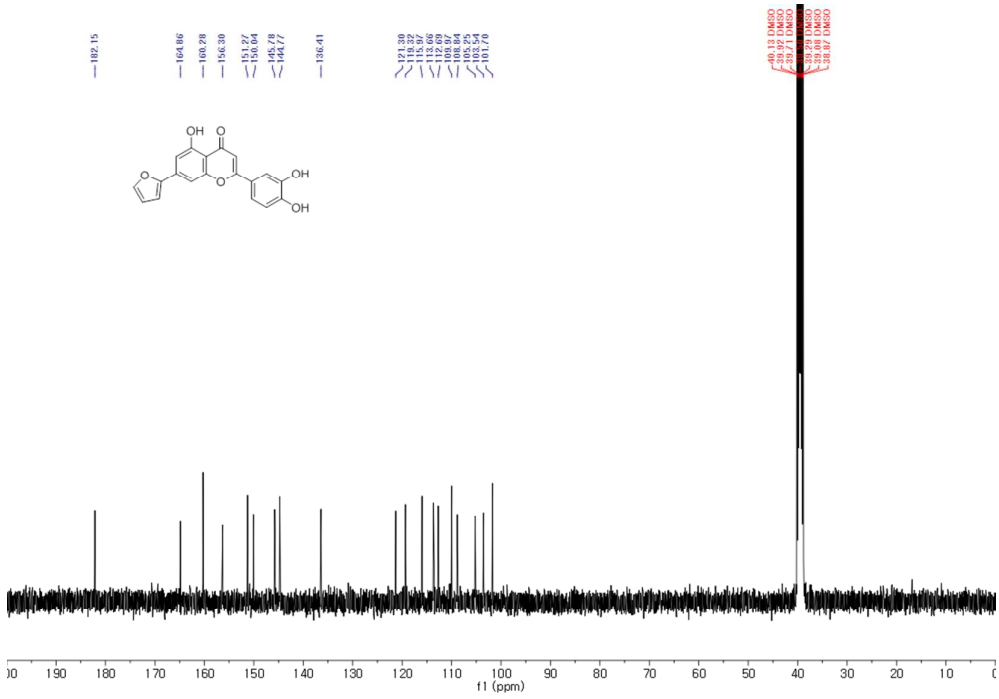


100 MHz, ^{13}C NMR in DMSO-d_6

2-(3,4-dihydroxyphenyl)-7-(furan-2-yl)-5-hydroxy-4H-chromen-4-one (10b)

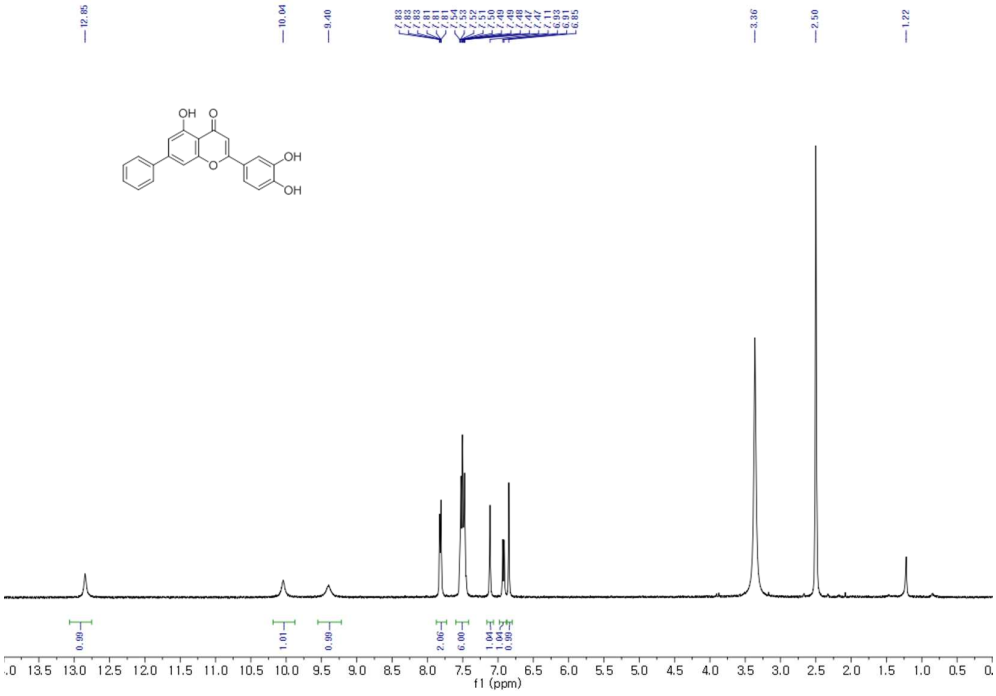


400 MHz, ^{1}H NMR in DMSO-d_6

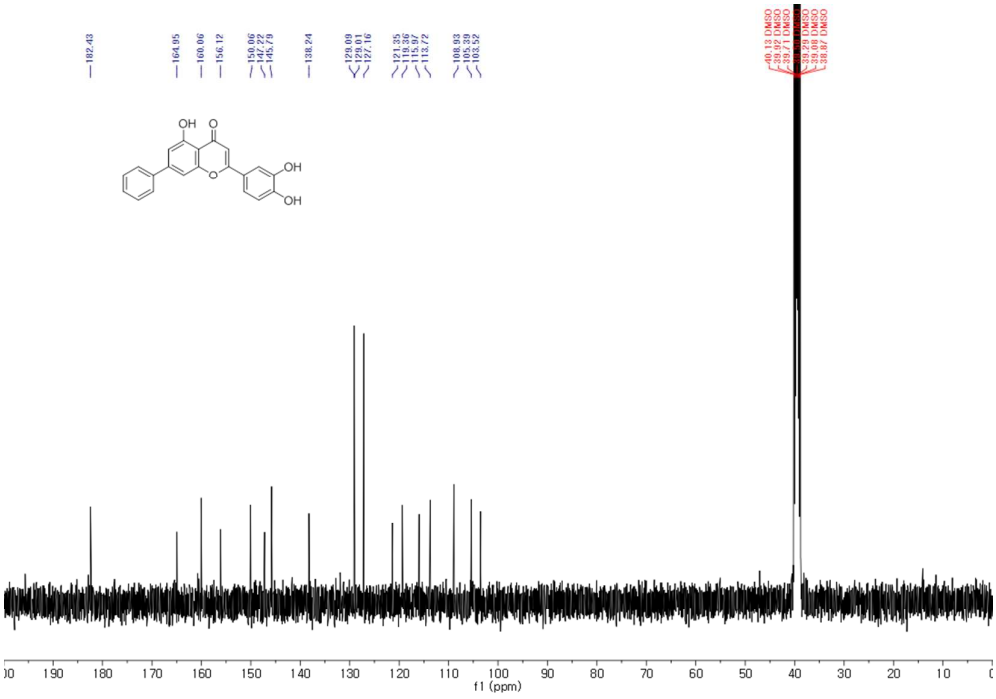


100 MHz, ^{13}C NMR in DMSO-d_6

2-(3,4-dihydroxyphenyl)-5-hydroxy-7-phenyl-4H-chromen-4-one (11b)

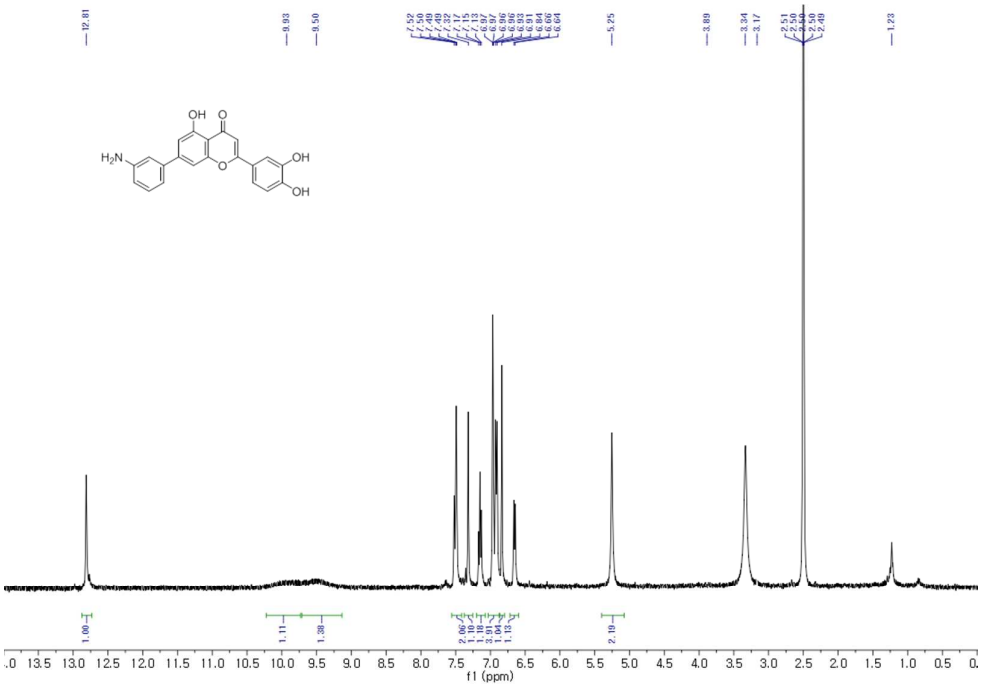


400 MHz, ^{1}H NMR in DMSO-d_6

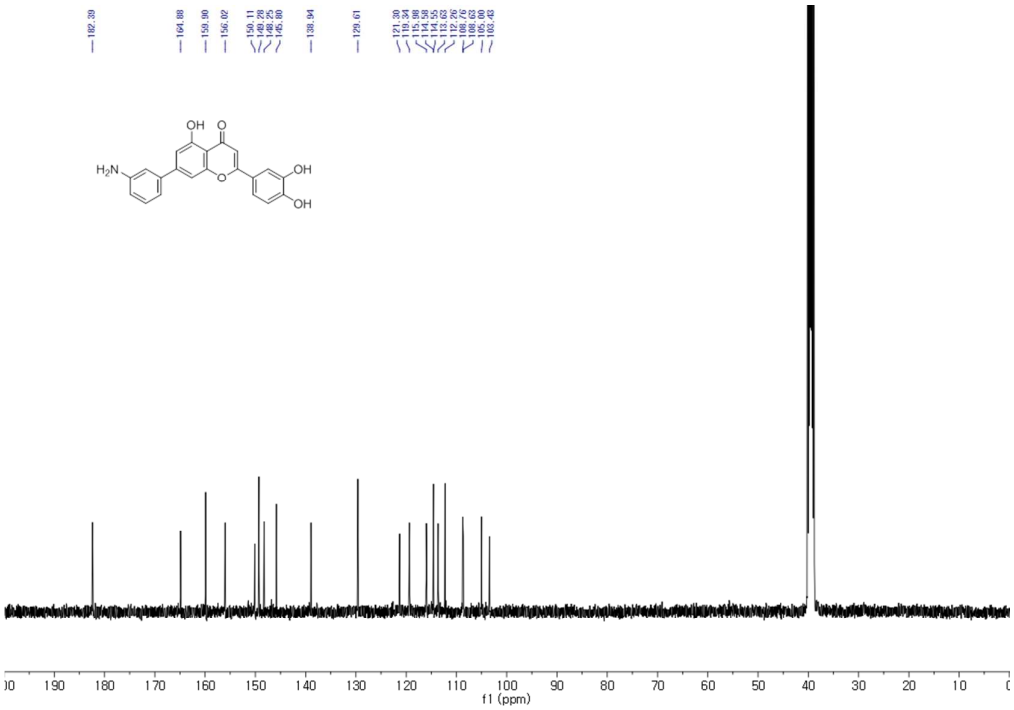


100 MHz, ^{13}C NMR in DMSO-d_6

7-(3-aminophenyl)-2-(3,4-dihydroxyphenyl)-5-hydroxy-4H-chromen-4-one (12b)



400 MHz, ^{1}H NMR in DMSO-d_6



100 MHz, ^{13}C NMR in DMSO-d_6