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Design and synthesis of novel anti-hyperalgesic agents based on 6-prenylnaringenin as the T-type calcium channel blockers

Huy Du Nguyen[a], Takuya Okada[a], Shun Kitamura[b], Sakura Yamaoka[c], Yamato Horaguchi[c], Yoshihito Kasanami[c], Fumiko Sekiguchi[c], Maho Tsubota[c], Shigeru Yoshida[d], Hiroyuki Nishikawa[c], Atsufumi Kawabata[c,*], Naoki Toyooka[a,e,*]

[a] Graduate School of Innovative Life Science, University of Toyama, Toyama 930-8555, Japan
[b] Faculty of Engineering, University of Toyama, 3190 Gofuku, Toyama 930-8555, Japan
[c] Faculty of Pharmacy, Kindai University, Higashi-Osaka 577-8502, Japan
[d] Faculty of Science and Engineering, Kindai University, Higashi-Osaka 577-8502, Japan
[e] Graduate School of Science and Engineering, University of Toyama, Toyama 930-8555, Japan

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ABSTRACT

Since 6-prenylnaringenin (6-PNG) was recently identified as a novel T-type calcium channel blocker with the IC_{50} value around 1 μM, a series of flavanone derivatives were designed, synthesized and subsequently evaluated for T-channel-blocking activity in HEK293 cells transfected with $Ca_v3.2$ T-type channels using a patch-clamp technique. As a result, several new flavanones blocked $Ca_v3.2$-dependent T-currents more potently than 6-PNG. In the synthesized compounds, 6-(3-ethylpent-2-enyl)-5,7-dihydroxy-2-(2-hydroxyphenyl)chroman-4-one **8j**, 6-(3-ethylpent-2-enyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one **11b**, 6-(2-cyclopentylideneethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one **11d**, and 6-(2-Cyclopentylethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one **12c** were more potent blocker than 6-PNG with the IC_{50} value of 0.39, 0.26, 0.46, and 0.50 μM, respectively. Among the above four derivatives, the compound **8j** provided the best result in the in vivo experiments; i.e. systemic administration of **8j** at the minimum dose completely restored neuropathic pain induced by partial sciatic nerve ligation in mice.

1. Introduction

Low voltage-activated or transient (T)-type calcium channels (T-channels) consist of three subtypes: $Ca_v3.1$, $Ca_v3.2$ and $Ca_v3.3$ channels, which have unique electrophysiological and pharmacological profiles distinct from high voltage-activated calcium channels.[1,2] These channels are abundantly expressed in the brain and the primary afferents, and implicated in regulation of neuronal excitation and neurotransmitter release.[3] Currently, T-channel-blocking compounds are considered useful as antiepileptics, anti-hyperalgesics and possibly antipsychotics. For example, T-channel blocker ethosuximide (IC_{50} = 600 μM) is clinically used as an antiepileptic drug,[4] and the analgesic or anti-hyperalgesic property of several T-channel blockers including ethosuximide have been demonstrated by preclinical studies.[5,6] A growing number of studies thus suggest the necessity of the discovery of more effective T-channel blockers. McCalmont et al. formulated T-channel blockers with the potency comparable to mibefradil (IC_{50} = 1 μM)[7] and a series of 3,4-dihydroquinazoline analogues were shown to block T-channels more potently than mibefradil.[8–11] It is also to be noted that T-channel blockers might be useful not only for pain therapies, but also to treat certain types of cancer.[12,13] However, the potential adverse effects of T-channel blockers such as sedation and cardiovascular dysfunction have to be taken into consideration; a well-known case for this matter is the drug interactions of mibefradil, leading to irregular heart rhythm.[14]

In 2016, we reported that the prenylflavanones (PFVNs) including sophoraflavanone G, 6-prenylnaringenin (6-PNG) and 8-prenylnaringenin (8-PNG) blocked T-channels with the IC_{50} values around 1 μM, while these PFVNs had little inhibitory effect on L-type calcium channels.[15] This evidence supports the previous reports showing the medical usefulness of PFVNs, which possess extensive biological activities, such as anti-oxidant, anti-cancer, immunomodulatory and estrogenic activity.[16,17] In addition, these PFVNs were structurally far different from known T-channel blockers, except valproic acid and

* Corresponding authors at: Faculty of Pharmacy, Kindai University, Higashi-Osaka 577-8502, Japan (A. Kawabata); Graduate School of Innovative Life Science, University of Toyama, Toyama 930-8555, Japan (N. Toyooka).
E-mail address: toyooka@eng.u-toyama.ac.jp (N. Toyooka).

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arundic acid. Several recent studies[18,19] attempted to discover the selective and potent inhibitors of T-channels for pain therapies, whereas they are not necessarily successful because of serious side effects.[13] Therefore, it is a new and unique approach to develop novel T-channel-blocking PFVNs useful as analgesic or anti-hyperalgesic drugs with minimum side effects.

PFVNs usually exhibit the bio-activities better than their flavanone skeletons. This phenomenon may be explained as follows: PFVNs are usually more lipophilic than their flavanone skeletons, which results in a higher affinity to biological membranes and a better interaction with target proteins.[20] Moreover, each T-channel contains an interactive pore for the selective passage of Ca^{2+} ions and a voltage sensor for controlling pore gating, so the T-channel blocking actions of PFVNs probably relate to their hydroxyl groups. These initial assumptions revealed that the relationship between the chemical structure of PFVNs and their channel-blocking actions may be rather complicated. Therefore, a series of the screening PFVNs should be synthesized and subsequently evaluated for their blocking effects on the $Ca_v3.2$ channels transfected into HEK293 cells to search out a lead compound. These screening PFVNs were designed as follows: the allyl-substituent at the 6-position of PFVNs was varied according to the length of carbon chain and the degree of saturation, and the hydroxyl groups of PFVNs were altered in the quantity and position or replaced with less polar functional groups, such as chloro, methoxyl or ethoxyl group, as shown in Fig. 1. This is a new requirement for the synthesis of designed derivatives, so several reaction sequences of previous studies will be applied or cleverly combined in order to suggest appropriate synthetic routes for the designed derivatives.

2. Results and discussions

2.1. Synthesis

According to our initial results, 6-PNG was able to inhibit the $Ca_v3.2$ channel transfected into HEK-293 cells, while the naringenin was inactive, so the prenyl group at the 6-position may play an important role in the blocking actions of 6-PNG. To explore the importance of substituent on the 6-position or the phenyl ring of flavanone nuclei (Fig. 1), we started the flexible synthesis of these derivatives including the 7-deoxy ones as shown in Scheme 1. The compounds **1a**[21] and **1b**[22] were converted to the corresponding chalcones **2a–o**,[23] which were transformed into the flavanones **3a–o**.[24] The Claisen rearrangement of **3a-o** provided the 6-allyl derivatives **4a–o**.[25] The 6-allyl derivatives of **4c** and **4g–n** were converted to the corresponding acetate **6c** and **6g–n** *via* the corresponding phenol **5c** and **5g–o**. The cross-metathesis reaction of **4a–b**, **5c**, **4d–f** and **5g–o** with appropriate olefin using Grubbs catalyst 2nd generation afforded the corresponding olefins **7a–q**. Finally, deprotection of acetyl group on **7c–d** and **7h–q** furnished **8c–d** and **8h–q**.

For more simple synthesis of the derivatives having the 4′-hydroxyphenyl ring on the flavanone, we selected the commercially available naringenin as the starting material. The synthesis began with the known di-acetate **9**, prepared from naringenin in 3 steps,[25] which was converted to the corresponding olefins **10a–d** by the cross-metathesis reaction with appropriate olefin using Grubbs catalyst 2nd generation. Finally, deprotection of acetyl group on **10a–d** provided **11a–d**, and hydrogenation of the resulting olefins **11a**, **11b** and **11d** furnished the saturated derivatives **12a–c** (Scheme 2).

2.2. In vitro biological evaluations

The effects of synthesized compounds on Ba^{2+} currents (T-currents) in human $Ca_v3.2$-HEK293 cells were evaluated using a whole cell patch clamp technique, and summarized in Table 1. On the deoxy-derivatives on the 7-position, allyl-derivatives **4d–f** showed good blockade than prenyl-derivatives **7e–g**. In the case of 7-hydroxy derivatives, effects of the blockade of allyl- (**5g** and **5n–o)** and prenyl-derivatives (**8h** and **8p–q**) were almost the same. However, derivatives with higher polarity, which have several hydroxyl groups on the phenyl ring on the flavanone, prenyl-derivatives (**8i** and **8k–o**) showed more potent blocking activity than allyl-derivatives **5h–m**. Overall, the prenyl-derivatives were superior to the allyl-derivatives. In the case of the derivatives having larger substituent on the 6-position (**8d** and **8j**), derivative **8j** was much better blocker than the corresponding prenyl-derivative **8i** and allyl-derivative **5h**. On the comparison of **8j** and its deoxy-derivative **8d**, derivative **8j** revealed much better effect than **8d**. According to these results, we anticipated that the structural element for potent blockers was slightly large substituent on the 6-position and presence of hydroxyl group on the 7-position. In addition, the derivatives having slightly large substituent on the 6-position **11b**, **11d** and its saturated derivatives **12a**, **12c** also showed good blocking effects.

2.3. In vivo biological evaluations

According to these results, we selected 8 compounds (**8c**, **8i**, **8j**, **8k**, **11b**, **11d**, and **12a**, **12c**) and conducted further evaluations for their IC_{50} values, and the results were summarized in Table 2. In the synthesized compounds, **12c**, **11d**, **8j**, and **11b** were more potent as T-channel blockers than 6-PNG, the IC_{50} value of which was 0.50 μM, 0.46 μM, 0.39 μM, and 0.26 μM, respectively. In the in vivo evaluations, as shown in Figs. 2–6, the compound **8j**, among the above four derivatives, most potently suppressed the mechanical allodynia induced by partial sciatic nerve ligation (PSNL) in mice, an animal model of neuropathic pain. It was particularly of interest that **8j** produced remarkable and significant anti-allodynic effect at a small dose, 10 mg/kg, at which 6-PNG had no effect, and that **8j** at 20 mg/kg achieved almost complete inhibition of the PSNL-induced neuropathy, as depicted in Figs. 2 and 3.

3. Conclusion

In summary, a series of 6-PNG derivatives were synthesized. The synthetic modifications were mainly explored on the prenyl group at the 6-position of 6-PNG. Among the synthesized derivatives, four compounds having a modified prenyl group (**8j**, IC_{50} = 0.39 μM, **11b**, IC_{50} = 0.26 μM, and **11d**, IC_{50} = 0.46 μM,) or saturated side chain (**12c**, IC_{50} = 0.50 μM) showed more potent blockade activity against human $Ca_v3.2$-HEK293 cells than 6-PNG (IC_{50} = ~1 μM). In addition, selected all four compounds suppressed the mechanical allodynia induced by

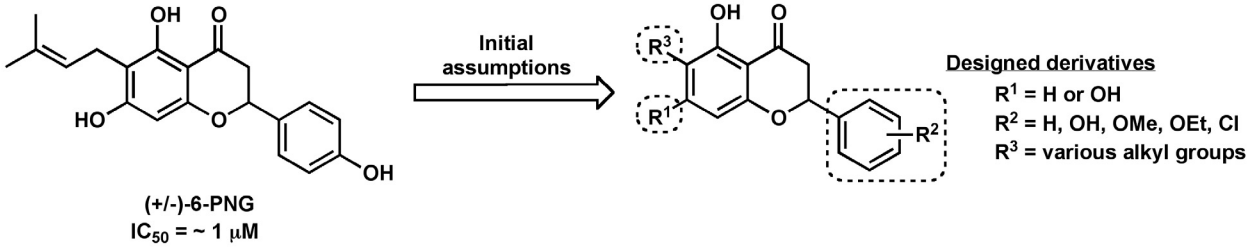
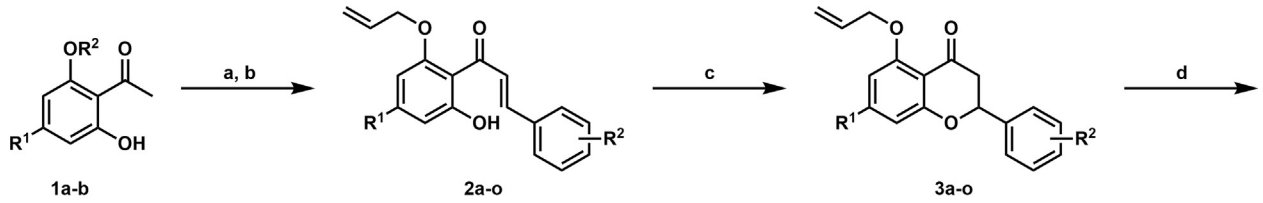


Fig. 1. The designation of screening derivatives.



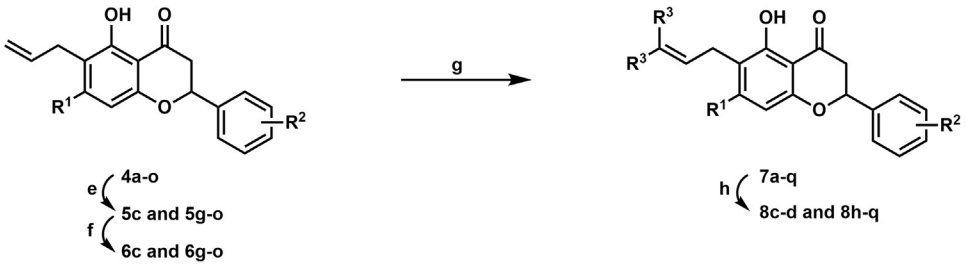
1a-b 2a-o 3a-o

1a : R^1=H, R^2=Allyl
1b : R^1=OMOM, R^2=H

2a : R^1=H, R^2=H
2b : R^1=H, R^2=4-Me
2c : R^1=H, R^2=2-OMOM
2d : R^1=H, R^2=4-OMe
2e : R^1=H, R^2=4-OEt
2f : R^1=H, R^2=4-Cl
2g : R^1=OMOM, R^2=H
2h : R^1=OMOM, R^2=2-OMOM
2i : R^1=OMOM, R^2=3-OMOM
2j : R^1=OMOM, R^2=2,3-di-OMOM
2k : R^1=OMOM, R^2=2,6-di-OMOM
2l : R^1=OMOM, R^2=3,4-di-OMOM
2m: R^1=OMOM, R^2=3,5-di-OMOM
2n : R^1=OMOM, R^2=4-OMe
2o : R^1=OMOM, R^2=4-Cl

3a : R^1=H, R^2=H
3b : R^1=H, R^2=4-Me
3c : R^1=H, R^2=2-OMOM
3d : R^1=H, R^2=4-OMe
3e : R^1=H, R^2=4-OEt
3f : R^1=H, R^2=4-Cl
3g : R^1=OMOM, R^2=H
3h : R^1=OMOM, R^2=2-OMOM
3i : R^1=OMOM, R^2=3-OMOM
3j : R^1=OMOM, R^2=2,3-di-OMOM
3k : R^1=OMOM, R^2=2,6-di-OMOM
3l : R^1=OMOM, R^2=3,4-di-OMOM
3m: R^1=OMOM, R^2=3,5-di-OMOM
3n : R^1=OMOM, R^2=4-OMe
3o : R^1=OMOM, R^2=4-Cl

Scheme 1. *Reagents and conditions*: a: AllylBr, K_2CO_3, acetone, 50 °C for **2g–o**; b: $Ba(OH)_2$, EtOH, H_2O, 40 °C; c: NaOAc, EtOH, H_2O, reflux; d: $Eu(fod)_3$, $ClCH_2CH_2Cl$, 100 °C, sealed tube; e: conc. HCl, MeOH, rt; f: Ac_2O, pyridine, rt; g: $(Me)_2C = CH_2$ or $(Et)_2C = CH_2$, Grubbs catalyst, 2nd Generation, benzene, 100 °C, sealed tube; h: K_2CO_3, MeOH, rt.



4a : R^1=H, R^2=H
4b : R^1=H, R^2=4-Me
4c : R^1=H, R^2=2-OMOM
4d : R^1=H, R^2=4-OMe
4e : R^1=H, R^2=4-OEt
4f : R^1=H, R^2=4-Cl
4g : R^1=OMOM, R^2=H
4h : R^1=OMOM, R^2=2-OMOM
4i : R^1=OMOM, R^2=3-OMOM
4j : R^1=OMOM, R^2=2,3-di-OMOM
4k : R^1=OMOM, R^2=2,6-di-OMOM
4l : R^1=OMOM, R^2=3,4-di-OMOM
4m: R^1=OMOM, R^2=3,5-di-OMOM
4n : R^1=OMOM, R^2=4-OMe
4o : R^1=OMOM, R^2=4-Cl

5c : R^1=H, R^2=2-OH
5g : R^1=OH, R^2=H
5h : R^1=OH, R^2=2-OH
5i : R^1=OH, R^2=3-OH
5j : R^1=OH, R^2=2,3-di-OH
5k : R^1=OH, R^2=2,6-di-OH
5l : R^1=OH, R^2=3,4-di-OH
5m: R^1=OH, R^2=3,5-di-OH
5n : R^1=OH, R^2=4-OMe
5o : R^1=OH, R^2=4-Cl

6c : R^1=H, R^2=2-OAc
6g : R^1=OAc, R^2=H
6h : R^1=OAc, R^2=2-OAc
6i : R^1=OAc, R^2=3-OAc
6j : R^1=OAc, R^2=2,3-di-OAc
6k : R^1=OAc, R^2=2,6-di-OAc
6l : R^1=OAc, R^2=3,4-di-OAc
6m: R^1=OAc, R^2=3,5-di-OAc
6n : R^1=OAc, R^2=4-OMe
6o : R^1=OAc, R^2=4-Cl

7a : R^1=H, R^2=H, R^3=Me
7b : R^1=H, R^2=4-Me, R^3=Me
7c : R^1=H, R^2=2-OAc, R^3=Me
7d : R^1=H, R^2=2-OAc, R^3=Et
7e : R^1=H, R^2=4-OMe, R^3=Me
7f : R^1=H, R^2=4-OEt, R^3=Me
7g : R^1=H, R^2=4-Cl, R^3=Me
7h : R^1=OAc, R^2=H, R^3=Me
7i : R^1=OAc, R^2=2-OAc, R^3=Me
7j : R^1=OAc, R^2=2-OAc, R^3=Et
7k : R^1=OAc, R^2=3-OAc, R^3=Me
7l : R^1=OAc, R^2=2,3-di-OAc, R^3=Me
7m: R^1=OAc, R^2=2,6-di-OAc, R^3=Me
7n : R^1=OAc, R^2=3,4-di-OAc, R^3=Me
7o : R^1=OAc, R^2=3,5-di-OAc, R^3=Me
7p : R^1=OAc, R^2=4-OMe, R^3=Me
7q : R^1=OAc, R^2=4-Cl, R^3=Me

8c : R^1=H, R^2=2-OH, R^3=Me
8d : R^1=H, R^2=2-OH, R^3=Et
8h : R^1=OH, R^2=H, R^3=Me
8i : R^1=OH, R^2=2-OH, R^3=Me
8j : R^1=OH, R^2=2-OH, R^3=Et
8k : R^1=OH, R^2=3-OH, R^3=Me
8l : R^1=OH, R^2=2,3-di-OH, R^3=Me
8m: R^1=OH, R^2=2,6-di-OH, R^3=Me
8n : R^1=OH, R^2=3,4-di-OH, R^3=Me
8o : R^1=OH, R^2=3,5-di-OH, R^3=Me
8p : R^1=OH, R^2=4-OMe, R^3=Me
8q : R^1=OH, R^2=4-Cl, R^3=Me

Scheme 2. *Reagents and conditions*: a: $(Me)_2C = CH_2$ or $(Et)_2C = CH_2$ or $(n\text{-}Pr)_2C = CH_2$, Grubbs catalyst, 2nd Generation, benzene, 100 °C, sealed tube; b: K_2CO_3, MeOH, rt; c: H_2, Pd/C, EtOAc, rt.

partial sciatic nerve ligation (PSNL) in mice, an animal model of neuropathic pain (Figs. 2–6). Especially, the 6-ethylpent-2-enyl instead of prenyl and 2-hydroxyphenyl instead of 4-hydroxyphenyl derivative, **8j**, showed remarkable and significant anti-allodynic effect at 10 mg/kg, which was a subeffective dose of 6-PNG, and achieved almost complete inhibition of the PSNL-induced neuropathy at 20 mg/kg.

Table 1
T-current suppression by the synthesized derivatives in human $Ca_v3.2$-HEK293 cells.

Compound	T-current at 3 μM (% control)	Compound	T-current at 3 μM (% control)	Compound	T-current at 3 μM (% control)
6-PNG	12.78 ± 1.74	**5m**	74.83 ± 14.73	**8k**	2.09 ± 0.54
4a	90.13 ± 13.62	**5n**	50.76 ± 9.35	**8l**	67.12 ± 12.61
4b	72.69 ± 10.84	**5o**	51.93 ± 7.57	**8m**	10.26 ± 4.71
5c	31.96 ± 8.22	**7a**	100.17 ± 15.09	**8n**	14.67 ± 4.73
4d	58.96 ± 4.40	**7b**	102.99 ± 13.58	**8o**	80.90 ± 8.16
4e	65.19 ± 11.66	**8c**	3.77 ± 2.71	**8p**	47.63 ± 7.62
4f	35.93 ± 8.89	**8d**	16.11 ± 7.59	**8q**	59.71 ± 5.94
5g	70.13 ± 7.71	**7e**	81.93 ± 17.55	**11b**	22.23 ± 7.76
5h	62.99 ± 12.79	**7f**	57.84 ± 8.63	**11c**	36.75 ± 3.21
5i	76.85 ± 8.95	**7g**	78.45 ± 15.83	**11d**	1.44 ± 0.28
5j	83.85 ± 16.87	**8h**	72.64 ± 9.52	**12a**	1.69 ± 0.50
5k	–	**8i**	2.04 ± 1.15	**12b**	10.09 ± 3.09
5l	86.67 ± 13.57	**8j**	0.33 ± 0.17	**12c**	5.42 ± 2.31

T-currents were determined at 1 μM.

Table 2
IC_{50} values of the selected 8 compounds T-current inhibition.

Compound	IC_{50} (μM)	Compound	IC_{50} (μM)
6-PNG	1.00	**11b**	0.26
8c	1.25	**11d**	0.46
8i	0.64	**12a**	0.48
8j	0.39	**12c**	0.50
8k	1.02		

4. Experimental

4.1. Chemistry

4.1.1. General information

Chemicals were purchased from Sigma-Aldrich, Merck, Nakalai Tesque, Wako Pure Chemicals, Tokyo Chemical Industry (TCI), and Kanto Chemicals, and used without further purification. Column chromatography was done on Cica silica gel 60N (spherical, neutral; particle size, 63–210 nm, Kanto Chemical Co., Inc., Tokyo, Japan), while thin-layer chromatography (TLC) was performed on Merck silica gel $60F_{254}$ plates (Merck KGaA, Darmstadt, Germany). Melting points were taken on a Yanaco micromelting point apparatus and are uncorrected. The nuclear magnetic resonance (NMR) spectra were acquired in the specified solvent, in a JEOL JNM-A400 (400 and 100 MHz for ^1H and ^{13}C, respectively) or JEOL JNM-ECX500 (500 and 125 MHz for ^1H and ^{13}C, respectively). The chemical shifts (δ) are reported in ppm downfield from TMS and coupling constants (J) are expressed in Hertz. IR spectra were measured with a JASCO FT/IR-460 Plus spectrophotometer (JASCO Corp.). The low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained with a Shimadzu GCMS-QP 500 mass spectrometer (Shimadzu Corp., Kyoto, Japan), JEOL D-200, or JEOL AX505 mass spectrometer (JEOL Ltd., Tokyo, Japan) in the electron impact mode at the ionization potential of 70 eV.

4.1.2. General procedure of allylation for 2g–o and Claisen-Schmidt condensation for 2a–o

To a stirred solution of **1b** (860 mg, 4.05 mmol) in acetone (12 mL) were added K_2CO_3 (300 mg, 2.43 mmol) and AllylBr (0.38 mL, 4.46 mmol), and the reaction mixture was stirred for 24 h at 50 °C. After cooling, K_2CO_3 was removed through a Celite pad and washed with acetone (3 mL × 3). The organic layer and washings were combined and evaporated to give a yellow oil, which was used directly in the next step.

To a stirred solution of acetophenone **1** (1.19 mmol) in EtOH (15 mL) and H_2O (3 mL) were added appropriate benzaldehyde (3.57 mmol) and $Ba(OH)_2{\cdot}8H_2O$ (4.28 mmol), and the reaction mixture was stirred for 20 h at 40 °C. After cooling, EtOH was evaporated and the aqueous mixture was extracted with CH_2Cl_2 (3 mL × 5). The organic extracts were combined, dried and evaporated to give an orange oil, which was chromatographed on SiO_2 (10 g, EtOAc/*n*-hexane = 1/10) to give **2a–o**.

4.1.2.1. 1-(2-Allyloxy-6-hydroxyphenyl)-3-phenylpropenone (2a). Yield: 87%; ^1H NMR (400 MHz $CDCl_3$) δ: 4.65 (2H, dt, J = 5.6, 1.2 Hz), 5.33 (1H, dd, J = 10.4, 1.2 Hz), 5.48 (1H, dd, J = 17.2, 1.2 Hz), 6.12 (1H, ddt, J = 17.2, 10.4, 5.6 Hz), 6.43 (1H, d, J = 8.6 Hz), 6.63 (1H, d, J = 8.6 Hz), 7.35 (1H, t, J = 8.6 Hz), 7.39–7.42 (3H, m), 7.58–7.62 (2H, m), 7.81 (1H, d, J = 15.6 Hz), 7.95 (1H, d, J = 15.6 Hz), 13.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 69.76, 102.57, 111.05, 112.21, 118.72, 127.71, 128.53, 128.84, 130.28, 132.30, 135.20, 135.85, 142.80, 159.90, 164.76, 194.50; IR (KBr): 1632, 1609, 1583, 1560,

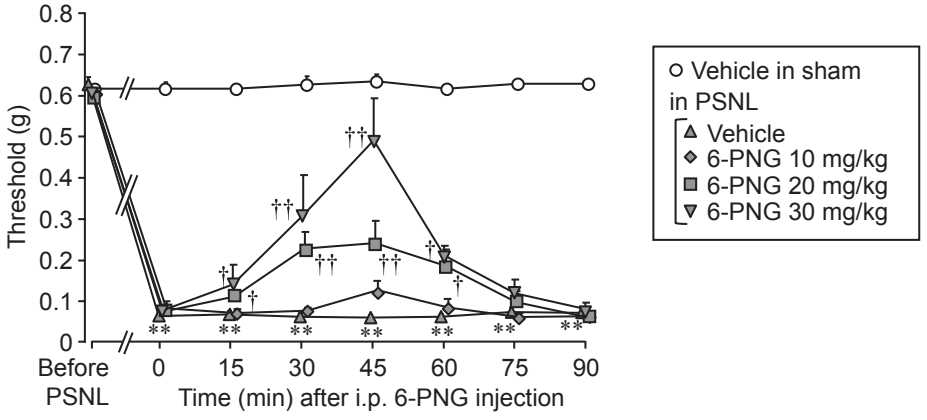


Fig. 2. 6-Prenylnaringenin (6-PNG) at 10–30 mg/kg or vehicle (V; 0.5% carboxymethyl cellulose) was administered i.p. to mice 7 days after partial sciatic nerve ligation (PSNL). Nociceptive threshold in the ipsilateral hindpaw was assessed by the von Frey test. Data show the mean with S.E.M. for 5–11 mice. $^{**}P < 0.01$ vs. vehicle in sham. $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$ vs. vehicle in PSNL.

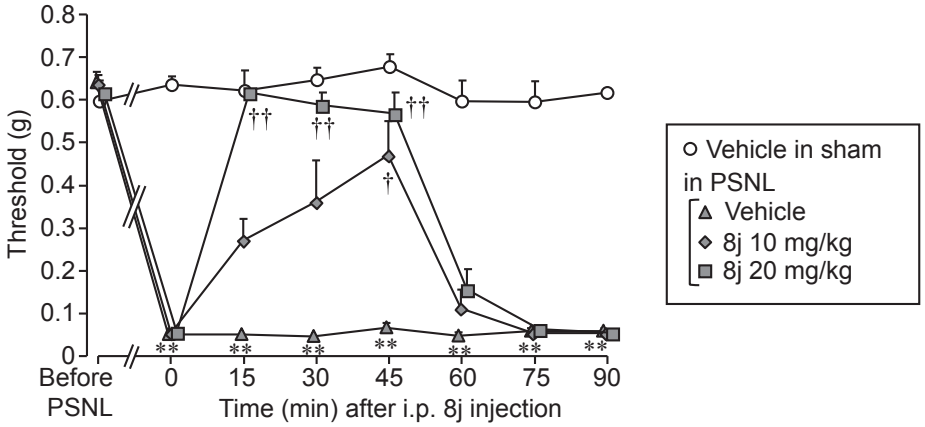


Fig. 3. 8j at 10 or 20 mg/kg or vehicle (V; 0.5% carboxymethyl cellulose) was administered i.p. to mice 7 days after partial sciatic nerve ligation (PSNL). Nociceptive threshold in the ipsilateral hindpaw was assessed by the von Frey test. Data show the mean with S.E.M. for 5–6 mice. $^{**}P < 0.01$ vs. vehicle in sham. $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$ vs. vehicle in PSNL.

1468, 1448, 1421, 1360, 1231, 1204, 1078, 984, 939, 874, 796, 735 cm^{-1}; mp: 76–78 °C; MS (EI): *m/z* 280 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_3$ 280.1099 (M^+); Found 280.1112.

*4.1.2.2. 1-(2-Allyloxy-6-hydroxyphenyl)-3-p-tolylpropenone (**2b**)*. Yield: 81%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.39 (3H, s), 4.65 (2H, d, *J* = 5.6 Hz), 5.34 (1H, dd, *J* = 10.4, 1.2 Hz), 5.48 (1H, dd, *J* = 17.2, 1.2 Hz), 6.12 (1H, ddt, *J* = 17.2, 10.4, 5.6 Hz), 6.42 (1H, d, *J* = 8.4 Hz), 6.62 (1H, d, *J* = 8.4 Hz), 7.21 (2H, d, *J* = 8.0 Hz), 7.34 (1H, t, *J* = 8.4 Hz), 7.51 (2H, d, *J* = 8.0 Hz), 7.81 (1H, d, *J* = 15.4 Hz), 7.95 (1H, d, *J* = 15.4 Hz), 13.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 21.48, 69.70, 102.52, 110.98, 112.20, 118.62, 126.65, 128.55, 129.57, 132.30, 132.43, 135.68, 140.80, 142.99, 159.84, 164.71, 194.48; IR (KBr): 1634, 1607, 1583, 1560, 1510, 1474, 1466, 1446, 1423, 1360, 1329, 1240, 1230, 1205, 1180, 1171, 1076, 1033, 983, 932, 876, 815, 746 cm^{-1}; mp: 75–77 °C; MS (EI): *m/z* 294 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_3$ 294.1256 (M^+); Found 294.1250.

*4.1.2.3. 1-(2-Allyloxy-6-hydroxyphenyl)-3-(2-methoxymethoxy-phenyl)propenone (**2c**)*. Yield: 56%; ^1H NMR (400 MHz $CDCl_3$) δ: 3.51 (3H, s), 4.66 (2H, dt, *J* = 6.8, 2.0 Hz), 5.28 (2H, s), 5.32 (1H, dd, *J* = 11.2, 2.0 Hz), 5.46 (1H, dd, *J* = 17.2, 2.0 Hz), 6.12 (1H, ddt, *J* = 17.2, 11.2, 6.8 Hz), 6.42 (1H, d, *J* = 8.0 Hz), 6.62 (1H, d, *J* = 8.0 Hz), 7.02 (1H, t, *J* = 8.0 Hz), 7.18 (1H, d, *J* = 8.0 Hz), 7.34 (2H, t, *J* = 8.0 Hz), 7.65 (1H, dd, *J* = 8.0, 2.0 Hz), 7.94 (1H, d, *J* = 15.6 Hz), 8.26 (1H, d, *J* = 15.6 Hz), 13.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.26, 69.71, 94.56, 102.61, 110.97, 111.96, 114.88, 118.51, 121.78, 124.85, 127.73, 127.81, 131.61, 132.36, 135.65, 137.59, 156.38, 159.85, 164.66, 194.70; IR (neat): 1629, 1598, 1577, 1570, 1558, 1485, 1472, 1457, 1448, 1355, 1235, 1200, 1153, 1078, 1028, 990, 754 cm^{-1}; MS (EI): *m/z* 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1311.

*4.1.2.4. 1-(2-Allyloxy-6-hydroxyphenyl)-3-(4-methoxyphenyl)-propenone (**2d**)*. Yield: 69%; ^1H NMR (400 MHz $CDCl_3$) δ: 3.85 (3H, s), 4.64 (2H, dt, *J* = 5.0, 1.2 Hz), 5.33 (1H, dd, *J* = 10.4, 1.2 Hz), 5.48 (1H, dd, *J* = 17.2, 1.2 Hz), 6.12 (1H, ddt, *J* = 17.2, 10.4, 5.0 Hz), 6.42 (1H, d, *J* = 8.0 Hz), 6.62 (1H, d, *J* = 8.0 Hz), 6.92 (2H, dt, *J* = 8.6, 2.4 Hz), 7.33 (1H, t, *J* = 8.0 Hz), 7.56 (2H, dt, *J* = 8.6, 2.4 Hz), 7.82 (2H, d, *J* = 5.4 Hz), 13.17 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 55.38, 69.71, 102.57, 111.04, 112.30, 114.32, 118.56, 125.36, 127.97, 130.32, 132.38, 135.54, 142.95, 159.82, 161.52, 164.70, 194.35; IR (KBr): 1632, 1607, 1578, 1560, 1512, 1473, 1466, 1458, 1447, 1421, 1362, 1261, 1232, 1171, 1074, 1028, 831 cm^{-1}; mp: 68–70 °C; MS (EI): *m/z* 310 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_4$ 310.1205 (M^+); Found 310.1195.

*4.1.2.5. 1-(2-Allyloxy-6-hydroxyphenyl)-3-(4-ethoxyphenyl)-propenone (**2e**)*. Yield: 51%; ^1H NMR (400 MHz $CDCl_3$) δ: 1.44 (3H, t, *J* = 7.0 Hz), 4.08 (2H, q, *J* = 7.0 Hz), 4.64 (2H, d, *J* = 5.6 Hz), 5.33 (1H, d, *J* = 10.4 Hz), 5.48 (1H, d, *J* = 17.2 Hz), 6.12 (1H, ddt, *J* = 17.2, 10.4, 5.6 Hz), 6.41 (1H, d, *J* = 8.0 Hz), 6.62 (1H, d, *J* = 8.0 Hz), 6.90 (2H, d, *J* = 8.4 Hz), 7.33 (1H, t, *J* = 8.0 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.82 (2H, d, *J* = 4.8 Hz), 13.17 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 14.72, 63.61, 69.71, 102.58, 111.03, 112.31, 114.79, 118.54, 125.22, 127.78, 130.34, 132.39, 135.51, 143.06, 159.81, 160.96, 164.69, 194.36; IR (KBr): 1622, 1607, 1578, 1545, 1512, 1474, 1458, 1423, 1362, 1258, 1236, 1198, 1177, 1076, 1032 cm^{-1}; mp: 76–78 °C; MS (EI): *m/z* 324 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_4$ 324.1362 (M^+); Found 324.1358.

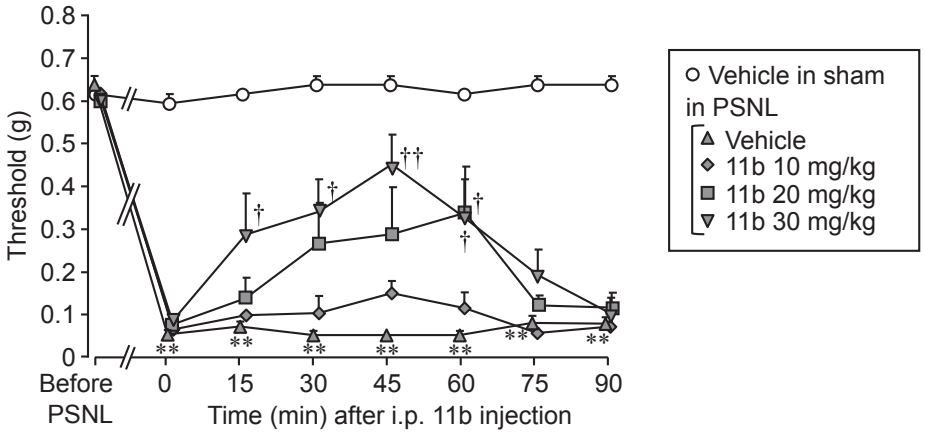


Fig. 4. 11b at 10–30 mg/kg or vehicle (V; 0.5% carboxymethyl cellulose) was administered i.p. to mice 7 days after partial sciatic nerve ligation (PSNL). Nociceptive threshold in the ipsilateral hindpaw was assessed by the von Frey test. Data show the mean with S.E.M. for 5–6 mice. $^{**}P < 0.01$ vs. vehicle in sham. $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$ vs. vehicle in PSNL.

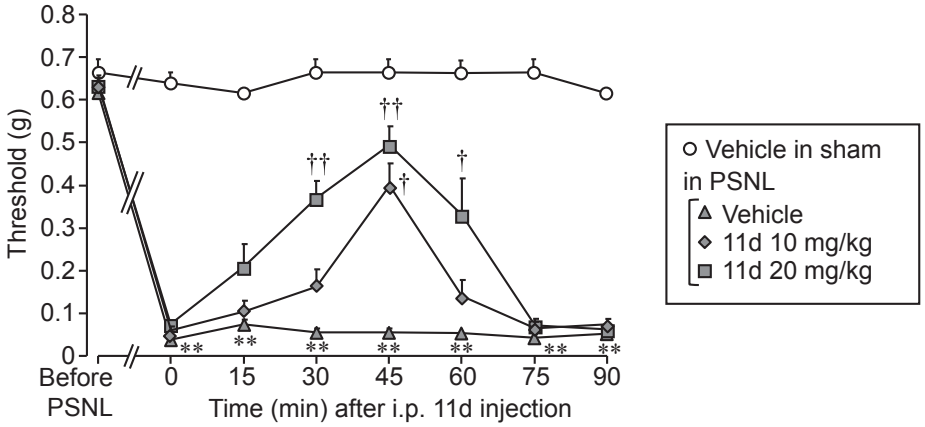


Fig. 5. 11d at 10 or 20 mg/kg or vehicle (V; 0.5% carboxymethyl cellulose) was administered i.p. to mice 7 days after partial sciatic nerve ligation (PSNL). Nociceptive threshold in the ipsilateral hindpaw was assessed by the von Frey test. Data show the mean with S.E.M. for 5–7 mice. $^{**}P < 0.01$ vs. vehicle in sham. $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$ vs. vehicle in PSNL.

*4.1.2.6. 1-(2-Allyloxy-6-hydroxyphenyl)-3-(4-chlorophenyl)-propenone **(2f)***. Yield: 61%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 4.64 (2H, d, J = 5.2 Hz), 5.34 (1H, d, J = 11.0, 1.2 Hz), 5.48 (1H, dd, J = 17.2, 1.2 Hz), 6.12 (1H, ddt, J = 17.2, 11.0, 5.2 Hz), 6.43 (1H, d, J = 8.6 Hz), 6.63 (1H, d, J = 8.6 Hz), 7.36 (1H, t, J = 8.6 Hz), 7.37 (2H, d, J = 8.6 Hz), 7.53 (2H, d, J = 8.6 Hz), 7.73 (1H, d, J = 16.0 Hz), 7.90 (1H, d, J = 16.0 Hz), 13.00 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 69.74, 102.53, 111.09, 112.11, 118.78, 128.24, 129.12, 129.60, 132.28, 133.71, 136.01, 136.11, 141.14, 159.86, 164.78, 194.24; IR (KBr): 1634, 1607, 1583, 1560, 1491, 1474, 1457, 1445, 1360, 1239, 1231, 1205, 1088, 1076, 1030, 986, 822, 748 cm^{-1}; mp: 68–70 °C; MS (EI): m/z 314 (M^+); HRMS (EI) Calcd for $C_{18}H_{15}ClO_3$ 314.0710 (M^+); Found 310.0713.

*4.1.2.7. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-phenylpropenone **(2g)***. Yield: 68% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.49 (3H, s), 4.62 (2H, dd, J = 5.2, 1.2 Hz), 5.20 (2H, s), 5.36 (1H, dd, J = 10.8, 1.2 Hz), 5.48 (1H, dd, J = 15.6, 1.2 Hz), 6.08 (1H, d, J = 2.0 Hz), 6.12 (1H, ddt, J = 15.6, 10.8, 5.2 Hz), 6.28 (1H, d, J = 2.0 Hz), 7.35–7.43 (3H, m), 7.54–7.62 (2H, m), 7.78 (1H, d, J = 15.2 Hz), 7.97 (1H, d, J = 15.2 Hz), 13.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.42, 69.77, 92.67, 94.01, 96.70, 107.16, 119.04, 127.62, 128.41, 128.78, 130.05, 132.09, 135.38, 142.28, 161.47, 163.57, 167.60, 192.88; IR (KBr): 1632, 1623, 1580, 1564, 1423, 1340, 1223, 1211, 1150, 1105, 1080, 1022, 976, 939, 824, 746 cm^{-1}; mp: 74–76 °C; MS (EI): m/z 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1327.

*4.1.2.8. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(2-methoxymethoxyphenyl)propenone **(2h)***. Yield: 85% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.49 (3H, s), 3.51 (3H, s), 4.62 (2H, d, J = 5.2 Hz), 5.20 (2H, s), 5.27 (2H, s), 5.34 (1H, d, J = 10.8 Hz), 5.47 (1H, d, J = 17.2 Hz), 6.07 (1H, d, J = 2.4 Hz), 6.11 (1H, ddt, J = 17.2, 10.8, 5.2 Hz), 6.27 (1H, d, J = 2.4 Hz), 7.01 (1H, t, J = 7.6 Hz), 7.18 (1H, d, J = 7.6 Hz), 7.33 (1H, td, J = 7.6, 1.6 Hz), 7.64 (1H, dd, J = 7.6, 1.6 Hz), 7.96 (1H, d, J = 15.6 Hz), 8.23 (1H, d, J = 15.6 Hz), 14.03 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.21, 56.37, 69.72, 92.65, 93.97, 94.52, 96.65, 107.22, 114.83, 118.83, 121.74, 125.02, 127.58, 127.69, 131.37, 132.14, 137.02, 156.22, 161.41, 163.41, 167.51, 193.09; IR (KBr): 1622, 1576, 1558, 1343, 1235, 1217, 1204, 1161, 1153, 1104, 1076, 1040, 991, 950, 835 cm^{-1}; mp: 94–96 °C; MS (EI): m/z 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

*4.1.2.9. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(3-methoxymethoxyphenyl)propenone **(2i)***. Yield: 90% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.43 (3H, s), 3.45 (3H, s), 4.56 (2H, d, J = 5.6 Hz), 5.15 (2H, s), 5.16 (2H, s), 5.30 (1H, d, J = 10.4 Hz), 5.42 (1H, d, J = 17.2 Hz), 6.02 (1H, d, J = 2.4 Hz), 6.10 (1H, ddt, J = 17.2, 10.4, 5.6 Hz), 6.22 (1H, d, J = 2.4 Hz), 7.07 (1H, d, J = 8.0 Hz), 7.23 (3H, m), 7.66 (1H, d, J = 15.6 Hz), 7.89 (1H, d, J = 15.6 Hz), 13.92 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 55.98, 56.39, 69.80, 92.61, 93.98, 94.32, 96.65, 107.10, 115.53, 118.06, 119.09, 122.36, 127.91, 129.75, 132.06, 136.82, 142.02, 157.54, 161.45, 163.57, 167.61, 192.77; IR (neat): 1653, 1634, 1623, 1617, 1577, 1569, 1558, 1505, 1343, 1218, 1151, 1082, 1025 cm^{-1}; MS (EI): m/z 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

*4.1.2.10. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(2,3-bismethoxymethoxyphenyl)propenone **(2j)***. Yield: 99% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.49 (3H, s), 3.51 (3H, s), 3.65 (3H, s), 4.61 (2H, d,

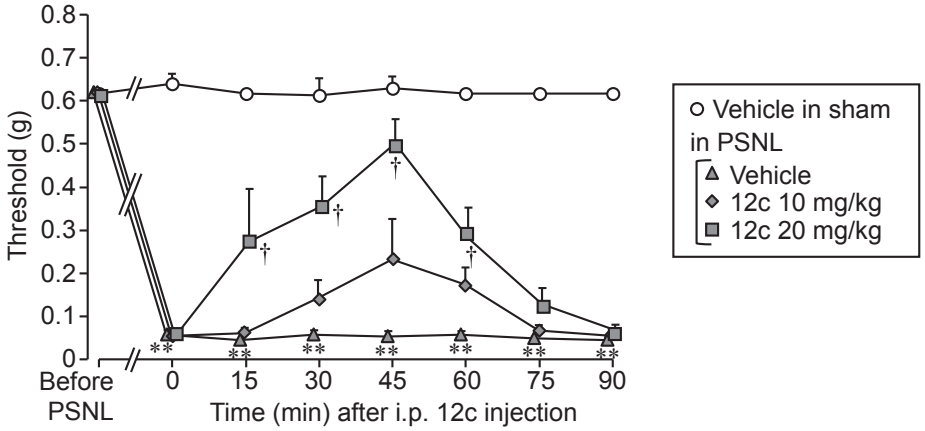


Fig. 6. 12c at 10 or 20 mg/kg or vehicle (V; 0.5% carboxymethyl cellulose) was administered i.p. to mice 7 days after partial sciatic nerve ligation (PSNL). Nociceptive threshold in the ipsilateral hindpaw was assessed by the von Frey test. Data show the mean with S.E.M. for 5 mice. $^{**}P < 0.01$ vs. vehicle in sham. $^{\dagger}P < 0.05$ vs. vehicle in PSNL.

J = 5.2 Hz), 5.18 (2H, s), 5.19 (2H, s), 5.22 (2H, s), 5.34 (1H, dd, J = 10.4, 1.2 Hz), 5.47 (1H, dd, J = 17.2, 1.2 Hz), 6.07 (1H, d, J = 2.4 Hz), 6.12 (1H, ddt, J = 17.2, 10.4, 5.2 Hz), 6.27 (1H, d, J = 2.4 Hz), 7.05 (1H, t, J = 8.0 Hz), 7.18 (1H, dd, J = 8.0, 1.2 Hz), 7.32 (1H, dd, J = 8.0, 1.2 Hz), 7.93 (1H, d, J = 15.6 Hz), 8.23 (1H, d, J = 15.6 Hz), 14.04 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.21, 56.35, 57.86, 69.73, 92.59, 93.94, 95.05, 96.60, 99.35, 107.11, 117.84, 118.97, 120.18, 124.29, 128.47, 130.54, 132.09, 137.13, 146.24, 150.26, 161.41, 163.45, 167.56, 192.81; IR (neat): 1653, 1624, 1617, 1577, 1570, 1565, 1559, 1480, 1461, 1262, 1223, 1210, 1155, 1083, 1030, 952 cm^{-1}; MS (EI): m/z 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1735.

4.1.2.11. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(2,6-bismethoxymethoxyphenyl)propenone ***(2k)***. Yield: 78% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.48 (6H, s), 3.49 (3H, s), 4.65 (2H, d, J = 4.8 Hz), 5.20 (1H, dd, J = 10.4, 1.2 Hz), 5.25 (6H, s), 5.39 (1H, dd, J = 17.2, 1.2 Hz), 6.02 (1H, ddt, J = 17.2, 10.4, 4.8 Hz), 6.06 (1H, d, J = 2.4 Hz), 6.27 (1H, d, J = 2.4 Hz), 6.85 (2H, d, J = 8.0 Hz), 7.23 (1H, t, J = 8.0 Hz), 8.26 (2H, d, J = 10.4 Hz), 14.02 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.27, 56.38, 69.68, 92.95, 94.01, 94.64, 96.66, 107.68, 108.12, 115.0, 117.61, 131.03, 132.41, 133.54, 157.74, 161.45, 163.16, 167.25, 194.48; IR (neat): 1623, 1595, 1577, 1573, 1558, 1472, 1334, 1202, 1152, 1100, 1083, 1037, 921 cm^{-1}; MS (EI): m/z 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1739.

4.1.2.12. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(3,4-bismethoxymethoxyphenyl)propenone ***(2l)***. Yield: 83% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.47 (3H, s), 3.51 (3H, s), 3.52 (3H, s), 4.60 (2H, d, J = 5.6 Hz), 5.18 (2H, s), 5.25 (2H, s), 5.26 (2H, s), 5.33 (1H, dd, J = 10.4, 1.2 Hz), 5.46 (1H, dd, J = 17.2, 1.2 Hz), 6.05 (1H, d, J = 2.4 Hz), 6.15 (1H, ddt, J = 17.2, 10.4, 5.6 Hz), 6.25 (1H, d, J = 2.4 Hz), 7.15 (1H, d, J = 8.4 Hz), 7.20 (1H, d, J = 8.4 Hz), 7.42 (1H, d, J = 1.6 Hz), 7.72 (1H, d, J = 16.4 Hz), 7.85 (1H, d, J = 16.4 Hz), 14.05 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.22, 56.29, 56.37, 69.80, 92.57, 93.98, 95.03, 95.36, 96.65, 107.11, 115.61, 115.97, 118.93, 124.02, 126.04, 129.84, 132.13, 142.31, 147.27, 149.06, 161.38, 163.39, 167.58, 192.66; IR (KBr): 1652, 1628, 1598, 1577, 1558, 1507, 1419, 1345, 1257, 1221, 1199, 1155, 1131, 1104, 1092, 1079, 1026, 1009, 997, 978 cm^{-1}; mp: 63–64 °C; MS (EI): m/z 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1718.

4.1.2.13. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(3,5-bismethoxymethoxyphenyl)propenone ***(2m)***. Yield: 87% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.49 (9H, s), 4.61 (2H, d, J = 5.2 Hz), 5.18 (4H, s), 5.20 (2H, s), 5.35 (1H, dd, J = 10.8, 1.2 Hz), 5.48 (1H, dd, J = 17.2, 1.2 Hz), 6.07 (1H, d, J = 2.4 Hz), 6.17 (1H, ddt, J = 17.2, 10.8, 5.2 Hz), 6.27 (1H, d, J = 2.4 Hz), 6.76 (1H, t, J = 2.4 Hz), 6.95 (2H, d, J = 2.4 Hz), 7.67 (1H, d, J = 15.2 Hz), 7.91 (1H, d, J = 15.2 Hz), 14.03 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.19, 56.54, 69.99, 92.73, 94.13, 94.54, 96.78, 106.83, 107.23, 109.71, 119.27, 128.31, 132.21, 137.57, 142.15, 158.59, 161.60, 163.74, 167.77, 192.86; IR (KBr): 1617, 1590, 1581, 1559, 1279, 1212, 1148, 1085, 1030, 948, 924 cm^{-1}; mp: 67–69 °C; MS (EI): m/z 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1739.

4.1.2.14. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(4-methoxyphenyl)propenone ***(2n)***. Yield: 41% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.48 (3H, s), 3.85 (3H, s), 4.61 (2H, d, J = 5.2 Hz), 5.19 (2H, s), 5.36 (1H, dd, J = 10.4, 1.2 Hz), 5.50 (1H, dd, J = 17.2, 1.2 Hz), 6.07 (1H, d, J = 2.4 Hz), 6.12 (1H, ddt, J = 17.2, 10.4, 5.2 Hz), 6.27 (1H, d, J = 2.4 Hz), 6.91 (2H, d, J = 8.4 Hz), 7.54 (2H, d, J = 8.4 Hz), 7.77 (1H, d, J = 15.2 Hz), 7.87 (1H, d, J = 15.2 Hz), 14.08 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 55.34, 56.40, 69.71, 92.63, 94.00, 96.70, 107.18, 114.25, 118.90, 125.24, 128.13, 130.16, 132.16, 142.41, 161.32, 161.38, 163.34, 167.53, 192.81; IR (KBr): 1624, 1589, 1564, 1560, 1512, 1421, 1346, 1288, 1256, 1225, 1177, 1151, 1103, 1080, 1022, 980, 949, 833, 825 cm^{-1}; mp: 57–59 °C; MS (EI): m/z 370 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_6$ 370.1416 (M^+); Found 370.1410.

4.1.2.15. 1-(2-Allyloxy-6-hydroxy-4-methoxymethoxyphenyl)-3-(4-chlorophenyl)propenone ***(2o)***. Yield: 77% in 2 steps; ^{1}H NMR (400 MHz $CDCl_3$) δ: 3.48 (3H, s), 4.59 (2H, d, J = 5.2 Hz), 5.19 (2H, s), 5.36 (1H, d, J = 10.0 Hz), 5.48 (1H, d, J = 17.4 Hz), 6.06 (1H, d, J = 2.4 Hz), 6.12 (1H, ddt, J = 17.4, 10.0, 5.2 Hz), 6.26 (1H, d, J = 2.4 Hz), 7.35 (2H, d, J = 8.4 Hz), 7.49 (2H, d, J = 8.4 Hz), 7.69 (1H, d, J = 16.0 Hz), 7.97 (1H, d, J = 16.0 Hz), 13.92 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 56.43, 69.75, 92.66, 94.01, 96.72, 107.07, 119.11, 128.17, 129.04, 129.48, 132.06, 133.90, 135.83, 140.63, 161.43, 163.59, 167.63, 192.57; IR (KBr): 1630, 1584, 1564, 1491, 1425, 1340, 1227, 1209, 1163, 1103, 1080, 1040, 1026, 978, 943, 926, 837, 822, 795 cm^{-1}; mp: 89–91 °C; MS (EI): m/z 374 (M^+); HRMS (EI) Calcd for $C_{20}H_{19}ClO_5$ 374.0921 (M^+); Found 374.0935.

4.1.3. General procedure for the synthesis of C-5-O-allyl ether flavanone intermediates ***3a–o***

To a stirred solution of **2a–o** (0.87 mmol) in EtOH (10 mL) and H_2O (1 mL) was added $NaOAc{\cdot}3H_2O$ (5.25 mmol), and the reaction mixture was reflexed for 24 h at 100 °C. After cooling, EtOH was evaporated, and then the aqueous mixture was extracted with CH_2Cl_2 (3 mL × 3). The organic extracts were combined, dried and evaporated to give an orange oil, which was chromatographed on SiO_2 (10 g, EtOAc/*n*-hexane = 1/10) to give the corresponding product **3a–o**.

4.1.3.1. 5-Allyloxy-2-phenylchroman-4-one ***(3a)***. Yield: 61%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.85 (1H, dd, J = 16.6, 2.9 Hz), 3.08 (1H, dd, J = 16.6, 13.2 Hz), 4.65 (2H, d, J = 4.8 Hz), 5.34 (1H, dd, J = 10.4, 1.2 Hz), 5.44 (1H, dd, J = 13.2, 2.9 Hz), 5.66 (1H, dd, J = 17.6, 1.2 Hz), 6.10 (1H, ddt, J = 17.6, 10.4, 4.8 Hz), 6.54 (1H, d, J = 8.8 Hz), 6.66 (1H, d, J = 8.8 Hz), 7.03–7.05 (6H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.95, 69.31, 78.86, 105.24, 110.14, 111.51, 117.47, 126.00, 128.55, 128.68, 132.24, 135.78, 138.64, 159.52, 163.02, 190.25; IR (KBr): 1680, 1603, 1570, 1474, 1456, 1450, 1379, 1333, 1263, 1231, 1124, 1072, 926, 783, 760, 733, 700 cm^{-1}; mp: 77–79 °C; MS (EI): m/z 280 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_3$ 280.1099 (M^+); Found 280.1110.

4.1.3.2. 5-Allyloxy-2-p-tolylchroman-4-one ***(3b)***. Yield: 55%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.38 (3H, s), 2.83 (1H, dd, J = 16.4, 3.2 Hz), 3.08 (1H, dd, J = 16.4, 13.0 Hz), 4.65 (2H, dt, J = 4.0, 1.6 Hz), 5.34 (1H, dd, J = 10.4, 1.6 Hz), 5.40 (1H, dd, J = 13.0, 3.2 Hz), 5.66 (1H, dd, J = 17.0, 1.6 Hz), 6.10 (1H, ddt, J = 17.0, 10.4, 4.0 Hz), 6.53 (1H, d, J = 7.2 Hz), 6.65 (1H, d, J = 7.2 Hz), 7.23 (2H, d, J = 8.0 Hz), 7.24 (1H, t, J = 7.2 Hz), 7.38 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 21.15, 45.89, 69.36, 78.86, 105.21, 110.23, 111.55, 117.51, 126.09, 129.37, 132.31, 135.69, 135.77, 138.52, 159.56, 163.17, 190.54; IR (KBr): 1686, 1597, 1574, 1472, 1454, 1325, 1256, 1225, 1119, 1065, 1042, 932, 893, 826, 791 cm^{-1}; mp: 85–87 °C; MS (EI): m/z 294 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_3$ 294.1256 (M^+); Found 294.1266.

4.1.3.3. 5-Allyloxy-2-(2-methoxymethoxyphenyl)chroman-4-one ***(3c)***. Yield: 45%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.91 (2H, d, J = 7.6 Hz), 3.34 (3H, s), 4.63 (2H, d, J = 4.0 Hz), 5.18 (2H, s), 5.32 (1H, d, J = 10.8 Hz), 5.66 (1H, d, J = 17.2 Hz), 5.80 (1H, t, J = 7.6 Hz), 6.07 (1H, ddt, J = 17.2, 10.8, 4.0 Hz), 6.51 (1H, d, J = 8.4 Hz), 6.65 (1H, d, J = 8.4 Hz), 7.07 (1H, t, J = 7.6 Hz), 7.12 (1H, d, J = 7.6 Hz), 7.28 (1H, t, J = 7.6 Hz), 7.35 (1H, t, J = 8.4 Hz), 7.60 (1H, d, J = 7.6 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.31, 56.20, 69.36, 74.12, 94.24, 105.18, 110.26, 111.89, 113.79, 117.48, 121.97, 126.35, 128.00, 129.31, 132.32, 135.70, 153.45, 159.68, 163.62, 191.04; IR (neat):

1694, 1684, 1602, 1575, 1558, 1507, 1490, 1472, 1457, 1259, 1153, 1078, 992 cm^{-1}; MS (EI): *m/z* 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1315.

4.1.3.4. 5-Allyloxy-2-(4-methoxyphenyl)chroman-4-one ***(3d)***. Yield: 32%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.82 (1H, dd, *J* = 16.4, 2.8 Hz), 3.08 (1H, dd, *J* = 16.4, 13.0 Hz), 3.83 (3H, s), 4.65 (2H, dt, *J* = 4.8, 1.6 Hz), 5.34 (1H, dd, *J* = 9.2, 1.6 Hz), 5.38 (1H, dd, *J* = 13.2, 2.8 Hz), 5.66 (1H, dd, *J* = 16.8, 1.6 Hz), 6.09 (1H, ddt, *J* = 16.8, 9.2, 4.8 Hz), 6.52 (1H, d, *J* = 8.4 Hz), 6.63 (1H, d, *J* = 8.4 Hz), 6.95 (2H, d, *J* = 8.4 Hz), 7.36 (1H, t, *J* = 8.4 Hz), 7.39 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.89, 55.33, 69.36, 78.72, 105.26, 110.26, 111.59, 114.12, 117.57, 127.67, 130.75, 132.35, 135.80, 159.62, 159.88, 163.22, 190.65; IR (KBr): 1684, 1603, 1576, 1558, 1516, 1472, 1456, 1256, 1231, 1175, 1123, 1082, 1073, 1030, 833, 775 cm^{-1}; mp: 74–76 °C; MS (EI): *m/z* 310 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_4$ 310.1205 (M^+); Found 310.1199.

4.1.3.5. 5-Allyloxy-2-(4-ethoxyphenyl)chroman-4-one ***(3e)***. Yield: 45%; ^1H NMR (400 MHz $CDCl_3$) δ: 1.42 (3H, t, *J* = 7.0 Hz), 2.81 (1H, dd, *J* = 16.4, 3.0 Hz), 3.08 (1H, dd, *J* = 16.4, 13.4 Hz), 4.05 (2H, q, *J* = 7.0 Hz), 4.64 (2H, d, *J* = 4.0 Hz), 5.34 (1H, dd, *J* = 10.4, 1.4 Hz), 5.37 (1H, dd, *J* = 13.4, 3.0 Hz), 5.66 (1H, dd, *J* = 17.0, 1.4 Hz), 6.09 (1H, ddt, *J* = 17.0, 10.4, 4.0 Hz), 6.52 (1H, d, *J* = 8.2 Hz), 6.63 (1H, d, *J* = 8.2 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 7.36 (1H, t, *J* = 8.2 Hz), 7.38 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 14.74, 45.81, 63.48, 69.38, 78.72, 105.21, 110.24, 111.57, 114.61, 117.51, 127.62, 130.54, 132.33, 135.75, 159.22, 159.58, 163.21, 190.62; IR (KBr): 1678, 1605, 1583, 1574, 1516, 1472, 1454, 1423, 1340, 1263, 1245, 1232, 1196, 1086, 1051, 824 cm^{-1}; mp: 85–87 °C; MS (EI): *m/z* 324 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_4$ 324.1362 (M^+); Found 324.1367.

4.1.3.6. 5-Allyloxy-2-(4-chlorophenyl)chroman-4-one ***(3f)***. Yield: 58%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.84 (1H, dd, *J* = 16.4, 2.8 Hz), 3.02 (1H, dd, *J* = 16.4, 13.0 Hz), 4.65 (2H, d, *J* = 4.0 Hz), 5.34 (1H, dd, *J* = 10.6, 1.6 Hz), 5.42 (1H, dd, *J* = 13.0, 2.8 Hz), 5.65 (1H, dd, *J* = 17.0, 1.6 Hz), 6.08 (1H, ddt, *J* = 17.0, 10.6, 4.0 Hz), 6.54 (1H, d, *J* = 8.0 Hz), 6.65 (1H, d, *J* = 8.0 Hz), 7.26–7.44 (5H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.77, 69.26, 78.01, 105.36, 110.01, 111.39, 117.46, 127.34, 128.79, 132.15, 134.24, 135.82, 137.17, 159.46, 162.70, 189.69; IR (KBr): 1732, 1676, 1601, 1574, 1491, 1472, 1458, 1329, 1279, 1259, 1252, 1225, 1121, 1078, 1015, 839, 787 cm^{-1}; mp: 71–73 °C; MS (EI): *m/z* 314 (M^+); HRMS (EI) Calcd for $C_{18}H_{15}ClO_3$ 314.0710 (M^+); Found 314.0715.

4.1.3.7. 5-Allyloxy-7-methoxymethoxy-2-phenylchroman-4-one ***(3g)***. Yield: 54%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.80 (1H, dd, *J* = 16.4, 3.0 Hz), 3.02 (1H, dd, *J* = 16.4, 13.2 Hz), 3.48 (3H, s), 4.65 (2H, dd, *J* = 6.0, 1.2 Hz), 5.18 (2H, s), 5.35 (1H, dd, *J* = 11.2, 1.2 Hz), 5.41 (1H, dd, *J* = 13.2, 3.0 Hz), 5.67 (1H, dd, *J* = 17.2, 1.2 Hz), 6.08 (1H, ddt, *J* = 17.2, 11.2, 6.0 Hz), 6.20 (1H, d, *J* = 2.0 Hz), 6.34 (1H, d, *J* = 2.0 Hz), 7.30–7.48 (5H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.73, 56.42, 69.40, 79.14, 94.07, 95.14, 96.25, 106.79, 117.69, 126.06, 128.60, 128.73, 132.12, 138.77, 161.11, 163.33, 164.60, 189.07; IR (KBr): 1674, 1611, 1572, 1456, 1435, 1261, 1248, 1221, 1209, 1148, 1124, 1105, 1084, 1055, 1034, 989 cm^{-1}; mp: 100–102 °C; MS (EI): *m/z* 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1327.

4.1.3.8. 5-Allyloxy-7-methoxymethoxy-2-(2-methoxymethoxy-phenyl)chroman-4-one ***(3h)***. Yield: 55%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.67 (2H, d, *J* = 7.2 Hz), 3.45 (3H, s), 3.48 (3H, s), 4.62 (2H, dd, *J* = 4.8, 1.6 Hz), 5.18 (2H, s), 5.19 (2H, s), 5.35 (1H, dd, *J* = 10.8, 1.6 Hz), 5.69 (1H, dd, *J* = 17.2, 1.6 Hz), 5.80 (1H, t, *J* = 7.2 Hz), 6.09 (1H, ddt, *J* = 17.2, 10.8, 4.8 Hz), 6.20 (1H, d, *J* = 2.4 Hz), 6.45(1H, d, *J* = 2.4 Hz), 7.09 (1H, t, *J* = 8.0 Hz), 7.13 (1H, d, *J* = 8.0 Hz), 7.30 (1H, td, *J* = 8.0, 2.0 Hz), 7.61 (1H, dd, *J* = 8.0, 2.0 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.00, 56.18, 56.36, 69.30, 74.26, 94.01, 94.18, 94.97, 96.23, 106.83, 113.07, 117.55, 121.91, 126.27, 128.00, 129.22, 132.09, 153.38, 161.13, 163.19, 165.05, 189.74; IR (KBr): 1683, 1669, 1608, 1576, 1559, 1490, 1458, 1437, 1355, 1257, 1251, 1233, 1215, 1153, 1126, 1111, 1053, 1046, 1035, 998, 993, 950, 925, 917, 826, 754 cm^{-1}; mp: 80–82 °C; MS (EI): *m/z* 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

4.1.3.9. 5-Allyloxy-7-methoxymethoxy-2-(3-methoxymethoxy-phenyl)chroman-4-one ***(3i)***. Yield: 56%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.79 (1H, dd, *J* = 17.2, 2.4 Hz), 3.00 (1H, dd, *J* = 17.2, 12.8 Hz), 3.48 (3H, s), 3.49 (3H, s), 4.61 (2H, d, *J* = 4.8 Hz), 5.17 (2H, d, *J* = 1.2 Hz), 5.20 (2H, d, *J* = 1.2 Hz), 5.34 (1H, dd, *J* = 10.4, 1.6 Hz), 5.37 (1H, dd, *J* = 12.8, 2.4 Hz), 5.66 (1H, dd, *J* = 17.2, 1.6 Hz), 6.07 (1H, ddt, *J* = 17.2, 10.4, 4.8 Hz), 6.19 (1H, d, *J* = 2.4 Hz), 6.34 (1H, d, *J* = 2.4 Hz), 7.04 (1H, dd, *J* = 8.0, 2.0 Hz), 7.08 (1H, d, *J* = 8.0 Hz), 7.13 (1H, t, *J* = 2.0 Hz), 7.33 (1H, t, *J* = 8.0 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.65, 55.96, 56.33, 69.32, 78.84, 93.99, 94.31, 95.09, 96.21, 106.70, 114.01, 116.11, 117.60, 119.34, 129.77, 132.06, 140.30, 157.46, 161.01, 163.25, 164.46, 188.90; IR (neat): 1683, 1680, 1608, 1573, 1436, 1259, 1211, 1150, 1124, 1107, 1083, 1055, 1031, 994 cm^{-1}; MS (EI): *m/z* 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

4.1.3.10. 5-Allyloxy-2-(3,4-bismethoxymethoxyphenyl)-7-methoxymethoxychroman-4-one ***(3j)***. Yield: 40%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.86 (1H, d, *J* = 3.2 Hz), 2.90 (1H, d, *J* = 12.8 Hz), 3.46 (3H, s), 3.47 (3H, s), 3.48 (3H, s), 4.60 (2H, d, *J* = 5.2 Hz), 5.12 (2H, s), 5.15 (2H, s), 5.18 (2H, s), 5.33 (1H, dd, *J* = 10.4, 1.6 Hz), 5.66 (1H, dd, *J* = 17.2, 1.6 Hz), 5.83 (1H, dd, *J* = 12.8, 3.2 Hz), 6.07 (1H, ddt, *J* = 17.2, 10.4, 5.2 Hz), 6.18 (1H, d, *J* = 2.4 Hz), 6.30 (1H, d, *J* = 2.4 Hz), 7.11 (1H, t, *J* = 8.0 Hz), 7.14 (1H, d, *J* = 8.0 Hz), 7.27 (1H, t, *J* = 8.0 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.10, 56.23, 56.37, 57.60, 69.38, 74.23, 94.03, 94.98, 95.07, 96.22, 99.26, 106.74, 116.38, 117.64, 119.73, 124.75, 132.14, 133.39, 143.91, 149.46, 161.09, 163.16, 164.84, 189.44; IR (neat): 1684, 1680, 1608, 1570, 1562, 1476, 1437, 1260, 1152, 1126, 1108, 1085, 1070, 1038, 1020, 959, 928 cm^{-1}; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1743.

4.1.3.11. 5-Allyloxy-2-(2,6-bismethoxymethoxyphenyl)-7-methoxymethoxychroman-4-one ***(3k)***. Yield: 27%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.54 (1H, dd, *J* = 17.2, 3.2 Hz), 3.44 (6H, s), 3.45 (3H, s), 3.82 (1H, dd, *J* = 17.2, 14.0 Hz), 4.62 (2H, d, *J* = 6.4 Hz), 5.14 (2H, d, *J* = 3.2 Hz), 5.17 (4H, s), 5.33 (1H, dd, *J* = 10.4, 1.2 Hz), 5.68 (1H, dd, *J* = 17.2, 1.2 Hz), 6.08 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.09 (1H, dd, *J* = 14.0, 3.2 Hz), 6.17 (1H, d, *J* = 2.4 Hz), 6.23 (1H, d, *J* = 2.4 Hz), 6.82 (2H, d, *J* = 8.4 Hz), 7.23 (1H, t, *J* = 8.4 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 42.12, 56.25, 56.34, 69.32, 71.66, 93.99, 94.55, 96.01, 106.80, 108.56, 115.63, 117.54, 130.41, 132.22, 156.56, 161.23, 162.96, 165.66, 190.86; IR (KBr): 1683, 1669, 1616, 1601, 1576, 1472, 1265, 1246, 1153, 1107, 1098, 1087, 1047, 1035, 919 cm^{-1}; mp: 79–81 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1718.

4.1.3.12. 5-Allyloxy-2-(3,4-bismethoxymethoxyphenyl)-7-methoxymethoxychroman-4-one ***(3l)***. Yield: 43%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.77 (1H, dd, *J* = 17.2, 3.2 Hz), 3.07 (1H, dd, *J* = 17.2, 13.6 Hz), 3.33 (2H, d, *J* = 6.0 Hz), 3.43 (3H, s), 3.50 (3H, s), 3.51 (3H, s), 4.94 (1H, dd, *J* = 10.4, 2.0 Hz), 4.99 (1H, dd, *J* = 17.2, 2.0 Hz), 5.18 (2H, d, *J* = 3.2 Hz), 5.23 (2H, s), 5.24 (2H, d, *J* = 3.2 Hz), 5.32 (1H, dd, *J* = 13.6, 3.2 Hz), 5.92 (1H, ddt, *J* = 17.2, 10.4, 6.0 Hz), 6.27 (1H, s), 7.02 (1H, dd, *J* = 8.4, 2.0 Hz), 7.18 (1H, d, *J* = 8.4 Hz), 7.24 (1H, d, *J* = 2.0 Hz), 12.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.16, 43.36, 56.17, 56.25, 56.36, 78.93, 93.42, 93.74, 95.26, 95.44, 103.34, 108.74, 114.23, 114.73, 116.57, 120.30, 132.52, 136.07, 147.40, 147.53,

160.68, 161.21, 162.87, 196.17; IR (KBr): 1653, 1636, 1577, 1559, 1521, 1516, 1507, 1433, 1261, 1157, 1130, 1091, 1076, 1057, 993, 962, 923 cm^{-1}; mp: 79–80 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1728.

*4.1.3.13. 5-Allyloxy-2-(3,5-bismethoxymethoxyphenyl)-7-methoxymethoxychroman-4-one (**3m**)*. Yield: 53%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.77 (1H, dd, *J* = 17.2, 2.4 Hz), 2.98 (1H, dd, *J* = 17.2, 13.6 Hz), 3.48 (9H, s), 4.62 (2H, d, *J* = 5.2 Hz), 5.18 (6H, s), 5.32 (1H, dd, *J* = 17.2, 2.4 Hz), 5.35 (1H, dd, *J* = 10.4, 1.2 Hz), 5.66 (1H, dd, *J* = 13.6, 1.6 Hz), 6.09 (1H, ddt, *J* = 17.2, 10.4, 5.2 Hz), 6.19 (1H, d, *J* = 2.4 Hz), 6.34 (1H, d, *J* = 2.4 Hz), 6.74 (1H, t, *J* = 2.4 Hz), 6.80 (2H, d, *J* = 2.4 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.70, 56.07, 56.38, 69.37, 78.88, 94.13, 94.54, 95.15, 96.27, 104.60, 106.73, 107.36, 117.65, 132.09, 141.13, 158.51, 161.04, 163.28, 164.44, 188.90; IR (neat): 1685, 1680, 1676, 1609, 1570, 1437, 1260, 1237, 1148, 1125, 1105, 1085, 1057, 1035, 924 cm^{-1}; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1739.

*4.1.3.14. 5-Allyloxy-7-methoxymethoxy-2-(4-methoxyphenyl)-chroman-4-one (**3n**)*. Yield: 28%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.76 (1H, dd, *J* = 16.8, 2.6 Hz), 3.03 (1H, dd, *J* = 16.8, 13.2 Hz), 3.47 (3H, s), 3.83 (3H, s), 4.60 (2H, dd, *J* = 5.2, 1.2 Hz), 5.17 (2H, d, *J* = 1.6 Hz), 5.34 (1H, dd, *J* = 9.2, 1.2 Hz), 5.38 (1H, dd, *J* = 13.2, 2.6 Hz), 5.67 (1H, dd, *J* = 17.2, 1.2 Hz), 6.07 (1H, ddt, *J* = 17.2, 9.2, 5.2 Hz), 6.19 (1H, d, *J* = 2.4 Hz), 6.31 (1H, d, *J* = 2.4 Hz), 6.94 (2H, d, *J* = 6.8 Hz), 7.38 (2H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.48, 55.27, 56.36, 69.34, 78.84, 94.01, 95.01, 96.20, 106.72, 114.02, 117.62, 127.61, 130.73, 132.10, 159.78, 161.05, 163.25, 164.64, 189.29; IR (KBr): 1672, 1611, 1587, 1572, 1516, 1437, 1421, 1337, 1271, 1254, 1227, 1207, 1180, 1157, 1146, 1111, 1087, 1065, 1034, 947, 835 cm^{-1}; mp: 95–97 °C; MS (EI): *m/z* 370 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_6$ 370.1416 (M^+); Found 370.1400.

*4.1.3.15. 5-Allyloxy-2-(4-chlorophenyl)-7-methoxymethox-ychroman-4-one (**3o**)*. Yield: 48%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.77 (1H, dd, *J* = 16.4, 2.8 Hz), 2.95 (1H, dd, *J* = 16.4, 13.0 Hz), 3.47 (3H, s), 4.60 (2H, dd, *J* = 4.8, 1.2 Hz), 5.18 (2H, d, *J* = 1.2 Hz), 5.34 (1H, dd, *J* = 9.2, 1.2 Hz), 5.38 (1H, dd, *J* = 13.0, 2.8 Hz), 5.65 (1H, dd, *J* = 16.8, 1.2 Hz), 6.07 (1H, ddt, *J* = 16.8, 9.2, 4.8 Hz), 6.19 (1H, d, *J* = 2.4 Hz), 6.31 (1H, d, *J* = 2.4 Hz), 7.35–7.42 (4H, br); ^{13}C NMR (100 MHz $CDCl_3$) δ: 45.60, 56.42, 69.40, 78.31, 94.05, 95.23, 96.19, 106.70, 117.71, 127.39, 128.88, 132.04, 134.33, 137.27, 161.10, 163.38, 164.30, 188.56; IR (KBr): 1680, 1608, 1570, 1495, 1437, 1423, 1337, 1269, 1223, 1207, 1149, 1109, 1086, 1063, 1032, 1015, 936, 814 cm^{-1}; mp: 90–92 °C; MS (EI): *m/z* 374 (M^+); HRMS (EI) Calcd for $C_{20}H_{19}ClO_5$ 374.0921 (M^+); Found 374.0937.

*4.1.4. General procedure for the synthesis of C-6 allylated flavanone intermediates **4a–o***

To a stirred solution of **3a–o** (0.69 mmol) in $ClCH_2CH_2Cl$ (5 mL) was added $Eu(fod)_3$ (0.07 mmol) under argon atmosphere, and the resulting solution was heated at 100 °C in a sealed tube for 12 h. After cooling, the solvent was evaporated and the residue was chromatographed on SiO_2 (10 g, acetone/*n*-hexane = 1/10) to give the corresponding product **4a–o**.

*4.1.4.1. 6-Allyl-5-hydroxy-2-phenylchroman-4-one (**4a**)*. Yield: 92%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.89 (1H, dd, *J* = 17.2, 3.0 Hz), 3.14 (1H, dd, *J* = 17.2, 13.2 Hz), 3.34 (2H, d, *J* = 6.4 Hz), 5.07 (1H, d, *J* = 10.4 Hz), 5.08 (1H, d, *J* = 17.2 Hz), 5.44 (1H, dd, *J* = 13.2, 3.0 Hz), 5.97 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.49 (1H, d, *J* = 8.8 Hz), 7.28 (1H, d, *J* = 8.8 Hz), 7.39–7.50 (5H, m), 11.98 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 32.60, 43.93, 79.06, 106.98, 107.76, 115.72, 120.28, 126.09, 128.85, 136.31, 138.37, 138.71, 159.45, 159.82, 198.19; IR (KBr): 1636, 1583, 1498, 1474, 1456, 1427, 1364, 1340, 1261, 1232, 1103, 1061, 1005, 924, 820, 779, 752, 700 cm^{-1}; mp: 90–92 °C; MS (EI): *m/z* 280 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_3$ 280.1099 (M^+); Found 280.1112.

*4.1.4.2. 6-Allyl-5-hydroxy-2-p-tolylchroman-4-one (**4b**)*. Yield: 95%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.38 (3H, s), 2.86 (1H, dd, *J* = 17.2, 2.8 Hz), 3.14 (1H, dd, *J* = 17.2, 13.0 Hz), 3.34 (2H, d, *J* = 6.8 Hz), 5.07 (1H, d, *J* = 10.4 Hz), 5.08 (1H, d, *J* = 17.2 Hz), 5.41 (1H, dd, *J* = 13.0, 2.8 Hz), 5.97 (1H, ddt, *J* = 17.2, 10.4, 6.8 Hz), 6.47 (1H, d, *J* = 8.8 Hz), 7.23 (1H, d, *J* = 8.8 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 11.99 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 21.18, 32.58, 43.81, 78.97, 106.97, 107.73, 115.68, 120.13, 126.12, 129.48, 135.36, 136.32, 138.65, 138.78, 159.43, 159.89, 198.37; IR (KBr): 1641, 1583, 1517, 1481, 1474, 1441, 1373, 1339, 1263, 1238, 1117, 1063, 999, 912, 814 cm^{-1}; mp: 75–77 °C; MS (EI): *m/z* 294 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_3$ 294.1256 (M^+); Found 294.1244.

*4.1.4.3. 6-Allyl-5-hydroxy-2-(2-methoxymethoxyphenyl)chroman-4-one (**4c**)*. Yield: 87%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.96 (1H, d, *J* = 4.8 Hz), 2.98 (1H, d, *J* = 12.4 Hz), 3.33 (2H, d, *J* = 6.0 Hz), 3.45 (3H, s), 5.05 (1H, dd, *J* = 10.0, 1.6 Hz), 5.07 (1H, dd, *J* = 17.2, 1.6 Hz), 5.20 (2H, d, *J* = 3.2 Hz), 5.80 (1H, dd, *J* = 12.4, 4.8 Hz), 5.96 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.47 (1H, d, *J* = 8.4 Hz), 7.09 (1H, t, *J* = 7.2 Hz), 7.14 (1H, d, *J* = 7.2 Hz), 7.26 (1H, d, *J* = 8.4 Hz), 7.31 (1H, td, *J* = 7.2, 1.2 Hz), 7.61 (1H, dd, *J* = 7.2, 1.2 Hz), 12.03 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 32.61, 43.12, 56.23, 74.23, 94.30, 106.95, 107.81, 113.92, 115.56, 120.09, 122.07, 126.47, 127.66, 129.54, 136.36, 138.55, 153.49, 159.50, 160.28, 198.88; IR (neat): 1651, 1644, 1639, 1634, 1494, 1455, 1442, 1435, 1362, 1234, 1154, 1080, 1061, 995, 755 cm^{-1}; MS (EI): *m/z* 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1327.

*4.1.4.4. 6-Allyl-5-hydroxy-2-(4-methoxyphenyl)chroman-4-one (**4d**)*. Yield: 89%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.85 (1H, dd, *J* = 17.0, 2.8 Hz), 3.15 (1H, dd, *J* = 17.0, 13.2 Hz), 3.35 (2H, d, *J* = 6.8 Hz), 3.84 (3H, s), 5.07 (1H, d, *J* = 8.8 Hz), 5.08 (1H, d, *J* = 17.8 Hz), 5.39 (1H, dd, *J* = 13.2, 2.8 Hz), 597 (1H, ddt, *J* = 17.8, 8.8, 6.8 Hz), 6.47 (1H, d, *J* = 8.4 Hz), 6.96 (2H, d, *J* = 7.8 Hz), 7.27 (1H, d, *J* = 8.4 Hz), 7.40 (2H, d, *J* = 7.8 Hz), 12.00 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 32.59, 43.75, 55.35, 78.83, 106.98, 107.74, 114.19, 115.68, 120.15, 127.69, 130.38, 136.33, 138.68, 159.45, 159.93, 160.01, 198.46; IR (neat): 1683, 1670, 1647, 1616, 1603, 1516, 1472, 1456, 1256, 1231, 1121, 1069, 1032 cm^{-1}; MS (EI): *m/z* 310 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_4$ 310.1205 (M^+); Found 310.1198.

*4.1.4.5. 6-Allyl-2-(4-ethoxyphenyl)-5-hydroxychroman-4-one (**4e**)*. Yield: 83%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.41 (3H, t, *J* = 7.0 Hz), 2.83 (1H, dd, *J* = 17.2, 2.6 Hz), 3.13 (1H, dd, *J* = 17.2, 13.0 Hz), 3.32 (2H, d, *J* = 6.8 Hz), 4.04 (2H, q, *J* = 7.0 Hz), 5.05 (1H, d, *J* = 9.6 Hz), 5.06 (1H, d, *J* = 17.2 Hz), 5.36 (1H, dd, *J* = 13.0, 2.6 Hz), 597 (1H, ddt, *J* = 17.2, 9.6, 6.8 Hz), 6.44 (1H, d, *J* = 8.2 Hz), 6.92 (2H, d, *J* = 8.8 Hz), 7.27 (1H, d, *J* = 8.2 Hz), 7.36 (2H, d, *J* = 8.8 Hz), 11.98 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 14.76, 32.56, 43.75, 63.54, 78.87, 106.98, 107.75, 114.72, 115.67, 120.13, 127.69, 130.19, 136.34, 138.66, 159.39, 159.45, 159.95, 198.49; IR (KBr): 1636, 1614, 1585, 1520, 1515, 1473, 1456, 1429, 1396, 1362, 1340, 1302, 1263, 1256, 1234, 1188, 1177, 1119, 1059, 1045, 993, 839, 820, 772 cm^{-1}; mp: 99–101 °C; MS (EI): *m/z* 324 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_4$ 324.1362 (M^+); Found 324.1377.

*4.1.4.6. 6-Allyl-2-(4-chlorophenyl)-5-hydroxychroman-4-one (**4f**)*. Yield: 90%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.87 (1H, dt, *J* = 17.0, 2.0 Hz), 3.07 (1H, ddd, *J* = 17.0, 13.0 Hz), 3.33 (2H, d, *J* = 6.0 Hz), 5.07 (1H, d, *J* = 10.4 Hz), 5.08 (1H, d, *J* = 16.8 Hz), 5.41 (1H, dt, *J* = 13.0, 2.0 Hz), 5.95 (1H, ddt, *J* = 16.8, 10.4, 6.0 Hz), 6.47 (1H, dd, *J* = 8.0 Hz), 7.28 (1H, d, *J* = 8.0 Hz), 7.40 (4H, d, *J* = 2.8 Hz), 11.94 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 32.59, 43.86, 78.28, 106.94, 107.70, 115.79, 120.54, 127.45, 129.05, 134.67, 136.23, 136.90, 138.78, 159.48, 159.51, 197.74; IR (KBr): 1635, 1585, 1491, 1445, 1429, 1362, 1338,

1304, 1261, 1238, 1190, 1168, 1107, 1079, 1062, 1056, 1015, 993, 906, 897, 831, 789 cm^{-1}; mp: 75–77 °C; MS (EI): *m/z* 314 (M^+); HRMS (EI) Calcd for $C_{18}H_{15}ClO_3$ 314.0710 (M^+); Found 314.0715.

4.1.4.7. 6-Allyl-5-hydroxy-7-methoxymethoxy-2-phenylchroman-4-one ***(4g)***. Yield: 96%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.83 (1H, dd, *J* = 17.2, 3.0 Hz), 3.09 (1H, dd, *J* = 17.2, 13.6 Hz), 3.36 (2H, d, *J* = 6.0 Hz), 3.46 (3H, s), 4.97 (1H, dd, *J* = 10.2, 1.6 Hz), 5.03 (1H, dd, *J* = 17.2, 1.6 Hz), 5.21 (2H, d, *J* = 2.8 Hz), 5.42 (1H, dd, *J* = 13.6, 3.0 Hz), 6.08 (1H, ddt, *J* = 17.2, 10.2, 6.0 Hz), 6.31 (1H, s), 7.37–7.48 (5H, m), 12.13(1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.21, 43.52, 56.41, 79.24, 93.45, 93.81, 103.41, 108.85, 114.31, 126.08, 128.83, 136.09, 138.40, 160.75, 161.28, 162.95, 196.14; IR (KBr): 1636, 1576, 1448, 1439, 1300, 1283, 1213, 1155, 1103, 1090, 1059, 964 cm^{-1}; mp: 101–103 °C; MS (EI): *m/z* 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1305.

4.1.4.8. 6-Allyl-5-hydroxy-7-methoxymethoxy-2-(2-methoxy-methoxyphe nyl)chroman-4-one ***(4h)***. Yield: 97%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.92 (1H, d, *J* = 4.4 Hz), 2.94 (1H, d, *J* = 12.4 Hz), 3.36 (2H, d, *J* = 6.0 Hz), 3.46 (3H, s), 3.47 (3H, s), 4.97 (1H, dd, *J* = 10.0, 1.6 Hz), 5.02 (1H, dd, *J* = 17.2, 1.6 Hz), 5.22 (4H, s), 5.78 (1H, dd, *J* = 12.4, 4.4 Hz), 5.95 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.32 (1H, s), 7.10 (1H, t, *J* = 8.0 Hz), 7.15 (1H, d, *J* = 8.0 Hz), 7.32 (1H, t, *J* = 8.0 Hz), 7.61 (1H, d, *J* = 8.0 Hz), 12.19 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.18, 42.72, 56.20, 56.37, 74.36, 93.38, 93.76, 94.25, 103.40, 108.63, 113.83, 114.24, 122.02, 126.41, 127.67, 129.45, 136.10, 153.42, 160.77, 161.69, 162.79, 196.86; IR (KBr): 1644, 1578, 1506, 1497, 1448, 1437, 1311, 1292, 1285, 1240, 1223, 1155, 1128, 1083, 1049, 997, 960, 913, 763 cm^{-1}; mp: 114–115 °C; MS (EI): *m/z* 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

4.1.4.9. 6-Allyl-5-hydroxy-7-methoxymethoxy-2-(3-methoxy-methoxyphe nyl)chroman-4-one ***(4i)***. Yield: 98%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.91 (1H, dd, *J* = 17.2, 2.4 Hz), 3.16 (1H, dd, *J* = 17.2, 13.6 Hz), 3.37 (2H, d, *J* = 6.4 Hz), 3.47 (3H, s), 3.49 (3H, s), 4.97 (1H, dd, *J* = 10.4, 1.2 Hz), 5.03 (1H, dd, *J* = 17.2, 1.2 Hz), 5.21 (2H, d, *J* = 1.2 Hz), 5.22 (2H, d, *J* = 2.4 Hz), 5.42 (1H, dd, *J* = 13.6, 2.4 Hz), 5.95 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.33 (1H, s), 7.06 (1H, dd, *J* = 8.0, 2.0 Hz), 7.09 (1H, d, *J* = 8.0 Hz), 7.15 (1H, s), 7.34 (1H, t, *J* = 8.0 Hz), 12.31 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.23, 43.85, 56.05, 56.40, 79.15, 93.49, 93.81, 94.39, 103.22, 108.88, 114.08, 114.30, 116.40, 119.41, 129.93, 136.08, 140.01, 157.58, 160.93, 161.31, 163.04, 196.67; IR (KBr): 1635, 1576, 1558, 1486, 1440, 1297, 1287, 1221, 1155, 1127, 1093, 1078, 1055, 1033, 966, 926 cm^{-1}; mp: 79–81 °C; MS (EI): *m/z* 400 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_7$ 400.1522 (M^+); Found 400.1529.

4.1.4.10. 6-Allyl-2-(2,3-bismethoxymethoxyphenyl)-5-hydroxy-7-methoxy methoxychroman-4-one ***(4j)***. Yield: 87%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.94 (1H, d, *J* = 3.6 Hz), 2.97 (1H, d, *J* = 12.8 Hz), 3.36 (2H, d, *J* = 6.0 Hz), 3.45 (3H, s), 3.50 (3H, s), 3.51 (3H, s), 4.97 (1H, dd, *J* = 10.4, 1.6 Hz), 5.04 (1H, dd, *J* = 17.2, 1.6 Hz), 5.15 (2H, s), 5.20 (2H, s), 5.21 (2H, s), 5.85 (1H, dd, *J* = 12.8, 3.6 Hz), 5.95 (1H, ddt, *J* = 17.2, 10.4, 6.0 Hz), 6.30 (1H, s), 7.14 (1H, t, *J* = 7.2 Hz), 7.16 (1H, d, *J* = 7.2 Hz), 7.27 (1H, dd, *J* = 7.2, 2.0 Hz), 12.18 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.21, 42.88, 56.28, 56.36, 57.57, 74.43, 93.39, 93.77, 95.07, 99.34, 103.34, 108.68, 114.29, 116.48, 119.68, 124.87, 133.08, 136.11, 143.90, 149.48, 160.75, 161.56, 162.78, 196.62; IR (KBr): 1653, 1640, 1577, 1477, 1448, 1438, 1296, 1287, 1275, 1219, 1156, 1128, 1089, 1060, 1040, 998, 962, 923 cm^{-1}; mp: 88–89 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1728.

4.1.4.11. 6-Allyl-2-(2,6-bismethoxymethoxyphenyl)-5-hydroxy-7-methoxy methoxychroman-4-one ***(4k)***. Yield: 80%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.59 (1H, dd, *J* = 17.2, 3.2 Hz), 3.36 (2H, d, *J* = 6.4 Hz), 3.45 (3H, s), 3.48 (6H, s), 3.92 (1H, dd, *J* = 17.2, 14.0 Hz), 4.97 (1H, d, *J* = 10.0 Hz), 5.04 (1H, dd, *J* = 17.2, 1.2 Hz), 5.20 (6H, s), 5.95 (1H, ddt, *J* = 17.2, 10.0, 6.4 Hz), 6.10 (1H, dd, *J* = 14.0, 3.2 Hz), 6.21 (1H, s), 6.85 (2H, d, *J* = 8.4 Hz), 7.26 (1H, t, *J* = 8.4 Hz), 12.32 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.22, 39.90, 56.34, 56.40, 71.63, 93.08, 93.77, 94.66, 108.20, 108.62, 114.26, 115.26, 130.71, 136.28, 156.66, 160.88, 162.40, 162.63, 197.99; IR (KBr): 1653, 1635, 1601, 1577, 1558, 1506, 1472, 1447, 1153, 1124, 1099, 1082, 1048 cm^{-1}; mp: 87–89 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1728.

4.1.4.12. 6-Allyl-2-(3,4-bismethoxymethoxyphenyl)-5-hydroxy-7-methoxy methoxychroman-4-one ***(4l)***. Yield: 96%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.77 (1H, dd, *J* = 17.2, 3.2 Hz), 3.07 (1H, dd, *J* = 17.2, 13.6 Hz), 3.33 (2H, d, *J* = 6.0 Hz), 3.43 (3H, s), 3.50 (3H, s), 3.51 (3H, s), 4.94 (1H, dd, *J* = 10.4, 1.2 Hz), 4.99 (1H, dd, *J* = 17.2, 1.2 Hz), 5.18 (2H, d, *J* = 3.2 Hz), 5.23 (2H, s), 5.24 (2H, d, *J* = 3.2 Hz), 5.32 (1H, dd, *J* = 13.6, 3.2 Hz), 5.92 (1H, ddt, *J* = 17.2, 10.4, 6.0 Hz), 6.27 (1H, s), 7.02 (1H, dd, *J* = 8.4, 2.0 Hz), 7.18 (1H, d, *J* = 8.4 Hz), 7.24 (1H, d, *J* = 2.0 Hz), 12.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.16, 43.36, 56.17, 56.25, 56.36, 78.93, 93.42, 93.74, 95.26, 95.44, 103.34, 108.74, 114.23, 114.73, 116.57, 120.30, 132.52, 136.07, 147.40, 147.53, 160.68, 161.21, 162.87, 196.17; IR (KBr): 1653, 1636, 1577, 1559, 1521, 1516, 1507, 1433, 1261, 1157, 1130, 1091, 1076, 1057, 993, 962, 923 cm^{-1}; mp: 79–80 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1739.

4.1.4.13. 6-Allyl-2-(3,5-bismethoxymethoxyphenyl)-5-hydroxy-7-methoxy methoxychroman-4-one ***(4m)***. Yield: 75%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.80 (1H, dd, *J* = 17.2, 3.2 Hz), 3.05 (1H, dd, *J* = 17.2, 13.6 Hz), 3.35 (2H, d, *J* = 6.0 Hz), 3.46 (3H, s), 3.48 (6H, s), 4.96 (1H, dd, *J* = 10.0, 1.2 Hz), 5.00 (1H, dd, *J* = 17.2, 1.6 Hz), 5.18 (4H, s), 5.21 (2H, d, *J* = 2.4 Hz), 5.33 (1H, dd, *J* = 13.6, 3.2 Hz), 5.94 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.31 (1H, s), 6.75 (1H, t, *J* = 2.4 Hz), 6.79 (2H, d, *J* = 2.4 Hz), 12.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.16, 43.48, 56.09, 56.36, 78.97, 93.47, 93.76, 94.42, 103.34, 104.80, 107.36, 108.81, 114.25, 136.05, 140.76, 158.59, 160.68, 161.09, 162.88, 195.97; IR (KBr): 1653, 1636, 1616, 1603, 1577, 1448, 1438, 1293, 1219, 1155, 1147, 1127, 1086, 1056, 968, 922 cm^{-1}; mp: 98–100 °C; MS (EI): *m/z* 460 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_9$ 460.1733 (M^+); Found 460.1739.

4.1.4.14. 6-Allyl-5-hydroxy-7-methoxymethoxy-2-(4-methoxy-phenyl)chr oman-4-one ***(4n)***. Yield: 84%; ^1H NMR (400 MHz $CDCl_3$) δ: 2.78 (1H, dd, *J* = 17.0, 2.8 Hz), 3.10 (1H, dd, *J* = 17.0, 13.2 Hz), 3.35 (2H, d, *J* = 6.0 Hz), 3.45 (3H, s), 3.83 (3H, s), 4.97 (1H, d, *J* = 9.6 Hz), 5.02 (1H, dd, *J* = 17.0, 1.2 Hz), 5.20 (2H, d, *J* = 3.6 Hz), 5.36 (1H, dd, *J* = 13.2, 2.8 Hz), 5.94 (1H, ddt, *J* = 17.0, 9.6, 6.0 Hz), 6.29 (1H, s), 6.95 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.8 Hz), 12.13 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.20, 43.32, 55.34, 56.39, 79.00, 93.41, 93.79, 103.38, 108.72, 114.16, 114.28, 127.67, 130.41, 136.11, 159.97, 160.72, 161.37, 162.92, 196.38; IR (neat): 1636, 1578, 1516, 1489, 1448, 1437, 1339, 1310, 1285, 1256, 1221, 1151, 1124, 1090, 1051, 959, 830 cm^{-1}; MS (EI): *m/z* 370 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_6$ 370.1416 (M^+); Found 370.1410.

4.1.4.15. 6-Allyl-2-(4-chlorophenyl)-5-hydroxy-7-methoxy-methoxychrom an-4-one ***(4o)***. Yield: 98%; ^1H NMR (400 MHz $CDCl_3$) δ: 3.43 (1H, d, *J* = 16.6 Hz), 3.48 (2H, d, *J* = 6.4 Hz), 3.54 (3H, s), 3.69 (1H, t, *J* = 16.6 Hz), 5.02 (1H, d, *J* = 10.4 Hz), 5.10 (1H, d, *J* = 17.2 Hz), 5.32 (2H, d, *J* = 3.6 Hz), 5.70 (1H, d, *J* = 12.8 Hz), 6.12 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.47 (1H, s), 7.37–7.48 (4H, m), 13.54 (1H, br); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.31, 44.09, 56.48, 78.71, 93.54, 93.89, 103.11, 109.18, 114.40, 127.46, 129.01, 134.61, 136.05, 137.01, 161.19, 161.26, 163.25, 196.87; IR (KBr): 1636, 1576, 1508, 1495, 1447, 1437, 1418, 1339, 1304, 1288, 1223, 1215, 1186, 1155, 1105,

1090, 1057, 962, 831 cm^{-1}; mp: 97–99 °C; MS (EI): *m/z* 374 (M^+); HRMS (EI) Calcd for $C_{20}H_{19}ClO_5$ 374.0921 (M^+); Found 374.0937.

*4.1.5. General procedure of deprotection of methoxymethyl group for **5c** and **5g–o***

To a stirred solution of **4c** or **4g–o** (0.64 mmol) in MeOH (5 mL) was added conc. HCl (5 drops). The reaction mixture was stirred at room temperature for 3 days. The reaction mixture was evaporated, and the crude product was chromatographed on SiO_2 (10 g, MeOH/CH_2Cl_2 = 1/50) to give the corresponding product **5c** or **5g–o**.

*4.1.5.1. 6-Allyl-5-hydroxy-2-(2-hydroxylphenyl)chroman-4-one **(5c)***. Yield: 93%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.93 (1H, dd, *J* = 17.2, 2.4 Hz), 3.19 (1H, dd, *J* = 17.2, 13.6 Hz), 3.30 (2H, d, *J* = 5.2 Hz), 5.00 (1H, d, *J* = 10.4 Hz), 5.06 (1H, d, *J* = 17.2 Hz), 5.84 (1H, dd, *J* = 13.6, 2.4 Hz), 5.95 (1H, ddt, *J* = 17.2, 10.4, 5.2 Hz), 6.49 (1H, d, *J* = 8.0 Hz), 6.93 (1H, t, *J* = 8.0 Hz), 6.94 (1H, d, *J* = 8.0 Hz), 7.21 (1H, t, *J* = 8.0 Hz), 7.32 (1H, d, *J* = 8.0 Hz), 7.54 (1H, d, *J* = 8.0 Hz), 8.77 (1H, s), 12.15 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 33.11, 43.02, 75.36, 107.73, 108.47, 115.81, 116.27, 120.42, 120.69, 126.23, 127.63, 130.20, 137.39, 139.18, 154.72, 160.18, 161.37, 200.18; IR (KBr): 1625, 1609, 1490, 1462, 1437, 1348, 1234, 755, 736 cm^{-1}; mp: 184–186 °C; MS (EI): *m/z* 296 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_4$ 296.1049 (M^+); Found 296.1044.

*4.1.5.2. 6-Allyl-5,7-dihydroxy-2-phenylchroman-4-one **(5g)***. Yield: 93%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.83 (1H, dd, *J* = 17.0, 3.0 Hz), 3.14 (1H, dd, *J* = 17.0, 12.8 Hz), 3.41 (2H, d, *J* = 6.0 Hz), 5.15 (1H, dd, *J* = 10.0, 1.2 Hz), 5.20 (1H, dd, *J* = 17.2, 1.2 Hz), 5.42 (1H, dd, *J* = 12.8, 3.0 Hz), 5.76 (1H, br), 5.98 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.03 (1H, s), 7.37–7.47 (5H, m), 12.39 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.68, 43.32, 79.90, 95.30, 103.03, 107.36, 114.54, 127.25, 129.35, 129.42, 136.98, 140.08, 162.03, 162.42, 164.92, 196.92; IR (KBr): 1651, 1630, 1585, 1485, 1452, 1304, 1252, 1219, 1182, 1161, 1124, 1086, 817 cm^{-1}; mp: 201–203 °C; MS (EI): *m/z* 296 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_4$ 296.1049 (M^+); Found 296.1044.

*4.1.5.3. 6-Allyl-5,7-dihydroxy-2-(2-hydroxylphenyl)chroman-4-one **(5h)***. Yield: 95%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.82 (1H, dd, *J* = 17.2, 3.2 Hz), 3.10 (1H, dd, *J* = 17.2, 13.2 Hz), 3.30 (2H, d, *J* = 6.4 Hz), 4.90 (1H, dd, *J* = 10.4, 2.0 Hz), 5.00 (1H, dd, *J* = 17.2, 2.0 Hz), 5.78 (1H, dd, *J* = 13.2, 3.2 Hz), 5.91 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.09 (1H, s), 6.93 (1H, d, *J* = 8.0 Hz), 6.93 (1H, t, *J* = 8.0 Hz), 7.21 (1H, td, *J* = 8.0, 2.0 Hz), 7.52 (1H, dd, *J* = 8.0, 2.0 Hz), 8.78 (1H, s), 9.62 (1H, s), 12.15 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.66, 42.50, 75.26, 95.25, 102.97, 107.21, 114.51, 116.21, 120.62, 126.34, 127.62, 130.10, 136.98, 154.70, 162.43, 164.77, 197.39; IR (KBr): 1653, 1646, 1635, 1616, 1591, 1558, 1506, 1497, 1490, 1472, 1457, 1340, 1312, 1300, 1218, 1158, 1118, 826 cm^{-1}; mp: 174–176 °C; MS (EI): *m/z* 312 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_5$ 312.0998 (M^+); Found 312.0986.

*4.1.5.4. 6-Allyl-5,7-dihydroxy-2-(3-hydroxylphenyl)chroman-4-one **(5i)***. Yield: 91%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.78 (1H, dd, *J* = 17.2, 3.2 Hz), 3.11 (1H, dd, *J* = 17.2, 12.8 Hz), 3.29 (2H, d, *J* = 6.0 Hz), 4.89 (1H, dd, *J* = 10.4, 1.6 Hz), 4.99 (1H, dd, *J* = 17.2, 1.6 Hz), 5.47 (1H, dd, *J* = 12.8, 3.2 Hz), 5.90 (1H, ddt, *J* = 17.2, 10.4, 6.0 Hz), 6.07 (1H, s), 6.84 (1H, dd, *J* = 8.0, 2.4 Hz), 6.99 (1H, d, *J* = 8.0 Hz), 7.02 (1H, d, *J* = 2.4 Hz), 7.25 (1H, t, *J* = 8.0 Hz), 8.55 (1H, br), 9.66 (1H, br), 12.44 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.66, 43.65, 79.74, 95.27, 103.02, 107.29, 114.09, 114.53, 116.22, 118.19, 130.52, 136.97, 141.59, 158.44, 161.99, 162.39, 164.88, 196.95; IR (KBr): 1635, 1593, 1558, 1506, 1490, 1472, 1456, 1339, 1303, 1280, 1215, 1154, 1120, 1078 cm^{-1}; mp: 168–170 °C; MS (EI): *m/z* 312 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_5$ 312.0998 (M^+); Found 312.0986.

*4.1.5.5. 6-Allyl-2-(2,3-dihydroxylphenyl)-5,7-dihydroxychroman-4-one **(5j)***. Yield: 99%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.81 (1H, dd, *J* = 17.2, 3.2 Hz), 3.12 (1H, dd, *J* = 17.2, 12.8 Hz), 3.30 (2H, dd, *J* = 6.0, 1.2 Hz), 4.89 (1H, dd, *J* = 10.4, 1.6 Hz), 5.00 (1H, dd, *J* = 17.2, 1.6 Hz), 5.79 (1H, dd, *J* = 12.8, 3.2 Hz), 5.91 (1H, ddt, *J* = 17.2, 10.4, 6.0 Hz), 6.07 (1H, s), 6.76 (1H, t, *J* = 8.0 Hz), 6.87 (1H, dd, *J* = 8.0, 1.2 Hz), 7.02 (1H, dd, *J* = 8.0, 1.2 Hz), 8.65 (1H, br), 12.49 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.66, 42.43, 75.30, 95.24, 103.00, 107.19, 114.50, 115.74, 118.42, 120.38, 126.57, 136.99, 143.29, 145.41, 162.43, 164.78, 197.42; IR (KBr): 1653, 1636, 1617, 1604, 1509, 1490, 1481, 1457, 1452, 1339, 1308, 1287, 1210, 1156 cm^{-1}; mp: 177–178 °C; MS (EI): *m/z* 328 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_6$ 328.0947 (M^+); Found 328.0947.

*4.1.5.6. 6-Allyl-2-(2,6-dihydroxylphenyl)-5,7-dihydroxychroman-4-one **(5k)***. Yield: 82%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.51 (1H, dd, *J* = 17.2, 2.4 Hz), 3.28 (2H, d, *J* = 6.0 Hz), 3.89 (1H, dd, *J* = 17.2, 13.6 Hz), 4.87 (1H, d, *J* = 10.0 Hz), 4.98 (1H, d, *J* = 17.2 Hz), 5.89 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.00 (1H, s), 6.02 (1H, dd, *J* = 13.6, 2.4 Hz), 6.44 (2H, d, *J* = 8.4 Hz), 7.00 (1H, t, *J* = 8.4 Hz), 8.55 (2H, s), 9.56 (1H, s), 12.57 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.20, 39.74, 72.64, 94.46, 102.25, 106.29, 107.67, 110.95, 113.71, 130.17, 136.33, 156.99, 161.84, 162.17, 163.86, 197.69; IR (KBr): 1653, 1635, 1601, 1558, 1506, 1472, 1456, 1451, 1447, 1312 cm^{-1}; mp: 214–216 °C; MS (EI): *m/z* 328 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_6$ 328.0947 (M^+); Found 328.0947.

*4.1.5.7. 6-Allyl-2-(3,4-dihydroxylphenyl)-5,7-dihydroxychroman-4-one **(5l)***. Yield: 100%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.70 (1H, dd, *J* = 17.2, 3.2 Hz), 3.13 (1H, dd, *J* = 17.2, 12.8 Hz), 3.28 (2H, dt, *J* = 6.0, 2.0 Hz), 4.88 (1H, dd, *J* = 10.0, 2.0 Hz), 4.98 (1H, dd, *J* = 17.2, 2.0 Hz), 5.36 (1H, dd, *J* = 12.8, 3.2 Hz), 5.90 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.03 (1H, s), 6.86 (2H, s), 7.02 (1H, s), 8.08 (2H, br), 9.62 (1H, br), 12.46 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.64, 43.57, 79.87, 95.19, 102.95, 107.09, 114.49, 114.63, 115.92, 119.15, 131.53, 137.00, 145.90, 146.27, 162.18, 162.34, 164.86, 197.30; IR (KBr): 1654, 1646, 1635, 1617, 1589, 1523, 1507, 1490, 1457, 1339, 1326, 1303, 1290, 1158, 1109 cm^{-1}; mp: 165–167 °C; MS (EI): *m/z* 328 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_6$ 328.0947 (M^+); Found 328.0947.

*4.1.5.8. 6-Allyl-2-(3,5-dihydroxylphenyl)-5,7-dihydroxychroman-4-one **(5m)***. Yield: 98%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 2.75 (1H, dd, *J* = 17.2, 2.8 Hz), 3.06 (1H, dd, *J* = 17.2, 12.8 Hz), 3.28 (2H, d, *J* = 6.4 Hz), 4.88 (1H, dd, *J* = 10.0, 1.6 Hz), 4.99 (1H, dd, *J* = 17.2, 1.6 Hz), 5.38 (1H, dd, *J* = 12.8, 2.8 Hz), 5.89 (1H, ddt, *J* = 17.2, 10.0, 6.4 Hz), 6.06 (1H, s), 6.35 (1H, t, *J* = 2.0 Hz), 6.50 (2H, d, *J* = 1.6 Hz), 8.55 (1H, br), 12.43 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.64, 43.61, 79.72, 95.23, 102.99, 103.34, 105.56, 107.21, 114.51, 136.97, 142.30, 159.56, 161.97, 162.34, 164.89, 196.97 cm^{-1}; mp: 121–123 °C; MS (EI): *m/z* 328 (M^+); HRMS (EI) Calcd for $C_{18}H_{16}O_6$ 328.0947 (M^+); Found 328.0947.

*4.1.5.9. 6-Allyl-5,7-dihydroxy-2-(4-methoxyphenyl)chroman-4-one **(5n)***. Yield: 79%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.79 (1H, dd, *J* = 17.2, 3.0 Hz), 3.10 (1H, dd, *J* = 17.2, 12.8 Hz), 3.41 (2H, dd, *J* = 6.0, 1.6 Hz), 3.83 (3H, s), 5.14 (1H, dd, *J* = 10.0, 1.6 Hz), 5.19 (1H, dd, *J* = 17.2, 1.6 Hz), 5.39 (1H, dd, *J* = 12.8, 3.0 Hz), 5.77 (1H, br), 5.97 (1H, ddt, *J* = 17.2, 10.0, 6.0 Hz), 6.01 (1H, s), 6.95 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.8 Hz), 12.40 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 26.20, 43.32, 55.34, 56.39, 79.00, 93.41, 93.79, 103.38, 108.72, 114.16, 114.28, 127.67, 130.41, 136.11, 159.97, 160.72, 161.37, 162.92, 196.38; IR (KBr): 1651, 1630, 1616, 1585, 1520, 1506, 1489, 1464, 1425, 1362, 1329, 1300, 1261, 1213, 1173, 1161, 1086, 835, 818 cm^{-1}; mp: 199–201 °C; MS (EI): *m/z* 326 (M^+); HRMS (EI) Calcd for $C_{19}H_{18}O_5$ 326.1154 (M^+); Found 326.1165.

*4.1.5.10. 6-Allyl-2-(4-chlorophenyl)-5,7-dihydroxychroman-4-one **(5o)***. Yield: 77%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.82 (1H, dd, *J* = 17.2, 3.0 Hz), 3.02

(1H, dd, J = 17.2, 12.8 Hz), 3.41 (2H, d, J = 5.6 Hz), 5.14 (1H, dd, J = 10.4, 1.2 Hz), 5.18 (1H, dd, J = 16.0, 1.2 Hz), 5.39 (1H, dd, J = 12.8, 3.0 Hz), 5.90–6.05 (3H, m), 7.34–7.45 (4H, m), 12.33 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 26.20, 43.31, 78.343, 95.49, 102.95, 105.68, 106.16, 127.47, 129.05, 134.67, 135.78, 136.92, 160.98, 161.52, 163.46, 195.46; IR (KBr): 1651, 1632, 1587, 1495, 1462, 1450, 1416, 1331, 1310, 1303, 1250, 1217, 1162, 1153, 1124, 1088, 825 cm^{-1}; mp: 185–187 °C; MS (EI): m/z 330 (M^+); HRMS (EI) Calcd for $C_{18}H_{15}ClO_4$ 330.0659 (M^+); Found 330.0672.

*4.1.6. General procedure of protection of acetyl group for **6c** and **6g–o***

To a stirred solution of **5c** or **5g–o** (0.46 mmol) in pyridine (5 mL) was added dropwise Ac_2O (2 eq. for the number of hydroxyl group on **5c** or **5g–o**) at room temperature. The reaction mixture was stirred for 12 h. The solvent was evaporated, and the residue was chromatographed on SiO_2 (10 g, EtOAc/hexane = 1/3) to give the corresponding product **6c** or **6g–o**.

*4.1.6.1. 6-Allyl-5-hydroxy-2-(2-acetoxyphenyl)chroman-4-one (**6c**)*. Yield: 99%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.27 (3H, s), 2.83 (1H, dd, J = 17.2, 2.4 Hz), 3.10 (1H, dd, J = 17.2, 13.6 Hz), 3.32 (2H, d, J = 6.4 Hz), 5.05 (1H, dd, J = 10.4, 1.8 Hz), 5.06 (1H, dd, J = 17.2, 1.8 Hz), 5.53 (1H, dd, J = 13.6, 2.4 Hz), 5.95 (1H, ddt, J = 17.2, 10.4, 6.4 Hz), 6.44 (1H, d, J = 8.0 Hz), 7.13 (1H, dd, J = 8.0, 1.2 Hz), 7.25 (1H, d, J = 8.0 Hz), 7.32 (1H, td, J = 8.0, 1.2 Hz), 7.40 (1H, td, J = 8.0, 1.6 Hz), 7.62 (1H, dd, J = 8.0, 1.6 Hz), 11.96 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.92, 32.59, 42.82, 74.32, 106.91, 107.66, 115.75, 120.49, 123.00, 126.55, 127.19, 129.76, 130.33, 136.22, 138.73, 147.72, 159.47, 159.72, 169.06, 198.02; IR (KBr): 1762, 1653, 1647, 1627, 1493, 1480, 1431, 1369, 1356, 1340, 1226, 1202, 1186, 1175, 1166, 1060, 919, 815 cm^{-1}; mp: 83–85 °C; MS (EI): m/z 338 (M^+); HRMS (EI) Calcd for $C_{20}H_{18}O_5$ 338.1154 (M^+); Found 338.1140.

*4.1.6.2. 7-Acetoxy-6-allyl-5-hydroxy-2-phenylchroman-4-one (**6g**)*. Yield: 82%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.30 (3H, s), 2.88 (1H, dd, J = 17.2, 3.0 Hz), 3.14 (1H, dd, J = 17.2, 13.2 Hz), 3.28 (2H, dd, J = 6.0, 1.6 Hz), 5.00 (1H, dd, J = 10.4, 1.6 Hz), 5.02 (1H, dd, J = 17.0, 1.6 Hz), 5.42 (1H, dd, J = 13.2, 3.0 Hz), 5.85 (1H, ddt, J = 17.0, 10.4, 6.0 Hz), 6.30 (1H, s), 7.37–7.47 (5H, m), 12.20 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.90, 27.05, 43.66, 79.13, 102.20, 106.12, 113.08, 115.06, 126.05, 128.84, 128.90, 135.16, 138.06, 156.69, 160.08, 161.21, 168.28, 197.23; IR (KBr): 1763, 1639, 1591, 1437, 1373, 1312, 1279, 1202, 1150, 1115, 1088, 1049, 993, 802 cm^{-1}; mp: 102–104 °C; MS (EI): m/z 338 (M^+); HRMS (EI) Calcd for $C_{20}H_{18}O_5$ 338.1154 (M^+); Found 338.1140.

*4.1.6.3. 7-Acetoxy-6-allyl-5-hydroxy-2-(2-acetoxyphenyl)-chroman-4-one (**6h**)*. Yield: 89%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.30 (3H, s), 2.31 (3H, s), 2.84 (1H, dd, J = 17.2, 3.2 Hz), 3.11 (1H, dd, J = 17.2, 13.6 Hz), 3.28 (2H, dd, J = 6.0, 1.2 Hz), 4.99 (1H, dd, J = 10.4, 1.2 Hz), 5.03 (1H, dd, J = 17.2, 1.2 Hz), 5.57 (1H, dd, J = 13.6, 3.2 Hz), 5.85 (1H, ddt, J = 17.2, 10.4, 6.0 Hz), 6.28 (1H, s), 7.14 (1H, dd, J = 7.6, 1.2 Hz), 7.34 (1H, td, J = 7.6, 1.2 Hz), 7.42 (1H, td, J = 7.6, 2.0 Hz), 7.62 (1H, dd, J = 7.6, 2.0 Hz), 12.19 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.85, 20.88, 27.01, 30.85, 42.52, 74.30, 102.19, 106.02, 113.30, 115.09, 122.95, 126.53, 127.10, 129.82, 135.06, 147.64, 156.64, 159.94, 161.21, 168.24, 169.06, 197.05; IR (KBr): 1771, 1653, 1635, 1587, 1558, 1505, 1436, 1373, 1270, 1192, 1178, 1138, 1083, 1055 cm^{-1}; mp: 104–106 °C; MS (EI): m/z 396 (M^+); HRMS (EI) Calcd for $C_{22}H_{20}O_7$ 396.1209 (M^+); Found 396.1213.

*4.1.6.4. 7-Acetoxy-6-allyl-5-hydroxy-2-(3-acetoxyphenyl)-chroman-4-one (**6i**)*. Yield: 88%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.28 (3H, s), 2.30 (3H, s), 2.87 (1H, dd, J = 17.2, 3.2 Hz), 3.07 (1H, dd, J = 17.2, 13.2 Hz), 3.26 (2H, d, J = 6.0 Hz), 4.98 (1H, dd, J = 9.6, 1.6 Hz), 5.00 (1H, dd, J = 17.2, 1.6 Hz), 5.43 (1H, dd, J = 13.2, 3.2 Hz), 5.83 (1H, ddt, J = 17.2, 9.6, 6.0 Hz), 6.30 (1H, s), 7.11 (1H, d, J = 8.0 Hz), 7.20 (1H, s), 7.28 (1H, d, J = 8.0 Hz), 7.42 (1H, t, J = 8.0 Hz), 12.14 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.89, 21.06, 27.03, 43.61, 78.38, 102.23, 106.06, 113.24, 115.08, 119.29, 122.05, 123.27, 129.88, 135.09, 139.77, 150.92, 156.69, 159.78, 161.19, 168.26, 169.27, 196.84; IR (KBr): 1768, 1652, 1640, 1635, 1586, 1436, 1371, 1198, 1138 cm^{-1}; mp: 71-73 °C; MS (EI): m/z 396 (M^+); HRMS (EI) Calcd for $C_{22}H_{20}O_7$ 396.1209 (M^+); Found 396.1213

*4.1.6.5. 7-Acetoxy-6-allyl-5-hydroxy-2-(2,3-diacetoxyphenyl)-chroman-4-one (**6j**)*. Yield: 89%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.28 (6H, s), 2.29 (3H, s), 2.82 (1H, dd, J = 17.2, 2.4 Hz), 3.09 (1H, dd, J = 17.2, 13.6 Hz), 3.24 (2H, d, J = 6.8 Hz), 4.97 (1H, dd, J = 10.4, 1.6 Hz), 5.00 (1H, dd, J = 17.2, 1.6 Hz), 5.52 (1H, dd, J = 13.6, 2.4 Hz), 5.83 (1H, ddt, J = 17.2, 10.4, 6.8 Hz), 6.25 (1H, s), 7.25 (1H, dd, J = 8.0, 1.6 Hz), 7.35 (1H, t, J = 8.0 Hz), 7.47 (1H, d, J = 8.0 Hz), 12.15 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.29, 20.64, 20.87, 27.03, 42.46, 74.18, 102.21, 106.00, 113.47, 115.13, 124.03, 124.28, 126.93, 132.12, 135.04, 139.65, 142.65, 156.68, 159.74, 161.24, 167.84, 168.01, 168.23, 196.76; IR (KBr): 1772, 1654, 1638, 1586, 1472, 1437, 1374, 1278, 1200, 1164, 1141, 1114 cm^{-1}; mp: 123–124 °C; MS (EI): m/z 454 (M^+); HRMS (EI) Calcd for $C_{24}H_{22}O_9$ 454.1264 (M^+); Found 454.1255.

*4.1.6.6. 7-Acetoxy-6-allyl-5-hydroxy-2-(2,6-diacetoxyphenyl)-chroman-4-one (**6k**)*. Yield: 65%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.25 (6H, s), 2.29 (3H, s), 2.71 (1H, dd, J = 17.2, 3.2 Hz), 3.27 (2H, d, J = 6.4 Hz), 3.56 (1H, dd, J = 17.2, 14.0 Hz), 5.00 (1H, dd, J = 10.4, 1.2 Hz), 5.03 (1H, dd, J = 17.2, 1.2 Hz), 5.59 (1H, dd, J = 14.0, 3.2 Hz), 5.85 (1H, ddt, J = 17.2, 10.4, 6.4 Hz), 6.22 (1H, s), 7.05 (2H, d, J = 8.0 Hz), 7.44 (1H, t, J = 8.0 Hz), 12.23 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.84, 27.08, 40.43, 72.23, 101.93, 105.79, 113.47, 115.19, 121.48, 122.48, 130.01, 135.04, 149.28, 156.77, 159.66, 161.36, 168.20, 168.96, 197.69; IR (KBr): 1771, 1653, 1646, 1635, 1616, 1558, 1507, 1436, 1192, 1139 cm^{-1}; mp: 72–74 °C; MS (EI): m/z 454 (M^+); HRMS (EI) Calcd for $C_{24}H_{22}O_9$ 454.1264 (M^+); Found 454.1255.

*4.1.6.7. 7-Acetoxy-6-allyl-5-hydroxy-2-(3,4-diacetoxyphenyl)-chroman-4-one (**6l**)*. Yield: 76%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.28 (3H, s), 2.29 (3H, s), 2.29 (3H, s), 2.87 (1H, dd, J = 17.2, 3.2 Hz), 3.05 (1H, dd, J = 17.2, 13.6 Hz), 3.26 (2H, d, J = 6.4 Hz), 4.98 (1H, d, J = 9.2 Hz), 4.99 (1H, d, J = 17.2 Hz), 5.41 (1H, dd, J = 13.6, 3.2 Hz), 5.83 (1H, ddt, J = 17.2, 9.2, 6.4 Hz), 6.29 (1H, d, J = 2.4 Hz), 7.23 (1H, d, J = 6.0 Hz), 7.24 (1H, d, J = 2.4 Hz), 7.30 (1H, d, J = 6.0 Hz), 12.13 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.57, 20.59, 20.89, 27.03, 43.60, 78.01, 102.21, 106.04, 113.35, 115.10, 121.30, 123.87, 124.07, 135.07, 136.86, 142.26, 142.30, 156.72, 159.69, 161.21, 168.04, 168.08, 168.24, 196.69; IR (KBr): 1769, 1751, 1653, 1647, 1637, 1507, 1436, 1374, 1262, 1216, 1201, 1137, 1115 cm^{-1}; mp: 97–99 °C; MS (EI): m/z 454 (M^+); HRMS (EI) Calcd for $C_{24}H_{22}O_9$ 454.1264 (M^+); Found 454.1261.

*4.1.6.8. 7-Acetoxy-6-allyl-5-hydroxy-2-(3,5-diacetoxyphenyl)-chroman-4-one (**6m**)*. Yield: 88%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.28 (6H, s), 2.29 (3H, s), 2.88 (1H, dd, J = 17.2, 2.8 Hz), 3.04 (1H, dd, J = 17.2, 12.8 Hz), 3.26 (2H, d, J = 6.4 Hz), 4.98 (1H, dd, J = 10.4, 1.6 Hz), 5.00 (1H, dd, J = 17.2, 1.6 Hz), 5.41 (1H, dd, J = 12.8, 2.8 Hz), 5.83 (1H, ddt, J = 17.2, 10.4, 6.4 Hz), 6.30 (1H, s), 6.94 (1H, t, J = 1.6 Hz), 7.07 (2H, d, J = 2.4 Hz), 12.11 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.91, 21.05, 27.05, 43.58, 77.94, 102.24, 106.04, 113.43, 115.13, 115.80, 116.52, 135.08, 140.52, 151.30, 156.74, 159.57, 161.22, 168.25, 168.79, 196.51; IR (KBr): 1772, 1653, 1640, 1586, 1436, 1369, 1282, 1197, 1140, 1125, 1052, 1025, 911, 900 cm^{-1}; mp: 145–147 °C; MS (EI): m/z 454 (M^+); HRMS (EI) Calcd for $C_{24}H_{22}O_9$ 454.1264 (M^+); Found 454.1255.

*4.1.6.9. 7-Acetoxy-6-allyl-5-hydroxy-2-(4-methoxyphenyl)-chroman-4-one (**6n**)*. Yield: 81%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.29 (3H, s), 2.84 (1H, dd, *J* = 17.2, 2.6 Hz), 3.14 (1H, dd, *J* = 17.2, 13.2 Hz), 3.28 (2H, d, *J* = 6.0 Hz), 3.83 (3H, s), 4.99 (1H, dd, *J* = 9.6, 1.2 Hz), 5.02 (1H, dd, *J* = 16.8, 1.2 Hz), 5.39 (1H, dd, *J* = 13.2, 2.6 Hz), 5.85 (1H, ddt, *J* = 16.8, 9.6, 6.0 Hz), 6.29 (1H, s), 6.95 (2H, d, *J* = 8.8 Hz), 7.37 (2H, d, *J* = 8.8 Hz), 12.21 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.87, 27.02, 43.42, 55.28, 78.89, 102.14, 106.08, 112.93, 114.14, 115.01, 127.65, 130.02, 135.17, 156.62, 160.00, 160.17, 161.16, 168.26, 197.48; IR (KBr): 1761, 1645, 1612, 1589, 1518, 1437, 1377, 1346, 1308, 1258, 1240, 1209, 1146, 1115, 1086, 1045 cm^{-1}; mp: 145–147 °C; MS (EI): *m/z* 368 (M^+); HRMS (EI) Calcd for $C_{21}H_{20}O_6$ 368.1260 (M^+); Found 368.1269.

*4.1.6.10. 7-Acetoxy-6-allyl-5-hydroxy-2-(4-chlorophenyl)-chroman-4-one (**6o**)*. Yield: 32%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 2.30 (3H, s), 2.86 (1H, dd, *J* = 17.2, 3.0 Hz), 3.08 (1H, dd, *J* = 17.2, 13.0 Hz), 3.28 (2H, d, *J* = 6.4 Hz), 5.00 (1H, dd, *J* = 10.4, 1.6 Hz), 5.02 (1H, dd, *J* = 17.2, 1.6 Hz), 5.43 (1H, dd, *J* = 13.0, 3.0 Hz), 5.85 (1H, ddt, *J* = 17.2, 10.4, 6.4 Hz), 6.31 (1H, s), 7.40 (4H, d, *J* = 4.4 Hz), 12.15 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.90, 27.03, 43.56, 78.34, 102.20, 106.05, 113.31, 115.11, 127.41, 129.04, 134.71, 135.08, 136.59, 156.72, 159.76, 161.22, 168.26, 196.76; IR (KBr): 1753, 1655, 1635, 1628, 1591, 1495, 1433, 1415, 1373, 1302, 1290, 1223, 1204, 1142, 1117, 1090, 1080, 1049, 908, 825 cm^{-1}; mp: 101–103 °C; MS (EI): *m/z* 372 (M^+); HRMS (EI) Calcd for $C_{20}H_{17}ClO_5$ 372.0765 (M^+); Found 372.0778.

*4.1.7. General procedure of cross-metathesis for **7a–q***

To a stirred solution of **4a–b, 6c, 4d–f** or **6g–o** (0.27 mmol) in benzene (5 mL) were added corresponding olefin (5.40 mmol) and Grubbs catalyst, 2nd Generation (11 mg, 0.014 mmol) under argon atmosphere. The reaction mixture was heated in the sealed tube at 100 °C for 20 h. After cooling, the solvent was removed under vacuum, the crude product was chromatographed on SiO_2 (10 g, EtOAc/hexane = 1/7) to give the corresponding product **7a–q**.

*4.1.7.1. 5-Hydroxy-6-(3-methylbut-2-enyl)-2-phenylchroman-4-one (**7a**)*. Yield: 98%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.72 (3H, s), 1.75 (3H, s), 2.88 (1H, dd, *J* = 17.2, 3.0 Hz), 3.14 (1H, dd, *J* = 17.2, 13.2 Hz), 3.28 (2H, d, *J* = 7.2 Hz), 5.28 (1H, tt, *J* = 7.2, 1.2 Hz), 5.43 (1H, dd, *J* = 13.2, 3.0 Hz), 6.46 (1H, d, *J* = 8.4 Hz), 7.27 (1H, d, *J* = 8.4 Hz), 7.39–7.49 (5H, m), 11.98 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.75, 25.77, 26.81, 43.98, 79.03, 106.81, 107.72, 121.80, 121.92, 126.10, 128.85, 128.90, 133.13, 135.68, 138.20, 138.43, 159.45, 198.23; IR (KBr): 1683, 1635, 1607, 1578, 1474, 1439, 1367, 1340, 1252, 1231, 1186, 1109, 1065, 698 cm^{-1}; mp: 72–74 °C; MS (EI): *m/z* 308 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_3$ 308.1412 (M^+); Found 308.1404.

*4.1.7.2. 5-Hydroxy-6-(3-methylbut-2-enyl)-2-p-tolylchroman-4-one (**7b**)*. Yield: 56%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.71 (3H, s), 1.74 (3H, s), 2.38 (3H, s), 2.84 (1H, dd, *J* = 17.2, 3.0 Hz), 3.12 (1H, dd, *J* = 17.2, 13.2 Hz), 3.27 (2H, d, *J* = 7.6 Hz), 5.28 (1H, tt, *J* = 7.6, 1.6 Hz), 5.37 (1H, dd, *J* = 13.2, 3.0 Hz), 6.44 (1H, d, *J* = 8.4 Hz), 7.23 (2H, d, *J* = 7.8 Hz), 7.26 (1H, d, *J* = 8.4 Hz), 7.35 (2H, d, *J* = 7.8 Hz), 11.98 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.75, 21.19, 25.76, 26.80, 43.86, 78.96, 106.81, 107.71, 121.78, 121.83, 126.13, 129.48, 133.08, 135.44, 138.15, 138.76, 159.43, 159.54, 198.40; IR (KBr): 1639, 1582, 1518, 1474, 1443, 1369, 1313, 1263, 1238, 1107, 1063, 814 cm^{-1}; mp: 57–59 °C; MS (EI): *m/z* 322 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_3$ 322.1569 (M^+); Found 322.1557.

*4.1.7.3. 5-Hydroxy-6-(3-methylbut-2-enyl)-2-(2-acetoxyphenyl)-chroman-4-one (**7c**)*. Yield: 85%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.64 (3H, s), 1.68 (3H, s), 2.22 (3H, s), 2.77 (1H, dd, *J* = 17.2, 3.2 Hz), 3.04 (1H, dd, *J* = 17.2, 13.2 Hz), 3.20 (2H, d, *J* = 7.6 Hz), 5.21 (1H, td, *J* = 7.6, 2.8 Hz), 5.46 (1H, dd, *J* = 13.2, 3.2 Hz), 6.36 (1H, d, *J* = 8.0 Hz), 7.07 (1H, d, *J* = 8.0 Hz), 7.19 (1H, d, *J* = 8.0 Hz), 7.27 (1H, t, *J* = 8.0 Hz), 7.34 (1H, td, *J* = 8.0, 1.2 Hz), 7.56 (1H, dd, *J* = 8.0, 1.2 Hz), 11.91 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.47, 20.93, 25.76, 26.83, 42.87, 74.30, 106.76, 107.63, 121.74, 122.12, 123.00, 126.55, 127.21, 129.74, 130.40, 133.15, 138.22, 147.73, 159.37, 159.48, 169.08, 198.06; IR (KBr): 1762, 1653, 1645, 1635, 1558, 1490, 1461, 1436, 1368, 1231, 1207, 1186, 1056, 790 cm^{-1}; mp: 93–95 °C; MS (EI): *m/z* 366 (M^+); HRMS (EI) Calcd for $C_{22}H_{22}O_5$ 366.1467 (M^+); Found 366.1485.

*4.1.7.4. 5-Hydroxy-6-(3-ethylpent-2-enyl)-2-(2-acetoxyphenyl)-chroman-4-one (**7d**)*. Yield: 80%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 0.98 (3H, t, *J* = 7.2 Hz), 1.00 (3H, t, *J* = 7.2 Hz), 2.05 (2H, q, *J* = 7.2 Hz), 2.12 (2H, q, *J* = 7.2 Hz), 2.27 (3H, s), 2.83 (1H, dd, *J* = 17.2, 3.2 Hz), 3.09 (1H, dd, *J* = 17.2, 13.4 Hz), 3.29 (2H, d, *J* = 7.2 Hz), 5.21 (1H, t, *J* = 7.2 Hz), 5.52 (1H, dd, *J* = 13.4, 3.2 Hz), 6.42 (1H, d, *J* = 8.0 Hz), 7.12 (1H, d, *J* = 8.0 Hz), 7.25 (1H, d, *J* = 8.0 Hz), 7.32 (1H, t, *J* = 8.0 Hz), 7.40 (1H, td, *J* = 8.0, 2.0 Hz), 7.62 (1H, dd, *J* = 8.0, 2.0 Hz), 11.96 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 12.80, 13.20, 20.93, 23.21, 26.13, 29.19, 42.87, 74.29, 106.76, 107.61, 119.61, 122.30, 123.00, 126.55, 127.21, 129.74, 130.42, 138.16, 144.47, 147.73, 159.36, 159.51, 169.10, 198.09; IR (KBr): 1771, 1768, 1653, 1646, 1635, 1490, 1456, 1436, 1368, 1226, 1201, 1187, 1111, 1064 cm^{-1}; mp: 72–74 °C; MS (EI): *m/z* 394 (M^+); HRMS (EI) Calcd for $C_{24}H_{26}O_5$ 394.1780 (M^+); Found 394.1794.

*4.1.7.5. 6-(3-Ethylpent-2-enyl)-5-hydroxy-2-(4-methoxyphenyl)-chroman-4-one (**7e**)*. Yield: 54%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.62 (3H, s), 1.65 (3H, s), 2.74 (1H, dd, *J* = 17.2, 2.4 Hz), 3.03 (1H, dd, *J* = 17.2, 13.2 Hz), 3.35 (2H, d, *J* = 7.4 Hz), 3.73 (3H, s), 5.19 (1H, t, *J* = 7.4 Hz), 5.26 (1H, dd, *J* = 13.2, 2.4 Hz), 6.34 (1H, d, *J* = 8.4 Hz), 6.85 (2H, d, *J* = 8.4 Hz), 7.16 (1H, d, *J* = 8.4 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 11.90 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.73, 25.75, 26.80, 43.77, 55.32, 78.77, 106.79, 107.69, 114.18, 121.76, 121.84, 127.67, 130.46, 133.06, 138.13, 159.43, 159.55, 159.98 198.45; IR (KBr): 1647, 1624, 1587, 1518, 1474, 1456, 1435, 1429, 1373, 1362, 1352, 1337, 1308, 1256, 1229, 1178, 1159, 1096, 1055, 1032, 833, 777 cm^{-1}; mp: 54–56 °C; MS (EI): *m/z* 338 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_4$ 338.1518 (M^+); Found 338.1508.

*4.1.7.6. 2-(4-Ethoxyphenyl)-6-(3-ethylpent-2-enyl)-5-hydroxy-chroman-4-one (**7f**)*. Yield: 64%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.43 (3H, t, *J* = 7.0 Hz), 1.71 (3H, s), 1.75 (3H, s), 2.83 (1H, dd, *J* = 17.2, 2.4 Hz), 3.13 (1H, dd, *J* = 17.2, 13.2 Hz), 3.27 (2H, d, *J* = 7.0 Hz), 4.05 (2H, q, *J* = 7.0 Hz), 5.28 (1H, t, *J* = 7.0 Hz), 5.36 (1H, dd, *J* = 13.2, 2.4 Hz), 6.44 (1H, d, *J* = 8.0 Hz), 6.94 (2H, d, *J* = 8.4 Hz), 7.25 (1H, d, *J* = 8.0 Hz), 7.37 (2H, d, *J* = 8.4 Hz), 11.99 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 14.77, 17.75, 25.76, 26.81, 43.80, 63.55, 78.84, 106.81, 107.71, 114.72, 121.77, 121.85, 127.67, 130.28, 133.08, 138.15, 159.38, 159.44, 159.60 198.52; IR (KBr): 1626, 1616, 1599, 1520, 1489, 1474, 1456, 1437, 1375, 1364, 1340, 1273, 1231, 1171, 1101, 1057, 831 cm^{-1}; mp: 105–107 °C; MS (EI): *m/z* 352 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_4$ 352.1675 (M^+); Found 352.1666.

*4.1.7.7. 2-(4-Chlorophenyl)-5-hydroxy-6-(3-methylbut-2-enyl)chroman-4-one (**7g**)*. Yield: 64%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.72 (3H, s), 1.75 (3H, s), 2.86 (1H, dd, *J* = 17.2, 2.8 Hz), 3.12 (1H, ddd, *J* = 17.2, 12.8 Hz), 3.27 (2H, d, *J* = 7.2 Hz), 5.28 (1H, t, *J* = 7.2 Hz), 5.40 (1H, dd, *J* = 12.8, 2.8 Hz), 6.45 (1H, dd, *J* = 8.2, 3.2 Hz), 7.27 (1H, d, *J* = 8.2 Hz), 7.40 (4H, d, *J* = 3.2 Hz), 11.94 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.75, 25.76, 26.81, 43.88, 78.23, 106.76, 107.66, 121.72, 122.17, 127.45, 129.03, 133.20, 134.62, 136.97, 138.25, 159.15, 159.47, 197.75; IR (KBr): 1647, 1628, 1495, 1475, 1435, 1362, 1339, 1259, 1228, 1097, 1055, 1016, 831, 820, 793 cm^{-1}; mp: 67–69 °C; MS (EI): *m/z* 342 (M^+); HRMS (EI) Calcd for $C_{20}H_{19}ClO_3$ 342.1023 (M^+); Found 342.1038.

*4.1.7.8. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-phenyl-chroman-4-one (**7h**)*. Yield: 51%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.68 (3H, s), 1.75 (3H, s), 2.30 (3H, s), 2.88 (1H, dd, J = 17.2, 2.8 Hz), 3.11 (1H, dd, J = 17.2, 13.0 Hz), 3.22 (2H, d, J = 6.8 Hz), 5.11 (1H, t, J = 6.8 Hz), 5.44 (1H, dd, J = 13.0, 2.8 Hz), 6.29 (1H, s), 7.38–7.45 (5H, m), 12.20 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.75, 20.90, 21.98, 25.67, 43.70, 79.09, 102.05, 106.18, 114.98, 115.06, 121.28, 126.05, 128.84, 132.16, 138.13, 156.44, 159.72, 161.22, 168.37, 197.23; IR (KBr): 1763, 1632, 1589, 1454, 1431, 1373, 1310, 1281, 1202, 1169, 1146, 1090, 1067, 999, 903, 793 cm^{-1}; mp: 82–84 °C; MS (EI): *m/z* 366 (M^+); HRMS (EI) Calcd for $C_{22}H_{22}O_5$ 366.1467 (M^+); Found 366.1485.

*4.1.7.9. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(2-acetoxyphenyl) chroman-4-one (**7i**)*. Yield: 78%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.64 (3H, s), 1.68 (3H, s), 2.28 (6H, s), 2.81 (1H, dd, J = 17.2, 3.2 Hz), 3.08 (1H, dd, J = 17.2, 13.2 Hz), 3.19 (2H, d, J = 7.2 Hz), 5.09 (1H, t, J = 7.2 Hz), 5.53 (1H, dd, J = 13.2, 3.2 Hz), 6.23 (1H, s), 7.12 (1H, d, J = 7.2 Hz), 7.32 (1H, t, J = 7.2 Hz), 7.40 (1H, td, J = 7.2, 1.6 Hz), 7.59 (1H, dd, J = 7.2, 1.6 Hz), 12.16 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.73, 20.85, 20.89, 21.95, 25.65, 42.58, 74.28, 102.06, 106.10, 115.20, 121.18, 122.97, 126.54, 127.13, 129.81, 130.10, 132.19, 147.68, 156.41, 159.61, 161.25, 168.34, 169.08, 197.08; IR (KBr): 1771, 1683, 1653, 1646, 1635, 1558, 1540, 1506, 1490, 1456, 1436, 1373, 1195, 1139 cm^{-1}; mp: 73–75 °C; MS (EI): *m/z* 424 (M^+); HRMS (EI) Calcd for $C_{24}H_{24}O_7$ 424.1522 (M^+); Found 424.1505.

*4.1.7.10. 7-Acetoxy-5-hydroxy-6-(3-ethylpent-2-enyl)-2-(2-acetoxyphenyl) chroman-4-one (**7j**)*. Yield: 77%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 0.94 (3H, t, J = 7.2 Hz), 1.03 (3H, t, J = 7.2 Hz), 2.00 (2H, q, J = 7.2 Hz), 2.18 (2H, q, J = 7.2 Hz), 2.22 (3H, s), 2.30 (3H, s), 2.84 (1H, dd, J = 17.2, 3.2 Hz), 3.10 (1H, dd, J = 17.2, 13.6 Hz), 3.25 (2H, d, J = 6.8 Hz), 5.04 (1H, t, J = 6.8 Hz), 5.55 (1H, dd, J = 13.6, 3.2 Hz), 6.25 (1H, s), 7.14 (1H, dd, J = 7.6, 1.2 Hz), 7.34 (1H, td, J = 7.6, 1.2 Hz), 7.42 (1H, td, J = 7.6, 2.0 Hz), 7.61 (1H, dd, J = 7.6, 2.0 Hz), 12.18 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 12.59, 13.07, 20.90, 20.94, 21.39, 23.27, 29.05, 42.65, 74.30, 102.12, 106.15, 115.45, 119.21, 122.98, 126.58, 127.15, 129.84, 130.15, 143.46, 147.70, 156.56, 159.65, 161.29, 168.36, 169.11, 197.11; IR (KBr): 1771, 1768, 1762, 1653, 1646, 1635, 1558, 1506, 1490, 1457, 1437, 1368, 1207, 1197, 1141, 1100, 1062 cm^{-1}; mp: 83–85 °C; MS (EI): *m/z* 452 (M^+); HRMS (EI) Calcd for $C_{26}H_{28}O_7$ 452.1835 (M^+); Found 452.1813.

*4.1.7.11. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(3-acetoxyphenyl) chroman-4-one (**7k**)*. Yield: 94%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.68 (3H, s), 1.75 (3H, s), 2.30 (3H, s), 2.32 (3H, s), 2.88 (1H, dd, J = 17.2, 3.2 Hz), 3.07 (1H, dd, J = 17.2, 13.2 Hz), 3.21 (2H, d, J = 7.2 Hz), 5.11 (1H, td, J = 7.2, 1.2 Hz), 5.43 (1H, dd, J = 13.2, 3.2 Hz), 6.29 (1H, s), 7.13 (1H, dd, J = 8.0, 1.2 Hz), 7.21 (1H, t, J = 1.2 Hz), 7.29 (1H, d, J = 8.0 Hz), 7.44 (1H, t, J = 8.0 Hz), 12.14 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.73, 20.87, 21.07, 21.96, 25.65, 43.66, 78.34, 102.06, 106.13, 115.15, 119.29, 121.21, 122.02, 123.27, 129.87, 132.19, 139.86, 150.93, 156.45, 159.43, 161.20, 168.34, 169.27, 196.84; IR (KBr): 1768, 1635, 1587, 1433, 1371, 1202, 1171, 1137, 1066 cm^{-1}; mp: 84–86 °C; MS (EI): *m/z* 424 (M^+); HRMS (EI) Calcd for $C_{24}H_{24}O_7$ 424.1522 (M^+); Found 424.1505.

*4.1.7.12. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(2,3-diacetoxyphenyl) chroman-4-one (**7l**)*. Yield: 89%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.65 (3H, s), 1.73 (3H, s), 2.27 (3H, s), 2.28 (6H, s), 2.81 (1H, dd, J = 17.2, 3.2 Hz), 3.07 (1H, dd, J = 17.2, 13.6 Hz), 3.19 (2H, d, J = 7.6 Hz), 5.08 (1H, tt, J = 7.6, 1.2 Hz), 5.50 (1H, dd, J = 13.6, 3.2 Hz), 6.22 (1H, s), 7.24 (1H, dd, J = 8.0, 1.6 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.46 (1H, dd, J = 8.0, 1.6 Hz), 12.13 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.88, 20.29, 20.64, 20.87, 22.09, 25.79, 42.62, 74.29, 102.21, 106.21, 115.48, 121.29, 124.16, 124.45, 127.07, 132.32, 132.37, 139.81, 142.81, 156.58, 159.54, 161.39, 168.00, 168.16, 168.48, 196.93; IR (KBr): 1772, 1654, 1646, 1635, 1629, 1507, 1470, 1431, 1374, 1205, 1171, 1160, 1137 cm^{-1}; mp: 56–58 °C; MS (EI): *m/z* 482 (M^+); HRMS (EI) Calcd for $C_{26}H_{26}O_9$ 482.1577 (M^+); Found 482.1576.

*4.1.7.13. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(2,6-diacetoxyphenyl)chroman-4-one (**7m**)*. Yield: 89%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.68 (3H, s), 1.75 (3H, s), 2.24 (6H, s), 2.29 (3H, s), 2.70 (1H, dd, J = 17.2, 3.2 Hz), 3.20 (2H, d, J = 7.6 Hz), 3.54 (1H, dd, J = 17.2, 14.0 Hz), 5.10 (1H, t, J = 7.6 Hz), 5.57 (1H, dd, J = 14.0, 3.2 Hz), 6.19 (1H, s), 7.05 (2H, d, J = 8.0 Hz), 7.43 (1H, t, J = 8.0 Hz), 12.21 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.71, 20.79, 20.83, 21.96, 25.65, 40.47, 72.20, 101.80, 105.85, 115.29, 121.09, 121.47, 122.51, 129.97, 132.25, 149.27, 156.50, 159.32, 161.36, 168.27, 168.97, 197.09; IR (KBr): 1771, 1653, 1646, 1635, 1616, 1558, 1506, 1472, 1465, 1436, 1373, 1192, 1138, 1032 cm^{-1}; mp: 68–70 °C; MS (EI): *m/z* 482 (M^+); HRMS (EI) Calcd for $C_{26}H_{26}O_9$ 482.1577 (M^+); Found 482.1576.

*4.1.7.14. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(3,4-diacetoxyphenyl)chroman-4-one (**7n**)*. Yield: 90%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.66 (3H, s), 1.73 (3H, s), 2.28 (6H, s), 2.29 (3H, s), 2.86 (1H, dd, J = 17.2, 3.2 Hz), 3.04 (1H, dd, J = 17.2, 13.6 Hz), 3.19 (2H, d, J = 7.6 Hz), 5.09 (1H, tt, J = 7.6, 1.2 Hz), 5.40 (1H, dd, J = 13.6, 3.2 Hz), 6.26 (1H, s), 7.23 (1H, d, J = 8.0 Hz), 7.24 (1H, s), 7.29 (1H, d, J = 8.0 Hz), 12.11 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.73, 20.57, 20.59, 20.87, 21.96, 25.65, 43.64, 77.95, 102.05, 106.09, 115.23, 121.18, 121.28, 123.85, 124.06, 132.20, 136.93, 142.23, 142.29, 156.45, 159.33, 161.21, 168.05, 168.09, 168.34, 196.68; IR (KBr): 1772, 1654, 1646, 1635, 1507, 1430, 1374, 1270, 1205, 1197, 1138 cm^{-1}; mp: 121–123 °C; MS (EI): *m/z* 482 (M^+); HRMS (EI) Calcd for $C_{26}H_{26}O_9$ 482.1577 (M^+); Found 482.1597.

*4.1.7.15. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(3,5-diacetoxyphenyl)chroman-4-one (**7o**)*. Yield: 84%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.66 (3H, s), 1.73 (3H, s), 2.29 (9H, s), 2.89 (1H, dd, J = 17.2, 2.8 Hz), 3.02 (1H, dd, J = 17.2, 13.2 Hz), 3.19 (2H, d, J = 7.6 Hz), 5.09 (1H, t, J = 7.6 Hz), 5.39 (1H, dd, J = 13.2, 2.8 Hz), 6.27 (1H, s), 6.94 (1H, t, J = 1.2 Hz), 7.06 (2H, d, J = 1.2 Hz), 12.10 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.78, 20.92, 21.09, 22.00, 25.68, 43.66, 77.91, 102.21, 106.13, 115.35, 115.80, 116.53, 121.18, 132.28, 140.61, 151.31, 156.50, 159.22, 161.25, 168.36, 168.83, 196.52; IR (KBr): 1772, 1653, 1646, 1635, 1507, 1435, 1369, 1195, 1138, 1062, 1025 cm^{-1}; mp: 130–132 °C; MS (EI): *m/z* 482 (M^+); HRMS (EI) Calcd for $C_{26}H_{26}O_9$ 482.1577 (M^+); Found 482.1576.

*4.1.7.16. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(4-methoxyphenyl) chroman-4-one (**7p**)*. Yield: 40%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.68 (3H, s), 1.75 (3H, s), 2.30 (3H, s), 2.83 (1H, dd, J = 17.0, 2.6 Hz), 3.13 (1H, dd, J = 17.0, 13.4 Hz), 3.21 (2H, d, J = 6.8 Hz), 3.83 (3H, s), 5.11 (1H, t, J = 6.8 Hz), 5.38 (1H, dd, J = 13.4, 2.6 Hz), 6.26 (1H, s), 6.95 (2H, d, J = 8.8 Hz), 7.37 (2H, d, J = 8.8 Hz), 12.19 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.74, 20.88, 21.97, 25.66, 43.50, 55.31, 78.86, 102.02, 106.17, 114.16, 114.84, 121.30, 127.66, 130.12, 132.13, 156.40, 159.84, 160.00, 161.19, 168.38, 197.50; IR (KBr): 1751, 1634, 1587, 1520, 1433, 1369, 1348, 1308, 1277, 1261, 1213, 1177, 1140, 1084, 1063 cm^{-1}; mp: 105–107 °C; MS (EI): *m/z* 396 (M^+); HRMS (EI) Calcd for $C_{23}H_{24}O_6$ 396.1573 (M^+); Found 396.1559.

*4.1.7.17. 7-Acetoxy-5-hydroxy-6-(3-methylbut-2-enyl)-2-(4-chlorophenyl) chroman-4-one (**7q**)*. Yield: 56%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.69 (3H, s), 1.75 (3H, s), 2.31 (3H, s), 2.85 (1H, dd, J = 17.0, 3.0 Hz), 3.06 (1H, dd, J = 17.0, 13.2 Hz), 3.21 (2H, d, J = 6.8 Hz), 5.10 (1H, t, J = 6.8 Hz), 5.41 (1H, dd, J = 13.2, 3.0 Hz), 6.28 (1H, s), 7.39 (4H, d, J = 4.8 Hz), 12.14 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 17.76, 20.90, 21.99, 25.68, 43.63, 78.33, 102.07, 106.13, 115.22, 121.19, 127.42, 129.05, 132.24, 134.71, 136.67, 156.48, 159.43, 161.25, 168.38, 196.78; IR (KBr): 1763, 1636, 1589, 1497, 1433, 1373, 1304, 1211, 1165, 1138, 1088, 1063, 822 cm^{-1}; mp: 105–107 °C; MS (EI): *m/z* 400

(M^+); HRMS (EI) Calcd for $C_{22}H_{21}ClO_5$ 400.1078 (M^+); Found 400.1083.

*4.1.8. General procedure for the synthesis of 6-PNG derivatives **8c–d** and **8h–q***

To a stirred solution of **7c–d** or **7h–q** (0.12 mmol) in MeOH (3 mL) was added K_2CO_3 (0.36 mmol) under argon atmosphere. The resulting solution was stirred at room temperature for 30 min. The reaction mixture was neutralized and evaporated. The crude product was chromatographed on SiO_2 (5 g, EtOAc/hexane = 1/1) to give the corresponding product **8c–d** or **8h–q**.

4.1.8.1. 5-Hydroxy-2-(2-hydroxyphenyl)-6-(3-methylbut-2-enyl)chroman-4-one (8c). Yield: 84%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.70 (6H, s), 2.93 (1H, dd, J = 17.2, 2.4 Hz), 3.18 (1H, dd, J = 17.2, 12.8 Hz), 3.25 (2H, d, J = 7.2 Hz), 5.29 (1H, tt, J = 7.2, 1.2 Hz), 5.83 (1H, dd, J = 12.8, 2.4 Hz), 6.47 (1H, d, J = 8.0 Hz), 6.92 (1H, t, J = 8.0 Hz), 6.94 (1H, d, J = 8.0 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.0 Hz), 7.54 (1H, dd, J = 8.0, 1.2 Hz), 8.77 (1H, s), 12.15 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.75, 25.82, 27.37, 43.07, 75.31, 107.57, 108.45, 116.26, 120.68, 121.93, 123.05, 126.30, 127.62, 130.17, 132.98, 138.73, 154.73, 160.18, 161.03, 200.19; IR (KBr): 1627, 1609, 1461, 1447, 1345, 1339, 1235, 1065, 735 cm^{-1}; mp: 172–174 °C; MS (EI): m/z 324 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_4$ 324.1362 (M^+); Found 324.1356.

4.1.8.2. 6-(3-Ethylpent-2-enyl)-5-hydroxy-2-(2-hydroxyphenyl)-chroman-4-one (8d). Yield: 84%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 0.99 (6H, t, J = 8.0 Hz), 2.05 (2H, q, J = 8.0 Hz), 2.17 (2H, q, J = 8.0 Hz), 2.93 (1H, dd, J = 17.2, 2.4 Hz), 3.19 (1H, dd, J = 17.2, 13.2 Hz), 3.28 (2H, d, J = 7.2 Hz), 5.25 (1H, t, J = 7.2 Hz), 5.84 (1H, dd, J = 13.2, 2.4 Hz), 6.48 (1H, d, J = 8.0 Hz), 6.93 (1H, t, J = 8.0 Hz), 6.94 (1H, d, J = 8.0 Hz), 7.21 (1H, td, J = 8.0, 2.0 Hz), 7.33 (1H, d, J = 8.0 Hz), 7.54 (1H, dd, J = 8.0, 2.0 Hz), 8.80 (1H, br), 12.16 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 13.16, 13.49, 23.65, 26.79, 43.08, 75.33, 107.61, 108.45, 116.28, 120.66, 121.09, 122.07, 126.31, 127.63, 130.18, 138.69, 144.44, 154.76, 160.21, 161.06, 200.23; IR (KBr): 2964, 1653, 1623, 1608, 1555, 1505, 1461, 1363, 1355, 1339, 1235, 1065, 740 cm^{-1}; mp: 112–114 °C; MS (EI): m/z 352 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_4$ 352.1675 (M^+); Found 352.1673.

4.1.8.3. 5,7-Dihydroxy-6-(3-methylbut-2-enyl)-2-phenylchroman-4-one (8h). Yield: 84%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.77 (3H, s), 1.83 (3H, s), 2.83 (1H, dd, J = 17.2, 2.4 Hz), 3.11 (1H, dd, J = 17.2, 12.8 Hz), 3.22 (2H, d, J = 7.0 Hz), 5.11 (1H, t, J = 7.0 Hz), 5.44 (1H, dd, J = 12.8, 2.4 Hz), 6.01 (1H, s), 6.13 (1H, d, J = 1.6 Hz), 7.38–7.45 (5H, m), 12.40 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.83, 21.60, 25.85, 43.68, 79.86, 95.33, 103.10, 109.16, 123.49, 127.25, 129.33, 129.43, 131.29, 140.14, 161.74, 162.24, 164.79, 196.89; IR (KBr): 1653, 1634, 1585, 1487, 1456, 1312, 1304, 1219, 1188, 1083, 1076 cm^{-1}; mp: 197–199 °C; MS (EI): m/z 324 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_4$ 324.1362 (M^+); Found 324.1366.

4.1.8.4. 5,7-Dihydroxy-2-(2-hydroxyphenyl)-6-(3-methylbut-2-enyl)chroman-4-one (8i). Yield: 87%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 2.81 (1H, dd, J = 17.2, 3.2 Hz), 3.08 (1H, dd, J = 17.2, 13.2 Hz), 3.24 (2H, d, J = 7.2 Hz), 5.23 (1H, tt, J = 7.2, 1.2 Hz), 5.77 (1H, dd, J = 13.2, 3.2 Hz), 6.08 (1H, s), 6.92 (1H, t, J = 7.6 Hz), 6.93 (1H, d, J = 7.6 Hz), 7.20 (1H, t, J = 7.6 Hz), 7.51 (1H, d, J = 7.6 Hz), 12.47 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.80, 21.59, 25.82, 42.55, 75.24, 95.27, 103.01, 109.01, 116.22, 120.60, 123.52, 126.41, 127.60, 130.08, 131.18, 154.74, 162.13, 162.24, 164.72, 197.37; IR (KBr): 1653, 1635, 1616, 1601, 1576, 1558, 1540, 1506, 1496, 1490, 1472, 1457, 1339, 1312, 1272, 1155, 1083, 751 cm^{-1}; mp: 174–176 °C; MS (EI): m/z 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1319.

4.1.8.5. 6-(3-Ethylpent-2-enyl)-5,7-dihydroxy-2-(2-hydroxy-phenyl)chroman-4-one (8j). Yield: 80%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 0.94 (3H, t, J = 7.2 Hz), 1.01 (3H, t, J = 7.2 Hz), 1.98 (2H, q, J = 7.2 Hz), 2.24 (2H, q, J = 7.2 Hz), 2.82 (1H, dd, J = 17.2, 3.2 Hz), 3.08 (1H, dd, J = 17.2, 12.8 Hz), 3.29 (2H, d, J = 7.2 Hz), 5.21 (1H, t, J = 7.2 Hz), 5.77 (1H, dd, J = 12.8, 3.2 Hz), 6.08 (1H, s), 6.91 (1H, t, J = 7.6 Hz), 6.94 (1H, d, J = 7.6 Hz), 7.20 (1H, td, J = 7.6, 1.2 Hz), 7.52 (1H, dd, J = 7.6, 1.2 Hz), 8.77 (1H, s), 9.62 (1H, s), 12.49 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 13.11, 13.47, 21.01, 23.62, 42.57, 75.26, 95.31, 103.07, 109.14, 116.25, 120.64, 121.55, 126.44, 127.64, 130.11, 142.61, 154.75, 162.17, 162.31, 164.73, 197.41; IR (KBr): 2964, 1653, 1635, 1616, 1595, 1559, 1507, 1496, 1490, 1472, 1457, 1339, 1309, 1302, 1272, 1156, 1082, 752 cm^{-1}; mp: 154–156 °C; MS (EI): m/z 368 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_5$ 368.1624 (M^+); Found 368.1637.

4.1.8.6. 5,7-Dihydroxy-2-(3-hydroxyphenyl)-6-(3-methylbut-2-enyl)chroman-4-one (8k). Yield: 73%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 2.77 (1H, dd, J = 17.2, 2.8 Hz), 3.10 (1H, dd, J = 17.2, 12.8 Hz), 3.34 (2H, d, J = 7.2 Hz), 5.22 (1H, td, J = 7.2, 1.2 Hz), 5.46 (1H, dd, J = 12.8, 2.8 Hz), 6.06 (1H, s), 6.84 (1H, d, J = 8.0 Hz), 6.99 (1H, d, J = 8.0 Hz), 7.02 (1H, s), 7.24 (1H, t, J = 8.0 Hz), 12.43 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.06, 20.83, 25.09, 42.92, 78.94, 94.56, 102.33, 108.33, 113.33, 115.45, 117.45, 122.73, 129.78, 130.48, 140.88, 157.67, 160.93, 161.45, 163.99, 196.14; IR (KBr): 1635, 1589, 1485, 1455, 1327, 1305, 1283, 1182, 1166, 1155, 1085, 1076 cm^{-1}; mp: 179–181 °C; MS (EI): m/z 340 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_5$ 340.1311 (M^+); Found 340.1311.

4.1.8.7. 2-(2,3-Dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chroman-4-one (8l). Yield: 95%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.64 (3H, s), 1.74 (3H, s), 2.81 (1H, dd, J = 17.2, 2.4 Hz), 3.10 (1H, dd, J = 17.2, 12.8 Hz), 3.25 (2H, d, J = 7.2 Hz), 5.23 (1H, t, J = 7.2 Hz), 5.78 (1H, dd, J = 12.8, 2.4 Hz), 6.06 (1H, s), 6.76 (1H, t, J = 8.0 Hz), 6.87 (1H, dd, J = 8.0, 1.2 Hz), 7.02 (1H, d, J = 8.0 Hz), 12.48 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.80, 21.59, 25.83, 42.48, 75.28, 95.26, 103.04, 108.98, 115.76, 118.38, 120.38, 123.53, 126.66, 131.18, 143.28, 145.43, 162.13, 162.24, 164.68, 197.39; IR (KBr): 1653, 1635, 1624, 1617, 1596, 1577, 1563, 1507, 1481, 1476, 1457, 1448, 1338, 1305, 1284, 1156, 1120, 1085 cm^{-1}; mp: 149–151 °C; MS (EI): m/z 356 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_6$ 356.1260 (M^+); Found 356.1273.

4.1.8.8. 2-(2,6-Dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chroman-4-one (8m). Yield: 97%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 2.51 (1H, dd, J = 17.2, 3.2 Hz), 3.24 (2H, d, J = 7.2 Hz), 3.89 (1H, dd, J = 17.2, 14.0 Hz), 5.23 (1H, t, J = 7.2 Hz), 6.00 (1H, s), 6.01 (1H, dd, J = 14.0, 3.2 Hz), 6.46 (2H, d, J = 8.0 Hz), 7.02 (1H, t, J = 8.0 Hz), 8.57 (2H, s), 12.58 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.79, 21.59, 25.82, 40.52, 73.38, 95.22, 103.03, 108.39, 108.84, 111.73, 123.62, 130.88, 131.09, 157.74, 162.39, 162.59, 164.51, 198.39; IR (KBr): 1653, 1635, 1603, 1559, 1506, 1472, 1456, 1451, 1447, 1309, 1150 cm^{-1}; mp: 244–246 °C; MS (EI): m/z 356 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_6$ 356.1260 (M^+); Found 356.1273.

4.1.8.9. 2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chroman-4-one (8n). Yield: 80%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.62 (3H, s), 1.73 (3H, s), 2.70 (1H, dd, J = 17.2, 3.2 Hz), 3.11 (1H, dd, J = 17.2, 12.8 Hz), 3.23 (2H, d, J = 7.2 Hz), 5.22 (1H, t, J = 7.2 Hz), 5.35 (1H, dd, J = 12.8, 3.2 Hz), 6.01 (1H, s), 6.85 (2H, s), 7.01 (1H, s), 8.19 (1H, br) 12.45 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.79, 21.56, 25.81, 43.60, 79.82, 95.24, 103.04, 108.92, 114.65, 115.95, 119.17, 123.51, 131.18, 131.64, 145.94, 146.28, 161.88, 162.17, 164.70, 197.26; IR (KBr): 1653, 1646, 1635, 1624, 1616, 1596, 1577, 1559, 1507, 1457, 1448, 1339, 1287, 1158,

1120, 1090 cm^{-1}; mp: 121–123 °C; MS (EI): *m/z* 356 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_6$ 356.1260 (M^+); Found 356.1273.

*4.1.8.10. 2-(3,5-Dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl) chroman-4-one (**8o**)*. Yield: 93%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 2.70 (1H, dd, *J* = 17.2, 2.4 Hz), 3.11 (1H, dd, *J* = 17.2, 12.8 Hz), 3.23 (2H, d, *J* = 7.6 Hz), 5.22 (1H, t, *J* = 7.6 Hz), 5.34 (1H, dd, *J* = 12.8, 2.4 Hz), 6.01 (1H, s), 6.85 (2H, s), 7.01 (1H, s), 8.17 (1H, br), 12.45 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 25.37, 38.85, 43.71, 49.04, 74.80, 79.70, 95.36, 103.09, 103.36, 105.62, 109.99, 123.49, 142.42, 159.59, 161.62, 162.31, 164.90, 196.97; IR (KBr): 1653, 1647, 1635, 1616, 1586, 1562, 1521, 1507, 1490, 1472, 1465, 1456, 1340, 1312, 1297, 1223, 1152, 1123, 833 cm^{-1}; mp: 196–199 °C; MS (EI): *m/z* 356 (M^+); HRMS (EI) Calcd for $C_{20}H_{20}O_6$ 356.1260 (M^+); Found 356.1273.

*4.1.8.11. 5,7-Dihydroxy-2-(4-methoxyphenyl)-6-(3-methylbut-2-enyl) chroman-4-one (**8p**)*. Yield: 98%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 2.73 (1H, dd, *J* = 17.0, 3.0 Hz), 3.17 (1H, dd, *J* = 17.2, 12.8 Hz), 3.24 (2H, d, *J* = 7.6 Hz), 3.81 (3H, s), 5.22 (1H, t, *J* = 7.6 Hz), 5.46 (1H, dd, *J* = 12.8, 3.0 Hz), 6.03 (1H, s), 6.98 (2H, d, *J* = 8.4 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 9.59 (1H, br), 12.46 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.80, 21.59, 25.82, 43.54, 55.57, 79.65, 95.28, 103.05, 109.03, 114.71, 123.53, 128.83, 131.22, 132.02, 160.87, 161.87, 162.22, 164.81, 197.18; IR (KBr): 1653, 1634, 1587, 1518, 1506, 1487, 1464, 1459, 1313, 1298, 1256, 1219, 1186, 1080, 1076, 827 cm^{-1}; mp: 155–157 °C; MS (EI): *m/z* 354 (M^+); HRMS (EI) Calcd for $C_{21}H_{22}O_5$ 354.1467 (M^+); Found 354.1463.

*4.1.8.12. 2-(4-Chlorophenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chroman-4-one (**8q**)*. Yield: 92%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.63 (3H, s), 1.74 (3H, s), 3.14 (1H, dd, *J* = 17.2, 12.8 Hz), 3.24 (2H, d, *J* = 7.2 Hz), 5.22 (1H, t, *J* = 7.2 Hz), 5.57 (1H, dd, *J* = 12.8, 3.0 Hz), 6.07 (1H, s), 7.48 (2H, d, *J* = 8.4 Hz), 7.59 (2H, d, *J* = 8.4 Hz), 9.63 (1H, br), 12.42 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 17.80, 21.60, 25.82, 43.55, 79.08, 95.36, 103.04, 109.29, 123.45, 129.04, 129.51, 131.29, 134.59, 139.10, 161.52, 162.24, 164.87, 196.61; IR (KBr): 1653, 1634, 1587, 1495, 1458, 1417, 1364, 1312, 1300, 1217, 1186, 1088, 1082, 1076, 826 cm^{-1}; mp: 183–185 °C; MS (EI): *m/z* 358 (M^+); HRMS (EI) Calcd for $C_{20}H_{19}ClO_4$ 358.0972 (M^+); Found 358.0971.

*4.1.9. General procedure of cross-metathesis for **10b–d***

To a stirred solution of **9** (0.1 g, 0.25 mmol) in benzene (5 mL) were added corresponding olefin (5.04 mmol) and Grubbs catalyst, 2nd Generation (11 mg, 0.012 mmol) under argon atmosphere. The reaction mixture was heated in the sealed tube at 100 °C for 20 h. After the solvent was removed under vacuum, the crude product was chromatographed on SiO_2 (10 g, EtOAc/hexane = 1/7) to give **10b–d**.

*4.1.9.1. 7-Acetoxy-5-hydroxy-6-(3-ethylpent-2-enyl)-2-(4-acetoxyphenyl) chroman-4-one (**10b**)*. Yield: 73%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 0.96 (3H, t, *J* = 7.2 Hz), 1.03 (3H, t, *J* = 7.2 Hz), 2.00 (2H, q, *J* = 7.2 Hz), 2.20 (2H, q, *J* = 7.2 Hz), 2.29 (3H, s), 2.31 (3H, s), 2.85 (1H, dd, *J* = 17.2, 2.8 Hz), 3.08 (1H, dd, *J* = 17.2, 13.2 Hz), 3.26 (2H, d, *J* = 7.2 Hz), 5.04 (1H, t, *J* = 7.2 Hz), 5.43 (1H, dd, *J* = 13.2, 2.8 Hz), 6.28 (1H, s), 7.15 (2H, d, *J* = 8.4 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 12.17 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 12.55, 13.05, 20.89, 21.07, 21.37, 23.25, 29.02, 43.69, 78.49, 102.06, 106.14, 115.31, 119.23, 122.02, 127.25, 135.71, 143.40, 150.85, 156.55, 159.57, 161.23, 168.35, 169.29, 197.01; IR (KBr): 2964, 1769, 1752, 1646, 1633, 1585, 1511, 1431, 1371, 1303, 1219, 1193, 1141, 1086, 1065, 900 cm^{-1}; mp: 70–72 °C; MS (EI): *m/z* 452 (M^+); HRMS (EI) Calcd for $C_{26}H_{28}O_7$ 452.1835 (M^+); Found 452.1826.

*4.1.9.2. 7-Acetoxy-5-hydroxy-6-(3-propylhex-2-enyl)-2-(4-acetoxyphenyl) chroman-4-one (**10c**)*. Yield: 23%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 0.82 (3H, t, *J* = 7.2 Hz), 0.93 (3H, t, *J* = 7.2 Hz), 1.28–1.45 (4H, m), 1.90 (2H, t, *J* = 7.2 Hz), 2.11 (2H, t, *J* = 7.2 Hz), 2.27 (3H, s), 2.30 (3H, s), 2.79 (1H, dd, *J* = 17.2, 2.8 Hz), 3.08 (1H, dd, *J* = 17.2, 12.8 Hz), 3.22 (2H, d, *J* = 7.0 Hz), 5.06 (1H, t, *J* = 7.0 Hz), 5.41 (1H, dd, *J* = 12.8, 2.8 Hz), 6.25 (1H, s), 7.13 (2H, d, *J* = 8.8 Hz), 7.44 (2H, d, *J* = 8.8 Hz), 12.13 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 13.90, 14.31, 20.95, 21.11, 21.17, 21.57, 32.33, 38.99, 43.75, 78.52, 102.06, 106.16, 115.39, 121.23, 122.05, 127.28, 135.74, 140.28, 150.88, 156.55, 159.59, 161.27, 168.38, 169.33, 197.03; IR (KBr): 2959, 1768, 1752, 1647, 1628, 1587, 1507, 1431, 1373, 1219, 1194, 1163, 1142, 1086, 1065 cm^{-1}; mp: 72–74 °C; MS (EI): *m/z* 480 (M^+); HRMS (EI) Calcd for $C_{28}H_{32}O_7$ 480.2148 (M^+); Found 480.2151.

*4.1.9.3. 7-Acetoxy-5-hydroxy-6-(2-cyclopentylidenethyl)-2-(4-acetoxyphenyl)chroman-4-one (**10d**)*. Yield: 96%; ^{1}H NMR (400 MHz $CDCl_3$) δ: 1.57 (2H, quin, *J* = 6.8 Hz), 1.67 (2H, quin, *J* = 6.8 Hz), 2.18 (2H, t, *J* = 6.8 Hz), 2.29 (3H, s), 2.30 (3H, s), 2.32 (2H, t, *J* = 6.8 Hz), 2.83 (1H, dd, *J* = 17.2, 3.2 Hz), 3.06 (1H, dd, *J* = 17.2, 13.6 Hz), 3.18 (2H, d, *J* = 6.8 Hz), 5.21 (1H, t, *J* = 6.8 Hz), 5.40 (1H, dd, *J* = 13.6, 3.2 Hz), 6.25 (1H, s), 7.13 (2H, d, *J* = 8.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 12.15 (1H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ: 20.93, 21.10, 23.41, 26.33, 26.41, 28.68, 33.56, 43.70, 78.51, 102.02, 106.16, 115.16, 116.61, 122.03, 127.27, 135.71, 144.20, 150.85, 156.43, 159.54, 161.24, 168.40, 169.32, 197.02; IR (KBr): 2962, 1769, 1751, 1653, 1646, 1636, 1586, 1559, 1507, 1436, 1369, 1198, 1137, 1087 cm^{-1}; mp: 67–69 °C; MS (EI): *m/z* 450 (M^+); HRMS (EI) Calcd for $C_{26}H_{26}O_7$ 450.1679 (M^+); Found 450.1682.

*4.1.10. General procedure for the synthesis of 6-PNG derivatives **11b-d***

To a stirred solution of **10b–d** (0.14 mmol) in MeOH (2 mL) was added K_2CO_3 (0.42 mmol) under argon atmosphere. The resulting solution was stirred at room temperature for 30 min. The reaction mixture was neutralized and evaporated. The crude product was chromatographed on SiO_2 (5 g, EtOAc/hexane = 1/1) to give the corresponding product **11b–d**.

*4.1.10.1. 6-(3-Ethylpent-2-enyl)-5,7-dihydroxy-2-(4-hydroxy-phenyl)chroman-4-one (**11b**)*. Yield: 86%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 0.93 (3H, t, *J* = 7.2 Hz), 1.01 (3H, t, *J* = 7.2 Hz), 1.98 (2H, q, *J* = 7.2 Hz), 2.23 (2H, q, *J* = 7.2 Hz), 2.70 (1H, dd, *J* = 17.2, 3.2 Hz), 3.16 (1H, dd, *J* = 17.2, 12.8 Hz), 3.28 (2H, d, *J* = 7.2 Hz), 5.19 (1H, t, *J* = 7.2 Hz), 5.42 (1H, dd, *J* = 12.8, 3.2 Hz), 6.02 (1H, s), 6.88 (2H, d, *J* = 8.4 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 8.53 (1H, br), 9.46 (1H, br), 12.48 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 12.35, 12.72, 20.32, 22.85, 28.94, 42.08, 79.07, 94.51, 102.30, 108.30, 115.34, 120.77, 128.20, 130.11, 141.84, 157.85, 161.20, 161.49, 164.00, 196.56; IR (KBr): 2965, 1653, 1646, 1635, 1616, 1587, 1558, 1521, 1517, 1507, 1490, 1457, 1447, 1337, 1309, 1297, 1170, 1153, 1085, 830 cm^{-1}; mp: 208–210 °C; MS (EI): *m/z* 368 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_5$ 368.1624 (M^+); Found 368.1637.

*4.1.10.2. 5,7-Dihydroxy-2-(4-hydroxyphenyl)-6-(3-propylhex-2-enyl)chroman-4-one (**11c**)*. Yield: 90%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 0.82 (3H, t, *J* = 7.4 Hz), 0.93 (3H, t, *J* = 7.4 Hz), 1.31–1.49 (4, m), 1.92 (2H, t, *J* = 7.4 Hz), 2.18 (2H, t, *J* = 7.4 Hz), 2.69 (1H, dd, *J* = 17.2, 2.8 Hz), 3.15 (1H, dd, *J* = 17.2, 12.8 Hz), 3.28 (2H, d, *J* = 7.6 Hz), 5.25 (1H, t, *J* = 7.6 Hz), 5.40 (1H, dd, *J* = 12.8, 2.8 Hz), 6.02 (1H, s), 6.88 (2H, d, *J* = 8.4 Hz), 7.37 (2H, d, *J* = 8.4 Hz), 12.48 (1H, br); ^{13}C NMR (100 MHz Acetone-d_6) δ: 14.11, 14.54, 21.29, 21.91, 22.33, 32.63, 39.72, 43.59, 79.83, 95.30, 103.35, 109.13, 116.11, 123.75, 128.97, 130.90, 139.29, 158.64, 161.88, 162.25, 164.77, 197.26; IR (KBr): 2959, 1638, 1616, 1601, 1518, 1491, 1456, 1340, 1310, 1252, 1215,

1153, 1086, 833 cm^{-1}; mp: 130–132 °C; MS (EI): *m/z* 396 (M^+); HRMS (EI) Calcd for $C_{24}H_{28}O_5$ 396.1937 (M^+); Found 396.1920.

*4.1.10.3. 6-(2-Cyclopentylidenethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one (**11d**)*. Yield: 98%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.55 (2H, quin, *J* = 7.2 Hz), 1.65 (2H, quin, *J* = 7.2 Hz), 2.15 (2H, t, *J* = 7.2 Hz), 2.39 (2H, t, *J* = 7.2 Hz), 2.70 (1H, dd, *J* = 17.2, 2.8 Hz), 3.15 (1H, dd, *J* = 17.2, 12.8 Hz), 3.22 (2H, d, *J* = 7.2 Hz), 5.32 (1H, tt, *J* = 7.2, 2.0 Hz), 5.40 (1H, dd, *J* = 12.8, 2.8 Hz), 6.02 (1H, s), 6.88 (2H, d, *J* = 8.4 Hz), 7.37 (2H, d, *J* = 8.4 Hz), 9.03 (2H, br), 12.47 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 23.02, 26.94, 27.04, 29.04, 34.08, 43.55, 79.81, 95.25, 103.06, 108.95, 116.10, 118.85, 128.96, 130.88, 143.13, 158.58, 161.92, 162.22, 164.70, 197.28; IR (KBr): 2969, 1653, 1646, 1635, 1616, 1586, 1559, 1521, 1517, 1507, 1497, 1490, 1472, 1457, 1448, 1437, 1339, 1310, 1296, 1245, 1220, 1160, 1085, 830 cm^{-1}; mp: 217–219 °C; MS (EI): *m/z* 366 (M^+); HRMS (EI) Calcd for $C_{22}H_{22}O_5$ 366.1467 (M^+); Found 366.1472.

*4.1.11. General procedure for the synthesis of 6-PNG derivatives **12a–c***

To a stirred solution of **11a, b** or **11d** (0.05 mmol) in EtOAc (3 mL) was added 10% Pd/C (5 mg), and the resulting mixture was hydrogenated at 1 atm for 20 h. The catalyst was removed through a Celite pad and washed with EtOAc (3 mL x 3). The filtrate and washings were combined and evaporated to give the corresponding product **12a–c**.

4.1.11.1. 5,7-Dihydroxy-2-(4-hydroxyphenyl)-6-(3-methylbutyl)-chroman-4-one (12a). Yield: 100%; ^{1}H NMR (400 MHz DMSO-d_6) δ: 0.88 (6H, d, *J* = 6.4 Hz), 1.28 (2H, q, *J* = 7.6 Hz), 1.42–1.54 (1H, m), 2.41 (1H, d, *J* = 7.6 Hz), 2.43 (1H, d, *J* = 7.6 Hz), 2.63 (1H, dd, *J* = 17.2, 2.8 Hz), 3.22 (1H, dd, *J* = 17.2, 12.8 Hz), 5.38 (1H, dd, *J* = 12.8, 2.8 Hz), 5.93 (1H, s), 6.77 (2H, d, *J* = 8.4 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 9.62 (1H, br), 12.41 (1H, s); ^{13}C NMR (100 MHz DMSO-d_6) δ: 19.47, 22.57, 27.59, 37.75, 42.12, 78.30, 94.41, 101.35, 108.59, 115.15, 128.31, 129.08, 157.70, 160.43, 160.74, 162.57, 196.28; IR (KBr): 2951, 1632, 1587, 1519, 1489, 1453, 1382, 1337, 1310, 1296, 1248, 1210, 1185, 1158, 1129, 1085, 1055, 830 cm^{-1}; mp: 217–219 °C; MS (EI): *m/z* 342 (M^+); HRMS (EI) Calcd for $C_{20}H_{22}O_5$ 342.1467 (M^+); Found 342.1475.

4.1.11.2. 6-(3-Ethylpentyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)-chroman-4-one (12b). Yield: 100%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 0.87 (6H, t, *J* = 7.2 Hz), 1.20–1.27 (1H, m), 1.31–1.41 (4H, m), 1.43–1.49 (2H, m), 2.52 (1H, d, *J* = 8.0 Hz), 2.54 (1H, d, *J* = 8.0 Hz), 2.70 (1H, dd, *J* = 17.2, 2.8 Hz), 3.16 (1H, dd, *J* = 17.2, 12.8 Hz), 5.41 (1H, dd, *J* = 12.8, 2.8 Hz), 6.01 (1H, s), 6.88 (2H, d, *J* = 8.4 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 8.52 (1H, br), 9.55 (1H, br), 12.46 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 11.16, 19.64, 26.06, 32.31, 41.33, 43.61, 79.84, 95.20, 103.01, 110.20, 116.10, 128.70, 130.90, 158.62, 161.83, 162.38, 164.89, 197.31; IR (KBr): 2960, 1635, 1587, 1518, 1489, 1458, 1338, 1308, 1296, 1261, 1244, 1186, 1161, 1105, 1084, 829 cm^{-1}; mp: 206–208 °C; MS (EI): *m/z* 370 (M^+); HRMS (EI) Calcd for $C_{22}H_{26}O_5$ 370.1780 (M^+); Found 370.1765.

*4.1.11.3. 6-(2-Cyclopentylethyl)-5,7-dihydroxy-2-(4-hydroxy-phenyl)chroman-4-one (**12c**)*. Yield: 100%; ^{1}H NMR (400 MHz Acetone-d_6) δ: 1.09–1.21 (2H, m), 1.44–1.54 (4H, m), 1.54–1.63 (2H, m), 1.76–1.85 (3H, m), 2.56 (1H, d, *J* = 8.0 Hz), 2.58 (1H, d, *J* = 8.0 Hz), 2.70 (1H, dd, *J* = 17.2, 2.8 Hz), 3.16 (1H, dd, *J* = 17.2, 12.8 Hz), 5.41 (1H, dd, *J* = 12.8, 2.8 Hz), 6.01 (1H, s), 6.88 (2H, d, *J* = 8.4 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 8.51 (1H, s), 9.48 (1H, s), 12.45 (1H, s); ^{13}C NMR (100 MHz Acetone-d_6) δ: 21.69, 25.83, 33.28, 36.19, 40.90, 43.61, 79.84, 95.19, 103.01, 110.04, 116.10, 128.98, 130.90, 158.61, 161.84, 162.43, 164.88, 197.31; IR (KBr): 2951, 1635, 1589, 1518, 1491, 1452, 1338, 1310, 1296, 1261, 1159, 1142, 1105, 1084, 829 cm^{-1}; mp: 224–226 °C; MS (EI): *m/z* 368 (M^+); HRMS (EI) Calcd for $C_{22}H_{24}O_5$ 368.1624 (M^+); Found 368.1637.

4.2. Biology

4.2.1. Assessment of T-currents by a patch-clamp technique in $Ca_v3.2$-expressing HEK293 cells

Measurements of T-type calcium channel-dependent membrane currents were performed in HEK293 cells that stably express human $Ca_v3.2$, using a whole cell patch-clamp technique, as described previously.[26] The cell membrane voltage was held at −90 mV, and whole-cell Ba^{2+} currents were elicited by a test pulse at 30 mV.

4.2.2. Animals, von Frey test and creation of a surgically induced neuropathic pain model in mice

Male ddY mice weighing 18–25 g (Kiwa Laboratory Animals Co. Ltd., Wakayama, Japan) were used with approval by the Committee for the Care and Use of Laboratory Animals at Kindai University, and all procedures employed were in accordance with the NIH guidelines (Guide for the Care and Use of Laboratory Animals, NIH Publication 86–23). Nociceptive threshold in the hindpaw was determined by von Frey test, employing the up-down method.[27] To create a surgically induced neuropathic pain model, the right sciatic nerve of the mouse was partially ligated under isoflurane anesthesia, according to the previously described method,[28] and used to detect anti-allodynic activity of test compounds one week after the surgery.

4.2.3. Drug administration to mice

All chemicals were suspended in 0.5% carboxymethyl cellulose sodium salt (CMC-Na) solution, and administered intraperitoneally (i.p.) to mice.

4.2.4. Data analysis

Data are shown as the mean ± S.E.M. Statistical significance was evaluated by non-parametric procedures; i.e. the data were analyzed by the Kruskal-Wallis *H* test followed by a least significant difference-type test. Significance was set at a $P < 0.05$ level.

A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.bmc.2018.07.023.

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