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Synthesis of Flavanones *via* Palladium(II)-Catalyzed One-Pot β-Arylation of Chromanones with Arylboronic Acids

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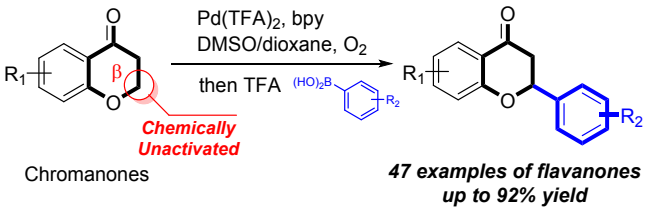


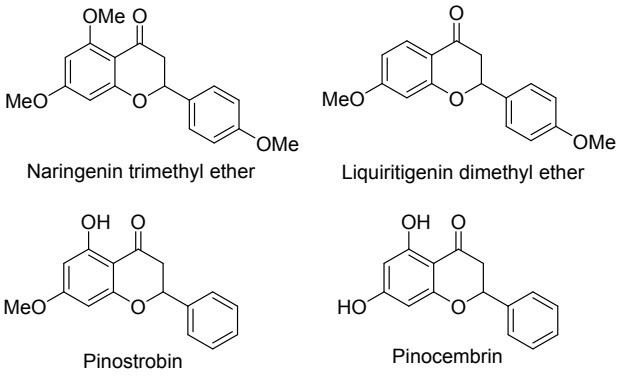
Abstract: A total of 47 flavanones were expediently synthesized *via* one-pot β-arylation of chromanones, a class of simple ketones possessing chemically unactivated β sites, with arylboronic acids *via* tandem palladium(II) catalysis. This reaction provides a novel route to various flavanones, including natural products such as naringenin trimethyl ether, in yields up to 92%.

INTRODUCTION

Flavonoids, which feature 15-carbon skeleton including 2 phenyl rings and 1 oxacycle, are a class of natural products from medicinal plants and their synthetic analogues.[1] For the past decades, flavonoids have been considered a privileged repository of various drug candidates due to their biological activities such as anti-oxidative, anti-inflammatory and anti-cancer effects.[2] Among flavonoids, flavanones, which are also known as 2-arylchroman-4-ones and include natural compounds such as naringenin trimethyl ether, have recently been identified as novel privileged structures with potent anti-cancer activity (Figure 1).[3] To date, the Claisen-Schmidt condensation of 2-hydroxyacetophenones and corresponding benzaldehydes has generally been used to provide chalcone intermediates that can be transformed into flavanones under acidic or basic refluxing conditions.[4] However, such conditions are harsh and not compatible with acid/base-labile compounds.

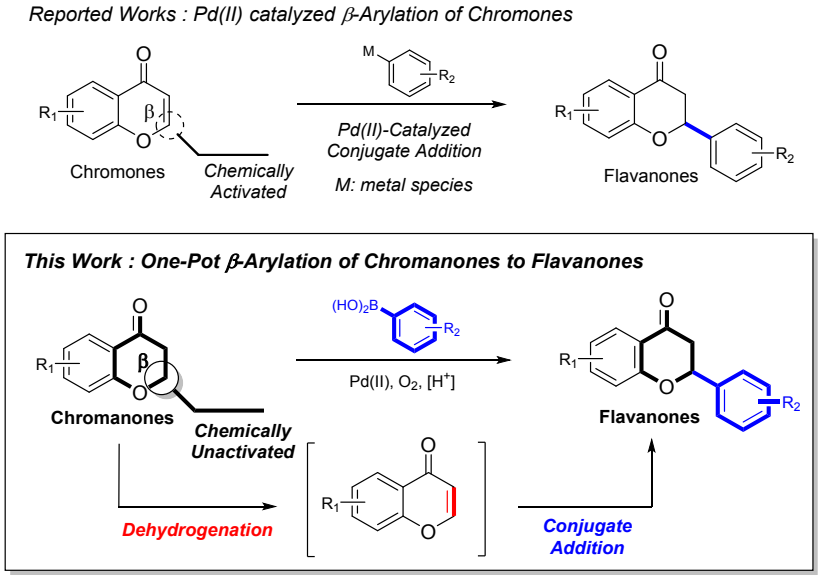
Therefore, novel synthetic routes for flavanones have been pursued.

Figure 1. Examples of natural flavanones



Recently, nucleophilic 1,4-addition to the electrophilic β sites of chromones, a class of enones, were reported for the synthesis of flavanones (Scheme 1).[5] These methods provided flavanones in good yields under mild conditions, mainly involving transition metal catalysis. In particular, they did not require acidic or basic refluxing conditions which were generally used in the Claisen-Schmidt condensation. Therefore, they showed good to excellent functional group compatibility and the feasibility of late-stage functionalization which has been central focus in the medicinal chemistry and chemical biology fields. However, chromones are sometimes prepared from chromanones,[6] a class of simple ketones, *via* additional oxidation processes[7] and generally not unmanageable because they possess reactive α,β-unsaturated carbonyl and enol ether which chromanones do not have. Therefore, chromanones might be applicable substrates to the synthesis of flavanones if it is possible to use them.

Scheme 1. One-Pot β-Arylation Strategy for Flavanones



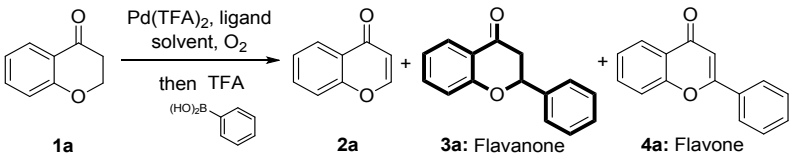
Thus, direct β-arylation of chromanones with aryl synthons would be a versatile approach to functionalized flavanones although a direct and transformative arylation of the chemically unactivated β-sites of various chromanones has not been reported. Recently, the MacMillan group and Dong group reported catalytic β-arylation of ketones with aryl synthons in the metal catalysis, respectively.[8] Furthermore, Li group reported palladium catalyzed β-arylation of ketones using arylboronic acid with *o*-iodoxybenzoic aicd (IBX) as an oxidant.[9] Inspired by these pioneering works, we aimed to develop novel methodologies that provide a diversity of privileged flavanones by one-pot arylation of chromanones *via* metal catalysis. In particular, an efficient transformation of a broad scope of substrates with high yields in the reaction would be expected to be desirable for the methodology towards flavanones. Herein, we report palladium(II)-catalyzed one-pot β-arylation of chromanones with arylboronic acids for the synthesis of flavanones.

RESULTS AND DISCUSSION

To obtain flavanones *via* β-arylation of chromanones in a one-pot sequence, we speculated that the overall reaction would involve oxidative chromone formation and sequential nucleophilic conjugate addition. Recently, preliminary reports suggested the potential of palladium(II) catalysis to enable dehydrogenation as well as conjugate addition of organoboron reagents, respectively.[5c, 5f, 8d, 10] Based on this speculation, we chose 4-chromanone **1a** and phenylboronic acid as the model compounds to

investigate the feasibility of a reaction in which they could be assembled into flavanones *via* palladium(II)-catalyzed dehydrogenation and sequential conjugate addition (Table 1). In our previous report on the synthesis of flavones from chromanones *via* a palladium(II) catalysis, we observed that the reaction with $Pd(TFA)_2$, 5-nitro-1,10-phenanthroline and DMSO solvent under an O_2 provided flavanone **3a** as a minor product (25%) along with flavone **4a** in 42% yield (entry 1).[11] For the successful conversion from chromanone to flavanone, we speculated that dehydrogenation would precede conjugate addition; however, formation of the flavone and arylboronic acid-derived byproducts should be avoided in the reaction.[12] For this purpose, we tried to screen many conditions and found that the yield of flavanone **3a** was significantly increased to 46% and that the yield of flavone, the oxidative boron-Heck product, was lowered to 14% (entry 2) when adding phenylboronic acid (conjugate addition) after complete conversion of chromanone into chromone **2a** (dehydrogenation). Given recent reports that protonolysis could induce conjugate addition rather than oxidative boron-Heck coupling in palladium(II) catalysis,[11, 13] we tried to add an acid in the conjugate addition step. In the presence of TFA, the yield of flavanone was increased to 60%, whereas the yield of flavone was lowered (14% to 10%), as anticipated (entry 3). Next, ligands were screened,[10a, 12d, 14] and 2,2′-bipyridine (bpy) was found to be superior to other ligands, providing flavanone in 65% isolated yield (entry 8). On the other hand, in the absence of ligand or with monodentate ligands such as DMAP, the reactions produced only trace amounts of the desired flavanones (entries 4-6). When TFA was changed to AcOH, the yield of the reaction was slightly reduced (entry 9).

Table 1. Optimization of the Reaction Condition[a]



				Yield (%)[b]		
Entry	Solvent	Ligand	Acid	**2a**	**3a**	**4a**
1[c]	DMSO	5-Nitro phen	-	1	25	42
2	DMSO	5-Nitro phen	-	1	46	14
3	DMSO	5-Nitro phen	TFA	4	60	10
4	DMSO	-	TFA	86	1	7
5	DMSO	DMAP	TFA	85	0	0

6	DMSO	Pyridine	TFA	76	1	1
7	DMSO	Phendione	TFA	35	11	1
8	DMSO	bpy	TFA	3	65	3
9	DMSO	bpy	AcOH	1	56	5
10	AcOH	bpy	TFA	26	4	0
11	Toluene	bpy	TFA	1	35	8
12	NMP	bpy	TFA	1	50	26
13	DMA	bpy	TFA	1	55	10
14	DMF	bpy	TFA	9	48	10
15	1,4-Dioxane	bpy	TFA	26	63	2
16[d]	*i*-PrOH	bpy	TFA	1	63	3
17	DMSO/*i*-PrOH(1:1)	bpy	TFA	4	76	2
18	DMSO/dioxane(1:1)	bpy	TFA	3	80	3
19	DMSO/dioxane(1:2)	bpy	TFA	3	81	4
20	DMSO/dioxane(1:3)	bpy	TFA	1	82	3
21	DMSO/dioxane(1:4)	bpy	TFA	1	85	3
22[e]	DMSO/dioxane(1:4)	bpy	TFA	1	73	2
23	DMSO/dioxane(1:8)	bpy	TFA	1	80	2

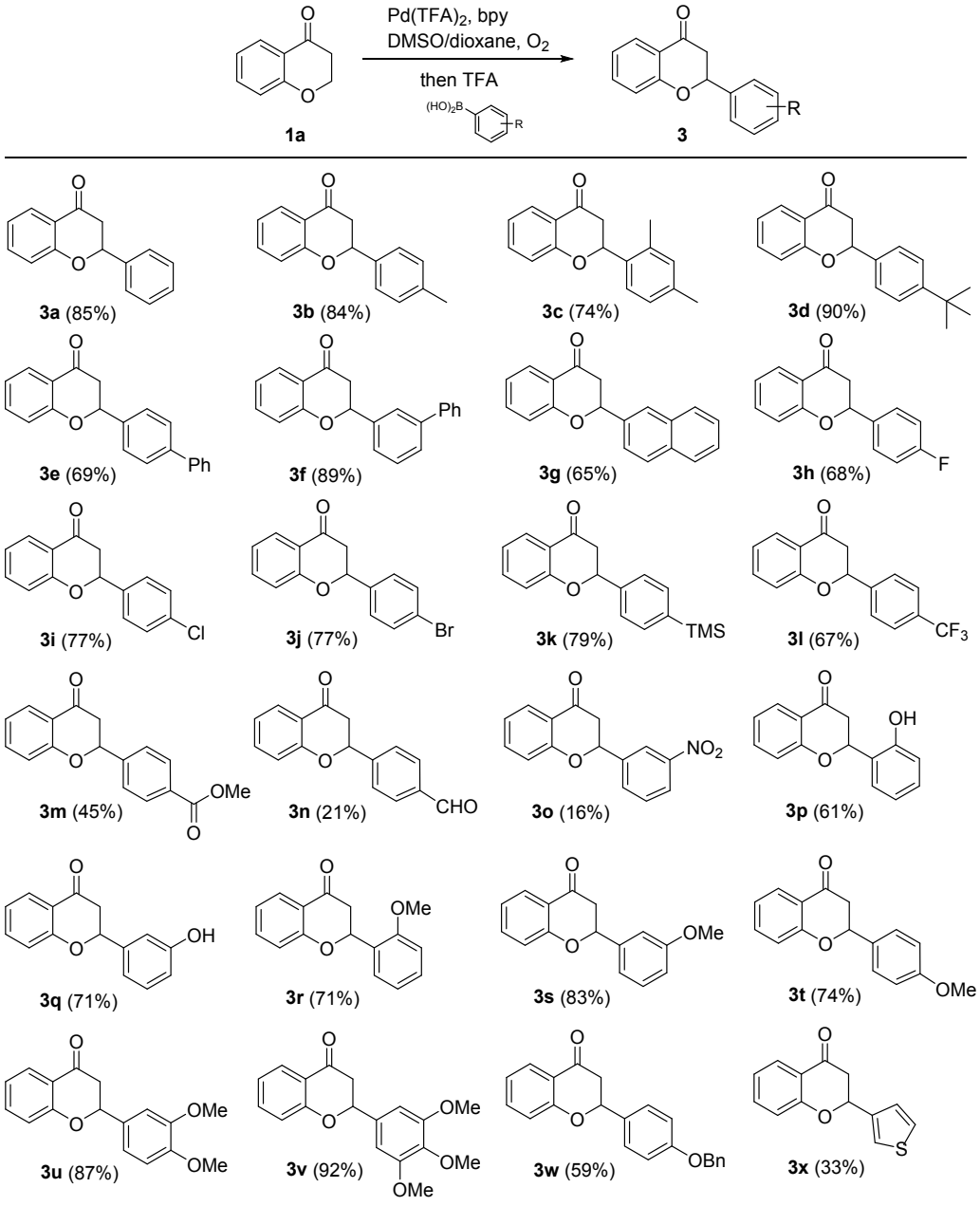
[a]Reaction conditions: **1a** (0.34 mmol), $Pd(TFA)_2$ (15 mol%), ligand (30 mol%), and solvent (0.5 mL) at 100 °C under O_2, 24-48 h; then phenylboronic acid (1.02 mmol), acid (0.34 mmol) and solvent (0.5 mL) at 80 °C under O_2, 4-48 h. [b]Isolated yield. [c]**1a** and phenylboronic acid were added simultaneously and the reaction was done at 100 °C. [d]80 °C. [e]$Pd(TFA)_2$ (10 mol%), bpy (20 mol%) and phenylboronic acid (0.51 mmol).

We also screened several solvents ranging from nonpolar to aprotic polar systems (entries 10-16). The reaction worked moderately in aprotic polar solvents while it did not in nonpolar toluene. Other solvents were not as good as DMSO, but 1,4-dioxane was similarly effective. *i*-PrOH was also moderate for the reaction (63%), but AcOH was not. Upon screening for the optimal condition, we observed that dehydrogenation from chromanone to chromone occurred faster and more smoothly in DMSO than in 1,4-dioxane and *i*-PrOH, while the conjugate addition in 1,4-dioxane and *i*-PrOH progressed well, compared that in DMSO. Based on this observation, we tried to screen the reaction conditions using co-solvents such as DMSO/dioxane. To our delight, compared to those in single solvents, the yields of flavanone in the reactions using co-solvent conditions were significantly increased (entries 17-23). Notably, the use of DMSO/dioxane (1:4) as a co-solvent system enables

the reaction to provide the desired flavanone **3a** with the highest yield of 85% within a shorter reaction time than those required under other conditions. In the case of decreasing loading amounts of catalyst, ligand, and phenylboronic acid, the yield for desired flavanone was slightly decreased.

Under the optimized condition, the reactions of chromanone **1a** with a series of arylboronic acids were performed to investigate the functional group tolerance of the reaction (Table 2). The reactions were successfully applied to synthesize a series of flavanones from **1a** with arylboronic acids possessing either electron-donating aryl or alkyl groups (**3b**-**g**) or electron-withdrawing groups (**3h**-**o**). Hydroxy (**3p** and **3q**) and methoxy (**3r**-**v**) flavanones mimicking natural flavanones were also readily synthesized using corresponding arylboronic acids. Furthermore, thiophene group (**3x**), a kind of heteroaryl group, was also tolerated in the reaction although the yield was slightly decreased. In particular, the highest yield of 92% was obtained for trimethoxy flavanone **3s**, while a relatively lower yield was obtained for nitro flavanone **3o**.

Table 2. Scope of Reactions Using Arylboronic Acids[a, b]

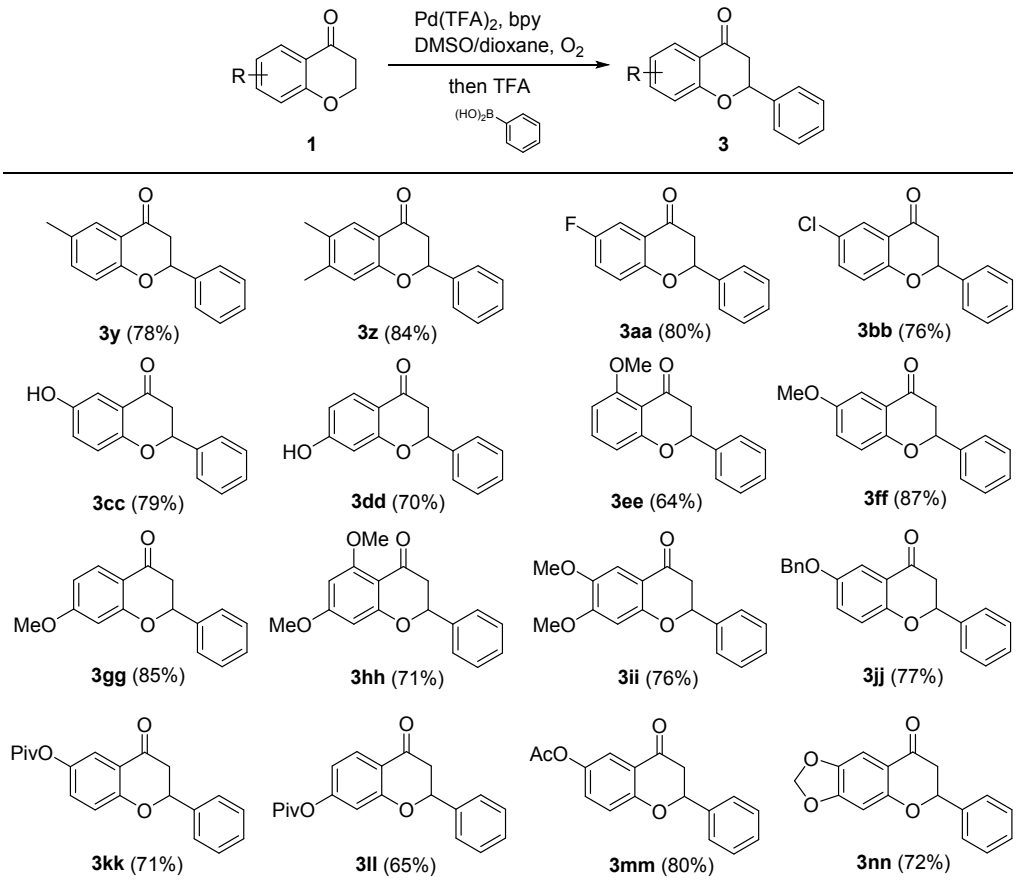


[a]Reaction conditions: **1a** (0.34 mmol), $Pd(TFA)_2$ (15 mol%), bpy (30 mol%), and DMSO/dioxane (1:4) (0.5 mL) at 100 °C under O_2, 16 h; then arylboronic acid (1.02 mmol), TFA (0.34 mmol) and DMSO/dioxane (1:4) (0.5 mL) at 80 °C under O_2, 4-24 h. [b]Isolated yield.

Subsequently, to further broaden the scope of the reaction, phenylboronic acid was reacted with a variety of chromanones under the optimized condition (Table 3). In the case of using chromanones with both electron-donating alkyl groups (**3y** and **3z**) and electron-withdrawing halogen substituents (**3aa** and **3bb**), the reactions progressed well. Hydroxy (**3cc** and **3dd**), methoxy (**3ee**-**ii**), and benzyloxy (**3jj**) flavanones were also expediently synthesized under the condition. In addition, OH^--

labile ester functional groups, such as those in (**3kk**-**mm**), and H^+-labile acetal group **3nn** were also tolerated in the reaction.

Table 3. Scope of Reactions Using Chromanones[a, b]

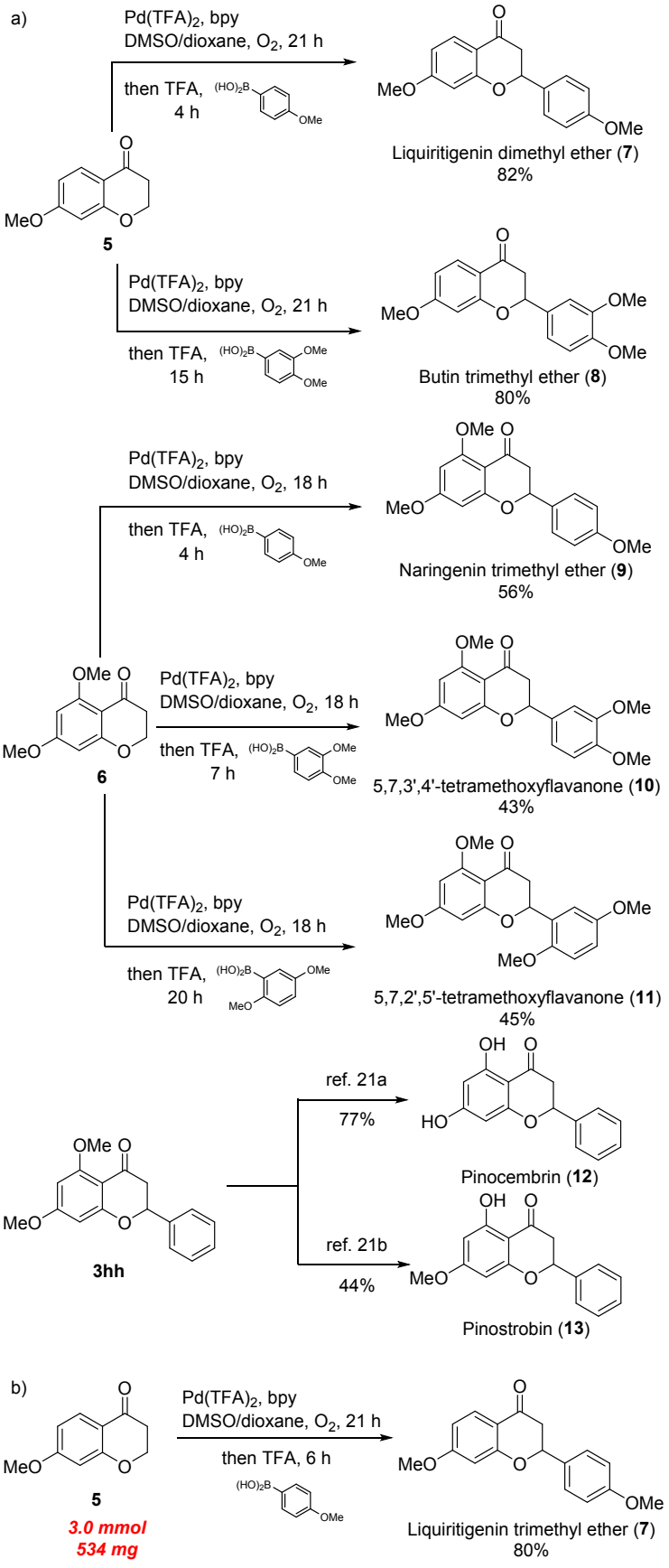


[a]Reaction conditions: **1** (0.34 mmol), $Pd(TFA)_2$ (15 mol%), bpy (30 mol%), and DMSO/dioxane (1:4) (0.5 mL) at 100 °C under O_2, 12-24 h; then phenylboronic acid (1.02 mmol), TFA (0.34 mmol) and DMSO/dioxane (1:4) (0.5 mL) at 80 °C under O_2, 4-24 h. [b]Isolated yield.

To further confirm the utility of our methodology, we tried to synthesize natural flavanones *via* the reaction (Scheme 2a).[15] First, we attempted to synthesize liquiritigenin dimethyl ether[16] **7** and butin trimethyl ether[17] **8** from 7-methoxy-4-chromanone **5**, and successfully obtained the desired flavanones in good yields of 82% and 80%, respectively. Furthermore, 3 natural flavanones (**9**-**11**),[18] were also obtained from 5,7-dimethoxy-4-chromanone **6** as a common intermediate. Among these natural compounds, compound **7** and **9** have been known to exhibit potent anti-cancer activity through cell cycle arrest, indicating that our methodology can be useful for further pharmacological studies by providing anti-cancer flavanones.[19] In addition, pinocembrin **12** and pinostrobin **13**,[20] natural hydroxyl

flavanones were readily converted from a common intermediate, **3hh**.[21] A scaled-up one-pot β-arylation using **5** and 4-methoxyphenylboronic acid as starting materials was also successfully performed, providing the desired anti-cancer flavanone **7** in 80% yield (Scheme 2b). Also, to expand the scope our methodology, we tried to synthesize α- or β-substituted flavanone (Scheme S2, ESI†). However, only trace amount of β-substituted product was isolated in the reaction with 2-methylchroman-4-one and no conjugate addition product was obtained with α-substituted chromanone, 3-methylchroman-4-one.

Scheme 2. Synthesis of Natural Flavanones and Scaled-Up Reaction

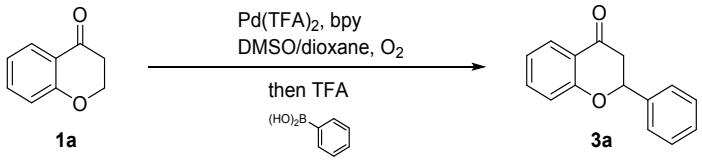


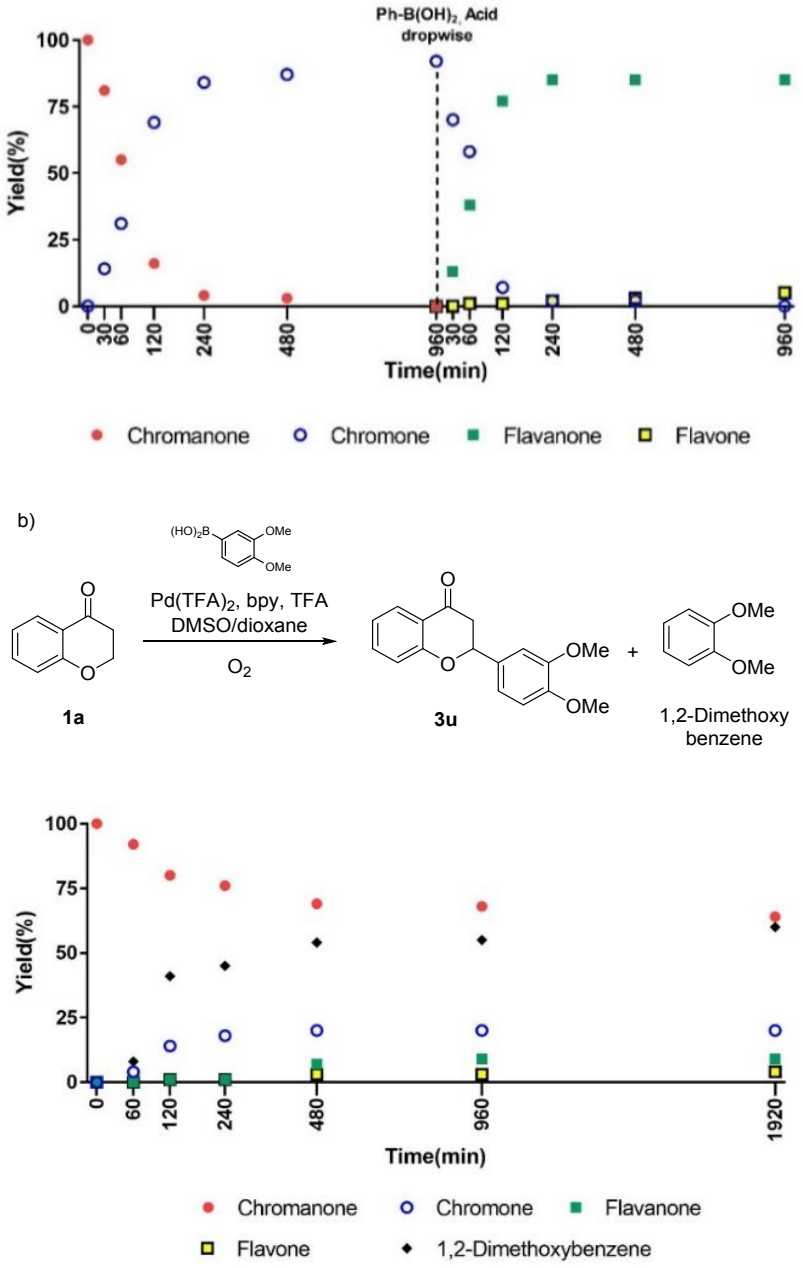
Next, to investigate the detailed mechanism of our methodology, we performed kinetic analysis of

the reaction by monitoring the time-dependent conversion of chromanone to chromone (dehydrogenation), eventually resulting in the formation of the flavanone (conjugate addition) under the optimal condition (Scheme 3a and Table S2, ESI†). During the first step of the reaction, chromanone **1a** was smoothly converted into chromone **2a**. Within 16 hours, chromanone was completely consumed, and chromone was concurrently produced in quantitative yield. After adding phenylboronic acid and TFA dropwise, chromone was subsequently converted into the desired flavanone **3a** by conjugate addition in a yield of 85% within 8 hours, along with a small amount of flavone **4a**. In addition, we confirmed whether an acid is beneficial in the reaction. In the dehydrogenation step, acidic condition resulted slightly lower conversion of chromanone to chromone with the yield of 84%, compared to 92% of optimized condition (Table S3, ESI†). Furthermore, in the absence of an acid, chromone was slowly converted to flavanone, and complete consumption of chromone took more than 16 hours with a decreased yield of 78% as a final output (Table S4, ESI†). These results suggested that acid is beneficial for the conjugate addition but not for dehydrogenation, compared to its absence. In this study, when chromanone, phenylboronic acid and TFA were reacted simultaneously, it was observed that a small amount of chromanone was converted into chromone, leading to only a trace amount of flavanone (Table S1 and S5, ESI†). Based on previous reports that arylboronic acid is undesirably transformed into arene through protodeboronation under acidic palladium(II) catalysis,[12a, 12b] we presumed that the all-in-one reaction would be sluggish due to the competitive protodeboronation of arylboronic acid. To validate our speculation, all-in-one β-arylation was executed, and its progress was analyzed by monitoring the conversion of chromanone into flavanone and byproducts (Scheme 3b). As anticipated, 1,2-dimethoxy benzene, the protodeboronated compound, was detected as a major product in yields up to 60% with little chromone and flavanone. Thus, tandem Pd(II) catalysis involving dehydrogenation and sequential conjugate addition would be more favorable than simultaneous catalysis for the conversion of chromanones into flavanones in the reaction.

Scheme 3. Mechanism Study by Kinetic Analysis

a)

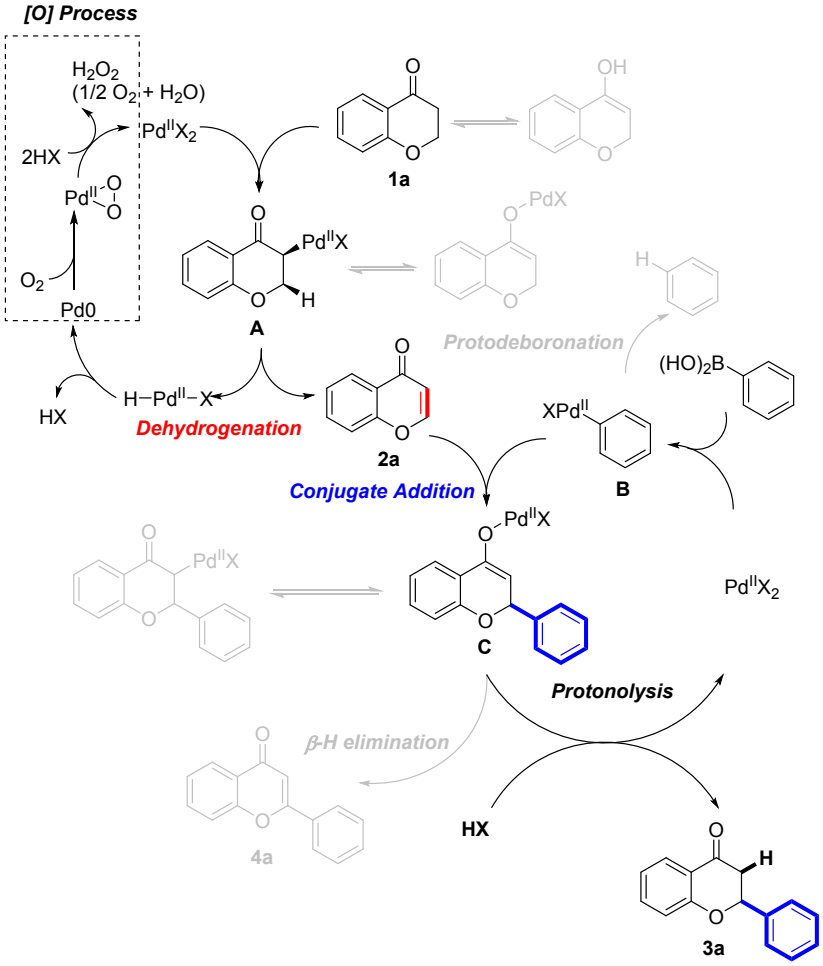




Based on mechanistic analysis, a plausible mechanism of the reaction is depicted in Scheme 4. In the first step, Pd(II) enolate **A** might be initially formed, followed by sequential β-hydride elimination.[10a, 10b, 22] As a result, enone intermediate chromone **2a** is formed, and its electrophilic β-site could be assembled with palladated intermediate **B** transformed from phenylboronic acid *via* transmetallation in the next step, resulting in intermediate **C**.[23] Finally, this intermediate is converted into the desired flavanone **3a** through concurrent protonolysis, along with the formation of a small amount of flavone **4a** as a byproduct by competitive β-hydride elimination.[24] During dehydrogenation, Pd(0) species formed in the reaction would be regenerated into Pd(II) *via* the [O] process, where O_2

works as the main oxidant in the reoxidation process.[25]

Scheme 4. A Plausible Mechanism of the Reaction



CONCLUSION

In conclusion, we developed a novel and efficient method to access a variety of flavanones *via* palladium(II)-catalyzed one-pot β-arylation of chromanones, possessing chemically unactivated β-sites, with arylboronic acids. This methodology has various advantages, including providing products in high yields (up to 92%), using easily accessible reagents, and offering good compatibilities with a wide range of functional groups. It also provides novel synthetic routes to diverse biologically active natural flavanones, such as liquiritigenin dimethyl ether. Further investigations on the biological studies of flavanones synthesized by our methodology are ongoing.

Experimental Section

General information. Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers (Aldrich, Acros Organics, Alfa Aesar, and TCI) and were used without further purification. All solvents used for routine isolation of products and chromatography were reagent grade. Reaction flasks were dried at 80 °C. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel glass plates with F-254 indicator, visualized by UV light (254 nm, 365 nm), in some cases stained with Hanessian's or *p*-anisaldehyde followed by heating. Flash column chromatography was performed using silica gel 60 (230-400 mesh) with the indicated solvents. NMR spectra were recorded and obtained using a Bruker 400 (400 MHz for ^{1}H-NMR) and Varian VNMRS500 (125 MHz for ^{13}C{1H}-NMR and 470 MHz for ^{19}F-NMR) spectrometer, respectively. ^{1}H, ^{13}C, and ^{19}F-NMR chemical shifts are reported in parts per million (ppm) relative to TMS (tetramethylsilane), with the residual solvent peak used as an internal reference. Signals are reported as m (multiplet), s (singlet), d (doublet), t (triplet), q (quartet), bs (broad singlet), bd (broad doublet), dd (doublet of doublets); the coupling constants (*J*) are reported in Hertz (Hz). High-resolution mass spectrometry (HRMS) data were obtained with a JEOL JMS-700 instrument (EI-quadrupole). 4-Chromanone derivatives **1,** starting materials for the synthesis of flavanones, were prepared, according to the reported procedures.[3e, 6c] All of the spectral data of the synthesized 4-chromanones were in accordance with the reported ones. The representative scheme for 4-chromanone synthesis was described in the supporting information.

General procedure for palladium(II)-catalyzed β-arylation to flavanones. To a 10 mL two neck round bottom flask, 4-chromanone **1** (0.337 mmol, 1.0 equiv.), $Pd(TFA)_2$ (0.051 mmol, 15 mol%), and 2,2′-bipyridine (0.102 mmol, 30 mol%) were added and then dissolved with anhydrous DMSO/dioxane (1:4) (0.5 mL). Under an oxygen (balloon) atmosphere, the reaction mixture was stirred at 100 °C in oil bath with reflux condenser until complete conversion of the starting material to chromone on TLC. Then, the reaction temperature was lowered to 80 °C and a solution of arylboronic acid (1.011 mmol, 3.0 equiv.) and TFA (0.337 mmol, 1.0 equiv.) in anhydrous DMSO/dioxane (1:4) (0.5 mL) was added dropwise to flask. The reaction mixture was stirred until complete consumption of chromone. Then, the reaction mixture was cooled to room temperature. 2*N* aq. HCl was added and the resulting mixture was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$,

filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography.

2-phenylchroman-4-one (3a). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 64.2 mg (85%) of compound **3a** as a white solid; mp 75-76 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.95 (dd, 1H, *J* = 7.9, 1.3 Hz), 7.57-7.35 (m, 6H), 7.11-7.01 (m, 2H), 5.49 (dd, 1H, *J* = 13.3, 2.7 Hz), 3.10 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.90 (dd, 1H, *J* = 16.9, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.1, 161.7, 138.9, 136.3, 129.0, 128.9, 127.2, 126.3, 121.7, 121.0. 118.3, 79.7. 44.8; HR-MS (EI+) calcd for $C_{15}H_{12}O_2$ 224.0837, found 224.0837.

2-(*p*-tolyl)chroman-4-one (3b). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-methylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 40) to afford 67.5 mg (84%) of compound **3b** as a white needle; mp 61-63 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 7.79 (dd, 1H, *J* = 8.0, 1.7 Hz), 7.59 (m, 1H), 7.43 (d, 2H, *J* = 8.0 Hz), 7.24 (d, 2H, *J* = 7.9 Hz), 7.12-7.06 (m, 2H), 5.63 (dd, 1H, *J* = 12.8, 2.8 Hz), 3.25 (dd, 1H, *J* = 16.8, 12.9 Hz), 2.80 (dd, 1H, *J* = 16.8, 2.9 Hz), 2.32 (s, 3H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.3, 161.8, 138.9, 136.3, 135.9, 129.6, 127.2, 126.3, 121.7, 121.1, 118.3, 79.7, 44.7, 21.4; HR-MS (EI+) calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0994.

2-(2,4-dimethylphenyl)chroman-4-one (3c). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 2,4-dimethylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 63.1 mg (74%) of compound **3c** as a white solid; mp 82-83 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.97 (dd, 1H, *J* = 7.7, 0.9 Hz), 7.55-7.42 (m, 2H), 7.13 (d, 1H, *J* = 7.8 Hz), 7.10-7.02 (m, 3H), 5.66 (dd, 1H, *J* = 13.7, 2.2 Hz), 3.10 (dd, 1H, *J* = 16.8, 13.8 Hz), 2.83 (dd, 1H, *J* = 16.9, 2.5 Hz), 2.37 (s, 3H), 2.36 (s, 3H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.6, 162.1, 138.6, 136.3, 135.3, 133.9, 131.8, 127.3, 127.2, 125.9, 121.7, 121.1, 118.3, 76.9, 43.7, 21.2, 19.1; HR-MS (EI+) calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1148.

2-(4-(*tert*-butyl)phenyl)chroman-4-one (3d). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-*tert*-butylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 85.4 mg (90%) of compound **3d** as a white solid; mp 99-100 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 7.80 (dd, 1H, *J* = 8.0, 1.7 Hz) 7.59 (m, 1H), 7.50-7.42 (m, 4H), 7.13-7.06 (m, 2H), 5.64 (dd, 1H, *J* = 12.8, 2.8 Hz), 3.27 (dd, 1H, *J* = 16.8, 12.9 Hz), 2.83 (dd, 1H, *J* = 16.9, 3.0 Hz), 1.29 (s, 9H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz)

δ 192.4, 161.8, 152.1, 136.3, 135.8, 127.2, 126.2, 125.9, 121.7, 121.1, 118.3, 79.7, 44.6, 34.8, 31.4; HR-MS (EI+) calcd for $C_{19}H_{20}O_2$ 280.1463, found 280.1467.

2-([1,1′-biphenyl]-4-yl)chroman-4-one (3e). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-biphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (DCM : methanol = 1 : 100) to afford 69.7 mg (69%) of compound **3e** as a white solid; mp 115-116 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, 1H, *J* = 7.8 Hz), 7.71-7.35 (m, 10H), 7.11-7.04 (m, 2H), 5.55 (dd, 1H, *J* = 13.3, 2.3 Hz), 3.15 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.95 (dd, 1H, *J* = 16.8, 2.7 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.1, 161.7, 142.0, 140.6, 137.8, 136.4, 129.0, 127.8, 127.7, 127.3, 127.2, 126.8, 121.8, 121.1, 118.3, 79.6, 44.7; HR-MS (EI+) calcd for $C_{21}H_{16}O_2$ 300.1150, found 300.1150.

2-([1,1″-biphenyl]-3-yl)chroman-4-one (3f). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3-biphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 90 mg (89%) of compound **3f** as a colorless oil; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.97 (m, 1H) 7.76-7.35 (m, 10H), 7.14-7.04 (m, 2H), 5.55 (dd, 1H, *J* = 13.4, 2.6 Hz), 3.16 (dd, 1H, *J* = 16.9, 13.5 Hz), 2.95 (dd, 1H, *J* = 16.9, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.0, 161.7, 142.1, 140.8, 139.4, 136.3, 129.4, 129.0, 127.7, 127.7, 127.3, 127.2, 125.1, 125.1, 121.8, 121.1, 118.3, 79.8, 44.9; HR-MS (EI+) calcd for $C_{21}H_{16}O_2$ 300.1150, found 300.1149.

2-(naphthalen-2-yl)chroman-4-one (3g). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 2-naphtylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 70) to afford 72 mg (65%) of compound **3g** as a white solid; mp 106-107 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.01-7.82 (m, 5H), 7.61 (d, 1H, *J* = 8.4 Hz), 7.58-7.49 (m, 3H), 7.15-7.03 (m, 2H), 5.66 (dd, 1H, *J* = 13.2, 2.3 Hz), 3.20 (dd, 1H, *J* = 16.8, 13.3 Hz), 2.99 (dd, 1H, *J* = 16.9, 2.7 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.0, 161.7, 136.4, 136.2, 133.5, 133.3, 128.9, 128.3, 127.9, 127.2, 126.7, 125.5, 123.8, 121.8, 121.1, 118.3, 79.8, 44.8; HR-MS (EI+) calcd for $C_{19}H_{14}O_2$ 274.0994, found 274.0994.

2-(4-fluorophenyl)chroman-4-one (3h). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-fluorophenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 55.4 mg (68%) of compound **3h** as a yellow solid; mp 74-75 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.94 (d, 1H, *J* = 7.6 Hz), 7.56-7.41

(m, 3H), 7.17-7.01 (m, 4H), 5.47 (dd, 1H, *J* = 13.2, 2.1 Hz), 3.07 (dd, 1H, *J* = 16.7, 13.4 Hz), 2.88 (dd, 1H, *J* = 16.8, 2.6 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.9, 163.0 (d, *J* = 246.2 Hz), 161.5, 136.4, 134.7 (d, *J* = 3.2 Hz), 128.2 (d, *J* = 8.3 Hz), 127.2, 121.9, 121.0, 118.2, 116.0 (d, *J* = 21.5 Hz), 79.1, 44.8; ^{19}F-NMR ($CDCl_3$, 470 MHz) δ −112.8 (m, 1F); HR-MS (EI+) calcd for $C_{15}H_{11}FO_2$ 242.0743, found 242.0741.

2-(4-chlorophenyl)chroman-4-one (3i). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-chlorophenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 67.5 mg (77%) of compound **3i** as a white solid; mp 79-80 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.93 (dd, 1H, *J* = 7.7, 1.1 Hz), 7.53 (m, 1H), 7.46-7.36 (m, 4H), 7.11-7.02 (m, 2H), 5.47 (dd, 1H, *J* = 13.1, 2.8 Hz), 3.05 (dd, 1H, *J* = 16.8, 13.2 Hz), 2.88 (dd, 1H, *J* = 16.8, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.7, 161.4, 137.4, 136.4, 134.7, 129.2, 127.7, 127.2, 122.0, 121.0, 118.2, 79.0, 44.7; HR-MS (EI+) calcd for $C_{15}H_{11}ClO_2$ 258.0448, found 258.0445.

2-(4-bromophenyl)chroman-4-one (3j). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-bromophenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 77.6 mg (77%) of compound **3j** as a yellow solid; mp 111-113 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 7.80 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.67-7.48 (m, 5H), 7.14-7.07 (m, 2H), 5.69 (dd, 1H, *J* = 12.9, 2.5 Hz), 3.25 (dd, 1H, *J* = 16.8, 13.0 Hz), 2.85 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.6, 161.4, 137.9, 136.5, 132.1, 127.9, 127.2, 122.9, 122.0, 121.0, 118.2, 79.0, 44.7; HR-MS (EI+) calcd for $C_{15}H_{11}BrO_2$ 301.9942, found 301.9944.

2-(4-(trimethylsilyl)phenyl)chroman-4-one (3k). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-trimethylsilylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 79 mg (79%) of compound **3k** as a yellow solid; mp 66-68 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.95 (dd, 1H, *J* = 8.0, 1.7 Hz), 7.62 (d, 2H, *J* = 7.9 Hz), 7.55-7.46 (m, 3H), 7.10-7.03 (m, 2H), 5.49 (dd, 1H, *J* = 13.4, 2.8 Hz), 3.12 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.91 (dd, 1H, *J* = 16.8, 2.9 Hz), 0.30 (s, 9H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.1, 161.7, 141.6, 139.2, 136.3, 134.0, 127.2, 125.6, 121.7, 121.1, 118.3, 79.8, 44.7, -1.0; HR-MS (EI+) calcd for $C_{18}H_{20}O_2Si$ 296.1233, found 296.1231.

2-(4-(trifluoromethyl)phenyl)chroman-4-one (3l). Prepared from 4-chromanone (50.0 mg, 0.34

mmol) and 4-trifluoromethylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 65.8 mg (67%) of compound **3l** as a white solid; mp 74-75 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.94 (dd, 1H, *J* = 8.1, 1.4 Hz), 7.71 (d, 2H, *J* = 8.2 Hz), 7.62 (d, 2H, *J* = 8.1 Hz), 7.54 (m, 1H), 7.13-7.02 (m, 2H), 5.56 (dd, 1H, *J* = 13.0, 2.9 Hz), 3.05 (dd, 1H, *J* = 16.8, 13.0 Hz), 2.92 (dd, 1H, *J* = 16.8, 3.1 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.3, 161.3, 142.8 (d, *J* = 1.2 Hz), 136.5, 131.0 (q, *J* = 32.4 Hz), 127.2, 126.5, 126.0 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 270.5 Hz), 122.1, 121.0, 118.2, 78.9, 44.8; ^{19}F-NMR ($CDCl_3$, 470 MHz) δ −62.6 (s, 3F); HR-MS (EI+) calcd for $C_{16}H_{11}F_3O_2$ 292.0711, found 292.0713.

methyl 4-(4-oxochroman-2-yl)benzoate (3m). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-methoxycarbonylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 20) to afford 43.0 mg (45%) of compound **3m** as a white solid; mp 133-134 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.14-8.08 (m, 2H), 7.94 (dd, 1H, *J* = 8.0, 1.8 Hz), 7.59-7.49 (m, 3H), 7.10-7.05 (m, 2H), 5.55 (dd, 1H, *J* = 13.0, 3.1 Hz), 3.94 (s, 3H), 3.05 (dd, 1H, *J* = 16.9, 13.0 Hz), 2.92 (dd, 1H, *J* = 16.9, 3.2 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.4, 166.7, 161.4, 143.8, 136.5, 130.5, 130.3, 127.2, 126.1, 122.0, 121.0, 118.2, 79.1, 52.4, 44.8; HR-MS (EI+) calcd for $C_{17}H_{14}O_4$ 282.0892, found 282.0894.

4-(4-oxochroman-2-yl)benzaldehyde (3n). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-formylphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 10) to afford 18.2 mg (21%) of compound **3n** as a white solid; mp 101-103 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 10.06 (s, 1H), 7.99-7.92 (m, 3H), 7.67 (d, 2H, *J* = 8.4 Hz), 7.55 (m, 1H), 7.12-7.07 (m, 2H), 5.58 (dd, 1H, *J* = 12.9, 3.3 Hz), 3.05 (dd, 1H, *J* = 16.9, 12.9 Hz), 2.94 (dd, 1H, *J* = 16.8, 3.3 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.8, 191.2, 161.3, 145.4, 136.6, 136.6, 130.4, 127.3, 126.7, 122.2, 121.1, 118.2, 79.0, 44.8; HR-MS (EI+) calcd for $C_{16}H_{12}O_3$ 252.0786, found 252.0772.

2-(3-nitrophenyl)chroman-4-one (3o). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3-nitrophenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 10) to afford 14.7 mg (16%) of compound **3o** as a white solid; mp 137-138 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.42 (t, 1H, *J* = 1.8 Hz), 8.26 (m, 1H), 7.95 (dd, 1H, *J* = 8.2, 1.8 Hz), 7.81 (d, 1H, *J* = 7.7 Hz), 7.64 (t, 1H, *J* = 8.0 Hz), 7.56 (m, 1H), 7.14-7.07 (m, 2H), 5.61 (dd, 1H, *J* = 12.9, 3.3 Hz), 3.07 (dd, 1H, *J* = 16.8, 12.9 Hz), 2.96 (dd, 1H, *J* =

16.8, 3.4 Hz); $^{13}C\{1H\}$-NMR ($CDCl_3$, 125 MHz) δ 190.9, 161.1, 148.8, 141.1, 136.7, 132.0, 130.1, 127.3, 123.7, 122.3, 121.3, 121.0, 118.2, 78.4, 44.8; HR-MS (EI+) calcd for $C_{15}H_{11}NO_4$ 269.0688, found 269.0680.

2-(2-hydroxyphenyl)chroman-4-one (3p). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 2-hydroxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 12) to afford 49.2 mg (61%) of compound **3p** as a yellow solid; mp 158-159 °C; 1H-NMR (DMSO-d_6, 400 MHz) δ 9.84 (bs, 1H), 7.80 (d, 1H, *J* = 7.6 Hz), 7.60 (t, 1H, *J* = 7.2 Hz), 7.48 (d, 1H, *J* = 7.5 Hz), 7.20 (t, 1H, *J* = 7.3 Hz), 7.14-7.05 (m, 2H), 6.92-6.83 (m, 2H), 5.79 (dd, 1H, *J* = 13.1, 2.3 Hz), 3.21 (dd, 1H, J = 16.6, 13.4 Hz), 2.78 (dd, 1H, J = 16.7, 2.3 Hz); $^{13}C\{1H\}$-NMR (CD_3OD, 125 MHz) δ 194.9, 163.7, 155.3, 137.5, 130.3, 127.8, 127.6, 126.9, 122.4, 122.0, 120.7, 119.2, 116.2, 76.4, 43.9; HR-MS (EI+) calcd for $C_{15}H_{12}O_3$ 240.0786, found 240.0786.

2-(3-hydroxyphenyl)chroman-4-one (3q). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3-hydroxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 5) to afford 57.5 mg (71%) of compound **3q** as a yellow solid; mp 135-136 °C; ^1H-NMR (DMSO-d_6, 400 MHz) δ 9.53 (s, 1H), 7.79 (dd, 1H, *J* = 8.1, 1.5 Hz), 7.59 (m, 1H), 7.21 (t, 1H, *J* = 8.1 Hz), 7.12-7.06 (m, 2H), 6.95-6.90 (m, 2H), 6.76 (m, 1H), 5.59 (dd, 1H, *J* = 12.6, 2.9 Hz), 3.19 (dd, 1H, *J* = 16.7, 12.6 Hz), 2.82 (dd, 1H, *J* = 16.8, 3.0 Hz); $^{13}C\{1H\}$-NMR (CD_3OD, 125 MHz) δ 194.1, 163.1, 158.8, 141.9, 137.5, 130.8, 127.7, 122.5, 122.0, 119.2, 118.3, 116.4, 114.1, 80.7, 45.4; HR-MS (EI+) calcd for $C_{15}H_{12}O_3$ 240.0786, found 240.0786.

2-(2-methoxyphenyl)chroman-4-one (3r). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 2-methoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 20) to afford 61.2 mg (71%) of compound **3r** as a yellow oil; ^1H-NMR ($CDCl_3$, 400 MHz) δ 7.95 (dd, 1H, *J* = 7.8, 1.6 Hz), 7.65 (dd, 1H, *J* = 7.6, 1.3 Hz), 7.51 (m, 1H), 7.35 (m, 1H), 7.10-7.03 (m, 3H), 6.93 (d, 1H, *J* = 8.1 Hz), 5.86 (dd, 1H, *J* = 12.4, 3.8 Hz), 3.84 (s, 3H), 3.02-2.86 (m, 2H); $^{13}C\{1H\}$-NMR ($CDCl_3$, 125 MHz) δ 192.8, 162.1, 155.9, 136.1, 129.5, 127.6, 127.2, 126.5, 121.5, 121.1, 121.0, 118.2, 110.6, 74.8, 55.4, 43.8; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

2-(3-methoxyphenyl)chroman-4-one (3s). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3-methoxyphenylboronic acid using the general procedure described above. The residue was purified

by silica gel column chromatography (DCM : methanol = 1 : 400) to afford 71.5 mg (83%) of compound **3s** as a white solid; mp 72-73 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.93 (dd, 1H, *J* = 8.1, 1.6 Hz), 7.51 (m, 1H), 7.35 (t, 1H, *J* = 8.2 Hz), 7.10-7.01 (m, 4H), 6.92 (dd, 1H, *J* = 8.2, 1.9 Hz), 5.45 (dd, 1H, *J* = 13.3, 2.8 Hz), 3.84 (s, 3H), 3.08 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.87 (dd, 1H, *J* = 16.8, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.0, 161.6, 160.0, 140.4, 136.3, 130.0, 127.1, 121.7, 121.0, 118.4, 118.2, 114.1, 112.0, 79.5, 55.4, 44.8; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

2-(4-methoxyphenyl)chroman-4-one (3t). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-methoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 5) to afford 63.6 mg (74%) of compound **3t** as a yellow solid; mp 82-83 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.93 (dd, 1H, *J* = 7.7, 0.9 Hz), 7.51 (m, 1H), 7.42 (d, 2H, *J* = 8.6 Hz), 7.08-7.01 (m, 2H), 6.96 (d, 2H, *J* = 8.6 Hz), 5.44 (dd, 1H, *J* = 13.3, 2.4 Hz), 3.84 (s, 3H), 3.11 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.86 (dd, 1H, *J* = 16.8, 2.7 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.4, 161.8, 160.1, 136.3, 130.9, 127.9, 127.2, 121.7, 121.0, 118.3, 114.3, 79.5, 55.5, 44.6; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

2-(3,4-dimethoxyphenyl)chroman-4-one (3u). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3,4-dimethoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 5) to afford 57.8 mg (87%) of compound **3u** as a yellow solid; mp 118-119 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.93 (dd, 1H, *J* = 7.9, 1.2 Hz), 7.51 (m, 1H), 7.09-6.95 (m, 4H), 6.91 (d, 1H, *J* = 7.9 Hz), 5.43 (dd, 1H, *J* = 13.3, 2.3 Hz), 3.92 (s, 3H), 3.90 (s, 3H), 3.12 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.87 (dd, 1H, *J* = 16.8, 2.6 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.2, 161.7, 149.6, 149.4, 136.3, 131.3, 127.2, 121.7, 121.0, 118.9, 118.3, 111.3, 109.5, 79.7, 56.1, 56.1, 44.7; HR-MS (EI+) calcd for $C_{17}H_{16}O_4$ 284.1049, found 284.1051.

2-(3,4,5-trimethoxyphenyl)chroman-4-one (3v). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3,4,5-trimethoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 6) to afford 97.4 mg (92%) of compound **3v** as a white solid; mp 98-100 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92 (dd, 1H, *J* = 8.1, 1.6 Hz), 7.51 (m, 1H), 7.09-7.02 (m, 2H), 6.70 (s, 2H), 5.40 (dd, 1H, *J* = 13.4, 2.7 Hz), 3.89 (s, 6H), 3.86 (s, 3H), 3.09 (dd, 1H, *J* = 16.9, 13.4 Hz), 2.87 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.9, 161.5, 153.6, 138.3, 136.3, 134.4, 127.1, 121.8, 120.9, 118.2, 103.3, 79.9,

60.9, 56.2, 44.9; HR-MS (EI+) calcd for $C_{18}H_{18}O_5$ 314.1154, found 314.1156.

2-(4-(benzyloxy)phenyl)chroman-4-one (3w). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 4-benzyloxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 65.2 mg (59%) of compound **3w** as a white solid; mp 105-106 °C; ^{1}H-NMR (CDCl3, 400 MHz) δ 7.95 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.51 (m, 1H), 7.49-7.32 (m, 7H), 7.09-6.99 (m, 4H), 5.43 (dd, 1H, *J* = 13.4, 2.7 Hz), 5.10 (s, 2H), 3.11 (dd, 1H, *J* = 16.8, 13.4 Hz), 2.87 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.3, 161.7, 159.2, 136.8, 136.2, 131.1, 128.7, 128.1, 127.8, 127.5, 127.1, 121.6, 121.0, 118.2, 115.2, 79.4, 70.1, 44.5; HR-MS (EI+) calcd for $C_{22}H_{18}O_3$ 330.1256, found 330.1259.

2-(thiophen-3-yl)chroman-4-one (3x). Prepared from 4-chromanone (50.0 mg, 0.34 mmol) and 3-thiopheneboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 40) to afford 25.8 mg (33%) of compound **3x** as a brown solid; mp 76-78 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92 (dd, 1H, *J* = 8.1, 1.7 Hz), 7.51 (m, 1H), 7.41-7.37 (m, 2H), 7.20 (m, 1H), 7.08-7.02 (m, 2H), 5.60 (dd, 1H, *J* = 12.1, 3.3 Hz), 3.12 (dd, 1H, *J* = 16.8, 12.1 Hz), 2.99 (dd, 1H, *J* = 16.8, 3.3 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.9, 161.4, 140.0, 136.3, 127.2, 127.0, 125.8, 123.0, 121.8, 121.2, 118.2, 75.7, 44.0; HR-MS (EI+) calcd for $C_{13}H_{10}O_2S$ 230.0402 found, 230.0401.

6-methyl-2-phenylchroman-4-one (3y). Prepared from 6-methyl-4-chromanone (55.0 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 62.0 mg (78%) of compound **3y** as a white solid; mp 103-104 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.73 (s, 1H), 7.52-7.30 (m, 6H), 6.96 (d, 1H, *J* = 8.4 Hz), 5.45 (dd, 1H, *J* = 13.3, 2.7 Hz), 3.07 (dd, 1H, *J* = 16.9, 13.4 Hz), 2.87 (dd, 1H, *J* = 17.0, 2.9 Hz), 2.33 (s, 3H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.3, 159.7, 139.0, 137.3, 131.1, 128.9, 128.8, 126.7, 126.2, 120.6, 118.0, 79.6, 44.8, 20.5; HR-MS (EI+) calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0996.

6,7-dimethyl-2-phenylchroman-4-one (3z). Prepared from 6,7-dimethyl-4-chromanone (56.0 mg, 0.32 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 50) to afford 67.5 mg (84%) of compound **3z** as a white solid; mp 78-79 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.67 (s, 1H), 7.51-7.35 (m, 5H), 6.85 (s, 1H), 5.43 (dd, 1H, *J* = 13.2, 2.8 Hz), 3.04 (dd, 1H, *J* = 16.9, 13.3 Hz), 2.84 (dd, 1H, *J* =

17.0, 2.9 Hz), 2.28 (s, 3H), 2.24 (s, 3H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.0, 160.0, 146.8, 139.1, 130.3, 128.9, 128.7, 127.0, 126.2, 118.8, 118.7, 79.6, 44.7, 20.6, 18.9; HR-MS (EI+) calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1148.

6-fluoro-2-phenylchroman-4-one (3aa). Prepared from 6-fluoro-4-chromanone (56.0 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 70) to afford 65.6 mg (80%) of compound **3aa** as a yellow solid; mp 71-73 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.58 (dd, 1H, *J* = 8.2, 3.2 Hz), 7.52-7.36 (m, 5H), 7.24 (m, 1H), 7.04 (m, 1H), 5.47 (dd, 1H, *J* = 13.4, 2.9 Hz), 3.08 (dd, 1H, *J* = 17.0, 13.4 Hz), 2.90 (dd, 1H, *J* = 16.9, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.2 (d, *J* = 1.8 Hz), 158.4, 157.8 (d, *J* = 1.7 Hz), 156.5, 138.5, 129.0, 126.2, 123.8 (d, *J* = 24.4 Hz), 121.5 (d, *J* = 6.5 Hz), 119.9 (d, *J* = 7.1 Hz), 112.1 (d, *J* = 23.2 Hz), 79.9, 44.4 (d, *J* = 1.0 Hz); ^{19}F-NMR ($CDCl_3$, 470 MHz) δ −121.0 (m, 1F); HR-MS (EI+) calcd for $C_{15}H_{11}FO_2$ 242.0743, found 242.0741.

6-chloro-2-phenylchroman-4-one (3bb). Prepared from 6-chloro-4-chromanone (62.0 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 70) to afford 65.4 mg (75%) of compound **3bb** as a yellow solid; mp 91-92 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, 1H, *J* = 2.6 Hz), 7.50-7.37 (m, 6H), 7.02 (d, 1H, *J* = 8.8 Hz), 5.47 (dd, 1H, *J* = 13.2, 3.0 Hz), 3.08 (dd, 1H, *J* = 16.8, 13.2 Hz), 2.91 (dd, 1H, *J* = 16.9, 3.0 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.9, 160.0, 138.4, 136.1, 129.1, 129.0, 127.3, 126.5, 126.3, 121.8, 120.0, 79.9, 44.4; HR-MS (EI+) calcd for $C_{15}H_{11}ClO_2$ 258.0448, found 258.0447.

6-hydroxy-2-phenylchroman-4-one (3cc). Prepared from 6-hydroxy-chroman-4-one (54.0 mg, 0.33 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (DCM : methanol = 100 : 1) to afford 62.3 mg (79%) of compound **3cc** as a yellow solid; mp 214-216 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 9.43 (s, 1H), 7.54 (s, 1H), 7.52 (s, 1H), 7.46-7.34 (m, 3H), 7.12 (d, 1H, *J* = 2.9 Hz), 7.04 (dd, 1H, *J* = 8.8, 3.0 Hz), 6.96 (d, 1H, *J* = 8.8 Hz), 5.55 (dd, 1H, *J* = 13.0, 2.6 Hz), 3.17 (dd, 1H, *J* = 16.8, 13.0 Hz), 2.77 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR (DMSO-d_6, 125 MHz) δ 191.7, 154.4, 151.6, 139.2, 128.5, 128.4, 126.6, 124.5, 120.8, 119.0, 109.9, 78.7, 43.7; HR-MS (EI+) calcd for $C_{15}H_{12}O_3$ 240.0786, found 240.0782.

7-hydroxy-2-phenylchroman-4-one (3dd). Prepared from 7-hydroxy-chroman-4-one (50.0 mg, 0.30 mmol) and phenylboronic acid using the general procedure described above. The residue was

purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 5) to afford 51.5 mg (70%) of compound **3dd** as a white solid; mp 185-186 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 10.64 (bs, 1H), 7.66 (d, 1H, *J* = 8.7 Hz), 7.53 (d, 2H, *J* = 7.0 Hz), 7.46-7.33 (m, 3H), 6.52 (dd, 1H, *J* = 8.7, 2.2 Hz), 6.37 (d, 1H, *J* = 2.2 Hz), 5.59 (dd, 1H, *J* = 12.7, 2.8 Hz), 3.12 (dd, 1H, *J* = 16.7, 12.8 Hz), 2.71 (dd, 1H, *J* = 16.8, 3.0 Hz); ^{13}C{1H}-NMR (CD_3OD, 125 MHz) δ 193.0, 166.9, 165.4, 140.7, 129.9, 129.7, 129.6, 127.3, 115.0, 111.9, 103.9, 81.0, 45.1; HR-MS (EI+) calcd for $C_{15}H_{12}O_3$ 240.0786, found 240.0786.

5-methoxy-2-phenylchroman-4-one (3ee). Prepared from 5-methoxy-4-chromanone (50.9 mg, 0.29 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 4) to afford 46.8 mg (64%) of compound **3ee** as a white solid; mp 141-143 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.49-7.33 (m, 6H), 6.66 (d, 1H, *J* = 8.3 Hz), 6.55 (d, 1H, *J* = 8.3 Hz), 5.44 (dd, 1H, *J* = 13.2, 2.8 Hz), 3.94 (s, 3H), 3.07 (dd, 1H, *J* = 16.4, 13.2 Hz), 2.85 (dd, 1H, *J* = 16.7, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.8, 163.3, 160.9, 138.8, 136.1, 128.9, 128.8, 126.2, 111.5, 110.3, 104.1, 79.0, 56.3, 46.0; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

6-methoxy-2-phenylchroman-4-one (3ff). Prepared from 6-methoxy-4-chromanone (55.0 mg, 0.31 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 30) to afford 68.5 mg (87%) of compound **3ff** as a pale yellow solid; mp 138-139 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.52-7.32 (m, 6H), 7.13 (dd, 1H, *J* = 9.0, 3.1 Hz), 7.00 (d, 1H, *J* = 9.0 Hz), 5.45 (dd, 1H, *J* = 13.4, 2.6 Hz), 3.82 (s, 3H), 3.08 (dd, 1H, *J* = 16.9, 13.5 Hz), 2.88 (dd, 1H, *J* = 16.9, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.1, 156.4, 154.3, 139.0, 128.9, 128.8, 126.2, 125.5, 120.9, 119.5, 107.4, 79.8, 55.9, 44.7; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

7-methoxy-2-phenylchroman-4-one (3gg). Prepared from 7-methoxy-4-chromanone (57.0 mg, 0.32 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 20) to afford 68.9 mg (85%) of compound **3gg** as a white solid; mp 84-86 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, 1H, *J* = 8.8 Hz), 7.50-7.35 (m, 5H), 6.62 (dd, 1H, *J* = 8.8, 2.4 Hz), 6.50 (d, 1H, *J* = 2.4 Hz), 5.47 (dd, 1H, *J* = 13.3, 2.9 Hz), 3.83 (s, 3H), 3.04 (dd, 1H, *J* = 16.9, 13.3 Hz), 2.83 (dd, 1H, *J* = 16.9, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.6, 166.3, 163.6, 138.9, 128.9, 128.8, 128.8, 126.2, 114.9, 110.3, 101.0, 80.1, 55.7, 44.4; HR-MS (EI+) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

5,7-dimethoxy-2-phenylchroman-4-one (3hh). Prepared from 5,7-dimethoxy-4-chromanone (62.6 mg, 0.3 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 3) to afford 61.0 mg (71%) of compound **3hh** as a yellow solid; mp 140-141 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.47-7.32 (m, 5H), 6.15 (d, 1H, *J* = 2.1 Hz), 6.08 (d, 1H, *J* = 2.1 Hz), 5.39 (dd, 1H, *J* = 13.1, 2.8 Hz), 3.88 (s, 3H), 3.80 (s, 3H), 3.00 (dd, 1H, *J* = 16.5, 13.2 Hz), 2.78 (dd, 1H, *J* = 16.6, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 189.4, 166.1, 165.1, 162.4, 138.9, 128.9, 128.8, 126.2, 106.1, 93.7, 93.3, 79.4, 56.3, 55.7, 45.7; HR-MS (EI+) calcd for $C_{17}H_{16}O_4$ 284.1049, found 284.1049.

6,7-dimethoxy-2-phenylchroman-4-one (3ii). Prepared from 6,7-dimethoxy-4-chromanone (70.0 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 6) to afford 73.1 mg (76%) of compound **3ii** as a yellow solid; mp 170-171 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.52-7.36 (m, 5H), 7.32 (s, 1H), 6.53 (s, 1H), 5.46 (dd, 1H, *J* = 13.5, 2.9 Hz), 3.91 (s, 3H), 3.90 (s, 3H), 3.04 (dd, 1H, *J* = 16.9, 13.5 Hz), 2.82 (dd, 1H, *J* = 16.9, 3.0 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.6, 158.0, 156.3, 144.7, 138.9, 128.9, 128.8, 126.2, 113.2, 106.7, 100.3, 80.3, 56.3, 56.2, 44.2; HR-MS (EI+) calcd for $C_{17}H_{16}O_4$ 284.1049, found 284.1049.

6-(benzyloxy)-2-phenylchroman-4-one (3jj). Prepared from 6-(benzyloxy)chroman-4-one (80.0 mg, 0.31 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 60) to afford 79.7 mg (77%) of compound **3jj** as a yellow solid; mp 103-104 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 7.54 (d, 2H, *J* = 7.2 Hz), 7.47-7.26 (m, 10H), 7.08 (d, 1H, *J* = 8.7 Hz), 5.61 (dd, 1H, *J* = 12.9, 2.5 Hz), 5.13 (s, 2H), 3.23 (dd, 1H, *J* = 16.8, 13.1 Hz), 2.82 (dd, 1H, *J* = 16.7, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 192.0, 156.5, 153.4, 138.9, 136.7, 128.9, 128.8, 128.7, 128.2, 127.7, 126.2, 126.0, 120.9, 119.6, 108.9, 79.8, 70.6, 44.6; HR-MS (EI+) calcd for $C_{22}H_{18}O_3$ 330.1256, found 330.1257.

4-oxo-2-phenylchroman-6-ylpivalate (3kk). Prepared from 4-oxochroman-7-yl pivalate (77.0 mg, 0.31 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 40) to afford 65.9 mg (65%) of compound **3kk** as a white solid; mp 106-107 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.59 (d, 1H, *J* = 2.7 Hz), 7.50-7.37 (m, 5H), 7.21 (dd, 1H, *J* = 8.9, 2.8 Hz), 7.07 (d, 1H, *J* = 8.9 Hz), 5.49 (dd, 1H, *J* = 13.3, 2.5 Hz), 3.09 (dd, 1H, *J* = 16.9, 13.5 Hz), 2.90 (dd, 1H, *J* = 16.9, 2.7 Hz), 1.36 (s, 9H); ^{13}C{1H}-NMR

($CDCl_3$, 125 MHz) δ 191.4, 177.3, 159.2, 145.3, 138.6, 130.1, 129.0, 129.0, 126.2, 121.3, 119.3, 119.2, 79.9, 44.5, 39.2, 27.2; HR-MS (EI+) calcd for $C_{20}H_{20}O_4$ 324.1362, found 324.1363.

4-oxo-2-phenylchroman-7-ylpivalate (3ll). Prepared from 4-oxochroman-7-ylpivalate (76.6 mg, 0.31 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 40) to afford 65.9 mg (65%) of compound **3ll** as a colorless oil; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, 1H, *J* = 8.6 Hz), 7.50-7.36 (m, 5H), 6.84-6.72 (m, 2H), 5.50 (dd, 1H, *J* = 13.3, 2.8 Hz), 3.08 (dd, 1H, *J* = 16.9, 13.3 Hz), 2.89 (dd, 1H, *J* = 16.9, 2.9 Hz), 1.35 (s, 9H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.0, 176.3, 162.5, 157.3, 138.6, 128.9, 128.9, 128.5, 126.2, 118.8, 115.8, 111.2, 80.0, 44.5, 39.3, 27.1, 27.1, 27.1; HR-MS (EI+) calcd for $C_{20}H_{20}O_4$ 324.1362, found 324.1360.

4-oxo-2-phenylchroman-6-yl acetate (3mm). Prepared from 6-acetoxy-chroman-4-one (69.5 mg, 0.34 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 30) to afford 76.0 mg (80%) of compound **3mm** as a yellow solid; mp 99-101 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.63 (d, 1H, *J* = 2.7 Hz), 7.51-7.36 (m, 5H), 7.24 (dd, 1H, *J* = 9.1, 2.9 Hz), 7.08 (d, 1H, *J* = 9.0 Hz), 5.48 (dd, 1H, *J* = 13.4, 2.5 Hz), 3.08 (dd, 1H, *J* = 16.9, 13.5 Hz), 2.89 (dd, 1H, *J* = 17.0, 2.9 Hz), 2.30 (s, 3H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 191.2, 169.6, 159.3, 144.8, 138.5, 130.0, 129.0, 126.2, 121.2, 119.4, 119.3, 79.9, 44.4, 21.0; HR-MS (EI+) calcd for $C_{17}H_{14}O_4$ 282.0892, found 282.0892.

6-phenyl-6,7-dihydro-8H-[1,3]dioxolo[4,5-g]chromen-8-one (3nn) Prepared from 6,7-methylenedioxy-chromanone (58.7 mg, 0.31 mmol) and phenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 30) to afford 58.7 mg (72%) of compound **3nn** as a yellow solid; mp 114-115 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.51-7.36 (m, 5H), 7.30 (s, 1H), 6.51 (s, 1H), 6.00 (d, 2H, *J* = 2.4 Hz), 5.43 (dd, 1H, *J* = 13.4, 2.5 Hz), 3.01 (dd, 1H, *J* = 16.8, 13.6 Hz), 2.82 (dd, 1H, *J* = 16.9, 2.7 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.4, 159.7, 154.5, 143.3, 138.8, 128.9, 128.8, 126.2, 114.7, 104.1, 102.1, 98.7, 80.2, 44.1; HR-MS (EI+) calcd for $C_{16}H_{12}O_4$ 268.0736, found 268.0740.

Liquiritigenin dimethyl ether (7). Prepared from 7-methoxy-4-chromanone (60.0 mg, 0.34 mmol) and 4-methoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 15) to afford 79.0 mg (82%) of compound **7** as a white solid; mp 87-88 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.85 (d, 1H, *J* = 8.8 Hz),

7.39 (d, 2H, *J* = 8.6 Hz), 6.94 (d, 2H, *J* = 8.6 Hz), 6.59 (dd, 1H, *J* = 8.8, 2.3 Hz), 6.46 (d, 1H, *J* = 2.2), 5.39 (dd, 1H, *J* = 13.2, 2.7 Hz), 3.81 (s, 3H), 3.80 (s, 3H), 3.03 (dd, 1H, *J* = 16.8, 13.3 Hz), 2.77 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.9, 166.3, 163.7, 160.1, 130.9, 128.8, 127.9, 114.9, 114.3, 110.3, 101.0, 79.9, 55.7, 55.5, 44.2; HR-MS (EI+) calcd for $C_{17}H_{16}O_4$ 284.1049, found 284.1050.

Butin trimethyl ether (8). Prepared from 7-methoxy-4-chromanone (60.0 mg, 0.34 mmol) and 3,4-dimethoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 6) to afford 85.2 mg (80%) of compound **8** as a yellow solid; mp 114-115 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, 1H, *J* = 8.8 Hz), 7.03-6.97 (m, 2H), 6.90 (d, 1H, *J* = 8.6 Hz), 6.61 (dd, 1H, *J* = 8.8, 2.4 Hz), 6.49 (d, 1H, *J* = 2.3 Hz), 5.41 (dd, 1H, *J* = 13.3, 2.7 Hz), 3.92 (s, 3H), 3.90 (s, 3H), 3.83 (s, 3H), 3.06 (dd, 1H, *J* = 16.8, 13.3 Hz), 2.80 (dd, 1H, *J* = 16.8, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.1, 166.2, 163.6, 149.5, 149.3, 131.3, 128.8, 118.9, 114.9, 111.2, 110.3, 109.5, 101.0, 80.0, 56.0, 56.0, 55.7, 44.3; HR-MS (EI+) calcd for $C_{18}H_{18}O_5$ 314.1154, found 314.1157.

Naringenin trimethyl ether (9). Prepared from 5,7-dimethoxy-4-chromanone (70.0 mg, 0.34 mmol) and 4-methoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 1) to afford 59.7 mg (56%) of compound **9** as a yellow solid; mp 86-87 °C ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 7.43 (d, 2H, *J* = 8.4 Hz), 6.96 (d, 2H, *J* = 8.5 Hz), 6.20 (d, 2H, *J* = 3.8 Hz), 5.45 (dd, 1H, *J* = 12.5, 2.2 Hz), 3.79 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.06 (dd, 1H, *J* = 16.2, 12.8 Hz), 2.58 (dd, 1H, *J* = 16.3, 2.5 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 189.6, 166.0, 165.2, 162.4, 160.0, 130.9, 127.8, 114.2, 106.1, 93.6, 93.2, 79.1, 56.3, 55.7, 55.4, 45.5; HR-MS (EI+) calcd for $C_{18}H_{18}O_5$ 314.1154, found 314.1157.

2-(3,4-dimethoxyphenyl)-5,7-dimethoxychroman-4-one (10). Prepared from 5,7-dimethoxy-4-chromanone (56.0 mg, 0.27 mmol) and 3,4-dimethoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 2 : 1) to afford 40.1 mg (43%) of compound **10** as a yellow solid; mp 152-153 °C ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.02-6.95 (m, 2H), 6.88 (d, 1H, *J* = 8.7 Hz), 6.15 (d, 1H, *J* = 2.2 Hz), 6.09 (d, 1H, *J* = 2.1 Hz), 5.35 (dd, 1H, *J* = 13.2, 2.7 Hz), 3.92 (s, 3H), 3.90 (s, 6H), 3.82 (s, 3H), 3.04 (dd, 1H, *J* = 16.4, 13.3 Hz), 2.77 (dd, 1H, *J* = 16.5, 2.8 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 189.5, 166.1, 165.1, 162.4, 149.5, 149.3, 131.3, 118.9, 111.2, 109.5, 106.1, 93.7, 93.3, 79.3, 56.3, 56.1, 56.1, 55.7, 45.6; HR-MS

(EI+) calcd for $C_{19}H_{20}O_6$ 344.1260, found 344.1262.

2-(2,5-dimethoxyphenyl)-5,7-dimethoxychroman-4-one (11). Prepared from 5,7-dimethoxy-4-chromanone (70.0 mg, 0.34 mmol) and 2,5-dimethoxyphenylboronic acid using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-hexane = 1 : 1) to afford 52.2 mg (45%) of compound **11** as a yellow solid; mp 117-118 °C ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.17 (d, 1H, *J* = 1.5 Hz), 6.86-6.79 (m, 2H), 6.18 (d, 1H, *J* = 2.3 Hz), 6.09 (d, 1H, *J* = 2.3 Hz), 5.75 (dd, 1H, *J* = 11.9, 4.2 Hz), 3.90 (s, 3H), 3.83 (s, 3H), 3.81 (s, 3H), 3.78 (s, 3H), 2.91-2.77 (m, 2H); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 190.0, 165.9, 165.5, 162.4, 153.9, 150.1, 128.7, 113.7, 112.6, 111.7, 106.2, 93.7, 93.2, 77.4, 56.3, 56.0, 55.9, 55.7, 44.9; HR-MS (EI+) calcd for $C_{19}H_{20}O_6$ 344.1260, found 344.1259.

Pinocembrin (12).[21a] Yield 21.1 mg (47%) from 50.0 mg (0.18 mmol) of **3hh** as a brown solid; mp 195-197 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 12.14 (s, 1H), 10.85 (s, 1H), 7.56-7.47 (m, 2H), 7.47-7.34 (m, 3H), 5.97-5.85 (m, 2H), 5.59 (dd, 1H, *J* = 12.5, 2.5 Hz), 3.27 (dd, 1H, *J* = 17.1, 12.7 Hz), 2.78 (dd, 1H, *J* = 17.1, 2.8 Hz); ^{13}C{1H}-NMR (CD_3OD, 125 MHz) δ 197.3, 168.4, 165.5, 164.7, 140.4, 129.7, 129.6, 127.3, 103.4, 97.2, 96.2, 80.4, 44.2; HR-MS (EI+) calcd for $C_{15}H_{12}O_4$ 256.0736, found 256.0735.

Pinostrobin (13).[21b] Yield 16.9 mg (77%) from 23.0 mg (0.08 mmol) of **3hh** as a yellow solid; mp 96-97 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 12.03 (s, 1H), 7.50-7.35 (m, 5H), 6.08 (d, 1H, *J* = 2.0 Hz), 6.08 (d, 1H, *J* = 3.9 Hz), 5.42 (dd, 1H, *J* = 13.0, 2.7 Hz), 3.81 (s, 3H), 3.09 (dd, 1H, *J* = 17.1, 13.1 Hz), 2.82 (dd, 1H, *J* = 17.1, 2.9 Hz); ^{13}C{1H}-NMR ($CDCl_3$, 125 MHz) δ 195.9, 168.1, 164.3, 162.9, 138.5, 129.0, 126.3, 103.3, 95.3, 94.4, 79.4, 55.8, 43.5; HR-MS (EI+) calcd for $C_{16}H_{14}O_4$ 270.0892, found 270.0895.

General procedure for scaled up palladium(II)-catalyzed β-arylation to 7. To a 25 mL two neck round bottom flask, 7-methoxy-4-chromanone **5** (535.0 mg, 3.0 mmol, 1.0 equiv.), $Pd(TFA)_2$ (150.0mg, 0.45 mmol, 15 mol%), and 2,2′-bipyridine (141.0mg, 0.90 mmol, 30 mol%) were added and then dissolved with anhydrous DMSO/dioxane (1:4) (4.0 mL). Under an oxygen (balloon) atmosphere, the reaction mixture was stirred at 100 °C in oil bath with reflux condenser until complete conversion of the starting material to chromone on TLC. Then, the reaction temperature was lowered to 80 °C and a solution of 4-methoxyphenylboronic acid (1.37 g, 9.0 mmol, 3.0 equiv.) and TFA (230.0 μL, 3.0

mmol, 1.0 equiv.) in anhydrous DMSO/dioxane (1:4) (4.0 mL) was added dropwise to flask. The reaction mixture was stirred until complete consumption of chromone. Then, the reaction mixture was cooled to room temperature. 2*N* aq. HCl was added and the resulting mixture was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to give liquiritigenin dimethyl ether **7** (679.7 mg, 80%).

General procedure for kinetic analysis of palladium(II)-catalyzed dehydrogenation of 4-chromanone in acidic condition. To a 10 mL two neck round bottom flask, 4-chromanone **1a** (50.0 mg, 0.337 mmol, 1.0 equiv.), $Pd(TFA)_2$ (17.0 mg, 0.051 mmol, 15 mol%), 2,2′-bipyridine (15.9 mg, 0.102 mmol, 30 mol%), and TFA (26.0 μL, 0.337 mmol, 1.00 equiv.) were added and then dissolved with anhydrous DMSO/dioxane (1:4) (1.0 mL). Under an oxygen (balloon) atmosphere, the reaction mixture was stirred at 100 °C in oil bath with reflux condenser for the indicated time. Then, the reaction mixture was cooled to room temperature. 2N aq. HCl was added and the resulting mixture was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography.

General procedure for kinetic analysis of palladium(II)-catalyzed β-arylation to flavanone 3a. To a 10 mL two neck round bottom flask, 4-chromanone **1a** (50.0 mg, 0.337 mmol, 1.0 equiv.), $Pd(TFA)_2$ (17.0 mg, 0.051 mmol, 15 mol%), and 2,2′-bipyridine (15.9 mg, 0.102 mmol, 30 mol%) were added and then dissolved with anhydrous DMSO/dioxane (1:4) (0.5 mL). Under an oxygen (balloon) atmosphere, the reaction mixture was stirred at 100 °C in oil bath with reflux condenser for the indicated time. After 960 minutes, the reaction temperature was lowered to 80 °C and a solution of phenylboronic acid (123.3 mg, 1.011 mmol, 3.0 equiv.) and TFA (26.0 μL, 0.337 mmol, 1.0 equiv.) in anhydrous DMSO/dioxane (1:4) (0.5 mL) was added dropwise to flask with stirring for the indicated time. Then, the reaction mixture was cooled to room temperature. 2*N* aq. HCl was added and the resulting mixture was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography.

General procedure for kinetic analysis of all-in-one palladium(II)-catalyzed β-arylation to flavanone 3u. To a 10 mL two neck round bottom flask, 4-chromanone **1a** (50.0 mg, 0.337 mmol, 1.0 equiv.), $Pd(TFA)_2$ (17.0 mg, 0.051 mmol, 15 mol%), 2,2′-bipyridine (15.9 mg, 0.102 mmol, 30 mol%),

3,4-dimethoxyphenylboronic acid (183.8 mg, 1.01 mmol, 3.00 equiv.), and TFA (26.0 μL, 0.337 mmol, 1.00 equiv.) were added and then dissolved with anhydrous DMSO/dioxane (1:4) (1.0 mL). Under an oxygen (balloon) atmosphere, the reaction mixture was stirred at 100 °C in oil bath with reflux condenser for the indicated time. Then, the reaction mixture was cooled to room temperature. 2N aq. HCl was added and the resulting mixture was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography.

ASSOCIATED CONTENT

Supporting Information

Reaction optimization and reaction profiles (PDF)

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Notes

The authors declare no competing financial interest.

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