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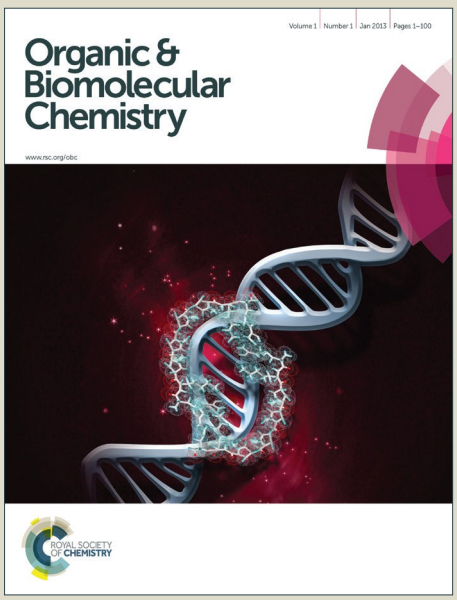

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ARTICLE

A versatile approach to flavones *via* one-pot Pd(II)-catalyzed dehydrogenation/oxidative boron-Heck coupling sequence of chromanones†

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A variety of flavones were expediently synthesized from readily accessible chromanones *via* a one-pot sequence involving Pd(II)-catalyzed dehydrogenation and oxidative boron-Heck coupling with arylboronic acid pinacol esters. Especially, the use of arylboronic acid pinacol esters was found to significantly improve the yield of the reaction.

Introduction

Flavones, a class of widely occurring natural products and their synthetic derivatives, have received enormous attention in the field of medicinal chemistry[1] due to their fascinating biological activities such as anti-oxidant, anti-inflammatory, anti-cancer and estrogen-related functions.[2] As representative routes to the structures of such privileged flavones, several synthetic methods, including intramolecular condensation of (2-hydroxyphenyl)-1, 3 diketones following the Baker-Venkataraman rearrangement, the oxidative cyclization of 2-hydroxychalcone, the Allan-Robinson reaction, and Pd(0)-catalyzed cyclization, have been conventionally used in recent decades.[3] These approaches have often been reported to possess the disadvantages of requiring multiple steps, using limited reagents or starting materials, operating under harsh reaction conditions, or providing low to moderate yields. Recently, a few reports on the preparation of flavones from chromone using Pd(II)-catalyzed C-H functionalization have been disclosed.[4] Among them, flavone synthesis *via* oxidative boron-Heck coupling[5] is interesting because it requires mild conditions, is conveniently available, uses a moderate amount of reagents, and provides good to excellent yields as well as regioselectivity.[4a,4b] This approach also showed significant feasibility of late stage functionalization to provide various substituted flavones. However, the preparation of various chromones, the starting materials of the reaction, might be sometimes difficult, partly due to their reactive α, β-unsaturated carbonyl and enol ether moieties. In these cases, the chromones have been occasionally synthesized and functionalized *via* other intermediates such as chromanones, which are readily available[6] and less reactive than chromones. Particularly, the oxidation process of chromanones has been used for concise conversion into chromones.[7]

In an effort to develop a more versatile approach to diverse flavones, we considered it worthwhile to explore an approach to flavone scaffolds using a Pd(II)-catalyzed reaction, directly from chromanones instead of chromones. In 2011, Stahl and his coworkers reported that Pd(II)-catalyzed dehydrogenation provided efficient transformation of simple ketones to enones.[8] In addition, a recent work about direct transformation of chromanones into flavones using simple arenes, reported by Hong and his coworkers, have shown the feasibility of one-pot Pd(II) catalysis.[4d] ~~Considering~~ Considering these previous reports that show the potential of Pd(II) species to proceed through further Pd(II)-catalysis ~~oxidative boron-Heck coupling~~ over dehydrogenation of the ketone, we envisaged that the chromanones could be assembled into the flavones *via* ~~chromones generated *in situ*~~ dehydrogenation and oxidative boron-Heck coupling in a one-pot ~~Pd(II) catalysis~~ sequence. Herein, we report a one-pot Pd(II)-catalyzed dehydrogenation/oxidative boron-Heck coupling sequence of chromanones as a concise and versatile approach to the synthesis of flavones. (Scheme 1)

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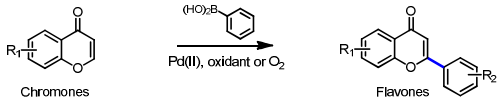

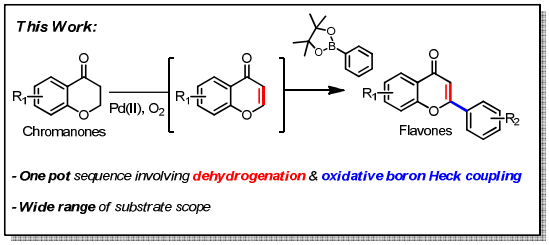

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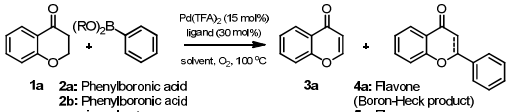
Scheme 1 One pot synthetic strategy toward flavones in this study

Result and Discussion

To investigate the feasibility of the Pd(II)-catalyzed dehydrogenation/oxidative boron-Heck coupling sequence for the synthesis of flavones, chromanone **1a** and phenylboronic acid **2a** were selected as the model compounds to screen and optimize the reaction conditions (Table 1). Based on the speculation that the dehydrogenation process might be a plausible starting point for the sequence, we initially tested the reaction condition with $Pd(TFA)_2$ catalyst, DMSO ligand and AcOH solvent under O_2 atmosphere, which are known to be optimal for Pd(II)-catalyzed dehydrogenation.[8] Use of ~~this condition~~these reaction conditions resulted in the formation of ~~the~~ desired flavone **4a**~~,~~ with 13% yield, and chromone **3a** as ~~a~~ the major product (34% yield, entry 1). This result indicated that chromanone could be dehydrogenated, but the resulting chromone might be poorly converted into the flavone under ~~the condition~~these reaction conditions.

Table 1. Optimization of the reaction conditions for one-pot dehydrogenation/oxidative boron-Heck coupling[a]



1a 2a: Phenylboronic acid 2b: Phenylboronic acid pinacol ester 3a 4a: Flavone (Boron-Heck product) 5a: Flavanone (Conjugate addition product)

Entry	2a or 2b	Ligand	Solvent	Yield (%)[b] 3a	4a (5a)
1	**2a**	DMSO	~~HOAc~~AcOH	34	13 (9)
2	**2a**		DMSO	43	0
3	**2a**	pyridine	DMSO	76	2
4	**2a**	DMAP	DMSO	70	2
5	**2a**	bipyridine	DMSO	35	11 (11)
6	**2a**	phenanthroline	DMSO	24	19 (9)
7	**2a**	5-nitro phen	DMSO	1	42 (25)
8	**2b**	5-nitro phen	DMSO	0	93 (1)
9	**2b**	5-nitro phen	toluene	57	2 (3)
10	**2b**	5-nitro phen	CH_3CN	52	4 (13)
11	**2b**	5-nitro phen	dioxane	51	1 (1)
12	**2b**	5-nitro phen	THF	72	3 (3)
13	**2b**	5-nitro phen	DMF	0	70
14[c]	**2b**	5-nitro phen	DMSO	0	72
15[d]	**2b**	5-nitro phen	DMSO	13	72 (1)
16[e]	**2b**	5-nitro phen	DMSO	0	70 (1)
17[f]	**2b**	5-nitro phen	DMSO	0	83 (1)

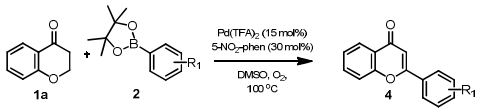
[a]Reaction conditions: **1a** (0.34 mmol, 1.0 equiv.), **2a** or **2b** (1.02 mmol, 3.0 equiv.), $Pd(TFA)_2$ (0.05 mmol, 15 mol-%), ligand (0.10 mmol, 30 mol-%), and solvent (1 mL)under O_2 for 48 hours. [b]Isolated yield. [c]1.5 equiv. **2b**. [d]10 mol-% $Pd(TFA)_2$ and 20 mol-% 5-nitro phen. [e]15 mol-% $Pd(OAc)_2$. [f]**1a** (6.84 mmol, 1.0 equiv.), **2b** (20.53 mmol, 3.0 equiv.), $Pd(TFA)_2$ (1.03 mmol, 15 mol%), 5-nitro phen (2.05 mmol, 30 mol%), and DMSO (10 mL) under O_2 for 48 hours.

In addition, most of the ligands used for boron-Heck reaction[4a,5a-k], such as phenanthroline, were already known to be ineffective for dehydrogenation in AcOH solvent.[8a] Therefore, we tried to optimize the reaction ~~condition~~ conditions using DMSO, another suitable solvent for the dehydrogenation process.[8a] In the presence of most of the ligands reported to improve the boron-Heck reaction[5a-k], low to moderate yields of the flavone were obtained (entry 2-7). Among them, the catalytic system including 5-nitro-1, 10 phenanthroline (5-nitro phen) as a ligand afforded flavone **4a** in 42% yield, along with flavanone **5a**, the conjugate addition product in 25% yield, indicating that it was better than the other ligands under incorporating conditions (entry 7).

In view of recent reports[4b,5d,5k] in which the conjugate addition product can be obtained in a higher amount as the acidity of an additive in the reaction increased, we supposed that the relatively acidic ~~property~~ nature of phenylboronic acid **2a** might increase the amount of flavanone **5a**, leading to decreased yield of ~~the~~ desired flavone **4a**. With this insight, we introduced phenylboronic acid pinacol ester **2b**, as a readily available and aprotic surrogate of phenylboronic acid **2a** to improve the reaction. To our delight, the use of **2b** in DMSO at 100 °C enables the reaction to exclusively provide flavone **4a** with the highest yield of 93% yield and flavanone **3a** in 1% yield. (entry 8).

Next, ~~we focused on an additional investigation regarding the solvent, the amount of the reagent and another Pd(II) catalyst~~the attention was focused in investigating the solvent, the amount of reagent and alternative Pd(II) catalysis. In the case of using DMF as a solvent, flavone was successfully formed with 70% yield. However, the use of other solvents, ~~another~~ alternative catalyst such as $Pd(OAc)_2$ and 1.5 equivalent of **2b** resulted in ~~a lower yield of the desired product~~lower yields of the desired product. ~~than yield under the optimized condition using **1a** (1.0 equiv.), **2b** (3.0 equiv.), $Pd(TFA)_2$ (15 mol %), 5-nitro phen (30 mol %), and DMSO (1 mL) under an O_2 atmosphere~~Hence, the optimized condition using **1a** (1.0 equiv.), **2b** (3.0 equiv.), $Pd(TFA)_2$ (15 mol%), 5-nitro phen (30 mol%), and DMSO (1 mL) under an O_2 atmosphere, were used.

Table 2. Dehydrogenation/oxidative boron Heck coupling of **1a** with various arylboronic acid pinacol esters[a]



1a 2 4

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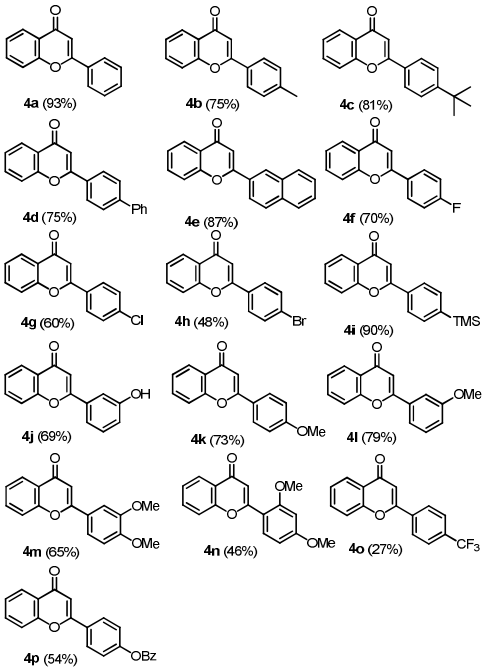


[a]Reaction conditions: **1a** (1.0 equiv.), arylboronic acid pinacol ester **2** (3.0 equiv.), $Pd(TFA)_2$ (15 mol-%), 5-nitro phen (30 mol-%), and DMSO under O_2 for 48 hours.

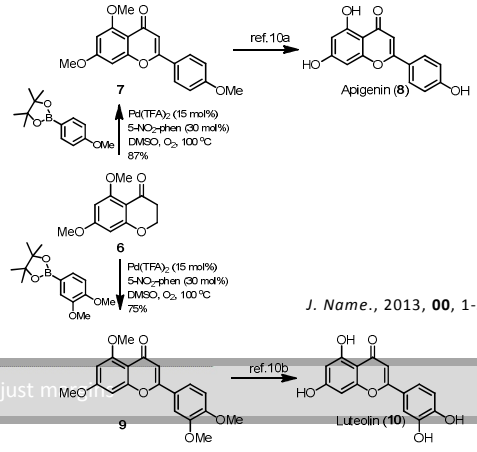
Using the optimized condition, we tested a variety of aryl boronic acid pinacol esters **2** to investigate the functional group compatibility of the reaction (Table 2). Notably, the reaction was widely applicable to the synthesis of flavones from chromanone **1a** with various arylboronic acid pinacol esters bearing either electron-donating groups such as methyl (**4b**), *tert*-butyl (**4c**), phenyl (**4d**), naphthyl (**4e**), hydroxyl (**4j**), and methoxy (**4k-n**) or electron withdrawing groups such as fluorine (**4f**), chlorine (**4g**) and bromine (**4h**). OH^--labile ester functional group (**4p**) were also tolerant in the reaction. The desired products were obtained in high yields, along with a small amount of flavanone as a side product. The highest yield of 90% was obtained by incorporating a trimethylsilyl phenyl group (**4j**). In the case of incorporating strongly electron withdrawing ~~trifluoromethyl group~~group, such as trifluoromethyl (**4o**), the reaction provided ~~the~~ desired flavone **4o** with relatively lower yield compared to others, along with chromone **3a** as ~~a~~ the major product (70%).[4a]

Table 3. Dehydrogenation/oxidative boron-Heck coupling of **2b** with various chromones[a]

[a]Reaction conditions: **1** (1.0 equiv.), **2b** (3.0 equiv.), $Pd(TFA)_2$ (15 mol-%), 5-nitro phen (30 mol-%), and DMSO under O_2 for 48 hours.

To further explore the scope and limitations of this procedure, the reaction with a series of chromanone **1** and phenylboronic acid pinacol ester **2b** was investigated under the given conditions. As shown in table 3, most of the chromanones could be readily transformed into the corresponding functionalized flavones in moderate to good yields, with both weakly and strongly electron withdrawing (**4q-s**) or donating substituents (**4t-w**) on the phenyl group of the chromanone. H^+-labile acetal group (**4x**) and OH^--labile ester functional group (**4y**) were tolerant in the reaction. More importantly, dimethoxy chromanones and catechol-derived arylboronic acid pinacol ester successfully underwent dehydrogenation/oxidative boron Heck coupling to provide the corresponding flavones (**4m-n**, and **4w-x**, respectively), indicating that this methodology could be extended to the synthesis of biologically active functionalized flavones bearing primarily dimethoxy or dihydroxyl groups.

To further demonstrate the potential utility of the one-pot dehydrogenation/oxidative boron-Heck coupling sequence for the synthesis of flavones, we attempted to synthesize apigenin (**8**), and luteolin (**10**)[9], natural flavones with significant biological activities[1], from readily available chromanone **6** using the methodology. As expected, each corresponding intermediate (**7** and **9**) for the synthesis of apigenin (**8**) and luteolin (**10**) was expediently synthesized in yields of 87% and 75%, respectively, *via* the one-pot dehydrogenation/oxidative boron-Heck coupling sequence.



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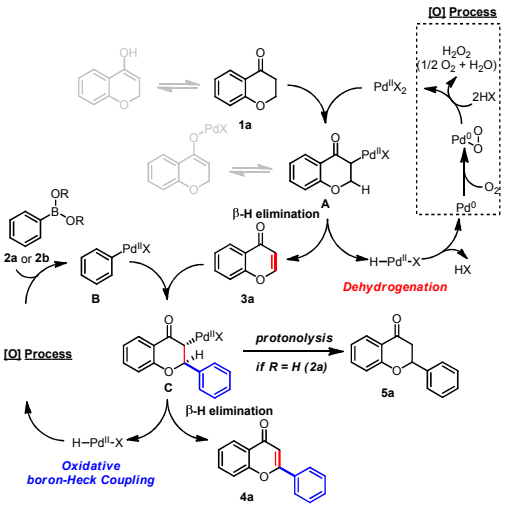
Scheme 2 Application of dehydrogenation/oxidative boron-Heck coupling to the synthesis of natural flavones[10]

A proposed mechanism of the sequential dehydrogenation/ oxidative boron-Heck coupling is depicted in scheme 3. First, the formation of a Pd(II) enolate ~~might follow~~might be followed by β-hydride elimination[11] to generate the enone product **3a** (dehydrogenation), which could be a starting material for the oxidative boron-Heck coupling. Next, the arylboronic acid pinacol ester would be transmetalated to form palladated aryl intermediate **B**, which inserts into the electrophilic alkene of **3a**, resulting in Pd/alkyl intermediate **C**. Then, this intermediate is converted into ~~the~~ desired coupled product **4a** by the subsequent β-hydride elimination (oxidative boron-Heck coupling). In an excess protic environment, flavanone **5a** might be produced through protonolysis of intermediate **C**. During both of the reactions, Pd(0) species formed in the reaction would be recycled into Pd(II) *via* [O] process, where O_2 plays a crucial role in the re-oxidation process of the catalyst.



Scheme 3 Proposed mechanism of the reaction

Conclusion

In summary, we developed a versatile approach to diverse flavones from readily available chromanones and arylboronic acid pinacol esters *via* a Pd(II)-catalyzed dehydrogenation and oxidative boron-Heck coupling reaction in a one-pot sequence. This approach has the advantages of convenience, including easily accessible reagents or starting materials and efficiency, providing high yields. This methodology also provides a facile route to biologically interesting flavones including natural products such as apigenin and luteolin. Additional investigations on broadening the scope of the reaction to afford other related compounds and to perform biological studies using the compounds are currently ongoing.

Experimental

General consideration

Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers (Aldrich, Alfa Aesar, and TCI) and were used without further purification. Tetrahydrofuran and Et_2O were distilled from sodium benzophenone ketyl. Dichloromethane, trimethylamine, acetonitrile and pyridine were freshly distilled from calcium hydride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried at 100 °C. Air and moisture sensitive reactions were performed under argon atmosphere. Flash column chromatography was performed using silica gel 60 (230-400 mesh) with the indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates. Optical rotations were measured using 100 nm cell of 1~2 mL capacity. ^{1}H NMR spectra were recorded and obtained using ~~on a~~ Bruker 400 (400 MHz for ^{1}H-NMR) and Varian VNMR S500 (~~;~~ 125 MHz for ^{13}C-NMR) spectrometer, respectively. ^{1}H and ^{13}C 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), dt (doublet of triplets), or dq (doublet of quartets); the coupling constants are reported in hertz (Hz). Mass spectra were obtained with VG Trio-2 GC-MS instrument. High resolution mass spectra were obtained with JEOL JMS-AX 505WA instrument.

General procedure for the synthesis of flavones. To a solution of $Pd(TFA)_2$ (0.05 mmol), and 5-nitro-1,10-phenanthroline (0.10 mmol) in anhydrous DMSO (1mL) were added chromanone (0.34 mmol) and phenyl boronic acid pinacol ester (1.02 mmol) under O_2 atmosphere. The reaction mixture was stirred at 100 °C until complete consumption of the starting material on TLC. Then, the reaction mixture was diluted with EtOAc and filtered through a pad of celite. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc/Hexanes).

2-phenyl-4H-chromen-4-one (4a). Prepared from 4-chromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 69 mg (93%) of compound **4a**~~.~~ as a white solid; mp 96-97°C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (dd, 1H, J = 7.9, 1.5 Hz), 7.91-7.88 (m, 2H), 7.68 (m, 1H), 7.55-7.48 (m, 4H), 7.39 (m, 1H), 6.80 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.6, 163.6, 156.5, 134.0, 132.0, 131.8, 129.3, 129.3, 126.5,

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126.5, 125.9, 125.5, 124.2, 118.3, 107.8; LR-MS (FAB) *m/z* 223 ($M+H^+$); HR-MS (FAB) calcd for $C_{15}H_{10}O_2$ ($M+H^+$) 223.0759; found 223.0762.

2-(*p*-tolyl)-4H-chromen-4-one (4b). Prepared from 4-chromanone and 4-tolylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 60 mg (75%) of compound **4b** as a pale yellow solid; mp 111-113 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, 1H, *J* = 7.9Hz), 7.82 (d, 2H, *J* = 8.2Hz), 7.69 (t, 1H, *J* = 8.2Hz), 7.56 (d, 1H, *J* = 8.4Hz), 7.41 (t, 1H, *J* = 7.5Hz), 7.32 (d, 1H, *J* = 8.0Hz), 6.80 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.7, 163.8, 156.5, 142.5, 133.9, 130.0, 130.0, 129.2, 126.5, 126.5, 125.9, 125.4, 124.2, 118.3, 107.2, 21.8.

2-(4-(*tert*-butyl)phenyl)-4H-chromen-4-one (4c). Prepared from 4-chromanone and 4-*t*-butylphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 76 mg (81%) of compound **4c** as a pale yellow solid; mp 97-99 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.23 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.86 (d, 2H, *J* = 6.8 Hz), 7.68 (td, 1H, *J* = 7.3, 1.6 Hz), 7.57-7.53 (m, 3H), 7.40 (t, 1H, *J* = 7.5 Hz), 6.81 (s, 1H), 1.37 (s, 9H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.7, 163.8, 156.5, 155.6, 133.9, 129.2, 126.4, 126.4, 126.3, 126.3, 125.9, 125.4, 124.2, 118.3, 107.3, 35.3, 31.4, 31.4, 31.4; LR-MS (FAB) *m/z* 279 ($M+H^+$); HR-MS (FAB) calcd for $C_{19}H_{18}O_2$ ($M+H^+$) 279.1385; found 279.1380.

2-([1,1'-biphenyl]-4-yl)-4H-chromen-4-one (4d). Prepared from 4-chromanone and 4-biphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 75 mg (75%) of compound **4d** as a pale yellow solid; mp 142-144 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, 1H, *J* = 7.9 Hz), 7.98 (d, 2H, *J* = 8.2 Hz), 7.74-7.63 (m, 5H), 7.57 (d, 1H, *J* = 8.4 Hz), 7.48 (t, 2H, *J* = 7.4 Hz), 7.43-7.38 (m, 2H), 6.86 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.6, 163.3, 156.5, 144.6, 140.0, 134.0, 130.7, 129.3, 129.3, 128.5, 127.9, 127.9, 127.4, 127.4, 127.0, 127.0, 126.0, 125.5, 124.3, 118.3, 107.7; LR-MS (FAB) *m/z* 299 ($M+H^+$); HR-MS (FAB) calcd for $C_{21}H_{14}O_2$ ($M+H^+$) 299.1072; found 299.1067.

2-(naphthalen-2-yl)-4H-chromen-4-one (4e). Prepared from 4-chromanone and naphthalene-2-boronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : n-Hexane = 1 : 2) to afford 80 mg (87%) of compound **4e**[4b] as a pale yellow solid; mp 148-150 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.45 (s, 1H), 8.24 (dd, 1H, *J* = 7.9 Hz, *J*=1.2 Hz), 8.00-7.83 (m, 4H), 7.71 (td, 1H, *J* = 7.8 Hz, *J*=1.4 Hz), 7.61 (d, 1H, *J* = 8.3Hz), 7.60-7.52 (m, 2H), 7.42 (t, 1H, *J* = 7.5 Hz), 6.94 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.7, 163.6, 156.6, 134.9, 134.1, 133.1, 129.3, 129.2, 129.1, 128.3, 128.1, 127.3, 127.2, 126.0, 125.5, 124.3, 122.7, 118.4, 108.1.

2-(4-fluorophenyl)-4H-chromen-4-one (4f). Prepared from 4-chromanone and 4-fluorophenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 57 mg (70%) of compound **4f**[35] as a yellow solid; mp 148-150 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.21 (dd, 1H, *J* = 7.9 Hz, *J*=1.5 Hz), 7.97-7.86 (m, 2H), 7.70 (td, 1H, *J* = 8.6 Hz, *J*=1.5 Hz), 7.55 (d, 1H, *J* = 8.4 Hz), 7.42 (t, 1H, *J* = 7.3 Hz), 7.20 (t, 2H, *J* = 8.6 Hz), 6.76 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 166.0, 164.0, 162.6, 156.4, 134.1, 128.8, 128.7, 128.2, 128.2, 125.9, 125.6, 124.1, 118.2, 116.6, 116.4, 107.6.

2-(4-chlorophenyl)-4H-chromen-4-one (4g). Prepared from 4-chromanone and 4-chlorophenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 52 mg (60%) of compound **4g** as a yellow solid; mp 188-190 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, 1H, *J* = 7.9 Hz), 7.86 (d, 2H, *J* = 7.6 Hz), 7.71 (m, 1H), 7.56 (d, 1H, *J* = 8.4 Hz), 7.50 (d, 2H, *J* = 7.6 Hz), 7.43 (t, 1H, *J* = 7.6 Hz), 6.79 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 162.4, 156.4, 138.1, 134.1, 130.5, 129.6, 129.6, 127.8, 127.8, 126.0, 125.6, 124.1, 118.3, 107.9; LR-MS (FAB) *m/z* 257 ($M+H^+$); HR-MS (FAB) calcd for $C_{15}H_9ClO_2$ ($M+H^+$) 257.0369; found 257.0372.

2-(4-bromophenyl)-4H-chromen-4-one (4h). Prepared from 4-chromanone and 4-bromo phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 49 mg (48%) of compound **4h** as a pale yellow solid; mp 164-166 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, 1H, *J* = 7.9 Hz), 7.79 (d, 2H, *J* = 8.4Hz), 7.74-7.63 (m, 3H), 7.56 (d, 1H, *J* = 8.4Hz), 7.43 (t, 1H, *J* = 7.5Hz), 6.80 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 162.5, 156.4, 134.2, 132.6, 132.6, 131.0, 127.9, 127.9, 126.6, 126.0, 125.6, 124.2, 118.3, 107.9.

2-(4-(trimethylsilyl)phenyl)-4H-chromen-4-one (4i). Prepared from 4-chromanone and 4-(Trimethylsilyl) phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 89 mg (90%) of compound **4i**[4b] as a pale yellow solid; mp 78-80 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (dd, 1H, *J* = 8.0 Hz, *J*=1.5 Hz), 7.87 (d, 2H, *J* = 8.2 Hz), 7.72-7.63 (m, 3H), 7.56 (d, 1H, *J* = 8.5 Hz), 7.40 (t, 1H, *J* = 7.4 Hz), 6.84 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.8, 163.7, 156.6, 145.7, 134.2, 134.0, 132.2, 126.0, 125.6, 125.5, 124.3, 118.4, 107.9, -1.1.

2-(3-hydroxyphenyl)-4H-chromen-4-one (4j). Prepared from 4-chromanone and 3-hydroxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 55 mg (69%) of compound **4j** as a white solid; mp 210 °C; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 9.93 (s, 1H), 8.07 (d, 1H, *J* = 7.8 Hz), 7.85 (m, 1H), 7.78 (m, 1H), 7.55-7.50 (m, 2H), 7.46 (m, 1H), 7.39 (t, 1H, *J* = 7.9 Hz), 7.02 (d, 1H, *J* = 8.1 Hz), 6.95 (s, 1H); ^{13}C-NMR (DMSO-d_6, 125 MHz) δ 177.8, 163.4, 158.6, 156.4, 135.0, 133.1, 131.0, 126.2, 125.5, 124.1, 119.6, 119.2, 117.9, 113.5, 107.6; LR-MS (FAB) *m/z* 239 ($M+H^+$); HR-MS (FAB) calcd for $C_{15}H_{10}O_3$ ($M+H^+$) 239.0708; found 239.0707.

2-(4-methoxyphenyl)-4H-chromen-4-one (4k). Prepared from 4-chromanone and 4-methoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 62 mg (73%) of compound **4k** as a white solid; mp 154-156 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.21 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.86 (d, 2H, *J* = 8.8 Hz), 7.67 (t, 1H, *J* = 7.6 Hz), 7.53 (d, 1H, *J* = 8.2 Hz), 7.39 (t, 1H, *J* = 7.6 Hz), 7.00 (d, 2H, *J* = 8.8 Hz), 6.73 (s, 1H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.6, 163.6, 162.6, 156.4, 133.8, 128.2, 128.2, 125.8, 125.3, 124.2, 124.1, 118.2, 114.7, 114.7, 106.4, 55.7; LR-MS (FAB) *m/z* 253 ($M+H^+$); HR-MS (FAB) calcd for $C_{16}H_{12}O_3$ ($M+H^+$) 253.0865; found 253.0863.

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2-(3-methoxyphenyl)-4H-chromen-4-one (4l). Prepared from 4-chromanone and 3-methoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 67 mg (79%) of compound **4l** as a white solid; mp 125-128 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.69 (td, 1H, *J* = 7.8, 1.7 Hz), 7.56 (d, 1H, *J* = 8.4 Hz), 7.49 (d, 1H, *J* = 7.9 Hz), 7.44-7.40 (m, 3H), 7.06 (m, 1H), 6.81 (s, 1H), 3.88 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.7, 163.4, 160.2, 156.5, 134.0, 133.3, 130.4, 125.9, 125.5, 124.2, 118.9, 118.3, 117.4, 112.0, 108.0, 55.7; LR-MS (FAB) *m/z* 253 (M+H$^+$); HR-MS (FAB) calcd for $C_{16}H_{12}O_3$ (M+H$^+$) 253.0865; found 253.0864.

2-(3,4-dimethoxyphenyl)-4H-chromen-4-one (4m). Prepared from 4-chromanone and 3,4-dimethoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 62 mg (65%) of compound **4m** as a pink solid; mp 144-146 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.21 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.68 (td, 1H, *J* = 7.8, 1.6 Hz), 7.56 (d, 2H, *J* = 8.4 Hz), 7.43-7.37 (m, 2H), 6.98 (d, 1H, *J* = 8.5 Hz), 6.75 (s, 1H), 3.98 (s, 3H), 3.96 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 163.6, 156.4, 152.3, 149.5, 133.8, 125.9, 125.3, 124.4, 124.1, 120.2, 118.2, 111.4, 109.0, 106.7, 56.3, 56.3; LR-MS (FAB) *m/z* 283 (M+H$^+$); HR-MS (FAB) calcd for $C_{17}H_{14}O_4$ (M+H$^+$) 283.0970; found 283.0967.

2-(2,4-dimethoxyphenyl)-4H-chromen-4-one (4n). Prepared from 4-chromanone and 2,4-dimethoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 44 mg (46%) of compound **4n** as a yellow solid; mp 127-129 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.90 (d, 1H, *J* = 8.8 Hz), 7.65 (td, 1H, *J* =7.9, 1.6 Hz), 7.50 (d, 1H, *J* = 8.4 Hz), 7.38 (t, 1H, *J* = 7.2 Hz), 7.15 (s, 1H), 6.63 (dd, 1H, *J* = 2.3 Hz), 6.55 (d, 1H, *J* = 2.3 Hz), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 179.2, 163.5, 161.1, 159.9, 156.6, 133.6, 130.7, 125.8, 125.0, 124.0, 118.1, 113.8, 111.6, 105.5, 99.1, 55.9, 55.8; LR-MS (FAB) *m/z* 283 (M+H$^+$); HR-MS (FAB) calcd for $C_{17}H_{14}O_4$ (M+H$^+$) 283.0970; found 283.0967.

2-(4-(trifluoromethyl)phenyl)-4H-chromen-4-one (4o). Prepared from 4-chromanone and 4-(Trifluoromethyl)phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 27 mg (27%) of compound **4o**[3w] as a brown solid; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.25 (dd, 1H, *J* = 7.9 Hz, ~~*J*~~=1.4 Hz), 8.05 (d, 2H, *J* = 8.2 Hz), 7.80 (d, 2H, *J* = 8.3 Hz), 7.74 (td, 1H, *J* = 7.8 Hz, ~~*J*~~=1.7 Hz), 7.60 (d, 1H, *J* = 8.4 Hz), 7.46 (t, 1H, *J* = 7.5 Hz), 6.88 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 161.9, 156.5, 135.5, 134.4, 133.5, 126.9, 126.4, 126.3, 126.3, 126.3, 126.1, 125.8, 124.2, 118.4, 109.0.

4-(4-oxo-4H-chromen-2-yl)phenyl benzoate (4p). Prepared from 4-chromanone and (4-(benzoyloxy)phenyl)boronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 63 mg (54%) of compound **4p** as a pale yellow solid; mp 124-125 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.27-8.18 (m, 3H), 8.01 (d, 2H, *J* = 8.7Hz), 7.75-7.64 (m, 2H), 7.61-7.50 (m, 3H), 7.47-7.37 (m, 3H), 6.84 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.6, 165.0, 162.8, 156.5, 153.8, 134.2, 134.1, 130.5, 130.5, 129.7, 129.3, 128.9, 128.9, 128.0, 128.0, 126.0, 125.6, 124.2, 122.8, 122.8, 118.3, 107.9.

6-nitro-2-phenyl-4H-chromen-4-one (4q). Prepared from 6-nitrochromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 35 mg (51%) of compound **4q** as a yellow solid; mp 184-187 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 9.10 (d, 1H, *J* = 2.8 Hz), 8.55 (dd, 1H, *J* = 9.2, 2.8 Hz), 7.95-7.93 (m, 2H), 7.75 (d, 1H, *J* = 9.2 Hz), 7.63-7.55 (m, 3H), 6.90 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.0, 164.4, 159.3, 145.1, 132.6, 131.0, 129.5, 129.5, 128.4, 126.7, 126.7, 124.3, 122.7, 120.1, 108.1; LR-MS (FAB) *m/z* 268 (M+H$^+$); HR-MS (FAB) calcd for $C_{15}H_9NO_4$ (M+H$^+$) 268.0610; found 268.0607.

6-fluoro-2-phenyl-4H-chromen-4-one (4r). Prepared from 6-fluorochromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 57 mg (79%) of compound **4r** as a yellow solid; mp 123-127 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.91 (dd, 2H, *J* = 7.8, 1.5 Hz), 7.86 (dd, 1H, *J* = 8.2, 3.1 Hz), 7.59-7.50 (m, 4H), 7.42 (m, 1H), 6.81 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.8, 163.9, 160.8, 158.9, 152.7, 132.0, 131.7, 129.3, 126.5, 125.4, 125.4, 122.2, 122.0, 120.4, 120.4, 111.0, 110.8, 107.1; LR-MS (FAB) *m/z* 241 (M+H$^+$); HR-MS (FAB) calcd for $C_{15}H_9FO_2$ (M+H$^+$) 241.0665; found 241.0661.

6-chloro-2-phenyl-4H-chromen-4-one (4s). Prepared from 6-chlorochromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 56 mg (80%) of compound **4s** as a yellow solid; mp 178-180 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.17 (d, 1H, *J* = 2.5 Hz), 7.91-7.88 (m, 2H), 7.63 (dd, 1H, *J* = 8.9, 2.6 Hz), 7.55-7.50 (m, 4H), 6.81 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.4, 163.9, 154.8, 134.2, 132.1, 131.6, 131.4, 129.4, 129.4, 126.6, 126.6, 125.4, 125.1, 120.1, 107.7; LR-MS (FAB) *m/z* 257 (M+H$^+$); HR-MS (FAB) calcd for $C_{15}H_9ClO_2$ (M+H$^+$) 257.0369; found 257.0368.

6-methoxy-2-phenyl-4H-chromen-4-one (4t~~4t~~). Prepared from 6-methoxychromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 52 mg (73%) of compound **4t** as a white solid; mp 165-167 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.90 (dd, 2H, *J* = 7.8, 2.8 Hz), 7.58 (d, 1H, *J* = 3.1 Hz), 7.55-7.47 (m, 4H), 7.27 (dd, 1H, *J* = 9.1, 3.1 Hz), 6.81 (s, 1H), 3.90 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.5, 163.4, 157.2, 151.3, 132.1, 131.7, 129.2, 129.2, 126.5, 126.5, 124.8, 124.0, 119.7, 107.0, 105.1, 56.1; LR-MS (FAB) *m/z* 253 (M+H$^+$); HR-MS (FAB) calcd for $C_{16}H_{12}O_3$ (M+H$^+$) 253.0865; found 253.0865.

7-methoxy-2-phenyl-4H-chromen-4-one (4u). Prepared from 7-methoxychromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 58 mg (82%) of compound **4u** as a white solid; mp 105-106 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 1H, *J* = 8.7 Hz), 7.91-7.87 (m, 2H), 7.53-7.49 (m, 3H), 6.99-6.93 (m, 2H), 6.75 (s, 1H), 3.92 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.1, 164.4, 163.2, 158.2, 132.1, 131.6, 129.2, 129.2, 127.3, 126.4, 126.4, 118.1, 114.7, 107.7, 100.6, 56.1; LR-MS (FAB) *m/z* 253 (M+H$^+$); HR-MS (FAB) calcd for $C_{16}H_{12}O_3$ (M+H$^+$) 253.0865; found 253.0865.

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6-methyl-2-phenyl-4H-chromen-4-one (4v). Prepared from 6-methylchromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 62 mg (85%) of compound **4v** as a pale yellow solid; mp 112-116 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.00 (s, 1H), 7.90 (dd, 2H, J = 7.5, 1.7 Hz), 7.54-7.43 (m, 5H), 6.80 (s, 1H), 2.44 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.8, 163.5, 154.8, 135.5, 135.3, 132.1, 131.8, 129.2, 129.2, 126.5, 126.5, 125.3, 123.8, 118.1, 107.6, 21.2; LR-MS (FAB) *m/z* 237 (M+H$^+$); HR-MS (FAB) calcd for $C_{16}H_{12}O_2$ (M+H$^+$) 237.0916; found 237.0914.

5,7-dimethoxy-2-phenyl-4H-chromen-4-one (4w). Prepared from 5,7-dimethoxychromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 43 mg (63%) of compound **4w** as a white solid; mp 200-203 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.88-7.83 (m, 2H), 7.52-7.45 (m, 3H), 6.67 (s, 1H), 6.56 (d, 1H, J = 2.3 Hz), 6.36 (d, 1H, J = 2.3 Hz), 3.95 (s, 3H), 3.91 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.8, 164.3, 161.2, 160.9, 160.2, 131.8, 131.4, 129.2, 129.2, 126.2, 126.2, 109.5, 109.3, 96.4, 93.1, 56.7, 56.0; LR-MS (FAB) *m/z* 283 (M+H$^+$); HR-MS (FAB) calcd for $C_{17}H_{14}O_4$ (M+H$^+$) 283.0970; found 283.0970.

6-phenyl-8H-[1,3]dioxolo[4,5-g]chromen-8-one (4x). Prepared from 6,7-methylenedioxy-chromanone and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 50 mg (72%) of compound **4x** as a yellow solid; mp 210-212 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.90-7.83 (m, 2H), 7.54-7.47 (m, 4H), 6.96 (s, 1H), 6.76 (s, 1H), 6.11 (s, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.6, 163.0, 153.8, 153.0, 146.4, 132.0, 131.6, 129.2, 129.2, 126.3, 126.3, 119.2, 107.2, 102.7, 102.6, 98.3; LR-MS (FAB) *m/z* 267 (M+H$^+$); HR-MS (FAB) calcd for $C_{16}H_{10}O_4$ (M+H$^+$) 267.0657; found 267.0657.

4-oxo-2-phenyl-4H-chromen-7-yl pivalate (4y). Prepared from 4-oxochroman-7-yl pivalate and phenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 34 mg (51%) of compound **4y**[12] as a pale yellow solid; mp 129-132°C; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.25 (d, 1H, J=8.7 Hz), 7.90 (dd, 2H, J=7.5 Hz, J=1.6 Hz), 7.56-7.47 (m, 3H), 7.39 (d, 1H, J=2.1 Hz), 7.14 (dd, 1H, J=8.7 Hz, J=2.1 Hz), 6.82 (s, 1H), 1.40 (s, 9H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 178.0, 176.6, 163.9, 157.0, 155.4, 132.0, 131.8, 129.3, 127.3, 126.5, 121.8, 119.7, 111.3, 107.9, 39.6, 27.3.

5,7-dimethoxy-2-(4-methoxyphenyl)-4H-chromen-4-one (7). Prepared from 5,7-dimethoxychromanone and 4-methoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 65 mg (87%) of compound **7**[13]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, 2H, J = 8.9 Hz), 6.98 (d, 2H, J = 8.9 Hz), 6.58 (s, 1H), 6.54 (d, 1H, J = 2.3 Hz), 6.35 (d, 1H, J = 2.2 Hz), 3.94 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.9, 164.1, 162.3, 161.1, 160.9, 160.0, 127.8, 127.8, 124.0, 114.6, 114.6, 109.4, 107.8, 96.3, 93.0, 56.6, 56.0, 55.7; LR-MS (FAB) *m/z* 313 (M+H$^+$); HR-MS (FAB) calcd for $C_{18}H_{16}O_5$ (M+H$^+$) 313.1076; found 313.1073.

2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4H-chromen-4-one (9). Prepared from 5,7-dimethoxychromanone and 3,4-dimethoxyphenylboronic acid pinacol ester using the general procedure described above. The residue was purified by silica gel column chromatography (EtOAc : *n*-Hexane = 1 : 2) to afford 62 mg (75%) of compound **9**[14]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.49 (dd, 1H, J = 8.5, 2.1 Hz), 7.30 (d, 1H, J = 2.0 Hz), 6.95 (d, 1H, J = 8.6 Hz), 6.60 (s, 1H), 6.55 (d, 1H, J = 2.2 Hz), 6.36 (d, 1H, J = 2.2 Hz), 3.97 (s, 3H), 3.95 (s, 6H), 3.92 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 177.8, 164.2, 161.1, 160.8, 160.0, 151.9, 149.4, 124.2, 119.7, 111.3, 109.4, 108.8, 108.1, 96.3, 93.1, 56.6, 56.3, 56.3, 56.0; LR-MS (FAB) *m/z* 343 (M+H$^+$); HR-MS (FAB) calcd for $C_{19}H_{18}O_6$ (M+H$^+$) 343.1182; found 343.1181.

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Notes and references

1. M. Singh, M. Kaur and O. Silakari, *Eur. J. Med. Chem.*, 2014, **84**, 206.
2. (a) B. Havsteen, *Biochem. Pharmacol.*, 1983, **32**, 1141; (b) J. A. Manthey, K. Grohmann and N. Guthrie, *Curr. Med. Chem.*, 2001, **8**, 135; (c) D. F. Birt, S. Hendrich and W. Wang, *Pharmacol. Ther.*, 2001, **90**, 157; (d) M. Lopez-Lazaro, *Curr. Med. Chem. Anticancer Agents*, 2002, **2**, 691; (e) H. P. Kim, K. H. Son, H. W. Chang and S. S. Kang, *J. Pharmacol. Sci.*, 2004, **96**, 229; (f) S. Chirumbolo, *Inflamm. Allergy Drug Targets*, 2010, **9**, 263; (g) C. Spatafora and C. Tringali, *Anticancer agents Med. Chem.*, 2012, **12**, 902; (h) Kumazawa, H. Takimoto, T. Matsumoto and K. Kawaguchi, *Curr. Parm. Des.*, 2014, **20**, 857.
3. (a) V. N. Kalinin, M. V. Shostakovsky and A. B. Ponomaryov, *Tetrahedron Lett.*, 1990, **31**, 4073; (b) M. Cushman and D. Nagarathnam, *Tetrahedron Lett.*, 1990, **31**, 6497; (c) L. W. Mcgarry and M. R. Detty, *J. Org. Chem.*, 1990, **55**, 4349; (d) P. G. Ciattini, E. Morera, G. Ortar and S. S. Rossi, *Tetrahedron*, 1991, **47**, 6449; (e) D. C. G. A. Pinto, A. M. S. Silva and J. A. S. Cavaleiro, *Tetrahedron Lett.*, 1994, **35**, 9459; (f) D. G. Powers, D. S. Casebier, D. Fokas, W. J. Ryan, J. R. Troth and D. L. Coffen, *Tetrahedron*, 1998, **54**, 4085; (g) D. E. Zembower and H. P. Zhang, *J. Org. Chem.*, 1998, **63**, 9300; (h) H. Miao and Z. Yang, *Org. Lett.*, 2000, **2**, 1765-1768; (i) P. Kumar and M. S. Bodas, *Org. Lett.*, 2000, **2**, 3821; (j) J. A. Seijas, M. P. Vazquez-Tato and R. Carballido-Reboredo, *J. Org. Chem.*, 2005, **70**, 2855; (k) B. Liang, M. W. Huang, Z. J. You, Z. C. Xiong, K. Lu, R. Fathi, J. H. Chen and Z. Yang, *J. Org. Chem.*, 2005, **70**, 6097; (l) A. K. Ganguly, S. Kaur, P. K. Mahata, D. Biswas, B. N. Pramanik and T. M. Chan, *Tetrahedron Lett.*, 2005, **46**, 4119; (m) E. Fillion, A. M. Dumas, B. A. Kuropatwa, N. R. Malhotra and T. C. Sitler, *J. Org. Chem.*, 2006, **71**, 409; (n) B. Kosmrlj and B. Sket, *Org. Lett.*, 2007, **9**, 3993; (o) K. H. Kumar and P. T. Perumal, *Tetrahedron*, 2007, **63**, 9531; (p) E. Awuah and A. Capretta, *Org. Lett.*, 2009, **11**, 3210; (q)

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DOI: 10.1039/C5OB01911G

M. Lorenz, M. S. Kabir and J. M. Cook, *Tetrahedron Lett.*, 2010, **51**, 1095; (r) Q. Yang and H. Alper, *J. Org. Chem.*, 2010, **75**, 948; (s) Z. Du, H. Ng, K. Zhang, H. Zeng and J. Wang, *Org. Biomol. Chem.*, 2011, **9**, 6930; (t) G. Maiti, R. Karmakar, R. N. Bhattacharya and U. Kayal, *Tetrahedron Lett.*, 2011, **52**, 5610; (u) J. Das and S. Ghosh, *Tetrahedron Lett.*, 2011, **52**, 7189; (v) T. M. Gogsig, R. H. Taaning, A. T. Lindhardt and T. Skrydstrup, *Angew. Chem. Int. Ed. ~~Engl.~~*, 2012, **51**, 798; (w) L. Klier, T. Bresser, T. A. Nigst, K. Karaghiosoff and P. Knochel, *J. Am. Chem. Soc.*, 2012, **134**, 13584; (x) K. V. Sashidhara, M. Kumar and A. Kumar, *Tetrahedron Lett.*, 2012, **53**, 2355; (y) X. F. Wu, H. Neumann and M. Beller, *Chem.-Eur. J.*, 2012, **18**, 12595.

4. (a) M. Khoobi, M. Alipour, S. Zarei, F. Jafarpour and A. Shafiee, *Chem. Commun.*, 2012, **48**, 2985; (b) D. Kim, K. Ham and S. Hong, *Org. Biomol. Chem.*, 2012, **10**, 7305; (c) K. H. Kim, H. S. Lee, S. H. Kim and J. N. Kim, *Tetrahedron Lett*, 2012, **53**, 2761; (d) Y. Moon, D. Kwon and S. Hong, *Angew. Chem. Int. Ed. ~~Engl.~~*, 2012, **51**, 11333.
5. (a) C. S. Cho and S. Uemura, *J. Organomet. Chem.*, 1994, **465**, 85; (b) K. S. Yoo, C. H. Yoon, R. K. Mishra, Y. C. Jung, S. W. Yi and K. W. Jung, *J. Am. Chem. Soc.*, 2006, **128**, 16384; (c) J. Lindh, P. A. Enquist, A. Pilotti, P. Nilsson and M. Larhed, *J. Org. Chem.*, 2007, **72**, 7957; (d) J. Ruan, X. Li, O. Saidi and J. Xiao, *J. Am. Chem. Soc.*, 2008, **130**, 2424; (e) D. C. Xiong, L. H. Zhang and X. S. Ye, *Org. Lett.*, 2009, **11**, 1709; (f) E. W. Werner and M. S. Sigman, *J. Am. Chem. Soc.*, 2010, **132**, 13981; (g) A. L. Gottumukkala, J. F. Teichert, D. Heijnen, N. Eisink, S. van Dijk, C. Ferrer, A. van den Hoogenband and A. J. Minnaard, *J. Org. Chem.*, 2011, **76**, 3498; (h) Y. Li, Z. Qi, H. Wang, X. Fu and C. Duan, *J. Org. Chem.*, 2012, **77**, 2053; (i) Z. He, S. Kirchberg, R. Frohlich and A. Studer, *Angew. Chem. Int. Ed.*, 2012, **51**, 3699; (j) C. Zheng, D. Wang and S. S. Stahl, *J. Am. Chem. Soc.*, 2012, **134**, 16496; (k) Y. W. Kim and G. I. Georg, *Org. Lett.*, 2014, **16**, 1574; (l) S. E. Walker, J. Boehnke, P. E. Glen, S. Levey, L. Patrick, J. A. Jordan-Hore and A. L. Lee, *Org. Lett.*, 2013, **15**, 1886.
6. (a) J. He, J. Zheng, J. Liu, X. She and X. Pan, *Org. Lett.*, 2006, **8**, 4637; (b)M. P. Hay, K. O. Hicks, K. Pchalek, H. H. Lee, A. Blaser, F. B. Pruijn, R. F. Anderson, S. S. Shinde, W. R. Wilson and W. A. Denny, *J. Med. Chem.*, 2008, **51**, 6853; (c) Y. L. Zhong, D. T. Boruta, D. R. Gauthier and D. Askin, *Tetrahedron Lett.*, 2011, **52**, 4824.
7. (a) P. G. Ciattini, E. Morera and G. Ortar, *J. Heterocyclic. Chem.*, 1982, **19**, 395; (b) C. G. Shanker, B. V. Mallaiah and G. Srimannarayana, *Synthesis*, 1983~~, **1983**~~, 310; (c) K. C. Nicolaou, T. Montagnon, P. S. Baran and Y. L. Zhong, *J. Am. Chem. Soc.*, 2002, **124**, 2245.
8. (a) T. N. Diao and S. S. Stahl, *J. Am. Chem. Soc.*, 2011, **133**, 14566; (b) Y. Izawa, D. Pun and S. S. Stahl, *Science*, 2011, **333**, 209.
9. D. Nagarathnam and M. Cushman, *J. Org. Chem.*, 1991, **56**, 4884.
10. (a) T. Liu and Y.Z. Hu, *Synthetic. Commun.*, 2004, **34**, 3209; (b) A. Ahond, J. Guilhem, J. Hamon, J. Hurtado, C. Poupat, J. Pusset, M. Pusset, T. Sevenet and P. Potier, *J. Nat. Prod.*, 1990, **53**, 875.
11. (a) J. P. Genet~~, J. P.,~~ Blart, M.E.~~,~~ Salvignac, ~~M.~~ *Synlett*, **1992**, 715; (b) N. Garg,~~ N.,~~ M. Larhed,~~ M.,~~ A. Hallberg,~~ A.~~ *J. Org. Chem.*, **1998**, *63*, 4158.
12. M. Min, H. Choe and S. Hong, *Asian J. Org. Chem.*, 2012, **1**, 47.
13. G. A. Kraus and V. Gupta, *Org. Lett.*, 2010, **12**, 527.
14. B. M. O'Keefe, N. Simmons and S. F. Martin, *Tetrahedron*, 2011, **67**, 4344.