

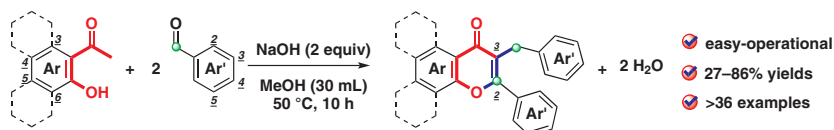
One-Pot Access to 2-Aryl-3-(arylmethyl)chromones




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-  easy-operational
-  27–86% yields
-  >36 examples

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Ar = Ph, 4-FC₆H₃, 4-ClC₆H₃, 4-BrC₆H₃, 1-naphthyl, 5-MeOC₆H₃, 4-MeOC₆H₃, 3-MeOC₆H₃, 5-BuOC₆H₃, 4-BuOC₆H₃, 3-BuOC₆H₃, 5-BnOC₆H₃, 4-BnOC₆H₃, 3-BnOC₆H₃, 4,6-Cl₂C₆H₂, 4,6-F₂C₆H₂, 4-MeC₆H₃, 2-naphthyl, 4-PhC₆H₃, 4-(4-FC₆H₄)C₆H₃, 4-(4-MeOC₆H₄)C₆H₃, 4-(2-naphthyl)C₆H₃, 4-(4-PhC₆H₄)C₆H₃
Ar' = pyridyl, phenyl, naphthyl, furyl, thienyl, benzofuryl, benzothienyl, quinolinyl

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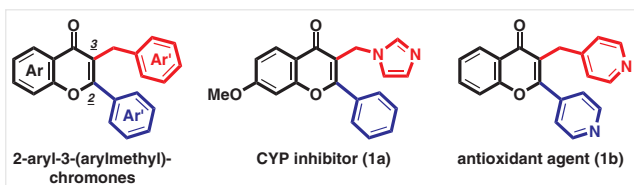
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Abstract Sodium hydroxide controlled intermolecular double aldol condensation of *o*-hydroxyacetophenones with 2 equivalents of arylaldehydes provides 2-aryl-3-(arylmethyl)chromones (a chimera of flavone and homoisoflavanone) in MeOH at 50 °C under mild conditions. The uses of various bases and solvents are investigated for one-pot facile and efficient transformation. A plausible mechanism is proposed.

Key words aldol condensation, *o*-hydroxyacetophenones, arylaldehydes, chromones, homoisoflavanone, benzopyran-4-one

The structure of a 2-aryl-3-(arylmethyl)chromone, having α -arylmethyl and β -aryl-conjugated groups, is a chimera of flavone and homoisoflavanone. On the basis of the same benzopyran-4-one skeleton (black), both flavone (blue, 2-aryl) and homoisoflavanone (red, 3-arylmethyl) possess an aryl motif and are the key members of benzofused oxacycles (Scheme 1). They are widely present in natural products and serve as multifunctionalized blocks in synthetic fields.¹ They exhibit diversified bioactive properties, such as antioxidant, anticancer, and antimicrobial activities.^{2,3}

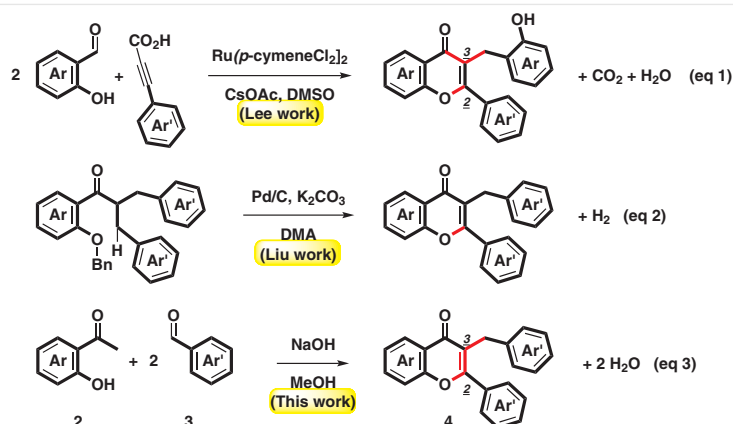


Scheme 1 Structures of 2-aryl-3-(arylmethyl)chromones

Therefore, a number of attempts to synthesize the skeletons of flavone and homoisoflavanone have been reported via various prepared protocols.^{4,5} Comparing two common

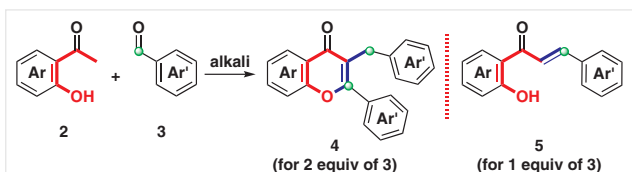
core skeletons, however, there are fewer studies on the related synthetic works and pharmaceutical properties of 2-aryl-3-(arylmethyl)chromones. So far, there are three main groups that have demonstrated the unique biological activities of 2-aryl-3-(arylmethyl)chromones. The Bisi group^{6a-c} reported that 2-phenyl-3-(imidazolylmethyl)chromones, e.g. **1a**, are suitable to serve as flavonoid-based cytochrome P450 (CYP) inhibitors. Lee and co-workers described that 2-pyridyl-3-(pyridylmethyl)chromone **1b** is an antioxidant agent.^{7a}

On the other hand, two attractive examples of the synthesis of 2-aryl-3-(arylmethyl)chromones with the structural hybrid of flavone and homoisoflavanone were described as follows (Scheme 2). They included: (1) Lee and co-workers investigated the ruthenium-catalyzed one-pot C–H activation of salicylaldehydes and decarboxylative coupling of alkynoic acids (eq 1),^{7a} and (2) Liu and co-workers explored the palladium-catalyzed dehydrogenation of *o*-acylphenols (eq 2).^{7b} They both showed novel transition-metal-promoted routes in the formation of 2-aryl-3-(arylmethyl)chromones. In spite of the advancements however, some problems exist, such as complicated catalytic conditions, lack of broad substrate generality, and prefunctionalized fragments. However, an operationally easy, inexpensive, open-vessel, and high-yield route for the preparation of 2-aryl-3-(arylmethyl)chromones with potential bioactive properties had not been reported until recently. As a result of the recent findings, further investigation of efficient synthetic methods for introducing both 2-aryl and 3-arylmethyl groups into the core scaffold of benzopyran-4-one is still highly desired. Herein, we present a one-pot synthesis of 2-aryl-3-(arylmethyl)chromones **4** via alkali-controlled intermolecular double aldol condensation of substituted *o*-hydroxyacetophenones **2** with arylaldehydes **3** (2 equiv) under warming alcoholic reaction conditions (eq 3).



Scheme 2 Synthetic routes toward 2-aryl-3-(arylmethyl)chromones

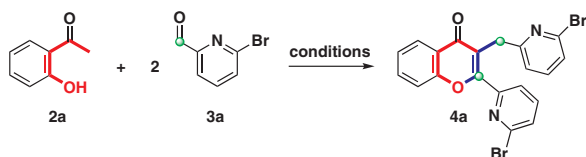
Continuing our synthetic research on the tandem aldol condensation/Michael addition of *o*-allylbenzaldehydes with different equivalents of substituted acetophenones (1, 2, and 3 equiv) for the preparation of diversified benzannulated molecules,⁸ a convenient route for synthesizing 2-aryl-3-(arylmethyl)chromones **4** was explored next. Using equal equivalents of starting materials, aldol condensation of substituted *o*-hydroxyacetophenones **2** (1 equiv) with arylaldehydes **3** (1 equiv) provided *o*-hydroxychalcones **5** under alkali-mediated traditional conditions.⁹ In particular, when the number of equivalents of arylaldehydes **3** was changed from 1 to 2 equiv, 2-aryl-3-(arylmethyl)chromones **4** displaced the expected *o*-hydroxychalcones **5** as the domain products in good yields (Scheme 3). In fact, to the best of our knowledge, so far no examples of the double aldol condensation of acetophenones **2** with arylaldehydes **3** have been reported. On the basis of these observations, initially, we utilized 6-bromopicolinaldehyde (**3a**) as the starting substrate to screen the reaction conditions since the bromo group could introduce a variety of functionalized groups by transition-metal cross-coupling, and the pyridyl ring could perform as a specific pharmacophore.¹⁰



Scheme 3 Alkali-mediated condensation of **2** and **3**

The study commenced with the treatment of model substrates **2a** (Ar = Ph, 1.0 mmol) and 6-bromopicolinaldehyde (**3a**, 2 equiv) in the presence of NaOH (2 equiv) in MeOH (30 mL) at 25 °C for 10 h (Table 1, entry 1). Under these reaction conditions, only trace amounts (8%) of **4a** were observed. Then, by controlling the temperature at 25

°C and increasing the time to 20, 30, and 40 h, **4a** was still isolated in low yields (14%, 16%, 15%, entries 2–4). Next, elevating the temperature to 50 °C and controlling the time at 10 h, the yield of **4a** was increased to 86% (entry 5). After increasing the time from 10 to 20 h, the yield (80%) of **4a** decreased slightly (entry 6). From the results, we found that temperature is a more important factor than time when affecting the formation of **4a**. To obtain better yields, we wanted to increase the temperature to reflux (65 °C), but this reflux condition provided a 71% yield of **4a** (entry 7). Furthermore, adjusting the reaction concentrations (0.033 → 0.10, 0.02 M) was examined. We found that concentrated solution (0.1 M) provided **4a** in a 25% yield along with major complex unknown products (entry 8). On the other hand, the diluted solution (0.02 M) could maintain the yield at 79% (entry 9). From the phenomenon, we understood that the factor of reaction concentration also affected the yield. Three alkalis with different basicity levels were examined next. Entries 10 and 11 show that no better yields were detected using LiOH and KOH (65% and 78%), respectively. Using K₂CO₃, the desired **4a** could not be generated (entry 12). By controlling the combination of 50 °C and 10 h, the solvent was adjusted from MeOH to EtOH, however only a 58% yield of **4a** was formed (entry 13). After elevating the temperature from 50 °C to 70 °C, the yield was still maintained at 68% (entry 14). Entries 15 and 16 show that *i*PrOH and *t*BuOH did not give better yields (37% and 12%) than MeOH (86%). By using H₂O as the solvent, no reaction was observed due to the poor solubility (entry 17). In entries 18 and 19, attempts to increase the number of equivalents (2 → 3 or 4) failed to afford higher yields (82% or 75%). Then, 1 equivalent of NaOH was tested, and only a 45% yield of **4a** was detected (entry 20). From our observations, we concluded that NaOH was the optimal alkali to yield **4a** under warming methanolic reaction conditions via one-pot facile intermolecular double condensation of **2a** and **3a**.

Table 1 Reaction Conditions^a

Entry	Alkali	Solvent (mL)	Temp (°C)	Time (h)	Yield ^b (%)
1	NaOH	MeOH (30)	25	10	8
2	NaOH	MeOH (30)	25	20	14
3	NaOH	MeOH (30)	25	30	16
4	NaOH	MeOH (30)	25	40	15
5	NaOH	MeOH (30)	50	10	86
6	NaOH	MeOH (30)	50	20	80
7	NaOH	MeOH (30)	reflux (65)	10	71
8	NaOH	MeOH (10)	50	10	25 ^c
9	NaOH	MeOH (50)	50	10	79
10	LiOH	MeOH (30)	50	10	65
11	KOH	MeOH (30)	50	10	78
12	K ₂ CO ₃	MeOH (30)	50	10	– ^d
13	NaOH	EtOH (30)	50	10	71
14	NaOH	EtOH (30)	70	10	68
15	NaOH	<i>i</i> PrOH (30)	50	10	37
16	NaOH	<i>t</i> BuOH (30)	50	10	12
17	NaOH	H ₂ O (30)	50	10	– ^d
18	NaOH ^e	MeOH (30)	50	10	82
19	NaOH ^f	MeOH (30)	50	10	75
20	NaOH ^g	MeOH (30)	50	10	45

^a Reaction conditions: **2a** (1.0 mmol), **3a** (2 equiv), alkali (2 equiv).

^b Isolated yields of **4a**.

^c Unknown mixture was isolated.

^d No product detected.

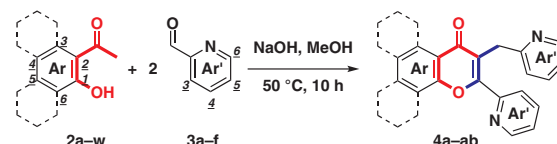
^e 3 equiv.

^f 4 equiv.

^g 1 equiv.

On the basis of our experimental results, a plausible mechanism for the formation of **4a** is illustrated in Scheme 4. Initially, NaOH (2 equiv) mediated deprotonation of **2a** provided a dianion intermediate. Following, in situ formed α -carbanion which attacked the carbonyl group of **3a** to lead to **A**. Then, an intramolecular proton exchange of **A** with two oxyanions yielded **B**. By the involvement of another **3a**, **B** was converted into **C** via a second intermolecular aldol reaction. Subsequently, **D** having the delocalized α -carbanion, was generated again by the repeated intramolecular proton exchange of **C**. After releasing the hydroxide ion on **D**, **E** with a conjugated enone moiety was formed. Furthermore, the oxyanion promoted the oxy-Michael reaction to the enone moiety followed by elimination of another hydroxide ion, and afforded (*E*)- or (*Z*)-homoisoflavone skeleton **F** via an intramolecular ring-closure process. Finally,

1,3-hydride migration on **F** from trisubstituted *exo*-olefin to tetrasubstituted *endo*-olefin furnished the construction of **4a**. On the other pathway, removal of the hydroxyl group of **B** provided **G** with a chalcone group. By intramolecular oxa-Michael annulation of **G** followed by intermolecular aldol

Table 2 Synthesis of **4a–4ab**^a

Entry	2 ^b Ar	3 ^c Ar'	Yield (%) ^d
1	2a , Ph	3a , 6-Br-2-pyridyl	4a , 86
2	2b , 4-FC ₆ H ₃	3a , 6-Br-2-pyridyl	4b , 86
3	2c , 4-ClC ₆ H ₃	3a , 6-Br-2-pyridyl	4c , 83
4	2d , 4-BrC ₆ H ₃	3a , 6-Br-2-pyridyl	4d , 80
5	2e , 1-naphthyl ^e	3a , 6-Br-2-pyridyl	4e , 76
6	2f , 5-MeOC ₆ H ₃	3a , 6-Br-2-pyridyl	4f , 72
7	2g , 4-MeOC ₆ H ₃	3a , 6-Br-2-pyridyl	4g , 80
8	2h , 3-MeOC ₆ H ₃	3a , 6-Br-2-pyridyl	4h , 70
9	2i , 5-BuOC ₆ H ₃	3a , 6-Br-2-pyridyl	4i , 83
10	2j , 4-BuOC ₆ H ₃	3a , 6-Br-2-pyridyl	4j , 80
11	2k , 3-BuOC ₆ H ₃	3a , 6-Br-2-pyridyl	4k , 64
12	2l , 5-BnOC ₆ H ₃	3a , 6-Br-2-pyridyl	4l , 80
13	2m , 4-BnOC ₆ H ₃	3a , 6-Br-2-pyridyl	4m , 73
14	2n , 3-BnOC ₆ H ₃	3a , 6-Br-2-pyridyl	4n , 70
15	2o , 4,6-Cl ₂ C ₆ H ₂	3a , 6-Br-2-pyridyl	4o , 78
16	2p , 4,6-F ₂ C ₆ H ₂	3a , 6-Br-2-pyridyl	4p , 80
17	2q , 4-MeC ₆ H ₃	3a , 6-Br-2-pyridyl	4q , 83
18	2r , 2-naphthyl ^f	3a , 6-Br-2-pyridyl	4r , 67
19	2s , 4-PhC ₆ H ₃	3a , 6-Br-2-pyridyl	4s , 80
20	2t , 4-(4-FC ₆ H ₄)C ₆ H ₃	3a , 6-Br-2-pyridyl	4t , 78
21	2u , 4-(4-MeOC ₆ H ₄)C ₆ H ₃	3a , 6-Br-2-pyridyl	4u , 78
22	2v , 4-(2-naphthyl)C ₆ H ₃	3a , 6-Br-2-pyridyl	4v , 76
23	2w , 4-(4-PhC ₆ H ₄)C ₆ H ₃	3a , 6-Br-2-pyridyl	4w , 74
24	2a , Ph	3b , 2-pyridyl	4x , 70
25	2a , Ph	3c , 5-F-2-pyridyl	4y , 74
26	2a , Ph	3d , 6-Cl-2-pyridyl	4z , 74
27	2a , Ph	3e , 6-Me-2-pyridyl	4aa , 80
28	2a , Ph	3f , 6-MeO-2-pyridyl	4ab , 78

^a Reaction conditions: **2a–2w** (1.0 mmol) **3a–3f** (2 equiv), NaOH (80 mg, 2 equiv), MeOH (30 mL), 50 °C, 10 h.

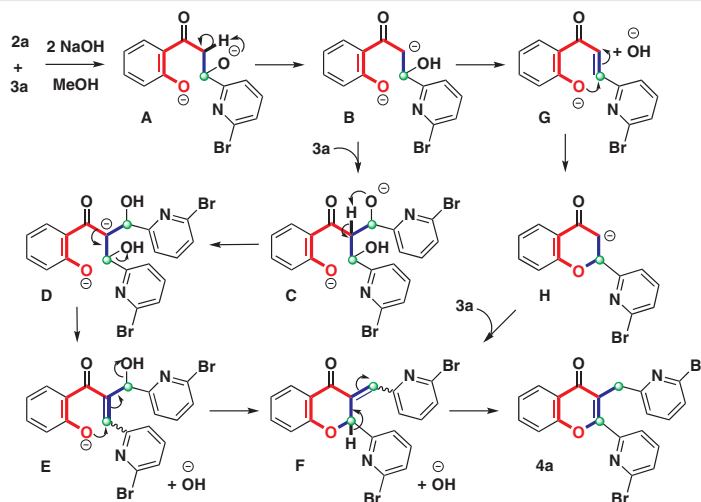
^b Ar is the substituted arene ring in 2-formylarene-1-ol (numbering shown).

^c Ar' is the substituted pyridine ring in 2-formylpyridine (numbering shown).

^d Isolated yields.

^e Substrate was 1-hydroxynaphthalene-2-carbaldehyde.

^f Substrate was 2-hydroxynaphthalene-1-carbaldehyde.

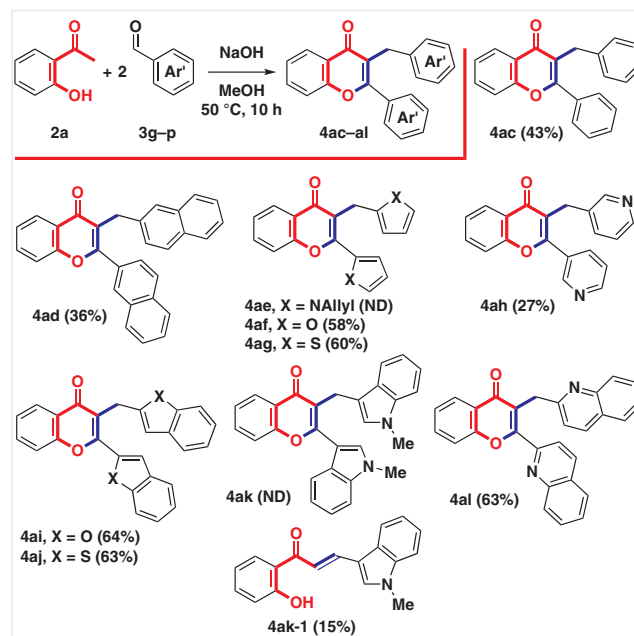


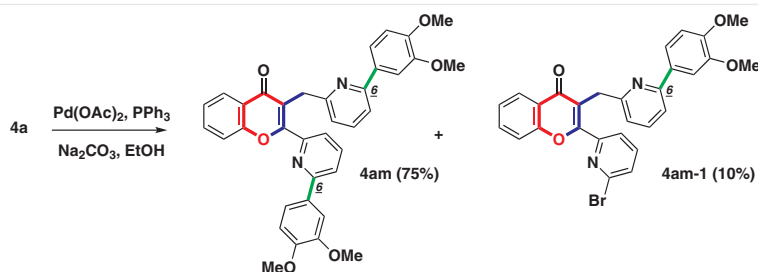
Scheme 4 Plausible mechanism

condensation of the resulting **H** with **3a**, **F** was achieved. Based on the above-mentioned procedure, **4a** was constructed. From the possible mechanism, we found that NaOH efficiently organized the continuous sequence of intermolecular aldol reactions and intramolecular ring-closures.

To study the scope and limitations of this approach, substituted *o*-hydroxyacetophenones **2a–2w** and 2-formylpyridines **3a–3f** were reacted with NaOH (2 equiv) to afford diversified 2-aryl-3-(arylmethyl)chromones **4a–4ab** under warming methanol (50 °C/10 h) conditions, as shown in Table 2. With optimal conditions established (Table 1, entry 5) and a plausible mechanism proposed (Scheme 4), we found that this route allowed direct double aldol condensation in moderate to good yields (64–86%). Among entries 1–28, efficient formation of **4a–4ab** showed that the two aryl substituents (**2**, Ar and **3**, Ar') did not affect the yields. The structures of **4a–4d**, **4g**, **4t**, and **4z** were determined by single-crystal X-ray crystallography.¹¹ For the electronic nature of aryl substituents (Ar) of **2**, not only haloaryl (bromo, chloro, dichloro) groups but also electron-neutral (methyl), electron-withdrawing (fluoro, difluoro) and electron-donating (methoxy, butoxy, benzyloxy) groups were appropriate. For the pyridyl substituents (Ar') of **3**, 6-bromo, 5-fluoro, 6-methyl, 6-chloro, and 6-methoxy groups were well-tolerated. Based on the results, after replacing the pyridyl group of **3a–3f** with benzaldehyde (**3g**) and 2-naphthaldehyde (**3h**), synthesis of **4ac–4ad** was examined next (Scheme 5). However, the desired **4ac** and **4ad** were formed in 43% and 36% yields, respectively. Next, when the monocyclic 2-formyl-heteroarenes were changed from 2-formylpyridines **3a–3f** to 1-allyl-2-formyl-1*H*-pyrrole (**3i**), 2-formylfuran (**3j**), 2-formylthiophene (**3k**), and 3-

formylpyridine (**3l**), **4af** and **4ag** were produced with moderate results (58% and 60% yields); surprisingly, the desired **4ae** could be not isolated. The structure of **4ag** was determined by single-crystal X-ray crystallography.¹¹ In particular, **4ah** was provided in only a 27% yield. Then, changing to bicyclic 2-formylbenzofuran (**3m**), 2-formylbenzothiophene (**3n**), and 3-formyl-1-methyl-1*H*-indole (**3o**), **4ai** and **4aj** were obtained in 64%, and 63% yields, respectively. However, the desired **4ak** could be not isolated, and only 15% yield of chalcone **4ak-1** was obtained. Furthermore, 2-formylquinoline (**3p**) produced 63% yield of **4al**.

Scheme 5 Synthesis of **4ac–4al** and **4ak-1**; ND = not detected

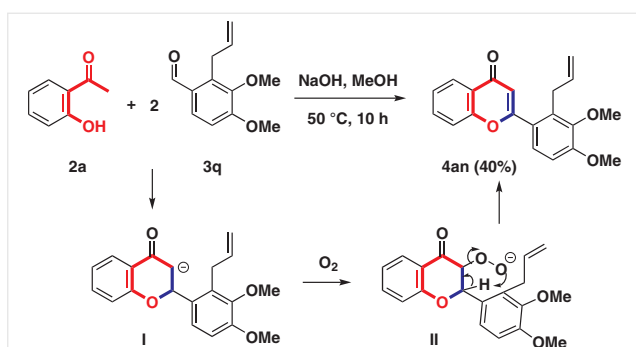


Scheme 6 Suzuki-Miyaura coupling of **4a**

From the results, we understand that hetero-monocyclic 2-azaarenes could produce better yields than benzaldehyde and naphthaldehyde, especially with substituted 2-formylpyridines. The putative explanations for the differences are that the aggregated intermediate adopts a bidentate coordination of the sodium ion by the nitrogen lone pair of 2-formylpyridine and the alkoxy anion such that this resulting complexation would necessitate the intermediate to coordinate with the second equivalent of 2-formylpyridine via the aldol reaction process.¹²

To elongate the side arm on the pyridyl ring of **4a**, Suzuki-Miyaura coupling of **4a** with 3,4-dimethoxyphenylboronic acid provided **4am** in a 75% yield along with a 10% yield of **4am-1**, as shown in Scheme 6. With the results, we envisioned that different aryl substituents could be installed into the 6-position of pyridine ring on **4a** to afford diversified aryl-pyridyl-conjugated homoisoflavanones.

On the other hand, a macrocyclic isoflavanone was examined (Scheme 7). Under the above conditions, a one-pot NaOH-controlled reaction of **2a** and **3q** with the *o*-allyl side chain provided flavone **4an** in a 40% yield. In particular, no desired homoisoflavanone was detected. The possible reason should be that the *o*-allyl group on **3q** exhibited a bulkier steric hindrance such that the second aldol condensation could not be generated. For the formation of **4an**, we thought that in situ generated **I** could trap molecular oxygen (from air) to lead **II**. Following, by the peroxyanion-mediated intramolecular deprotonation of **II**, **4an** was accomplished.



Scheme 7 Synthesis of **4an**

In summary, we have developed an NaOH-controlled synthesis of 2-aryl-3-(arylmethyl)chromones via intermolecular double aldol condensation of *o*-hydroxyacetophenones with 2 equivalents of an arylaldehyde under warming MeOH reaction conditions in moderate to good yields. The process provides a cascade pathway of C–C and then, C–O bond formations. The uses of various bases and solvents are investigated for one-pot facile and efficient transformation. Related plausible mechanisms have been proposed. The structures of the key products were confirmed by X-ray crystallography. Further investigations regarding the synthetic applications of *o*-hydroxyacetophenones will be conducted and published in due course.

All reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry air with magnetic stirring. The heating mantle is used to provide a stable heat source. Products in organic solvents were dried with anhydrous MgSO_4 before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. ^1H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 400 and at 100 MHz, respectively. HRMS were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf-Nonius FR-590 diffractometer (CAD4, Kappa CCD).

For the starting compounds **2a–2w** and **3a–3r**, these reagents were obtained from commercial sources and used without further purification.

2-Aryl-3-(arylmethyl)chromen-4-ones **4a–4ad**, **4af–4aj**, **4ak-1**, and **4al**; General Procedure

NaOH (80 mg, 2.0 mmol) was added to a solution of **2a–2w** (1.0 mmol) in MeOH (30 mL) at 25 °C. The mixture was stirred at 25 °C for 10 min. Arylaldehyde **3a–3p** (2.0 mmol) was added to the mixture at 25 °C and it was stirred at 50 °C for 10 h. The mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (2×10 mL), dried (MgSO_4), filtered and evaporated to afford crude product under reduced pressure. The remaining mixture was separated by column chromatography (silica gel, hexanes/EtOAc 20:1–3:1) affording the title compounds.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-chromen-4-one (4a)

Colorless solid; yield: 404 mg (86%); mp 179–180 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.21 (dd, *J* = 8.0, 1.6 Hz, 1 H), 8.06 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.69 (dd, *J* = 8.8, 2.0 Hz, 1 H), 7.56 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.51 (dd, *J* = 8.8, 0.8 Hz, 1 H), 7.42 (dt, *J* = 8.0, 1.2 Hz, 1 H), 7.37 (d, *J* = 7.6 Hz, 1 H), 7.23 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.21 (dd, *J* = 8.0, 0.4 Hz, 1 H), 4.32 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.2, 161.2, 158.4, 155.8, 152.1, 141.4, 141.0, 138.9, 138.8, 134.0, 129.3, 126.0, 125.2, 125.2, 123.2, 122.8, 121.8, 120.4, 118.1, 32.9.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₁₃Br₂N₂O₂: 470.9344; found: 470.9338.

Single-crystal X-ray diagram: crystal of compound **4a** was grown by slow diffusion of EtOAc into a solution of compound **4a** in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group *Pbca*, *a* = 11.6446(3) Å, *b* = 14.7976(4) Å, *c* = 19.6780(6) Å, *V* = 3390.76(16) Å³, *Z* = 8, *d*_{calcd} = 1.850 g/cm³, *F*(000) = 1856, 2θ range 2.070–26.456°, *R* indices (all data) *R*1 = 0.0233, *wR*2 = 0.0499.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-fluorochromen-4-one (4b)

Colorless solid; yield: 420 mg (86%); mp 190–191 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.05 (d, *J* = 7.2 Hz, 1 H), 7.81 (dd, *J* = 8.0, 3.2 Hz, 1 H), 7.71 (t, *J* = 8.0 Hz, 1 H), 7.55 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.51 (dd, *J* = 9.2, 4.0 Hz, 1 H), 7.43–7.36 (m, 2 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 4.31 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 177.5 (d, *J* = 2.3 Hz), 160.9, 159.5 (d, *J* = 245.6 Hz), 158.2, 152.0 (d, *J* = 1.5 Hz), 151.8, 141.4, 141.0, 139.0, 138.5, 129.4, 125.3, 123.8 (d, *J* = 8.6 Hz), 123.3, 122.2 (d, *J* = 25.7 Hz), 121.9, 120.3 (d, *J* = 7.6 Hz), 119.8, 110.7 (d, *J* = 23.5 Hz), 32.7.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₁₂Br₂FN₂O₂: 488.9250; found: 488.9244.

Single-crystal X-ray diagram: crystal of compound **4b** was grown by slow diffusion of EtOAc into a solution of compound **4b** in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group *P2₁/c*, *a* = 14.5142(8) Å, *b* = 19.8390(9) Å, *c* = 12.2505(6) Å, *V* = 3521.0(3) Å³, *Z* = 4, *d*_{calcd} = 1.849 g/cm³, *F*(000) = 1920, 2θ range 1.406–26.451°, *R* indices (all data) *R*1 = 0.0658, *wR*2 = 0.01105.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-chlorochromen-4-one (4c)

Colorless solid; yield: 418 mg (83%); mp 188–189 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.15 (d, *J* = 2.8 Hz, 1 H), 8.06 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.62 (dd, *J* = 8.8, 2.8 Hz, 1 H), 7.56 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.47 (d, *J* = 8.8 Hz, 1 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 7.22 (d, *J* = 7.6 Hz, 1 H), 4.31 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 177.1, 160.8, 158.6, 154.1, 151.8, 141.4, 141.1, 139.0, 138.5, 134.2, 131.1, 129.5, 125.4, 125.3, 123.7, 123.3, 122.0, 120.6, 119.9, 32.8.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₁₂Br₂ClN₂O₂: 504.8954; found: 504.8950.

Single-crystal X-ray diagram: crystal of compound **4c** was grown by slow diffusion of EtOAc into a solution of compound **4c** in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group *P* $\bar{1}$, *a* = 7.5481(3) Å, *b* = 10.3357(4) Å, *c* =

13.1031(5) Å, *V* = 896.64(6) Å³, *Z* = 2, *d*_{calcd} = 1.876 g/cm³, *F*(000) = 496, 2θ range 1.682–26.413°, *R* indices (all data) *R*1 = 0.0208, *wR*2 = 0.0475.

6-Bromo-2-(6-bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)chromen-4-one (4d)

Colorless solid; yield: 438 mg (80%); mp 175–176 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.33 (d, *J* = 2.4 Hz, 1 H), 8.08 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.77 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.73 (t, *J* = 8.0 Hz, 1 H), 7.58 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.42 (d, *J* = 8.8 Hz, 1 H), 7.40 (t, *J* = 8.0 Hz, 1 H), 7.24 (d, *J* = 7.6 Hz, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 4.30 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 176.9, 160.8, 158.6, 154.6, 151.8, 141.5, 141.1, 139.0, 138.5, 136.9, 129.5, 128.6, 125.4, 124.1, 123.4, 122.0, 120.7, 120.1, 118.6, 32.8.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₁₂Br₃N₂O₂: 548.8449; found: 548.8446.

Single-crystal X-ray diagram: crystal of compound **4d** was grown by slow diffusion of EtOAc into a solution of compound **4d** in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group *P* $\bar{1}$, *a* = 7.5768(5) Å, *b* = 10.4119(7) Å, *c* = 13.2517(9) Å, *V* = 915.93(11) Å³, *Z* = 2, *d*_{calcd} = 1.998 g/cm³, *F*(000) = 532, 2θ range 1.666–26.479°, *R* indices (all data) *R*1 = 0.0292, *wR*2 = 0.0593.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-benzo[h]chromen-4-one (4e)

Colorless solid; yield: 395 mg (76%); mp 223–224 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.50 (d, *J* = 8.0 Hz, 1 H), 8.19 (d, *J* = 8.0 Hz, 1 H), 8.15 (d, *J* = 8.0 Hz, 1 H), 7.93 (d, *J* = 7.6 Hz, 1 H), 7.81–7.65 (m, 4 H), 7.60 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.27 (d, *J* = 7.6 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 4.44 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 177.9, 161.2, 157.7, 152.2, 141.5, 141.1, 139.1, 138.5, 138.7, 136.0, 129.4, 129.3, 128.2, 127.2, 125.5, 125.2, 123.9, 123.2, 122.4, 121.90, 121.88, 121.0, 119.2, 32.9.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₄H₁₅Br₂N₂O₂: 520.9500; found: 520.9496.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-7-methoxychromen-4-one (4f)

Colorless solid; yield: 360 mg (72%); mp 198–199 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.12 (d, *J* = 8.8 Hz, 1 H), 8.07 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.56 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.25 (d, *J* = 8.8 Hz, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 6.98 (dd, *J* = 8.8, 2.4 Hz, 1 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 4.28 (s, 2 H), 3.91 (s, 3 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 177.4, 164.4, 161.3, 158.1, 147.7, 152.2, 141.5, 141.0, 138.9, 138.5, 129.3, 127.4, 125.2, 123.3, 121.9, 120.3, 116.9, 114.9, 100.1, 55.9, 32.9.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₁H₁₅Br₂N₂O₃: 500.9450; found: 500.9444.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-methoxychromen-4-one (4g)

Colorless solid; yield: 400 mg (80%); mp 177–178 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.01 (d, *J* = 7.6 Hz, 1 H), 7.68 (t, *J* = 7.6 Hz, 1 H), 7.52–7.50 (m, 2 H), 7.41 (d, *J* = 9.2 Hz, 1 H), 7.36 (t, *J* = 7.6 Hz, 1 H), 7.25 (dd, *J* = 8.8, 2.8 Hz, 1 H), 7.20 (d, *J* = 7.6 Hz, 2 H), 4.32 (s, 2 H), 3.84 (s, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.9, 161.3, 158.0, 156.9, 152.0, 150.6, 141.2, 140.9, 138.9, 138.4, 129.2, 125.1, 124.1, 123.2, 123.1, 121.7, 119.50, 119.45, 104.7, 55.8, 32.9.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}_3$: 500.9450; found: 500.9444.

Single-crystal X-ray diagram: crystal of compound **4g** was grown by slow diffusion of EtOAc into a solution of compound **4g** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P21/c$, $a = 4.4683(4)$ Å, $b = 22.3901(19)$ Å, $c = 18.7910(16)$ Å, $V = 1879.6(3)$ Å 3 , $Z = 4$, $d_{\text{calcd}} = 1.774$ g/cm 3 , $F(000) = 992$, 2θ range 1.415–26.411°, R indices (all data) $R1 = 0.0443$, $wR2 = 0.0972$.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-5-methoxychromen-4-one (4h)

Colorless solid; yield: 350 mg (70%); mp 187–188 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.08 (d, $J = 7.6$ Hz, 1 H), 7.71 (t, $J = 7.6$ Hz, 1 H), 7.58 (d, $J = 8.4$ Hz, 1 H), 7.56 (d, $J = 8.4$ Hz, 1 H), 7.37 (t, $J = 7.6$ Hz, 1 H), 7.26 (d, $J = 7.6$ Hz, 1 H), 7.21 (d, $J = 8.0$ Hz, 1 H), 7.07 (dd, $J = 8.4, 0.8$ Hz, 1 H), 6.81 (d, $J = 8.0$ Hz, 1 H), 4.23 (s, 2 H), 3.97 (s, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.7, 161.4, 159.8, 157.9, 156.8, 152.0, 141.4, 140.9, 138.9, 138.5, 134.0, 129.2, 125.1, 123.3, 122.1, 121.5, 113.6, 110.1, 106.2, 56.4, 32.9.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}_3$: 500.9450; found: 500.9445.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-7-butoxychromen-4-one (4i)

Colorless solid; yield: 450 mg (83%); mp 140–141 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.10 (d, $J = 9.2$ Hz, 1 H), 8.06 (dd, $J = 8.0, 0.8$ Hz, 1 H), 7.71 (t, $J = 8.0$ Hz, 1 H), 7.56 (dd, $J = 8.0, 0.8$ Hz, 1 H), 7.39 (t, $J = 7.6$ Hz, 1 H), 7.24 (t, $J = 7.6$ Hz, 1 H), 7.23 (d, $J = 7.6$ Hz, 1 H), 6.97 (dd, $J = 8.8, 2.4$ Hz, 1 H), 6.89 (d, $J = 2.4$ Hz, 1 H), 4.28 (s, 2 H), 4.05 (t, $J = 6.4$ Hz, 2 H), 1.86–1.79 (m, 2 H), 1.56–1.49 (m, 2 H), 0.99 (t, $J = 7.6$ Hz, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.4, 163.9, 161.4, 158.1, 157.7, 152.2, 141.4, 141.0, 138.9, 138.5, 129.2, 127.3, 125.2, 123.3, 121.9, 120.3, 116.7, 115.3, 100.5, 68.5, 32.9, 31.0, 19.2, 13.8.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{21}\text{Br}_2\text{N}_2\text{O}_3$: 542.9919; found: 542.9916.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-butoxychromen-4-one (4j)

Colorless solid; yield: 434 mg (80%); mp 124–125 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.05 (d, $J = 8.4$ Hz, 1 H), 7.72 (t, $J = 8.0$ Hz, 1 H), 7.56 (d, $J = 8.8$ Hz, 1 H), 7.55 (s, 1 H), 7.45 (d, $J = 9.2$ Hz, 1 H), 7.38 (t, $J = 7.6$ Hz, 1 H), 7.29 (dd, $J = 9.2, 3.2$ Hz, 1 H), 7.24 (d, $J = 8.0$ Hz, 2 H), 4.32 (s, 2 H), 4.05 (t, $J = 6.4$ Hz, 2 H), 1.83–1.76 (m, 2 H), 1.55–1.45 (m, 2 H), 0.98 (t, $J = 7.6$ Hz, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.1, 161.4, 158.2, 156.6, 152.3, 150.6, 141.4, 141.0, 139.9, 138.5, 129.3, 125.2, 124.6, 123.4, 123.3, 121.8, 119.6, 119.5, 106.5, 68.4, 33.0, 31.1, 19.2, 13.8.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{21}\text{Br}_2\text{N}_2\text{O}_3$: 542.9919; found: 542.9916.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-5-butoxychromen-4-one (4k)

Colorless solid; yield: 347 mg (64%); mp 170–171 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.01 (d, $J = 8.4$ Hz, 1 H), 7.69 (t, $J = 7.6$ Hz, 1 H), 7.55 (d, $J = 8.4$ Hz, 1 H), 7.53 (d, $J = 8.4$ Hz, 1 H), 7.35 (d, $J = 7.6$ Hz, 1 H), 7.21 (d, $J = 7.6$ Hz, 1 H), 7.20 (d, $J = 7.6$ Hz, 1 H), 7.04 (d, $J = 8.4$ Hz, 1 H), 6.80 (d, $J = 8.4$ Hz, 1 H), 4.29 (s, 2 H), 4.10 (t, $J = 6.4$ Hz, 2 H), 1.95–1.88 (m, 2 H), 1.60–1.50 (m, 2 H), 0.98 (t, $J = 7.6$ Hz, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.4, 161.6, 159.4, 157.8, 156.4, 152.1, 141.3, 140.9, 138.8, 138.4, 133.9, 129.1, 125.0, 123.0, 121.8, 121.3, 113.8, 109.7, 107.3, 69.3, 32.7, 31.0, 19.2, 13.8.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{21}\text{Br}_2\text{N}_2\text{O}_3$: 542.9919; found: 542.9915.

7-Benzyloxy-2-(6-bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)chromen-4-one (4l)

Colorless solid; yield: 461 mg (80%); mp 216–217 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.13 (d, $J = 9.2$ Hz, 1 H), 8.06 (d, $J = 7.6$ Hz, 1 H), 7.71 (t, $J = 8.0$ Hz, 1 H), 7.56 (dd, $J = 8.0, 0.8$ Hz, 1 H), 7.46–7.34 (m, 6 H), 7.24 (d, $J = 7.6$ Hz, 2 H), 7.06 (dd, $J = 8.8, 2.4$ Hz, 1 H), 6.98 (d, $J = 2.4$ Hz, 1 H), 5.17 (s, 2 H), 4.28 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.4, 163.4, 161.3, 158.2, 157.6, 152.1, 141.4, 141.0, 138.9, 138.5, 135.6, 129.3, 128.8 (2 ×), 128.4, 127.52, 127.47 (2 ×), 125.2, 123.3, 121.9, 120.4, 117.0, 115.4, 101.1, 70.5, 32.9.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_3$: 576.9763; found: 576.9757.

6-Benzyloxy-2-(6-bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)chromen-4-one (4m)

Colorless solid; yield: 420 mg (73%); mp 184–185 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.05 (dd, $J = 7.6, 0.4$ Hz, 1 H), 7.72 (t, $J = 7.6$ Hz, 1 H), 7.68 (d, $J = 2.8$ Hz, 1 H), 7.56 (dd, $J = 8.0, 0.8$ Hz, 1 H), 7.48–7.34 (m, 8 H), 7.24 (d, $J = 7.6$ Hz, 2 H), 5.14 (s, 2 H), 4.33 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.0, 161.3, 158.3, 156.1, 152.2, 150.8, 141.4, 141.0, 138.9, 138.5, 136.2, 129.3, 128.6 (2 ×), 128.2, 127.7 (2 ×), 125.2, 124.7, 123.4, 123.3, 121.8, 119.7, 119.6, 106.1, 70.6, 33.0.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_3$: 576.9763; found: 576.9757.

5-Benzyloxy-2-(6-bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)chromen-4-one (4n)

Colorless solid; yield: 403 mg (70%); mp 203–204 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.03 (dd, $J = 7.6, 0.4$ Hz, 1 H), 7.70 (t, $J = 8.0$ Hz, 1 H), 7.57–7.53 (m, 3 H), 7.51 (t, $J = 8.0$ Hz, 1 H), 7.40–7.36 (m, 3 H), 7.29 (t, $J = 7.2$ Hz, 1 H), 7.23 (dt, $J = 8.0, 0.4$ Hz, 1 H), 7.07 (dd, $J = 8.4, 0.4$ Hz, 2 H), 6.83 (d, $J = 8.0$ Hz, 1 H), 5.30 (s, 2 H), 4.32 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.4, 161.5, 158.6, 157.9, 156.5, 152.1, 141.4, 140.9, 138.9, 138.5, 136.4, 133.8, 129.2, 128.6 (2 ×), 127.7, 126.7 (2 ×), 125.1, 123.1, 121.9, 121.5, 114.2, 110.4, 108.4, 70.9, 32.8.

HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_3$: 576.9763; found: 576.9758.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6,8-dichlorochromen-4-one (4o)

Colorless solid; yield: 420 mg (78%); mp 216–217 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.13 (dd, J = 7.6, 0.8 Hz, 1 H), 8.11 (d, J = 2.4 Hz, 1 H), 7.76 (t, J = 8.0 Hz, 1 H), 7.75 (d, J = 8.8 Hz, 1 H), 7.57 (dd, J = 8.0, 0.8 Hz, 1 H), 7.38 (t, J = 8.0 Hz, 1 H), 7.22 (d, J = 8.0 Hz, 1 H), 7.20 (dd, J = 7.6, 0.8 Hz, 1 H), 4.51 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 176.7, 160.7, 157.8, 151.7, 150.1, 141.22, 141.16, 139.2, 138.4, 134.0, 130.9, 129.7, 125.3, 124.4, 124.3, 124.2, 123.1, 121.7, 121.1, 32.5.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{20}\text{H}_{11}\text{Br}_2\text{Cl}_2\text{N}_2\text{O}_2$: 538.8564; found: 538.8560.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6,8-difluorochromen-4-one (4p)

Colorless solid; yield: 405 mg (80%); mp 155–156 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.09 (dd, J = 7.6, 0.8 Hz, 1 H), 7.74 (t, J = 8.0 Hz, 1 H), 7.65 (dt, J = 8.0, 2.8 Hz, 1 H), 7.57 (dd, J = 8.0, 0.8 Hz, 1 H), 7.39 (t, J = 7.6 Hz, 1 H), 7.27 (dt, J = 8.0, 2.8 Hz, 1 H), 7.20 (d, J = 7.6 Hz, 2 H), 4.41 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 176.5 (t, J = 3.1 Hz), 160.6, 158.3 (dd, J = 9.8, 247.9 Hz), 158.0, 151.6, 151.4 (dd, J = 11.4, 256.2 Hz), 141.4 (d, J = 2.3 Hz), 141.3, 141.1, 139.1, 138.5, 129.7, 125.3, 124.8 (d, J = 8.3 Hz), 123.2, 121.8, 120.6, 109.3 (dd, J = 20.5, 28.8 Hz), 106.2 (dd, J = 4.6, 23.5 Hz), 32.5.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{20}\text{H}_{11}\text{Br}_2\text{F}_2\text{N}_2\text{O}_2$: 506.9155; found: 506.9151.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-methylchromen-4-one (4q)

Colorless solid; yield: 402 mg (83%); mp 163–164 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.02 (d, J = 7.6 Hz, 1 H), 7.97 (t, J = 0.4 Hz, 1 H), 7.70 (t, J = 7.6 Hz, 1 H), 7.53 (d, J = 8.0 Hz, 1 H), 7.49 (dd, J = 8.4, 2.0 Hz, 1 H), 7.39 (d, J = 8.4 Hz, 1 H), 7.35 (d, J = 7.6 Hz, 1 H), 7.22 (d, J = 8.0 Hz, 2 H), 4.32 (s, 2 H), 2.43 (s, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.2, 161.3, 158.2, 154.1, 152.1, 141.3, 141.0, 138.9, 138.4, 135.23, 135.20, 129.2, 125.2, 125.1, 123.2, 122.4, 121.7, 120.2, 117.8, 32.9, 20.9.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}_2$: 484.9500; found: 484.9493.

3-(6-Bromopyridin-2-yl)-2-(6-bromopyridin-2-ylmethyl)-benzo[*f*]chromen-1-one (4r)

Colorless solid; yield: 348 mg (67%); mp 177–178 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 10.03 (d, J = 8.0 Hz, 1 H), 8.14 (dd, J = 8.4, 0.8 Hz, 1 H), 8.12 (d, J = 7.6 Hz, 1 H), 7.92 (d, J = 8.0 Hz, 1 H), 7.75 (t, J = 8.0 Hz, 1 H), 7.74 (t, J = 8.0 Hz, 1 H), 7.63 (dt, J = 8.0, 1.2 Hz, 1 H), 7.59 (d, J = 8.8 Hz, 1 H), 7.58 (dd, J = 7.6, 0.8 Hz, 1 H), 7.41 (d, J = 7.6 Hz, 1 H), 7.29 (d, J = 8.0 Hz, 1 H), 7.25 (d, J = 7.6 Hz, 1 H), 4.42 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 179.5, 161.4, 157.1, 156.3, 152.0, 141.5, 141.1, 139.0, 138.6, 135.9, 130.6, 130.4, 129.4, 129.3, 128.3, 127.1, 126.7, 125.2, 123.3, 123.0, 121.8, 117.6, 116.2, 33.2.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{24}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}_2$: 520.9500; found: 520.9495.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-phenylchromen-4-one (4s)

Colorless solid; yield: 437 mg (80%); mp 174–175 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.43 (d, J = 2.4 Hz, 1 H), 8.09 (dd, J = 7.6, 0.8 Hz, 1 H), 7.94 (dd, J = 8.4, 2.4 Hz, 1 H), 7.73 (t, J = 7.6 Hz, 1 H), 7.67–7.64 (m, 2 H), 7.583 (t, J = 8.0 Hz, 1 H), 7.580 (t, J = 8.0 Hz, 1 H), 7.48–7.44 (m, 2 H), 7.42–7.36 (m, 2 H), 7.26 (d, J = 8.4 Hz, 1 H), 7.24 (dd, J = 8.0, 0.4 Hz, 1 H), 4.36 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.2, 161.2, 158.4, 155.3, 152.1, 141.4, 141.1, 139.2, 139.0, 138.5, 138.4, 132.9, 129.4, 129.0 (2 \times), 127.8, 127.1 (2 \times), 125.2, 123.8, 123.3, 122.9, 121.9, 120.5, 118.6, 32.9.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{26}\text{H}_{17}\text{Br}_2\text{N}_2\text{O}_2$: 546.9657; found: 546.9652.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-(4-fluorophenyl)chromen-4-one (4t)

Colorless solid; yield: 440 mg (78%); mp 191–192 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.37 (d, J = 2.4 Hz, 1 H), 8.09 (dd, J = 7.6, 0.8 Hz, 1 H), 7.88 (dd, J = 8.4, 2.4 Hz, 1 H), 7.73 (t, J = 7.6 Hz, 1 H), 7.62–7.56 (m, 4 H), 7.40 (t, J = 7.6 Hz, 1 H), 7.26 (d, J = 7.6 Hz, 1 H), 7.24 (d, J = 7.6 Hz, 1 H), 7.18–7.13 (m, 2 H), 4.35 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.2, 162.7 (d, J = 246.3 Hz), 161.1, 158.5, 155.2, 152.0, 141.4, 141.1, 139.0, 138.5, 137.4, 135.4 (d, J = 3.1 Hz), 132.7, 129.4, 128.8 (d, J = 8.4 Hz, 2 \times), 125.3, 123.7, 123.3, 122.9, 121.9, 120.5, 118.7, 115.9 (d, J = 21.2 Hz, 2 \times), 32.9.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{26}\text{H}_{16}\text{Br}_2\text{FN}_2\text{O}_2$: 564.9563; found: 564.9557.

Single-crystal X-ray diagram: crystal of compound **4t** was grown by slow diffusion of EtOAc into a solution of compound **4t** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group $P\bar{1}$, a = 7.4478(6) Å, b = 10.0187(8) Å, c = 15.9674(13) Å, V = 1079.68(15) Å 3 , Z = 2, d_{calcd} = 1.742 g/cm 3 , $F(000)$ = 560, 2θ range 1.315–26.402°, R indices (all data) R_1 = 0.0221, wR_2 = 0.0517.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-(4-methoxyphenyl)chromen-4-one (4u)

Colorless solid; yield: 449 mg (78%); mp 162–163 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.36 (d, J = 2.4 Hz, 1 H), 8.07 (d, J = 7.2 Hz, 1 H), 7.89 (dd, J = 8.4, 2.4 Hz, 1 H), 7.72 (t, J = 7.6 Hz, 1 H), 7.60–7.53 (m, 4 H), 7.39 (t, J = 7.6 Hz, 1 H), 7.24 (t, J = 7.6 Hz, 2 H), 6.98 (d, J = 8.8 Hz, 2 H), 4.36 (s, 2 H), 3.85 (s, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.3, 161.3, 159.5, 158.3, 154.8, 152.1, 141.3, 141.0, 138.9, 138.5, 138.0, 132.5, 131.7, 129.3, 128.2 (2 \times), 125.2, 123.2, 123.0, 122.9, 121.8, 120.4, 118.5, 114.4 (2 \times), 55.3, 32.9.

HRMS (ESI-TOF): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_3$: 576.9763; found: 576.9756.

2-(6-Bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)-6-naphthalen-2-ylchromen-4-one (4v)

Colorless solid; yield: 453 mg (76%); mp 182–183 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.56 (d, J = 2.0 Hz, 1 H), 8.11 (dd, J = 8.0, 1.6 Hz, 1 H), 8.08 (s, 1 H), 8.07 (d, J = 8.8, 2.4 Hz, 1 H), 7.96–7.76 (m, 4 H), 7.72 (t, J = 7.6 Hz, 1 H), 7.62 (d, J = 8.8 Hz, 1 H), 7.57 (dd, J = 8.0, 0.8 Hz, 1 H), 7.53–7.46 (m, 2 H), 7.41 (t, J = 7.6 Hz, 1 H), 7.28 (d, J = 7.6 Hz, 1 H), 7.23 (d, J = 8.8 Hz, 1 H), 4.38 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.3, 161.2, 158.4, 155.3, 152.1, 141.4, 141.1, 139.0, 138.5, 138.3, 136.5, 133.6, 133.0, 132.8, 129.4, 128.7, 128.3, 127.6, 126.5, 126.3, 126.1, 125.3, 125.1, 124.0, 123.3, 123.0, 121.9, 120.5, 118.7, 33.0.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₃₀H₁₉Br₂N₂O₂: 596.9813; found: 596.9816.

6-(Biphenyl-4-yl)-2-(6-bromopyridin-2-yl)-3-(6-bromopyridin-2-ylmethyl)chromen-4-one (4w)

Colorless solid; yield: 460 mg (74%); mp 212–213 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.47 (d, J = 2.4 Hz, 1 H), 8.08 (d, J = 7.6 Hz, 1 H), 7.98 (dd, J = 8.8, 2.4 Hz, 1 H), 7.74–7.55 (m, 9 H), 7.48–7.35 (m, 4 H), 7.26 (t, J = 7.6 Hz, 1 H), 7.25 (t, J = 8.0 Hz, 1 H), 4.38 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.2, 161.2, 158.3, 155.2, 152.0, 141.4, 141.1, 140.6, 140.3, 138.9, 138.5, 138.0, 137.8, 132.7, 129.3, 128.8 (2 ×), 127.6 (2 ×), 127.5, 127.4 (2 ×), 127.0 (2 ×), 125.2, 123.6, 123.3, 122.9, 121.9, 120.5, 118.7, 32.9.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₃₂H₂₁Br₂N₂O₂: 622.9970; found: 622.9974.

2-(Pyridin-2-yl)-3-(pyridin-2-ylmethyl)chromen-4-one (4x)

Colorless solid; yield: 220 mg (70%); mp 145–146 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.67 (dd, J = 4.8, 0.8 Hz, 1 H), 8.40 (dd, J = 4.8, 0.8 Hz, 1 H), 8.19 (dd, J = 8.4, 1.2 Hz, 1 H), 7.99 (d, J = 8.0 Hz, 1 H), 7.78 (dt, J = 8.0, 1.6 Hz, 1 H), 7.64 (dt, J = 8.4, 1.6 Hz, 1 H), 7.50 (d, J = 8.4 Hz, 1 H), 7.49 (dt, J = 8.0, 1.6 Hz, 1 H), 7.35 (dt, J = 8.4, 1.2 Hz, 1 H), 7.33 (dt, J = 8.8, 1.2 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 1 H), 7.00 (dd, J = 8.0, 1.2 Hz, 1 H), 4.37 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.4, 159.9, 159.8, 155.9 (2 ×), 151.6, 149.4, 148.8, 136.6, 136.0, 133.6, 125.9, 124.9, 124.5, 124.3, 122.8, 120.8, 120.6, 118.0, 33.4.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₀H₁₅N₂O₂: 315.1134; found: 315.1129.

2-(5-Fluoropyridin-2-yl)-3-(5-fluoropyridin-2-ylmethyl)chromen-4-one (4y)

Colorless solid; yield: 259 mg (74%); mp 149–150 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.55 (d, J = 2.8 Hz, 1 H), 8.27 (d, J = 2.8 Hz, 1 H), 8.21 (dd, J = 8.0, 1.6 Hz, 1 H), 8.15 (ddd, J = 8.8, 4.4, 0.4 Hz, 1 H), 7.69 (dt, J = 8.4, 1.6 Hz, 1 H), 7.56 (ddd, J = 8.8, 7.6, 2.8 Hz, 1 H), 7.52 (dd, J = 8.8, 0.8 Hz, 1 H), 7.40 (dt, J = 8.0, 1.2 Hz, 1 H), 7.30 (dt, J = 8.4, 4.4 Hz, 1 H), 7.26 (dt, J = 8.8, 2.8 Hz, 1 H), 4.36 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.4, 159.6 (d, J = 260.0 Hz), 158.8, 158.0 (d, J = 251.7 Hz), 155.9, 155.8 (d, J = 3.8 Hz), 147.9 (d, J = 4.6 Hz), 138.0 (d, J = 23.5 Hz), 136.8 (d, J = 22.8 Hz), 133.9, 126.1, 125.8 (d, J = 5.3 Hz), 125.1, 123.9 (d, J = 3.7 Hz), 123.5, 123.2 (d, J = 25.0 Hz), 122.9 (d, J = 1.5 Hz), 120.7, 118.0, 32.6 (d, J = 1.5 Hz).

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₀H₁₃F₂N₂O₂: 351.0945; found: 351.0938.

2-(6-Chloropyridin-2-yl)-3-(6-chloropyridin-2-ylmethyl)chromen-4-one (4z)

Colorless solid; yield: 283 mg (74%); mp 164–165 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.15 (dd, J = 8.0, 1.6 Hz, 1 H), 7.997 (dd, J = 7.6, 0.4 Hz, 1 H), 7.77 (t, J = 8.0 Hz, 1 H), 7.63 (dt, J = 8.8, 1.6 Hz, 1 H), 7.45 (dd, J = 8.0, 1.6 Hz, 1 H), 7.43 (d, J = 7.6 Hz, 1 H), 7.35 (dt, J = 8.0, 0.8 Hz, 1 H), 7.33 (dt, J = 8.0, 1.2 Hz, 1 H), 7.16 (dt, J = 7.2, 0.4 Hz, 1 H), 7.02 (dd, J = 8.0, 0.8 Hz, 1 H), 4.33 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.0, 160.6, 158.2, 155.6, 151.5, 150.7, 150.1, 139.3, 138.6, 133.8, 125.8, 125.4, 125.1, 122.7, 122.6, 121.3, 121.2, 120.3, 117.9, 32.7.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₀H₁₃Cl₂N₂O₂: 383.0354; found: 383.0348.

Single-crystal X-ray diagram: crystal of compound **4z** was grown by slow diffusion of EtOAc into a solution of compound **4z** in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group $P\bar{1}$, a = 8.0551(5) Å, b = 10.7878(6) Å, c = 11.1421(6) Å, V = 815.63(8) Å³, Z = 2, d_{calcd} = 1.560 g/cm³, $F(000)$ = 392, 2θ range 2.043–26.470°, R indices (all data) $R1$ = 0.0404, $wR2$ = 0.1033.

2-(6-Methylpyridin-2-yl)-3-(6-methylpyridin-2-ylmethyl)chromen-4-one (4aa)

Colorless solid; yield: 274 mg (80%); mp 77–78 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.22 (dd, J = 8.0, 1.6 Hz, 1 H), 7.76 (dd, J = 8.0, 0.4 Hz, 1 H), 7.68 (t, J = 7.6 Hz, 1 H), 7.65 (dd, J = 8.4, 0.8 Hz, 1 H), 7.51 (d, J = 8.4 Hz, 1 H), 7.38 (t, J = 8.0 Hz, 1 H), 7.37 (t, J = 8.0 Hz, 1 H), 7.20 (d, J = 7.6 Hz, 1 H), 6.96 (d, J = 8.0 Hz, 1 H), 6.88 (d, J = 7.6 Hz, 1 H), 4.30 (s, 2 H), 2.49 (s, 3 H), 2.46 (s, 3 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.6, 160.4, 159.4, 158.4, 157.2, 156.0, 150.9, 136.7, 136.4, 133.6, 126.0, 124.9, 124.2, 123.0, 121.3, 120.4, 120.2, 119.1, 118.0, 33.6, 24.4, 24.3.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₂H₁₉N₂O₂: 343.1447; found: 343.1442.

2-(6-Methoxypyridin-2-yl)-3-(6-methoxypyridin-2-ylmethyl)chromen-4-one (4ab)

Colorless solid; yield: 292 mg (78%); mp 124–125 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.23 (dd, J = 8.0, 1.6 Hz, 1 H), 7.71–7.62 (m, 3 H), 7.51 (dd, J = 8.4, 0.4 Hz, 1 H), 7.38 (dt, J = 8.0, 0.8 Hz, 1 H), 7.36 (t, J = 7.6 Hz, 1 H), 6.80 (dd, J = 8.0, 0.8 Hz, 1 H), 6.76 (d, J = 6.8 Hz, 1 H), 6.45 (d, J = 8.4 Hz, 1 H), 4.53 (s, 2 H), 3.73 (s, 3 H), 3.65 (s, 3 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.6, 163.2, 163.1, 159.2, 157.7, 155.8, 149.3, 138.8, 138.5, 133.6, 126.0, 124.8, 122.8, 120.2, 117.8, 116.9, 114.7, 112.6, 10.3, 53.4, 52.9, 32.6.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₂H₁₉N₂O₄: 375.1345; found: 375.1337.

3-Benzyl-2-phenylchromen-4-one (4ac)

Colorless solid; yield: 134 mg (43%); mp 82–83 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.27 (dd, J = 8.0, 1.6 Hz, 1 H), 7.67 (dt, J = 8.4, 1.6 Hz, 1 H), 7.58–7.56 (m, 2 H), 7.52–7.46 (m, 3 H), 7.41 (dt, J = 8.0, 0.8 Hz, 1 H), 7.25–7.21 (m, 2 H), 7.17–7.13 (m, 4 H), 3.98 (s, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.2, 162.9, 156.2, 140.1, 133.5, 133.2, 130.4, 128.6 (2 ×), 128.5 (2 ×), 128.4 (2 ×), 128.1 (2 ×), 126.1, 125.9, 124.9, 123.0, 120.6, 117.9, 31.2.

HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₂H₁₇O₂: 313.1229; found: 313.1221.

2-(Naphthalen-2-yl)-3-(naphthalen-2-ylmethyl)chromen-4-one (4ad)

Colorless solid; yield: 148 mg (36%); mp 144–145 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.34 (dd, J = 8.0, 1.6 Hz, 1 H), 8.06 (s, 1 H), 7.93 (d, J = 8.4 Hz, 1 H), 7.91 (d, J = 8.8 Hz, 1 H), 7.81–7.67 (m, 6 H), 7.61–7.52 (m, 4 H), 7.47–7.35 (m, 4 H), 4.20 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.4, 163.2, 156.3, 138.0, 133.9, 133.6, 132.5, 132.1, 130.4, 129.1, 128.7, 128.4, 128.0, 127.8, 127.6 (3 \times), 127.5, 127.1, 126.8, 126.2 (2 \times), 125.8, 125.18, 125.17, 125.0, 123.1, 120.8, 118.0, 31.6.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{30}\text{H}_{21}\text{O}_2$: 413.1542; found: 413.1536.

2-(Furan-2-yl)-3-(furan-2-ylmethyl)chromen-4-one (4af)

Colorless solid; yield: 169 mg (58%); mp 111–112 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.21 (dd, J = 8.0, 1.6 Hz, 1 H), 7.66 (dd, J = 1.6, 0.4 Hz, 1 H), 7.64 (dt, J = 8.8, 1.2 Hz, 1 H), 7.46 (dd, J = 8.4, 0.8 Hz, 1 H), 7.37 (dt, J = 8.0, 0.8 Hz, 1 H), 7.27 (dd, J = 1.6, 0.8 Hz, 1 H), 7.17 (dd, J = 3.6, 0.8 Hz, 1 H), 6.60 (dd, J = 3.6, 1.6 Hz, 1 H), 6.23 (dd, J = 3.2, 1.6 Hz, 1 H), 6.05 (dd, J = 3.2, 0.8 Hz, 1 H), 4.31 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.6, 155.5, 153.2, 152.2, 146.7, 145.4, 140.9, 133.6, 126.0, 124.8, 122.7, 117.7, 116.0, 115.3, 112.1, 110.3, 105.8, 23.2.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{18}\text{H}_{13}\text{O}_4$: 293.0814; found: 293.0809.

2-(Thiophen-2-yl)-3-(thiophen-2-ylmethyl)chromen-4-one (4ag)

Colorless solid; yield: 194 mg (60%); mp 138–139 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.25 (dd, J = 8.0, 1.6 Hz, 1 H), 7.68 (dd, J = 7.2, 1.6 Hz, 1 H), 7.64 (dd, J = 8.0, 1.2 Hz, 1 H), 7.61 (dd, J = 8.8, 0.8 Hz, 1 H), 7.50 (dd, J = 8.0, 0.8 Hz, 1 H), 7.40 (dt, J = 8.0, 0.8 Hz, 1 H), 7.16 (dd, J = 4.8, 4.0 Hz, 1 H), 6.12 (dd, J = 4.8, 1.2 Hz, 1 H), 6.90–6.87 (m, 2 H), 4.36 (d, J = 0.8 Hz, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.6, 156.6, 155.7, 142.0, 134.4, 133.7, 130.6, 130.1, 127.9, 126.8, 126.1, 125.0, 124.7, 123.6, 122.6, 119.0, 117.8, 26.2.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{18}\text{H}_{13}\text{O}_2\text{S}_2$: 325.0357; found: 325.0352.

Single-crystal X-ray diagram: crystal of compound **4ag** was grown by slow diffusion of EtOAc into a solution of compound **4ag** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P2_1/n$, a = 9.1253(10) Å, b = 9.1493(10) Å, c = 18.386(2) Å, V = 1512.1(3) Å 3 , Z = 4, d_{calcd} = 1.425 g/cm 3 , $F(000)$ = 672, 2θ range 2.249–26.551°, R indices (all data) $R1$ = 0.0339, $wR2$ = 0.0734.

2-(Pyridin-3-yl)-3-(pyridin-3-ylmethyl)chromen-4-one (4ah)

Colorless gum; yield: 85 mg (27%).

^1H NMR (400 MHz, CDCl_3): δ = 8.78 (dd, J = 1.6, 0.8 Hz, 1 H), 8.73 (dd, J = 4.8, 1.6 Hz, 1 H), 8.35 (d, J = 3.6 Hz, 1 H), 8.26 (d, J = 1.6 Hz, 1 H), 8.20 (dd, J = 8.0, 1.6 Hz, 1 H), 7.79 (dt, J = 8.0, 2.4 Hz, 1 H), 7.67 (dt, J = 8.4, 1.6 Hz, 1 H), 7.45–7.38 (m, 4 H), 7.10 (dd, J = 8.0, 4.8 Hz, 1 H), 3.91 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.5, 160.1, 156.0, 151.4, 149.2, 149.0, 147.5, 135.8, 135.6, 135.0, 134.0, 128.9, 125.9, 125.3, 123.3 (2 \times), 122.7, 120.6, 117.9, 28.4.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{20}\text{H}_{15}\text{N}_2\text{O}_2$: 315.1134; found: 315.1136.

2-(Benzofuran-2-yl)-3-(benzofuran-2-ylmethyl)chromen-4-one (4ai)

Colorless solid; yield: 251 mg (64%); mp 186–187 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.27 (dd, J = 8.4, 1.6 Hz, 1 H), 7.72 (dt, J = 8.4, 1.6 Hz, 1 H), 7.69 (dd, J = 8.0, 0.8 Hz, 1 H), 7.59 (dd, J = 8.0, 0.8 Hz, 1 H), 7.58 (s, 1 H), 7.56 (dd, J = 8.4, 0.8 Hz, 1 H), 7.45–7.39 (m, 4 H), 7.32 (dt, J = 8.0, 0.8 Hz, 1 H), 7.17 (dt, J = 8.8, 1.6 Hz, 1 H), 7.12 (dt, J = 8.0, 1.6 Hz, 1 H), 6.47 (d, J = 1.2 Hz, 1 H), 4.61 (d, J = 0.8 Hz, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.5, 156.5, 155.7, 155.6, 154.7, 152.5, 148.2, 134.0, 128.9, 127.3, 126.9, 126.1, 125.2, 123.9, 123.1, 122.7, 122.4, 122.2, 120.3, 117.8, 117.3, 111.9, 111.5, 110.8, 102.9, 23.9.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{26}\text{H}_{17}\text{O}_4$: 393.1127; found: 393.1122.

2-(Benzo[b]thiophen-2-yl)-3-(benzo[b]thiophen-2-yl)methylchromen-4-one (4aj)

Colorless solid; yield: 267 mg (63%); mp 195–196 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.29 (dd, J = 8.0, 1.6 Hz, 1 H), 7.89 (dd, J = 8.0, 2.0 Hz, 1 H), 7.88 (s, 1 H), 7.83 (dd, J = 8.4, 1.6 Hz, 1 H), 7.76 (d, J = 8.0 Hz, 1 H), 7.72 (dt, J = 8.8, 2.0 Hz, 1 H), 7.63 (dd, J = 8.8, 1.6 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H), 7.46–7.39 (m, 3 H), 7.29 (dt, J = 8.4, 1.2 Hz, 1 H), 7.25 (dt, J = 8.4, 1.2 Hz, 1 H), 7.12 (s, 1 H), 4.49 (d, J = 0.8 Hz, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 177.5, 156.9, 155.8, 143.1, 140.8, 140.1, 139.6, 138.9, 134.0, 133.9, 127.8, 126.3, 126.2, 125.3, 125.0 (2 \times), 124.1, 123.6, 123.0, 122.6, 122.2, 122.1, 121.3, 119.7, 117.9, 27.2.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{26}\text{H}_{17}\text{O}_2\text{S}_2$: 425.0670; found: 425.0678.

1-(2-Hydroxyphenyl)-3-(1-methyl-1H-indol-3-yl)prop-2-en-1-one (4ak-1)

Colorless solid; yield: 42 mg (15%); mp 208–209 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 13.30 (s, 1 H), 8.19 (d, J = 15.2 Hz, 1 H), 8.03–8.00 (m, 1 H), 7.96 (dd, J = 8.4, 1.6 Hz, 1 H), 7.65 (d, J = 15.2 Hz, 1 H), 7.50 (s, 1 H), 7.48 (dt, J = 7.6, 2.0 Hz, 1 H), 7.41–7.33 (m, 3 H), 7.03 (dd, J = 8.4, 0.8 Hz, 1 H), 6.96 (dt, J = 8.0, 1.2 Hz, 1 H), 3.85 (s, 3 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 193.6, 163.5, 139.4, 138.4, 135.6, 135.4, 129.3, 126.1, 123.4, 121.9, 120.8, 120.3, 118.6, 115.5, 114.5, 113.1, 110.3, 33.4.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{18}\text{H}_{16}\text{NO}_2$: 278.1181; found: 278.1188.

2-(Quinolin-2-yl)-3-(quinolin-2-ylmethyl)chromen-4-one (4al)

Colorless solid; yield: 145 mg (35%); mp 122–123 °C (hexanes/EtOAc).

^1H NMR (400 MHz, CDCl_3): δ = 8.27 (dd, J = 8.0, 1.6 Hz, 1 H), 8.25 (d, J = 9.2 Hz, 1 H), 8.10 (d, J = 8.4 Hz, 1 H), 7.98 (d, J = 8.4 Hz, 1 H), 7.92 (dd, J = 8.4, 3.2 Hz, 1 H), 7.80 (dd, J = 8.0, 0.8 Hz, 1 H), 7.71–7.53 (m, 7 H), 7.46 (d, J = 8.8 Hz, 1 H), 7.43–7.38 (m, 2 H), 4.71 (s, 2 H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 178.6, 160.7, 160.1, 156.0, 151.5, 147.7, 147.3, 136.7, 135.9, 133.7, 130.0, 129.9, 128.9, 128.8, 127.9, 127.8, 127.4, 127.3, 126.7, 126.1, 125.4, 125.1, 123.0, 121.2, 121.0, 120.8, 118.0, 34.3.

HRMS (ESI-TOF): m/z [M + H] $^+$ calcd for $\text{C}_{28}\text{H}_{19}\text{N}_2\text{O}_2$: 415.1447; found: 415.1446.

2-[6-(3,4-Dimethoxyphenyl)pyridin-2-yl]-3-[6-(3,4-dimethoxyphenyl)pyridin-2-ylmethyl]chromen-4-one (4am)

3,4-Dimethoxyphenylboronic acid (180 mg, 1.0 mmol), $\text{Pd}(\text{OAc})_2$ (45 mg, 20 mol%), PPh_3 (130 mg, 0.5 mmol), and Na_2CO_3 (53 mg, 0.5 mmol) were added stepwise to a solution of **4a** (235 mg, 0.5 mmol) in EtOH (15 mL) at 25 °C. The mixture was stirred at reflux for 8 h (TLC

monitoring). The mixture was cooled to 25 °C, concentrated, and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford the crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc 8:1–2:1) afforded **4am** as a colorless gum; yield: 220 mg (75%).

¹H NMR (400 MHz, CDCl₃): δ = 8.24 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.93 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 7.76 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.70 (dt, *J* = 8.4, 1.6 Hz, 1 H), 7.56–7.52 (m, 4 H), 7.45–7.37 (m, 4 H), 7.17 (d, *J* = 7.6 Hz, 1 H), 6.83 (d, *J* = 8.4 Hz, 1 H), 6.79 (d, *J* = 8.8 Hz, 1 H), 4.70 (s, 2 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.71 (s, 3 H), 3.70 (s, 3 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.7, 159.7, 159.6, 156.6, 156.0, 155.8, 151.7, 150.2, 149.5, 149.1, 148.9, 137.3, 136.8, 133.7, 132.6, 131.2, 126.0, 124.9, 122.9, 121.7, 121.0, 120.5 (2 ×), 119.6, 119.0, 117.9, 116.8, 111.0, 110.7, 110.0, 109.9, 55.84, 55.81, 55.7, 55.5, 33.5.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₃₆H₃₁N₂O₆: 587.2182; found: 587.2188.

2-(6-Bromopyridin-2-yl)-3-[6-(3,4-dimethoxyphenyl)pyridin-2-ylmethyl]chromen-4-one (**4am-1**)

Colorless solid; yield: 26 mg (10%); mp 188–190 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.20 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.89 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.84 (d, *J* = 7.6 Hz, 1 H), 7.73 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.67 (dt, *J* = 8.4, 1.2 Hz, 1 H), 7.52 (d, *J* = 8.4 Hz, 1 H), 7.42 (d, *J* = 2.0 Hz, 1 H), 7.38 (t, *J* = 7.6 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 7.26 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.20 (d, *J* = 7.6 Hz, 1 H), 7.14 (d, *J* = 7.6 Hz, 1 H), 6.85 (d, *J* = 8.4 Hz, 1 H), 4.60 (s, 2 H), 3.89 (s, 3 H), 3.78 (s, 3 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 178.4, 161.8, 159.9, 156.5, 155.8, 151.2, 150.2, 149.0, 141.0, 138.4, 137.4, 133.8, 131.0, 125.8, 125.0 (2 ×), 122.7, 121.6, 120.9, 120.7, 119.7, 119.5, 117.9, 111.0, 109.7, 55.8, 55.7, 33.3.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₈H₂₂BrN₂O₄: 529.0763; found: 529.0769.

2-(2-Allyl-3,4-dimethoxyphenyl)chromen-4-one (**4an**)

NaOH (80 mg, 2.0 mmol) was added to a solution of **2a** (136 mg, 1.0 mmol) in MeOH (30 mL) at 25 °C and the mixture was stirred at 25 °C for 10 min. Compound **3q** (412 mg, 2.0 mmol) was added to the mixture at 25 °C and then the mixture was stirred at 50 °C for 10 h. The mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford the crude product under reduced pressure. Purification (silica gel, hexanes/EtOAc 10:1–4:1) afforded **4an** as a colorless solid; yield: 129 mg (40%); mp 208–209 °C (hexanes/EtOAc).

¹H NMR (400 MHz, CDCl₃): δ = 8.28 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.69 (dt, *J* = 8.4, 1.6 Hz, 1 H), 7.49 (dd, *J* = 8.4, 0.8 Hz, 1 H), 7.43 (dt, *J* = 8.0, 0.8 Hz, 1 H), 7.36 (d, *J* = 8.4 Hz, 1 H), 6.95 (d, *J* = 8.4 Hz, 1 H), 6.42 (s, 1 H), 5.95–5.85 (m, 1 H), 4.91–4.82 (m, 2 H), 3.94 (s, 3 H), 3.87 (s, 3 H), 3.51 (dt, *J* = 6.4, 1.6 Hz, 2 H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 173.2, 155.6, 154.4, 147.8, 147.7, 138.4, 136.6, 133.9, 133.5, 126.5, 125.5, 124.5, 123.0, 121.2, 118.4, 115.2, 110.2, 60.8, 55.8, 31.8.

HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₁₉O₄: 323.1283; found: 323.1288.

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Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0039-1690760>. Included are scanned photocopies of NMR spectral data for all compounds and X-ray analysis data of **4a–4d**, **4g**, **4t**, **4z** and **4ag**.

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