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Synthesis of substituted 2-aroyl-3-methylchromen-4-ones from isovanillin via 2-aroyl-3-methylchroman intermediates

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ABSTRACT

The synthesis of substituted 2-aroyl-3-methylchromen-4-one from isovanillin is described. *O*-Allylphenol (**2**) prepared from isovanillin (**1**) was allowed to react with various α-bromoacetophenone (**3**) to produce 2-(2-allyl-3,4-dimethoxy)phenoxy-1-aroylethanones (**4**). The resultant **4** were treated with 2 equiv of potassium *tert*-butoxide to afford the substituted 2-aroyl-3-methylchromans (**5**) through an isomerization of an allylic double bond and a carbanion–olefin intramolecular 6-*endo*-*trig* cyclization reaction. Subsequently, resultant **5** were oxidized with DDQ to yield the title compound **6**, in good over-all yields.

1. Introduction

1-Chromen-4-one (4*H*-1-benzopyran-4-one) is a core and common framework of naturally occurring bioactive flavones, flavonols, and isoflavones, which are closely related oxygen benzoheterocyclic compounds.[1] Because they exhibit diverse biological activities, the studies of these compounds either from nature products or from synthetic methods are still an attractive topic. The major biological activities of flavones including anti-aggregatory and anti-inflammatory activities,[2] cytostatic activity,[3] antibacterial and antiviral activity,[4] anti-allergic activity,[5] estrogenic activity,[6] hepatoprotective activity,[7] aldose reductase inhibitory activity,[8] as well as other activities[9] have been disclosed. Furthermore, it have been reported that flavanol derivatives exhibit cardioprotective activity,[10] antioxidative activity,[11] and antiplatelet activity.[12] Moreover, the major biological activities of isoflavones reported are estrogenic activity,[13] antiviral activity,[14] and aldose reductase inhibitory activity.[15] In addition, certain synthetic chromen-4-one derivatives have been reported to possess antimicrobial activity,[16] anti-breast cancer activity,[17] and nonsteroidal antiestrogens activity,[18] as well as other activities. Even various synthetic chromen-4-ones were developed, but their major strategies were derived from the traditional method by the cyclization of the common intermediate 1-(2-hydroxyphenyl)-3-aryl-1,3-propanediones and followed by the dehydration with diverse conditions.[19] In addition, certain unique methods for the preparation of chromen-4-ones include the carbonylation coupling of *o*-iodophenols with terminal acetylenes,[20] the coupling of acid chlorides with terminal alkynes,[21] the Pd-catalyzed carbonylation of *o*-iodophenols in the presence of acetylenes,[22] and the cyclization of α-oxoketene and phenylacetylene.[23] However, some disadvantages still exist on those reported methods including the tedious reaction condition, multi-synthetic steps, and low yields. Moreover 2-aroylchromen-4-ones exhibiting potential biological activities were disclosed in previous studies.[24] Therefore, to develop a unique, concise, and high yield approaches for substituted chromen-4-ones are requisite and significant from both chemical and biological viewpoints. In continuing our previous studies on benzoheterocyclic and benzocarbocyclic compounds utilizing isovanillin as starting material,[25] herein we disclose a new synthetic method for substituted 1-chromen-4-ones (Scheme 1). Our strategy involves the utilization of isovanillin (**1**) as starting material, and through a sequence of an O-allylation, Claisen rearrangement, O-methylation, and H_2O_2 oxidation to give 2-allyl-3,4-dimethoxyphenol (**2**).[26] Followed by the reaction of resultant phenol with various α-bromoacetophenones (**3a**–**e**), 2-(2-allyl-3,4-dimethoxy)-phenolxy-1-aryloylethanones (**4a**–**e**) were produced. Then, the resultant ethanones were treated with 2 equiv of potassium *tert*-butoxide to undergo a series of reactions including the formation of

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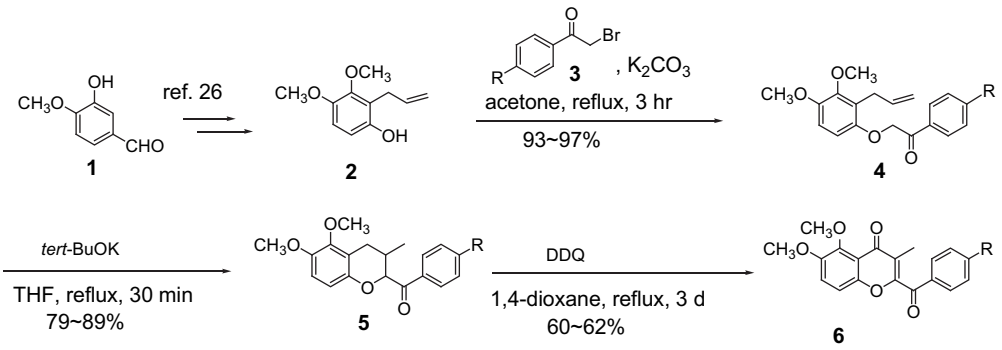
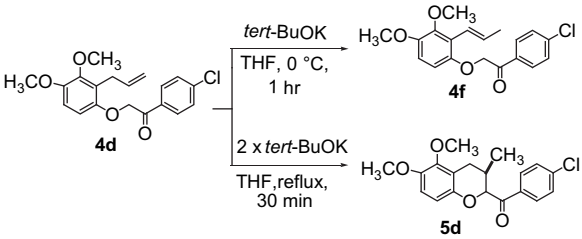


Scheme 1. Synthesis of substituted 2-aroyl-3-methylchromen-4-ones from vanillin.

dianions, isomerization of an allylic double bond, and a carbanion–olefinic intra-molecular 6-*endo-trig* cyclization reaction to generate substituted 2-aroyl-3-methyl-1-chroman (2-aroyl-3-methyl-3,4-dihydro-2*H*-benzopyrans) (**5a**–**e**) in diasteromeric mixtures as key intermediate. With separation or without separation of diastereomeric mixtures, **5** was oxidized with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) to yield the title compounds, substituted 2-aroyl-3-methylchromen-4-ones (**6a**–**e**) in one pot.

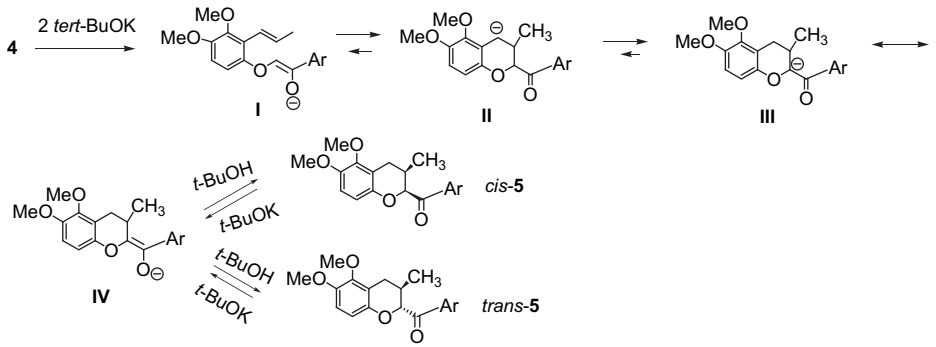
2. Results and discussion

2-Allyl-3,4-dimethoxyphenol (**2**), which was prepared from isovanillin through 3 steps,[26] was allowed to react with various α-bromoacetophenones (**3a**–**d**) in the presence of dried K_2CO_3 in the refluxing acetone for 3 h to produce 2-(2-allyl-3,4-dimethoxy)-phenoxy-1-aroylethanones (**4a**–**d**) in 93–97% yield. The formation of $-OCH_2C(=O)-$ bond where singlet signal appeared at δ 5.12–5.19 in ^{1}H NMR spectrum, briefly proved the success of the formation of **4a**–**d**. Subsequently, in the model reaction, while treatment of **4d** with potassium *tert*-butoxide at 0 °C in THF for 1 h, the product with lower R_f value than that of starting material was obtained. The resultant product (**4f**), in which double bond of allyl group was isomerized and migrated to the position to conjugate with the benzene ring, was proven by physical and spectral data.[27] Nevertheless, at the same reaction condition but using 2 equiv of potassium *tert*-butoxide and elevation of the reaction temperature to the reflux for 30 min, the products with higher R_f value than that of starting material were afforded. The products, which were cyclized to give a diastereomeric mixture, were carefully separated into *trans*-**5d**, and *cis*-**5d** isomers in the ratio of 1.7:1 by silica gel column chromatography (ethyl acetate/*n*-hexane=1:20). The given result showed this intramolecular carbanion–olefin cyclization which is stereo-specific to 6-*endo-trig* cyclization and is favor to the stable *trans*-product. The reaction described above was depicted in Scheme 2.



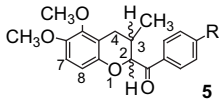
Scheme 2. The formation of **4f** or **5d** from the reaction of **4d** with one or 2 equiv of potassium *tert*-butoxide.

The discrimination of *trans*-**5d** and *cis*-**5d** isomers was briefly achieved by examining the coupling constant of H-2, which coupled with H-3 in ^{1}H NMR spectrum. For instance, the signal of H-2 (doublet) at δ 4.96 with coupling constant J=7.2 Hz indicates that is the *trans*-isomer of **5d**. On the other hand, the signal of H-2 (doublet) at δ 5.35 with coupling constant J=2.0 Hz indicates that is the *cis*-isomer of **5d**. Thereby, the mechanism for the generation of compound **5** is rationally proposed and shown below. The allylic proton and proton near the carbonyl group of **4** are abstracted by 2 equiv of potassium *tert*-butoxide to isomerize the double bond of allyl group to form a more stable one and to generate a carbanion which is subsequently isomerized to the initial enolate **I**. The initial enolate subsequently undergoes the intramolecular carbanion–olefinic *6-endo-trig* cyclization reaction to give an unstable and transient intermediate **II**. Because of thermodynamic controlled reaction, **II** is isomerized to the cyclized carbanion **III** via a protonation–deprotonation with *t*-BuOH/*t*-BuOK. Then, the stable enolate **IV**, which has resonance with **III**, is formed and subsequently picks up a proton from α-carbon to produce the mixture of *trans*- and *cis*-2-aroyl-3-methyl-3,4-dihydro-2*H*-benzopyran (chroman) **5** (Scheme 3). The reaction condition for the formation of **5d** is applied to the preparation of other chromans **5a**–**e** from **4**. The



Scheme 3. The mechanism for the formation of *trans*-**5** and *cis*-**5** from **4**.

Table 1
The ratio of *trans*- and *cis*-isomer, % yield, and typical protons of **5a–e** obtained from **4a–e**



5

a. R = H,
b. R = OCH_3,
c. R = CH_3,
d. R = Cl,
e. R = Br

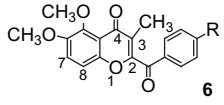
Compound	*cis*/*trans* Ratio[a]	Yield[b] (%)	H-2 (δ) *trans*- *cis*-	CH_3-3 (δ) *trans*- *cis*-
5a	1/2.2	86	4.96 (d, J=7.2 Hz) 5.35 (d, J=2.0 Hz)	1.09 (d, J=6.4 Hz) 0.92 (d, J=6.8 Hz)
5b	1/3.2	84	4.88 (d, J=7.2 Hz) 5.29 (d, J=2.0 Hz)	1.07 (d, J=6.4 Hz) 0.93 (d, J=6.8 Hz)
5c	1/2.7	89	4.93 (d, J=7.6 Hz) 5.33 (d, J=2.4 Hz)	1.07 (d, J=6.0 Hz) 0.91 (d, J=6.8 Hz)
5d	1/1.7	79	4.84 (d, J=7.6 Hz) 5.24 (d, J=2.4 Hz)	1.08 (d, J=6.4 Hz) 0.93 (d, J=6.8 Hz)
5e	1/2.8	80	4.84 (d, J=7.6 Hz) 5.23 (d, J=2.0 Hz)	1.08 (d, J=6.0 Hz) 0.93 (d, J=7.2 Hz)

[a] The ratio of *cis*/*trans* is determined by the isolated yield, which is separated from column chromatography.
[b] % Yield of **5** are the diastereomeric mixture obtained.

ratio of the resultant diasteromeric mixtures, % yield, and typical protons in ^{1}H NMR spectra are summarized in Table 1. Besides our preliminary study,[28] the cyclization of enolate to the non-activated C=C double bond was also reported by other groups.[29]

Because of the thermodynamic driving force of this cyclization, the ratio of *cis*-**5**/*trans*-**5** is determined by the stability of these isomers. This can be verified by heating pure *cis*-**5b** with *t*-BuOK in *t*-BuOH for 4 h to yield the mixture of *cis*-**5b** and *trans*-**5b** in ratio of 1:2.7 by GC–MS analysis. Then, the diastereomeric mixtures **5a–e** were, respectively, oxidized by DDQ (2,3-dichloro-5,6-dicyano *p*-benzoquinone) in refluxing dioxane for 3 days to yield the desired chromen-4-ones (**6a–e**) in one pot. Besides the disappearance of H-2, H-3, and H-4 signals from ^{1}H NMR spectra and the appearance of carbonyl groups at 1631–1649 cm^{-1} in IR spectra, other data such as EIMS and EA, which are the correct connectivity required for compound **6a–e**. The % yield, melting point (mp), selected signals of ^{1}H NMR spectra, ESI-HRMS data, and elemental analyses (EA) of 2-aroyl-3-methylchromen-4-ones (**6a–e**) are depicted in Table 2.

Table 2
The % yield, melting point (mp), selected signals of ^{1}H NMR, EIMS, and elemental analysis (EA) of 2-aroyl chroman-4-ones (**6a–e**)



6

a. R = H,
b. R = OCH_3,
c. R = CH_3,
d. R = Cl,
e. R = Br

Compound	Yield (%)	Mp (°C)	^{1}H NMR[a] CH_3-3, H-7, H-8	EA calcd. found (C%, H%)	ESI-HRMS calcd found
6a	62	118–120	2.02 7.31, 7.15	70.36, 4.97 70.12, 5.01	$C_{19}H_{16}O_5Na$ 347.0895 347.0897
6b	57	171–173	1.99 7.31, 7.16	67.79, 5.12 67.74, 5.12	$C_{20}H_{18}O_6Na$ 377.1001 377.1002
6c	60	153–155	2.00 7.31, 7.16	70.99, 5.36 70.85, 5.35	$C_{20}H_{18}O_5Na$ 361.1052 361.1050
6d	60	161–162	2.04 7.32, 7.14	63.61, 4.21 63.27, 4.29	$C_{19}H_{15}ClO_5Na$ 381.0506 381.0503
6e	69	178–180	2.04 7.32, 7.14	56.59, 3.75 56.44, 3.77	$C_{19}H_{15}BrO_5Na$ 425.0001 424.9999

[a] The chemical shift of proton H-7, which links with the signal of CH_3O at the position 6 in the structure of **6**, is determined by NOESY technique.

3. Conclusion

We have established a novel synthetic route for 2-aroyl-5,6-dimethoxy-3-methylchromen-4-ones through the DDQ oxidation of 2-aroyl-3-methyl-1-chroman, which prepared from isovanillin via a 6-*endo*-*trig* carbanion–olefin cyclization reaction. The screening of biological activities of the resultant 2-aroyl-3-methyl-1-benzopyran-4-ones is in progress under the cooperation with other laboratories.

4. Experimental

4.1. General

Melting points (Yanaco micro melting point apparatus) were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Varian Gemini-200 or Varian Unity plus 400 Spectrometer. Chemical shifts are indicated in parts per million with respect to TMS. Elemental analyses were recorded on a Heraeus CHN-O Rapid analyzer. Mass spectra were recorded on a Chem/hp/middle spectrometer connected to a Hewlett Packard series II model gas–liquid chromatography. HRMS spectra were performed on a JEOL JMS SX/SX 102A instrument. Silica gel (230–400 mesh) for column chromatography and precoated silica gel plates (60 F-254) for TLC was purchased from E. Merck Co. UV light (254 nm) was used to detect spots on TLC plates after development.

4.2. General procedure for the preparation of 2-(2-allyl-3,4-dimethoxyphenoxy)-1-arylethanones (4a–e)

As the general procedure, the mixture of 2-allyl-3,4-dimethoxyphenol (**2**) (1.9 g, 10.0 mmol) and K_2CO_3 (2.1 g, 15 mmol) in anhydrous acetone (20 mL) was stirred and heated to the reflux. To the refluxing mixture, α-bromoacetophenones (**3a–e**) (10 mmol) was added in drops. The reaction mixture was continually heated to the reflux for 3 h. At the end of reaction, which was monitored by TLC, the mixture was cooled down to room temperature and was filtered. The resultant filtrate, which was concentrated in vacuo to remove the solvent was further purified from silica gel chromatography (ethyl acetate/*n*-hexane=1:20) to give pure **4a–e** in yield of 93–98%, respectively.

*4.2.1. 2-(2-Allyl-3,4-dimethoxyphenoxy)-1-phenylethan-one (**4a**).* Compound **4a** (2.93 g, 94%) was obtained as yellow liquid, R_f=0.58 (ethyl acetate/*n*-hexane=1:4), IR (KBr) cm^{-1}, ν_{max}: 3067, 2936, 2832, 1702, 1636, 1595, 1485, 1446, 1254, 1222, 1128, 1086, 1035, 983, 913, 791, 757, 728, 691; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.49 (dt, J=6.4, 1.6 Hz, 2H, ArCH_2CH=CH_2), 3.81, 3.82 (each s, 2×3H, 2×OCH_3), 4.96 (ddt, J=10.0, 1.6, 1.6 Hz, 1H, $ArCH_2CH$=CH_aH_b), 4.98 (ddt, J=16.8, 1.6, 1.6 Hz, 1H, $ArCH_2CH$=CH_aH_b), 5.19 (s, 2H, $ArOCH_2COAr'$), 5.99 (ddt, J=16.8, 10.0, 6.4 Hz, 1H, $ArCH_2CH$=CH_2), 6.51 (d, J=8.8 Hz, 1H, ArH), 6.69 (d, J=8.8 Hz, 1H, ArH), 7.47–7.50 (m, 2H, ArH), 7.59–7.63 (m, 1H, ArH), 8.00 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.3, 56.1, 60.9, 72.1, 107.1, 110.0, 114.7, 123.8, 128.3, 128.7, 133.7, 134.7, 137.0, 147.9, 148.1, 150.6, 195.2; EIMS (70 eV) *m*/*z* (rel intensity, %): 312 (M^+, 19), 294 (31), 193 (21), 192 (100), 191 (33), 178 (21), 177 (38), 105 (17); HRMS (ESI) calcd for $C_{19}H_{20}O_4Na$ $[M+Na]^+$: 335.1259. Found: 335.1260.

*4.2.2. 2-(2-Allyl-3,4-dimethoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (**4b**).* Compound **4b** (3.34 g, 98%) was obtained as yellow liquid, R_f=0.43 (ethyl acetate/*n*-hexane=1:4), IR (KBr) cm^{-1}, ν_{max}: 3057, 2926, 2836, 1694, 1560, 1476, 1246, 1115, 1024, 797, 592; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.49 (dt, J=6.4, 1.6 Hz, 2H, ArCH_2CH=CH_2), 3.80,

3.81, 3.88 (each s, 3×3H, 3×OCH_3), 4.96 (ddt, J=10.0, 1.6, 1.6 Hz, 1H, $ArCH_2CH{=}CH_aH_b$), 4.99 (ddt, J=16.8, 1.6, 1.6 Hz, 1H, $ArCH_2CH{=}CH_aH_b$), 5.12 (s, 2H, $ArO{-}CH_2COAr$), 6.00 (ddt, J=16.8, 10.0, 6.4 Hz, 1H, $ArCH_2CH{=}CH_2$), 6.51 (d, J=9.2 Hz, 1H, ArH), 6.68 (d, J=9.2 Hz, 1H, ArH), 6.94 (d, J=9.2 Hz, 2H, ArH), 8.00 (d, J=9.2 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.4, 55.5, 56.1, 60.9, 72.1, 107.1, 110.2, 113.9, 114.7, 123.8, 127.8, 130.8, 137.1, 147.9, 148.2, 150.8, 164.0, 193.8; EIMS (70 eV) m/z (rel intensity, %) 342 (M^+, 15), 324 (51), 193 (29), 192 (100), 191 (24), 177 (34), 135 (66); ESI-HRMS calcd for $C_{20}H_{22}O_5Na$ $[M+Na]^+$: 365.1365. Found: 165.1363.

*4.2.3. 2-(2-Allyl-3,4-dimethoxyphenoxy)-1-(p-tolyl)-ethanone (**4c**).* (3.03 g, 93%) was obtained as yellow liquid, R_f=0.58 (ethyl acetate: n-hexane=1: 4), IR (KBr) cm^{-1}, ν_{max}: 3065, 2934, 2830, 1698, 1604, 1484, 1254, 1127, 1037, 991, 911, 790; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (s, 3H, CH_3), 3.50 (dt, J=6.0, 1.6 Hz, 2H, $ArCH_2CH{=}CH_2$), 3.80, 3.81 (each s, 2×3H, 2×OCH_3), 4.96 (ddt, J=10.0, 1.6, 1.6 Hz, 1H, $ArCH_2CH{=}CH_aH_b$), 4.99 (ddt, J=16.8, 1.6, 1.6 Hz, 1H, $ArCH_2CH{=}CH_aH_b$), 5.16 (s, 2H, $ArOCH_2COAr$), 6.00 (ddt, J=16.8, 10.0, 6.0 Hz, 1H, $ArCH_2CH{=}CH_2$), 6.50 (d, J=9.0 Hz, 1H, ArH), 6.68 (d, J=9.0 Hz, 1H, ArH), 7.27 (d, J=8.0 Hz, 2H, ArH), 7.90 (d, J=8.0 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7, 28.3, 56.1, 60.9, 72.1, 107.2, 110.1, 114.7, 123.8, 128.4, 129.4, 132.2, 137.0, 144.7, 147.9, 148.1, 150.7, 194.8; EIMS (70 eV) m/z (rel intensity, %) 326 (M^+, 33), 308 (33), 193 (24), 192 (100), 191 (27), 177 (35), 119 (30); HRMS (ESI) Calcd for $C_{20}H_{22}O_4Na$ $[M+Na]^+$: 349.1417. Found: 349.1416.

*4.2.4. 2-(2-Allyl-3,4-dimethoxyphenoxy)-1-(4-chloro-phenyl)-ethanone (**4d**).* Compound **4d** (3.25 g, 94%) was obtained as colorless crystal, mp 78–79 °C, R_f=0.61 (ethyl acetate/n-hexane=1:4), IR (KBr) cm^{-1}, ν_{max}: 3086, 2933, 2836, 1705, 1590, 1486, 1486, 1258, 1090, 987, 956, 926, 826, 799, 742; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.47 (dt, J=6.0, 1.6 Hz, 2H, $ArCH_2CH{=}CH_2$), 3.81, 3.81 (each s, 2×3H, 2×OCH_3), 4.93–4.98 (m, 2H, $ArCH_2CH{=}CH_2$), 5.12 (s, 2H, $ArOCH_2COAr$), 5.97 (ddt, J=15.6, 9.6, 6.0 Hz, 1H, $ArCH_2CH{=}CH_2$), 6.49 (d, J=8.8 Hz, 1H, ArH), 6.69 (d, J=8.8 Hz, 1H, ArH), 7.45 (d, J=8.4 Hz, 2H, ArH), 7.95 (d, J=8.4 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.3, 56.1, 60.9, 72.2, 107.0, 110.0, 114.7, 123.7, 129.1, 129.9, 133.0, 136.9, 140.2, 148.0, 148.2, 150.4, 194.4; EIMS (70 eV) m/z (rel intensity, %) 348 ($[M+2]^+$, 8), 346 (M^+, 21), 193 (20), 192 (100), 191 (27), 178 (20), 177 (38); HRMS (ESI) calcd for $C_{19}H_{19}ClO_4Na$ $[M+Na]^+$: 369.0870. Found: 369.0873. Anal. Calcd for $C_{19}H_{19}ClO_4$: C, 65.80%; H, 5.52%. Found: C, 65.74%; H, 5.51%.

*4.2.5. 2-(2-Allyl-3,4-dimethoxyphenoxy)-1-(4-bromo-phenyl)-ethanone (**4e**).* Compound **4e** (3.80 g, 97%) was obtained as colorless crystal, mp 80–81 °C, R_f=0.59 (ethyl acetate/n-hexane=1:4), IR (KBr) cm^{-1}, ν_{max}: 3085, 2933, 2836, 1705, 1587, 1486, 1255, 1224, 1127, 1073, 986, 956, 925, 821; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.47 (dt, J=6.0, 1.6 Hz, 2H, $ArCH_2CH{=}CH_2$), 3.81, 3.81 (each s, 2×3H, 2×OCH_3), 4.93–4.98 (m, 2H, $ArCH_2CH{=}CH_2$), 5.12 (s, 2H, $ArOCH_2COAr$), 5.97 (ddt, J=15.6, 9.6, 6.0 Hz, 1H, $ArCH_2CH{=}CH_2$), 6.49 (d, J=8.8 Hz, 1H, ArH), 6.69 (d, J=8.8 Hz, 1H, ArH), 7.62 (d, J=9.0 Hz, 2H, ArH), 7.87 (d, J=9.0 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.3, 56.1, 60.9, 72.2, 107.0, 110.0, 114.7, 123.7, 129.0, 130.0, 132.0, 133.4, 136.9, 148.0, 148.2, 150.4, 194.7; EIMS (70 eV) m/z (rel intensity, %) 392 ($[M+2]^+$, 8), 390 (M^+, 11), 374 (12), 372 (12), 207 (19), 193 (20), 192 (100), 191 (24), 178 (18), 177 (35); HRMS (ESI) calcd for $C_{19}H_{19}BrO_4Na$ $[M+Na]^+$: 413.0364. Found: 413.0363. Anal. Calcd for $C_{19}H_{19}BrO_4$: C, 58.33%; H, 4.89%. Found: C, 58.19%; H, 4.85%.

4.3. General procedure for the preparation of *trans*- and *cis*-2-aryloyl-5,6-dimethoxy-3-methylchroman (5a–e)

Under the protection of N_2, **4a–e** (10.0 mmol) dissolved in THF (20.0 mL) was stirred and heated to the reflux. To this refluxing solution, potassium *tert*-butoxide (2.3 g, 20.5 mmol) in THF (20 mL) was added in drops. The reaction mixture was continually kept at the reflux for 30 min until TLC analysis showed complete consumption of the starting material. After cooling to room temperature, the reaction mixture was quenched with an aqueous saturated NH_4Cl solution (25 mL), and concentrated in *vacuo* to remove THF. The water suspension that was obtained was extracted with CH_2Cl_2 (20 mL×3). The organic extracts were combined, washed with brine (10 mL×2), and dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated in vacuo to remove the solvent. The residue was purified by silica gel column (ethyl acetate/n-hexane=1:5) to obtain a diasteromeric mixture **5a–e**, which was directly used for next oxidation reaction. For spectrometric data and the ratio of resultant isomers, a batch of diasteromeric mixture was further subjected to silica gel column chromatography (ethyl acetate/n-hexane=1:20) to give *trans*-**5a–e** as major and *cis*-**5a–e** as minor compounds, respectively.

*4.3.1. The diasteromeric mixture of 2-benzoyl-5,6-dimethoxy-3-methylchroman (**5a**).* Compound **5a** (2.69 g, 86%) was obtained as yellow liquid. *trans*-2-Benzoyl-5,6-dimethoxy-3-methylchroman (*trans*-**5a**) (1.85 g, 59%) was obtained as yellow liquid, R_f=0.61 (ethyl acetate/n-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.09 (d, J=6.4 Hz, 3H, CH_3), 2.44–2.52 (m, 1H, H-3), 2.44–2.52 (m, 1H, H-4a), 2.89 (dd, J=19.6, 8.4 Hz, 1H, H-4b), 3.82, 3.83 (each s, 2×3H, 2×OCH_3), 4.96 (d, J=7.2 Hz, 1H, H-2), 6.62 (d, J=9.0 Hz, 1H, ArH), 6.74 (d, J=9.0 Hz, 1H, ArH), 7.47 (t, J=9.2 Hz, 2H, ArH), 7.59 (t, J=7.2 Hz, 1H, ArH), 8.04 (d, J=8.0 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 26.3, 28.4, 56.3, 60.2, 82.0, 110.9, 111.6, 115.9, 128.6, 129.0, 133.5, 135.2, 146.6, 146.9, 147.6, 197.2; *cis*-**5**a (0.84 g, 27%) was obtained as yellow liquid, R_f=0.56 (ethyl acetate/n-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.92 (d, J=6.8 Hz, 3H, CH_3), 2.59–2.68 (m, 1H, H-3), 2.74 (dd, J=17.2, 2.8 Hz, 1H, H-4a), 3.08 (dd, J=17.2, 6.0 Hz, 1H, H-4b), 3.84, 3.84 (each s, 2×3H, 2×OCH_3), 5.35 (d, J=2.0 Hz, 1H, H-2), 6.72 (d, J=8.8 Hz, 1H, ArH), 6.76 (d, J=8.8 Hz, 1H, ArH), 7.49 (t, J=7.6 Hz, 2H, ArH), 7.61 (t, J=7.2 Hz, 1H, ArH), 7.97 (d, J=7.6 Hz, 2H, ArH), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.5, 28.0, 28.5, 56.3, 60.2, 79.5, 111.5, 111.6, 115.6, 128.5, 128.7, 133.4, 135.6, 147.8, 147.9, 196.9; EIMS (70 eV) m/z (rel intensity, %) 312 (M^+, 36), 207 (100), 192 (26), 179 (18), 176 (16), 151 (25); ESI-HRMS calcd for $C_{19}H_{20}O_4Na$ $[M+Na]^+$: 335.1259. Found: 335.1261.

*4.3.2. The diasteromeric mixture of 2-(4-methoxyl-benzoyl)-5,6-dimethoxy-3-methylchroman (**5b**).* Compound **5b** (2.88 g, 84%) was obtained as yellow viscous liquid. *trans*-2-(4-Methoxylbenzoyl)-5,6-dimethoxy-3-methylchroman (*trans*-**5b**) (2.18 g, 64%) was obtained as yellowish crystal, mp 109–111 °C, R_f=0.51 (ethyl acetate/n-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.07 (d, J=6.4 Hz, 3H, CH_3-3), 2.42–2.49 (m, 1H, H-3), 2.42–2.49 (m, 1H, H_a-4), 2.91 (dd, J=20.0, 8.8 Hz, 1H, H_b-4), 3.82, 3.83, 3.87 (each s, 3×3H, 3×OCH_3), 4.88 (d, J=7.6 Hz, 1H, H-2), 6.62 (d, J=9.2 Hz, 1H, ArH), 6.74 (d, J=9.2 Hz, 1H, ArH), 7.94 (d, J=8.8 Hz, 2H, ArH), 8.05 (d, J=8.8 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 26.7, 28.6, 55.5, 56.4, 60.2, 82.1, 110.9, 111.7, 113.8, 116.1, 128.2, 131.5, 146.5, 146.9, 147.8, 163.8, 195.5; *cis*-**5b** (0.70 g, 20%) was obtained as brownish liquid, δ 0.93 (d, J=6.8 Hz, 3H, CH_3-3), 2.59–2.66 (m, 1H, H-3), 2.73 (dd, J=17.2, 2.8 Hz, 1H, H_a-4), 3.07 (dd, J=17.2, 6.4 Hz, 1H, H_b-4), 3.82, 3.83, 3.88 (each s, 3×3H, 3×OCH_3), 5.29 (d, J=2.0 Hz, 1H, H-2), 6.71 (d, J=8.8 Hz, 1H, ArH), 6.75 (d, J=8.8 Hz, 1H, ArH), 6.96 (d, J=8.8 Hz, 2H, ArH), 7.99 (d, J=8.8 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.5, 28.0, 29.7, 55.5, 56.4, 60.2, 79.3, 111.5, 111.6, 113.8, 115.7, 128.4, 131.0, 146.7, 147.4, 148.0, 163.7, 195.2; EIMS (70 eV) m/z (rel intensity, %) 342 (M^+, 37), 207 (100), 192 (59), 179 (25), 176 (22), 151 (33), 136 (26), 135 (76); ESI-HRMS calcd for $CH_{18}O_3Na$ $[M+Na]^+$: 365.1365. Found: 365.1363.

*4.3.3. The diasteromeric mixture of 2-(4-methyl-benzoyl)-5,6-dimethoxy-3-methylchroman (**5c**).* Compound **5c** (2.90 g, 89%) was

obtained as viscous yellow liquid. *trans*-2-(4-methylbenzoyl)-5,6-dimethoxy-3-methylchroman (*trans*-**5c**) (2.1 g, 64%) was obtained as yellowish crystal, mp 120–121 °C, R_f=0.61 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.07 (d, *J*=6.0 Hz, 3H, CH_3-3), 2.42 (s, 3H, CH_3-4′), 2.43–2.50 (m, 1H, H-3), 2.47 (dd, *J*=20.0 Hz, 8.4 Hz, 1H, H_a-4), 2.89 (dd, *J*=20.0 Hz, 8.4 Hz, 1H, H_b-4), 3.82, 3.82 (each s, 2×3H, 2×OCH_3), 4.93 (d, *J*=7.6 Hz, 1H, H-2), 6.62 (d, *J*=8.8 Hz, 1H, ArH), 6.74 (d, *J*=8.8 Hz, 1H, ArH), 7.27 (d, *J*=8.4 Hz, 2H, ArH), 7.95 (d, *J*=8.4 Hz, 2H, ArH), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 21.7, 26.4, 28.5, 56.4, 60.2, 81.9, 110.9, 111.7, 116.0, 129.2, 129.3, 132.7, 144.4, 146.5, 146.9, 147.7, 196.7; *cis*-**5c** (0.81 g, 25%) was obtained as yellow liquid, R_f=0.56 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 (d, *J*=6.8 Hz, 3H, CH_3-3), 2.43 (s, 3H, CH_3-4′), 2.59–2.66 (m, 1H, H-3, H-3), 2.73 (dd, *J*=17.2, 2.8 Hz, 1H, H_a-4), 3.01 (dd, *J*=17.2, 6.4 Hz, 1H, H_b-4), 3.82, 3.84 (each s, 2×3H, 2×OCH_3), 5.33 (d, *J*=2.4 Hz, 1H, H-2), 6.72 (d, *J*=9.0 Hz, 1H, ArH), 6.76 (d, *J*=9.0 Hz, 1H, ArH), 7.28 (d, *J*=8.8 Hz, 2H, ArH), 7.87 (d, *J*=8.8 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.5, 21.7, 28.0, 28.5, 56.3, 60.2, 79.5, 111.5, 111.6, 115.6, 128.5, 128.7, 133.4, 135.6, 147.8, 147.4, 147.9, 196.9; EIMS (70 eV) *m*/*z* (rel intensity, %) 326 (M^+, 71), 207 (100), 192 (38), 179 (21), 176 (18), 151 (28), 119 (17); ESI-HRMS calcd for $C_{20}H_{22}O_4Na$ $[M+Na]^+$: 349.1416. Found: 349.1414.

*4.3.4. The diasteromeric mixture of 2-(4-chlorobenzoyl)-5,6-dimethoxy-3-methylchroman (**5d**).* Compound **5d** (2.74 g, 79%) was obtained as viscous yellow liquid. *trans*-2-(4-chloro-benzoyl)-5,6-dimethoxy-3-methylchroman (*trans*-**5d**) (1.73 g, 50%) was obtained as orange color crystal, mp 101–102 °C, R_f=0.62 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (d, *J*=6.4 Hz, 3H, CH_3-3), 2.43–2.50 (m, 1H, H-3), 2.46 (dd, *J*=20.4, 8.8 Hz, 1H, H_a-4), 2.88 (dd, *J*=20.4, 8.8 Hz, 1H, H_b-4), 3.82, 3.83 (each s, 2×3H, 2×OCH_3), 4.84 (d, *J*=7.6 Hz, 1H, H-2), 6.60 (d, *J*=8.8 Hz, 1H, ArH), 6.74 (d, *J*=8.8 Hz, 1H, ArH), 7.44 (d, *J*=8.4 Hz, 2H, ArH), 8.01 (d, *J*=8.8 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 26.6, 28.3, 56.4, 60.2, 82.5, 110.9, 111.8, 116.0, 128.9, 130.6, 133.6, 140.0, 146.7, 146.9, 147.4, 196.1; *cis*-**5d** (1.01 g, 29%) was obtained as yellow liquid, R_f=0.57 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (d, *J*=6.8 Hz, 3H, CH_3-3), 2.60–2.65 (m, 1H, H-3), 2.74 (dd, *J*=16.8, 2.8 Hz, 1H, H_a-4), 3.06 (dd, *J*=16.8, 6.0 Hz, 1H, H_b-4), 3.82, 3.84 (each s, 2×3H, 2×OCH_3), 5.24 (d, *J*=2.4 Hz, 1H, H-2), 6.69 (d, *J*=9.2 Hz, 1H, ArH), 6.75 (d, *J*=9.2 Hz, 1H, ArH), 7.46 (d, *J*=8.6 Hz, 2H, ArH), 7.94 (d, *J*=8.6 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6, 27.9, 28.4, 56.4, 60.2, 79.7, 111.4, 111.7, 115.7, 129.0, 130.2, 133.9, 139.8, 146.9, 147.4, 147.7, 196.0; EIMS (70 eV) *m*/*z* (rel intensity, %) 348 ($[M+2]^+$, 9), 346 (M^+, 26), 207 (100), 192 (22), 179 (17), 151 (20); ESI-HRMS calcd for $C_{19}H_{19}ClO_4Na$ $[M+Na]^+$: 369.0870. Found: 369.0871.

*4.3.5. The diasteromeric mixture of 2-(4-bromo-benzoyl)-5,6-dimethoxy-3-methylchroman (**5e**).* Compound **5e** (3.12 g, 80%) was obtained as viscous yellow liquid. *trans*-2-(4-bromobenzoyl)-5,6-dimethoxy-3-methylchroman (*trans*-**5e**) (2.29 g, 59%) was obtained as orange color crystal, mp 99–100 °C, R_f=0.59 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (d, *J*=6.0 Hz, 3H, CH_3-3), 2.43–2.50 (m, 1H, H-3), 2.46 (dd, *J*=20.4, 8.4 Hz, 1H, H_a-4), 2.93 (dd, *J*=20.4, 8.4 Hz, 1H, H_b-4), 3.82, 3.83 (each s, 2×3H, 2×OCH_3), 4.84 (d, *J*=7.6 Hz, 1H, H-2), 6.60 (d, *J*=9.0 Hz, 1H, ArH), 6.74 (d, *J*=9.0 Hz, 1H, ArH), 7.61 (d, *J*=8.6 Hz, 2H, ArH), 7.93 (d, *J*=8.6 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 26.5, 28.3, 56.4, 60.2, 82.5, 110.9, 111.7, 116.0, 128.7, 130.7, 131.9, 133.9, 146.7, 146.9, 147.3, 196.3; *cis*-**5e** (0.83 g, 21%) was obtained as yellow liquid, R_f=0.55 (ethyl acetate/*n*-hexane=1:4), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (d, *J*=7.2 Hz, 3H, CH_3-3), 2.60–2.65 (m, 1H, H-3), 2.74 (dd, *J*=16.8, 2.8 Hz, 1H, H_a-4), 3.06 (dd, *J*=16.8, 6.4 Hz, 1H, H_b-4), 3.82, 3.84 (each s, 2×3H, 2×OCH_3), 5.23 (d, *J*=2.0 Hz, 1H, H-2), 6.69 (d, *J*=8.6 Hz, 1H, ArH), 6.75 (d, *J*=8.6 Hz, 1H, ArH), 7.63 (d, *J*=8.8 Hz, 2H, ArH), 7.86 (d, *J*=8.8 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6, 27.9, 28.4, 56.3, 60.2, 79.7, 111.4, 111.6, 115.7, 128.6, 130.2, 132.0, 134.4, 146.9, 147.4, 147.7, 196.2; EIMS (70 eV) *m*/*z* (rel intensity, %) 392 ($[M+2]^+$, 15), 390 (M^+, 21), 207 (100), 192 (23), 179 (14), 151 (18); ESI-HRMS calcd for $C_{19}H_{19}BrO_4Na$ $[M+Na]^+$: 413.0364. Found: 413.0362.

4.4. General procedure for the preparation of 2-benzoyl-5,6-dimethoxy-3-methylchromen-4-ones (6a–e)

The diastereomeric mixture of **5a**–**e** (5.0 mmol) dissolved in 1,4-dioxane (10.0 mL) was stirred and added DDQ (3.4 g, 15.0 mmol). The resultant mixture was heated to the reflux for 3 days until TLC analysis showed the consumption of the starting material. The resultant mixture, which was cooled to room temperature was added water (30 mL) and extracted with dichloromethane (20 mL×3). The organic extracts were combined, washed with brine (10 mL×2), and dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated in vacuo to remove the solvent. The residue was purified by silica gel column chromatography (ethyl acetate/*n*-hexane=1:5) to give **6a**–**e**.

*4.4.1. 2-Benzoyl-5,6-dimethoxy-3-methyl-1-chromen-4-one (**6a**).* Pure **6a** (1.0 g, 62%) was obtained as yellow crystal, mp 118–120 °C, R_f=0.44 (ethyl acetate/*n*-hexane=1:2), IR (KBr) cm^{-1}, ν_{max}: 2932, 1646, 1482, 1368, 1260, 1168, 1095, 1054, 1012, 936, 800, 716; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03 (s, 3H, CH_3), 3.93, 3.99 (each s, 2×3H, 2×OCH_3), 7.15 (d, *J*=9.6 Hz, 1H, H-8), 7.31 (d, *J*=9.6 Hz, 1H, H-7), 7.51–7.56 (m, 2H, H-3′), 7.66–7.70 (m, 1H, H-4′), 7.91–7.94 (m, 2H, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.1, 57.1, 61.8, 113.5, 118.4, 119.4, 119.5, 129.0, 130.0, 134.7, 134.9, 147.6, 150.1, 150.6, 154.1, 177.8, 188.9; EIMS (70 eV) *m*/*z* (rel intensity, %) 324 (M^+, 49), 310 (21), 309 (100), 295 (34), 281 (36), 105 (43), 77 (19); ESI-HRMS calcd for $C_{19}H_{16}O_5Na$ $[M+Na]^+$: 347.0895. Found: 347.0897. Anal. Calcd for $C_{19}H_{16}O_5$: C, 70.36%; H, 4.97%. Found: C, 70.12%; H, 5.01%.

*4.4.2. 5,6-Dimethoxy-2-(4-methoxybenzoyl)-3-methyl-1-chromen-4-one (**6b**).* Pure **6b** (1.01 g, 57%) was obtained as yellow crystal, mp 171–173 °C, R_f=0.24 (ethyl acetate/*n*-hexane=1:2), IR (KBr) cm^{-1}, ν_{max}: 2931, 2837, 1652, 1599, 1479, 1429, 1367, 1256, 1168, 1096, 1052, 1012, 934, 837, 799; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.99 (s, 3H, CH_3), 3.91, 3.93, 3.99 (each s, 3×3H, 3×OCH_3), 6.99 (d, *J*=8.8 Hz, 2H, H-3′), 7.16 (d, *J*=8.8 Hz, 1H, H-8), 7.31(d, *J*=8.8 Hz, 1H, H-7), 7.91 (d, *J*=8.8 Hz, 2H, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.4, 55.9, 57.3, 62.0, 113.8, 114.5, 114.6, 118.7, 119.0, 119.5, 128.0, 132.8, 147.8, 150.3, 151.0, 155.0, 165.2, 187.5; EIMS (70 eV) *m*/*z* (rel intensity, %) 354 (M^+, 51), 340 (21), 339 (100), 325 (18), 311 (28), 135 (76), 77 (14); ESI-HRMS calcd for $C_{20}H_{18}O_6Na$ $[M+Na]^+$: 377.1001. Found: 377.1002. Anal. Calcd for $C_{20}H_{18}O_6$: C, 67.79%; H, 5.12%. Found: C, 67.74%; H, 5.12%.

*4.4.3. 5,6-Dimethoxy-3-methyl-2-(4-methylbenzoyl)-1-chromen-4-one (**6c**).* Pure **6c** (1.02 g, 60%) was obtained as brown crystal, mp 153–155 °C, R_f=0.40 (ethyl acetate/*n*-hexane=1:2), IR (KBr) cm^{-1}, ν_{max}: 2933, 1631, 1478, 1425, 1368, 1264, 1163, 1095, 1054, 1003, 931, 799, 764, 616; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.00 (s, 3H, CH_3-3), 2.46 (s, 3H, CH_3-4′), 3.94, 4.00 (each s, 2×3H, 2×OCH_3), 7.16 (d, *J*=9.2 Hz, 1H, H-8), 7.32 (d, *J*=9.2 Hz, 1H, H-7), 7.33 (d, *J*=8.0 Hz, 2H, H-3′), 7.83 (d, *J*=8.4 Hz, 2H, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.1, 21.9, 57.0, 61.7, 113.5, 118.4, 119.1, 119.3, 129.70, 130.1, 132.3, 146.0, 147.6, 150.0, 150.6, 154.4, 177.8, 188.4; EIMS (70 eV) *m*/*z* (rel intensity, %) 338 (M^+, 35), 324 (20), 323 (100), 309 (15) 295 (29), 119 (41), 91 (19); ESI-HRMS calcd for $C_{20}H_{18}O_5Na$ $[M+Na]^+$: 361.1052. Found: 361.1050. Anal. Calcd for $C_{20}H_{18}O_5$: C, 70.99%; H, 5.36%. Found: C, 70.85%; H, 5.35%.

*4.4.4. 2-(4-Chlorobenzoyl)-5,6-dimethoxy-3-methyl-1-chromen-4-one (**6d**).* Pure **6d** (1.08 g, 60%) was obtained as yellow crystal, mp 161–162 °C, R_f=0.46 (ethyl acetate/*n*-hexane=1:2), IR (KBr) cm^{-1},

ν_{max}: 2943, 1646, 1579, 1581, 1481, 1366, 1236, 1167, 1087, 1050, 1001, 927, 844, 799, 769, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04 (s, 3H, CH_3), 3.93, 3.99 (each s, 2×3H, 2×OCH_3), 7.14 (d, J=9.2 Hz, 1H, H-8), 7.32 (d, J=9.2 Hz, 1H, H-7), 7.51 (d, J=8.4 Hz, 2H, H-3′), 7.86 (d, J=8.4 Hz, 2H, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.1, 57.0, 61.8, 113.4, 118.4, 119.4, 120.0, 129.4, 131.3, 133.3, 141.3, 147.6, 150.1, 150.5, 153.5, 177.7, 187.7; EIMS (70 eV) m/z (rel intensity, %) 360 ([M+2]$^+$, 16), 358 (M$^+$, 44), 345 (33), 343 (100), 329 (24), 315 (36), 139 (45); ESI-HRMS calcd for $C_{19}H_{15}ClO_5Na$ [M+Na]$^+$: 381.0506. Found: 381.0503. Anal. Calcd for $C_{19}H_{15}ClO_5$: C, 63.61%; H, 4.21%. Found: C, 63.27%; H, 4.29%.

*4.4.5. 2-(4-Bromobenzoyl)-5,6-dimethoxy-3-methyl-1-chromen-4-one (**6e**).* Pure **6e** (1.39 g, 69%) was obtained as yellow crystal, mp 178–180 °C, R_f=0.47 (ethyl acetate/n-hexane=1:2), IR (KBr) cm^{-1}, ν_{max}: 2953, 1649, 1579, 1478, 1368, 1236, 1167, 1058, 1004, 932, 806, 770; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04 (s, 3H, CH_3), 3.93, 3.99 (each s, 2×3H, 2×OCH_3), 7.14 (d, J=9.6 Hz, 1H, H-8), 7.32 (d, J=9.2 Hz, 1H, H-7), 7.68 (d, J=8.4 Hz, 2H, H-3′), 7.78 (d, J=8.4 Hz, 2H, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.1, 57.0, 61.8, 113.4, 118.4, 119.4, 120.0, 130.1, 131.3, 132.4, 133.7, 147.6, 150.1, 150.4, 153.4, 177.7, 182.0; EIMS (70 eV) m/z (rel intensity, %) 404 ([M+2]$^+$, 39), 402 (M$^+$, 40), 389 (97), 387 (100), 361 (31), 359 (33), 185 (46), 183 (46); ESI-HRMS calcd for $C_{19}H_{15}BrO_5Na$ [M+Na]$^+$: 425.0001. Found: 424.9999. Anal. Calcd for $C_{19}H_{15}BrO_5$: C, 56.59%; H, 3.75%. Found: C, 56.44%; H, 3.77%.

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