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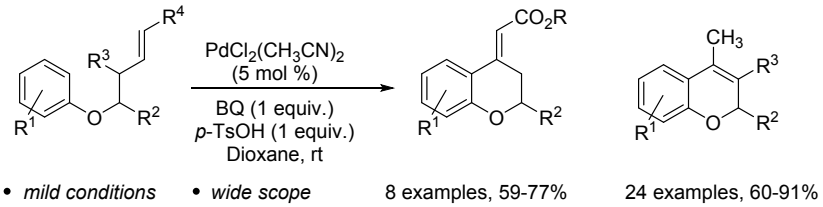


Abstract. The intramolecular Pd(II)-catalyzed alkenylation of aryl homoallyl ethers constitutes a mild, versatile, and efficient procedure for the synthesis of highly and diversely substituted chromanes, and 2*H*-chromenes. The use of *p*-TsOH as additive allows more efficient reactions that could be carried out a room temperature in most cases. The procedure has a wide scope, allowing the synthesis of alkylidenechromanes and 2*H*-chromenes substituted at C-2 or C-3 of the chromene moiety, thus accessing relevant flavenes and isoflavenes, and even coumarins, in high yields (59 to 91%, 32 examples)

Introduction

Carbon-carbon bond formation through transition metal-catalyzed cross-coupling reactions constitutes one of the most powerful tools both in industry and academic organic synthesis.[1] Oxidative-coupling reactions,[2] particularly palladium (II)-catalyzed intramolecular C-H alkenylation reaction of arenes and heteroarenes, provide a direct route to carbocyclic and heterocyclic frameworks.[3] In contrast to the

Mizoroki-Heck reaction, this atom-economical approach eliminates the need for preactivated coupling partners (halides or triflates), although a stoichiometric oxidant is required to regenerate the Pd(II) active species. The intramolecular variant is mainly limited to C-H alkenylation of electron-rich heteroarenes (e.g. indole and pyrrole) and/or to the construction of five-membered rings. Representative examples include aerobic oxidative annulations of indoles and pyrroles for the construction of five-, six- and even seven-membered rings[4] and cyclization of allyl aryl ethers for the synthesis of benzofuran derivatives.[5] The potential of these Pd(II)-catalyzed alkenylations has also been shown in the synthesis of pyrrole-containing natural products, such as (±)-rhazinal[6] or dragmacidins.[7]

Depending on the structural features of the substrate and the experimental conditions, different mechanistic pathways can operate (i.e. arene metalation-alkene insertion or alkene activation-arene insertion), which in turn may lead to different regioisomeric products. For example, Pd(II)-catalyzed intramolecular reactions of *N*-phenylacrylamides in the presence of Pd(II) catalysts and oxidants has been reported to afford oxindoles,[8] and even when β-hydride elimination is not allowed, the Ar-Pd(II)-intermediate undergoes a 5-*exo*-trig cyclization followed by nucleophile capture[9] or subsequent C-H alkylation.[10] However, the reaction can be directed to the β–position, achieving the selective intramolecular C–H alkenylation of related *N*-alkyl substituted *N*-phenylacrylamides to give 4-substituted quinolin-2[*1H*]-ones.[11]

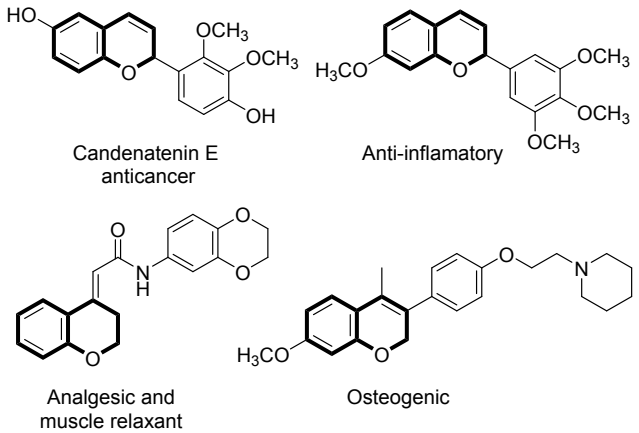
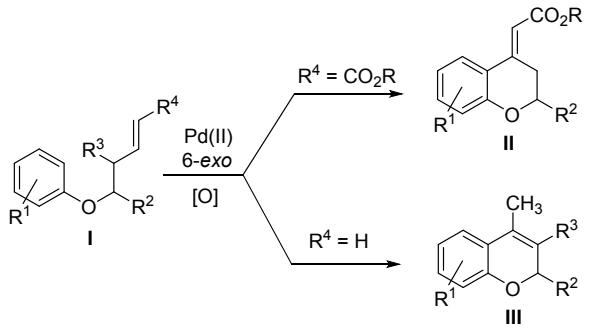


Figure 1. Biologically active 2*H*-chromene and chromane derivatives

To expand the synthetic utility of this procedure, we decided to investigate C–H alkenylation reactions for the synthesis of oxygen heterocycles, such as chromanes. The chromane and 2*H*-chromene moieties are important structural motifs present in a wide variety of bioactive natural products,[12] pharmaceuticals[13] and photochromic materials for different applications (laser dyes, fluorescence probes, etc.).[14] For example, 4-alkylidenechromanes have shown their potential as antagonists of transient receptor type 1 (TRPV1)[15] for pain relief[16] and as muscle relaxants.[17] Besides, they are used as building blocks in the synthesis of 6-oxastereoid derivatives.[18] On the other hand, flav-2-enes, (2-aryl-2*H*-chromenes), have shown anticancer, anti-inflammatory or antiviral activity,[19] while isoflavenes (3-ary-2*H*-chromenes) have been recently identified as novel potential osteogenic agents[20] (Figure 1). Therefore, rapid access to chromenes bearing substituents at specific positions is of great interest to both synthetic and medicinal chemistry. Chromenes have been prepared via intramolecular cyclization of advanced intermediates using metal-free Bronsted and Lewis acid/base catalysis and transition-metal catalyzed reactions,[21] although only a few examples of oxidative C-H alkenylation reactions have been described for the synthesis of chromenes. Youn reported the Pd(II)-catalyzed oxidative cyclization of ally aryl ethers to obtain benzofurans, through a Claisen rearrangement followed by an oxidative 5-*exo*-trig cyclization. The procedure could also be extended to homoallyl ethers, obtaining *2H*-chromenes after isomerization of the initially formed exocyclic double bond.[22] Besides, the carbonylative cyclization of aryl homoallyl ethers has also been reported for the synthesis of 4-substituted chromanes.[23] We have recently described the use of Pd(II)-catalyzed intramolecular alkenylation reaction of *N*-protected homoallyl anilines to access quinolines and dihydroquinolines, through 6-*exo* cyclization processes. Thus, starting from the same precursor, conditions could be selected to favor the one pot formation of 4-substituted quinolines. Under milder reaction conditions, 1,2-dihydroquinolines were obtained after isomerization of the double bond.[24] This procedure would be complementary to the related Mizoroki-Heck reaction that led to the formation of 4-methylidenetetrahydroquinolines.[25]

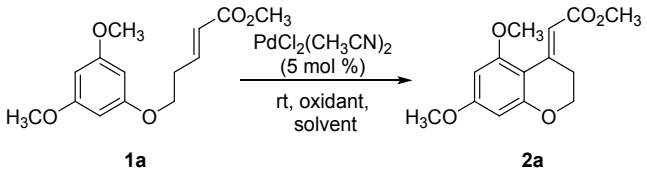
Results and Discussion

In connection with our interest in palladium catalyzed cyclization reactions,[11,24,25,26] our goal was to expand the synthetic utility of this type of 6-*exo* intramolecular alkenylation reaction into the synthesis of chromanes and 2*H*-chromenes. We reasoned that a Pd(II)-oxidative cyclization could be applied for the synthesis of 4-akylidenechromanes, avoiding the isomerization of the double bond. Thus, if a 5-aryloxypent-2-enoate such as **I** ($R^4 = CO_2R$) (Scheme 1) is selected as a substrate, the presence of the conjugated alkoxycarbonyl group would prevent the exocyclic/endocyclic isomerization of the double bond, leading to the formation of **II.** Without the presence of the ester group ($R^4 = H$), the initially formed exocyclic double bond would be expected to isomerize to the more stable endocyclic double bond, leading to the formation of 2*H*-chromenes. We decided to study the applicability of this reaction to the synthesis of diversely substituted chromanes **I** and 2*H*-chromenes **II**, including flavenes ($R^2 = Ar$) and isoflavenes ($R^3 = Ar$)



Scheme 1. Pd(II)-catalyzed cyclization of 5-aryloxypent-2-enoates ($R^4 = CO_2R$) and homoallyl ethers ($R^4 = H$)

Table 1. Cyclization of **1a**.



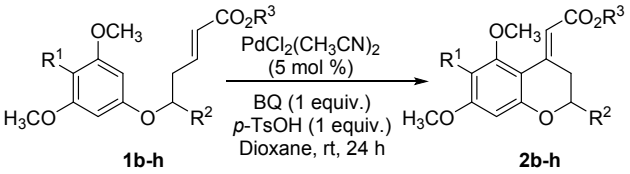
	[O][a]	additive [a]	solvent	t (h)	**2a**(%)[b]
1	$PhCO_3tBu$[c]	p-TsOH	AcOH	24	[d]
2	F+[c]	*p*-TsOH	AcOH	24	[d]
3	F+[c]	*p*-TsOH	mesitylene	24	[d]
4	*p*-BQ	Na_2CO_3	dioxane	96	[e]
5	*p*-BQ[f]	Na_2CO_3	dioxane	48	[e]
6	*p*-BQ[g]	Na_2CO_3	dioxane[h]	24	[e]
7	*p*-BQ	-	dioxane	48	74
8	Ag(OAc)	-	dioxane	120	[e]
9	*p*-BQ	Ag_2CO_3	dioxane	24	56
10	*p*-BQ	*p*-TsOH	dioxane	24	73

[a]1 equiv. [b]Yield of isolated pure compound. [c]$Cu(OAc)_2$ (5 mol %) was used as co-oxidant. [d]Decomposition. [e]Unreacted **1a** (95-100%) was recovered. [f]$Pd(OAc)_2$ (5 mol %) was used. [g]$Pd(OAc)_2$ (10 mol %) was used. [h]The reaction was performed at 70 ºC

First, 5-aryloxypent-2-enoate **1a** was selected as a substrate to test the reaction (Table 1). For that purpose we started from the conditions previously optimized for the obtention of quinolones[11] (Table 1, entry 1) or quinolines[24] (Table 1, entry 2) using $PdCl_2(CH_3CN)_2$ (5 mol %) as catalyst, in the presence of *p*-TsOH and using *t*-butyl perbenzoate or *N*-fluoro-2,4,6-trimethylpyridinium triflate (F^+) as oxidant. However, only decomposition was observed in acetic acid or in mesitylene (entry 3) at room temperature. Next, we tested the conditions previously reported for the cyclization of homoallyl ethers,[22] in the presence of a base and using *p*-benzoquinone as the oxidant (entry 4), but no evolution of the substrate was achieved. No reactivity was observed when $Pd(OAc)_2$ was used as catalyst (entry 5), not

even with higher catalyst loading and at 70ºC (entry 6). In fact, the base had a detrimental effect as **2a** was obtained in a good yield with complete regio- and diastereoselectivity with no base over 48 h (entry 7). The use of silver (I) as an oxidant was not efficient (entry 8), while in combination with *p*-benzoquinone gave a moderate yield of **2a** after 24 h (entry 9). Finally, the addition of *p*-TsOH enhanced the reactivity, probably generating a more electrophilic Pd(II) species,[27] and the reaction time could be shortened to 24 h, with no loss of yield (entry 10 *vs*. 7).

Table 2. Synthesis of chromanes **2b-h**



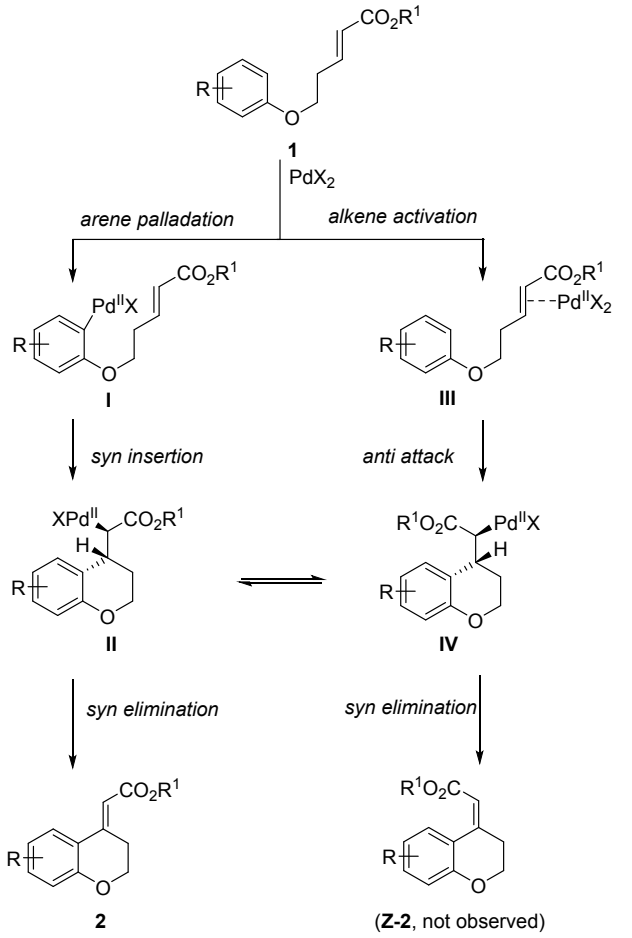
	1	R^1	R^2	R^3	**2**	Yield (%)[a]
1	**1b**	H	CH_3	CH_3	**2b**	80
2	**1c**	H	Ph	CH_3	**2c**	59
3	**1d**	H	H	Et	**2d**	49
4	**1d**[b]	H	H	Et	**2d**	77
5	**1e**	H	H	*n*-Bu	**2e**	44
6	**1e**[b]	H	H	*n*-Bu	**2e**	70
7	**1f**	H	H	*t*-Bu	**2f**	35
8	**1f**[b]	H	H	*t*-Bu	**2f**	59
9	**1g**[b]	H	CH_3	*t*-Bu	**2g**	69
10	**1h**[b]	OCH_3	CH_3	CH_3	**2h**	60

[a]Yield of isolated pure compound. [b] $PdCl_2(CH_3CN)_2$ (10 mol %) was used.

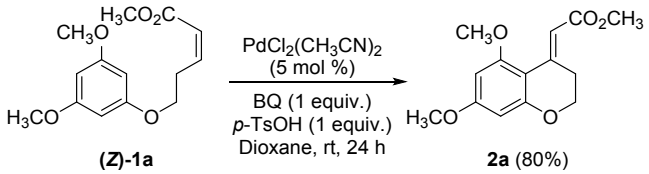
Once the reaction conditions had been selected, we extended the reaction into the synthesis of different chromanes **2b-h** (Table 2). Substitution at C-2 is tolerated (Table 2, entries 1, 9, 10) and, thus, flavan **2c** could also be accessed (Table 2, entry 2). Different substitution at the ester moiety is also allowed;

however, the reactions did not proceed to full conversion in 24 h (Table 2, entries 3, 5, 7), so an increase of the catalyst loading (10 mol %) was required to obtain good yields within the same reaction time (Table 2, entries 4, 6, 8). Besides, the reaction could also extended to a 6,7,8-trimethoxy substituted chromane, such as **2h** (entry 10). All chromanes **2a-h** were obtained with complete stereoselectivity, as *E* diastereomers, and as single regioisomers.

Two related reaction mechanisms could be proposed for this cyclization (Scheme 2). On one hand, C-H electrophilic palladation of the aromatic ring with a cationic palladium species (favored by the addition of *p*-TSOH) could occur to obtain an aryl palladium (II) intermediate **I**, which would undergo a *syn* olefin insertion to afford **II**. Subsequent *syn* β-hydride elimination is possible to give the observed *E* stereochemistry for the alkene in **2**. This mechanism has been proposed for related alkenylations of electron rich aromatic systems,[5,11] so this reaction would be considered as an intramolecular Fujiwara-Moritani reaction or dehydrogenative Heck reaction.[28] On the other hand, a Pd(II) alkene activation followed by *anti* nucleophilic attack of the arene to the Pd(II) π complex,[22,29] would lead to a diastereomeric intermediate such as **IV**. In this case, alignment of the C(sp^3)-Pd(II) and C(sp^3)-H bonds required for the direct *syn* β-hydride elimination on **IV** would give the *Z*-configured **2** (**Z-2**), which is not detected in any case. An *anti* elimination would thus be required for the obtention of **2,** with the observed *E*-configuration, from **IV**. However, **IV** could undergo epimerization at the α carbon through the formation of an oxo-π-allylpalladium(II) intermediate[29b] to form **II**, allowing the *syn* β- elimination to obtain **2** with the observed *E*-configuration. To check if this was possible, we carried out the cyclization of **(*Z*)-1a** and, under the same reaction conditions, **2a** was obtained in comparable yield with complete diastereoselectivity (Scheme 3). Thus, the reaction is not stereospecific. This does not rule out either mechanism, but shows that palladium enolate intermediate could epimerize, to give the more stable *E* diastereomer after *syn*-elimination.



Scheme 2. Possible pathways for palladation**:** arene palladation *vs*. alkene activation

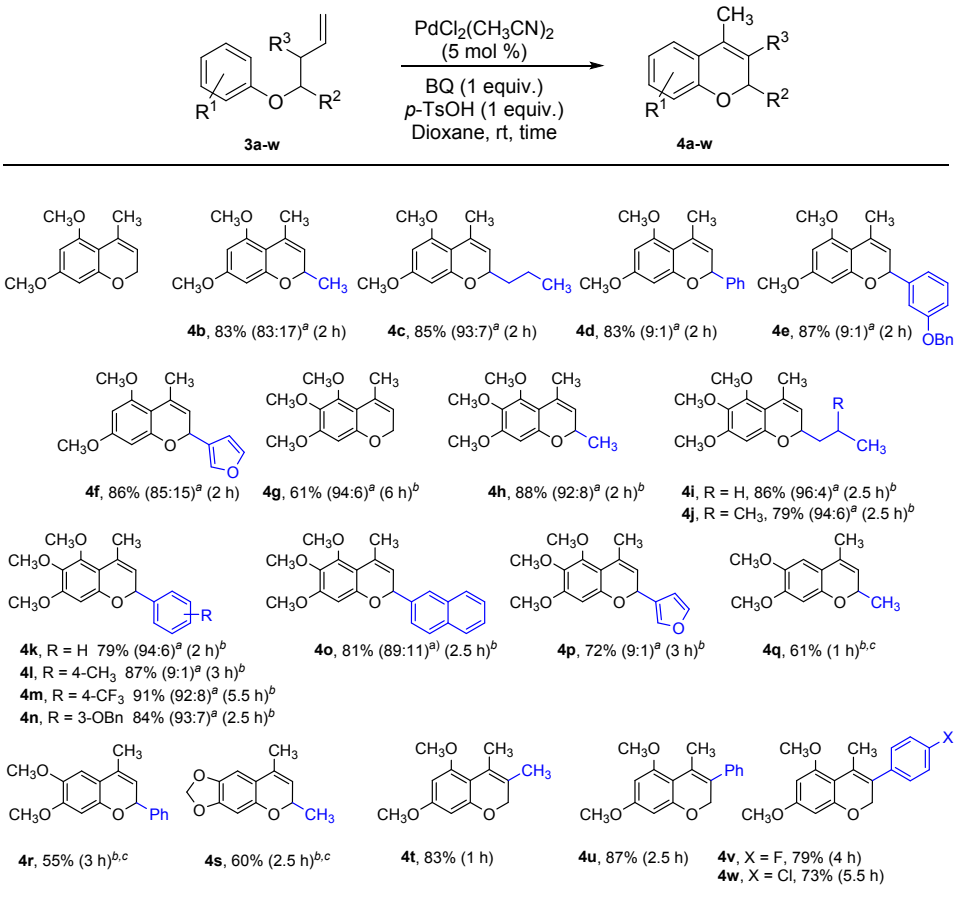


Scheme 3. Intramolecular C-H alkenylation of (*Z*)-**1a**

We next decided to expand the scope of the reaction to non substituted alkenes tethered to the aromatic ring. Thus, a series of substituted homoallyl aryl ethers **3a-w** were selected in order to access highly and diversely substituted 2*H*-chromenes **4a-w** (Table 3). First, the cyclization of unsubstituted homoallyl aryl ether **3a** was tested. In this case, the reaction was much faster, and it was completed in 2 h at rt,

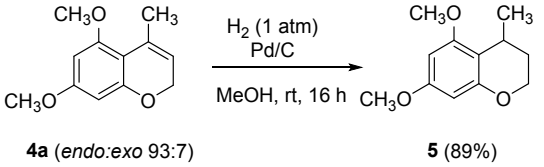
obtaining 2*H*-chromene **4a,** as expected, with a good isolated yield (74%) (Table 3). However, the ^{1}H and ^{13}C NMR spectra showed the presence of a minor amount of the regioisomeric methylenechromane, with an exocyclic double bond. A 93:7 *endo/exo* ratio was established by ^{1}H NMR. This was confirmed, as hydrogenation of the regioisomeric mixture gave 4-methylchromane **5a** in high yield a single product (Scheme 4). 2-Substitued chromenes, including flavenes **4d** or **4e** or a heteroaryl analog **4f**, were efficiently obtained under these reaction conditions (Table 3), in high isolated yields. The reaction could also be extended to different substitution patterns on the aromatic ring, obtaining 5,6,7-trimethoxy substituted chromenes **4g-4p**, although an increase of the catalyst loading was required to maintain the reactivity. Thus, a series of both alkyl and aryl substituted 2*H*-chromenes were easily accessed.

Table 3. Synthesis of chromenes **4a-w**



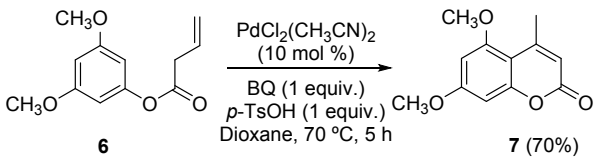
[a]Yield of isolated compound. *Endo*/*exo* regioisomer ratio determined by ^{1}H NMR. [b] $PdCl_2(CH_3CN)_2$ (10 mol %) was used. [c]Performed at 70 ºC.

This type of alkenylation reaction requires an activated electron rich aromatic ring. We have previously shown that non substituted or alkyl substituted aromatic rings gave only low yields of the cyclized compounds on related reactions.[11,24] However, the reaction works efficiently with different oxygenated substitution patterns on the aromatic ring. The 6,7-disubstituted chromenes **4q-s** were obtained as single regioisomers by this procedure. This is interesting, as previous reports showed that, under related conditions, catalyst loadings up to 20 and 25 % mol were required to obtain comparable yields with this type of substitution on the aromatic ring.[22] When a substituent is present on the position 3 of the homoallyl ether (**3t-w**, R^3 = Me, aryl), the reaction completed in just 1 to 5 hours with 5 mol % of catalyst. The endocyclic double bond is favored by this substitution pattern, and 3-substituted 2*H*-chromenes, including isoflavenes **4u-w** were obtained in high yield with complete regioselectivity. The structure of the 2*H*-chromenes was unambiguously confirmed by single-crystal X-ray analysis of **4v** (See Supporting information).[30] Finally, we tested this intramolecular alkenylation on an aryl butenoate, such as **6,** to check the applicability of this procedure for the synthesis of coumarins. Thus, coumarin **7** was obtained, although heating to 70 ºC was required to obtain full conversion in a reasonable reaction time (Scheme 5).



4a (*endo:exo* 93:7) **5** (89%)

Scheme 4. Hydrogenation of **4a**.



6 **7** (70%)

Scheme 5. Synthesis of coumarin **7**

In conclusion, an improved and mild protocol for Pd(II)-catalyzed C-H alkenylation of aryl homoallyl ethers has been developed. The use of *p*-TsOH as additive accelerates the reaction, probably generating more electrophilic Pd(II) species, and gives the procedure a significant improvement in substrate scope and reaction conditions. Thus, in most cases, the reactions could be run at room temperature using catalyst loadings of 5-10 mol % depending on the aromatic substitution pattern. This procedure would be complementary to the related Mizoroki-Heck reaction that led to the formation of 4-methylidene chromanes, with exocyclic double bonds,[31] with the advantage that it does not require the prior functionalization of the substrates. An additional feature of the process is the easy preparation of the substrates, the polysubstituted aryl homoallyl ethers **3**, which in most cases can be prepared in one step by a Mitsunobu reaction between readily available alcohols and phenols. A cross-metathesis is required to prepare the pent-2-enoates **1** (See Experimental Section). The procedure is very versatile, since it allows the synthesis of alkylidenechromanes **2** and *2H*-chromenes **4** with different types of substituents (alkyl, electron-rich and electron-deficient aryl, heteroaryl) at C-2 or C-3 of the chromene moiety, thus accessing relevant flavenes and isoflavenes, and even coumarins. Therefore, this procedure would be an efficient alternative to previously reported catalytic approaches,[21] which usually give access either to 2-substituted[32] or to 3-substituted chromene derivatives.[33,34]

Experimental Section

General experimental methods. Melting points were determined in unsealed capillary tubes and are uncorrected. IR spectra were obtained using an ATR. NMR spectra were recorded at 20-25 ˚C, at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C or at 500 MHz for ^{1}H and 125.7 MHz for ^{13}C in $CDCl_3$ solutions. Assignments of individual ^{13}C and ^{1}H resonances are supported by DEPT experiments and 2D correlation experiments (COSY, HSQCed or HMBC). Mass spectra were recorded under electron impact (EI) at 70 eV or with an ESI^{+} source. Exact mass was obtained using a TOF detector. TLC was carried out with 0.2 mm thick silica gel plates. Visualization was accomplished by UV light. Flash column chromatography was performed on silica gel (230-400 mesh). All solvents used in reactions

were anhydrous and purified according to standard procedures. All air- or moisture-sensitive reactions were performed under argon; the glassware was dried (130 ˚C) and purged with argon. Palladium catalysts were commercially available, and were used without further purification: $PdCl_2(CH_3CN)_2$, 99% purity; $Pd(OAc)_2$ 98% purity.

Synthesis aryl homoallyl ethers 3a-w. General Procedure. Over a solution of the corresponding homoallylic alcohol (1 mmol) in THF (3.3 mL) the corresponding phenol (3 mmol), PPh_3 (1.3 mmol) and DEAD (40 % wt solution in toluene) (1.3 mmol) were added under argon atmosphere. The resulting solution was heated at reflux for 3-16 h. The reaction mixture was allowed to cool down to room temperature and it was concentrated *in vacuo*. Purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1 or 8/2) afforded the corresponding aryl alkenyl ethers **3a-w.**

1-(But-3-en-1-yloxy)-3,5-dimethoxybenzene (3a).[22] Prepared from 3-buten-1-ol (0.17 mL, 2.0 mmol), 3,5-dimethoxyphenol (0.92 g, 6.0 mmol), PPh_3 (0.68 g, 2.6 mmol) and DEAD (1.1 g, 2.6 mmol) in THF (6.6 mL). The reaction mixture was heated at reflux for 4 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3a** was obtained as an oil (0.35 g, 83 %): IR (ATR) 2937, 3078 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.53 (q, J = 6.7 Hz, 2H), 3.77 (s, 6H), 3.98 (t, J = 6.7 Hz, 2H), 5.07-5.22 (m, 2H), 5.90 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 6.09 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 33.6, 55.3, 67.2, 93.0, 93.4, 117.0, 134.4, 160.8, 161.5; MS (EI) *m/z* (rel intensity): 208.1 (M^+, 28), 154.1 (100), 126.1 (62). HRMS (ESI-TOF) calcd. for $C_{12}H_{17}O_3$ [MH^+], 209.1178; found, 209.1169.

1,3-Dimethoxy-5-(pent-4-en-2-yloxy)benzene (3b).[23] Prepared from 4-penten-2-ol (0.14 mL, 1.4 mmol), 3,5-dimethoxyphenol (0.64 g, 4.1 mmol), PPh_3 (0.47 g, 1.8 mmol) and DEAD (0.78 g, 1.8 mmol) in THF (4.6 mL). The reaction mixture was heated at reflux for 3 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3b** was obtained as an oil (0.22 g, 73 %): IR (ATR) 2841, 2934, 2970, 3002, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (d, J = 6.1 Hz, 3H), 2.26-2.59 (m, 2H), 3.77 (s, 6H), 4.16-4.34 (m, 1H), 5.02-5.21 (m, 2H), 5.86 (ddt, J = 17.2, 10.2, 7.0 Hz, 1H), 6.06-6.14 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.4, 40.5, 55.3, 73.2, 92.9, 94.7,

117.5, 134.2, 159.8, 161.5; MS (EI) *m/z* (rel intensity): 222.1 (M^+, 12), 181.1 (15), 154.1 (100), 153.1 (18), 125.1 (65); HRMS (ESI-TOF): calcd. for $C_{13}H_{19}O_3$ [MH^+], 223.1334, found, 223.1335.

1-(Hept-1-en-4-yloxy)-3,5-dimethoxybenzene (3c). Prepared from 1-hepten-4-ol (0.10 mg, 0.90 mmol), 3,5-dimethoxyphenol (0.42 g, 2.7 mmol), PPh_3 (0.30 g, 1.2 mmol) and DEAD (0.51 g, 1.2 mmol) in THF (3.0 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3c** was obtained as an oil (0.14 g, 63 %): IR (ATR) 2841, 2934, 2959, 3006, 3081 cm^{-1} ;^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95 (t, *J* = 7.3 Hz, 3H), 1.30-1.76 (m, 4H), 2.35-2,52 (m, 2H), 3.77 (s, 6H), 4.18-4.33 (m, 1H), 5.04-5.19 (m, 2H), 5.87 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 6.07-6.12 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 18.7, 35.9, 38.2, 55.3, 77.0, 92.8, 94.7, 117.4, 134.2, 160.3, 161.5; MS (ESI) *m/z* (rel intensity): 251.2 (MH^+, 100), 155.1 (30); HRMS (ESI-TOF): calcd. for $C_{15}H_{23}O_3$ [MH^+], 251.1647; found, 251.1650.

1,3-Dimethoxy-5-((1-phenylbut-3-en-1-yl)oxy)benzene (3d)[22] Prepared from 4-phenyl-1-buten-4-ol (0.25 mg, 1.7 mmol), 3,5-dimethoxyphenol (0.79 g, 5.1 mmol), PPh_3 (0.58 g, 2.2 mmol) and DEAD (0.96 g, 2.2 mmol) in THF (5.7 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3d** was obtained as an oil (0.23 g, 47 %): IR (ATR) 2837, 2898, 2937, 2991, 3002, 3066 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.52-2.87 (m, 2H), 3.71 (s, 6H), 5.04-5.21 (m, 3H), 5.88 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 6.05 (t, *J* = 2.0, 1H), 6.08 (d, *J* = 2.0 Hz, 2H), 7.23-7.42 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.8, 55.2, 79.9, 93.1, 94.9, 117.6, 126.0, 127.6, 128.6, 134.1, 141.4, 160.0, 161.3; MS (EI) *m/z* (rel intensity): 284.2 (M^+, 6), 155.1 (10), 154.0 (100), 131.1 (42), 129.1 (32), 125.1 (30), 115.1 (23), 91.1 (38); HRMS (ESI-TOF): calcd. for $C_{18}H_{21}O_3$ [MH^+], 285.1491; found, 285.1495.

5-((1-(3-(Benzyloxy)phenyl)but-3-en-1-yl)oxy)-1,3-dimethoxybenzene (3e). Prepared from 1-(3-(benzyloxy)phenyl)but-3-en-1-ol (0.17 g, 0.68 mmol), 3,5-dimethoxyphenol (0.31 g, 2.0 mmol), PPh_3 (0.23 g, 0.88 mmol) and DEAD (0.39 g, 0.88 mmol) in THF (2.3 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3e** was obtained as an oil (0.13 g, 50 %): IR (ATR) 2841, 2901, 2934, 3009, 3031, 3074 cm^{-1}; ^{1}H

NMR (300 MHz, $CDCl_3$): δ 2.70 (m, 2H), 3.73 (s, 6H), 5.02-5.25 (m, 5H), 5.90 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H,), 6.07-6.10 (m, 1H), 6.12 (d, *J* = 2.1 Hz, 2H), 6.82-7.08 (m, 3H), 7.20-7.51 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.8, 55.3, 70.0, 79.8, 93.2, 94.9, 112.6, 113.9, 117.6, 118.7, 127.6, 128.0, 128.6, 129.7, 134.1, 137.0, 143.2, 159.1, 160.0, 161.4; MS (ESI) *m/z* (rel intensity): 391.2 (MH^+, 76), 156.1 (5), 155.1 (100); HRMS (ESI-TOF): calcd. for $C_{25}H_{27}O_4$ [MH^+], 391.1909; found, 391.1907.

3-(1-(3,5-Dimethoxyphenoxy)but-3-en-1-yl)furan (3f). Prepared from 1-(furan-3-yl)but-3-en-1-ol[35] (0.21 g, 1.5 mmol), 3,5-dimethoxyphenol (0.70 g, 4.5 mmol), PPh_3 (0.51 g, 2.0 mmol) and DEAD (0.85 g, 2.0 mmol) in THF (5.0 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3f** was obtained as an oil (0.12 g, 29 %): IR (ATR) 2841, 2901, 2941, 2999, 3074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.52-2.83 (m, 2H,), 3.77 (s, 6H), 5.04-5.23 (m, 3H), 5.85 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 6.06-6.10 (m, 1H), 6.12 (d, *J* = 1.9 Hz, 2H), 6.41 (s, 1H), 7.38 (s, 1H), 7.40 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 40.9, 55.3, 72.9, 93.3, 94.9, 108.9, 117.8, 125.6, 133.7, 139.7, 143.3, 159.9, 161.4; MS (ESI) *m/z* (rel intensity): 275.1 (MH^+, 100), 233.1 (9), 155.1 (31); HRMS (ESI-TOF): calcd. for $C_{16}H_{19}O_4$ [MH^+], 275.1283; found, 275.1289.

5-(But-3-en-yloxy)-1,2,3-trimethoxybenzene (3g).[22] Prepared from 3-buten-1-ol (0.22 mL, 2.5 mmol), 3,4,5-trimethoxyphenol (1.4 g, 7.6 mmol), PPh_3 (0.86 g, 3.3 mmol) and DEAD (1.4 g, 3.3 mmol) in THF (8.4 mL). The reaction mixture was heated at reflux for 5.5 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3g** was obtained as an oil (0.47 g, 78 %): IR (ATR) 2833, 2934, 2995, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.49 (q, *J* = 6.7 Hz, 2H), 3.75 (s, 3H), 3.79 (s, 6H), 3.94 (t, *J* = 6.7 Hz, 2H), 5.02-5.21 (m, 2H), 5.87 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 6.12 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 33.7, 56.0, 60.9, 67.5, 92.3, 117.0, 132.3, 134.4, 153.7, 155.5; MS (EI) *m/z* (rel intensity): 238.1 (M^+, 91), 223.1 (22), 184.0 (32), 169.00 (89), 153.1 (10), 141.0 (36), 55.1 (100); HRMS (ESI-TOF): calcd. for $C_{13}H_{19}O_4$ [MH^+], 239.1283, found, 239.1292.

1,2,3-Trimethoxy-5-(pent-4-en-2-yloxy)benzene (3h). Prepared from 4-penten-2-ol (0.12 mL, 1.2 mmol), 3,4,5-trimethoxyphenol (0.66 g, 3.6 mmol), PPh_3 (0.41 g, 1.6 mmol) and DEAD (0.68 g, 1.6

mmol) in THF (4.0 mL). The reaction mixture was heated at reflux for 6 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3h** was obtained as an oil (0.24 g, 78 %): IR (ATR) 2844, 2977, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (d, *J* = 6.1 Hz, 3H), 2.26-2.55 (m, 2H), 3.77 (s, 3H), 3.81 (s, 6H), 4.27-4.39 (m, 1H), 5.05-5.18 (m, 2H), 5.85 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.5, 40.6, 56.0, 60.7, 73.9, 93.9, 117.5, 132.4, 134.2, 153.7, 154.4; MS (EI) *m/z* (rel intensity): 252.1 (M^+, 36), 184.1 (43), 169.0 (100), , 141.0 (27); HRMS (ESI-TOF): calcd. for $C_{14}H_{21}O_4$ [MH^+], 253.1440; found, 253.1449.

5-(Hept-1-en-4-yloxy)-1,2,3-trimethoxybenzene (3i). Prepared from 1-hepten-4-ol (0.10 mg, 0.90 mmol), 3,4,5-trimethoxyphenol (0.49 g, 2.7 mmol), PPh_3 (0.30 g, 1.2 mmol) and DEAD (0.51 g, 1.2 mmol) in THF (3.0 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3i** was obtained as an oil (0.16 g, 63 %): IR (ATR) 2841, 2872, 2937, 2962, 3074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.30-1.76 (m, 4H), 2.28-2.50 (m, 2H), 3.77 (s, 3H), 3.81 (s, 6H), 4.13-4.28 (m, 1H), 5.02-5.19 (m, 2H), 5.85 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 18.7, 36.0, 38.3, 56.0, 61.0, 77.7, 93.9, 117.4, 132.3, 134.2, 153.7, 154.9; MS (EI) *m/z* (rel intensity): 281.2, 280.2 (M^+, 28), 184.0 (62), 169.0 (100), 141.0 (18), 69.0 (15); HRMS (ESI-TOF): calcd. for $C_{16}H_{25}O_4$ [MH^+], 281.1753; found, 281.1753.

1,2,3-Trimethoxy-5-((6-methylhept-1-en-4-yl)oxy)benzene (3j). Prepared from 6-methylhept-1-en-4-ol[36] (0.12 mg, 0.95 mmol), 3,4,5-trimethoxyphenol (0.52 g, 2.9 mmol), PPh_3 (0.32 g, 1.2 mmol) and DEAD (0.54 g, 1.2 mmol) in THF (3.2 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3j** was obtained as an oil (0.10 g, 36 %): IR (ATR) 2833, 2872, 2934, 2959, 3070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.91 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.30-1.49 (m, 1H), 1.55-1.90 (m, 2H), 2.39 (t, *J* = 6.1 Hz, 2H), 3.78 (s, 3H), 3.82 (s, 6H), 4.15-4.32 (m, 1H), 5.04-5.18 (m, 2H), 5.85 (ddt, *J* = 17.4, 10.4, 7.1 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 22.5, 23.1, 24.6, 38.6, 43.1, 56.0, 61.0, 76.0,

93.7, 117.5, 132.2 (C_4), 134.1, 153.7, 154.8; MS (EI) *m/z* (rel intensity): 294.2 (M^+, 23), 184.1 (64), 169.0 (100); HRMS (ESI-TOF): calcd. for $C_{17}H_{27}O_4$ [MH^+], 295.1909; found, 295.1910.

1,2,3-Trimethoxy-5-((1-phenylbut-3-en-1-yl)oxy)benzene (3k). Prepared from 4-phenyl-1-buten-4-ol (0.39 g, 2.6 mmol), 3,4,5-trimethoxyphenol (1.4 g, 7.9 mmol), PPh_3 (0.89 g, 3.4 mmol) and DEAD (1.5 g, 3.4 mmol) in THF (8.7 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3k** was obtained as an oil (0.37 g, 41 %): IR (ATR): 2841, 2901, 2937, 2959, 2987, 3070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.50-2.88 (m, 2H), 3.72 (s, 6H), 3.74 (s, 3H), 5.02-5.21 (m, 3H), 5.76-5.96 (m, 1H), 6.11 (s, 2H), 7.20-7.44 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.8, 55.9, 60.9, 80.5, 93.9, 117.6, 126.0, 127.7, 128.6, 132.2, 134.5, 141.5, 153.5, 154.7; MS (EI) *m/z* (rel intensity): 314.1 (M^+, 13), 184.1 (100), 169.0 (85), 131.1 (33), 129.1 (35), 115.0 (27), 91.1 (38); HRMS (ESI-TOF): calcd. for $C_{19}H_{23}O_4$ [MH^+], 315.1596; found, 315.1602.

1,2,3-Trimethoxy-5-((1-(*p*-tolyl)but-3-en-1-yl)oxy)benzene (3l). Prepared from 1-(4-methylphenyl)-3-buten-1-ol (0.29 g, 1.8 mmol), 3,4,5-trimethoxyphenol (1.0 g, 5.4 mmol), PPh_3 (0.62 g, 2.3 mmol) and DEAD (1.0 g, 2.3 mmol) in THF (6.0 mL). The reaction mixture was stirred at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3l** was obtained as an oil (0.23 g, 42 %): IR (ATR) 2837, 2937 (^{sp3}C-H), 3002, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 2.51-2.83 (m, 2H), 3.73 (s, 9H), 5.01-5.17 (m, 3H), 5.86 (ddt, J = 24.1, 10.6, 6.9 Hz, 1H), 6.11 (s, 2H), 7.15 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.1, 42.8, 55.9, 60.9, 80.3, 93.8, 117.5, 126.0, 129.3, 132.2, 134.2, 137.4, 138.5, 153.4, 154.7; MS (ESI) *m/z* (rel intensity): 329.2 (MH^+, 18), 186.1 (7), 185.1 (100). HRMS (ESI-TOF): calcd. for $C_{20}H_{25}O_4$ [MH^+], 329.1753; found, 329.1759.

1,2,3-Trimethoxy-5-((1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)oxy)benzene (3m). Prepared from 1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol[37] (0.40 g, 1.9 mmol), 3,4,5-trimethoxyphenol (1.0 g, 5.6 mmol), PPh_3 (0.64 g, 2.4 mmol) and DEAD (1.1 g, 2.4 mmol) in THF (6.2 mL). The reaction mixture was stirred at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum

ether/AcOEt 8/2), **3m** was obtained as an oil (0.49 g, 68 %): IR (ATR) 2833, 2941, 3002, 3077 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$): δ 2.50-2.85 (m, 2H), 3.73 (s, 6H), 3.74 (s, 3H), 5.04-5.18 (m, 3H), 5.83 (ddt, *J* = 16.7, 9.7, 7.0 Hz, 1H), 6.07 (s, 3H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.5, 56.0, 60.9, 79.7, 93.8, 118.2, 124.3 (q, *J* = 271.3 Hz), 125.6 (q, *J* = 3.7 Hz), 126.4, 130.4 (q, *J* = 32.5 Hz), 132.6 133.3, 145.5, 153.6, 154.2; MS (ESI) *m/z* (rel intensity): 383.1 (MH^+, 100), 185.1 (21). HRMS (ESI-TOF): calcd. for $C_{20}H_{22}F_3O_4$ [MH^+], 383.1470; found: 383.1479.

5-((1-(3-(Benzyloxy)phenyl)but-3-en-1-yl)oxy)-1,2,3-trimethoxybenzene (3n). Prepared from 1-(3-(benzyloxy)phenyl)but-3-en-1-ol (0.21 g, 0.83 mmol), 3,4,5-dimethoxyphenol (0.46 g, 2.5 mmol), PPh_3 (0.28 g, 1.1 mmol) and DEAD (0.47 g, 1.1 mmol) in THF (2.8 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3n** was obtained as an oil (0.16 g, 45 %): IR (ATR): 2841, 2934, 2970, 3002, 3077 cm^{-1} ;^1H NMR (300 MHz, $CDCl_3$): δ 2.50-2.85 (m, 2H), 3.73 (s, 6H), 3.77 (s, 3H), 5.00-5.23 (m, 5H), 5.88 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 6.12 (s, 2H), 6.82-7.08 (m, 3H), 7.20-7.51 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.7, 55.9, 61.0, 70.0, 80.4, 93.8, 112.6, 114.0, 117.6, 118.7, 127.9, 128.0, 128.6, 129.7, 132.3, 134.1, 136.9, 143.3, 153.9, 154.7, 159.1; MS (EI) *m/z* (rel intensity): 420.2 (M^+, 2), 184.1 (49), 169.0 (26), 91.1 (100); HRMS (ESI-TOF): calcd. for $C_{26}H_{29}O_5$ [MH^+], 421.2015; found, 421.2014.

2-(1-(3,4,5-Trimethoxyphenoxy)but-3-en-1-yl)naphthalene (3o). Prepared from 1-(naphthalen-2-yl)but-3-en-1-ol[38] (0.21 g, 1.1 mmol), 3,4,5-trimethoxyphenol (0.60 g, 3.2 mmol), PPh_3 (0.37 g, 1.4 mmol) and DEAD (0.61 g, 1.4 mmol) in THF (3.6 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3o** was obtained as an oil (0.12 g, 31 %): IR (ATR) 2851, 2930, 2959, 2999, 3060, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.62-2.95 (m, 2H), 3.73 (s, 6H), 3.75 (s, 3H), 5.04-5.37 (m, 3H), 5.92 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 6.19 (s, 2H), 7.43-7.60 (m, 3H), 7.79-7.90 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 42.7, 56.0, 60.9, 80.7, 94.0, 117.8, 123.9, 125.1, 126.0, 126.3, 127.8, 127.9, 128.6, 132.4, 133.1, 133.3, 134.0, 139.0, 153.5, 154.7; MS (ESI) *m/z* (rel intensity): 365.2 (MH^+, 15), 185.1 (100). HRMS (ESI-TOF): calcd. for $C_{23}H_{25}O_4$ [MH^+], 365.1753; found: 365.1754.

3-(1-(3,4,5-Trimethoxyphenoxy)but-3-en-1-yl)furan (3p). Prepared from 1-(furan-3-yl)but-3-en-1-ol[35] (0.38 g, 2.7 mmol), 3,4,5-trimethoxyphenol (1.5 g, 8.2 mmol), PPh_3 (0.93 g, 3.6 mmol) and DEAD (1.5 g, 3.6 mmol) in THF (9.1 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3p** was obtained as an oil (0.22 g, 27 %): IR (ATR) 2841, 2934, 2987, 3009, 3074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.50-2.83 (m, 2H), 3.76 (s, 3H), 3.77 (s, 6H), 5.04-5.21 (m, 3H), 5.73-5.95 (m, 1H), 6.15 (s, 2H), 6.41 (s, 1H), 7.38 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 41.0, 56.0, 60.9, 73.5, 94.1, 108.7, 117.9, 125.8, 132.6, 133.7, 139.7, 143.4, 153.3, 154.5; MS (EI) *m/z* (rel intensity): 304.1 (M^+, 7), 263.1 (17), 184.1 (100), 169.0 (85), 91.1 (56); HRMS (ESI-TOF): calcd. for $C_{17}H_{21}O_5$ [MH^+], 305.1389; found: 305.1398.

1,2-Dimethoxy-4-(pent-4-en-2-yloxy)benzene (3q). Prepared from 4-penten-2-ol (0.28 mL, 3.3 mmol), 3,4-dimethoxyphenol (1.5 g, 9.8 mmol), PPh_3 (1.1 g, 4.2 mmol) and DEAD (1.8 g, 4.2 mmol) in THF (10.9 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3q** was obtained as an oil (0.49 g, 67 %): IR (ATR) 2833, 2908, 2930, 2977, 3002, 3070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.26 (d, J = 6.1 Hz, 3H), 2.21-2.55 (m, 2H,), 3.80 (s, 3H), 3.81 (s, 3H), 4.29 (h, J = 6.1 Hz, 1H), 5.00-5.18 (m, 2H), 5.84 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H), 6.39 (dd, J = 8.7, 2.5 Hz, 1H), 6.49 (d, J = 2.5 Hz, 1H), 6.74 (d, J = 8.7, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.5, 40.6, 55.8, 56.4, 74.1, 102.5, 106.0, 111.9, 117.4, 134.3, 143.5, 149.9, 152.3; MS (EI) *m/z* (rel intensity): 222.1 (M^+, 41), 154.1 (100), 139.0 (88), 111.0 (23); HRMS (ESI): calcd. for $C_{13}H_{19}O_3$ [MH^+], 223.1334; found: 223.1334.

1,2-Dimethoxy-4-((1-phenylbut-3-en-1-yl)oxy)benzene (3r). Prepared from 4-phenyl-1-buten-4-ol (0.64 mL, 4.3 mmol), 3,4-dimethoxyphenol (2.0 g, 13.0 mmol), PPh_3 (1.5 g, 5.6 mmol) and DEAD (2.6 g, 5.6 mmol) in THF (14.4 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2), **3r** was obtained as an oil (0.38 g, 31 %): IR (ATR) 2830, 2937, 3006, 3031, 3077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.52-2.90 (m, 2H), 3.77 (s, 3H), 3.80 (s, 3H), 5.00-5.23 (m, 3H), 5.88 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H), 6.30 (dd, J = 8.8, 2.8 Hz, 1H), 6.54 (d, J = 2.8 Hz, 1H), 6.65 (d, J = 8.8, 1H), 7.20-7.42 (m, 5H); ^{13}C NMR (75.5

MHz, $CDCl_3$): δ 42.8, 55.7, 56.3, 80.6, 102.1, 106.1, 111.7, 117.9, 126.1, 127.6, 128.5, 134.3, 141.6, 143.5, 149.7, 152.6; MS (EI) *m/z* (rel intensity): 284.1 (M^+, 6), 154,1 (100), 139.0 (36), 131.1 (24), 129.1 (23), 91.1 (29); HRMS (ESI-TOF): calcd. for $C_{18}H_{20}O_3Na$ [MNa^+], 307.1310; found: 307.1315.

5-(Pent-4-en-2-yloxy)benzo[*d*][1,3]dioxole (3s). Prepared from 4-penten-2-ol (0.17 mL, 2.0 mmol), sesamol (0.83 g, 6.0 mmol), PPh_3 (0.69 g, 2.6 mmol) and DEAD (1.1 g, 2.6 mmol) in THF (6.7 mL). The reaction mixture was heated at reflux for 8 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3s** was obtained as an oil (0.36 g, 86 %): IR (ATR) 2833, 2908, 2930, 2977, 3002, 3070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 1.28 (d, *J* = 6.1 Hz, 3H), 2.24-2.55 (m, 2H), 4.26 (h, *J* = 6.1 Hz, 1H), 5.05-5.21 (m, 2H), 5.91 (s, 2H), 5.75-5.99 (m, 1H), 6.35 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.51 (d, *J* = 2.5 Hz, 1H), 6.70 (d, *J* = 8.4, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.4, 40.6, 74.9, 99.8, 101.1, 108.0, 108.3, 117.4, 134.3, 141.8, 148.2, 153.3; MS (EI) *m/z* (rel intensity): 206.1 (M^+, 24), 138.0 (100), 137.0 (54); HRMS (ESI-TOF): calcd. for $C_{12}H_{15}O_3$ [MH^+], 207.1021; found, 207.1022.

1,3-Dimethoxy-5-((2-methylbut-3-en-1-yl)oxy)benzene (3t). Prepared from 2-methyl-3-buten-1-ol (0.23 mL, 2.6 mmol), 3,5-dimethoxyphenol (1.2 g, 7.9 mmol), PPh_3 (0.90 g, 3.4 mmol) and DEAD (1.5 g, 3.4 mmol) in THF (8.8 mL). The reaction mixture was heated at reflux for 3.5 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3t** was obtained as an oil (0.47 g, 79 %): IR (ATR) 2841, 2872, 2912, 2926, 2959, 2987, 3005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.15 (d, *J* = 6.8 Hz, 3H), 2.59-2.80 (m, 1H), 3.77 (s, 6H), 3.69-3.94 (m, 2H), 5.04-5.25 (m, 2H), 5.88 (ddd, *J* = 17.3, 10.4, 6.8 Hz, 1H), 6.10 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 16.5, 37.3, 55.3, 72.4, 93.0, 93.5, 114.7, 140.4, 161.0, 161.5; MS (EI) *m/z* (rel intensity): 222.1 (M^+, 10), 154.0 (100), 126.1 (37), 125.1 (43); HRMS (ESI-TOF): calcd. for $C_{13}H_{19}O_3$ [MH^+], 223.1334; found: 223.1328.

1,3-Dimethoxy-5-((2-phenylbut-3-en-1-yl)oxy)benzene (3u).[22] Prepared from 2-phenylbut-3-en-1-ol[39] (0.35 g, 2.4 mmol), 3,5-dimethoxyphenol (1.1 g, 7.1 mmol), PPh_3 (0.81 g, 3.1 mmol) and DEAD (1.3 g, 3.1 mmol) in THF (7.9 mL). The reaction mixture was heated at reflux for 16 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3u** was obtained as an oil (0.20 g, 30 %): IR (ATR) 2841, 2880, 2930, 2955, 3002, 3063, 3085 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.76

(s, 6H), 3.84 (q, J = 7.0 Hz, 1H), 4.11-4.23 (m, 2H), 5.11-5.28 (m, 2H), 6.01-6.21 (m, 4H), 7.20-7.42 (m. 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 49.0, 55.3, 71.1, 93.0, 93.6, 116.5, 126.9, 128.1, 128.6, 138.3, 140.4 ($C_{1'}$), 160.7, 161.5; MS (ESI) *m/z* (rel intensity): 285.2 (MH^+, 100), 15.1 (6); HRMS (ESI-TOF): calcd. for $C_{18}H_{21}O_3$ [MH^+], 285.1491; found: 285.1501.

1-((2-(4-Fluorophenyl)but-3-en-1-yl)oxy)-3,5-dimethoxybenzene (3v). Prepared from 2-(4-fluorophenyl)but-3-en-1-ol[40] (0.34, 2.0 mmol), 3,5-dimethoxyphenol (0.95 g, 6.1 mmol), PPh_3 (0.70 g, 2.7 mmol) and DEAD (1.2 g, 2.7 mmol) in THF (6.8 mL). The reaction mixture was heated at reflux for 5 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3v** was obtained as an oil (0.18 g, 30 %): IR (ATR) 2841, 2926, 2959, 3006, 3081 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (s, 6H), 3.84 (q, J = 6.9 Hz, 1H), 4.11-4.23 (m, 2H), 5.09-5.32 (m, 2H), 6.01-6.21 (m, 4H), 7.05 (t, J = 8.7 Hz, 2H), 7.27 (dd, J = 8.7, 5.4 Hz, 2H $_{'}$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 48.2, 55.3, 71.0, 93.3, 93.6, 115.4 (d, J = 21.2 Hz), 116.7, 129.6 (d, J = 7.9 Hz), 136.4 (d, J = 3.2 Hz), 138.0, 160.6, 161.5, 161.8 (d, J = 247.4 Hz); MS (ESI) *m/z* (rel intensity): 303.1 (MH^+, 100), 155.1 (7). HRMS (ESI-TOF): calcd. for $C_{18}H_{20}O_3F$ [MH^+], 303.1396; found: 303.1395.

1-((2-(4-Chlorophenyl)but-3-en-1-yl)oxy)-3,5-dimethoxybenzene (3w). Prepared from 2-(4-chlorophenyl)but-3-en-1-ol[41] (0.32, 1.8 mmol), 3,5-dimethoxyphenol (0.81 g, 5.3 mmol), PPh_3 (0.60 g, 2.3 mmol) and DEAD (0.99 g, 2.3 mmol) in THF (5.8 mL). The reaction mixture was heated at reflux for 5 h. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 9/1), **3w** was obtained as an oil (0.13 g, 23 %): IR (ATR) 2841, 2876, 2934, 2955, 3006, 3085 cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 6H), 3.77-3.85 (m, 1H), 4.04-4.23 (m, 2H), 5.09-5.26 (m, 2H), 5.95-6.15 (m, 4H), 7.22 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 48.3, 55.3, 70.8, 93.3, 93.6, 116.9, 128.7, 129.5, 132.6, 137.7, 139.3, 160.5, 161.5; MS (ESI) *m/z* (rel intensity): 321.1 (MH^+ + 2, 28), 319.1 (MH^+, 100), 155.1 (4). HRMS (ESI-TOF): calcd. for $C_{18}H_{20}O_3Cl$ [MH^+], 319.1101; found: 319.1099.

Synthesis aryl aryloxypentenoates 1a-h. General Procedure. Over a solution of the corresponding aryl alkenyl ether **3** (1 mmol) and acrylate (20 mmol) in dry CH_2Cl_2 (2 mL), 2nd generation Grubbs

catalyst (0.05 mmol) was added under argon atmosphere. The reaction mixture was stirred at room temperature for 24 h, after which DMSO (2.5 mmol) was added. The resulting mixture was further stirred for 20 h. The volatile compounds were evaporated *in vacuo* and the residue obtained was purified by flash column chromatography (petroleum ether/AcOEt 8/2 or 9/1) to obtain the corresponding esters **1a-h**.

Methyl (*E*)-5-(3,5-dimethoxyphenoxy)pent-2-enoate (1a). Prepared from **3a** (0.27 g, 1.3 mmol), methyl acrylate (2.3 mL, 25.4 mmol) and 2nd generation Grubbs catalyst (54.0 mg, 0.06 mmol) in dry CH_2Cl_2 (2.6 mL). After stirring the reaction mixture for 24 h, DMSO (0.23 mL, 3.2 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 9/1), **3a** was obtained as a solid (0.29 g, 87 %): mp (CH_2Cl_2) 47-49 ºC; IR (ATR) 1724 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.64-2.70 (m, 2H), 3.74 (s, 3H), 3.76 (s, 6H), 4.03 (t, *J* = 5.8 Hz, 2H), 5.95 (d, *J* = 15.7 Hz, 1H,), 6.07 (s, 3H), 7.03 (dt, *J* = 15.7, 6.9 Hz, 1H,); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 32.0, 51.5, 55.3, 65.9, 93.2, 93.4, 123.0, 144.5, 160.4, 161.5, 166.; MS (EI) *m/z* (rel intensity): 266.1 (M^+, 38), 154.1 (96), 126.1 (50), 113.1 (100); HRMS (ESI-TOF): calcd. for $C_{14}H_{19}O_5$ [MH^+], 267.1233; found: 267.1232.

Methyl (*Z*)-5-(3,5-dimethoxyphenoxy)pent-2-enoate [(*Z*)-1a]. Obtained as a side-product in the obtention of **1a** (19 mg, 6 %): mp (CH_2Cl_2) 62-64 ºC; IR (ATR) 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.07-3.19 (m, 2H), 3.72 (s, 3H), 3.76 (s, 6H), 4.04 (t, *J* = 5.8 Hz, 2H), 5.91 (d, *J* = 11.5 Hz, 1H), 6.09 (s, 3H), 6.40 (dt, *J* = 11.5, 7.3 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 29.1, 51.1, 55.3, 66.8, 93.2, 93.4, 121.2, 146.1, 160.7, 161.5, 166.6; MS (EI) *m/z* (rel intensity): 266.2 (M^+, 24), 154.1 (84), 113.1 (100), 81.1 (34); HRMS (ESI-TOF): calcd. for $C_{14}H_{19}O_5$ [MH^+], 267.1233; found: 267.1232.

Methyl (*E*)-5-(3,5-dimethoxyphenoxy)hex-2-enoate (1b). Prepared from 1 **3b** (1.9 g, 8.4 mmol), methyl acrylate (15.1 mL, 0.17 mol) and 2nd generation Grubbs catalyst (0.36 g, 0.42 mmol) in dry CH_2Cl_2 (16.7 mL). After stirring the reaction mixture for 24 h, DMSO (1.5 mL, 20.9 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 8/2), **1b** was obtained

as an oil (1.3 g, 55 %): IR (ATR) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (d, *J* = 6.1 Hz, 3H), 2.42-2.69 (m, 2H), 3.72 (s, 3H), 3.75 (s, 6H), 4.45 (h, *J* = 6.0 Hz , 1H), 5.91 (dt, *J* = 15.7, 1.4 Hz, 1H), 6.06 (s, 3H), 6.99 (dt, *J* = 15.7, 7.3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.6, 38.8, 51.5, 55.3, 72.2, 93.2, 93.7, 123.5, 144.5, 159.3, 161.6, 166.7; MS (EI) *m/z* (rel intensity): 280.1 (M^+, 20), 207.1 (28), 181.1 (29), 154.0 (100), 127.1 (72), 125.1 (74), 95.1 (32); HRMS (ESI-TOF): calcd. for $C_{15}H_{21}O_5$ [MH^+], 281.1389; found: 281.1399.

Methyl (*E*)-5-(3,5-dimethoxyphenoxy)-5-phenylpent-2-enoate (1c). Prepared from **3d** (0.30 g, 1.1 mmol), methyl acrylate (1.9 mL, 21.2 mol) and 2nd generation Grubbs catalyst (45.0 mg, 0.053 mmol) in dry CH_2Cl_2 (2.1 mL). After stirring the reaction mixture for 24 h, DMSO (0.19 mL, 2.6 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 8/2), **1c** was obtained as a solid (0.27 g, 75 %): mp (CH_2Cl_2) 67-69 ºC; IR (ATR) 1713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.62-2.95 (m, 2H), 3.69 (s, 6H), 3.72 (s, 3H), 5.20 (dd, *J* = 7.6, 5.0 Hz, 1H), 5.90 (d, *J* = 15.7 Hz, 1H), 6.03 (s, 3H), 7.01 (dt, *J* = 15.7, 7.6 Hz, 1H), 7.20-7.39 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 41.1, 51.5, 55.5, 78.6, 93.3, 94.9, 123.6, 125.8, 127.9, 128.8, 140.6, 144.3, 159.6, 161.3, 166.6; MS (ESI) *m/z* (rel intensity): 343.2 (MH^+, 60), 155.1 (100); HRMS (ESI-TOF): calcd. for $C_{20}H_{23}O_5$ [MH^+], 343.1546; found: 343.1557.

Ethyl (*E*)-5-(3,5-dimethoxyphenoxy)pent-2-enoate (1d). Prepared from **3a** (0.30 g, 1.5 mmol), ethyl acrylate (3.2 mL, 29.1 mmol) and 2nd generation Grubbs catalyst (61.7 mg, 0.07 mmol) in dry CH_2Cl_2 (2.9 mL). After stirring the reaction mixture for 24 h, DMSO (0.26 mL, 3.6 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 8/2), **1d** was obtained as an oil (0.23 g, 57 %): IR (ATR) 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, *J* = 7.1 Hz, 3H), 2.64-2.70 (m, 2H), 3.76 (s, 6H), 4.03 (t, *J* = 5.8 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 5.95 (d, *J* = 15.7 Hz, 1H), 6.07 (s, 3H), 7.02 (dt, *J* = 15.7, 6.9 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 31.9, 55.3, 60.3, 65.9,

93.2, 93.4, 123.5, 144.5, 160.5, 161.5, 166.3; MS (ESI) *m/z* (rel intensity): 281.1 (MH^+, 100), 127.1 (35); HRMS (ESI-TOF): calcd. for $C_{15}H_{21}O_5$ [MH^+], 281.1389; found: 281.1390.

Butyl (*E*)-5-(3,5-dimethoxyphenoxy)pent-2-enoate (1e). Prepared from **3a** (0.49 g, 2.4 mmol), *n*-butyl acrylate (6.8 mL, 47.1 mmol) and 2nd generation Grubbs catalyst (99.9 mg, 0.12 mmol) in dry CH_2Cl_2 (4.7 mL). After stirring the reaction mixture for 24 h, DMSO (0.42 mL, 5.9 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 9/1), **1e** was obtained as an oil (0.59 g, 82 %): IR (ATR) 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.93 (t, *J* = 7.3 Hz, 3H), 1.28-1.47 (m, 2H), 1.54-1.70 (m, 2H), 2.59-2.71 (m, 2H), 3.75 (s, 6H), 4.02 (t, *J* = 6.4 Hz, 2H), 4.13 (t, *J* = 6.7 Hz, 2H), 5.94 (dt, *J* = 15.7, 1.5 Hz, 1H), 6.04-6.10 (s, 3H), 7.01 (dt, *J* = 15.7, 6.8 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7, 19.2, 30.7, 31.9, 55.3, 64.2, 65.9, 93.2, 93.4, 123.4, 144.5, 160.5, 161.5, 166.4; MS (ESI) *m/z* (rel intensity): 309.2 (MH^+, 100), 155.1 (23); HRMS (ESI-TOF): calcd. for $C_{17}H_{25}O_5$ [MH^+], 309.1702; found: 309.1703.

***t*-Butyl (*E*)-5-(3,5-dimethoxyphenoxy)pent-2-enoate (1f).** Prepared from **3a** (0.41 g, 2.0 mmol), *tert*-butyl acrylate (5.8 mL, 39.3 mmol) and 2nd generation Grubbs catalyst (83.4 mg, 0.098 mmol) in dry CH_2Cl_2 (4.0 mL). After stirring the reaction mixture for 24 h, DMSO (0.35 mL, 4.9 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 9/1), **1f** was obtained as an oil (0.44 g, 73 %): IR (ATR) 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.47 (s, 9H), 2.52-2.68 (m, 2H), 3.74 (s, 6H), 4.00 (t, *J* = 6.4 Hz , 2H), 5.86 (dt, *J* = 15.7, 1.4 Hz, 1H), 6.06 (s, 3H), 6.90 (dt, *J* = 15.7, 6.8 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 28.1, 31.8, 55.3, 66.0, 80.2, 93.2, 93.4, 125.1, 143.2, 160.5, 161.5, 165.6; MS (ESI) *m/z* (rel intensity): 309.2 (MH^+, 15), 253.1 (100); HRMS (ESI-TOF) calcd. for $C_{17}H_{25}O_5$ [MH^+], 309.1702; found: 309.1697.

***t*-Butyl (*E*)-5-(3,5-dimethoxyphenoxy)hex-2-enoate (1g).** Prepared from **3b** (0.27 g, 1.2 mmol), *tert*-butyl acrylate (3.5 mL, 23.8 mmol) and 2nd generation Grubbs catalyst (50.6 mg, 0.060 mmol) in dry CH_2Cl_2 (2.4 mL). After stirring the reaction mixture for 24 h, DMSO (0.21 mL, 2.9 mmol) was added

and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 9/1), **1g** was obtained as an oil (0.33 g, 87 %): IR (ATR) 1713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (d, *J* = 6.1 Hz, 3H), 1.50 (s, 9H), 2.40-2.67 (m, 2H), 3.78 (s, 6H), 4.37-4.53 (m, 1H), 5.74-5.92 (m, 1H), 6.09 (s, 3H), 6.79-6.98 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.6, 28.1, 38.7, 55.3, 72.3, 80.3, 93.2, 94.7, 125.7, 142.8, 159.4, 161.5, 165.6; MS (ESI) *m/z* (rel intensity): 323.2 (MH^+, 19), 268.1 (13), 267.1 (100), 155.1 (10); HRMS (ESI-TOF): calcd. for $C_{18}H_{27}O_5$ [MH^+], 323.1858; found, 323.1859.

Methyl (*E*)-5-(3,4,5-trimethoxyphenoxy)hex-2-enoate (1h). Prepared from **3h** (0.29 g, 1.1 mmol), methyl acrylate (2.1 mL, 23.0 mmol) and 2nd generation Grubbs catalyst (48.8 mg, 0.057 mmol) in dry CH_2Cl_2 (2.3 mL). After stirring the reaction mixture for 24 h, DMSO (0.2 mL, 2.9 mmol) was added and the resulting solution was further stirred for 20 h. After evaporating the volatile compounds *in vacuo* and purification by flash column chromatography (petroleum ether/AcOEt 8/2), **1h** was obtained as an oil (0.29 g, 83 %): IR (ATR) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.22 (d, *J* = 6.0 Hz, 3H), 2.33-2.59 (m, 2H), 3.62 (s, 3H), 3.68 (s, 3H), 3.72 (s, 6H), 4.26-4.44 (m, 1H), 5.82 (d, *J* = 15.7 Hz, 1H), 6.06 (s, 2H), 6.91 (dt, *J* = 15.7, 7.3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.6, 38.8, 51.3, 55.9, 60.8, 72.8, 94.0, 123.4, 132.5, 144.5, 153.6, 153.9, 166.5; MS (EI) *m/z* (rel intensity): 310.1 (M^+, 23), 184.0 (34), 169.0 (100), 127.1 (57), 69.0 (22); HRMS (ESI-TOF): calcd. for $C_{16}H_{23}O_6$ [MH^+], 311.1495; found, 311.1499.

Pd(II)-Catalyzed cyclization of 1 and 3. Synthesis of chromanes 2a-h and 2*H*-chromenes 4a-w. A solution of the corresponding ester **1a-h** or ether **3a-w** (1 mmol), *p*-TsOH (1 mmol), *p*-benzoquinone (1 mmol) and $PdCl_2(CH_3CN)_2$ (0.05 or 0.1 mmol) in 1,4-dioxane (66.7 mL) was stirred at room temperature (or 70 ºC) for 1 to 24 h. Then, the reaction was quenched by addition of water and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2 or 9/1) the corresponding chromanes **1a-h** or 2*H*-chromenes **4a-w** were obtained.

Methyl *(E)*-2-(5,7-dimethoxychroman-4-ylidene)acetate (2a). Prepared from **1a** (43.8 mg, 0.16 mmol), *p*-TsOH (31.8 mg, 0.16 mmol), *p*-benzoquinone (18.2 mg, 0.16 mmol) and $PdCl_2(CH_3CN)_2$ (2.1 mg, 0.008 mmol) in 1,4-dioxane (11.0 mL), 24 h at rt. **2a** was obtained as a solid (31.5 mg, 73 %): mp (CH_2Cl_2) 96-98 ºC; IR (ATR) 1706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.36 (t , J = 6.0 Hz, 2H), 3.71 (s, 3H,), 3.77 (s, 3H), 3.84 (s, 3H), 4.16 (t, J = 6.0 Hz, 2H), 6.04 (s, 1H), 6.07 (s, 1H), 6.92 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 27.3, 50.9, 55.3, 55.6, 65.8, 92.7, 93.9, 104.8, 112.4, 145.6, 159.4, 160.7, 162.0, 168.5; MS (EI) *m/z* (rel intensity): 264.2 (M^+, 75), 233.1 (100), 191.1 (80), 175.1 (20); HRMS (ESI-TOF): calcd. for $C_{14}H_{17}O_5$ [MH^+], 265.1076; found, 265.1073.

Methyl *(E)*-2-(5,7-dimethoxy-2-methyl-chroman-4-ylidene)acetate (2b). Prepared from **1b** (89.6 mg, 0.32 mmol), *p*-TsOH (60.8 mg, 0.32 mmol), *p*-benzoquinone (34.6 mg, 0.32 mmol) and $PdCl_2(CH_3CN)_2$ (4.2 mg, 0.016 mmol) in 1,4-dioxane (21.3 mL), 24 h at rt. **2b** was obtained as a solid (71.1 mg, 80 %): mp (CH_2Cl_2) 76-78 ºC; IR (ATR) 1695 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.40 (d, J = 6.2 Hz, 3H), 2.52-2.69 (m, 1H), 3.71 (s, 3H), 3.77 (s, 3H), 3.84 (s, 3H), 3.82-3.92 (m, 1H), 4.06-4.24 (m, 1H), 6.98-6.10 (m, 2H), 6.93 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8, 33.9, 50.9, 55.3, 55.6, 72.1, 92.6, 93.9, 104.4, 112.5, 145.9, 159.4, 160.6, 162.1, 168.4; MS (ESI) *m/z* (rel intensity): 279.1 (MH^+, 100), 247.1 (23); HRMS (ESI-TOF): calcd. for $C_{15}H_{19}O_5$ [MH^+], 279.1233; found, 279.1236.

Methyl *(E)*-2-(5,7-dimethoxy-2-phenylchroman-4-ylidene)acetate (2c). Prepared from **1c** (65.2 mg, 0.19 mmol), *p*-TsOH (36.2 mg, 0.19 mmol), *p*-benzoquinone (20.6 mg, 0.19 mmol) and $PdCl_2(CH_3CN)_2$ (2.5 mg, 0.01 mmol) in 1,4-dioxane (12.7 mL) 24 h at rt. **2c** was obtained as a solid (38.3 mg, 59 %): mp (CH_2Cl_2) 142-144 ºC; IR (ATR) 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.86-3.03 (m, 1H), 3.71 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 4.10-4.25 (m, 1H), 5.00-5.14 (m, 1H), 6.13 (d, J = 2.1 Hz, 1H), 6.18 (d, J = 2.1 Hz, 1H), 6.99 (s, 1H), 7.27-7.51 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 34.1, 50.9, 55.4, 55.6, 77.6, 93.0, 94.1, 104.5, 112.9, 126.2, 128.2, 128.5, 140.1, 145.5, 159.5, 160.7, 162.2, 168.4; MS (ESI) *m/z* (rel intensity): 341.1 (MH^+, 100), 309.1 (13); HRMS (ESI-TOF): calcd. for $C_{20}H_{21}O_5$ [MH^+], 341.1389; found, 341.1388.

Ethyl *(E)*-2-(5,7-dimethoxychroman-4-ylidene)acetate (2d). Prepared from **1d** (68.3, 0.24 mmol), *p*-TsOH (46.3 mg, 0.24 mmol), *p*-benzoquinone (26.3 mg, 0.24 mmol) and $PdCl_2(CH_3CN)_2$ (6.3 mg, 0.024 mmol) in 1,4-dioxane (24.6 mL) 24 h at rt. **2d** was obtained as a solid (51.7 mg, 77 %): mp (CH_2Cl_2) 107-108 ºC; IR (ATR)1739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.30 (t, *J* = 7.1 Hz, 3H), 3.37 (t, *J* = 5.8 Hz, 2H), 3.78 (s, 3H), 3.85 (s, 3H), 4.08-4.25 (m, 4H), 6.05 (d, *J* = 2.3 Hz, 1H), 6.08 (d, *J* = 2.3 Hz, 1H), 6.91 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 27.3, 55.3, 55.6, 59.5, 65.8, 92.7, 93.9, 104.8, 112.9, 145.2, 159.3, 160.7, 161.9, 168.1; MS (ESI) *m/z* (rel intensity):, 279.1 (MH^+, 100), 233.1 (3); HRMS (ESI) Calcd. for $C_{15}H_{19}O_5$ [MH^+], 279.1233; found, 279.1240.

***n*-Butyl *(E)*-2-(5,7-dimethoxychroman-4-ylidene)acetate (2e).** Prepared from **1e** (0.11, 0.37 mmol), *p*-TsOH (70.1 mg, 0.37 mmol), *p*-benzoquinone (39.8 mg, 0.37 mmol) and $PdCl_2(CH_3CN)_2$ (9.6 mg, 0.037 mmol) in 1,4-dioxane (24.6 mL) 24 h at rt. **2e** was obtained as a solid (79.2 mg, 70 %): mp (CH_2Cl_2) 81-82 ºC; IR (ATR) 1691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.95 (t, *J* = 7.3 Hz, 3H), 1.32-1.49 (m, 2H), 1.56-1.73 (m, 2H), 3.27-3.41 (m, 2H), 3.77 (s, 3H), 3.84 (s, 3H), 4.11 (t, *J* = 6.8 Hz, 2H), 4.17 (t, *J* = 6.0 Hz, 2H), 6.04 (d, *J* = 2.4 Hz, 1H), 6.07 (d, *J* = 2.4 Hz, 1H), 6.90 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.8, 19.3, 27.3, 30.9, 55.3, 55.6, 63.5, 65.2, 92.7, 93.9, 104.8, 113.0, 145.1, 159.3, 160.7, 161.9, 168.2; MS (ESI) *m/z* (rel intensity): 307.2 (MH^+, 100), 305.1 (3); HRMS (ESI-TOF): calcd. for $C_{17}H_{23}O_5$ [MH^+], 307.1546; found, 307.1546.

***t*-Butyl *(E)*-2-(5,7-dimethoxychroman-4-ylidene)acetate (2f).** Prepared from **1f** (0.13 g, 0.42 mmol), *p*-TsOH (79.5 mg, 0.42 mmol), *p*-benzoquinone (45.2 mg, 0.42 mmol) and $PdCl_2(CH_3CN)_2$ (10.8 mg, 0.042 mmol) in 1,4-dioxane (28.0 mL) 24 h at rt. **2f** was obtained as an oil (75.8 mg, 59 %): IR (ATR) 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.52 (s, 9H), 3.28-3.42 (m, 2H), 3.79 (s, 3H), 3.86 (s, 3H), 4.18 (t, *J* = 6.0 Hz, 2H), 6.05 (d, *J* = 2.3 Hz, 1H), 6.09 (d, *J* = 2.3 Hz, 1H), 6.84 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 27.2, 28.4, 55.3, 55.6, 65.2, 79.5, 92.6, 93.9, 104.9, 115.0, 143.8, 159.1, 160.6, 161.7, 167.7; MS (ESI) *m/z* (rel intensity): 307.2 (MH^+, 100), 251.1 (76); HRMS (ESI-TOF): calcd. for $C_{17}H_{23}O_5$ [MH+], 307.1546; found, 307.1563.

***t*-Butyl *(E)*-2-(5,7-dimethoxy-2-methylchroman-4-ylidene)acetate (2g).** Prepared from **1g** (0.11 g, 0.33 mmol), *p*-TsOH (63.0 mg, 0.33 mmol), *p*-benzoquinone (35.8 mg, 0.33 mmol) and $PdCl_2(CH_3CN)_2$ (8.6 mg, 0.033 mmol) in 1,4-dioxane (22.1 mL) 24 h at rt. **2g** was obtained as a solid (74.1 mg, 69 %): mp (CH_2Cl_2) 83-84 ºC; IR (ATR) 1685 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.40 (d, *J* = 6.2 Hz, 3H), 1.50 (s, 9H), 2.55 (ddd, *J* = 15.8, 11.3, 1.8 Hz, 1H), 3.76 (s, 3H), 3.84 (s, 3H), 3.81-3.89 (m, 1H), 4.08-4.23 (m, 1H), 6.04 (d, *J* = 2.3 Hz, 1H), 6.06 (d, *J* = 2.3 Hz, 1H), 6.83 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9, 28.4, 33.8, 55.3, 55.6, 72.1, 79.4, 92.6, 93.8, 104.5, 115.0, 144.2, 159.3, 160.5, 161.7, 167.8; MS (ESI) *m/z* (rel intensity): 321.2 (MH^+, 100), 284.1 (6); 265.1 (62). HRMS (ESI-TOF): calcd. for $C_{18}H_{25}O_5$ [MH^+], 321.1702; found, 321.1708.

Methyl *(E)*-2-(5,6,7-trimethoxy-2-methyl-chroman-4-ylidene)acetate (2h). Prepared from **1h** (0.11 g, 0.38 mmol), *p*-TsOH (73.0 mg, 0.38 mmol), *p*-benzoquinone (41.5 mg, 0.38 mmol) and $PdCl_2(CH_3CN)_2$ (10.0 mg, 0.038 mmol) in 1,4-dioxane (25.6 mL) 24 h at rt. **2h** was obtained as a solid (67.4 mg, 60 %): mp (CH_2Cl_2) 90-92 ºC; IR (ATR) 1706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.38 (d, *J* = 6.2 Hz, 3H), 2.48-2.64 (m, 1H), 3.70 (s, 3H), 3.78 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 3.48-3.96 (m, 1H), 4.04-4.23 (m, 1H), 6.19 (s, 1H), 6.97 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8, 33.7, 50.9, 55.8, 60.2, 61.0, 72.2, 96.6, 107.7, 112.7, 136.9, 145.8, 153.4, 154.1, 155.5, 168.4; MS (ESI) *m/z* (rel intensity): 309.1 (MH^+, 100), 277.1 (27); HRMS (ESI-TOF): calcd. for $C_{16}H_{21}O_6$ [MH^+], 309.1338; found, 309.1347.

5,7-Dimethoxy-4-methyl-*2H*-chromene (4a).[22] Prepared from **3a** (0.14 g, 0.66 mmol), *p*-TsOH (0.12 g, 0.66 mmol), *p*-benzoquinone (71.6 mg, 0.66 mmol) and $PdCl_2(CH_3CN)_2$ (8.7 mg, 0.033 mmol) in 1,4-dioxane (44.6 mL) 2 h at rt. **4a** was obtained and as an oil (0.10 g, 74 %) (mixture of regioisomers 93:7): IR (ATR) 2837, 2959, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.15 (s, 3H), 3.78 (s, 6H), 4.42-4.54 (m, 2H), 5.35-5.47 (m, 1H), 6.09 (d, *J* = 2.3 Hz, 1H), 6.12 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.8, 55.3, 55.4, 65.0, 92.9, 93.8, 108.0, 115.2, 131.7, 157.2, 158.2, 160.6; MS (ESI) *m/z* (rel intensity): 207.1 (MH^+, 100), 205.1 (3). HRMS (ESI-TOF): calcd. for $C_{12}H_{15}O_3$ [MH^+], 207.1021; found, 207.1022.

5,7-Dimethoxy-2,4-dimethyl-*2H*-chromene (4b). Prepared from **3b** (0.15 g, 0.67 mmol), *p*-TsOH (0.13 g, 0.67 mmol), *p*-benzoquinone (72.3 mg, 0.67 mmol) and $PdCl_2(CH_3CN)_2$ (8.7 mg, 0.034 mmol) in 1,4-dioxane (44.6 mL) 2 h at rt. **4b** was obtained as an oil (0.13 g, 86 %) (mixture of regioisomers 83:17): IR (ATR) 2837, 2934, 2966, 2999, 3034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (d, J = 6.6 Hz, 3H), 2.15 (s, 3H), 3.77 (s, 6H), 4.61-4.74 (m, 1H), 5.22-5.26 (m, 1H), 6.08 (d, J = 2.4 Hz, 1H), 6.12 (d, J = 2.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.4, 21.8, 55.2, 55.3, 71.1, 92.8, 94.0, 107.5, 121.0, 130.9, 156.8, 158.2, 161.5; MS (ESI) *m/z* (rel intensity): 221.1 (MH^+, 100), 219.1 (10). HRMS (ESI-TOF): calcd. for $C_{13}H_{17}O_3$ [MH^+], 221.1178; found, 221.1178.

5,7-Dimethoxy-4-methyl-2-propyl-*2H*-chromene (4c). Prepared from **3c** (73.8 mg, 0.29 mmol), *p*-TsOH (56.1 mg, 0.29 mmol), *p*-benzoquinone (31.9 mg, 0.29 mmol) and $PdCl_2(CH_3CN)_2$ (3.8 mg, 0.015 mmol) in 1,4-dioxane (19.7 mL) 2 h at rt. **4c** was obtained as an oil (62.0 mg, 85 %) (mixture of regioisomers 93:7): IR (ATR) 2841, 2872, 2937, 2959, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.98 (t, J = 7.1 Hz, 3H), 1.40-1.90 (m, 4H), 2.17 (s, 3H), 3.79 (s, 6H), 4.51-4.60 (m, 1H), 5.30 (d, J = 1.6 Hz, 1H), 6.09 (d, J = 2.1 Hz, 1H), 6.14 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0, 18.3, 21.9, 36.5, 55.3, 55.4, 74.6, 92.7, 94.0, 107.6, 120.0, 130.8, 156.7, 158.1, 160.5; MS (ESI) *m/z* (rel intensity): 249.1 (MH^+, 100), 247.1 (3); HRMS (ESI-TOF): calcd. for $C_{15}H_{21}O_3$ [MH^+], 249.1491; found, 249.1489.

5,7-Dimethoxy-4-methyl-2-phenyl-*2H*-chromene (4d). Prepared from **3d** (77.2 mg, 0.27 mmol), *p*-TsOH (51.6 mg, 0.27 mmol), *p*-benzoquinone (29.4 mg, 0.27 mmol) and $PdCl_2(CH_3CN)_2$ (3.5 mg, 0.014 mmol) in 1,4-dioxane (18.0 mL) 2h at rt. **4d** was obtained as an oil (63.4 mg, 83 %) (mixture of regioisomers 90:10): IR (ATR) 2837, 2930, 2973, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 5.41-5.46 (m, 1H), 5.60-5.64 (m, 1H), 6.11 (d, J = 2.4 Hz, 1H), 6.18 (d, J = 2.4 Hz, 1H), 7.24-7.54 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 22.0, 55.3, 55.4, 76.8, 93.0, 94.1, 107.2, 119.1, 127.1, 128.1, 128.5, 131.4, 140.9, 156.2, 158.3, 160.8; MS (ESI) *m/z* (rel intensity): 283.1 (MH^+, 100), 155.1 (3); HRMS (ESI-TOF): calcd. for $C_{18}H_{19}O_3$ [MH^+], 283.1334; found, 283.1337.

2-(3-(Benzyloxy)phenyl)-5,7-dimethoxy-4-methyl-*2H*-chromene (4e). Prepared from **3e** (0.10 g, 0.26 mmol), *p*-TsOH (50.0 mg, 0.26 mmol), *p*-benzoquinone (28.4 mg, 0.26 mmol) and $PdCl_2(CH_3CN)_2$ (3.4 mg, 0.013 mmol) in 1,4-dioxane (17.5 mL) 2h at rt. **4e** was obtained as an oil (88.3 mg, 87 %) (mixture of regioisomers 90:10): IR (ATR) 2837, 2930, 2959, 2999, 3031, 3066 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 3.77 (s, 3H), 3.79 (s, 3H), 5.07 (s, 2H), 5.38-5.41 (m, 1H), 5.56-5.59 (m, 1H), 6.09 (d, *J* = 2.4 Hz, 1H), 6.16 (d, *J* = 2.4 Hz, 1H), 6.86-7.17 (m, 3H), 7.22-7.51 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 22.0, 55.3, 55.4, 70.0, 76.6, 93.0, 94.1, 107.2, 112.7, 113.5, 114.3, 118.7, 127.6, 128.0, 128.6, 129.6, 131.4, 137.0, 142.6, 156.2, 158.3, 159.0, 160.8; MS (ESI) *m/z* (rel intensity): 389.2 (MH^+, 100), 363.2 (2); HRMS (ESI-TOF): calcd. for $C_{25}H_{25}O_4$ [MH^+], 389.1753; found, 389.1749.

2-(Furan-3-yl)-5,7-dimethoxy-4-methyl-*2H*-chromene (4f). Prepared from **3f** (77.2 mg, 0.27 mmol), *p*-TsOH (51.6 mg, 0.27 mmol), *p*-benzoquinone (29.4 mg, 0.27 mmol) and $PdCl_2(CH_3CN)_2$ (3.5 mg, 0.014 mmol) in 1,4-dioxane (18.0 mL) 2h at rt. **4f** was obtained as an oil (63.4 mg, 86 %) (mixture of regioisomers 85:15): IR (ATR) 2841, 2926, 2962, 2991, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.21 (t, *J* = 1.5 Hz, 3H), 3.76 (s, 3H), 3.78 (s, 3H), 5.38-5.47 (m, 1H), 5.50-5.59 (m, 1H), 6.09 (d, *J* = 2.4 Hz, 1H), 6.13 (d, *J* = 2.4 Hz, 1H), 6.47-6.49 (m, 1H), 7.38 (t, *J* = 1.7 Hz, 1H ·), 7.44-7.46 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.9, 55.3, 55.4, 69.2, 93.0, 94.2, 107.4, 109.6, 117.9, 125.2, 131.8, 140.8, 143.3, 156.0, 158.3, 160.8; MS (ESI): *m/z* (rel intensity): 273.1 (MH^+, 100), 171.1 (2). HRMS (ESI-TOF): calcd. for $C_{16}H_{17}O_4$ [MH^+], 273.1127; found, 273.1123.

5,6,7-Trimethoxy-4-methyl-*2H*-chromene (4g). Prepared from **3g** (0.13 g, 0.53 mmol), *p*-TsOH (0.10 g, 0.53 mmol), *p*-benzoquinone (57.4 mg, 0.53 mmol) and $PdCl_2(CH_3CN)_2$ (13.8 mg, 0.053 mmol) in 1,4-dioxane (35.4 mL) 6 h at rt. **4g** was obtained as an oil (76.5 mg, 61 %) (mixture of regioisomers 94:6): IR (ATR) 2833, 2934, 2966, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 3.85 (s, 3H), 4.48 (d, *J* = 2.2 Hz, 2H), 5.46 (bs, 1H), 6.28 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.1, 55.9, 60.9, 61.2, 64.9, 96.3, 111.7, 117.0, 131.1, 137.1, 151.4, 151.7, 153.4; MS (ESI) *m/z* (rel intensity): 237.1 (MH^+, 100), 236.1 (3). HRMS (ESI-TOF): calcd. for $C_{13}H_{17}O_4$ [MH^+], 237.1127; found, 237.1126.

5,6,7-Trimethoxy-2,4-dimethyl-*2H*-chromene (4h). Prepared from **3h** (0.11 g, 0.43 mmol), *p*-TsOH (81.0 mg, 0.43 mmol), *p*-benzoquinone (46.0 mg, 0.43 mmol) and $PdCl_2(CH_3CN)_2$ (11.0 mg, 0.043 mmol) in 1,4-dioxane (28.4 mL) 2 h at rt. **4h** was obtained as an oil (94.2 mg, 88 %) (mixture of regioisomers 92:8): IR (ATR) 2833, 2930, 2970, 3034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (d, J = 6.6 Hz, 3H), 2.15 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 3.85 (s, 3H), 4.58-4.71 (m, 1H), 5.25-5.33 (m, 1H), 6.27 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.4, 21.1, 55.8, 60.9, 61.2, 70.9, 96.4, 111.2, 122.6, 130.3, 136.9, 151.2, 151.3, 153.4; MS (ESI) *m/z* (rel intensity): 251.1 (MH^+, 100). HRMS (ESI-TOF): calcd. for $C_{14}H_{19}O_4$ [MH^+], 251.1283; found, 251.1293.

5,6,7-Trimethoxy-4-methyl-2-propyl-*2H*-chromene (4i). Prepared from **3i** (50.0 mg, 0.18 mmol), *p*-TsOH (34.0 mg, 0.18 mmol), *p*-benzoquinone (19.3 mg, 0.18 mmol) and $PdCl_2(CH_3CN)_2$ (4.6 mg, 0.018 mmol) in 1,4-dioxane (12.0 mL) 2.5 h at rt. **4i** was obtained as an oil (42.9 mg, 86 %) (mixture of regioisomers 96:4): IR (ATR) 2869, 2934, 2959 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, J = 7.1 Hz, 3H), 1.40-1.88 (m, 4H), 2.17 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 3.87 (s, 3H), 4.53-4.59 (m, 1H), 5.35 (d, J = 1.6 Hz, 1H), 6.29 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0, 18.3, 21.2, 36.5, 55.8, 60.9, 61.2, 74.4, 96.5, 111.2, 121.7, 130.2, 136.8, 151.2, 151.3, 153.3; MS (ESI) *m/z* (rel intensity): 279.2 (MH^+, 100), 278.2 (1), 235.1 (1); HRMS (ESI-TOF): calcd. for $C_{16}H_{23}O_4$ [MH^+], 279.1596; found, 279.1601.

2-Isobutyl-5,6,7-trimethoxy-4-methyl-*2H*-chromene (4j). Prepared from **3j** (99.2 mg, 0.34 mmol), *p*-TsOH (64.2 mg, 0.34 mmol), *p*-benzoquinone (36.5 mg, 0.34 mmol) and $PdCl_2(CH_3CN)_2$ (8.8 mg, 0.034 mmol) in 1,4-dioxane (22.5 mL) 2.5 h at rt. **4j** was obtained as an oil (78.1 mg, 79 %) (mixture of regioisomers 94:6): IR (ATR) 2833, 2872, 2934, 2955, 2987, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.93 (d, J = 3.4 Hz, 3H), 0.95 (d, J = 3.4 Hz, 3H), 1.28-1.48 (m, 1H), 1.66-1.98 (m, 2H), 2.15 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 3,85 (s, 3H), 4.50-4.64 (m, 1H), 5.26-5.39 (m, 1H), 6.26 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.2, 22.3, 23.1, 24.4, 43.3, 55.8, 60.9, 61.2, 73.0, 96.5, 111.4, 121.9, 130.1, 136.8, 151.1, 151.3, 153.3; MS (ESI) *m/z* (rel intensity): 293.2 (MH^+, 100), 292.2 (1). HRMS (ESI-TOF): calcd. for $C_{17}H_{25}O_4$ [MH^+], 293.1753; found, 293.1762.

5,6,7-Trimethoxy-4-methyl-2-phenyl-*2H*-chromene (4k). Prepared from **3k** (0.12 g, 0.40 mmol), *p*-TsOH (75.2 mg, 0.40 mmol), *p*-benzoquinone (42.7 mg, 0.40 mmol) and $PdCl_2(CH_3CN)_2$ (10.3 mg, 0.040 mmol) in 1,4-dioxane (26.4 mL) 2 h at rt. **4k** was obtained as an oil (98.4 mg, 79 %) (mixture of regioisomers 94:6): IR (ATR) 2841, 2934, 2966, 3034, 3063 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 3.89 (s, 3H), 5.42-5.52 (m, 1H), 5.57-5.66 (m, 1H), 6.32 (s, 1H), 7.25-7.51 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.3, 55.9, 60.9, 61.3, 76.8, 96.6, 110.8, 120.9, 127.1, 128.2, 128.5, 130.9, 137.1, 140.7, 150.7, 151.4, 153.7; MS (ESI) *m/z* (rel intensity): 313.1 (MH^+, 100); HRMS (ESI-TOF): calcd. for $C_{19}H_{21}O_4$ [MH^+], 313.1440; found, 313.1451.

5,6,7-Trimethoxy-4-methyl-2-(*p*-tolyl)-2*H*-chromene (4l). Prepared from **3l** (0.12 g, 0.37 mmol), *p*-TsOH (70.6 mg, 0.37 mmol), *p*-benzoquinone (40.1 mg, 0.37 mmol) and $PdCl_2(CH_3CN)_2$ (9.6 mg, 0.037 mmol) in 1,4-dioxane (24.7 mL) 3 h at rt. **4l** was obtained as an oil (0.11, 87 %) (mixture of regioisomers 92:8): IR (ATR) 2841, 2934, 2959, 2987, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 2.36 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 3.89 (s, 3H), 5.42-5.52 (m, 1H), 5.52-5.62 (m, 1H), 6.31 (s, 1H), 7.19 (d, J = 7.9 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.2, 21.3, 55.8, 60.9, 61.3, 76.3, 96.7, 110.8, 120.9, 127.2, 129.2, 130.8, 137.0, 137.7, 138.0, 150.7, 151.4, 153.6; MS (ESI) *m/z* (rel intensity): 327.2 (MH^+, 100), 326.2 (2); HRMS (ESI-TOF): calcd. for $C_{20}H_{23}O_4$ [MH^+], 327.1596; found, 327.1600.

5,6,7-Trimethoxy-4-methyl-2-(4-(trifluoromethyl) phenyl)-2*H*-chromene (4m). Prepared from **3m** (0.12 g, 0.32 mmol), *p*-TsOH (61.2 mg, 0.32 mmol), *p*-benzoquinone (34.8 mg, 0.32 mmol) and $PdCl_2(CH_3CN)_2$ (8.3 mg, 0.032 mmol) in 1,4-dioxane (21.4 mL) 5.5 h at rt. **4m** was obtained as an oil (0.11 g, 91 %) (mixture of regioisomers 92:8): IR (ATR) 2841, 2937, 2987, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.81 (s, 6H), 3.89 (s, 3H), 5.45 (d, J = 1.6 Hz, 1H), 5.65 (d, J = 1.6 Hz, 1H), 6.32 (s, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.3 (CH_3), 55.9, 60.9, 61.3, 75.8, 96.6, 110.7, 119.8, 124.3 (q, J = 272.5 Hz), 125.5 (q, J = 3.8 Hz), 127.2, 130.2 (q, J = 32.7 Hz), 131.5, 137.3, 144.7, 150.3, 151.5, 151.9; MS (ESI) *m/z* (rel intensity):

382.1 (MH^+, 100), 380.1 (2); HRMS (ESI-TOF): calcd. for $C_{20}H_{20}F_3O_4$ [MH^+], 381.1314; found, 381.1311.

2-(3-(Benzyloxy)phenyl)-5,6,7-trimethoxy-4-methyl-2*H*-chromene (4n). Prepared from **3n** (0.14 g, 0.34 mmol), *p*-TsOH (64.1 mg, 0.34 mmol), *p*-benzoquinone (36.4 mg, 0.34 mmol) and $PdCl_2(CH_3CN)_2$ (8.7 mg, 0.034 mmol) in 1,4-dioxane (22.5 mL) 2.5 h at rt. **4n** was obtained as an oil (0.12, 84 %) (mixture of regioisomers 93:7): IR (ATR) 2851, 2934, 2962, 2991, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 3.89 (s, 3H), 5.07 (s, 2H), 5.46 (d, J = 1.6 Hz, 1H), 5.58 (bs, 1H), 6.33 (s, 1H), 6.89-7.17 (m, 3H), 7.20-7.49 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.3, 55.9, 60.9, 61.3, 70.0, 76.6, 96.6, 110.8, 113.6, 114.6, 119.7, 120.8, 127.6, 128.0, 128.6, 129.6, 130.9, 136.9, 137.1, 142.4, 150.7, 151.5, 153.7, 159.0; MS (ESI) *m/z* (rel intensity): 419.2 (MH^+, 100), 235.1 (1). HRMS (ESI-TOF): calcd. for $C_{26}H_{27}O_5$ [MH^+], 419.1859; found, 419.1862.

5,6,7-Trimethoxy-4-methyl-2-(naphthalene-2-yl)-*2H*-chromene (4o). Prepared from **3o** (0.12 g, 0.34 mmol), *p*-TsOH (64.6 mg, 0.34 mmol), *p*-benzoquinone (36.7 mg, 0.34 mmol) and $PdCl_2(CH_3CN)_2$ (8.8 mg, 0.034 mmol) in 1,4-dioxane (22.7 mL) 2.5 h at rt. **4o** was obtained as an oil (0.10 g, 81 %) (mixture of regioisomers 89:11): IR (ATR) 2837, 2934, 2962, 3056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.31 (t, J = 1.5 Hz, 3H), 3.81 (s, 3H), 3.85 (s, 3H), 3.93 (s, 3H), 5.56-5.67 (m, 1H), 5.72-5.83 (m, 1H), 6.36 (s, 1H), 7.41-7.53 (m, 2H), 7.62 (dd, J = 8.5, 1.6 Hz, 1H), 7.81-7.94 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.4, 55.9, 60.9 (OCH_3), 61.3, 76.8, 96.7, 110.9, 120.7, 125.1, 126.1, 126.2, 127.7, 128.2, 128.4, 131.1, 133.2, 133.3, 137.1, 138.0, 150.7, 151.5, 153.8; MS (ESI) *m/z* (rel intensity): 363.2 (MH^+, 100); HRMS (ESI-TOF): calcd. for $C_{23}H_{23}O_4$ [MH^+], 363.1596; found, 363.1592.

2-(Furan-3-yl)-5,6,7-trimethoxy-4-methyl-2*H*-chromene (4p). Prepared from **3p** (0.11 g, 0.37 mmol), *p*-TsOH (69.5 mg, 0.37 mmol), *p*-benzoquinone (39.5 mg, 0.37 mmol) and $PdCl_2(CH_3CN)_2$ (9.5 mg, 0.037 mmol) in 1,4-dioxane (24.4 mL) 3 h at rt. **4p** was obtained as an oil (80.2 mg, 72 %) (mixture of regioisomers 92:8): IR (ATR): 2851, 2934, 2962, 2991, 3009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 3.80 (s, 3H), 3.80 (s, 3H), 3.87 (s, 3H), 5.47-5.51 (m, 1H), 5.52-5.56 (m, 1H), 6.29 (s, 1H), 6.46 (bs, 1H), 7.39 (bs, 1H), 7.43 (bs, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.2, 55.8, 60.9, 61.2, 69.0, 96.7,

109.5, 111.0, 119.7, 125.1, 131.3, 137.1, 140.8, 143.4, 150.4, 151.4, 153.6; MS (ESI) *m/z* (rel intensity): 303.1 (MH^+, 100), 302.1 (2). HRMS (ESI-TOF): calcd. for $C_{17}H_{19}O_5$ [MH^+], 303.1233; found, 303.1240.

6,7-Dimethoxy-2,4-dimethyl-*2H*-chromene (4q). Prepared from **3q** (0.12 g, 0.53 mmol), *p*-TsOH (0.10 g, 0.53 mmol), *p*-benzoquinone (56.9 mg, 0.53 mmol) and $PdCl_2(CH_3CN)_2$ (13.7 mg, 0.053 mmol) in 1,4-dioxane (35.1 mL) 1 h at 70 ºC. **4q** was obtained as an oil (71.0 mg, 61 %): IR (ATR) 2837, 2858, 2934, 2970, 3088 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.40 (d, *J* = 6.5 Hz, 3H), 1.99 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 4.78-4.94 (m, 1H), 5.28-5.38 (m, 1H), 6.45 (s, 1H), 6.69 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.0, 21.1, 55.9, 56.8, 71.4, 100.7, 107.6, 115.8, 121.1, 129.4, 143.2, 148.3, 149.6; MS (ESI) *m/z* (rel intensity): 221.1 (MH^+, 100), 220.1 (5), 219.1 (32); HRMS (ESI-TOF): calcd. for $C_{13}H_{17}O_3$ [MH^+], 221.1178; found, 221.1182.

6,7-Dimethoxy-4-methyl-2-phenyl-*2H*-chromene (4r). Prepared from **3r** (0.11 g, 0.39 mmol), *p*-TsOH (74.6 mg, 0.39 mmol), *p*-benzoquinone (42.4 mg, 0.39 mmol) and $PdCl_2(CH_3CN)_2$ (10.2 mg, 0.039 mmol) in 1,4-dioxane (26.1 mL) 3 h at 70 ºC. **4r** was obtained as an oil (60.5 mg, 55 %): IR (ATR) 2833, 2855, 2920, 2955, 3002, 3031, 3060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.10 (s, 3H), 3.84 (s, 3H), 3.89 (s, 3H), 5.50-5.55 (m, 1H), 5.79-5.83 (m, 1H), 6.49 (s, 1H), 6.76 (s, 1H), 7.2-7.54 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.1, 55.9, 56.8, 77.3, 100.7, 107.6, 115.3, 119.2, 127.0, 128.2, 128.6, 129.8, 141.3, 143.3, 147.9, 149.9; MS (ESI) *m/z* (rel intensity): 281.1 ($[M-H]^+$, 100), 267.1 (1). HRMS (ESI-TOF): calcd. for $C_{18}H_{17}O_3$ $[M-H]^+$: 281.1178; found, 281.1172.

6,8-Dimethyl-6*H*-[1,3]dioxolo[4,5-*g*]chromene (4s). Prepared from **3s** (81.5 mg, 0.40 mmol), *p*-TsOH (75.2 mg, 0.40 mmol), *p*-benzoquinone (42.7 mg, 0.40 mmol) and $PdCl_2(CH_3CN)_2$ (10.3 mg, 0.040 mmol) in 1,4-dioxane (26.3 mL) 2.5 h at 70 ºC. **4s** was obtained as an oil (48.3 mg, 60 %): IR (ATR) 2895, 2923, 2973, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (d, *J* = 6.5 Hz, 3H), 1.98 (s, 3H), 4.77-4.92 (m, 1H), 5.30-5.40 (m, 1H), 5.92 (s, 2H), 6.43 (s, 1H), 6.68 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.3, 20.8, 71.4, 98.6, 101.0, 103.2, 117.0, 121.1, 129.7, 141.7, 147.3, 149.1; MS (ESI) *m/z*

(rel intensity): 203.1 ([M - H]$^+$, 100), 189.1 (1). HRMS (ESI-TOF): calcd. for $C_{12}H_{11}O_3$ [M - H]$^+$: 203.0708; found, 203.0717.

5,7-Dimethoxy-3,4-dimethyl-*2H*-chromene (4t).[42] Prepared from **3t** (0.11 g, 0.51 mmol), *p*-TsOH (97.4 mg, 0.51 mmol), *p*-benzoquinone (55.3 mg, 0.51 mmol) and $PdCl_2(CH_3CN)_2$ (6.6 mg, 0.026 mmol) in 1,4-dioxane (34.1 mL) 1.5 h at rt. **4t** was obtained as a solid (93.2 mg, 83 %): mp (CH_2Cl_2) 56-58 ºC; IR (ATR) 2841, 2934, 2962, 2991 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.83 (s, 3H), 2.11 (s, 3H), 3.79 (s, 3H), 3.81 (s,3H), 4.38 (s, 2H), 6.09-6.20 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 15.9, 16.0, 55.3, 55.4, 69.8, 93.2, 93.6, 109.3, 122.5, 123.6, 156.7, 158.0, 159.7; MS (ESI) *m/z* (rel intensity): 221.1 (MH$^+$, 100). HRMS (ESI-TOF): calcd. for $C_{13}H_{17}O_3$ [MH$^+$], 221.1178; found, 221.1181.

5,7-Dimethoxy-4-methyl-3-phenyl-*2H*-chromene (4u). Prepared from **3u** (96.3 mg, 0.34 mmol), *p*-TsOH (64.4 mg, 0.34 mmol), *p*-benzoquinone (36.6 mg, 0.34 mmol) and $PdCl_2(CH_3CN)_2$ (4.4 mg, 0.017 mmol) in 1,4-dioxane (22.6 mL) 2.5 h at rt. **4u** was obtained as an oil (83.3 mg, 87 %): IR (ATR) 2837, 2934, 2966, 3002, 3060, 3077 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (t, *J* = 1.4 Hz, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 4.69 (q, *J* = 1.4 Hz, 2H), 6.17 (d, *J* = 2.4 Hz, 1H), 6.20 (d, *J* = 2.4 Hz, 1H), 7.22-7.46 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.0, 55.4, 55.5, 69.8, 93.3, 93.5, 109.5, 126.4, 126.8, 128.3, 128.4, 129.4, 139.1, 157.3, 158.5, 160.6; MS (ESI) *m/z* (rel intensity): 283.1 (MH$^+$, 100), 282.1 (7), 281.1 (37). HRMS (ESI-TOF): calcd. for $C_{18}H_{19}O_3$ [MH$^+$], 283.1334; found, 283.1334.

3-(4-Fluorophenyl)-5,7-dimethoxy-4-methyl-*2H*-chromene (4v). Prepared from **3v** (0.11 g, 0.35 mmol), *p*-TsOH (67.3 mg, 0.35 mmol), *p*-benzoquinone (38.2 mg, 0.35 mmol) and $PdCl_2(CH_3CN)_2$ (4.6 mg, 0.018 mmol) in 1,4-dioxane (23.6 mL) 4 h at rt. **4v** was obtained as a solid (83.7 mg, 79 %): mp (CH_2Cl_2) 94-95 ºC; IR (ATR) 2851, 2923, 2952, 2970, 2995, 3049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 4.65 (s, 2H), 6.17 (d, *J* = 2.3 Hz, 1H), 6.19 (d, *J* = 2.3 Hz, 1H), 7.07 (t, *J* = 8.7 Hz, 2H), 7.25-7.33 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.0, 55.3, 55.4, 69.7, 93.3, 93.5, 109.3, 115.2 (d, *J* = 21.3 Hz), 126.7, 127.3, 131.0 (d, *J* = 7.9 Hz), 134.9 (d, *J* = 3.4 Hz), 157.3,

158.5, 160.7, 161.7 (d, J = 248.1 Hz); MS (ESI) *m/z* (rel intensity): 301.1 (MH^+, 100), 299.1 (20), 287.1 (4); HRMS (ESI-TOF): calcd. for $C_{18}H_{18}FO_3$ [MH^+], 301.1240; found, 301.1235.

3-(4-Chlorophenyl)-5,7-dimethoxy-4-methyl-*2H*-chromene (4w). Prepared from **3w** (94.0 mg, 0.29 mmol), *p*-TsOH (56.1 mg, 0.29 mmol), *p*-benzoquinone (31.9 mg, 0.29 mmol) and $PdCl_2(CH_3CN)_2$ (3.8 mg, 0.015 mmol) in 1,4-dioxane (19.7 mL) 5.5 h at rt. **4w** was obtained as a solid (68.6 mg, 73 %): mp (CH_2Cl_2) 101-102 ºC; IR (ATR) 2837, 2855, 2901, 2934, 2952, 2977, 2995, 3006, 3056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.10 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 4.64 (s, 2H), 6.16 (d, J = 2.2 Hz, 1H), 6.19 (d, J = 2.2 Hz, 1H), 7.26 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.0, 55.3, 55.4, 69.6, 93.4, 93.5, 109.3, 127.1, 127.2, 128.5, 130.8, 132.6, 137.5, 157.3, 158.5, 160.7; MS (ESI) *m/z* (rel intensity): 319.1 (MH^+ + 2, 24), 317.1 (MH^+, 100), 316.1 (11), 315.1 (25); HRMS (ESI-TOF): calcd. for $C_{18}H_{18}ClO_3$ [MH^+], 317.0944; found, 317.0930.

Hydrogenation of 4a. Over a solution of **4a** (*endo:exo* 93:7) in dry MeOH (3 mL), Pd-C (7.4 mg) (5% in 50% water) was added under argon atmosphere. The reaction flask was evacuated and refilled with H_2 twice and the reaction mixture was stirred vigorously under H_2 atmosphere for 16 h. The resulting mixture was filtered through Celite® and washed with MeOH. The solvent was evaporated *in vacuo* and purification by flash column chromatography (silica gel, petroleum ether/AcOEt 19/1) afforded the corresponding chromane **5**[42] as an oil (21.7 mg, 89%): IR (ATR) 2841, 2880, 2923, 2955, 3006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.23 (d, J = 6.9 Hz, 3H), 1.54-1.60 (m, 1H), 1.94-2.12 (m, 1H), 2.96-3.08 (m, 1H), 3.75 (s, 3H), 3.79 (s, 3H), 4.05-4.16 (m, 1H), 4.17-4.25 (m, 1H), 6.02 (d, J = 2.3 Hz, 1H), 6.05 (d, J = 2.3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.2, 22.9, 29.1, 55.2, 55.3, 60.0, 91.3, 93.2, 108.9, 155.3, 158.9, 159.2; MS (ESI) *m/z* (rel intensity): 209.1 (MH^+, 100); HRMS (ESI-TOF): calcd. for $C_{12}H_{17}O_3$ [MH^+], 209.1178; found, 209.1178.

3,5-Dimethoxyphenyl but-3-enoate (6). Over a solution of 3-butenoic acid (0.40 mL, 4.7 mmol) in CH_2Cl_2 (4.7 mL), were added subsequently 3,5-dimethoxyphenol (0.87 g, 5.6 mmol), *N,N´*-dicyclohexylcarbodiimide (DCC) (1.2 g, 6.5 mmol) and 4-dimethylaminopyrine (DMAP) (69.0 mg, 0.47 mmol). The reaction mixture was stirred at room temperature for 5 h. After that time, the reaction

mixture was filtered and the filtrate was washed with a 1 M aqueous solution of NaOH (2 × 20 mL) and the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification by flash column chromatography (petroleum ether/AcOEt 8/2), afforded **6** as an oil (0.95 g, 91 %): IR (ATR) 1739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.32 (d, J = 6.8 Hz), 3.75 (s, 6H), 5.19-5.35 (m, 2H), 5.92-6.12 (m, 1H), 6.28-6.31 (m, 2H), 6.34-6.38 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 39.1, 55.4. 98.3, 100.1, 119.2, 129.6, 152.2, 161.2, 169.8; MS (ESI) *m/z* (rel intensity): 245.1 (MNa^+, 33), 242.1 (12), 155.1 (100); HRMS (ESI-TOF): calcd. for $C_{12}H_{14}O_4Na$ [MNa^+], 245.0790; found: 245.0783.

5,7-Dimethoxy-4-methyl-2H-chromen-2-one (7). A solution of ester **6** (0.10, 0.46 mmol), *p*-TsOH (86.6 mg, 0.46 mmol), *p*-benzoquinone (49.2 mg, 0.46 mmol) and $PdCl_2(CH_3CN)_2$ (11.8 mg, 0.046 mmol) in 1,4-dioxane (30.4 mL) was stirred at 70 ºC for 5 h. Then, the reaction was quenched by addition of water and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with an aqueous 1M solution of NaOH (3 × 15 mL) and with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. After purification by flash column chromatography (silica gel, petroleum ether/AcOEt 8/2) coumarin **7** was obtained as a solid (70.1 mg, 70 %): mp (CH_2Cl_2) 166-168 ºC [Lit.[43] mp (methanol) 168-170 ºC]; IR (ATR) 1724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.50 (d, J = 1.2 Hz, 3H), 3.82 (s, 3H), 3.83 (s, 3H), 5.91 (s, 1H), 6.26 (d, J = 2.4 Hz, 1H), 6.39 (d, J = 2.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 24.2, 55.6, 55.7, 93.4, 95.4, 104.8, 111.3, 154.5, 156.9, 159.1, 162.8, 161.0; MS (EI) *m/z* (rel intensity): 220.1 (M^+, 100), 193.1 (11), 192.1 (91), 178.1 (10), 177.1 (73), 149.0 (13); HRMS (ESI-TOF): calcd. for $C_{12}H_{13}O_4$ [MH^+], 221.0814; found: 221.0811.

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Supporting Information Available. X-ray structure determination of **4v** (CCDC 1872267), and copies of ^{1}H and ^{13}C NMR spectra of compounds **1a-h, 2a-h, 3a-w, 4a-w, 5-7**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For representative reviews, see: (a) de Meijere, A.; Bräse, S.; Oestreich, M., Eds. *Metal-Catalyzed Cross-Coupling Reactions and More*; Wiley-VCH: Wenheim, Germany, 2014; Vol.1-3. (b) Shen, C. H. Selected Applications of Transition Metal-Catalyzed Carbon–Carbon Cross-Coupling Reactions in the Pharmaceutical Industry. In *Applications of Transition Metal Catalysis in Drug Discovery and Development: An Industrial Perspective*; Crawley, M. L.; Trost B. M., Eds.; Wiley: Hoboken, 2012; pp. 25-95.

(2) Lei, A.; Shi, W.; Liu, W.; Zhang, H.; He, C. *Oxidative Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2017.

(3) Suna, E.; Shubin, K. Intramolecular Coupling via C(sp^2)-H Activation. In *Science of Synthesis. Cross Coupling and Heck-Type Reactions 3. Metal-Catalyzed Heck-Type Reactions and C-H Couplings via C-H Activation*; Larhed, M. Ed.; Georg Thieme Verlag: Stuttgart, 2013; pp. 643–653.

(4) (a) Ferreira, E. M.; Stoltz, B. M. Catalytic C-H Bond Functionalization with Palladium(II): Aerobic Oxidative Annulations of Indoles. *J. Am. Chem. Soc.* **2003**, *125*, 9578-9579. (b) Abbiati, G.; Beccalli, E. M.; Broggini, G.; Zoni, C. Regioselectivity on the Palladium-Catalyzed Intramolecular Cyclization of Indole Derivatives. *J. Org. Chem*. **2003**, *68*, 7625-7628. (c) Kong, A.; Han, X.; Lu, X. Highly Efficient Construction of Benzene Ring in Carbazoles by Palladium-Catalyzed *endo*-Mode Oxidative Cyclization of 3-(3'-Alkenyl)indoles. *Org. Lett*. **2006**, *8*, 1339-1342. (d) Schiffner, J. A.; Machotta, A. B.;

Oestreich, M. A Catalytic Asymmetric Fujiwara-Moritani Cyclization. *Synlett* **2008**, *15*, 2271-2274; (e) Schiffner, J. A.; Woste, T. H.; Oestreich, M. Enantioselective Fujiwara–Moritani Indole and Pyrrole Annulations Catalyzed by Chiral Palladium(II)–NicOx Complexes. *Eur. J. Org. Chem*. **2010**, 174-182. (f) Donets, P. A.; Van der Eycken, E. V. Synthesis of the Azepinoindole Framework via Oxidative Heck (Fujiwara-Moritani) Cyclization. *Synthesis* **2011**, 2147-2153.

(5) (a) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. Direct Oxidative Heck Cyclizations: Intramolecular Fujiwara–Moritani Arylations for the Synthesis of Functionalized Benzofurans and Dihydrobenzofurans. *Angew. Chem. Int. Ed.* **2004**, *43*, 6144-6148. (b) Ferreira, E. M.; Zhang, H.; Stoltz, B. M. C-H Bond Functionalizations with Palladium(II): Intramolecular Oxidative Annulations of Arenes. *Tetrahedron* **2008**, *64*, 5987-6001. (c) Gao, Y.; Gao, Y.; Wu, W.; Jiang, H.; Yang, X.; Liu, W.; Li, C.-J. Palladium-Catalyzed Tandem Oxidative Arylation/Olefination of Aromatic Tethered Alkenes/Alkynes. *Chem. Eur. J*. **2017**, *23*, 793-797.

(6) Bowie, A. L.; Trauner, D. Total Synthesis of (±)-Rhazinal Using Novel Palladium-Catalyzed Cyclizations. *J. Org. Chem*. **2009**, *74*, 1581-1586.

(7) Garg, N. K.; Stoltz, B. M. A Unified Synthetic Approach to the Pyrazinone Dragmacidins. *Chem. Commun.* **2006**, 3769-3779.

(8) Schiffner, J. A.; Oestreich, M. All-Carbon-Substituted Quaternary Carbon Atoms in Oxindoles by an Aerobic Palladium(II)-Catalyzed Ring Closure onto Tri- and Tetrasubstituted Double Bonds. *Eur. J. Org. Chem.* **2011**, 1148-1154.

(9) (a) Han, X.; Lu, X. Novel Palladium-Catalyzed Acyloxylation/Cyclization of 2-(3'-Alkenyl)indoles. *Org. Lett.* **2009**, *11*, 2381-2384. (b) Jaegli, S.; Dufour, J.; Wei, H.-I.; Piou, T.; Duan, X.-H.; Vors, J.-P.; Neuville, L.; Zhu, J. Palladium-Catalyzed Carbo-Heterofunctionalization of Alkenes for the Synthesis of Oxindoles and Spirooxindoles. *Org. Lett.* **2010**, *12*, 4498-4501. (c) Mu, X.; Wu, T.; Wang, H.-Y.;

Guo, Y.-I.; Liu, G. Palladium-Catalyzed Oxidative Aryltrifluoromethylation of Activated Alkenes at Room Temperature. *J. Am. Chem. Soc*. **2012**, *134*, 878-881.

(10) Wu, T.; Mu, X.; Liu, G. Palladium-Catalyzed Oxidative Arylalkylation of Activated Alkenes: Dual C-H Bond Cleavage of an Arene and Acetonitrile. *Angew. Chem. Int. Ed.* **2011**, *50*, 12578-12581.

(11) Ortiz-de-Elguea, V.; Sotomayor, N.; Lete, E. Two Consecutive Pd(II)-promoted C-H Alkenylation Reactions for the Synthesis of Substituted 3-Alkenylquinolones. *Adv. Synth. Catal.* **2015**, *357*, 463-473.

(12) Costa, M.; Dias, T. A.; Brito, A.; Proença, F. Biological Importance of Structurally Diversified Chromenes. *Eur. J. Med. Chem.* **2016**, *123*, 487-507.

(13) Pratap, R.; Ram, V. J. Natural and Synthetic Chromenes, Fused Chromenes, and Versatility of Dihydrobenzo[*h*]chromenes in Organic Synthesis. *Chem. Rev*. **2014**, *114*, 10476−10526.

(14) Paramonov, S. V.; Lokshin, V.; Fedorova, O. A. Spiropyran, Chromene or Spirooxazine Ligands: Insights into Mutual Relations between Complexing and Photochromic Properties. *J. Photochem. Pthobiol., C:Photochem. Rev.* **2011**, *12*, 209-236.

(15) Uchida, H.; Kosuga, N.; Satoh, T.; Hotta, D.; Kamino, T.; Maeda, Y.; Amano, K.-I.; Akada Y. (Mochida Pharmaceutical Co., Ltd., Japan) Preparation of Novel 2-(Bicyclic Heterocyclidene)acetamide Derivatives as Antagonists of Transient Receptor Potential Type 1 (TRPV1). PCT Int. Appl. WO 2007010383 A1 20070125, Jan 25, 2007; *Chem. Abstr.* **2007**, *146*, 163039.

(16) Lee, Y.; Hong, S.; Cui, M.; Sharma, P. K.; Lee, J.; Choi, S. Transient Receptor Potential Vanilloid Type 1 Antagonists: A Patent Review (2011 - 2014). *Expert. Opin. Ther. Pat*. **2015**, *25*, 291-318.

(17) Kelley, J. L.; Rigdon, G. C.; Cooper, B. R.; McLean, E. W.; Musso, D. L.; Orr, G. F.; Selph, J. L.; Styles V. L. (Glaxo Wellcome Inc., USA) Preparation of Indanylideneacetamides, Naphthylideneacetamides, and Benzopyranylideneacetamides as Muscle Relaxants. US 6124284 A 20000926, Sep 26, 2000; *Chem. Abstr.* **2000**, *133*, 252177..

(18) Halskov, K. S.; Donslund, B. S.; Barfüsser, S.; Jørgensen, K. A. Organocatalytic Asymmetric Formation of Steroids. *Angew. Chem. Int. Ed*. **2014**, *53*, 4137-4141.

(19) Thomas, N.; Zachariah, S. M. Pharmacological Activities of Chromene Derivatives: An Overview. *Asian J. Pharm. Clin. Res.* **2013**, *6 (Suppl. 2)*, 11-15.

(20) Gupta, A.; Ahmad, I.; Kureel, J.; Hasanain, M.; Pandey, P.; Singh, S.; John, A. A.; Sarkar, J.; Singh, D. Induction of Targeted Osteogenesis with 3-Aryl-2*H*-Benzopyrans and 3-Aryl-3*H*-Benzopyrans: Novel Osteogenic Agents *J. Steroid Biochem. Mol. Biol.* **2016**, *153*, 63-75.

(21) Majumdar, N.; Paul, N. D.; Mandal, S.; de Bruin, B.; Wulff, W. D. Catalytic Synthesis of 2*H*-Chromenes. *ACS Catal.* **2015**, *5*, 2329−2366.

(22) Youn, S. W.; Eom, J. I. Facile Construction of the Benzofuran and Chromene Ring Systems via Pd^{II}-Catalyzed Oxidative Cyclization. *Org. Lett*. **2005**, *7*, 3355-3358.

(23) Li, S.; Li, F.; Gong, J.; Yang, Z. Palladium-Catalyzed Carbonylative Cyclization of Aryl Alkenes/Alkenols: A New Reaction Mode for the Synthesis of Electron-Rich Chromanes. *Org. Lett*. **2015**, *17*, 1240-1243.

(24) Carral-Menoyo, A.; Ortiz-de Elguea, V.; Martínez-Nunes, M.; Sotomayor, N.; Lete, E. Palladium-Catalyzed Dehydrogenative Coupling: An Efficient Synthetic Strategy for the Construction of the Quinoline Core. *Mar. Drugs* **2017**, *15*, 276.

(25) Martínez-Estíbalez, U.; García-Calvo, O.; Ortiz-de-Elguea, V.; Sotomayor, N.; Lete, E. Intramolecular Mizoroki-Heck Reaction in the Regioselective Synthesis of 4-Alkylidene Tetrahydroquinolines. *Eur. J. Org. Chem.* **2013**, 3013-3022.

(26) (a) Coya, E.; Sotomayor, N.; Lete, E. Enantioselective Palladium-catalyzed Heck–Heck Cascade Reactions. Ready Access to the Tetracyclic Core of Lycorane Alkaloids. *Adv. Synth. Catal.* **2015**, *357*, 3206-3214. (b) Coya, E.; Sotomayor, N.; Lete, E. Intramolecular Direct Arylation and Heck Reactions

in the Formation of Medium Sized Rings. Selective Synthesis of Fused Indolizine, Pyrroloazepine and Pyrroloazocine Systems. *Adv. Synth. Catal.* **2014**, *356*, 1853-1865. (c) Lage, S.; Martínez-Estíbalez, U.; Sotomayor, N.; Lete, E. Intramolecular Palladium-catalyzed C-H Activation vs Heck Reactions. Synthesis of Pyrroloisoquinolines and Isoindoles. *Adv. Synth. Catal.* **2009**, *351*, 2460-2468.

(27) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. Selective Pd-Catalyzed Oxidative Coupling of Anilides with Olefins through C-H Bond Activation at Room Temperature. J. *Am. Chem. Soc.* **2002**, *124*, 1586–1587.

(28) For selected recent reviews, see: (a) Le Bras, J.; Muzart, J. Intermolecular Dehydrogenative Heck Reactions. *Chem. Rev.* **2011**, *111*, 117-1214. (b) Rauf, W.; Brown, J. M. Reactive Intermediates in Catalytic Alkenylation; Pathways for Mizoroki–Heck, Oxidative Heck and Fujiwara–Moritani Reactions. *Chem. Commun.* **2013**, *49*, 8430-8440. (c) Zhou, L.; Lu, W. Towards Ideal Synthesis: Alkenylation of Aryl C-H Bonds by a Fujiwara–Moritani Reaction. *Chem. Eur. J.* **2014**, *20*, 634-642. (d) Kitamura, T.; Fujiwara Y. Dehydrogenative Heck-type Reactions: The Fujiwara–Moritani Reaction. In *From C-H to C-C Bonds: Cross-Dehydrogenative-Coupling*; Li, C.-J., Ed.; Royal Society of Chemistry: London, 2015; pp. 33-54. (e) Topczewski, J. J.; Sanford, M. S. Carbon-Hydrogen (C-H) Bond Activation at Pd^{IV}: A Frontier in C-H Functionalization Catalysis. *Chem. Sci.* **2015**, *6*, 70-76. (f) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. Mild Metal-Catalyzed C–H Activation: Examples and Concepts. *Chem. Soc. Rev.* **2016**, *45*, 2900-2936.

(29) (a) Liu, C.; Widenhoefer, R. A. Palladium-Catalyzed Cyclization/Carboalkoxylation of Alkenyl Indoles. *J. Am. Chem. Soc.* **2004**, *126*, 10250-10251. b) Kandukuri, S. R.; Schiffner, J. A.; Oestreich, M. Aerobic Palladium(II)-Catalyzed 5-endo-trig Cyclization: An Entry into the Diastereoselective C-2 Alkenylation of Indoles with Tri- and Tetrasubstituted Double Bonds. *Angew. Chem. Int. Ed.* **2012**, *51*, 1265-1269.

(30) CCDC 1872267 contains the supplementary crystallographic data for **4v**. These data can be obtained from The Cambridge Crystallographic Data Centre.

(31) Hornillos, V.; van Zijl, A. W.; Feringa, B. L. Catalytic Asymmetric Synthesis of Chromenes and Tetrahydroquinolines *via* Sequential Allylic Alkylation and Intramolecular Heck Coupling. *Chem. Commun.* **2012**, 3712-3714.

(32) For selected examples of preparation of flavenes via transition-metal catalyzed methods, see, for example: (a) Pastine, S. J.; Youn, S. W.; Sames, D. Pt^{IV}-Catalyzed Cyclization of Arene−Alkyne Substrates via Intramolecular Electrophilic Hydroarylation. *Org. Lett.* **2003**, *5*, 1055-1058. (b) Scheidt, K. A.; Zeng, B.-S. Catalytic Enantioselective Synthesis of 2-ArylChromenes and Related Phosphoramidite Ligands and Catalyst Compounds. U.S. Pat. Appl. 20150315168 A1 20151105, Nov 5, 2015; *Chem. Abstr.* **2015**, *163*, 676768. (c) Iridium-catalyzed Allylic Etherification/RCM: He, H.; Ye, K. Y.; Wu, Q. F.; Dai, L. X.; You, S. L. Iridium-catalyzed Asymmetric Allylic Etherification and Ring-Closing Metathesis Reaction for Enantioselective Synthesis of Chromene and 2,5-Dihydrobenzo[*b*]oxepine Derivatives. *Adv. Synth. Catal.* **2012**, *354*, 1084-1094.

(33) See for example: Ma, L.; Li, W.; Xi, H.; Bai, X.; Ma, E.; Yan, X.; Li, Z. $FeCl_3$-Catalyzed Ring-Closing Carbonyl-Olefin Metathesis. *Angew. Chem. Int. Ed.* **2016**, *55*, 10410-10413.

(34) Isoflavenes are usually prepared by sequences that involve stoichiometric steps, such as an intramolecular Wittig reaction (Erhardt, P. W.; Khupse, R. S.; Luniwal, A. (The University of Toledo, USA) Methods for Synthesizing Glycinols, Glyceollins I and II and Isoflavenes and Chromanes using a Wittig Reaction, and Compositions made therewith. U.S. Pat. Appl. 20120115942 A1 20120510, May 10, 2012; *Chem. Abstr.* **2012**, *156*, 613224) or by transformation of other chromane derivatives, such as the chroman-4-ones (see for example, ref. 20).

(35) Yoo, J.; Oh, K. E.; Keum, G.; Kang, S. B.; Kim, Y. Indium-mediated Monoallylation of Carbonyl Compounds with Allylic Chlorides and Bisallylation of 2-Pyridyl Carboxylates with Allylic Halides in Aqueous Media. *Polyhedron*, **2000**, *19*, 549-551.

(36) Reetz, M. T.; Steinbach, R.; Westermann, J.; Peter, R. Chemo- and Diastereoselective Addition of Alkyl and Aryl Titanium(IV) Compounds to Aldehydes and Ketones. *Angew. Chem*. **1980**, *92*, 1044-1045.

(37) Li, L.-H.; Chan, T. H. Organometallic Reactions in Aqueous Media. Antimony-mediated Allylation of Carbonyl Compounds with Fluoride Salts. *Tetrahedron Lett.* **2000**, *41*, 5009-5012.

(38) Grigg, R.; Putnikovic, B.; Urch, C. J. Electrochemically driven Catalytic Pd(0)/Cr(II) mediated Coupling of Organic Halides with Aldehydes. The Nozaki-Hiyama-Kishi Reaction. *Tetrahedron Lett.* **1997**, *38*, 6307-6308.

(39) Lu, J.-T.; Shi, Z.-F.; Cao, X.-P. Total Synthesis of (-)-Chanoclavine I and an Oxygen-Substituted Ergoline Derivative. *J. Org. Chem.* **2017**, *82*, 7774-7782.

(40) Miura, T.; Takahashi, Y.; Murakami, M. Rhodium-catalysed Substitutive Arylation of *Cis*-Allylic Diols with Arylboroxines. *Chem. Commun.* **2007**, 595-597.

(41) Ent, H.; De Koning, H.; Speckamp, W. N. 2-Azonia-Cope Rearrangement in *N*-Acyliminium Cyclizations. *J. Org. Chem.* **1986**, *51*, 1687-1691.

(42) Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. Gold-catalyzed Hydroarylation of Allenes: A Highly Regioselective Carbon-Carbon Bond Formation Producing Six-Membered Rings. *Org. Lett*. **2007**, *9*, 4821-4824.

(43) Trost, B. M.; Toste, F. D.; Greenman, K. Atom Economy. Palladium-Catalyzed Formation of Coumarins by Addition of Phenols and Alkynoates via a Net C−H Insertion. *J. Am. Chem. Soc.* **2003**, *125*, 4518-4526.