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Pt(IV)-catalyzed generation and [4+2]-cycloaddition reactions of *o*-quinone methides

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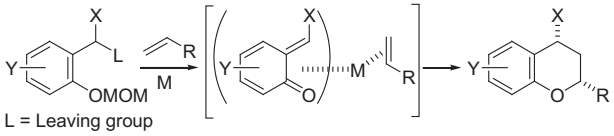
ABSTRACT

Novel intermolecular and intramolecular generations of *ortho*-quinone methides and their formal [4+2]-cycloaddition reactions with olefins catalyzed by $PtCl_4$ and $AuCl_3$ under mild conditions have been developed. Good to excellent yields (up to 99%) and diastereoselectivity (up to >99:1) of the chromans were obtained. $PtCl_4$ was found to be effective and compatible with various functional groups present in the substrates. A mechanism accounting for its catalytic cycle is proposed and discussed.

1. Introduction

Metal-catalyzed reactions have revolutionized modern synthetic methodologies and their development has made possible total syntheses of structurally complex natural products. In recent years, platinum and gold salts/complexes have drawn much attention and their use as catalysts for various organic transformations have been developed.[1] The chemistry of Pt(II), Pt(IV), Au(I), and Au(III) and their use in organic synthesis has been studied and reported.[1f–i] However, chemistry of these metal salts/complexes has largely involved activation of the π-system of the alkyne rather than that of the olefin.[1e–i]

A number of methods have been developed to generate the transient highly reactive *ortho*-quinone methides (*o*-QMs). In addition to thermal and base initiation, some Lewis acids and transition metal salts/complexes of Os, Rh, Ir, Mn, and Pd were reported to mediate the generation of *o*-QMs.[2] Recently, our research group has been involved with acid-mediated generation of *o*-QMs and their cycloaddition reactions using *p*-TsOH immobilized on silica (PTS–Si).[3] The resulting 2-aryl chromans can be functionalized to provide the core structures of natural and synthetic compounds exhibiting a wide array of biological properties.[4] Herein, we report, for the first time, a novel Pt(IV)- and Au(III)-catalyzed generation of *o*-QMs and their cycloaddition reactions via Pt(IV)- and Au(III)-activation of olefin and coordination with *o*-QM (Scheme 1).



Scheme 1. Metal-catalyzed generation of *o*-QMs and cycloaddition reactions.

2. Results and discussion

We envisioned that, upon coordination with metal salts/complexes, the *o*-QM may be stabilized for the subsequent cycloaddition reactions to provide the chroman products. One drawback, albeit a minor one, of our previously developed method for the generation of *o*-QM and its cycloaddition reactions using PTS–Si was the required stoichiometric amount of the acid, which may not be compatible with a number of functional groups present on the *o*-QM precursor or the olefin. Taken together, with appropriate metal salts/complexes, a catalytic process may be developed to circumvent the drawback.

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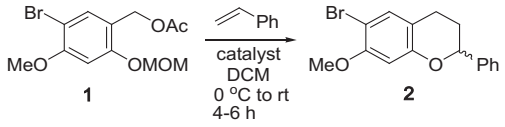
2.1. Intermolecular [4+2]-cycloaddition reactions

Our preliminary data using PTS–Si to generate *o*-QMs showed that compound **1** gave the best results and was thus chosen as the *o*-QM precursor for the screening of Lewis acids and transition metal salts/complexes.[3,5] As summarized in Table 1, it was found that stoichiometric amount of $AlCl_3$, $TiCl_3$, $TiCl_4$, $ZrCl_4$, $FeCl_3$, $ZnCl_2$, AuCl, $AuCl_3$, $InCl_3$, $PtCl_2$, and $PtCl_4$ gave the desired product **2** in 26–85% yields while catalytic amount (10–30 mol %) of only $PtCl_4$, $AuCl_3$, and $InCl_3$,[6] furnished the chroman in 62–88% yields. In a larger scale reaction, the required amount of the $PtCl_4$ could be reduced to 4 mol %, which gave the product in a slightly lower yield (76%). In fact, the reactions using catalytic amount of metal salts proceeded more cleanly than those using stoichiometric amount, giving the product in higher yields (entries 7 and 10). An increase in electrophilicity, rather than the oxidation state, of the metal center (Pt) is an important factor responsible for the successful catalysis of generating *o*-QMs and mediating cycloaddition reactions. Whilst possessing the same oxidation state (Pt(IV)) and ligand (Cl), $PtCl_4$, but not K_2PtCl_6, is a useful catalyst (entries 10 and 11). Previous work suggested that an increase in oxidation state increases the electrophilicity of the metal center, resulting in increasing the reactivity of the catalyst.[1h] Thus, successful catalysis of $PtCl_4$ may be due to its higher Lewis acidity.

Table 1
Screening of the metal salts/complexes for *o*-QMs and cycloaddition reactions with styrene[a]



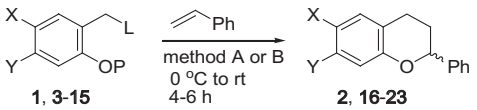
Entry	Catalyst	mol (%)	Yield (%)[b]
1[c]	$AlCl_3$	100	26
2[c]	$TiCl_3$	100	48
3[c]	$TiCl_4$	100	68
4[c]	$ZrCl_4$	100	39
5[c]	$FeCl_3$	100	63
6[c]	$ZnCl_2$	100	83
7[d]	AuCl	30	84 (75)
8[e]	$AuCl_3$	10	84 (85)
9[c]	$PtCl_2$	100	62
10	$PtCl_4$	10	88 (75)
11	K_2PtCl_6	10	0
12	$InCl_3$	10	62 (41)
13[f]	PTS–Si	100	81

[a] Unless otherwise noted, all reactions were performed in DCM, using 10 equiv of styrene.
[b] Isolated yields. Numbers in parenthesis are yields of **2** when using stoichiometric amount of catalysts.
[c] Substoichiometric (30–50 mol %) and catalytic (10–30 mol %) amounts of catalysts resulted in no reaction with recovery of *o*-QM precursor.
[d] Compound **2** (91%) was obtained (based on recovered starting materials) if 10 mol % of AuCl was employed.
[e] The reaction using 10 mol % $AuCl_3$ required 36 h to complete.
[f] For reference, the reaction using PTS–Si was performed in toluene.

The use of dichloromethane (DCM) as solvent was important.[7] Toluene, which was the solvent of choice when PTS–Si was employed, gave no desired product with complete recovery of **1** regardless of the metal salts/complexes under current investigation. Because of the higher yield, shorter reaction time, and easier handling, $PtCl_4$ was chosen as catalyst for the subsequent studies.

The effects of substituents on the aromatic ring as well as those of the leaving group at the benzylic position and the phenol protecting groups were also investigated. As summarized in Table 2, both compound **1** (with the acetate) and **3**[8] (with the *tert*-butyldimethylsilyloxy (OTBDMS) group) gave better yields (88%) than compound **4**[8] containing a hydroxy group (58%) as the leaving group at the benzylic position under similar conditions (entries 1–3). The importance of MOM as a phenol protecting group was evident as compound **5**, with an *i*-Pr group, failed to give any product while compound **6**,[8] with a MEM group, gave the product only in 49% yield (entries 4 and 5).

Table 2
Effects of the substituents on the aromatic ring, the leaving group, the phenol protecting groups, and the method to generate the *o*-QMs and mediate their cycloaddition reactions[a]



Entry	Compound	X	Y	L	P	Product	Method[b]	Yield (%)[c]
1	**1**	Br	OMe	OAc	MOM	**2**	A	88
							B	81
2	**3**	Br	OMe	OTBDMS	MOM	**2**	A	88
							B	44
3	**4**	Br	OMe	OH	MOM	**2**	A	58
							B	46
4	**5**	Br	OMe	OAc	*i*-Pr	**2**	A	0[d]
							B	0[e]
5	**6**	Br	OMe	OAc	MEM	**2**	A	49
6	**7**	Br	H	OAc	MOM	**16**	A	trace[d]
							B	46
7	**8**	F	OMe	OAc	MOM	**17**	A	75
							B	66
8	**9**	OMe	OMe	OAc	MOM	**18**	A	84
							B	60
9	**10**	OMe	OMe	OTBDMS	MOM	**18**	A	56
10	**11**	OMe	H	OAc	MOM	**19**	A	46
							B	17
11	**12**	OMe	Br	OAc	MOM	**20**	A	91
							B	39
12	**13**	CO_2Me	OMe	OTBDMS	MOM	**21**	A	88
							B	23
13	**14**	H	OMe	OAc	MOM	**22**	A	0[d]
							B	0[d]
14	**15**	H	H	OAc	MOM	**23**	A	23[d]
							B	48

[a] Unless otherwise noted, all reactions were performed using 10 equiv of styrene.
[b] Method A=$PtCl_4$ (10 mol %) in DCM; method B=PTS–Si (1.1 equiv) in toluene.
[c] Isolated yields.
[d] The reactions gave complex mixtures of unidentifiable products.
[e] Starting material was not consumed.

In order to investigate the effects of the substituents, *o*-QM precursors **7**–**15** were synthesized[8] for the cycloaddition reactions leading to the expected chromans **16**–**23**. In general, $PtCl_4$ can tolerate a range of substituent X on the aromatic ring with different electronic properties, such as halogens (F and Br), electron-donating group (EDG; OMe), and electron-withdrawing group (EWG; CO_2Me). In case of Y=H, the effects of substituent X on the reactions using $PtCl_4$ were evident for compounds **7**, **11**, and **15**. If the result of compound **15** (X=Y=H) was considered as a point of reference (23% yield; entry 14), a substrate bearing an EWG (**7**; X=Br; Y=H) gave only trace amounts of the corresponding product **16** and thus had a detrimental effect on the reaction yield (entry 6). Compound **11** (X=OMe; Y=H), on the other hand, with an EDG gave the product **19** in moderate 46% yield (entry 10). Such a trend was not observed for the reactions using PTS–Si as similar yields were obtained for compounds **7** and **15** (46–48%) while a much lower yield was observed for compound **11** (17% yield), suggesting that similar *o*-QMs may be generated by different mechanisms when $PtCl_4$ or PTS–Si was employed.

The position of an EDG on the aromatic ring appeared crucial for the successful generation of the corresponding *o*-QMs and the subsequent cycloaddition reactions. Compound **14** (X=H; Y=OMe) gave no desired product **22** regardless of whether PTS–Si or $PtCl_4$

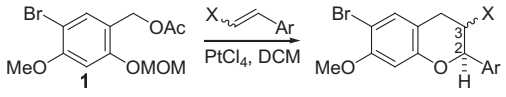
was employed. A mixture of products presumably arising from the displacement of acetate by styrene followed by partial polymerization of the resulting intermediate(s) with other styrene molecule(s) was obtained. In these cases, the presence of OMe *para* to the benzyl acetate rendered the system too reactive. Upon protonation (PTS–Si) or coordination ($PtCl_4$), the *p*-quinone methide (*p*-QM) might be formed as a result of the departure of acetate before the cleavage of the MOM group to generate the *o*-QM. Subsequently, styrene reacted with the *p*-QM to yield the carbocation-like intermediate, which underwent further reaction(s) with other styrene molecule(s).

When substituents X and Y are not hydrogen, the yields (75–91%) from the reactions using $PtCl_4$ were largely unaffected by the nature of these substituents (entries 1, 7, 8, 11, and 12). Switching of Br and OMe (**12**, entry 11) does not seem to affect the reactions; the corresponding chroman product **20** was furnished in high yield (91%). Interestingly, a good yield (84%) of the product **18** was obtained from **9**, which contain the methoxy groups as both substituents (entry 8). Replacing Br with F only gave a slightly lower yield of the product (entry 7). Even with a strong EWG in **13**, a good yield (88%) of the product **21** was obtained (entry 12). Thus, it appears that the effects of substituents X and Y should not be considered separately; both substituents may altogether modulate electron density in the aromatic ring for the generation of *o*-QMs as well as in the *o*-QM intermediates for their cycloaddition reactions.

In contrast to the reactions for substrates bearing no hydrogen as substituents X and Y using $PtCl_4$ as the catalyst, the reactions using PTS–Si gave lower yields of the corresponding products (23–81%). All the changes in substituents X and Y presumably changed the electron density in the aromatic ring. In addition, some side reactions presumably from O–Si cleavage also occurred when PTS–Si was used with compound **3**, resulting in a lower yield (44%; entry 2).

Due to the ease of preparation, the *o*-QM precursor **1** was used as the substrate for the subsequent studies. As summarized in Table 3, moderate to excellent yields (33–99%) and diastereoselectivity of the 2,3-disubstituted chromans **24**–**28** were obtained. The *trans* olefins gave the products as single diastereomers while the *cis* olefin provided the product as a 1:1[9] mixture of diastereomers. Cinnamyl benzoate furnished **26** in 99% yield as a single diastereomer.[10,11] In addition, even with an electron-withdrawing group (CO_2Et) in *trans*-ethyl cinnamate, **27** was obtained in moderate 33% yield;[12] a better yield (76%) of **28**, as a single diastereomer, was obtained with the (*p*-OMe)Ph *trans*-ethyl cinnamate.[10] The CH_2OBz and CO_2Et groups in **26**–**28** at C3 allow further modifications on the 2-aryl chromans.

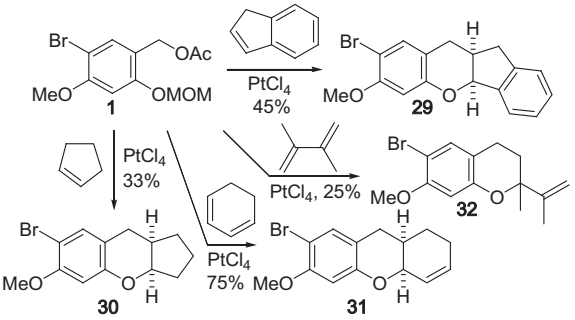
Table 3
Stereoselective $PtCl_4$-catalyzed cycloaddition reactions of *o*-QMs for 2,3-disubstituted chromans[a]



Entry	X	Ar	Olefin	Prod	Yield (%)[b]	dr (trans:cis)
1	*n*-Pr	Ph	*cis*	**24a**	78	1:1
2	*n*-Pr	Ph	*trans*	**24b**	72	>99:1
3	Me	Ph	*trans*	**25**	99	>99:1
4	CH_2OBz	Ph	*trans*	**26**	99	>99:1
5	CO_2Et	Ph	*trans*	**27**	33	>99:1
6[c]	CO_2Et	Ph(OMe-*p*)	*trans*	**28**	76	>99:1

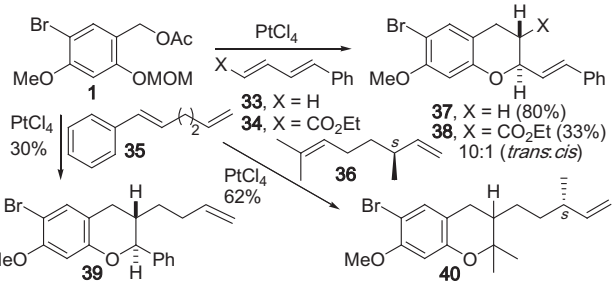
[a] Unless otherwise noted, all reactions were performed using 10 mol % of $PtCl_4$ and 10 equiv of styrenes.
[b] Isolated yields.
[c] Cinnamate (2 equiv) was used.

As shown in Scheme 2, the ring-fused *cis*-styrene (indene) reacted to provide **29** in 45% yield as a single diastereomer.[12] Simple non-conjugated alkene, such as cyclopentene furnished the corresponding product **30** albeit in lower yield.[13] The addition of *p*-TsOH on silica (PTS–Si) accelerated the reactions but gave only a slightly better yield of the product. Conjugated 1,3-cyclohexadiene gave a better yield of the corresponding product **31** in 75% as a single regioisomer and diastereomer. However, a non-cyclic conjugated 2,3-dimethyl-1,3-butadiene gave **32** only in 25% yield.



Scheme 2. $PtCl_4$-catalyzed generation and cycloaddition of *o*-QMs with other olefins.

To further investigate the effects of conjugation on the dienophile, dienes **33**–**36** were employed in the reactions (Scheme 3). Interestingly, both diene **33**[8] and **34**,[8] which contain a 1,3-diene system in conjugation with an aryl system, furnished the corresponding products **37** and **38** in 80% and 33% yields, respectively, as single regioisomers. The reactions occurred exclusively on the terminal olefin of the conjugated system. The presence of an EWG at the end of diene **34** had no effect on the regioselectivity of the reaction but dramatically affected the yield (33%) and diastereoselectivity (a 10:1 mixture of diastereomers favoring the C2–C3 *trans* relationship) of the resulting chroman **38**. When a non-conjugated diene **35**[8] was employed, the product **39** arising solely from the reaction on the styrene moiety was obtained albeit in low yield (30%). Moreover, non-styrene non-conjugated diene **36** furnished the corresponding product **40** as a single isomer (dr>99:1) from the reaction occurring exclusively on the more substituted olefin in moderate 62% yield.[14]

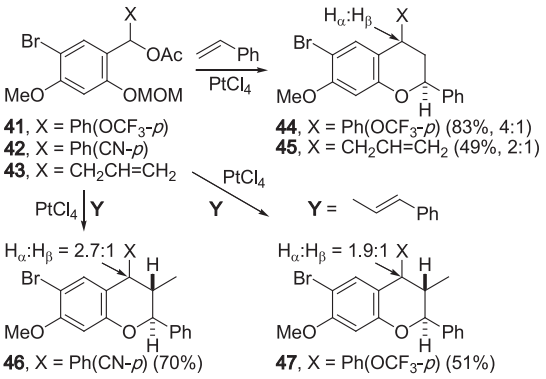


Scheme 3. $PtCl_4$-catalyzed generation and cycloaddition of *o*-QMs with other olefins.

The precursors **41**–**43**[8] furnished the 2,4-disubstituted and 2,3,4-trisubstituted chroman systems **44**–**47** in moderate to good yields but only in moderate diastereoselectivity favoring the 2,4-*cis* relationship (Scheme 4). For comparison, **44** was previously synthesized from **41** in 51% yield as a single diastereomer.[3a] Thus, the use of $PtCl_4$ for the 2,4-disubstituted chromans improved the yield but lowered the diastereoselectivity.

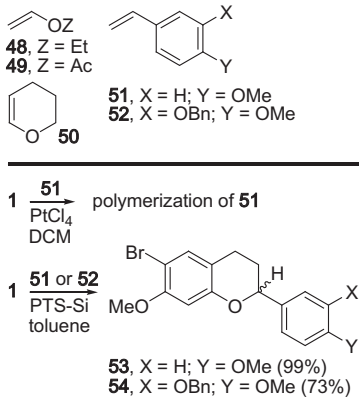
2.2. Scope and limitation of using $PtCl_4$ as catalyst

Even though the use of a catalytic amount of $PtCl_4$ in the generation of *o*-QMs and their cycloaddition reactions appears general,



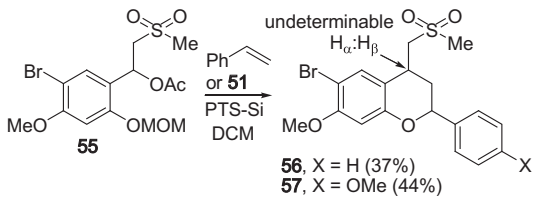
Scheme 4. 2,4-Disubstituted and 2,3,4-trisubstituted chromans from $PtCl_4$-catalyzed generation and cycloaddition of *o*-QMs with styrenes.

there are a few exceptions. Electron-rich dienophiles (**48**–**52**, Scheme 5), such as enol ethers and oxygenated aromatic systems did not furnish any chroman products. A ^{1}H NMR study suggested that *p*-methoxystyrene **51** underwent a facile $PtCl_4$-mediated polymerization under the reaction condition. It also appeared that polymerization occurred at a faster rate than the generation of the *o*-QM from the precursor. Reactions of precursor **1** with **48**–**50** using PTS–Si gave similar results. However, the use of PTS–Si, in case of the oxygenated aromatic systems **51** and **52**, gave the desired products **53** and **54**, respectively, in good to excellent yields (73%–99%).



Scheme 5. Electron-rich dienophiles **53**–**56** and cycloaddition reactions.

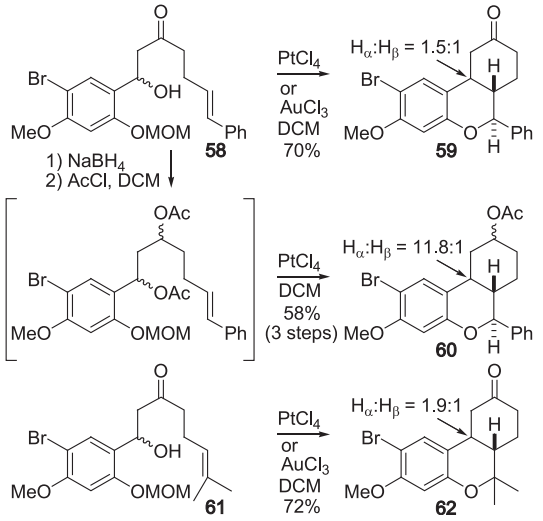
It should be noted also that the presence of sulfone appeared incompatible with $PtCl_4$. Generation of the *o*-QM from the precursor **55**[8] containing sulfone and its cycloaddition reaction with styrene using $PtCl_4$ gave no desired product. However, when similar reactions were performed with styrene or **51** using PTS–Si, the corresponding chromans **56** and **57** were obtained in 37% and 44% yields, respectively (Scheme 6). The stereoselectivity at C2–C4 cannot be determined due to the complex and overlapping ^{1}H NMR signals.



Scheme 6. Reactions of precursor **55** containing sulfone with styrene derivatives.

2.3. Intramolecular [4+2]-cycloaddition reactions

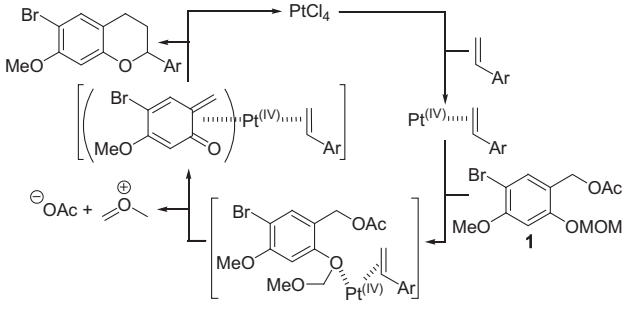
Both $PtCl_4$ and $AuCl_3$ effectively catalyzed the intramolecular cycloaddition reactions of the *o*-QM tethered with styrene or simple olefin (Scheme 7).[15] The alcohol **58**[3b] could be used directly in the reactions to furnish the corresponding tricyclic ketone **59** in one step and 70% yield (as a 1.5:1 mixture of diastereomers). Alternatively, conversion of the β-hydroxyketone to the corresponding bis-acetate intermediate, which upon generating the *o*-QM and the ensuing cycloaddition reaction, gave the chroman **60** in 58% yields over 3 steps (as an 11.8:1 mixture of diastereomers). Thus, the direct use of precursor **58** furnished the tricyclic system in better yield and in fewer chemical steps albeit in lower diastereoselectivity. A similar reaction with precursor **61** containing simple non-styrene olefin gave the corresponding chroman **62** in 72% yield as a 1.9:1 mixture of diastereomers. Thus, the 3,4-*trans* isomers are the major products from these intramolecular reactions.



Scheme 7. Intramolecular $PtCl_4$- or $AuCl_3$-catalyzed generation and cycloaddition reactions of *o*-QMs with tethered alkenes.

2.4. Mechanistic studies of the generation of *o*-QMs and [4+2]-cycloaddition reactions via $PtCl_4$

A plausible mechanism was proposed to involve first the coordination of Pt(IV) to the π-system of olefin (Scheme 8). This Pt(IV)-olefin complex then mediated the generation of *o*-QM from the precursor **1**. In these reactions, it appears that $PtCl_4$ also serves as a mild Lewis acid, which facilitates the ensuing cycloaddition reaction.[16] The product chroman was produced in concomitant with the regeneration of the catalytic species, completing the catalytic cycle.



Scheme 8. A proposed catalytic cycle of the Pt(IV)-catalyzed generation of *o*-QM and cycloaddition reactions.

Some supporting evidence for this mechanism was as follows. Sequential addition of olefin to the reaction after premixing $PtCl_4$ with **1** was not successful, giving an unidentifiable mixture of products and signifying the first step of Pt(IV)-π coordination. In addition, in the complete absence of styrene, a similar unidentifiable mixture of products was obtained, suggesting that the *o*-QM was formed from **1** in the presence of $PtCl_4$ alone.[17] Thus, it is likely that the *o*-QM remains bound to Pt(IV) for the subsequent cycloaddition reaction.[18] The bound state of Pt(IV) to the *o*-QM intermediate might account for the moderate diastereoselectivity for some substrates, presumably due to the steric demand and the positioning of the metal center.[19] The role of $PtCl_4$ in the cleavage of the MOM group as Lewis acid was evident from the facile cleavage of the MOM ether of salicylaldehyde by $PtCl_4$ under similar reaction condition to provide salicylaldehyde in 92% yield. Interestingly, no reactions occurred when styrene and $PtCl_4$ were mixed with nucleophile (phenol) or electrophile (BnOH/BnOAc) or both,[20] implying that the reaction proceeded via the intermediacy of *o*-QM rather than a stepwise addition/substitution reaction mechanism.

In order to follow the reactions in more detail, ^{1}H NMR studies were performed. As shown in Figs. 1 and 2, the NMR studies of the reactions both in the absence and in the presence of styrene with **1** using $PtCl_4$ as catalyst were conducted. In the absence of styrene, it is evident that the signals of protons belonging to the MOM (singlets at δ 3.45 and 5.19) and the acetate (a singlet at δ 2.03) groups in the precursor **1** slowly disappeared and the new sets of signals could be observed. In particular, the observation of a sharp singlet at δ 9.67 and a broad one at δ 8.25 was remarkable because the increment of these peaks at the beginning of the reaction corresponded with the diminishing height of the sets of peaks of the MOM and acetate groups. In addition, these peaks started to disappear after t=30 min, implying that the nature of the intermediate giving rise to these signals is only transient. Together with the observation that the new sets of signals around δ 2.01–2.15 were likely to correspond to the acetate group(s), these singlets at δ 8.25 and 9.67 were tentatively assigned to an intermediate either (1) resulting from the $PtCl_4$-mediated cleavage of the MOM group or (2) possessing a highly unshielded quinone methide-type moiety. Thus, a $PtCl_4$-catalyzed cleavage of the MOM group of the MOM ether-containing benzaldehyde (similar structure to compound **1** with the aldehyde moiety in place of the benzyl acetate) was carried out to clarify whether the $PtCl_4$-catalyzed MOM cleavage process alone without the possibility of generating any *o*-QM intermediate could generate some species with a signal at δ 9.67 (See Supplementary data for the overlay of the spectra). The cleavage of the MOM group alone by $PtCl_4$ did not generate any singlets at δ 8.25 or 9.67. However, some similar peaks were observed between the two reactions, especially those new sets of signals around δ 3.30–5.30, suggesting a similar course of reaction for the MOM cleavage. Thus, it is reasonable to postulate that the singlets at 8.25 and 9.67 may come from the Pt(IV)-stabilized *o*-QM intermediate.

In the presence of styrene, to our delight, a similar reaction course occurred. The singlets at δ 8.25 and 9.67 were still observed, suggesting the formation of the Pt(IV)-stabilized *o*-QM intermediate. In addition, the presence of styrene made the overall reaction proceed at a faster rate. Such observation was in good accordance with the role of styrene as dienophile trapping the *o*-QM, thus driving the reaction to completion faster. Taken together, the mechanisms of the reactions both in the absence and in the presence of styrene proceeded via the intermediacy of *o*-QM.

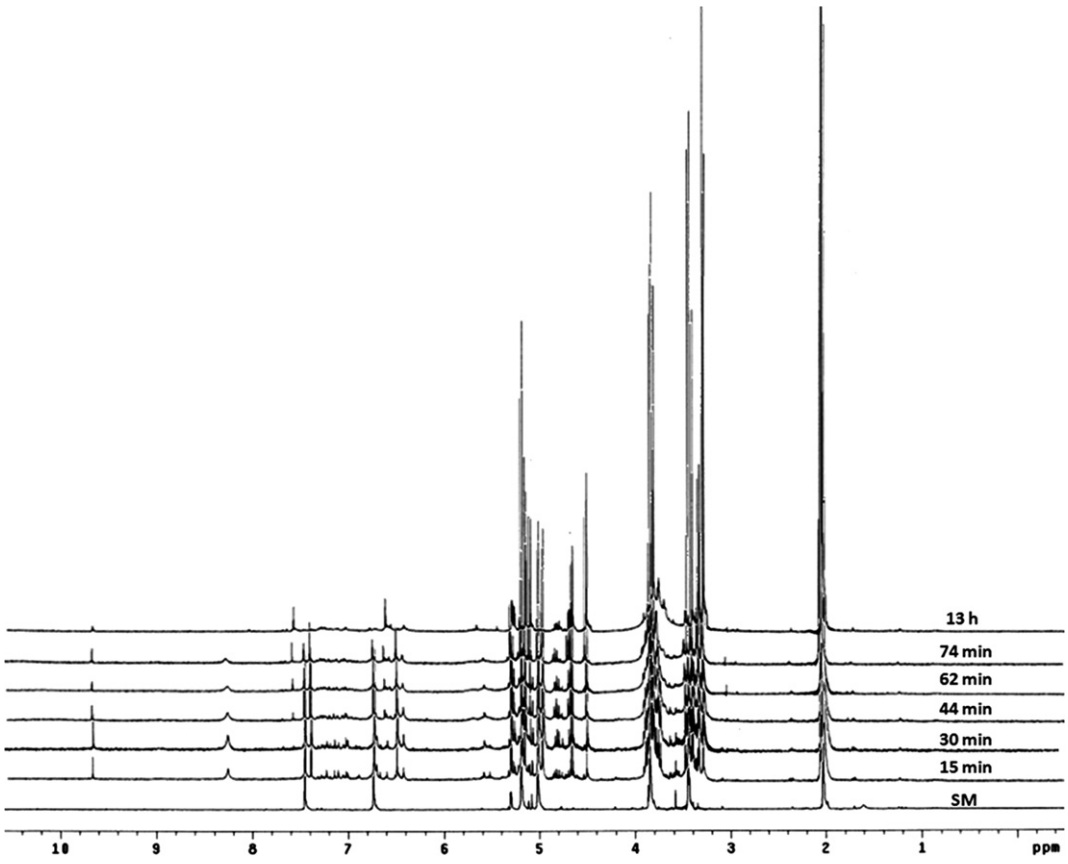


Fig. 1. ^{1}H NMR study of the reaction between the precursor **1** and $PtCl_4$ in the absence of styrene in CD_2Cl_2.

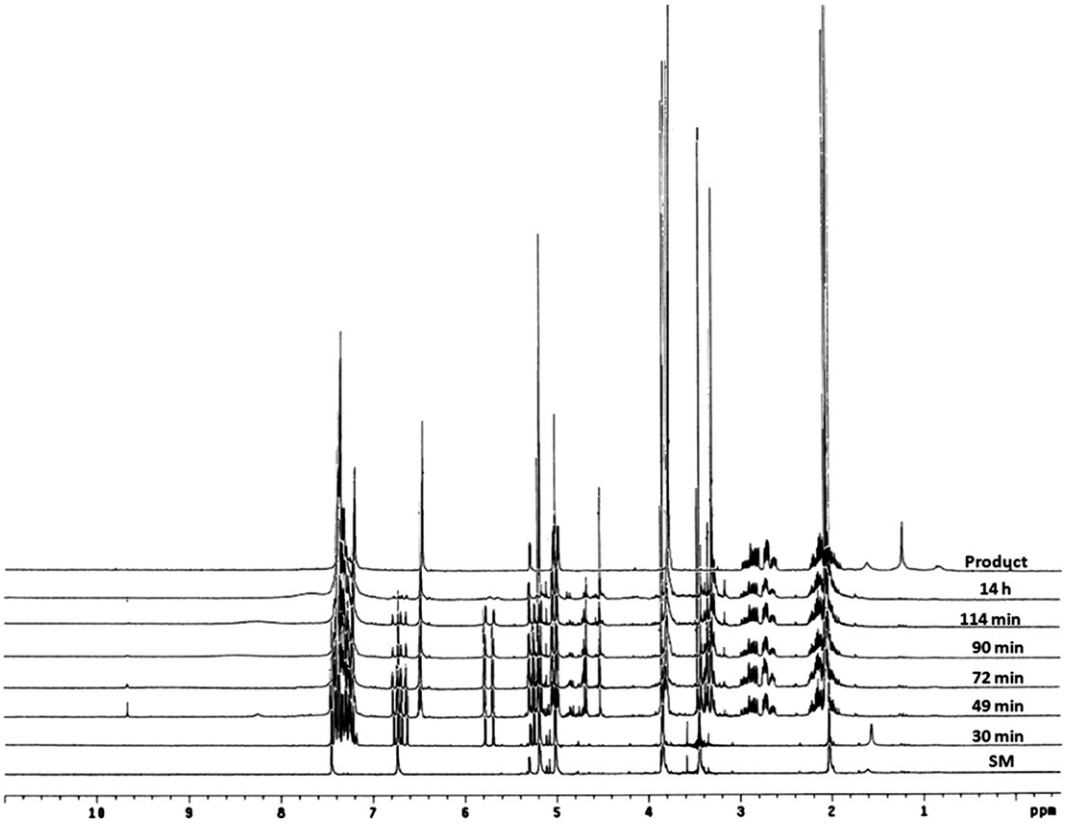


Fig. 2. ^{1}H NMR study of the reaction between the precursor **1** and $PtCl_4$ in the presence of styrene in CD_2Cl_2.

3. Conclusion

In summary, the mild and facile generation of *o*-QMs under the catalysis of $PtCl_4$ and their formal [4+2]-cycloaddition reactions with styrenes and other activated olefins have been successfully developed. The reactions furnished the 2-alkyl or 2-aryl chromans in moderate to excellent yields and moderate to excellent diastereoselectivity. When compared with our previously reported method using PTS–Si, this novel Pt(IV)-catalyzed process provided some significant advantages of wider range of the substituents on the aromatic ring of the *o*-QM precursors including better functional group compatibility. In addition, most dienophiles, with a few exceptions, gave the products in higher yields when $PtCl_4$ was employed. However, it should be noted that use of $PtCl_4$ led to somewhat lower diastereoselectivity at C2–C4. For the intramolecular reactions, the conversion of benzyl alcohol to the corresponding benzyl acetate was not necessary when using $PtCl_4$, thus resulting in fewer chemical steps in the synthesis of the desired chroman systems. The intermediacy of *o*-QM in the reactions under the $PtCl_4$ catalysis was also proposed and the Pt(IV)-stabilized *o*-QM involved in the reactions was detected spectroscopically.

4. Experimental section

4.1. General procedure for the hetero-Diels–Alder reactions of 2-arylchroman products

To a stirred solution of *o*-QM precursors (1.0 equiv) in CH_2Cl_2 (10 mL/mmol of benzyl acetates) were added styrene derivatives (2.0–10.0 equiv) at room temperature. The resulting mixture was stirred at 0 °C for 10 min, and then Lewis acids, transition metal salts or complexes (stoichiometric 100 mol %; substoichiometric 30–50 mol %, and catalytic 10–30 mol %) were added. The reaction mixture was stirred until all *o*-QM precursors were consumed as indicated by TLC (4–6 h). At that time, the reaction mixture was concentrated under reduced pressure to give a crude product mixture, which was further purified by preparative TLC (10–30% EtOAc/hexanes) to furnish the desired products.

*4.1.1. 6-Bromo-7-methoxy-2-phenylchroman (**2**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.018 g, 0.058 mmol, 88%, using $PtCl_4$; 0.016 g, 0.053 mmol, 81%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.72. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.97–2.28 (m, 2H), 2.66–2.79 (m, 1H), 2.84–3.01 (m, 1H), 3.85 (s, 3H), 5.05 (dd, J=9.4, 3.0 Hz, 1H), 6.52 (s, 1H), 7.26 (s, 1H), 7.35–7.44 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.1, 29.6, 56.2, 78.0, 101.1, 101.8, 115.2, 125.9, 128.0, 128.6, 133.0, 141.1, 154.8, 155.1. TOF-HRMS calcd for $C_{16}H_{16}BrO_2$ ($M+H^+$) 319.0328, found 319.0327. These spectroscopic data were identical to those reported previously.[3a]

*4.1.2. 6-Bromo-2-phenylchroman (**16**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (trace, using $PtCl_4$; 0.010 g, 0.035 mmol, 46%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.55. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.94–2.24 (m, 2H), 2.67–2.80 (m, 1H), 2.86–3.03 (m, 1H), 5.02 (dd, J=9.6, 2.8 Hz, 1H), 6.78 (d, J=9.6 Hz, 1H), 7.20 (m, 2H), 7.27–7.38 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.8, 29.4, 77.8, 112.3, 118.7, 124.0, 125.9, 127.9, 128.5, 130.1, 131.9, 141.1, 154.2. TOF-HRMS calcd for $C_{15}H_{12}BrO$ ($M-H^+$) 287.0063, found 287.0077. These spectroscopic data were identical to those reported previously.[3a]

*4.1.3. 6-Fluoro-7-methoxy-2-phenylchroman (**17**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.013 g, 0.048 mmol, 75%, using $PtCl_4$; 0.012 g, 0.046 mmol, 66%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.58. IR (neat): ν_{max} 2928, 1631, 1515, 1446, 1274, 1216, 1195,

1162, 1118 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.95–2.23 (m, 1H), 2.62–3.00 (m, 1H), 3.82 (s, 3H), 5.00 (dd, J=9.8, 2.8 Hz, 1H), 6.53 (d, J=7.6 Hz, 1H), 6.80 (d, J=11.4 Hz, 1H), 7.28–7.44 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.4, 29.7, 56.2, 77.9, 102.2, 112.9 (d, J_{C-F}=3.2 Hz), 115.7 (d, J_{C-F}=19.2 Hz), 126.0, 127.9, 128.5, 141, 146.5 (d, J_{C-F}=12.8 Hz), 146.8 (d, J_{C-F}=235.9 Hz), 150.9. LRMS (EI) m/z (rel intensity) 259 ($M+H^+$, 17), 258 (M^+, 100), 227 (20), 167 (30), 154 (28), 104 (73), 91 (33). TOF-HRMS calcd for $C_{16}H_{15}FO_2$ (M^+) 258.1051, found 258.1055.

*4.1.4. 6,7-Dimethoxy-2-phenylchroman (**18**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as yellowish oil (0.014 g, 0.052 mmol, 84%, using $PtCl_4$; 0.012 g, 0.045 mmol, 60%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.61. IR (neat): ν_{max} 2929, 2849, 1736, 1619, 1511, 1450, 1413, 1261, 1224, 1193, 1170, 1125, 1018 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.98–2.25 (m, 2H), 2.65–3.03 (m, 2H), 3.83 (s, 3H), 3.84 (s, 3H), 4.99 (dd, J=9.5, 2.9 Hz, 1H), 6.51 (s, 1H), 6.59 (s, 1H), 7.32–7.45 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.7, 30.1, 55.9, 56.5, 77.8, 101.1, 112.2, 126.0, 127.8, 128.3, 128.5, 141.7, 143.1, 148.3, 148.9. LRMS (EI) m/z (rel intensity) 270 (M^+, 100), 239 (13), 166 (40), 138 (16), 91 (11). TOF-HRMS calcd for $C_{17}H_{19}O_3$ ($M+H^+$) 271.1329, found 271.1325.

*4.1.5. 6-Methoxy-2-phenylchroman (**19**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.011 g, 0.047 mmol, 46%, using $PtCl_4$; 0.003 g, 0.014 mmol, 17%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.57. IR (neat): ν_{max} 3338, 2927, 2851, 1612, 1494, 1431, 1268, 1220, 1149, 1067, 1048, 1035, 1000 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.97–2.25 (m, 2H), 2.71–3.09 (m, 2H), 3.77 (s, 3H), 5.01 (dd, J=9.6, 3.0 Hz, 1H), 6.64 (d, J=3.0 Hz, 1H), 6.71 (dd, J=8.8, 3.0 Hz, 1H), 6.85 (d, J=8.8 Hz, 1H), 7.29–7.45 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.5, 30.0, 55.8, 77.6 (superimposed with $CDCl_3$), 113.4, 114.0, 117.5, 122.3, 126.0, 127.7, 128.5, 141.8, 153.2, 153.3. LRMS (EI) m/z (rel intensity) 240 (M^+, 100), 149 (41), 136 (89), 108 (31), 91 (25). TOF-HRMS calcd for $C_{16}H_{17}O_2$ ($M+H^+$) 241.1223, found 241.1218.

*4.1.6. 7-Bromo-6-methoxy-2-phenylchroman (**20**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.017 g, 0.052 mmol, 91%, using $PtCl_4$; 0.008 g, 0.024 mmol, 39%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.51. IR (neat): ν_{max} 3027, 2927, 2847, 1603, 1490, 1401, 1312, 1194, 1046, 1006 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.96–2.27 (m, 1H), 2.67–3.05 (m, 1H), 3.83 (s, 3H), 5.01 (dd, J=9.8, 2.8 Hz, 1H), 6.62 (s, 1H), 7.14 (s, 1H), 7.31–7.41 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.2, 29.6, 56.9, 77.6, 109.6, 112.7, 121.5, 127.6, 127.9, 128.3, 128.5, 141.3, 149.4, 149.8. LRMS (EI) m/z (rel intensity) 320 (M^++2, 87), 318 (M^+, 88), 216 (66), 214 (70), 178 (49), 148 (58), 104 (48), 91 (97), 81 (53), 77 (57), 69 (100). TOF-HRMS calcd for $C_{16}H_{15}BrO_2$ (M^+) 318.0250, found 318.0235.

*4.1.7. Methyl 7-methoxy-2-phenylchroman-6-carboxylate (**21**).* Follo wing the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.012 g, 0.042 mmol, 88%, using $PtCl_4$; 0.006 g, 0.020 mmol, 23%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.38. IR (neat): ν_{max} 2923, 2853, 1722, 1697, 1619, 1573, 1495, 1434, 1280, 1260, 1193, 1144, 1079 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.98–2.30 (m, 2H), 2.68–3.01 (m, 2H), 3.855 (s, 3H), 3.862 (s, 3H), 5.10 (dd, J=9.9, 2.5 Hz, 1H), 6.51 (s, 1H), 7.33–7.42 (m, 5H), 7.68 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.0, 29.7, 51.7, 56.0, 78.4, 100.5, 111.8, 113.4, 125.9, 128.0, 128.5, 133.6, 140.8, 159.5, 166.2. LRMS (EI) m/z (rel intensity) 299 ($M+H^+$, 19), 298 (M^+, 93), 239 (89), 179 (43), 178 (61), 149 (52), 104 (51), 91 (52), 71 (68), 57 (100). TOF-HRMS calcd for $C_{18}H_{19}O_4$ ($M+H^+$) 299.1278, found 299.1282.

*4.1.8. 2-Phenylchroman (**23**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.005 g, 0.021 mmol, 23%, using $PtCl_4$; 0.009 g, 0.044 mmol, 48%, using PTS–Si). R_f (30% EtOAc/hexanes) 0.66. ^1H NMR (200 MHz, $CDCl_3$): δ 2.01–2.32 (m, 2H), 2.75–2.89 (m, 1H), 2.95–3.12 (m, 1H), 5.09 (dd, J=9.4, 3.0 Hz, 1H), 6.87–6.96 (m, 2H), 7.10–7.21 (m, 2H), 7.34–7.48 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.1, 29.9, 77.7, 116.9, 120.3, 121.8, 126.0, 127.3, 127.8, 128.5, 129.5, 141.7, 155.1. TOF-HRMS calcd for $C_{15}H_{15}O$ ($M+H^+$) 211.1117, found 211.1114. These spectroscopic data were identical to those reported previously.[3a]

*4.1.9. 1:1 Mixture of cis- and trans-6-bromo-7-methoxy-2-phenyl-3-propylchroman (**24a**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as a 1:1 mixture of 2,3-*cis* and 2,3-*trans* diastereomers as colorless oil (0.018 g, 0.048 mmol, 78%). R_f (30% EtOAc/hexanes) 0.68. IR (neat): ν_{max} 2957, 2929, 2871, 1610, 1575, 1496, 1443, 1430, 1311, 1282, 1200, 1155, 1058 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J=7.04 Hz, 3H, trans), 0.81 (t, J=7.13 Hz, 3H, cis), 1.01–1.45 (m, 4H), 2.04–2.13 (m, 1H, trans), 2.16–2.22 (m, 1H, cis), 2.48 (dd, J=16.1, 9.9 Hz, 1H, trans), 2.61 (dd, J=16.1, 4.4 Hz, 1H, cis), 2.81 (dd, J=16.2, 5.0 Hz, 1H, trans), 2.97 (dd, J=16.1, 5.4 Hz, 1H, cis), 3.81 (s, 3H, trans), 3.85 (s, 3H, cis), 4.71 (d, J=8.6 Hz, 1H, trans), 5.22 (d, J=2.6 Hz, 1H, cis), 6.47 (s, 1H, trans), 6.52 (s, 1H, cis), 7.23 (s, 1H, trans), 7.24 (s, 1H, cis), 7.28–7.41 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 19.5 (trans), 20.5 (cis), 28.2 (cis), 28.4 (cis), 29.4 (trans), 33.8 (trans), 36.5 (cis), 37.1 (trans), 56.2, 80.2 (cis), 83.2 (trans), 100.7 (trans), 100.8 (cis), 101.8 (cis), 101.9 (trans), 114.5 (cis), 115.2 (trans), 125.9 (cis), 127.0 (trans), 127.3 (cis), 128.1 (cis), 128.2 (trans), 128.5 (trans), 133.0 (trans), 133.5 (cis), 139.6 (cis), 140.0 (trans), 154.8, 154.9. LRMS (EI) m/z (rel intensity) 362 (M^++2, 43), 360 (M^+, 44), 271 (60), 269 (63), 190 (100), 117 (97), 115 (40), 104 (38), 91(42). TOF-HRMS calcd for $C_{19}H_{22}BrO_2$ ($M+H^+$) 361.0798, found 361.0798.

*4.1.10. trans-6-Bromo-7-methoxy-2-phenyl-3-propylchroman (**24b**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.016 g, 0.044 mmol, 72%). R_f (30% EtOAc/hexanes) 0.63. ^1H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, J=3.61 Hz, 3H), 1.01–1.45 (m, 4H), 2.01–2.13 (m, 1H), 2.48 (d, J=16.1, 9.9 Hz, 1H), 2.81 (d, J=16.2, 5.1 Hz, 1H), 3.82 (s, 3H), 4.71 (d, J=8.6 Hz, 1H), 6.47 (s, 1H), 7.23 (s, 1H), 7.33–7.41 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 19.5, 29.4, 33.8, 37.1, 56.2, 83.2, 100.7, 101.8, 115.3, 127.0, 128.2, 128.6, 133.1, 140.1, 154.8, 154.9. TOF-HRMS calcd for $C_{19}H_{22}BrO_2$ ($M+H^+$) 361.0798, found 361.0812. These spectroscopic data were identical to those reported previously.[3a]

*4.1.11. trans-6-Bromo-7-methoxy-3-methyl-2-phenylchroman (**25**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.020 g, 0.061 mmol, 99%). R_f (30% EtOAc/hexanes) 0.68. IR (neat): ν_{max} 2925, 1611, 1575, 1496, 1443, 1404, 1310, 1281, 1201, 1156, 1051, 1019 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.83 (d, J=6.8 Hz, 3H), 2.11–2.23 (m, 1H), 2.54 (dd, J=16.1, 10.8 Hz, 1H), 2.77 (dd, J=16.2, 5.1 Hz, 1H), 3.81 (s, 3H), 4.58 (d, J=9.3 Hz, 1H), 6.47 (s, 1H), 7.22 (s, 1H), 7.33–7.41 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.7, 32.6, 32.8, 56.2, 84.4, 100.8, 101.8, 115.4, 127.1, 128.3, 128.5, 132.8, 139.7, 154.8, 155.0. LRMS (EI) m/z (rel intensity) 334 (M^++2, 37), 332 (M^+, 38), 162 (33), 118 (42), 117 (100), 115 (34), 91 (73). TOF-HRMS calcd for $C_{17}H_{18}BrO_2$ ($M+H^+$) 333.0485, found 333.0475.

*4.1.12. trans-(6-Bromo-7-methoxy-2-phenylchroman-3-yl)methyl benzoate (**26**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the product was obtained as colorless oil (0.029 g, 0.063 mmol, 99%). R_f (15% EtOAc/hexanes) 0.34. IR (neat): ν_{max} 2920, 2853, 1718, 1495, 1268, 1109 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 2.75–2.55 (m, 1H), 2.88 (d, J=7.8 Hz, 2H), 3.83 (s, 3H), 4.07 (dd, J=11.4, 6.0 Hz, 1H), 4.28 (dd, J=11.3, 4.7 Hz, 1H),

5.04 (d, *J*=8.4 Hz, 1H), 6.52 (s, 1H), 7.63–7.25 (m, 9H), 8.00–7.92 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.9, 37.7, 56.3, 65.0, 79.9, 100.9, 102.4, 114.2, 126.0, 126.3, 126.4, 126.7, 127.2, 128.4, 128.6, 128.8, 129.5, 129.7, 133.1, 138.9, 154.5, 155.1, 166.2. LRMS (EI) *m*/*z* (rel intensity) 454 (M+2, 15), 452 (M^+, 13), 332 (30), 330 (24), 251 (21), 115 (26), 105 (90), 91 (22), 77 (100), 51 (43). TOF-HRMS calcd for $C_{24}H_{22}BrO_4$ ($M+H^+$) 453.0696, found 453.0706.

*4.1.13. trans-Ethyl 6-bromo-7-methoxy-2-phenylchroman-3-carboxylate (**27**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the product was obtained as colorless oil (0.010 g, 0.024 mmol, 33%). R_f (15% EtOAc/hexanes) 0.32. IR (neat): ν_{max} 2925, 1728, 1612, 1442, 1151, 1024 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.96 (t, *J*=7.2 Hz, 3H), 3.25–2.83 (m, 3H), 3.82 (s, 3H), 3.94 (q, *J*=7.2 Hz, 2H), 5.07 (d, *J*=8.4 Hz, 1H), 7.27 (s, 1H), 7.40–7.35 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.8, 27.7, 29.7, 45.5, 56.2, 60.8, 79.3, 101.0, 102.7, 113.5, 127.0, 128.5, 128.7, 132.8, 138.3, 154.3, 155.1, 172.1. LRMS (EI) *m*/*z* (rel intensity) 392 (M^++2, 99), 390 (M^+, 100), 346 (81), 344 (84), 265 (96), 238 (60), 237 (56), 131 (55), 91 (93), 77 (66). TOF-HRMS calcd for $C_{19}H_{20}BrO_4$ ($M+H^+$) 391.0539, found 391.0532.

*4.1.14. trans-Ethyl 6-bromo-7-methoxy-2-(4-methoxyphenyl)chroman-3-carboxylate (**28**).* Following the general procedure and purification PTLC (15% EtOAc/hexanes), the desired product was obtained as colorless oil (0.020 g, 0.048 mmol, 76%). R_f (15% EtOAc/hexanes) 0.21. IR (neat): ν_{max} 2933, 1721, 1612, 1574, 1515, 1447, 1372, 1243, 1201, 1186, 1153, 1032. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (t, *J*=7.1 Hz, 3H), 2.92 (dd, *J*=15.6, 4.9 Hz, 1H), 3.02 (ddd, *J*=10.9, 9.3, 4.9 Hz, 1H), 3.19 (dd, *J*=15.5, 11.0 Hz, 1H), 3.81 (s, 6H), 3.947 (q, *J*=7.1 Hz, 1H), 3.953 (q, *J*=7.1 Hz, 1H), 5.00 (d, *J*=9.3 Hz, 1H), 6.48 (s, 1H), 6.90 (AA′BB′, *J*=8.7 Hz, 2H), 7.26 (s, 1H), 7.32 (AA′BB′, *J*=8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 28.0, 45.4, 55.3, 56.2, 60.7, 79.0, 101.0, 102.5, 113.5, 113.9, 128.4, 130.3, 132.8, 154.5, 155.1, 159.9, 172.2. LRMS (EI) *m*/*z* (rel intensity) 422 (M^++2, 76), 421 ($M+H^+$, 18), 420 (M^+, 77), 376 (97), 374 (100), 295 (46), 269 (42), 267 (60), 206 (35), 161 (83), 134 (92), 121 (52). TOF-HRMS calcd for $C_{20}H_{21}BrO_5$ (M^+) 420.0572, found 420.0575.

*4.1.15. 8-Bromo-7-methoxy-4b,10,10a,11-tetrahydroindeno[1,2-b]chromene (**29**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.008 g, 0.024 mmol, 45%). R_f (15% EtOAc/hexanes) 0.51. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.46–2.58 (m, 1H), 2.73–3.13 (m, 4H), 3.79 (s, 3H), 5.48 (d, *J*=5.8 Hz, 1H), 6.45 (s, 1H), 7.19 (s, 1H), 7.23–7.30 (m, 3H), 7.48–7.52 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.7, 36.6, 37.5, 56.1, 81.5, 101.5, 101.7, 116.0, 125.1, 125.2, 126.9, 128.9, 132.5, 142.2, 142.6, 154.7, 155.2. TOF-HRMS calcd for $C_{17}H_{16}BrO_2$ ($M+H^+$) 331.0328, found 331.0325. These spectroscopic data were identical to those reported previously.[3a]

*4.1.16. 7-Bromo-6-methoxy-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene (**30**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.008 g, 0.027 mmol, 33%). R_f (15% EtOAc/hexanes) 0.71. IR (neat): ν_{max} 2941, 1496, 1445, 1200, 1160, 1053 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46–1.35 (m, 2H), 2.00–1.64 (m, 4H), 2.31–2.22 (m, 1H), 2.55 (dd, *J*=8.2, 1.4 Hz, 1H), 2.94 (dd, *J*=8.4, 3.2 Hz, 1H), 3.82 (s, 3H), 4.36 (dt, *J*=2.8, 1.0 Hz, 1H), 6.39 (s, 1H), 7.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 25.5, 28.1, 32.9, 37.5, 56.1, 79.6, 101.1, 101.6, 114.3, 133.2, 154.4, 154.6. LRMS (EI) *m*/*z* (rel intensity) 284 (M^++2, 100), 282 (M^+, 99), 217 (36), 215 (33), 203 (17). TOF-HRMS calcd for $C_{13}H_{15}BrO_2$ (M^+) 282.0250, found 282.0244.

*4.1.17. 7-Bromo-6-methoxy-2,4a,9,9a-tetrahydro-1H-xanthene (**31**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.011 g, 0.037 mmol, 75%). R_f (30% EtOAc/hexanes) 0.63. IR (neat): ν_{max} 2924, 2853, 1677, 1610, 1576, 1496, 1443, 1476, 1198, 1160, 1051 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.53–1.59 (m, 1H), 1.63–1.73 (m, 1H), 2.09–2.26 (m, 4H), 2.50 (dd, *J*=16.4, 3.5 Hz, 1H), 2.96 (dd, *J*=16.4, 6.6 Hz, 1H), 3.81 (s, 3H), 4.48 (t, *J*=3.6 Hz, 1H), 5.92–5.96 (m, 1H), 6.01 (td, *J*=10.0, 3.4 Hz, 1H), 6.41 (s, 1H), 7.18 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 23.0, 25.0, 28.7, 30.4, 56.1, 70.6, 100.8, 101.6, 113.9, 125.8, 132.9, 133.1, 1153.5, 1154.7. LRMS (EI) *m*/*z* (rel intensity) 296 (M^++2, 47), 294 (M^+, 48), 217 (91), 215 (98), 97 (38), 92 (49), 91 (36), 83 (40), 80 (70), 79 (100). TOF-HRMS calcd for $C_{14}H_{16}BrO_2$ ($M+H^+$) 295.0328, found 295.0324.

*4.1.18. 6-Bromo-7-methoxy-2-methyl-2-(prop-1-en-2-yl)chroman (**32**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the product was obtained as colorless oil (0.005 g, 0.016 mmol, 25%). R_f (30% EtOAc/hexanes) 0.61. IR (neat): ν_{max} 2924, 2851, 1610, 1574, 1496, 1443, 1200, 1149, 1090, 1051 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.46 (s, 3H), 1.77 (s, 3H), 1.68–1.83 (m, 1H), 2.11 (dt, *J*=13.6, 4.9 Hz, 1H), 2.56 (dd, *J*=4.8, 8.0 Hz, 2H), 3.84 (s, 3H), 4.85 (s, 1H), 4.90 (s, 1H), 6.44 (s, 1H), 7.15 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 35.3, 37.4, 41.0, 43.6, 62.1, 78.9, 94.1, 94.3, 101.7, 104.2, 116.9, 126.5, 132.1, 132.6. LRMS (EI) *m*/*z* (rel intensity) 298 (M^++2, 41), 296 (M^+, 42), 217 (71), 215 (51), 178 (100). TOF-HRMS calcd for $C_{14}H_{18}BrO_2$ ($M+H^+$) 297.0485, found 297.0485.

*4.1.19. (E)-6-Bromo-7-methoxy-2-styrylchroman (**37**).* Following the general procedure and purification by PTLC (20% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.026 g, 0.074 mmol, 80%). R_f (20% EtOAc/hexanes) 0.50. IR (neat): ν_{max} 3020, 2960, 2925, 2854, 1723, 1610, 1572, 1495, 1443, 1403, 1307, 1261, 1187, 1154, 1047, 1028 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.81–2.00 (m, 1H), 2.06–2.17 (m, 1H), 2.73–2.83 (m, 2H), 3.84 (s, 3H), 4.66–4.73 (m, 1H), 6.31 (dd, *J*=16.1, 6.3 Hz, 1H), 6.48 (s, 1H) 6.72 (d, *J*=16.0 Hz, 1H), 7.11–7.44 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 23.4, 27.8, 56.2, 101.1, 101.9, 115.2, 126.0, 127.9, 128.2, 128.5, 131.9, 133.1, 136.3, 154.5, 154.9. LRMS (EI) *m*/*z* (rel intensity) 346 (M^++2, 53), 345 ($M+H^+$, 18), 344 (M^+, 54), 265 (22), 216 (14), 215 (13), 174 (19), 143 (32), 142 (54), 141 (15), 137 (23), 130 (57), 129 (100), 128 (34), 115 (45), 91 (59). TOF-HRMS calcd for $C_{18}H_{18}BrO_2$ ($M+H^+$) 345.0485, found 345.0492.

*4.1.20. (E)-Ethyl 6-bromo-7-methoxy-2-styrylchroman-3-carboxylate (**38**).* Following the general procedure and purification by PTLC (10% EtOAc/hexanes), the desired compound was obtained as a 10:1 mixture of C2–C3 *trans*:*cis* diastereomers as colorless oil (0.014 g, 0.034 mmol, 33%). R_f (10% EtOAc/hexanes) 0.29. IR (neat): ν_{max} 2980, 2937, 1729, 1612, 1575, 1496, 1443, 1256, 1200, 1187, 1154, 1018 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.17 (t, *J*=7.1 Hz, 3H), 1.27 (t, *J*=7.2 Hz, 3H, minor), 2.79–3.00 (m, 2H), 3.06–3.21 (m, 1H), 3.83 (s, 3H), 3.85 (s, 3H, minor), 4.13 (q, *J*=7.1 Hz, 3H), 4.76 (app t, *J*=7.9 Hz, 1H), 5.21–5.24 (m, 1H, minor), 6.19 (dd, *J*=16.0, 6.6 Hz, 1H, minor), 6.26 (dd, *J*=15.8, 7.4 Hz, 1H), 6.64 (d, *J*=16.6 Hz, 1H, minor), 6.73 (dd, *J*=16.0 Hz, 1H), 7.25–7.43 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.2, 23.5 (minor), 26.9, 42.0 (minor), 44.1, 56.2, 61.1, 75.5 (minor), 77.6 (superimposed with $CDCl_3$), 100.9, 102.6, 113.4, 125.5, 126.7, 128.2, 128.5, 132.8, 134.2, 135.9, 153.6, 155.1, 172.1. LRMS (EI) *m*/*z* (rel intensity) 418 (M^++2, 64), 417 ($M+H^+$, 18), 416 (M^+, 66), 372 (57), 370 (53), 281 (100), 279 (88), 204 (55), 202 (49), 129 (63), 128 (61), 115 (39). TOF-HRMS calcd for $C_{21}H_{22}BrO_4$ ($M+H^+$) 417.0696, found 417.0708.

*4.1.21. 6-Bromo-3-(but-3-enyl)-7-methoxy-2-phenylchroman (**39**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.009 g, 0.023 mmol, 30%). R_f (15% EtOAc/hexanes) 0.52. IR (neat): ν_{max} 2930, 2854, 1611, 1576, 1496, 1444, 1201, 1158, 1053 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13–1.37 (m, 2H),

1.88–2.01 (m, 2H), 2.05–2.17 (m, 2H), 2.49 (dd, 1H, *J*=4.9, 8.1 Hz), 2.82 (dd, 1H, *J*=2.2, 8.4 Hz), 3.82 (s, 3H), 4.73 (d, 1H, *J*=4 Hz), 4.92 (d, 1H, *J*=4.4 Hz), 4.95 (d, 1H, *J*=8 Hz), 5.61–5.72 (m, 1H), 6.47 (s, 1H), 7.23 (s, 1H), 7.30–7.41 (m, 5H). ^{13}C NMR (100 MHz, CDCl3): δ 29.3, 30.5, 30.8, 36.6, 56.1, 83.0, 100.7, 101.8, 115.0, 115.1, 126.9, 128.3, 128.6, 133.0, 137.9, 139.9, 154.7, 154.9. LRMS (EI) *m*/*z* (rel intensity) 374 (M^++1, 17), 372 (M^+−1, 17), 241 (14), 239 (17), 217 (24), 215 (24), 178 (51), 161 (30), 149 (30), 117 (100), 91 (53), 71 (46), 69 (88). TOF-HRMS calcd for $C_{20}H_{22}BrO_2$ ($M+H^+$) 373.0798, found 373.0793.

*4.1.22. 6-Bromo-7-methoxy-2,2-dimethyl-3-((S)-3-methyl pent-4-enyl)chroman (**40**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.022 g, 0.062 mmol, 62%). R_f (15% EtOAc/hexanes) 0.60. IR (neat): ν_{max} 2931, 2865, 1610, 1577, 1486, 1497, 1315, 1203, 1161, 1134, 1054 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (d, 3H, *J*=2.2 Hz), 1.02 (d, 3H, *J*=2.2 Hz), 1.13 (s, 3H), 1.14 (s, 3H), 1.20–1.72 (m, 2H), 2.06–2.16 (m, 1H), 2.26–2.37 (m, 1H), 2.77 (td, 1H, *J*=7.8, 2.5 Hz), 3.82 (s, 3H), 4.94 (d, 1H, *J*=4.6 Hz), 4.97 (d, 1H, *J*=8.3 Hz), 5.60–5.75 (m, 1H), 6.36 (s, 1H), 7.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9, 20.4, 20.5, 20.7, 27.1, 27.2, 27.5, 27.6, 28.2, 28.3, 34.3, 34.5, 37.8, 37.9, 40.6, 41.0, 56.1, 78.2, 78.3, 101.2, 112.8, 113.1, 115.0, 132.9, 144.1, 144.5, 153.7, 154.9. LRMS (EI) *m*/*z* (rel intensity) 354 (M^++2, 23), 352 (M^+, 24), 217 (95), 215 (100). TOF-HRMS calcd for $C_{18}H_{26}BrO_2$ ($M+H^+$) 353.1111, found 353.1112.

*4.1.23. 6-Bromo-7-methoxy-2-phenyl-4-(4-(trifluoromethoxy)phenyl)chroman (**44**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the desired compound was obtained as a 4:1 mixture of C2-C4 *cis*:*trans* diastereomers as colorless oil (0.019 g, 0.039 mmol, 83%). R_f (30% EtOAc/hexanes) 0.63. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.17 (ddd, *J*=11.9, 11.8, 11.8 Hz, 1H), 2.38 (ddd, *J*=13.8, 5.9, 1.8 Hz, 1H), 2.42–2.48 (m, 1H, minor), 3.85 (s, 3H), 3.89 (s, 3H, minor), 4.17 (dd, *J*=5.5, 3.3 Hz, 1H, minor), 4.31 (dd, *J*=12.0, 5.8 Hz, 1H), 4.98 (dd, *J*=10.5, 2.2 Hz, 1H, minor), 5.17 (dd, *J*=11.4, 1.5 Hz, 1H), 6.54 (s, 1H), 6.60 (s, 1H, minor), 6.89 (s, 1H), 7.12 (s, 1H, minor), 7.14–7.26 (m, 4H), 7.31–7.47 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.5, 42.1, 56.2, 78.4, 101.1, 102.6, 113.6 (minor), 118.5, 121.0 (minor), 121.3, 126.0, 128.3, 128.57 (minor), 128.65, 129.6, 129.8 (minor), 133.1, 134.0 (minor), 140.3, 142.6, 148.1, 155.4, 155.7. TOF-HRMS calcd for $C_{23}H_{18}BrF_3O_3$ (M^+) 478.0386, found 478.0379. These spectroscopic data were identical to those reported previously.[3a]

*4.1.24. 4-Allyl-6-bromo-7-methoxy-2-phenylchroman (**45**).* Following the general procedure and purification by PTLC (15% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.013 g, 0.033 mmol, 49%). R_f (15% EtOAc/hexanes) 0.52. IR (neat): ν_{max} 2916, 2853, 1609, 1568, 1488, 1443, 1199, 1156, 1052 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98–2.14 (m, 1H), 2.17–2.29 (m, 2H), 2.27–2.44 (m, minor), 2.53–2.61 (m, minor), 2.68–2.475 (m, 1H), 2.80–2.88 (m, minor), 3.07–3.17 (m, 1H), 3.82 (s, 3H), 3.83 (s, minor), 4.98–5.15 (m, 3H), 5.71–5.90 (m, 1H), 6.49 (s, 1H), 6.51 (s, minor), 7.31–7.45 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.8, 33.1, 33.8, 36.4, 38.8, 41.9, 73.9, 78.4, 101.1(minor), 101.3, 102.3, 117.4 (minor), 117.5, 118.8, 118.9 (minor), 125.9 (minor), 126.0, 128.0 (minor), 128.1, 128.6, 131.1, 133.1, 135.2, 135.9, 141.1, 154.9, 155.5. LRMS (EI) *m*/*z* (rel intensity) 360 (M^++2, 18), 358 (M^+, 19), 319 (89), 317 (93), 238 (100), 223 (26), 115 (40), 104 (33), 91 (58). TOF-HRMS calcd for $C_{19}H_{20}BrO_2$ ($M+H^+$) 359.0641, found 359.0650.

*4.1.25. 6-Bromo-7-methoxy-3-methyl-2-phenyl-4-(4-cyanophenyl) chroman (**46**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the desired compound was obtained as a 2.7:1 mixture of C2-C4 *cis*:*trans* diastereomers as colorless oil (0.015 g, 0.034 mmol, 70%). R_f (30% EtOAc/hexanes) 0.54. IR (neat): ν_{max} 2960, 2228, 1608, 1574, 1486, 1443, 1399, 1311, 1261, 1197, 1159, 1052, 1020 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.54 (d, *J*=7.0 Hz, 3H, minor), 0.58 (d, *J*=6.6 Hz, 3H), 2.17–2.27 (m, 1H), 2.45–2.55 (m, 1H, minor), 3.81 (d, *J*=10.8 Hz, 1H), 3.813 (s, 3H), 3.86 (s, 3H, minor), 4.08 (d, *J*=5.4 Hz, 1H, minor), 4.73 (d, *J*=10.1 Hz, 1H), 4.75 (d, *J*=10.0 Hz, 1H, minor), 6.51 (s, 1H), 6.58 (s, 1H, minor), 6.69 (d, *J*=0.8 Hz, 1H), 7.05 (s, 1H, minor), 7.22–7.42 (m, 5H), 7.62 (AA′BB′, *J*=8.4 Hz, 2H), 7.64 (AA′BB′, *J*=8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.2 (minor), 15.4, 36.8 (minor), 40.8, 45.8 (minor), 50.4, 56.2, 79.3 (minor), 84.3, 100.7 (minor), 100.9, 102.7 (minor), 102.8, 110.8 (minor), 111.1, 116.7(minor), 118.4 (minor), 118.7, 125.5 (minor), 127.1 (minor), 127.4, 128.5, 128.6 (minor), 128.7, 128.8, 130.0, 130.8 (minor), 131.9 (minor), 132.6, 133.3, 133.6 (minor), 138.8, 139.1 (minor), 147.2 (minor), 149.0, 154.8 (minor), 155.4, 155.5, 155.8 (minor). LRMS (EI) *m*/*z* (rel intensity) 435 (M^++2, 98), 433 (M^+, 100), 344 (40), 342 (42), 317 (46), 316 (88), 315 (43), 314 (72), 263 (46), 118 (74), 117 (74). TOF-HRMS calcd for $C_{24}H_{21}BrNO_2$ ($M+H^+$) 434.0750, found 434.0749.

*4.1.26. 6-Bromo-7-methoxy-3-methyl-2-phenyl-4-(4-(trifluoromethoxy)phenyl) chroman (**47**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the desired compound was obtained as a 1.9:1 mixture of C2-C4 *cis*:*trans* diastereomers as colorless oil (0.010 g, 0.020 mmol, 51%). R_f (30% EtOAc/hexanes) 0.62. IR (neat): ν_{max} 2928, 1608, 1572, 1488, 1440, 1399, 1310, 1256, 1195, 1153, 1119, 1053, 1019 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.54 (d, *J*=7.0 Hz, 3H, minor), 0.58 (d, *J*=6.6 Hz, 3H), 2.16–2.26 (m, 1H), 2.40–2.50 (m, 1H, minor), 3.75 (d, *J*=10.8 Hz 1H), 3.81 (s, 3H), 3.85 (s, 3H, minor), 4.03 (d, *J*=5.2 Hz, 1H, minor), 4.73 (d, *J*=10.1 Hz, 1H), 4.79 (d, *J*=10.1 Hz, 1H, minor), 6.50 (s, 1H), 6.57 (s, 1H, minor), 6.77 (d, *J*=0.9 Hz, 1H), 7.09–7.46 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.2 (minor), 15.4, 36.9 (minor), 40.9, 45.1 (minor), 49.6, 56.2, 79.3 (minor), 84.5, 100.6 (minor), 100.8, 102.6, 117.7 (minor), 119.3, 120.5 (minor), 121.1, 125.5 (minor), 127.2, 127.4, 128.4, 128.6 (minor), 128.7, 130.5, 131.3 (minor), 133.5, 133.7 (minor), 139.1, 140.3 (minor), 141.9, 154.8 (minor), 155.2, 155.5. LRMS (EI) *m*/*z* (rel intensity) 494 (M^++2, 19), 492 (M^+, 19), 191 (27), 289 (27), 278 (33), 277 (100), 117 (57), 91(26). TOF-HRMS calcd for $C_{24}H_{21}BrF_3O_3$ ($M+H^+$) 493.0621, found 493.0618.

*4.1.27. 6-Bromo-7-methoxy-2-(4-methoxyphenyl)chroman (**53**).* Following the general procedure and purification by PTLC (20% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.032 g, 0.092 mmol, 99%). R_f (20% EtOAc/hexanes) 0.56. IR (neat): ν_{max} 3000, 2929, 2852, 1732, 1611, 1573, 1514, 1495, 1443, 1403, 1305, 1246, 1193, 1153, 1034 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.92–2.21 (m, 2H), 2.65–3.00 (m, 2H), 3.82 (s, 6H), 4.97 (dd, *J*=9.6, 3.0 Hz, 1H), 6.48 (s, 1H), 6.93 (app. td, *J*=8.8, 2.6 Hz, 2H), 7.24 (s, 1H), 7.34 (app. td, *J*=8.8, 1.8 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 29.2, 29.5, 55.3, 56.2, 77.8, 101.3, 102.0, 114.0, 115.3, 127.4, 133.0, 133.5, 155.0, 155.3, 159.5. LRMS (EI) *m*/*z* (rel intensity) 351 (M^++3, 14), 350 (M^++2, 78), 349 ($M+H^+$, 17), 348 (M^+, 80), 271 (8), 269 (31), 134 (62), 121 (36), 91 (100). TOF-HRMS calcd for $C_{17}H_{18}BrO_3$ ($M+H^+$) 349.0434, found 349.0435.

*4.1.28. 2-(3-Benzyloxy-4-methoxy)phenyl-6-bromo-7-methoxychroman (**54**).* Following the general procedure and purification by PTLC (20% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.037 g, 0.082 mmol, 73%). R_f (20% EtOAc/hexanes) 0.44. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.92–2.21 (m, 2H), 2.64–2.76 (m, 1H), 2.82–3.04 (m, 1H), 3.86 (s, 3H), 3.93 (s, 3H), 4.96 (dd, *J*=9.4, 2.2 Hz, 1H), 5.20 (s, 2H), 6.50 (s, 1H), 6.92–7.03 (m, 3H), 7.29–7.50 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.0, 29.4, 56.1, 56.2, 71.2, 77.8, 101.1, 101.9, 111.9, 112.4, 115.2, 119.1, 127.4, 127.8, 128.5, 133.0, 133.7,

137.0, 148.3, 149.6, 154.9, 155.1. TOF-HRMS calcd for $C_{24}H_{24}BrO_4$ ($M+H^+$) 455.0852, found 455.0866. These spectroscopic data were identical to those reported previously.[3a]

*4.1.29. 6-Bromo-7-methoxy-4-(methylsulfonylmethyl)-2-phenyl chroman (**56**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.007 g, 0.018 mmol, 37%). R_f (30% EtOAc/hexanes) 0.22. IR (neat): ν_{max} 2924, 2854, 1609, 1568, 1488, 1443, 1400, 1300, 1197, 1153, 1051 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.9–2.3 (m, 2H), 2.60–2.86 (m, 1H), 3.02 (s, 3H), 3.06–3.16 (m, 1H), 3.35–3.66 (m, 1H), 3.61 (dd, 1H, J=3.0, 13.6 Hz), 3.85 (s, 3H), 5.07 (ddd, 1H, J=15.6, 11.3, 1.7 Hz), 6.52 (s, 1H), 7.30–7.48 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 33.4, 36.8, 42.3, 42.5, 56.3, 59.8, 60.0, 73.7, 101.4, 101.8, 102.9, 115.3, 126.0, 126.1, 128.3, 128.4, 128.7, 130.9, 132.7, 140.0, 155.7, 155.8. LRMS (EI) m/z (rel intensity) 412 (20, M^++2), 410 (19, M^+), 330 (77), 332 (74), 315 (97), 317 (100), 148 (84), 104 (86), 91 (84), 77 (74). TOF-HRMS calcd for $C_{18}H_{20}BrO_4S$ ($M+H^+$) 411.0260, found 411.0262.

*4.1.30. 6-Bromo-7-methoxy-2-(4-methoxyphenyl)-4-(methyl sulfonylmethyl)chroman (**57**).* Following the general procedure and purification by PTLC (30% EtOAc/hexanes), the desired compound was obtained as colorless oil (0.013 g, 0.029 mmol, 44%). R_f (30% EtOAc/hexanes) 0.20. IR (neat): ν_{max} 2926, 2846, 1610, 1514, 1489, 1300, 1247, 1197, 1154, 1051, 1030 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.93–2.34 (m, 1H), 2.55–2.84 (m, 1H), 3.02 (s, 3H), 3.07–3.70 (m, 2H), 3.83 (s, 6H), 5.02 (dd, 1H, J=11.4, 15.0 Hz), 6.50 (s, 1H), 6.93 (d, 2H, J=8.8 Hz), 7.34 (s, 1H), 7.35 (d, 2H, J=8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 33.2, 36.6, 42.2, 42.5, 55.4, 56.3, 59.9, 60.2, 73.4, 77.4, 101.4, 101.8, 102.8, 114.1, 115.3, 115.6, 127.4, 127.5, 130.8, 132.1, 132.7, 155.2, 155.6, 156.0, 159.6. LRMS (EI) m/z (rel intensity) 442 (M^++2, 10), 440 (M^+, 10), 362 (26), 360 (27), 347 (34), 345 (32), 134 (100), 119 (39), 91 (38), 77 (20). TOF-HRMS calcd for $C_{19}H_{22}BrO_5S$ ($M+H^+$) 441.0366, found 441.0376.

*4.1.31. 2-Bromo-3-methoxy-6-phenyl-7,8,10,10a-tetrahydro-6H-benzo[c]chromen-9(6aH)-one (**59**).* Following the general procedure and purification by PTLC (20% EtOAc/hexanes), the C3-C4 *trans* isomer was obtained as a white solid (0.042 g, 0.11 mmol, 42%, using $PtCl_4$; 0.035 g, 0.09 mmol, 44%, using $AuCl_3$). R_f (20% EtOAc/hexanes) 0.29. IR (neat): ν_{max} 2953, 1713, 1609, 1488, 1443, 1202, 1052 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (ddd, J=25.7, 13.4, 4.8 Hz, 1H), 1.57–1.63 (m, 1H), 2.13–2.04 (m, 1H), 2.25–2.35 (m, 2H), 2.45 (dq, J=15.1, 2.4 Hz, 1H), 2.98–3.04 (m, 1H), 3.06 (ddd, J=13.3, 4.3, 2.0 Hz, 1H), 3.82 (s, 3H), 4.79 (d, J=10.0 Hz, 1H,), 6.50 (s, 1H), 7.24 (s, 1H), 7.46–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.6, 39.1, 40.3, 42.0, 44.9, 56.2, 83.0, 100.9, 102.4, 117.4, 127.2, 128.8, 128.9, 129.5, 138.7, 154.6, 155.5, 208.8. LRMS (EI) m/z (rel intensity) 388 (M^++2, 93), 386 (M^+, 100), 307 (37), 293 (25), 291 (26), 230 (25), 228 (25), 216 (26), 117 (16), 115 (20), 91 (13), 77 (4). TOF-HRMS calcd for $C_{20}H_{20}BrO_3$ ($M+H^+$) 387.0596, found, 387.0591.

The C3–C4 *cis* isomer was obtained as colorless oil (0.028 g, 0.072 mmol, 28%, using $PtCl_4$; 0.022 g, 0.057 mmol, 27%, using $AuCl_3$). R_f (20% EtOAc/hexanes) 0.23. IR (neat): ν_{max} 2945, 2099, 1715, 1609, 1488, 1443, 1199, 1158, 1053 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.66–1.74 (m, 1H), 1.87–1.96 (m, 1H), 2.27–2.40 (m, 2H), 2.48–2.54 (m, 1H), 2.62–2.75 (m, 2H), 3.18–3.23 (m, 1H), 3.82 (s, 3H), 5.22 (d, J=8.6 Hz, 1H), 6.50 (s, 1H), 7.24 (s, 1H), 7.36–7.44 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 35.0, 36.7, 37.6, 45.6, 56.2, 77.8, 101.0, 102.6, 117.3, 126.5, 128.6, 128.8, 132.0, 139.2, 153.9, 155.5, 209.1. LRMS (EI) m/z (rel intensity) 388 (M^++2, 100), 386 (M^+, 97), 307 (28), 230 (32), 228 (37), 216 (41), 178 (29), 149 (49), 117 (33), 91 (25). TOF-HRMS calcd for $C_{20}H_{20}BrO_3$ ($M+H^+$) 387.0596, found 387.0588.

*4.1.32. 2-Bromo-3-methoxy-6-phenyl-6a,7,8,9,10,10a-hexahydro-6H-benzo[c]chromen-9-yl acetate (**60**).* To a solution of compound **58** (0.067 g, 0.15 mmol) in MeOH (3 mL) was added $NaBH_4$ (0.0060 g, 0.16 mmol) at room temperature and then stirred for 30 min. After removal of solvent, the residue was added with H_2O and extracted with EtOAc (2×10 mL). The combined organic phases were washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum to give an alcohol crude product. This crude product was dissolved in CH_2Cl_2 (0.15 mL), followed by addition of DMAP (0.045 g, 0.37 mmol), and the reaction mixture was stirred until completely dissolved. Acetyl chloride (0.03 mL, 0.37 mmol) was added dropwise into this solution and then the reaction was stirred vigorously overnight. To this mixture was added $PtCl_4$ (0.0050 g, 0.01 mmol) and the resulting mixture was stirred at room temperature for 5 h. Following concentration under reduced pressure, the residue was purified by flash chromatography on silica gel to yield compound **60** as a white solid (0.037 g, 0.085 mmol, 58%). R_f (20% EtOAc/hexanes) 0.48. IR (neat): ν_{max} 2944, 1732, 1610, 1444, 1243 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.05–1.71 (m, 6H), 1.96–2.06 (m, 1H), 2.07 (s, 3H), 2.10 (s, 3H, minor), 2.60–2.68 (m, 1H), 2.88–3.02 (m, 1H, minor), 3.82 (s, 3H), 4.74 (d, J=10.0 Hz, 1H), 4.80 (d, J=10.6 Hz, 1H, minor), 4.84–4.95 (m, 1H), 5.22–5.26 (m, 1H, minor), 6.47 (s, 1H), 7.30–7.42 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.35, 21.44, 22.6, 26.1, 29.0, 30.8, 33.7, 35.0, 37.4, 42.5, 42.8, 56.2, 68.8, 72.2, 83.4, 100.8, 101.8, 101.9, 118.0, 118.6, 127.17, 127.23, 128.6, 129.5, 139.1, 154.6, 154.8, 155.0, 155.1, 170.4, 170.6. LRMS (EI) m/z (rel intensity) 432 (M^++2, 91), 430 (M^+, 100), 372 (31), 370 (37), 291 (30), 281 (56), 279 (65), 200 (20). TOF-HRMS calcd for $C_{22}H_{24}BrO_4$ ($M+H^+$) 431.0852 found 431.0859.

*4.1.33. 1-(5-Bromo-4-methoxy-2-(methoxymethoxy)phenyl)-1-hydroxy-7-methyloct-6-en-3-one (**61**).* To a stirred solution of LDA prepared by treating a solution of *i*-Pr_2NH (0.59 mL, 4.22 mmol) in THF (20 mL) and *n*-BuLi (2.06 M in hexane, 2.05 mL, 4.22 mmol) at 0 °C was added 6-methylhept-5-en-2-one (0.50 mL, 3.38 mmol) dropwise at −78 °C. After 1 h, a solution of 5-bromo-4-methoxy-2-(methoxymethoxy)benzaldehyde (0.76 g, 2.81 mmol) in THF (3 mL) was added, and the resulting mixture was stirred for 1 h at −78 °C. The reaction was quenched with H_2O at −78 °C, and then the mixture was extracted with EtOAc, washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated at reduced pressure. The residue was purified by flash chromatography on silica gel (30% EtOAc/hexanes) to give compound **61** (0.97 g, 2.42 mmol, 86%) as colorless oil. R_f (30% EtOAc/hexanes) 0.30. IR (neat): ν_{max} 3486, 2960, 1706, 1603, 1492, 1287, 1142 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.59 (s, 3H), 1.66 (s, 3H), 2.16–2.30 (m, 2H), 2.41–2.49 (m, 2H), 2.68 (B of ABX, J_{BA}=17.6 Hz, J_{BX}=8.8 Hz, 1H), 2.82 (A of ABX, J_{AB}=17.2 Hz, J_{AX}=3.4 Hz, 1H), 3.46 (s, 3H), 3.48 (d, J=3.8 Hz, 1H), 3.84 (s, 3H), 4.99–5.06 (m, 1H), 5.17 (s, 2H), 5.35 (app dt, J=8.8, 3.4 Hz, 1H), 6.70 (s, 1H), 7.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 22.1, 25.6, 43.4, 49.5, 56.1, 56.2, 64.1, 94.7, 99.3, 103.5, 122.4, 125.2, 130.4, 132.9, 153.5, 155.6, 211.4. TOF-HRMS calcd for $C_{18}H_{25}BrNaO_5$ ($M+Na^+$) 423.0778, found 423.0787.

*4.1.34. 2-Bromo-3-methoxy-6,6-dimethyl-7,8,10,10a-tetrahydro-6H-benzo[c]chromen-9(6aH)-one (**62**).* Following the general procedure, the C3-C4 *trans* isomer was obtained as a white solid (0.052 g, 0.15 mmol, 47%, using $PtCl_4$; 0.047 g, 0.14 mmol, 44%, using $AuCl_3$). R_f (30% EtOAc/hexanes) 0.39. IR (neat): ν_{max} 2926, 2860, 1716, 1609, 1488, 1199, 1055 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (s, 3H), 1.48 (s, 3H), 1.53–1.42 (m, 1H), 1.84 (td, J=12.1, 3.0 Hz, 1H), 2.15 (qt, J=6.5, 2.6 Hz, 1H), 2.25 (t, J=13.6 Hz, 1H), 2.41 (td, J=14.4, 6.5 Hz, 1H), 2.54 (dm, J=14.8 Hz, 1H), 2.78 (td, J=12.1, 4.3 Hz, 1H), 3.01 (ddd, J=14.2, 4.3, 2.0 Hz, 1H), 3.82 (s, 3H), 6.38 (s, 1H), 7.19 (d, J=0.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 27.0, 27.9, 35.3, 40.6, 45.5, 45.8, 56.1, 77.8, 101.3, 101.9, 117.0, 129.8, 153.3, 155.4,

209.0. LRMS (EI) *m*/*z* (rel intensity) 340 (M^++2, 97), 338 (M^+, 100), 257 (36), 254 (46), 230 (31), 228 (32). TOF-HRMS calcd for $C_{16}H_{20}BrO_3$ (M+H^+) 339.0590, found 339.0594.

The C3–C4 *cis* isomer was obtained as a white solid (0.028 g, 0.083 mmol, 25%, using $PtCl_4$; 0.025 g, 0.073 mmol, 23%, using $AuCl_3$). R_f (30% EtOAc/hexanes) 0.34. IR (neat): ν_{max} 2893, 1717, 1607, 1489, 1443, 1166, 1150, 1054 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 3H), 1.45 (s, 3H), 1.67–1.56 (m, 1H), 2.07–2.02 (m, 1H), 2.17–2.10 (m, 1H), 2.27 (dm, *J*=14.6 Hz, 1H), 2.37 (td, *J*=13.9, 6.4 Hz, 1H), 2.72 (dd, *J*=14.9, 6.0 Hz, 1H), 2.98 (dt, *J*=14.9, 2.5 Hz, 1H), 3.63 (br s, 1H), 3.81 (s, 3H), 6.36 (s, 1H), 7.36 (d, *J*=0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.9, 26.3, 26.6, 34.0, 39.6, 39.9, 42.7, 56.1, 101.3, 102.3, 114.0, 131.2, 153.3, 155.5, 209.4. LRMS (EI) *m*/*z* (rel intensity) 340 (M^++2, 100), 338 (M^+, 99.6), 270 (14), 250 (34), 230 (30), 228 (31). TOF-HRMS calcd for $C_{16}H_{20}BrO_3$ (M+H^+) 339.0590, found 339.0585.

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Supplementary data

General methods, detailed characterization and copies of ^1H and ^{13}C NMR of all new compounds as well as the overlay of ^1H NMR (not shown in the manuscript). Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.03.059. These data include MOL files and InChiKeys of the most important compounds described in this article.

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5. These Lewis acids or transition metal salts/complexes did not give any product: $BF_3{\cdot}Et_2O$, $SnCl_4$, $CoCl_2$, Ag_2O, $NiCl_2$, $YbCl_3{\cdot}6H_2O$, $Pd(OAc)_2$, K_2PdCl_6, $Pd(PPh_3)_2Cl_2$, $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$, $Ti(O{-}i{-}Pr)_3Cl$, $Y(C_5H_7O_2)_3$, [(COD)Ir(PCy_3)Py)]PF_6, and $Mg(ClO_4)_2$. For comparison, Nafion® NR50 and montmorillonite K 10, the proton source, gave the product **2** in low yields (25% and 30%, respectively).
6. $InCl_3$-catalyzed aqueous Diels–Alder reactions, in which $InCl_3$ served as Lewis acid, have been reported. See: (a) Loh, T.-P.; Pei, J.; Lin, M. *Chem. Commun.* **1996**, 2315–2316; (b) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439–455.
7. Except for MeOH, which gave no product, use of THF, $CHCl_3$, and $(CH_2Cl)_2$ furnished the product in 22%, 26%, and 83% yields, respectively, but the reactions took 18 h. In MeCN, the reaction required 72 h to complete, giving the product in moderate 46% yield. Thus, solubility does not seem to be an important contributing factor, which accounts for the difference in yields. In addition, toluene gave no product regardless of the Lewis acids or transition metal salts/complexes under investigation.
8. See the Supplementary data for the detailed preparation of **3**, **4**, **6**–**15**, **33**–**35**, **41**–**43**, **55**, and **58**.
9. In contrast to the proposed [4+2]-cycloaddition of the reaction using *trans* olefin, the 1:1 mixture of diastereomeric **24a** from the reaction using *cis* olefin may suggest a stepwise mechanism. In a separate experiment, it was found that the *cis* olefin did not isomerize to the *trans* olefin under the reaction condition. Thus, the *trans* product is likely to arise from the stepwise nature of the reaction.
10. Cinnamyl acetate and methyl cinnamyl ether gave no product under similar reaction conditions using $PtCl_4$.
11. Under acid-mediated conditions (Ref. 3), cinnamyl benzoate, cinnamyl acetate, and methyl cinnamyl ether as well as both *trans*-ethyl cinnamates gave no desired products.
12. In addition to the products **27** and **29**, only the baseline unidentified materials were obtained.
13. Better yields were obtained with SnCl4 when employed with other systems. See: Schmidt, R. R. *Tetrahedron* **1969**, *10*, 5279–5282.
14. The structure of chroman **40** contains a known '*s*' stereocenter on the sidechain at C3. However, the relative as well as absolute configuration at C3 has not been determined. Compound **40** exhibited optical activity ($[\alpha]_D^{29.3}$ −4.22 (*c* 1.43, $CHCl_3$)). The compound was obtained as a single diastereomer (dr>99:1). Determination of the absolute configuration is underway in our laboratory.
15. Similar yields and stereoselectivity were obtained with $AuCl_3$.
16. The role of Pt(IV) as a mild Lewis acid in the cycloaddition may be similar to that of $InCl_3$ in the Diels–Alder reactions (see Ref. 6)
17. Under other acid-mediated conditions (Ref. 3) to generate *o*-QMs, it is known that, once generated in the reactions without the appropriate dienophiles (olefins), the *o*-QMs similar to those in the current study are not stable and decompose very rapidly.
18. The exact position of Pt(IV) coordination on the *o*-QM has not been fully determined and is currently under our investigation.
19. In the bound state of *o*-QM with Pt(IV), the metal may position itself between the *o*-QM and dienophile to disfavor the otherwise favorable *endo* transition state. See Supplementary data for more details.
20. Both phenol and BnOH/BnOAc are the functional groups similar to those present in the reactions under $PtCl_4$ catalysis.