JOC The Journal of Organic Chemistry

Article

Cite This: J. Org. Chem. XXXX, XXX, XXX−XXX

pubs.acs.org/joc

Access to Electron-Deficient 2,2-Disubstituted Chromanes: A Highly Regioselective One-Pot Synthesis via an Inverse-Electron-Demand [4 + 2] Cycloaddition of *ortho*-Quinone Methides

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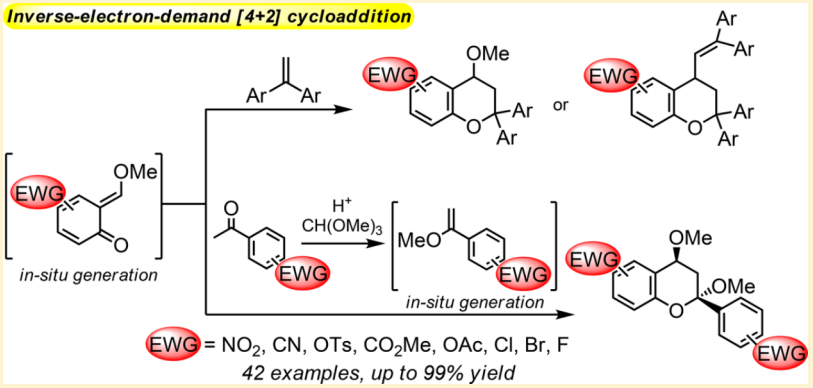
Supporting Information



ABSTRACT: We report the one-pot synthesis of 2,2-disubstituted chromanes with electron-withdrawing substituents. This reaction provides a simple yet efficient route to a wide range of electron-deficient chromanes in high yield and excellent regioselectivity. The reaction of salicylaldehyde with 1,1-disubstituted ethylenes smoothly furnishes these electron-deficient chromanes, which can be further transformed into functionalized chromanes or chromene. For example, **BW683C** was effectively synthesized from 5-chlorosalicylaldehyde with 4-chlorostyrene in two steps in excellent yield. The present reaction thus provides versatile access to functionalized electron-deficient chromanes and chromenes and therefore constitutes a promising tool for the synthesis of biologically and photochemically active molecules.

INTRODUCTION

Owing to their unique biological properties, the development of efficient synthetic methods for chromanes has attracted significant attention in organic chemistry and medicinal science.[1] Most biologically active chromanes contain multiple substituents, especially electron-donating moieties such as the methoxy group.[1] Based on the characteristic features of these compounds, a number of research groups have explored the synthesis of chromanes that bear electron-donating moieties (Scheme 1a).[2] In comparison, chromanes substituted with electron-withdrawing groups have received substantially less attention. Some chromanes that bear electron-withdrawing substituents exhibit biological (for example, antirhinoviral, antihypertensive, and antimicrobial) activity (Figure 1).[3] Despite the number of reports on these functionalized chromanes, the synthesis of such electron-deficient compounds has been much less explored. In addition, the previously reported synthetic methods suffer from requirements such as laborious reaction procedures and functionalization with strongly electron-withdrawing groups.[3,4] Recently, Ohwada and co-workers have demonstrated that 4*H*-1,2-benzoxazines with various electron-withdrawing substitutes react with ethylenes to furnish the corresponding chromanes.[5] This sequence successfully provides chromanes that bear strongly electron-withdrawing groups such as NO_2, CN, and CF_3.

We have previously developed an acid-catalyzed synthesis of *ortho*-quinone methides (*o*-QMs) from salicylaldehyde in the presence of trimethyl orthoformate under mild conditions.[6] During that study, we investigated the inverse-electron-demand [4 + 2] cycloaddition reaction of in situ-generated strongly electron-withdrawing *o*-QMs with arylalkynes, which afforded 2*H*-chromenes.[7] To expand the access to chromanes with electron-withdrawing substituents, we report herein a highly regioselective one-pot synthesis of electron-deficient 2,2-disubstituted chromanes using easily available substrates (Scheme 1b). This reaction provides a simple yet efficient route to a wide range of electron-deficient chromanes.

RESULTS AND DISCUSSION

Initially, we screened the reaction of 5-nitrosalicylaldehyde (**1a**) with 1,1-diphenylethylene (**2a**) using a variety of acid

Received: July 25, 2019
Published: October 3, 2019

DOI: 10.1021/acs.joc.9b02036
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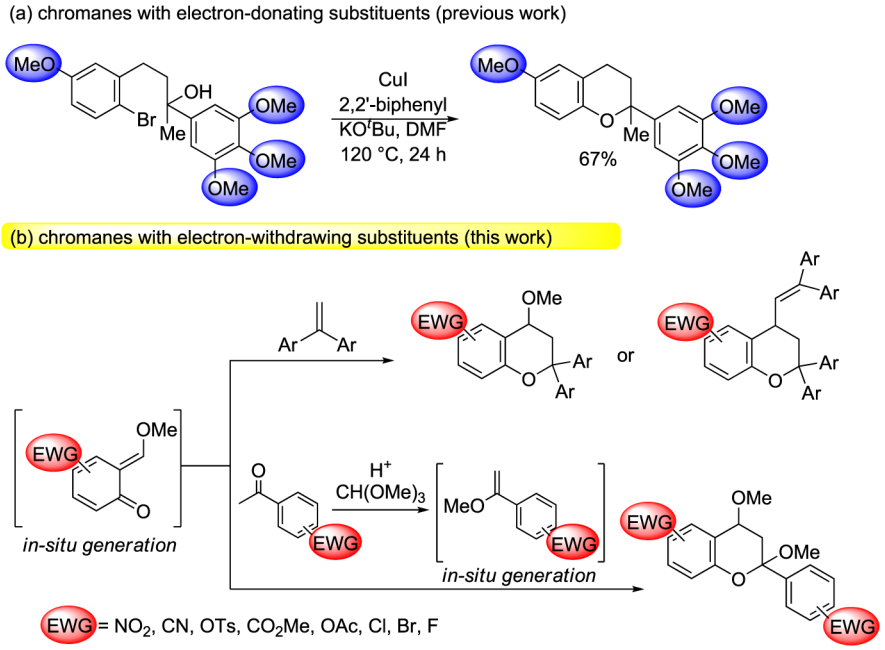
Scheme 1. Synthesis of Chromanes with Various Substituents



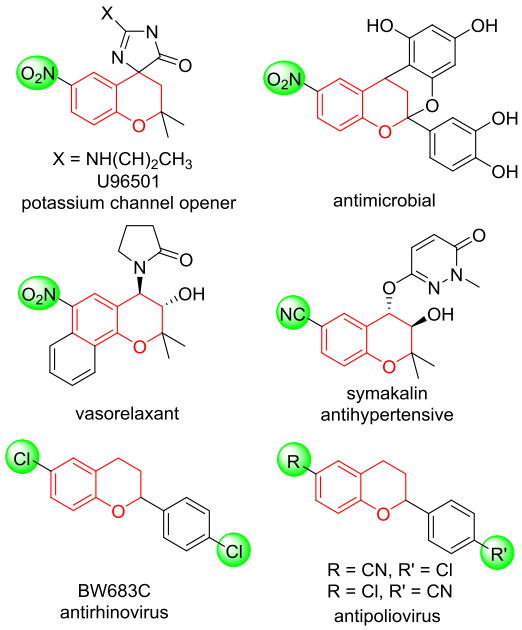
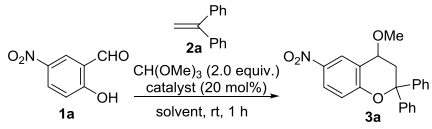


Figure 1. Selected examples of bioactive chromanes with electron-withdrawing substituents.

catalysts and solvents at room temperature (Table 1). When polar solvents such as dimethylformamide (DMF) and MeOH were used in the presence of catalytic amounts of trifluoromethanesulfonic acid (TfOH; 20 mol %), the reaction did not afford any of the targeted products (entries 1 and 2). However, CH_3CN efficiently promotes the reaction, providing the desired chromane (**3a**) in 69% yield (entry 3). In addition, moderately polar to nonpolar solvents such as tetrahydrofuran (THF), CH_2Cl_2, and toluene are also suitable (entries 4–6), whereby especially toluene effectively increased the product yield to 85%. Other Brønsted acids did not efficiently provide the product (entries 7–13).[8] Subsequently, we confirmed that the strong Brønsted acid TfOH smoothly promotes the

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	solvent	yield (%)[b]
1	TfOH	MeOH	nr[c]
2	TfOH	DMF	nr[c]
3	TfOH	CH_3CN	69
4	TfOH	THF	25
5	TfOH	CH_2Cl_2	79
6	TfOH	toluene	85
7	$PhSO_3H$	toluene	32
8	$MeSO_3H$	toluene	15
9	*p*-TsOH·H_2O	toluene	8
10	HBF_4·OEt_2	toluene	18
11	TFA	toluene	nr[c]
12	CSA[d]	toluene	nr[c]
13	$PhCO_2H$	toluene	nr[c]
14	$Pd(OAc)_2$	toluene	nr[c]
15	$Sc(OTf)_3$	toluene	15
16	$Al(OTf)_3$	toluene	26
17	BF_3·OEt_2	toluene	trace
18[e]	TfOH	toluene	71
19[f]	TfOH	toluene	63
20[g]	TfOH	toluene	0

[a]All reactions were carried out using **1a** (0.5 mmol), **2a** (1.5 mmol), $CH(OMe)_3$ (1.0 mmol), and the corresponding catalyst (20 mol %) in the specified solvent (5.0 mL) at room temperature for 1 h. [b]Isolate yield. [c]nr: no reaction. [d]CSA: (+)-10-camphorsulfonic acid. [e]Amount of **2a**: 1.0 mmol. [f]Amount of TfOH: 10 mol %. [g]From room temperature (1 h) to 100 °C (1 h).

generation of an *o*-QM from salicylaldehyde **1a**. The use of $Pd(OAc)_2$, which is a soft Lewis acid, was not successful (entry 14), while $Sc(OTf)_3$, which is a hard Lewis acid catalyst that has been used in the [4 + 2] cycloaddition of salicylaldehydes

DOI: 10.1021/acs.joc.9b02036
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with ethylenes by Yadav and co-workers,[9] affords the product in 15% yield (entry 15). TfOH is an inexpensive organic catalyst that is much easier to handle than $Sc(OTf)_3$. Other hard Lewis acid catalysts afforded low product yields (entries 16 and 17), while decreasing the amounts of **2a** or TfOH did not improve the product yield (entries 18 and 19). Next, we examined the effect of reaction temperature on the yield. When the reaction mixture was initially stirred at room temperature (1 h) and then heated to 100 °C (1 h), 4-alkenylchromane **4a** was obtained in 74% yield instead of 4-methoxychromane **3a** (entry 20, Figure 2). This result suggests that the elimination

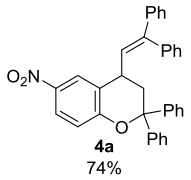

Figure 2. 4-Alkenylchromane **4a**.

of the methoxy group from chromane **3a** under acidic conditions at 100 °C furnishes a dihydropyrylium salt, which could react with 1,1-disubstituted ethylene to yield the corresponding 4-alkenylchromane. This synthetic strategy constitutes a new method to control the formation of carbon−carbon or carbon−oxygen bonds via controlling the reaction temperature. The thus-obtained chromanes, which contain carbon−carbon or carbon−oxygen bonds at the 4-position, represent important structural motifs in natural products and medicinal chemistry.[10] Against this background, we examined the scope of this selective, direct, and temperature-controlled synthetic route to 4-alkoxy and 4-alkenylchromanes.

With the optimized conditions in hand, we examined the scope and limitations of the formation of 4-methoxychromanes and 4-alkenylchromanes (Table 2). Salicylaldehydes with strongly to moderately electron-withdrawing groups were well tolerated, under both conditions A and B (**3a−f**, **4a−f**). 2-Hydroxy-1-naphthoaldehyde furnished **3g** together with chromene **5g** as an inseparable mixture in 33 and 32% yields, respectively. When the quantitative ratio of the starting materials was optimized (**1**/**2** = 2:1), chromene **5g** was selectively obtained in 66% yield. Chromene **5g** is a photochromic material,[11] which suggests that the present method may also represent a facile and efficient one-pot approach to the synthesis of chromene-based photochromic materials from easily available starting materials.[12] In addition, high yield was obtained under condition B (**4g**). The parent salicylaldehyde is also a good substrate for the formation of chromanes **3h** and **4h**. The 1,1-diphenylethylene with *p*-chloro groups afforded the corresponding products (**3i** and **4i**) in good yield. The reaction using a 1,1-dialkylethylene, that is, 1-methyl-1-phenylethylene, proceeded under condition A (**3j** and **3k**).[10,13,14] Interestingly, spiro compounds were obtained when 9-methylene-9*H*-thioxanthene and 5-methylene-5*H*-dibenzo[*a*,*d*][7]annulene were used as the dienophile (**3l** and **3m**). Styrene was also a good substrate under condition A,[14] suggesting that the reaction can be applied to not only 1,1-disubstituted olefins but also monosubstituted ones. Diarylethylenes were suitable under condition B, while other ethylenes furnished complex mixtures (**4j−n**), which suggests that the bisphenyl groups may effectively stabilize the benzyl cation of the intermediate (vide infra).[15]

Subsequently, we examined the corresponding reactions between acetophenones and salicylaldehydes. Under acidic conditions, in the presence of trimethyl orthoformate, acetophenone **A** is converted into 1-methoxy-1-phenyl ethylene **C** via acetal **B** (Scheme 2).[16] Initially, when 4′-nitroacetophenone was treated with 5-nitrosalicylaldehyde, the desired cycloadduct (**6a**) was obtained in high yield (Table 3). Although acetophenones that bear strongly electron-withdrawing groups are usually unsuitable dienophile substrates for inverse-electron-demand Diels−Alder reactions, this reaction proceeded smoothly to give the desired chromanes.[17] This may tentatively be ascribed to the fact that the methoxy group on ethylene **C** (Scheme 2) effectively promotes the reaction as an electron-donating group. Fortunately, single crystals suitable for an X-ray diffraction analysis were obtained, from which the relative stereochemistry of *cis*- and *trans*-chromanes **6a** was determined.[18] The separation of cis/trans isomers can be achieved by column chromatography, and the isolated ratio is shown in Table 3. When we examined the use of 3 equiv (excess) of acetophenone, the mixture of the desired product and acetophenone could not be completely separated by column chromatography. Therefore, we examined the amount of salicylaldehyde used, and optimal results were obtained for 2 equiv, that is, the consumption of acetophenone was virtually complete and only the desired chromane was isolated. 4′-Nitrileacetophenone also readily undergoes this transformation (**6b**). Halogen-functionalized derivatives are also good substrates to afford **6c−e**. Salicylaldehydes that bear strongly to moderately electron-withdrawing groups also furnished the corresponding cycloadducts in good yield (**6f−k**). The parent salicylaldehyde was also suitable for the reaction (**6l**). It is noteworthy that this reaction is applicable to various substrates with electron-withdrawing groups, which stereoselectively give electron-deficient 2,2-disubstituted chromanes.

Further transformations of chromane **3a** are shown in Scheme 3. When **3a** was treated with $TsNH_2$ in the presence of $FeCl_3$, 4-aminochromane **7a** was obtained in high yield. Moreover, the reaction of **3a** with allyltrimethylsilane afforded 4-alkylchromane **8a**. 4-Amino- and 4-alkylchromanes are found in natural products and biologically active compounds, with, for example, antimicrobial, potassium-channel-opening, and other bio-organic properties.[3,19] The hydrogenation of **3a** furnished 6-aminochromane **9a** in good yield. 6-Aminochromanes also exhibit diverse bioactivity.[20] Interestingly, when **3a** was treated with *N*-bromosuccinimide (NBS), 3-bromochromene **10a** was obtained in 75% yield. This reaction thus provides a new synthetic route to 3-bromochromenes,[21] which may lead to photochromic 2,2,3-triaryl-2*H*-chromenes.[22] It should be noted here that this reaction represents a feasible route to chromenes, leading to the effective synthesis of photochemically active molecules. For example, **BW683C** is a highly effective inhibitor of the replication of certain serotypes of rhinovirus.[3a] Recently, the synthesis of **BW683C** has been reported, including a modular synthesis of 2-alkyl- and 2-arylchromans via a three-step sequence and a regioselective domino synthesis of 2-alkylflavans via a hidden Brønsted acid catalysis.[23] To demonstrate the synthetic utility of the method presented herein, we synthesized **BW683C** in two steps in 90% yield from 5-chlorosalicylaldehyde with 4-chlorostyrene (Scheme 4). It should be noted here that this method is

DOI: 10.1021/acs.joc.9b02036
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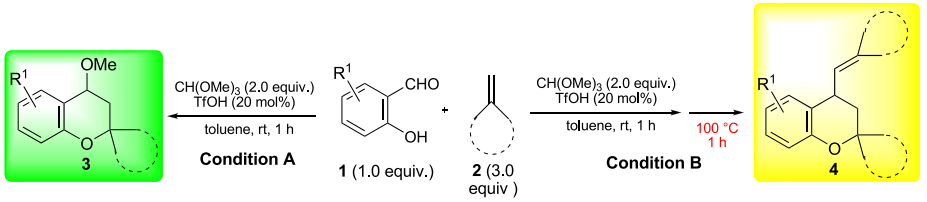
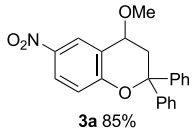
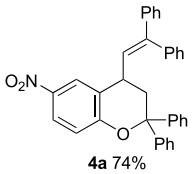
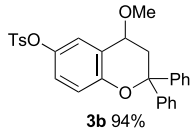
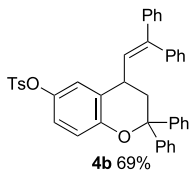
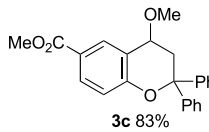
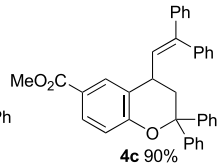
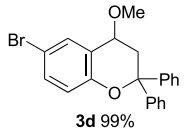
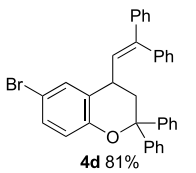
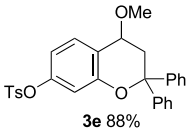
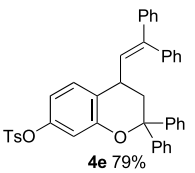
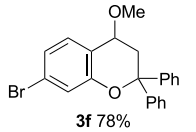
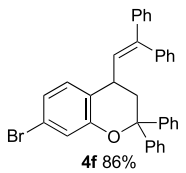
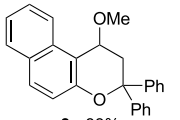
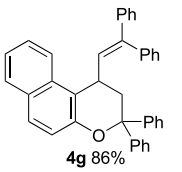
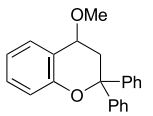
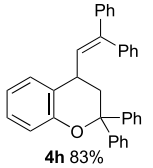
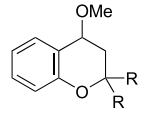
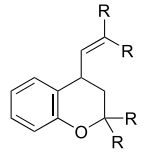
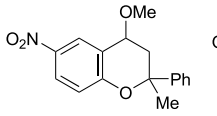
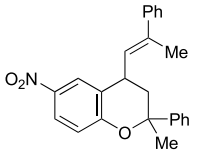
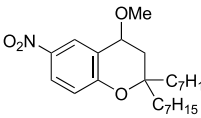
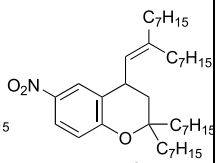
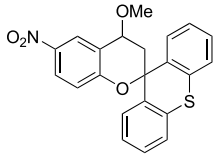
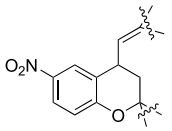
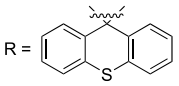
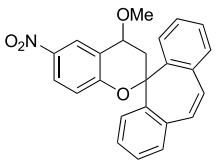
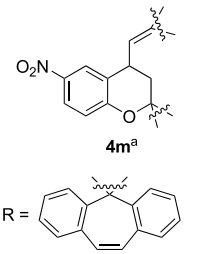
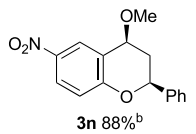
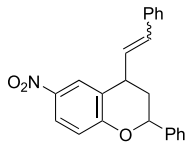
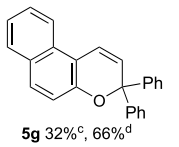
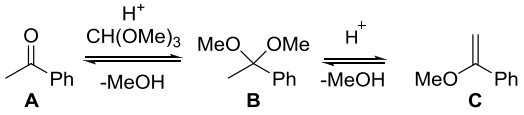
Table 2. Synthesis of 4-Methoxychromanes 3 and 4-Alkenylchromanes 4[e]



Condition A	Condition B	Condition A	Condition B	Condition A	Condition B
 **3a** 85%	 **4a** 74%	 **3b** 94%	 **4b** 69%	 **3c** 83%	 **4c** 90%
 **3d** 99%	 **4d** 81%	 **3e** 88%	 **4e** 79%	 **3f** 78%	 **4f** 86%
 **3g** 33%	 **4g** 86%	 **3h** 83%	 **4h** 83%	 **3i** R = C_6H_4-*p*-Cl 63%	 **4i** R = C_6H_4-*p*-Cl 70%
 **3j** 85% (dr = 3:2)	 **4j**[a]	 **3k** 15%	 **4k**[a]	 **3l** 99%>	 **4l**[a] 
 **3m** 98%	 **4m**[a]	 **3n** 88%[b] (cis / trans = 93:7)	 **4n**[a]	 **5g** 32%[c], 66%[d]	

[a]A complex mixture was obtained. [b]Salicylaldehyde (2.0 mmol) and the 1,1-disubstituted ethylene (1.0 mmol) were stirred for 24 h. The product yield is given with respect to the ethylene. [c]^{1}H NMR yield. [d]Salicylaldehyde (2.0 equiv) and ethylene (1.0 equiv) were reacted for 6 h. The product yield was calculated on the basis of the ethylene. [e]Condition A: **1** (0.5 mmol), **2** (1.5 mmol), $CH(OMe)_3$ (1.0 mmol), and TfOH (20 mol %) in toluene (5.0 mL) at room temperature for 1 h; condition B: **1** (0.5 mmol), **2** (1.5 mmol), $CH(OMe)_3$ (1.0 mmol), and TfOH (20 mol %) in toluene (5.0 mL) at room temperature (1 h) and then at 100 °C (1 h).

Scheme 2. Generation of 1-Phenyl-1-methoxy Ethylene C in the Presence of an Acid Catalyst



based on easily available substrates and inexpensive catalysts and provides the products in excellent yield.[3a,23]

A mechanism for the present reaction is proposed in Scheme 5. An *o*-QM is generated from salicylaldehyde **12** with trimethyl orthoformate via acetal **13** under acidic conditions. An inverse-electron-demand Diels–Alder reaction of the *o*-QM with a 1,1-disubstituted ethylene (**14**) affords chromane **15**, probably via a concerted mechanism and an endo addition.[13,14,24] The formation of 4-alkenylchromane **4a** from 4-methoxychromane **3a** under the reaction conditions outlined in Scheme 6 (1) strongly suggests that the retro-Diels–Alder reaction occurs at 100 °C and regenerates the starting compounds *o*-QM and 1,1-diphenylethylene in situ [Scheme

DOI: 10.1021/acs.joc.9b02036
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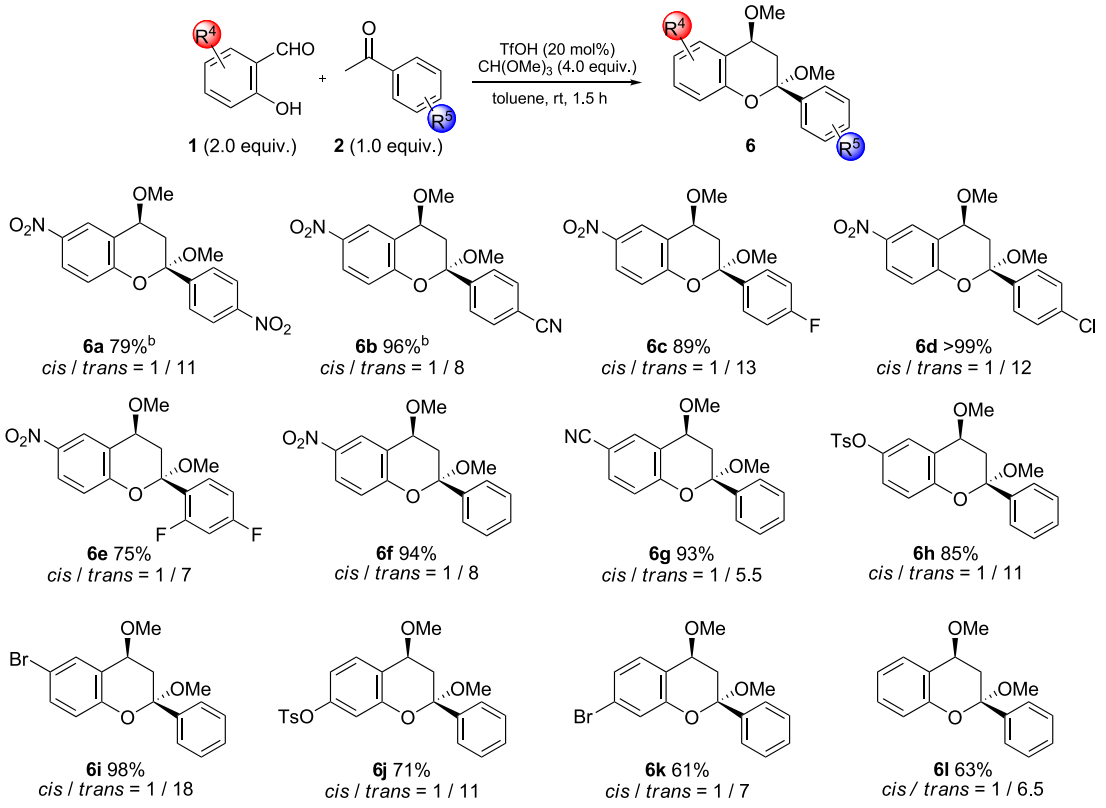
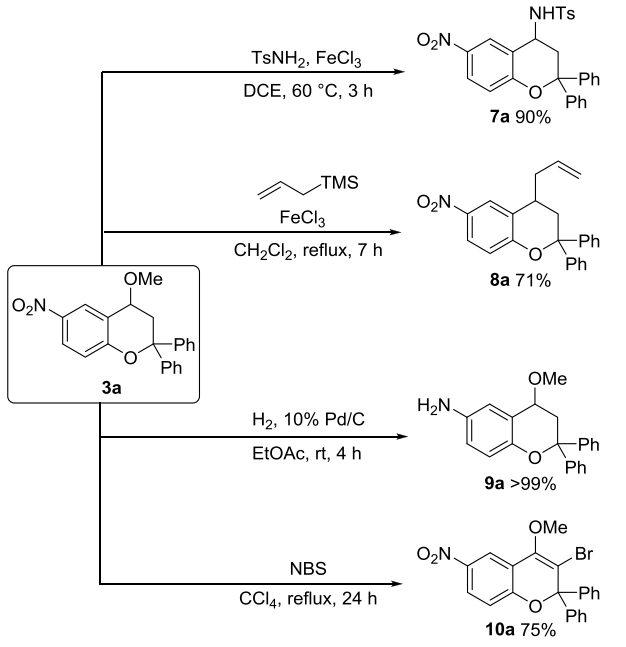
Table 3. Reaction of Acetophenones with Salicylaldehydes[a]

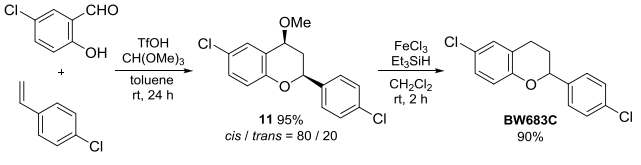


[a]The ratio of cis/trans isomers was determined by ^{1}H NMR spectroscopy. [b]Reaction conducted at 40 °C for 24 h.

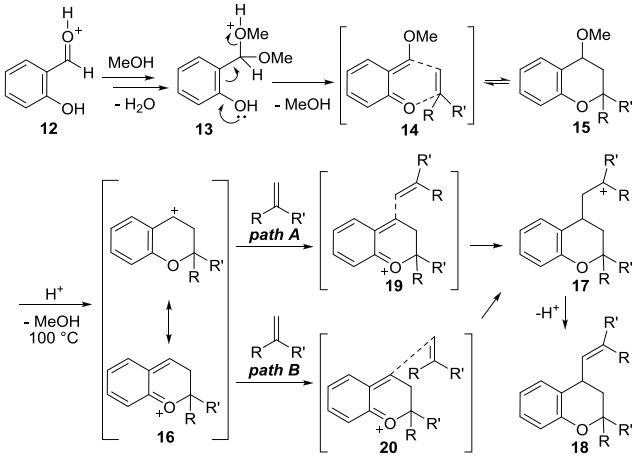
Scheme 3. Further Transformations of Chromane 3a



Scheme 4. Two-Step Synthesis of BW683C



Scheme 5. Proposed Mechanism for the Reaction of Salicylaldehyde (12) with 1,1-Disubstituted Ethylenes



6 (2)]. The elimination of the methoxy group on chromane **15** under acidic conditions would then afford cationic intermediate **16**, before **17** could be generated via either path A or B. Intermediate **16** could be attacked from the exo side of the dihydrobenzopyrylium ring by the 1,1-disubstituted ethylene to yield the stable dibenzyl cation **17** (path A).[25] Dihydropyrylium **16** could also react with the 1,1-disubstituted ethylene via an endo approach to give **17** (path B).[26] Based on density functional theory (DFT) calculations at the theoretical level of B3LYP with the 6-31G(d,p) basis set, path A might be energetically more favorable than path B.[27] Finally, the loss of a proton from **17** would afford the desired product (**18**). Further

DOI: 10.1021/acs.joc.9b02036
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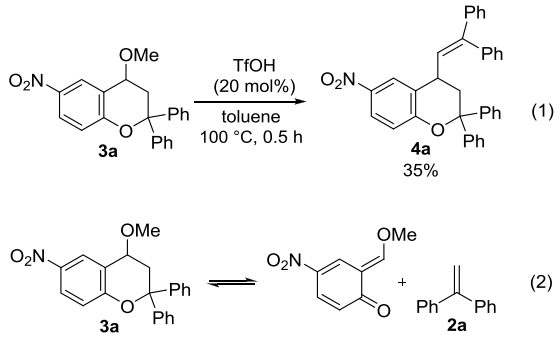
Scheme 6. Reaction of Chromane 3a in the Absence of 1,1-Diphenyl Ethylenes



studies on the scope and mechanism of this reaction are currently in progress and will be reported in due course.

CONCLUSIONS

We have developed a highly regioselective one-pot method for the generation of electron-deficient 2,2-disubstituted chromanes via an inverse-electron-demand [4 + 2] cycloaddition. When 1,1-disubstituted ethylenes or acetophenones are reacted with salicylaldehydes that bear electron-withdrawing groups, the desired chromanes are obtained in high yield and excellent regioselectivity. The reaction of salicylaldehydes with 1,1-disubstituted ethylenes generates 4-methoxychromanes at room temperature, whereas 4-alkenylchromanes are obtained when the reaction is carried out at room temperature and then at 100 °C. Further transformations of the electron-deficient chromanes furnished functionalized chromanes or chromene. For example, **BW683C** was synthesized from 5-chlorosalicylaldehyde and 4-chlorostyrene in 90% yield in two steps. The present reaction thus provides versatile access to functionalized electron-deficient chromanes and chromenes and therefore constitutes a promising tool for the synthesis of biologically and photochemically active molecules.

EXPERIMENTAL SECTION

General Information. Infrared (IR) spectra were recorded on JASCO FT/IR-4100. ^{1}H NMR spectra were recorded on a Bruker DRX-300 (300 MHz) spectrometer, a Bruker DRX-500 (500 MHz) spectrometer, or a JEOL ECA-500 (500 MHz) spectrometer with tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in ppm relative to TMS (δ 0). NMR data are reported as follows: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constants, integration. ^{13}C{^{1}H} NMR spectra were recorded on a Bruker DRX-500 (126 MHz) spectrometer or a JEOL ECA-500 (126 MHz) spectrometer under complete proton decoupling. Chemical shifts are reported in ppm relative to the solvent resonance of $CDCl_3$ (δ 77.0). High-resolution mass spectra (HRMS) were recorded on a Hitachi High-Technologies Nanofrontier LD Spectrometer [electrospray ionization (ESI)/time-of-flight]. Column chromatography was carried out on Cica-reagent silica gel 60 N (spherical; particle size: 63−210 μm). Thin-layer chromatography (TLC) was carried out on Merck TLC plates with silica gel (60 F_{254}). Single-crystal X-ray diffraction analyses were performed at 223 K using a Rigaku XtaLAB P200 diffractometer with a graphite-monochromated Cu Kα radiation (λ = 1.54187 Å). Unless otherwise noted, commercially purchased reagents were used as received. 1,1-Disubstituted ethylenes were prepared according to published methods.[28−38]

1,1-Bis(4-chlorophenyl)ethylene. Yellow solid (572.1 mg, 77% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35−7.20 (m, 8H), 5.45 (s, 2H). The spectroscopic data were consistent with literature values.[33]

1,1-Bis(3-fluorophenyl)ethylene. Yellow oil (455.3 mg, 13% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.27 (m, 2H), 7.13−7.07 (m, 2H), 7.05−7.00 (m, 4H), 5.51 (s, 2H). The spectroscopic data were consistent with literature values.[34]

1,1-Bis(4-methoxyphenyl)ethylene. White solid (1.0934 g, 91% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.24 (m, 4H), 6.90−6.83 (m, 4H), 5.29 (s, 2H), 3.83 (s, 6H). The spectroscopic data were consistent with literature values.[35]

2-Heptyl-1-nonene. Colorless liquid (742.3 mg, 66% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.68 (s, 2H), 1.99 (t, J = 6.8 Hz, 4H), 1.46−1.36 (m, 4H), 1.28 (m, 16H), 0.88 (t, J = 7.2 Hz, 6H). The spectroscopic data were consistent with literature values.[32]

9-Methylene-9H-thioxanthene. Yellow solid (143.6 mg, 15% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65−7.61 (m, 2H), 7.37−7.34 (m, 2H), 7.28−7.24 (m, 4H), 5.55 (s, 2H). The spectroscopic data were consistent with literature values.[36]

5-Methylene-5H-dibenzo[a,d][7]annulene. White solid (685.5 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42−7.23 (m, 8H), 6.83 (s, 2H), 5.26 (s, 2H). The spectroscopic data were consistent with literature values.[37]

General Procedure for the Synthesis of Chromanes. *Synthesis of Chromane 3.* Salicylaldehyde **1** (0.50 mmol), 1,1-disubstituted ethylene **2** (1.5 mmol), and trimethyl orthoformate (1.0 mmol) were dissolved in dry toluene (5.0 mL) under an atmosphere of nitrogen before trifluoromethanesulfonic acid (20 mol %) was added to the reaction mixture. After stirring at room temperature for 1 h, the reaction mixture was neutralized with 5% aqueous (aq) $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic phases were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 50/1, v/v) to afford chromane **3**.

Synthesis of Chromane 4. Salicylaldehyde **1** (0.50 mmol), 1,1-disubstituted ethylene **2** (1.5 mmol), and trimethyl orthoformate (1.0 mmol) were dissolved in dry toluene (5.0 mL) under an atmosphere of nitrogen before trifluoromethanesulfonic acid (20 mol %) was added to the reaction mixture. After stirring at room temperature for 1 h, the reaction mixture was heated to 100 °C (oil bath) and stirred for 1 h. Then, every 15 min, a three-way stopcock was carefully opened three times to quickly discharge gaseous methanol. After the reaction was completed, the reaction mixture was neutralized with 5% aq $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic phases were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane) to afford chromane **4**.

Synthesis of Chromane 6. Salicylaldehyde **1** (2.0 mmol), acetophenone **2** (1.0 mmol), and trimethyl orthoformate (4.0 mmol) were dissolved in dry toluene (5.0 mL) under an atmosphere of nitrogen before trifluoromethanesulfonic acid (20 mol %) was added to the reaction mixture. After stirring at room temperature for 1.5 h, the reaction mixture was neutralized with 5% aq $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic phases were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 20/1, v/v) to afford chromane **6**.

Characterization Data for the Chromanes. *4-Methoxy-6-nitro-2,2-diphenylchromane (**3a**).* 5-Nitrosalicylaldehyde (84.3 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow solid (154.2 mg, 85% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (dd, J = 2.8, 0.9 Hz, 1H), 8.13 (dd, J = 9.0, 2.6 Hz, 1H), 7.45−7.27 (m, 10H), 7.14 (d, J = 9.0 Hz, 1H), 4.28 (dd, J = 10.9, 5.7 Hz, 1H), 3.54 (s, 3H), 3.34 (dd, J = 13.4, 5.5 Hz, 1H), 2.46 (dd, J = 13.4, 10.7 Hz 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.8, 144.1, 141.9, 141.7, 128.9, 128.4, 128.0, 127.8, 125.8, 125.7, 125.0, 124.3, 124.1,

DOI: 10.1021/acs.joc.9b02036
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117.5, 84.4, 71.1, 56.5, 36.3; IR [attenuated total reflection (ATR)]: 1585, 1516, 1478, 1432, 1338, 1253, 1098, 1081, 1017, 900, 752, 697 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{19}NO_4Na$ ($[M + Na]^+$): 384.1206, found: 384.1226.

*4-Methoxy-2,2-diphenyl-6-tosyloxychromane (**3b**).* 2-Hydroxy-5-tosyloxybenzaldehyde (145.4 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (226.9 mg, 94% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.66 (d, J = 7.6 Hz, 2H), 7.43−7.37 (m, 4H), 7.35−7.22 (m, 8H), 6.97 (dd, J = 3.0, 0.8 Hz, 1H), 6.92 (d, J = 8.9 Hz, 1H), 6.80−6.75 (m, 1H), 4.21 (dd, J = 10.9, 5.7 Hz, 1H), 3.35 (s, 3H), 3.19 (dd, J = 13.2, 5.7 Hz, 1H), 2.48−2.36 (m, 4H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.2, 145.0, 144.9, 143.0, 142.5, 132.4, 129.6, 128.6, 128.5, 128.2, 127.6, 127.4, 126.0, 125.6, 124.3, 122.9, 121.2, 117.6, 83.0, 71.2, 55.6, 36.2, 21.6; IR (ATR): 1486, 1449, 1364, 1173, 1132, 1091, 1026, 943, 892, 838, 808, 735, 663 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{29}H_{26}O_5NaS$ ($[M + Na]^+$): 509.1393, found: 509.1383.

*4-Methoxy-6-methoxycarbonyl-2,2-diphenylchromane (**3c**).* Methyl 3-formyl-4-hydroxybenzoate (90.4 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (156.8 mg, 83% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.47−7.40 (m, 4H), 7.35−7.19 (m, 6H), 7.09 (d, J = 8.5 Hz, 1H), 4.29 (dd, J = 10.4, 5.7 Hz, 1H), 3.83 (s, 3H), 3.48 (s, 3H), 3.28 (dd, J = 13.2. 5.4 Hz, 1H), 2.50−2.546 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 166.7, 157.5, 144.7, 142.4, 130.7, 129.6, 128.6, 128.3, 127.7, 127.5, 125.9, 125.7, 123.3, 122.7, 117.0, 83.4, 71.4, 56.1, 51.7, 36.5; IR (ATR): 1707, 1585, 1493, 1448, 1296, 1262, 1212, 1117, 1093, 1025, 928, 766, 708 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{24}H_{22}O_4Na$ ($[M + Na]^+$): 397.1410, found: 397.1415.

*6-Bromo-4-methoxy-2,2-diphenylchromane (**3d**).* 5-Bromosalicylaldehyde (99.7 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (219.7 mg, quant.). ^1H NMR (300 MHz, $CDCl_3$): δ 7.47−7.38 (m, 5H), 7.38−7.16 (m, 8H), 6.94 (d, J = 8.7 Hz, 1H), 4.26 (dd, J = 10.6, 5.7 Hz, 1H), 3.48 (s, 3H), 3.24 (dd, J = 13.4, 5.8 Hz), 2.44 (dd, J = 13.4, 10.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.7, 145.0, 142.5, 132.0, 130.0, 128.7, 128.3, 127.7, 127.5, 126.1, 125.8, 125.4, 118.8, 113.0, 83.0, 71.5, 56.1, 36.5; IR (ATR): 1474, 1264, 1217, 1100, 1060, 1020, 915, 888, 829, 699 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{19}O_2Na^{79}Br$ ($[M + Na]^+$): 417.0461, found: 417.0451.

*4-Methoxy-2,2-diphenyl-7-tosyloxychromane (**3e**).* 2-Hydroxy-4-tosyloxybenzaldehyde (84.3 mg, 0.49 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (210.6 mg, 88% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.2 Hz, 2H), 7.40−7.35 (m, 4H), 7.32−7.26 (m,6H), 7.25−7.19 (m, 3H), 6.73−6.69 (m, 1H), 6.54 (d, J = 8.5 H, 1H), 4.23 (dd, J = 10.4, 5.4 Hz, 1H), 3.43 (s, 3H), 3.22 (dd, J = 11.8, 5.8 Hz, 1H), 2.45−2.38 (m, 4H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 154.1, 149.7, 145.2, 144.7, 142.4, 132.3, 129.6, 128.5, 128.5, 128.2, 128.2, 127.6, 127.4, 126.0, 125.6, 122.4, 114.6, 110.8, 83.2, 71.3, 56.0, 36.5, 21.6; IR (ATR): 1594, 1492, 1370, 1191, 1177, 1110, 1090, 963, 811, 698 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{29}H_{26}O_5NaS$ ($[M + Na]^+$): 509.1393, found: 509.1393.

*7-Bromo-4-methoxy-2,2-diphenylchromane (**3f**).* 4-Bromosalicylaldehyde (84.3 mg, 0.51 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow solid (157.1 mg, 78% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 7.42 (m, 4H), 7.34−7.29 (m, 4H), 7.27−7.21 (m, 3H), 7.18 (dd, J = 8.2, 1.0 Hz, 1H), 7.02 (dd, J = 8.2, 1.9 Hz, 1H), 4.25 (dd, J = 10.7, 5.7 Hz, 1H), 3.45 (s, 3H), 3.23 (dd, J = 13.6, 5.7 Hz, 1H), 2.44 (dd, J = 13.6, 10.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 154.4, 144.9, 142.5, 128.7, 128.3, 127.7, 127.5, 126.1, 125.7, 123.9, 122.4, 122.0, 119.9, 83.2, 71.4, 55.9, 36.6; IR (ATR): 1598, 1477, 1406, 1225, 1090, 1016, 814, 700 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{19}O_2Na^{79}Br$ ($[M + Na]^+$): 417.0461, found: 417.0449.

*2,3-Dihydro-1-methoxy-3,3-diphenyl-1H-naphto[2,1-b]pyran (**3g**).* 2-Hydroxy-1-naphthaldehyde (86.1 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (61.0 mg, 33% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.87 (d, J = 8.7 Hz, 1H), 7.74−7.70 (m, 2H), 7.53−7.39 (m, 5H), 7.33−7.14 (m, 8H), 4.97 (t, J = 6.6 Hz, 1H), 3.39 (s, 3H), 3.21−3.13 (m, 1H), 3.07−2.99 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.4, 144.7, 143.5, 132.8, 130.5, 129.5, 128.4, 128.3, 128.1, 127.4, 127.2, 126.5, 126.3, 125.8, 123.9, 123.4, 119.3, 114.1, 82.1, 69.9, 54.2, 36.5; IR (ATR): 1737, 1624, 1446, 1233, 1215, 1095, 1079, 1060, 908, 814, 733, 696 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{26}H_{22}O_2Na$ ($[M + Na]^+$): 389.1512, found: 389.1522.

*4-Methoxy-2,2-diphenylchromane (**3h**).* Salicylaldehyde (48.3 μL, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (131.5 mg, 83% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.52−7.39 (m, 4H), 7.35−7.18 (m, 8H), 7.05 (dd, J = 8.3, 1.1 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 4.33 (dd, J = 10.6, 5.7 Hz, 1H), 3.47 (s, 3H), 3.24 (dd, J = 13.6, 5.7 Hz, 1H), 2.49 (dd, J = 13.2, 10.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.6, 145.4, 143.0, 129.0, 128.5, 128.2, 127.4, 127.3, 127.2, 126.2, 125.8, 123.2, 120.7, 116.9, 82.5, 71.8, 55.8, 36.8; IR (ATR): 1581, 1486, 0445, 1228, 1216, 1096, 1020, 757, 700 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{20}O_2Na$ ($[M + Na]^+$): 339.1356, found: 339.1360.

*2,2-Bis(4-chlorophenyl)-4-methoxychromane (**3i**).* Salicylaldehyde (48.3 μL, 0.50 mmol), 1,1-bis(4-chlorophenyl)ethylene (373.7 mg, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (122.1 mg, 63% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.40−7.32 (m, 5H), 7.32−7.23 (m, 5H), 7.20 (dt, J = 7.3, 0.9 Hz, 1H), 7.03 (dd, J = 7.9, 1.1 Hz, 1H), 6.92 (td, J = 7.4, 1.1 Hz, 1H), 4.30 (dd, J = 10.2, 5.7 Hz, 1H), 3.46 (s, 3H), 3.12 (dd, J = 13.4, 5.8 Hz, 1H), 2.47 (dd, J = 13.6, 10.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.1, 143.4, 141.4, 133.5, 133.5, 129.3, 128.9, 128.5, 127.6, 127.5, 127.2, 122.9, 121.2, 116.9, 81.6, 71.5, 55.9, 36.6; IR (ATR): 1486, 1455,1230, 1091, 1011, 816, 753 cm^{-1}; HRMS (ESI +) m/z calcd for $C_{22}H_{18}O_2Na^{35}Cl_2$ ($[M + Na]^+$): 407.0576, found: 407.0573.

*4-Methoxy-2-methyl-6-nitro-2-phenylchromane (**3j**).* 5-Nitrosalicylaldehyde (83.6 mg, 0.50 mmol), α-methylstyrene (195 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow oil (127.2 mg, 85% yield, diastereomeric ratio 3:2). ^1H NMR (500 MHz, $CDCl_3$): (major) δ 8.38 (d, J = 2.8 Hz, 1H), 8.10 (m, 1H), 7.47−7.38 (m, 1H), 7.34−7.23 (m, 4H), 7.04 (dd, J = 10.7, 9.1 Hz, 1H), 4.57 (dd, J = 9.1, 5.7 Hz, 1H), 3.45 (s, 3H), 2.54 (ddd, J = 13.6, 5.7, 1.6 Hz, 1H), 2.20 (dd, J = 13.6, 9.1 Hz, 1H), 1.69 (s, 3H); (minor) δ 8.26 (dd, J = 2.8 Hz, 1H), 8.11 (m, 1H), 7.47−7.38 (m, 1H), 7.34−7.23 (m, 4H), 7.04 (dd, J = 10.7, 9.1 Hz, 1H), 4.02 (dd, J = 10.6, 5.5 Hz, 1H), 3.48 (s, 3H), 2.90 (dd, J = 13.4, 5.5 Hz, 1H), 2.09 (dd, J = 13.4, 10.6 Hz, 1H), 1.74 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): (mixture) δ 158.9, 158.6, 145.0, 143.6, 141.2, 141.1, 128.7, 128.3, 127.3, 124.9, 124.8, 124.8, 124.1, 124.0, 123.0, 117.7, 117.1, 81.2, 80.3, 70.9, 70.7, 56.2, 56.1, 37.8, 36.8, 31.2, 26.4; IR (ATR) (mixture): 1586, 1514, 1477, 1336, 1324, 1259, 1102, 1085, 749, 698 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{17}NO_4Na$ ($[M + Na]^+$): 322.1050, found: 322.1062.

*2,2-Diheptyl-4-methoxy-6-nitrochromane (**3k**).* 5-Nitrosalicylaldehyde (83.6 mg, 0.50 mmol), 2-heptyl-1-nonene (432 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow oil (30.4 mg, 15% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 8.34 (dd, J = 3.0, 0.8 Hz, 1H), 8.05 (dd, J = 9.0, 3.0 Hz, 1H), 6.84 (d, J = 9.0 Hz, 1H), 4.41 (dd, J = 8.5, 5.8 Hz, 1H), 3.52 (s, 3H), 2.20 (dd, J = 13.6, 5.7 Hz, 1H), 1.88 (dd, J = 13.6, 8.7 Hz, 1H), 1.75−1.51 (m, 4H), 1.37−1.22 (m, 20H), 0.92−0.84 (m, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 159.2, 140.9, 125.0, 123.0, 117.7, 81.9, 71.0, 56.5, 37.7, 36.3, 33.0, 31.8, 31.7, 29.9, 29.9, 29.2, 29.1, 23.3, 23.2, 22.6, 22.6, 14.1, 14.0; IR (ATR): 2926, 2855, 1586, 1518, 1479, 1334, 1260, 1085, 750 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{24}H_{40}NO_4$ ($[M + H]^+$): 406.2952, found: 406.2948.

DOI: 10.1021/acs.joc.9b02036
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*4-Methoxy-6-nitrospiro[chromane-2,9′-thioxanthene] (**3l**).* 5-Nitrosalicylaldehyde (36.5 mg, 0.22 mmol), 9-methylene-9*H*-thioxanthene (143.6 mg, 0.68 mmol), trimethyl orthoformate (50 μL, 0.46 mmol), and dry toluene (2.2 mL). White solid (95.4 mg, quant.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (dd, *J* = 2.9, 1.2 Hz, 1H), 8.28 (dd, *J* = 9.2, 2.9 Hz, 1H), 7.78 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.55−7.53 (m, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.37−7.34 (m, 2H), 7.32−7.27 (m, 2H), 7.25−7.18 (m, 2H), 3.92 (dd, *J* = 10.6, 4.9 Hz, 1H), 3.29 (s, 3H), 3.19−3.15 (m, 1H), 1.76 (dd, *J* = 13.2, 10.3 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.4, 141.9, 138.2, 135.9, 129.8, 127.8, 127.8, 127.6, 127.2, 126.9, 126.7, 125.5, 124.9, 124.7, 124.3, 123.8, 116.7, 81.2, 70.2, 56.3, 31.0; IR (ATR): 1586, 1434, 1335, 1255, 1240, 1087, 1020, 747 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{22}H_{18}NO_4S$ ([M + H]$^+$): 392.0951, found: 392.0969.

*4-Methoxy-6-nitrospiro[chromane-2,5′-dibenzo[a,d][7]annulene] (**3m**).* 5-Nitrosalicylaldehyde (83.2 mg, 0.50 mmol), 5-methylene-5*H*-dibenzo[*a*,*d*][7]annulene (306.4 mg, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (188.9 mg, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29−8.20 (m, 2H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.49−7.46 (m, 1H), 7.43−7.39 (m, 4H), 7.35−7.26 (m, 3H), 7.13 (s, 2H), 3.65 (dd, *J* = 10.6, 4.9 Hz, 1H), 3.48−3.44 (m, 1H), 3.27 (s, 3H), 1.76 (dd, *J* = 13.5, 10.6 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.4, 141.7, 139.7, 137.4, 131.9, 131.7, 130.9, 130.0, 129.9, 129.2, 128.9, 127.2, 127.1, 125.2, 124.7, 124.3, 123.8, 123.3, 117.0, 82.8, 70.5, 56.0, 29.2; IR (ATR): 1473, 1376, 1262, 1034, 908, 739, 575 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{24}H_{20}NO_4$ ([M + H]$^+$): 386.1387, found: 386.1377.

(2S,4S*)-4-Methoxy-6-nitro-2-phenylchromane (**3n**).* 5-Nitrosalicylaldehyde (166.6 mg, 1.0 mmol), styrene (58 μL, 0.50 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL) for 24 h. Yellow solid (125.0 mg, 88% yield, cis/trans = 93/7). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 2.8 Hz, 1H), 8.06 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.52−7.37 (m, 5H), 6.93 (d, *J* = 8.5 Hz, 1H), 5.25 (dd, *J* = 12.0, 1.9 Hz, 1H), 4.75 (dd, *J* = 10.7, 5.7 Hz, 1H), 3.55 (s, 3H), 2.65 (ddd, *J* = 13.1, 5.8, 2.2 Hz, 1H), 2.14−2.02 (m, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.8, 141.5, 139.3, 128.7, 128.6, 126.0, 124.8, 124.4, 123.9, 117.1, 78.0, 72.9, 56.3, 34.4; IR (ATR): 2929, 1584, 1512, 1342, 1253, 1080, 749 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{16}H_{15}NO_4$ ([M + H]$^+$): 286.1074, found: 286.1075.

*6-Nitro-2,2-diphenyl-4-(2,2-diphenylvinyl)chromane (**4a**).*[38] 5-Nitrosalicylaldehyde (82.3 mg, 0.49 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow solid (185.6 mg, 74% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09−8.03 (m, 2H), 7.43−7.23 (m, 15H), 7.16−7.03 (m, 6H), 6.08 (d, *J* = 9.4 Hz, 1H), 3.68−3.55 (m, 1H), 2.87 (dd, *J* = 14.3, 5.3 Hz, 1H), 2.35 (dd, *J* = 14.1, 12.6 Hz, 1H).

*2,2-Diphenyl-4-(2,2-diphenylethenyl)-6-tosyloxychromane (**4b**).* 2-Hydroxy-5-tosyloxybenzaldehyde (143.4 mg, 0.49 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (165.6 mg, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68−7.61 (m, 2H), 7.41−7.31 (m, 5H), 7.31−7.18 (m, 8H), 7.16−7.04 (m, 9H), 6.95 (d, *J* = 9.1 Hz, 1H), 6.89−6.79 (m, 1H), 6.64 (d, *J* = 2.8 Hz, 1H), 5.89 (d, *J* = 9.5 Hz, 1H), 3.49−3.37 (m, 1H), 2.75 (dd, *J* = 14.0, 5.5 Hz, 1H) 2.26−2.21 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.2, 145.4, 145.0, 144.8, 143.1, 142.2, 141.1, 139.4, 132.6, 129.5, 129.4, 129.2, 128.6, 128.4, 128.3, 128.2, 128.2, 127.5, 127.4, 127.3, 127.0, 126.2, 125.8, 125.6, 122.1, 121.8, 118.0, 81.9, 38.4, 34.0, 21.5; IR (ATR): 1483, 1370, 1175, 1092, 948, 832, 695 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{42}H_{34}O_4NaS$ ([M + Na]$^+$): 657.2070, found: 657.2076.

*4-(2,2-Diphenylethenyl)-6-methoxycarbonyl-2,2-diphenyl-chromane (**4c**).* Methyl-3-formyl-4-hydroxybenzoate (89.0 mg, 0.49 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (231.2 mg, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89−7.82 (m, 2H), 7.43−7.32 (m, 5H), 7.30−7.16 (m, 10H), 7.10−7.04 (m, 6H), 6.13 (d, *J* = 9.5 Hz, 1H), 3.84 (s, 3H), 3.59 (t, *J* = 12.9 Hz, 1H), 2.81 (dd, *J* = 13.9, 5.4 Hz, 1H), 2.37−2.28 (m, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 166.8, 157.7, 145.2, 144.8, 142.2, 141.1, 139.5, 130.8, 129.7, 129.7, 129.3, 128.6, 128.3, 128.2, 127.4, 127.2, 127.1, 127.0, 126.0, 125.6, 124.8, 122.6, 117.2, 82.4, 51.7, 38.6, 33.8; IR (ATR): 1713, 1491, 1285, 1259, 763, 695 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{37}H_{31}O_3$ ([M + H]$^+$): 523.2268, found: 523.2267.

*6-Bromo-4-(2,2-diphenylethenyl)-2,2-diphenylchromane (**4d**).*[38] 5-Bromosalicylaldehyde (99.7 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (218.4 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41−7.33 (m, 5H), 7.30−7.17 (m, 12H), 7.12−7.04 (m, 5H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.09 (d, *J* = 9.8 Hz, 1H), 3.58−3.50 (m, 1H), 2.77 (dd, *J* = 14.2, 5.4 Hz, 1H), 2.29 (dd, *J* = 14.0, 12.5 Hz, 1H).

*2,2-Diphenyl-4-(2,2-diphenylethenyl)-7-tosyloxychromane (**4e**).* 2-Hydroxy-4-tosyloxybenzaldehyde (145.3 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (250.3 mg, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78−7.70 (m, 2H), 7.42−7.18 (m, 17H), 7.14−7.05 (m, 3H), 7.05−6.99 (m, 3H), 6.62 (d, *J* = 2.5 Hz, 1H), 6.55 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.04 (d, *J* = 9.3 Hz, 1H), 3.55−3.46 (m, 1H), 2.77 (dd, *J* = 13.9, 5.4 Hz, 1H), 2.46 (s, 3H), 2.27 (dd, *J* = 14.0, 12.5 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 154.1, 148.9, 145.3, 145.2, 144.5, 142.2, 141.2, 139.5, 132.6, 130.0, 129.7, 129.5, 129.3, 128.6, 128.6, 128.3, 128.3, 128.2, 127.5, 127.5, 127.3, 127.1, 127.0, 126.2, 125.6, 123.9, 114.6, 111.2, 82.1, 38.6, 33.7, 21.7; IR (ATR): 1489, 1349, 1174, 1091, 963, 828, 820, 809, 695 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{42}H_{35}O_4S$ ([M + H]$^+$): 635.2251, found: 635.2271.

*7-Bromo-4-(2,2-diphenylethenyl)-2,2-diphenylchromane (**4f**).*[6c] 4-Bromosalicylaldehyde (99.3 mg, 0.49 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (230.7 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40−7.32 (m, 5H), 7.32−7.18 (m, 11H), 7.13−7.07 (m, 5H), 7.01−6.94 (m, 2H), 6.06 (d, *J* = 9.5 Hz, 1H), 3.49 (ddd, *J* = 12.4, 9.5, 5.5 Hz, 1H), 2.79 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.29 (dd, *J* = 13.9, 12.3 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 154.4, 145.4, 144.5, 142.3, 141.2, 139.5, 130.1, 130.0, 129.3, 128.6, 128.4, 128.3, 128.2, 127.5, 127.4, 127.3, 127.1, 127.0, 126.2, 125.6, 124.0, 123.7, 120.6, 120.2, 82.1, 38.6, 33.7; IR (ATR): 1508, 1445, 1228, 1031, 759, 695 cm^{-1}; LRMS (EI+) *m*/*z* calcd for $C_{35}H_{28}{}^{79}BrO$ ([M + H]$^+$): 543.1318, found: 543.1.

*2,3-Dihydro-1-(2,2-dipenylethenyl)-3,3-diphenyl-1H-naphto[2,1-b]pyran (**4g**).* 2-Hydroxy-1-naphthaldehyde (85.8 mg, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (220.6 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.57−7.51 (m, 2H), 7.49−7.45 (m, 3H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.33−7.10 (m, 13H), 7.08−7.04 (m, 3H), 6.07 (d, *J* = 9.1 Hz, 1H), 3.99−3.91 (m, 1H), 2.97 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.56 (dd, *J* = 14.2, 10.1 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 151.6, 145.5, 142.6, 141.4, 140.7, 139.9, 134.0, 133.1, 129.7, 129.4, 128.8, 128.8, 128.4, 128.3, 128.2, 128.1, 127.4, 127.2, 127.1, 127.1, 126.9, 126.3, 125.9, 125.7, 124.3, 123.1, 119.7, 116.9, 81.1, 40.0, 32.5; IR (ATR): 1058, 1248, 1228, 1033, 821, 697 cm^{-1}; HRMS (ESI+) *m*/*z* calcd for $C_{39}H_{31}O$ ([M + H]$^+$): 515.2369, found: 515.2345.

*4-(2,2-Diphenylethenyl)-2,2-diphenylchromane (**4h**).* Salicylaldehyde (48.3 μL, 0.50 mmol), 1,1-diphenylethylene (264 μL, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). White solid (192.0 mg, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43−7.33 (m, 5H), 7.31−7.20 (m, 10H), 7.19−7.03 (m, 8H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.13 (d, *J* = 9.4 Hz, 1H), 3.61−3.52 (m, 1H), 2.80 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.33 (dd, *J* = 13.9, 12.3 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.6, 146.0, 144.1, 142.8, 141.5, 139.7, 130.8, 129.4, 128.8, 128.5, 128.3, 128.2, 128.2, 127.8, 127.3, 127.3, 127.2, 127.0, 126.9, 126.3, 125.7, 124.8, 120.6, 117.3, 81.5, 38.8, 34.0; IR (ATR): 1483, 1444, 4091, 1015, 759, 750, 698

DOI: 10.1021/acs.joc.9b02036
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cm^{-1}; HRMS (ESI+) m/z calcd for $C_{35}H_{29}O$ ($[M + H]^+$): 465.2213, found: 465.2198.

*2,2-Bis(4-chlorophenyl)-4-(2,2-bis(4-chlorophenyl)ethenyl)-chromane (**4i**).*[38] Salicylaldehyde (48.3 μL, 0.50 mmol), 1,1-bis(4-chlorophenyl)ethylene (371.8 mg, 1.5 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL). Yellow solid (285.7 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, J = 7.5 Hz, 2H), 7.30−7.23 (m, 6H), 7.20−6.98 (m, 11H), 6.89 (t, J = 7.4 Hz, 1H), 6.12 (d, J = 9.8 Hz, 1H), 3.45−3.38 (m, 1H), 2.61 (dd, J = 13.9, 5.4 Hz, 1H), 2.31−2.23 (m, 1H).

*3,3-Diphenyl-3H-naphto[2,1-b]pyran (**5g**).* 2-Hydroxy-1-naphthaldehyde (172.6 mg, 1.0 mmol), 1,1-diphenylethylene (87.8 μL, 0.50 mmol), trimethyl orthoformate (109 μL, 1.0 mmol), and dry toluene (5.0 mL) for 6 h. White solid (110.5 mg, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.7 Hz, 1H), 7.52−7.43 (m, 5H), 7.34−7.27 (m, 6H), 7.27−7.22 (m, 2H), 7.20 (d, J = 8.8 Hz, 1H), 6.25 (d, J = 9.7 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.5, 144.8, 129.8, 129.8, 129.3, 128.5, 128.1, 127.7, 127.5, 127.0, 126.6, 123.6, 121.3, 119.5, 118.3, 114.0, 82.5; IR (ATR): 1737, 1260, 1216, 1093, 1008, 802, 697 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{25}H_{19}O$ ($[M + H]^+$): 335.1430, found: 335.1439.

(2S,4S*)-2,4-Dimethoxy-6-nitro-2-(4-nitrophenyl)chromane (**6a**).* 5-Nitrosalicylaldehyde (334.6 mg, 2.0 mmol), 4′-nitroacetophenone (163.5 mg, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL) at 40 °C for 24 h. Yellow solid (282.0 mg, 79% yield, cis/trans = 1/11). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49−8.46 (m, 1H), 8.33 (d, J = 7.9 Hz, 2H), 8.18 (dd, J = 8.8, 2.8 Hz, 1H), 7.82−7.78 (m, 2H), 7.13 (d, J = 9.1 Hz, 1H), 4.87 (dd, J = 10.9, 6.2 Hz, 1H), 3.55 (s, 3H), 3.10 (s, 3H), 2.77 (dd, J = 13.1, 6.2 Hz, 1H), 1.85 (dd, J = 13.2, 11.0 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.1, 148.3, 146.1, 142.7, 127.3, 125.2, 125.0, 124.0, 123.9, 117.6, 102.9, 70.6, 56.9, 50.9, 38.4; IR (ATR): 1509, 1344, 1086, 749 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{16}N_2O_7Na$ ($[M + Na]^+$): 383.0850, found: 383.0867.

(2S,4S*)-2-(4-Cyanophenyl)-2,4-dimethoxy-6-nitrochromane (**6b**).* 5-Nitrosalicylaldehyde (334.8 mg, 2.0 mmol), 4′-cyanoacetophenone (144.2 mg, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL) at 40 °C for 24 h. Yellow solid (325.0 mg, 96% yield, cis/trans = 1/8). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, J = 2.8 Hz, 1H), 8.17 (dd, J = 8.8, 2.8 Hz, 1H), 7.79−7.75 (m, 2H), 7.75−7.71 (m, 2H), 7.11 (d, J = 9.1 Hz, 1H), 4.86 (dd, J = 11.0, 6.3 Hz, 1H), 3.54 (s, 3H), 3.08 (s, 3H), 2.74 (dd, J = 13.2, 6.3 Hz, 1H), 1.82 (dd, J = 13.2, 11.0 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.1, 144.3, 142.6, 132.6, 126.9, 125.2, 124.9, 123.8, 118.3, 117.5, 112.9, 102.9, 70.6, 56.8, 50.9, 38.4; IR (ATR): 3492, 2932, 2232, 1516, 1341, 1258, 1030, 839, 758 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{18}H_{16}N_2O_5Na$ ($[M + Na]^+$): 363.0951, found: 363.0961.

(2S,4S*)-2-(4-Fluorophenyl)-2,4-dimethoxy-6-nitrochromane (**6c**).* 5-Nitrosalicylaldehyde (332.9 mg, 2.0 mmol), 4′-fluoroacetophenone (121 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (295.5 mg, 89% yield, cis/trans = 1/13). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, J = 2.8 Hz, 1H), 8.14 (dd, J = 8.8, 2.8 Hz, 1H), 7.63−7.54 (m, 2H), 7.18−7.08 (m, 3H), 4.86 (dd, J = 11.2, 6.2 Hz, 1H), 3.54 (s, 3H), 3.08 (s, 3H), 2.77 (dd, J = 13.1, 6.2 Hz, 1H), 1.83 (dd, J = 13.2, 11.0 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 162.8 (d, J = 248.9 Hz), 156.6, 142.3, 135.1 (d, J = 2.8 Hz), 127.9 (d, J = 8.3 Hz), 125.3, 124.7, 123.7, 117.5, 115.5 (d, J = 22.0 Hz), 103.3, 70.7, 56.6, 50.5, 38.7; IR (ATR): 1509, 1218, 1024, 842, 751 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{16}NO_5FNa$ ($[M + Na]^+$): 356.0905, found: 356.0897.

(2S,4S*)-2-(4-Chlorophenyl)-2,4-dimethoxy-6-nitrochromane (**6d**).* 5-Nitrosalicylaldehyde (335.0 mg, 2.0 mmol), 4′-chloroacetophenone (123 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (352.0 mg, quant., cis/trans = 1/12). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (dd, J = 2.8, 1.0 Hz, 1H), 8.20−8.12 (m, 1H), 7.56−7.50 (m, 2H), 7.47−7.40 (m, 2H), 7.10 (d, J = 8.8 Hz, 1H), 4.84 (dd, J = 11.0, 6.3 Hz, 1H), 3.54 (s, 3H), 3.07 (s, 3H), 2.75 (dd, J = 13.1, 6.2 Hz, 1H), 1.82 (dd, J = 13.2, 11.0 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.5, 142.4, 137.8, 134.8, 128.8, 127.5, 125.3, 124.7, 123.7, 117.5, 103.2, 70.7, 56.7, 50.6, 38.5; IR (ATR): 1509, 1332, 1104, 1027, 892 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{16}NO_5Na^{35}Cl$ ($[M + Na]^+$): 372.0609, found: 372.0602.

(2S,4S*)-2-(2,4-Difluorophenyl)-2,4-dimethoxy-6-nitrochromane (**6e**).* 5-Nitrosalicylaldehyde (333.0 mg, 2.0 mmol), 2′,4′-difluoroacetophenone (126 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (264.7 mg, 75% yield, cis/trans = 1/7). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47−8.42 (m, 1H), 8.15 (dd, J = 8.8, 2.8 Hz, 1H), 7.72 (dt, J = 8.8, 6.3 Hz, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.97 (t, J = 8.2 Hz, 1H), 6.93−6.88 (m, 1H), 4.85 (dd, J = 11.0, 6.3 Hz, 1H), 3.56 (s, 3H), 3.13 (s, 3H), 3.05 (dd, J = 13.1, 6.2 Hz, 1H), 1.89 (dd, J = 13.1, 11.2 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.4 (dd, J = 252.0, 11.9 Hz), 160.0 (dd, J = 254.8, 11.9 Hz), 156.0, 142.4, 130.0 (dd, J = 9.2, 4.6 Hz), 125.4, 124.8, 123.8, 122.0 (dd, J = 11.0, 4.6 Hz), 117.5, 111.3 (dd, J = 21.1, 3.7 Hz), 105.0 (t, J = 26.1 Hz), 101.8 (d, J = 3.7 Hz), 70.4, 56.8, 50.8, 36.2 (d, J = 2.8 Hz); IR (ATR): 1515, 1343, 1102, 851 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{15}NO_5F_2Na$ ($[M + Na]^+$): 374.0811, found: 374.0795.

(2S,4S*)-2,4-Dimethoxy-6-nitro-2-phenylchromane (**6f**).* 5-Nitrosalicylaldehyde (334.0 mg, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (294.9 mg, 94% yield, cis/trans = 1/8). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (dd, J = 2.7, 1.1 Hz, 1H), 8.15 (dd, J = 9.0, 2.7 Hz, 1H), 7.60−7.56 (m, 2H), 7.52−7.45 (m, 2H), 7.45−7.41 (m, 1H), 7.10 (d, J = 8.8 Hz, 1H), 4.86 (dd, J = 11.2, 6.2 Hz, 1H), 3.53 (s, 3H), 3.09 (s, 3H), 2.78 (dd, J = 13.2, 6.3 Hz, 1H), 1.85 (dd, J = 13.2, 11.4 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.9, 142.4, 139.2, 128.8, 128.7, 126.0, 125.4, 124.8, 123.8, 117.6, 103.7, 70.8, 56.7, 50.6, 38.7; IR (ATR): 1519, 1331, 1103, 1027, 893, 746 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{17}NO_5Na$ ($[M + Na]^+$): 338.0999, found: 338.1013.

(2S,4S*)-6-Cyano-2,4-dimethoxy-2-phenylchromane (**6g**).* 5-Cyanosalicylaldehyde (292.2 mg, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (273.6 mg, 93% yield, cis/trans = 1/5.5). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, J = 1.0 Hz, 1H), 7.62−7.56 (m, 2H), 7.52 (dd, J = 8.5, 1.9 Hz, 1H), 7.49−7.38 (m, 3H), 7.08 (d, J = 8.5 Hz, 1H),4.83 (dd, J = 11.2, 6.2 Hz, 1H), 3.50 (s, 3H), 3.08 (s, 3H), 2.75 (dd, J = 13.2, 6.3 Hz, 1H), 1.83 (dd, J = 13.1, 11.1 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 155.2, 139.4, 132.8, 131.9, 128.7, 128.6, 125.9, 125.8, 119.1, 117.9, 105.0, 103.3, 70.7, 56.5, 50.5, 38.7; IR (ATR): 2246, 1255, 1026, 701 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{18}H_{18}NO_3$ ($[M + H]^+$): 296.1281, found: 296.1286.

(2S,4S*)-2,4-Dimethoxy-2-phenyl-6-tosyloxychromane (**6h**).* 2-Hydroxy-5-tosyloxybenzaldehyde (290.7 mg, 1.0 mmol), acetophenone (58 μL, 0.50 mmol), trimethyl orthoformate (219 μL, 2.0 mmol), and dry toluene (2.5 mL). Yellow solid (187.6 mg, 85% yield, cis/trans = 1/11). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81−7.74 (m, 2H), 7.61−7.55 (m, 2H), 7.45−7.40 (m, 2H), 7.39−7.36 (m, 1H), 7.33 (d, J = 8.51 Hz, 2H), 7.17−7.12 (m, 1H), 6.92−6.86 (m, 1H), 6.86−6.82 (m, 1H), 4.77 (dd, J = 11.0, 6.3 Hz, 1H), 3.35 (s, 3H), 3.04 (s, 3H), 2.63 (dd, J = 12.9, 6.3 Hz, 1H), 2.46 (s, 3H), 1.80 (dd, J = 13.1, 11.2 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.2, 145.1, 143.6, 140.0, 132.6, 129.7, 128.5, 128.5, 126.0, 125.3, 122.7, 121.0, 117.6, 102.6, 71.0, 55.8, 50.3, 38.5, 21.6; IR (ATR): 2970, 1371, 1176, 947, 838, 730 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{24}H_{24}O_6NaS$ ($[M + Na]^+$): 463.1186, found: 463.1202.

(2S,4S*)-6-Bromo-2,4-dimethoxy-2-phenylchromane (**6i**).* 5-Bromosalicylaldehyde (403.2 mg, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (342.9 mg, 98% yield, cis/trans = 1/18). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68−7.52 (m, 3H), 7.46−7.28 (m, 4H), 6.89 (d, J = 8.6 Hz, 1H), 4.82 (dd, J = 10.9, 6.3 Hz, 1H), 3.46 (s, 3H), 3.05 (s, 3H), 2.68 (dd, J = 13.5, 6.5 Hz, 1H), 1.82 (dd, J = 12.9, 11.2 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.7, 140.1, 131.7, 129.9, 128.5, 126.3, 126.0, 118.7, 113.9, 102.5, 71.2,

DOI: 10.1021/acs.joc.9b02036
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56.3, 50.3, 38.8; IR (ATR): 2937, 1483, 1237, 1027, 908, 700 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{17}O_3Na^{79}Br$ ($[M + N]^+$): 371.0253 found: 371.0269.

(2S,4S*)-2,4-Dimethoxy-2-phenyl-7-tosyloxychromane (**6j**).* 2-Hydroxy-4-tosyloxybenzaldehyde (574.1 mg, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (312.3 mg, 71% yield, cis/trans = 1/11). ^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, J = 8.6 Hz, 2H), 7.56 (d, J = 7.2 Hz, 2H), 7.48−7.33 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 6.74−6.67 (m, 1H), 6.65−6.60 (m, 1H), 4.78 (dd, J = 10.9, 6.3 Hz, 1H), 3.44 (s, 3H), 3.01 (s, 3H), 2.68 (dd, J = 12.9, 6.0 Hz, 1H), 2.42 (s, 3H), 1.80 (dd, J = 13.2, 10.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.1, 149.6, 145.2, 139.8, 132.3, 129.7, 128.5, 128.4, 127.9, 125.9, 123.3, 115.2, 111.1, 102.8, 71.1, 56.2, 50.2, 38.9, 21.6; IR (ATR): 2939, 2360, 1373, 1091, 963, 825, 702 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{24}H_{24}O_6NaS$ ($[M + Na]^+$): 463.1186, found: 463.1195.

(2S,4S*)-7-Bromo-2,4-dimethoxy-2-phenylchromane (**6k**).* 4-Bromosalicylaldehyde (410.1 mg, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (214.6 mg, 61% yield, cis/trans = 1/7). ^1H NMR (500 MHz, $CDCl_3$): δ 7.60−7.56 (m, 2H), 7.46−7.41 (m, 2H), 7.40−7.35 (m, 2H), 7.20 (d, J = 1.72 Hz, 1H), 7.15 (dd, J = 8.3, 2.0 Hz, 1H), 4.79 (dd, J = 11.5, 6.3 Hz, 1H), 3.46 (s, 3H), 3.07 (s, 3H), 2.69 (dd, J = 12.9, 6.0 Hz, 1H), 1.83 (dd, J = 12.9, 11.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.4, 140.0, 128.5, 128.5, 126.0, 124.6, 123.4, 121.7, 120.0, 102.8, 71.1, 56.1, 50.4, 38.9; IR (ATR): 3350, 2935, 1409, 1224, 991, 699 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{17}O_3Na^{79}Br$ ($[M + Na]^+$): 371.0253, found: 371.0258.

(2R,4S*)- and (2S*,4S*)-2,4-Dimethoxy-2-phenylchromane (**6l**).* Salicylaldehyde (244 μL, 2.0 mmol), acetophenone (117 μL, 1.0 mmol), trimethyl orthoformate (438 μL, 4.0 mmol), and dry toluene (5.0 mL). Yellow solid (169.2 mg, 63% yield, cis/trans = 1/6.5). ^1H NMR (500 MHz, $CDCl_3$) (trans): δ 7.68−7.60 (m, 2H), 7.51 (d, J = 7.6 Hz, 1H), 7.47−7.41 (m, 2H), 7.41−7.35 (m, 1H), 7.27−7.22 (m, 1H), 7.09−7.00 (m, 2H), 4.87 (dd, J = 11.0, 6.3 Hz, 1H), 3.47 (s, 3H), 3.07 (s, 3H), 2.69 (dd, J = 13.1, 6.2 Hz, 1H), 1.88 (dd, J = 13.0, 11.0 Hz, 1H); (cis): δ 7.60−7.56 (m, 2H), 7.43−7.39 (m, 3H), 7.38−7.33 (m, 1H), 7.30−7.27 (m, 1H), 7.08−7.01 (m, 2H), 4.23 (dd, J = 5.7, 3.5 Hz, 1H), 3.54 (s, 3H), 3.11 (s, 3H), 2.63 (dd, J = 13.7, 3.6 Hz, 2H), 2.23 (dd, J = 14.7, 5.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) (trans): δ 151.6, 140.6, 128.8, 128.4, 128.3, 127.0, 126.1, 124.2, 121.4, 116.8, 102.3, 71.5, 56.0, 50.2, 39.2; (cis): δ 151.8, 140.9. 129.5, 129.5, 128.4, 128.2, 126.2, 123.0, 121.4, 117.4, 100.7, 71.8, 57.0, 50.4, 39.3; IR (ATR) (trans): 2938, 1449, 1213, 1092, 1025, 907, 751 cm^{-1}; (cis): 1450, 1228, 1147, 1095, 1016, 808, 755, 565 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{17}H_{18}O_3Na$ ($[M + Na]^+$) (trans): 293.1148, found: 293.1159; (cis): 293.1148, found: 293.1158.

Transformation of Chromane 3a. *Transformation of 4-Methoxy-6-nitro-2,2-diphenylchromane (**3a**) into 6-Nitro-2,2-diphenyl-4-tosylamidechromane (**7a**).* 4-Methoxy-6-nitro-2,2-diphenylethylene (**3a**, 89.3 mg, 0.25 mmol), *p*-toluenesulfonamide (429.1 mg, 2.5 mmol), and $FeCl_3$ (20 mol %) were dissolved in dry dichloroethane (3.0 mL) under an atmosphere of nitrogen. After stirring for 3 h at 60 °C, the reaction mixture was neutralized with H_2O. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic phases were washed with brine, dried over Na_2SO_4, and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5/1, v/v) to afford 6-nitro-2,2-diphenyl-4-tosylamidechromane (**7a**, 111.6 mg, 90% yield) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.03 (dd, J = 9.1, 2.5 Hz, 1H), 7.94−7.90 (m, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.34−7.23 (m, 10H), 7.09 (d, J = 9.1 Hz, 1H), 5.19 (s, 1H), 4.34 (td, J = 10.3, 5.5 Hz, 1H), 3.06 (dd, J = 13.7, 5.5 Hz, 1H), 2.50−2.41 (m, 4H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 159.0, 144.3, 143.2, 141.5, 141.2, 136.9, 130.0, 128.9, 128.4, 128.0, 128.0, 127.1, 125.7, 125.6, 125.1, 124.1, 123.0, 117.9, 84.2, 46.8, 38.9, 21.5; IR (ATR): 3251, 1513, 1316, 1158, 667, 556 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{28}H_{24}N_2O_5NaS$ ($[M + Na]^+$): 523.1298, found: 523.1318.

*Transformation of 4-Methoxy-6-nitro-2,2-diphenylchromane (**3a**) into 4-Allyl-6-nitro-2,2-diphenylchromane (**8a**).* 4-Methoxy-6-nitro-2,2-diphenylethylene (**3a**, 38.1 mg, 0.11 mmol), allyltrimethylsilane (159 μL, 1.0 mmol), and $FeCl_3$ (10 mol %) were dissolved in CH_2Cl_2 (1.0 mL). After stirring at reflux for 7 h, the reaction mixture was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic layer was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by preparative TLC on silica gel (hexane) to afford 4-allyl-6-nitro-2,2-diphenylchromane (**8a**, 27.8 mg, 71% yield) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J = 2.7, 1.1 Hz, 1H), 8.07 (ddd, J = 8.8, 2.8, 0.6 Hz, 1H), 7.45−7.40 (m, 2H), 7.40−7.27 (m, 7H), 7.25−7.21 (m, 1H), 7.15 (d, J = 9.1 Hz, 1H), 5.84−5.74 (m, 1H), 5.21−5.13 (m, 2H), 2.99 (dd, J = 14.2, 5.4 Hz, 1H), 2.89−2.76 (m, 2H), 2.41−2.30 (m, 1H), 2.18 (dd, J = 14.2, 12.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 159.7, 144.9, 142.4, 141.4, 134.6, 128.7, 128.4, 127.7, 127.6, 126.1, 125.9, 125.7, 123.8, 123.6, 118.4, 118.0, 83.6, 37.9, 37.5, 31.2; IR (ATR): 2925, 1577, 1506, 1250, 1095, 1009, 748, 699 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{24}H_{21}NO_3Na$ ($[M + Na]^+$): 394.1414, found: 394.1426.

*Transformation of 4-Methoxy-6-nitro-2,2-diphenylchromane (**3a**) to 6-Amino-4-methoxy-2,2-diphenylchromane (**9a**).* To 4-Methoxy-6-nitro-2,2-diphenylethylene (**3a**, 91.1 mg, 0.25 mmol) in EtOAc (2.5 mL), palladium on charcoal (10%, 14.9 mg) was added. After being stirred under hydrogen for 4 h, the reaction mixture was filtered. The filtrate was concentrated in vacuo to afford 6-amino-4-methoxy-2,2-diphenylchromane (**9a**, 86.1 mg, quant.) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.45−7.40 (m, 4H), 7.32−7.18 (m, 6H), 6.87 (d, J = 8.8 Hz, 1H), 6.66 (d, J = 2.8 Hz, 1H), 6.57 (dd, J = 8.5, 3.2 Hz, 1H), 4.26 (dd, J = 10.4, 5.7 Hz, 1H), 3.45 (s, 3H), 3.20 (dd, J = 13.2, 6.0 Hz, 1H), 3.06 (s, 2H), 2.46 (dd, J = 13.2, 10.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.7, 145.7, 143.1, 139.8, 128.4, 128.2, 127.3, 127.1, 126.3, 125.8, 123.5, 117.6, 116.9, 113.5, 82.1, 71.9, 55.6, 36.8; IR (ATR): 3356, 2818, 1493, 1216, 1089, 1018, 797, 735, 698 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{22}NO_2$ ($[M + H]^+$): 332.1645, found: 332.1656.

*Transformation of 4-Methoxy-6-nitro-2,2-diphenylchromane (**3a**) to 3-Bromo-4-methoxy-6-nitro-2,2-diphenyl-2H-chromene (**10a**).* A mixture of 4-methoxy-6-nitro-2,2-diphenylethylene (**3a**, 91.4 mg, 0.25 mmol) and NBS (136.0 mg, 0.76 mmol) was stirred at reflux for 24 h in CCl_4 (5.0 mL) under an atmosphere of nitrogen. After that, the reaction mixture was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane) to afford 3-bromo-4-methoxy-6-nitro-2,2-diphenyl-2*H*-chromene (**10a**, 83.4 mg, 75% yield) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, J = 2.8 Hz, 1H), 8.06 (dd, J = 8.8, 2.8 Hz, 1H), 7.43−7.38 (m, 4H), 7.37−7.32 (m, 6H), 6.99 (d, J = 8.8 Hz, 1H), 3.91 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 157.9, 149.7, 142.6, 141.4, 128.7, 128.6, 127.9, 126.0, 120.1, 118.3, 117.7, 111.2, 89.6, 60.1; IR (ATR): 2962, 1519, 1341, 1260, 1069, 967, 907, 800, 751, 695 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{22}H_{17}NO_4{}^{79}Br$ ($[M + H]^+$): 438.0336, found: 438.0344.

Synthesis of 11. 5-Chlorosalicylaldehyde (155.6 mg, 0.99 mmol), *p*-chlorostyrene (64 μL, 0.5 mmol), and trimethyl orthoformate (109 μL, 1.0 mmol) were dissolved in dry toluene (5.0 mL) under an atmosphere of nitrogen before trifluoromethanesulfonic acid (20 mol %) was added. After stirring at room temperature for 24 h, the reaction mixture was neutralized with 5% aq $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (5.0 mL × 3). The combined organic phases were washed with brine, dried over $MgSO_4$, and filtered before the filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane/chloroform = 3/1, v/v) to afford (2*S**,4*S**)-6-chloro-2-(4-chlorophenyl)-4-methoxychromane

DOI: 10.1021/acs.joc.9b02036
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(**11**, 146.9 mg, 95% yield, cis/trans = 80/20) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (dd, J = 2.5, 1.0 Hz, 1H), 7.38 (s, 4H), 7.13 (dd, J = 8.7, 2.7 Hz, 1H), 6.80 (d, J = 8.5 Hz, 1H), 5.10 (dd, J = 12.0, 1.9 Hz, 1H), 4.71 (dd, J = 10.7, 6.0 Hz, 1H), 3.49 (s, 3H), 2.51 (ddd, J = 13.2, 6.1, 1.9 Hz, 1H), 2.07−1.97 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.1, 138.9, 134.1, 129.0, 128.8, 127.4, 127.2, 126.0, 124.9, 118.0, 76.4, 73.3 56.1, 34.9; IR (ATR): 2962, 1477, 1248, 1092, 814 cm^{-1}; HRMS (ESI+) m/z calcd for $C_{15}H_{11}O^{35}Cl_2$ ([M − OMe]$^+$): 277.0182, found: 277.0179.

Synthesis of BW683C. (2*S**,4*S**)-6-Chloro-2-(4-chlorophenyl)-4-methoxychromane (**11**, 74.3 mg, 0.24 mmol), triethylsilane (60 μL, 0.375 mmol), and $FeCl_3$ (10 mol %) were dissolved in dichloroethane (3.0 mL). After stirring at room temperature for 2 h, the reaction mixture was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered, and the filtrate was concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 30/1, v/v) to afford 6-chloro-2-(4-chlorophenyl)chromane (**BW683C**, 60.1 mg, 90% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.32 (m, 4H), 7.09−7.05 (m, 2H), 6.82 (d, J = 8.4 Hz, 1H), 5.02 (dd, J = 10.0, 2.6 Hz, 1H), 2.95 (ddd, J = 16.8, 11.0, 6.0 Hz, 1H), 2.78−2.73 (m, 1H), 2.21−2.15 (m, 1H), 2.02 (dtd, J = 13.8, 10.6, 5.2 Hz, 1H).[21]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b02036.

Crystallographic data for compound *cis*-**6a** (CIF)

Crystallographic data for compound *trans*-**6a** (CIF)

Crystallographic data for compound *cis*-**3n** (CIF)

NMR spectra of new compounds, X-ray crystallographic data of chromanes (*cis*-**3n** and **6a**); characterization of **3n**; computational data (PDF)

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Notes

The authors declare no competing financial interest.

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