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# Triflic-Acid-Catalyzed Tandem Allylic Substitution–Cyclization Reaction of Alcohols with Thiophenols—Facile Access to Polysubstituted Thiochromans

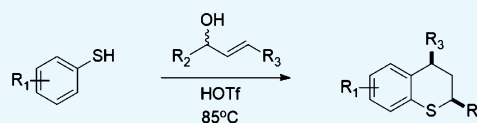
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## Supporting Information

**ABSTRACT:** Hitherto inaccessible multisubstituted thiochroman derivatives were constructed via the one-pot reaction of thiophenols with allylic alcohols catalyzed by 0.2 equiv triflic acid under metal-free conditions. A variety of thiochroman derivatives can be obtained by this straightforward protocol that allows the introduction of up to four substituents at various locations on the thiochroman skeleton. Relative conformations of all isolated products were confirmed by NOESY NMR studies, and a stepwise mechanism, proceeding via an allylic substitution-intramolecular cyclization protocol, is proposed on the basis of NMR experiments.



## INTRODUCTION

3,4-Dihydro-2*H*-1-benzothiopyrans (commonly known as thiochromans) are one of the least explored sulfur-based heterocycles in terms of synthetic methodologies.<sup>1</sup> This is indeed surprising because several thiochroman compounds, as well as their derivatives such as thiochromones, thiochromenes, and thiochroman-4-ones, have exhibited interesting biological activities.<sup>2</sup> However, the synthetic protocols available for accessing the core thiochroman motif remain relatively limited and usually entail the use of drastic conditions (Scheme 1). The very first report in the literature involves a ZnI<sub>2</sub>-mediated intermolecular cycloaddition between allyl alcohols and arenethiols.<sup>3</sup> A protocol reported by Jensen et al. (2000) requires the use of epoxide and a strong base BuLi as key reagents.<sup>4</sup> In 2001, Katritzky proposed a new method for the synthesis of polysubstituted thiochromans via the cationic cycloaddition of  $\alpha$ -(benzotriazolyl)methyl thioether with styrenes.<sup>5</sup> In 2003, Skarzewski et al. reported an alternative route which however requires an enantiopure starting material for selective *cis*-thiochroman formation via rearrangement–racemization steps.<sup>6</sup> Nishibayashi et al., Zhao et al. (2008), and Arai et al. (2014) have separately reported asymmetric synthesis routes, which gave excellent yields and enantiomeric excess.<sup>7</sup> Many of these aforementioned protocols however often involve elaborate preformed catalysts and substrates and/or are limited to substrates with good Michael-acceptor ability, viz., nitroalkenes. The products in the latter case need to undergo further reactions for removal of the directing group. Recently, Xu et al. have reported an efficient chiral NHC-catalyzed sulfa-Michael/Michael/lactonization cascade to synthesize a series of chiral thiochromans bearing three chiral centers.<sup>8</sup>

In view of our broad interest in C–X (X = N, P, As) bond formation protocols<sup>9</sup> and motivated by results from our work on functionalizing allylic alcohols by anilines using Cu(OTf)<sub>2</sub>,<sup>10</sup> as well as a study by Wu et al. using Ga(OTf)<sub>3</sub> involving direct substitution of alcohols using sulfur nucleophiles,<sup>11</sup> we decided to explore a new synthetic route involving substituted thiophenols and allylic alcohols using triflic acid as the catalyst with the hope of achieving the heterocycle of interest under metal-free conditions (Scheme 1). Such a method is also attractive because the direct use of readily available and low-cost allylic alcohols avoids the formation of stoichiometric amounts of waste that is typically associated with synthesis of activated substrates.

## RESULTS AND DISCUSSION

As aforementioned, we had previously demonstrated the use of copper(II) triflate, for the direct and selective synthesis of *C*-allylanilines via a direct allylic amination protocol from relevant allylic alcohols and anilines.<sup>10</sup> The 2-allylanilines can then be readily converted under mild conditions to give substituted quinolines via an oxidative cycloaddition reaction. We therefore decided to explore the possibility of developing a similar protocol involving C–S bond formation to access the targeted thiochroman motifs. Our initial study focused on the reaction between 2,4-dimethyl thiophenol (**1a**) and *trans*-1,3-diphenyl-2-propen-1-ol (**2a**) under acidic media in refluxing 1,2-dichloroethane (DCE) solvent (Table 1).

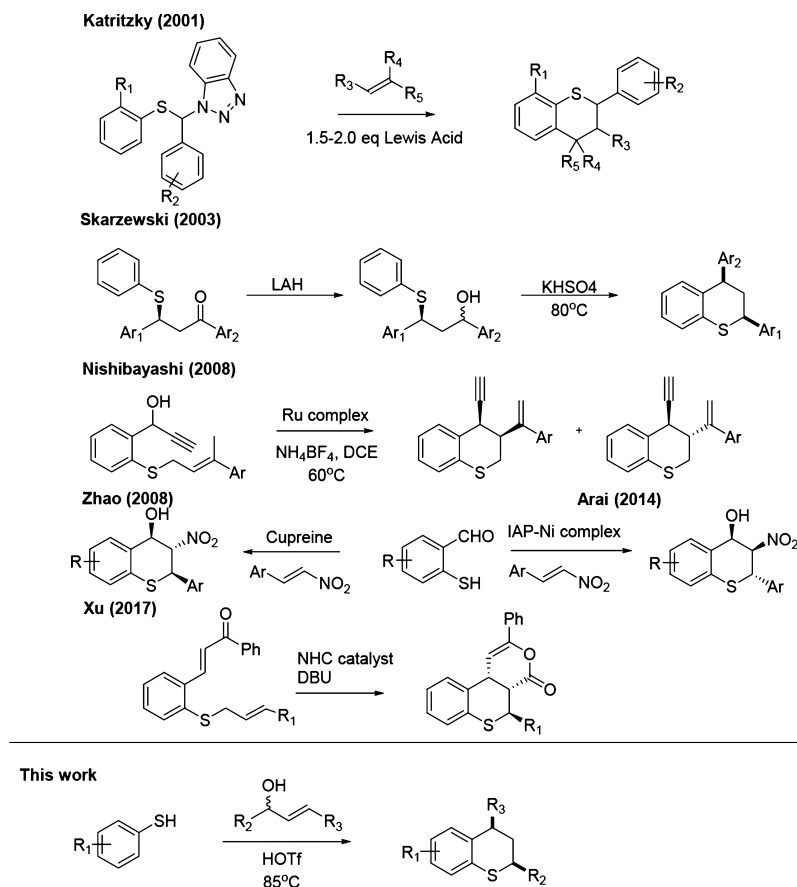
Both Lewis and Brønsted acids were tested under the same conditions (entries 1–6). The results showed that only copper

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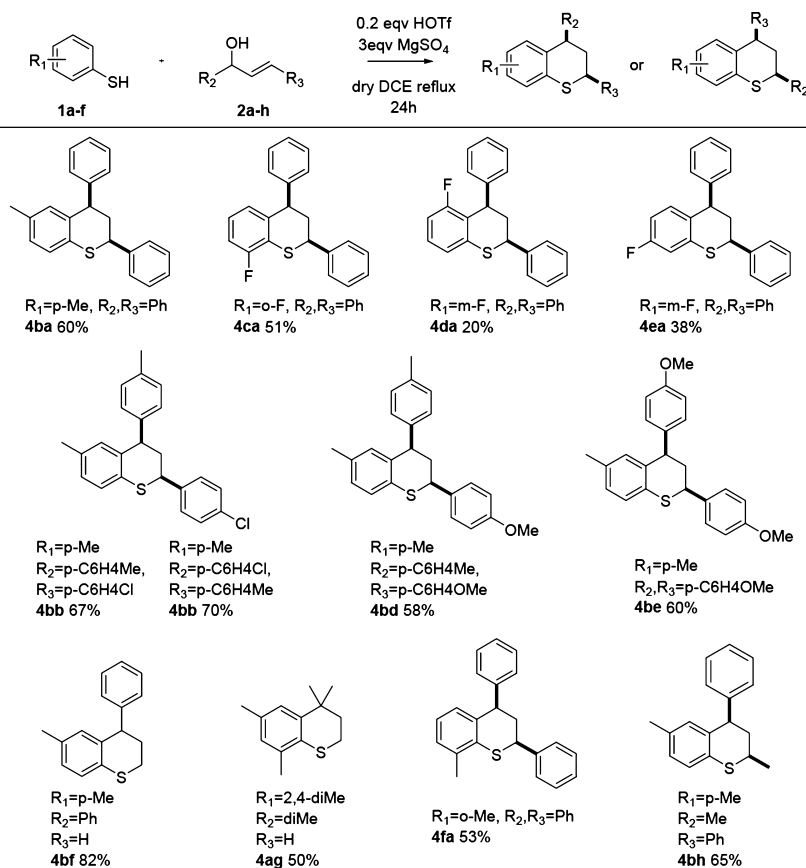
## Scheme 1. Selected Recent Literature Methods for Thiochroman Synthesis

Table 1. Optimization of Reaction Conditions<sup>a,b</sup>

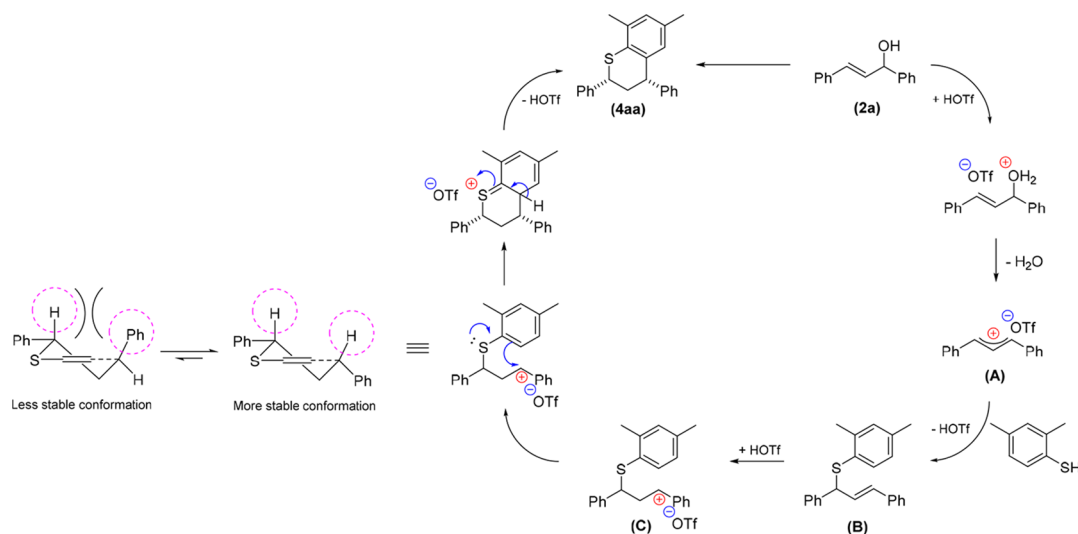
entry	catalyst (equiv)	solvent (0.1 M)	temperature (°C)	yield <sup>c</sup> of 3aa (%)	yield <sup>c</sup> of 4aa (%)
1	AlCl <sub>3</sub> (0.10)	DCE	85	71	
2	BF <sub>3</sub> ·Et <sub>2</sub> O (0.20)	DCE	85	70	
3	CF <sub>3</sub> COOH (0.20)	DCE	85	90	
4	MSA (0.20)	DCE	85	49	15
5	PTSA (0.20)	DCE	85	51	18
6	Cu(OTf) <sub>2</sub> (0.10)	DCE	85		40
7	HOTf (0.10)	DCE	85		40
8	HOTf (0.20)	DCE	85		51
9	HOTf (0.20)	DCE	25	82	
10	HOTf (0.20)	DCE	50	85	
11	HOTf (0.20)	toluene	100		50
12	HOTf (0.20)	MeCN	85	23	
13	HOTf (0.20)	DMF	100	25	
14	HOTf (0.20)	EtOH	80	40	
15	HOTf (0.20)	DCE/H <sub>2</sub> O	85	87	
16 <sup>c</sup>	HOTf (0.20)	DCE	85		50
17 <sup>d</sup>	HOTf (0.20)	DCE	85		60

<sup>a</sup>MSA: methanesulfonic acid; PTSA: *p*-toluenesulfonic acid. <sup>b</sup>All reactions were done in the stoichiometry of 0.75 mmol (**1a**)/0.50 mmol (**2a**) with stirring (24 h) under reflux conditions (open air). <sup>c</sup>Reaction was conducted in a sealed tube, under an inert atmosphere (N<sub>2</sub>) for direct comparison with entry 8. <sup>d</sup>Drying agent (MgSO<sub>4</sub> or molecular sieves) added. <sup>e</sup>Yield was calculated from crude NMR, using internal standard 1,3,5-trimethoxybenzene.

Scheme 2. Successfully Synthesized Thiochromans

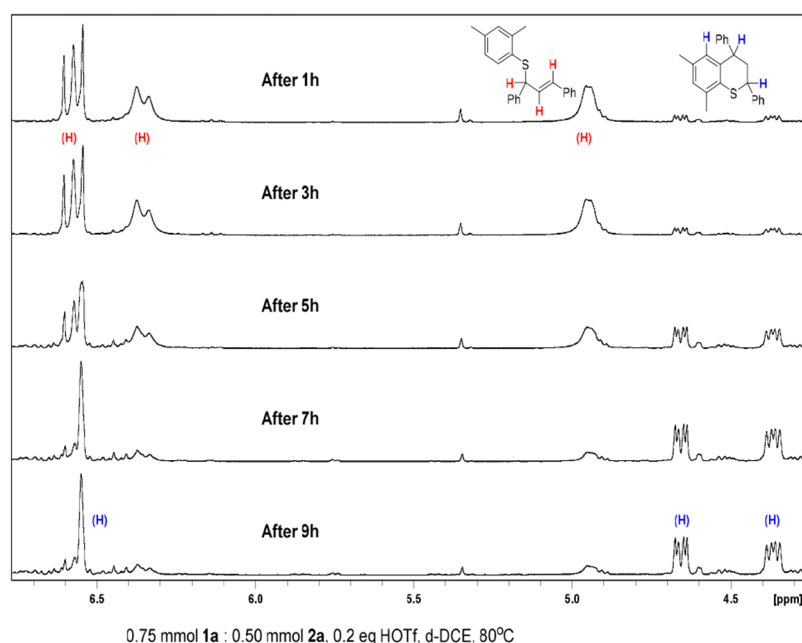


Scheme 3. Proposed Reaction Mechanism



triflate ( $\text{Cu}(\text{OTf})_2$ ) successfully catalyzed the formation of the desired product **4aa** (entry 6). The other Brønsted acids merely facilitated C–S bond coupling via nucleophilic substitution to form product **3aa**. Copper triflate in particular and triflate salts in general have been implicated as a hidden source of triflic acid (HOTf) in halogenated solvents.<sup>12</sup> It was observed that, with 0.1 equiv catalyst loading of HOTf, the reaction gave the same yield as that obtained when copper triflate was used (entry 6 vs entry 7). Although different solvents and various temperatures were screened (entries 11–

15), only aprotic or nonproton-acceptor solvents together with a temperature above 80 °C induced the cyclization. Interestingly, although thiols are known to have a propensity for oxidation, we observed insignificant differences in resultant yields for trials done using inert conditions in comparison to those conducted in air (entry 8 vs entry 16). The mixture of DCE and trace amounts of water failed to facilitate the formation of **4aa** (entry 15) because triflic acid should probably remain solubilized only in the aqueous phase. Subsequently, the reaction was conducted with the addition



**Figure 1.** NMR spectra of reaction between **1a** and **2a** over 9 h.

of common drying agents such as molecular sieves and magnesium sulfate (entry 17) with only 0.2 equiv of triflic acid. This resulted in a 10% increase in yield (to 60%), and it was thus chosen as the optimum condition for the reaction.

The structure of **4aa** was confirmed by NMR, High-resolution mass spectrometry (HRMS), and single-crystal X-ray crystallography (see [Supporting Information](#)). It needs to be noted that only the *cis* isomer of **4aa** was selectively obtained from the reaction. The  $^1\text{H}$  NMR spectra of the crude also confirmed this selectivity. With the optimized conditions in hand, we proceeded to screen for substrate tolerance for this protocol ([Scheme 2](#)). The highest yield of 82% was observed in the reaction between alcohol **2f** and thiophenol **1b**. In general, *ortho*-substituted thiophenols showed slightly lower reactivity than the *para*-substituted isomer (**4ba** and **4fa**). In addition, thiols-bearing electron-withdrawing groups gave relatively low yields (**4ca**, **4da**, and **4ea**). The reaction also showed its applicability toward non-aromatic substituted alcohol (**4ag**). For *meta*-substituted thiophenol, the regioselectivity control was not significant (**4da** and **4ea**). Fluoro-substituted thiols gave generally lower yields. Various alcohol substrates with aryl substituents such as  $-\text{OMe}$  were tolerated with appreciable yields therefore providing access to further functionalization of the basic skeleton at desired positions. Reaction of 2-methylbut-3-en-2-ol with 2,4-dimethylbenzenethiol allowed the generation of a thiochroman skeletal core with four methyl substituents (**4ag**) via this protocol. The relative conformation of all the isolated products was confirmed by NOESY NMR experiments (see [Supporting Information](#)). Although the possibility of the *trans*-isomer being formed cannot be conclusively ruled out in the case of **4bb**, **4bd**, and other unsymmetrically substituted allylic alcohols, we were unable to isolate pure *trans*-isomer in any of the cases and conclusive evidence of their presence could not be ascertained from the crude NMR.

A plausible mechanism of the reaction is illustrated in [Scheme 3](#). Initial protonation of the OH functionality in the presence of acid transforms it into a good leaving group,

forming the  $\pi$ -allyl cationic species (**A**).<sup>13</sup> Following which, nucleophilic addition of the thiol occurs to yield the allyl thioether adduct (**B**). For reaction trials conducted with unsymmetrical alcohol substrates, the regioselectivity for nucleophilic attack appeared to be largely dependent on steric control, in which thiol addition occurred at the sterically less hindered carbon site (**4bf**, **4ag**, and **4bh**).<sup>13</sup> In cases with less significant steric disparity, the regioselective pathway could have then therefore been facilitated by electronic factors, attributed to the resultant stabilization of the electrophilic carbocationic site via resonance from lone-pair electron donation of the respective *p*-Cl and *p*-OMe substituents (**4bb** and **4bd**). Subsequent protonolysis of the allylic thioether furnishes a carbocationic species (**C**) that can be better stabilized by the corresponding adjacent R group from the alcohol substrate. The reaction pathway then further translates into an intramolecular cyclization for the eventual formation of the cyclized product (**4aa**). With respect to the cyclization step, the relative selectivity could be explained by exertion of thermodynamic control that favored the stable conformation of the *cis* product, which in turn minimizes steric interaction between the two pseudo-axial substituents. This is postulated to occur via a possible reversible C–C bond formation involving an equilibrium process as depicted.

In order to obtain experimental proof to better elucidate the mechanism,  $^1\text{H}$  NMR experiments using deuterated DCE as the solvent were conducted. Under the reaction conditions at 80 °C, the formation of intermediate (**C**) was initially observed ([Figure 1](#)); subsequently, it undergoes an intramolecular cyclization to form (**E**) over time. Product (**E**) was not observed at any temperature lower than 80 °C.

## CONCLUSIONS

In conclusion, a one-pot, metal-free synthesis protocol for a hitherto inaccessible range of multisubstituted thiochroman heterocycles from easily accessible thiophenols and allylic alcohols has been developed. The simple triflic-acid-catalyzed protocol allows the direct use of allylic alcohols without the



need for any activation. Although the yields obtained are moderate, the newly developed synthetic approach to these less studied heterocyclic motifs will potentially spur further studies into developing more efficient methods. Further studies are currently underway to evaluate the synthesized compounds obtained in this study and their derivatives for biological activity.

## EXPERIMENTAL SECTION

**General Information.** All the reactions were conducted in open air condition (unless otherwise specified). Chemical reagents were obtained from commercial sources and were used without further purification. DCE was dried by molecular sieves prior to use. The reactions were monitored by TLC (Silica gel 60 F<sub>254</sub>) and visualized by UV (254 nm). Column chromatography was done using Silicagel 60 (size 40–63  $\mu\text{m}$ ) as the stationary phase. HRMS spectra were recorded on a time-of-flight machine. NMR spectra were recorded at 400 and 300 MHz for <sup>1</sup>H; 100 and 75 MHz for <sup>13</sup>C. Chemical shifts (ppm) of all the peaks in <sup>1</sup>H NMR were calibrated to the TMS residue peak (0 ppm) in CDCl<sub>3</sub>. The X-ray diffraction experiment was conducted with Mo K $\alpha$  radiation ( $\lambda = 0.7107 \text{ \AA}$ ).

**Representative Procedure for the Thiochroman Synthesis.** Trifluoromethanesulfonic acid (0.2 mmol, 0.2 equiv, 17.6  $\mu\text{L}$ ) was added into the solution of substituted thiophenol (1.5 mmol) and allylic alcohol (1.0 mmol) in dry DCE. Magnesium sulfate powder (3.0 equiv) was subsequently added. The mixture was refluxed at 85  $^{\circ}\text{C}$  for 24 h. Subsequently, filtration was done to remove any insoluble residue. DCE solvent was also removed by using a rotary evaporator. The crude product was then further purified by flash column chromatography using hexane/ethyl acetate mixture as the eluent. After removing the solvent, the final product was recrystallized by slow diffusion of diethyl ether into its saturated solution in chloroform.

***cis*-6,8-Dimethyl-2,4-diphenylthiochromane (4aa).** Light yellow solid; yield 60%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.44–7.20 (m, 10H), 6.82 (s, 1H), 6.43 (s, 1H), 4.57–4.52 (m, 1H), 4.28–4.23 (m, 1H), 2.57–2.51 (m, 2H), 2.26 (s, 3H), 2.09 (s, 3H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  145.78, 141.59, 136.62, 133.99, 132.90, 130.76, 129.09, 128.78, 128.76, 128.72, 128.38, 127.82, 127.65, 126.63, 48.22, 45.99, 41.63, 20.83, 20.10. HR-MS (ESI) *m/z*: calcd for C<sub>23</sub>H<sub>23</sub>S<sup>+</sup> [(M + H)<sup>+</sup>], 331.1520; found, 331.1516.

***cis*-6-Methyl-2,4-diphenylthiochromane (4ba).** White solid; yield 60%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.42–7.21 (m, 10H), 7.05 (d, 1H, <sup>3</sup>J<sub>HH</sub> = 9 Hz), 6.90 (d, 1H, <sup>3</sup>J<sub>HH</sub> = 9 Hz), 6.56 (s, 1H), 4.59 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 6 Hz, <sup>3</sup>J<sub>HH</sub> = 9 Hz), 4.22 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 6 Hz, <sup>3</sup>J<sub>HH</sub> = 9 Hz), 2.58–2.50 (m, 2H), 2.11 (s, 3H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  145.25, 141.42, 136.71, 133.90, 131.14, 130.62, 128.75, 127.78, 126.72, 126.17, 47.80, 46.12, 42.05, 20.97. HR-MS (ESI) *m/z*: calcd for C<sub>22</sub>H<sub>21</sub>S<sup>+</sup> [(M + H)<sup>+</sup>], 317.1364; found, 317.1360.

***cis*-8-Fluoro-2,4-diphenylthiochromane (4ca).** Light orange solid; yield 51%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.46–7.21 (m, 10H), 6.88–6.84 (m, 2H), 6.57–6.54 (m, 1H), 4.60–4.55 (m, 1H), 4.32–4.26 (m, 1H), 2.60–2.54 (m, 2H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  144.81, 140.61, 138.86, 128.81, 128.63, 127.63, 126.92, 125.62, 125.58, 124.17, 124.06, 112.82, 112.54, 47.75, 45.18, 41.05. HR-MS (ESI) *m/z*: calcd for C<sub>21</sub>H<sub>18</sub>FS<sup>+</sup> [(M + H)<sup>+</sup>], 321.1113; found, 321.1111.

***cis*-5-Fluoro-2,4-diphenylthiochromane (4da).** White solid; yield 20%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.36–7.19 (m, 12H), 6.71–6.64 (m, 1H), 4.48 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, <sup>3</sup>J<sub>HH</sub> = 11 Hz), 4.36 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 2 Hz, <sup>3</sup>J<sub>HH</sub> = 12 Hz), 2.81–2.74 (m, 1H), 2.57–2.44 (m, 1H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  162.16 (<sup>1</sup>J<sub>CF</sub> = 249 Hz), 146.28, 139.94, 138.09, 128.80, 128.58, 127.97, 127.78, 127.65, 127.59, 127.00, 126.28, 124.04 (<sup>2</sup>J<sub>CF</sub> = 14.25 Hz), 122.98 (<sup>3</sup>J<sub>CF</sub> = 3.75 Hz), 112.26 (<sup>2</sup>J<sub>CF</sub> = 22.5 Hz), 46.08, 44.28, 42.80 (<sup>3</sup>J<sub>CF</sub> = 1.5 Hz). HR-MS (ESI) *m/z*: calcd for C<sub>21</sub>H<sub>18</sub>FS<sup>+</sup> [(M + H)<sup>+</sup>], 321.1113; found, 321.1087.

***cis*-7-Fluoro-2,4-diphenylthiochromane (4ea).** White solid; yield 38%; <sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.42–7.10 (m, 10H), 6.86 (dd, 1H, <sup>4</sup>J<sub>HF</sub> = 4 Hz, <sup>3</sup>J<sub>HH</sub> = 8 Hz), 6.68 (dd, 1H, <sup>2</sup>J<sub>HF</sub> = 8 Hz, <sup>4</sup>J<sub>HH</sub> = 8 Hz), 6.61–6.56 (m, 1H), 4.63 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 4 Hz, <sup>3</sup>J<sub>HH</sub> = 12 Hz), 4.19 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 4 Hz, <sup>3</sup>J<sub>HH</sub> = 12 Hz), 2.58–2.50 (m, 2H). <sup>13</sup>C NMR (100 MHz; CDCl<sub>3</sub>):  $\delta$  161.08 (<sup>1</sup>J<sub>CF</sub> = 245 Hz), 144.86, 140.71, 131.49 (<sup>3</sup>J<sub>CF</sub> = 8 Hz), 128.87, 128.85, 128.63, 128.50, 128.02, 127.89, 127.59, 126.95, 112.34 (<sup>2</sup>J<sub>CF</sub> = 23 Hz), 111.32 (<sup>2</sup>J<sub>CF</sub> = 21 Hz), 47.26, 46.23, 41.56. HR-MS (ESI) *m/z*: calcd for C<sub>21</sub>H<sub>18</sub>FS<sup>+</sup> [(M + H)<sup>+</sup>], 321.1113; found, 321.1113.

***cis*-2-(4-Chlorophenyl)-6-methyl-4-(*p*-tolyl)thiochromane (4bb).** White solid; yield 70%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.34–6.88 (m, 10H), 6.57 (s, 1H), 4.55 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 3 Hz, <sup>3</sup>J<sub>HH</sub> = 12 Hz), 4.16 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 6 Hz, <sup>3</sup>J<sub>HH</sub> = 12 Hz), 2.51–2.42 (m, 1H), 2.35 (s, 3H), 2.32–2.27 (m, 1H), 2.12 (s, 3H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  141.93, 140.04, 136.84, 136.32, 134.06, 133.41, 130.67, 130.57, 129.47, 128.95, 128.87, 128.56, 127.58, 126.10, 47.23, 45.44, 41.98, 21.12, 20.96. HR-MS (ESI) *m/z*: calcd for C<sub>23</sub>H<sub>22</sub>ClS<sup>+</sup> [(M + H)<sup>+</sup>], 365.1131; found, 365.1122.

***cis*-2-(4-Methoxyphenyl)-6-methyl-4-(*p*-tolyl)thiochromane (4bd).** White solid; yield 58%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.33–6.78 (m, 10H), 6.56 (s, 1H), 4.58–4.54 (m, 1H), 4.12–4.14 (m, 1H), 3.80 (s, 3H), 2.55–2.50 (m, 2H), 2.22 (s, 3H), 1.54 (s, 3H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  158.33, 138.47, 137.43, 137.32, 137.08, 133.77, 131.22, 130.51, 129.65, 129.39, 127.47, 127.41, 126.07, 114.10, 55.28, 46.97, 45.85, 42.07, 21.13, 20.97. HR-MS (ESI) *m/z*: calcd for C<sub>24</sub>H<sub>25</sub>OS<sup>+</sup> [(M + H)<sup>+</sup>], 361.1626; found, 361.1625.

***cis*-2,4-Bis(4-methoxyphenyl)-6-methylthiochromane (4be).** Pink solid; yield 60%; <sup>1</sup>H NMR (300 MHz; CDCl<sub>3</sub>):  $\delta$  7.34–6.84 (m, 10H), 6.56 (s, 1H), 4.58–4.53 (m, 1H), 4.19–4.13 (m, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 2.52–2.45 (m, 2H), 2.13 (s, 3H). <sup>13</sup>C NMR (75 MHz; CDCl<sub>3</sub>):  $\delta$  159.09, 158.31, 137.33, 136.96, 133.75, 133.49, 131.23, 130.53, 129.63, 128.61, 127.45, 126.01, 114.09, 55.30, 55.27, 47.01, 45.50, 42.20, 20.94. HR-MS (ESI) *m/z*: calcd for C<sub>24</sub>H<sub>25</sub>O<sub>2</sub>S<sup>+</sup> [(M + H)<sup>+</sup>], 377.1575; found, 377.1575.

**6-Methyl-4-phenylthiochromane (4bf).** Colourless liquid; yield 82%; <sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.28–7.24 (m, 2H), 7.20–7.15 (m, 1H), 7.05 (d, 3H, <sup>3</sup>J<sub>HH</sub> = 8 Hz), 6.91–6.89 (m, 1H), 6.71 (s, 1H), 4.16 (t, 1H, <sup>3</sup>J<sub>HH</sub> = 4 Hz), 2.90–2.77 (m, 2H), 2.29–2.25 (m, 2H), 2.14 (s, 3H). <sup>13</sup>C NMR (100 MHz; CDCl<sub>3</sub>):  $\delta$  145.35, 135.10, 133.56, 131.98, 129.97, 128.68, 128.51, 128.01, 126.42, 126.39, 44.24, 30.92, 23.34, 20.89. HR-MS (ESI) *m/z*: calcd for C<sub>16</sub>H<sub>17</sub>S<sup>+</sup> [(M + H)<sup>+</sup>], 241.1051; found, 241.1051.

**4,4,6-Trimethylthiochromane (4ag).** Colourless liquid; yield 50%; <sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.05 (s, 1H), 6.78 (s, 1H), 2.99–2.96 (m, 2H), 2.24 (s, 3H), 2.21 (s, 3H),

1.92–1.90 (m, 2H), 1.30 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz;  $\text{CDCl}_3$ ):  $\delta$  141.89, 134.13, 132.47, 128.63, 127.72, 124.84, 37.76, 33.18, 30.73, 22.93, 21.05, 20.47. HR-MS (ESI)  $m/z$ : calcd for  $\text{C}_{13}\text{H}_{19}\text{S}^+$  [(M + H) $^+$ ], 207.1207; found, 207.1209.

**cis-8-Methyl-2,4-diphenylthiochromane (4fa).** White solid; yield 53%;  $^1\text{H}$  NMR (300 MHz;  $\text{CDCl}_3$ ):  $\delta$  7.46–7.21 (m, 10H), 6.98 (d, 1H,  $^3J_{\text{HH}} = 9$  Hz), 6.81 (m, 1H), 6.61 (d, 1H,  $^3J_{\text{HH}} = 9$  Hz), 4.62–4.57 (m, 1H), 4.33–4.27 (m, 1H), 2.59–2.53 (m, 2H), 2.29 (s, 3H).  $^{13}\text{C}$  NMR (75 MHz;  $\text{CDCl}_3$ ):  $\delta$  145.60, 141.39, 136.71, 134.23, 134.04, 128.78, 128.72, 128.71, 127.94, 127.86, 127.73, 127.63, 126.66, 123.35, 48.22, 46.02, 41.18, 20.16. HR-MS (ESI)  $m/z$ : calcd for  $\text{C}_{22}\text{H}_{21}\text{S}^+$  [(M + H) $^+$ ], 317.1364; found, 317.1372.

**cis-4,6-Dimethyl-2-phenylthiochromane (4bh).** Colourless liquid; yield 65%;  $^1\text{H}$  NMR (300 MHz;  $\text{CDCl}_3$ ):  $\delta$  7.33–7.15 (m, 5H), 6.99 (d, 1H,  $^3J_{\text{HH}} = 9$  Hz), 6.83 (d, 1H,  $^3J_{\text{HH}} = 9$  Hz), 6.48 (s, 1H), 4.03 (dd, 1H,  $^3J_{\text{HH}} = 9$  Hz,  $^3J_{\text{HH}} = 12$  Hz), 3.52–3.46 (m, 1H), 2.35–2.28 (m, 1H), 2.06 (s, 3H), 2.01–1.92 (m, 1H), 1.30 (d, 3H,  $^3J_{\text{HH}} = 9$  Hz).  $^{13}\text{C}$  NMR (75 MHz;  $\text{CDCl}_3$ ):  $\delta$  145.66, 136.70, 133.58, 130.75, 130.66, 128.82, 128.78, 127.52, 126.68, 126.28, 47.43, 43.10, 36.49, 21.88, 21.00. HR-MS (ESI)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{19}\text{S}^+$  [(M + H) $^+$ ], 255.1207; found, 255.1207.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b01305.

Physical data;  $^1\text{H}$ ,  $^{13}\text{C}$ , and NOESY spectra for all new compounds; and 2D NMR analysis spectral data and single crystal X-ray diffraction data for selected compounds (PDF)

Crystallographic information file (CIF)

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### Notes

The authors declare no competing financial interest.

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