

# A facile and highly diastereoselective synthesis of *cis*-2,4-diarylthiochromans

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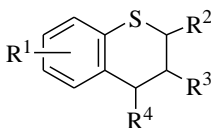
## Abstract

A simple methodology has been developed for diastereoselective synthesis of *cis*-2,4-diarylthiochromans in three steps starting from chalcones. The methodology involves reduction of the conjugate addition product of thiophenol to chalcones followed by Amberlyst-15 catalyzed cyclization of those reduction products.

**Keywords:** *cis*-2,4-Diarylthiochromans, diastereoselective synthesis, chalcones, thiophenol, amberlyst-15

## Introduction

Thiochromans (3,4-dihydro-2*H*-1-benzothiopyrans) (**1**) form a useful class of heterocyclic compounds. Derivatives of **1** have been reported to show a wide range of biological activities, the important ones of which may include their diuretic, anti-inflammatory, antipyretic, analgesic, antidepressant, antihypertensive, anti-amoebic and antimicrobial activities.<sup>1</sup> They are also used as agents against angina pains and as oral infertility agents.<sup>1</sup> Besides, they find a good number of important industrial applications, *e.g.*, they are commonly used as fuel additives, resins, dyes, solvent clathrates and in uranium extraction.<sup>1,2</sup> Regarding their synthetic utilities, thiochroman derivatives are found to be useful synthons for some sesquiterpenoids, the key step in the transformation being Raney nickel induced desulfurization.<sup>3,4</sup>



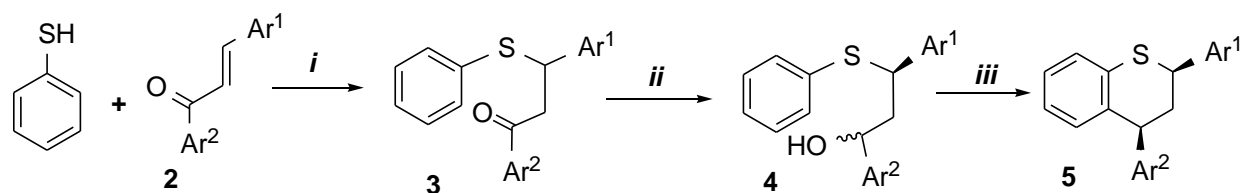
**1**

All the above applications of thiochromans have made them important synthetic targets for organic chemists. This has led to the development of a number of methodologies for their synthesis, which may be mainly categorized as (i) intramolecular electrophilic aromatic substitution of aryl thioethers with functional groups like carbonyl,<sup>1,5</sup> chlorine,<sup>3,4</sup> thioacetal<sup>6</sup> and alcohol,<sup>7,8</sup> (ii) thio-Claisen rearrangement of allyl phenyl sulphides,<sup>1,8-10</sup> (iii) reduction of the corresponding thiochromones and thiochromanones,<sup>1,11,12</sup> (iv) Diels-Alder cycloaddition,<sup>13,14</sup> (v) cationic cycloaddition involving a benzotriazolyl thioether derivative,<sup>15</sup> (vi) a thermal rearrangement, possibly involving substitution of chlorine by a thiol,<sup>1</sup> (vii) thermal cyclization using an oxirane ring<sup>2</sup> and (viii) acid and base catalysed cyclization of the corresponding alcohols.<sup>16</sup>

In continuation of our recent studies on development of new methodologies for synthesis of thiochroman derivatives,<sup>17,18</sup> we report here a simple synthesis of *cis*-2,4-diarylthiochromans in a highly diastereoselective manner using common starting materials like chalcones and thiophenol and involving the use of the sulfonated polystyrene resin amberlyst-15 as a catalyst in the final step.

## Results and Discussion

The present work began by using unsubstituted chalcone (**2a**) as the starting material. In the first step it was reacted with thiophenol under iodine catalyzed condition.<sup>19</sup> The conjugate addition product **3a** was obtained in good yield. Sodium borohydride reduction of **3a** gave a mixture of two diastereomeric alcohols (**4a**) (approximately in 1:1 ratio, as assessed by <sup>1</sup>H NMR) in very good yield. The mixture was directly used for the next step without separating its components. Treatment of the alcohol mixture with amberlyst-15 in dry toluene at 80 °C afforded the *cis*-2,4-diphenylthiochroman (**5a**) as the only product (Scheme-1).



- a:** Ar<sup>1</sup>= Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **b:** Ar<sup>1</sup>=C<sub>6</sub>H<sub>4</sub>-Me-*p*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **c:** Ar<sup>1</sup>=C<sub>6</sub>H<sub>4</sub>-OMe-*m*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;  
**d:** Ar<sup>1</sup>=C<sub>6</sub>H<sub>4</sub>-OMe-*p*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **e:** Ar<sup>1</sup>=C<sub>6</sub>H<sub>4</sub>-Cl-*p*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **f:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>4</sub>-NO<sub>2</sub>-*m*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;  
**g:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>4</sub>-NO<sub>2</sub>-*p*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **h:** Ar<sup>1</sup>= piperonyl, Ar<sup>2</sup>= C<sub>6</sub>H<sub>5</sub>;      **i:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>5</sub>, Ar<sup>2</sup>= C<sub>6</sub>H<sub>4</sub>-Me-*p*;  
**j:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>4</sub>-Cl-*p*, Ar<sup>2</sup>= C<sub>6</sub>H<sub>4</sub>-Me-*p*;      **k:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>5</sub>, Ar<sup>2</sup>=C<sub>6</sub>H<sub>4</sub>-OMe-*p*;      **l:** Ar<sup>1</sup>= C<sub>6</sub>H<sub>4</sub>-Cl-*p*, Ar<sup>2</sup>=C<sub>6</sub>H<sub>4</sub>-OMe-*p*

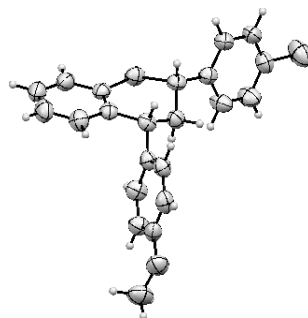
**i:** I<sub>2</sub>, 6-10 °C, 1-1.5 h; **ii:** NaBH<sub>4</sub>, Dry MeOH, r.t., 6-8 h; **iii:** Amberlyst-15, Dry toluene, 80 °C, 1-2 h

**Scheme 1.** Synthetic route to *cis*-2,4-diarylthiochromans (**5**).

The *cis* stereochemistry has been assigned on the basis of  $^1\text{H}$  NMR spectral features of the product. Thus, the two doublet of doublets appearing at 4.26 ( $J = 10.2$  and 6.3 Hz) and 4.64 ( $J = 9.9$  and 4.5 Hz) are characteristic of the pseudoaxial H-4 and axial H-2, respectively, as reported earlier.<sup>15</sup> Extending this study by involving eleven other chalcones, analogous results were obtained (Table 1). X-Ray crystallographic study done on **5l** confirmed the *cis* stereochemistry (ORTEP diagram given in Figure 1)<sup>20</sup>.

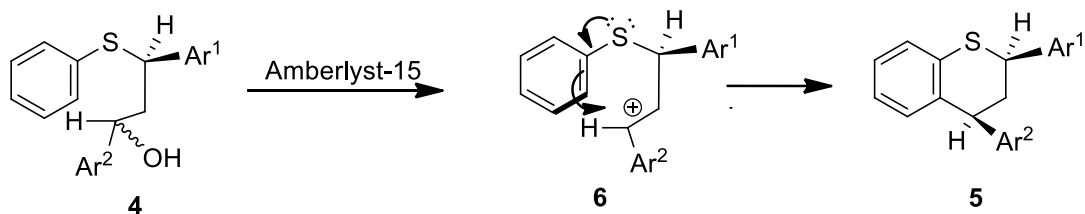
**Table 1.** Results of synthesis of *cis*-2,4-diarylthiochromans (**5**) from chalcones (**2**)

Entry	Chalcone ( <b>2</b> )	Thiochroman ( <b>5</b> )	Stepwise Yield (%)	Overall Yield (%)
1	<b>2a</b>	<b>5a</b>	80, 88, 70	49
2	<b>2b</b>	<b>5b</b>	64, 89, 79	45
3	<b>2c</b>	<b>5c</b>	61, 87, 76	40
4	<b>2d</b>	<b>5d</b>	57, 85, 74	36
5	<b>2e</b>	<b>5e</b>	58, 83, 76	37
6	<b>2f</b>	<b>5f</b>	74, 96, 82	58
7	<b>2g</b>	<b>5g</b>	50, 95, 86	41
8	<b>2h</b>	<b>5h</b>	82, 87, 76	54
9	<b>2i</b>	<b>5i</b>	71, 97, 74	51
10	<b>2j</b>	<b>5j</b>	72, 97, 88	61
11	<b>2k</b>	<b>5k</b>	76, 94, 79	56
12	<b>2l</b>	<b>5l</b>	64, 85, 88	48



**Figure 1.** ORTEP diagram of compound **5l**.

The formation of only one diastereoisomer of 2,4-diarylthiochroman in each case clearly indicates that under the influence of amberlyst-15 a common stable carbocation **6** is formed from both the diastereoisomers of **4**. Cyclization of this carbocation is highly stereoselective and the stereoselectivity is controlled by the existing chirality in it. For rationalization of the result, it may be considered that the transition state for the cyclization is formed through an approach of the thiophenoxy moiety in the way shown in Scheme-2.



**Scheme 2.** Plausible mechanism for diastereoselective formation of *cis*-2,4-diarylthiochromans (**5**).

There are two previous reports of cyclization of 1,3-diaryl-3-phenylsulfanylpropan-1-ols (**4**) leading to 2,4-diarylthiochromans. Jensen *et al.*<sup>2</sup> first performed the cyclization of **4** (prepared in a different way) by refluxing them in toluene with added TsOH and obtained only *cis*-2,4-diarylthiochromans (**5**). They considered the possibility of occurrence of different mechanisms and finally concluded that the process is a case of aromatic electrophilic substitution. Few years later, Skarzewski *et al.*<sup>16</sup> reported a detailed study of cyclization of **4** with KHSO<sub>4</sub> in toluene as well as with MesCl/Et<sub>3</sub>N by using both optically active and racemic varieties of the substrates. It was their observation that both *cis* and *trans* products were formed along with products from 1,3-phenyl shift (through involvement of a cyclic four membered sulfonium ion). In between these two reports, Katritzky and Button reported the synthesis of **5** and some related compounds by a Lewis acid catalyzed reaction involving  $\alpha$ -(benzotriazolyl)methyl thioethers and styrenes<sup>15</sup>. It may be mentioned here that their results show that *cis* product was exclusively formed only in two out of seven cases studied.

## Conclusions

We report here a simple method for synthesis of *cis*-2,4-diarylthiochromans in a highly diastereoselective manner.

## Experimental Section

**General.** Mps were recorded on a K fner block and are uncorrected. IR spectra were recorded on Perkin Elmer FT-IR Spectrophotometer (Spectrum BX II) as KBr pellets. <sup>1</sup>H and <sup>13</sup>C NMR

spectra were obtained in CDCl<sub>3</sub> on Bruker AV-300 (300 MHz), Bruker AC-200 (200 MHz), Bruker DPX-300 (300 MHz) and Bruker DPX-500 (500 MHz) spectrometers using TMS as an internal standard. Mass spectrum was acquired on a Waters QTOF Micro YA263 Mass Spectrometer. Analytical samples were dried *in vacuo* at room temperature. Column chromatography was performed on silica gel (100-200 mesh) using petroleum ether (60-80 °C) and petroleum ether-ethyl acetate mixtures as eluents. TLC was done with silica gel G.

### General method for preparation of 1,3-diaryl-3-phenylsulfanyl-1-propanones (3)

To a mixture of chalcone (**2**) (2 mmole) and thiophenol (2.4 mmole) a pinch of iodine was added and the reaction mixture was kept at 6-10 °C for 1-1.5 h. Excess iodine was removed by treatment with ice cold saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution and the organic material was extracted with dichloromethane (3×15 ml). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. Chromatography of the concentrate over silica gel gave **3** in pure state (yield: 50-82%). Mps: **3a**, 118-120 °C (lit. 119-120 °C)<sup>21</sup>; **3b**, 70-72 °C; **3c**, 84-86 °C (lit. 82-84.5 °C)<sup>20</sup>; **3d**, 110-112 °C; **3e**, 87-89 °C; **3f**, 108-110 °C; **3g**, 102-104 °C; **3h**, 66-68 °C; **3i**, 60-62 °C; **3j**, 89-91 °C; **3k**, 117-119 °C; **3l**, 94-96 °C. Analytical and spectral data of one representative member **3a** were as follows: IR (KBr) cm<sup>-1</sup>: 1679 (C=O), 1581, 1480, 1364, 1231, 1170, 1086, 1074, 981, 954, 918. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 3.54-3.71 (2H, m), 4.95 (1H, t, *J* = 7.0 Hz), 7.16-7.28 (6H, m), 7.33 (4H, m), 7.43 (2H, t, *J* = 7.5 Hz), 7.55 (1H, t, *J* = 7.5 Hz), 7.87 (2H, d, *J* = 7.5 Hz). Anal. Calcd. for C<sub>21</sub>H<sub>18</sub>SO: C, 79.21; H, 5.70. Found: C, 79.43; H, 5.48.

### General method for preparation of 1,3-diaryl-3-phenylsulfanyl-1-propanols (4)

To a solution of compound **3** (2 mmole) in dry methanol (25 mL), NaBH<sub>4</sub> (137 mg, 3.7 mmole) was added and the mixture was stirred at room temperature for 6-8 h. Work up of the reaction mixture in the usual way afforded 1,3-diaryl-3-phenylsulfanyl-1-propanol (**4**) as a mixture of diastereomers (yield: 83-97%). Spectral data of compound **4a**: IR (KBr) cm<sup>-1</sup>: 3435, 3060, 3028, 2361, 2342, 1490, 1407, 1090, 1014. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.17-2.48 (2H, m, CH<sub>2</sub>), 4.25 (approx. 0.5H, t, *J* = 7.5 Hz), 4.28 (approx. 0.5H, dd, *J* = 9.9 and 5.7 Hz), 4.55 (approx. 0.5H, dd, *J* = 9.6 and 3.6 Hz), 4.90 (approx. 0.5H, dd, *J* = 7.8 and 5.8 Hz), 7.18-7.35 (15H, m, Ar-H).

### General method for preparation of *cis*-2,4-diarylthiochromans (5)

A mixture of diastereomers of 1,3-diaryl-3-phenylsulfanyl-1-propanol (**4**) (1mmole) obtained in the previous step was dissolved in dry toluene (20 mL) and to it amberlyst-15 (100 mg) was added and the mixture was heated at 80 °C for 1-2 h. The crude product obtained after removal of the solvent by distillation under reduced pressure was crystallized from dichloromethane-petroleum ether when pure **5** was obtained (yield: 35-60%). The analytical and spectral data of twelve *cis*-2,4-diarylthiochromans (**5a-l**) thus synthesized were as follows:

***cis*-2,4-Diphenylthiochroman (5a)**. Colorless crystalline solid, mp 128-130 °C [Lit.<sup>16</sup> 129-132 °C]; IR (KBr) cm<sup>-1</sup>: 3058, 2914, 1600, 1584, 1491, 1453, 1052, 762. <sup>1</sup>H NMR (300 MHz,

CDCl<sub>3</sub>):  $\delta$  2.53-2.60 (2H, m, CH<sub>2</sub>), 4.26 (1H, dd,  $J$  = 10.2 and 6.3 Hz, H-4), 4.64 (1H, dd,  $J$  = 9.9 and 4.5 Hz, H-2), 6.74 (d,  $J$  = 7.8 Hz, 1H), 6.91 (1H, t,  $J$  = 7.5 Hz), 7.08 (1H, t,  $J$  = 7.5 Hz), 7.16 (1H, d,  $J$  = 7.5 Hz), 7.23-7.37 (8H, m), 7.44 (2H, d,  $J$  = 7.1 Hz). Anal. Calcd for C<sub>21</sub>H<sub>18</sub>S (302.43): C, 83.40; H, 6.00. Found: C, 83.24; H, 6.16.

**cis-2-(4-Methylphenyl)-4-phenylthiochroman (5b)**. Light brown crystalline solid, mp 135-137 °C; IR (KBr) cm<sup>-1</sup>: 3053, 2904, 2355, 1903, 1652, 1514, 1493, 1084, 1015, 832, 747. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  2.36 (3H, s, -CH<sub>3</sub>), 2.50-2.59 (2H, m, CH<sub>2</sub>), 4.22 (1H, dd,  $J$  = 9.0 and 7.4 Hz, H-4), 4.64 (1H, dd,  $J$  = 9.0 and 4.8 Hz, H-2), 6.74 (1H, d,  $J$  = 7.0 Hz), 6.90 (1H, t,  $J$  = 8.0 Hz), 7.03-7.44 (11H, m). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 21.1, 41.6, 46.1, 47.3, 124.2, 126.0, 126.5, 127.5, 127.8, 128.5, 128.7, 129.4, 129.9, 134.6, 136.3, 137.0, 141.2, 142.0. TOF MS ES<sup>+</sup> (M+K)<sup>+</sup>: Calcd 355.0923, Found 355.0438. Anal. Calcd for C<sub>22</sub>H<sub>20</sub>S (316.46): C, 83.50; H, 6.37. Found: C, 83.34; H, 6.17.

**cis-2-(3-Methoxyphenyl)-4-phenylthiochroman (5c)**. Colourless crystalline solid, mp 118-120 °C; IR (KBr) cm<sup>-1</sup>: 3048, 2914, 2360, 1600, 1560, 1470, 1241, 1045, 821, 747. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.51-2.59 (2H, m, CH<sub>2</sub>), 3.80 (3H, s, -OCH<sub>3</sub>), 4.25 (1H, dd,  $J$  = 11.1 and 5.7 Hz, H-4), 4.62 (1H, dd,  $J$  = 10.6 and 4.1 Hz, H-2), 6.73 (1H, d,  $J$  = 7.8 Hz), 6.82 (1H, dd,  $J$  = 8.1 and 2.4 Hz), 6.90 (1H, t,  $J$  = 7.5 Hz), 6.98 (1H, br. s), 6.99-7.26 (7H, m), 7.28 (1H, d,  $J$  = 4.5 Hz), 7.35 (1H, d,  $J$  = 6.9 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 41.6, 46.1, 47.7, 55.2, 113.1, 113.3, 119.8, 124.2, 126.1, 126.6, 126.7, 127.8, 128.7, 129.7, 129.9, 134.6, 136.8, 142.8, 145.0, 159.9. Anal. Calcd for C<sub>22</sub>H<sub>20</sub>OS (332.46): C, 79.48; H, 6.06. Found: C, 79.26; H, 6.02.

**cis-2-(4-Methoxyphenyl)-4-phenylthiochroman (5d)**. Off-white crystalline solid, mp 142-144 °C; IR (KBr) cm<sup>-1</sup>: 3047, 2913, 2360, 1602, 1586, 1455, 1045, 1015, 821, 794. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.50-2.57 (2H, m, CH<sub>2</sub>), 3.82 (3H, s, -OCH<sub>3</sub>), 4.20 (1H, dd,  $J$  = 10.6 and 5.8 Hz, H-4), 4.65 (1H, dd,  $J$  = 10.5 and 4.5 Hz, H-2), 6.76 (1H, d,  $J$  = 7.8 Hz), 6.86- (3H, m), 7.06 (1H, t,  $J$  = 7.5 Hz), 7.13-7.17 (3H, m), 7.24-7.44 (5H, m). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  12.3, 29.8, 41.8, 46.3, 47.1, 55.4, 114.3, 124.3, 126.2, 126.7, 127.7, 127.9, 128.9, 129.8, 130.0, 134.8, 137.1, 137.4. Anal. Calcd for C<sub>22</sub>H<sub>20</sub>OS (332.46): C, 79.48; H, 6.06. Found: C, 79.34; H, 6.20.

**cis-2-(4-Chlorophenyl)-4-phenylthiochroman (5e)**. Colourless crystalline solid, mp 146-148 °C [Lit.<sup>16</sup> 146-147 °C]; IR (KBr) cm<sup>-1</sup>: 3060, 3028, 1585, 1490, 1453, 1434, 1090, 1015, 864, 702. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.50-2.58 (2H, m, CH<sub>2</sub>), 4.28 (1H, dd,  $J$  = 11.1 and 4.8 Hz, H-4), 4.64 (1H, dd,  $J$  = 10.8 and 3.6 Hz, H-2), 6.76 (1H, d,  $J$  = 8.1 Hz), 6.93 (1H, t,  $J$  = 7.8 Hz), 7.10-7.40 (11H, m). Anal. Calcd for C<sub>21</sub>H<sub>17</sub>ClS (336.88): C, 74.87; H, 5.09. Found: C, 74.62; H, 4.87.

**cis-2-(3-Nitrophenyl)-4-phenylthiochroman (5f)**. Light yellow crystalline solid, mp 156-158 °C; IR (KBr) cm<sup>-1</sup>: 3061, 2940, 2358, 1590, 1530, 1350, 1095, 1072, 902, 809, 752. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.52-2.64 (2H, m, CH<sub>2</sub>), 4.26 (1H, dd,  $J$  = 11.5 and 5.0 Hz, H-4), 4.74 (1H, dd,  $J$  = 11.4 and 3.8 Hz, H-2), 6.75 (1H, d,  $J$  = 7.8 Hz), 6.94 (1H, br. t, 7.9 Hz) 7.08-7.18 (2H, m), 7.23-7.38 (5H, m), 7.52 (1H, t,  $J$  = 8.0 Hz), 7.76 (1H, d,  $J$  = 7.8 Hz), 8.15 (1H, d,  $J$  = 8.4 Hz), 8.31 (1H, s). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  41.3, 45.4, 47.4, 122.7, 122.9, 124.7, 126.2,

126.8, 127.0, 128.7, 128.9, 129.7, 130.0, 133.5, 133.9, 136.8, 143.6, 144.3, 148.5. Anal. Calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>2</sub>S (347.43): C, 72.60; H, 4.93; N, 4.03. Found: C, 72.49; H, 4.81; N, 3.88.

**cis-2-(4-Nitrophenyl)-4-phenylthiochroman (5g).** Light yellow crystalline solid, mp 164-166 °C; IR (KBr) cm<sup>-1</sup>: 3062, 2911, 2360, 1590, 1532, 1351, 1096, 1051, 810, 751. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 2.48-2.61 (2H, m, CH<sub>2</sub>), 4.25 (1H, dd, *J* = 11.5 and 5.0 Hz, H-4), 4.75 (1H, dd, *J* = 11.0 and 3.6 Hz, H-2), 6.74 (1H, d, *J* = 7.8 Hz, ArH), 6.91 (1H, t, *J* = 6.8 Hz, ArH), 6.98-7.36 (7H, m), 7.58 (2H, d, *J* = 8.6 Hz), 8.18 (2H, d, *J* = 8.6 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 41.1, 45.5, 47.3, 124.0, 124.7, 126.1, 126.8, 127.0, 128.5, 128.6, 128.8, 129.9, 133.4, 136.9, 144.2, 147.4, 148.8. TOF MS ES<sup>+</sup> (M+K)<sup>+</sup>: Calcd. 386.0617. Found 386.2152. Anal. Calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>2</sub>S (347.43): C, 72.60; H, 4.93; N, 4.03. Found: C, 72.38; H, 4.72; N, 4.16.

**cis-2-(3,4-Dioxymethylene)-4-phenylthiochroman (5h).** Colourless crystalline solid, mp 186-188 °C; IR (KBr) cm<sup>-1</sup>: 2861, 1955, 1610, 1509, 1302, 1251, 1174, 1032, 832, 766. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 2.50-2.61 (2H, m, CH<sub>2</sub>), 4.24 (1H, dd, *J* = 10.5 and 6.3 Hz, -H-4), 4.65 (1H, dd, *J* = 10.0 and 4.5 Hz, H-2), 5.99 (2H, s, -OCH<sub>2</sub>O-), 6.72-6.81 (4H, m), 6.96 (1H, br. t, *J* = 7.5 Hz), 7.02-7.20 (2H, m), 7.30-7.48 (5H, m). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 41.6, 46.0, 47.4, 100.9, 108.2, 108.7, 121.9, 124.2, 126.1, 126.6, 127.5, 127.8, 128.7, 129.9, 134.6, 136.8, 138.8, 141.1, 146.3, 147.9. TOF MS ES<sup>+</sup> (M+Na)<sup>+</sup>: Calcd. 369.0925. Found 369.4673, Anal. Calcd. for C<sub>22</sub>H<sub>18</sub>O<sub>2</sub>S (346.44): C, 76.27; H, 5.24. Found: C, 76.01; H, 5.09.

**cis-2-Phenyl-4-(4-Methylphenyl)-thiochroman (5i).** Off-white crystalline solid, mp 146-148 °C [Lit.<sup>15</sup> 148 °C]; IR (KBr) cm<sup>-1</sup>: 3055, 2902, 2358, 1906, 1650, 1517, 1498, 1091, 802, 752. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.37 (3H, s, -CH<sub>3</sub>), 2.54-2.61 (2H, m, CH<sub>2</sub>), 4.24 (1H, dd, *J* = 9.9 and 6.6 Hz, H-4), 4.66 (1H, dd, *J* = 9.6 and 4.8 Hz, H-2), 6.77 (1H, d, *J* = 8.1 Hz), 6.92 (1H, br. t, *J* = 7.5 Hz.), 7.08 (1H, br. t, *J* = 7.6 Hz), 7.14-7.19 (4H, m), 7.25-7.38 (4H, m) 7.45 (2H, d, *J* = 8.1 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.1, 41.6, 46.1, 47.3, 124.2, 126.1, 126.5, 127.5, 127.8, 128.6, 128.7, 129.4, 129.9, 134.6, 136.3, 137.0, 141.2, 142.0. Anal. Calcd for C<sub>22</sub>H<sub>20</sub>S (316.46): C, 83.50; H, 6.37. Found: C, 83.25; H, 6.13.

**cis-2-(4-Chlorophenyl)-4-(4-Methylphenyl)-thiochroman (5j).** Colourless crystalline solid, mp 149-151 °C; IR (KBr) cm<sup>-1</sup>: 3002, 2908, 2833, 2360, 1610, 1513, 1251, 1037, 832, 751. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.35 (3H, s, -CH<sub>3</sub>), 2.41-2.58 (2H, m, CH<sub>2</sub>), 4.21 (1H, dd, *J* = 11.2 and 5.5 Hz, H-4), 4.60 (1H, dd, *J* = 10.8 and 3.9 Hz, H-2), 6.75 (1H, br. d, *J* = 8.1 Hz), 6.90 (1H, br. t, *J* = 8.2 Hz), 7.05 (1H, br. d, *J* = 7.8 Hz), 7.09 (1H, s), 7.15 (1H, s), 7.17 (1H, s), 7.26 (1H, s), 7.29 (1H, s), 7.30 (1H, s), 7.34 (1H, s), 7.37 (1H, s), 7.17 (1H, s). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.1, 41.5, 45.4, 47.2, 124.3, 126.0, 126.6, 128.5, 128.8, 128.9, 129.4, 129.9, 133.4, 134.2, 136.4, 136.8, 139.8, 141.7. Anal. Calcd for C<sub>22</sub>H<sub>19</sub>ClS (350.90): C, 75.30; H, 5.46. Found: C, 75.10; H, 5.19.

**cis-2-Phenyl-4-(4-methoxyphenyl)-thiochroman (5k).** Off-white crystalline solid, mp 156-158 °C [Lit.<sup>16</sup> 158-159 °C]; IR (KBr) cm<sup>-1</sup>: 3027, 2942, 2359, 1600, 1586, 1455, 1242, 821, 765. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 2.42-2.59 (2H, m, CH<sub>2</sub>), 3.82 (3H, s, -OCH<sub>3</sub>), 4.20 (1H, dd, *J* = 9.8 and 7.0 Hz, H-4), 4.65 (1H, dd, *J* = 9.0 and 4.6 Hz, H-2), 6.75 (1H, d, *J* = 7.8 Hz), 6.90 (2H, d, *J* = 8.4 Hz), 7.03-7.11 (3H, m), 7.15 (2H, d, *J* = 8.6 Hz), 7.25-7.45 (5H, m). <sup>13</sup>C NMR (75 MHz,

CDCl<sub>3</sub>):  $\delta$  41.6, 46.1, 46.9, 55.3, 114.1, 124.2, 126.0, 126.5, 127.5, 127.8, 128.7, 129.6, 129.9, 134.6, 137.0, 137.2, 141.3, 158.4. Anal. Calcd for C<sub>22</sub>H<sub>20</sub>OS (332.46): C, 79.48; H, 6.06. Found: C, 79.27; H, 6.01.

**cis-2-(4-Chlorophenyl)-4-(4-methoxyphenyl)-thiochroman (5I)**. Off-white crystalline solid, mp 166-168 °C; IR (KBr) cm<sup>-1</sup>: 3040, 2913, 2360, 1586, 1486, 1243, 1037, 930, 823, 764. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  2.43-2.54 (2H, m, CH<sub>2</sub>), 3.82 (3H, s, -OCH<sub>3</sub>), 4.20 (1H, dd, *J* = 10.8 and 5.6 Hz, H-4), 4.62 (1H, dd, *J* = 10.4 and 4.4 Hz, H-2), 6.75 (1H, d, *J* = 7.8 Hz), 6.88 (2H, d, *J* = 8.6 Hz), 6.86-6.95 (1H, m), 7.03-7.16 (2H, m), 7.13 (2H, d, *J* = 8.6 Hz), 7.30 (2H, d, *J* = 8.7 Hz), 7.35 (2H, d, *J* = 8.8 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  41.5, 45.5, 46.7, 55.2, 114.1, 124.3, 126.0, 126.6, 128.8, 128.9, 129.6, 129.9, 133.4, 134.1, 136.7, 137.1, 139.8, 158.4. Anal. Calcd for C<sub>22</sub>H<sub>19</sub>ClOS (366.90): C, 72.02; H, 5.22. Found: C, 72.21; H, 5.01.

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20. Crystallographic data collection and refinement: A suitable single crystal of compound **51** (crystallized from acetone) was mounted on a thin glass fiber with commercially available super glue. X-ray single crystal data collection was performed at room temperature using "Bruker SMART" diffractometer, equipped with a normal focus, sealed tube X-ray source with graphite monochromated Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was solved by SHELXS 97. Structure refinement was carried out using SHELXL 97. The relevant data are given in **Table-2**. "CCDC 882530" contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

**Table 2.** Important crystallographic data for Compound **5I**

Molecular formula	C <sub>22</sub> H <sub>19</sub> ClOS
$f_w$ (g. mol <sup>-1</sup> )	366.88
Space group	Pbca
$\mu$ (Mo-K $\alpha$ )	0.330 mm <sup>-1</sup>
F (000)	1536
a = 17.9005(4) Å	$\alpha = 90^\circ$
b = 8.3965(2) Å	$\beta = 90^\circ$
c = 24.2979(5) Å	$\gamma = 90^\circ$
Theta Min-Max	1.68, 25.00
Vol [Å <sup>3</sup> ]	3652.01(14)
Z	8
D <sub>calc</sub> (g.cm <sup>-3</sup> )	1.335
Index range	-21 <= h <= 21 -9 <= k <= 9 -28 <= l <= 28
Number of data measured	3206
Number of unique data	2324
Goodness-of-fit	1.083
Final R indices	R1 = 0.0605, wR2 = 0.0926

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