# Stereoselective Synthesis of Thiochroman-4-ones by Ring Transformation of Chiral 5-Ylidene-1,3-dioxan-4-ones with 2-Bromothiophenol via Bromo−Lithium Exchange

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The reaction of (*E*)- or (*Z*)-5-ylidene-1,3-dioxan-4-one **(1)** and 2-bromothiophenol, followed by bromo-lithium exchange with *n*BuLi, provides a new access to optically active thiochroman-4-ones **4** and **5**. Stereoselective conjugate addition occurs in the first step and the resulting 5-(1-phenylsulfanylalkyl)-1,3-dioxan-4-ones **2** and **3** undergo ring transformation to thiochroman-4-ones by attack of the lithiated phenyl ring at the dioxanone carbonyl carbon atom, cleaving off pivalaldehyde. If reactants with a (*Z*)-configuration are used, a retro-aldol reaction occurs in the ring transformation step, thus affording the 3-unsubstituted thiochroman-4-ones **5** rather than 3-(1-hydroxyethyl)-thiochroman-4-ones **4**. This phenomenon can be rationalized by the steric congestion in the intermediate enolate **7**.

## Introduction

Thiochroman-4-ones are sulfur analogues of naturally occurring chromanones and are of interest in the synthesis of pharmacologically active compounds such as Dilthiazem-related chiral CNS drugs.[1,2] The existence of thiochroman-4-ones has been known about for a long time[3,4] and a number of syntheses have been developed. The unsubstituted compound is commercially available. The most versatile route to thiochroman-4-ones is based on the addition of arylthiols to α,β-unsaturated carboxylic acids or their derivatives, followed by intramolecular Friedel-Craft acylation of the resulting β-arylthiopropionic acids.[3,5,6] The latter can also be obtained in other ways such as by the ring opening of β-lactones.[5] The only reported synthesis of optically active thiochroman-4-ones uses the cyclization of (*R*)-β-phenylthiocarboxylic acids which were obtained from optically active β-hydroxy esters and thiophenol.[1] Racemic 2-phenyl-thiochroman-4-one has been resolved by formation of its chiral hydrazone.[7] Treatment of 2-methylthio or 2-(4-methoxybenzylthio)chalcones with acids represents another ring closure synthesis of thiochroman-4-ones.[4,8] Finally, this class of heterocycles can also be obtained by addition reactions to thiochromones.[4,6,9,10]

Here we report a new stereoselective synthesis of thiochroman-4-ones using 2-bromothiophenol as a binucleophilic S−C−C building block. Since a strongly nucleophilic carbon atom can be generated by bromo−lithium exchange, this reagent should be particularly useful for asymmetric syntheses requiring mild conditions. 2-Bromothiophenol undergoes conjugate addition in Michael systems[11,12] but has not been used further as a binucleophilic S−C−C building block in these cases. On the other hand, the 5-ylidene-1,3-dioxanones **(*E*)-1** and **(*Z*)-1**, available from naturally occurring poly-(3*R*)-hydroxybutyrate,[13−15] have become versatile starting materials in Michael systems, allowing the stereoselective synthesis of several heterocyclic products such as benzothiazepones and pyrrolidones by reaction with binucleophiles or by cycloadditions.[16−19] Addition reactions to the double bond follow a predictable mode, i.e. in cases of **(*E*)-1** attack from the *re*-face[15,17] (e.g. cuprates, silanes, nitromethane) unless stereoelectronic factors force an attack from the more sterically hindered side, i.e. the *si*-face of **(*E*)-1**[18] (e.g. 2-aminothiophenol, because of hydrogen bonding of the amino group with the lone pairs of the oxygen atoms of the dioxanone ring).

## Results and Discussion

The reaction of 2-bromothiophenol with 5-ylidene-1,3-dioxanone **(1)** in the presence of 1 mol-% *n*BuLi in THF at −78 °C gave a clean addition to the C−C double bond. As expected, the preferred mode of attack occurred from the bottom side, i.e. from the *re*-face of **(*E*)-1** and the *si*-face of **(*Z*)-1**, while the protonation took place from the *si*-face (*anti*-addition). Obviously, the stereochemical mode of protonation is governed by 1,2-asymmetric induction exerted by the Me group at the C-6 position of the dioxanone ring. Diastereoselectivities between 70:30 and 95:5 were achieved. The major diastereomers, i.e. adducts **2** starting from **(*E*)-1** and adducts **3** starting from **(*Z*)-1** could be obtained in an analytically pure form by flash chromatography of the diastereomeric mixture (Scheme 1, Table 1). The diastereoselectivities were lower with the (*Z*)-isomer

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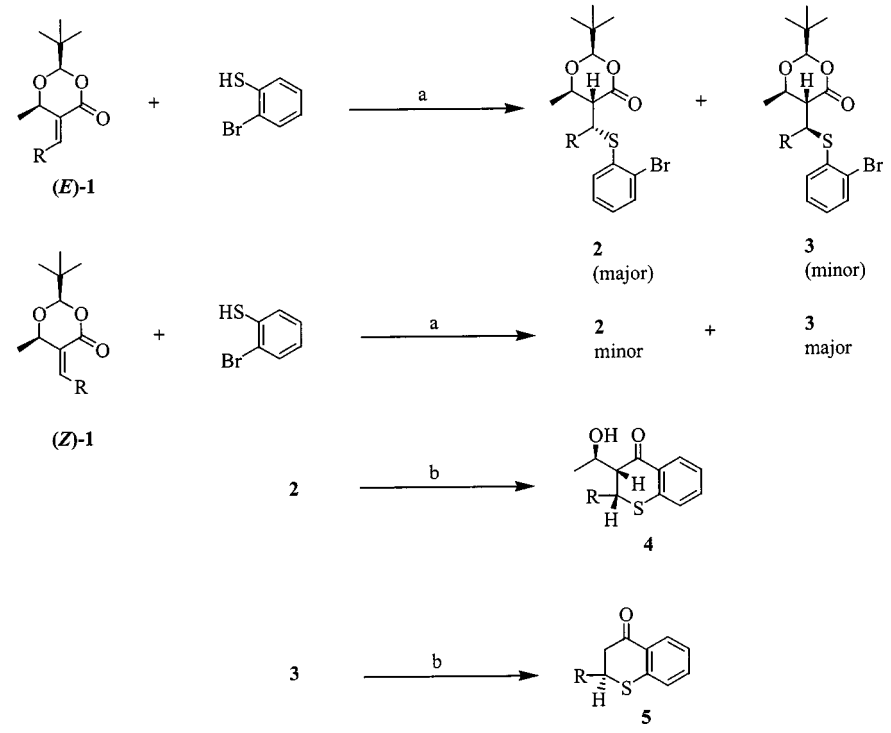


| R | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Me | a | a | a | a |
| Et | b | b | b | b |
| *i*Pr | c | c | c | c |
| $(CH_2)_2Ph$ | d | d | d | d |
| Ph | e | e | e | - |
| *c*Hex | f | f | f | - |

Scheme 1. (a) *n*BuLi (cat.), THF, −78 to 0 °C; (b) *n*BuLi, THF, −100 to −78 °C

Table 1. Adducts **2**, **3** and thiochroman-4-ones **4** and **5**

| Entry | R | Geometry of reactant **1** | Adducts **2**+**3** (% yield)[a] | *dr* **2**/**3** | Thiochromanones **4** or **5** (% yield)[b] |
|---|---|---|---|---|---|
| 1 | Me | *E* | **2a/3a** (92) | 80:20 | **4a** (76) |
| 2 | Me | *Z* | **2a/3a** (90) | 30:70 | **5a** (76) |
| 3 | Et | *E* | **2b/3b** (91) | 80:20 | **4b** (73) |
| 4 | Et | *Z* | **2b/3b** 90 | 30:70 | **5b** (75) |
| 5 | *i*Pr | *E* | **2c/3c** (86) | 90:10 | **4c** (72) |
| 6 | *i*Pr | *Z* | **2c/3c** (85) | 20:80 | **5c** (78) |
| 7 | $(CH_2)_2Ph$ | *E* | **2d/3d** (92) | 90:10 | **4d** (73) |
| 8 | $(CH_2)_2Ph$ | *Z* | **2d/3d** (92) | 20:80 | **5d** (75) |
| 9 | Ph | *E* | **2e/3e** (86) | 95:05 | **4e** (70) |
| 10 | *c*Hex | *E* | **2f/3f** (85) | 70:30 | **4f** (78) |

[a] Major isomer could be obtained in analytically pure form by flash chromatography. − [b] Obtained from pure adducts **2** or **3**, respectively.

than with the corresponding (*E*)-isomer. After separation, pure adducts **2** and **3** were submitted to bromo−lithium exchange by treatment with *n*BuLi in THF at −100 °C. To our surprise, different types of cyclization products appeared depending on the configuration at the 1′-position of the 5-(1-phenylsulfanylalkyl)-1,3-dioxan-4-ones **2** and **3**. Adducts **2**, derived as the main products from **(*E*)-1**, gave the expected 2-substituted 3-(1-hydroxyethyl)-thiochroman-4-ones **4** by attack of the lithiated ring position at the carbonyl carbon atom, opening of the dioxanone ring and subsequent loss of the pivalaldehyde moiety. The diastereomeric adducts **3**, predominantly derived from the (*Z*)-starting material **(*Z*)-1**, additionally lose the hydroxyethyl moiety in the *n*BuLi-assisted cyclization reaction affording the 3-unsubstituted thiochroman-4-ones **5**. Obviously, a retro-aldol reaction has occurred. So far, this type of reaction has only been observed with 1,3-dioxan-4-ones possessing a quaternary carbon atom at position 5 — sterically less-congested analogues with a tertiary carbon at position 5 keep the hydroxyethyl group.[16−19] In order to rationalize the different reaction behavior of **2** and **3**, the structures of the likely enolate intermediates **6a** and **7a**, derived from the intramolecular attack of the lithiated phenyl ring at the dioxanone carbonyl carbon and cleaving off of pivalaldehyde, were geometry optimized by MM2 force field calculations (see Figure 1 and 2). It turned out that a steric repulsion between the two methyl groups exists in enolate **7a,** which would cause a retro-aldol reaction releasing the hydroxyethyl group as acetaldehyde. Enolate **6a** lacks this repulsive driving force (minimum energy 17.98 kcal/mol compared to 26.50 kcal/mol in case of **7a**) and the aldol structure survives.

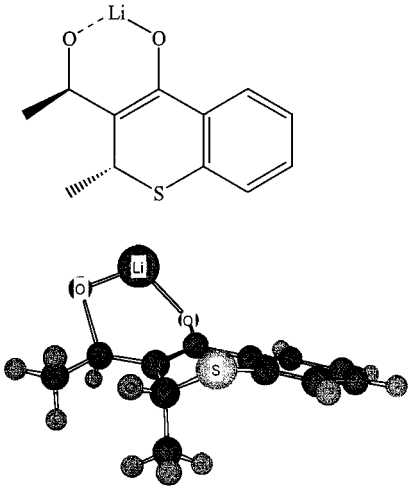


Figure 1. Intermediate enolate **6a** (formula and MM2-optimized structure, total energy 17.98 kcal/mol) formed in the conversion of **2a** to **4a**

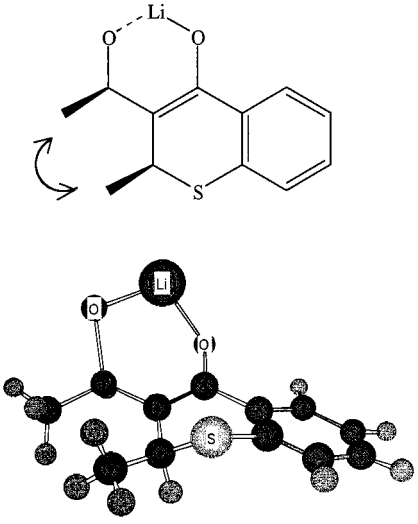


Figure 2. Intermediate enolate **7a** (formula and MM2-optimized structure, total energy 26.50 kcal/mol) formed in the conversion of **3a** to **5a**

The structural elucidation of compounds **2**−**4** is based on an X-ray crystal analysis of adduct **2b** (see Figure 3)[20] and similar CD spectra in this series (see Figure 4). The coupling constants $J < 4$ Hz observed in the $^1$H NMR spectra are in accordance with the *cis*-configuration of the substituents in thiochromanones **4**. The C*H*S protons of adducts **2** exhibit a slight downfield shift and a somewhat greater coupling constant with C*H*C=O than in the corresponding diastereomer **3**. The latter compounds possess higher $R_f$ values.

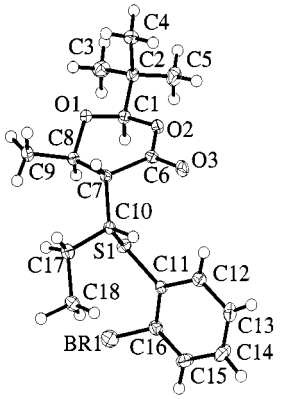


Figure 3. X-ray crystal analysis of **2b**

In summary, a new straightforward asymmetric synthesis of thiochromanones was found by the two step-reaction of 5-alkylidene-1,3-dioxan-4-ones with 2-bromothiophenol. Similar to the known synthesis of thiochroman-4-ones from thiophenols with α,β-unsaturated esters, conjugate addition occurs in the first step and the thiopyran ring is established by nucleophilic attack of the aryl ring at the carbonyl carbon atom and ring transformation. However, the application of 2-bromo-thiophenol instead of thiophenol allows the cyclization step to run under much milder conditions since the nucleophilicity of the aryl ring is enhanced by bromo−lithium exchange.

## Experimental Section

**General Remarks:** $^1$H NMR and $^{13}$C NMR (including DEPT) spectra were recorded at 300 and 75.5 MHz, respectively on a Bruker AC-300 in $CDCl_3$ with TMS as internal standard. 2D NMR experiments include $^1$H,$^1$H COSY and HMQC. Optical rotations were determined with a Perkin−Elmer polarimeter 241 ($c$ = 1, $CHCl_3$, d = 1 mm). Circular dichroism in terms of ellipticity Theta (in deg)

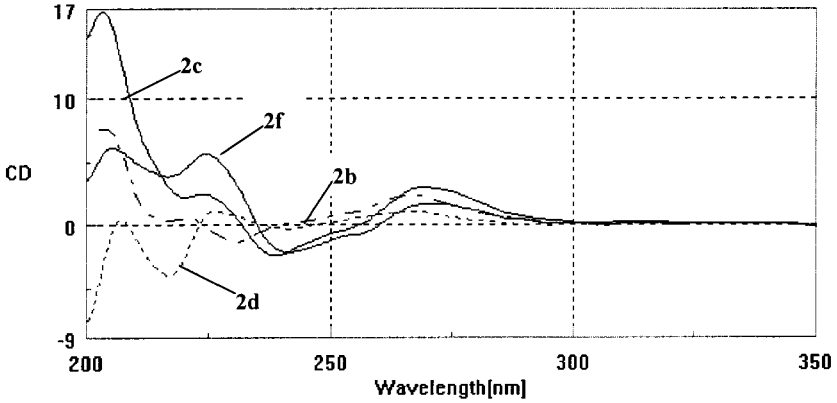


Figure 4. CD spectra for compounds **2b, 2c, 2d** and **2f** in $CH_3OH$

was measured on a Jasco J710 spectrometer (minimum wave length 190 nm). For preparative column chromatography, silica (0.04−0.063 mm, Merck) was used. Starting materials **1a−1f** were obtained following or adapting literature procedures.[13−15,18] ChemOffice version 5 was used for MM2-force field calculations.

**General Procedure for the Michael Addition of 2-Bromothiophenol:** A solution of 2-bromothiophenol (378 mg, 2 mmol) in dry THF (5 mL) was added to an ice-cold solution of *n*BuLi (1.6 M in hexane, 0.04 mmol) in dry THF (5 mL). The resulting solution was stirred at 0 °C for 45 min and then cooled to −78 °C. A solution of the ylidenedioxanone **1** (1 mmol) in THF (10 mL) was added dropwise over a period of 20 min. The reaction mixture was slowly warmed to 0 °C overnight, quenched with aqueous 2 M NaOH (10 mL) solution and was extracted with $CH_2Cl_2$ (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated to give a pale yellow oil, which was purified by flash chromatography (silica gel, *n*-hexane/$Et_2O$, 5:1).

**(1′*R*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanylethyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2a):** Yield: 286 mg (74%). − $R_f$ = 0.32 (hexane/$Et_2O$, 4:1). − Colorless crystals. M.p. 52−53 °C. − $[\alpha]_D^{20}$ = +8.5 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.88 [s, 9 H, C(C$H_3$)$_3$], 1.33 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 1.37 (d, *J* = 7.1 Hz, 3 H, C$H_3$CHS), 2.67 (dd, *J* = 3.0, 9.0 Hz, 1 H, C*H*C=O), 3.82 (dq, *J* = 3.0, 7.1 Hz, 1 H, CHS), 4.06 (dq, *J* = 6.4, 9.0 Hz, 1 H, CHO), 4.94 (s, 1 H, OC*H*O), 7.03 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.19 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.46 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.50 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 20.60 (*C*$H_3$CHS), 22.09 (*C*$H_3$CHO), 23.84 [C(*C*$H_3$)$_3$], 35.01 [*C*(CH$_3$)$_3$], 44.31 (CHS), 53.89 (CH=O), 73.01 (CHO), 107.47 (O*C*HO), 127.42 (C, Ar), 127.98, 128.96, 133.33, 133.75 (CH, Ar), 135.46 (C, Ar), 169.35 (C=O). − $C_{17}H_{23}BrO_3S$ (387.33): calcd. C 52.72, H 5.99, S 8.28, Br 20.63; found C 52.53, H 6.19, S 8.19, Br 20.50.

**(1′*S*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanylethyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (3a):** Yield: 244 mg (63%). − $R_f$ = 0.38 (hexane/$Et_2O$, 4:1). − Colorless oil. − $[\alpha]_D^{20}$ = +47.5 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.89 [s, 9 H, C(C$H_3$)$_3$], 1.32 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 1.45 (d, *J* = 7.1 Hz, 3 H, C$H_3$CHS), 2.67 (dd, *J* = 2.6, 9.4 Hz, 1 H, C*H*C=O), 3.86 (dq, *J* = 2.6, 7.1 Hz, 1 H, CHS), 4.01 (dq, *J* = 6.4, 9.4 Hz, 1 H, CHO), 4.89 (s, 1 H, OC*H*O), 7.02 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.23 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.40 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.51 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 18.78 (*C*$H_3$CHS), 21.58 (*C*$H_3$CHO), 23.84 [C(*C*$H_3$)$_3$], 35.13 [*C*(CH$_3$)$_3$], 41.63 (CHS), 52.19 (*C*HC=O), 72.60 (CHO), 107.97 (O*C*HO), 125.47 (C, Ar), 128.08, 128.12, 131.14, 133.46 (CH, Ar), 135.83 (C, Ar), 169.25 (C=O). − $C_{17}H_{23}BrO_3S$ (387.33): calcd. C 52.72, H 5.99, S 8.28, Br 20.63; found C 52.46, H 6.23, S 8.10, Br 20.42.

**(1′*R*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanylpropyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2b):** Yield: 292 mg (73%). − $R_f$ = 0.37 (hexane/$Et_2O$, 4:1). − Colorless crystals. M.p. 75−76 °C. − $[\alpha]_D^{20}$ = +41.6 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.88 [s, 9 H, C(C$H_3$)$_3$], 0.98 (t, *J* = 7.1 Hz, 3 H, C$H_3$CH$_2$), 1.33 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 1.61−1.80 (m, 2 H, CH$_2$), 2.77 (dd, *J* = 2.6, 9.0 Hz, 1 H, C*H*C=O), 3.81 (ddd, *J* = 2.6, 7.1, 8.6 Hz, 1 H, CHS), 4.10 (dq, *J* = 6.0, 9.0 Hz, 1 H, CHO), 4.99 (s, 1 H, OC*H*O), 6.99 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.18 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.46 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.49 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 12.44 (*C*H$_3$CH$_2$), 22.21 (*C*$H_3$CHO), 23.83 [C(*C*H$_3$)$_3$], 28.86 (CH$_2$), 34.98 [*C*(CH$_3$)$_3$], 52.20 (CHS), 52.43 (*C*HC=O), 72.89 (CHO), 107.31 (O*C*HO), 126.03 (C, Ar), 128.03, 128.36, 132.66, 133.15 (CH, Ar), 136.07 (C, Ar), 170.20 (C=O). − $C_{18}H_{25}BrO_3S$ (401.36): calcd. C 53.87, H 6.28, S 7.99, Br 19.91; found C 53.85, H 6.39, S 8.02, Br 19.70.

**(1′*S*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sufanylpropyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (3b):** Yield: 253 mg (63%). − $R_f$ = 0.44 (hexane/$Et_2O$, 4:1). − Colorless oil. − $[\alpha]_D^{20}$ = +40.6 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.88 [s, 9 H, C(C$H_3$)$_3$], 1.03 (t, *J* = 7.1 Hz, 3 H, C$H_3$CH$_2$), 1.30 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 1.74−1.99 (m, 2 H, CH$_2$), 2.70 (dd, *J* = 2.2, 9.8 Hz, 1 H, C*H*C=O), 3.52 (ddd, *J* = 2.2, 6.8, 8.6 Hz, 1 H, CHS), 3.96 (dq, *J* = 6.0, 9.8 Hz, 1 H, CHO), 4.91 (s, 1 H, OC*H*O), 7.01 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.22 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.39 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.50 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 12.78 (*C*H$_3$CH$_2$), 21.12 (*C*$H_3$CHO), 23.86 [C(*C*H$_3$)$_3$], 26.57 (CH$_2$), 35.12 [*C*(CH$_3$)$_3$], 49.18 (CHS), 51.21 (*C*HC=O), 72.99 (CHO), 108.0 (O*C*HO), 125.15 (C, Ar), 127.74, 128.12, 130.59, 133.44 (CH, Ar), 136.67 (C, Ar), 169.20 (C=O). − $C_{18}H_{25}BrO_3S$ (401.36): calcd. C 53.87, H 6.28, S 7.99, Br 19.91; found C 53.63, H 6.43, S 7.78, Br 19.84.

**(1′*R*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanylisobutyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2c):** Yield: 321 mg (77%). − $R_f$ = 0.44 (hexane/$Et_2O$, 4:1). − Colorless crystals. M.p. 125−126 °C. − $[\alpha]_D^{20}$ = +61.4 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.88 [s, 9 H, C(C$H_3$)$_3$], 0.98 and 1.02 [each d, *J* = 6.4 Hz, 2 × 3 H, CH(C$H_3$)$_2$], 1.37 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 1.88 [m, 1 H, C*H*(CH$_3$)$_2$], 2.98 (dd, *J* = 3.0, 9.0 Hz, 1 H, C*H*C=O), 3.74 (dd, *J* = 3.0, 10.5 Hz, 1 H, CHS), 4.15 (dq, *J* = 6.0, 9.0 Hz, 1 H, CHO), 5.0 (s, 1 H, OC*H*O), 6.96 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.20 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.45 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.51 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 21.33 and 21.63 [CH(*C*H$_3$)$_2$], 22.13 (*C*$H_3$CHO), 23.85 [C(*C*H$_3$)$_3$], 33.58 [*C*H(CH$_3$)$_2$], 34.97 [*C*(CH$_3$)$_3$], 51.04 (*C*HC=O), 58.74 (CHS), 73.25 (CHO), 107.17 (O*C*HO), 124.44 (C, Ar), 127.71, 128.14, 131.46, 133.03 (CH, Ar), 137.24 (C, Ar), 170.99 (C=O). − $C_{19}H_{27}BrO_3S$ (415.39): calcd. C 54.94, H 6.55, S 7.72, Br 19.24; found C 55.26, H 6.62, S 7.40, Br 19.04.

**(1′*S*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanylisobutyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (3c):** Yield: 283 mg (68%). − $R_f$ = 0.48 (hexane/$Et_2O$, 4:1). − Colorless oil. − $[\alpha]_D^{20}$ = +19.6 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.87 [s, 9 H, C(C$H_3$)$_3$], 1.05 and 1.12 [each d, *J* = 6.8 Hz, 2 × 3 H, CH(C$H_3$)$_2$], 1.25 (d, *J* = 6.0 Hz, 3 H, C$H_3$CHO), 2.35 [m, 1 H, C*H*(CH$_3$)$_2$], 2.80 (dd, *J* = 1.5, 10.1 Hz, 1 H, C*H*C=O), 3.06 (dd, *J* = 1.5, 10.5 Hz, 1 H, CHS), 3.85 (dq, *J* = 6.0, 10.1 Hz, 1 H, CHO), 4.96 (s, 1 H, OC*H*O), 6.97 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.21 (ddd, *J* = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.33 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.48 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 20.29 and 21.66 [CH(*C*H$_3$)$_2$], 22.14 (*C*$H_3$CHO), 23.91 [C(*C*H$_3$)$_3$], 32.06 [*C*H(CH$_3$)$_2$], 35.08 [*C*(CH$_3$)$_3$], 51.51 (*C*HC=O), 55.34 (CHS), 73.46 (CHO), 107.88 (O*C*HO), 124.40 (C, Ar), 127.28, 128.09, 129.78, 133.45 (CH, Ar), 138.37 (C, Ar), 168.73 (C=O). − $C_{19}H_{27}BrO_3S$ (415.39): calcd. C 54.94, H 6.55, S 7.72, Br 19.24; found C 54.73, H 6.75, S 7.52, Br 19.06.

**(1′*R*,2*R*,5*R*,6*R*)-5-{1′-[(2-Bromophenyl)sulfanyl]-3′-phenylpropyl}-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2d):** Yield: 396 mg (83%). − $R_f$ = 0.35 (hexane/$Et_2O$, 4:1). − Colorless crystals. M.p. 114−115 °C. − $[\alpha]_D^{20}$ = +11.9 (*c* = 1, $CHCl_3$). − $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.87 [s, 9 H, C(C$H_3$)$_3$], 1.28 (d, *J* = 6.4 Hz, 3 H,

C$H_3$CHO), 1.86−2.08 (m, 2 H, C$H_2$CH$_2$Ph), 2.55 (ddd, $J$ = 6.4, 9.0, 13.5 Hz, 1 H, CH$_2$C$H_2$Ph), 2.78 (dd, $J$ = 2.6, 9.0 Hz, 1 H, C$H$C=O), 2.82 (ddd, $J$ = 5.2, 9.0, 13.5 Hz, 1 H, CH$_2$C$H_2$Ph), 3.84 (ddd, $J$ = 2.6, 5.6, 8.6 Hz, 1 H, CHS), 4.08 (dq, $J$ = 6.0, 9.0 Hz, 1 H, CHO), 4.97 (s, 1 H, OC$H$O), 6.96−7.02 (m, 3 H, ArH), 7.08−7.20 (m, 4 H, ArH), 7.40 (dd, $J$ = 1.5, 7.9 Hz, 1 H, ArH), 7.48 (dd, $J$ = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 22.13 (*C*H$_3$CHO), 23.86 [C(*C*H$_3$)$_3$], 33.71 (CH$_2$*C*H$_2$Ph), 35.03 [*C*(CH$_3$)$_3$], 37.71 (*C*H$_2$CH$_2$Ph), 49.71 (CHS), 53.07 (*C*HC=O), 72.97 (CHO), 107.44 (O*C*HO), 126.08 (C, Ar), 126.25, 128.11, 128.43 (× 2), 128.48, 128.55 (× 2), 132.76, 133.21 (CH, Ar), 136.04, 140.57 (C, Ar), 169.84 (C=O). − $C_{24}H_{29}BrO_3S$ (477.46): calcd. C 60.37, H 6.12, S 6.71, Br 16.74; found C 60.05, H 6.16, S 6.86, Br 16.80.

**(1′*S*,2*R*,5*R*,6*R*)-5-{1′[(2-Bromophenyl)sufanyl]-3′-phenylpropyl}-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (3d):** Yield: 352 mg (74%). − $R_f$ = 0.42 (hexane/Et$_2$O, 4:1). − Colorless oil. − $[\alpha]_D^{20}$= +42.6 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.87 [s, 9 H, C(C$H_3$)$_3$], 1.21 (d, $J$ = 6.4 Hz, 3 H, C$H_3$CHO), 2.12 and 2.27 (each m, 2 × H, C$H_2$CH$_2$Ph), 2.65−2.85 (m, 2 H, CH$_2$C$H_2$Ph), 2.70 (dd, $J$ = 1.9, 9.8 Hz, 1 H, C$H$C=O), 3.52 (ddd, $J$ = 1.9, 6.4, 8.3 Hz, 1 H, CHS), 3.91 (dq, $J$ = 6.0, 9.8 Hz, 1 H, CHO), 4.88 (s, 1 H, OC$H$O), 6.98 (ddd, $J$ = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.05−7.23 (m, 7 H, ArH), 7.48 (dd, $J$ = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 20.95 (*C*H$_3$CHO), 23.90 [C(*C*H$_3$)$_3$], 33.75 (CH$_2$*C*H$_2$Ph), 35.02 (*C*H$_2$CH$_2$Ph), 35.16 [*C*(CH$_3$)$_3$], 49.53 (CHS), 51.49 (*C*HC=O), 73.14 (CHO), 108.07 (O*C*HO), 125.32 (C, Ar), 126.29, 127.91, 128.15, 128.50 (× 2), 128.55 (× 2), 130.79, 133.51 (CH, Ar), 136.41, 140.50 (C, Ar), 168.92 (C=O). − $C_{24}H_{29}BrO_3S$ (477.46): calcd. C 60.37, H 6.12, S 6.71, Br 16.74; found C 60.13, H 6.37, S 6.50, Br 16.59.

**(1′*S*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanyl(phenyl)methyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2e):** Yield: 368 mg (82%). − $R_f$ = 0.34 (hexane/Et$_2$O, 4:1). − Colorless crystals. M.p. 61−62 °C. − $[\alpha]_D^{20}$ = −70.2 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.81 (d, $J$ = 6.0 Hz, 3 H, C$H_3$CHO), 0.88 [s, 9 H, C(C$H_3$)$_3$], 3.03 (dd, $J$ = 3.7, 9.0 Hz, 1 H, C$H$C=O), 4.01 (dq, $J$ = 6.0, 9.0 Hz, 1 H, CHO), 4.86 (s, 1 H, OC$H$O), 4.99 (d, $J$ = 3.7 Hz, 1 H, CHS), 6.88−6.94 (m, 1 H, ArH), 6.97−7.08 (m, 2 H, ArH), 7.15−7.28 (m, 3 H, ArH), 7.42−7.45 (m, 3 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 21.24 (*C*H$_3$CHO), 23.85 [C(*C*H$_3$)$_3$], 35.02 [*C*(CH$_3$)$_3$], 52.75 (CHS), 55.45 (*C*HC=O), 73.09 (CHO), 107.54 (O*C*HO), 125.26 (C, Ar), 127.88, 128.02, 128.20 (× 2), 128.88 (× 2), 129.39, 131.39, 133.01 (CH, Ar), 135.88, 138.39 (C, Ar), 169.07 (C=O). − $C_{22}H_{25}BrO_3S$ (449.40): calcd. C 58.80, H 5.61, S 7.13, Br 17.78; found C 58.78, H 5.66, S 6.16, Br 17.76.

**(1′*R*,2*R*,5*R*,6*R*)-5-[1′-(2-Bromophenyl)sulfanyl(cyclohexyl)methyl]-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one (2f):** Yield: 271 mg (59%). − $R_f$ = 0.54 (hexane/Et$_2$O, 4:1). − Colorless crystals. M.p. 84−85 °C. − $[\alpha]_D^{20}$ = +47.7 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.72−0.77 (m, 1 H, cyclohexyl), 0.93 [s, 9 H, C(C$H_3$)$_3$], 1.05−1.24 (m, 4 H, cyclohexyl), 1.39 (d, $J$ = 6.0 Hz, 3 H, C$H_3$CHO), 1.46−1.56 (m, 1 H, cyclohexyl), 1.59−1.80 (m, 4 H, cyclohexyl), 2.18−2.22 (m, 1 H, cyclohexyl), 3.10 (dd, $J$ = 2.6, 9.0 Hz, 1 H, C$H$C=O), 3.83 (dd, $J$ = 2.6, 10.5 Hz, 1 H, CHS), 4.19 (dq, $J$ = 6.0, 9.0 Hz, 1 H, CHO), 5.07 (s, 1 H, OC$H$O), 7.0 (ddd, $J$ = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.25 (ddd, $J$ = 1.5, 7.9, 9.0 Hz, 1 H, ArH), 7.49 (dd, $J$ = 1.5, 7.9 Hz, 1 H, ArH), 7.55 (dd, $J$ = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 22.03 (*C*H$_3$CHO), 23.86 [C(*C*H$_3$)$_3$], 25.90, 25.96, 26.16, 31.42, 31.60 (CH$_2$, cyclohexyl), 34.96 [*C*(CH$_3$)$_3$], 42.43 (CH, cyclohexyl), 50.10 (*C*HC=O), 57.36 (CHS), 73.26 (CHO), 107.12 (O*C*HO), 124.20 (C, Ar), 127.53, 128.09, 131.18, 132.99 (CH, Ar), 137.35 (C, Ar), 171.10 (C=O). − $C_{22}H_{31}BrO_3S$ (455.45): calcd. C 58.02, H 6.86, S 7.04, Br 17.54; found C 58.18, H 6.97, S 6.88, Br 17.46.

**General Procedure for the Ring Transformation of Adducts 2 and 3:** A solution of the adduct **2** or **3** (1 mmol) in dry THF (30 mL) was cooled to −100 °C under an argon atmosphere. *n*BuLi (1.6 M in hexane, 0.88 mL, 1.4 mmol) was added rapidly carefully maintaining the reaction temperature below −90 °C. The reaction mixture was stirred at −100 °C for 2 h and then it was warmed slowly to −78 °C. Stirring was continued for a further 4 h before the reaction was quenched with a saturated $NH_4Cl$ solution (10 mL) and the mixture extracted with diethyl ether (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated to give a pale yellow oil, which was purified by flash chromatography (silica gel, *n*-hexane/Et$_2$O, 4:1 for **4** and 9:1 for **5**).

**(+)-(1′*R*,2*R*,3*R*)-3-(1′-Hydroxyethyl)-2-methylthiochroman-4-one (4a):** Yield: 169 mg (76%). − $R_f$ = 0.30 (hexane/Et$_2$O, 3:1). − Colorless crystals. M.p. 35−36 °C. − $[\alpha]_D^{20}$ = +81.9 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 1.24 (d, $J$ = 6.4 Hz, 3 H, C$H_3$CHO), 1.29 (d, $J$ = 7.1 Hz, 3 H, C$H_3$CHS), 2.97 (dd, $J$ = 3.7, 7.9 Hz, 1 H, C$H$C=O), 3.39 (dq, $J$ = 3.7, 7.1 Hz, 1 H, CHS), 3.81 (br s, 1 H, OH), 4.18 (dq, $J$ = 6.4, 7.9 Hz, 1 H, CHO), 7.10 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.15 (dd, $J$ = 1.1, 7.9, Hz, 1 H, ArH), 7.34 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.98 (dd, $J$ = 1.1, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 15.92 (*C*H$_3$CHS), 19.50 (*C*H$_3$CHO), 37.43 (CHS), 59.05 (*C*HC=O), 66.35 (CHO), 124.72, 127.84, 128.80 (CH, Ar), 130.34 (C, Ar), 134.09 (CH, Ar), 139.69 (C, Ar), 198.34 (C=O). − $C_{12}H_{14}O_2S$ (222.30): calcd. C 64.84, H 6.35, S 14.42; found C 64.85, H 6.65, S 14.18.

**(+)-(1′*R*,2*R*,3*R*)-2-Ethyl-3-(1′-hydroxyethyl)thiochroman-4-one (4b):** Yield: 173 mg (73%). − $R_f$ = 0.33 (hexane/Et$_2$O, 3:1). − Colorless oil. − $[\alpha]_D^{20}$ = +101.6 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.96 (t, $J$ = 7.1 Hz, C$H_3$CH$_2$), 1.23 (d, $J$ = 6.4 Hz, 3 H, C$H_3$CHO), 1.35−1.48 (m, 1 H, CH$_2$), 1.50−1.61 (m, 1 H, CH$_2$), 3.03 (dd, $J$ = 3.7, 7.5 Hz, 1 H, C$H$C=O), 3.09 (ddd, $J$ = 3.7, 6.8, 11.0 Hz, 1 H, CHS), 3.76 (br s, 1 H, OH), 4.27 (dq, $J$ = 6.4, 7.5 Hz, 1 H, CHO), 7.09 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.15 (dd, $J$ = 1.1, 7.9, Hz, 1 H, ArH), 7.33 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.97 (dd, $J$ = 1.1, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 13.08 (*C*H$_3$CH$_2$), 19.60 (*C*H$_3$CHO), 21.61 (CH$_2$), 45.81 (CHS), 59.24 (*C*HC=O), 66.21 (CHO), 124.72, 127.81, 128.74 (CH, Ar), 130.86 (C, Ar), 133.98 (CH, Ar), 139.79 (C, Ar), 198.20 (C=O). − $C_{13}H_{16}O_2S$ (236.33): calcd. C 66.07, H 6.82, S 13.57; found C 66.02, H 6.94, S 13.42.

**(+)-(1′*R*,2*R*,3*R*)-3-[1′-Hydroxyethyl]-2-isopropylthiochroman-4-one (4c):** Yield: 180 mg (72%). − $R_f$ = 0.35 (hexane/Et$_2$O, 3:1). − Colorless oil. − $[\alpha]_D^{20}$ = +149.6 ($c$ = 1, CHCl$_3$). − $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.78 and 0.94 [each d, $J$ = 6.8 Hz, 2 × 3 H, CH(C$H_3$)$_2$], 1.27 (d, $J$ = 6.4 Hz, 3 H, C$H_3$CHO), 2.05 [m, 1 H, C$H$(CH$_3$)$_2$], 3.02 (dd, $J$ = 3.7, 7.9 Hz, 1 H, C$H$C=O), 3.33 (dd, $J$ = 3.7, 11.6, Hz, 1 H, CHS), 3.70 (br s, 1 H, OH), 4.41 (dq, $J$ = 6.4, 7.9 Hz, 1 H, CHO), 7.06 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.17 (dd, $J$ = 1.1, 7.9, Hz, 1 H, ArH), 7.29 (ddd, $J$ = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.94 (dd, $J$ = 1.1, 7.9 Hz, 1 H, ArH). − $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ = 18.46 (*C*H$_3$CHO), 20.31 and 20.81 [CH(*C*H$_3$)$_2$], 29.55 [*C*H(CH$_3$)$_2$], 50.49 (CHS), 56.82 (*C*HC=O), 66.25 (CHO), 124.54, 126.71, 128.50 (CH, Ar), 131.34 (C, Ar), 133.56 (CH, Ar), 141.53 (C, Ar), 198.24 (C=O). − $C_{14}H_{18}O_2S$ (250.36): calcd. C 67.17, H 7.25, S 12.81; found C 67.11, H 7.48, S 12.68.

**(+)-(1′*R*,2*R*,3*R*)-3-[1′-Hydroxyethyl]-2-phenylethyl)thiochroman-4-one (4d):** Yield: 228 mg (73%). − $R_f$ = 0.34 (hexane/$Et_2O$, 3:1). − Colorless crystals. M.p. 67−68 °C. − $[\alpha]_D^{20}$ = +194.4 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.4 Hz, 3 H, C*H*$_3$CHO), 1.72−1.80 (m, 2 H, C*H*$_2$CH$_2$Ph), 2.56−2.66 (m, 2 H, CH$_2$C*H*$_2$Ph), 2.96 (dd, *J* = 3.7, 7.9 Hz, 1 H, C*H*C=O), 3.06 (ddd, *J* = 3.7, 5.6, 9.4 Hz, 1 H, CHS), 3.72 (br s, 1 H, OH), 4.15 (dq, *J* = 6.4, 7.9 Hz, 1 H, CHO), 6.97−7.13 (m, 4 H, ArH), 7.17−7.22 (m, 3 H, ArH), 7.33 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.96 (dd, *J* = 1.1, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 19.13 (*C*H$_3$CHO), 29.67 (*C*H$_2$CH$_2$Ph), 33.68 (CH$_2$*C*H$_2$Ph), 42.11 (CHS), 58.96 (*C*HC=O), 66.14 (CHO), 124.88, 126.38, 127.94, 128.55(× 2), 128.61 (× 2), 128.85 (CH, Ar), 130.83 (C, Ar), 134.09 (CH, Ar), 139.51, 140.26 (C, Ar), 198.10 (C=O). − $C_{19}H_{20}O_2S$ (312.43): calcd. C 73.04, H 6.45, S 10.26; found C 72.84, H 6.46, S 9.98.

**(+)-(1′*R*,2*S*,3*R*)-3-[1′-Hydroxyethyl]-2-phenylthiochroman-4-one (4e):** Yield: 199 mg (70%). − $R_f$ = 0.30 (hexane/$Et_2O$, 3:1). − Colorless crystals. M.p. 125−126 °C. − $[\alpha]_D^{20}$ = +211.4 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.14 (d, *J* = 6.8 Hz, 3 H, $CH_3$), 3.37 (dd, *J* = 3.8, 9.8 Hz, 1 H, C*H*C=O), 3.54 (br s, 1 H, OH), 3.82 (dq, *J* = 6.8, 9.8 Hz, 1 H, CHO), 4.56 (d, *J* = 3.8 Hz, 1 H, CHS), 7.10−7.18 (m, 2 H, ArH), 7.23−7.30 (m, 3 H, ArH), 7.33−7.38 (m, 3 H, ArH), 8.0 (dd, *J* = 1.5, 8.6 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 Hz, $CDCl_3$): δ = 19.09 ($CH_3$), 47.70 (CHS), 58.86 (*C*H$_2$C=O), 66.81 (CHO), 125.26, 126.94, 127.83 (× 2), 128.51, 129.07 (× 2), 129.39 (CH, Ar), 130.95 (C, Ar), 133.99 (CH, Ar), 137.33, 141.44 (C, Ar), 197.48 (C=O). − $C_{17}H_{16}O_2S$ (284.37): calcd. C 71.80, H 5.67, S 11.27; found C 71.77, H 5.78, S 11.51.

**(+)-(1′*R*,2*R*,3*R*)-2-Cyclohexyl-3-[1′-hydroxyethyl]thiochroman-4-one (4f):** Yield: 226 mg (78%). − $R_f$ = 0.38 (hexane/$Et_2O$, 3:1). − Colorless crystals. M.p. 92−93 °C. − $[\alpha]_D^{20}$ = +178.8 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.87−1.03(m, 3 H, cyclohexyl), 1.13−1.19 (m, 1 H, cyclohexyl), 1.26 (d, *J* = 6.4 Hz, 3 H, $CH_3$), 1.35−1.54 (m, 4 H, cyclohexyl), 1.65−1.69 (m, 3 H, cyclohexyl), 3.0 (dd, *J* = 3.7, 7.6 Hz, 1 H, C*H*C=O), 3.29 (dd, *J* = 3.7, 11.2 Hz, 1 H, CHS), 3.82 (br s, 1 H, OH), 4.39 (dq, *J* = 6.4, 7.6 Hz, 1 H, CHO), 7.06 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.17 (dd, *J* = 1.5, 7.9, Hz, 1 H, ArH), 7.30 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.94 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 20.36 ($CH_3$), 25.71, 25.92 (× 2), 26.16, 31.53 ($CH_2$, cyclohexyl), 39.42 (CH, cyclohexyl), 49.80 (CHS), 57.52 (*C*H$_2$C=O), 66.26 (CHO), 124.50, 126.72, 128.50 (CH, Ar), 131.36 (C, Ar), 133.55 (CH, Ar), 141.43 (C, Ar), 198.19 (C=O). − $C_{17}H_{22}O_2S$ (290.42): calcd. C 70.31, H 7.64, S 11.04; found C 70.28, H 7.95, S 10.84.

**(−)-(2*S*)-2-Methyl-2,3-thiochroman-4-one (5a):** Data for the racemic **5a**[5,6,9] and (2*R*)-**5a**[1] have been reported earlier. Yield: 135 mg (76%). − $R_f$ = 0.43 (hexane/$Et_2O$, 6:1). − Colorless oil. − $[\alpha]_D^{20}$ = −200.5 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.37 (d, *J* = 6.8 Hz, 3 H, $CH_3$), 2.69 (dd, *J* = 11.3, 16.2 Hz, 1 H, C*H*$_2$C=O), 2.95 (dd, *J* = 3.0, 16.2 Hz, 1 H, C*H*$_2$C=O), 3.56 (ddq, *J* = 3.0, 6.8, 11.3 Hz, 1 H, CHS), 7.09 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.18 (dd, *J* = 1.5, 7.9, Hz, 1 H, ArH), 7.31 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 8.02 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR: (75.5 Hz, $CDCl_3$): δ = 20.45 ($CH_3$), 36.43 (CHS), 47.82 (*C*H$_2$C=O), 124.91, 127.48, 128.96 (CH, Ar), 130.36 (C, Ar), 133.47 (CH, Ar), 141.79 (C, Ar), 194.66 (C=O). − $C_{10}H_{10}OS$ (178.25): calcd. C 66.38, H 5.65, S 17.99; found C 66.21, H 5.69, S 17.82.

**(−)-(2*S*)-2-Ethylthiochroman-4-one (5b):** Data for the racemic **5b** have been reported earlier.[9] − Yield: 144 mg (75%). − $R_f$ = 0.50 (hexane/$Et_2O$, 6:1). − Colorless oil. − $[\alpha]_D^{20}$ = −205.7 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 1.69 (m, 2 H, $CH_3$C*H*$_2$), 2.73 (dd, *J* = 10.9, 16.2 Hz, 1 H, C*H*$_2$C=O), 2.98 (dd, *J* = 3.0, 16.2 Hz, 1 H, C*H*$_2$C=O), 3.36 (ddt, *J* = 3.0, 7.1, 10.9 Hz, 1 H, CHS), 7.09 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.20 (dd, *J* = 1.5, 7.9, Hz, 1 H, ArH), 7.31 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 8.0 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 11.35 ($CH_3$), 27.62 ($CH_3$*C*H$_2$), 43.28 (CHS), 45.90 (*C*H$_2$C=O), 124.83, 127.64, 128.88 (CH, Ar), 130.64 (C, Ar), 133.44 (CH, Ar), 141.64 (C, Ar), 194.75 (C=O). − $C_{11}H_{12}OS$ (192.28): calcd. C 68.71, H 6.29, S 16.67; found C 68.76, H 6.49, S 16.42.

**(−)-(2*S*)-2-Isopropylthiochroman-4-one (5c):** Yield: 161 mg (78%). − $R_f$ = 0.56 (hexane/$Et_2O$, 6:1). − Colorless oil. − $[\alpha]_D^{20}$ = −191.5 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.99 and 1.01 [each d, *J* = 6.8 Hz, 2 × 3 H, CH(C*H*$_3$)$_2$], 1.88 [m, 1 H, C*H*(CH$_3$)$_2$], 2.77 (dd, *J* = 12.0, 16.2 Hz, 1 H, C*H*$_2$C=O), 2.94 (dd, *J* = 3.0, 16.2 Hz, 1 H, C*H*$_2$C=O), 3.30 (ddd, *J* = 3.0, 6.4, 12.0 Hz, 1 H, CHS), 7.07 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.20 (dd, *J* = 1.5, 7.9, Hz, 1 H, ArH), 7.29 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.99 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 19.60 and 19.79 [CH(*C*H$_3$)$_2$], 31.99 [*C*H(CH$_3$)$_2$], 43.76 (*C*H$_2$C=O), 48.46 (CHS), 124.71, 127.69, 128.84 (CH, Ar), 130.59 (C, Ar), 133.35 (CH, Ar), 142.07 (C, Ar), 195.22 (C=O). − $C_{12}H_{14}OS$ (206.30): calcd. C 69.86, H 6.84, S 15.54; found C 69.66, H 7.06, S 15.32.

**(−)- (2*S*)-2-Phenethylthiochroman-4-one (5d):** Yield: 201 mg (75%). − $R_f$ = 0.42 (hexane/$Et_2O$, 6:1). − Colorless oil. − $[\alpha]_D^{20}$ = −178 (*c* = 1, $CHCl_3$). − $^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.89−1.97 (m, 2 H, C*H*$_2$CH$_2$Ph), 2.58−2.77 (m, 3 H, CH$_2$C*H*$_2$Ph and C*H*$_2$C=O), 2.95 (dd, *J* = 3.0, 16.2 Hz, 1 H, C*H*$_2$C=O), 3.35 (m, 1 H, CHS), 7.02−7.11 (m, 4 H, ArH), 7.15−7.20 (m, 3 H, ArH), 7.27 (ddd, *J* = 1.1, 7.1, 8.3 Hz, 1 H, ArH), 7.97 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH). − $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 32.76 (CH$_2$*C*H$_2$Ph), 35.94 (*C*H$_2$CH$_2$Ph), 40.69 (CHS), 46.10 (*C*H$_2$C=O), 124.99, 126.29, 127.73, 128.44 (× 2), 128.60 (× 2), 128.93 (CH, Ar), 130.66 (C, Ar), 133.54 (CH, Ar), 140.52, 141.23 (C, Ar), 194.37 (C=O). − $C_{17}H_{16}OS$ (268.37): calcd. C 76.08, H 6.01, S 11.95; found C 75.81, H 6.28, S 11.72.

**X-ray Crystal Analysis of 2b:**[20] A single crystal of **2b** with the dimensions 0.80 × 0.80 × 0.40 mm was measured on a STOE Ipds diffractometer using Mo-$K_\alpha$ radiation (λ = 0.71073 Å). Crystal data: $C_{18}H_{25}BrO_3S$, *M* = 401.36, orthorhombic space group $P2_12_12_1$, *a* = 7.3753 (9) Å, *b* = 10.617 (3) Å, *c* = 24.180 (3) Å, α = 90°, β = 90°, γ = 90°, *V* = 1893.4 (6) Å$^3$, *Z* = 5, $D_c$ = 1.408 g/cm$^3$, *F* (000) = 832, μ(Mo-$K_\alpha$) = 2.293 mm$^{-1}$. At 180 (2) K in the range 1.68 < θ < 25.23°, 2276 reflections were measured, 1990 were unique ($R_{int}$ = 0.0143). The final residuals were $wR_{2(all)}$ = 0.0661, $R_{1(all)}$ = 0.0400 and $R_{1(obs)}$ = 0.0286. The maximum and minimum peaks in the final difference map were 0.330 and −0.243 e Å$^{-3}$, respectively.

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[20] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-147766. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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