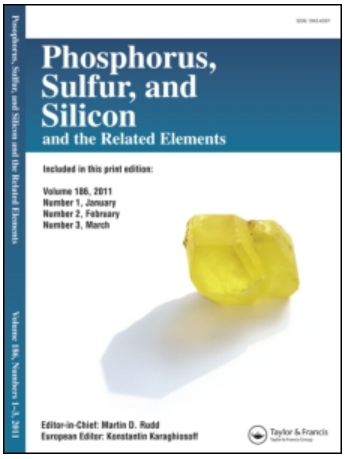

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Novel Chiral, Sulfur-Containing Heteroarotinoids with Liquid Crystal Properties

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NOVEL CHIRAL, SULFUR-CONTAINING HETEROAROTINOIDS WITH LIQUID CRYSTAL PROPERTIES

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*Synthetic methods were developed to prepare ethyl (E)-4-[2-(3, 4-dihydro-2-n-octyl-1-oxy-2H-1-benzothio-pyran-6-yl)-1-propenyl]-benzoate (**1**) and ethyl (E)-4-[2-(3,4-dihydro-2-n-octyl-2H-1-benzothiopyran-6-yl)-1-propenyl]benzoate (**10**). These are the first examples of heteroarotinoids which possess properties of liquid crystals. The properties were evaluated using differential scanning calorimetry and by use of polarizing micrography. Both displayed textures which are typical of a smectic or cholesteric phase.*

Keywords: Chiral liquid crystals; DSC data; ethyl (*E*)-4-[2-(3,4-dihydro-2-*n*-octyl-1-oxy-2*H*-1-benzothiopyran-6-yl)-1-propenyl]benzoate; ethyl (*E*)-4-[2-(3,4-dihydro-2-*n*-octyl-2*H*-1-benzothiopyran-6-yl)-1-propenyl]benzoate; NMR data

In working to develop a methodology to obtain heteroarotinoids for chemotherapeutic applications,[1] it occurred to us that properly designed members of this heterocyclic family might well exhibit liquid crystal (LC) properties. Calimitic liquid crystalline compounds have a rigid core and flexible ends that enable the molecules to order in one or two dimensions at temperatures above the freezing point. The heteroarotinoids have rigid stilbene units in the center and can be substituted with flexible ends. Moreover, chiral units can be incorporated into heteroarotinoid structures. Some of the most useful applications of liquid crystals, such as cholesteric thermochromic devices, fast-switching

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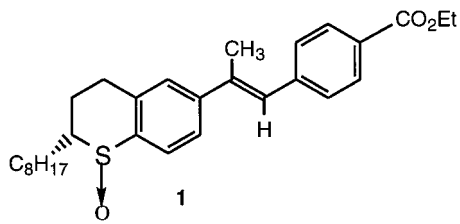
ferroelectric light valves, and active matrix ferroelectric LC displays, are due to chirality.[2] The synthesis of ferroelectric liquid crystals (FLCs) has been of interest since the discovery of bistable, fast-switching, electrooptic light valves.[2] Lengths of terminal chains are important parameters in LC formation.[3] The net polarization of a molecule is markedly affected by the strength of the lateral dipoles associated with an optically active center.[3,4] Many FLCs contain a chiral center at the terminus of a molecule, but this is somewhat undesirable since at such a position the chiral center is free to rotate independent of the highly polarizable central core with the delocalized π electrons. Thus, the contribution of the core to the dipole associated with the chiral center is reduced. Restriction of rotation of the chiral center with respect to the rest of the compound could increase the strength of the spontaneous polarization.[2]

RESULTS AND DISCUSSION

We have constructed a sulfur-containing heteroarotinoid systems **1** and have investigated its LC properties using differential scanning calorimetry (DSC) and optical microscopy with polarized light, the latter being utilized to characterize mesophases.[3] Sulfoxide **1**, as well as the precursor sulfide, exhibited the focal conic structure typical of a smetic or cholesteric meso-phase. The synthesis of **1** is outlined (Scheme 1), being initiated from **2**. A modified Sharpless oxidation of the sulfur atom in **2** led to **3** (82%) as a light yellow oil. Alkylation of the ring holding the sulfoxide group, via deprotonation of the alpha position with LDA, proved difficult but led to the new sulfoxide **4** (40%). Deoxygenation of the sulfur atom proceeded smoothly with NaI in TFAA to give **5** (95%) as an oil. Acetylation of the aryl ring with acetic anhydride in CS_2:H_3CNO_2 produced ketone **6** in high yield (quantitative, after chromatography). Reduction of the carbonyl group in **6** with $LiAlH_4$ as a suspension in dry ether gave alcohol **7** as an oil which was used at once to prepare the phosphonium salt **8** (quantitative) as illustrated.



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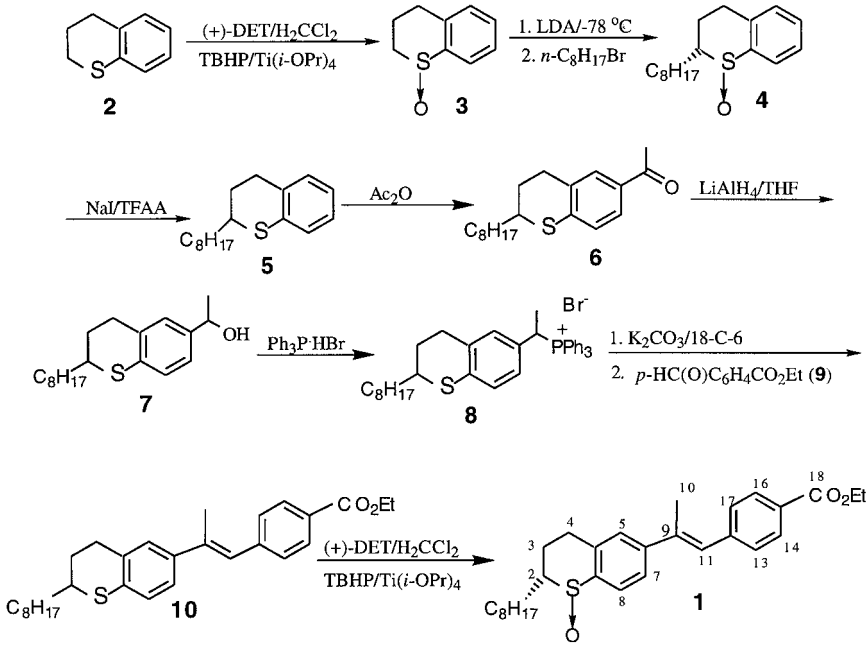

SCHEME 1

Potassium carbonate in the presence of 18-C-6 generated the corresponding anion from **8** which was then treated with ethyl 4-formylbenzoate (**9**) in H_2CCl_2 to yield **10** (79%). Oxidation of **10** with a modified Sharpless approach gave chiral sulfoxide **1** in moderate yield after repeated recrystallization.

The absolute configurations at S-1 and C-2 have not been determined since all attempts have proven futile to obtain adequate crystals of **1** (or of **10**) for an x-ray diffraction study. The stereochemistry of **1** depends on the formation of the α-sulfinyl carbanion from **10** via kinetic acidity or thermodynamic acidity.[5] Using THF and $-20^{\circ}C$ suggests that the former parameter can be neglected.[5] The alpha carbanion should have sufficient time to form the most stable configuration prior to reaction with the electrophile.[5,6] In view of the large size of the complex in the modified Sharpless oxidation, attack from the least hindered side is expected to occur.[7] The argument is supported by the increased ee% in the α-alkylation of sulfoxides as the alkyl group enlarged.[8] Although the ^1H NMR signal for H-8 was used with $Eu(dpm)_3$ to estimate the cis:trans ratio of isomers in **4**,[9] the complex nature of the ^1H NMR signals for **1** prevented such an analysis, particularly in the region of aryl protons. However, the narrow melting range of **1** (and of the precursor

TABLE I Phase Transition Temperatures and Enthalpies (cal/g) for **1** and **10** From DSC

Transition Temperatures and Transition Enthalpies for **1**	
Heating:	333.7 (0.05) → 346.5 (1.09) → 374.9 (0.84) → 384.5 (2.02) → 390.3 (0.13)
Cooling:	366 (−3.34) → 337 (−0.34) → 328 (−0.72)
Transition Temperatures and Transition Enthalpies for **10**	
Heating:	338.8 (0.22) → 356.7 (10.83)
Cooling:	341.5 (−0.54)

10) implies the presence of only one compound which we tentatively label as the trans isomer, as illustrated, or its enantiomeric form.

LC phase transitions were observed for **1** by a polarizing microscopy and by DSC (Table I). Slightly different heating curves (Figure 1) were noted for the first and second heating of **1**. In contrast, the cooling curves essentially remained unchanged. No mesophase was detected during the first heating of **1**, but the phase observed on cooling of **1** (Figure 1) did exhibit a focal conic or spherulitic texture of a mesophase or crystal (Figure 2).[10] This is not unusual. The small (−0.5 cal/g) exotherm at 341.5 K on cooling and the large (10.8 cal/g) exotherm on heating of **1** suggest that the transition on cooling to 341.5 K forms a metastable phase which undergoes a transition to a more stable LC or crystalline phase while at <310 K between cooling and heating experiments. Since

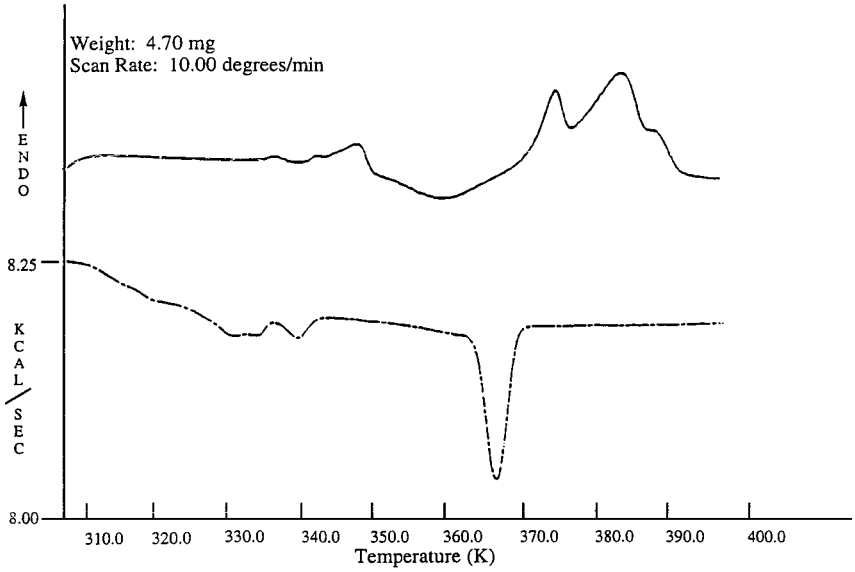

FIGURE 1 DSC thermogram of **1** after cycling.

FIGURE 2 Polarizing micrograph of **1** at 339 K, cooled from the isotropic liquid at 2°C/min.

crystalline **1** contains some nonstoichiometric amount of water, the loss of such may account for part of the transition.

A similar examination of **10** (Table I), the precursor of **1**, revealed fewer phase transitions (Figure 3). Although the first and second

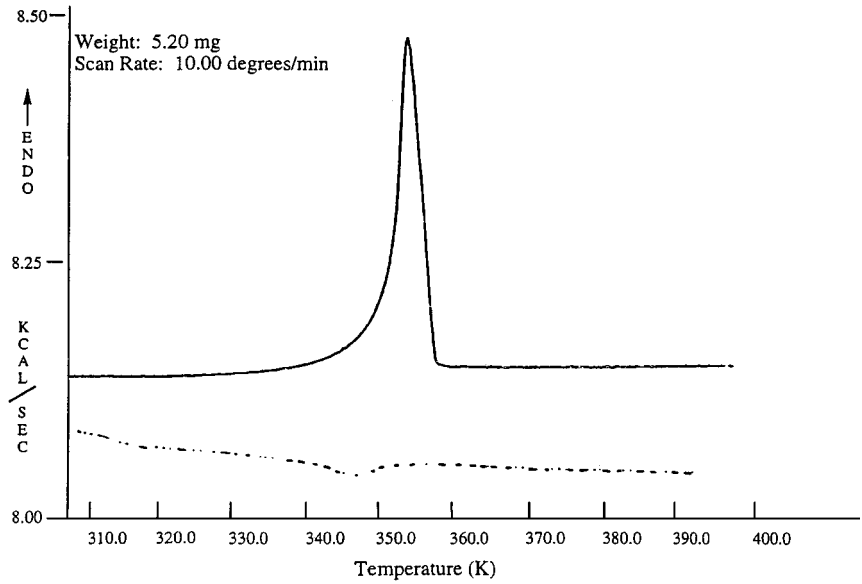

FIGURE 3 DSC thermogram of **10** after cycling.

heating curves varied slightly, the cooling curves for **10** were essentially identical (Figure 3). Under a polarizing microscope, **10**, upon cooling, exhibited a focal conic texture (Figure 4), typical of a smectic or cholesteric phase.[11,12]

In summary, we have obtained two heteroarotinoids with LC properties. The field is virtually unexplored, but the work herein may provide a background for future development.

EXPERIMENTAL

General Methods

All reactions were performed under N_2 with magnetic stirring unless otherwise specified. IR spectra were recorded on a Perkin-Elmer 681 spectrophotometer as films or from KBr pellets. NMR spectral data were obtained on solutions ($DCCl_3$) using a Varian XL-300 spectrometer with ^1H and ^{13}C data being taken at 299.99 MHz and 75.4 MHz, respectively, and on a Varian XL-400 NMR BB spectrometer with ^1H and ^{13}C data being taken at 399.99 MHz and 100.5 MHz respectively. References were to TMS in δ values or ppm respectively. Mass spectral data were recorded on a VG analytical instrument, model ZAB-2SE. Melting points were determined on a Fischer-Johns melting point

FIGURE 4 Polarizing micrograph of **10** at 337 K, cooled from the isotropic liquid at 2°C/min.

apparatus and a Thomas-Hoover melting point apparatus and were uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. A standard check was made with a glucose solution which had $\alpha = 2.582^\circ$ [l = 10 dm, c = 4.92 g/100 mL, H_2O] and $[\alpha] = +52.5^\circ$ [lit.[13]

$[\alpha] = +52.5^\circ$]. Differential Scanning Calorimetry (DSC) measurements were performed with a Perkin-Elmer DSC-2 instrument equipped with a TADs 3600 data station. The phase transitions and mesomorphic textures were observed with a Nikon OPTIPHOT-POL microscope with crossed polarizer and equipped with a Instec hot stage (Boulder, CO). RT = room temperature. Reagent grade solvents were used without further purification. Chromatography was performed using the Chromatotron (Harrison Research, model 7924) with silica gel (pF 254 containing gypsum, EM Science) plates (2 mm and 4 mm thick). All elemental analyses were performed by Galbraith Laboratories, Knoxville, TN 37921.

*Ethyl (***E***)-4-[2-(3,4-Dihydro-2-*n*-octyl-1-oxy-2*H*-1-benzothiopyran-6-yl)-1-propenyl]benzoate (1)*

Water (41 μL) was introduced in a single portion to a stirred mixture of Ti(O-*i*-Pr)$_4$ (3.7 mL, 2.2 mmol) and (+)-diethyl *L*-tartrate (0.46 g, 4.5 mmol) in H_2CCl_2 (50 mL) (N_2). The mixture was stirred to a homogeneous solution. To this was added sulfide **10** (1.02 g, 2.2 mmol) (dropwise-addition funnel). To the cooled (-20°C, dry ice-CCl_4) mixture was introduced dropwise a solution of TBHP (0.19 g, 2.2 mmol) in H_2CCl_2 (0.7 mL). Stirring was continued at -20°C (4 h), and 4 mL of water was then added dropwise (10 min). Stirring was continued at -20°C (1 h) and then at RT (1 h). A white gel was filtered off (filter aid used), and the filtrate was dried (Na_2SO_4) and evaporated to give sulfoxide **1** (light yellow solid). Recrystallized (ethanol) product was a white **1** (0.2 g, 30%); m.p. 122–124°C. ^{1}H NMR ($DCCl_3$, 300 MHz) δ 0.9 [t, $^3J_{HCCH} = 7.3$ Hz, 3 H, $(CH_2)_7CH_3$], 1.15 1.1–2.0 [m, 18 H, $(CH_2)_7CH_3$, OCH_2CH_3 and H(3)], 2.2–2.3 [s, 3 H, H(10)], 2.4–2.6 [m, 1 H, H(3)], 2.7–3.2, [m, 3 H, H(2) and H(4)], 4.3 [q, $^3J_{HCCH} = 7.4$ Hz, 2 H, H(19)], 6.8 [s, 1 H, H(11)], 7.25–8.05 [m, 7 H, Ar-H]. ^{13}C NMR ($DCCl_3$, 75 MHz) ppm aliphatic-C: 16.85, 17.11, 20.33, 25.40, 28.57, 28.65, 29.36, 30.50, 31.95, 32.05, 32.17, 34.57, 62.19, 63.75; ArC and vinylic C: 127.12, 128.12, 129.59, 131.61, 131.75, 1131.79, 132.30, 139.30, 140.32, 140.71, 144.83, 150.27; 168.80 [C(18)]. $[\alpha] = +29.9^\circ$ (acetone). Anal. Calcd for $C_{29}H_{38}O_3S$: C, 74.64; H, 8.21; S, 6.86. Anal. Calcd for $C_{29}H_{38}O_3S{\cdot}0.5\ H_2O$: C; 73.22; H, 8.24. Found: C, 73.09; H, 8.14.

*3,4-Dihydro-2*H*-1-benzothiopyran (2)*

In a standard setup chemicals were added in the following order of thiochroman-4-one[14] (3.0 g, 18 mmol), toluene (75 ml), water (120 mL), conc HCl (60 mL), and the Clemmenson-Martin[15] amalgam (50 g, prepared by shaking for 5 min a mixture of mossy Zn [50 g, 765 g atom], mercuric chloride [5 g, 18 mmol], conc HCl [2.5 mL], and water [75 mL.]) The heterogeneous mixture was boiled and stirred for 72 h, adding

20-mL portions of conc HCl at intervals of about 6 h to maintain a total volume of 500 mL. The mixture was allowed to cool to RT (1 h) and was filtered. The aqueous layer was extracted (toluene, 2 × 50 mL). Combined organic layers were separated and washed with saturated $NaHCO_3$ (2 × 50 mL), water (2 × 50 mL), and saturated NaCl (50 mL). Then the solution was dried ($MgSO_4$). Evaporation of the solvent gave **2** as a yellow oil (2.7 g, 98%) which was used directly to prepare sulfoxide **3**. IR (neat) 3020 (Ar-H), 2940 (alkyl-H) cm^{-1}; ^1H NMR ($DCCl_3$, 400 MHz) δ 2.1 [quintet, $^3J_{HCCH} = 6.1$ Hz, 2 H, H(3)], 2.8 [t, $^3J_{HCCH} = 6.2$ Hz, 2 H, H(4)], 3.0 [t, $^3J_{HCCH} = 6.0$ Hz, 2 H, H(2)], 7.05–7.2 [m, 4 H, ArH]; ^{13}C NMR ($DCCl_3$, 100 MHz) ppm 22.75 [C(3)], 27.46 [C(4)], 29.56 [C(2)]; ArC: 123.79, 126.28, 126.45, 129.87, 132.77, 133.73. Only two properties have been reported for **2**:[9] b.p. 81.5–82.5°C/1.2 mm; ^1H NMR ($DCCl_3$) δ 1.90, 2.92, and 6.90.

*3,4-Dihydro-2*H*-1-benzothiopyran-1-oxide (3)*

A solution of Ti(O-*i*-Pr)$_4$ (43 mL, 40.6 g, 143 mmol) and (+)-diethyl *L*-tartrate (49 mL, 58.9 g, 286 mmol) was dissolved in H_2CCl_2 (250 mL). Water (2.6 mL) was introduced, and the resulting mixture was stirred (20 min) to a homogeneous solution. To this solution was added in a single portion sulfide **2** (21.45 g, 143 mmol). The mixture was cooled to −20°C (dry ice, CCl_4), and a 3.1 *M* solution of TBHP (180 mmol) in H_2CCl_2 (51 mL) was introduced dropwise (5 min). Stirring was continued for 4 h at −20°C, and 25 mL of water was then added dropwise (10 min). Stirring was continued at −20°C for another hour and then for 1 h at RT. A white gel formed and was filtered off (filter aid used), and the filtrate was dried (Na_2SO_4) and evaporated. The resulting mixture was separated on silica gel (ethyl acetate:hexane, 85:15, 100% MeOH). The fraction from methanol was evaporated to yield thiochroman-S-oxide **3** (19 g, 82%) as a yellow oil. ^1H NMR ($DCCl_3$, 300 MHz) δ 2.0–2.2 [m, 1 H, H(3)], 2.4–2.7 [m, 1 H, H(3)], 2.8–3.3 [m, 4 H, H(2) and H(4)], 7.2–7.9 [m, 4 H, ArH]; ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 14.12 [C(3)], 28.43 [C(4)], 46.37 [C(2)]; ArC: 127.42, 130.51, 130.81, 131.65, 136.01, 138.04. The optical rotation of **3** was taken in cells (l cm × 10 cm) on a Perkin-Elmer 241 polarimeter. At 26°C $[\alpha]_D = -114.15°$ (acetone). Our procedure was much easier to employ than that reported.[9] The only recorded properties[9] of **3** are: b.p. 117–120°C/0.04 mm, ^1H NMR δ 1.09–3.50 and 7.20–7.90 as well as a specific rotation $[\alpha]_D = -21.8°$ (acetone) at 25°C.[16]

*3,4-Dihydro-2-*n*-octyl-2*H*-1-benzothiopyran-1-oxide (4)*

To a cooled (−78°C, dry ice-acetone) solution of diisopropylamine (4.8 mL, 34 mmol) in THF (50 mL) was added dropwise *n*-butyllithium

(22 mL, 1.6 *M* in hexanes) over a period of 1 h. The resulting solution was stirred at RT for 1 h. After the solution was again cooled to −78°C, sulfoxide **3** (5.72 g, 30 mmol) in THF (50 mL) was added (15 min). The solution was then allowed to warm to −30°C (1 h) and again cooled to −78°C. Then *n*-octyl bromide (5.4 mL, 34 mmol) was added via syringe in a single portion. Stirring was continued for another 12 h after which time 5% hydrochloric acid (50 mL) was added, and the solution was extracted with $HCCl_3$ (3 × 50 mL). Combined extracts were washed with water (1 × 50 mL), $NaHCO_3$ (2 × 50 mL), water (50 mL), and brine (50 mL). When dried (Na_2SO_4), the solution was concentrated to give a brown oil which was separated on a silica gel column (hexane:$HCCl_3$:ethyl acetate = 4:1:1). The second fraction gave the alkylated product **3** (R = *n*-octyl, 3.2 g, 40%) as a light yellow oil. ^{1}H NMR ($DCCl_3$, 300 MHz) δ 0.9 [t, $^3J_{HCCH}$ = 0.7 Hz, 3 H, CH_3], 1.2–1.4 [bs, 12 H, (CH_2)$_6$$CH_3$], 1.4–1.7 [m, 2 H, $CH_2(CH_2)_6$], 1.85 [m, 1 H, H(3)], 2.45 [m, 1 H, H(3)], 2.8–3.1 [m, 3 H, H(2) and H(4)], 7.1–7.8 [m, 4 H, ArH]; ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 14.06 [C(3)]; aliphatic-C: 20.75, 22.54, 26.32, 26.53, 28.31, 29.08, 29.25, 29.40, 31.71; 57.99 [C(2)]; ArC: 127.2, 129.18, 129.46, 130.67, 135.47, 140.0. The only recorded[9] property of **3** is: ^{1}H NMR ($DCCl_3$) δ 0.88, 1.1–3.10, and 7.24–8.10.

*3,4-Dihydro-2-*n*-octyl-2*H*-1-benzothiopyran (5)*

To a stirred mixture of the sulfoxide **4** (1.7 g, 6 mmol) and NaI (2.2 g, 15 mmol) in acetone at 0°C (ice-water bath) was slowly added trifluoroacetic anhydride (2.5 ml, 18 mmol) in acetone. The reaction mixture was stirred (1 h) at 0°C. Acetone was evaporated, water (50 mL) was added, and the mixture was extracted with ether (3 × 25 mL). The ether extracts were washed with water (50 mL), saturated $Na_2S_2O_3$ (3 × 50 mL), water (50 mL) and saturated NaCl (50 mL). After drying ($MgSO_4$), the solvent was evaporated. The red oil obtained was passed through a short silica gel column with hexane as eluent. Hexane was evaporated to give sulfide **5** (1.5 g, 95%) as a light yellow oil which was used directly to make **6**. ^{1}H NMR ($DCCl_3$, 300 MHz) δ 0.88 [t, $^3J_{HCCH}$ = 0.7 Hz, 3 H, CH_3], 1.2–1.5 [bs, 12 H, (CH_2)$_6$$CH_3$], 1.6–1.8 [m, 3 H, $CH_2(CH_2)_6$ and H(3)], 2.2–2.3 [m, 1 H, H(3)], 2.75–2.9 [m, 2 H, H(4)], 3.25–3.57 [m, 1 H, H(2)], 6.9–7.1 [m, 4 H, ArH]; ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 13.67 [CH_3]; aliphatic-C: 22.22, 22.37, 25.40, 26.70, 28.88, 29.13, 29.27, 31.43, 33.92, 37.21; ArC: 123.14, 123,31, 125.89, 125.92, 126.05, 129.44. Only the proton NMR spectrum has been recorded[9] for **5**: ^{1}H NMR ($DCCl_3$) δ 1.03, 1.43, 1.8–2.62, 2.80–3.10, 3.15–3.57, and 6.97–7.3.

*6-Acetyl-2-*n*-octylthiochroman (6)*

Acetic anhydride (0.5 mL, 6 mmol) was added to a stirred suspension of $AlCl_3$ (1.4 g, 9 mmol) in nitromethane [50 mL, 0°C (ice-water bath]. To the above stirred mixture was added (5 min) a solution of 2-octylthiochroman **5** (1.5 g, 6 mmol) in CS_2:nitromethane (1:5, 25 mL). The solution was stirred at 0°C for 1 h and then allowed to warm to RT while stirring was continued for 48 h. The solution was then cooled to 0°C (ice-water bath) and finally quenched with water (50 mL, 15 min). The aqueous layer was extracted with $HCCl_3$ (4 × 50 mL). Combined organic extracts were washed with saturated $NaHCO_3$ (3 × 50 mL), water (2 × 50 mL) and saturated NaCl (1 × 50 mL). After drying (Na_2SO_4), the solution was evaporated to a red oil which was separated on a silica gel column (hexane:ether = 20:80) to give ketone **6** (quantitative) as an orange oil. IR (neat) 1680 (C=O) cm^{-1}; ^1H NMR ($DCCl_3$, 300 MHz) δ 0.9 [t, $^3J_{HCCH}$ = 0.7 Hz, 3 H, CH_3], 1.35–1.45 [m 14 H, $(CH_2)_7CH_3$], 2.0 [m, 1 H, H(3)], 2.3 [m, 1 H, H(3)], 2.7 [s, 3 H, $CH_3C(O)$], 2.9–3.3 [m, 3 H, H(2) and H(4)], 7.2–7.7 [m, 3 H, ArH]; ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 14.07 [CH_3]; aliphatic-C: 22.62, 22.90, 25.11, 27.99, 29.37, 29.42, 29.51, 29.62, 31.82, 34.19, 37.67; ArC: 126.29, 126.34, 129.56, 132.67, 137.75, 139.89; 197.42 [C(O)]. The ketone **6** was used at once to make **7**.

*2-*n*-Octylthiochroman-6-ethanol (7)*

A solution of ketone **6** (1.5 g, 6 mmol) in dry ether (15 mL) was added (10 min) to a stirred suspension of $LiAlH_4$ (0.38 g, 9 mmol) in dry ether (10 mL). This mixture was heated at reflux for 6 h. It was then cooled to 0°C (ice-water bath), and ethyl acetate (25 mL) was slowly added (~0.5 h) followed by 5% HCl (10 mL, 10 min). The mixture was stirred for 5 min. The aqueous layer was extracted with ether (3 × 25 mL). Combined organic layers were washed with saturated $NaHCO_3$ (2 × 25 mL), water (25 mL), and saturated NaCl (25 mL). After drying ($MgSO_4$), the solvent was evaporated to give an orange oil which was separated on a silica gel column (hexane:ether = 1:1) to give alcohol **7** (1.2 g, 80%) as a yellow oil and which was used immediately to make **8**. IR (neat) 3350 (O–H) cm^{-1}; ^1H NMR ($DCCl_3$, 300 MHz) δ 0.9 [t, $^3J_{HCCH}$ = 0.7 Hz, 3 H, CH_3], 1.1–1.6 [m 17 H, $(CH_2)_7CH_3$ and $CH_3C(OH)$], 1.75–1.95 [m, 2 H, OH and H(3)], 2.0–2.2 [m, 1 H, H(3)], 2.8 [m, 2 H, H(4)], 3.1–3.15 [m, 1 H, H(2)], 4.65–4.8 [m, 1 H, $CH_3CH(OH$], 6.9–7.1 [m, 3 H, ArH]; ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 14.07 [CH_3]; aliphatic-C: 22.62, 22.70, 25.68, 25.70, 27.11, 29.27, 29.55, 29.64, 31.83, 34.34, 37.75; 70.05 [$CH_3C(OH)$]; ArC: 123.540, 123.62, 126.50, 126.92, 126.98, 139.08, 141.01.

1-[(2-n-Octylthiochroman-6-yl)ethyl]-triphenylphosphonium Bromide (8)

A solution of alcohol **7** (4.4 g, 14 mmol) and triphenylphosphonium hydrobromide (5.0 g, 14 mmol) in H_2CCl_2 (50 mL) was stirred at RT (24 h). The solvent was then evaporated, and the oil obtained was triturated (RT) with dry ether (50 mL) to obtain **8** as a white solid (9.0 g, 98%); m.p. 67–68°C. ^{1}H NMR ($DCCl_3$, 400 MHz) δ 0.9 [t, $^3J_{HCCH}$ = 6.6 Hz, 3 H, CH_3], 1.1–1.6 [m 14 H, $(CH_2)_7CH_3$], 1.7–1.95 [m, 4 H, CH_3CH and H(3)], 2.0–2.2 [m, 1 H, H(3)], 2.5–2.7 [m, 1 H, H(4)], 2.8 [m, 1 H, H(4)], 3.0–3.1 [m, 1 H, H(2)], 6.55 [m, 1 H, CH_3CH], 6.9–7.1 [m, 3 H, ArH], 7.3–7.7 [m, 15 H]; ^{13}C NMR ($DCCl_3$, 100 MHz) ppm 14.15 [CH_3]; aliphatic-C: 16.89, 17.29, 22.68, 26.74, 26.95, 29.36, 29.44, 29.50, 29.74, 31.9, 34.12; 37.55 [CH_3C(H)]; ArC: 117.42, 117.52, 118.24, 118.33, 126.88, 128.55, 128.67, 129.26, 129.36, 130.04, 130.08, 130.12, 130.16, 130.21, 130.24, 132.11, 132.21, 133.82, 133.97, 134.64, 134.67, 134.73, 134.76, 134.82. Salt **8** was used directly to prepare **10**.

Ethyl 4-Formylbenzoate (9)

A solution of ethyl *p*-toluate (5.8 g, 35 mmol) in freshly distilled acetic anhydride (50 mL) and glacial acetic acid (50 mL) was cooled to 0°C (ice-salt water bath). To the stirred solution was added conc H_2SO_4 (2.5 mL). To this solution was added (1 h) slowly CrO_3(10.6 g, 100 mmol). Care was taken to maintain the temperature below 5°C during the addition. When the addition was complete, a dark green reaction mixture remained which was stirred (2 h) at 0°C. Decomposition was effected by slowly pouring the mixture onto crushed ice (250 g) and then adding (very slowly) 250 mL of cold water. A green-colored solution formed, and this was extracted with ether (4 × 50 mL). Combined ether extracts were washed with water (2 × 50 mL), 5% Na_2CO_3 (4 × 50 mL), and brine (50 mL). When dried (Na_2SO_4), the solution was evaporated to obtain the diacetate (4.7 g, 48%) as a yellow oil. To the diacetate was added water (30 mL), 95% ethanol (30 mL), and conc H_2SO_4 (2 mL). The resulting solution was boiled for 6 h. After allowing to cool to RT (30 min), the solution was treated with water (20 mL), and the aqueous phase was extracted with $HCCl_3$ (3 × 50 mL). The combined extracts were washed with water (1 × 50 mL), 10% $NaHCO_3$ (2 × 50 mL), water (1 × 50 mL), and saturated NaCl (50 mL). When dried (Na_2SO_4), the solution was evaporated to give **9** (2.3 g, 44%) as a colorless oil which appeared to be reactive and was thus used immediately in the Wittig reaction. Properties of **9** are: IR (neat) 1740 (C=O) cm^{-1}; ^{1}H NMR ($DCCl_3$, 100 MHz) δ 1.4 (t, J = 7.5 Hz, 3 H, CH_3), 4.4 (q, J = 7.5 Hz, 2 H, CH_2), 7.9–8.2 (m, 4 H, Ar-H), 10.1 (s, 1 H, CHO). ^{13}C NMR ($DCCl_3$, 75 MHz) ppm 14.15 [CH_3], 61.48 [CH_2]; ArC: 129.36, 130.02, 135.33,

138.97, 166.91 [C(O)OEt], 191 .57 [C(O)H]. The b.p. (143°C/13 mm) of **9** has been reported.[17]

*Ethyl (***E***)-4-[2-(3,4-Dihydro-2-***n***-octyl-2***H***-1-benzothiopyran-6-yl)-1-propenyl]benzoate (10)*

To a boiling mixture of phosphonium salt **8** (2.0 g, 3 mmol), K_2CO_3 (0.4 g, 3 mmol) and 18-C-6 (30 mg), in H_2CCl_2 (15 mL) was added ethyl 4-formylbenzoate (**9**, 0.5 g, 3 mmol) in H_2CCl_2 (10 mL) in a single portion. The mixture was boiled for 12 h and was then concentrated to yield an orange oil which was treated with hexane (150 mL). A suspension formed and was filtered. The filtrate was washed with saturated NaCl (50 mL), dried (Na_2SO_4), and concentrated to give a yellow oil which was separated on a silica gel column (hexane:ethylacetate = 1:1) to give the sulfide **10** (1.1 g, 79%) as a white solid; m.p. 72–73°C. IR (neat) 1750 cm^{-1} (C=O); ^1H NMR ($DCCl_3$, 400 MHz) δ 0.95 [t, J = 7.5 Hz, 3 H, $(CH_2)_7CH_3$], 1.1–1.7 [m, 17 H, $(CH_2)_7CH_3$ and OCH_2CH_3], 2.8–2.95 [m, 1 H, H(3)], 2.15–2.3 [m, 4 H, H(3) and H(10)], 2.8–2.9 [m, 2 H, H(4)], 3.1–3.2 [m, 1 H, H(2)], 4.3 [q, J = 7.5 Hz, 2 H, OCH_2CH_3], 6.8 [s, 1 H, H(11)], 7.0–8.1 [m, 7 H, ArH]; ^{13}C NMR ($DCCl_3$, 100 MHz) ppm 14.05 [$(CH_2)_3CH_3$]; aliphatic-C: 14.31, 17.46, 22.61, 25.55, 27.08, 29.26, 29.54, 29.63, 31.87, 36.83, 37.83, 42.31; 60.79 [C(19)]; ArC and vinylic C: 124.03, 125.63, 126.34, 127.39, 128.93, 129.36, 132.08, 148.01, 149.10, 149.32, 143.8; 168.82 [C(18)]. Mass spectral (EI) data: Calcd for $C_{29}H_{38}O_2S$ *m/z* ($M^{+\cdot}$): 450.2593; Found: 450.2595. Anal. Calcd for $C_{29}H_{38}O_2S$: C, 77.29; H, 8.51; Found: C, 77.61; H, 8.31.

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