Ring Contractions of Thiochroman-4-ones and Thiochromen-4-ones

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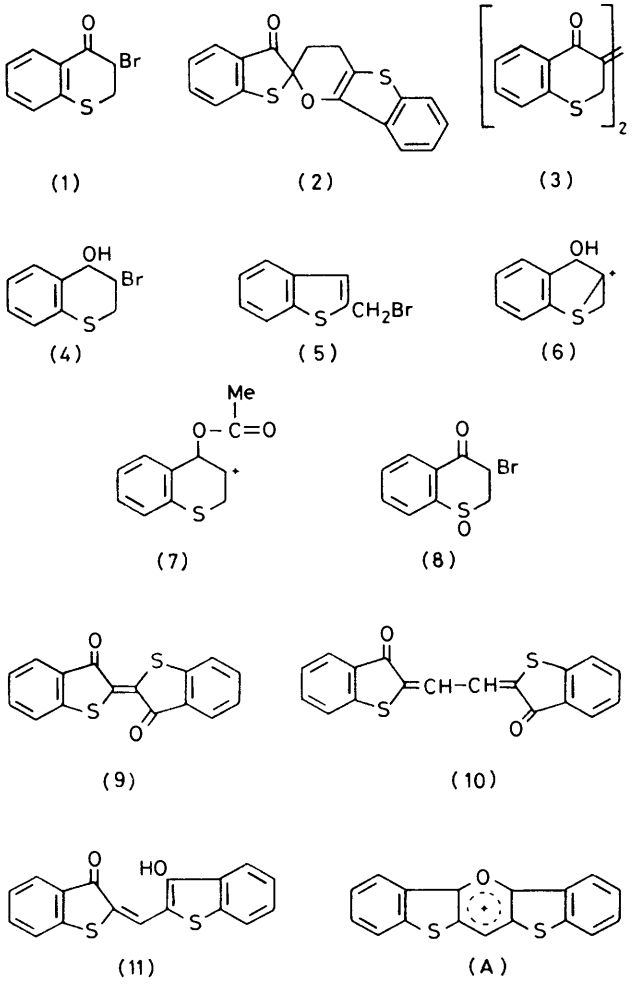
3-Bromothiochroman-4-one and its *S*-oxide undergo ring contraction on heating, especially in the presence of sodium acetate, to give mixtures which include thioindigo (9) and the ethanediylidenethioindigo (10). Brominated 2,2-dimethylthiochroman-4-one reacts on silica gel to form thioindigo, thioindirubin, and the bis(benzothieno)pyran (17).

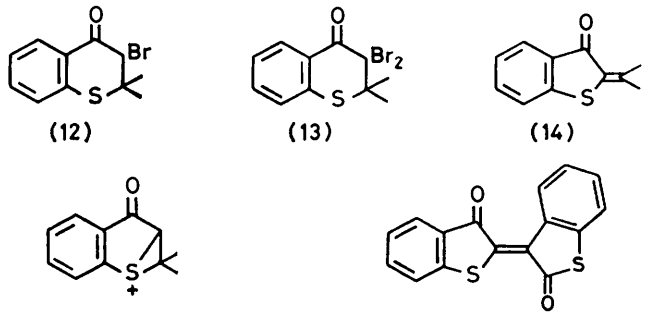
Bromination of thiochromanone gives a number of products, including 2,3-dibromothiochromen-4-one *S*-oxide which, on heating with sodium acetate in acetic acid, is converted efficiently into thioindigo. The mechanism of this reaction is investigated.

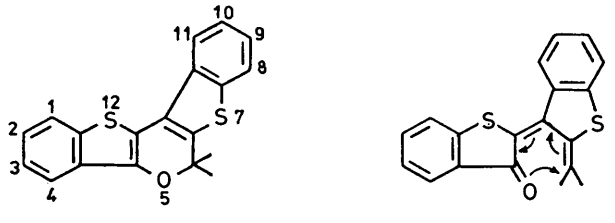
WE showed [1] recently that one of the products of the reaction of 3-bromothiochroman-4-one (1) with sodium acetate is the spiroketone (2) and not the diketone (3), as formerly thought.[2] This demonstrates the tendency of thiochroman-4-ones (and related compounds [3,4]) to undergo thermal ring-contraction, a tendency which is specially evident in compounds brominated at C-3. The C-3 bromine permits the formation of a thi-iranium cation which then rearranges. Such a rearrangement was first reported by Hofmann and Salbeck [5] in the ring contraction, in hot dioxan, of the bromothiochromanol (4) to the benzothiophen derivative (5). Thus, compound (4) proceeds to the thiophen (5) by way of the intermediate (6), and it is noteworthy that the acetate of compound (4) remained unchanged on heating in dioxan, implying that the cation (7) is stabilised by the adjacent acetate group rather than by the sulphur atom. We now describe a number of ring contractions of thiochromen-4-one and thiochroman-4-one derivatives.



Like the thiochroman-4-one (1), the corresponding sulphoxide (8) also undergoes ring contraction readily. Compound (8) was best prepared from compound (1) by oxidation with *m*-chloroperbenzoic acid, as bromination of thiochroman-4-one *S*-oxide leads only to deoxygenation of the sulphoxide.[6] The bromosulphoxide (8) turned red on melting and the melt contained ' vinylenethioindigo ' (10). On brief heating in dimethylformamide, compound (8) formed a complex mixture from which we could isolate thioindigo (9) (10%), ' vinylenethioindigo ' (10) (8%), and 3-bromothiochromen-4-one (8%). On heating with sodium acetate in acetic acid an even more complex mixture was formed which was not investigated, apart from the isolation of the relatively insoluble compound (11) in 18% yield. This was originally obtained [7] by heating 3-hydroxybenzothiophen-2-carbaldehyde in ethanol with dilute sulphuric acid, and by condensing 3-hydroxybenzothiophen-2-carbaldehyde with thioindoxyl; the formation of these precursors from compound (8) can be envisaged. It is of interest that the base peak in the mass spectrum is at *m/e* 293 (M^+ — HO), which can be attributed to the ion (A).

As both compounds (1) and (8) tend to give a number of products on ring contraction, attention was turned to the dimethyl homologue (12) in the hope of obtaining a simpler product mixture. However, compound (12) was not obtained in the pure form. Bromination of 2,2-dimethylthiochroman-4-one proceeded smoothly to give, essentially, the product (12), containing a little of the dibromo-compound (13) and starting material. When this mixture was heated briefly with sodium acetate in acetic acid it gave mainly the enone (14) (65%) presumably by way of the thi-iranium cation (15). However, attempts to purify the bromothiochromanone (12) by silica gel chromatography were unsuccessful because





a; X = Cl
b; X = Br

reactions occurred on the silica, again involving ring contractions.

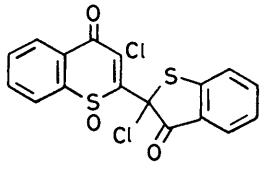
When the bromination mixture was adsorbed onto silica and left for some time, examination (t.l.c.) after 4 h showed that extensive reaction had occurred, the main product being the enone (14). After 7 days the silica became black and contained a very complex mixture from which we could isolate thioindigo (9) (17%), its isomer thioindirubin (16) (8%), and the pentacyclic pyran (17) (20%). A similar mixture, in different proportions, was obtained from the dibromothiochromanone (13) (purified by crystallisation) under the same conditions. The pyran (17) has a benzothiophen-type u.v. spectrum, the ^{1}H n.m.r. spectrum consists of CMe_2 and aromatic signals only, while in the mass spectrum the base peak is at *m/e* 307 (M^+ — Me), with major fragments at 190 and 175 corresponding to losses of a benzothiophen moiety from both M^+ and M^+ — Me.

In the formation of compounds (9), (16), and (17) from the thiochromanones (12) and (13) it is not certain how far the reactions proceed on silica gel before elution and work-up, but judging by the intense colour developed it seems likely that thioindigo (9), at least, is formed in the solid support. Bearing in mind that water is always present in silica gel and that there was probably some hydrogen bromide in the bromination mixture, it can be suggested that thioindigo is formed from compound (12) by way of the cation (15), which reacts with water followed by a retro-aldol reaction. This would give thioindoxyl and hence thioindigo by oxidation. A similar sequence starting from compound (13) would lead to 2-bromothioindoxyl from which thioindigo could also be derived. Alternatively, hydrolysis of 2-bromothioindoxyl and oxidation would form thionaphthenequinone, a precursor of thioindirubin (16) by condensation with thioindoxyl. The pyran (17) probably arises as shown from compound (18), the condensation product of the enone (14) with thioindoxyl.

While working with thiochroman-4-one derivatives we have noticed, on occasions,[8] the formation of minor amounts of thioindigo (9). In particular, during attempts to tetrabrominate the parent compound using bromine (4 mol) and sodium acetate (8 mol) in boiling acetic acid, thioindigo was obtained in 10% yield which could be increased to >20% by addition of a little water. It is obvious that the first step in this reaction must be bromination, one or more of the initial products being subsequently converted into thioindigo. Possible intermediate compounds are 3-bromo- and 3,3-dibromothiochroman-4-one, and thiochromen-4-one and when these were treated with appropriate amounts of bromine and sodium acetate under the same conditions thioindigo was again obtained in yields of 12, 4, and 0.5%, respectively. More useful information was obtained when the original bromination of thiochroman-4-one was repeated, the reaction being stopped as soon as all the bromine was consumed. As the reaction mixture was cooled, a mixture of bromo-compounds separated which were identified as 2,3-dibromothiochromen-4-one and its *S*-oxide (19b), and 3,3-dibromothiochroman-4-one *S*-oxide. The key compound was 2,3-dibromothiochromen-4-one *S*-oxide because when that was refluxed in acetic acid with sodium acetate thioindigo was obtained in 81% yield.[9] Neither of the other compounds gave thioindigo under these conditions, and the reaction failed with the *S*-oxide (19b) in the absence of acetate.

As the dibromo-compound (19b) is not readily accessible further work was carried out using the dichloro-analogue (19a) which was easily obtained by reaction of thiochromanone *S*-oxide with an excess of chlorine to give the tetrachloro-derivative (20) followed by heating with sodium iodide in acetone. Surprisingly, there is no significant deoxygenation during the chlorination (*cf.* the bromination of thiochromanone *S*-oxide, described above). The dichloro *S*-oxide (19a) gave thioindigo in 80% yield on heating with sodium acetate in acetic acid for 15 min. Clearly, in the conversion of (19a) into thioindigo (9) there are many steps and, to study this further, the reaction was carried out in dry acetonitrile with silver acetate by stirring overnight in the cold. Under these conditions, with 1 and 2 mol of silver acetate the yields of thioindigo were 29 and 54%, respectively; using 2 mol of sodium benzoate the yield was 52% (the 29% yield does not allow for unchanged starting material). When the cold reactions were monitored by t.l.c. traces of colourless compounds could be detected,

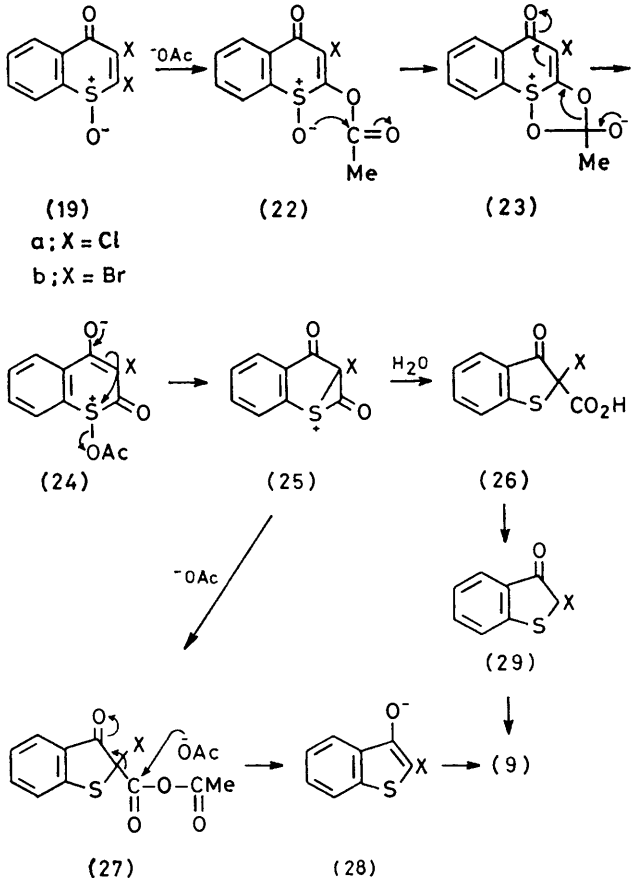
but all attempts to isolate these, under mild conditions, led to thioindigo except on two occasions when we were able to isolate another compound in trace amounts. It had the formula $C_{17}H_8Cl_2O_3S_2$, and, on the basis of its mass spectrum, structure (21) (or the 2,3-isomer) seems



(21)

likely. This compound, which is stable, is evidently not involved in the route to thioindigo. No intermediates on the main pathway could be isolated and the reaction proceeded equally well in the dark or in the presence of cyclohexene (added as a carbene trap).

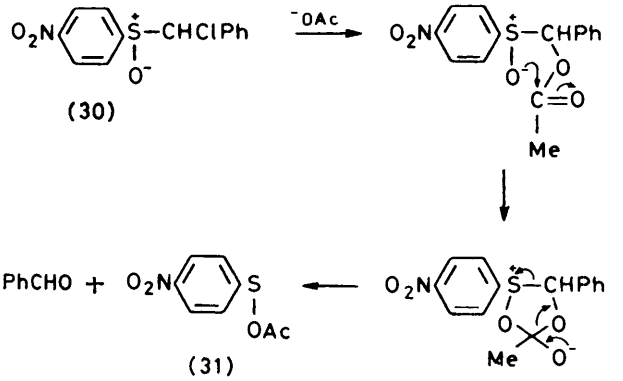
Scheme 1 is consistent with these observations. Nucleophilic displacement of halogen at C-2 gives the



SCHEME 1 X = Br or Cl

acetate (22) which can rearrange to the *S*-acetate (24) by way of the ortho-ester (23). Intramolecular displacement of acetate from compound (24) removes the original (but essential) *S*-oxide to form a reactive thi-iranium cation (25) which will react with any available nucleophile. In the hot acetic acid reactions this could be water which would give the β-keto-acid (26) and hence 2-halogenothioindoxyl which is known [10] to yield thioindigo in the presence of acetate. The evolution of carbon dioxide was confirmed. The alternative nucleophile is acetate and the only one available in the dry acetonitrile reaction. This would give the mixed anhydride (27) which, on reaction with a second mol of acetate, would collapse to form the enolate (28) (and diacetyl carbonate), and hence thioindigo. The less likely attack by acetate on the other anhydride carbonyl of compound (27) would produce acetic anhydride and the anion of compound (26).

The acyl migration (22) ⟶ (24) between adjacent oxygens is similar to glycerol monoester rearrangements,[11] but has not been observed before in sulphoxides. Another sulphoxide example is provided in Scheme 2.



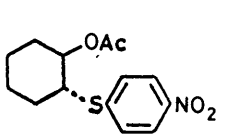
SCHEME 2

Heating the α-chlorosulphoxide (30) with sodium acetate in refluxing acetic acid gave benzaldehyde in 72% yield. The *p*-nitrophenylsulphenyl acetate (31), said to be stable at −20 °C,[12] was not observed. However, by repeating the reaction on a steam-bath in the presence of cyclohexene it was possible to trap compound (31) as its adduct (32) in low yield.

In principle, it should be possible to initiate the reactions in Scheme 1 starting from the 2-acetoxy-3-halogenothiochromen-4-one (33) which might be oxidised with a peracid to form the sulphoxide (22). However, efforts to obtain the acetate (33a) as a model compound were unsuccessful. The ' parent ' compound, 2-hydroxythiochromen-4-one, is tautomeric with 4-hydroxythiocoumarin (34b) which is reported [13] to give exclusively the 4-*O*-acetate on acetylation. Acetylation in cold pyridine gave a crystalline compound containing nitrogen (not pursued), and at least three other compounds which turned pink during p.l.c. on silica gel. The red compound was thioindigo. Heating 3-bromo-4-hydroxythiocoumarin (34a) with sodium acetate in acetic acid also gave thioindigo in small amounts.

We also attempted to test Scheme 1 starting with 2-chloro-3-methylthiochromen-4-one *S*-oxide (35) which should react with acetate to give either 2-methylthio-

indoxyl (29; X = Me) or the dimer (36). Reaction of 3-methylthiochromanone with an excess of chlorine gave a mixture which included the dichloro-derivative (37), but no trichloro-compound [*cf.* compound (20)]. Dehydrochlorination of compound (37) with various bases



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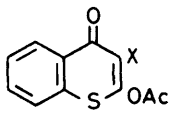
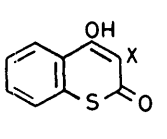
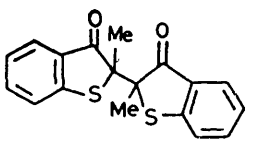


(33)
a; X = H



(34)
a; X = Br
b; X = H

(35)



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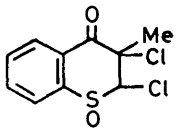

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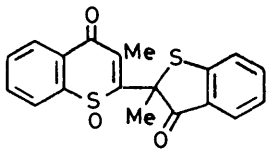
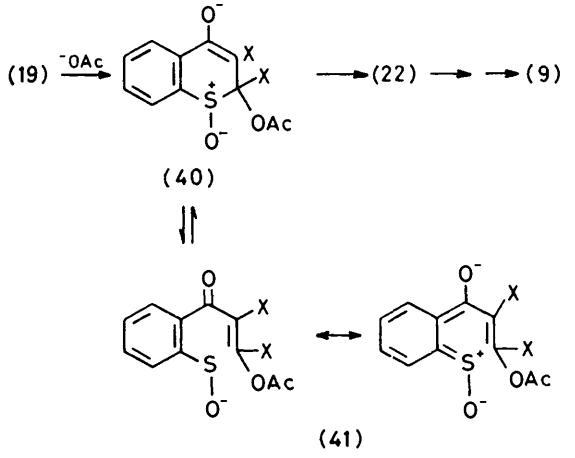


(39)

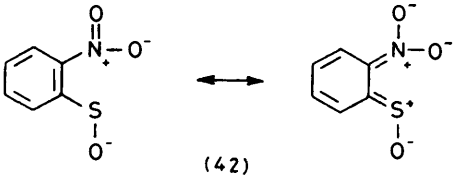
(sodium acetate, sodium methoxide, and lithium di-isopropylamide) did not yield compound (35) and the attempted preparation of compound (35) by chlorination of 3-methylthiochromanone *S*-oxide gave 2-chloro-3-methylthiochromen-4-one *S*-dioxide (38). Consequently, the dichloro-sulphoxide (37) was heated with an



SCHEME 3

excess (3 mol) of sodium acetate in acetic acid (or acetonitrile) in order to form compound (35) *in situ*, which should then react further with acetate, according to Scheme 1. However, the only product isolated was the unsymmetrical dimer (39) which is an analogue of compound (31).

An interesting feature of the conversion of 2,3-dichlorothiochromen-4-one *S*-oxide into thioindigo in cold acetonitrile is the appearance of a bright blue colour ($\lambda_{max.}$ 600 nm) after *ca.* 5 min, which persists for *ca.* 10 min and then disappears. We attribute this colour to the formation of the sulphenate anion (41) by analogy with the *o*-nitrosulphenate anion (42) ($\lambda_{max.}$ 588 nm).[14] The first intermediate (40) can either lose a chloride ion to form compound (22) or break the C–S bond to give compound (41) (Scheme 3). The colour is transient because compound (41) is in equilibrium with the sulphoxide (40) which is consumed as thioindigo formation proceeds. An attempt to trap the blue sulphenate as its



(42)

methyl ester by addition of methyl fluorosulphonate resulted in immediate decolourisation, but the only compound isolated was 2,3-dichlorothiochromen-4-one.

EXPERIMENTAL

N.m.r. spectra were measured for solutions in deuteriochloroform, and i.r. spectra for KBr discs unless otherwise stated. Merck Kieselgel 100 (70—230 mesh) was used for dry column chromatography and GF_{254} for p.l.c. Known compounds were identified by direct comparison with authentic samples unless indicated otherwise.

Preparation of Thiochroman-4-ones and Thiochromen-4-ones.—Thiochroman-4-one,[15] 3-methyl-[16] and 2,2-dimethylthiochroman-4-one,[17] and 3-bromo-[2] and 3,3-dibromothiochroman-4-one [15] were made by literature methods.

Thiochroman-4-one S-Oxide.—*m*-Chloroperbenzoic acid (85%, 10.15 g) in chloroform (100 ml) was added, as drops, during 1 h to thiochromanone (8.20 g) in chloroform (100 ml). After filtration the solution was washed successively with aqueous sodium hydrogencarbonate and water, dried, and evaporated. The residue was chromatographed on a column of dry silica in chloroform–ethyl acetate (4 : 1) to give an oil which slowly crystallised. The *sulphoxide* formed needles, m.p. 47—50 °C (from carbon tetrachloride) (7.14 g, 79%) (Found: C, 60.1; H, 4.7; S, 17.6. $C_9H_8O_2S$ requires C, 60.0; H, 4.5; S, 17.8%); $\nu_{max.}$ 1 685 cm^{-1}; δ 8.08 (1 H, m, ArH), 7.67 (3 H, m, ArH), 3.44 (3 H, m), and 2.90 (1 H, m); *m/e* 180 (M^+, 5%), 164 (11), 152 (100), and 136 (35).

3-Bromothiochroman-4-one S-Oxide (8).—*m*-Chloroperbenzoic acid (0.26 g) in chloroform (10 ml) was added, as drops, to a stirred solution of 3-bromothiochromanone (0.36 g) in chloroform (25 ml) in 20 min. After being stirred for a further 30 min the solution was washed with aqueous sodium hydrogencarbonate, dried, and evaporated. The residue crystallised from methanol to give the S-*oxide* (8) as needles, m.p. 160—161 °C (lit.,[18] 159—160 °C) (0.36 g, 88%) (Found: C, 41.9; H, 2.6; Br, 30.4; S, 12.4. Calc. for $C_9H_7BrO_2S$: C, 41.9; H, 2.7; Br, 30.6; S, 12.4%); $\nu_{max.}$ 1 692 cm^{-1}; *m/e* 260 (M^+, 0.9%), 258 (M^+, 0.9), 179 (32), 162 (16), 152 (100), 136 (63), 120 (5), 108 (16), and 104 (10).

2,3-*Dichlorothiochromen*-3-*one*. (*With* Dr. R. M. Christie).—Thiochromanone (6.56 g) was dissolved in acetic acid (250 ml) containing chlorine (14.2 g), and left in a stoppered flask in the dark for 14 d. The solution was poured into water and the precipitate was crystallised from ethanol to give 2,2,3,3-*tetrachlorothiochroman*-4-*one* as prisms, m.p. 96.5—98 °C (2.75 g, 27%) (Found: C, 35.9; H, 1.4; Cl, 46.9; S, 10.6. $C_9H_4Cl_4OS$ requires C, 35.8; H, 1.3; Cl, 47.0; S, 10.6%); $\nu_{max.}$ 1 705 cm^{-1}; δ 8.30 (1 H, m, ArH) and 7.43 (3 H, m, ArH); *m/e* 300 (M^+, 5%), 265 (11), 230 (28), 202 (16), 195 (5), 136 (100), and 108 (25); correct Cl isotope clusters. The tetrachloro-compound (15.1 g) was refluxed in acetone (250 ml) with sodium iodide (8.25 g) for 2 h. The mixture was reduced to 50 ml, diluted with water, and extracted with diethyl ether to give 2,3-*dichlorothiochromen* 4-*one* as needles, m.p. 171—172 °C (from ethanol) (7.03 g, 61%) (Found: C, 46.8; H, 1.8; Cl, 30.8; S, 13.5. $C_9H_4Cl_2OS$ requires C, 46.8; H, 1.7; Cl, 30.7; S, 13.9%); $\nu_{max.}$ 1 635 cm^{-1}; δ 8.45 (1 H, m, ArH) and 7.50 (3 H, m, ArH); *m/e* 234 (M^+, 9%), 232 (56), 230 (94), 206 (5), 204 (28), 202 (45), 197 (7), 195 (20), 169 (5), 167 (22), 136 (100), and 108 (28).

2,3-*Dichlorothiochromen*-4-*one* S-*Oxide* (19a).—An excess of chlorine (9.2 g) was passed into a solution of thiochromanone *S*-oxide (2 g) in acetic acid (100 ml). The flask was stoppered. After 4 d the solution was poured into ice–water to precipitate 2,2,3,3-*tetrachlorothiochroman*-4-*one* S-*oxide* (20) which crystallised from light petroleum (b.p. 80—100 °C) as needles, m.p. 130—133 °C (3.25 g, 92%) (Found: C, 33.7; H, 1.3; Cl, 44.4; S, 9.9. $C_9H_4Cl_4O_2S$ requires C, 34.0; H, 1.3; Cl, 44.6; S, 10.1%); $\nu_{max.}$ 1 710 cm^{-1}; δ 8.33 (1 H, d, *J* 8 Hz, ArH) and 7.85 (3 H, m, ArH); *m/e* 316 (M^+, 0.3%), 281 (0.9), 230 (3), 183 (13), 152 (100), 136 (13), 108 (25), and 104 (13); correct Cl isotope clusters. The tetrachloro-compound (31.8 g) and sodium iodide (30.0 g) were refluxed in acetone (700 ml) for 3 h. The solution was concentrated to 200 ml and the product, which was deposited when the mixture was cooled, was collected and washed with cold acetone and water. It crystallised from methanol to give the *dichloro* S-*oxide* (19a) as pale yellow needles, m.p. 203—204 °C (13.5 g, 55%) (Found: C, 43.8; H, 1.7; Cl, 28.5; S, 12.7. $C_9H_4Cl_2O_2S$ requires C, 43.8; H, 1.6; Cl, 28.7; S, 13.0%); $\nu_{max.}$ 1 670 cm^{-1}; δ 8.30 (1 H, d, *J* 8 Hz, ArH) and 7.87 (3 H, m, ArH); *m/e* 246 (M^+, 3 peaks 0.4%), 230 (5.5), 211 (1.5), 185 (28), 183 (100), 163 (20), 155 (13), 152 (13), 136 (14), 108 (8), and 104 (9).

3-*Bromo*-4-*hydroxythiocoumarin* (34a).—To 4-hydroxythiocoumarin [19] (634 mg) in acetic acid (10 ml) was added, as drops, a solution of bromine (0.18 ml) in acetic acid (5 ml). The mixture was warmed to 50 °C and allowed to cool. The product was collected and recrystallised from aqueous methanol as *needles*, m.p. 179 °C (700 mg, 77%) (Found: C, 41.9; H, 2.0; Br, 31.3; S, 12.6%; M^+, 255.9195. $C_9H_5{}^{79}BrSO_2$ requires C, 42.0; H, 1.95; Br, 31.1; S, 12.5%; *M*, 255.9193); $\nu_{max.}$ 3 280, 1 605, and 1 581 cm^{-1}; *m/e* 258 (M^+, 90%), 256 (M^+, 90), 230 (35), 228 (35), 177 (100), 149 (5), 137 (50), 136 (67), 121 (40), 120 (32), and 109 (22).

Reactions of 3-*Bromothiochroman*-4-*one* S-*Oxide* (8).—(*a*) 3-Bromothiochroman-4-one *S*-oxide (8) (0.2 g) in dimethylformamide (5 ml) was refluxed for 2 min and then evaporated to dryness under reduced pressure. T.l.c. showed that the residue was a complex mixture. P.l.c. in chloroform gave (i) thioindigo (9) as red needles, m.p. >300 °C (from acetic acid) (12 mg, 10%), u.v. and i.r. spectra in agreement with ref. 20; (ii) 2,2′-ethanediylidenebis{benzo[*b*]thiophen-3(2*H*)-one} (10) as red needles, m.p. 294—296 °C (from acetic acid) (10 mg, 8%), identical with a sample prepared by condensing thioindoxyl with glyoxal,[21] u.v. and i.r. spectra as in ref. 20. The *leucodiacetate*, prepared by heating with zinc dust and acetic anhydride, formed needles, m.p. 217—222 °C (from methanol) (Found: C, 64.5; H, 3.9; S, 15.8%. $C_{22}H_{16}O_4S_2$ requires C, 64.7; H, 3.9; S, 15.7%); $\nu_{max.}$ 1 775 cm^{-1}; δ 7.70 (2 H, m, ArH), 7.39 (6 H, m, ArH), 7.0 (2 H, s, CH=), and 2.45 (6 H, s, OAc); *m/e* 408 (M^+, 9%), 366 (25), 324 (100), 187 (18), 175 (11), 162 (32), and 159 (16); (iii) 3-bromothiochromen-4-one as needles, m.p. 137—139 °C (from methanol) (16 mg, 8%).

(*b*) 3-Bromothiochroman-4-one *S*-oxide (0.2 g) was refluxed in acetic acid (3 ml) with anhydrous sodium acetate (0.32 g) for 1 h, cooled, and diluted with water. The dried precipitate was stirred (twice) with a little diethyl ether and the insoluble portion was crystallised from a large volume of ethanol to give 2-(3-hydroxybenzothienylmethylene)-thioindoxyl (11) as violet-red needles, m.p. 260—262 °C (decomp.) [lit.,[22] 271—274 °C (decomp.)] (21 mg, 18%) (Found: S, 20.4%; M^+, 310.0123. $C_{17}H_{10}O_2S_2$ requires S, 20.6%; *M*, 310.0125); $\lambda_{max.}$ (EtOH–H^+) 215, 249, 290, 338—353, and 480 nm (log ε 4.43, 4.05, 4.14, 4.12, and 4.45); $\lambda_{max.}$ (EtOH–HO^-) 586 nm; $\nu_{max.}$ (Nujol) 1 638 cm^{-1} (spectrum in close agreement with published [22] curve); δ [$(CD_3)_2SO$] 8.52 (1 H, s, CH=) and 8.0—7.3 (8 H, m, ArH); *m/e* 310 (M^+, 56%), 293 (100), 281 (3), 253 (4), 221 (4.5), and 174 (13).

3,3-*Dibromo*-2,2-*dimethylthiochroman*-4-*one* (13).—Bromine (0.25 g, 1.6 mmol) in chloroform (15 ml) was added, as drops, to a stirred solution of 2,2-dimethylthiochromanone (0.15 g, 0.78 mmol) in chloroform during 30 min. The solution was then evaporated to give a solid which crystallised from light petroleum (b.p. 40—60 °C) as pale yellow needles (0.25 g, 92%), m.p. 69.5—71.5 °C (Found: C, 37.9; H, 3.2; Br, 45.6; S, 9.1. $C_{11}H_{10}Br_2OS$ requires C, 37.7; H, 2.9; Br, 45.7; S, 9.1%); $\nu_{max.}$ 1 693 cm^{-1}; δ 8.24 (1 H, dd, *J* 8 and 2 Hz, ArH), 7.34 (3 H, m, ArH), and 1.76 (6 H, s, CMe_2); *m/e* 352 (M^+, 0.9%), 350 (M^+, 2), 348 (M^+, 0.9), 271 (8), 269 (8), 190 (100), 175 (6), 163 (6), 147 (18), and 136 (18).

2-*Isopropylidenethioindoxyl* (14).—Bromine (84 mg, 0.52 mmol) in chloroform (10 ml) was added, as drops, to 2,2-dimethylthiochroman-4-one (100 mg, 0.52 mmol) in chloroform (15 ml) in 15 min. The solution was evaporated to dryness under reduced pressure and anhydrous sodium acetate (214 mg, 2.6 mmol) in acetic acid (20 ml) was added to the residue. The mixture was heated on a steam-bath for 5 min and then evaporated to dryness under reduced pressure. The residue was chromatographed on a dry column of silica in toluene and then crystallised from light petroleum (b.p. 80—100 °C) as yellow needles, m.p. 102—103 °C (lit.,[3] 103—105 °C) (64 mg, 65%); $\nu_{max.}$ 1 670 cm^{-1}; *m/e* 190 (M^+, 100%), 175 (4), 162 (3), and 148 (14).

Reaction of Brominated 2,2-*Dimethylthiochroman*-4-*one on Silica Gel*.—Bromine (0.21 g, 1.3 mmol) in chloroform (15 ml) was added, as drops, to 2,2-dimethylthiochromanone (0.25 g, 1.3 mmol) in chloroform (25 ml) in 30 min. T.l.c. then showed the presence of starting material, the 3,3-dibromo-derivative, and a major spot, presumably 3-bromo-2,2-dimethylthiochroman-4-one. Silica gel (2 g) was then added to the reaction mixture, the solvent was removed under reduced pressure, and the residue was left in a stoppered flask. After 4 h t.l.c. showed that fairly extensive reaction had occurred, the major product being 2-isopropyl-

idenethioindoxyl (14). After 7 d, the mixture was black and very complex (t.l.c.), but did not include the enone (14). It was extracted with chloroform and separated on a column of dry silica gel (in chloroform) followed by p.l.c. (in toluene and then hexane) to give (i) 6,6-*dimethyl*-6H-*bis*[1]*benzothieno*[3,2-*b*;3',2'-d]*pyran* (17) as needles, m.p. 160—161 °C (from toluene) (40 mg, 20%) (Found: C, 70.5; H, 4.6; S, 19.7%; M^+, 322.0485. $C_{19}H_{14}OS_2$ requires C, 70.8; H, 4.35; S, 19.9%; M, 322.0485); $\lambda_{max.}$ (MeOH) 213, 240, 280, 293, and 303 nm (log ε 4.58, 4.55, 3.77, 3.77, and 3.78); $\nu_{max.}$ 1 605, 1 570, 1 538, 1 369, and 1 116 cm^{-1}; δ 8.0—7.2 (8 H, m, ArH) and 1.83 (6 H, s, CMe_2); *m/e* 322 (M^+, 3%), 307 (100), 190.0451 (11, $C_{11}H_{10}OS$ requires 190.0452), 175 (6), 153.5(5), and 105 (28); (ii) thioindirubin (16) as red needles, m.p. 208—209 °C (lit.,[23] 206—207 °C) (from acetic acid) (15 mg, 8%); (iii) thioindigo as red needles, m.p. >300 °C (lit.,[24] >280 °C) (from acetic acid) (32 mg, 17%).

Similarly, 3,3-dibromo-2,2-dimethylthiochroman-4-one (0.48 g) in chloroform (30 ml) was adsorbed onto silica gel (2 g), evaporated, and left for 7 d in a stoppered flask. Work-up of the black mixture gave the pyran (17) (27 mg, 12%), thioindigo (52 mg, 25%), and thioindirubin (20 mg, 10%).

Bromination of Thiochroman-4-one.—A mixture of thiochroman-4-one (0.82 g, 5 mmol), bromine (3.2 g, 20 mmol), and anhydrous sodium acetate (3.3 g, 40 mmol) in acetic acid (25 ml) was stirred and refluxed until the solution became colourless (*ca.* 3—4 h). After being cooled, the precipitate was collected, dried, and chromatographed on a column of dry silica in chloroform to give (i) 2,3-*dibromothiochromen-4-one* as needles, m.p. 183 °C (from methanol) (55 mg, 34%) (Found: C, 31.8; H, 1.2; Br, 52.8; S, 9.7. $C_9H_4Br_2OS$ requires C, 31.8; H, 1.2; Br, 52.9; S, 9.4%); $\nu_{max.}$ 1 640 cm^{-1}; δ 8.54 (1 H, m, ArH) and 7.61 (3 H, m, ArH); *m/e* 322 (M^+, 40%), 320 (M^+, 100), 318 (M^+, 40), 294 (6), 292 (17), 290 (5.5), 241 (45), 239 (45), 213 (9), 211 (8), 160 (6), 136 (20), 132 (100), and 108 (6); (ii) 2,3-*dibromothiochromen-4-one* S-*oxide* (19b) as needles, m.p. 207—210 °C (from methanol) (0.2 g, 12%) (Found: C, 30.2; H, 1.0; Br, 50.6; S, 9.2. $C_9H_4BrO_2S$ requires C, 30.3; H, 1.1; Br, 5.6; S, 9.0%); $\nu_{max.}$ 1 663 and 1 070 cm^{-1}; *m/e* 338 (M^+, 0.8), 336 (M^+, 1.5), 334 (M^+, 0.8), 322 (10), 320 (25), 318 (10), 241 (6), 239 (5.5), 229 (100), 227 (100), 209 (18), 207 (18), 152 (13), 136 (14), 132 (28), 120 (8), and 108 (6); (iii) 3,3-*dibromothiochroman-4-one* S-*oxide* as needles, m.p. 131—133 °C (from methanol) (50 mg, 3%) (Found: C, 30.2; H, 1.9; Br, 50.2; S, 8.8. $C_9H_6Br_2O_2S$ requires C, 30.2; H, 1.7; Br, 50.3; S, 8.9%); $\nu_{max.}$ 1 705 and 1 033 cm^{-1}; δ 8.35 (1 H, dd, *J* 9 and 2 Hz, ArH), 7.82 (3 H, m, ArH), 4.82 and 4.21 (each 1 H, d, *J* 14 Hz, CH_2); *m/e* 340 (M^+, 0.9%), 338 (2), 336 (0.9), 259 (60), 257 (56), 178 (50), 162 (40), 152 (100), 136 (63), 120 (40), 108 (22), and 104 (20).

Thioindigo Preparations.—(*a*) (*With* Dr. R. M. Christie). A mixture of thiochromanone (164 mg, 1 mmol), bromine (640 mg, 4 mmol), and anhydrous sodium acetate (650 mg, 8 mmol) in acetic acid (5 ml) was stirred and refluxed for 1.5 h, and allowed to cool. After dilution with water the precipitate was collected, washed with ethyl acetate, and crystallised from acetic acid to give thioindigo as red needles, m.p. >300 °C (15 mg, 10%). Repeating this reaction with the addition of a drop of water increased the yield to 31 mg (21%).

(*b*) A mixture of 3,3-dibromothiochroman-4-one (332 mg, 1 mmol), bromine (320 mg, 2 mmol), and anhydrous sodium acetate (328 mg, 4 mmol) in acetic acid (10 ml) was stirred and refluxed for 4 h. The solution was cooled, poured into water, and extracted with ethyl acetate. The extracts were washed successively with aqueous sodium hydrogencarbonate and water, dried ($MgSO_4$), and evaporated. The residue, in chloroform, was chromatographed on a column of dry silica to give thioindigo (6 mg, 4%) and 3-bromothiochromen-4-one as needles, m.p. 140—141 °C (142 mg, 59%).

(*c*) Repeating (*b*) with 3-bromothiochroman-4-one (243 mg, 1 mmol), bromine (480 mg, 3 mmol), and anhydrous sodium acetate (660 mg, 8 mmol) gave thioindigo in 12% yield.

(*d*) Repeating (*c*) using thiochromen-4-one (162 mg, 1 mmol) gave a trace of thioindigo and 3-bromothiochromen-4-one (170 mg, 71%). Using the latter as starting material gave only a trace of thioindigo.

(*e*) 2,3-Dibromothiochromen-4-one *S*-oxide (100 mg, 0.3 mmol) was refluxed with anhydrous sodium acetate (50 mg, 0.6 mmol) in acetic acid (5 ml) for 15 min, cooled, and diluted with water. The precipitate was collected, dried, and crystallised from acetic acid to give thioindigo (36 mg, 81%). In the absence of sodium acetate only the starting material was recovered. Repeating the reaction using 2,3-dibromothiochromen-4-one afforded only the starting material.

(*f*) Repeating (*e*) with 2,3-dichlorothiochromen-4-one *S*-oxide (200 mg, 0.81 mmol) and anhydrous sodium acetate (130 mg, 1.63 mmol) in acetic acid (5 ml) gave thioindigo (95 mg, 80%). The reaction was repeated in a stream of nitrogen and with refluxing for 30 min. The effluent gases were passed into saturated aqueous calcium hydroxide to give a precipitate of calcium carbonate (55%).

(*g*) A mixture of 2,3-dichlorothiochromen-4-one *S*-oxide (200 mg, 0.81 mmol) and silver acetate (136 mg, 0.81 mmol) in acetonitrile (15 ml, freshly distilled over calcium hydride) was stirred overnight (15 h) at room temperature with the exclusion of moisture. The mixture became blue within 5 min and colourless again after 15 min. After filtration, t.l.c. showed the presence of thioindigo, starting material, and an unknown compound. After concentration under reduced pressure (without heating) further spots were detectable. Purification by p.l.c. afforded only thioindigo (35 mg, 29%). This reaction was repeated several times and on two occasions only it was possible to isolate trace amounts of 3-*chloro*-2-{2-*chloro*-3(2H)-*oxobenzo*[b]*thien*-2-*yl*}*thiochromen*-4-*one* S-*oxide* (21) (Found: M^+, 393.9292. $C_{17}H_8{}^{35}Cl_2O_3S_2$ requires M, 393.9292); $\nu_{max.}$ 1 668 cm^{-1}; *m/e* 394 (M^+, 3 lines, 0.3), 377.9346 (1.5, $C_{17}H_8{}^{35}Cl_2O_2S_2$ requires 377.9343), 343 (2), 308 (0.4), 210.9617 (0.9, $C_9H_4{}^{35}ClO_2S$ requires 210.9620), 195 (1), 185 (33), 182.9760 (100, $C_9H_4{}^{35}ClO$. requires 182.9671), 167 (2.5), 155 (22), 132 (6), and 104 (2).

The amount of blue anion was estimated as follows: 2,3-dichlorothiochromen-4-one *S*-oxide (1.23 mg) and silver acetate (1.67 mg) were stirred in acetonitrile (9 ml) until the blue colour appeared. The mixture was immediately filtered into a u.v. cell and the spectrum measured [$\lambda_{max.}$ 600 nm (ε, 504, assuming 100% conversion)]. Extinction coefficients for related sulphenate anions [14] are between 5×10^3 and 10^4, suggesting that 5—10% of the starting compound was present as the blue anion.

(*h*) Repeating (*g*) with silver acetate (2 mol) gave thioindigo in 54% yield (65 mg).

(*i*) 2,3-Dichlorothiochromen-4-one *S*-oxide (200 mg, 0.81 mmol) and sodium benzoate (234 mg, 1.62 mmol) were stirred overnight in freshly distilled acetonitrile (15 ml) at

room temperature with the exclusion of moisture. The mixture became blue after 45 min and colourless again after 2 h. Stirring was continued for 3 h. Work-up gave thioindigo (52%) and a trace of compound (21).

(*j*) Reaction (*g*) was repeated with the addition of methyl fluorosulphonate (93 mg, 0.81 mmol) when the mixture became blue. It became colourless immediately and was left to stir overnight. After filtration and evaporation under reduced pressure the residue was purified by p.l.c. to give 2,3-dichlorothiochromen-4-one, m.p. 170—172 °C (from methanol) (130 mg, 65%).

Replacing methyl fluorosulphonate by methyl iodide gave only thioindigo (30 mg, 26%).

(*k*) 3-Bromo-4-hydroxythiocoumarin (782 mg) and anhydrous sodium acetate (792 mg) were heated in refluxing acetic acid (20 ml) containing water (1 drop) for 3 h. The mixture was poured into water and extracted with chloroform which was washed successively with aqueous sodium hydrogencarbonate and water, and then dried ($MgSO_4$). The residue, after evaporation, was purified by p.l.c. in chloroform to give thioindigo (18 mg, 4%).

α-Chlorobenzyl 4-Nitrophenyl Sulphoxide (30) *and its Reaction with Acetate*.—Iodobenzene dichloride (4.49 g) in dry pyridine (10 ml) was added, as drops, at −40 °C to a stirred solution of benzyl 4-nitrophenyl sulphide (2 g) in 20% aqueous pyridine (13 ml). The mixture was kept at −40 °C for 1 h, out of direct sunlight, and then at room temperature overnight. Chloroform (50 ml) was added, and the solution was shaken with dilute sulphuric acid and water, dried, and evaporated. The residue was purified by chromatography on a column of dry silica in diethyl ether–light petroleum (b.p. 40—60 °C) (1 : 1) followed by p.l.c. (same solvents) to give (i) benzyl 4-nitrophenyl sulphone as needles, m.p. 173—174 °C (lit.,[25] 169 °C) (from methanol) (50 mg, 2%) (Found: C, 56.0; H, 4.1; N, 5.5; S, 11.85. Calc. for $C_{13}H_{11}NO_4S$: C, 56.3; H, 4.0; N, 5.5; S, 11.55%); δ 8.26 (2 H, d, *J* 9 Hz, ArH), 7.75 (2 H, d, *J* 9 Hz, ArH), 7.20 (5 H, m, ArH), and 4.37 (2 H, s, CH_2); *m/e* 91 (100%); (ii) α-chlorobenzyl 4-nitrophenyl sulphoxide as needles, m.p. 151—153 °C (lit.,[26] 151—152 °C) (from methanol) (0.4 g, 19%); δ 8.15 (2 H, d, *J* 9 Hz, ArH), 7.23 (7 H, m, ArH), and 5.60 (1 H, s, CHCl); *m/e* 127 (25%), 125 (100), and 91 (32); (iii) *benzyl 4-nitrophenyl sulphoxide* as needles, m.p. 163—165 °C (from methanol) (70 mg, 3%) (Found: C, 59.7; H, 4.3; N, 5.9; S, 12.3. $C_{13}H_{11}NO_3S$ requires C, 59.8; H, 4.2; N, 5.4; S, 12.3%); δ 8.23 (2 H, d, *J* 9 Hz, ArH), 7.48 (2 H, d, *J* 9 Hz, ArH), 7.3 and 6.9 (total 5 H, m, ArH), and 4.12 (2 H, s, CH_2); *m/e* (%) 170 (3) and 91 (100).

Reaction with acetate. (*a*) A mixture of α-chlorobenzyl 4-nitrophenyl sulphoxide (100 mg, 0.34 mmol) and sodium acetate (55 mg, 0.68 mmol) in acetic acid (15 ml) was refluxed for 3 h, cooled, and the solvent then removed under reduced pressure. The residue, after p.l.c. in chloroform, gave benzaldehyde (26 mg, 72%) which was isolated as its 2,4-dinitrophenylhydrazone, m.p. 237—238 °C (lit.,[24] 237 °C).

(*b*) The sulphoxide (100 mg, 0.34 mmol), anhydrous sodium acetate (42 mg, 0.68 mmol), and cyclohexene (0.4 ml) in acetic acid (3 ml) were heated on a steam-bath for 7 h, poured into water, and extracted with diethyl ether. The extract was washed successively with aqueous sodium hydrogencarbonate and water, dried ($MgSO_4$), and evaporated. T.l.c. of the residue showed several spots including the starting material, benzaldehyde, and the desired acetate which was isolated by p.l.c. in chloroform as a low melting solid identified as *trans*-2-acetoxycyclohexyl 4-nitrophenyl sulphide (32) (9 mg) by direct comparison (t.l.c., n.m.r. and mass spectra) with authentic material (see below).

trans-2-*Acetoxycyclohexyl 4-Nitrophenyl Sulphide* (32) (cf. *Ref.* 27).—*trans*-2-Chlorocyclohexyl 4-nitrophenyl sulphide[28] (0.4 g) and anhydrous sodium acetate (0.4 g) were heated in refluxing acetic acid (10 ml) for 30 h. The mixture was diluted with diethyl ether and shaken successively with water, aqueous sodium hydrogencarbonate, and water, and then dried. Evaporation left a semisolid which crystallised from methanol in pale yellow plates, m.p. 56—57 °C (0.33 g, 76%) (Found: C, 57.2; H, 5.6; S, 10.7%; M^+, 295.0878. $C_{14}H_{17}NO_4S$ requires C, 56.9; H, 5.8; S, 10.8%; *M*, 295.0878); $\nu_{max.}$ 1 721 cm^{-1}; δ 8.09 (2 H, d, *J* 9 Hz, ArH), 7.47 (2 H, d, *J* 9 Hz, ArH), 4.82 (1 H, m, C*H*OAc), 3.44 (1 H, m, C*H*SAr), 1.86 (3 H, s, OCOMe), and 2.25—1.35 (10 H, m, CH_2); *m/e* 295 (M^+, 0.2%) and 235 (100).

Chlorination of 3-Methylthiochroman-4-one.—An excess of chlorine (7 g) was passed into a solution of 3-methylthiochroman-4-one (3 g) in acetic acid (50 ml). The flask was stoppered and, after 2 d, the solution was evaporated to dryness under reduced pressure. The residue was dissolved in chloroform, washed with aqueous sodium hydrogencarbonate, dried, and evaporated. The solid obtained was chromatographed on a column of dry silica in chloroform to give (i) 3-methylthiochromen-4-one as small prisms, m.p. 103—104 °C (lit.,[29] 104—105 °C) (from methanol–water) (1.2 g, 40%); (ii) *2-chloro-3-methylthiochromen-4-one S-dioxide* (38) as needles, m.p. 186—187 °C (from methanol) (0.04 g, 1%) (Found: C, 49.7; H, 3.20; Cl, 14.2; S, 13.0%; M^+, 241.9803. $C_{10}H_7ClO_3S$ requires C, 49.6; H, 2.9; Cl, 14.7; S, 13.2%; *M*, 241.9805); *m/e* 244 (M^+, 0.3%), 242 (M^+, 0.8), 212 (28), 210 (100), 187 (14), 185 (89), 147 (32), 136 (28), 108 (11), and 104 (7); (iii) 3-methylthiochroman-4-one *S*-oxide as needles, m.p. 116—117 °C (from light petroleum, b.p. 40—60 °C) (lit.,[17] 116—117 °C) (0.5 g, 15%); (iv) *2,3-dichloro-3-methylthiochroman-4-one S-oxide* (37) as prisms, m.p. 99—101 °C (from ethyl acetate–light petroleum, b.p. 40—60 °C) (0.5 g, 12%) (Found: C, 45.7; H, 3.1; Cl, 26.5; S, 12.4%; M^+, 261.9621. $C_{10}H_8Cl_2O_2S$ requires C, 45.8; H, 3.1; Cl, 26.9; S, 12.2%; *M*, 261.9621); δ 8.24 (1 H, dd, *J* 9 and 2 Hz, ArH), 8.0—7.62 (3 H, m, ArH), 5.62 (1 H, s, CHCl), and 2.09 (3 H, s, Me); *m/e* 262 (M^+, 2%), 227 (25), 176 (11), 152 (100), and 136 (13).

2-Chloro-3-methylthiochromen-4-one S-Dioxide (38).—An excess of chlorine (0.5 g) was passed into a solution of 3-methylthiochroman-4-one *S*-oxide (0.25 g) in acetic acid (25 ml). The reaction mixture was left overnight and worked-up as above to give the *S*-dioxide (38) (0.17 g, 57%), identical with the sample described above.

3-Methyl-2-{2-methyl-3(2H)-oxobenzo[b]thien-2-yl}thiochromen-4-one S-Oxide (39).—2,3-Dichloro-3-methylthiochroman-4-one *S*-oxide (0.1 g) and anhydrous sodium acetate (62 mg) were refluxed in acetic acid (or acetonitrile) (10 ml) for 20 h. The reaction mixture was evaporated to dryness under reduced pressure and the residue (in the case of acetic acid, after being washed with aqueous sodium hydrogencarbonate and dried) was chromatographed on a dry column of silica in chloroform–toluene (4 : 1) to give the *dimer* (39) as small prisms, m.p. 172—175 °C (from carbon tetrachloride) (6 mg, 36%)* (Found: M^+, 354.0383. $C_{19}H_{14}O_3S_2$ requires *M*, 354.0383); δ 8.31 (1 H, m, ArH), 7.84—7.64 (4 H, m, ArH), 7.51 (1 H, m, ArH), 7.32 (2 H, m, ArH), 2.56 (3 H, s, =CMe), and 2.35 (3 H, s, CMe); *m/e* 354

* Based on recovered starting material.

(M^+, 10%), 338 (63), 295 (4), 191 (35), 188 (20), 175 (13), 163 (100), 147 (100), 135 (14), and 91 (22).

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