Synthesis and Conformation of Substituted Isothiochromans and Derivatives. *X*-Ray Analysis of *cis*-1,4-Dimethylisothiochroman 2,2-Dioxide, an *S*-Heterocycle with Preferred Boat Conformation

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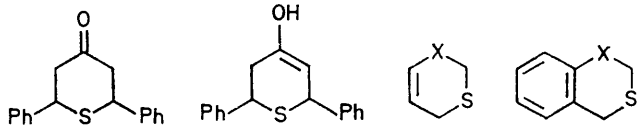
Stereoselective syntheses for *cis*-1,4- and *cis*-1,3-dimethylisothiochromans and their 2,2-dioxides are described. In the 1,4- and 1,3-dimethyl sulphones, the *cis*- and *trans*-forms, respectively, are shown to be the more thermodynamically stable stereoisomers. A preferred boat conformation is inferred for these compounds, and is demonstrated for the *cis*-1,4-dimethyl sulphone (16) by *X*-ray analysis; crystals are monoclinic, space group $P2_1/c$, with $Z = 4$ in a unit cell $a = 8{\cdot}44 \pm 0{\cdot}01$, $b = 15{\cdot}90 \pm 0{\cdot}02$, $c = 8{\cdot}22 \pm 0{\cdot}01$ Å, $\beta = 114{\cdot}37 \pm 0{\cdot}2°$. The structure was solved by Patterson and Fourier methods and refined by least squares to R 0·081 for 1320 independent reflections measured on a diffractometer. 1-Methyl and 1,3-dimethylisothiochroman-4-ones intermediate in the synthesis are unstable to light, rearranging on irradiation to thiochroman-3-ones. Some heterocycles containing the 5,6-dihydro-2*H*-thiopyran ring are reported.

STUDIES [1] on the kinetics of the formation of *cis*- and *trans*-2,6-diphenyltetrahydrothiopyran-4-one (1) from dibenzylideneacetone and hydrogen sulphide in basic media have shown that the thermodynamically less stable *trans*-isomer is produced faster. Ring closure in this reaction may involve the enol (2), or its anion, as the first product. Examination of a molecular model of the thiacyclohex-3-ene ring contained in (2) indicates a preference for a boat (or twist boat) conformation. Thus in enol (2) the *trans*-isomer can have two equatorial

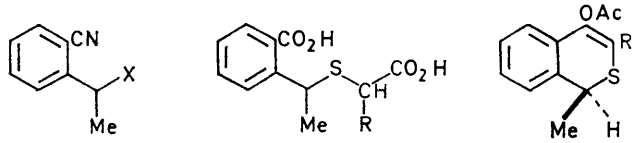


(1) (2) (3) (4)

substituents, in a boat ring, and is expected to be more stable than the *cis*-isomer. However on ketonisation, with change to a chair conformation, both substituents in the *cis*-isomer can take the equatorial orientation, and this isomer is then the more stable.

Further study of molecular models suggested that in ring systems of types (3) (X = CH_2, NH, O, or S) and (4) (X = CH_2, NH, or S), and certain relatives, the boat or twist conformation is subject to less angle strain in the ring than in the chair forms. We set out to synthesise suitable derivatives of systems (3) and (4) in order to study their preferred conformation, and to test the validity of the argument from molecular models. At the start of this work, few such compounds had been prepared. We now describe [2] stereoselective syntheses of the *cis*-1,4- and *cis*-1,3-dimethylisothiochromans (15) and (27), and their corresponding sulphones and report on their relative stabilities and stereochemistry.

To this end, *o*-ethylbenzonitrile [3] (5) was treated with *N*-bromosuccinimide, under u.v. irradiation, and the resulting *o*-(α-bromoethyl)benzonitrile (87%) (6) was converted into *S*-[α-(2-cyanophenyl)ethyl]thioglycolic acid (7) (95%) by reaction with thioglycolic acid in alkali. Hydrolysis of the nitrile function with aqueous alkali gave the crystalline dicarboxylic acid (8), (81%), which cyclised,[4] with decarboxylation, to the enol

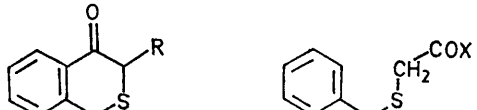


(5) X = H
(6) X = Br
(7) X = S·CH_2·CO_2H
(21) X = S·CH(Me)·CO_2H

(8) R = H
(22) R = Me

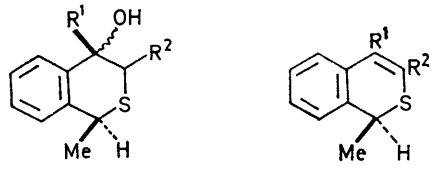
(9) R = H
(23) R = Me

acetate (9) (61%) on heating with sodium acetate in acetic anhydride. Hydrolysis of the enol acetate afforded the 1-methylisothiochroman-4-one (10) (61%) as a solid, m.p. 90—91°, 2,4-dinitrophenylhydrazone, m.p. 194°. This ketone has previously been reported [5] as a liquid, contaminated by isomers, prepared in low yield *via* Friedel–Crafts cyclisation of the acid (11) or its



(10) R = H
(24) R = Me

(11) X = OH
(12) X = Cl



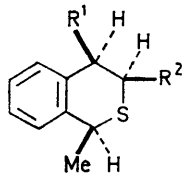
(13) R^1 = Me, R^2 = H
(25) R^1 = H, R^2 = Me

(14) R^1 = Me, R^2 = H
(26) R^1 = H, R^2 = Me

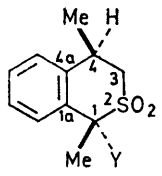
chloride (12); we were unable to obtain any of the isothiochroman-4-one by this method, using a wide range of catalysts and experimental conditions.

[1] C. A. R. Baxter and D. A. Whiting, *J. Chem. Soc.* (*C*), 1968, 1174.
[2] Preliminary communication, D. A. Whiting and D. A. Pulman, *Chem. Comm.*, 1971, 831.
[3] J. M. Stuart, I. Klundt, and K. Peacock, *J. Org. Chem.*, 1960, **25**, 913.
[4] *Cf.* R. Lesser and A. Mehrlander, *Ber.*, 1923, **56**, 1642.
[5] P. Cagniant, G. Jecko, and D. Cagniant, *Bull. Soc. chim. France*, 1959, 1998.

Treatment of the ketone (10) with methylmagnesium iodide gave a mixture of the stereoisomers of the alcohol (13) (84%). The isomers were separated and characterised, but stereochemical assignment from the spectroscopic data could not be made with certainty. Both isothiochromanols (13) were dehydrated (71%) by refluxing in benzene with a little toluene-*p*-sulphonic acid. The resulting isothiochromen (14) was hydrogenated over 10% palladium–carbon at 80° and 40 atm. The product (91%) was the *cis*-1,4-dimethylisothiochroman (15), hydrogen addition taking place specifically from the less hindered face of the molecule. No other compound was

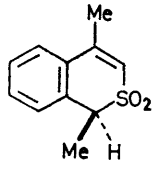


(15) R^1 = Me, R^2 = H
(27) R^1 = H, R^2 = Me



(16) Y = H
(17) Y = D

detected in the hydrogenation product by chromatographic and spectroscopic examination, both of the isothiochroman itself and of its crystalline mercury(II) chloride adduct. The isothiochroman (15) was oxidised with potassium permanganate to the corresponding *cis*-dimethyl sulphone (16). The latter could also be prepared *via* oxidation of the isothiochromen (14) with hydrogen peroxide to yield the isothiochromen sulphone



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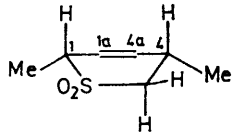


(19)

TABLE 1

$J_{3.3}$	13 Hz
$J_{4.3ax}$	12 Hz
$J_{4.3eq}$	5 Hz

(18), which could be hydrogenated (at ambient temperature and pressure) to the sulphone (16) (99%). This hydrogenation was also highly specific; no *trans*-1,4-dimethyl isomer was detected.

If the heterocyclic ring of the *cis*-1,4-dimethyl sulphone (16) were to assume a quasi-chair conformation, the two methyl substituents would adopt axial and equatorial orientations. It would then be expected that the *trans*-isomer would be more stable than the *cis*-, since both methyl groups in the former could then be equatorial. However, the *cis*-arrangement is preferred, since no epimerisation at C-1 was detected in aqueous sodium hydroxide–pyridine, although the 1-deuteriated compound (17) was obtained from treatment with deuterium oxide–sodium deuterioxide–pyridine, thus demonstrating 1-H exchange. This suggests that the sulphone (16) preferentially takes up the boat conformation (19) with the *cis*-1,4-substituents equatorial.

This suggestion was confirmed (at least for the solid state) by a crystallographic study of the sulphone (16), $C_{11}H_{14}O_2S$, which crystallised as prisms from aqueous ethanol, m.p. 119—120 °C in space group $P2_1/c$. Intensity data were collected on linear diffractometer, and 1320 reflections were finally considered observed. Crystallographic details and discussion of the solution of the crystal structure are contained in the Experimental section. The structure was refined to R 0·081, excluding hydrogen atoms, and with anisotropic temperature factors. The final molecular structure is shown in Figure 1(a)—(c). The *cis*-stereochemistry is

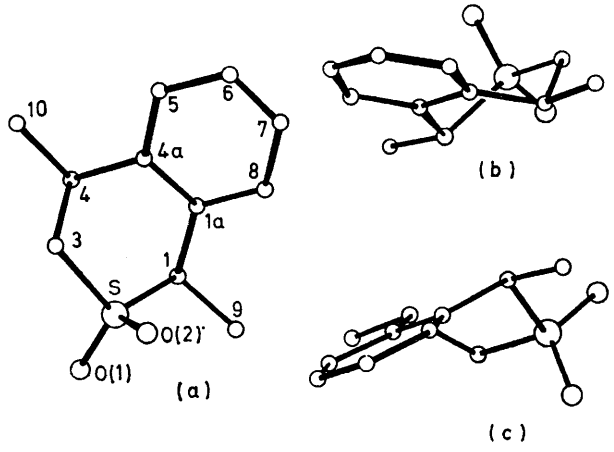


FIGURE 1 Projections along (a) *b* axis, (b) *a* axis, (c) *c* axis

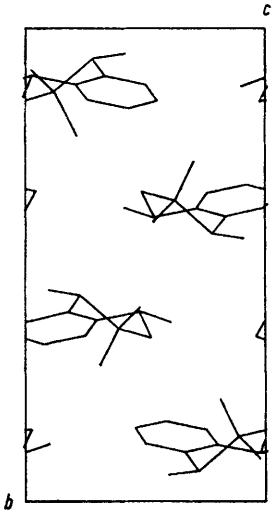
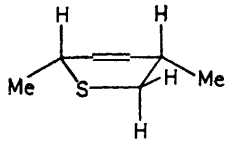


FIGURE 2 Unit cell projected along the *a* axis

confirmed, and a classical boat conformation is revealed. C(1) and C(4) are closely coplanar with the aromatic ring, and C(3) and S are on the same side of that plane, with the C(3)–S bond nearly parallel to the C(1a)–C(4a) bond. The two methyl groups are disposed equatorially. It seems likely that the length of C(1)–S and C(3)–S bonds [1·82 and 1·79 Å], and the size of the C(1)–S–C(3) angle (103·4°, less than the tetrahedral angle) contribute to angle strain in the more flattened quasi-chair form which is relieved in the boat conformation. The packing of molecules in the cell is shown in Figure 2.

The n.m.r. spectrum of the sulphone (16) is in accord with this molecular shape; the coupling constants * germane to this consideration are shown in Table 1 and may be compared with those for the *cis*-1,4-dimethylisothiochroman shown (Table 2) in the boat shape. In



(20)

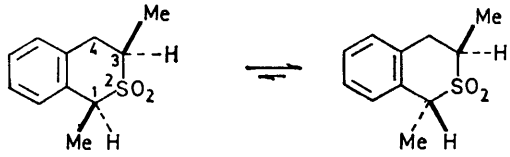
TABLE 2

$J_{3.3}$	13 Hz
$J_{4.3ax}$	13 Hz
$J_{4.3eq}$	4 Hz

both cases coupling constants are of the order expected for a system which is not involved in rapid conformational inversion, *i.e.* with fixed H-3*ax*,H-4*ax* and H-3*eq*,H-4*ax* relationships. The spectrum of neither of these two was temperature dependant in [$^2H_6$]dimethyl sulphoxide solution in the range −100 to +100 °C. These data point to a solution conformation which is stationary, and therefore has both methyl groups equatorial and is likely to be the same boat structure as found in the crystalline state. Other details of the n.m.r. spectra are given in the Experimental section.

A related set of experiments was also carried out with 1,3-dimethylisothiochroman-4-one, prepared by a route similar to that described for its 1,4-dimethyl isomer. In this case *o*-(α-bromoethyl)benzonitrile (6) was treated with thiolactic acid, in the presence of sodium hydroxide, to form the diastereomers of *S*-[α-(2-cyanophenyl)ethyl]-thiolactic acid (21) (72%), which on hydrolysis gave a mixture of the diastereomers of the diacid (22) (70%).

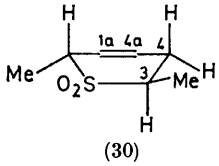
These stereoisomers were separated by fractional crystallisation. Both isomers cyclised in acetic anhydride with sodium acetate to the enol acetate (23) (92%). The latter was hydrolysed to *cis*- and *trans*-1,3-dimethylisothiochromanones (24) (73%). We could not separate these ketones by chromatography. Reduction to the alcohols (25) (98%) was followed by dehydration to 1,3-dimethylisothiochromen (26) (91%). Hydrogenation of the isothiochromen over 10% palladium–carbon, at 80° under 40 atm, yielded the isothiochroman (27). The reduction proceeded slowly at room temperature and pressure, giving rise to the same product, which was shown to be homogeneous by chromatographic and spectroscopic examination of the total hydrogenation product and its mercurichloride, and comparison with the purified materials. This compound is the *cis*-1,3-dimethylisothiochroman (27), derived by stereospecific addition of hydrogen to the less hindered face of the isothiochromene (26). Oxidation to the corresponding *cis*-sulphone (28) was accomplished with potassium permanganate.



(28) (29)

If the heterocyclic ring of *cis*-sulphone (28) assumes a boat conformation in preference to the quasi-chair form, then one methyl substituent must be equatorial and the other axial. It would then be expected that the corresponding *trans*-isomer would be more thermodynamically stable, since both methyl groups could be equatorial. In accordance with this view, the *cis*-1,3-dimethyl sulphone (28) equilibrated in pyridine containing aqueous alkali with a new isomeric product, which proved to be the *trans*-isomer (29). Data supporting this structure are detailed in the Experimental section. The *cis* ⟶ *trans* isomerisation was followed in the n.m.r. probe, in pyridine–sodium deuterioxide–deuterium oxide at 30°. At equilibrium the *trans*-isomer (29) predominated by 2 : 1 and is the more stable isomer, although only by a relatively small margin. The two isomers were separated by fractional crystallisation; the *cis*-form had m.p. 83—85° and the *trans* m.p. 84—87° (mixed m.p. 70—75°).

The *trans*-isomer (29) is assigned the diequatorial boat conformation (30). Relevant coupling constants are shown in Table 3. The spectrum was temperature-independent in the range −100 to +100°.

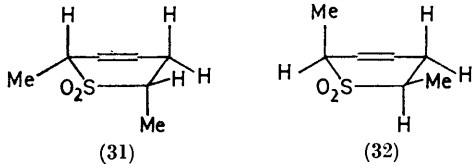


(30)

TABLE 3

$J_{4.4}$	11 Hz
$J_{3.4ax}$	11 Hz
$J_{3.4eq}$	7 Hz

If the *cis*-1,3-dimethylsulphone (28) also has the boat conformation it is likely to be in equilibrium between the two possible boat forms (31) and (32), both with one equatorial and one axial methyl group and of very similar energy. Similar arguments applied to the corresponding *cis*-1,3-dimethylisothiochroman (27). However the mag-



(31) (32)

nitudes of the spin couplings between protons at C-3 and C-4, in both compounds (see Table 4) suggest that the 3-H is fixed in the axial orientation. Further the n.m.r. spectra of (27) and (28) are temperature inde-

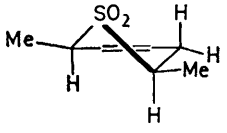
* The coupling constants referred to here, and those in Tables 2—4, were obtained from 100 MHz spectra from which the H-3,CH_3 (or H-4,CH_3) vicinal coupling was cut out by double irradiation. The 3,4-proton group was treated as an ABX system, and coupling constants were extracted by using standard formulae. Also, in the cases of sulphones (19), (30), and (33) the spectra were simplified to first-order by altering the chemical shifts with tris(dipivaloylmethanato)europium(III) complex.

pendent (−100 to +100°). It could be argued that these data show conformation (32) to be favoured over (31), in the case of the sulphone (28), with a parallel situation

TABLE 4

Compound:	(28)	(27)
$J_{4,4}$	16 Hz	15 Hz
$J_{3,4ax}$	10 Hz	8 Hz
$J_{3,4eq}$	5 Hz	4 Hz

for the isothiochroman (27). However, it appears more reasonable to invoke quasi-chair conformations, (33) and (34), for these two compounds; where both methyl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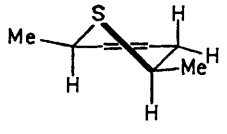
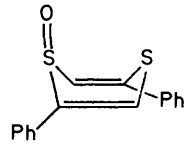

(34)

groups are equatorial. No inversion to the diaxial chair conformation is then likely. The equilibrium (28) ⇌ (29) is thus between the chair *cis*-1,3-dimethyl sulphone [(33); less stable] and the boat *trans*-1,3-dimethyl sulphone [(3); more stable].

Boat conformations are rarely favoured in six-membered rings, but a few cases involving sulphur in the ring are known. Thus, *X*-ray crystallographic studies of 2,5-diphenyl-1,4-dithiin 1-oxide [6] (35), 3-methyl-2-thioxo-1,3-thiazine-4-one [7] (36), and tetramethyltetrathian [8] (37) revealed the boat conformations shown. The last case has been intensively examined [9] by n.m.r. Boat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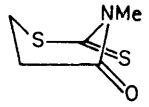
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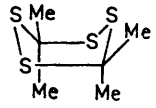
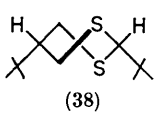

(37)

and twist-boat conformations have also been suggested, on the basis of spectroscopic data, for *cis*-2,5-di-t-butyl-1,3-dithian [10] (38), *t*-4,*t*-6-dimethyl-*r*-2-t-butyl-1,3-dithian [10] (39), and certain steroid fused cyclic sulphites.[11]

Attempts were made to extend this investigation to the unfused thiacyclohex-3-ene ring. Both geometric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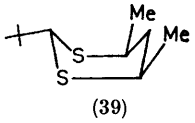
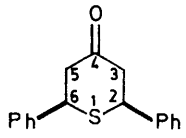

(39)

isomers of 2,6-diphenyltetrahydrothiopyran-4-one (40) and (41) are known,[1] and we now briefly describe the synthesis from them of several 3,4-unsaturated derivatives, although we were not able to demonstrate the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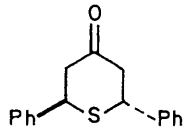
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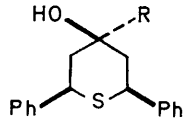
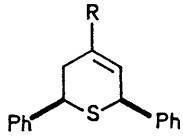

(42) R = Me
(45) R = Ph

thermodynamically preferred stereochemistry in any of these cases.

Reaction of the *cis*-tetrahydrothiopyrone (40) with methylmagnesium iodide gave the alcohol (42) as major product,[1] which on dehydration afforded the *cis*-olefin (43). Oxidation of the latter with hydrogen peroxide gave the corresponding sulphone (44). Attempts to equilibrate the stereoisomers of the sulphone in base were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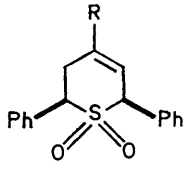
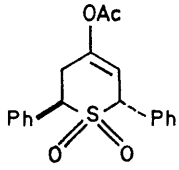
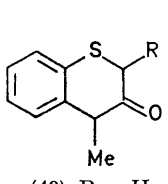
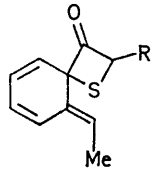

(44) R = Me
(47) R = Ph


(48)

unsatisfactory, since the mixture of products could not be separated and characterised. The corresponding 4-phenyl analogues (45)—(47) were similarly prepared, but the reaction of (47) with base was complex and was not resolved.

Both thiopyranones (40) and (41) could be oxidised to their corresponding sulphones; the *trans*-sulphone readily afforded a crystalline enol acetate (48) on reacton with acetic anhydride in chloroform containing perchloric acid. However the isomeric *cis*-sulphone could


(49) R = H
(50) R = Me


(51)

not be persuaded to yield such a derivative under a variety of conditions.

Finally we record our observations on the rearrangement of 1-methylisothiochroman-4-one (10) and 1,3-dimethylisothiochroman-4-one (24). Both these compounds were prepared in the syntheses already described,

[6] G. Bandolini, D. A. Clemente, and C. Panattoni, *Chem. Comm.*, 1970, 1143.
[7] V. Amirthalingam and V. S. Jakkal, *Chem. Comm.*, 1970, 1356.
[8] A. Frega, *Acta Chem. Scand.*, 1958, **12**, 891.
[9] C. H. Bushweller, *J. Amer. Chem. Soc.*, 1967, **89**, 5978.
[10] E. L. Eliel and R. O. Hutchins, *J. Amer. Chem. Soc.*, 1969, **91**, 2703.
[11] A. T. Rowlands, T. B. Adams, H. W. Atland, W. S. Creasy, S. A. Dressner, and T. M. Dyott, *Tetrahedron Letters*, 1970, **50**, 4405.

and were unstable to light. U.v. irradiation in solution rearranged both compounds (10) and (24) to the isomeric thiochroman-3-ones (49) and (50) (mixture of stereoisomers), respectively. Similar rearrangements of isothiochromanones substituted only in the aromatic ring have been reported by Lumma and Berchtold,[12] and are believed to implicate intermediates such as (51).

EXPERIMENTAL

Unless otherwise stated, the following generalisations apply. M.p.s were measured with a Kofler hot-stage apparatus. I.r. spectra were recorded for chloroform solutions; u.v. spectra were measured for solutions in ethanol ($\log_{10}$ ε in parentheses). ^{1}H N.m.r. measurements used tetramethylsilane as internal standard. Mass spectra were obtained with an A.E.I. MS 902 spectrometer (with direct insertion at 70 eV). T.l.c. was carried out with silica gel G (Merck–Stahl); chromatograms were developed with iodine vapour. P.l.c. was performed with silica gel HF 254 (Merck–Stahl) in 0·5 × 200 × 200 mm layers. Solutions were dried over mangesium sulphate and evaporated under reduced pressure. Molecular weights were measured by mass spectrometry.

o-*Ethylbenzonitrile*.—Sodium disulphite (66·3 g) and sodium hydroxide (43·8 g) in water (500 cm^3) were added to a solution of hydrated copper sulphate (312·5 g) and sodium chloride (81·3 g) in water (1 dm^3) at 70° with stirring. The precipitated copper(I) chloride was washed by decantation, suspended in water (500 cm^3), and stirred while sodium cyanide (162·5 g) in water (250 cm^3) was added, yielding a copper(I) cyanide solution. Conc. hydrochloric acid (250 cm^3) was added to *o*-ethylaniline (121 g), and the resultant hydrochloride was crushed and stirred with ice (800 g). Sodium nitrite (70 g) in water (200 ml) was added during 20 min, the temperature being maintained at 0—5° with ice. The solution was then neutralised (litmus) with sodium carbonate. The copper(I) cyanide solution was cooled in an ice-bath, and toluene (250 cm^3) was added. The mixture was stirred vigorously while the cold neutralised diazonium solution was added (during 30 min). Stirring was continued for 30 min at 0° and 6 h at ambient temperature. After being heated to 50° the solution was set aside overnight. The organic layer was collected and steam distilled. The distillate contained a yellow oil, which was separated, dried, and distilled, to yield *o*-ethylbenzonitrile (84 g, 65%), b.p. 45° at 0·5 mmHg (lit.,[3] b.p. 91—93° at 12 mmHg), $\nu_{max.}$ (film) 2240 cm^{-1}, τ (CCl_4) 2·4—2·9 (4H, m, ArH), 7·15 (2H, q), and 8·70 (3H, t).

o-(α-*Bromoethyl*)*benzonitrile*.—A mixture of *o*-ethylbenzonitrile (1 g), *N*-bromosuccinimide (1·36 g), benzoyl peroxide (50 mg), and carbon tetrachloride (20 cm^3) was refluxed for 3 h under u.v. irradiation. The mixture was cooled, filtered, and distilled. The fraction b.p. 83—87° at 0·5 mmHg afforded *o*-(α-bromoethyl)benzonitrile (6) (1·40 g, 87%), (lit.,[3] b.p. 99° at 2—3 mmHg), $\nu_{max.}$ (film) 2230 cm^{-1}, τ 2·2—2·8 (4H, m, ArH), 4·53 (1H, q, CHBr), and 7·94 (3H, d, *J* 7 Hz, Me).

S-[α-(2-*Cyanophenyl*)*ethyl*]*thioglycolic Acid*.—Thioglycolic acid (0·438 g) dissolved in a solution of potassium hydroxide (0·534 g) in water (5 cm^3) was added slowly to the bromobenzonitrile (6) (1 g) in ethanol (15 cm^3). After 30 min at ambient temperature the solution was refluxed for 45 min. Most of the ethanol was distilled off and water (20 cm^3) was added. The solution was washed with ether. Acidification of the aqueous fraction gave an oil which was collected into ether and washed with water. The dried ethereal solution was evaporated to yield the *cyano-acid* (7) as a liquid (1 g, 95%), b.p. 130° at 0·06 mmHg (Found: C, 59·4; H, 4·85; N, 5·9; S, 14·6. $C_{11}H_{11}NO_2S$ requires C, 59·7; H, 5·0; N, 6·35; S, 14·5%), $\nu_{max.}$ 3350—2500br, 2250, 1720, 1455, 1295, and 1135 cm^{-1}, τ ($CDCl_3$) −0·62 (1H, s, OH), 2·43 (4H, m, ArH), 5·37 (1H, q, *J* 7 Hz, C*H*·CH_3), 6·88 (2H, s), and 8·36 (3H, d, *J* 7 Hz); *methyl ester*, b.p. 130—132° at 0·4 mmHg (treatment with diazomethane) (Found: C, 61·05; H, 5·75; N, 5·6; S, 13·6. $C_{12}H_{13}NO_2S$ requires C, 61·2; H, 5·55; N, 5·95; S, 13·6%), $\nu_{max.}$ (film) 2240, 1730, and 1280 cm^{-1}, $\lambda_{max.}$ 202 (4·49), 2·26 (4·00), 280 (3·12), and 286 nm (3·12), τ (CCl_4) 2·54 (4H, m, ArH), 5·42 (1H, q, *J* 7 Hz, C*H*·CH_3), 6·34 (3H, s, OMe), 7·03 (2H, s), and 8·39 (3H, d, *J* 7 Hz).

S-[α-(2-*Carboxyphenyl*)*ethyl*]*thioglycolic Acid*.—The cyano-acid (7) (37·5 g) was dissolved in aqueous 20% sodium hydroxide (250 ml) and heated on steam until evolution of ammonia ceased (*ca.* 24 h). The solution was acidified and deposited slowly crystals. The aqueous solution was extracted with ether, and the dried ether layers were evaporated. The residue crystallised. The total solid product was recrystallised from water, forming the *dicarboxylic acid* (8) (81%), m.p. 122·5°, homogeneous on t.l.c. (benzene–dioxan–acetic acid, 18 : 5 : 0·5) (Found: C, 55·05; H, 5·05. $C_{11}H_{12}O_4S$ requires C, 55·0; H, 5·05%), $\nu_{max.}$ 3500—2500br, 1700, 1420, and 1300 cm^{-1}, $\lambda_{max.}$ 277 nm (2·94), τ ($CDCl_3$) −2·80 (2H, s, OH), 4·58 (1H, q, *J* 7 Hz, CH), 7·14 (2H, q, J_{AB} 15 Hz), and 8·42 (3H, d, *J* 7 Hz).

Enol Acetate of 1-*Methylisothiochroman*-4-*one*.—Fused sodium acetate (55 g), acetic anhydride (200 cm^3), and the dicarboxylic acid (8) (55 g) were heated together at 130° for 1·5 h, after which effervescence had ceased. The cooled mixture was diluted with ethanol (250 cm^3) and refluxed for 3 h, then poured into water (400 cm^3) and extracted with ether. The ether extracts were washed with aqueous sodium carbonate and water, and dried. Evaporation of the solvent left a solid, which gave the *enol acetate* (9), m.p. 90° [from ethanol (charcoal)] (37·1 g, 61%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 65·65; H, 5·45. $C_{12}H_{12}O_2S$ requires C, 65·4; H, 5·5%), $\nu_{max.}$ 1750, 1625, 1370, and 1115 cm^{-1}, $\lambda_{max.}$ 208 (4·34), 239 (3·91), and 319 (3·77) nm, τ (CCl_4) 2·83 (4H, m, ArH), 4·02 (1H, d, *J* 2 Hz, 3-H), 6·17 (1H, dq, *J* 2 and 7 Hz, 1-H), 7·80 (3H, s, Ac), and 8·43 (3H, d, *J* 7 Hz, 1-Me).

1-*Methylisothiochroman*-4-*one*.—Sodium hydroxide (7·5 g) in water (50 cm^3) was added slowly with shaking to a solution of the enol acetate (9) (37 g) in ethanol (250 cm^3). The solution was heated to 60° and most of the ethanol was evaporated off. Water (100 cm^3) was added and the mixture extracted with ether (250 cm^3). The organic extracts were evaporated and the residue was crystallised from ethanol to give 1-*methylisothiochroman*-4-*one* (10), m.p. 90—91° (30 g, 90%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 67·45; H, 5·7%; *M*, 178. $C_{10}H_{10}OS$ requires C, 67·35; H, 5·65%; *M*, 178), $\nu_{max.}$ 1675, 1600, 1455, and 1275 cm^{-1}, $\lambda_{max.}$ 206 (4·28), 250 (3·93), 291 (3·23), and 347 nm (2·38), τ ($CDCl_3$), 2·10 (1H, m, ArH), 2·6—3·0 (3H, m, ArH), 6·01 (1H, q, *J* 7 Hz, 1-H) 6·56 (2H, q, J_{AB} 16 Hz, 3-H_2), and 8·27 (3H, d, *J* 7 Hz, 1-Me); 2,4-*dinitrophenylhydrazone*, m.p. 194° (Found: C, 53·7; H, 4·3;

[12] W. C. Lumma and G. A. Berchtold, *J. Org. Chem.*, 1969, **34**, 1566.

N, 15·5; S, 8·3. $C_{16}H_{14}N_4O_4S$ requires C, 53·6; H, 3·95; N, 15·5; S, 8·95%).

1-*Methylisothiochroman*-4-*one* 2,2-*Dioxide*.—1-Methylisothiochromanone (10) (2·0 g) was dissolved in acetic acid (20 cm³) and acetic anhydride (10 cm³) and cooled to 0°. Hydrogen peroxide (100 vol; 10 cm³) was added with stirring. The temperature was allowed to rise to ambient and stirring was continued for 4 h. The solution was diluted with ice-cold water (150 cm³) and extracted with methylene chloride. The washed and dried extracts were evaporated. The residue crystallised from ethanol giving 1-*methylisothiochroman*-4-*one* 2,2-*dioxide*, m.p. 154° (78%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 57·6; H, 4·75; S, 14·5. $C_{10}H_{10}O_3S$ requires C, 57·1; H, 4·8; S, 15·25%), $\nu_{max.}$ 1685, 1600, 1455, and 1330 cm^{-1}, $\lambda_{max.}$ 206 (4·34), 253 (4·04), and 291 nm (3·23), τ ($CDCl_3$) 1·77 (1H, m, ArH), 2·5 (3H, m, ArH), 5·58 (1H, q, J 7 Hz, 1-H), 5·78 (2H, q, J_{AB} 15 Hz, 3-H), and 8·16 (3H, d, J 7 Hz, 1-Me).

Reaction of 1-*Methylisothiochroman*-4-*one with Methylmagnesium Iodide*.—Methylmagnesium iodide was prepared in ether (60 cm³) from magnesium (3·5 g) and a slight excess of methyl iodide. 1-Methylisothiochromanone (14·80 g) in dry ether (200 cm³) was added, dropwise with stirring. Refluxing was maintained for 2 h. After addition of water and hydrochloric acid, the ether layer was separated and dried. Evaporation of the solvent afforded a mixture of the alcohols (13) (84%). Part (0·3 g) of the mixture was separated by p.l.c. (chloroform–ethyl acetate, 8 : 1). The band of lower R_F gave, after extraction and crystallisation from light petroleum, 1,4-*dimethylisothiochroman*-4-*ol* (13), m.p. 120—120·5°, (194 mg) (Found: C, 67·85; H, 7·15; S, 15·9. $C_{11}H_{14}OS$ requires C, 68·0; H, 7·25; S, 16·5%), $\nu_{max.}$ 3600, 3500, 1375, 1335, and 1075 cm^{-1}, $\lambda_{max.}$ 205 (4·03), 262 (2·32), 268 (2·19), and 272 nm (2·17), τ ($CDCl_3$) 2·37 (1H, m, ArH), 2·65—2·9 (3H, m, ArH), 6·10 (1H, q, J 7 Hz, 1-H), 7·07 (2H, q, J_{AB} 14 Hz, 3-H_2), 7·40 (1H, s, OH), 8·36 (3H, s, 4-Me), and 8·36 (3H, d, J 7 Hz, 1-Me). The band of higher R_F gave the isomeric liquid *alcohol* (80 mg) (Found: C, 68·05; H, 7·0%), $\nu_{max.}$ 3570br, 1380, 1340, and 1080 cm^{-1}, τ ($CDCl_3$) 2·35 (1H, m, ArH), 2·6—2·9 (3H, m, ArH), 6·11 (1H, dq, J 1 and 7 Hz, 1-H), 7·03 (2H, m, J_{AB} 14 Hz, $J_{1,3}$ 1 Hz, 3-H_2), 8·33 (3H, s, 4-Me), and 8·39 (3H, d, J 7 Hz, 1-Me).

1,4-*Dimethyl*-1H-*isothiochromen*.—A mixture of the alcohols (13) (250 mg) and toluene-*p*-sulphonic acid (40 mg) was refluxed in benzene (25 cm³) with continuous water separation (Dean–Stark). The solution was washed with aqueous sodium carbonate, dried, and evaporated. The residue crystallised from light petroleum to yield the *isothiochromen* (14), m.p. 76—78° (71%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 74·9; H, 6·6. $C_{11}H_{12}S$ requires C, 74·95; H, 6·8%), $\nu_{max.}$ 1600, 1485, 1455, 1380, and 1368 cm^{-1}, $\lambda_{max.}$ 209 (4·31), 239 (3·87), 248 (3·78), and 318 nm (3·77), τ (CCl_4), 2·85 (4H, m, ArH), 3·92 (1H, m, J 1 and 2 Hz, 3-H), 6·19 (1H, dq, J 2 and 7 Hz, 1-H), 7·83 (3H, d, J 1 Hz, 4-Me), and 8·57 (3H, d, J 7 Hz, 1-Me).

1,4-*Dimethyl*-1H-*isothiochromen* 2,2-*Dioxide*.—The isothiochromen (14) (1·50 g) in glacial acetic acid (30 cm³) was cooled while hydrogen peroxide (100 vol) was added (excess). The solution was set aside for 24 h and then kept at 0° overnight. The precipitate was collected and recrystallised from 50% aqueous ethanol to give the *sulphone* (18), m.p. 110° (1·4 g), homogeneous on t.l.c. (benzene–dioxan–acetic acid, 36 : 10 : 1) (Found: C, 63·55; H, 5·9. $C_{11}H_{12}O_2S$ requires C, 63·4; H, 5·8%), $\nu_{max.}$ 1615, 1455, 1300, and 1120 cm^{-1}, $\lambda_{max.}$ 208 (4·19), 214 (4·18), 219 (4·19), and 273 nm (3·88), τ ($CDCl_3$) 2·57 (4H, m, ArH), 3·57 (1H, m, J 1·5 and 1·5 Hz, 3-H), 5·86 (1H, dq, J 1·5 and 7 Hz, 1-H), 7·70 (3H, d, J 1·5 Hz, 4-Me), and 8·36 (3H, d, J 7 Hz, 1-Me).

cis-1,4-*Dimethylisothiochroman*.—The chromen (14) (1·25 g) in ethanol (100 cm³) was heated at 80° under hydrogen (40 atm) over 10% palladium–carbon (1·3 g) for 4 h. After filtration and evaporation, the residual liquid product was purified *via* the mercurichloride (see later) to yield cis-1,4-*dimethylisothiochroman* (15), (0·97 g, 77%), b.p. 110—115° at 0·4 mmHg, homogeneous on t.l.c. (benzene–light petroleum, 2 : 5) (Found: C, 74·1; H, 7·95; S, 17·95%; M, 178. $C_{11}H_{14}S$ requires C, 74·1; H, 7·9; S, 18·0%; M, 178), $\nu_{max.}$ 1605, 1495, 1465, 1380, 1100, and 1035 cm^{-1}, $\lambda_{max.}$ 209 (4·03), 258 (2·56), 263 (2·57), and 270 nm (2·43), τ [$(CD_3)_2CO$] 2·81 (4H, m, ArH), 5·99 (1H, q, J 7 Hz, 1-H), 6·94 (1H, m, 4-H), 6·98 (1H, m, 4*eq*-H), 7·61 (1H, m, 4*ax*-H), 8·44 (3H, d, J 7 Hz, 1-Me), and 8·57 (3H, d, J 7 Hz, 4-Me). Other coupling constants are shown in Table 2. The total hydrogenation product was spectroscopically and chromatographically very similar to the purified material. The *mercurichloride derivative* was prepared from the initial reaction product (0·2 g) in ethanol (5 cm³) by treating with mercury(II) chloride (1 g) in water (30 cm³) for 2 h; m.p. 127° (Found: C, 29·2; H, 3·0. $C_{11}H_{14}Cl_2HgS$ requires C, 29·35; H, 3·15%). The m.p. was not raised by recrystallisation. Shaking the derivative with ether (5 cm³) and aqueous 5% sodium hydroxide (10 cm³) for 5 h released the purified isothiochroman (15), which was isolated from the ether layer (0·15 g).

cis-1,4-*Dimethylisothiochroman* 2,2-*Dioxide*.—The isothiochroman (15) (140 mg) in acetic acid (10 cm³) was mixed with potassium permanganate (0·4 g) in 2M-sulphuric acid (15 cm³) and left for 2 h. Sodium disulphite (0·5 g) in 4M-hydrochloric acid (20 cm³) was added, and the solution was extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate and water. Evaporation of the dried solution gave a solid, crystallising from aqueous ethanol to yield the *sulphone* (16), m.p. 119—120° (68%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 62·85; H, 6·8; S, 14·75%; M, 210. $C_{11}H_{14}O_2S$ requires C, 62·8; H, 6·7; S, 15·25%; M, 210), $\nu_{max.}$ 1460, 1315, 1295, and 1115 cm^{-1}, $\lambda_{max.}$ 211 (3·87), 258 (2·32), 267 (2·25), and 271 nm (2·17), τ [$(CD_3)_2CO$] 2·65 (4H, m, ArH), 5·74 (1H, q, J 7 Hz, 1-H), 6·40 (1H, m, 4-H), 6·61 (1H, m, 3*eq*-H), 7·18 (1H, m, 3*ax*-H), 8·32 (3H, d, J 7 Hz, 1-Me), and 8·48 (3H, d, J 6·5 Hz, 4-Me). Other coupling constants are given in Table 1. The n.m.r. spectrum was measured in dry pyridine (0·3 cm³) containing 30% sodium deuterioxide in deuterium oxide (0·1 cm³). Deuterium incorporation at C-1 was complete in 10 min, with disappearance of the quartet (τ 5·8) and collapse of the 1-Me signal to a singlet. No new bands appeared in 2 h. Repetition of the experiment with pyridine–aqueous sodium hydroxide and isolation of the product produced only unchanged sulphone, m.p. 119—120°.

Hydrogenation of 1,4-*Dimethylisothiochromen* 2,2-*Dioxide*.—The sulphone (18) (100 mg) was dissolved in ethanol (10 ml) and hydrogenated at ambient temperature and pressure over 10% palladium–carbon (100 mg). After filtration and concentration, the *cis*-sulphone (16) crystallised (100 mg, 99%), m.p. 119—120°, identical (spectra and t.l.c.) with the foregoing sample.

S-[α-(2-*Cyanophenyl*)*ethyl*]*thiolactic Acid*.—Thiolactic acid

(2·53 g) and potassium hydroxide (2·67 g) in water (19 cm³) were added to *o*-(α-bromoethyl)benzonitrile (5 g) in ethanol (50 cm³). The mixture was shaken (30 min) and then refluxed for 2 h. After evaporation of ethanol and dilution with water, the mixture was extracted with ether (15 cm³). The aqueous layer was separated and acidified. The precipitated oil was collected in ether and dried. Evaporation afforded the *cyano-acid* (21) (4·0 g, 72%) as a viscous oil, b.p. 168—172° at 0·01 mmHg, homogeneous on t.l.c. (benzene–dioxan–acetic acid, 36 : 10 : 1) although a mixture of diastereoisomers (Found: C, 61·0; H, 5·45; N, 6·25. $C_{12}H_{13}NO_2S$ requires C, 61·25; H, 5·55; N, 5·95%), τ ($CDCl_3$) −1·23 (OH), 2·40 (m, ArH), 5·33 (q, CHAr), 5·37 (q, CHAr), 6·58 (q, C*H*Me), 6·93 (q, C*H*Me), and 8·35, 8·40, 8·55, and 8·65 (all d, Me).

S-[α-(2-*Carboxyphenyl*)*ethyl*]*thiolactic Acid*.—The cyano-acid (21) (4·0 g) in aqueous 20% sodium hydroxide (80 cm³) was heated on a steam-bath overnight. The solution was cooled, acidified, and set aside at 0° overnight. The solid was filtered off and crystallised from aqueous 20% ethanol to give the dicarboxylic acid (22) (3·0 g). Fractional crystallisation from water separated the two diastereoisomers; the less soluble *acid* (22) had m.p. 148—149° (Found: C, 56·5; H, 5·6; S, 12·3. $C_{12}H_{14}O_4S$ requires C, 56·65; H, 5·55; S, 12·6%), $\nu_{max.}$ 3200—2500br, 1682, 1455, 1370, 1290, and 1260 cm⁻¹, τ ($CDCl_3$) −2·44 (2H, s, OH), 2·40 (4H, m, ArH), 4·58 (1H, q, *J* 7 Hz, ArCH), 7·28 (1H, q, *J* 7 Hz, C*H*Me), 8·43 (3H, d, *J* 7 Hz, Me), and 8·74 (3H, d, *J* 7 Hz, Me). The more soluble *diacid* had m.p. 133—134° (Found: C, 56·95; H, 5·75; S, 12·1%), $\nu_{max.}$ 3200—2500br, 1700, 1670, 1460, 1300, and 1270 cm⁻¹, τ ($CDCl_3$) −2·44 (2H, s, OH), 2·35 (4H, m, ArH), 4·43 (1H, q, *J* 7 Hz, ArCH), 6·35 (1H, q, *J* 7 Hz, C*H*Me), 8·30 (3H, d, *J* 7 Hz, Me), and 8·68 (3H, d, *J* 7 Hz, Me).

Enol Acetate of 1,3-*Dimethylisothiochroman*-4-*one*.—A mixture of the dicarboxylic acids (22) (0·85 g), fused sodium acetate (0·85 g), and acetic anhydride (3 cm³) was heated at 130° for 75 min. Ethanol (15 cm³) was added, and the solution refluxed for 1 h. After dilution of the mixture with water it was extracted with ether. The extracts were washed with aqueous sodium carbonate and water, and dried. Evaporation of the solvent produced the *enol acetate* (23), m.p. 86° (from ethanol) (92%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 66·45; H, 6·0%; *M*, 234. $C_{13}H_{14}O_2S$ requires C, 66·6; H, 6·05%; *M*, 234), $\nu_{max.}$ 1750, 1623, 1490, 1450, 1375, 1115, and 1080 cm⁻¹, $\lambda_{max.}$ 208 (4·61), 238 (3·92), and 313 nm (3·82), τ (CCl_4) 2·82 (4H, s, ArH), 6·20 (1H, q, *J* 7 Hz, 1-H), 7·83 (3H, s, Ac), 8·10 (3H, s, 3-Me), and 8·46 (3H, d, 1-Me).

1,3-*Dimethylisothiochroman*-4-*one*.—The enol acetate (23) (2·5 g) in ethanol (50 cm³) with aqueous 10% sodium hydroxide (10 cm³) was set aside for 30 min and diluted with water (200 cm³). The mixture was extracted with ether. The dried extracts were evaporated to yield 1,3-*dimethylisothiochroman*-4-*one* (24) as a mixture of *cis*- and *trans*-isomers, b.p. 120° at 0·05 mmHg (Found: C, 68·55; H, 6·25%; *M*, 192. $C_{11}H_{12}OS$ requires C, 68·7; H, 6·25%; *M*, 192), $\nu_{max.}$ 1680 cm⁻¹, τ ($CDCl_3$) 1·95 (m, ArH), 2·5—2·9 (m, ArH), 5·5—6·4 (m, C*H*Me), and 8·22, 8·39, 8·54, and 8·66 (all d, Me).

1,3-*Dimethylisothiochromen*.—The ketone (24) (5 g) in ethanol (75 cm³) was treated with sodium borohydride (1·35 g) for 2 h. Most of the ethanol was evaporated off and water (30 cm³) was added. Extraction of the solution with ether and evaporation of the dried extracts gave an oily mixture of the stereoisomers of the alcohol (25) (98%). The alcohols (0·4 g) were refluxed in light petroleum (b.p. 100—120°; 50 cm³) with phosphorus pentoxide (3 g) for 90 min. The solution was decanted and evaporated. Distillation of the residue gave 1,3-*dimethylisothiochromen* (26), b.p. 72° at 0·03 mmHg (0·33 g, 91%), homogeneous on t.l.c. (light petroleum–benzene, 5 : 2) (Found: C, 74·5; H, 6·75; S, 17·7%; *M*, 176. $C_{11}H_{12}S$ requires C, 74·95; H, 6·8; S, 18·2%; *M*, 176), $\nu_{max.}$ 1616, 1495, 1460, 1375, and 1135 cm⁻¹, $\lambda_{max.}$ 207 (4·39), 236 (3·82), 242 (3·80), 303 (3·70), and 313 nm (3·72), τ (CCl_4) 3·04 (4H, m, ArH), 3·66 (1H, m, 4-H), 6·18 (1H, q, *J* 7 Hz, 1-H), 8·01 (3H, d, *J* 2 Hz, 3-Me), and 8·66 (3H, d, *J* 7 Hz, 1-Me).

cis-1,3-*Dimethylisothiochroman*.—The thiochromen (26) (200 mg) in ethanol (20 cm³) was hydrogenated over 10% palladium–carbon (200 mg) under ambient conditions for 72 h. Removal of catalyst and solvent gave a mixture with two components (t.l.c.; light petroleum–benzene, 1 : 1). P.l.c. gave unchanged starting material (higher R_F) and the hydrogenated product (100 mg). The latter was purified *via* the mercurichloride, as described for the 1,4-dimethyl isomer, to yield cis-1,3-*dimethylisothiochroman* (27), b.p. 105° at 0·05 mmHg (Found: C, 74·5; H, 8·05; S, 18·0%; *M*, 178. $C_{11}H_{14}S$ requires C, 74·1; H, 7·9; S, 18·0%; *M*, 178), $\nu_{max.}$ 1600, 1450, and 1255 cm⁻¹, τ [$(CD_3)_2CO$] 2·81 (4H, m, ArH), 5·90 (1H, q, *J* 7 Hz, 1-H), 6·62 (1H, m, 3-H), 6·96 (1H, m, 4*eq*-H), 7·22 (1H, m, 4*ax*-H), 8·45 (3H, d, *J* 7 Hz, 1-Me), and 8·89 (3H, d, *J* 6·5 Hz, 3-Me). Other coupling constants are given in Table 4. Reaction with mercury(II) chloride in ethanol gave the *mercurichloride*, m.p. 150—152° (from aqueous ethanol) (Found: C, 29·4; H, 3·1. $C_{11}H_{14}Cl_2HgS$ requires C, 29·4; H, 3·15%).

cis-1,3-*Dimethylisothiochroman* 2,2-*Dioxide*.—The isothiochroman (27) was oxidised with potassium permanganate, as described for the 1,4-dimethyl isomer. The cis-1,3-*dimethyl sulphone* (28) had m.p. 83—84° (from aqueous ethanol), homogeneous on t.l.c. (benzene–dioxan–acetic acid, 36 : 10 : 1) (Found: C, 63·0; H, 6·75%; *M*, 210. $C_{11}H_{14}O_2S$ requires C, 62·8; H, 6·7%; *M*, 210), $\nu_{max.}$ 1465, 1380, 1315, 1275, 1235, and 1135 cm⁻¹, $\lambda_{max.}$ 211 (3·91), 258 (2·35), 263 (2·40), and 272 nm (2·28), τ [$(CD_3)_2CO$] 2·78 (4H, m, ArH), 5·65 (1H, q, *J* 7 Hz, 1-H), 6·51 (1H, m, 3-H), 6·57 (1H, m, 4*eq*-H), 6·91 (1H, m, 4*ax*-H), 8·32 (3H, d, *J* 7 Hz, 1-Me) and 8·73 (3H, d, *J* 7 Hz, 3-Me). Other coupling constants are given in Table 4.

trans-1,3-*Dimethylisothiochroman* 2,2-*Dioxide*.—The *cis*-1,3-dimethyl sulphone (28) (0·5 g) in pyridine (5 cm³) and aqueous 5% sodium hydroxide (0·5 cm³) was kept at room temperature for 4 h and then diluted with 2M-hydrochloric acid (25 cm³) at 0°. The solution was extracted with ether (30 cm³) and the extracts were washed with aqueous sodium carbonate and water. Evaporation of the dried extracts gave an oil which crystallised from 95% ethanol. Repeated recrystallisation afforded the trans-1,3-*dimethyl isomer* (29) (196 mg), m.p. 84—87°, mixed m.p. with the *cis*-isomer 75° (Found: C, 62·55; H, 6·85%; *M*, 210), $\nu_{max.}$ 1310, 1290, 1260, 1125, and 1115 cm⁻¹, τ [$(CD_3)_2CO$] 2·71 (4H, m, ArH), 5·78 (1H, q, *J* 7 Hz, 1-H), 6·75 (3H, m, 3-H, 4-H_2), 8·34 (3H, d, *J* 7 Hz, 1-Me), and 8·63 (3H, d, *J* 6 Hz, 3-Me). The 3-H and 4-H_2 signals were resolved on adding tris-(dipivaloylmethanato)europium(III) to the sample. Coupling constants are shown in Table 3.

Irradiation of 1-*Methylisothiochroman*-4-*one*.—The ketone (10) (1·51 g) in cyclohexane (450 cm³) was irradiated for 5 h

with a 450 W medium-pressure mercury lamp (Pyrex filter). The solution was filtered free of polymeric precipitate and evaporated. T.l.c. showed a complex mixture, from which the major component was separated by repeated p.l.c., to yield 4-*methylthiochroman*-3-*one* (49) as an oil (50 mg) (Found: C, 67·45; H, 5·9%; *M*, 178. $C_{10}H_{10}OS$ requires C, 67·35; H, 5·65%; *M*, 178), $\nu_{max.}$ 1710, 1470, and 1385 cm^{-1}, τ ($CDCl_3$) 2·60 (4H, m, ArH), 6·17 (1H, q, *J* 7 Hz, 4-H), 6·65 (2H, s, 2-H_2), and 8·46 (3H, d, *J* 7 Hz, 4-Me). Similar irradiation of the ketone (24) (1·2 g) gave the stereoisomers of the ketone (50) (160 mg), $\nu_{max.}$ 1710 cm^{-1}, τ ($CDCl_3$) 2·77 (4H, m, ArH), 6·1—6·8 (2H, 4 quartets, *J* 7 Hz), and 8·4—8·7 (3H, 4 doublets, *J* 7 Hz).

5,6-*Dihydro*-4-*methyl*-2,6-*diphenyl*-2H-*thiopyran* 1,1-*Dioxide*.—Methylmagnesium iodide was prepared from magnesium (0·39 g), ether (20 cm^3), and excess of methyl iodide. To the cooled solution was added *cis*-2,6-diphenyltetrahydrothiopyran-4-one,[1] m.p. 113° (0·76 g), in ether (10 cm^3) with stirring. After 30 min ice was added, followed by dil. hydrochloric acid. The ethereal layer was removed, washed with aqueous sodium carbonate and water, and dried. Evaporation of the ether and crystallisation of the residue from light petroleum gave the alcohol (42) (0·4 g), m.p. 85—86° (lit.,[1] 85—86°). A mixture of this alcohol (1·2 g) with phosphorus pentoxide (1·5 g) in light petroleum (b.p. 80—100°; 50 cm^3) was refluxed for 1 h. The solution was decanted and evaporated to yield the dihydrothiopyran (43) (0·62 g) (from light petroleum), m.p. 75—76° (lit.,[13] 83—84°), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 81·4; H, 6·85. Calc. for $C_{18}H_{18}S$: C, 81·15; H, 6·8%), τ ($CDCl_3$) 2·70 (10H, m, ArH), 4·31 (1H, m, 3-H), 5·12 (1H, m, 2-H), 5·79 (1H, m, 6-H), 7·50 (2H, m, 5-H_2), and 8·18 (3H, s, 4-Me). Oxidation of the dihydrothiopyran (43) (0·5 g) in acetic acid (15 cm^3) with hydrogen peroxide (100 vol) for 72 h at 0° gave a crystalline precipitate of the *sulphone* (44) (0·3 g), m.p. 179—181° (from aqueous ethanol) (Found: C, 72·35; H, 6·25; S, 9·6%; *M*, 298. $C_{18}H_{18}O_2S$ requires C, 72·5; H, 6·1; S, 10·75%; *M*, 298), $\nu_{max.}$ 1610, 1320, and 1125 cm^{-1}, $\lambda_{max.}$ 209 (4·34), 253 (2·74), 259 (2·82), 265 (2·73), and 270 nm (2·53), τ ($CDCl_3$) 2·60 (10H, m, ArH), 4·52 (1H, m, 3-H), 4·93 (1H, m, 2-H), 5·54 (1H, m, $J_{5.6}$ 4 and 12 Hz, 6-H), 6·63 (1H, m, J_{AB} 18, $J_{5.6}$ 12 Hz, 5-H), 7·32 (1H, m, J_{AB} 18, $J_{5.6}$ 4 Hz, 5-H), and 8·10 (3H, s, 4-Me).

5,6-*Dihydro*-2,4,6-*triphenyl*-2H-*thiopyran* 1,1-*Dioxide*.—The ketone (40) (3·5 g) in ether (75 cm^3) was added dropwise with stirring to phenylmagnesium bromide prepared in ether (20 cm^3) from magnesium (0·635 g) and bromobenzene (4·2 cm^3). The solution was refluxed for 2 h and shaken with cold dil. hydrochloric acid. The washed, dried, ether layer was evaporated to afford the *alcohol* (45), m.p. 153° (from ethanol) (98%), homogeneous on t.l.c. (benzene–chloroform, 1 : 1) (Found: C, 79·75; H, 6·3. $C_{23}H_{22}OS$ requires C, 79·75; H, 6·4%), $\nu_{max.}$ 3640, 3460, 1600, 1505, and 1460 cm^{-1}, τ ($CDCl_3$) 2·68 (15H, m, ArH), 5·35 (2H, m, 2-H and 6-H), 7·65 (4H, m, 3-H_2 and 5-H_2), and 8·28 (1H, s, OH). A mixture of the alcohol (1·7 g) and phosphorus pentoxide (4 g) in light petroleum (b.p. 80—100°; 100 cm^3) was refluxed for 4 h. The solution was decanted and evaporated to yield the dihydrothiopyran (46) as an oil. The latter (0·5 g) in glacial acetic acid (10 cm^3) was mixed with excess of hydrogen peroxide (100 ml) and set aside at 0°. Filtration gave the *sulphone* (47) m.p. 227° (0·42 g), homogeneous on t.l.c. (benzene–dioxan–acetic acid, 36 : 10 : 1) (Found: C, 77·1; H, 5·6%; *M*, 360. $C_{23}H_{20}O_2S$ requires C, 76·65; H, 5·6%; *M*, 360), $\lambda_{max.}$ 223 (4·43) and 244 nm (4·09), τ ($CDCl_3$) 2·45 (15H, m, ArH), 3·88 (1H, m, 3-H), 4·24 (1H, m, 2-H), 4·96 (1H, m, *J* 5 and 12 Hz, 6-H), 6·17 (1H, m, J_{AB} 18, $J_{5.6}$ 12 Hz, 5-H), and 6·71 (1H, m, J_{AB} 18, $J_{5.6}$ 5 Hz, 5-H).

Enol Acetate of trans-2,6-*Diphenyltetrahydrothiopyrone* 1,1-*Dioxide*.—The *trans*-ketone (41) was oxidised to the corresponding sulphone (as just described), m.p. 184—185° (lit.,[14] 196°) (Found: C, 68·15; H. 5·15. Calc. for $C_{17}H_{16}O_3S$: C, 68·0; H, 5·35%), $\nu_{max.}$ 1715, 1600, 1324, and 1125 cm^{-1}, τ ($CDCl_3$) 2·60 (10H, m, ArH), 5·47 (2H, q, *J* 4·5 and 9 Hz, 2-H and 6-H), and 6·57 (4H, m, J_{AB} 16 Hz). On keeping a mixture of the sulphone (150 mg) in chloroform (5 cm^3) and acetic anhydride (0·4 cm^3) with 60% perchloric acid (0·1 cm^3) for 4 h, washing with aqueous alkali and water, and evaporating, the *enol acetate* (48) was obtained, m.p. 219—221° (60 mg) (Found: C, 66·45; H, 5·3. $C_{19}H_{18}O_4S$ requires C, 66·65; H, 5·3%), $\nu_{max.}$ 1745 cm^{-1}, τ ($CDCl_3$) 2·60 (10H, m, ArH), 4·37 (1H, dd, *J* 1·5 and 5 Hz, 3-H), 5·27 (1H, d, *J* 5 Hz, 2-H), 5·65 (1H, m, 6-H), 6·61 (1H, m, J_{AB} 17·5, $J_{5.6}$ 9 Hz, 5-H), 6·95 (1H, m, J_{AB} 17·5, $J_{5.6}$ 6 Hz, 5-H), and 7·80 (3H, s, Me).

Crystal Structure Determination

cis-1,4-Dimethylisothiochroman 2,2-dioxide crystallised from aqueous ethanol in prisms. Preliminary oscillation and Weissenberg photographs were taken about the *a* and *b* axes. For intensity measurements a crystal was mounted about the *b* axis on a Hilger and Watts linear diffractometer. With Mo-K_α radiation data were collected on the levels *h*0—16*l* by the moving-crystal–stationary-counter scan method. Each reflection was measured twice and the mean taken in data reduction. Reflections with a mean net count $< 3\sigma$ were considered unobserved. 1345 Reflections were observed. No absorption corrections were made. Data reduction and subsequent crystallographic calculations were performed by use of programs of Ahmed *et al.*[15] Atomic scattering factors were taken from ref. 16.

Crystal Data.—$C_{11}H_{14}O_2S$, $M = 210$, Monoclinic, $a = 8·44 \pm 0·01$, $b = 15·90 \pm 0·02$, $c = 8·22 \pm 0·01$ Å, $\beta = 114·37 \pm 0·2°$, $U = 1005$ Å^3, $D_m = 1·35$, $Z = 4$, $D_c = 1·39$, $F(000)$ 448. Space group $P2_1/c$ from systematic absences: $0k0$ when $k = 2n + 1$, $h0l$ when $l = 2n + 1$. Mo-K_α radiation, $\lambda = 0·7107$ Å; μ(Mo-K_α) = 2·8 cm^{-1}.

Structure Determination.—The sulphur co-ordinates were found from a Patterson synthesis by use of the observed intensity data sharpened by Lorentz polarisation corrections, and were used to calculate trial phases for the data. A three-dimensional Fourier map then revealed all non-hydrogen atom positions. Four cycles of block-diagonal least-squares refinement of atomic co-ordinates with isotropic temperature factors for all observed data with unit weights, gave *R* 0·14. Anisotropic thermal parameters were then introduced, and two cycles of refinement brought *R* to 0·091. At this stage a weighting scheme of the form $w = 1/\{1 + [(|F_o| - P_2)/P_1]^2\}$ with $P_1 = 10$ and $P_2 = 7·5$ was introduced, and 25 reflections on the threshold of

[13] F. Arndt and E. Schauder, *Ber.*, 1930, **63**, 313.
[14] F. Arndt, P. Natchwey, and J. Pusch, *Ber.*, 1925, **58**, 1633.
[15] F. R. Ahmed, S. R. Hall, M. E. Pippy, and C. P. Saunderson, Programs for Crystallographic Analysis, National Research Council (Ottowa).
[16] 'International Tables for *X*-Ray Crystallography, vol. III, Kynoch Press, Birmingham, 1962.

observation were omitted from refinement. Three more cycles of refinement were calculated, when R was reduced to 0·081. No further reduction of R was obtained on further least-squares refinement. The final atomic co-ordinates and anisotropic temperature factors with their standard deviation are given in Tables 5 and 6. Bond lengths and angles are shown in Tables 7 and 8. Observed and calculated structure factors are listed in supplementary Publication No. SUP 20590 (9 pp., 1 microfiche).*

TABLE 5

Atomic co-ordinates

Atom	x/a	y/b	z/c
S(1)	0·0536(2)	0·1343(1)	0·1170(2)
O(1)	−0·1079(6)	0·0893(4)	0·0270(7)
O(2)	0·0426(7)	0·2122(4)	0·1944(7)
C(1)	0·2035(10)	0·0649(5)	0·2750(9)
C(1a)	0·3867(9)	0·1024(4)	0·3323(8)
C(3)	0·1600(10)	0·1534(6)	−0·0180(9)
C(4)	0·3308(9)	0·0992(5)	0·0285(8)
C(4a)	0·4501(9)	0·1178(4)	0·2094(8)
C(5)	0·6231(10)	0·1510(5)	0·2554(11)
C(6)	0·7264(11)	0·1681(6)	0·4274(12)
C(7)	0·6607(11)	0·1544(6)	0·5442(11)
C(8)	0·4901(11)	0·1198(5)	0·4984(10)
C(9)	0·1325(12)	0·0550(6)	0·4097(11)
C(10)	0·4126(12)	0·1218(7)	−0·0963(10)

TABLE 6

Thermal parameters ($\times 10^4$) *

Atom	B_{11}	B_{22}	B_{33}	B_{23}	B_{13}	B_{12}
S(1)	168(3)	42(1)	135(3)	−18(3)	98(5)	2(3)
O(1)	152(10)	61(3)	235(11)	−73(9)	111(7)	−48(9)
O(2)	260(12)	52(3)	191(10)	−46(9)	51(18)	59(9)
C(1)	208(15)	41(3)	150(12)	45(10)	194(22)	21(11)
C(1a)	182(14)	37(3)	115(10)	3(9)	114(19)	19(10)
C(3)	196(16)	81(5)	140(12)	75(13)	137(22)	20(14)
C(4)	196(15)	60(4)	112(11)	0(10)	143(21)	−0(13)
C(4a)	184(14)	31(3)	155(12)	−2(9)	133(20)	−1(10)
C(5)	183(15)	38(4)	284(19)	−9(12)	160(27)	−19(11)
C(6)	216(18)	56(4)	274(21)	−41(15)	74(31)	18(14)
C(7)	223(18)	65(5)	208(16)	−59(14)	−43(27)	60(15)
C(8)	261(18)	53(5)	137(11)	−9(11)	63(23)	71(14)
C(9)	326(22)	70(5)	235(17)	53(15)	408(34)	26(16)
C(10)	330(22)	97(6)	186(16)	20(16)	346(31)	−28(19)

* In the form: $\exp -(h^2B_{11} + k^2B_{22} + l^2B_{33} + hkB_{12} + hlB_{13} + klB_{23})$.

TABLE 7

Bond lengths (Å)

S–C(1)	1·817(8)	C(8)–C(7)	1·44(1)
S–C(3)	1·788(9)	C(7)–C(6)	1·37(1)
S–O(1)	1·452(6)	C(6)–C(5)	1·43(1)
S–O(2)	1·436(6)	C(5)–C(4a)	1·45(1)
C(1)–C(1a)	1·54(1)	C(4a)–C(4)	1·52(1)
C(1)–C(9)	1·54(1)	C(4)–C(3)	1·58(1)
C(1a)–C(8)	1·39(1)	C(4)–C(10)	1·56(1)
C(1a)–C(4a)	1·41(1)		

TABLE 8

Bond angles (°)

O(1)–S–O(2)	117·0(0·4)	C(1a)–C(8)–C(7)	119·6(0·8)
O(1)–S–C(1)	108·7(0·4)	C(8)–C(7)–C(6)	121·3(0·8)
O(1)–S–C(3)	109·7(0·4)	C(7)–C(6)–C(5)	120·4(0·9)
O(2)–S–C(1)	108·7(0·4)	C(6)–C(5)–C(4a)	118·1(0·8)
O(2)–S–C(3)	108·6(0·4)	C(5)–C(4a)–C(4)	121·4(0·7)
C(1)–S–C(3)	103·4(0·4)	C(5)–C(4a)–C(1a)	120·4(0·7)
S–C(1)–C(9)	106·2(0·6)	C(4)–C(4a)–C(1a)	118·2(0·6)
S–C(1)–C(1a)	107·7(0·5)	C(4a)–C(4)–C(3)	107·7(0·6)
C(9)–C(1)–C(1a)	116·4(0·7)	C(4a)–C(4)–C(10)	113·5(0·7)
C(1)–C(1a)–C(8)	122·2(0·7)	C(4)–C(3)–S	112·9(0·6)
C(4a)–C(1a)–C(8)	120·1(0·7)		
C(1)–C(1a)–C(4a)	117·6(0·6)	C(10)–C(4)–C(3)	108·2(0·6)

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* For details see Notice to Authors No. 7 in *J. Chem. Soc.* (*A* 1970, Issue No. 20 (items less than 10 pp. are sent as full size copies).