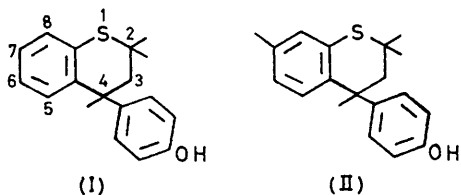


## Synthesis and X-Ray Structural Analysis of 4-*p*-Hydroxyphenyl-2,2,4,7-tetramethylthiochroman

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The title compound has been prepared and its crystal and molecular structure determined by three dimensional X-ray analysis. Crystals are orthorhombic,  $a = 11.777(1)$ ,  $b = 16.501(2)$ ,  $c = 8.479(1)$  Å,  $Z = 4$ , space group  $P2_12_12_1$ . The structure was solved by a combination of conventional Patterson and direct methods, and refined by least-squares methods to a final  $R$  of 0.091, employing 1 136 diffractometer data. The crystal structure possesses infinite chains of molecules linked head-to-tail by  $\text{OH} \cdots \text{S}$  hydrogen bonds of length 3.34 Å, such that no voids are left for solvent inclusion.

In connection with a series of studies on clathrate formation, we have recently given a preliminary account<sup>1</sup> concerning structural modification of the known<sup>2</sup> versatile clathrate host 4-*p*-hydroxyphenyl-2,2,4-trimethylthiochroman (I). Introduction of a single additional methyl group at either the 6- or at the 8-position<sup>3</sup> gave new clathrate hosts, whereas the 7-methyl isomer (II) was found to crystallise without inclusion of solvent. In order to establish the packing arrangement of (II) in the crystal, and also to obtain detailed information about its molecular structure, we have performed a single-crystal X-ray diffraction analysis on this compound.



### EXPERIMENTAL

**Preparation of (II).**—A mixture of phenol (34.6 g) and 4-methyl-4-(*m*-tolylthio)pentan-2-one, prepared<sup>4</sup> from *m*-thiocresol and mesityl oxide was saturated (6 h) at 0 °C with dry hydrogen chloride. The resulting dark-green viscous liquid was then set aside in a flask fitted with a drying tube; after 4 months, the excess of phenol was extracted with boiling water (5 × 150 ml) leaving a pale brown glass. Chromatography on Mallinckrodt silicic acid (ratio 55 : 1, eluant 50% ethyl acetate in benzene) gave a pale yellow oil which defied crystallisation. Final purification was achieved by gel permeation chromatography (200 × 2.5 cm column of Sephadex LH-20 modified<sup>5</sup> with Nedox 1114, elution with methanol) which gave a colourless oil having a s.e.v. of ca. 150. Crystallisation was induced by suddenly cooling a sample dissolved in the minimum volume of hot light petroleum with simultaneous scratching, whereupon fine white crystals were deposited. Recrystallisation from cyclopentane gave single, colourless, unsolvated prisms, m.p. 114–115 °C (43%) (Found: C, 76.28; H, 7.32.  $\text{C}_{19}\text{H}_{22}\text{OS}$  requires C, 76.48; H, 7.43%;  $M$ ,

298);  $m/e$  298 ( $M^+$ );  $\nu_{\text{max}}$  (KBr) 3 335  $\text{cm}^{-1}$  (OH);  $\tau$  ( $\text{CDCl}_3$ ) 2.7–3.5 (7 H, m), 5.22 (1 H, s), 7.75 (2 H, ABq,  $\delta_{\text{AB}}$  0.30 p.p.m.  $J$  14 Hz), and 7.73, 8.26, 8.59, and 8.92 (each 3 H, all singlets).

Compound (II) was also found to crystallise unsolvated from cyclohexane, methylcyclohexane, and benzene.

### X-Ray Crystal Structure Analysis of (II)

**Crystal Data.**— $\text{C}_{19}\text{H}_{22}\text{OS}$ ,  $M = 298.4$ , recrystallised from cyclopentane, orthorhombic,  $a = 11.777(1)$ ,  $b = 16.501(2)$ ,  $c = 8.479(1)$  Å,  $Z = 4$ ,  $U = 1\ 647.7$  Å<sup>3</sup>,  $D_c = 1.20$  g  $\text{cm}^{-3}$ ,  $F(000) = 640$ . Mo- $K_\alpha$  radiation,  $\lambda = 0.710$  7 Å,  $\mu(\text{Mo-}K_\alpha) = 1.90$   $\text{cm}^{-1}$ . Space group  $P2_12_12_1$ . The crystal used was a colourless prism of dimensions ca. 0.81 × 0.62 × 0.44 mm.

**Crystallographic Measurements.**—Least-squares best cell dimensions were obtained by a treatment of the  $\theta, \chi, \phi$ , setting angles of 12 reflections measured on a Hilger and Watts automatic diffractometer. Intensities were measured by the  $\theta$ – $2\theta$  step scan procedure with Zr-filtered Mo- $K_\alpha$  radiation. Background counts were taken at each end of the scan range. The intensities of three standard reflections were monitored after every 50 intensity measurements, and the results used to place the reflections on a common scale. Reflections were surveyed out to  $\theta \leq 28^\circ$ . The intensity values were corrected for Lorentz polarisation effects, but not for absorption, and a total of 2 269 independent reflections were obtained [1 136 reflections having  $I/\sigma(I) > 2.0$  were considered observed].

**Structure Analysis.**—The co-ordinates of the sulphur atom were found from a sharpened three-dimensional Patterson map. A three-dimensional electron-density distribution phased on this atom ( $R$  45.5%) could not be unambiguously interpreted, and so the phases appropriate to the heavy atom were used as a starting point for tangent formula refinement (by use of the direct methods programme TANGEN of the 'X-Ray '72' system<sup>6</sup>). A starting set of 83 reflections ( $|E| \geq 2.00$ ) was used to derive the phases of 228 reflections with  $|E| \geq 1.60$ . The subsequent  $E$  map revealed the positions of 19 of the 21 non-hydrogen atoms in the asymmetric unit, and the two remaining carbon atoms were found in a later difference electron-density distribution. These approximate atomic parameters were adjusted by several cycles of full-matrix

<sup>1</sup> A. D. U. Hardy, J. J. McKendrick, and D. D. MacNicol, *J.C.S. Chem. Comm.*, 1974, 972.

<sup>2</sup> D. D. MacNicol, *Chem. Comm.*, 1969, 836; D. D. MacNicol, H. H. Mills, and F. B. Wilson, *ibid.*, p. 1332; D. D. MacNicol and F. B. Wilson, *ibid.*, 1971, 786.

<sup>3</sup> For a report of the crystal structure of 4-*p*-hydroxyphenyl-2,2,4,8-tetramethylthiochroman see, D. D. MacNicol, A. D. U. Hardy, and J. J. McKendrick, *Nature*, 1975, 256, 343.

<sup>4</sup> D. D. MacNicol and J. J. McKendrick, *J.C.S. Perkin I*, 1974, 2493.

<sup>5</sup> J. Ellingboe, E. Nystrom, and J. Sjoval, *Biochim. Biophys. Acta*, 1968, 152, 803; *J. Lipid Res.*, 1970, 11, 266.

<sup>6</sup> 'X-Ray '72' suit of programmes, J. M. Stewart, G. J. Kruger, M. L. Ammon, C. Dickenson, and S. R. Hall, 1972, Technical Report TR 192, Computer Science Centre, University of Maryland.

least-squares calculations, and with anisotropic temperature factors for all atoms  $R$  was reduced to 12.7%.

The twenty-two hydrogen atoms in the molecule were

TABLE 1

Atomic co-ordinates ( $\times 10^4$ ), with estimated standard deviations in parentheses

	$x$	$y$	$z$
S(1)	0 740(2)	-2 335(1)	1 893(3)
C(2)	1 682(9)	-2 897(5)	0 547(12)
C(3)	2 763(8)	-3 177(6)	1 414(11)
C(4)	2 762(7)	-3 282(6)	3 213(12)
C(5)	3 169(8)	-2 139(8)	5 173(14)
C(6)	2 943(10)	-1 382(9)	5 782(12)
C(7)	2 086(9)	-0 909(7)	5 258(15)
C(8)	1 471(8)	-1 218(6)	3 979(13)
C(9)	1 669(7)	-1 972(5)	3 361(10)
C(10)	2 547(8)	-2 457(6)	3 948(11)
C(11)	1 934(8)	-3 920(6)	3 734(11)
C(12)	1 878(7)	-4 692(6)	3 076(12)
C(13)	1 114(9)	-5 277(6)	3 538(14)
C(14)	0 366(8)	-5 118(6)	4 750(12)
C(15)	0 416(7)	-4 380(7)	5 492(12)
C(16)	1 177(8)	-3 787(6)	5 008(12)
C(17)	3 967(8)	-3 621(7)	3 657(13)
C(18)	0 952(11)	-3 598(7)	-0 057(14)
C(19)	2 016(10)	-2 374(8)	-0 828(13)
C(20)	1 845(10)	-0 098(7)	5 954(15)
O(21)	-0 412(5)	-5 669(4)	5 301(8)

TABLE 2

Interatomic distances ( $\text{\AA}$ ), with standard deviations in parentheses

S(1)-C(2)	1.843 (10)	C(6)-C(7)	1.350 (17)
S(1)-C(9)	1.762 (9)	C(7)-C(8)	1.400 (16)
C(2)-C(3)	1.541 (14)	C(7)-C(20)	1.491 (17)
C(2)-C(18)	1.528 (15)	C(8)-C(9)	1.369 (13)
C(2)-C(19)	1.503 (15)	C(9)-C(10)	1.400 (13)
C(3)-C(4)	1.536 (14)	C(11)-C(12)	1.393 (14)
C(4)-C(10)	1.519 (14)	C(11)-C(16)	1.417 (13)
C(4)-C(11)	1.501 (13)	C(12)-C(13)	1.377 (14)
C(4)-C(17)	1.571 (13)	C(13)-C(14)	1.378 (15)
C(5)-C(6)	1.379 (19)	C(14)-C(15)	1.372 (15)
C(5)-C(10)	1.375 (15)	C(14)-O(21)	1.373 (12)
C(15)-C(16)	1.390 (14)		

Mean C( $sp^3$ )-H 0.95, mean C( $sp^2$ )-H 0.94; O-H 0.90.

TABLE 3

Valency angles ( $^\circ$ ), with standard deviations in parentheses

C(9)-S(1)-C(2)	103.6(4)	C(3)-C(2)-S(1)	110.6(7)
C(18)-C(2)-S(1)	104.5(7)	C(19)-C(2)-S(1)	110.4(7)
C(18)-C(2)-C(3)	113.4(8)	C(19)-C(2)-C(3)	109.0(9)
C(19)-C(2)-C(18)	108.8(9)	C(4)-C(3)-C(2)	120.4(8)
C(10)-C(4)-C(3)	107.8(8)	C(11)-C(4)-C(3)	111.9(8)
C(17)-C(4)-C(3)	106.1(8)	C(11)-C(4)-C(10)	113.5(8)
C(17)-C(4)-C(10)	111.8(7)	C(17)-C(4)-C(11)	105.5(8)
C(10)-C(5)-C(6)	121.7(10)	C(7)-C(6)-C(5)	123.0(11)
C(8)-C(7)-C(6)	115.5(11)	C(20)-C(7)-C(6)	122.1(11)
C(20)-C(7)-C(8)	122.3(10)	C(9)-C(8)-C(7)	122.6(9)
C(8)-C(9)-S(1)	118.3(7)	C(10)-C(9)-S(1)	121.0(7)
C(10)-C(9)-C(8)	120.6(8)	C(9)-C(10)-C(5)	116.4(9)
C(9)-C(10)-C(4)	119.4(8)	C(5)-C(10)-C(4)	124.2(9)
C(12)-C(11)-C(4)	123.6(8)	C(16)-C(11)-C(4)	121.6(8)
C(16)-C(11)-C(12)	114.7(8)	C(13)-C(12)-C(11)	123.9(9)
C(14)-C(13)-C(12)	119.7(9)	C(15)-C(14)-C(13)	118.9(9)
O(21)-C(14)-C(13)	123.6(9)	O(21)-C(14)-C(15)	117.4(9)
C(16)-C(15)-C(14)	121.1(9)	C(15)-C(16)-C(11)	121.4(9)

Means: H-C( $sp^3$ )-H 107.5, C( $sp^2$ )-C( $sp^2$ )-H 118.9, C( $sp^2$ )-C( $sp^3$ )-H 107.3, and C( $sp^3$ )-C( $sp^3$ )-H 108.3; C( $sp^2$ )-O-H 107.3.

located in a difference electron-density distribution, and were included in subsequent least-squares calculations with isotropic temperature factors. After further cycles of least-squares adjustment (with the hydrogen atoms having their temperature factors fixed, all other atomic parameters

being refined), employing only the 1136 observed reflections, the final  $R$  value was 9.1% ( $R'$  8.1%). The

TABLE 4

Torsion angles ( $^\circ$ ), with standard deviations in parentheses

C(9)-S(1)-C(2)-C(3)	24.0(8)
C(9)-S(1)-C(2)-C(19)	-96.8(8)
C(2)-S(1)-C(9)-C(10)	-40.5(8)
C(18)-C(2)-C(3)-C(4)	-93.2(11)
C(2)-C(3)-C(4)-C(10)	-63.5(11)
C(2)-C(3)-C(4)-C(17)	176.6(8)
C(3)-C(4)-C(10)-C(9)	46.8(11)
C(11)-C(4)-C(10)-C(9)	-77.7(11)
C(17)-C(4)-C(10)-C(9)	163.1(8)
C(3)-C(4)-C(11)-C(16)	-133.6(9)
C(10)-C(4)-C(11)-C(16)	-11.2(13)
C(17)-C(4)-C(11)-C(16)	111.5(10)
C(6)-C(5)-C(10)-C(4)	179.3(10)
C(5)-C(6)-C(7)-C(8)	-3.5(18)
C(6)-C(7)-C(8)-C(9)	4.2(16)
C(7)-C(8)-C(9)-S(1)	173.3(8)
S(1)-C(9)-C(10)-C(4)	5.1(12)
C(8)-C(9)-C(10)-C(4)	-178.6(9)
C(4)-C(11)-C(12)-C(13)	-179.3(9)
C(4)-C(11)-C(16)-C(15)	-179.6(9)
C(11)-C(12)-C(13)-C(14)	-1.9(16)
C(12)-C(13)-C(14)-O(21)	-179.0(9)
O(21)-C(14)-C(15)-C(16)	-179.9(9)
C(9)-S(1)-C(2)-C(18)	146.4(7)
C(2)-S(1)-C(9)-C(8)	143.2(8)
S(1)-C(2)-C(3)-C(4)	23.8(11)
C(19)-C(2)-C(3)-C(4)	145.4(9)
C(2)-C(3)-C(4)-C(11)	62.0(11)
C(3)-C(4)-C(10)-C(5)	-132.7(10)
C(11)-C(4)-C(10)-C(5)	102.7(11)
C(17)-C(4)-C(10)-C(5)	-16.5(13)
C(3)-C(4)-C(11)-C(12)	49.6(12)
C(10)-C(4)-C(11)-C(12)	172.0(9)
C(17)-C(4)-C(11)-C(12)	-65.3(11)
C(10)-C(5)-C(6)-C(7)	1.7(19)
C(6)-C(5)-C(10)-C(9)	-0.3(16)
C(5)-C(6)-C(7)-C(20)	178.9(11)
C(20)-C(7)-C(8)-C(9)	-178.2(10)
C(7)-C(8)-C(9)-C(10)	-3.1(15)
S(1)-C(9)-C(10)-C(5)	-175.3(8)
C(8)-C(9)-C(10)-C(5)	1.0(14)
C(16)-C(11)-C(12)-C(13)	3.7(14)
C(12)-C(11)-C(16)-C(15)	-2.6(14)
C(12)-C(13)-C(14)-C(15)	-1.1(15)
C(13)-C(14)-C(15)-C(16)	2.2(15)
C(14)-C(15)-C(16)-C(11)	-0.2(15)

weighting scheme employed throughout the least-squares calculations was  $w = 1/\sigma^2(F)$ .

Calculations were carried out on IBM 370/158 and 370/168 computers at Edinburgh and Newcastle. Observed and calculated structure factors, hydrogen atom co-

TABLE 5

Displacements ( $\text{\AA}$ ) of relevant atoms from planes through various sets of atoms

Plane (A): C(5)-(10)	
C(5) 0.003, C(6) 0.010, C(7) -0.021, C(8) 0.016, C(9) -0.005,	
C(10) -0.002, C(20) -0.036, C(4) 0.006, S(1) -0.135	
Plane (B): C(11)-(16)	
C(11) -0.019, C(12) 0.017, C(13) 0.0, C(14) -0.015, C(15)	
0.010, C(16) 0.007, O(21) -0.013, C(4) -0.015	
Plane (C): C(9), C(10), C(4), S(1)	
C(9) -0.023, C(10) 0.028, C(4) -0.014, S(1) 0.001, C(2)	
-1.085, C(3) -1.148	

ordinates, and all thermal parameters are listed in Supplementary Publication No. SUP 22026 (19 pp., 1 microfiche).\*

\* For details of Supplementary Publications see Notice to Authors No. 7, in *J.C.S. Perkin II*, 1976, Index issue.

atoms were taken from ref. 7, those for hydrogen from ref. 8. The anomalous dispersion was allowed for in the least-squares calculations, with values of  $\Delta f'$  and  $\Delta f''$  for sulphur taken from ref. 9. The atomic fractional coordinates of the 21 non-hydrogen atoms are listed in Table 1, and various parameters connected with the compound's molecular geometry in Tables 2–5. Figure 1

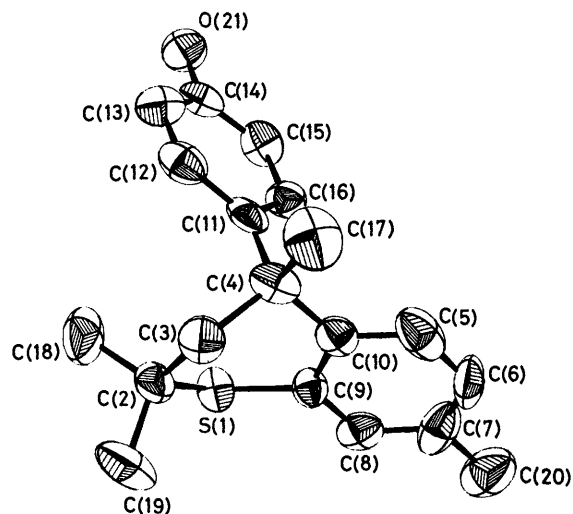


FIGURE 1 An ORTEP drawing showing a general view of the molecular structure of compound (II) in the crystal (hydrogen atoms omitted for clarity)

shows a general view of the molecular structure (for clarity all hydrogen atoms have been omitted), and Figure 2 shows the packing arrangement in the crystal, as viewed perpendicular to the  $ab$  plane, with dotted lines denoting intermolecular hydrogen bonds.

#### DISCUSSION

An interesting feature of the molecular structure of (II) is the boat conformation of the sulphur containing ring (see Figure 1); the atoms C(2) and C(3) are displaced from the mean-plane defined by the atoms C(9), C(10), C(4), and S(1) by  $-1.08$  and  $-1.15$  Å respectively. This contrasts with the corresponding displacements of  $0.25$  and  $-0.47$  Å found for the same atoms in the isomer 4-*p*-hydroxyphenyl-2,2,4,8-tetramethylthiochroman,<sup>3</sup> which has a distorted half-chair conformation for the heterocyclic ring. A less-distorted half-chair conformation of this ring has been found in the parent (I),<sup>2</sup> the displacements of C(2) and C(3) being  $0.38$  and  $-0.34$  Å.

This overall change in ring conformation is accom-

<sup>7</sup> D. T. Cromer and J. B. Mann, *Acta Cryst.*, 1968, **A24**, 321.  
<sup>8</sup> R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

panied by a change in the torsion angle C(11)–C(4)–C(10)–C(9), which is  $-77.7$  for (II),  $-104.5$  for its 8-isomer, and  $-108.2^\circ$  for the parent (I). Small but significant changes are also found in the torsion angle C(10)–C(4)–C(11)–C(16), corresponding values being  $-11.2$ ,  $-7.9$ , and  $3.5^\circ$ .

The molecular packing arrangement of (II) is illustrated in Figure 2. The molecules are linked in infinite chains in a head-to-tail manner by O–H $\cdots$ S hydrogen bonds. These chains run parallel and anti-parallel to the  $b$ -axis direction, with only van der Waals attractive forces acting between adjacent chains. The dimensions of the chain hydrogen bond [S $\cdots$ O  $3.34(1)$  and S $\cdots$ H  $2.45(8)$  Å, and O–H $\cdots$ S  $168.5(6.2)^\circ$ ] are compatible with weak hydrogen-bonding interactions.<sup>10</sup>

The structure of the parent (I) and the 8-substituted analogue contain discrete groups of six molecules, the hydroxy-groups of which are linked by O–H $\cdots$ O hydrogen bonds such that the oxygen atoms form a hexagon.<sup>3</sup> Such sextets are stacked on top of one another to form infinite columns containing closed cages between sextets. The substitution of an additional

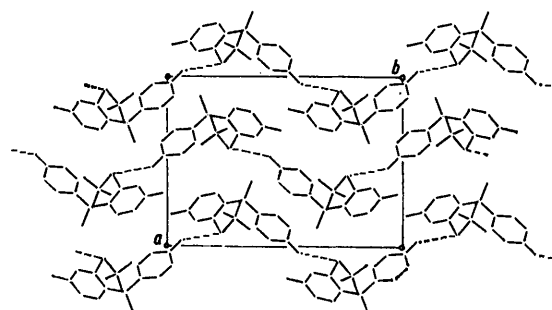


FIGURE 2 A view normal to the  $ab$  plane showing the molecular packing of (II) in the crystal. Intermolecular hydrogen bonds are denoted by broken lines

methyl group at the 7-position of (I) to give (II) results in the complete break-up of the open structure and gives a packing arrangement which leaves no voids for solvent inclusion. It is noteworthy, however, that cages are formed by both enantiomers of (I) and its 8-substituted analogue, whereas the crystallisation of (II) involves spontaneous resolution.

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<sup>9</sup> 'International Tables for X-ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

<sup>10</sup> See e.g. Lj. Manojlovic-Muir, *Acta Cryst.*, 1975, **B31**, 135, and references therein.