9-(Cyclohexylmethyl)thioxanthene 10,10-Dioxide

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Abstract. $C_{20}H_{22}O_2S$, monoclinic, $P2_1/c$, $Z=4$, M.W. 326·5, $a=6\cdot845(1)$, $b=14\cdot967(3)$, $c=16\cdot839(1)$ Å, $\beta=103\cdot24(1)°$, $D_x=1\cdot29$, $D_m=1\cdot28$ g cm^{-3} (by flotation), λ(Cu $K\alpha$)$=1\cdot5418$ Å, μ(Cu $K\alpha$)$=17\cdot13$ cm^{-1}. Final residual $R=0\cdot049$.

Introduction. Samples of 9-(cyclohexylmethyl)thioxanthene 10,10-dioxide (I) were obtained through the courtesy of Dr A. L. Ternay Jr of the Chemistry Department of the University of Texas at Arlington. Single crystals in the form of clear prisms were grown from an ethyl alcohol solution. The space group, $P2_1/c$, was deduced from systematic absences ($h0l$ absent with l odd and $0k0$ absent with k odd). Three-dimensional X-ray diffraction data were collected on a Datex-Syntex automatic diffractometer in the Biophysics and Biochemistry Department of the Texas A & M University, College Station, Texas. A crystal approximately $0\cdot27 \times 0\cdot22 \times 0\cdot51$ mm was mounted along the c axis. A $\theta/2\theta$ time variable scanning mode with Cu $K\alpha$ radiation was used to measure 1713 independent reflections with 2θ values below 100°, of which 1563 were considered as observed by the criterion $I > 3\sigma(I)$, where $\sigma(I)$ was determined from counting statistics. The intensity data were reduced to structure factors by the application of Lorentz and polarization factors, and no absorption corrections were applied. The data were scaled by means of a Wilson plot.
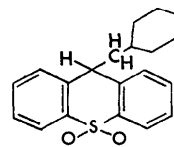
(I)

The structure was determined by the heavy-atom method. The refinement procedure, the atomic scattering factors, and the computer programs used in this analysis were the same as those described in the preceding paper by Chu & Mangion (1975). The final R index ($\sum |F_o| - |F_c| / \sum |F_o|$) was 0·049. The magnitude of $[\sum w(F_o - F_c)^2/(m-n)]^{1/2}$, where m is the number of reflections and n is the number of parameters refined, was 0·91. There were five low-order strong reflections (002, 032, 102, 131, $\bar{1}02$), whose calculated structure amplitudes were much higher than the observed values owing to extinction. They were given zero weight in the least-squares refinement and were excluded in the calculation of the final disagreement index. The final

Table 1. *Fractional atomic coordinates and thermal parameters* ($\times 10^4$)

The estimated standard deviations are given in parentheses and refer to the last positions of respective values. The expression for the temperature factor exponent consistent with β values is $-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
S	8394 (1)	1761 (1)	408 (0)	181 (2)	41 (0)	47 (0)	1 (1)	27 (1)	3 (0)
O(1)	9118 (3)	2505 (2)	17 (1)	216 (5)	60 (1)	69 (1)	−22 (2)	45 (2)	10 (1)
O(2)	9836 (3)	1096 (2)	765 (2)	246 (6)	61 (1)	69 (1)	32 (2)	24 (2)	6 (1)
C(1)	2936 (5)	1242 (2)	−963 (2)	312 (9)	57 (2)	41 (1)	−30 (3)	10 (3)	13 (1)
C(2)	3279 (6)	447 (2)	−1332 (2)	419 (11)	65 (2)	41 (1)	−76 (4)	15 (3)	1 (1)
C(3)	5126 (6)	62 (2)	−1191 (2)	510 (13)	60 (2)	42 (1)	−48 (4)	57 (4)	−5 (1)
C(4)	6728 (5)	468 (2)	−659 (2)	365 (10)	49 (2)	49 (1)	−4 (3)	58 (3)	5 (1)
C(5)	8197 (5)	2141 (2)	1962 (2)	354 (10)	40 (2)	50 (2)	−9 (3)	6 (3)	5 (1)
C(6)	7223 (7)	2456 (2)	2543 (2)	580 (14)	51 (2)	42 (2)	−6 (4)	41 (4)	1 (1)
C(7)	5337 (7)	2784 (2)	2313 (2)	627 (16)	49 (2)	54 (2)	10 (4)	92 (4)	−3 (1)
C(8)	4333 (5)	2822 (2)	1498 (2)	384 (11)	46 (2)	59 (2)	12 (3)	74 (4)	7 (1)
C(9)	4164 (4)	2528 (2)	1 (2)	197 (7)	40 (1)	45 (1)	1 (3)	22 (3)	8 (1)
C(11)	4501 (4)	1673 (2)	−424 (2)	219 (8)	45 (2)	34 (1)	−15 (3)	17 (2)	10 (1)
C(12)	6372 (4)	1265 (2)	−286 (2)	258 (8)	41 (2)	37 (1)	−10 (3)	38 (2)	3 (1)
C(13)	7185 (4)	2165 (2)	1148 (2)	261 (8)	33 (1)	40 (1)	−6 (3)	18 (3)	2 (1)
C(14)	5251 (4)	2501 (2)	894 (2)	249 (8)	31 (1)	46 (1)	0 (3)	46 (3)	2 (1)
C(15)	4751 (4)	3379 (2)	−442 (2)	224 (8)	44 (2)	57 (2)	−8 (3)	22 (3)	10 (1)
C(16)	3043 (4)	3803 (2)	−1062 (2)	215 (7)	37 (1)	45 (1)	2 (2)	29 (2)	2 (1)
C(17)	3878 (5)	4477 (2)	−1571 (2)	276 (8)	52 (2)	46 (1)	6 (3)	36 (3)	2 (1)
C(18)	2243 (5)	4999 (2)	−2170 (2)	357 (10)	55 (2)	45 (1)	−5 (3)	22 (3)	4 (1)
C(19)	825 (5)	5442 (2)	−1726 (2)	340 (10)	48 (2)	51 (2)	20 (3)	9 (3)	3 (1)
C(20)	−102 (5)	4765 (2)	−1262 (2)	266 (9)	56 (2)	68 (2)	17 (3)	31 (3)	−4 (1)
C(21)	1532 (5)	4262 (2)	−655 (2)	276 (9)	49 (2)	51 (1)	13 (3)	50 (3)	8 (1)

Table 1 (cont.)

Hydrogen atomic coordinates ($\times 10^3$)

	x	y	z
H(1)	156 (4)	157 (2)	−102 (2)
H(2)	212 (5)	21 (2)	−162 (2)
H(3)	523 (5)	−55 (2)	−145 (2)
H(4)	808 (4)	27 (2)	−56 (2)
H(5)	958 (5)	183 (2)	206 (2)
H(6)	796 (6)	241 (2)	313 (2)
H(7)	467 (6)	305 (2)	268 (2)
H(8)	290 (5)	303 (2)	132 (2)
H(9)	261 (4)	257 (2)	−5 (2)
H(15)1	514 (4)	386 (2)	−2 (2)
H(15)2	589 (4)	321 (2)	−66 (2)
H(16)	238 (4)	332 (2)	−140 (2)
H(17)1	473 (4)	413 (2)	−186 (2)
H(17)2	476 (4)	493 (2)	−117 (2)
H(18)1	283 (5)	543 (2)	−243 (2)
H(18)2	125 (4)	457 (2)	−259 (2)
H(19)1	164 (4)	590 (2)	−135 (2)
H(19)2	−23 (5)	579 (2)	−214 (2)
H(20)1	−98 (4)	437 (2)	−167 (2)
H(20)2	−97 (4)	507 (2)	−94 (2)
H(21)1	88 (4)	377 (2)	−38 (2)
H(21)2	234 (4)	474 (2)	−22 (2)

positional and thermal parameters are given in Table 1.*

Discussion. The determination of the crystal structure of 9-(cyclohexylmethyl)thioxanthene 10,10-dioxide is a continuation of the studies on a series of thioxanthene derivatives. The 9-(cyclohexylmethyl)thioxanthene molecule is related to methixene [(II), Chu, 1973] in that it is formed by the substitution of the *N*-methyl group in the piperidyl ring of the methixene by a CH_2 group. Methixene is known to possess anticholinergic, antispasmodic, and antiparkinsonism activities; however, 9-(cyclohexylmethyl)thioxanthene shows no pharmacological activities (Ternay, 1974). The determination of the structure of 9-(cyclohexylmethyl)thioxanthene 10,10-dioxide in this work showed that the configuration of the 9-(cyclohexylmethyl) substituent is identical with that of the 9-(*N*-methyl-3-piperidylmethyl) substituent in methixene. Therefore, the *N*-methyl group is a required structure unit for the pharmacological activity of methixene. The sulfone derivative of 9-(cyclohexylmethyl)thioxanthene rather than the sulfide itself was examined in order to compare the bonding characteristics of sulfur with other thioxanthene sulfone derivatives (Chu, 1975).

(II)
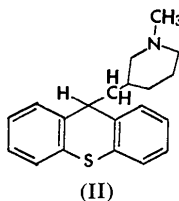
* A table of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31024 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

The configuration of a 9-(cyclohexylmethyl)thioxanthene 10,10-dioxide molecule and the identification of the atoms are shown in the *ORTEP* (Johnson, 1965) drawing, Fig. 1, which also gives the bond lengths and bond angles with their standard deviations. The mean values of the two C–S and the two S–O bond lengths are
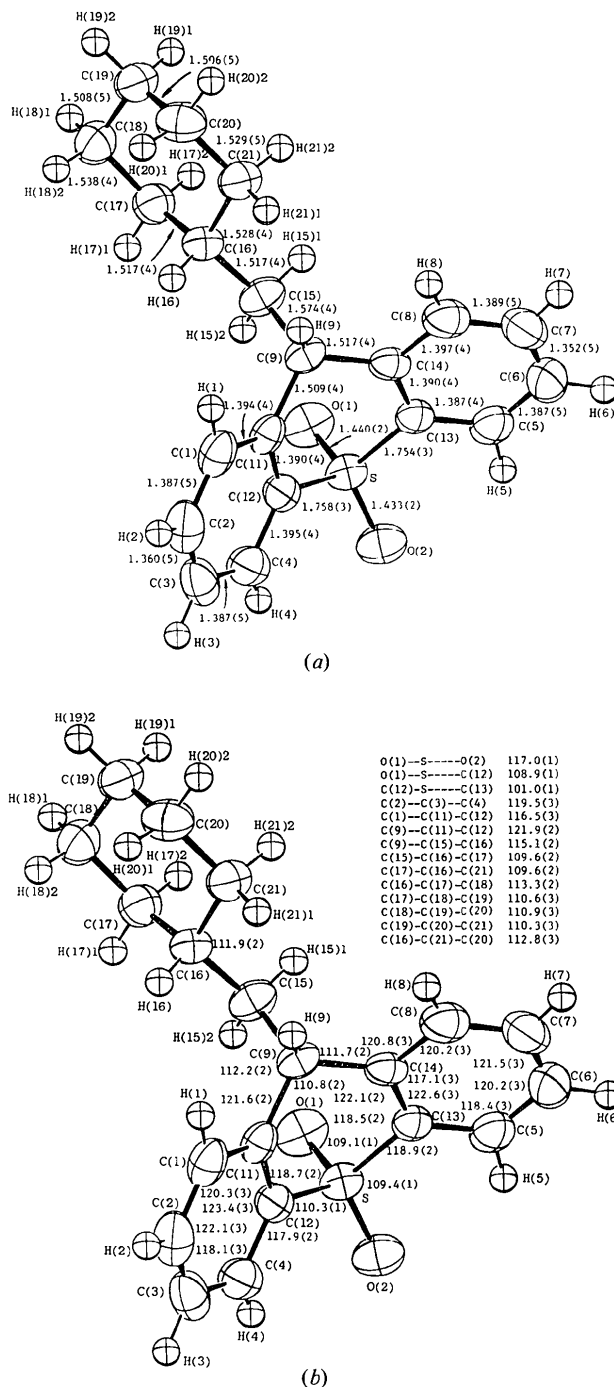

(a)

O(1)—S----O(2)	117.0(1)
O(1)—S----C(12)	108.9(1)
C(12)-S----C(13)	101.0(1)
C(2)—C(3)—C(4)	119.5(3)
C(1)—C(11)-C(12)	116.5(3)
C(9)—C(11)-C(12)	121.9(2)
C(9)—C(15)-C(16)	115.1(2)
C(15)-C(16)-C(17)	109.6(2)
C(17)-C(16)-C(21)	109.6(2)
C(16)-C(17)-C(18)	113.3(2)
C(17)-C(18)-C(19)	110.6(3)
C(18)-C(19)-C(20)	110.9(3)
C(19)-C(20)-C(21)	110.3(3)
C(16)-C(21)-C(20)	112.8(3)

(b)

Fig. 1. The structure of one molecule of 9-(cyclohexylmethyl)-thioxanthene 10,10-dioxide with (a) bond lengths (Å), (b) bond angles (°) and e.s.d.'s in parentheses.

1.756 ± 0.003 Å and 1.437 ± 0.002 Å, respectively, and the C–S–C and the mean value of the two C–S–O bond angles are $101.0 \pm 0.1°$ and $109.4 \pm 0.1°$, respectively. These values are in good agreement with other thioxanthene derivatives when the coordination number of the sulfur atom is four (Chu, 1975). The C–H bond lengths range from 0.93 to 1.08 Å with a mean value of 1.00 Å and a root-mean-square standard deviation of 0.03 Å. The C–C–H bond angles involving benzene rings range from 111 to 127° with a mean value of 120°, and the C–C–H and H–C–H bond angles involving tetrahedral carbon atoms range from 103 to 114° with a mean value of 109°. The root-mean-square standard deviation of these bond angles is 2°.

The dihedral angles between the least-squares planes of the two benzene rings is 133.7°. The 9-(cyclohexylmethyl) substituent is in a 'boat axial' conformation. These results are the same as those obtained by the n.m.r. spectroscopic study of the thioxanthene derivatives in solution (Evans & Ternay, 1974). The packing of the molecules in the crystal, projected down the a axis, is shown in Fig. 2. There is no intermolecular distance less than the van der Waals interaction.

The conformation angles of the cyclohexyl ring are given in Table 2, and the torsion angles about the C(9)–C(15) and C(15)–C(16) bonds are shown in Fig. 3. (The conformation and torsion angles are calculated from the coordinates for the enantiomorph given in Table 1.) These torsion angles have the same magnitude as those in methixene (Chu, 1973), which are also shown in Fig. 3 for comparison. Therefore, the 9-(cyclohexylmethyl) group in (I) and the 9-(N-methyl-3-piperidylmethyl) group in (II) have the same configuration.
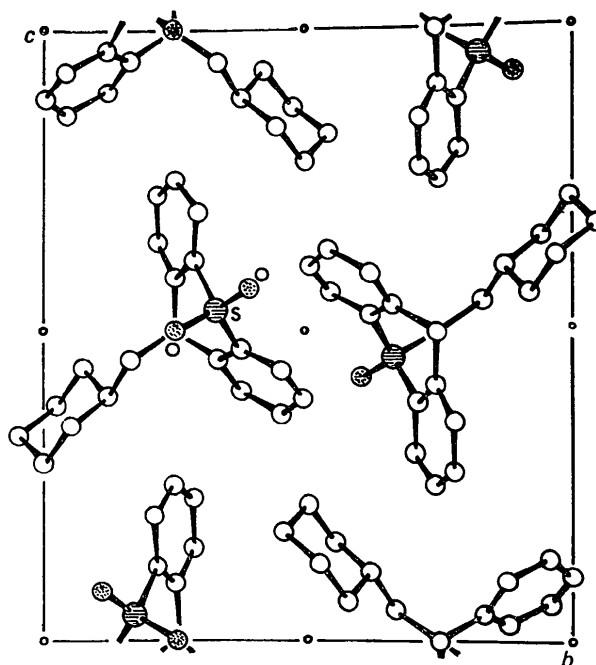
Table 2. *Conformation angles within the cyclohexyl ring*

Bond	Reference atoms	Conformation angle
C(16) → C(17)	C(21)C(16)C(17)C(18)	−52.0
C(17) → C(18)	C(16)C(17)C(18)C(19)	54.7
C(18) → C(19)	C(17)C(18)C(19)C(20)	−56.8
C(19) → C(20)	C(18)C(19)C(20)C(21)	58.0
C(20) → C(21)	C(19)C(20)C(21)C(16)	−56.8
C(21) → C(16)	C(20)C(21)C(16)C(17)	53.0

The conformation angle of a directed bond C(17) → C(18) is defined as the angle that the projection of the bond C(16) → C(17) makes with respect to the projection of the bond C(18) → C(19). The angle is positive if it is measured clockwise.

Fig. 2. The packing of the molecules, excluding hydrogen atoms, in the unit cell projected down the a axis.

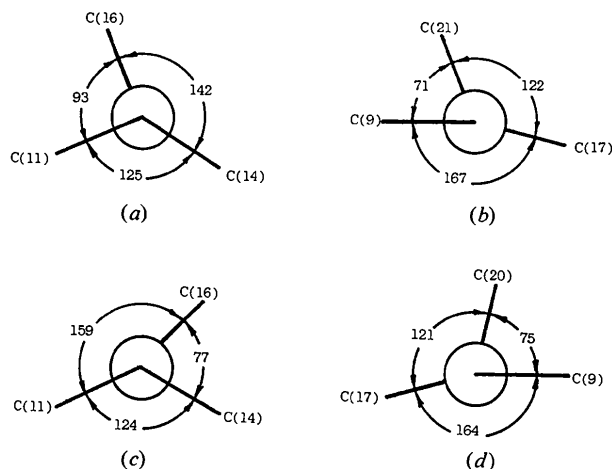*(a)*   *(b)*

(c)   *(d)*

Fig. 3. Comparison of torsion angles between the (a) C(9)–C(15) and (b) C(15)–C(16) bonds in 9-(cyclohexylmethyl)-thioxanthene 10,10-dioxide and the (c) C(9)–C(15) and (d) C(15)–C(16) bonds in methixene.

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