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Spirolactone of Xanthene. II.[1] Synthesis and Molecular Structure of 2′,5,7′-Trichlorospiro[benzofuran-3(2*H*),9′-[9*H*]xanthen]-2-one

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The title compound has been synthesized by the novel condensation reaction of *p*-chlorophenol with oxalic and sulfuric acids; its crystal and molecular structures have been determined by the single crystal X-ray diffraction method. The space group is *C*2/*c*. There are eight molecules of the title compound in the unit cell of dimensions a=21.316(9), b=17.267(4), c=9.158(6) Å, and β=94.05(5)°. The structure was solved by the direct method and refined by the block-diagonal least-squares method to a value of 0.088 for R using 1993 independent observed reflections with $F_o > 3\sigma(F_o)$. The molecule possesses three phenyl rings fused to spirolactone and the dihedral angles between the phenyl rings are 73.60°, 83.60°, and 22.81°.

In a previous communication,[1] it has been reported that, in the studies of the reactivity of xanthene, the reaction of 1-naphthol with oxalic and sulfuric acids accompanying the loss of four molecules of water gave a novel spirolactone (**1**) of dibenzo[*c*,*h*]xanthene in excellent yield (70—75%), and the molecular structure of **1** has been established by the single crystal X-ray diffraction method (Cu *Kα* radiation) as shown in Fig. 1. In order to increase the examples of this novel reaction and to get some information about the reaction mechanism, further studies concerning the synthesis of derivatives were performed by utilizing substituted phenols in place of 1-naphthol. Reaction of *p*-chlorophenol with oxalic and sulfuric acids gave the corresponding novel spirolactone (**3**), whose molecular structure could not be well established on the basis of chemical and spectroscopic data described in the experimental section. Accordingly, the X-ray analysis of **3** has been undertaken in order to elucidate the correct structure. The established molecular structure for **3** resembles the well known fluoran (**5**),[2] except for the lactone moiety, which is formed by the reaction of phenols with phthalic anhydride in the presence of dehydrating agents as in Scheme 1 (fluorescein if *R* is OH in **5**).

Experimental

*Preparation of 2′,5,7′-Trichlorospiro[benzofuran-3(2*H*),9′-[9*H*]xanthen]-2-one (3).* To a mixture of *p*-chlorophenol (11.0 g) and oxalic acid (8.0 g), conc. sulfuric acid (8.0 g) was added cautiously, and the resulting mixture was heated gently for 4 h at 140—145 °C in an oil bath. After cooling,

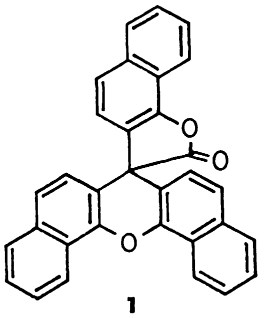

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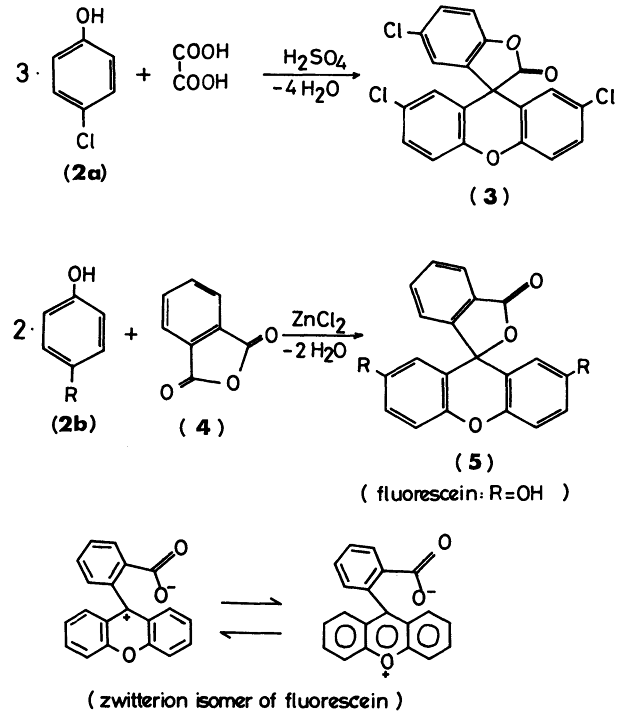
Fig. 1. Spiro[7*H*-dibenzo[*c*,*h*]xanthene-7,3′(2′*H*)-naphtho- [1,2-*b*]furan]-2′-one



Scheme 1.

Table 1. Crystal data

Mol. formula	$C_{20}H_9O_3Cl_3$
Mol. wt.	403.64
Space group	*C*2/*c*
Cell dimensions	
a/Å	21.316(9)
b/Å	17.267(4)
c/Å	9.158(6)
β/°	94.05(5)
Unit cell volume/Å^3	3362.2
Z-value	8
Dc/g cm^{-3}	1.59
μ/cm^{-1} (Cu $K\alpha$)	51.96

the reaction mixture was poured into water and extracted with chloroform (100 ml). The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and concentrated under vacuum. The crude oily products were chromatographed over 300 g of silica gel (using chloroform as eluent) to give 1.5 g of **3**. Crystals suitable for X-ray analysis were obtained by slow evaporation of a xylene solution of **3** at room temperature. Mp 237 °C; IR ν_{max}^{KBr} cm^{-1} 1630, 1790 (C=O); MS m/z 402 (M$^+$), 374 (M$^+$−CO), 357 (M$^+$−CO−OH), 339 (M$^+$−CO−OH−H_2O). ^{1}H-NMR ($CDCl_3$) δ=7.5—6.3 (m for three aromatic ring protons).

Collection and Reduction of Crystallographic Data. The crystal selected for the measurement of the lattice parameters and intensity data was a cleaved fragment which had approximate dimensions of 0.20×0.15×0.25 mm. A preliminary examination of the crystal carried out on a Rigaku AFC diffractometer showed it to be monoclinic. Systematic absences of $h+k=2n+1$ for hkl and $l=2n+1$ for $h0l$ showed the space group to be Cc or $C2/c$. The correct space group was later confirmed to be $C2/c$ by the successful refinement of the structure. The unit cell parameters at room temperature were refined by the least-squares method using the Bragg angles (Cu $K\alpha$ λ=1.54178 Å) of thirty reflections (20°<2θ<35°). The unit cell dimensions and other data are summarized in Table 1. Intensity data were collected at room temperature on the Rigaku AFC diffractometer utilizing nickel-filtered Cu $K\alpha$ radiation. The 2θ—ω scans were employed with a scan speed of 4° min^{-1} in 2θ and scan range which was varied by 1.2°+0.15° tanθ. Background counts were taken at both ends of the scan with a displacement of 3.0° from the $K\alpha$ peak; the time of each measurement was one-third of the scan time. A total of 2823 unique reflections was measured in the range of 0°<2θ<120°. The intensities of three standard reflections were measured after every 57 reflections; three intensities dropped by an average of a few percent over the period of data collection, but no correction factor was applied because the decrease was not considered significant. Lorentz and polarization corrections were applied to convert intensities to structure amplitudes, but no absorption corrections were applied. Standard deviations in the structure amplitudes, $\sigma(F_o)$, were derived from counting statistics.

Solution and Refinement of the Structure. The structure was solved by the direct method using MULTAN[3] to calculate phases for the 300 reflections with $|E_o|>1.60$. The E-map computed from the phases with the largest combined figure of merit (2.59) revealed all the non-hydrogen atoms. The 1993 observed reflections for which $|F_o|$ were greater than $3\sigma(F_o)$ were used for the block-diagonal least-squares refinement of the structure. The function minimized was $\Sigma w(|F_o|-|F_c|)^2$, where w is the unit weight for $0<|F_o|\leq 20$ and $w=(20/|F_o|)^{-2}$ for $|F_o|>20$. An initial refinement using individual isotropic temperature factors for the non-hydrogen atoms led to a conventional $R=(\Sigma||F_o|-|F_c||)/\Sigma|F_o|$ of 0.143. After the successive refinement with the anisotropic temperature factors for all the non-hydrogens, all the hydrogen atoms were readily located from the difference Fourier map. In the further refinement positional and isotropic thermal parameters for the hydrogen atoms were included. The refinement, after 6 cycles of block-diagonal least-squares calculation, converged to an R of 0.088 and a weighted $R_w=(\Sigma w(|F_o|-|F_c|)^2/\Sigma w|F_o|^2)^{1/2}$ of 0.088. An extinction parameter was refined because extinction effects were considered significant. The refinement was completed when the largest shift in any parameters among the non-hydrogen atoms was less than 0.01% of standard deviations, while the largest shift for the hydrogen atoms was 0.09%. The final positional and thermal parameters[†] are given in Table 2. The largest peak in the final difference map, 0.2 eÅ^{-3}, was located near the chlorine atoms. The atomic scattering factors for Cl, O, and C were those of Cromer and Weber[4] and for H, the

TABLE 2. FINAL POSITIONAL AND THERMAL PARAMETERS OF NON-HYDROGEN AND HYDROGEN ATOMS WITH ESTIMATED STANDARD DEVIATIONS

$$B_{eq}=\frac{1}{3}(U_{11}+U_{22}+U_{33})$$

Atoms	x	y	z	B_{eq} or B/Å^2
CL1	0.2463(2)	0.1307(2)	0.5068(2)	6.71
CL2	−0.0900(2)	0.3244(2)	−0.1451(2)	7.10
CL3	0.0673(2)	0.4861(2)	0.3778(2)	7.93
C1	0.1177(5)	0.2286(6)	0.0752(5)	4.09
C2	0.0523(5)	0.2116(6)	0.0188(5)	3.91
C3	0.0153(5)	0.2706(6)	−0.0324(6)	4.78
C4	−0.0434(5)	0.2502(6)	−0.0856(6)	5.05
C5	−0.0636(5)	0.1754(7)	−0.0918(6)	5.33
C6	−0.0269(6)	0.1157(7)	−0.0407(6)	6.01
C7	0.0301(6)	0.1367(6)	0.0158(6)	5.10
O8	0.0655(4)	0.0745(4)	0.0669(5)	6.62
C9	0.1091(5)	0.0921(6)	0.1676(6)	5.09
C10	0.1272(6)	0.0291(6)	0.2525(7)	6.30
C11	0.1712(6)	0.0416(6)	0.3558(6)	5.81
C12	0.1951(5)	0.1143(6)	0.3699(6)	5.15
C13	0.1775(5)	0.1778(6)	0.2858(6)	4.51
C14	0.1338(5)	0.1646(6)	0.1795(5)	4.02
O15	0.1786(4)	0.1718(5)	−0.1354(4)	6.77
C16	0.1653(5)	0.2248(6)	−0.0557(6)	4.88
O17	0.1961(4)	0.2946(5)	−0.0682(4)	5.73
C18	0.1715(5)	0.3459(6)	0.0393(6)	4.57
C19	0.1880(6)	0.4197(7)	0.0552(7)	6.32
C20	0.1592(6)	0.4626(6)	0.1583(7)	6.45
C21	0.1085(7)	0.4297(6)	0.2500(7)	7.83
C22	0.0919(6)	0.3526(6)	0.2376(6)	5.22
C23	0.1269(5)	0.3095(6)	0.1232(5)	3.80
HC3	0.031(5)	0.330(6)	−0.032(5)	2.5
HC5	−0.108(8)	0.162(10)	−0.136(9)	3.9
HC6	−0.052(5)	0.058(6)	−0.009(6)	3.5
HC10	0.110(5)	−0.026(6)	0.245(6)	2.3
HC11	0.186(7)	−0.005(8)	0.423(8)	3.5
HC13	0.209(5)	0.232(6)	0.265(6)	2.5
HC19	0.225(6)	0.444(7)	−0.017(7)	3.4
HC20	0.172(5)	0.552(5)	0.155(5)	1.5
HC22	0.057(5)	0.328(6)	0.326(6)	2.7

[†] Tables of the final thermal parameters and the observed and the calculated structure factors are deposited as Document No. 8510 at the Office of the Editor of the Bulletin of the Chemical Society of Japan.

scattering factors of Stewart, Davidson, and Simpson5) were used. Computations were performed by the crystallographic program system UNICS.6)

Discussion

The molecular structure and the labeling sequence of **3** is presented in the ORTEP drawing of Fig. 2. The molecule of **3** has a T-like shape with the benzofuranone moiety nearly perpendicular to the xanthene plane. The gross molecular conformation and the configuration around the spiro-carbon atom (C1) of **3** are similar to the corresponding part of **1**. The bond distances and angles of **3** are presented in Table 3. The average C–C bond lengths in the benzene rings A, C, and E are 1.376, 1.391, and 1.392 Å, respectively, which are normal compared with the values usually found for the C–C distances in aromatic rings (1.395 Å). In Fig. 3 the geometry of the important parts of **3** and of fluorescein are compared. In fluorescein,2) the bond length (1.525 Å) between the spiro-carbon and oxygen atoms (corresponding to C1–C16 in **3**) is exceptionally long and indicates weakness in the bond which is consistent with the behaviour of fluorescein in solution, where the ready cleavage of that bond yields the fluorescent zwitterion isomer (as shown in Scheme 1). On the other hand, the distance of C1–C23 in **3** (1.482 Å) is typical of C–C sp^2—sp^3 bond, and does not show comparable weakness of the bond. In comparison with related compounds with three fused rings, two C–O bond distances (C7–O8=1.411 and C9–O8=1.389 Å) in

TABLE 3. BOND LENGTHS (l/Å) AND ANGLES (ϕ/°) IN **3**

(a) Bond lengths for non-hydrogen atoms

CL1-C12	1.744(6)	CL2-C4	1.732(9)	CL3-C21	1.717(8)
C1-C2	1.549(11)	C1-C14	1.516(9)	C1-C16	1.517(8)
C1-C23	1.482(11)	C2-C3	1.390(11)	C2-C7	1.379(13)
C3-C4	1.420(12)	C4-C5	1.364(15)	C5-C6	1.395(13)
C6-C7	1.402(13)	C7-O8	1.411(11)	O8-C9	1.389(8)
C9-C10	1.408(11)	C9-C14	1.365(13)	C10-C11	1.396(11)
C11-C12	1.364(14)	C12-C13	1.407(10)	C13-C14	1.414(8)
O15-C16	1.193(8)	C16-O17	1.375(12)	O17-C18	1.398(8)
C18-C19	1.334(14)	C18-C23	1.337(9)	C19-C20	1.318(10)
C20-C21	1.438(12)	C21-C22	1.385(14)	C22-C23	1.448(8)

(b) Bond lengths involving hydrogen atoms

HC3-C3	1.08(9)	HC5-C5	1.08(13)	HC6-C6	1.16(9)
HC10-C10	1.02(9)	HC11-C11	1.08(9)	HC13-C13	1.16(9)
HC19-C19	1.08(8)	HC20-C20	1.07(9)	HC22-C22	1.15(6)

(c) Bond angles

C23-C1-C16	100.4(6)	C23-C1-C14	117.4(4)
C23-C1-C2	114.7(7)	C16-C1-C14	107.4(7)
C16-C1-C2	107.2(4)	C14-C1-C2	108.8(7)
C7-C2-C3	118.5(8)	C7-C2-C1	120.2(7)
C3-C2-C1	121.4(8)	C4-C3-C2	118.0(9)
C5-C4-C3	122.6(8)	C5-C4-CL2	119.8(7)
C3-C4-CL2	117.6(7)	C6-C5-C4	119.9(8)
C7-C6-C5	117.1(9)	O8-C7-C6	115.0(8)
O8-C7-C2	121.0(8)	C6-C7-C2	123.9(8)
C9-O8-C7	116.9(6)	C14-C9-C10	122.8(7)
C14-C9-O8	122.3(6)	C10-C9-O8	114.9(8)
C11-C10-C9	118.6(9)	C12-C11-C10	118.6(7)
C13-C12-C11	123.4(6)	C13-C12-CL1	118.1(7)
C11-C12-CL1	118.3(5)	C14-C13-C12	117.7(8)
C13-C14-C9	118.7(6)	C13-C14-C1	120.4(7)
C9-C14-C1	120.8(5)	O17-C16-O15	122.1(6)
C1-C16-O17	108.5(6)	O15-C16-C1	129.3(8)
C18-O17-C16	110.0(5)	C23-C18-C19	124.7(6)
C23-C18-O17	108.9(7)	C19-C18-O17	126.4(6)
C20-C19-C18	120.2(8)	C21-C20-C19	119.3(9)
C22-C21-C20	121.2(7)	C22-C21-CL3	118.7(6)
C20-C21-CL3	120.1(7)	C22-C23-C1	112.1(5)
C18-C23-C1	112.1(5)		

ring D of **3** are comparable with 1.382 and 1.369 Å of 4-azaphenoxathiin,[6] 1.401 and 1.386 Å of phenoxathiin,[7] and 1.378 and 1.377 Å of fluorescein[2] within the experimental errors.

In Table 4 the best least-squares planes are given together with the displacement of the atoms from the best planes. The lactone ring B is coplanar with ring A, and its orientation is almost perpendicular to the xanthene ring, which is similar to that observed in **1**.[1] The dihedral angles between rings A—C, rings A—E, and rings C—E are 73.6°, 83.6°, and 22.81°, respectively, which may be compared with those of **1** (81.4°, 86.9°, and 5.9° in order).[1] The great difference in the butterfly angles of the xanthene rings in **1** and **3** (22.81° and 5.9°) seems to be caused by electron-withdrawing effects of the chlorine atoms and the lesser steric hindrance of the phenyl ring of **3** in comparison with the bulky naphthalene ring of **1**.

Table 4. Least-squares planes and deviations (d/Å) of atoms from the planes

Plane A: Defined by the atoms C18-C23

$-0.7151X+0.2669Y-0.6461Z+1.2829=0$[a)]

C18 0.013; C19 0.001; C20 −0.019

C21 0.019; C22 −0.005; C23 −0.009

Plane B: Defined by the atoms C1, C16, O17, C18, and C23

$-0.7323X+0.3150Y-0.6038Z+1.0369=0$

C1 −0.008; C16 0.014; O17 −0.014

C18 0.006; C23 0.002; O15 −0.005

Plane C: Defined by the atoms C2-C7

$0.3902X-0.1095Y-0.9142Z+0.1252=0$

C2 0.008; C3 0.004; C4 −0.016

C5 0.008; C6 0.012; C7 −0.011

Plane E: Defined by the atoms C9-C14

$-0.6944X+0.2179Y+0.6859Z+0.3037=0$

C9 0.011; C10 −0.000; C11 −0.004

C12 −0.002; C13 0.007; C14 −0.013

a) Expressed in an orthogonal coordinate system in Å units.

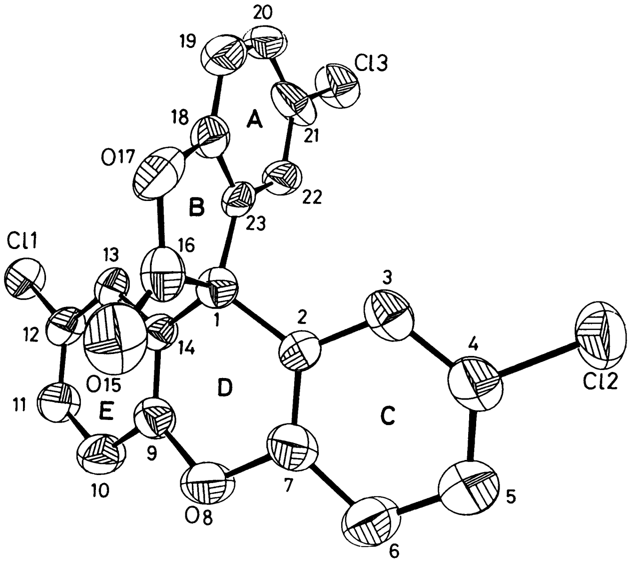
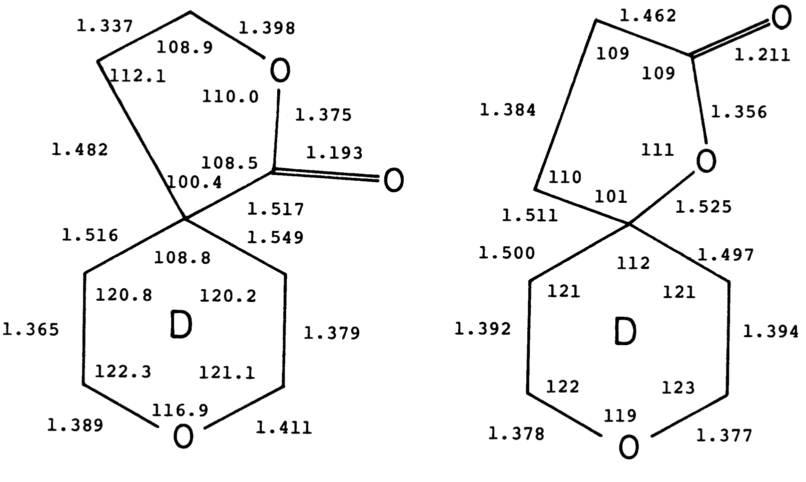


Fig. 2. ORTEP drawing of the title compound ---- Thermal ellipsoids are drawn at the 50% probability level.

Table 5. Intermolecular distances less than 4 Å

CL2···C3[a)]	3.385(5)
C6···O8[b)]	3.400(12)
C16···O17[c)]	3.257(10)
O17···C13[c)]	3.270(8)
C18···O15[c)]	3.388(11)
C19···O15[c)]	3.380(13)

Symmetry code	Symmetry operation
a	$-x, y, 1/2-z$
b	$-x, -y, -z$
c	$1/2-x, 1/2-y, -z$



3 fluorescein[2)]

Fig. 3. The selected bond lengths and angles around the spiro carbon atom of **3** and fluorescein. The standard deviations are described in Table 3.

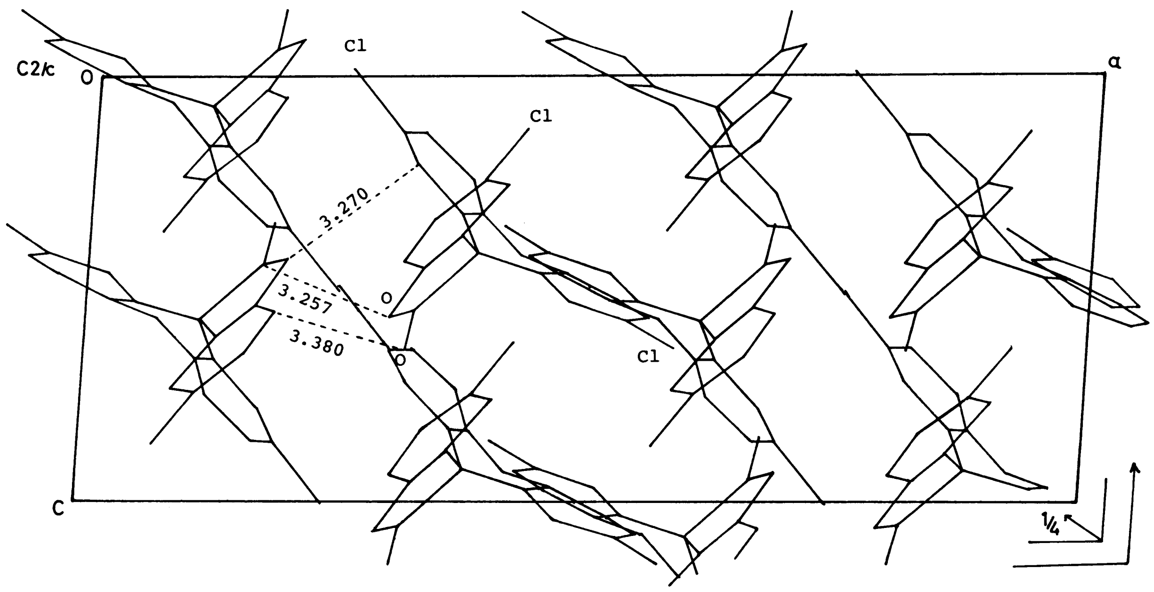
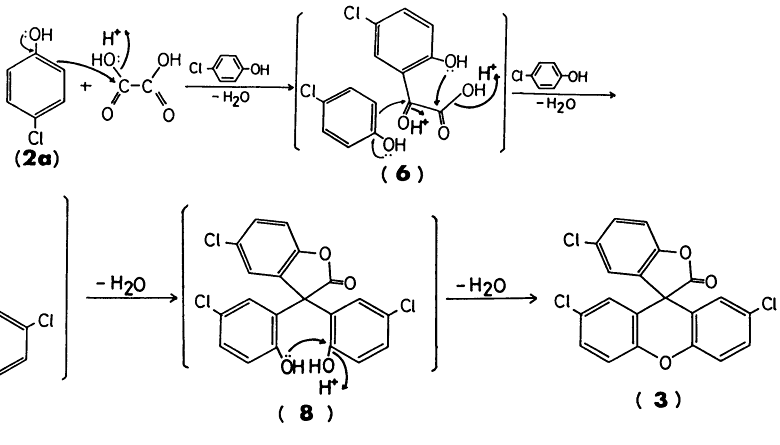


Fig. 4. Projection of the structure along the b-axis.



Scheme 2.

On the other hand, the corresponding value of 9.4° for fluorescein is comparable with that of **1** (5.9°). The projection of the crystal structure along the b-axis is shown in Fig. 4, and the shortest intermolecular distances are given in Table 5. There are no unusually close contacts of atoms in the unit cell, and all the intermolecular van der Waals distances are larger than 3.26 Å.

As the molecular structure of **3** has been elucidated by the X-ray diffraction method, a plausible reaction mechanism leading to the formation of **3** could be infered as shown in Scheme 2. The initial step probably involves a Friedel-Crafts type reaction between phenols (**2a**) and oxalic acid to form the oxalophenols (**6**). Subsequently, the nucleophilic attack of another phenols (**2a**) to the protonated carbonyl carbon atom of **7** forms the intermediates (**8**) with three phenol rings connected by the lactone moiety. Further, the intermediates (**8**) proceed by the intramolecular cyclization to the xanthene ring accompanying the loss of one molecule of water to reach **3**. Thus the reaction mechanism to form **3** seems to be based on the nucleophilic approach of the electron localized ortho-position of phenols to the carbonyl carbon atom, which results in the loss of four molecules of water.

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