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9-(2-Methylphenyl)-3,4,5,6,9,10-hexahydroxanthene-1,8(2H,7H)-dione

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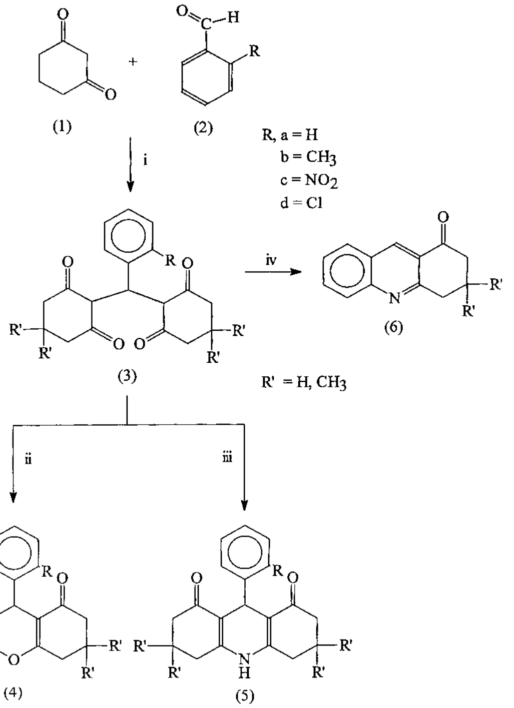
Several 9-(2-R phenyl)xanthenediones have been synthesized and the x-ray diffraction structure for the 2-methylphenyl derivative (**4b**) has been determined. This compound crystallizes in the monoclinic system, space group $P2_1/n$, with a = 11.729 (3), b = 9.674 (3), c = 14.628 (4) Å, and β = 106.30°. It presents a partially hydrogenated xanthene system in distorted boat conformation for the heterocyclic central ring, and an almost ideal envelope conformation for the outer rings. The aromatic substituent at the ninth position is at 84° in angle with the xanthene system.

KEY WORDS: X-ray diffraction; xanthenedione; heterocyclic fused rings.

Experimental section

Our general approach uses 1,3-cyclohexanedione (**1**) and *ortho* substituted benzaldehydes (**2a–d**) as starting materials, which were condensed with KOH in EtOH—H_2O media to generate intermediate (**3**), which is further reacted with sodium methoxide solution at room temperature to afford (**4**). This reaction can also be carried out straightforwardly by reacting (**1**) and (**2**) with sodium methoxide solution to directly produce (**4**) in 60% yield. The ^1H NMR spectroscopy displays similar signal pattern in agreement with the X-ray structure obtained. Thus, for (**4b**) ($CDCl_3$): δ 2.0 (4H, t), 2.3 (4H, m), 2.7 (4H, t), 2.9 (3H, s), 5.0 (1H, s), 7.0–7.6 (4H, m). It is noteworthy to mention that the dimeric intermediate (**3**), which we have been able to isolate, is a key intermediate for the preparation of the heterocyclic



Scheme. Reagents and conditions: (i) KOH/EtOH-H_2O, reflux, 2h; (ii) MeONa/MeOH, RT, 3h; (iii) NaN_3-HC1/THF, RT, 3h; (iv) Fe-AcOH/CH_2Cl_2, RT, 3h.

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Table 1. Crystal Data and Structure Refinement

Empirical formula	$C_{20}H_{20}O_3$
CCDC deposit no.	CCDC-1003/5630
Formula weight	308.4
Temperature (K)	298 (2)
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	
$a = 11.729$ (3) Å $\alpha = 90.0°$	
$b = 9.674$ (3) Å $\beta = 106.30$ (2)°	
$c = 14.628$ (4) Å $\gamma = 90.0°$	
Volume	$V = 1593.1$ (8) Å^3
Z	4
Density (calc.)	1.286 mg/m^3
Absorption coefficient	0.085 mm^{-1}
Diffractometer/scan	Siemens P4/PC; $\theta/2\theta$
Radiation/wavelength	Mo$K\alpha$ (graphite monochrom.)/ $\lambda = 0.71073$ Å
$F(000)$	656
Crystal size (mm)	$0.78 \times 0.66 \times 0.56$
θ range for data collection	2.0 to 27.5°
Index ranges	$0 \le h \le 15$; $0 \le k \le 12$; $-19 \le l \le 18$
Reflections collected	3842
Independent/observed refls.	3666 (Rint = 0.0277)/2430 ([$I > 2\sigma(I)$])
Absorption correction	Semi-empirical
Max. and min. transmission	0.9538 and 0.9364
Refinement method	Full matrix least-squares on F^2
Computing	SHELXTL PLUS (PC version)
Data/parameters	3666/209
Goodness-of-fit on F^2	1.034
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0588$, $wR2 = 0.1673$
R indices (all data)	$R1 = 0.0877$, $wR2 = 0.1926$
Extinction coefficient	0.006(3)
Largest diff. peak and hole	0.78 and -0.30 eÅ^{-3}

three ring systems (**4**), (**5**), and (**6**) that we have reported so far. Therefore, depending on the system requested (either the xanthendione (**4**), the acridindione (**5**), or the acridone (**6**) derivatives), the intermediate (**3**) must be treated with sodium methoxide solution, with amines or sodium azide, and with iron in acid, respectively.

The structure of the title compound was solved by direct methods. Refinement was based on full-matrix least-squares methods, with anisotropic displacement parameters for all non-H atoms and a global fixed isotropic displacement parameter for H atoms. H atoms were included at calculated positions, using a riding model. Table 1 shows crystal data and the structure refinement parameters corresponding to the x-ray diffraction analysis.

Table 2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients (Å $\times$ 10^3) for the Title Compound

	x	y	z	U(eq)^a
C(1)	6460(2)	−610(3)	4525(2)	51(1)
O(1)	6817(2)	572(2)	4614(1)	77(1)
C(2)	6506(3)	−1514(3)	5383(2)	71(1)
C(3)	5658(3)	−2697(3)	5183(2)	74(1)
C(4)	5743(2)	−3521(3)	4333(2)	52(1)
C(4A)	5728(2)	−2584(2)	3516(1)	41(1)
C(4B)	5590(2)	−2641(2)	1879(1)	42(1)
C(5)	5421(3)	−3620(3)	1063(2)	58(1)
C(6)	5200(3)	−2813(3)	133(2)	65(1)
C(7)	6124(3)	−1699(3)	214(2)	57(1)
C(8)	6248(2)	−757(2)	1059(2)	43(1)
O(8)	6658(2)	−397(2)	1088(1)	60(1)
C(8A)	5894(2)	−1314(2)	1880(1)	38(1)
C(9)	5934(2)	−363(2)	2706(1)	36(1)
C(9A)	6005(2)	−1244(2)	3577(1)	39(1)
O(10)	5395(2)	−3282(2)	2663(1)	49(1)
C(1′)	4836(2)	−579(2)	2445(1)	35(1)
C(2′)	4915(2)	2025(2)	2415(1)	42(1)
C(3′)	3860(3)	2783(3)	2119(2)	53(1)
C(4′)	2772(2)	2157(3)	1862(2)	58(1)
C(5′)	2691(2)	737(3)	1902(2)	56(1)
C(6′)	3723(2)	−42(2)	2188(2)	43(1)
C(7′)	6083(3)	2774(3)	2673(2)	63(1)

[a] U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Results and discussion

We previously reported the synthesis and X-ray structure of acridindione[1] (**5**) and acridone[2] (**6**) derivatives, which have been indicated as potential acetilcholinesterease inhibitors in the treatment of Alzheimer[3] and Malaria disease.[4] In continuation of our studies oriented in preparing heterocyclic three-ring dione systems, herein we describe the synthesis of series of 9-(2-R phenyl)xanthenediones (**4a–d**) and the tridimensional analysis for the 2-methylphenyl derivative (**4b**) referred to above.

Fractional atomic coordinates for non-hydrogen atoms of the title compound are given in Table 2. Bond lengths and angles are given in Table 3. The molecular structure (Fig. 1) can be described as a xanthenedione group bonded to a methylphenyl substituent. The xanthene system is roughly planar (mean planes define angles of 8.0, 10.2, and 8.0° between the central and the outer rings, and between the outer rings, respectively). The aromatic substituent is almost perpendicular to the xanthenedione group, as indicated by the angle between their mean

Table 3. Bond Lengths (Å) and Angles (°)

C(1)−O(1)	1.212(3)	C(9A)−C(4A)−O(10)	122.7(2)
C(1)−C(9A)	1.472(3)	C(9A)−C(4A)−C(4)	126.0(2)
C(1)−C(2)	1.518(3)	O(10)−C(4A)−C(4)	111.3(2)
C(2)−C(3)	1.491(5)	C(8A)−C(4B)−O(10)	122.6(2)
C(3)−C(4)	1.505(4)	C(8A)−C(4B)−C(5)	126.0(2)
C(4)−C(4A)	1.495(3)	O(10)−C(4B)−C(5)	111.4(2)
C(4A)−C(9A)	1.334(3)	C(4B)−C(5)−C(6)	109.9(2)
C(4A)−O(10)	1.375(3)	C(7)−C(6)−C(5)	110.9(2)
C(4B)−C(8A)	1.333(3)	C(6)−C(7)−C(8)	113.4(2)
C(4B)−O(10)	1.379(3)	O(8)−C(8)−C(8A)	120.4(2)
C(4B)−C(5)	1.492(3)	O(8)−C(8)−C(7)	122.1(2)
C(5)−C(6)	1.526(4)	C(8A)−C(8)−C(7)	117.4(2)
C(6)−C(7)	1.509(4)	C(4B)−C(8A)−C(8)	119.1(2)
C(7)−C(8)	1.510(3)	C(4B)−C(8A)−C(9)	122.5(2)
C(8)−O(8)	1.211(3)	C(8)−C(8A)−C(9)	118.4(2)
C(8)−C(8A)	1.478(3)	C(8A)−C(9)−C(9A)	108.2(2)
C(8A)−C(9)	1.508(3)	C(8A)−C(9)−C(1′)	109.1(2)
C(9)−C(9A)	1.516(3)	C(9A)−C(9)−C(1′)	112.7(2)
C(9)−C(1′)	1.536(3)	C(4A)−C(9A)−C(1)	119.0(2)
C(1′)−C(6′)	1.388(3)	C(4A)−C(9A)−C(9)	122.3(2)
C(1′)−C(2′)	1.403(3)	C(1)−C(9A)−C(9)	118.6(2)
C(2′)−C(3′)	1.398(3)	C(4A)−O(10)−C(4B)	117.6(2)
C(2′)−C(7′)	1.502(3)	C(6′)−C(1′)−C(2′)	119.2(2)
C(3′)−C(4′)	1.366(4)	C(6′)−C(1′)−C(9)	118.0(2)
C(4′)−C(5′)	1.379(4)	C(2′)−C(1′)−C(9)	122.7(2)
C(5′)−C(6′)	1.387(3)	C(3′)−C(2′)−C(1′)	118.2(2)
		C(3′)−C(2′)−C(7′)	119.4(2)
O(1)−C(1)−C(9A)	121.1(2)	C(1′)−C(2′)−C(7′)	122.5(2)
O(1)−C(1)−C(2)	121.6(2)	C(4′)−C(3′)−C(2′)	122.0(2)
C(9A)−C(1)−C(2)	117.3(2)	C(3′)−C(4′)−C(5′)	120.0(2)
C(3)−C(2)−C(1)	114.4(2)	C(4′)−C(5′)−C(6′)	119.3(2)
C(2)−C(3)−C(4)	111.9(2)	C(5′)−C(6′)−C(1′)	121.4(2)
C(4A)−C(4)−C(3)	110.5(2)		

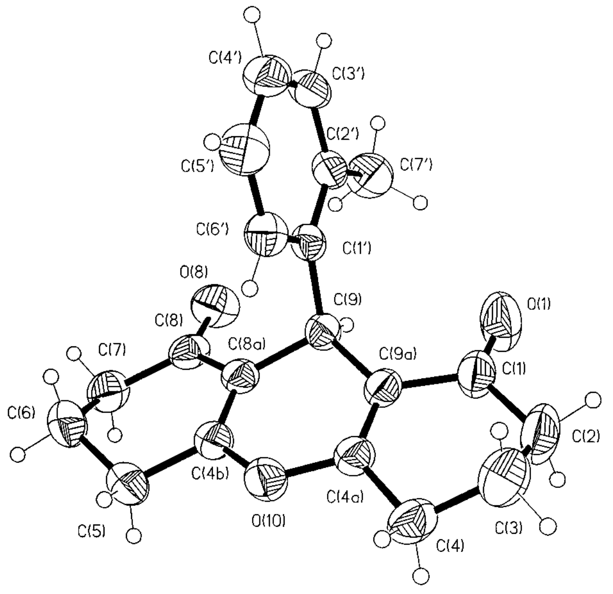

Fig. 1.

planes (84°) and is shown in the unit cell view (Fig. 2). The mean $C_{sp2}-C_{sp2}$ bond length within the planar phenyl ring of the substituent is 1.39 (1) Å.

The molecules are held together by weak C−H···O[5] and C−H···π-ring interactions (the shortest hydrogen bond has d(C···O) = 3.350(4) Å and d(H···O) = 2.59 Å), which contribute to the stabilization of the molecular and crystal structure. The shortest contacts are given in Table 4.

By comparing the acridindione[1] derivative recently reported with the present xanthenedione compound, we observe a high homology in terms of conformation. The outer rings of both the acridine moiety and the xanthene group have an almost ideal envelope conformation (with puckering parameters[6]: Q = 0.462 and 0.435 Å, θ = 123.5 and 121.5°, φ = 300.6 and 298.8°, and Q = 0.472 and 0.471 Å, θ = 120.0 and 119.8°, and φ = 302.8 and 302.3°, for the acridindione and xanthenedione derivatives, respectively). Also, in both cases, the heterocyclic central ring presents a distorted boat conformation (Q =

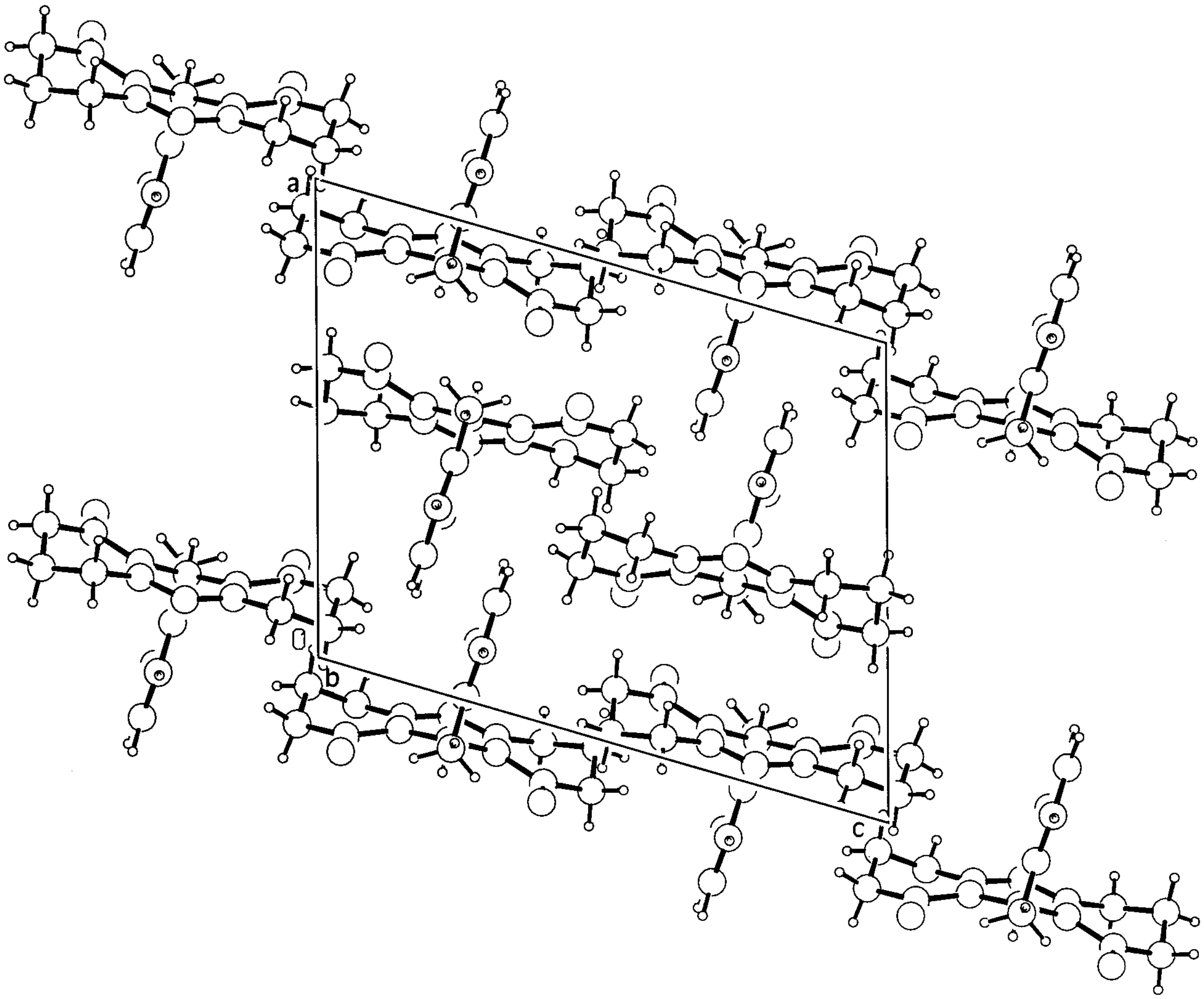

Fig. 2.

Table 4. Shortest Intermolecular Contacts (in Å and °)[a]

D—H···A	D—H	H···A		D···A	D—H···A
C(6)—H(6A)···O(8) #1	0.96	2.59		3.350(4)	136
D—H···Cg (Ring)	H···Cg	H-Perp	γ	D···Cg	D—H···Cg
C(2)—H(2A)···Cg(A.S.) #2	2.97	2.91	11.2	3.720	136
C(7)—H(7A)···Cg(A.S.) #1	2.75	2.74	4.8	3.506	136

[a] Cg(A.S.) is the center of gravity of the aromatic substituent ring, H-Perp. is the distance from the hydrogen to the ring and γ is the angle between the H ··· Cg direction and the normal to the ring. Symmetry transformations used to generate equivalent atoms are: #1: $1 - x, -y, -z$; #2: $1 - x, -y, 1 - z$.

0.094 and 0.213 Å, $\theta = 103.8$ and 101.0°, and $\varphi = 352.4$ and 365.2°, for the acridindione and xanthenedione derivatives, respectively).

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