

Structure of (\pm)-6-Methyl-6,12-methano-6*H*,12*H*,13*H*-[1]benzopyran- [4,3-*d*][1,3]benzodioxocin-13-one

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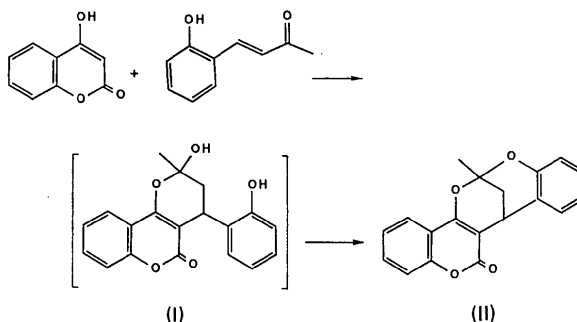
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Abstract. A derivative of warfarin, racemic $C_{19}H_{14}O_4$, $M_r = 306.32$, monoclinic, Cc , $a = 9.594$ (2), $b = 20.437$ (4), $c = 7.793$ (2) Å, $\beta = 109.94$ (3)°, $V = 1436.4$ (11) Å³, $Z = 4$, $D_x = 1.416$ g cm⁻³, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu = 7.742$ cm⁻¹, $F(000) = 640$, $T = 293$ K, final $R = 0.053$ for 1224 observations. The title molecule, formed by spontaneous dehydration of 2'-hydroxywarfarin, is a cyclic ketal in which the side-chain phenyl is disposed pseudoaxially and is linked through a 2'-oxygen to the ketal carbon in a fixed *cis* 1,3-diaxial configuration. Two dihydropyran rings are formed; one fused with the benzopyran ring adopts an *e,f*-diplanar conformation, the other is a chroman and is in a similar conformation.

Introduction. As part of a continuing study of the structures of dihydropyran derivatives containing various 2-oxygen substituents, the compound described here is one of a series of crystalline warfarin derivatives. Warfarins generally crystallize as hemiketal 2-hydroxy-2-methyl-3,4-dihydro-2*H*,5*H*-pyrano[3,2-*c*]-[1]benzopyran-5-ones with varying 4-substituents; 4-phenyl is the parent in the series. A number of 2-hydroxy and 2-methoxy analogs have been made and studied crystallographically, revealing an operative anomeric effect in the uniform axial disposition of the 2-oxygen substituents, local influences on C–O bond lengths and conformational preferences associated with the exoanomeric effect (Valente, Eggleston & Schomaker, 1986). This contribution describes the structure of a 2-aryloxy warfarin ketal.

Experimental. Warfarin derivatives are made by Michael-type addition of unsaturated ketones to 4-hydroxycoumarin (Ikawa, Stahmann & Link, 1944). Synthesis of 2'-hydroxywarfarin (I) by this method leads instead to a higher melting compound (II) which is not soluble in dilute alkali. An initial assignment of the structure required revision in the light of spectroscopic evidence and knowledge of the tendency of

warfarins to form cyclic hemiketal structures (Porter & Trager, 1977).



This material proves to be a conveniently prepared 2-aryloxy warfarin ketal, and colorless crystals were obtained from ethanol solutions as plates, m.p. 531–534 K. A specimen, 0.2 × 0.4 × 0.4 mm, was chosen for data collection on a CAD-4 diffractometer. Cell constants were determined from 25 accurately centered reflections with $60 \leq 2\theta \leq 70^\circ$ and intensities were measured with variable speed θ - 2θ scans to $2\theta = 136^\circ$ (h : -11 to 11, k : 0 to 24, l : 0 to 9). The data (1404 unique) were corrected for coincidence and polarization, and symmetry equivalent data were averaged (agreement 2.6% on I). Three intensities were periodically monitored over the 15 h data collection period; average change -0.5 (1.1)%, no correction for deterioration was made. An extinction coefficient of the type defined by Zachariasen (1963), $g = 7.03$ (1) × 10⁻⁶ was later applied and refined. Through the systematic absences (hkl : $h+k = 2n+1$; $h0l$: $l = 2n+1$), and the structure solution, the space group was confirmed. The structure was discovered with *MULTAN* (Germain, Main & Woolfson, 1971). Non-H-atom positions were refined with U_{iso} 's by full-matrix least squares on F minimizing $\sum w(|F_o| - |F_c|)^2$, then with U_{ij} 's. H-atom positions were fixed at 1.0 Å from their adjacent atoms with B 's fixed at approximately

Table 1. Positions and B_{eq} for (II) with e.s.d.'s in parentheses
$$B_{eq} = \frac{1}{3} \sum_i \sum_j B_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	$B(\text{\AA}^2)$
O1	0.790	0.0772 (1)	0.440	3.58 (5)
O2	0.8314 (3)	0.1834 (1)	0.4506 (4)	4.71 (7)
O3	1.2107 (3)	0.0401 (1)	0.7964 (3)	3.21 (5)
O4	1.4052 (3)	0.0988 (1)	0.7614 (3)	3.57 (5)
C2	0.8845 (4)	0.1297 (2)	0.5051 (5)	3.28 (7)
C3	1.0292 (4)	0.1173 (2)	0.6258 (4)	2.90 (6)
C4	1.0757 (3)	0.0549 (2)	0.6803 (4)	2.59 (6)
C5	1.0183 (4)	-0.0654 (2)	0.6583 (5)	3.15 (6)
C6	0.9175 (4)	-0.1140 (2)	0.5807 (5)	3.79 (8)
C7	0.7797 (5)	-0.0997 (2)	0.4611 (6)	4.22 (8)
C8	0.7374 (4)	-0.0353 (2)	0.4112 (6)	3.86 (8)
C9	0.8387 (4)	0.0134 (2)	0.4902 (5)	2.97 (6)
C10	0.9775 (4)	0.0005 (2)	0.6106 (4)	2.63 (5)
C11	1.1383 (4)	0.1728 (2)	0.6965 (5)	3.25 (7)
C12	1.2391 (4)	0.1547 (2)	0.8871 (5)	3.29 (7)
C13	1.3174 (4)	0.0914 (2)	0.8755 (4)	3.07 (6)
C14	1.4179 (5)	0.0634 (2)	1.0500 (5)	4.20 (8)
C15	1.2345 (4)	0.1811 (2)	0.5786 (4)	3.04 (6)
C16	1.2007 (5)	0.2238 (2)	0.4310 (5)	3.90 (8)
C17	1.2929 (5)	0.2301 (2)	0.3289 (6)	4.85 (9)
C18	1.4214 (5)	0.1934 (2)	0.3760 (6)	4.59 (8)
C19	1.4568 (4)	0.1503 (2)	0.5202 (5)	3.87 (7)
C20	1.3631 (4)	0.1441 (2)	0.6203 (5)	3.08 (6)

1.3 times the B_{eq} for the attached carbon. Scattering factors were from *International Tables for X-ray Crystallography* (1974) except for H (Stewart, Davidson & Simpson, 1965). No parameter shifted in the final cycle. Final agreement factors for (II): $R = 0.053$, $wR = 0.068$, $GOF = 2.2$ for the 1224 intensities with $I \geq 3\sigma(I)$. Least-squares weights were taken as $4F_o^2/\sigma^2(I)$ where $\sigma^2(I) = \sigma^2(I)_c + 0.05(I)_c^2$ and the differences in structure factors were minimized for the 209 variables; scale factor = 0.135; maximum final $|\Delta\rho|$ excursions were less than 0.32 e \AA^{-3} . Other programs used were from the locally modified Enraf-Nonius (1987) *Structure Determination Package* (V.3.0).

Discussion. Final atom positions and equivalent isotropic vibrational amplitudes for non-H atoms are given in Table 1.* Bond distances and angles are given in Table 2. Referring to the plot of the molecular structure given in Fig. 1, the 2- and 4-substituents on the dihydropyran ring composed of C3/C4/O3/C13/C12/C11 are constrained to a diaxial configuration. This dihydropyran has an *ef*-diplanar conformation and ring displacement asymmetry parameter $\Delta C_2 = 0.138 (2)$ (Nardelli, 1983), and shows the largest dihydropyran ring distortion observed in the warfarin series. The C13—O4 bond length, 1.426 (5) Å, is more like the C13—O3 length, 1.448 (4) Å, than in the warfarin

* Lists of H-atom positions, anisotropic vibrational amplitudes and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51799 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Principal bond distances (Å) and angles (°) with e.s.d.'s in parentheses

O1—C2	1.383 (4)	C7—C8	1.392 (6)
O1—C9	1.395 (4)	C8—C9	1.380 (5)
O2—C2	1.223 (4)	C9—C10	1.368 (4)
O3—C4	1.338 (4)	C11—C12	1.517 (5)
O3—C13	1.448 (4)	C11—C15	1.517 (6)
O4—C13	1.426 (5)	C12—C13	1.514 (5)
O4—C20	1.388 (4)	C13—C14	1.487 (5)
C2—C3	1.408 (4)	C15—C16	1.391 (5)
C3—C4	1.370 (4)	C15—C20	1.388 (5)
C3—C11	1.514 (5)	C16—C17	1.383 (8)
C4—C10	1.438 (4)	C17—C18	1.381 (7)
C5—C6	1.374 (5)	C18—C19	1.377 (6)
C5—C10	1.417 (5)	C19—C20	1.383 (7)
C6—C7	1.365 (5)		
C2—O1—C9	120.6 (2)	C5—C10—C9	118.7 (3)
C4—O3—C13	120.3 (2)	C3—C11—C12	107.7 (3)
C13—O4—C20	119.4 (3)	C3—C11—C15	110.6 (3)
O1—C2—O2	115.2 (3)	C12—C11—C15	107.7 (3)
O1—C2—C3	118.5 (3)	C11—C12—C13	108.3 (3)
O2—C2—C3	126.3 (3)	O3—C13—O4	107.1 (3)
C2—C3—C4	121.1 (3)	O3—C13—C12	110.6 (3)
C2—C3—C11	120.6 (3)	O3—C13—C14	104.7 (3)
C4—C3—C11	118.3 (3)	O4—C13—C12	110.9 (3)
O3—C4—C3	123.9 (3)	O4—C13—C14	105.9 (3)
O3—C4—C10	116.0 (3)	C12—C13—C14	117.0 (3)
C3—C4—C10	120.1 (3)	C11—C15—C16	123.5 (3)
C6—C5—C10	118.8 (3)	C11—C15—C20	118.2 (3)
C5—C6—C7	121.2 (3)	C16—C15—C20	118.2 (4)
C6—C7—C8	121.1 (4)	C15—C16—C17	121.3 (4)
C7—C8—C9	117.6 (3)	C16—C17—C18	119.1 (4)
O1—C9—C8	115.7 (3)	C17—C18—C19	120.9 (5)
O1—C9—C10	121.6 (3)	C18—C19—C20	119.5 (4)
C8—C9—C10	122.7 (3)	O4—C20—C15	123.0 (4)
C4—C10—C5	123.3 (3)	O4—C20—C19	116.0 (3)
C4—C10—C9	118.0 (3)	C15—C20—C19	121.0 (3)

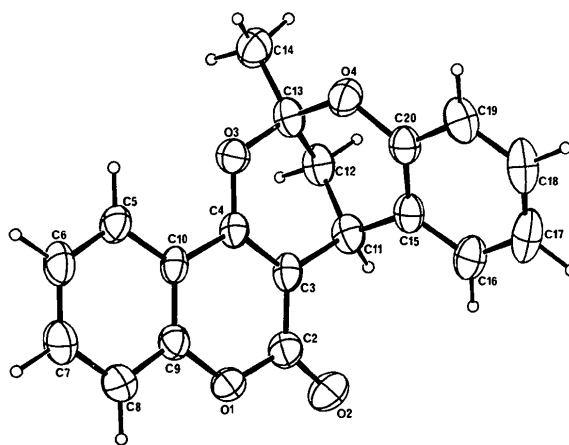


Fig. 1. An ORTEP (Johnson, 1976) drawing of (II) showing 50% probability vibrational ellipsoids for the non-H atoms.

methyl ketals and hemiketals (Valente, Eggleston & Schomaker, 1986) in which comparable lengths are 1.40 and 1.47 Å, respectively. Both the dihydropyran ring conformation and the better charge-accepting character of the 2-phenoxy group in (II), relative to warfarin or its methyl ketals, tend increasingly to populate double bond—no bond resonance structures

shortening C13—O3 and lengthening C13—O4. The ring formed by the dehydration of (I), C15/C20/O4/C13/C12/C11, is a chroman dihydropyran, which also has a half-chair conformation distorted towards the *ef*-diplanar form. The displacement asymmetry parameter $\Delta C_2 = 0.155$ (2).

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The Mono Diels–Alder Adduct of 1,4-Bis(2,4-cyclopentadien-1-ylidene)cyclohexane and Dimethyl Butynedioate

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Abstract. Dimethyl 7-[4-(2,4-cyclopentadien-1-ylidene)cyclohexylidene]bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate, C₂₂H₂₂O₄, $M_r = 350.4$, triclinic, $P\bar{1}$, $a = 8.215$ (1), $b = 10.6297$ (9), $c = 11.545$ (2) Å, $\alpha = 70.976$ (9), $\beta = 75.48$ (1), $\gamma = 85.245$ (8)°, $V = 922.7$ (1) Å³, $Z = 2$, $D_x = 1.261$ Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.54184$ Å, $\mu = 0.658$ mm⁻¹, $F(000) = 372$, $T = 296$ K, $R = 0.044$ for 3275 data having $F_o^2 > 3\sigma(F_o^2)$. The strained double bond *exo* to the bicyclo[2.2.1]hepta-2,5-diene has a normal bond length, 1.330 (1) Å. However, this double bond exhibits severe distortion from sp^2 hybridized geometry at the bond angle endocyclic to the bicyclo[2.2.1]hepta-2,5-diene, which is 94.76 (6)°. The cyclopentadienyliidene ring is planar, with maximum deviation of 0.004 (2) Å.

Introduction. The mono Diels–Alder adduct of 1,4-bis(2,4-cyclopentadien-1-ylidene)cyclohexane and dimethyl butynedioate, shown in Fig. 1, is one of three isomeric products expected from the stoichiometry of this reaction. Other isomers from further intramolecular Diels–Alder cycloadditions of this bifunctional dienophile to the other diene system are not observed. Dimethyl butynedioate is known to act as a bifunctional dienophile for bifunctional Diels–Alder dienes (Paquette, Wyvrat, Berk & Moerck, 1978).

The structure of the title compound is being probed to determine whether there is cooperativity of the two 'isolated' chromophores, the fulvene and the strained double bond.

Experimental. The title compound is prepared by refluxing excess 1,4-bis(2,4-cyclopentadien-1-ylidene)cyclohexane with dimethyl butynedioate in chloroform for 72 hours. Clear, yellow-orange crystals, m.p. 370 K, suitable for single-crystal X-ray structure determination were crystallized from hexane/ether at room temperature. The X-ray structure determination supports all standard spectroscopic measurements.

Intensity data were obtained from an irregular fragment of dimensions 0.25 × 0.45 × 0.50 mm mounted in a random orientation on an Enraf–Nonius CAD-4 diffractometer. Cell dimensions were determined at 296 K by a least-squares fit to setting angles of 25 reflections having $25 < \theta < 30^\circ$. A hemisphere of data having $4 < 2\theta < 150^\circ$, $0 \leq h \leq 10$, $-13 \leq k \leq 13$,

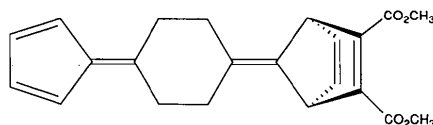


Fig. 1. The mono Diels–Alder adduct of 1,4-bis(2,4-cyclopentadien-1-ylidene)cyclohexane and dimethyl butynedioate.

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