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9,10-Dihydroxy-4,4-dimethyl-5,8-dihydroanthracen-1(4H)-one

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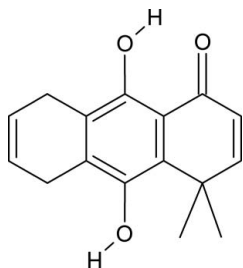
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Key indicators: single-crystal X-ray study; $T = 150$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.044; wR factor = 0.118; data-to-parameter ratio = 10.7.

In the title molecule, $\text{C}_{16}\text{H}_{16}\text{O}_3$, the ring system is planar and an intramolecular hydrogen bond is present. The molecular packing is dominated by an intermolecular hydrogen bond and by π -stacking interactions [interplanar separation 3.8012 Å].

Related literature

For related literature, see: Allen (2002); Araya-Maturana *et al.* (2006, 2007); Desiraju (2002); Joshi *et al.* (1997); Valderrama *et al.* (1993).



Experimental

Crystal data

 $\text{C}_{16}\text{H}_{16}\text{O}_3$ $M_r = 256.29$ Orthorhombic, $Pnma$

$a = 8.5944$ (5) Å
 $b = 7.6024$ (5) Å
 $c = 19.2949$ (12) Å
 $V = 1260.69$ (14) Å³

 $Z = 4$

Mo $K\alpha$ radiation
 $\mu = 0.09$ mm⁻¹
 $T = 150$ (2) K
 $0.43 \times 0.38 \times 0.08$ mm

Data collection

Siemens SMART CCD area-detector diffractometer
 Absorption correction: multi-scan (*SADABS* in *SAINT-NT*; Bruker, 1999)
 $T_{\min} = 0.961$, $T_{\max} = 0.993$

7422 measured reflections
 1198 independent reflections
 948 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.043$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.118$
 $S = 1.01$
 1198 reflections

112 parameters
 H-atom parameters constrained
 $\Delta\rho_{\max} = 0.33$ e Å⁻³
 $\Delta\rho_{\min} = -0.29$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$O2-H2\cdots O1$	0.84	1.77	2.5172 (18)	147
$O3-H3\cdots O1^i$	0.84	2.03	2.8022 (18)	152

Symmetry code: (i) $x - 1, y, z$.

Data collection: *SMART-NT* (Bruker, 2001); cell refinement: *SAINT-NT* (Bruker, 1999); data reduction: *SAINT-NT*; program(s) used to solve structure: *SHELXTL-NT* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL-NT*; molecular graphics: *SHELXTL-NT*; software used to prepare material for publication: *SHELXTL-NT*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HG2395).

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supporting information

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9,10-Dihydroxy-4,4-dimethyl-5,8-dihydroanthracen-1(4H)-one

Oney Ramírez-Rodríguez, Maximiliano Martínez-Cifuentes, Andres Ibañez, Andrés Vega and Ramiro Araya-Maturana

S1. Comment

The title hydroquinone **I** is a potent antioxidant (Araya-Maturana *et al.*, 2007) and respiration inhibitor of cancer cells (Araya-Maturana *et al.*, 2006). In mouse mammary adenocarcinoma TA3 and their multidrug-resistant variant TA3-MTX-*R* lines exhibit IC₅₀ values below 10⁻⁴M. Moreover, this compound inhibits the growth of the human tumor U937 cell line at low micromolar concentrations (Araya-Maturana *et al.*, 2006).

The molecule consists of three six-membered carbon rings fused through atoms 4a, 9a in a side and through carbons 8a, 10a in the other, to give rise to an anthracene skeleton, substituted with an oxo, a *gem*-dimethyl and two hydroxyl groups at positions 1, 4, 9 and 10 respectively, as shown in Scheme 1. The central ring is aromatic, and double bonds are also found between carbons 2 - 3 and 6 - 7. This double bond distribution leads to the core to be strictly planar. In fact, all the carbon atoms in the skeleton lie on the crystallographic mirror plane *m* from space group *Pnma*. The same happens with the oxo oxygen atom O1 and the hydroxyl groups O2 and O3. Interestingly, the hydroxyl hydrogen atoms H2 and H3 display a *trans* correlation. The planarity of the molecule together with the proximity of the oxo oxygen atom (O1) and the hydroxyl hydrogen atom (H2) leads to the presence of an intramolecular O—H...O hydrogen bond with O...O of 2.5172 (18) Å, suggesting a rather strong bond (Desiraju, 2002), which is present still in CDCl₃ solution, as indicated by NMR (Araya-Maturana *et al.*, 2007). Few structures with this or some closely related pattern of substitution could be found in Cambridge Structural database (v 5.29, Allen, 2002), being 1,4-Dihydro-9,10-anthrahydroquinone the best, probably the one to the best of our knowledge, example (Joshi *et al.*, 1997).

The molecular packing is also dominated by the hydrogen bond, this time between vicinal molecules. As depicted in Figure 2, a planar chain is produced by means of the interaction of the "terminal" hydroxyl hydrogen atom H3 with the oxo oxygen O1 from the nearest molecule (*x* - 1, *y*, *z*), in a "head to tail" arrangement in the [100] direction. The O...O distance, 2.8022 (18) Å, suggests a weaker interaction. Layers of molecules are defined in the packing by putting these chains one together the other, with no strong interaction between them. Any of the chains is contained in the *x*, 1/4, *z* plane. The next layer, *x*, 3/4, *z* is separated from the first in *b*/2, 3.8012 Å, a typical value for the aromatic π -stacking interaction.

S2. Experimental

The molecule was synthesized by the Diels–Alder reaction between 8,8-dimethylnaphthalene-1,4,5(8*H*)-trione and butadiene. The cycloaddition takes place exclusively at the external quinone double bond affording the corresponding adduct **I-a** (See Scheme 2). Enolization of the adduct **I-a** with silicagel in toluene yields the hydroquinone **I**. (Valderrama *et al.*, 1993). The ¹H-NMR spectrum in CDCl₃ of **I** exhibits a sharp singlet at 13.08 p.p.m. indicating that hydrogen bonding is also present in solution. This characteristic is important regarding antitumor and antioxidant properties.

S3. Refinement

The hydrogen atoms positions were calculated after each cycle of refinement with *SHELXL* (Bruker, 1999) using a riding model for each structure, with C—H distances in the range 0.95 to 0.99 Å and O—H equal to 0.84 Å. $U_{\text{iso}}(\text{H})$ values were set equal to $1.5U_{\text{eq}}$ of the parent carbon atom for methyl groups and hydroxyl hydrogen atoms, while $1.2U_{\text{eq}}$ for the others.

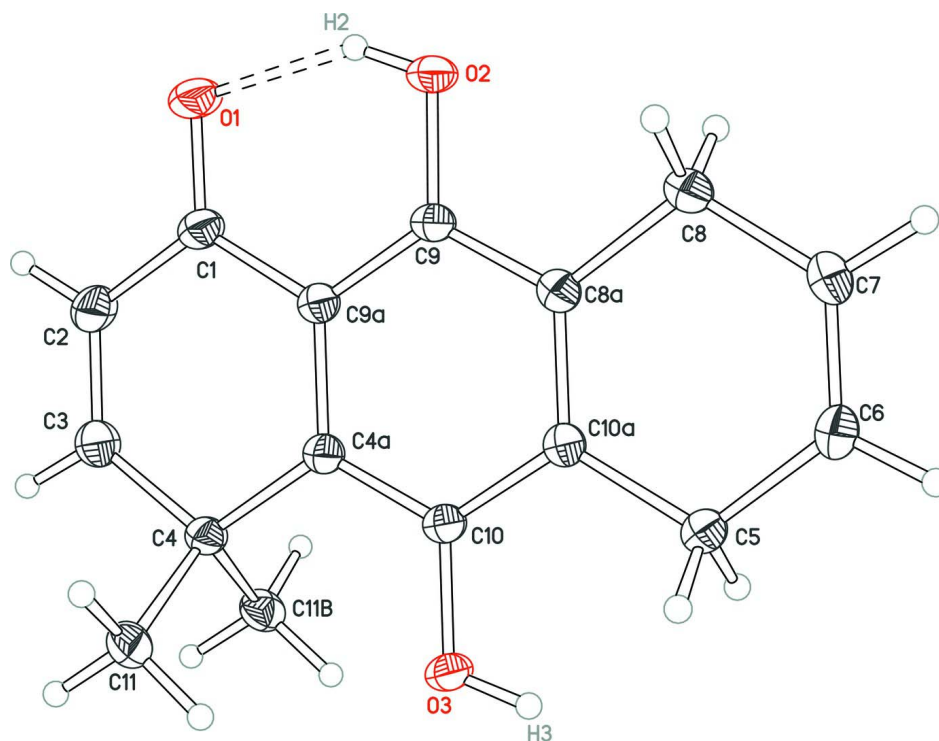


Figure 1

Molecular structure diagrams for **I** showing atom numbering scheme. Displacement ellipsoids are at 33% probability level and H atoms are shown as spheres of arbitrary radii. Letter a corresponds to the names of fused carbon atoms according to the nomenclature rules. Letter B to symmcode $x, -y + 1/2, z$.

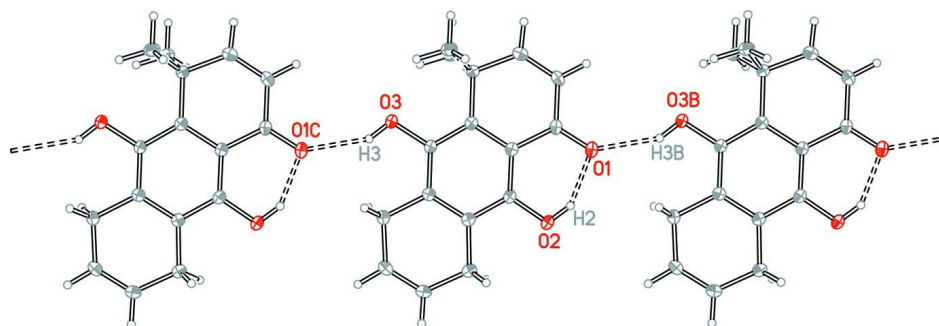
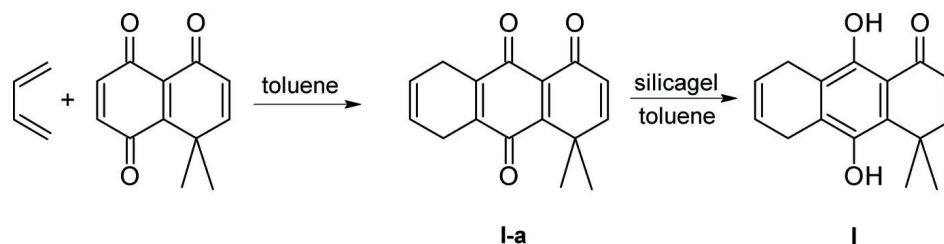


Figure 2

Molecular packing view for **I** along [010]. [symmetry codes: (B) $x + 1, y, z$; (C) $x - 1, y, z$].

**Figure 3**

The formation of the title compound.

9,10-Dihydroxy-4,4-dimethyl-5,8-dihydroanthracen-1(4H)-one

Crystal data

$C_{16}H_{16}O_3$

$M_r = 256.29$

Orthorhombic, *Pnma*

Hall symbol: -P 2ac 2n

$a = 8.5944$ (5) Å

$b = 7.6024$ (5) Å

$c = 19.2949$ (12) Å

$V = 1260.69$ (14) Å³

$Z = 4$

$F(000) = 544$

$D_x = 1.350$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 2361 reflections

$\theta = 2.6$ – 25.0°

$\mu = 0.09$ mm⁻¹

$T = 150$ K

Plate, orange

$0.43 \times 0.38 \times 0.08$ mm

Data collection

Siemens SMART CCD area-detector
diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

φ and ω scans

Absorption correction: multi-scan

(*SADABS* in *SAINT-NT*; Bruker, 1999)

$T_{\min} = 0.961$, $T_{\max} = 0.993$

7422 measured reflections

1198 independent reflections

948 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.043$

$\theta_{\max} = 25.0^\circ$, $\theta_{\min} = 2.1^\circ$

$h = -10 \rightarrow 10$

$k = -9 \rightarrow 9$

$l = -22 \rightarrow 22$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.044$

$wR(F^2) = 0.118$

$S = 1.01$

1198 reflections

112 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: inferred from
neighbouring sites

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0796P)^2]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.33$ e Å⁻³

$\Delta\rho_{\min} = -0.29$ e Å⁻³

Special details

Experimental. 10 s by frame separated by 0.3°

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$	Occ. (<1)
O1	1.23661 (15)	0.2500	0.97450 (7)	0.0430 (4)	
C1	1.1134 (2)	0.2500	0.93987 (9)	0.0316 (5)	
C2	1.1204 (2)	0.2500	0.86508 (10)	0.0394 (5)	
H2B	1.2188	0.2500	0.8427	0.047*	
C3	0.9915 (2)	0.2500	0.82719 (10)	0.0366 (5)	
H3A	1.0040	0.2500	0.7783	0.044*	
C4	0.8283 (2)	0.2500	0.85428 (9)	0.0276 (5)	
C11	0.74913 (15)	0.41540 (18)	0.82447 (7)	0.0319 (4)	
H11A	0.7543	0.4123	0.7737	0.048*	
H11B	0.8027	0.5206	0.8415	0.048*	
H11C	0.6400	0.4184	0.8392	0.048*	
C4A	0.8227 (2)	0.2500	0.93365 (10)	0.0250 (4)	
C10	0.68158 (19)	0.2500	0.96919 (10)	0.0257 (5)	
O3	0.54736 (14)	0.2500	0.93053 (6)	0.0349 (4)	
H3	0.4700	0.2500	0.9571	0.052*	
C10A	0.67531 (19)	0.2500	1.04249 (9)	0.0246 (5)	
C5	0.5186 (2)	0.2500	1.07767 (10)	0.0293 (5)	
H5A	0.4600	0.3551	1.0623	0.035*	0.50
H5B	0.4600	0.1449	1.0623	0.035*	0.50
C6	0.5260 (2)	0.2500	1.15519 (10)	0.0302 (5)	
H6A	0.4305	0.2500	1.1800	0.036*	
C7	0.6566 (2)	0.2500	1.19124 (10)	0.0299 (5)	
H7A	0.6495	0.2500	1.2404	0.036*	
C8	0.8143 (2)	0.2500	1.15932 (10)	0.0311 (5)	
H8A	0.8718	0.1448	1.1755	0.037*	0.50
H8B	0.8718	0.3552	1.1755	0.037*	0.50
C8A	0.8116 (2)	0.2500	1.08099 (9)	0.0252 (4)	
C9	0.9537 (2)	0.2500	1.04619 (9)	0.0257 (5)	
O2	1.08404 (15)	0.2500	1.08586 (6)	0.0356 (4)	
H2	1.1629	0.2500	1.0602	0.053*	
C9A	0.9614 (2)	0.2500	0.97343 (10)	0.0255 (5)	

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0199 (7)	0.0740 (12)	0.0351 (8)	0.000	-0.0021 (6)	0.000
C1	0.0210 (10)	0.0430 (12)	0.0310 (11)	0.000	-0.0009 (8)	0.000
C2	0.0246 (10)	0.0629 (14)	0.0306 (12)	0.000	0.0075 (9)	0.000
C3	0.0322 (11)	0.0527 (13)	0.0248 (10)	0.000	0.0037 (8)	0.000
C4	0.0232 (9)	0.0384 (12)	0.0213 (10)	0.000	-0.0015 (7)	0.000

C11	0.0346 (8)	0.0375 (8)	0.0237 (7)	-0.0025 (6)	-0.0025 (5)	0.0023 (6)
C4A	0.0230 (10)	0.0287 (10)	0.0232 (10)	0.000	-0.0008 (7)	0.000
C10	0.0211 (10)	0.0313 (11)	0.0246 (10)	0.000	-0.0020 (7)	0.000
O3	0.0189 (7)	0.0610 (10)	0.0247 (7)	0.000	-0.0024 (5)	0.000
C10A	0.0243 (10)	0.0264 (10)	0.0233 (10)	0.000	0.0004 (7)	0.000
C5	0.0226 (10)	0.0377 (11)	0.0276 (11)	0.000	0.0003 (7)	0.000
C6	0.0286 (10)	0.0335 (11)	0.0286 (10)	0.000	0.0069 (8)	0.000
C7	0.0354 (11)	0.0323 (11)	0.0221 (10)	0.000	0.0021 (8)	0.000
C8	0.0291 (10)	0.0395 (12)	0.0247 (10)	0.000	-0.0036 (8)	0.000
C8A	0.0262 (10)	0.0261 (10)	0.0233 (10)	0.000	-0.0012 (7)	0.000
C9	0.0222 (9)	0.0307 (11)	0.0243 (10)	0.000	-0.0039 (7)	0.000
O2	0.0215 (7)	0.0583 (9)	0.0271 (8)	0.000	-0.0058 (6)	0.000
C9A	0.0225 (10)	0.0291 (10)	0.0248 (10)	0.000	-0.0008 (7)	0.000

Geometric parameters (Å, °)

O1—C1	1.252 (2)	O3—H3	0.8400
C1—C2	1.444 (3)	C10A—C8A	1.387 (2)
C1—C9A	1.458 (2)	C10A—C5	1.508 (2)
C2—C3	1.327 (3)	C5—C6	1.497 (3)
C2—H2B	0.9500	C5—H5A	0.9900
C3—C4	1.497 (2)	C5—H5B	0.9900
C3—H3A	0.9500	C6—C7	1.320 (3)
C4—C4A	1.532 (3)	C6—H6A	0.9500
C4—C11 ⁱ	1.5410 (16)	C7—C8	1.489 (3)
C4—C11	1.5410 (16)	C7—H7A	0.9500
C11—H11A	0.9800	C8—C8A	1.512 (3)
C11—H11B	0.9800	C8—H8A	0.9900
C11—H11C	0.9800	C8—H8B	0.9900
C4A—C10	1.393 (2)	C8A—C9	1.394 (2)
C4A—C9A	1.418 (2)	C9—O2	1.357 (2)
C10—O3	1.374 (2)	C9—C9A	1.405 (3)
C10—C10A	1.415 (3)	O2—H2	0.8400
O1—C1—C2	119.87 (16)	C10—C10A—C5	118.94 (16)
O1—C1—C9A	121.38 (17)	C6—C5—C10A	114.34 (15)
C2—C1—C9A	118.75 (16)	C6—C5—H5A	108.7
C3—C2—C1	121.05 (17)	C10A—C5—H5A	108.7
C3—C2—H2B	119.5	C6—C5—H5B	108.7
C1—C2—H2B	119.5	C10A—C5—H5B	108.7
C2—C3—C4	126.13 (18)	H5A—C5—H5B	107.6
C2—C3—H3A	116.9	C7—C6—C5	124.20 (17)
C4—C3—H3A	116.9	C7—C6—H6A	117.9
C3—C4—C4A	112.24 (15)	C5—C6—H6A	117.9
C3—C4—C11 ⁱ	106.46 (10)	C6—C7—C8	123.79 (17)
C4A—C4—C11 ⁱ	111.05 (10)	C6—C7—H7A	118.1
C3—C4—C11	106.46 (10)	C8—C7—H7A	118.1
C4A—C4—C11	111.05 (10)	C7—C8—C8A	113.53 (15)

C11 ⁱ —C4—C11	109.37 (14)	C7—C8—H8A	108.9
C4—C11—H11A	109.5	C8A—C8—H8A	108.9
C4—C11—H11B	109.5	C7—C8—H8B	108.9
H11A—C11—H11B	109.5	C8A—C8—H8B	108.9
C4—C11—H11C	109.5	H8A—C8—H8B	107.7
H11A—C11—H11C	109.5	C10A—C8A—C9	118.81 (17)
H11B—C11—H11C	109.5	C10A—C8A—C8	123.28 (16)
C10—C4A—C9A	117.74 (17)	C9—C8A—C8	117.91 (15)
C10—C4A—C4	121.29 (15)	O2—C9—C8A	116.85 (16)
C9A—C4A—C4	120.97 (15)	O2—C9—C9A	121.64 (16)
O3—C10—C4A	117.62 (16)	C8A—C9—C9A	121.50 (16)
O3—C10—C10A	120.71 (15)	C9—O2—H2	109.5
C4A—C10—C10A	121.67 (16)	C9—C9A—C4A	120.08 (16)
C10—O3—H3	109.5	C9—C9A—C1	119.07 (16)
C8A—C10A—C10	120.20 (16)	C4A—C9A—C1	120.86 (16)
C8A—C10A—C5	120.86 (17)		
C2—C3—C4—C11	121.70 (9)	C11—C4—C4A—C9A	-119.04 (10)
C11—C4—C4A—C10	60.96 (10)		

Symmetry code: (i) $x, -y+1/2, z$.

Hydrogen-bond geometry ($\text{\AA}, ^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O2—H2 \cdots O1	0.84	1.77	2.5172 (18)	147
O3—H3 \cdots O1 ⁱⁱ	0.84	2.03	2.8022 (18)	152

Symmetry code: (ii) $x-1, y, z$.