

# 11-Hydroxy-3,3-dimethyl-7,12-dioxo-3,4,6,6a,7,12,12a,12b-octahydro-benz[*a*]anthracen-1-yl acetate

Tomas Rozek,<sup>a</sup> John H. Bowie,<sup>a</sup> Brian W. Skelton<sup>b\*</sup> and Allan H. White<sup>b</sup>

<sup>a</sup>Department of Chemistry, University of Adelaide, South Australia 5005, Australia, and <sup>b</sup>Department of Chemistry, University of Western Australia, 35 Stirling Highway, Crawley, Western Australia 6009, Australia  
Correspondence e-mail: bws@crystal.uwa.edu.au

Received 27 May 2003

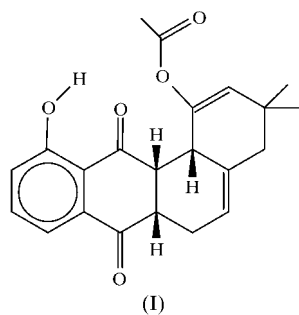
Accepted 16 June 2003

Online 12 July 2003

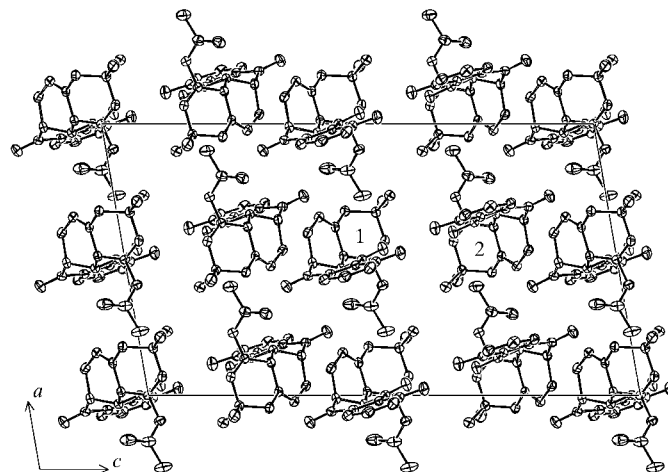
The Diels–Alder reaction between 5-hydroxy-1,4-naphthoquinone and 5,5-dimethyl-3-vinyl-1,2-cyclohexadienyl acetate by *endo* addition gives the title compound, C<sub>22</sub>H<sub>22</sub>O<sub>5</sub>, in 68% yield. This racemic diastereoisomer has the opposite regiochemistry to ochromycinone analogues produced previously and may allow access to a new type of anticancer-active saquayamycin analogue.

## Comment

The results of the low-temperature single-crystal X-ray study of the title compound, (I), as presented in Figs. 1 and 2 and Table 1, are consistent with the given formulation, stoichiometry and stereochemistry. Although non-centrosymmetric, the individual crystals are racemic; the asymmetric unit of the structure consists of two independent molecules of similar geometry and conformation, with an interesting pseudosymmetry evident in their packing (Figs. 1 and 2).



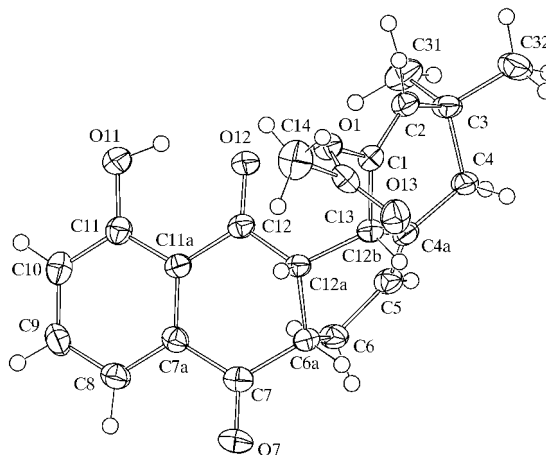
The fused tetracyclic ring system (ring *D*) has been recorded previously with diverse combinations of hydroxy and keto moieties at the 7,12-sites, with phenol substituents at the 8- rather than the 11-position, and with a diversity of double-bond and/or epoxide functionalities variously associated with



**Figure 1**

The unit cell of (I), projected along *b*. Displacement ellipsoids for non-H atoms are shown at the 50% probability level.

rings *A* and *B*. A brominated adduct (Rozek *et al.*, 2001) corresponding to the present combination of substituents has also been reported (see Kim *et al.*, 1992; Rozek, Janowski *et al.*, 1998; Rozek, Tiekink *et al.*, 1998; Sasaki *et al.*, 1998; Apponyi *et al.*, 2002). In (I), the combination of ring fusions and functionalities results in a curved or 'dished' molecule, with dihedral angles between the planes about the C<sub>n</sub>1=C<sub>n</sub>2 and C<sub>n</sub>5=C<sub>n</sub>4a double bonds of 29.7 (1) and 27.7 (2)° (*n* = 1 or 2), the angles between these planes and those of the aromatic rings being 84.8 (2) and 85.8 (2)° for C<sub>n</sub>1=C<sub>n</sub>2, and 75.6 (1) and 76.6 (1)° for C<sub>n</sub>5=C<sub>n</sub>4a. The pendant C<sub>2</sub>O<sub>2</sub> acetate planes are twisted to lie at dihedral angles of 115.4 (2) and 115.3 (2)° to the C<sub>n</sub>1=C<sub>n</sub>2 environment planes in molecules 1 and 2, respectively. Hydrogen-bonding details are given in Table 1. The pronounced asymmetry in the exocyclic angles at C<sub>n</sub>11, suggestive of O···O repulsion, is more pronounced than at C<sub>n</sub>12 (or C<sub>n</sub>7).



**Figure 2**

Molecule 1 of (I) (molecule 2 is similar), showing the atomic numbering scheme (molecule numbers, *n*, have been omitted). H atoms are represented by circles of arbitrary radii (0.1 Å).

## Experimental

A mixture of 5-hydroxy-1,4-naphthoquinone (317 mg) and 5,5-dimethyl-3-vinyl-1,2-cyclohexadienyl acetate (350 mg) in anhydrous toluene (60 ml) was heated under reflux for 60 h. The reaction mixture was allowed to cool to 293 K; the solvent was concentrated to 2 ml *in vacuo*, and the product was precipitated following dropwise addition of diethyl ether at 273 K. The product (550 mg) was purified by flash chromatography on silica, eluting with hexane/diethyl ether (2:1), and was crystallized from dichloromethane/diethyl ether (1:1), yielding the title compound (yield 450 mg, 68%) as colourless crystals (m.p. 461–463 K).

### Crystal data

$C_{22}H_{22}O_5$	$D_x = 1.298 \text{ Mg m}^{-3}$
$M_r = 366.41$	Mo $K\alpha$ radiation
Monoclinic, $Cc$	Cell parameters from 6110 reflections
$a = 13.774 (2) \text{ \AA}$	$\theta = 2.4\text{--}20.3^\circ$
$b = 11.233 (2) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$c = 24.595 (4) \text{ \AA}$	$T = 153 (2) \text{ K}$
$\beta = 99.792 (2)^\circ$	Fragment, colourless
$V = 3750.0 (11) \text{ \AA}^3$	$0.32 \times 0.21 \times 0.17 \text{ mm}$
$Z = 8$	

### Data collection

Bruker SMART CCD diffractometer	4771 independent reflections
$\omega$ scans	4288 reflections with $F > 2\sigma(F)$
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)	$R_{\text{int}} = 0.044$
$T_{\text{min}} = 0.87$ , $T_{\text{max}} = 0.96$	$\theta_{\text{max}} = 29^\circ$
21 857 measured reflections	$h = -18 \rightarrow 18$
	$k = -15 \rightarrow 15$
	$l = -32 \rightarrow 32$

### Refinement

Refinement on $F$	All H-atom parameters refined
$R = 0.044$	$w = 1/(\sigma^2 F + 0.0005 F^2)$
$wR = 0.046$	$(\Delta/\sigma)_{\text{max}} = 0.016$
$S = 1.11$	$\Delta\rho_{\text{max}} = 0.34 \text{ e \AA}^{-3}$
4288 reflections	$\Delta\rho_{\text{min}} = -0.23 \text{ e \AA}^{-3}$
661 parameters	

**Table 1**

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

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
O111—H111 $\cdots$ O112	0.88 (6)	1.83 (5)	2.618 (4)	148 (4)
O211—H211 $\cdots$ O212	0.92 (4)	1.77 (4)	2.586 (4)	147 (3)

H atoms were located from difference Fourier maps and refined without constraints, giving C—H distances in the range 0.90 (5)–1.08 (5)  $\text{\AA}$  and O—H distances of 0.88 (6) and 0.92 (4)  $\text{\AA}$ .

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *Xtal3.5* (Hall *et al.*, 1995); program(s) used to solve structure: *Xtal3.5*; program(s) used to refine structure: *CRYLSQ* in *Xtal3.5*; molecular graphics: *Xtal3.5*; software used to prepare material for publication: *BONDLA* and *CIFIO* in *Xtal3.5*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1412). Services for accessing these data are described at the back of the journal.

## References

- Apponyi, M. A., Bowie, J. H., Skelton, B. W. & White, A. H. (2002). *Aust. J. Chem.* **55**, 343–348.
- Hall, S. R., King, G. S. D. & Stewart, J. M. (1995). *Xtal3.5 User's Manual*. University of Western Australia, Perth: Lamb.
- Kim, K., Reibenspies, J. & Sulikowski, G. (1992). *J. Org. Chem.* **57**, 5557–5559.
- Rozek, T., Bowie, J. H., Pyke, S. M., Skelton, B. W. & White, A. H. (2001). *J. Chem. Soc. Perkin Trans. 1*, pp. 1826–1830.
- Rozek, T., Janowski, W., Hevko, J. M., Tiekink, E. R. T., Dua, S., Stone, D. J. M. & Bowie, J. H. (1998). *Aust. J. Chem.* **51**, 515–523.
- Rozek, T., Tiekink, E. R. T., Taylor, D. K. & Bowie, J. H. (1998). *Aust. J. Chem.* **51**, 1057–1060.
- Sasaki, T., Gomi, S., Sezaki, M., Takeuchi, Y., Kodama, Y. & Kawamura, K. (1998). *J. Antibiot.* **41**, 843–800.
- Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
- Siemens (1995). *SMART* and *SAINT*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.