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4-Hydroxy-17a-oxa-17a-homoandrost-4-ene-3,17-dione

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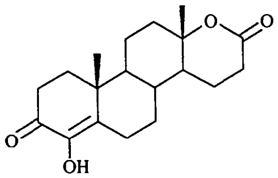
Abstract

The dihedral angles between ring planes of the title compound, $C_{19}H_{26}O_4$, a *D*-ring lactone, indicate a slightly curved molecular profile. All ring junctions are *trans*. A hydrogen bond between the hydroxyl group of ring *A* and the carbonyl group of ring *D* links the molecules head-to-tail in helical chains parallel to the 2_1 screw axis along **a**.

Comment

The title compound, (I), is a new potential aromatase inhibitor which was synthesized (Tavares da Silva *et al.*, 1997) through oxidation in two sequential steps followed by isomerization of the previously prepared 3α,4β-dihydroxy-5α-androstan-17-one (Tavares da Silva, Sá e Melo & Campos Neves, 1996).



(I)

The X-ray analysis gives bond lengths and angles in good agreement with expected values. The mean C_{sp^3}—C_{sp^3} bond length is 1.526 (10) Å, with only C9—C10 clearly different from this value. A similar feature for steroids with a double C═C bond in ring *A* has been reported (Rohrer, Duax & Segaloff, 1978; Rohrer, Strong, Duax & Segaloff, 1978; Griffin *et al.*, 1980; Honda *et al.*, 1996).

An *ORTEP*II (Johnson, 1976) drawing of (I) is shown in Fig. 1. The distance between the terminal O atoms, O3 and O17, is 11.037 (4) Å. The pseudo-torsion angle C19—C10···C13—C18 is 1.95 (17)°. All ring junctions are *trans*. The dihedral angles between rings *A* and *D* and the least-squares plane defined by the atoms of rings *B* and *C* are, respectively, 23.79 (5) and 17.08 (9)°, indicating a slightly curved molecular profile. The conformation of the molecule may be described by the asymmetry parameters (Duax & Norton, 1975) calculated from the intramolecular torsion angles. The presence of a double bond between C4 and C5 gives rise to a 1α,2β-half-chair conformation distorted towards 1α-sofa, with asymmetry parameters $\Delta C_2(1,2)$ = 8.8 (3), $\Delta C_s(1)$ = 15.6 (2) and $\Delta C_2(2,3)$ = 50.5 (3)°. Rings *B* and *C* have slightly distorted chair conformations [average torsion angles are 52 (3) and 56 (1)°, respectively]. The six-membered ring *D* characteristic of a γ-lactone has a conformation midway between a 13β,14α-half-chair [$\Delta C_2(13,14)$ = 16.4 (3)°] and a 14α-sofa [$\Delta C_s(14)$ = 18.0 (2)°], with $\Delta C_2(15,16)$ = 71.0 (3)°. Atoms C2, C3, C4 and O3 of ring *A* are coplanar within experimental error, as are atoms C16, C17, O17 and O17*A* of ring *D* [the sum of the bond angles around C3 and C17 equals 359.9 (4)°].

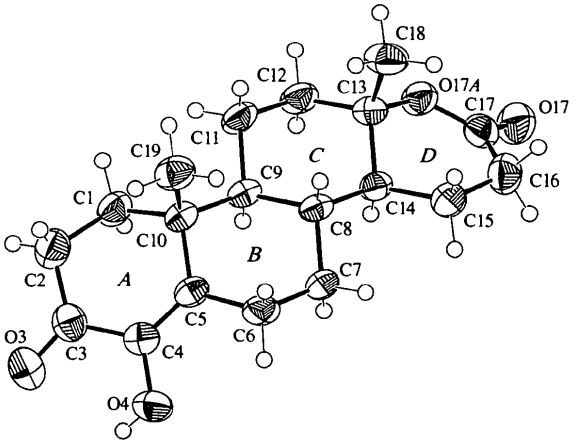


Fig. 1. *ORTEP*II (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% level, except for H atoms, which were given arbitrary radii.

Hydrogen-bonding details are given in Table 2. The H atom of the hydroxyl group is shared between the carbonyl O3 atom (intramolecular bond) and the carbonyl O17 atom of a neighbouring molecule. The sum of the three bond angles around the shared proton is 358.9 (2) Å. The O4···O17($x-\frac{1}{2}$, $\frac{3}{2}-y$, $1-z$) bond joins molecules head-to-tail in infinite one-dimensional helical chains parallel to the *a* axis.

It should be stated that the absolute configuration was chosen to give the correct chirality of the molecule that was known beforehand from the synthesis route. Due to the absence of a strong enough anomalous scatterer at the molybdenum wavelength, the absolute configuration could not be confirmed from the X-ray data.

Experimental

Details of the synthesis, IR, NMR and mass spectroscopy data will be published elsewhere (Tavares da Silva *et al.*, 1997). Crystals of good quality suitable for X-ray analysis were grown from ethyl acetate–isopropyl ether solution.

Crystal data

$C_{19}H_{26}O_4$
$M_r = 318.40$
Orthorhombic
$P2_12_12_1$
$a = 7.433\,(3)$ Å
$b = 12.128\,(5)$ Å
$c = 17.826\,(4)$ Å
$V = 1607.0\,(10)$ Å^3
$Z = 4$
$D_x = 1.316$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 8\text{–}16°$
$\mu = 0.091$ mm^{-1}
$T = 293\,(2)$ K
Prismatic
0.49 × 0.24 × 0.24 mm
Transparent

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
Absorption correction: none
7285 measured reflections
2784 independent reflections
2054 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.040$

$\theta_{\max} = 25.0°$
$h = -7 \rightarrow 8$
$k = -14 \rightarrow 14$
$l = -21 \rightarrow 21$
3 standard reflections every 300 reflections intensity decay: 1.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.032$
$wR(F^2) = 0.078$
$S = 1.043$
2784 reflections
204 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0289P)^2 + 0.2378P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.125$ e Å^{-3}
$\Delta\rho_{\min} = -0.113$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

C2—C3	1.489 (3)	C9—C10	1.559 (3)
C3—O3	1.220 (2)	C16—C17	1.495 (3)
C3—C4	1.463 (3)	C17—O17	1.207 (2)
C4—C5	1.335 (3)	C17—O17*A*	1.333 (2)
C4—O4	1.367 (2)		
O3—C3—C4	120.4 (2)	O17A—C13—C12	103.18 (15)
O3—C3—C2	123.14 (19)	O17A—C13—C18	107.17 (15)
C4—C3—C2	116.44 (19)	O17A—C13—C14	108.56 (15)
C5—C4—O4	121.41 (17)	O17—C17—O17*A*	117.5 (2)
C5—C4—C3	123.12 (19)	O17—C17—C16	123.0 (2)
O4—C4—C3	115.35 (17)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4···O3	0.82	2.27	2.676 (2)	110.9
O4—H4···O17$^{\rm i}$	0.82	2.21	2.938 (2)	148.3

Symmetry code: (i) $x - \frac{1}{2}, \frac{3}{2} - y, 1 - z$.

The title structure was solved by direct methods. The H atoms were placed at calculated positions and refined as riding using *SHELXL*97 (Sheldrick, 1997) defaults. Examination of the crystal structure with *PLATON* (Spek, 1995) showed that there are no solvent-accessible voids in the crystal lattice. All calculations were performed on a Pentium 150 MHz PC running LINUX.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *SDP-Plus* (Frenz, 1985). Program(s) used to solve structure: *MULTAN*11/82 (Main *et al.*, 1982). Program(s) used to refine structure: *SHELXL*97. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1137). Services for accessing these data are described at the back of the journal.

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