

9 β ,11 β -Epoxy-3 β -hydroxy-5 α -androstan-17-one

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Key indicators

Single-crystal X-ray study
 $T = 293\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$
 R factor = 0.036
 wR factor = 0.103
Data-to-parameter ratio = 10.0

For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

In the title compound, $\text{C}_{19}\text{H}_{28}\text{O}_3$, the ester linkage in ring *A* is equatorial. The six-membered rings *A* and *B* have chair conformations, but ring *C* can be better described as a half-chair. The five-membered ring *D* adopts a 14α -envelope conformation. The *A/B*, *B/C* and *C/D* ring junctions are all *trans*. The packing of the molecules is assumed to be dictated mainly by intermolecular hydrogen bonds. There is an intramolecular $\text{C}-\text{H}\cdots\text{O}$ interaction between the O11 atom of the epoxy group and the methyl C18 group.

Comment

Corticosteroids have demonstrated substantial topical anti-inflammatory potency. In particular, betamethasone 17-benzoate has been in clinical practice for a long time (Lutsky *et al.*, 1979). The strategy and importance for the synthesis of these compounds have antecedents in similar structures, with anabolic and/or androgenic activity, replacing the positions 9α and 11β with fluorine and hydroxyl, respectively (Shapiro *et al.*, 1987). An example of this is 9α -fluoro- $11\beta,17\alpha$ -dihydroxy- 17α -methyl-4-androsten-3-one (halotestin), a commercial compound 20 times more androgenic and 10 times more anabolic than methyltestosterone. In connection with our studies on the synthesis and characterization of bioactive steroids, the structure of the title compound, (I), could allow us to predict the possibility of presenting/displaying anabolic and/or androgenic properties. The absolute configuration was assumed to be the same as that predicted beforehand from the synthesis route.

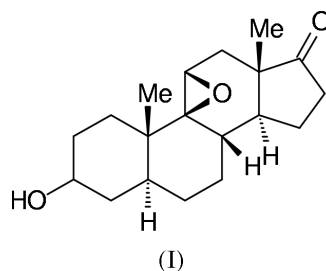


Fig. 1 shows the molecular structure of (I), with the corresponding numbering scheme. The $\text{C}3-\text{O}3$ bond of the hydroxy group is equatorially oriented and (–)antiperiplanar to the $\text{C}3-\text{C}4$ bond. The presence of OH bonded to C3 does not disturb the chair conformation in the ring *A* of the steroid nucleus. Ring *A* has a highly symmetrical chair conformation with all asymmetry parameters (Duax *et al.*, 1976) below $4.3(3)^\circ$. The average magnitude of the torsion angles is $55.08(10)^\circ$. Ring *B* displays a chair conformation, as expected (Pfeiffer *et al.*, 1985), but this is not the case for ring *C*, which

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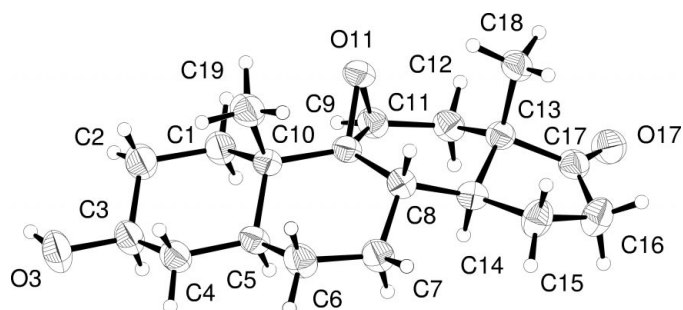


Figure 1

Plot showing the atomic numbering scheme for the title compound. Displacement ellipsoids are drawn at 50% probability level for non-H atoms. H atoms have been omitted for clarity.

has a half-chair conformation. The five-membered ring *D* adopts a 14α -envelope conformation (Altona *et al.*, 1968). The *A/B*, *B/C* and *C/D* ring junctions are all *trans*. Bond distances and valence angles are close to expected values (Honda *et al.*, 1996). The packing of the molecules is assumed to be dictated mainly by intermolecular $O3-H3A \cdots O17$ hydrogen bonds. There is an intramolecular $C-H \cdots O$ interaction between the O11 atom of the epoxy group and the methyl C18 group (Taylor & Kennard, 1982).

Experimental

The synthesis of the title compound is described by Ruíz (1997). Crystals (m.p. 529 K) were grown by slow evaporation from ethanol.

Crystal data

$C_{19}H_{28}O_3$
 $M_r = 304.41$
 Orthorhombic, $P2_12_12_1$
 $a = 7.3171$ (3) Å
 $b = 10.6462$ (6) Å
 $c = 21.0401$ (14) Å
 $V = 1639.01$ (16) Å³
 $Z = 4$
 $D_x = 1.234$ Mg m⁻³

Cu $K\alpha$ radiation
 Cell parameters from 40 reflections
 $\theta = 10.5$ – 28.0°
 $\mu = 0.64$ mm⁻¹
 $T = 293$ (2) K
 Prism, colourless
 $0.64 \times 0.46 \times 0.28$ mm

Data collection

Siemens *P4* four-circle diffractometer
 $\omega/2\theta$ scans
 Absorption correction: ψ scan (North *et al.*, 1968)
 $T_{\min} = 0.615$, $T_{\max} = 0.835$
 2214 measured reflections
 2031 independent reflections
 1987 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.043$
 $\theta_{\text{max}} = 69.1^\circ$
 $h = -8 \rightarrow 1$
 $k = -1 \rightarrow 12$
 $l = -1 \rightarrow 25$
 3 standard reflections every 100 reflections
 intensity decay: none

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.036$
 $wR(F^2) = 0.103$
 $S = 1.07$
 2031 reflections
 203 parameters
 H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0626P)^2 + 0.3007P]$
 where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\text{max}} = 0.006$
 $\Delta\rho_{\text{max}} = 0.21$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.16$ e Å⁻³
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.0148 (11)
 Absolute structure: Flack (1983);
 388 Friedel pairs
 Flack parameter = -0.3 (3)

Table 1

Hydrogen-bonding geometry (Å, °).

<i>D</i> –H··· <i>A</i>	<i>D</i> –H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> –H··· <i>A</i>
$O3-H3A \cdots O17^i$	0.82	2.02	2.828 (2)	171
$C18-H18B \cdots O11$	0.96	2.32	2.990 (3)	126

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

H atoms were calculated geometrically and included in the refinement, but were constrained to ride on their parent atoms. The isotropic displacement parameters of the H atoms were fixed to $1.3U_{\text{eq}}$ of their parent atoms.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PLATON* (Spek, 1990), *PARST* (Nardelli, 1983, 1995) and *PARSTCIF* (Nardelli, 1991).

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