

9 α -Chloro-3 β ,11 β -dihydroxy-5 α -androstan-17-one

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Key indicators

Single-crystal X-ray study
 $T = 293\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.004\text{ \AA}$
 R factor = 0.033
 wR factor = 0.099
Data-to-parameter ratio = 8.9

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

In the title compound, $\text{C}_{19}\text{H}_{29}\text{ClO}_3$, the hydroxyl linkage in ring *A* is equatorial. The six-membered rings *A*, *B* and *C* have chair conformations. The five-membered ring *D* adopts a 14α envelope conformation. The *A/B*, *B/C* and *C/D* ring junctions are *trans*. The packing of the molecules is assumed to be dictated mainly by two strong intermolecular hydrogen bonds of the type $\text{O}-\text{H}\cdots\text{O}$.

Comment

Topical corticosteroids became available for medical use in the 1950's when hydrocortisone was introduced demonstrating substantial topical anti-inflammatory potency. Modification of the basic corticosteroid molecule, *e.g.* by halogenation or the optimization of the vehicle, enhances their effectiveness, the former by raising the potency and the latter by increasing the percutaneous absorption (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 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 the prediction of the possibility of a compound of presenting/displaying anabolic and/or androgenic properties. The absolute configuration turned out to be the same as that predicted beforehand from the synthesis route.

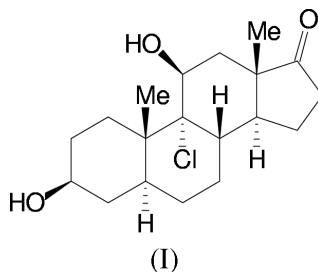


Fig. 1 shows the molecular structure of the title compound, with the corresponding numbering scheme. The $\text{C}3-\text{O}3$ bond of the hydroxy group is equatorially oriented and (–)-antiperiplanar to the $\text{C}4-\text{C}5$ bond. The presence of OH bonded to C3 does not disturb the chair conformation in the ring *A* of the steroidal nucleus. Ring *A* has a chair conformation with all asymmetry parameters (Duax *et al.*, 1976) below $9.2(3)^\circ$. The average magnitude of the torsion angles is

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54.27 (12)°. Ring *B* displays a chair conformation, as does ring *C* (Pfeiffer *et al.*, 1985). The five-membered ring *D* adopts a 14 α -envelope conformation (Altona *et al.*, 1968). The *A/B*, *B/C* and *C/D* ring junctions are *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 two intermolecular hydrogen bonds (Table 1).

Experimental

The synthesis of the title compound has been described by Ruíz (1997). Crystals (m.p. 399 K) were grown by slow evaporation from ethanol.

Crystal data

C ₁₉ H ₂₉ ClO ₃	$D_x = 1.297 \text{ Mg m}^{-3}$
$M_r = 340.87$	Cu $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 40 reflections
$a = 8.3450 (3) \text{ \AA}$	$\theta = 10.5\text{--}28.0^\circ$
$b = 8.5536 (3) \text{ \AA}$	$\mu = 2.04 \text{ mm}^{-1}$
$c = 12.6875 (5) \text{ \AA}$	$T = 293 (2) \text{ K}$
$\beta = 105.482 (3)^\circ$	Prism, colourless
$V = 872.77 (6) \text{ \AA}^3$	$0.64 \times 0.46 \times 0.28 \text{ mm}$
$Z = 2$	

Data collection

Siemens <i>P4</i> four-circle diffractometer	$R_{\text{int}} = 0.051$
$\omega/2\theta$ scans	$\theta_{\text{max}} = 69.2^\circ$
Absorption correction: ψ scan (North <i>et al.</i> , 1968)	$h = -10 \rightarrow 1$
$T_{\text{min}} = 0.247$, $T_{\text{max}} = 0.356$	$k = -1 \rightarrow 10$
2286 measured reflections	$l = -15 \rightarrow 15$
1893 independent reflections	3 standard reflections every 100 reflections
1862 reflections with $I > 2\sigma(I)$	intensity decay: none

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0628P)^2 + 0.1216P]$
$R[F^2 > 2\sigma(F^2)] = 0.033$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.099$	$(\Delta/\sigma)_{\text{max}} = 0.009$
$S = 1.10$	$\Delta\rho_{\text{max}} = 0.21 \text{ e \AA}^{-3}$
1893 reflections	$\Delta\rho_{\text{min}} = -0.28 \text{ e \AA}^{-3}$
213 parameters	Extinction correction: <i>SHELXL97</i>
H atoms treated by a mixture of independent and constrained refinement	Extinction coefficient: 0.032 (2)
	Absolute structure: Flack (1983)
	Flack parameter = 0.012 (17)

Table 1

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

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
$\text{O3--H3A}\cdots\text{O17}^i$	0.82	2.08	2.874 (3)	164
$\text{O11--H11A}\cdots\text{O3}^{ii}$	0.82	2.05	2.862 (3)	171

Symmetry codes: (i) $x - 1, 1 + y, z$; (ii) $1 - x, y - \frac{1}{2}, -z$.

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. The torsion angles about the C—OH and C—CH₃ bonds were allowed to refine. Number of Friedel pairs used: 232. Friedel pairs were treated as independent data.

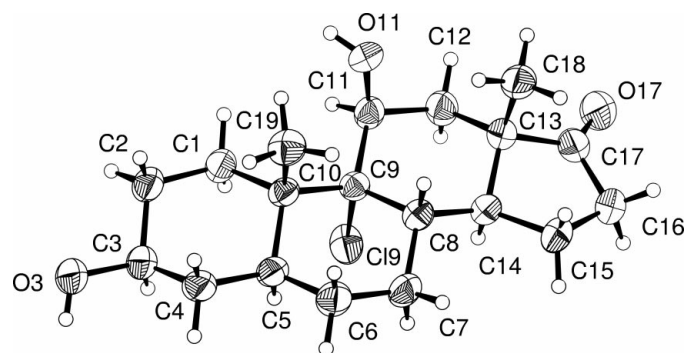


Figure 1

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