

**3 $\alpha$ ,4 $\beta$ -Dihydroxy-5 $\beta$ -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 = 0.035

$wR$  factor = 0.108

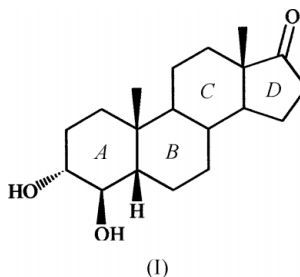
Data-to-parameter ratio = 8.8

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

The ring conformation of the title compound,  $\text{C}_{19}\text{H}_{30}\text{O}_3$ , is similar to that of the  $5\alpha$ -epimer except for the *cis* *A/B* ring junction. Ring *D* adopts a  $13\beta,14\alpha$ -half chair conformation. The molecules are linked together by a two-dimensional network of hydrogen bonds involving the carbonyl and hydroxyl groups.

**Comment**

The title compound, 3 $\alpha$ ,4 $\beta$ -dihydroxy-5 $\beta$ -androstan-17-one, (I), is a 3,4-*trans*-diequatorial diol which has been prepared as a potential intermediate for the synthesis of the potent aromatase inhibitor Formestane (Tavares da Silva *et al.*, 2002), clinically used as an anti-tumor agent in the treatment of estrogen-dependent breast cancers. Preparation of the above-mentioned diol results from the abnormal ring opening of the 3 $\beta$ ,4 $\beta$ -epoxide precursor recently studied through X-ray and deuterium-labeling experiments (Tavares da Silva *et al.*, 2002). Following our work on the elucidation of several androstane structures as potential aromatase inhibitors and intermediates in their syntheses, the present X-ray analysis aims to contribute to the elucidation of the reactivity of these compounds.

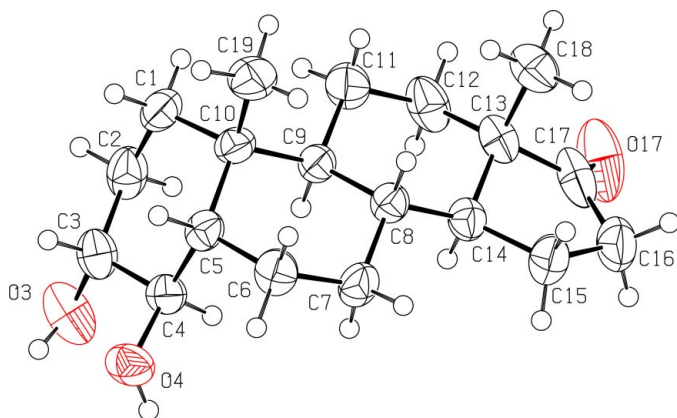


From the X-ray analysis of (I), a  $\beta$  configuration for this molecule was evident, with a *cis* junction between rings *A* and *B*. An *ORTEP*II (Johnson, 1976) drawing of the molecule with the corresponding atomic numbering scheme is shown in Fig. 1. Bond lengths and angles are within the expected ranges (Allen *et al.*, 1987), with average values:  $\text{Csp}^3-\text{Csp}^3$  1.533 (11),  $\text{Csp}^3-\text{Csp}^2$  1.519 (4),  $\text{C}=\text{O}$  1.206 (3) and  $\text{C}-\text{O}$  1.428 (5) Å. Rings *A*, *B* and *C* have slightly flattened chair conformations, with average torsion angles of 53.7 (9), 55.4 (8) and 55.0 (15)°, respectively. Ring *D* adopts a  $13\beta,14\alpha$ -half-chair conformation, with puckering parameters (Cremer & Pople, 1975) calculated using the atom sequence C13,C14,...,C17 of  $q_2 = 0.435$  (3) Å and  $\varphi_2 = 199.7$  (4)° [pseudo-rotation (Altona *et al.*, 1968) and asymmetry parameters:  $\Delta = 2.4$  (4),  $\varphi_m = 44.7$  (1),  $\Delta C_s(14) = 15.5$  (3) and

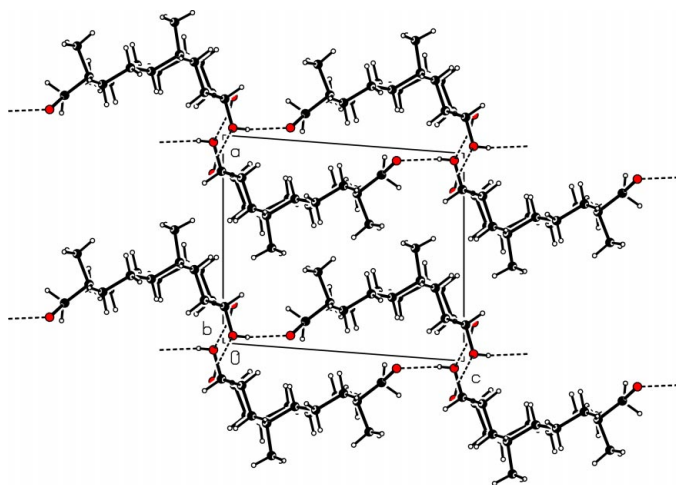
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**Figure 1**  
ORTEPII (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% probability level.



**Figure 2**  
View (Spek, 2003) of the unit cell along the *b* axis, showing the molecular packing and hydrogen-bond network.

$\Delta C_2(13,14) = 1.6(2)^\circ$ . The unusual *D*-ring conformation is very similar to that found for the  $5\alpha$ -epimer of this compound (Paixão *et al.*, 1998). The environment around C17 is planar, *viz.* atoms C13, C16, C17 and O17 are coplanar. The bowing angle between the *A* ring and the least-squares plane that includes the atoms of the *B*, *C* and *D* rings is  $67.62(5)^\circ$ ; the distance between terminal O atoms (O3...O17) is  $8.691(4) \text{ \AA}$  and the pseudo-torsion angle C19–C10–C13–C18 is  $-2.8(2)^\circ$ , showing that the molecule is only slightly twisted. The crystal packing is stabilized by a two-dimensional network of hydrogen bonds involving the hydroxyl and carbonyl groups, linking the molecules in planes parallel to (001) (Fig. 2). The  $3\alpha$ -hydroxyl group takes part in two intermolecular hydrogen bonds, one as a donor to the carbonyl group, the other as an acceptor from the  $4\beta$ -hydroxyl group. The two bonds have approximately the same length; the  $3\alpha$ -hydroxyl to the  $4\beta$ -hydroxyl intermolecular bond links two molecules head-to-head and the bond *via* the carbonyl group links two molecules head-to-tail. In addition, there is a short contact between atoms O3 and O4 [ $2.853(3) \text{ \AA}$ ,  $100(3)^\circ$  at H3] that may correspond to an intramolecular interaction between the two hydroxyl groups.

## Experimental

The title compound has been prepared and characterized according to a procedure recently described in the literature (Tavares da Silva *et al.*, 2002). Crystals suitable for X-ray experiments were obtained by slow evaporation of a solution of the steroid in methanol.

### Crystal data

$C_{19}H_{30}O_3$   
 $M_r = 306.43$   
Monoclinic,  $P2_1$   
 $a = 9.798(3) \text{ \AA}$   
 $b = 7.7742(11) \text{ \AA}$   
 $c = 11.372(4) \text{ \AA}$   
 $\beta = 94.36(2)^\circ$   
 $V = 863.7(4) \text{ \AA}^3$   
 $Z = 2$

$D_x = 1.178 \text{ Mg m}^{-3}$   
Cu  $K\alpha$  radiation  
Cell parameters from 25 reflections  
 $\theta = 17.4\text{--}31.4^\circ$   
 $\mu = 0.61 \text{ mm}^{-1}$   
 $T = 293(2) \text{ K}$   
Prism, colourless  
 $0.48 \times 0.37 \times 0.37 \text{ mm}$

### Data collection

Enraf–Nonius MACH-3 diffractometer  
Profile data from  $\omega$ - $2\theta$  scans  
Absorption correction:  $\psi$  scan (North *et al.*, 1968)  
 $T_{\min} = 0.713$ ,  $T_{\max} = 0.798$   
3519 measured reflections  
1827 independent reflections  
1794 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.017$   
 $\theta_{\text{max}} = 71.9^\circ$   
 $h = -12 \rightarrow 12$   
 $k = 0 \rightarrow 9$   
 $l = -14 \rightarrow 14$   
3 standard reflections  
frequency: 120 min  
intensity decay: 1.6%

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.035$   
 $wR(F^2) = 0.108$   
 $S = 1.09$   
1827 reflections  
208 parameters  
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0599P)^2 + 0.1172P]$   
where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} < 0.001$   
 $\Delta\rho_{\text{max}} = 0.24 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\text{min}} = -0.13 \text{ e \AA}^{-3}$   
Extinction correction: SHELXL97  
Extinction coefficient: 0.0148 (16)

**Table 1**

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

<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>
O4–H4...O3 <sup>i</sup>	0.83(3)	1.93(3)	2.751(3)	168(3)
O3–H3...O17 <sup>ii</sup>	0.84(4)	2.04(4)	2.792(3)	149(4)

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

All H atoms were refined as riding on their parent atoms using SHELXL97 (Sheldrick, 1997) defaults, except for those of the hydroxyl groups, which had their coordinates freely refined with  $U_{\text{iso}} = 1.2U_{\text{eq}}$  of the O atoms. The absolute configuration was not determined from the X-ray data, but it was known from the synthetic route. Friedel pairs were merged, as there was no significant anomalous dispersion.

Data collection: CAD-4 Software (Enraf–Nonius, 1989); cell refinement: CAD-4 Software; data reduction: HELENA (Spek, 1997); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEPII (Johnson, 1976); software used to prepare material for publication: SHELXL97.

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