Compound (2)

Crystal data

$C_9H_{15}N_3O_3$
$M_r = 213.24$
Orthorhombic
$P2_12_12_1$
$a = 7.835$ (2) Å
$b = 8.144$ (1) Å
$c = 16.820$ (5) Å
$V = 1073.3$ (4) Å^3
$Z = 4$
$D_x = 1.320$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 750 reflections
$\theta = 2.78$–$28.81°$
$\mu = 0.100$ mm^{-1}
$T = 293$ (2) K
Prism
0.20 × 0.15 × 0.10 mm
White

Data collection

Enraf–Nonius FAST area-detector diffractometer
Rotation scans
Absorption correction: none
1568 measured reflections
1568 independent reflections

1380 reflections with $I > 2\sigma(I)$
$\theta_{\max} = 28.81°$
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.107$
$S = 1.074$
1568 reflections
136 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0629P)^2 + 0.1546P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = -0.001$
$\Delta\rho_{\max} = 0.296$ e Å^{-3}
$\Delta\rho_{\min} = -0.227$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

D—H···A	D—H	H···A	D···A	D—H···A
C6—H61···O1^{i}	0.97	2.572 (2)	3.350 (2)	137.4 (2)
C7—H71···O3^{ii}	0.96	2.667 (3)	3.305 (3)	124.3 (2)
C7—H73···O2^{iii}	0.96	2.876 (3)	3.493 (3)	123.0 (2)
C8—H81···O1^{iv}	0.96	2.604 (3)	3.299 (3)	129.5 (2)
C8—H82···O3^{v}	0.96	2.728 (3)	3.340 (3)	122.2 (2)

Symmetry codes: (i) $x, y-1, z$; (ii) $-x, \frac{1}{2}+y, \frac{3}{2}-z$; (iii) $x-1, y, z$; (iv) $\frac{1}{2}+x, \frac{5}{2}-y, 2-z$; (v) $\frac{1}{2}+x, \frac{3}{2}-y, 2-z$.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989) for (1); *MADNES* (Pflugrath & Messerschmidt, 1989) for (2). Cell refinement: *CAD*-4 *Software* for (1); *MADNES* for (2). Data reduction: *CAD*-4 *Software* for (1); *MADNES* for (2). For both compounds, program(s) used to solve structures: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ORTEP*II (Johnson, 1976) and *PLUTO* (Motherwell & Clegg, 1978); software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OA1038). Services for accessing these data are described at the back of the journal.

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3α,4β-Dihydroxy-5α-androstan-17-one

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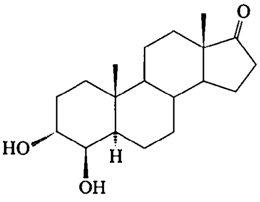
Abstract

The ring conformation of the title compound, 3α,4β-dihydroxy-5α-androstan-17-one, $C_{19}H_{30}O_3$, is similar to that of the 5β-epimer except for the *trans A*/*B* ring junction and the geometry of ring *D*, which adopts a slightly deformed 13,14-half-chair conformation instead of the more common 14α-envelope conformation. The molecules are linked together by a two-dimensional network of hydrogen bonds involving the carbonyl and hydroxyl groups.

Comment

The title steroid, (I), is one of the intermediate compounds obtained during the synthesis of formestane (Tavares da Silva, Sá e Melo & Campos Neves, 1996), an irreversible aromatase inhibitor which is known to be a very effective drug in the treatment of breast cancer. This work is part of a project to study the conformation and intermolecular interactions of steroids related to formestane. The crystal structure of the 5β-epimer, also obtained as an intermediate in the formestane syn-



(I)

thesis, was recently reported by us (Ramos Silva *et al.*, 1996).

The ring conformation of (I) (Fig. 1) is very similar to that found for its 5β-epimer (Ramos Silva *et al.*, 1996), with the exception of the *trans A*/*B* ring junction and a change in the *D* ring conformation described below (Fig. 2). The internal degree of isostructurality (Kálman, Argay, Scharfenberg-Pfeiffer, Höhne & Ribár, 1991) between the two epimers is I = 99.4 and 98.8% for distances and angles, respectively. Rings *A*, *B* and *C* all have slightly flattened chair conformations, with average torsion angles of 53 (1), 55 (3) and 56 (2)°, respectively. A short C2—C3 bond distance, common to other related steroids (Ramos Silva *et al.*, 1996; Paixão *et al.*, 1997; Andrade *et al.*, 1997), was also found in the present compound. The distance between the terminal O atoms, O3 and O17, is 9.260 (3) Å, slightly shorter than that in the 5β-epimer [9.966 (4) Å]. The bowing angle between the *A* ring and the least-squares plane that includes the atoms of the *B*, *C* and *D* rings is 16.47 (8)° [58.91 (6)° in the 5β-epimer]. The pseudo-torsion angle C19—C10···C13—C18 is 2.19 (14)°. The *D* ring adopts a slightly deformed 13,14-half-chair conformation, instead of the more common 14α-envelope conformation found in the 5β-epimer, as can be inferred from the asymmetry parameters $\Delta C_s(14)$ = 13.0 (2) and $\Delta C_2(13,14)$ = 4.4 (2)° (Duax & Norton, 1975), and Δ = −7.5 (4) and φ_m = 43.7 (2)° (Altona, Geise & Romers, 1968).

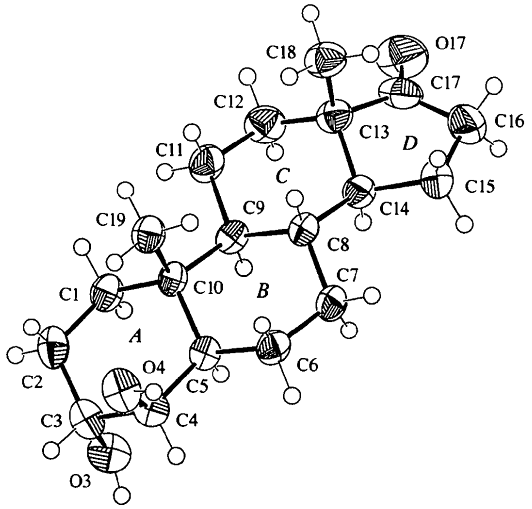
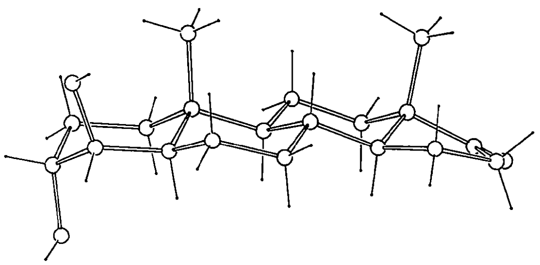
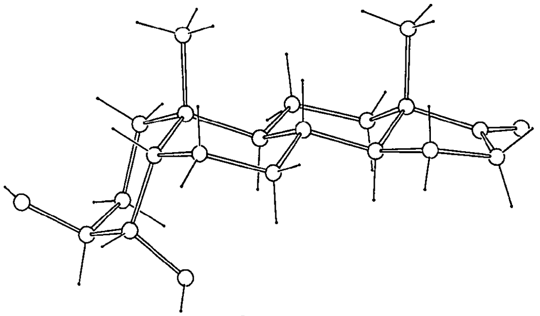


Fig. 1. *ORTEP*II (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% probability level, except for H atoms which were given arbitrary radii.



5α-epimer



5β-epimer

Fig. 2. Side view of the molecules of the 5α- (this work) and 5β-epimers (Ramos Silva *et al.*, 1996) of 3α,4β-dihydroxy-5(α,β)-androstan-17-one.

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). This differs from the crystal structure of the 5β-epimer where the hydrogen bonding extends over a three-dimensional network. The geometry of the hydrogen bonds is detailed in Table 2. The 3α-hydroxyl group takes part in two intermolecular hydrogen bonds, one as a donor towards the carbonyl group, the other as an acceptor from the 4β-hydroxyl group. The two bonds have approximately the same length; the 3α-hydroxyl to 4α-hydroxyl intermolecular bond links two molecules head-to-head and the bond *via* the carbonyl group links two molecules head-to-tail. There is in addition a short intramolecular contact between the C19 and O4 atoms with a geometry that would qualify as a weak C—H···O bond [C—H···O 3.080 (3), H···O 2.411 (6) Å and C—H···O 126.4 (7)°].

It should be pointed out that because none of the atoms is a strong enough anomalous scatterer at the Mo *K*α wavelength, the absolute configuration was not determined from the X-ray data, and the chirality assigned to the molecule is that determined from the synthesis route.

Experimental

The title compound was prepared by oxidation of 5α-androst-3-en-17-one with performic acid generated *in situ*. The compound 5α-androst-3-en-17-one was easily obtained from the available androst-4-ene-3,17-dione in the presence of Zn/AcOH under ultrasonic irradiation (Salvador, Sá e Melo & Campos Neves, 1993). The main product of this reaction has been isolated and identified by IR, MS, and ^{1}H and ^{13}C NMR as the title compound 3α,4β,-dihydroxy-5α-androstan-17-one (Tavares da Silva, Sá e Melo & Campos Neves, 1996). Good quality crystals suitable for X-ray diffraction were obtained by slow evaporation of the steroid in a mixture of acetone and hexane.

Crystal data

$C_{19}H_{30}O_3$
$M_r = 306.43$
Orthorhombic
$P2_12_12_1$
$a = 6.068\,(2)$ Å
$b = 11.118\,(3)$ Å
$c = 24.925\,(5)$ Å
$V = 1681.4\,(8)$ Å^3
$Z = 4$
$D_x = 1.210$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.70930$ Å
Cell parameters from 25 reflections
$\theta = 8–15°$
$\mu = 0.080$ mm^{-1}
$T = 293\,(2)$ K
Prismatic
0.49 × 0.32 × 0.24 mm
Colourless transparent

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile method from ω–2θ scans
Absorption correction: none
7399 measured reflections
2922 independent reflections
2202 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.029$
$\theta_{\rm max} = 25.0°$
$h = 0 \rightarrow 7$
$k = -13 \rightarrow 13$
$l = -29 \rightarrow 29$
3 standard reflections every 120 reflections intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.089$
$S = 1.056$
2922 reflections
203 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0422P)^2 + 0.2017P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.194$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.123$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

C2—C3	1.507 (3)	C13—C17	1.501 (3)
C3—O3	1.434 (2)	C16—C17	1.511 (3)
C3—C4	1.519 (3)	O17—C17	1.215 (3)
C4—O4	1.429 (2)		
C17—C13—C14—C15	43.7 (2)	C14—C13—C17—C16	−33.7 (2)
C13—C14—C15—C16	−37.6 (2)	C15—C16—C17—C13	11.3 (2)
C14—C15—C16—C17	16.3 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O17$^{\rm i}$	0.82	2.05 (2)	2.857 (3)	167 (1)
O4—H4···O3$^{\rm ii}$	0.82	2.048 (6)	2.847 (2)	165 (3)

Symmetry codes: (i) $x, y-1, z$; (ii) $1+x, y, z$.

The title structure was solved by direct methods. The H atoms were placed at calculated positions and refined as riding using *SHELXL*93 (Sheldrick, 1993) defaults; O—H 0.82, C—H 0.93 Å and U(H) = $1.5U_{\rm iso}$(parent atom). Examination of the crystal structure with *PLATON* (Spek, 1995) showed that there are no solvent-accessible voids in the unit cell. 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). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BS1035). Services for accessing these data are described at the back of the journal.

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