

5 α -Androst-3-en-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 = 0.040

wR factor = 0.109

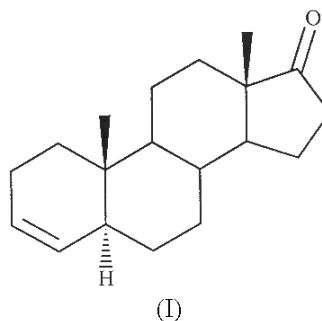
Data-to-parameter ratio = 11.4

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

In the title 6–6–6–5 fused ring compound, $\text{C}_{19}\text{H}_{28}\text{O}$, all the ring junctions are *trans*. The unsaturated ring *A* shows a conformation intermediate between a 10β -sofa and a $1\alpha,10\beta$ -half-chair.

Comment

Following our work on several androstane derivatives (Andrade *et al.*, 1999) as potential aromatase inhibitors and intermediates of their syntheses, the present study aims to contribute towards the elucidation of the different reactivities of the 5α - and 5β -androst-3-en-17-one, upon treatment with performic acid generated *in situ* in dichloromethane. The title compound, (I), was prepared from androst-4-ene-3,17-dione, through a modification of the McKenna process (McKenna *et al.*, 1959), as starting material for the synthesis of the potent and clinically useful antitumor steroid 4-hydroxy-androst-4-ene-3,17-dione (Tavares da Silva *et al.*, 1996) and its ring *D* modified derivative 4-hydroxy-17 α -oxa-17 α -homoandrost-4-ene-3,17-dione (Tavares da Silva *et al.*, 1997; Paixão *et al.*, 1998). The difference between the two epimers, 5α and 5β , is in the absolute configuration at C5. A 5β -isomer would have a *cis* junction of rings *A* and *B*; the rings are fused *trans* in a 5α -isomer. The X-ray analysis unequivocally establishes the molecular structure of (I) as an α configuration.



All ring junctions are *trans* (Fig. 1). The unsaturated ring *A* takes an intermediate conformation between 10β -sofa and $1\alpha,10\beta$ half-chair [Cremer & Pople (1975) puckering parameters: $Q = 0.508(3)\text{ \AA}$, $\theta = 50.3(3)^\circ$, $\varphi = 312.0(4)^\circ$; Duax & Norton (1975) asymmetry parameters: $\Delta C_s(3) = 9.6(3)^\circ$, $\Delta C_2(3,4) = 15.8(4)^\circ$ and $\Delta C_2(1,2) = 51.7(4)^\circ$]. Rings *B* and *C* have slightly flattened chair conformations, as shown by the mean values of their torsion angles [$57(2)$ and $55(3)^\circ$, respectively]. Ring *D* assumes a 14α -envelope conformation with puckering parameters $q_2 = 0.422(3)\text{ \AA}$ and $\varphi_2 = 214.1(4)^\circ$ [pseudo-rotation (Altona *et al.*, 1968) and asymmetry parameters (Duax & Norton, 1975): $\Delta = -31.4(4)^\circ$, $\varphi_m = 43.2(1)^\circ$,

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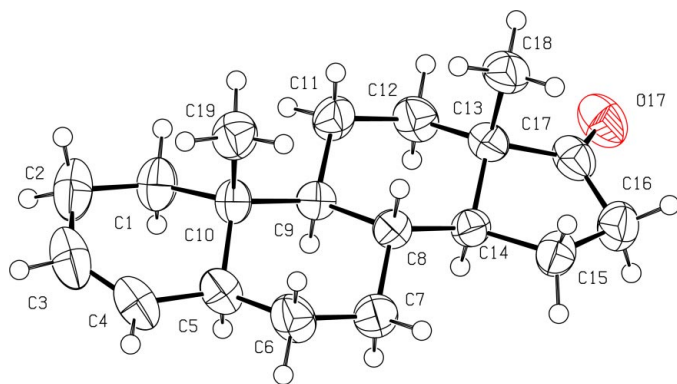


Figure 1
ORTEPII (Johnson, 1976) plot of (I). Displacement ellipsoids are drawn at the 50% probability level.

$\Delta C_s(14) = 2.0 (2)^\circ$, $\Delta C_2(13,14) = 18.5 (2)^\circ$]. The value of the pseudo-torsion angle $C19-C10-C13-C18$ of $0.01 (19)^\circ$ shows that the molecule is not twisted. The dimension of the present steroid molecule may be measured by the distance between the C3 and O17 atoms, $9.560 (4) \text{ \AA}$. The crystal structure contains no hydrogen bonds and thus cohesion is mainly achieved by van der Waals interactions (Fig. 2).

Experimental

To prepare the title compound, (I), zinc dust (3.0 g, 325 mesh Aldrich) was added in several portions during 10 min to a boiling solution of androstenedione (500 mg, 1.75 mmol) in glacial acetic acid (30 ml) after which the reaction was complete (thin-layer chromatography control). The zinc suspension was filtered, the zinc was washed with glacial acetic acid and the filtrate was evaporated to dryness. The residue was diluted with water (100 ml) and extracted with diethyl ether ($3 \times 100 \text{ ml}$). The organic layers were washed with aqueous 10% NaHCO_3 ($3 \times 100 \text{ ml}$) and water ($3 \times 100 \text{ ml}$), dried (MgSO_4) and evaporated to dryness to give a colourless crystalline solid (476 mg) composed of an isomeric mixture of 5α - and 5β -androst-3-en-17-one (70:30). Crystallization from methanol gave the pure 5α compound [(I); 285 mg, 1.05 mmol] in 60% yield; m.p. 398–399 K, literature 397–399 K (McKenna *et al.*, 1959). Crystals of (I) suitable for X-ray experiments were obtained by slow evaporation of an *n*-hexane solution.

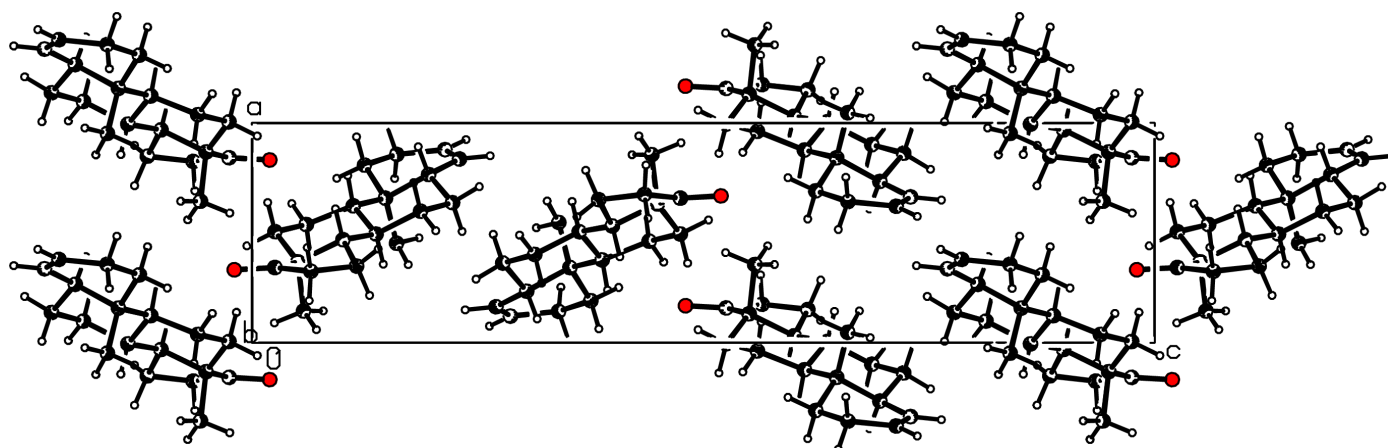


Figure 2
Packing diagram of (I) viewed along the *b* axis.

Crystal data

$\text{C}_{19}\text{H}_{28}\text{O}$
 $M_r = 272.41$
Orthorhombic, $P2_12_12_1$
 $a = 6.451 (3) \text{ \AA}$
 $b = 9.2109 (9) \text{ \AA}$
 $c = 26.558 (8) \text{ \AA}$
 $V = 1578.0 (10) \text{ \AA}^3$
 $Z = 4$
 $D_x = 1.147 \text{ Mg m}^{-3}$

Mo $K\alpha$ radiation
Cell parameters from 25 reflections
 $\theta = 5.9\text{--}10.3^\circ$
 $\mu = 0.07 \text{ mm}^{-1}$
 $T = 293 (2) \text{ K}$
Block, colourless
 $0.50 \times 0.45 \times 0.30 \text{ mm}$

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω - 2θ scans
3713 measured reflections
2091 independent reflections
1607 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.048$

$\theta_{\text{max}} = 27.5^\circ$
 $h = 0 \rightarrow 8$
 $k = 0 \rightarrow 11$
 $l = -34 \rightarrow 34$
3 standard reflections
frequency: 180 min
intensity decay: 1.4%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.040$
 $wR(F^2) = 0.109$
 $S = 1.07$
2091 reflections
184 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0409P)^2 + 0.3113P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.19 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.14 \text{ e \AA}^{-3}$
Extinction correction: SHELXL97
Extinction coefficient: 0.0101 (18)

Table 1

Selected geometric parameters (\AA).

O17–C17	1.212 (3)	C2–C3	1.482 (4)
C5–C4	1.496 (3)	C4–C3	1.315 (4)

H atoms were placed at calculated positions and constrained as riding. The absolute configuration was chosen to give the correct chirality of the molecule that was known beforehand from the synthesis route (McKenna *et al.*, 1959).

Data collection: CAD-4 Software (Enraf–Nonius, 1989); cell refinement: CAD-4 Software; data reduction: PLATON (Spek, 1995); 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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