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16-(4-Isopropylbenzylidene)androst-4-ene-3,17-dione

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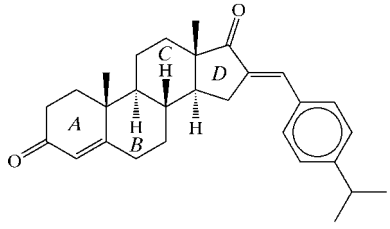
In the title compound, $C_{29}H_{36}O_2$, the outer cyclohexene ring of the steroid nucleus has a conformation that lies about halfway between a half-chair and an envelope, while the central and outer cyclohexane rings of the steroid nucleus have slightly distorted chair conformations. The steroidal cyclopentane ring adopts a 13β,14α-half-chair conformation. The benzylidene moiety has an *E* configuration with respect to the carbonyl group on the cyclopentane ring. The dihedral angle between the mean planes of the steroid nucleus and the benzylidene moiety is 35.54 (9)°. The packing of the molecules is assumed to be dictated mainly by weak intermolecular C—H···O interactions.

Comment

The present study is part of an ongoing investigation of the crystal structures of a series of androstene derivatives (Thamotharan *et al.*, 2002, 2004; Hema *et al.*, 2003). We are particularly interested in studying the conformational flexibilities of the steroid nucleus resulting from various substitutions at the C3, C16 and C17 positions. The crystals of the title compound, (I), are enantiomerically pure; however, because of the absence of any significant anomalous scatterers in the compound, the absolute configuration of the molecule has not been determined from the X-ray diffraction experiment and the assumed chirality of the molecule was determined from the synthesis route.

Both methyl groups of the steroid nucleus adopt the expected staggered arrangements. The *B*/*C* and *C*/*D* ring junctions are all-*trans* (see scheme and Fig. 1). In (I), the cyclohexene ring, *A*, has a conformation that lies about halfway between a half-chair and an envelope [puckering parameters (Cremer & Pople, 1975) Q = 0.454 (3) Å, q_2 = 0.360 (3) Å, q_3 = 0.277 (3) Å, θ = 52.4 (4)° and φ_2 = 12.7 (5)° for the atom sequence C1—C2—C3—C4—C5—C10]. Distorted half-chair conformations have been reported for the conformation of ring *A* in the two related structures androst-4-ene-3,17-dione (Busetta *et al.*, 1972) and 16-(3-pyridylmethylene)androst-4-ene-3,17-dione (Vasuki, Thamotharan *et al.*, 2002), while an envelope conformation has been reported in another related compound (Vasuki, Parthasarathi *et al.*, 2002). The C4═C5 (Csp^2—Csp^2) distance [1.338 (4) Å] confirms the localization of a double bond at this position.



(I)

The steroidal cyclohexane rings, *B* and *C*, have slightly distorted chair conformations, as shown by their puckering parameters [ring *B*: Q = 0.534 (3) Å, q_2 = 0.084 (3) Å, q_3 = 0.528 (3) Å, θ = 8.9 (3)° and φ_2 = 146.1 (19)° for the atom sequence C5—C6—C7—C8—C9—C10; ring *C*: Q = 0.584 (3) Å, q_2 = 0.046 (3) Å, q_3 = 0.582 (3) Å, θ = 4.3 (3)° and φ_2 = 282 (3)° for the atom sequence C8—C9—C11—C12—C13—C14]. The cyclopentane ring, *D*, of the steroid nucleus adopts a 13β,14α-half-chair conformation, with a pseudo-rotation angle of 6.5 (2)° and a maximum torsion angle of 43.2 (1)° (Rao *et al.*, 1981) for the atom sequence C13—C14—C15—C16—C17. In a related structure, in which atom C16 has no substitution, ring *D* has a 14α-envelope conformation (Busetta *et al.*, 1972).

The C3···C16 distance [8.849 (4) Å], which is a measure of the length of the steroid nucleus, indicates that the steroid nucleus is in a completely extended form (Karle, 1970). The distance between terminal atoms O3 and C27*A* is 14.330 (4) Å. The C19—C10···C13—C18 pseudo-torsion angle, which gives a measure of the molecular twist, is 9.0 (2)°.

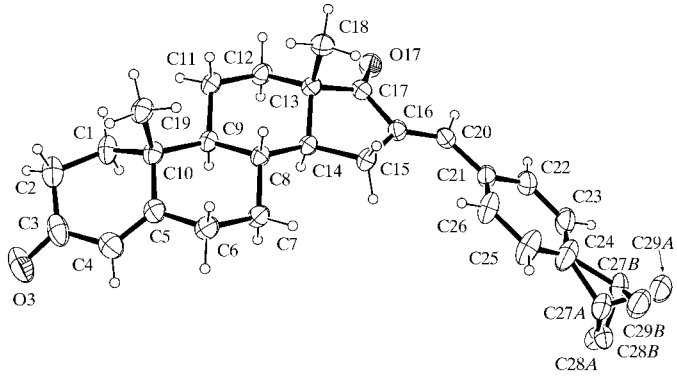


Figure 1
A perspective view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. For clarity, all H atoms of the disordered isopropyl moiety have been omitted. The other H atoms are shown as small circles of arbitrary radii.

† Deceased.

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The value of the C17—C16—C20—C21 torsion angle [−176.6 (3)°] indicates that the benzylidene ring has an *E* configuration with respect to the carbonyl group at position C17. The C15—C16—C20 exocyclic angle [131.2 (2)°] is slightly larger than the normal value, possibly as a consequence of steric repulsion between atoms H15*B* and H26 (H···H = 2.26 Å). The dihedral angle between the mean planes of the steroid nucleus and the benzylidene moiety is 35.54 (9)°. In (I), the skeletal bond angles are close to the expected values (Duax *et al.*, 1976). Additionally, the isopropyl group is disordered over two orientations, with the major conformation existing in 59.5 (7)% of the molecules.

In (I), atom C1 acts as a donor for a weak intermolecular C—H···O interaction with carbonyl atom O17 of an adjacent molecule. This interaction links the molecules into a chain that runs parallel to the *y* axis and has a graph-set motif of *C*(9) (Bernstein *et al.*, 1995). One of the disordered methyl atoms (C28*A*) of the isopropyl group is involved in an intermolecular C—H···O interaction with the other carbonyl O atom (O3) of a different adjacent molecule. This interaction links the molecules into a chain, which also runs parallel to the *y* axis and which has a graph-set motif of *C*(18) (Table 1).

Experimental

16-(4-Isopropylbenzylidene)-17-oxo-5-androsten-3β-ol (1.0 g) was dissolved in dry toluene (150 ml) under reflux, and then cyclohexanone (10 ml) was added. Traces of moisture were removed by azeotropic distillation. The distillation was continued at a slow rate while adding dropwise a solution of aluminium isopropoxide (1.0 g) in dry toluene (15 ml). The reaction mixture was refluxed for 4 h and then allowed to stand overnight at room temperature. The slurry was filtered and the residue was washed thoroughly with dry toluene. The combined filtrate and washings were steam distilled until the complete removal of organic solvents was affected. The solid residue was collected by filtration the next day, dried and crystallized from acetone at low temperature, affording crystals of (I) (yield 0.80 g, 80.39%; m.p. 453–459 K). UV_{max}(MeOH): 305.6 (logε = 4.48) and 233.6 nm (logε = 4.36); IR_{max} (cm^{-1}): 2975, 1705, 1690, 1600, 900; ^{1}H NMR ($CDCl_3$): δ 1.01 (*s*, 3H, 18-CH_3), 1.25 (*s*, 3H, 19-CH_3), 1.26 [*d*, 6H, $CH(CH_3)_2$], 2.91 [*m*, 1H, $CH(CH_3)_2$], 5.76 (*s*, 1H, 4-CH), 7.44 [*s*, 1H, vinyl H of 16-(4-isopropylbenzylidene)], 7.27–7.30 (*d*, 2H, J_o = 8.2, 3-CH and 5-CH aromatic H atom) and 7.47–7.49 (*d*, 2H, J_o = 8.2, 2-CH and 6-CH aromatic H atom).

Crystal data

$C_{29}H_{36}O_2$
M_r = 416.58
Orthorhombic, $P2_12_12_1$
a = 6.1318 (2) Å
b = 17.3938 (5) Å
c = 22.3210 (7) Å
V = 2380.65 (13) Å^3
Z = 4
D_x = 1.162 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2447 reflections
θ = 2.0–25.0°
μ = 0.07 mm^{-1}
T = 160 (2) K
Prism, colourless
0.25 × 0.20 × 0.18 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans with κ offsets
22 900 measured reflections
2437 independent reflections
2000 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
θ_{max} = 25.0°
$h = -7 \rightarrow 7$
$k = -20 \rightarrow 20$
$l = -26 \rightarrow 26$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.116
S = 1.04
2436 reflections
315 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0635P)^2 + 0.3105P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.028 (5)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1*A*···O17^{i}	0.99	2.57	3.321 (4)	132
C28*A*—H28*A*···O3^{ii}	0.98	2.57	3.32 (2)	134

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

The isopropyl group is disordered over two sites. Two sets of positions were defined for all atoms of this group, and constrained refinement of the site-occupation factors led to a value of 0.595 (7) for the major conformation. Similarity restraints were applied to all 1,2- and 1,3-distances involving disordered atoms, so as to maintain similar geometry about the chemically equivalent atoms. This treatment led to non-ideal angles about atom C24, and it is likely that the disorder extends into the phenyl ring, particularly as atoms C23, C24 and C25 show slightly elongated atomic displacement ellipsoids. However, attempts to model disorder for the ring, even by employing extensive restraints, proved fruitless. Methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å), with U_{iso}(H) values of 1.5U_{iso}(C), but were allowed to rotate freely about the C—C bonds. All remaining H atoms were placed in idealized positions (C—H = 0.95–1.00 Å) and constrained to ride on their parent non-H atoms, with U_{iso}(H) values of 1.2U_{iso}(C). Because of the absence of any significant anomalous scatterers in (I), attempts to confirm the absolute structure by refinement of the Flack (1983) parameter in the presence of 1757 sets of Friedel pairs led to an inconclusive value of −0.1 (19) (Flack & Bernardinelli, 2000). Therefore, the Friedel pairs were merged before the final refinement and the absolute configuration was assigned to correspond to the known chiral centres in a precursor molecule, which remained unchanged during the synthesis of (I). Reflection 020 was partially obscured by the beam stop and was omitted.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1688). Services for accessing these data are described at the back of the journal.

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