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16-[3-Methoxy-4-(2-piperidin-1-yl-ethoxy)benzylidene]-17-oxoandrost-5-en-3β-yl acetate monohydrate

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The title compound, $C_{36}H_{49}NO_5\cdot H_2O$, has the outer two six-membered rings of the steroid nucleus in chair conformations. The central ring *B* of the steroid nucleus is in an 8β,9α-half-chair conformation, while ring *D* of the steroid adopts a slightly distorted 13β,14α-half-chair conformation. The piperidine ring is in a chair conformation. The methoxybenzylidene moiety has an *E* configuration with respect to the carbonyl group at position 17. Intermolecular O—H···O and O—H···N hydrogen bonds link the steroid and water molecules into chains which run parallel to the *b* axis.

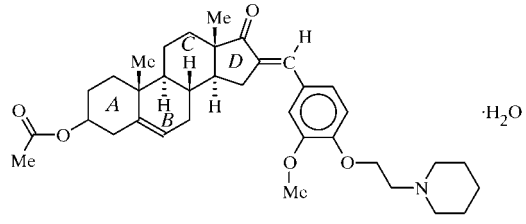
Comment

The present study of the title compound, (I), is the 10th in our series of X-ray crystal structure analyses of new synthetic androstene derivatives (Vasuki *et al.*, 2001; Hema *et al.*, 2002; Vasuki, Parthasarathi, Ramamurthi, Jindal & Dubey, 2002; Vasuki, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002*a*,*b*,*c*; Vasuki, Thamotharan, Parthasarathi, Ramamurthi, Jindal & Dubey, 2002; Vasuki, Thamotharan, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002; Vasuki, Parthasarathi, Ramamurthi, Piplani & Jindal, 2002). In our studies, we are particularly interested in the conformational flexibilities of the steroids resulting from variations in the substituents at the C3, C16 and C17 positions.

The crystals of (I) are enantiomerically pure. However, due to the absence of significant anomalous scatterers in the compound, the absolute configuration of the molecule has not been determined by the X-ray diffraction experiment. The enantiomer used in the refinement was assigned to correspond with the configuration of the known chiral centres in a precursor molecule which remained unchanged during the synthesis of (I).

† Deceased.

Fig. 1 shows the asymmetric unit of (I) with the steroid numbering scheme and ring labels. Among the few conformational options, both methyl groups of the steroid nucleus adopt the expected staggered arrangements. The geometry at both the *B*/*C* and *C*/*D* ring junctions is *trans*. The distance between the terminal C atoms, C39 and C34, is 20.213 (3) Å. The C5—C6 distance of 1.332 (3) Å confirms the presence of a localized double bond at this position (Kálmán *et al.*, 1992; Vasuki *et al.*, 2001; Hema *et al.*, 2002; Vasuki, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002*a*,*b*; Vasuki, Thamotharan, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002). Rings *A* and *C* are slightly flattened, the mean values of their ring torsion angles being 53.68 (8) and 54.53 (8)°, respectively. Both ring conformations are close to that of a chair, as shown by the values of the Cremer & Pople (1975) puckering parameters [ring *A*: Q = 0.548 (2) Å, θ = 5.7 (2)° and φ = 85 (2)° for the atom sequence C1—C2—C3—C4—C5—C10; ring *C*: Q = 0.568 (2) Å, θ = 11.9 (2)° and φ = 266.4 (10)° for the atom sequence C8—C9—C11—C12—C13—C14]. Thus, the presence of the acetoxy group bonded to atom C3 does not disturb the usual chair conformation of ring *A* of the steroid nucleus; the 3β-acetoxy group is planar. The C3—O37 bond is oriented equatorially and is (−)antiperiplanar to the C3—C4 bond. The dihedral angle between the planes of the acetoxy group and the steroid nucleus is 83.45 (12)°.



(I)

Due to the C5═C6 double bond, the environment of atom C5 is planar, and hence ring *B* adopts the 8β,9α-half-chair conformation generally found in steroids containing a C5═C6 double bond (Caira *et al.*, 1995; Andrade *et al.*, 2001; Vasuki *et al.*, 2001; Hema *et al.*, 2002; Vasuki, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002*a*,*b*; Vasuki, Thamotharan, Parthasarathi, Ramamurthi, Dubey & Jindal, 2002); puckering parameters Q = 0.494 (2) Å, θ = 51.7 (2)° and φ = 209.2 (3)° for the atom sequence C5—C6—C7—C8—C9—C10. The five-membered ring *D* exhibits a distorted 13β,14α-half-chair conformation; Δ = 3.9° and φ_m = 38.8 (1)° for the atom sequence C13—C14—C15—C16—C17 (Altona *et al.*, 1968). The piperidine ring adopts a chair conformation, as is evident from the puckering parameters; Q = 0.576 (2) Å, θ = 4.6 (2)° and φ = 345 (3)° for the atom sequence N31—C32—C33—C34—C35—C36. Atoms N31 and C34 are on opposite sides of the C32/C33/C35/C36 plane and displaced from it by 0.691 (2) and 0.649 (3) Å, respectively.

The C17—C16—C20—C21 torsion angle of 172.55 (17)° indicates that the methoxybenzylidene moiety has an *E* configuration with respect to the carbonyl group at position 17. The C15—C16—C20 exocyclic angle of 130.56 (18)° is significantly larger than the normal value of 120°, and this may

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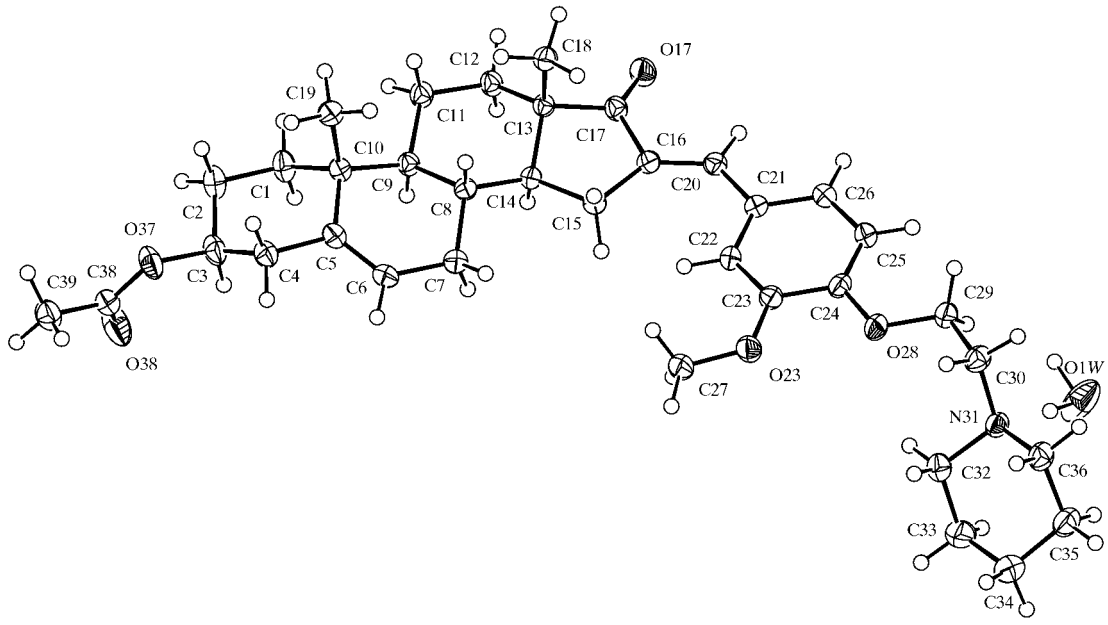

Figure 1
View of the asymmetric unit of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary radii.

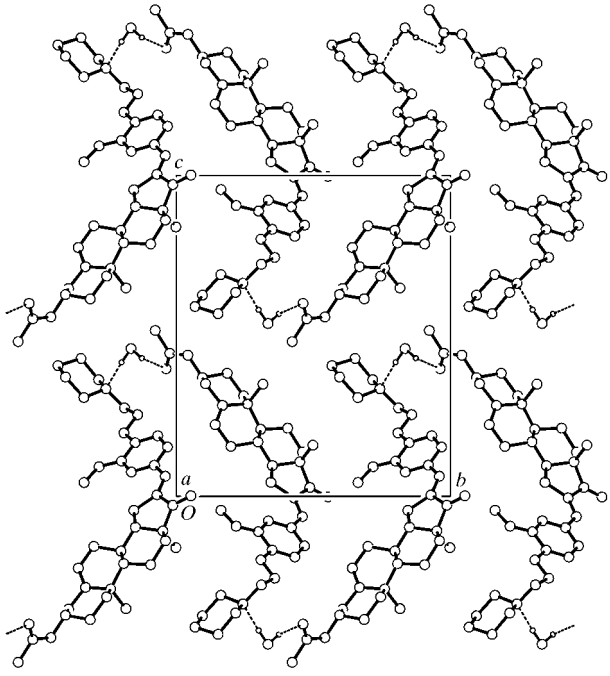

Figure 2
The molecular packing in (I), projected down the *a* axis, showing the hydrogen-bonding scheme. H atoms bonded to C atoms have been omitted for clarity.

be due to steric repulsion between atoms H15*A* and H22 (2.31 Å), and between atoms H15*B* and H22 (2.12 Å).

The pseudo-torsion angle C19—C10···C13—C18 has a value of 12.53 (15)°. The steroid nucleus and the average plane of the piperidine ring are oriented at angles of 6.38 (4) and 68.93 (8)°, respectively, with respect to the 3-methoxybenzylidene ring. In (I), the angles C8—C14—C15 of 118.63 (15)° and C14—C13—C17 of 100.81 (15)° are close to the expected values of 119.3 and 99.2°, respectively (Duax *et al.*, 1976). [In Hema *et al.* (2002), we inadvertently gave the upper limit for these angles, instead of the expected values.]

The water molecule forms an intermolecular hydrogen bond with the N atom of the piperidine ring of a neighbouring steroid molecule, as well as with the carbonyl O atom of the ester group of a different neighbouring steroid molecule (Table 1). These interactions link the steroid and water molecules alternately into chains, which run parallel to the *b* axis and have a binary graph-set motif (Bernstein *et al.*, 1995) of $C_2^2(24)$ (Fig. 2).

Experimental

A mixture of 16-[3-methoxy-4-(2-piperidin-1-ylethoxy)benzylidene]-17-oxo-5-androsten-3β-ol (0.5 g, 0.868 mmol), acetic anhydride (1.0 ml) and dry pyridine (2.0 ml) was heated on a steam bath for 2 h. The contents of the reaction mixture were then poured into ice-cold water and basified with liquid ammonia. The precipitate obtained was filtered off, washed with water, dried and crystallized from hexane (333–353 K), affording crystals of the title compound (institution code: DPJ-RG-1111) (yield: 0.38 g, 70.5%; m.p. 399–401 K).

Crystal data

$C_{36}H_{49}NO_5\cdot H_2O$
M_r = 593.78
Monoclinic, $P2_1$
a = 6.1726 (1) Å
b = 14.9068 (2) Å
c = 17.6465 (3) Å
β = 97.724 (1)°
V = 1608.99 (4) Å^3
Z = 2
D_x = 1.226 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4884 reflections
θ = 2.0–30.0°
μ = 0.08 mm^{-1}
T = 160 (2) K
Tablet, colourless
0.25 × 0.25 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer	R_{int} = 0.062
φ and ω scans with κ offsets	θ_{max} = 30.0°
42 238 measured reflections	$h = 0 \rightarrow 8$
4878 independent reflections	$k = -20 \rightarrow 20$
3793 reflections with $I > 2\sigma(I)$	$l = -24 \rightarrow 24$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0606P)^2 + 0.0106P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.042	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.105	$\Delta\rho_{max}$ = 0.24 e Å^{-3}
S = 1.03	$\Delta\rho_{min}$ = −0.18 e Å^{-3}
4878 reflections	Extinction correction: *SHELXL*97
401 parameters	Extinction coefficient: 0.016 (3)
H atoms treated by a mixture of independent and constrained refinement	

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

D—H···A	D—H	H···A	D···A	D—H···A
O1W—H1W···N31^{i}	0.97 (5)	1.88 (5)	2.847 (3)	174 (4)
O1W—H2W···O38^{ii}	1.04 (5)	1.94 (5)	2.961 (3)	167 (4)

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

The positions of the water H atoms were determined from a difference Fourier map and refined freely along with their isotropic displacement parameters. The methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å), with U_{iso}(H) = 1.5U_{eq}(C), but were allowed to rotate freely about the C—C bonds. All remaining H atoms were placed in geometrically idealized positions (C—H = 0.95–1.00 Å) and were constrained to ride on their parent non-H atoms, with U_{iso}(H) = 1.2U_{eq}(C). Due to the absence of any significant anomalous scatterers in the compound, attempts to confirm the absolute structure by refinement of the Flack (1983) parameter, in the presence of 4331 sets of Friedel equivalents, led to an inconclusive value (Flack & Bernardinelli, 2000) of −0.5 (7). Therefore, the Friedel pairs were merged before the final refinement and the absolute configuration was assigned to correspond with that of the known chiral centres in a precursor molecule which remained unchanged during the synthesis of the title compound. Reflection 002 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: *WinGX* (Version 1.64.02; Farrugia, 1999); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2002).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1582). Services for accessing these data are described at the back of the journal.

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