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16-(4-Cyanobenzylidene)-17-oxo-androst-5-en-3β-ol

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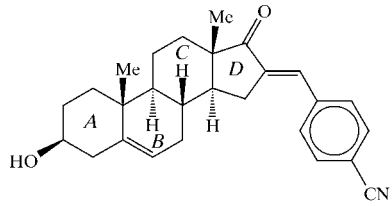
In the title compound, 4-(3β-hydroxy-17-oxoandrost-5-en-16-ylidenemethyl)benzonitrile, $C_{27}H_{31}NO_2$, rings *A* and *C* of the steroid nucleus are in chair conformations. The central six-membered ring *B* is in an 8β,9α-half-chair conformation, while the five-membered ring *D* adopts a 13β,14α-half-chair conformation. The cyanobenzylidene moiety has an *E* configuration with respect to the carbonyl group at position C17. The dihedral angle between the planes of the steroid nucleus and the cyanobenzylidene moiety is 22.61 (15)°. Intermolecular O—H···N hydrogen bonds formed between the hydroxyl group of the steroid and the N atom of the cyanobenzylidene moiety of symmetry-related molecules link the steroid molecules into chains which run parallel to the *b* axis.

Comment

The present study of the title compound, (I), is the 11th in our series of X-ray crystal structure analyses of androstene and its derivatives (Thamotharan *et al.*, 2002, and references therein). The conformations of steroids having a flexible unsaturated ring and/or substituents are of interest, and we are particularly interested in studying the conformational flexibilities of the steroids resulting from various substitutions 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 to those of the known chiral centres in a precursor molecule, namely dehydroepiandrosterone (Weeks *et al.*, 1971), which remained unchanged during the synthesis of (I).

Among the few conformational options, both methyl groups of the steroid nucleus adopt the expected staggered arrangements. The geometry of the rings is *trans* at the *B*/*C* and *C*/*D* ring junctions (see *Scheme* and Fig. 1).



(I)

The C5—C6 distance of 1.318 (6) Å is comparable with the corresponding distance in a related structure (Bhacca *et al.*, 1996) and confirms the localization of the double bond at this position. Rings *A* and *C* are slightly flattened, the mean values of their torsion angles being 52.5 (2) and 55.2 (2)°, 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 = 0.538 (5) Å, θ = 9.3 (5)° and φ = 81 (3)° for the atom sequence C1—C2—C3—C4—C5—C10; ring C: Q = 0.565 (5) Å, θ = 5.8 (5)° and φ = 266 (6)° for the atom sequence C8—C9—C11—C12—C13—C14]. Thus, the presence of the hydroxyl group at C3 has not disturbed the usual chair conformation of ring *A* of the steroid nucleus. The C3—O31 bond is oriented equatorially and (+)antiperiplanar with respect to the C3—C4 bond. The dihedral angle between the planes of the cyanobenzylidene group and the steroid nucleus is 22.61 (15)°.

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 with a C5═C6 double bond (Thamotharan *et al.*, 2002, and references therein), with puckering parameters Q = 0.464 (2) Å, θ = 49.8 (6)° and φ = 217.9 (7)° for the atom sequence C5—C6—C7—C8—C9—C10. The five-membered ring *D* exhibits a 13β,14α-half-chair conformation, whereas this ring adopts a 14α-envelope conformation in the unsubstituted dehydroxy steroid nucleus. It seems that the bulky cyanobenzylidene substituent causes the conformational change observed in ring

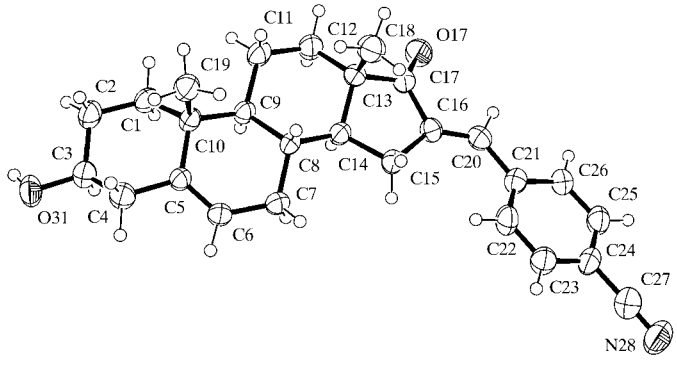


Figure 1
View of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by circles of arbitrary radii.

† Deceased.

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D in (I); $\Delta = 0.3\ (4)^\circ$ and $\varphi_m = 42.9\ (3)^\circ$ for the atom sequence C13—C14—C15—C16—C17 (Altona *et al.*, 1968).

The C17—C16—C20—C21 torsion angle of 171.1 (4)° indicates that the cyanobenzylidene moiety has an *E* configuration with respect to the carbonyl group at position C17, as has been observed in a previous compound (Thamotharan *et al.*, 2002). The C15—C16—C20 exocyclic angle of 133.0 (4)° is significantly larger than the normal value of 120° and this may be due to steric repulsion between atoms H15*B* and H22 (2.41 Å). In (I), the skeletal bond angles are close to the expected values (Duax *et al.*, 1976).

In the crystal structure, the steroid nucleus forms head-to-tail chains of O—H···N intermolecular hydrogen bonds involving the O—H group and the N atom of the cyanobenzylidene moiety of a symmetry-related molecule (Table 1 and Fig. 2). These interactions link the steroid molecules into chains, running parellel to the [$\bar{1}$10] direction, which can be described by a *C*(18) graph-set motif (Bernstein *et al.*, 1995).

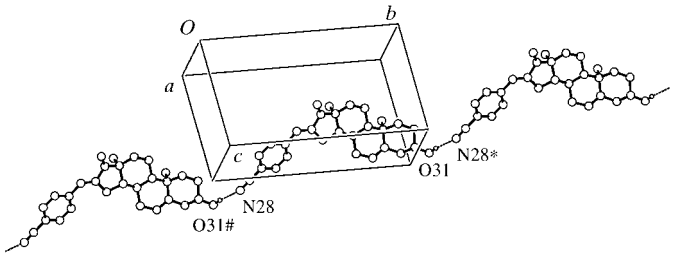

Figure 2
Part of the crystal structure of (I), showing the formation of a chain through O—H···N interactions. Atoms marked with a hash (#) or asterisk (*) are at the symmetry positions $(1 + x, -1 + y, z)$ and $(-1 + x, 1 + y, z)$, respectively.

Experimental

A mixture of a dehydroepiandrosterone (0.5 g), sodium hydroxide (0.75 g) and 4-cyanobenzaldehyde (0.75 g) in methanol (10 ml) was stirred for 1.5 h at room temperature. The reaction mixture was added to ice-cold water. The precipitate was filtered off, washed thoroughly with water and crystallized from methanol to afford crystals of (I); yield: 0.23 g (43%) and m.p. 565–571 K. Analysis, UV_{max}(MeOH): 296.2 nm ($\log\varepsilon = 4.35$); IR_{max}: 2980, 2210. 1720, 1640 and 900 cm^{-1}; ^1H NMR: 0.99 (*s*, 3H, 18-CH_3), 1.08 (*s*, 3H, 19-CH_3), 3.50 (*m*, 1H, 3-H), 5.40 (*d*, 1H, 6-CH), 3.9 (*s*) and 7.4 (*s*) [0.29:1 area ratio, 1H, vinyl-H of 16-(4-cyanobenzylidene)], 7.60 (*d*, 2H, J_o = 8.4 Hz, 2-CH and 6-CH aromatic proton), 7.70 p.p.m. (*d*, 2H, J_o = 8.2 Hz, 3-CH and 5-CH aromatic proton); calculated for $C_{27}H_{31}NO_2$: C 80.8, H 7.8, N 3.5%; found: C 80.8, H 7.8, N 3.6%.

Crystal data

$C_{27}H_{31}NO_2$
$M_r = 401.53$
Monoclinic, $P2_1$
$a = 6.005\ (3)$ Å
$b = 17.448\ (4)$ Å
$c = 10.453\ (5)$ Å
$\beta = 93.846\ (4)^\circ$
$V = 1092.8\ (8)$ Å^3
$Z = 2$
$D_x = 1.220$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 20$–30°
$\mu = 0.08$ mm^{-1}
$T = 293\ (2)$ K
Block, pale yellow
0.25 × 0.20 × 0.15 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
$T_{min} = 0.981$, $T_{max} = 0.989$
2184 measured reflections
1986 independent reflections
1520 reflections with $I > 2\sigma(I)$
$R_{int} = 0.033$
$\theta_{max} = 25.0^\circ$
$h = 0 \rightarrow 7$
$k = 0 \rightarrow 20$
$l = -12 \rightarrow 12$
2 standard reflections
frequency: 60 min
intensity decay: 4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.136$
$S = 1.05$
1986 reflections
276 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.082P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O31—H31···N28^{i}	0.81 (2)	2.18 (2)	2.980 (7)	172 (6)

Symmetry code: (i) $x - 1, 1 + y, z$.

The methyl H atoms were constrained to an ideal geometry (C—H = 0.96 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 constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C), except for the hydroxyl H atom, which was located in a difference Fourier map and refined using the DFIX option in *SHELXL*97 (Sheldrick, 1997), with H31—O31 = 0.81 (2) Å, and included in the structure-factor calculations with U_{iso}(H31) = 1.2U_{eq}(O31). Friedel pairs were merged before the final refinement and the absolute configuration was assigned to correspond with those of the known chiral centres in a precursor molecule, namely dehydroepiandrosterone (Weeks *et al.*, 1971), which remained unchanged during the synthesis of the title compound.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); 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: GD1244). Services for accessing these data are described at the back of the journal.

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