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16-(4-Cyanobenzylidene)-3β-pyrrolidinoandrost-5-en-17β-ol monohydrate

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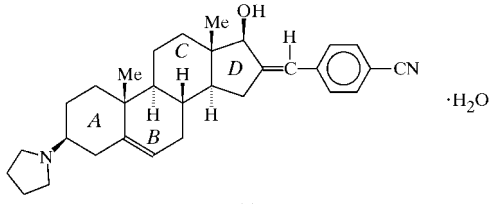
In the title compound, $C_{31}H_{40}N_2O\cdot H_2O$, the outer two six-membered rings are in chair conformations, while the central ring is in an 8β,9α-half-chair conformation. The five-membered ring adopts a 13β-envelope conformation and the cyanobenzylidene moiety has an *E* configuration with respect to the hydroxyl group at position 17. The steroid nuclei are linked by intermolecular O—H···O and O—H···N hydrogen bonds to form a molecular network. The molecular packing has an interesting feature, with the steroids aligned parallel to the *b* axis, forming a closed loop through hydrogen bonds linked *via* water molecules.

Comment

The X-ray investigation of the title compound, (I), was undertaken as part of a study of the structures and conformations of new synthetic steroid derivatives. We are particularly interested in the conformational flexibilities of steroids as a result of substitutions at the C3, C16 and C17 positions, as it is well known that steroid receptors are able to modify the mode of binding at ring *D* to accommodate several different types of C17 substitution (Duax & Norton, 1975). The absolute configuration of (I) was not determined from the X-ray data, but is based on the known chirality of the starting material used in the synthesis, namely 16-(4-cyanobenzylidene)androst-4-ene-3,17-dione.



(I)

The C5—C6 distance of 1.332 (4) Å confirms the localization of a double bond at this position (Kálmán *et al.*, 1992; Vasuki *et al.*, 2001). The puckering parameters [ring *A*: Q = 0.542 (3) Å, θ = 2.7 (3)° and Φ = 42.8 (7)°; ring *C*: Q = 0.562 (3) Å, θ = 8.6 (3)° and Φ = 235.0 (2)°; Cremer & Pople, 1975] show that rings *A* and *C* adopt chair conformations. The presence of the pyrrolidine group bonded to C3 does not disturb the usual chair conformation of ring *A* of the steroidal nucleus. Due to the C5═C6 double bond, the environment of atom C5 is planar, and hence ring *B* adopts the half-chair conformation generally found in steroids with a C5═C6 double bond (Caira *et al.*, 1995; Andrade *et al.*, 2001), with puckering parameters Q = 0.490 (3) Å, θ = 49.4 (4)° and Φ = 202.5 (5)°.

The conformation of ring *D* can be expressed by two parameters, a pseudo-rotation angle, Δ, and a maximum torsion angle, φ_m (Altona *et al.*, 1968). In compound (I), ring *D* exhibits a 13β-envelope conformation, with Δ = 28.5° and φ_m = 48.2 (2)°.

Atoms C8 and C9 are on opposite sides of the C10/C5/C6/C7 plane, displaced from it by 0.2631 (3) and 0.2155 (3) Å, respectively. The C17—C16—C20—C21 torsion angle of −177.7 (3)° indicates that the cyanobenzylidene moiety has an *E* configuration with respect to the hydroxyl group at position 17. The C15—C16—C20 exocyclic angle of 131.0 (3)° is significantly larger than the normal value, and this may be due to steric repulsion between atoms H15*A* and H26 (2.293 Å) and between atoms H15*B* and H26 (2.354 Å).

The pseudo-torsion angle C19—C10···C13—C18 has a value of 12.41 (3)°. The 4-cyanobenzylidene group is oriented at an angle of 11.14 (10)° with respect to the central steroid nucleus. The equatorially substituted pyrrolidine group at C3 is oriented at an angle of 22.64 (12)° with respect to the central steroid nucleus. The geometry of the rings is *trans* at ring junctions *B*/*C* and *C*/*D*. In (I), the valency angles C8—C14—C15 [119.5 (2)°] and C14—C13—C17 [98.8 (2)°] are close to the expected values of 121.2 and 101.4°, respectively (Duax & Norton, 1975).

The 17β-OH group is attached equatorially at C17 and the pyrrolidine group is substituted equatorially at C3. The structure of (I) is stabilized by a network of O—H···O and O—H···N intermolecular hydrogen bonds (Table 1). The hydroxyl O atom takes part in intermolecular hydrogen bonds as donor, while the O atom of the water molecule acts as acceptor. The water molecule links three different steroid molecules, acting as a hydrogen-bond acceptor from atom O17

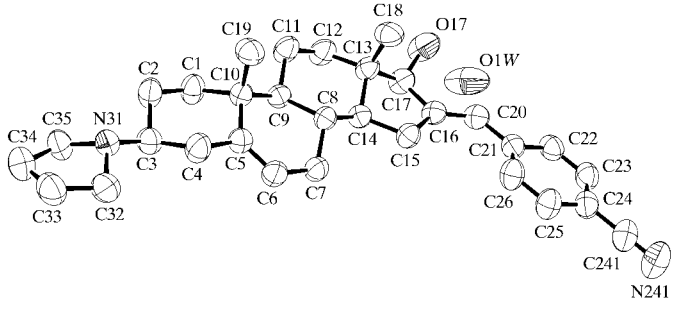


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

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of one steroid molecule and as a donor to the N atoms of the pyrrolidine and 4-cyanobenzylidene groups of two other steroid molecules. In Fig. 2, we see that the steroid molecules are aligned parallel to the *b* axis, forming a closed loop through hydrogen bonds linked *via* water molecules.

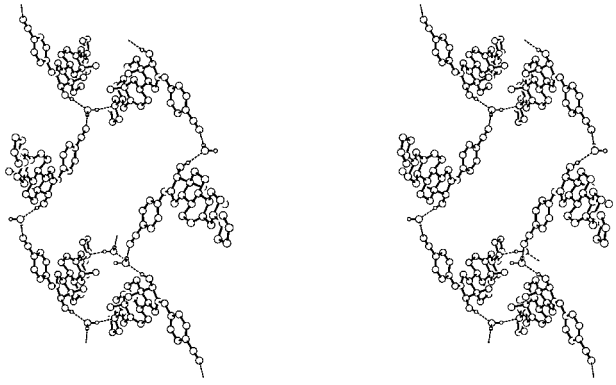

Figure 2
A stereoview of the molecular packing of (I) viewed down the *b* axis.

Experimental

Freshly distilled pyrrolidine was added to a refluxing solution of 16-(4-cyanobenzylidene)androst-4-ene-3,17-dione (0.5 g, 1.25 mmol) in methanol (50 ml). After refluxing for 15 min, the precipitate obtained was cooled in ice, filtered and washed with methanol to obtain 16-(4-cyanobenzylidene)-3-pyrrolidinoandrosta-3,5-dien-17-one (0.4 g). This was immediately suspended in methanol (50 ml) and reduced with sodium borohydride (1.0 g), while stirring at room temperature. The stirring was continued for 4 h, excess methanol was removed under reduced pressure and ice-cold water was added. The precipitate obtained was filtered, washed with water, dried and crystallized from acetone to obtain (I) (0.23 g, 56.99%; m.p. 501–507 K). Spectroscopic analysis, UV_{max} (MeOH): 282.2 nm (log ε = 4.47); IR, ν_{max} (KBr, cm^{-1}): 3350, 2980, 2200, 1595; ^{1}H NMR ($CDCl_3$ + DMSO, δ, p.p.m.): 0.69 (*s*, 3H, 18-CH_3), 1.02 (*s*, 3H, 19-CH_3), 2.61 (*s*, 4H, *N*-methylene of the pyrrolidine function), 4.02 (*m*, 1H, 3α-H), 5.36 (*s*, 2H, 6-CH), 6.55 [*s*, 1H, vinyl H of 16-(4-cyanobenzylidene)], 7.47 (*d*, 2H, J_o = 8.3 Hz, 2-CH and 6-CH aromatic H), 7.67 (*d*, 2H, J_o = 8.3 Hz, 3-CH and 5-CH aromatic H); MS: *m*/*z* (mass/relative intensity): 456 [M^+].

Crystal data

$C_{31}H_{40}N_2O\cdot H_2O$
M_r = 474.67
Orthorhombic, $P2_12_12_1$
a = 7.2171 (6) Å
b = 18.541 (3) Å
c = 20.176 (6) Å
V = 2699.8 (9) Å^3
Z = 4
D_x = 1.168 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 20–30°
μ = 0.56 mm^{-1}
T = 293 (2) K
Plate, colourless
0.30 × 0.25 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.850, T_{max} = 0.946
2916 measured reflections
2898 independent reflections
2580 reflections with $I > 2\sigma(I)$
R_{int} = 0.016
θ_{max} = 68°
h = −8 → 2
k = −22 → 9
l = −24 → 10
2 standard reflections
every 100 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.123
S = 1.09
2898 reflections
318 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0626P)^2 + 0.6312P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0021 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*W*—H1*W*···N241^{i}	0.81	2.20	3.008 (5)	176
O1*W*—H2*W*···N31^{ii}	0.97	1.93	2.892 (3)	168
O17—H17*A*···O1*W*^{iii}	0.82	1.97	2.740 (4)	155

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

All H atoms were fixed with geometrical considerations (C—H = 0.93–0.98 Å and O—H = 0.82 Å, except water H atoms, for which the overall displacement parameters were refined.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structure: *DIRDIF*99 (Beurskens *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *WinGX* (Farrugia, 1999); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: VJ1164). Services for accessing these data are described at the back of the journal.

References

Altona, C., Geise, H. J. & Romers, C. (1968). *Tetrahedron*, **24**, 13–32.
Andrade, L. C. R., Paixão, J. A., de Almeida, M. J. M., Martins, R. M. L. M., Soares, H. I. M., Morais, G. J. R., Moreno, M. J. S. M., Sá e Melo, M. L. & Campos Neves, A. S. (2001). *Acta Cryst.* C**57**, 587–589.
Beurskens, P. T., Beurskens, G., de Gelder, R., García-Granda, S., Israel, R., Gould, R. O. & Smits, J. M. M. (1999). *The DIRDIF*99 *Program System*. Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.
Caira, M. R., Guillory, K. J. & Chang, L. (1995). *J. Chem. Crystallogr.* **25**, 393–400.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Duax, W. L. & Norton, D. A. (1975). In *Atlas of Steroid Structures*. New York: Plenum.
Enraf–Nonius (1994). *CAD*-4 *EXPRESS*. Version 5.1/1.2. Enraf–Nonius, Delft, The Netherlands.
Fair, C. K. (1990). *MolEN*. Enraf–Nonius, Delft, The Netherlands.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Kálmán, A., Argay, G., Živanov-Stakić, D. & Ribár, B. (1992). *Acta Cryst.* B**48**, 812–819.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Vasuki, G., Parthasarathi, V., Ramamurthi, K., Jindal, D. P. & Dubey, S. (2001). *Acta Cryst.* C**57**, 1062–1063.