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16-Cyano-13α-(5-methyl-1,3,4-oxadiazol-2-yl)-13,16-seco-17-norandrost-5-en-3β-yl acetate

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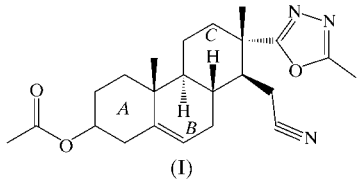
In the title compound, $C_{23}H_{31}N_3O_3$, the outer cyclohexane rings have chair conformations, while the central cyclohexene ring adopts a half-chair conformation. In the solid state, intra- and intermolecular C—H···N interactions are observed.

Comment

There are several reports highlighting the fact that steroid molecules containing heteroatoms or fused heterocyclic ring systems exhibit favourable biological activity, such as anti-inflammatory effects (Singh *et al.*, 1991, and references therein; Gupta *et al.*, 1996; Jindal *et al.*, 1996). The present study of the title compound, (I), 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 interested in the stereochemistry and conformational flexibilities of the steroid nucleus resulting from various substitutions at the C3, C16 and C17 positions. As far as the authors are aware, there seem to be no structures of related androst-5-ene derivatives reported in the literature to date.



(I)

The crystals of (I) are enantiomerically pure. However, due to the absence of any significant anomalous scatterers in the compound, the absolute configuration of the molecule has not been determined by the present 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).

A perspective view of the molecule of (I) with the steroid numbering scheme is shown in Fig. 1. The methyl groups at C18 and C19 are in the expected staggered arrangement. The geometries at the *A*/*B* and *B*/*C* ring junctions are quasi-*trans* and *trans*, respectively.

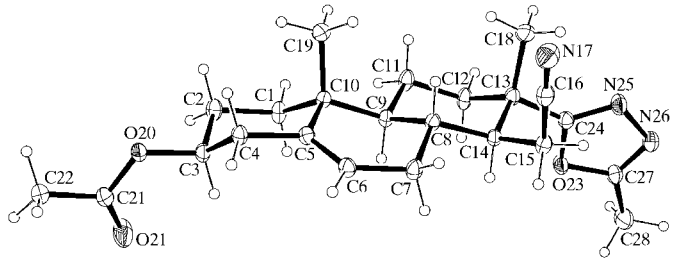


Figure 1
A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.

In (I), rings *A* and *C* of the steroid nucleus adopt distorted chair and chair conformations, respectively, with puckering parameters (Cremer & Pople, 1975) for the atom sequence C1–C5/C10 of ring *A* of Q = 0.560 (2) Å, q_2 = 0.107 (2) Å, q_3 = 0.550 (2) Å, θ = 11.0 (2)° and φ_2 = 105.4 (12)°, and for the atom sequence C8/C9/C11–C14 of ring *C* of Q = 0.563 (2) Å, q_2 = 0.055 (2) Å, q_3 = 0.561 (2) Å, θ = 4.7 (2)° and φ_2 = 206 (2)°. The 3β-acetoxy group is planar. Thus, the presence of an acetoxy group bonded to atom C3 slightly affects the usual chair conformation of ring *A* of the steroid nucleus. The C3—O20 bond is oriented equatorially and is (−)anticlinal to the C3—C4 bond; in contrast, it lies (−)antiperiplanar to the C3—C4 bond in a related structure with this substitution reported previously (Thamotharan *et al.*, 2002). The acetoxy group, oxadiazole moiety and nitrile group are oriented nearly perpendicular to the plane of the atoms of steroid rings *A*/*B*/*C*, the dihedral angles being 79.5 (2), 73.6 (1) and 73.6 (1)°, respectively.

The C5═C6 (Csp^2—Csp^2) distance of 1.324 (3) Å confirms the localization of the double bond at this position. This double bond imposes an 8β,9α-half-chair conformation on ring *B* of the steroid nucleus [the puckering parameters are Q = 0.486 (2) Å, q_2 = 0.379 (2) Å, q_3 = 0.304 (2) Å, θ = 51.3 (3)° and φ_2 = 216.0 (3)° for the atom sequence C5–C10]. The C9—C10 bond tends to be longer in several derivatives of testosterone; for example, it is 1.590 (7) and 1.580 (8) Å for the two molecules in 8-isotestosterone (Chakrabarti *et al.*, 1981). A slight lengthening is observed in the present structure, the value of this bond being 1.564 (2) Å. The observed lengthening may be attributed to steric strain present at the quaternary atom C10.

‡ Deceased.

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The oxadiazole moiety in (I) is in an α-equatorial position, while C15—C16≡N17 is β-equatorial. Taking C13—C14—C15 as the reference plane, the C18 methyl group and C16 nitrile group are in a *syn* orientation. The C19—C10···C13—C18 pseudo-torsion angle has a value of 7.02 (17)°, which gives a quantitative measure of the molecular twist.

In the crystalline state of (I), atom C15 is involved in a weak intramolecular C—H···N interaction with atom N25 of the oxadiazole moiety and this interaction leads to an *S*(6) loop motif (Bernstein *et al.*, 1995). Atom C28 participates in a weak intermolecular C—H···N interaction with atom N25 of an adjacent molecule. This interaction links the steroid molecules into a chain that runs parallel to the *a* axis and which has a graph-set motif of *C*(5) (Table 1).

Table 1
Intra- and intermolecular C—H···N interactions (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C15—H15*B*···N25	0.99	2.61	3.371 (3)	134
C28—H28*B*···N25^{i}	0.98	2.48	3.443 (3)	167

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

Experimental

A solution of 3β-hydroxy-16-oximino-5-androsten-17-one hydrazone (4 g, 12 mmol) in acetic anhydride (40 ml) was refluxed for 45 min, poured into ice-cold water, filtered, washed, dried and purified by fractional crystallization from ethanol to afford crystals of (I) (institution code DPJ-177) (yield 2 g, 42%; m.p. 501–502 K).

Crystal data

$C_{23}H_{31}N_3O_3$
M_r = 397.51
Monoclinic, $P2_1$
a = 6.1855 (1) Å
b = 7.5511 (1) Å
c = 22.6406 (4) Å
β = 95.9439 (10)°
V = 1051.80 (3) Å^3
Z = 2
D_x = 1.255 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3282 reflections
θ = 2.0–30.0°
μ = 0.08 mm^{-1}
T = 160 (2) K
Prism, colourless
0.30 × 0.28 × 0.20 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
27 570 measured reflections
3279 independent reflections
2778 reflections with $I > 2\sigma(I)$
R_{int} = 0.046
θ_{max} = 30.0°
$h = -8 \rightarrow 8$
$k = -10 \rightarrow 10$
$l = -31 \rightarrow 31$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.108
S = 1.05
3276 reflections
267 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0511P)^2 + 0.1624P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.026 (5)

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 atoms. Due to 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 2812 sets of Friedel equivalents led to an inconclusive value (Flack & Bernardinelli, 2000) of 0.4 (11). 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 (I). Reflections 003, 011 and 102 were partially obscured by the beam stop and were 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 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

RG thanks Cipla Ltd, Mumbai, India, for the generous supply of the title steroid.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1690). Services for accessing these data are described at the back of the journal.

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