Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

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

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Key indicators

Single-crystal X-ray study
T = 273 K
Mean σ(C–C) = 0.005 Å
R factor = 0.059
wR factor = 0.160
Data-to-parameter ratio = 7.7

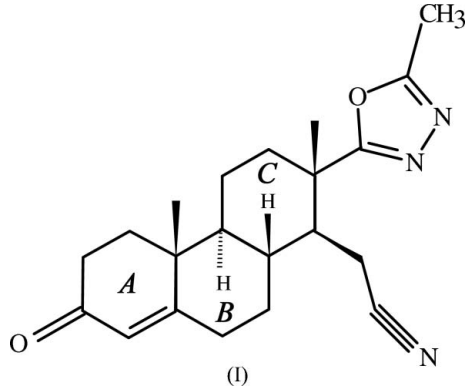
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 6 February 2006
Accepted 8 February 2006

In the title compound, a seco steroid derivative, $C_{21}H_{27}N_3O_2$, the cyclohexane rings of the steroid nucleus are in chair conformations, while the cyclohexene ring adopts a 1α-sofa conformation. In the crystal structure, intermolecular C—H···N interactions link the molecules into extended chains, parallel to the c axis, with graph-set motif $C(5)$. The structure is further stabilized by weak intermolecular C—H···O interactions which can be described as $C(4)$ chains running parallel to the b axis.

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 (Thamotharan *et al.*, 2004, and references therein). We are interested in the stereochemistry and conformational flexibilities of the steroid nucleus resulting from various substituents at the C3, C16 and C17 positions. The X-ray crystal structure determination of the title compound, (I), has been undertaken in order to understand the influence of structural modifications on the overall molecular geometry and conformation.



(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

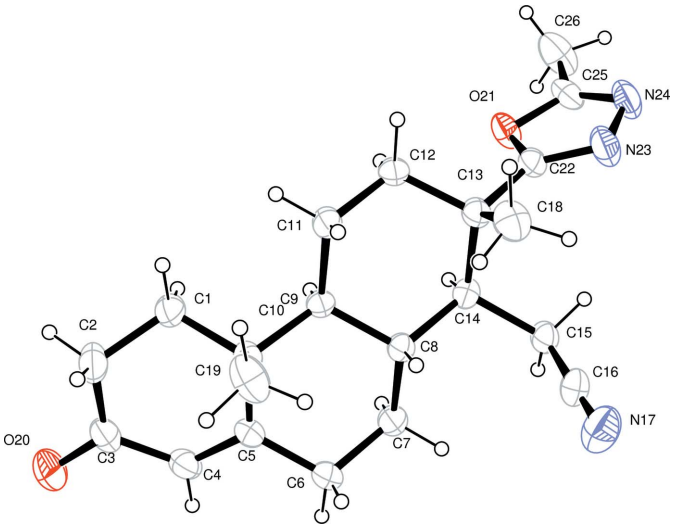


Figure 1
A view of the molecular structure of (I) with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as circles of arbitrary radii.

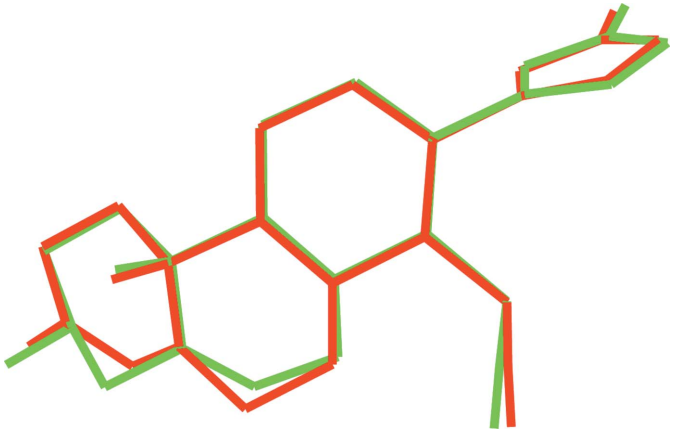


Figure 2
A superimposed fit of non-H atoms of (I) (red) and corresponding atoms of (II) (green).

geometries at the *A*/*B* and *B*/*C* ring junctions are quasi-*trans* and *trans*, respectively. In (I), rings *B* and *C* of the steroid nucleus adopt chair conformations, with puckering parameters (Cremer & Pople, 1975) Q = 0.533 (4) Å, q_2 = 0.066 (4) Å, q_3 = 0.528 (4) Å, θ = 7.2 (4)° and φ_2 = 163 (4)° for the atom sequence C5–C6–C7–C8–C9–C10 of ring *B*, and Q = 0.569 (4) Å, q_2 = 0.025 (4) Å, q_3 = 0.568 (4) Å, θ = 2.0 (4)° and φ_2 = 206 (9)° for the atom sequence C8–C9–C11–C12–C13–C14 of ring *C*. The C4—C5 (Csp^2—Csp^2) distance of 1.324 (3) Å confirms the localization of the double bond at this position. This double bond imposes a 1α-sofa conformation on ring *A* of the steroid nucleus, with atom C1 at the flap position. The puckering parameters are Q = 0.445 (4) Å, q_2 = 0.376 (4) Å, q_3 = 0.238 (4) Å, θ = 57.6 (5)° and φ_2 = 5.7 (7)° for the atom sequence C1–C2–C3–C4–C5–C10. The different conformations of rings *A* (sofa) and *B* (chair) in (I) and those observed for rings *A* (chair) and *B* (half-chair) in the related structure 16-cyano-3α-(5-methyl-1,3,4-oxadiazol-2-yl)-13,16-seco-17-norandrost-5-en-3β-yl acetate, (II) (Thamotharan *et al.*, 2004), caused by the shifting of the double bond from C4═C5 in (I) to C5═C6 in (II), lead to significant differences in the steroid skeleton geometry in the region of rings *A* and *B*. This is evident from the C19—C10···C13—C18 pseudo-torsion angle of 4.0 (4)° in (I), compared to 7.0 (1)° for the corresponding angle in (II). This also leads to a smaller molecular twist of (I). A similar observation has been made for the structures of 3β-acetoxy-17-methyl-17-oxo-16,17-seco-5-androstene-16-carbonitrile and 17-methyl-3,17-dioxo-16,17-seco-4-androstene-16-carbonitrile (Lazar *et al.*, 2004).

A slight lengthening is observed in the C9—C10 bond [1.559 (5) Å]. This may be attributed to steric strain present at the quaternary atom C10. A similar observation has been made for the structure (II). A superimposed fit of the non-H atoms common to the structures (I) and (II) gives an r.m.s. deviation of 0.248 Å (Fig. 2). The oxadiazole ring in (I) is in the α-equatorial position, while C15—C16≡N17 is β-equatorial.

In the crystalline state in (I), atom C26 is involved in a weak intermolecular C—H···N interaction with atom N23 of the oxadiazole ring; this interaction links the molecules into a chain running parallel to the *b* axis that can described by the graph-set motif $C(5)$ (Bernstein *et al.*, 1995). Atom C4 participates in a weak intermolecular C—H···O interaction with atom O20 of an adjacent molecule. This interaction links the steroid molecules into a chain that runs parallel to the *b* axis and can be represented by graph-set motif $C(4)$. The details are presented in Table 1.

Experimental

A solution of 16-cyano-13α-(5-methyl-1,3,4-oxadiazol-2-yl)-13,16-seco-17-nor-androst-5-en-3-ol (0.5 g, 1.4 mmol) in cyclohexanone (5 ml) and toluene (250 ml) was slowly distilled as aluminium isopropoxide (2.0 g) in toluene (30 ml) was added dropwise. The mixture was refluxed for 4 h and allowed to stand overnight. The solution was filtered and steam distilled. The aqueous solution obtained was extracted with chloroform. The product obtained after removal of solvent was crystallized from ethyl acetate to afford crystals of (I) (yield 0.18 g, 35%; m.p. 453–457 K).

Crystal data

$C_{21}H_{27}N_3O_2$
M_r = 353.46
Monoclinic, $P2_1$
a = 6.0831 (11) Å
b = 7.6736 (14) Å
c = 20.614 (4) Å
β = 95.796 (3)°
V = 957.3 (3) Å^3
Z = 2
D_x = 1.226 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3439 reflections
θ = 2.8–25.1°
μ = 0.08 mm^{-1}
T = 273 (2) K
Block, colourless
0.19 × 0.11 × 0.09 mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: none
9075 measured reflections
1823 independent reflections
1650 reflections with $I > 2\sigma(I)$
R_{int} = 0.039
θ_{max} = 25.0°
$h = -7 \rightarrow 7$
$k = -9 \rightarrow 9$
$l = -24 \rightarrow 24$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.1021P)^2 + 0.0266P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.059$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.160$	$\Delta\rho_{max} = 0.31$ e Å^{-3}
$S = 1.23$	$\Delta\rho_{min} = -0.18$ e Å^{-3}
1823 reflections	
238 parameters	
H-atom parameters constrained	

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

D—H···A	D—H	H···A	D···A	D—H···A
C4—H4···O20^{i}	0.93	2.45	3.329 (5)	157
C26—H26*C*···N23^{ii}	0.96	2.50	3.423 (7)	162

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

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, with U_{iso}(H) = 1.2U_{eq}(C). In the absence of any significant anomalous scatterers in (I), Friedel pairs were merged before the final refinement.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997), *PLATON* (Spek, 2003) and *Qmol* (Gans & Shalloway, 2001); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

TVS thanks Mrs R. Hema, School of Physics, Bharathidasan University, for fruitful discussions and RB thanks the late Professor D. P. Jindal for his guidance and help in the synthesis of the title compound.

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