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20-Hydroxyimino-5 α -pregna-9(11),16-dien-3 β -yl acetate and 17-oxo-5 α -androst-9(11)-en-3 β -yl acetate

Héctor Novoa de Armas *et al.*

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20-Hydroxyimino-5 α -pregna-9(11),16-dien-3 β -yl acetate and 17-oxo-5 α -androst-9(11)-en-3 β -yl acetate

Héctor Novoa de Armas,^{a*} Oswald M. Peeters,^a
Norbert M. Blaton,^a Camiel J. De Ranter,^a José A. Ruíz
García,^b Mayra Reyes Moreno^b and Yoanna M. Alvarez
Ginarte^b

^aLaboratorium voor Analytische Chemie en Medicinale Fysicochemie, Faculteit Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium, and ^bCentro de Química Farmacéutica, Laboratorio de Síntesis Química, Apartado 16042, La Habana, Cuba
Correspondence e-mail: hector.novoa@farm.kuleuven.ac.be

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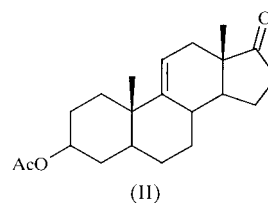
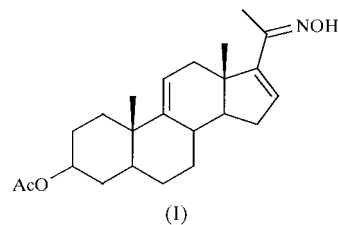
In the title compounds, C₂₃H₃₃NO₃ and C₂₁H₃₀O₃, respectively, the ester linkage in ring *A* is equatorial. In these steroids, the six-membered rings *A* and *B* have chair conformations, but ring *C* can be better described as a half-chair. The five-membered ring *D* adopts a 14 α -envelope conformation. The *A/B*, *B/C* and *C/D* ring junctions are *trans*.

Comment

Corticosteroids have demonstrated substantial topical anti-inflammatory potency. In particular, betamethasone 17-benzoate has been in clinical practice for a long time (Lutsky *et al.*, 1979). The strategy and importance for the synthesis of these compounds have their antecedents in similar structures, with anabolic and/or androgenic activity, replacing the positions 9 α and 11 β with fluorine and hydroxyl, respectively (Shapiro *et al.*, 1987). An example of this is the 9 α -fluoro-11 β ,17 α -dihydroxy-17 α -methyl-4-androsten-3-one (halotestin), a commercial compound 20 times more androgenic and 10 times more anabolic than methyltestosterone. In connection with our studies on the synthesis and characterization of bioactive steroids, the structures of the obtained compounds (I) and (II) could allow us to predict the possibility of presenting/displaying anabolic and/or androgenic properties.

The absolute configuration was assumed to be the same as the one predicted beforehand from the synthesis route; it was not reliably determined from the X-ray data. The C3—O31 bond of the acetoxy group is equatorially oriented and (–)-antiperiplanar to the C3—C4 bond for both compounds. The presence of the acetoxy bounded to C3 does not disturb the chair conformation in the ring *A* of the steroidal nucleus. Ring *A* has a highly symmetrical chair conformation with all

asymmetry parameters (Duax *et al.*, 1976) below 8.3 (3)^o [2.4 (4)^o, for compound (II)]. Rotational symmetry is dominant, a pseudo-C₂ axis intercepts the C3—C4 bond with asymmetry parameters $\Delta C_2(C3-C4) = 3.3$ (3), $\Delta C_5(C1) = 5.3$ (2) and $\Delta C_5(C3) = 1.4$ (2)^o [for compound (II): $\Delta C_2(C3-C4) = 1.5$ (5), $\Delta C_5(C1) = 1.6$ (4) and $\Delta C_5(C3) = 0.6$ (4)^o]. The average magnitude of the torsion angles is 55.1 (1)^o [55.6 (2)^o]. Ring *B* in both structures displays a chair conformation, as expected (Pfeiffer *et al.*, 1985), but this is not the case for ring *C* which has a half-chair conformation. The five-membered



ring *D*, in both structures, adopts a 14 α -envelope conformation (Altona *et al.*, 1968). The *A/B*, *B/C* and *C/D* ring junctions are *trans*. Bond distances and valence angles are close to expected values (Honda *et al.*, 1996). In (I), the packing of the molecules is assumed to be dictated mainly by intermolecular hydrogen bonds O—H...O. There is an intramolecular C—H...O interactions between the O17 atom of the oxime group and the terminal C172 atom of the methyl group (Taylor & Kennard, 1982). The molecules are linked forming an infinite one-dimensional network with base vector [001], by means of the O—H...O hydrogen bonds. There are no intermolecular hydrogen bonds in (II); however, an intermolecular C—H...O interaction between the atom O32 of the acetoxy group and the carbon C15 is present (Taylor & Kennard, 1982). The packing of the molecules is assumed to be dictated by this interaction and van der Waals forces in (II).

Experimental

The synthesis of (I) and (II) is described by Ruíz (1997). M.p.: 536–538 K for (I) and 469–479 K for (II). Crystals were grown from ethanol by slow evaporation.

Compound (I)

Crystal data

C₂₃H₃₃NO₃
M_r = 371.51
Orthorhombic, P2₁2₁2₁
a = 7.0198 (2) Å
b = 12.0153 (5) Å
c = 24.669 (2) Å
V = 2080.7 (2) Å³
Z = 4
D_x = 1.186 Mg m⁻³

Cu K α radiation
Cell parameters from 46 reflections
 $\theta = 7.36$ – 34.23 ^o
 $\mu = 0.610$ mm⁻¹
T = 293 K
Block, colourless
0.38 × 0.30 × 0.20 mm

Data collection

Siemens P4 four-circle diffractometer
 $\omega/2\theta$ scans
 Absorption correction: ψ scan (North *et al.*, 1968)
 $T_{\min} = 0.765$, $T_{\max} = 0.885$
 2846 measured reflections
 2614 independent reflections
 2318 reflections with $F^2 > 2\sigma(F^2)$

$R_{\text{int}} = 0.022$
 $\theta_{\max} = 69.21^\circ$
 $h = -1 \rightarrow 7$
 $k = -1 \rightarrow 14$
 $l = -29 \rightarrow 1$
 3 standard reflections every 100 reflections
 intensity decay: none

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.0389$
 $wR(F^2) = 0.1110$
 $S = 1.057$
 2614 reflections
 250 parameters
 H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0605P)^2 + 0.2543P]$
 where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.15 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.12 \text{ e } \text{\AA}^{-3}$
 Extinction correction: *SHELXL97* (Sheldrick, 1997)
 Extinction coefficient: 0.0039 (4)
 Absolute structure: Flack (1983), 227 Friedel pairs
 Flack parameter = 0.1 (5)

Table 1

Selected geometric parameters (\AA , $^\circ$) for (I).

O17–N17	1.410 (3)	O32–C31	1.204 (3)
O31–C3	1.467 (3)	N17–C171	1.285 (4)
O31–C31	1.329 (3)		
C3–O31–C31	119.9 (2)	O32–C31–C32	124.5 (3)
O17–N17–C171	110.2 (2)	O31–C31–O32	123.2 (2)
O31–C3–C2	110.62 (19)	N17–C171–C17	117.3 (2)
O31–C3–C4	104.51 (19)	N17–C171–C172	123.0 (2)
O31–C31–C32	112.3 (2)		

Table 2

Hydrogen-bonding geometry (\AA , $^\circ$) for (I).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
O17–H17 \cdots O32 ⁱ	0.82	1.94	2.745 (3)	165
C172–H17A \cdots O17	0.96	2.17	2.586 (4)	104

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

Compound (II)

Crystal data

$C_{21}H_{30}O_3$
 $M_r = 330.45$
 Monoclinic, $P2_1$
 $a = 10.112$ (1) \AA
 $b = 7.7821$ (6) \AA
 $c = 12.0922$ (9) \AA
 $\beta = 91.73$ (1) $^\circ$
 $V = 951.1$ (1) \AA^3
 $Z = 2$

$D_x = 1.154 \text{ Mg m}^{-3}$
 Cu $K\alpha$ radiation
 Cell parameters from 36 reflections
 $\theta = 11.03$ – 23.49°
 $\mu = 0.590 \text{ mm}^{-1}$
 $T = 293 \text{ K}$
 Plate, colourless
 $0.44 \times 0.30 \times 0.02 \text{ mm}$

Data collection

Siemens P4 four-circle diffractometer
 $\omega/2\theta$ scans
 Absorption correction: ψ scan (North *et al.*, 1968)
 $T_{\min} = 0.825$, $T_{\max} = 0.988$
 2465 measured reflections
 2109 independent reflections
 1395 reflections with $F^2 > 2\sigma(F^2)$

$R_{\text{int}} = 0.024$
 $\theta_{\max} = 68.79^\circ$
 $h = -1 \rightarrow 12$
 $k = -8 \rightarrow 1$
 $l = -14 \rightarrow 14$
 3 standard reflections every 100 reflections
 intensity decay: none

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.0479$
 $wR(F^2) = 0.1470$
 $S = 1.055$
 2109 reflections
 221 parameters
 H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0758P)^2 + 0.0881P]$
 where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.17 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.18 \text{ e } \text{\AA}^{-3}$
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.0031 (9)
 Absolute structure: Flack (1983), 501 Friedel pairs
 Flack parameter = -0.3 (4)

Table 3

Selected geometric parameters (\AA , $^\circ$) for (II).

O17–C17	1.221 (6)	O31–C31	1.326 (6)
O31–C3	1.461 (4)	O32–C31	1.205 (6)
C3–O31–C31	116.6 (3)	O17–C17–C16	125.5 (4)
O31–C3–C2	111.2 (3)	O31–C31–O32	123.7 (3)
O31–C3–C4	106.8 (3)	O31–C31–C32	112.9 (4)
O17–C17–C13	125.7 (5)	O32–C31–C32	123.3 (4)

Table 4

Hydrogen-bonding geometry (\AA , $^\circ$) for (II).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
C15–H15A \cdots O32 ⁱ	0.97	2.49	3.163 (6)	126

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

Data collection, cell refinement and data reduction: *XSCANS* (Siemens, 1996); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); refine structure: *SHELXL97* (Sheldrick, 1997); software used to prepare material for publication: *PLATON* (Spek, 1990), *PARST* (Nardelli, 1995) and *PARSTCIF* (Nardelli, 1991).

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