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16α-Hydroxy-20-oxopregn-5-en-3β-yl acetate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.041
wR factor = 0.119
Data-to-parameter ratio = 10.1

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

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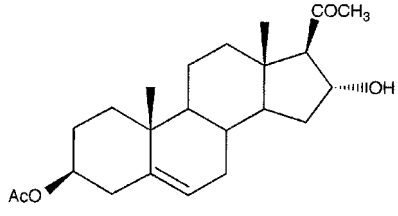
In the title compound, $C_{23}H_{34}O_4$, the two saturated six-membered rings have slightly flattened chair conformations and the unsaturated ring assumes a 8β,9α-half chair conformation distorted towards a 8β-sofa. The five-membered ring has an unusual conformation close to a 13β-envelope. The acetoxy and methyl ketone substituents are twisted with respect to the average molecular plane of the steroid nucleus. The molecules are hydrogen-bonded head-to-head *via* the hydroxy and methyl ketone groups forming dimers, which are stacked in planes perpendicular to the *b* axis.

Comment

As part of an ongoing project to clarify the behaviour of steroidal 16α,17α-epoxy ketones towards reactions with broad scope in the synthesis of bioactive steroids (Moreno, Costa *et al.*, 1998), 16α-hydroxy-20-oxopregn-5-en-3β-yl acetate, (I), was prepared from the corresponding 16α,17α-epoxide by selective reductive opening with aluminium amalgam under ultrasonic conditions (Moreno *et al.*, 1993; Moreno, Sá e Melo & Campos Neves, 1998). A comparative structural study of the steroidal 16α-hydroxy and 16α,17α-epoxy ketones with those functionalized at C21 or C15 is relevant for the purpose of correlating the observed differences in chemical reactivity (Moreno *et al.*, 1993) with the effects of the stereochemistry of the substituents on molecular conformation.



(I)

The X-ray diffraction study of the title compound indicates that all rings are fused *trans*. An *ORTEP*II (Johnson, 1976) drawing of the molecule with the corresponding atomic numbering scheme and ring labels is shown in Fig. 1. Bond lengths and angles are within the range of expected values (Allen *et al.*, 1987), with averages Csp^3-Csp^3 1.532 (4), Csp^3-Csp^2 1.504 (7) and Csp^2-Csp^2 1.321 (4) Å, except for a larger than ususal Csp^2-Csp^3 bond, *i.e.* C5—C10 [1.531 (4) Å].

Rings *A* and *C* have slightly flattened chair conformations, the mean values of their torsion angles being 53 (3) and

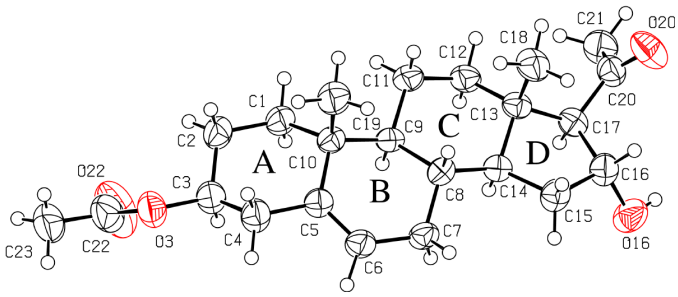


Figure 1
*ORTEP*II (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% probability level except for H atoms which were given arbitrary radii.

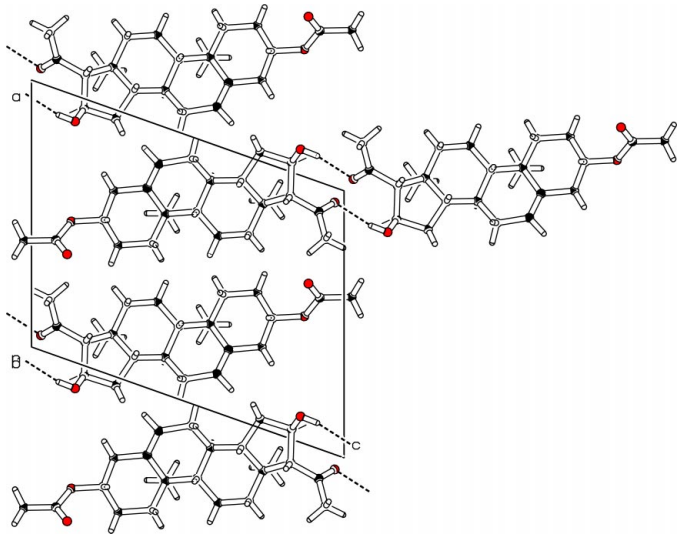


Figure 2
Packing diagram showing the unit-cell contents viewed along the *b* axis and the hydrogen-bonding scheme.

53.9 (15)°, respectively. As reported in a previous crystallographic work on the closely related 16α,17α-epoxy derivative (Andrade *et al.*, 2001), the acetoxy group bonded to C3 does not disturb the usual chair conformation of the A ring of the steroid nucleus. The 3β-acetoxy group is planar and oriented equatorially. The dihedral angle between the acetoxy group and the mean molecular plane is 57.2 (2)°, showing that it is twisted around the C3—O3 bond. Due to the double C5═C6 bond, the environment of the C5 atom is planar [sum of the valence angles around C5 is 360.0 (5)°]. Consequently, ring *B* is highly distorted assuming an 8β,9α-half chair conformation distorted towards a 8β-sofa [asymmetry parameters (Duax & Norton, 1975) are ΔC_2(5,6) = 6.7 (4), ΔC_S(6) = 16.3 (3) and ΔC_2 = 47.8 (4)°]. The five-membered *D* ring assumes an unusual conformation close to 13β-envelope, with puckering parameters (Cremer & Pople, 1975) q_2 = 0.483 (3) Å, φ_2 = 188.2 (4)° [pseudo-rotation (Altona *et al.*, 1968) and asymmetry parameters (Duax & Norton, 1975): Δ = 18.5 (6)°, φ_m = 48.7 (2)°, ΔC_s(13) = 9.3 (3) and ΔC_2(13,14) = 12.4 (4)°].

The conformation of the substituent group at C17 is characterized by a torsion angle C13—C17—C20—O20 of 84.9 (3)°, slightly lower, but close to the values reported by Weeks *et al.* (1973) in a comparative study of six corticosteroids with a similar side chain at C17. The 17β-methyl ketone group is not coplanar with the mean molecular plane, the dihedral angle being 55.59 (14)°. The pseudo-torsion angle C19—C10—C13—C18 which measures the twist of the molecule is 3.4 (3)°, much smaller than the twist observed in the 16α,17α-epoxy steroid molecule [10.4 (2)°]. The linear dimension of the molecule given by the distance between terminal C21 and C23 atoms [13.680 (14) Å] is slightly smaller in the hydroxy- than in the epoxy-substituted steroid molecule [14.873 (4) Å].

The molecules are hydrogen bonded head-to-head *via* the hydroxy and methyl ketone groups. No weak C—H···O short contacts with suitable geometry to be classified as weak intermolecular interactions are found in the structure. Interestingly, the carbonyl O22 atom of the 3β-acetoxy group, which is a potential strong acceptor, is not involved in hydrogen bonding. This may be the reason of an increased librational motion or slight disorder of this atom, deduced from the enhanced displacement parameters of O22 when compared to those of neighbouring atoms.

It should be noted that the absolute configuration of the molecule was not determined from the X-ray data but was chosen to give the correct chirality that was known beforehand from the synthetic route (Moreno *et al.*, 1993).

Experimental

16α,17α-Epoxy-20-oxopregn-5-en-3β-yl acetate, required for introduction of the 16α-hydroxy group, was easily prepared from commercially available 20-oxopregna-5,16-dien-3β-yl acetate through a two-step reaction (Kirk & Sá e Melo, 1979; Andrade *et al.*, 2001). Synthesis of 16α-hydroxy-20-oxopregn-5-en-3β-yl acetate, (I), was efficiently accomplished by sonochemical reductive opening of the 16α,17α-epoxy ketone with aluminium amalgam (Moreno *et al.*, 1993; Moreno, Sá e Melo & Campos Neves, 1998). The product of this reaction was isolated and identified as the title compound (I) from IR, ^{1}H and ^{13}C NMR spectroscopy (Moreno *et al.*, 1993). Crystals suitable for X-ray analysis were obtained by slow evaporation of a solution of the steroid in methanol.

Crystal data

$C_{23}H_{34}O_4$
M_r = 374.50
Monoclinic, $P2_1$
a = 12.110 (9) Å
b = 6.084 (3) Å
c = 15.024 (11) Å
β = 109.54 (11)°
V = 1043.1 (12) Å^3
Z = 2
D_x = 1.192 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 6.1–11.3°
μ = 0.08 mm^{-1}
T = 293 (2) K
Plate, colourless
0.48 × 0.25 × 0.12 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
5099 measured reflections
2553 independent reflections
1631 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 27.5°
$h = -15 \rightarrow 15$
$k = 0 \rightarrow 7$
$l = -19 \rightarrow 19$
3 standard reflections
frequency: 180 min
intensity decay: 7.2%

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.041$	$w = 1/[\sigma^2(F_o^2) + (0.0722P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.119$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.00$	$\Delta\rho_{max} = 0.16$ e Å^{-3}
2553 reflections	$\Delta\rho_{min} = -0.19$ e Å^{-3}
254 parameters	

Table 1
Selected geometric parameters (Å, °).

C10—C5	1.531 (4)	C4—C5	1.517 (4)
C6—C5	1.321 (4)	O22—C22	1.187 (5)
O20—C20—C17—C13	84.9 (3)	C3—O3—C22—O22	2.4 (5)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O16—H16···O20^{i}	0.82 (4)	2.01 (4)	2.817 (4)	169 (3)

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

The H atoms were placed at calculated positions and refined as riding using *SHELXL*97 defaults, except for atom H16, involved in hydrogen bonding, which was refined isotropically with U_{iso}(H16) = $1.2U_{eq}$(O16). Examination of the crystal structure with *PLATON* (Spek, 2001) showed that there are no solvent-accessible voids in the crystal lattice.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

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