

16 α ,17 α -Epoxy-20-oxopregn-5-ene-3 β ,21-diyl diacetate

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Key indicators

Single-crystal X-ray study

$T = 293\text{ K}$

Mean $\sigma(\text{C}-\text{C}) = 0.005\text{ \AA}$

R factor = 0.050

wR factor = 0.154

Data-to-parameter ratio = 9.2

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

The title compound, $\text{C}_{25}\text{H}_{34}\text{O}_6$, has a 3 β ,21-configuration, with the epoxy O atom at 16 α ,17 α . Rings *A* and *C* have chair conformations which are slightly flattened. Because of the presence of a double bond, ring *B* assumes an 8 β ,9 α -half chair conformation. Ring *D* has a conformation close to a 14 α -envelope. Cohesion of the crystal can be attributed to van der Waals interactions and weak C—H \cdots O interactions.

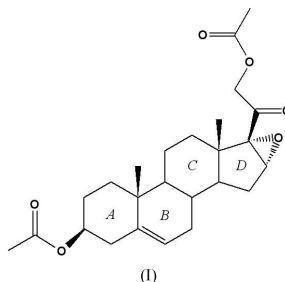
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Comment

Epoxides are very reactive compounds and, owing to the possibility of performing ring opening both regio- and stereospecifically, they are used as versatile synthetic intermediates in the preparation of complex bioactive molecules. Therefore, our interest in preparing new steroids for biological screening (Moreno *et al.*, 1998; Campos Neves *et al.* 1999) led us to the title compound, (I), a key intermediate in the bis-oxidation, at atoms C16 and C21, of 20-oxopregnenes.



Compound (I) was obtained from 20-oxopregne-5,16-dien-3 β -yl acetate in a four-stage synthesis: stereoselective epoxidation of the C16 double bond (Moreno *et al.*, 1998); careful oxidation at C21 with $\text{PhI}(\text{OAc})_2$ (Kamernitzky *et al.*, 1985); subsequent hydrolysis of the corresponding 21-hydroxyketone dimethyl acetal (Kamernitzky *et al.*, 1985) and acetylation of the 3 β -OH and 21-OH. According to the X-ray analysis of the title compound, (I), all rings are *trans* fused. An *ORTEPII* (Johnson, 1976) drawing of the molecule with the atomic numbering scheme is shown in Fig. 1. The distance between the terminal O atoms, O22 \cdots O24, is 13.761 (6) \AA , and between the terminal C atoms, C23 \cdots C25, is 17.363 (7) \AA . Bond lengths and angles are within the expected ranges (Allen *et al.*, 1987), with average values $\text{Csp}^3-\text{Csp}^3 = 1.528$ (13), $\text{Csp}^3-\text{Csp}^2 = 1.497$ (15), $\text{Csp}^2=\text{Csp}^2 = 1.332$ (4) and $\text{C}=\text{O} = 1.209$ (15) \AA . It is worth mentioning a small but significant asymmetry between the two $\text{C}=\text{O}$ acetoxy bond lengths [1.232 (6) and 1.191 (6) \AA] and the two C—O epoxy bond lengths [1.424 (5) and 1.461 (4) \AA]. Similar asymmetries were also found in the 3 β -yl acetate of this compound (Andrade *et al.*, 2001). Rings *A* and *C* are slightly flattened, the mean values of their torsion angles being 51.8 (2) and 55.9 (1)°,

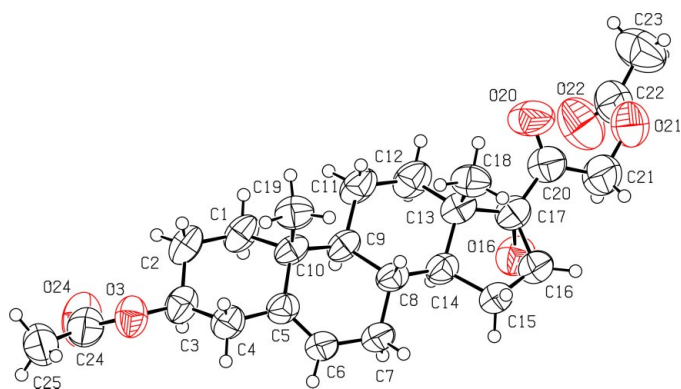


Figure 1
The molecular structure of (I), showing 50% displacement ellipsoids.

respectively. The presence of the acetoxy group bonded to C3 does not disturb the usual chair conformation of ring A of the steroid nucleus. Due to the C5=C6 double bond, the environment of atom C5 is planar (the sum of the valence angles around this atom is 359.9°) and consequently ring B is distorted, assuming an 8β,9α-half-chair conformation with asymmetry parameters (Duax & Norton, 1975) $\Delta C_2(5,6) = 3.1(4)^\circ$, $\Delta C_2(5,10) = 48.6(4)^\circ$ and $\Delta C_s(6) = 20.0(3)$. The five-membered ring D assumes a 14α-envelope conformation, with puckering parameters (Cremer & Pople, 1975) $q_2 = 0.388(4) \text{ \AA}$ and $\varphi_2 = 213.6(6)^\circ$ [pseudo-rotation (Altona *et al.*, 1968) and asymmetry parameters: $\Delta = -31.4(7)$, $\tau_m = 39.5(2)$, $\Delta C_s(14) = 1.8(4)$ and $\Delta C_2(13,14) = 16.9(4)^\circ$]. The 3β-acetoxy group attached to ring A is planar. The C3—O3 bond is oriented equatorially. The dihedral angle between the plane of the 3β-acetoxy group and the mean molecular plane is 61.3(1)°. The dihedral angle between the plane of the epoxy group and the average molecular plane comprising rings A, B, C and D is 87.8(2)°. As reported for a similar structure (Andrade *et al.*, 2001), the epoxide link on ring D may be responsible for the unusual conformation of the substituent group at C17, where the C13—C17 bond almost eclipses the C20—O20 bond [C13—C17—C20—O20 $-5.8(6)^\circ$]. This conformation might be responsible for the relatively large value of the pseudo-torsion angle C18—C13—C10—C19 12.4(2)°. The 17β group may be divided into an acetyl group and an acetoxy group. The dihedral angles between the planes of the acetyl group and the acetoxy group with the average molecular plane comprising rings A, B, C and D are 28.9(2) and 59.0(2)°, respectively. The environments of atoms C20 and C22 are planar (the sums of the valence angles around these C atoms are both 360.0°). However, the angle between the plane of the acetyl group and the plane of the acetoxy group, 82.5(2)°, shows a twist of the two groups around the C21—O21 bond.

The molecule lacks a strong hydrogen donor, so no classical hydrogen bonds are present in the structure and its cohesion is mainly achieved by van der Waals interactions. One intramolecular C—H...O short contact between the O atom of the 17β-group and a neighbouring H atom of a methyl group is present, C18—H18...O20 at 3.107(5) Å. The bent angle

defined by these atoms, 116°, and the weak acidic character of the methyl group suggest that this interaction is probably destabilizing and should not be classified as a weak hydrogen bond. There is, in addition, an intermolecular C—H...O short contact between two atoms of the 17β-group: C16—H16...O22ⁱ [C16...O22ⁱ 3.127(6) Å and C16—H16...O22ⁱ 115°; symmetry code: (i) 1 + x, y, z].

Experimental

Stereoselective epoxidation of the C16 double bond of the commercially available 20-oxopregne-5,16-dien-3β-yl acetate, with hydrogen peroxide in alkaline conditions, was performed according to the literature (Moreno *et al.*, 1998; Andrade *et al.*, 2001). Crystals suitable for X-ray analysis were obtained by slow evaporation of a solution of the steroid in methanol/ethyl acetate.

Crystal data

C₂₅H₃₄O₆
M_r = 430.52
 Orthorhombic, *P*2₁2₁2₁
a = 5.988(1) Å
b = 10.668(1) Å
c = 36.511(3) Å
V = 2332.4(5) Å³
Z = 4
D_x = 1.226 Mg m⁻³

Cu Kα radiation
 Cell parameters from 25 reflections
 $\theta = 18.8\text{--}26.5^\circ$
 $\mu = 0.70 \text{ mm}^{-1}$
T = 293(2) K
 Prism, colourless
 0.49 × 0.14 × 0.13 mm

Data collection

Enraf–Nonius MACH-3 diffractometer
 Profile data from ω -2 θ scans
 Absorption correction: ψ scan (North *et al.*, 1968)
 $T_{\min} = 0.887$, $T_{\max} = 0.913$
 6910 measured reflections
 2624 independent reflections
 1949 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.068$
 $\theta_{\text{max}} = 72.6^\circ$
 $h = -7 \rightarrow 7$
 $k = -13 \rightarrow 13$
 $l = 0 \rightarrow 45$
 3 standard reflections
 frequency: 200 min
 intensity decay: 37.0%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.050$
 $wR(F^2) = 0.154$
 $S = 1.03$
 2624 reflections
 284 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0947P)^2 + 0.2153P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} = 0.005$
 $\Delta\rho_{\text{max}} = 0.29 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.19 \text{ e \AA}^{-3}$

Intensities were corrected for the large (linear) decay of 37%, which appears to be due to radiation damage. The H atoms were placed at calculated idealized positions and refined as riding on their parent atoms using *SHELXL97* defaults. The absolute configuration of the molecule is known from the synthesis route. Due to the lack of significant anomalous scattering, the Friedel pairs were merged before refinement. Examination of the crystal structure with *PLATON* shows that the crystal structure does not contain voids which might be occupied by solvent molecules.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

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