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21-Acetoxy-17α-4-pregnene-3,20-dione

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.006 Å
R factor = 0.054
wR factor = 0.155
Data-to-parameter ratio = 7.6

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

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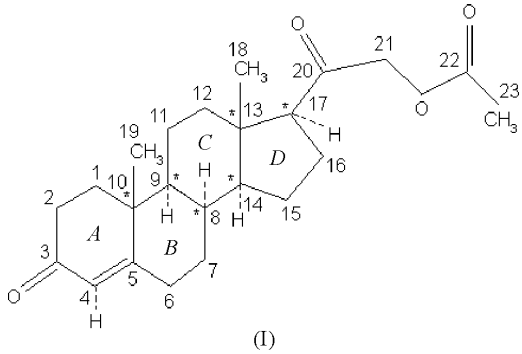
The synthetic steroid 21-acetoxy-17α-4-pregnene-3,20-dione, $C_{23}H_{32}O_4$, crystallizes with a single molecule in the asymmetric unit. The molecule contains four fused rings, typical of steroids. The cyclohexene ring A has nearly the conformation of a boat. One saturated six-membered ring, B, is intermediate between chair and half-chair conformations, while the other six-membered ring, C, is essentially a chair. The five-membered ring D tends towards a twist conformation. The ring junction A/B is quasi-*trans*, whereas the ring junctions B/C and C/D are both *trans*. The molecule is slightly convex towards the β side.

Comment

Corticosteroids are produced uniquely in the adrenal cortex. The functions of these steroids are mediated through binding with the corresponding target proteins. The corticosteroid hormones, *e.g.* cortisol, corticosterone, cortisone and aldosterone, act by binding with intracellular receptors such as glucocorticoid receptors or mineralocorticoid receptors, or by binding with corticosteroid binding globulin (CBG). Glucocorticoids and mineralocorticoids differ not only in their secretion rates and plasma concentrations, but also in the extent to which they are protein-bound in plasma (Schoenmakers *et al.*, 1999). Steroid hormones are usually transported by serum proteins (Sandberg *et al.*, 1966; Seal *et al.*, 1966; Westphal, 1983), characteristic responses of which require their binding to specific proteins in target tissues (Jensen & Jacobsen, 1970). The title compound 21-acetoxy-17α-4-pregnene-3,20-dione is a synthetic corticosteroid, the structure of which is reported here. The structural information could be used to study its binding interactions with the target protein using techniques of molecular modelling.



(I)

The asymmetric C atoms of the title compound, (I), are indicated by asterisks in the scheme. Fig. 1 shows the molecular structure. Ring A has approximately a boat confor-

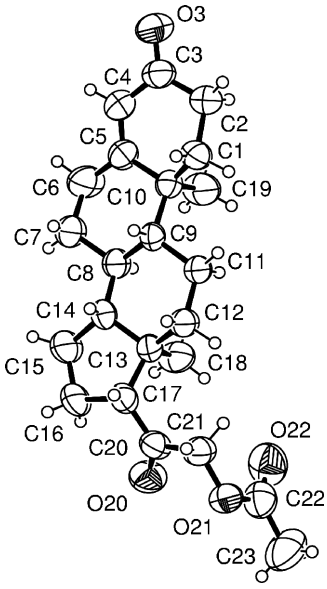


Figure 1
Molecular structure, with displacement ellipsoids drawn at the 50% probability level.

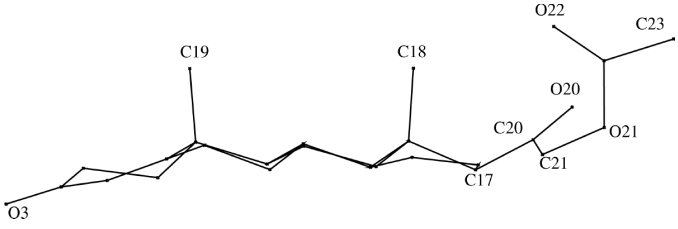


Figure 2
Projection of the molecule on to the C5–C17 mean plane. H atoms have been omitted.

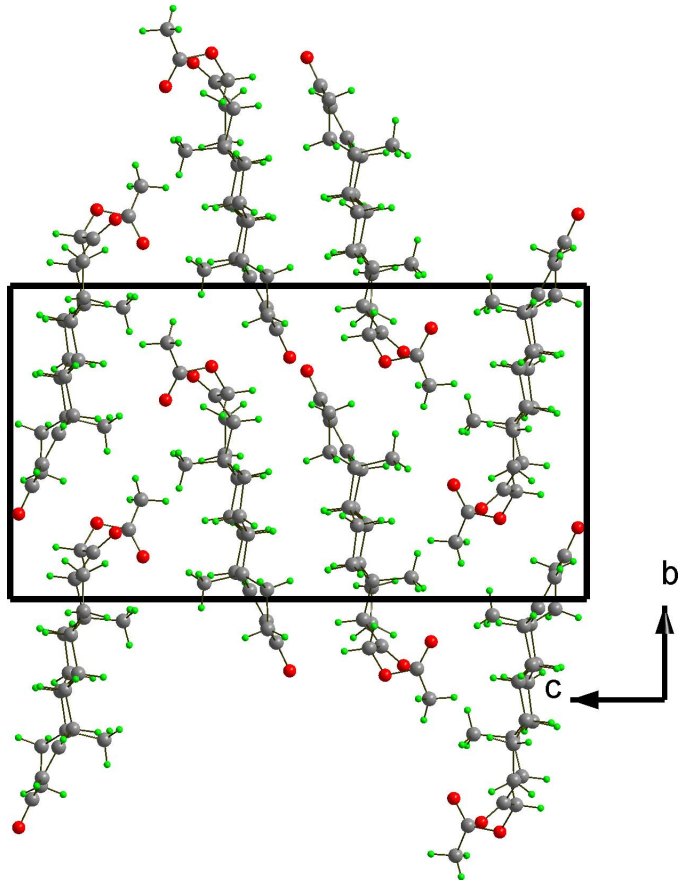


Figure 3
Molecular packing, viewed down the *a* axis.

mation, with an α-hydrogen at C4. Ring *B* is intermediate between chair and half-chair conformations, and contains a β-hydrogen at C8 and an α-hydrogen at C9. Ring *C* has approximately a chair conformation, with an α-hydrogen at C14. Ring *D* tends towards a twist conformation (Spek, 2003). The ring junction *A*/*B* is quasi-*trans* in nature, whereas the ring junctions *B*/*C* and *C*/*D* are *trans* (Bucourt, 1974). The quasi-characteristic of the ring junction *A*/*B* is due to the trigonal carbon C5. A list of endocyclic torsion angles about the three ring junctions supporting the above ring junction characteristics is given in Table 1.

The twist of the molecule about its length is determined by the pseudo-torsion angle C19—C10···C13—C18 [−6.3 (4)°], which implies that the molecule is slightly twisted anti-clockwise by that amount. Moreover, the molecule is slightly convex towards the β side, with an angle of 8.3 (2)° between the C10—C19 and C13—C18 vectors. Bond lengths and angles agree well with published values (Duax *et al.*, 1975). A list of functional groups with their orientations, deviations from the C5–C17 mean plane (determined by all the atoms of the *B*, *C* and *D* rings) and angles subtended with the C5–C17 mean plane is given in Table 2. Here, the angle subtended by a functional group with the C5–C17 mean plane is obtained by calculating the angle between the normal to this mean plane towards the β side and the line joining the functional group to its bonded C atom. It is well known that the *A* ring conformation is considered to be a key factor in binding steroids to their receptors (Duax *et al.*, 1984). Since this class of steroids exhibits a certain degree of flexibility in the region of the *A* ring, the title compound can be accommodated in the ligand-binding domain of the receptor by changing the orientation of the *A* ring relative to the C5–C17 mean plane. The O3–plane distance is normally used as a measure of bow in all 4-en-3-one steroid molecules (Galdecki *et al.*, 1989). The bowing of the *A* ring relative to the remainder of the steroid (*A*/*B*–*C*–*D*) is 17.0 (2)°. The projection of the steroid molecule viewed parallel to the C5–C17 mean plane is shown in Fig. 2. The C13—C17—C20—O20 and C16—C17—C20—O20 torsion angles are −109.6 (5) and 10.3 (6)°, respectively, suggesting that atom O20 is in the anticlinal position with respect to atom C13 and in the synperiplanar position with respect to atom C16. Again, the values 71.7 (4) and −168.5 (4)° of the respective torsion angles C13—C17—C20—C21 and C16—C17—C20—C21 clearly show the conformation of atom C21 relative to atoms C13 and C16 to be described by the qualitative descriptors synclinal and antiperiplanar, respectively (Klyne & Prelog, 1960). The acetoxy group at C21 is almost planar and inclined at an angle of 72.5 (2)° to the least-squares plane passing through the steroid nucleus. The 17β side chain

is composed of two planes, one containing atoms C17, C20, O20 and C21 (with deviations ±0.01 Å), and the other containing atoms C21, O21, C22, O22 and C23 (with deviations ±0.02 Å), with a dihedral angle of 80.2 (3)° between them. The β-orientation of the side chain at C17 is probably dictated by packing forces.

The side-chain conformations in 21-acetoxy-17α-hydroxy-4-pregnene-3,11,20-trione (PR21) (Declercq *et al.*, 1972) and the title compound were compared. The O20—C20—C21—O21 and C17—C20—C21—O21 torsion angles are −10.6 and 168.5° for PR21, and −3.3 (6) and 175.5 (3)° for the title compound. These observations indicate an almost identical side-chain conformation for the two steroid compounds containing an acetoxy group at C21.

Experimental

The synthetic compound 21-acetoxy-17α-4-pregnene-3,20-dione, purchased from Sigma, was crystallized from ethanol. Data were collected about 15 years ago and are inferior, especially regarding data completeness, to modern methods and standards.

Crystal data

$C_{23}H_{32}O_4$
M_r = 372.49
Orthorhombic, $P2_12_12_1$
a = 7.590 (2) Å
b = 12.098 (3) Å
c = 22.228 (4) Å
V = 2041.1 (8) Å^3
Z = 4
D_x = 1.212 Mg m^{-3}
D_m = 1.23 Mg m^{-3}
D_m measured by flotation in benzene/bromoform
Cu $K\alpha$ radiation
Cell parameters from 50 reflections
θ = 4.0–71.0°
μ = 0.65 mm^{-1}
T = 293 (2) K
Parallelepiped, colorless
0.42 × 0.35 × 0.30 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
1885 measured reflections
1885 independent reflections
1882 reflections with $I > 2\sigma(I)$
θ_{max} = 71.0°
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 14$
$l = 0 \rightarrow 27$
3 standard reflections
every 150 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.155
S = 1.00
1885 reflections
247 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0939P)^2 + 0.6818P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Endocyclic torsion angles (°) about the ring junctions.

Junction	Atoms	Torsion angle	Characteristics
A/*B*	C4—C5—C10—C1	21.7 (5)	Quasi-*trans*
	C6—C5—C10—C9	−44.6 (5)	
B/*C*	C7—C8—C9—C10	−58.2 (4)	*trans*
	C14—C8—C9—C11	50.3 (4)	
C/*D*	C12—C13—C14—C8	63.4 (4)	*trans*
	C17—C13—C14—C15	−44.2 (4)	

Table 2
Functional groups with their orientations, deviations from the C5–C17 mean plane (Å) and angles subtended to the C5–C17 mean plane (°).

Functional group	Orientation	Deviation	Angle
C18	β-axial	1.894 (4)	87.6 (2)
C19	β-axial	1.678 (4)	79.3 (2)
O3	α-axial	−1.290 (4)	19.5 (2)
O20	β-axial	1.223 (4)	37.5 (3)
C22	β-axial	1.980 (4)	72.4 (2)

All H atoms were included in the riding-model approximation, with C—H distances in the range 0.93–0.98 Å and with U_{iso}(H) = 1.2U_{eq}(C). The data set contains no Friedel pairs; the absolute configuration is known from the synthesis.

Data collection: *XDS* (Kabsch, 1988); cell refinement: *XDS*; data reduction: *XDS*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *DIAMOND* (Brandenburg, 2004); software used to prepare material for publication: *SHELXL97*.

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