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1-β-Hydroxycorticosterone hemihydrate

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.003 Å
R factor = 0.038
wR factor = 0.089
Data-to-parameter ratio = 8.6

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

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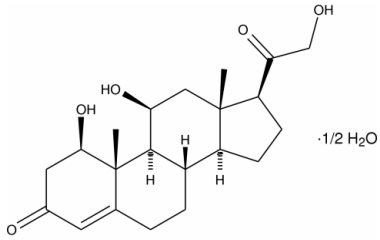
The title compound, 4-pregnene-1β,11β,21-triol-3,20-dione hemihydrate, $C_{21}H_{30}O_5\cdot0.5H_2O$, has two independent steroid molecules and one water molecule in the asymmetric unit, and these steroid molecules have nearly identical conformations. In each, the two OH groups attached to the ring system form an intramolecular hydrogen bond, with O···O distances 2.738 (3) and 2.768 (3) Å.

Comment

The C1 hydroxylation of steroids remains a rare biological event, limited largely to microbial transformations (Dodson *et al.*, 1962) and, to a lesser extent, liver microsomal metabolism (Ford *et al.*, 1975). Synthetic access to C1-hydroxlated steroids and derivatives has been reported for testosterone (Sharma & Akhila, 1991; Mann & Pietrzak, 1989), cholesterol (Mihailovic *et al.*, 1977) and corticosterone (Kime, 1975). Of these steroids, 1-α-hydroxycorticosterone, (II), represents a distinct C1-hydroxylated steroid that exhibits biological activity, and has been identified as a major corticosteroid hormone of the elasmobranch fish (Idler & Kane, 1980; Kime, 1977). As part of our ongoing efforts to study the production of this steroid from shark interrenal gland and to subsequently quantify blood plasma levels, we established a new and efficient five-step synthesis of 1α-hydroxycorticosterone, (II), in addition to the title compound, 1β-hydroxycorticosterone, (I), from corticosterone. The structures of (I) and (II) were elucidated and partially confirmed by the combination of two-dimensional NMR techniques, including H-COSY, H-NOSEY, HMQC and HMBC. However, the configuration of the C1-hydroxy group could not be assigned unequivocally for (I) or (II). X-ray analysis of a crystalline sample of the hemihydrate of (I) clearly demonstrates that it is the 1β epimer.



(I)

There are two independent steroid molecules and one water molecule in the asymmetric unit. Both steroid molecules exhibit intramolecular hydrogen bonding, with the OH group at C11 as donor and that at C1 as acceptor, as detailed in Table 1. For both *A* and *B* molecules, the ketone at C3 is involved in hydrogen bonding, but the ketone at C20 is not.

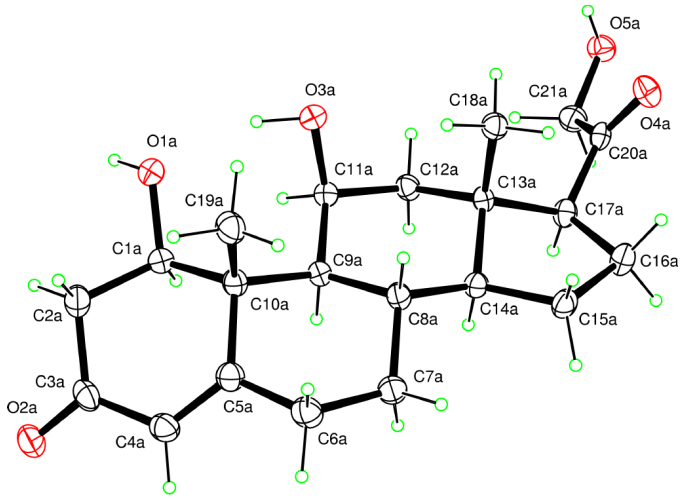


Figure 1
Numbering scheme and displacement ellipsoids at the 50% probability level for molecule *A* of (I).

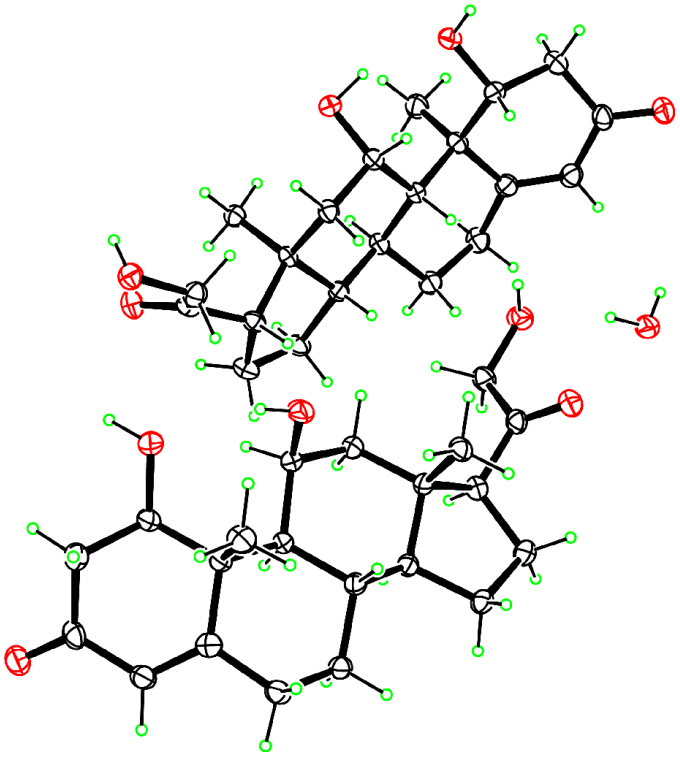


Figure 2
The asymmetric unit, with displacement ellipsoids drawn at the 50% probability level.

The conformations of the two independent molecules are virtually identical. Their endocyclic torsion angles, given in Table 2, exhibit an r.m.s. deviation of only 1.7°, with a maximum difference of 3.8 (6)° for C2—C3—C4—C5. This conformation is also quite similar to that of corticosterone (Campsteyn *et al.*, 1973), which lacks the OH group at C1. Endocyclic torsion angles for that structure are also given in Table 2 for comparison.

Experimental

Compound (I) was synthesized from corticosterone in a five-step sequence; its synthesis will be reported in a separate communication. Analytical data: m.p. 473–475 K (acetone–hexane); $[\alpha]_D^{25}$ = +136° (*c* = 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$ with 20 µl D_2O for OH exchange): δ 5.75 (*s*, 1H), 4.48 (*d*, *J* = 2.5 Hz, 1H), 4.20 (*dd*, *J* = 18.9, 18.9 Hz, 2H), 4.14 (*dd*, *J* = 5.9, 12.1 Hz, 1H), 2.60 (*m*, 2H), 2.60 (*m*, 1H), 2.43 (*t*, *J* = 9.2 Hz, 1H), 2.37 (*dd*, *J* = 3.6, 14.3 Hz, 1H), 2.25 (*m*, 1H), 2.22 (*dd*, *J* = 2.1, 13.7 Hz, 1H), 2.05 (*m*, 2H), 1.82 (*m*, 2H),1.64 (*dd*, *J* = 3.8, 13.7 Hz, 1H), 1.60 (*bs*, 1H), 1.45 (*s*, 3H), 1.12 (*m*, 2H), 1.05 (*dd*, *J* = 4.0, 11.2 Hz), 0.92 (*s*, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.30, 198.21, 170.60, 122.72, 73.34, 69.58, 69.58, 59.78, 57.40, 57.12, 46.67, 45.46, 43.84, 43.59, 32.95, 32.57, 32.27, 25.12, 22.77, 15.49, 14.84. Analysis for dehydrated material, calculated for $C_{21}H_{30}O_5$: C 69.59, H 8.34%; found: C 69.15, H 8.28%.

Crystal data

$C_{21}H_{30}O_5{\cdot}0.5H_2O$
M_r = 371.46
Triclinic, *P*1
a = 7.781 (2) Å
b = 10.598 (3) Å
c = 12.432 (4) Å
α = 95.131 (11)°
β = 107.490 (12)°
γ = 97.32 (2)°
V = 960.9 (5) Å^3
Z = 2
D_x = 1.284 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 4095 reflections
θ = 2.5–27.5°
μ = 0.09 mm^{-1}
T = 100 K
Needle, colorless
0.50 × 0.10 × 0.07 mm

Data collection

Nonius KappaCCD diffractometer (with an Oxford Cryosystems Cryostream cooler)
ω scans with κ offsets
21 194 measured reflections
4338 independent reflections
3588 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 27.5°
h = −10 → 9
k = −13 → 13
l = −16 → 16

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.089
S = 1.02
4338 reflections
507 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0516P)^2 + 0.0079P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*A*—H10*A*···O1*W*^{i}	0.93 (4)	1.84 (4)	2.759 (3)	174 (3)
O3*A*—H30*A*···O1*A*	0.91 (3)	1.88 (3)	2.738 (3)	158 (3)
O5*A*—H50*A*···O2*A*^{ii}	0.82 (4)	1.89 (4)	2.687 (3)	163 (3)
O1*B*—H10*B*···O1*W*^{ii}	1.01 (4)	1.75 (4)	2.760 (3)	176 (3)
O3*B*—H30*B*···O1*B*	0.79 (4)	2.06 (4)	2.768 (3)	150 (3)
O5*B*—H50*B*···O2*B*^{iii}	1.01 (3)	1.67 (3)	2.659 (3)	166 (3)
O1*W*—H1*W*···O5*A*^{iv}	0.84 (4)	1.95 (4)	2.733 (3)	156 (3)
O1*W*—H2*W*···O5*B*	0.89 (4)	1.89 (4)	2.743 (3)	162 (3)

Symmetry codes: (i) 1 + *x*, *y*, *z*; (ii) 1 + *x*, *y*, 1 + *z*; (iii) *x*, *y*, *z* − 1; (iv) *x* − 1, *y*, *z* − 1.

Table 2
Endocyclic torsion angles (°) in (I) and corticosterone (Campsteyn *et al.*, 1973).

D—H···*A*	Molecule *A*	Molecule *B*	Corticosterone
C1—C2—C3—C4	42.7 (3)	45.7 (3)	35.6
C2—C3—C4—C5	−10.6 (4)	−14.4 (4)	−7.6
C3—C4—C5—C10	−7.9 (4)	−6.7 (4)	−1.7
C4—C5—C10—C1	−7.7 (3)	−6.2 (3)	−18.0
C5—C10—C1—C2	40.8 (3)	39.4 (3)	46.1
C10—C1—C2—C3	−58.9 (3)	−59.4 (3)	−55.6
C10—C5—C6—C7	−50.0 (3)	−53.2 (3)	−55.9
C5—C6—C7—C8	46.8 (3)	50.4 (3)	56.6
C6—C7—C8—C9	−52.2 (3)	−53.5 (3)	−55.2
C7—C8—C9—C10	61.3 (2)	59.0 (2)	52.7
C8—C9—C10—C5	−61.3 (2)	−58.4 (2)	−49.0
C9—C10—C5—C6	55.1 (3)	55.3 (3)	50.8
C8—C9—C11—C12	43.8 (3)	43.3 (3)	47.6
C9—C11—C12—C13	−49.9 (3)	−47.8 (3)	−48.4
C11—C12—C13—C14	56.8 (2)	55.4 (3)	54.0
C12—C13—C14—C8	−60.7 (2)	−62.2 (2)	−62.3
C13—C14—C8—C9	54.6 (3)	58.2 (2)	61.8
C14—C8—C9—C11	−45.1 (3)	−47.2 (3)	−53.2
C13—C14—C15—C16	−32.5 (2)	−32.5 (2)	−34.2
C14—C15—C16—C17	5.0 (3)	5.6 (2)	9.1
C15—C16—C17—C13	23.5 (2)	22.8 (2)	18.5
C16—C17—C13—C14	−42.1 (2)	−41.5 (2)	−38.1
C17—C13—C14—C15	46.3 (2)	45.8 (2)	44.8

The absolute configuration could not be determined from the X-ray data but was assigned from the known configuration of steroids. Friedel pairs were averaged. H atoms on C atoms were placed in idealized positions, with C—H bond distances 0.98–1.00 Å, and thereafter treated as riding, with displacement parameters assigned as $U_{iso} = 1.2U_{eq}$ of the attached atom. A torsional parameter was refined for each methyl group. H atoms on O atoms were positioned from difference maps, and their positions were refined, with $U_{iso} = 1.5U_{eq}(O)$.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SIR* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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