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Dexamethasone at 119 K

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Key indicators

Single-crystal X-ray study
T = 119 K
Mean σ(C–C) = 0.002 Å
R factor = 0.041
wR factor = 0.115
Data-to-parameter ratio = 20.3

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

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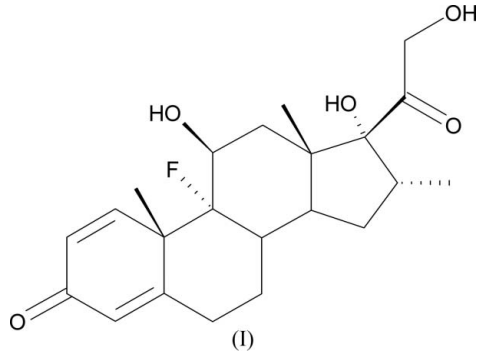
The structure of the title compound, $C_{22}H_{29}FO_5$, has been redetermined at 119 K. It crystallizes with two molecules in the asymmetric unit and the molecules form rippled layers held together by hydrogen bonds.

Comment

Steroids are used in the treatment of many conditions including various cancers (Mourits & de Bock, 2006; Yano *et al.*, 2006), skin disorders (Katelaris & Peake, 2006), asthma (Sadowska *et al.*, 2006), and laryngeal nodes and scarring (Mortensen & Woo, 2006). The title compound (Fig. 1), (I), is a glucocorticoid, also known by the brand name Decadron (Merck), used as an anti-emetic in cancer treatments (Sharma *et al.*, 2005) and as a stand-alone treatment for multiple myeloma (Sidra *et al.*, 2006; Jimenez-Zepeda & Dominguez-Martinez, 2006).



(I)

The room-temperature structure of (I) was previously reported (Van den Bossche, 1971; Rohrer & Duax, 1977). However, we redetermined the structure at 119 K in order to generate accurate restraints for the refinement of a protein-ligand complex and to provide a more reliable model for docking studies. As it turned out, the structures are very similar, the largest difference in equivalent dihedral angles being 5.9°.

The structure of (I) is stabilized by hydrogen bonds (Table 1). There are hydrogen bonds between molecules in the asymmetric unit, and the hydrogen-bond network extends further through interaction between carbonyl atoms from the A rings (Figs. 2 and 3) and the hydroxyl groups from neighboring molecules. The strongest hydrogen bonds produce a sheet with two planes of molecules staggered such that every other row is coplanar. These sheets are further stabilized by weaker hydrogen bonds between the O5*B* hydoxyl group and carbonyl atom O1*B* from a neighboring molecule.

Dexamethasone has been successfully cocrystallized with human glucocorticoid receptor (Bledsoe *et al.*, 2002; Kauppi *et al.*, 2003). The conformation of (I) in the protein binding site is very similar to that reported in our paper (Fig. 4). In the protein structure (PDB code: 1M2*Z*) all hydroxyl groups are involved in hydrogen-bonding interactions, as they are in the crystal structure reported here. Moreover, both carbonyl O atoms are acceptors of hydrogen bonds. The carbonyl O atom from ring A is an acceptor of two hydrogen bonds (Fig. 5), while the carbonyl O atom from the acetate group participates in a less frequently observed hydrogen bond, in which the H atom is donated by the Cα atom from Cys 736 of the glucocorticoid receptor, and the distance between the Cα atom and the O atom is 3.1 Å.

Experimental

Dexamethasone ((11β,16α)-9-fluoro-11,17,21-trihyrdoxy-16-methylpregna-1,4-diene-3,20-dione) was purchased from SIGMA (lot 016 K1452). Crystallization was performed at room temperature and the crystals used for X-ray diffraction experiments were obtained by slow evaporation of a solution in methanol.

Crystal data

$C_{22}H_{29}FO_5$
M_r = 392.45
Orthorhombic, $P2_12_12_1$
a = 10.364 (1) Å
b = 16.157 (1) Å
c = 23.206 (1) Å
V = 3885.9 (5) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 119 (2) K
0.34 × 0.34 × 0.15 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.97, T_{max} = 0.99
131111 measured reflections
10251 independent reflections
9109 reflections with $I > 2\sigma(I)$
R_{int} = 0.038

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.115
S = 1.04
10251 reflections
505 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.50 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O3*A*—H3*A*···O1*B*^{i}	0.82	2.15	2.937 (1)	160
O3*B*—H3*B*···O1*A*^{ii}	0.82	1.99	2.782 (1)	163
O2*B*—H2*B*···O5*A*	0.82	2.02	2.814 (1)	163
O5*B*—H5*B*···O1*B*^{iii}	0.82	2.65	3.192 (2)	125
O2*A*—H2*A*···O5*B*	0.82	2.07	2.823 (2)	153

Symmetry codes: (i) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (ii) $-x, y-\frac{1}{2}, -z+\frac{1}{2}$; (iii) $-x+\frac{1}{2}, -y+1, z-\frac{1}{2}$.

All H atoms were placed in calculated positions (O—H = 0.82 Å and C—H = 0.93–0.98 Å) and refined using a riding-model approximation [U_{iso}(H) = 1.5U_{eq}(C,O)]. The absolute configuration could not be determined (there is no atom heavier than F in the structure), and Friedel pairs were merged.

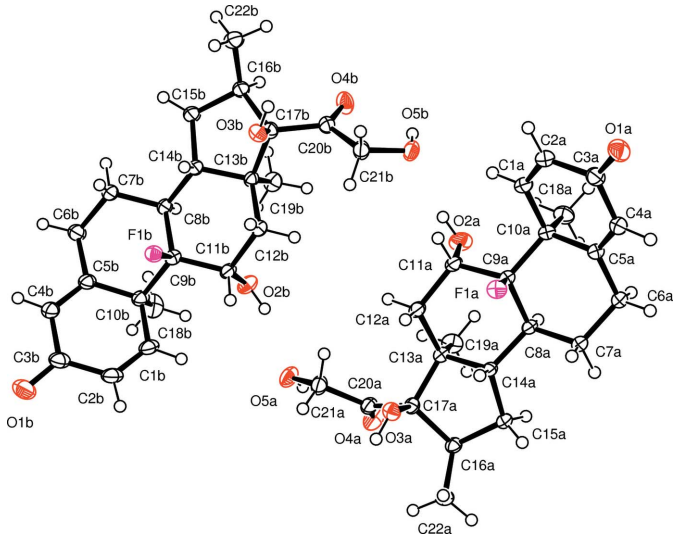


Figure 1
The asymmetric unit of (I). Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as spheres of an arbitrary radius.

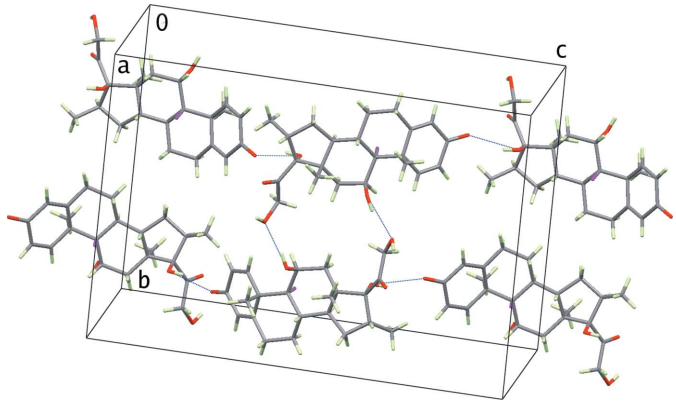


Figure 2
The layer formed by dexamethasone molecules. Hydrogen bonds are shown in blue.

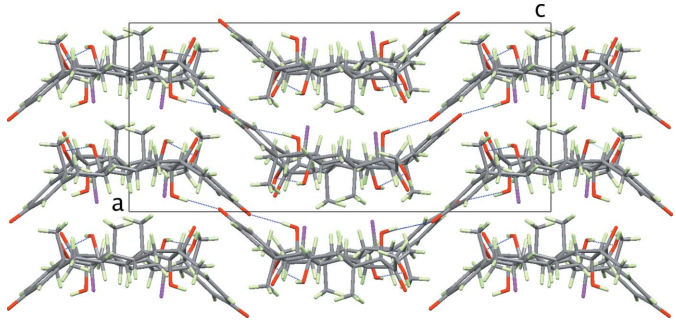


Figure 3
The arrangement of the dexamethasone layers, viewed along [010]. Hydrogen bonds are shown in blue.

Data collection: *HKL-2000* (Otwinowski & Minor, 1997); cell refinement: *HKL-2000*; data reduction: *HKL-2000*; program(s) used to solve structure: *HKL-3000SM* (Minor *et al.*, 2006) and *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *HKL-3000SM*

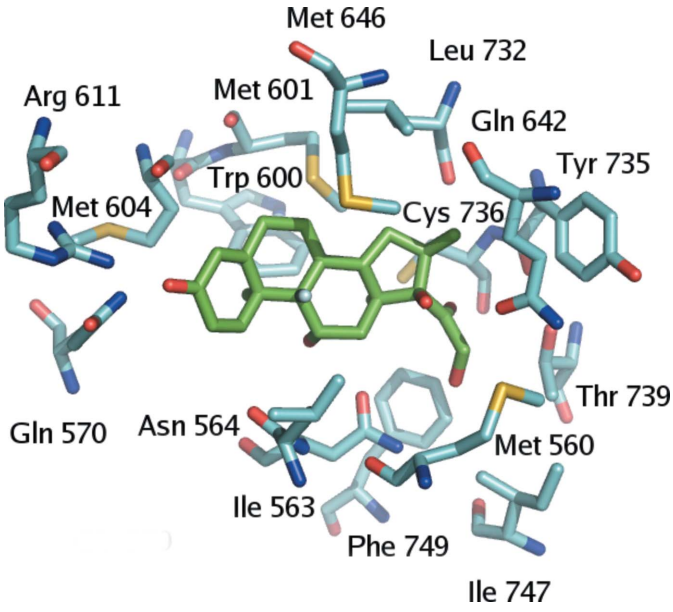


Figure 4
The dexamethasone molecule in the binding site in human glucocorticoid receptor (Bledsoe *et al.*, 2002).

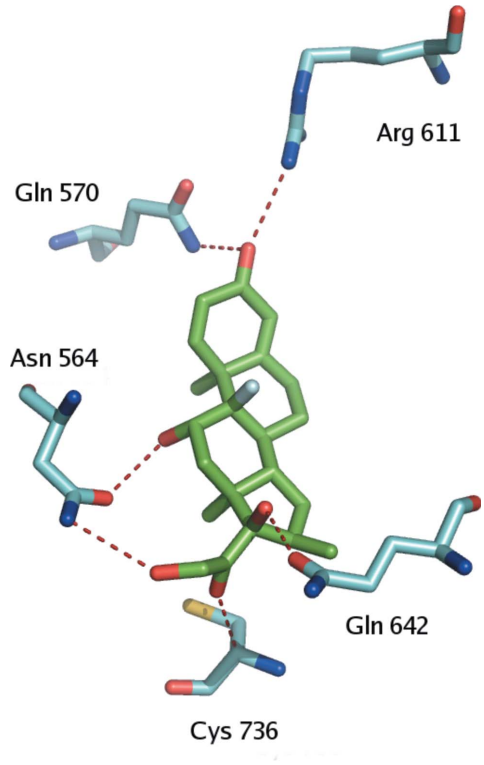


Figure 5
Hydrogen bonds between the dexamethasone and residues forming the binding site of the receptor.

and *SHELXL97* (Sheldrick, 1997); molecular graphics: *HKL-3000SM*, *ORTEPIII* (Burnett & Johnson, 1996), *ORTEP-3* (Farrugia, 1997), *Mercury* (Macrae *et al.*, 2006) and *PYMOL* (DeLano, 2002); software used to prepare material for publication: *HKL-3000SM*.

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