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Triamcinolone acetonide methanol 0.67-solvate at 170 K

Inke Jeß and Christian Näther*

Institut für Anorganische Chemie, Christian-Albrechts-Universität Kiel, Olshausenstrasse 40, D-24098 Kiel, Germany

Correspondence e-mail: cnaether@ac.uni-kiel.de

Key indicators

Single-crystal X-ray study
T = 170 K
Mean σ(C–C) = 0.004 Å
H-atom completeness 94%
Disorder in solvent or counterion
R factor = 0.037
wR factor = 0.095
Data-to-parameter ratio = 8.7

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

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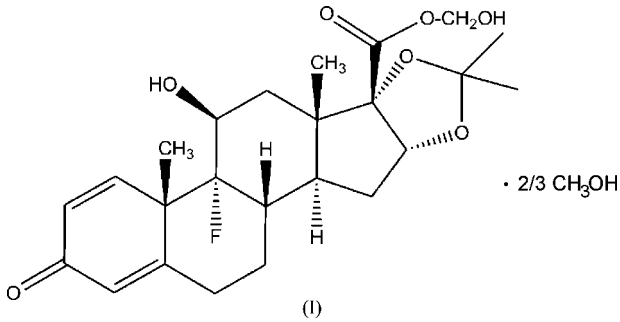
In the crystal structure of the title compound (systematic name: 9α-fluoro-11β,21-dihydroxy-16α,17α-isopropylidenedioxypregna-1,4-diene-3,20-dione methanol 0.67-solvate), $C_{24}H_{31}FO_6 \cdot 0.67CH_3OH$, the molecules are connected *via* O—H···O hydrogen bonding. In this arrangement, channels are formed which are elongated in the direction of the crystallographic *c* axis. In these channels, methanol molecules are included with the C atoms located on the threefold axis. Therefore, the O atoms are disordered over three orientations. One of the two crystallographically independent solvent molecules is connected to the triamcinolone acetonide molecules *via* O—H···O hydrogen bonding.

Comment

Triamcinolone acetonide is a synthetic glucocorticoid widely used in therapy against inflammatory and immune responses (Barnes, 1998; Buttgereit, 2000; Falkenstein *et al.*, 2000). We have investigated this drug as part of a project on the polymorphism and pseudopolymorphism of glucocorticoids. During these investigations, we have isolated two polymorphic modifications as well as the pseudopolymorph triamcinolone acetonide methanol solvate. The structure of this compound was first determined by Surcouf (1979) at room temperature, but two H atoms were not located and considered in the structure refinement. This included one C—H H atom as well as the O—H H atom at O6, which should be involved in O—H···O hydrogen bonding. Furthermore, some of the C—H H atoms showed a really unusual geometry. In addition, all C and O atoms of the methanol molecules were located on a threefold axis and the H atoms of the solvent were not located. Therefore, we have redetermined this structure at a lower temperature and we have located all H atoms of the triamcinolone acetonide molecule and one O—H H atom of the solvent. In addition, we have found a different disorder model for one of the solvent molecules.



(I)

In the crystal structure of the title compound, (I) (Fig. 1), the molecules are connected *via* O—H···O hydrogen bonding

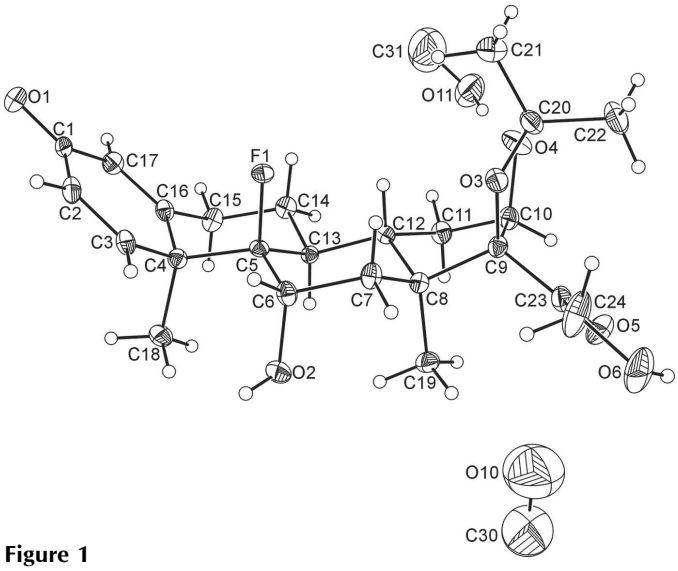


Figure 1
View of the the title compound, with the atom labelling and displacement ellipsoids drawn at the 50% probability level. Only one disorder component is shown.

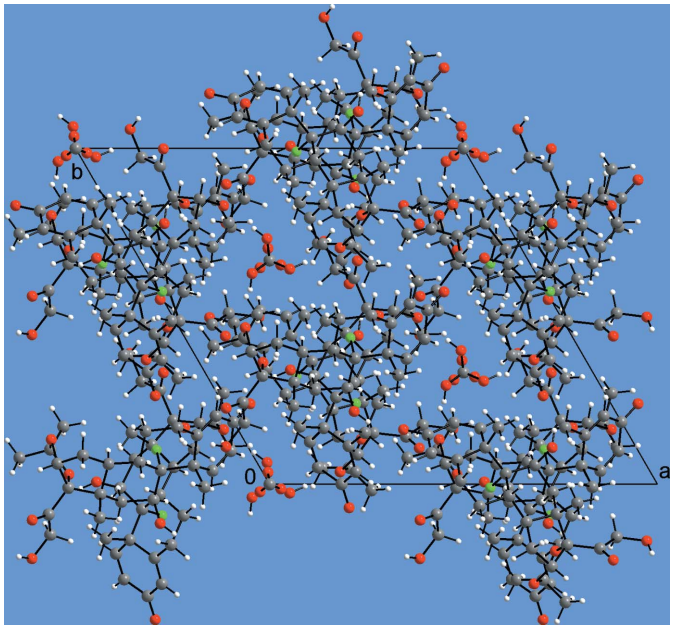


Figure 2
Crystal structure of the title compound, viewed along the *c* axis. The hydrogen bonding is not shown, but the disorder of the solvent molecules is shown.

between the hydroxyl H atom at O2 and carbonyl atom O1. The O—H distance of 2.03 Å, the O···O distance of 2.806 (3) Å and the O—H···O angle of 154° show that this is a relatively strong interaction (Table 1). Atom O2 is, in addition, a hydrogen-bond acceptor for the O—H H atom attached to O6, which was not located in the previous structure report (Surcouf, 1979). However, the intermolecular O···H distance is relatively long and this is therefore a much weaker interaction (Table 1). Channels are formed in the direction of the *c* axis in which the methanol molecules are located (Fig. 2).

There are two crystallographically independent methanol molecules in the asymmetric unit, both of which are located on a threefold axis. In the previous structure report, both C atoms and one of the two crystallographically independent O atoms are located exactly on the threefold axis, whereas the second O atom occupies a general position. Starting from this model, we obtained large anisotropic displacement parameters for the O atom in the special position and some residual electron density which was located at this O atom. If the structure was refined with this O atom (O10) in a general position, the anisotropic displacement parameters decreased, showing that this atom should not be located exactly on the threefold axis. In this case, this atom is disordered over three different positions due to symmetry. Each of these disordered O atoms has a short distance [2.56 (6) Å] to the hydroxyl atom O6, and an O—H···O hydrogen-bonding interaction can therefore be assumed. Unfortunately, the O—H H atom was not located in a difference map, possibly because it is disordered due to symmetry. In contrast, the H atom attached to the methanol atom O11 was located in a difference map; this was not the case in the previous structure report (Surcouf, 1979). This H atom exhibits a relatively strong hydrogen bond to carbonyl atom O4, with an O···H distance of 2.25 Å, an O···O distance of 3.073 (9) Å and an O—H···O angle of 168°.

Experimental

The title compound was obtained from HPP (Hommel Pharmaceuticals Production GmbH, Germany) as an enantiomerically pure compound and was recrystallized from methanol. The homogeneity was checked by X-ray powder diffraction. The compound decomposes at room temperature within a few hours.

Crystal data

$C_{24}H_{31}FO_6\cdot0.67CH_4O$
M_r = 455.85
Trigonal, *R*3
a = 17.8570 (9) Å
c = 18.0528 (11) Å
V = 4985.3 (5) Å^3
Z = 9
D_x = 1.367 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 6326 reflections
θ = 2.5–28°
μ = 0.10 mm^{-1}
T = 170 (2) K
Block, colourless
0.4 × 0.3 × 0.2 mm

Data collection

Stoe IPDS-1 diffractometer
φ scans
Absorption correction: none
6326 measured reflections
2667 independent reflections
2394 reflections with $I > 2\sigma(I)$
R_{int} = 0.030
θ_{max} = 28.0°
h = −23 → 16
k = −23 → 23
l = −22 → 23

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.095
S = 1.03
2667 reflections
305 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.067P)^2 + 0.8013P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0049 (6)

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

D—H···A	D—H	H···A	D···A	D—H···A
O2—H1*O*2···O1^{i}	0.84	2.03	2.806 (3)	154
O6—H1*O*6···O2^{ii}	0.84	2.50	3.307 (3)	161
O11—H11*O*···O4	0.84	2.25	3.073 (9)	168

Symmetry codes: (i) $-y+1, x-y-1, z$; (ii) $-y, x-y-1, z$.

All H atoms of the triamcinolone acetonide were found in a difference map. However, the C—H H atoms of the triamcinolone acetonide molecule were repositioned with idealized geometry and were refined with fixed isotropic displacement parameters, with U_{iso}(H)= 1.5U_{eq}(C) for methyl H atoms and U_{iso}(H) = 1.2U_{eq}(C) for methine, aromatic and methylene H atoms, using a riding model with C—H = 0.98 Å for methyl, 1.00 Å for methine, 0.99 Å for methylene and 0.95 Å for aromatic H atoms. The O—H H atoms were located in a difference map, their bond lengths set to ideal values and were refined with fixed isotropic displacement parameters [U_{iso}(H)= 1.5U_{eq}(O)], using a riding model with O—H = 0.94 Å. The methyl H atoms of both, and the O—H H atom of one of the two crystallographically independent methanol molecules were not located. In the absence of significant anomalous scattering, Friedel pairs were merged. The absolute configuration was assigned according to the known absolute configuration of the starting material.

Data collection: *IPDS Program Package* (Stoe & Cie, 1998); cell refinement: *IPDS Program Package*; data reduction: *IPDS Program Package*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997; program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL* (Bruker, 1998); software used to prepare material for publication: *CIFTAB* in *SHELXTL*.

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