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Triamcinolone diacetate chloroform solvate

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In the crystal structure of the title compound, 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione chloroform solvate, $C_{25}H_{31}FO_8\cdot CHCl_3$, the molecules are connected *via* O—H···O hydrogen bonding. Channels, in which the chloroform molecules are located, are formed in the direction of the crystallographic *a* axis.

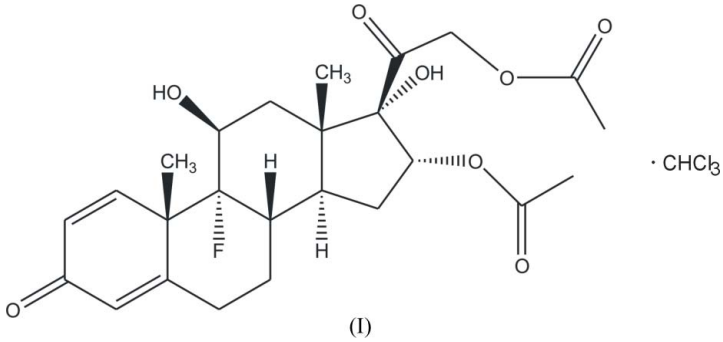
Key indicators

Single-crystal X-ray study
T = 170 K
Mean σ(C–C) = 0.004 Å
R factor = 0.047
wR factor = 0.122
Data-to-parameter ratio = 17.7

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

Comment

Triamcinolone diacetate, also known as 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxyl-1,4-pregnadiene-3,20-dione or 9α-fluoro-16α-prednisolone-16α,21-diacetate, belongs to the class of glucocorticoids which are adrenal cortical hormones.



(I)

Synthetic and natural glucocorticoids are amongst the most effective drugs against inflammatory and immune responses (Barnes, 1998; Buttgereit, 2000; Falkenstein *et al.*, 2000). They are essential for chronic inflammatory disease therapy for multiple sclerosis, rheumatoid arthritis, allergic asthma and Morbus Crohn, and also for severe symptoms of psoriasis and allergic dermatitis. In the human body, glucocorticoids are a part of many catabolic processes. This is the reason why, in long-term treatment, glucocorticoids show some adverse effects, such as decomposition of skeletal muscles and skin atrophy. In some cases, a reallocation of adipose tissues (Cushing's syndrome) and osteoporosis are observed. One very important glucocorticoid is triamcinolone, which has been used in therapy for several decades, mainly as the acetonide and the diacetate. Despite their great importance, no crystal structures are available in the Cambridge Structural Database (CSD) for the diacetate or the pure triamcinolone (Allen, 2002; *ConQuest* Version 1.6, CSD Version 5.26 of November 2004). The acetonide has been structurally characterized only as a methanol solvate (Surcouf, 1979).

The structure determination of the title compound was performed as a part of a project on the polymorphism of glucocorticoids. During these investigations we have isolated triamcinolone diacetate as a chloroform solvate.

In the crystal structure of the title compound, (I) (Fig. 1), the molecules are connected *via* O—H···O hydrogen bonding between the hydroxyl H atom at O2 and carbonyl atom O8, and between the hydroxyl H atom at O3 and carbonyl atom O1 (Fig. 2 and Table 1). The O···O distances and O—H···O angles show that these are strong interactions (Table 1). In the direction of the *a* axis, channels are formed in which the chloroform molecules are located (Fig. 2).

Experimental

The title compound was obtained from HPP (Hommel Pharmaceuticals Production GmbH, Germany) as an enantiopure compound and was recrystallized from chloroform. The homogeneity was confirmed by X-ray powder diffraction. The compound decomposes at room temperature within a few days.

Crystal data

$C_{25}H_{31}FO_8{\cdot}CHCl_3$
M_r = 597.87
Orthorhombic, $P2_12_12_1$
a = 8.0465 (4) Å
b = 14.5972 (7) Å
c = 23.7454 (14) Å
V = 2789.0 (3) Å^3
Z = 4
D_x = 1.424 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 8000 reflections
θ = 11.6–25°
μ = 0.38 mm^{-1}
T = 170 (2) K
Block, colourless
0.2 × 0.2 × 0.15 mm

Data collection

Stoe IPDS-1 diffractometer
φ scans
Absorption correction: none
17821 measured reflections
6150 independent reflections
4683 reflections with $I > 2\sigma(I)$
R_{int} = 0.054
θ_{max} = 27.1°
$h = -10 \rightarrow 8$
$k = -18 \rightarrow 16$
$l = -30 \rightarrow 30$

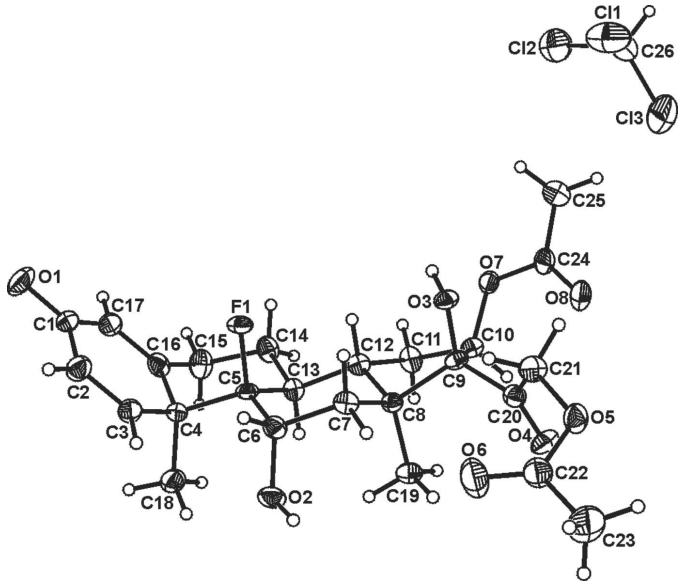


Figure 1
View of the asymmetric unit of (I), showing the atom labelling scheme and with displacement ellipsoids drawn at the 50% probability level.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.122
S = 1.03
6150 reflections
347 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0585P)^2 + 1.0803P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.59 e Å^{-3}
$\Delta\rho_{min}$ = −0.45 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0083 (12)
Absolute structure: Flack (1983), with 2672 Friedel pairs
Flack parameter: 0.06 (8)

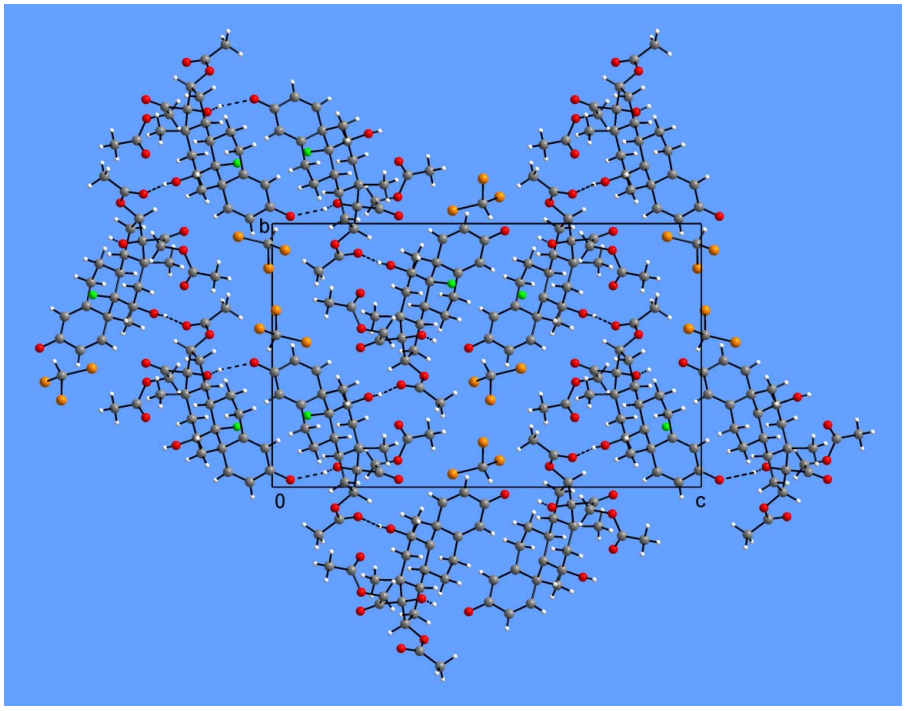


Figure 2
The crystal structure of (I), viewed along the *a* axis (hydrogen bonds are shown as dashed lines).

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

D—H···A	D—H	H···A	D···A	D—H···A
O2—H1$O2$···O8^{i}	0.84	1.92	2.750 (3)	169
O3—H1$O3$···O1^{ii}	0.84	1.95	2.747 (3)	157

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

The H atoms were positioned with idealized geometry and were refined with fixed isotropic displacement parameters [U_{iso}(H) = 1.2U_{eq}(C)] using a riding model, with C—H = 0.95 Å for olefin, 1.00 Å for methine and 0.99 Å for methylene H atoms. The positions of the methyl (except C18 and C19) and hydroxy H atoms were idealized (C—H = 0.98 Å and O—H = 0.84 Å), then refined with fixed isotropic displacement parameters [U_{iso}(H)= 1.5U_{eq}(C,O)] as rigid groups allowed to rotate but not tip. Although the absolute configuration was known in advance, it was additionally determined on the basis of anomalous scattering effects.

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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