

## Betamethasone dipropionate

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## Key indicators

Single-crystal X-ray study  
 T = 293 K  
 Mean  $\sigma(\text{C}-\text{C}) = 0.006 \text{ \AA}$   
 Disorder in main residue  
 R factor = 0.059  
 wR factor = 0.174  
 Data-to-parameter ratio = 8.8

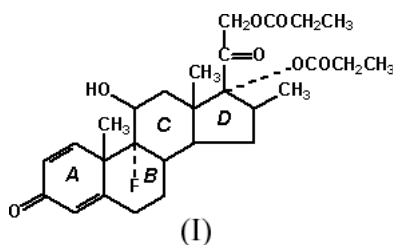
For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

The title compound (systematic name: 9 $\alpha$ -fluoro-11 $\beta$ ,17 $\alpha$ ,21-trihydroxy-16 $\beta$ -methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropionate, BMDP),  $\text{C}_{28}\text{H}_{37}\text{FO}_7$ , crystallizes in the orthorhombic space group  $P2_12_12_1$ . The overall shape of the steroid skeleton is similar to that of other anti-inflammatory steroids. Ring A is planar due to the 1,4-dien-3-one moiety, rings B and C have normal chair conformations and ring D adopts an envelope conformation.

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## Comment

Betamethasone dipropionate, an anti-inflammatory steroid, has been synthesized and used as an asthma drug since 1979 (Piitaa, 1979). Compared with beclomethasone dipropionate, another efficient asthma drug (Duax *et al.*, 1981), the present compound contains a smaller F atom in place of a Cl atom at the 9 $\alpha$  position. We report here the crystal structure of BMDP, (I), which was elucidated by X-ray diffraction analysis.



Compound (I) crystallizes in the orthorhombic space group  $P2_12_12_1$  and the overall shape of the steroid skeleton is similar to that of beclomethasone dipropionate (Duax *et al.*, 1981) and some other anti-inflammatory steroids, such as dexamethasone (Rohrer & Duax, 1977) or a 1,4-dien-3-one-6 $\alpha$ -hydroxy steroid (Nakai, 1991). As shown in Fig. 1, ring A is planar due to the 1,4-dien-3-one moiety, rings B and C have normal chair conformations and ring D adopts an envelope conformation. All the bond lengths and valence angles are comparable to those observed in other steroid compounds (Duax & Norton, 1975). Substitution at the 17 $\alpha$  and 23 positions restricts the conformational flexibility of the 17 $\alpha$  side chain, resulting in a C16–C17–C18–O3 torsion angle of  $-36.0(5)^\circ$ , which is in the range observed for other 17 $\alpha$ -substituted steroids (Duax *et al.*, 1980).

## Experimental

BMDP was obtained from Tianjin Tianyao Pharmaceutical Co. Ltd. Colorless single crystals were obtained by slow diffusion of hexane into an acetone solution of (I) (m.p.: 451–453 K); analysis calculated

for  $C_{28}H_{37}FO_7$ ; C 66.59, H 7.33%; found: C 66.26, H 7.45%. IR (KBr): 3300 (s), 2940 (s), 1733 (vs), 1663 (vs), 1607 (vs), 1461 (m), 1392 (s), 1289 (m), 1204 (m), 1144 (w), 1066 (s), 1034 (m), 1012 (m), 983 (w), 957 (w), 888 (s), 811 (w), 696 (s), 629 (w)  $cm^{-1}$ .

#### Crystal data

$C_{28}H_{37}FO_7$   
 $M_r = 504.58$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 11.883$  (4) Å  
 $b = 13.833$  (4) Å  
 $c = 15.737$  (5) Å  
 $V = 2587$  (1) Å<sup>3</sup>  
 $Z = 4$   
 $D_x = 1.296$  Mg m<sup>-3</sup>

Mo  $K\alpha$  radiation  
 Cell parameters from 983 reflections  
 $\theta = 3.0\text{--}25.5^\circ$   
 $\mu = 0.10$  mm<sup>-1</sup>  
 $T = 293$  (2) K  
 Block, colorless  
 $0.26 \times 0.24 \times 0.24$  mm

#### Data collection

Bruker SMART CCD area-detector diffractometer  
 $\varphi$  and  $\omega$  scans  
 Absorption correction: multi-scan (SADABS; Sheldrick, 1996; Blessing, 1995)  
 $T_{min} = 0.975$ ,  $T_{max} = 0.977$   
 14862 measured reflections

2982 independent reflections  
 2310 reflections with  $I > 2\sigma(I)$   
 $R_{int} = 0.036$   
 $\theta_{max} = 26.4^\circ$   
 $h = -6 \rightarrow 14$   
 $k = -17 \rightarrow 16$   
 $l = -19 \rightarrow 19$

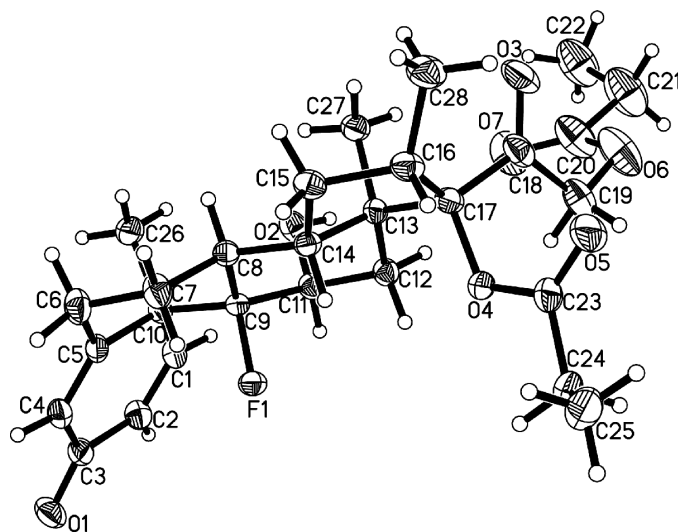
#### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.059$   
 $wR(F^2) = 0.174$   
 $S = 1.09$   
 2982 reflections  
 339 parameters  
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0998P)^2 + 0.9843P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} = 0.002$   
 $\Delta\rho_{max} = 0.63$  e Å<sup>-3</sup>  
 $\Delta\rho_{min} = -0.37$  e Å<sup>-3</sup>

H atoms were positioned geometrically and refined using a riding model, with O—H distances of 0.82 Å and C—H distances in the range 0.93–0.98 Å, and with  $U_{iso}(H) = 1.2U_{eq}(O)$  and  $1.5U_{eq}(C)$ . The propionyl group in (I) is disordered and was refined isotropically with restraints containing EADP C21 C22, C21' C22' and C20 C20'; DFIX 1.24 0.01 O7 C20 O7' C20', 1.54 0.01 C20 C21 C21 C22 C20' C21' C21' C22', 2.52 0.01 C20 C22 C20' C22', 1.4 0.01 O6 C20 O6 C20', 1.45 0.01 O6 C19 and FLAT 0.01 O6 O7 C20 C21, O6 O7' C20' C21', resulting in occupancy factors of 23 and 77% for the two parts, respectively. In the absence of significant anomalous scattering effects, the Friedel pairs were merged.

Data collection: SMART (Bruker, 1998); cell refinement: SMART; data reduction: SAINT (Bruker, 1998); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine



**Figure 1**

Molecular structure of the title compound with the atom-labeling scheme. Displacement ellipsoids are drawn at the 30% probability level and the minor disorder components have been omitted.

structure: SHELXL97 (Sheldrick, 1997); molecular graphics: SHELXTL (Bruker, 1998); software used to prepare material for publication: SHELXTL.

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