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16β-Bromo-17α-hydroxypregn-4-ene-3,11,20-trione methanol solvate

Zhang Haitao,* Qiang Nie, Ying Chen, Jingkang Wang and Lina Zhou

School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, People's Republic of China

Correspondence e-mail: cheny_79@yahoo.com.cn

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.036
wR factor = 0.081
Data-to-parameter ratio = 19.0

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

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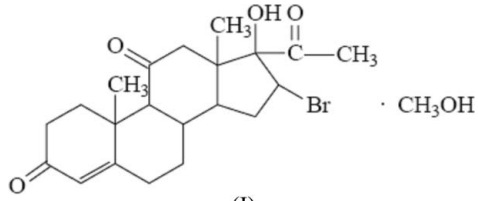
16β-Bromo-17α-hydroxy-pregn-4-ene-3,11,20-trione, $C_{21}H_{27}BrO_4\cdot CH_4O$, is an important intermediate in the synthesis of hormone pharmaceuticals. The crystal structure of its methanol solvate is reported in this paper. The structure is stabilized by strong intermolecular O—H···O hydrogen bonds.

Comment

The main molecule of the title compound is an important steroid compound, which serves as an intermediate for many hormone pharmaceuticals (Xu, 2001). It was first reported in 1955 during the the syntheses of some corticosteroids (Ercoli *et al.*, 1955). Later, ^{1}H and ^{13}C NMR data were used to establish the atomic connectivity (Duddeck *et al.*, 1986; Kirk *et al.*, 1990), but its single-crystal strucure has not yet been reported.



(I)

Here we report the crystal structure of the methanol solvate, (I), which crystallizes in the non-centrosymmetric space group $P2_12_12_1$. The asymmetric unit consists of one steroid molecule and one methanol molecule (Fig. 1). The main molecule shows a typical steroid skeleton with three six-membered rings, *viz.* *A* (C1–C5/C10), *B* (C5–C10) and *C* (C8/C9/C11–C14) and one five-membered ring, *D* (C13–C17). Ring *A* has a 1α-sofa conformation, while rings *B* and *C* are in chair conformations; the puckering parameters (Cremer & Pople, 1975) are φ_2 = 14.83 (1)°, θ_2 = 53.8 (2)° and Q_T =

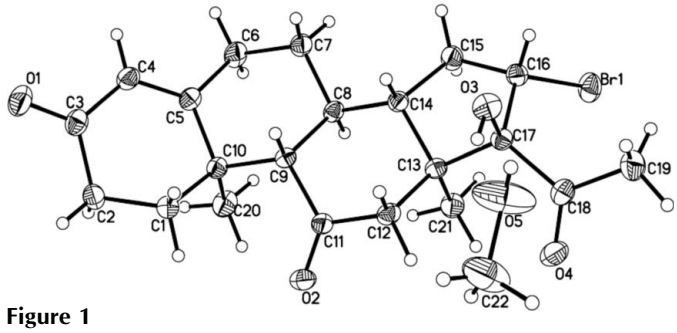


Figure 1
The molecular structure (I) with displacement ellipsoids drawn at the 30% probability level (arbitrary spheres for H atoms).

0.452 (1) Å for ring *A*, φ_2 = 169.44 (2)°, θ_2 = 8.2 (2)° and Q_T = 0.531 (1) Å for ring *B*, and φ_2 = 107.56 (1)°, θ_2 = 10.3 (2)° and Q_T = 0.574 (1) Å for ring *C*. Refinement of the Flack (1983) parameter indicated that the well defined chiral centres in the main molecule in (I) have the following configurations: C8 *S*, C9 *S*, C10 R, C13 *S*, C14 *S*, C16 *S* and C17 *R*.

O—H···O hydrogen bonds (Table 1) help to establish the crystal packing in (I). Atom O5 of the methanol solvent is involved in a pair of hydrogen bonds: in one of them it acts as the acceptor atom and in the other as the donor. In this way, a [100] molecular chain arising from the helicoidal 2_1 axis is generated.

Experimental

11α-Hydroxy-16α,17-epoxyprogesterone (1.0 g, provided by Tianjin Tianyao Pharmaceutical Co. Ltd.) was dissolved in pyridine (10.0 ml) and treated with chromium trioxide (0.25 g) at room temperature overnight. The product was purified by column chromatography and recrystallization from acetone–hexane (1:2 *v*/*v*, 30 ml). The product was then treated with hydrobromic acid (2.0 ml, 40%) in acetic acid (10 ml) solution. The product was crystallized and dried. Colorless prismatic single crystals of (I) suitable for X-ray diffraction were obtained by slow natural evaporation of a methanol solution (5 ml) at room temperature. The melting point determined by DSC is 472 K; before melting a desolvation occurs at 418 K.

Crystal data

$C_{21}H_{27}BrO_4\cdot CH_4O$
M_r = 455.38
Orthorhombic, $P2_12_12_1$
a = 8.6030 (17) Å
b = 12.235 (2) Å
c = 20.001 (4) Å
V = 2105.3 (7) Å^3
Z = 4
D_x = 1.437 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 1.98 mm^{-1}
T = 293 (2) K
Block, colorless
0.24 × 0.24 × 0.22 mm

Data collection

Rigaku R-AXIS RAPID IP area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)
T_{min} = 0.648, T_{max} = 0.670
20576 measured reflections
4815 independent reflections
4133 reflections with $I > 2\sigma(I)$
R_{int} = 0.054
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.081
S = 0.97
4815 reflections
254 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.030P)^2 + 0.8713P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.40 e Å^{-3}
Absolute structure: Flack (1983), 2065 Friedel pairs
Flack parameter: 0.016 (8)

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

D—H···A	D—H	H···A	D···A	D—H···A
O5—H5···O1^{i}	0.82	2.06	2.823 (4)	155
O3—H3A···O5	0.82	1.93	2.674 (3)	150

Symmetry code: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, -z+2$.

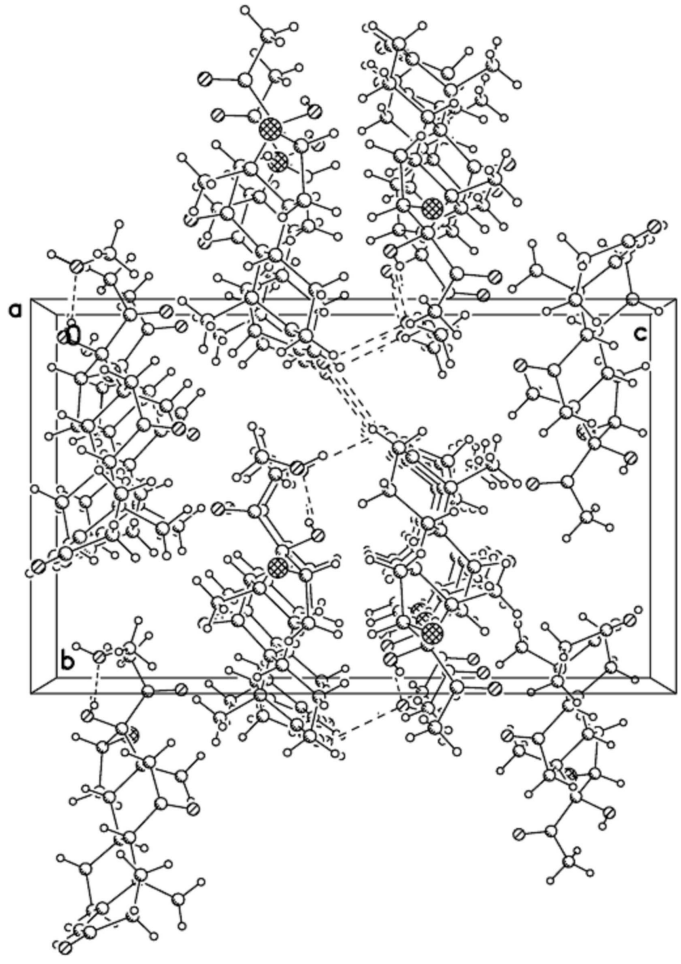


Figure 2
The molecular packing of (I), viewed along the *a* axis, with H bonds indicated by dashed lines.

H atoms were placed in calculated positions (O—H = 0.82 Å, C—H = 0.93–0.98 Å) and refined as riding with U_{iso}(H) = 1.2U_{eq}(C,O) or 1.5U_{eq}(methyl C).

Data collection: *RAPID-AUTO* (Rigaku, date); cell refinement: *RAPID-AUTO*; data reduction: *RAPID-AUTO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL97* (Bruker, 1998); software used to prepare material for publication: *SHELXTL97*.

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