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

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The title compound (systematic name: 17-acetyl-16-bromo-17-hydroxy-10,13-dimethyl-1,6,7,8,9,10,12,13,14, 15,16,17-dodecahydro-2*H*-cyclopenta[*a*]phenanthrene-3,11-dione chloroform solvate), $C_{21}H_{27}BrO_4\cdot CHCl_3$, is an important intermediate in the synthesis of hormone pharmaceuticals. The asymmetric unit consists of one steroid and one chloroform molecule. The crystal structure is predominantly stabilized by strong intermolecular O—H···O hydrogen bonds.

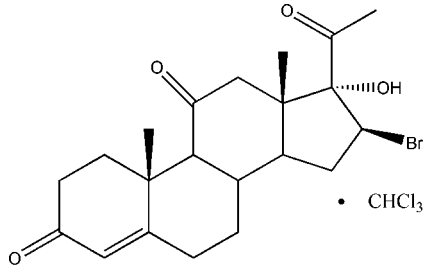
Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
R factor = 0.042
wR factor = 0.091
Data-to-parameter ratio = 14.7

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

Comment

The title compound, (I), is an important steroid compound which serves as an intermediate of many hormone pharmaceuticals (Xu, 2001). It was first reported in 1955 for the syntheses of some corticosteroids (Ercoli *et al.*, 1955). Until now, only ^{1}H and ^{13}C NMR spectra have been measured to determine its chemical structure (Duddeck *et al.*, 1986; Kirk *et al.*, 1990). The single-crystal structure has not previously been reported.



(I)

The asymmetric unit contains one steroid and one chloroform molecule (Fig. 1). Bond lengths and angles (Table 1) are in normal ranges (Allen *et al.*, 1987). The steroid molecule has a typical structure 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 = 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*.

The crystal structure is predominantly stabilized by intermolecular O—H···O hydrogen bonds, as well as Cl1′···O3 [3.105 (3) Å] close contacts (Table 2 and Fig. 2).

Experimental

11α-Hydroxy-16α,17-epoxyprogesterone (1.0 g, 3 mmol) (provided by Tianjin Tianyao Pharmaceutical Co. Ltd) was dissolved in pyridine

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(10 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 resulting product was treated with hydrobromic acid (2 ml, 40%) in an acetic acid (10 ml) solution, crystallized and dried. Colorless single crystals suitable for X-ray diffraction were obtained by slow natural evaporation of a chloroform solution (5 ml) at room temperature. The melting point determined by DSC is 472.2 K and, before melting, desolvation occurs at 368.2 K.

Crystal data

$C_{21}H_{27}BrO_4\cdot CHCl_3$	$Z = 4$
$M_r = 542.70$	$D_x = 1.480$ Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 10.443$ (2) Å	$\mu = 2.04$ mm^{-1}
$b = 12.324$ (3) Å	$T = 296$ (2) K
$c = 18.927$ (4) Å	Plate, colorless
$V = 2435.9$ (9) Å^3	0.23 × 0.18 × 0.05 mm

Data collection

Rigaku R-AXIS RAPID IP area-detector diffractometer	20190 measured reflections
φ ω scans	4527 independent reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)	3310 reflections with $I > 2\sigma(I)$
$T_{min} = 0.648$, $T_{max} = 0.901$	$R_{int} = 0.082$
	$\theta_{max} = 25.5°$

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} = 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.042$	$\Delta\rho_{max} = 0.27$ e Å^{-3}
$wR(F^2) = 0.091$	$\Delta\rho_{min} = -0.30$ e Å^{-3}
$S = 0.95$	Extinction correction: *SHELXL97*
4527 reflections	Extinction coefficient: 0.0070 (11)
309 parameters	Absolute structure: Flack (1983), with 1972 Friedel pairs
H-atom parameters constrained	Flack parameter: 0.01 (1)
$w = 1/[\sigma^2(F_o^2) + (0.0364P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	

Table 1
Selected geometric parameters (Å, °).

Br1—C16	1.964 (3)	C3—O1	1.285 (12)
Cl1—C22	1.709 (6)	C11—O2	1.225 (4)
Cl2—C22	1.802 (5)	C17—O3	1.421 (4)
Cl3—C22	1.765 (7)	C18—O4	1.211 (4)
O1—C3—C4	115.8 (8)	C18—C17—C16	115.2 (3)
O2—C11—C9	122.8 (3)	O3—C17—C13	106.5 (2)
C15—C16—Br1	111.4 (2)	O4—C18—C17	122.7 (3)
C17—C16—Br1	113.8 (2)	Cl1—C22—Cl3	100.0 (4)
O3—C17—C18	104.7 (3)	Cl1—C22—Cl2	88.2 (5)
O3—C17—C16	109.5 (3)	Cl3—C22—Cl2	105.5 (5)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3*A*···O2^{i}	0.82	2.01	2.819 (3)	169

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

H atoms were positioned geometrically, with O—H = 0.82 Å and C—H = 0.93, 0.96, 0.97 and 0.98 Å for aromatic, methyl, methylene and methine H atoms, respectively, and constrained to ride on their parent atoms, with $U_{iso}(H) = xU_{eq}(C,O)$, where $x = 1.2$ for aromatic and methylene H atoms, and $x = 1.5$ for all other H atoms. The refinement of the Flack (1983) parameter confirms that, as expected, the chiral centers retain their original configurations during the synthesis. Atom O1 in the steroid molecule and the three Cl atoms of the chloroform solvent molecule were refined with statistical disorder over two positions, with partial site occupancies of 0.488 (9) for Cl1, Cl2, Cl3 and O1, and 0.512 (9) for Cl1′, Cl2′, Cl3′ and O1′.

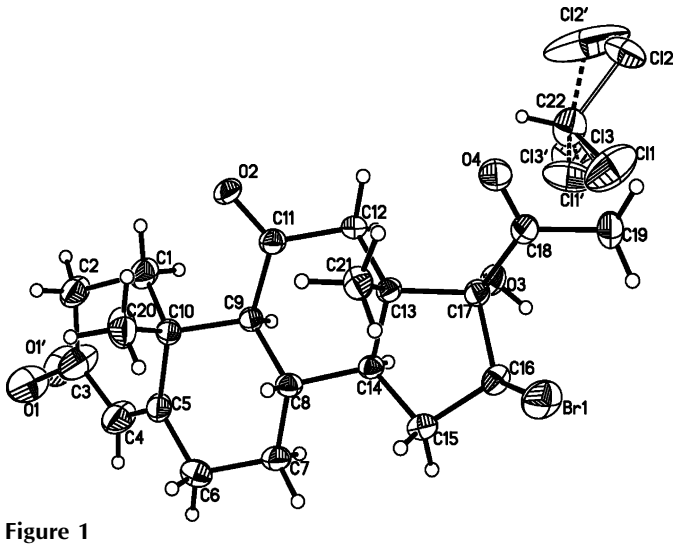

Figure 1
The asymmetric unit, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Both disorder components are shown.

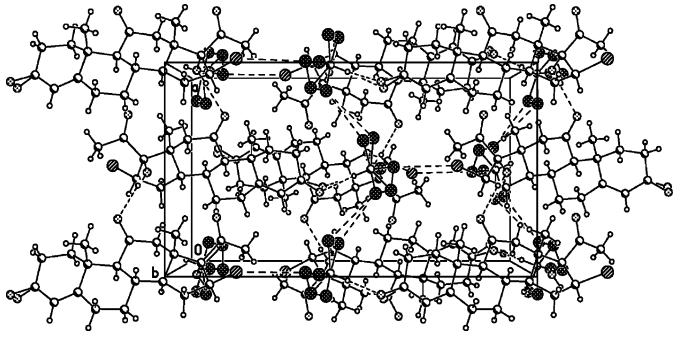

Figure 2
A packing diagram of (I), viewed down the *b* axis. Hydrogen bonds and close contacts are shown as dashed lines. Only one disorder component is shown.

Data collection: *RAPID-AUTO* (Rigaku, 2004); 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: *SHELXTL* (Bruker, 1998); software used to prepare material for publication: *SHELXTL*.

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References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.

Bruker (1998). *SMART*, *SAINT* and *SHELXTL*. Bruker AXS Inc., Madison. Wisconsin, USA.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Duddeck, H., Rosenbaum, D., Hani, M., Elgamal, A. & Fayez, M. B. E. (1986). *Magn. Reson. Chem.* **24**, 999–1003.
Ercoli, A., De Ruggieri, P. & Della Morte, D. (1955). *Gazz. Chim. Ital.* **85**, 628–638.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Kirk, D. N., Toms, H. C., Douglas, C., White, K. A., Smith, K. E., Latif, S. & Hubbard, R. W. P. (1990). *J. Chem. Soc. Perkin Trans. 2*, pp. 1567–1594.
Rigaku (2004). *RAPID-AUTO*. Rigaku Corporation, Tokyo, Japan.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Xu, G. (2001). *Handbook of Pharmaceutical Intermediates II*, p.143. Beijing: Chemical Industry Press. (In Chinese.)