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Methyl 4β-bromo-7α-cathyloxy-3-oxo-5β-cholanoate

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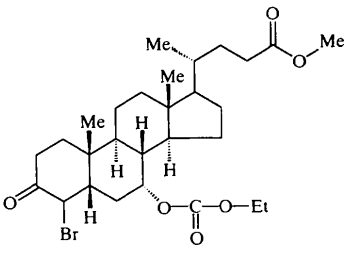
Abstract

In the title compound, methyl 4β-bromo-7α-ethoxycarbonyloxy-3-oxo-5β-cholanoate, $C_{28}H_{43}BrO_6$, the Br—C4 bond is oriented equatorially and (−)-antiperiplanar with respect to the C5—C10 bond. The six-membered rings (*A*, *B* and *C*) have the usual chair conformations, while the five-membered ring (*D*) adopts a distorted 13β,14α-half-chair conformation. The *A*/*B* ring junction is *cis*, and the *B*/*C* and *C*/*D* ring junctions are both *trans*.

Comment

Reduction of bromoketones and elimination reactions involving the halohydrines obtained allows the introduction of double bonds in specific positions of a molecule (Cristol & Rademacher, 1959). This procedure has been used to obtain analogues of brassinosteroids with a 3,4-diol moiety in the *A* ring from 3α,7α-dihydroxy-5β-cholanoic acid (chenodeoxycholic acid) (data not published). We report here the crystal structure of methyl 4β-bromine-7α-cathyloxy-3-oxo-5β-cholanoate, (I), the starting material used in the synthesis of analogues of brassinosteroids.



(I)

The absolute configuration, determined from the refinement of the Flack (1983) parameter in the X-ray analysis, confirmed that predicted beforehand from the synthesis route. The Br—C4 bond is oriented equatorially and (−)-antiperiplanar with respect to the C5—C10 bond. The presence of the Br atom does not disturb the chair conformation in ring *A* of the steroidal nucleus. Ring *A* has a symmetrical chair conformation, with all asymmetry parameters below 8.8 (5)° (Duax *et al.*, 1976). Rotational symmetry is dominant; a pseudo-C_2 axis intercepts the C1—C2 bond [asymmetry parameters: ΔC_2(C1—C2) = 2.5 (5), ΔC_S(C1) = 3.2 (4) and ΔC_S(C3) = 8.0 (4)°]. The modulus of the ring *A* torsion angles is in the range 46.59 (5)–57.76 (6)°. Rings *B* and *C* have the expected chair conformations (Pfeiffer *et al.*, 1985). The five-membered ring (*D*) adopts a distorted 13β,14α-half-chair conformation (Altona *et al.*, 1968). The *A*/*B* ring junction is *cis*, and the *B*/*C* and *C*/*D* ring junctions are both *trans*. The packing of the molecules is assumed to be dictated by van der Waals interactions, and by intramolecular and intermolecular C—H···O hydrogen bonds (Taylor & Kennard, 1982).

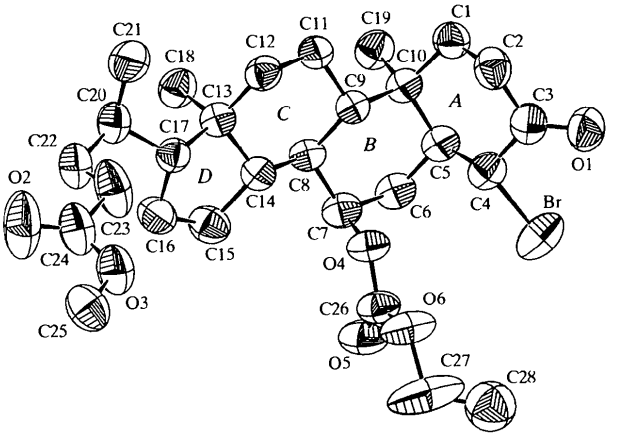


Fig. 1. Plot showing the atomic numbering scheme of the title compound. Displacement ellipsoids are drawn at the 50% probability level for non-H atoms and H atoms have been omitted for clarity.

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Experimental

The title compound was synthesized from methylchenodeoxycholic acid by cathylation, selective deprotection, oxidation and bromination procedures. The dicathylate was obtained by reaction of methyl chenodeoxycholanate with ethyl chloroformate, followed by selective deprotection with potassium carbonate and methanol to afford 3α-hydroxy-7α-cathyloxy-5β-cholanoic acid. Oxidation of the monocathylate with Jones' reagent yielded the ketone, which was brominated with bromine and acetic acid to afford 4β-bromo-7α-cathyloxy-3-oxo-5β-cholanoic acid. The bromoketone compound was purified by column chromatography and crystals were obtained by slow evaporation of an *n*-hexane/ethyl acetate (1:1) solution.

Crystal data

$C_{28}H_{43}BrO_6$
M_r = 555.55
Orthorhombic
$P2_12_12_1$
a = 7.7585 (5) Å
b = 15.606 (1) Å
c = 22.8759 (9) Å
V = 2769.8 (3) Å^3
Z = 4
D_x = 1.3322 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 78 reflections
θ = 7.7–56.3°
μ = 2.335 mm^{-1}
T = 293 (2) K
Prism
0.40 × 0.24 × 0.14 mm
Colourless

Data collection

Siemens *P*4 four-circle diffractometer
$2\theta/\omega$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.373, T_{max} = 0.721
3609 measured reflections
3092 independent reflections (plus 306 Friedel-related reflections)

2803 reflections with $F > 2\sigma(F)$
R_{int} = 0.027
θ_{max} = 68.99°
$h = -1 \rightarrow 8$
$k = -1 \rightarrow 18$
$l = -27 \rightarrow 1$
3 standard reflections
every 100 reflections
intensity decay: <1.0%

Refinement

Refinement on F^2
$R(F)$ = 0.044
$wR(F^2)$ = 0.138
S = 1.071
3398 reflections
320 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0727P)^2 + 1.1796P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.304 e Å^{-3}
$\Delta\rho_{min}$ = −0.344 e Å^{-3}

Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0052 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = −0.01 (3)

Table 1. *Selected geometric parameters (Å, °)*

Br—C4	1.946 (5)	O4—C7	1.473 (6)
O1—C3	1.212 (6)	O4—C26	1.325 (7)
O2—C24	1.181 (7)	O5—C26	1.186 (7)
O3—C24	1.311 (8)	O6—C26	1.334 (8)
O3—C25	1.433 (6)	O6—C27	1.475 (11)
C24—O3—C25	116.8 (4)	O4—C7—C6	109.0 (4)
C7—O4—C26	115.8 (4)	O4—C7—C8	106.2 (4)
C26—O6—C27	114.7 (6)	O2—C24—O3	123.3 (5)
C2—C1—C10	115.5 (4)	O2—C24—C23	125.6 (6)
O1—C3—C2	122.1 (6)	O3—C24—C23	111.1 (5)
O1—C3—C4	123.3 (5)	O4—C26—O5	127.7 (6)
Br—C4—C3	110.2 (3)	O4—C26—O6	105.7 (5)
Br—C4—C5	111.1 (3)	O5—C26—O6	126.6 (6)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2*B*···O5^{i}	0.97	2.51	3.383 (7)	150
C4—H4···O4	0.98	2.30	3.002 (6)	128
C6—H6*A*···Br	0.97	2.74	3.285 (5)	116
C17—H17···O1^{ii}	0.98	2.45	3.382 (6)	158
C23—H23*A*···O1^{ii}	0.97	2.60	3.493 (7)	153
C25—H25*A*···O6^{ii}	0.96	2.50	3.253 (9)	135
C27—H27*B*···O5	0.97	2.24	2.686 (11)	107

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

The title structure was solved by direct methods and Fourier synthesis. Non-H atoms were refined anisotropically by full-matrix least-squares techniques. H atoms were calculated geometrically and included in the refinement, but were restrained to ride on their parent atoms. The isotropic displacement parameters of the H atoms were fixed at $1.3U_{eq}$ of the parent atoms. The C28 atom of the terminal methyl group was located from the ΔF map and was found to be disordered; it was placed in two positions, each with 50% occupancy. The H atoms of the disordered C28 atom were not located.

Data collection: *XSCANS* (Siemens, 1996). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*a*). Molecular graphics: *DIAMOND* (Bergerhoff, 1996). Software used to prepare material for publication: *PLATON* (Spek, 1990), *PARST* (Nardelli, 1983, 1995) and *PARSTCIF* (Nardelli, 1991).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1393). Services for accessing these data are described at the back of the journal.

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(25*R*)-6β-Acetoxy-3β-bromo-5α-spirostan-23-one

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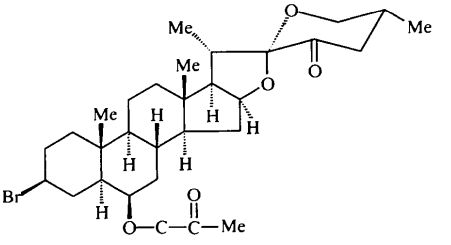
Abstract

In the title compound [systematic name: (25*R*)-3β-bromo-23-oxo-5α-spirostan-6-yl acetate, $C_{29}H_{43}BrO_5$], the C3—Br bond is oriented equatorially and (–)-antiperiplanar with respect to the C4—C5 bond. The six-membered *B*, *C* and *F* rings have chair conformations, as is usual in this type of compound. The five-membered *D* ring adopts a 14α-envelope conformation and the *E* ring adopts a C22β,O3α-half-chair conformation. The *A*/*B*, *B*/*C* and *C*/*D* ring junctions are *trans*.

Comment

In connection with our studies on the synthesis and characterization of bioactive steroids, we need, for reference purposes, the detailed molecular geometry of (25*R*)-6β-acetoxy-3β-bromo-5α-spirostan-23-one, (I), which is being used extensively as a starting material for the synthesis of different spirostanic analogues of brasinosteroids. The title compound was obtained by treatment of an acetic acid solution of the previously reported steroid (25*R*)-5α-spirostan-2α,3α,6β-triol triacetate (Iglesias-Arteaga *et al.*, 1998).



(I)

The absolute configuration, determined from refinement of the Flack (1983) parameter in the X-ray analysis, confirmed that predicted beforehand from the synthesis route. The molecular structure of the title compound with the atomic numbering scheme is shown in Fig. 1. The C3—Br bond is oriented equatorially and (–)-antiperiplanar with respect to the C4—C5 bond. The presence of the Br atom does not disturb the chair conformation in ring *A* of the steroidal nucleus. Ring *A* has a highly symmetrical chair conformation with all asymmetry parameters below 2.70 (9)° (Duax *et al.*, 1976). Mirror symmetry is dominant, with asymmetry parameters ΔC_S(C3) = 0.6 (7), ΔC_S(C5) = 1.2 (8) and ΔC_2(C4—C5) = 2.70 (9)°. The average of the torsion angles is 56.50 (9)°. Rings *B*, *C* and *F* have chair conformations, as expected (Pfeiffer *et al.*, 1985). Ring *D* has a 14α-envelope conformation (Altona *et al.*, 1968). Ring *E* has a C22β,O3α-half-chair conformation. The *A*/*B*, *B*/*C* and *C*/*D* ring junctions are *trans*. Bond distances and valence angles are close to expected values (Honda *et al.*, 1996). The packing of the molecules is assumed to be dictated by van der Waals interactions and by intramolecular and intermolecular C—H···O hydrogen bonds (Taylor & Kennard, 1982).

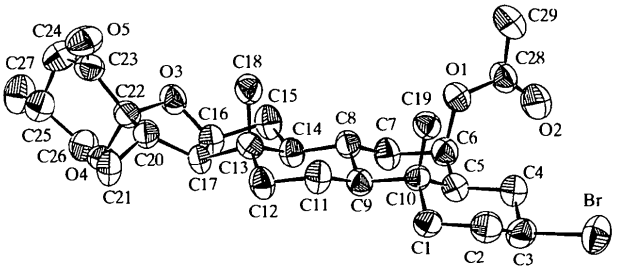


Fig. 1. Plot showing the atomic numbering scheme of (I). Displacement ellipsoids are drawn at the 50% probability level for non-H atoms and H atoms have been omitted for clarity.

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