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# Androstane-3$\beta$,5$\alpha$,6$\beta$,17$\beta$-tetrol trihydrate

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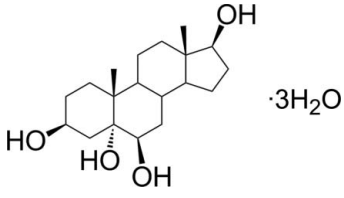
Key indicators: single-crystal X-ray study; $T$ = 293 K; mean $\sigma$(C–C) = 0.003 Å; $R$ factor = 0.031; $wR$ factor = 0.082; data-to-parameter ratio = 8.6.

The title hydrated tetrol, $C_{19}H_{32}O_4\cdot 3H_2O$, was synthesized by stereoselective reduction of the compound 3$\beta$,5$\alpha$,6$\beta$-trihydroxyandrostan-17-one. All rings are fused *trans*. The organic molecules are connected head-to-tail along the *c* axis *via* O—H···O hydrogen bonds. Layers of water molecules in the *ab* plane interconnect these chains. A quantum chemical *ab initio* Roothan Hartree–Fock calculation of the isolated molecule gives values for the molecular geometry close to experimentally determined ones, apart from the C—O bond lengths, whose calculated values are significantly smaller than the measured ones, probably a consequence of the involvement of the C—OH groups in the hydrogen-bonding network.

## Related literature

For the synthesis of the title compound, see: Carvalho, Silva, Moreira *et al.* (2010); Carvalho, Silva & Sá e Melo (2010); Luche *et al.* (1978). For related structures, see: Andrade *et al.* (2011). For puckering parameters, see: Cremer & Pople (1975). For asymmetry parameters, see: Duax & Norton (1975); Altona *et al.* (1968). For reference bond-length data, see: Allen *et al.* (1987). For the program *GAMESS* used to perform the quantum chemical calculations, see: Schmidt *et al.* (1993).




## Experimental

### Crystal data

$C_{19}H_{32}O_4\cdot 3H_2O$
$M_r$ = 378.49
Triclinic, $P\overline{1}$
$a$ = 5.8420 (2) Å
$b$ = 7.3366 (2) Å
$c$ = 12.7922 (3) Å
$\alpha$ = 74.560 (1)°
$\beta$ = 83.091 (1)°
$\gamma$ = 68.930 (1)°
$V$ = 492.97 (2) Å$^3$
$Z$ = 1
Mo $K\alpha$ radiation
$\mu$ = 0.10 mm$^{-1}$
$T$ = 293 K
0.40 × 0.30 × 0.24 mm

### Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2000)
$T_{min}$ = 0.973, $T_{max}$ = 0.982
14489 measured reflections
2222 independent reflections
2132 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.017

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.082
$S$ = 1.05
2222 reflections
259 parameters
9 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.20 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.18 e Å$^{-3}$

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O3—H3···O17$^{i}$ | 0.82 | 1.98 | 2.787 (2) | 169 |
| O5—H5···*OW*1 | 0.82 | 2.08 | 2.891 (2) | 170 |
| O6—H6···O5$^{ii}$ | 0.82 | 2.26 | 2.9897 (16) | 149 |
| O17—H17···*OW*3 | 0.82 | 1.94 | 2.718 (3) | 159 |
| *OW*1—*HW*11···O3$^{iii}$ | 0.80 (2) | 2.15 (2) | 2.944 (2) | 170 (4) |
| *OW*1—*HW*12···*OW*2$^{i}$ | 0.82 (2) | 2.19 (2) | 2.977 (3) | 160 (4) |
| *OW*2—*HW*21···O17 | 0.83 (2) | 2.05 (2) | 2.862 (2) | 168 (4) |
| *OW*2—*HW*22···O3$^{iv}$ | 0.81 (2) | 2.14 (2) | 2.921 (2) | 161 (4) |
| *OW*3—*HW*31···*OW*1$^{v}$ | 0.81 (2) | 2.05 (2) | 2.850 (3) | 169 (5) |
| *OW*3—*HW*32···*OW*2$^{vi}$ | 0.82 (2) | 2.11 (2) | 2.921 (3) | 173 (5) |

Symmetry codes: (i) $x, y, z+1$; (ii) $x+1, y, z$; (iii) $x, y-1, z$; (iv) $x-1, y, z-1$; (v) $x-1, y+1, z-1$; (vi) $x, y+1, z$.

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2006); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BT5554).

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# supplementary materials

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# Androstane-3$\beta$,5$\alpha$,6$\beta$,17$\beta$-tetrol trihydrate

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## Comment

Following our interest in oxysterols and their cytotoxicity (Carvalho, Silva, Moreira *et al.*, 2010), we were able to synthesize the title compound, (I), by stereoselective reduction of compound 3β,5α,6β-trihydroxyandrostan-17-one (Andrade *et al.*, 2011). Evaluation of the cytotoxicity of compound (I) towards HT-29 cancer cells (Carvalho, Silva, Moreira *et al.*, 2010) indicates no relevant values ($IC_{50}$>50$\mu M$), in contrast to other 3β,5α,6β-trihydroxy steroids, namely cholestane-3β,5α,6β-triol. Such result points to the importance of a C-17 cholesteryl-type side chain for cytoxicity. Determination of the three-dimensional structure of compound (I) by X-ray crystallography will contribute to correlate the importance of this side chain influence on the overall steroid geometry with such biological effect. Determined interatomic distances and valency angles agree well with expected values reported by Allen *et al.* (1987), except for C2–C3 bond [1.514 (3) Å] which is significantly shorter than average $C_{sp}^3$–$C_{sp}^3$ bond length [1.535 Å], a common feature with 3β,5α,6β-trihydroxyandrostan-17-one (Andrade *et al.*, 2011). Rings A, B and C have slightly flattened chair conformations [weighted average torsion angles 55.9 (8)°, 54.5 (4)°, 56.4 (9)°, respectively]. Ring D adopts a conformation in between 13β-envelope and 13β,14α-half chair [Cremer & Pople (1975) parameters $q_2$ = 0.480 (2) Å and $\varphi_2$ = 191.2 (3)°; asymmetry parameters (Duax & Norton, 1975; Altona *et al.*, 1968) $\Delta C_s(14)$ = 24.64 (18)°; $\Delta C_s(13)$ = 11.80 (19)°; $\Delta C_2(13,14)$ = 9.1 (2)°; $\varphi_m$ = 48.8 (1)°; $\Delta$ = 13.5 (3)°]. All rings are fused *trans*. The pseudo torsion angle C19—C10—C13—C18 is 2.86 (14)°, showing that the molecule is only slightly twisted.

There is an extensive hydrogen bonding network in the crystal sructure. The steroid molecules are linked head to tail *via* the O17 and O3 atoms, through a direct H bond where the O3 atom acts as a donor and through two additional H bonds mediated by a water molecule. The chains, aligned along the *c* axis, are further linked together *via* the two remaining water molecules. Interestingly the three water molecules are located in layers in the *ab* plane.

*Ab-initio* Roothan Hartree-Fock calculations of the free steroid molecule were performed using the computer code GAMESS (Schmidt *et al.*, 1993) in order to access the influence in the molecular geometry of the crystalline field, in particular of the solvent water molecules involved in H-bonding. These calculations gave values of the bond lengths,valency and torsion angles very close to those observed in the crystalline environment, except for the C–O bond lengths of the C—O—H groups, whose calculated values were significantely smaller than the measured ones, an effect that can be attributed to the influence of the hydrogen bonds (C17–O17 calc. 1.402, exp. 1.438 (2); C3–O3 calc. 1.408, exp. 1.4472 (18); C5–O5 calc. 1.423, exp. 1.4495 (19); C6–O6 calc. 1.405, exp. 1.426 (2) Å).

## Experimental

Synthesis of the title compound was performed using Luche conditions ($NaBH_4$/$CeCl_3$) (Luche *et al.*, 1978). Reduction of the carbonyl in position C17 revealed to be stereoselective rendering the 17β–OH in good yield (Carvalho, Silva & Sá e Melo, 2010). Crystallization from ethanol at room temperature afforded colourless crystals suitable for X-ray analysis. Analytical data of the title compound is in accordance with the literature (Carvalho, Silva & Sá e Melo, 2010). To a solution

of 3β,5α,6β-trihydroxy-androstan-17-one (100 mg, 0.310 mmol) and $CeCl_3.7H_2O$ (173.3 mg, 0.465 mmol) in THF (5 ml) and MeOH (5 ml) at 273 K, was slowly added $NaBH_4$ (35.2 mg, 0.930 mmol). The mixture was stirred for 15 minutes, stopped with the addition of acetone, neutralized with $Et_3N$ and concentrated under vacuum. The residue was dissolved in ethyl acetate, filtrated and evaporated again. Flash chromatography (chloroform, ethanol 9:1) afforded the pure androstan-3β,5α,6β,17β-tetrol (I, 76.5 mg, 76%). *M*.p. 547 K (EtOH). IR (film) 3365, 2936, 2872, 1158, 1123, 1047, 1001, 960, 874, 745 $cm^{-1}$. $^1H$ NMR (300 MHz, DMSO–*d6*) δ p.p.m. 0.61 (3*H*, s, 18–$CH_3$), 1.02 (3*H*, s, 19$CH_3$), 1.85 (1*H*, dd, *J*=12.9, 11.2 Hz), 3.29 (1*H*, td, *J*=3.9, 3.3, 3.3 Hz, 6α–H), 3.43 (1*H*, dd, *J*=8.7, 4.5 Hz, 17α–H), 3.65 (1*H*, s, 5–OH), 3.79 (1*H*, tt, *J*=11.1, 5.7 Hz, 3α–H), 4.20 (1*H*, d, *J*=5.7 Hz, OH), 4.40 (1*H*, d, *J*=4.5 Hz, 17–OH), 4.41 (1*H*, d, *J*=3.3 Hz, 6–OH). $^{13}C$ NMR (75 MHz, DMSO-*d6* δ p.p.m. 11.4, 16.3, 20.3 ($CH_2$), 23.1 ($CH_2$), 29.9 ($CH_2$), 30.1, 31.1 ($CH_2$), 32.0 ($CH_2$), 34.1 ($CH_2$), 36.8 ($CH_2$), 37.9 (C), 40.9 ($CH_2$), 42.6 (C), 44.8, 50.4, 65.7, 74.0, 74.3 (C–5), 80.1. MS m/*z* (%): 323.2 (28) $[M–H]^+$, 311.6 (11), 294.1 (70), 281.5 (17), 266.3 (100), 263.7 (15), 98.8 (20).

### Refinement

All hydrogen atoms were refined as riding on their parent atoms using *SHELXL97* defaults except for those of the water molecules whose coordinates were refined from the starting coordinates obtained from a difference Fourier synthesis with $U_{eq}$(H)=1.5$U_{eq}$(O) using a *DFIX* restraint for the O—H bond of 0.82 Å and those of the C—OH groups which were positioned and refined with a SELXL97 HFIX 147 instruction.

The absolute configuration was not determined from the X-ray data, as the molecule lacks any strong anomalous scatterer atom at the Mo Kα wavelength, but was known from the synthetic route. Friedel pairs were merged before refinement.

### Figures

Fig. 1. *ORTEPII* plot of the title compound. Displacement ellipsoids are drawn at the 50% level.

Fig. 2. Projection of the crystal structure along the *a* axis, showing the H-bond network.

### Androstane-3β,5α,6β,17β-tetrol trihydrate

*Crystal data*

| | |
|---|---|
| $C_{19}H_{32}O_4·3H_2O$ | $Z$ = 1 |
| $M_r$ = 378.49 | $F$(000) = 208 |
| Triclinic, $P\overline{1}$ | $D_x$ = 1.275 Mg $m^{-3}$ |
| Hall symbol: P -1 | Melting point: 547 K |
| $a$ = 5.8420 (2) Å | Mo $K\alpha$ radiation, λ = 0.71073 Å |
| $b$ = 7.3366 (2) Å | Cell parameters from 9795 reflections |
| $c$ = 12.7922 (3) Å | θ = 3.1–27.9° |
| α = 74.560 (1)° | μ = 0.10 $mm^{-1}$ |
| β = 83.091 (1)° | $T$ = 293 K |
| γ = 68.930 (1)° | Prism, colourless |
| $V$ = 492.97 (2) $Å^3$ | 0.40 × 0.30 × 0.24 mm |

*Data collection*

| | |
|---|---|
| Bruker APEXII CCD area-detector diffractometer | 2222 independent reflections |
| Radiation source: fine-focus sealed tube | 2132 reflections with $I > 2\sigma(I)$ |
| graphite | $R_{int} = 0.017$ |
| φ and ω scans | $\theta_{max} = 27.9°$, $\theta_{min} = 1.7°$ |
| Absorption correction: multi-scan (*SADABS*; Sheldrick, 2000) | $h = -7\rightarrow7$ |
| $T_{min} = 0.973$, $T_{max} = 0.982$ | $k = -9\rightarrow9$ |
| 14489 measured reflections | $l = -16\rightarrow16$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | Primary atom site location: structure-invariant direct methods |
| Least-squares matrix: full | Secondary atom site location: difference Fourier map |
| $R[F^2 > 2\sigma(F^2)] = 0.031$ | Hydrogen site location: inferred from neighbouring sites |
| $wR(F^2) = 0.082$ | H atoms treated by a mixture of independent and constrained refinement |
| $S = 1.05$ | $w = 1/[\sigma^2(F_o^2) + (0.0531P)^2 + 0.0525P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| 2222 reflections | $(\Delta/\sigma)_{max} = 0.001$ |
| 259 parameters | $\Delta\rho_{max} = 0.20$ e Å$^{-3}$ |
| 9 restraints | $\Delta\rho_{min} = -0.18$ e Å$^{-3}$ |

*Special details*

**Geometry**. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on $F^2$, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative $F^2$. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on $F^2$ are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| O3 | 0.6825 (3) | 0.6903 (2) | 1.01710 (10) | 0.0341 (3) |
| H3 | 0.5888 | 0.6824 | 1.0699 | 0.051* |
| O5 | 0.5070 (2) | 0.4040 (2) | 0.81009 (10) | 0.0274 (3) |
| H5 | 0.5466 | 0.3118 | 0.8646 | 0.041* |
| O6 | 1.1265 (2) | 0.3581 (2) | 0.69231 (12) | 0.0327 (3) |
| H6 | 1.1957 | 0.3562 | 0.7449 | 0.049* |

| | | | | |
|---|---|---|---|---|
| O17 | 0.3382 (3) | 0.6345 (2) | 0.18191 (10) | 0.0322 (3) |
| H17 | 0.2368 | 0.7464 | 0.1812 | 0.048* |
| C8 | 0.7075 (3) | 0.4785 (2) | 0.54354 (13) | 0.0190 (3) |
| H8 | 0.8405 | 0.5298 | 0.5122 | 0.023* |
| C9 | 0.5052 (3) | 0.6405 (2) | 0.59165 (13) | 0.0184 (3) |
| H9 | 0.3762 | 0.5836 | 0.6216 | 0.022* |
| C10 | 0.5997 (3) | 0.6831 (2) | 0.68858 (13) | 0.0189 (3) |
| C4 | 0.7953 (3) | 0.5133 (3) | 0.87369 (14) | 0.0235 (3) |
| H4A | 0.8595 | 0.3850 | 0.9256 | 0.028* |
| H4B | 0.9271 | 0.5678 | 0.8518 | 0.028* |
| C5 | 0.7073 (3) | 0.4805 (2) | 0.77394 (13) | 0.0200 (3) |
| C11 | 0.3867 (3) | 0.8294 (3) | 0.50259 (14) | 0.0265 (4) |
| H11A | 0.5074 | 0.8931 | 0.4723 | 0.032* |
| H11B | 0.2534 | 0.9239 | 0.5346 | 0.032* |
| C13 | 0.4866 (3) | 0.6246 (2) | 0.36183 (13) | 0.0203 (3) |
| C14 | 0.5959 (3) | 0.4377 (2) | 0.45415 (13) | 0.0209 (3) |
| H14 | 0.4580 | 0.3953 | 0.4884 | 0.025* |
| C1 | 0.3880 (3) | 0.8233 (3) | 0.74519 (14) | 0.0283 (4) |
| H1A | 0.3224 | 0.9529 | 0.6945 | 0.034* |
| H1B | 0.2578 | 0.7667 | 0.7651 | 0.034* |
| C3 | 0.5877 (3) | 0.6566 (3) | 0.92717 (14) | 0.0285 (4) |
| H3A | 0.4634 | 0.5936 | 0.9554 | 0.034* |
| C6 | 0.9057 (3) | 0.3161 (2) | 0.72770 (14) | 0.0233 (3) |
| H6A | 0.9462 | 0.1899 | 0.7840 | 0.028* |
| C7 | 0.8106 (3) | 0.2850 (2) | 0.63067 (14) | 0.0240 (3) |
| H7A | 0.6831 | 0.2264 | 0.6555 | 0.029* |
| H7B | 0.9434 | 0.1898 | 0.5988 | 0.029* |
| C2 | 0.4682 (4) | 0.8545 (3) | 0.84738 (15) | 0.0326 (4) |
| H2A | 0.5831 | 0.9268 | 0.8266 | 0.039* |
| H2B | 0.3261 | 0.9360 | 0.8822 | 0.039* |
| C12 | 0.2867 (3) | 0.7820 (3) | 0.41083 (14) | 0.0267 (4) |
| H12A | 0.1527 | 0.7327 | 0.4392 | 0.032* |
| H12B | 0.2230 | 0.9044 | 0.3547 | 0.032* |
| C18 | 0.6775 (3) | 0.7118 (3) | 0.29715 (15) | 0.0293 (4) |
| H18A | 0.7901 | 0.6159 | 0.2601 | 0.044* |
| H18B | 0.7658 | 0.7405 | 0.3457 | 0.044* |
| H18C | 0.5963 | 0.8335 | 0.2450 | 0.044* |
| C19 | 0.7914 (3) | 0.7860 (3) | 0.64653 (14) | 0.0266 (4) |
| H19A | 0.7130 | 0.9184 | 0.6024 | 0.040* |
| H19B | 0.9156 | 0.7081 | 0.6040 | 0.040* |
| H19C | 0.8654 | 0.7961 | 0.7069 | 0.040* |
| C17 | 0.3951 (3) | 0.5244 (3) | 0.29226 (14) | 0.0262 (4) |
| H17A | 0.2486 | 0.4975 | 0.3281 | 0.031* |
| C15 | 0.7529 (4) | 0.2761 (3) | 0.39465 (15) | 0.0302 (4) |
| H15A | 0.7737 | 0.1420 | 0.4394 | 0.036* |
| H15B | 0.9131 | 0.2880 | 0.3739 | 0.036* |
| C16 | 0.6017 (4) | 0.3220 (3) | 0.29381 (17) | 0.0376 (5) |
| H16A | 0.7037 | 0.3314 | 0.2283 | 0.056* |
| H16B | 0.5340 | 0.2169 | 0.2990 | 0.056* |

| | | | | |
|---|---|---|---|---|
| OW1 | 0.6011 (4) | 0.1107 (3) | 1.01617 (15) | 0.0493 (4) |
| HW11 | 0.607 (7) | −0.002 (3) | 1.021 (3) | 0.074* |
| HW12 | 0.468 (5) | 0.163 (6) | 1.045 (3) | 0.074* |
| OW2 | 0.1512 (3) | 0.3921 (3) | 0.09832 (16) | 0.0519 (4) |
| HW21 | 0.186 (7) | 0.466 (5) | 0.128 (3) | 0.078* |
| HW22 | 0.042 (6) | 0.488 (5) | 0.067 (3) | 0.078* |
| OW3 | 0.0382 (5) | 1.0250 (4) | 0.1259 (2) | 0.0762 (7) |
| HW31 | −0.074 (7) | 1.048 (8) | 0.088 (4) | 0.114* |
| HW32 | 0.074 (9) | 1.124 (6) | 0.124 (4) | 0.114* |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| O3 | 0.0427 (8) | 0.0482 (8) | 0.0175 (6) | −0.0188 (7) | −0.0037 (5) | −0.0118 (6) |
| O5 | 0.0313 (7) | 0.0332 (7) | 0.0210 (6) | −0.0191 (6) | −0.0032 (5) | 0.0002 (5) |
| O6 | 0.0222 (6) | 0.0420 (8) | 0.0344 (7) | −0.0078 (6) | −0.0039 (5) | −0.0129 (6) |
| O17 | 0.0371 (7) | 0.0358 (7) | 0.0209 (6) | −0.0056 (6) | −0.0087 (5) | −0.0087 (5) |
| C8 | 0.0199 (7) | 0.0185 (8) | 0.0183 (7) | −0.0047 (6) | −0.0020 (6) | −0.0058 (6) |
| C9 | 0.0200 (7) | 0.0207 (8) | 0.0148 (7) | −0.0058 (6) | −0.0022 (6) | −0.0055 (6) |
| C10 | 0.0209 (7) | 0.0195 (8) | 0.0160 (6) | −0.0053 (6) | −0.0032 (6) | −0.0047 (6) |
| C4 | 0.0259 (8) | 0.0263 (9) | 0.0183 (7) | −0.0089 (7) | −0.0057 (6) | −0.0033 (6) |
| C5 | 0.0220 (8) | 0.0226 (8) | 0.0174 (7) | −0.0103 (7) | −0.0022 (6) | −0.0037 (6) |
| C11 | 0.0323 (9) | 0.0218 (8) | 0.0200 (8) | 0.0007 (7) | −0.0083 (7) | −0.0069 (7) |
| C13 | 0.0207 (7) | 0.0232 (8) | 0.0164 (7) | −0.0049 (6) | −0.0025 (6) | −0.0063 (6) |
| C14 | 0.0229 (8) | 0.0214 (8) | 0.0193 (7) | −0.0068 (7) | −0.0018 (6) | −0.0069 (6) |
| C1 | 0.0283 (9) | 0.0310 (10) | 0.0220 (8) | −0.0006 (8) | −0.0056 (7) | −0.0118 (7) |
| C3 | 0.0307 (9) | 0.0420 (11) | 0.0185 (8) | −0.0157 (8) | −0.0036 (7) | −0.0107 (7) |
| C6 | 0.0265 (9) | 0.0190 (8) | 0.0210 (7) | −0.0040 (7) | −0.0076 (6) | −0.0016 (6) |
| C7 | 0.0291 (9) | 0.0182 (8) | 0.0234 (8) | −0.0033 (7) | −0.0071 (6) | −0.0066 (6) |
| C2 | 0.0360 (10) | 0.0354 (11) | 0.0238 (8) | −0.0019 (8) | −0.0052 (8) | −0.0154 (8) |
| C12 | 0.0249 (8) | 0.0302 (9) | 0.0200 (8) | 0.0007 (7) | −0.0065 (6) | −0.0092 (7) |
| C18 | 0.0314 (9) | 0.0339 (10) | 0.0243 (9) | −0.0149 (8) | −0.0006 (7) | −0.0050 (7) |
| C19 | 0.0348 (9) | 0.0245 (9) | 0.0245 (8) | −0.0157 (7) | −0.0044 (7) | −0.0033 (7) |
| C17 | 0.0288 (8) | 0.0328 (10) | 0.0198 (8) | −0.0113 (7) | −0.0026 (6) | −0.0089 (7) |
| C15 | 0.0393 (10) | 0.0234 (9) | 0.0251 (8) | −0.0024 (8) | −0.0064 (7) | −0.0104 (7) |
| C16 | 0.0535 (12) | 0.0304 (10) | 0.0286 (9) | −0.0064 (9) | −0.0088 (8) | −0.0145 (8) |
| OW1 | 0.0636 (11) | 0.0451 (10) | 0.0416 (9) | −0.0261 (9) | −0.0069 (8) | −0.0015 (7) |
| OW2 | 0.0525 (10) | 0.0546 (11) | 0.0552 (11) | −0.0203 (9) | −0.0148 (8) | −0.0151 (8) |
| OW3 | 0.0667 (14) | 0.0515 (12) | 0.107 (2) | −0.0064 (11) | −0.0284 (13) | −0.0217 (12) |

*Geometric parameters (Å, °)*

| | | | |
|---|---|---|---|
| O3—C3 | 1.4473 (18) | C1—C2 | 1.538 (2) |
| O3—H3 | 0.8200 | C1—H1A | 0.9700 |
| O5—C5 | 1.4496 (19) | C1—H1B | 0.9700 |
| O5—H5 | 0.8200 | C3—C2 | 1.513 (3) |
| O6—C6 | 1.426 (2) | C3—H3A | 0.9800 |
| O6—H6 | 0.8200 | C6—C7 | 1.520 (2) |
| O17—C17 | 1.438 (2) | C6—H6A | 0.9800 |

| | | | |
|---|---|---|---|
| O17—H17 | 0.8200 | C7—H7A | 0.9700 |
| C8—C14 | 1.5248 (19) | C7—H7B | 0.9700 |
| C8—C7 | 1.525 (2) | C2—H2A | 0.9700 |
| C8—C9 | 1.547 (2) | C2—H2B | 0.9700 |
| C8—H8 | 0.9800 | C12—H12A | 0.9700 |
| C9—C11 | 1.535 (2) | C12—H12B | 0.9700 |
| C9—C10 | 1.5603 (18) | C18—H18A | 0.9600 |
| C9—H9 | 0.9800 | C18—H18B | 0.9600 |
| C10—C19 | 1.537 (2) | C18—H18C | 0.9600 |
| C10—C1 | 1.542 (2) | C19—H19A | 0.9600 |
| C10—C5 | 1.557 (2) | C19—H19B | 0.9600 |
| C4—C3 | 1.520 (3) | C19—H19C | 0.9600 |
| C4—C5 | 1.537 (2) | C17—C16 | 1.537 (3) |
| C4—H4A | 0.9700 | C17—H17A | 0.9800 |
| C4—H4B | 0.9700 | C15—C16 | 1.545 (2) |
| C5—C6 | 1.535 (2) | C15—H15A | 0.9700 |
| C11—C12 | 1.539 (2) | C15—H15B | 0.9700 |
| C11—H11A | 0.9700 | C16—H16A | 0.9700 |
| C11—H11B | 0.9700 | C16—H16B | 0.9700 |
| C13—C12 | 1.527 (2) | OW1—HW11 | 0.802 (19) |
| C13—C18 | 1.532 (2) | OW1—HW12 | 0.820 (19) |
| C13—C17 | 1.537 (2) | OW2—HW21 | 0.825 (19) |
| C13—C14 | 1.540 (2) | OW2—HW22 | 0.809 (19) |
| C14—C15 | 1.535 (2) | OW3—HW31 | 0.81 (2) |
| C14—H14 | 0.9800 | OW3—HW32 | 0.82 (2) |
| C3—O3—H3 | 109.5 | O3—C3—H3A | 108.6 |
| C5—O5—H5 | 109.5 | C2—C3—H3A | 108.6 |
| C6—O6—H6 | 109.5 | C4—C3—H3A | 108.6 |
| C17—O17—H17 | 109.5 | O6—C6—C7 | 106.88 (14) |
| C14—C8—C7 | 110.14 (12) | O6—C6—C5 | 114.35 (13) |
| C14—C8—C9 | 108.20 (12) | C7—C6—C5 | 110.36 (13) |
| C7—C8—C9 | 111.03 (13) | O6—C6—H6A | 108.4 |
| C14—C8—H8 | 109.1 | C7—C6—H6A | 108.4 |
| C7—C8—H8 | 109.1 | C5—C6—H6A | 108.4 |
| C9—C8—H8 | 109.1 | C6—C7—C8 | 113.45 (13) |
| C11—C9—C8 | 111.15 (13) | C6—C7—H7A | 108.9 |
| C11—C9—C10 | 114.18 (13) | C8—C7—H7A | 108.9 |
| C8—C9—C10 | 111.71 (12) | C6—C7—H7B | 108.9 |
| C11—C9—H9 | 106.4 | C8—C7—H7B | 108.9 |
| C8—C9—H9 | 106.4 | H7A—C7—H7B | 107.7 |
| C10—C9—H9 | 106.4 | C3—C2—C1 | 111.83 (15) |
| C19—C10—C1 | 108.27 (14) | C3—C2—H2A | 109.2 |
| C19—C10—C5 | 111.98 (13) | C1—C2—H2A | 109.2 |
| C1—C10—C5 | 107.37 (13) | C3—C2—H2B | 109.2 |
| C19—C10—C9 | 109.47 (13) | C1—C2—H2B | 109.2 |
| C1—C10—C9 | 111.07 (13) | H2A—C2—H2B | 107.9 |
| C5—C10—C9 | 108.69 (12) | C13—C12—C11 | 111.20 (14) |
| C3—C4—C5 | 111.29 (14) | C13—C12—H12A | 109.4 |
| C3—C4—H4A | 109.4 | C11—C12—H12A | 109.4 |

| | | | |
|---|---|---|---|
| C5—C4—H4A | 109.4 | C13—C12—H12B | 109.4 |
| C3—C4—H4B | 109.4 | C11—C12—H12B | 109.4 |
| C5—C4—H4B | 109.4 | H12A—C12—H12B | 108.0 |
| H4A—C4—H4B | 108.0 | C13—C18—H18A | 109.5 |
| O5—C5—C6 | 105.43 (13) | C13—C18—H18B | 109.5 |
| O5—C5—C4 | 107.34 (13) | H18A—C18—H18B | 109.5 |
| C6—C5—C4 | 111.83 (13) | C13—C18—H18C | 109.5 |
| O5—C5—C10 | 106.41 (12) | H18A—C18—H18C | 109.5 |
| C6—C5—C10 | 114.03 (12) | H18B—C18—H18C | 109.5 |
| C4—C5—C10 | 111.26 (12) | C10—C19—H19A | 109.5 |
| C9—C11—C12 | 112.56 (14) | C10—C19—H19B | 109.5 |
| C9—C11—H11A | 109.1 | H19A—C19—H19B | 109.5 |
| C12—C11—H11A | 109.1 | C10—C19—H19C | 109.5 |
| C9—C11—H11B | 109.1 | H19A—C19—H19C | 109.5 |
| C12—C11—H11B | 109.1 | H19B—C19—H19C | 109.5 |
| H11A—C11—H11B | 107.8 | O17—C17—C16 | 109.69 (14) |
| C12—C13—C18 | 110.92 (15) | O17—C17—C13 | 116.41 (15) |
| C12—C13—C17 | 115.43 (13) | C16—C17—C13 | 105.03 (14) |
| C18—C13—C17 | 109.95 (14) | O17—C17—H17A | 108.5 |
| C12—C13—C14 | 108.13 (13) | C16—C17—H17A | 108.5 |
| C18—C13—C14 | 113.66 (13) | C13—C17—H17A | 108.5 |
| C17—C13—C14 | 98.26 (13) | C14—C15—C16 | 103.10 (15) |
| C8—C14—C15 | 119.76 (14) | C14—C15—H15A | 111.1 |
| C8—C14—C13 | 114.15 (12) | C16—C15—H15A | 111.1 |
| C15—C14—C13 | 103.82 (13) | C14—C15—H15B | 111.1 |
| C8—C14—H14 | 106.0 | C16—C15—H15B | 111.1 |
| C15—C14—H14 | 106.0 | H15A—C15—H15B | 109.1 |
| C13—C14—H14 | 106.0 | C17—C16—C15 | 105.92 (14) |
| C2—C1—C10 | 112.90 (14) | C17—C16—H16A | 110.6 |
| C2—C1—H1A | 109.0 | C15—C16—H16A | 110.6 |
| C10—C1—H1A | 109.0 | C17—C16—H16B | 110.6 |
| C2—C1—H1B | 109.0 | C15—C16—H16B | 110.6 |
| C10—C1—H1B | 109.0 | H16A—C16—H16B | 108.7 |
| H1A—C1—H1B | 107.8 | HW11—OW1—HW12 | 104 (4) |
| O3—C3—C2 | 110.35 (15) | HW21—OW2—HW22 | 90 (4) |
| O3—C3—C4 | 109.14 (14) | HW31—OW3—HW32 | 114 (6) |
| C2—C3—C4 | 111.63 (15) | | |
| C14—C8—C9—C11 | −54.42 (17) | C19—C10—C1—C2 | −64.85 (19) |
| C7—C8—C9—C11 | −175.41 (13) | C5—C10—C1—C2 | 56.22 (19) |
| C14—C8—C9—C10 | 176.76 (13) | C9—C10—C1—C2 | 174.93 (15) |
| C7—C8—C9—C10 | 55.78 (17) | C5—C4—C3—O3 | −177.17 (13) |
| C11—C9—C10—C19 | −59.18 (19) | C5—C4—C3—C2 | −54.92 (19) |
| C8—C9—C10—C19 | 68.02 (17) | O5—C5—C6—O6 | −176.93 (13) |
| C11—C9—C10—C1 | 60.3 (2) | C4—C5—C6—O6 | −60.60 (18) |
| C8—C9—C10—C1 | −172.47 (13) | C10—C5—C6—O6 | 66.72 (16) |
| C11—C9—C10—C5 | 178.24 (14) | O5—C5—C6—C7 | 62.55 (17) |
| C8—C9—C10—C5 | −54.57 (16) | C4—C5—C6—C7 | 178.88 (14) |
| C3—C4—C5—O5 | −57.61 (18) | C10—C5—C6—C7 | −53.80 (17) |
| C3—C4—C5—C6 | −172.78 (14) | O6—C6—C7—C8 | −71.50 (18) |

| | | | |
|---|---|---|---|
| C3—C4—C5—C10 | 58.43 (18) | C5—C6—C7—C8 | 53.39 (19) |
| C19—C10—C5—O5 | 177.61 (14) | C14—C8—C7—C6 | −175.01 (14) |
| C1—C10—C5—O5 | 58.90 (15) | C9—C8—C7—C6 | −55.17 (18) |
| C9—C10—C5—O5 | −61.33 (15) | O3—C3—C2—C1 | 174.34 (15) |
| C19—C10—C5—C6 | −66.61 (16) | C4—C3—C2—C1 | 52.8 (2) |
| C1—C10—C5—C6 | 174.68 (13) | C10—C1—C2—C3 | −55.1 (2) |
| C9—C10—C5—C6 | 54.45 (16) | C18—C13—C12—C11 | −69.96 (18) |
| C19—C10—C5—C4 | 61.00 (17) | C17—C13—C12—C11 | 164.15 (15) |
| C1—C10—C5—C4 | −57.72 (16) | C14—C13—C12—C11 | 55.30 (19) |
| C9—C10—C5—C4 | −177.94 (14) | C9—C11—C12—C13 | −55.6 (2) |
| C8—C9—C11—C12 | 54.8 (2) | C12—C13—C17—O17 | 81.80 (19) |
| C10—C9—C11—C12 | −177.68 (14) | C18—C13—C17—O17 | −44.6 (2) |
| C7—C8—C14—C15 | −56.0 (2) | C14—C13—C17—O17 | −163.54 (14) |
| C9—C8—C14—C15 | −177.54 (15) | C12—C13—C17—C16 | −156.68 (16) |
| C7—C8—C14—C13 | −179.93 (14) | C18—C13—C17—C16 | 76.94 (18) |
| C9—C8—C14—C13 | 58.54 (17) | C14—C13—C17—C16 | −42.02 (17) |
| C12—C13—C14—C8 | −59.23 (17) | C8—C14—C15—C16 | −165.07 (15) |
| C18—C13—C14—C8 | 64.39 (18) | C13—C14—C15—C16 | −36.31 (18) |
| C17—C13—C14—C8 | −179.50 (13) | O17—C17—C16—C15 | 146.74 (16) |
| C12—C13—C14—C15 | 168.66 (14) | C13—C17—C16—C15 | 20.9 (2) |
| C18—C13—C14—C15 | −67.72 (17) | C14—C15—C16—C17 | 9.3 (2) |
| C17—C13—C14—C15 | 48.38 (16) | C19—C10—C13—C18 | 2.85 (14) |

*Hydrogen-bond geometry (Å, °)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O3—H3···O17$^{i}$ | 0.82 | 1.98 | 2.787 (2) | 169 |
| O5—H5···OW1 | 0.82 | 2.08 | 2.891 (2) | 170 |
| O6—H6···O5$^{ii}$ | 0.82 | 2.26 | 2.9897 (16) | 149 |
| O17—H17···OW3 | 0.82 | 1.94 | 2.718 (3) | 159 |
| OW1—HW11···O3$^{iii}$ | 0.80 (2) | 2.15 (2) | 2.944 (2) | 170 (4) |
| OW1—HW12···OW2$^{i}$ | 0.82 (2) | 2.19 (2) | 2.977 (3) | 160 (4) |
| OW2—HW21···O17 | 0.83 (2) | 2.05 (2) | 2.862 (2) | 168 (4) |
| OW2—HW22···O3$^{iv}$ | 0.81 (2) | 2.14 (2) | 2.921 (2) | 161 (4) |
| OW3—HW31···OW1$^{v}$ | 0.81 (2) | 2.05 (2) | 2.850 (3) | 169 (5) |
| OW3—HW32···OW2$^{vi}$ | 0.82 (2) | 2.11 (2) | 2.921 (3) | 173 (5) |

Symmetry codes: (i) *x*, *y*, *z*+1; (ii) *x*+1, *y*, *z*; (iii) *x*, *y*−1, *z*; (iv) *x*−1, *y*, *z*−1; (v) *x*−1, *y*+1, *z*−1; (vi) *x*, *y*+1, *z*.

**Fig. 1**

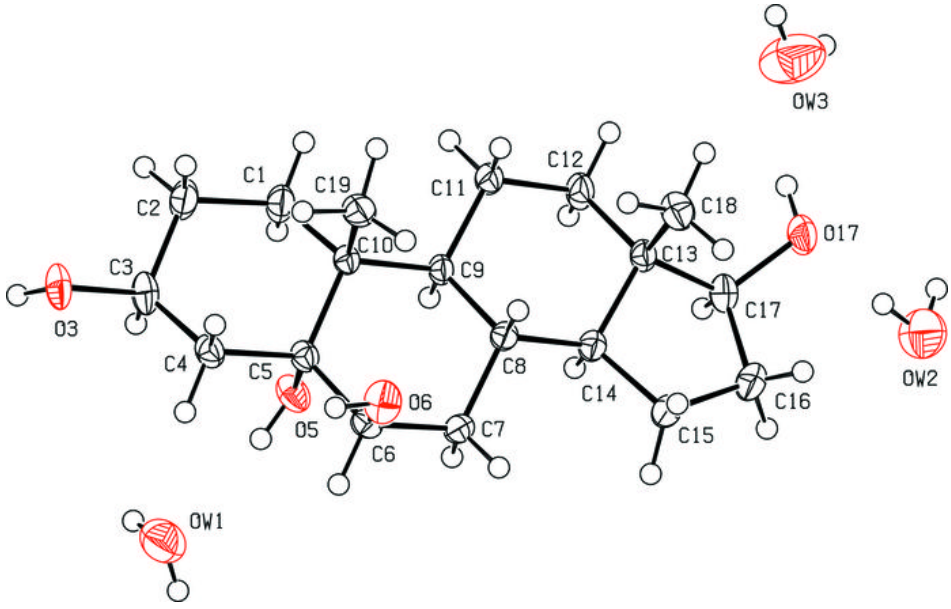
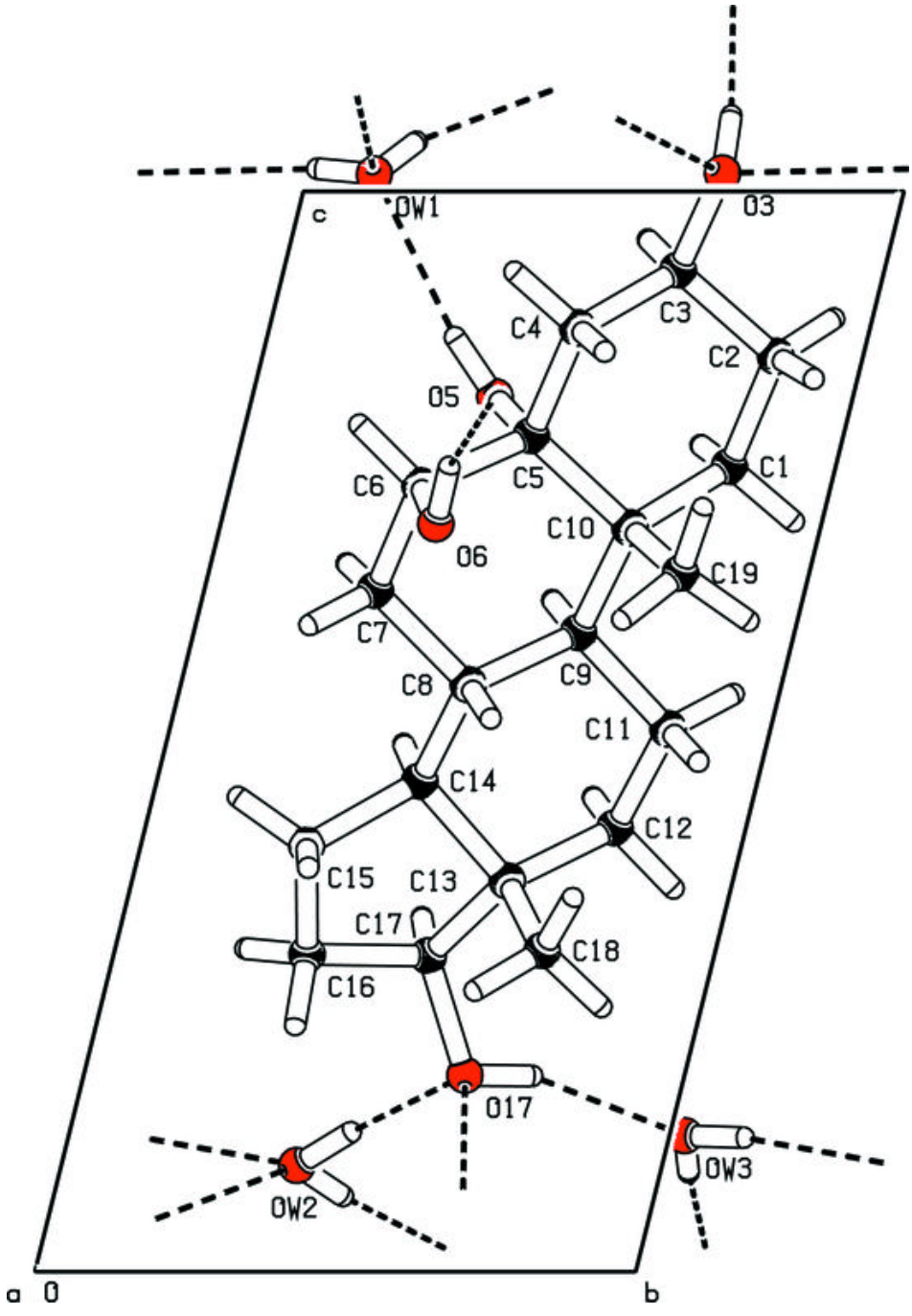

OW3
C1
C19
C11
C12
C2
C18
O17
C10
C13
C3
C9
C17
O3
C4
C5
C8
C14
C16
OW2
O6
O5
C7
C6
C15
OW1

**Fig. 2**


c
OW1
O3
C4
C3
C2
O5
C6
C5
C1
C10
O6
C19
C7
C8
C9
C11
C14
C12
C15
C13
C17
C18
C16
O17
OW3
OW2
a
0
b