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Biotransformation, spectroscopic investigation, crystal structure and electrostatic properties of 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one monohydrate studied using transferred electron-density parameters

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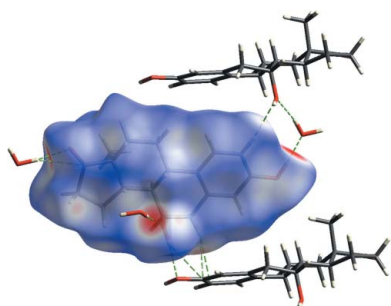
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The biologically transformed product of estradiol valerate, namely 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one monohydrate, C₁₈H₂₂O₃·H₂O, has been investigated using UV–Vis, IR, ¹H and ¹³C NMR spectroscopic techniques, as well as by mass spectrometric analysis. Its crystal structure was determined using single-crystal X-ray diffraction based on data collected at 100 K. The structure was refined using the independent atom model (IAM) and the transferred electron-density parameters from the ELMAM2 database. The structure is stabilized by a network of hydrogen bonds and van der Waals interactions. The topology of the hydrogen bonds has been analyzed by the Bader theory of ‘Atoms in Molecules’ framework. The molecular electrostatic potential for the transferred multipolar atom model reveals an asymmetric character of the charge distribution across the molecule due to a substantial charge delocalization within the molecule. The molecular dipole moment was also calculated, which shows that the molecule has a strongly polar character.

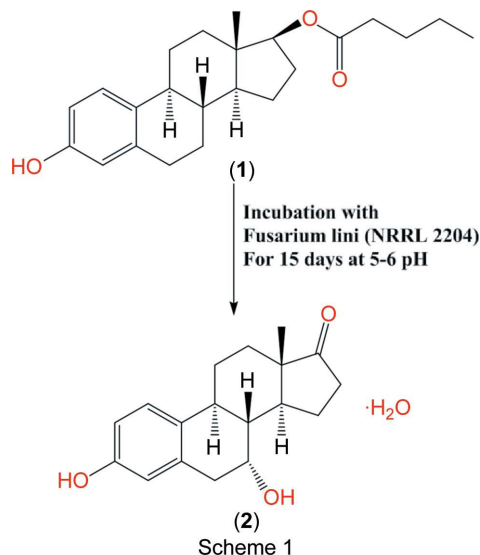
1. Introduction

Biocatalytic approaches are a growing interdisciplinary area of chemistry, genetic engineering and microbiology (Borges *et al.*, 2009). Microbial biotransformations (Hegazy *et al.*, 2015) are structural modifications carried out either by whole bacterial or fungal organisms (Nankai *et al.*, 1997) or by whole cells (Wang *et al.*, 2008). These are the structural analogues of the starting material produced as a result of enzyme-catalyzed reactions (Lilly, 1994; Shah *et al.*, 2013). Biotransformation reactions have many advantages over classical chemical reactions due to high stereo-, regio- and chemoselectivity (Ahmad *et al.*, 2016). Biotransformation or biocatalysis is an important tool with great potential for the synthesis of new derivatives and structure analogues of active pharmaceutical ingredients (APIs). These reactions are cost effective and ecologically friendly (Borges *et al.*, 2009), can be carried out in aqueous medium at neutral pH (Hussain *et al.*, 2016) and can therefore be considered green chemistry (Borges *et al.*, 2009; Baydoun *et al.*, 2014).

Estradiol valerate (also known as oestradiol valerate), (**1**), is a steroid available under the brand names Prognova, Prognon Depot and Delestrogen, and is well known for the treatment of typical symptoms associated with menopause in women. It is a synthetic estrogen hormone and has great



therapeutic importance associated with post-menopausal complications (Düsterberg & Nishino, 1982). In the current study, the *Fusarium lini*-induced structural modification of estradiol valerate, (**1**), yielded 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one monohydrate, (**2**), through the loss of the valerate moiety and hydroxylation at C7; (**2**) is a known metabolite previously reported by Iriarte and co-workers (Iriarte *et al.*, 1958). We have investigated the structure and electrostatic properties of crystals of compound (**2**) in order to understand the nature and intensity of the intermolecular interactions contributing to the structural stability in the crystal lattice.



The charge–density distribution (Coppens, 1998; Jayatilaka, 2012) at the surface of a molecule is helpful in understanding the chemical properties of the molecule, including rationalizing the site of chemical reactions. In addition, interactions with proteins and enzymes in biosystems can be better understood, therefore contributing towards a better understanding of biological activity and structure–activity relationship studies. The commonly used independent atom model (IAM) lacks thorough information related to intra- and intermolecular interactions, which can likely produce serious systematic errors in the refined atomic structure (Ruysink & Vos, 1974).

The transferable aspherical atom model (TAAM) is used to achieve the multipolar modelling of low-resolution single-crystal X-ray diffraction data (SC-XRD) because the experimental charge–density calculations require the refinement of multipolar parameters, for which the diffraction data should be collected at high resolution using crystals capable of diffraction at large angles. These methods help in the quantitative modelling of the distortion of the atomic electron distribution arising because of bonding effects and intermolecular interactions. However, operational thermal displacement deconvolution and significant electron-density distributions can be achieved at lower resolution through the transfer of the atomic parameters from an electron-density database (Pichon-Pesme *et al.*, 1995; Jelsch *et al.*, 1998; Dittrich *et al.*, 2004, 2005, 2007; Bąk *et al.*, 2011). The transfer of

electron-density parameters allows the atomic coordinates to be found at their expected values. The ‘transferability principle’ was first reported by Brock *et al.* (1991).

The TAAM was initiated from an IAM refinement against experimental data and later from the experimental library of multipolar atom models using the ELMAM2 database (Domagała *et al.*, 2012), which is used for the study of common organic molecules. Least-squares refinements were performed using the *MoPro* software (Guillot *et al.*, 2001; Jelsch *et al.*, 2005), which uses the Hansen & Coppens (1978) multipolar atom formalism (Coppens, 1998) built with the ELMAM2 database for the automated transfer of a suitable model for the desired structure. In this software, various atoms in a molecule are distinguished with respect to their nature and the number of attached neighbours. The valence and core spherical electron densities were taken from the relativistic Dirac–Fock wave functions of Su & Coppens (1992). Anomalous dispersion coefficients were derived from Kissel *et al.* (1995). The transferability principle for a multipolar model was practiced on the molecule under study with the intention of better refining the structural parameters, *i.e.* the displacement parameters, scale factors and atomic coordinates of all the atoms (except for H atoms attached to C atoms). After appropriate electron-density modelling, residual Fourier maps are improved and residual electron-density peaks localized on the covalent bonds disappear.

2. Experimental

2.1. Microbial culture preparation

Cultures of the fungus *Fusarium lini* (NRRL 2204) (Baydoun *et al.*, 2013) were cultivated on Sabouraud dextrose agar at 298 K and kept at 277 K. The broth medium was made by dissolving peptone (50.0 g), NaCl (50.0 g), glucose (100.0 g), yeast extract (30.0 g), KH_2PO_4 (50.0 g) and glycerol (100.0 ml) in distilled water (10 l) for the growth of the fungi and then suspended in an Erlenmeyer flask. The growth medium was autoclaved and inoculated in the medium. After the mature growth of the culture, compound (**1**) (2.0 g) was allowed to dissolve in acetone (100 ml) and was transferred to the grown culture flasks.

2.2. Fermentation, purification and crystallization

Flasks containing compound (**1**) were incubated for 15 d with the culture of *Fusarium lini*. After this time, filtration of the fungal mass was followed by extraction with ethyl acetate and evaporation of the extract under reduced pressure, resulting in a crude gummy brown material (20 g). The crude material was subjected to silica-gel column chromatography and fractionated using increasing polarities of petroleum ether with acetone. The fraction obtained on elution with 45% acetone in petroleum ether was rechromatographed on silica gel and yielded 10 mg of (**2**) on elution with dichloromethane and methanol (97:3 v/v). Colourless crystals were obtained at room temperature after slow evaporation of the solvent mixture. Crystalline compound (**2**) was further washed with

MeOH–H₂O (1:1 v/v) and dried to obtain crystals suitable for SC-XRD analysis.

2.3. Analytical data for (2)

Colourless crystalline solid: m.p. 532–534 K; $\alpha_D = +4.6$ ($c = 0.01$, CH₃OH); UV [CH₃OH, λ_{\max} nm, log(I)]: 283 (7.9); IR (KBr, ν_{\max} , cm⁻¹): 3418 (OH), 1716 (C=O), 1662 (C=C); EI-MS m/z (relative intensity, %): 286 [M^+] (38), 255 (20), 211 (39); HREI-MS m/z (286.1564, calculated 286.1569): 286.1564 (C₁₈H₂₂O₃, 286.1569).

¹H NMR (500 MHz, CD₃OD): δ 0.90 (3H, *s*, H₃-18), 1.42, 1.81 (2H, *m*, H₂-12), 1.50, 2.50 (2H, *m*, H₂-11), 1.63 (1H, *m*, H-8), 1.79 (1H, *m*, H-14), 1.80, 2.13 (2H, *m*, H₂-15), 2.18, 2.48 (2H, *m*, H-16), 2.68 (1H, *m*, H-9), 2.80, 3.05 (2H, *m*, H₂-6), 4.17 (1H, *brs*, H-7), 6.50 (1H, *brs*, H-4), 6.56 (2H, *dd*, $J_{2,1} = 8.4$ Hz; $J_{2,4} = 2.0$ Hz, H-2), 7.10 (1H, *d*, $J_{1,2} = 8.4$ Hz, H-1).

¹³C NMR (125 MHz, CD₃OD): δ 127.3 (C-1), 114.1 (C-2), 156.3 (C-3), 116.7 (C-4), 136.1 (C-5), 39.3 (C-6), 65.8 (C-7), 43.5 (C-8), 37.0 (C-9), 131.5 (C-10), 27.1 (C-11), 32.8 (C-12), 49.0 (C-13), 47.4 (C-14), 21.9 (C-15), 36.7 (C-16), 223.8 (C-17), 14.1 (C-18).

2.4. Data collection

Single-crystal X-ray diffraction analysis of compound (2) was performed at 100 K using Cu $K\alpha$ radiation ($\lambda = 1.54178$ Å) on a Bruker D8 Venture diffractometer equipped with a PHOTON II detector. The crystal was mounted on a loop using Paratone oil and placed on a Kappa four-circle goniometer under a stream of cold nitrogen gas in order to cool it from room temperature to 100 K during the course of the experiment. Bragg intensities were collected using a 1.0° ω -scan width and a 10 s per frame exposure time, resulting in a total of 2931 reflections and up to a $\sin\theta/\lambda = 0.62$ Å⁻¹.

2.5. Structure solution and SHELXL refinement

Table 1 summarizes the crystal data, data collection and structure refinement details of the transferred model. Most of the H atoms could be located in difference Fourier maps. However, a riding model (Allen & Bruno, 2010) was used for H atoms attached to C atoms, while those attached to O atoms were refined freely. The structure was found to be noncentrosymmetric in nature, with four stereocentres (Jones, 1986). After SHELXL refinement, the R factor was 0.040, a weighted R factor was 0.111 and the goodness-of-fit was 1.10. The highest difference peak and deepest hole were at 0.34 and -0.27 e Å⁻³, respectively. The Flack parameter (Flack, 1983; Flack & Bernardinelli, 2000) refined to a value of -0.01 (7), establishing the correct absolute configuration.

2.6. Independent atom model (IAM) refinement using MoPro

The previously refined model was imported into the least-squares refinement package MoPro (Version 1609; Jelsch *et al.*, 2005). Using the independent atom model (IAM), a full-matrix least-squares refinement was performed in accordance with the intensity data. In order to have a goodness-of-fit close to unity, a SHELXL-type weighting scheme was adopted, *i.e.*

Table 1

Experimental details for the transferred model of (2).

Crystal data	
Chemical formula	C ₁₈ H ₂₂ O ₃ ·H ₂ O
M_r	304.37
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, b, c (Å)	6.143 (3), 8.4833 (17), 14.767 (3)
β (°)	91.94 (2)
V (Å ³)	769.2 (4)
Z	2
Radiation type	Cu $K\alpha$
μ (mm ⁻¹)	0.74
Crystal size (mm)	0.46 × 0.22 × 0.12
Data collection	
Diffractometer	Bruker D8 Venture PHOTON II Detector
Absorption correction	Multi-scan (SADABS; Krause <i>et al.</i> , 2015)
T_{\min}, T_{\max}	0.727, 0.916
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	9196, 2931, 2905
R_{int}	0.043
($\sin\theta/\lambda$) _{max} (Å ⁻¹)	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.040, 0.111, 1.10
No. of reflections	2931
No. of parameters	216
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max}, \Delta\rho_{\min}$ (e Å ⁻³)	0.34, -0.27
Absolute structure	Flack x determined using 1292 quotients $[(I^+) - (I^-)] / [(I^+) + (I^-)]$ (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	-0.01 (7)

Computer programs: APEX2 (Bruker, 2014), SAINT (Bruker, 2014), SIR92 (Altomare *et al.*, 1993) in WinGX (Farrugia, 2012), SHELXL2014 (Sheldrick, 2015), Mercury (Macrae *et al.*, 2008) and publCIF (Westrip, 2010).

$\{w = 1/[\delta^2(F_o^2) + (aP)^2 + bP]\}$, where $P = (F_o^2 + 2F_c^2)/3$, with $a = 0.06$ and $b = 0.05$. Initially, the scale factor was refined, followed by the refinement of the positions of all atoms and displacement parameters, excluding the H atoms. The C–H bond lengths were constrained to standard values of neutron distances from the *International Tables of Crystallography*

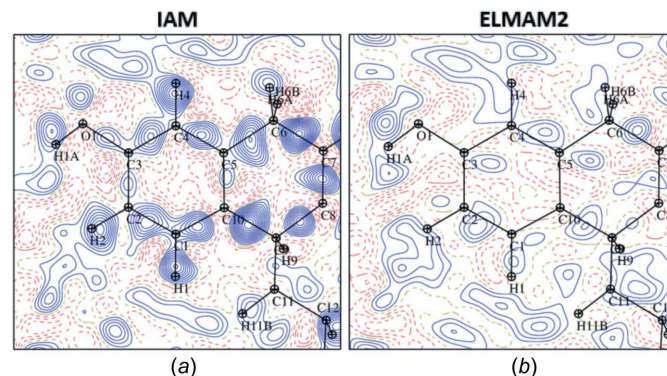


Figure 1
The residual electron-density maps of compound (2) after (a) IAM and (b) ELMAM2 for selected portions of the molecule. Contour level: 0.05 e Å⁻³.

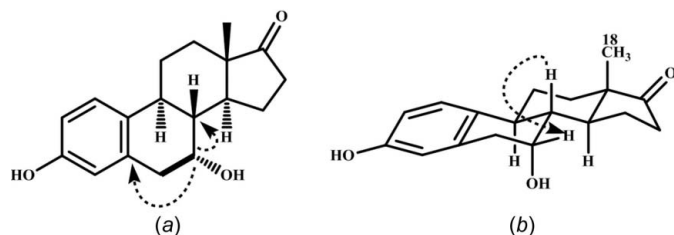


Figure 2
(a) HMBC and (b) NOESY correlations of compound (2).

(Allen & Bruno, 2010), whereas the O–H distances were refined freely. The anisotropic displacement parameters for the H atoms were constrained to calculated values from the *SHADE* server (Madsen, 2006). The scattering form factors for C, H and O are taken from Clementi & Roetti (1974). The refinement was continued until convergence. The residual electron-density maps after the IAM refinement are shown in Fig. 1(a). As a result of IAM refinement, the *R* factor was 0.046, a weighted *R* factor was 0.0681 and the goodness-of-fit was 1.698. The minimum and maximum electron-density peaks and the r.m.s. deviation values were -0.472 , 0.476 and $0.145 \text{ e} \text{ \AA}^{-3}$, respectively.

2.7. ELMAM2 refinement using *MoPro*

The spherical atomic scattering factors of the Hansen and Coppens model (Hansen & Coppens, 1978) were transferred from the ELMAM2 library (Experimental Library of Multipolar Atom Model; Domagała *et al.*, 2012) using the automated mode in *MoPro*. Later, the asymmetric unit was neutralized electrically. The structural parameters, for instance, the scale factor, displacement parameters and position parameters, were refined until convergence, although the electron-density parameters were retained throughout the ELMAM2 refinement. H atoms were treated in a similar way to that described earlier for the IAM refinement. The residual electron-density maps after the ELMAM2 refinement are shown in Fig. 1(b). The crystallographic *R* factor $R[F^2 > 2\sigma(F^2)]$ was 0.032, the weighted *R* factor $[wR(F^2)]$ was 0.044 and the goodness-of-fit (*S*) was 1.10. The minimum and maximum electron-density peaks and the r.m.s. deviation value were -0.263 , 0.281 and $0.0614 \text{ e} \text{ \AA}^{-3}$, respectively. Hence, the ELMAM2-refined model was found to be of significantly better quality than the IAM-refined model.

3. Results and discussion

3.1. Structure elucidation

The HREI-MS (high-resolution electron ionization mass spectrometry) of metabolite (2) showed an M^+ peak at m/z 286.1564, indicating the formula $C_{18}H_{22}O_3$ (calculated 286.1569), consistent with eight degrees of unsaturation, which is consistent with hydrolysis of the ester, followed by oxidation and hydroxylation of compound (1). The IR absorbances at 3418, 1716 and 1662 cm^{-1} indicated the presence of hydroxy, ketonic carbonyl and aromatic groups, respectively. Metabo-

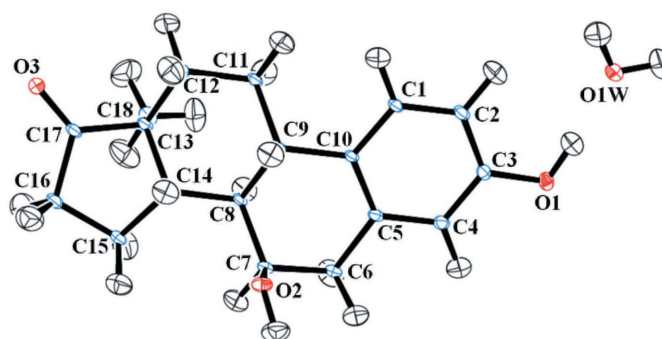


Figure 3
The molecular structure of the title compound, showing the atom-numbering scheme for the non-H atoms. Displacement ellipsoids are drawn at the 50% probability level.

lite (2) showed a characteristic fluorescence in the UV spectrum at 230, 278 and 283 nm, which indicates the presence of a benzene ring in the molecule. The ^1H and ^{13}C NMR spectra showed an additional downfield methine signal at δ 4.17 (*brs*) and δ 69.2, indicating a hydroxy-substituted methine C atom. A new downfield quaternary carbon signal appeared at δ 223.8, indicating the presence of a ketonic functionality in the transformed metabolite. The positions of the hydroxy and ketone functionalities were assigned on the basis of COSY (correlated spectroscopy) and HMBC (heteronuclear multiple bond correlation) correlations. The HMBC correlations of H-7 (δ 4.17, *brs*) with C-6 (δ 39.3) and C-5 (δ 136.1) supported the presence of a hydroxy group at C-7 (Fig. 2). The position of the hydroxy group was further supported by COSY correlations of H₂-6 (δ 2.80, *d*; 3.05, *dd*) with H-7 (δ 4.17, *brs*). The presence of a ketonic functionality at C-17 was deduced from HMBC correlation of H-18 (δ 0.90, *s*) with C-17 (δ 223.8). NOESY (nuclear Overhauser effect spectroscopy) correlations of H-7 (δ 4.17, *brs*) with H-8 (δ 1.63, *m*) supported the stereochemistry of the hydroxy group at C-7 as α (Fig. 2). Finally, metabolite (2) was identified as 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one.

3.2. Crystal structure and packing

The crystal structure of (2), including H atoms, is shown in Fig. 3, while Fig. 1 presents the residual electron-density maps after IAM (Fig. 1a) and ELMAM2 (Fig. 1b) refinements for selected parts of the molecule. IAM maps show that well-defined electron-density peaks are positioned on the covalent bonds, whereas the maps obtained after the ELMAM2 refinement are quite featureless. This result shows the advantage of using the transferred parameters, as it indicates that the bonding electron densities have been taken into account. The compound crystallized as a water solvate having a single independent molecule of 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one along with a molecule of water. It exhibits the fundamental configuration of the estrane (C_{18}) steroid, with a fused four-ring assembly consisting of two cyclohexane [C5–C10 (ring *B*) and C8/C9/C11–C14 (ring *C*)], a phenyl (C1–C5/C10, *A*) and a cyclopentane ring (C13–C17, *D*). Cyclohexane rings *B* and *C* are nonplanar in nature. Ring

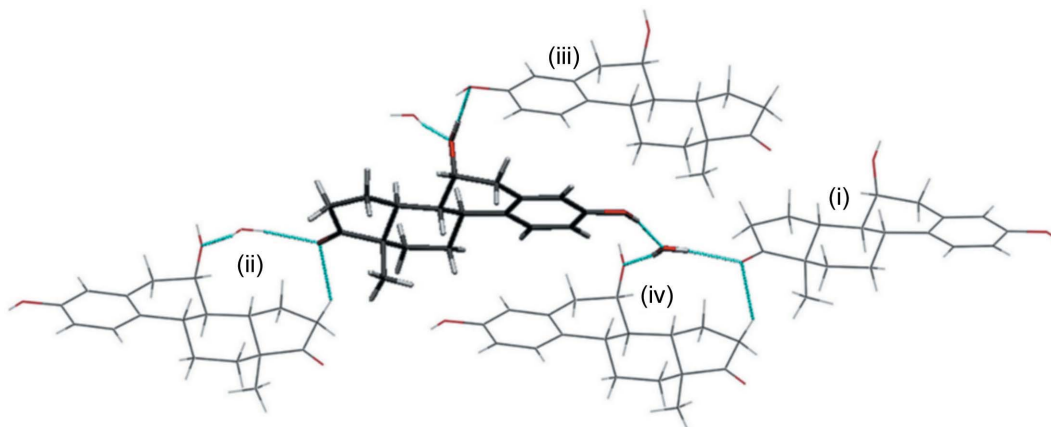
Table 2
 Hydrogen-bond geometry (Å, °) for (2).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1A \cdots O1W	0.87 (4)	1.82 (4)	2.672 (3)	167 (4)
O2—H2A \cdots O1 ⁱ	0.87 (5)	2.00 (5)	2.858 (3)	166 (4)
O1W—H1W \cdots O3 ⁱⁱ	0.81 (4)	2.00 (4)	2.809 (3)	173 (4)
O1W—H2W \cdots O2 ⁱⁱⁱ	0.81 (4)	1.95 (4)	2.758 (3)	171 (4)
C16—H16B \cdots O3 ^{iv}	0.99	2.53	3.353 (3)	141

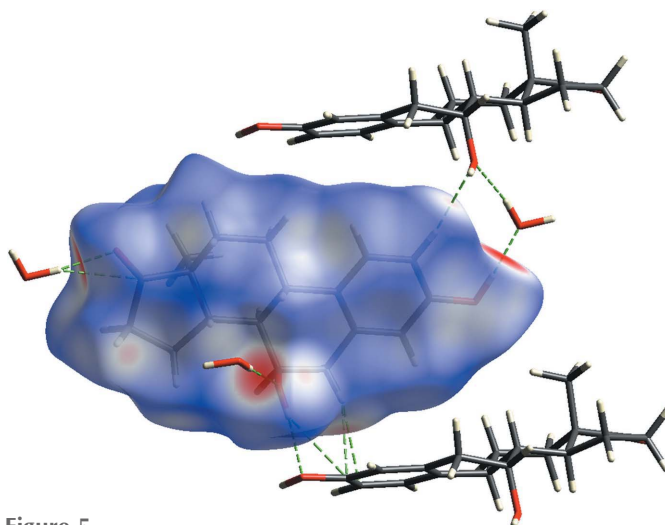
Symmetry codes: (i) $-x + 1, y + \frac{1}{2}, -z + 1$; (ii) $x, y, z + 1$; (iii) $-x + 2, y - \frac{1}{2}, -z + 1$; (iv) $-x + 2, y + \frac{1}{2}, -z$.

B adopts a half-chair conformation due to the olefinic bond between atoms C5 and C10, along with a pseudo-axially oriented hydroxy substituent, attached at C7. The puckering parameters for ring *B* have φ , θ and Q values of 154.7417°, 46.72° and 0.4861 Å, respectively (Cremer & Pople, 1975). Cyclohexane ring *C* has a classical chair conformation, while cyclopentane ring *D* was found to be *trans*-fused to ring *C* along the C13—C14 bond, and displays a 14 β ,17 α -envelope conformation having φ and Q puckering parameters of 210.3238° and 0.4249 Å, respectively (Cremer & Pople, 1975). The torsion angle (C1—C10—C5—C6) at the ring *A/B* intersection is -178.13 (14)°, the torsion angle (C10—C9—C8—C14) at the ring *B/C* intersection is 175.03 (17)° and the torsion angle (C12—C13—C14—C15) at the ring *C/D* intersection is 165.8 (7)°. The 7-hydroxy group has an α configuration, with a C9—C8—C7—O2 torsion angle of 60.35 (18)°. The C13-methyl group has a β -configuration, with a C8—C14—C13—C18 torsion angle of 64.49 (18)°.

In the crystal packing, the molecules are arranged in a stacking order, in parallel sheets and in zigzag chains along the *a*, *b* and *c* axes, respectively, by means of different interactions; Fig. 4 presents a view along the *a* axis. The molecular assembly is built principally on the basis of strong and a number of weak intermolecular hydrogen bonds (Table 2 and Table S1 of the supporting information). The crystal structure can be referred to as a donor–acceptor adduct, in which the carbonyl and hydroxy groups play an essential role in the hydrogen-bonding pattern. The molecule of (2) is in contact with four neighbouring molecules (Fig. 4). Each O atom is involved in the


Figure 4

A view of the molecular packing along an *a* axis, showing the strong intermolecular hydrogen bonds. [Symmetry codes: (i) $-x + 2, y - \frac{1}{2}, -z + 1$; (ii) $-x + 2, y + \frac{1}{2}, -z$; (iii) $-x + 1, y + \frac{1}{2}, -z + 1$; (iv) $-x + 2, y - \frac{1}{2}, -z + 1$.]


Figure 5

A Hirshfeld surface of the parent molecule, showing the interacting molecules.

formation of a strong hydrogen bond. The water molecule plays a bridging role in the crystal packing through the formation of strong intermolecular interactions (Table 2 and Fig. 4). Water atom O1W is directly linked with hydroxy atom H1A of an adjacent molecule and carbonyl atom O3 of another adjacent molecule. There are conventional hydrogen bonds involving the hydroxy and carbonyl groups of the O—H \cdots O and C—H \cdots O types. All the O—H \cdots O interactions are characterized by short distances (≈ 1.8 Å) and the angles are quite linear, while the C—H \cdots O interactions have comparatively longer interatomic distances (≈ 2.5 Å) and the angle is nonlinear. The role of H \cdots H and H \cdots π interactions in the discussion of crystal assembly cannot be underestimated. The molecular assembly is rich in these van der Waal interactions. Table S1 (see supporting information) lists the H \cdots H interactions for which the interatomic distance is shorter than double the van der Waals radius for an H atom. Matta and co-workers (Matta *et al.*, 2003) observed that such contacts have a stabilizing role in the molecular assembly. The results in the following section will reveal that these inter-

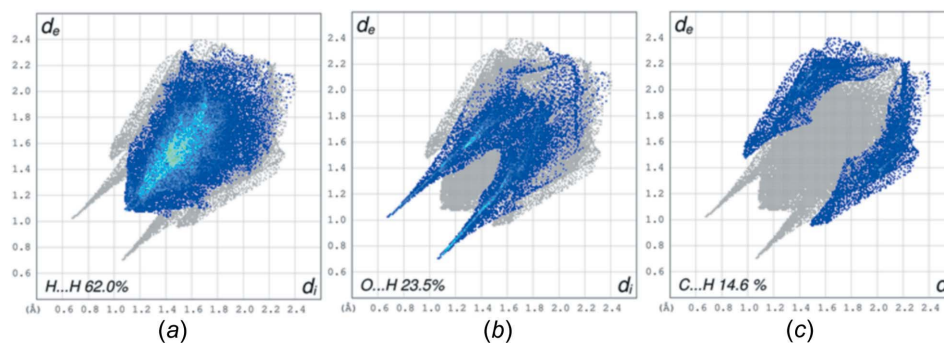


Figure 6
Fingerprint plots showing the percentages of interactions present in the molecule.

actions constitute the major proportion of all the contributing interactions.

3.3. Hirshfeld surface analysis

Hirshfeld surface analysis provides a convenient way to study intermolecular interactions (Spackman & Byrom, 1997; Spackman & Jayatilaka, 2009). The quantity d_{norm} is the ratio of the distance of any surface point to the nearest interior (d_i) and exterior (d_e) atom and the van der Waals radii of the atoms (McKinnon *et al.*, 2007). If d_{norm} is negative, the sum $d_i + d_e$, *i.e.* the contact distance, is shorter than the sum of the van der Waals radii of the atoms. *CrystalExplorer* (Wolff *et al.*, 2012) was used to generate Hirshfeld surfaces recorded over the d_{norm} property of (2), excluding the water molecule (Fig. 5). The red colour shows the region where the intermolecular distance between two atoms is shorter than the sum of their van der Waals radii. The fingerprint plots list the relative contributions of the various interactions of the molecule under discussion. Three kinds of interactions are involved in the crystal packing: H...H interactions account for 62.0%, O...H for 23.5% and C...H for 14.5%, as shown in Fig. 6. The enrichment ratio (ER) was calculated (Jelsch *et al.*, 2014) and shows that H...H contacts are preferred, with an ER value of 1.2315, over O...H and C...H interactions, with ER values of 0.6165 and 0.6165, respectively.

3.4. Electrostatic potential and dipole moment

The prevalence of possible electrostatic contacts close to the molecule can be defined qualitatively using an electrostatic potential map (ESP) on the electron-density isosurface. This helps in the description, as well as the understanding, of the inter- and intramolecular interactions (Drissi *et al.*, 2015). The electrostatic potential is considered predictive of chemical reactivity because regions of negative potential are expected to be sites of potential protonation and nucleophilic attack, while regions of positive potential may indicate electrophilic sites. The electrostatic potential can be measured on the basis of electron-density distribution (Su & Coppens, 1992). Fig. 7 illustrates the three-dimensional electron-density surface, coloured according to electrostatic potential, calculated individually for each fragment in the electrically neutralized asymmetric unit. The maps show that electron density is

accumulated on all the O atoms. The electronegative electrostatic potential spreads over a wide surface from atoms O1 to O2. The intensity of the red colour around carbonyl atom O3 shows a high concentration of negative charge. Likewise, the O1W atom shows a strong negative electrostatic potential and its H atoms are strongly positive. The resulting hydrogen bonds involving atoms O1, O3 and O1W are thus very short in length and provide a backbone to the molecular assembly (Table 2 and Table S1 in the supporting information). The molecule of (2), as well as the whole asymmetric unit, have a highly polar character, as shown by their dipole moment values of 4.42 and 4.28 Debye, respectively (Fig. 8). The dipole moment was calculated using *MoProViewer* (Guillot, 2011) for electrically neutralized individual moieties (grey arrows), as well as for an electrically neutralized asymmetric unit (blue arrow).

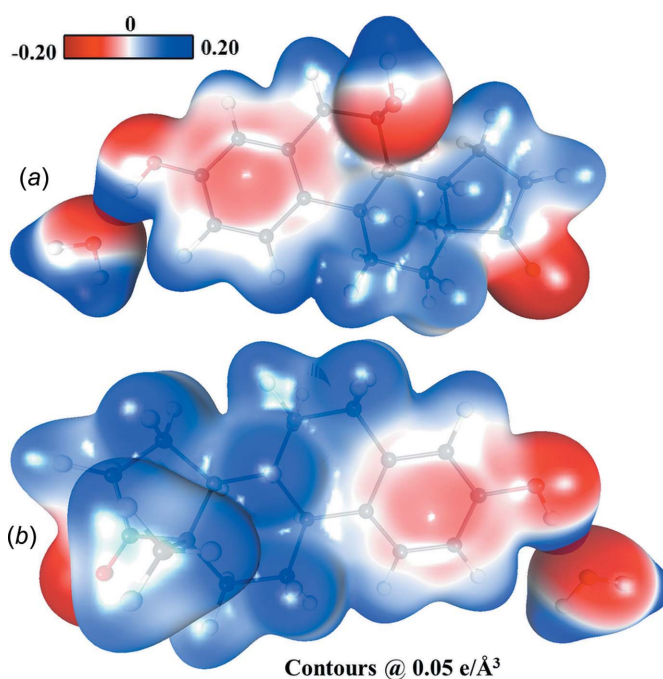


Figure 7
A three-dimensional electron-density isosurface generated at an electron-density value of $0.05 \text{ e} \text{ \AA}^{-3}$, coloured according to electrostatic potential.

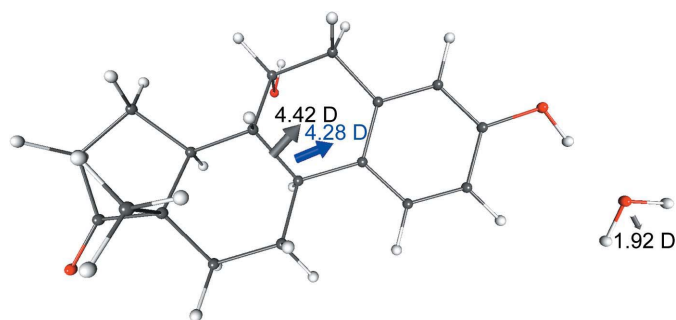


Figure 8
The arrow shows the direction of the total dipole moment (4.28 D) of (2), computed on the basis of transferred parameters.

3.5. Topology of hydrogen bonds

Table S1 (see supporting information) lists the topological parameters of the strong hydrogen bonds. The analysis was performed using Bader's Quantum Theory of Atoms in Molecules (QTAIM; Bader, 1990). The transferred model has the advantage that a quantitative analysis of the bond properties can be established to a reliable extent. The topological analysis confirms that all the O atoms are involved in the formation of strong hydrogen bonds. A survey of Table S1 shows that there are four hydrogen bonds displaying significant values of the electron density at the critical point ($>0.23 \text{ e } \text{Å}^{-3}$), all of them involving either the water molecule as hydrogen-bond donor and acceptor, or hydroxy atom O1. These bonds are characterized by very short distances and high electron-density values at the critical points. The values of the kinetic and potential energy densities for these interactions are also quite high compared to other interactions. The rest of the hydrogen bonds are medium-to-weak in terms of the hydrogen-bond length and the values of the electron density at the critical points are also much lower. As discussed above for the $\text{H} \cdots \text{H}$ interactions, the interatomic distance is shorter than the sum of their van der Waals radii. The electron-density values at the critical points for the $\text{H} \cdots \text{H}$ interactions range from 0.03 to $0.05 \text{ e } \text{Å}^{-3}$. All these CPs have positive Laplacian values, a characteristic of closed-shell interactions.

4. Conclusions

The biotransformation of estradiol valerate has provided very interesting results. During the process, the valerate moiety was consumed by the fungus. Spectroscopic and spectrometric analyses confirmed the molecular structure, which was further authenticated by single-crystal X-ray diffraction analysis. The transferred aspherical atom model of the crystal gives valuable quantitative information about the intra- and intermolecular interactions present. The molecular assembly is stabilized by very strong classical hydrogen bonds, as well as by weak van der Waals contacts. The dissymmetric character of the charge distribution generating a dipole moment along the molecule was established. The calculation of electrostatic potential validates the polar nature of the molecule and highlights the

regions of charge concentration and charge depletion which anchor the inter- and intramolecular hydrogen-bond network. Besides this, it has been observed that the aspherical atom model refinement gives superior refinement statistics to the classical spherical atom model refinement. The findings strongly encourage the use of the database transfer approach in routine crystal structure determinations and in investigations of quantitative crystal engineering in the absence of high-resolution diffraction data, given the simplicity involved in the whole procedure. We are currently attempting to explore the bioactivities of the biotransformed product *vis-à-vis* its parent molecule and its potential as a drug *via in silico* and *in vitro* studies.

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References

- Ahmad, M. S., Zafar, S., Yousuf, S., Wahab, A. T., Rahman, A. U. & Choudhary, M. I. (2016). *Steroids*, **112**, 62–67.
- Allen, F. H. & Bruno, I. J. (2010). *Acta Cryst.* **B66**, 380–386.
- Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. (1993). *J. Appl. Cryst.* **26**, 343–350.
- Bader, R. F. W. (1990). In *Atoms in Molecules: A Quantum Theory*. Oxford: Clarendon Press.
- Båk, J. M., Domagała, S., Hübschle, C., Jelsch, C., Dittrich, B. & Dominiak, P. M. (2011). *Acta Cryst.* **A67**, 141–153.
- Baydoun, E., Bibi, M., Iqbal, M. A., Wahab, A., Farran, D., Smith, C., Sattar, S. A., Rahman, A. U. & Choudhary, M. I. (2013). *Chem. Cent. J.* **7**, article No. 57.
- Baydoun, E., Karam, M., Atia-tul-Wahab, Khan, M. S., Ahmad, M. S., Samreen, Smith, C., Abdel-Massih, R. & Choudhary, M. I. (2014). *Steroids*, **88**, 95–100.
- Borges, K. B., de Souza Borges, W., Durán-Patrón, R., Pupo, M. T., Bonato, P. S. & Collado, I. G. (2009). *Tetrahedron Asymmetry*, **20**, 385–397.
- Brock, C. P., Dunitz, J. D. & Hirshfeld, F. L. (1991). *Acta Cryst.* **B47**, 789–797.
- Bruker (2014). *APEX2*. Bruker AXS Inc., Madison, Wisconsin, USA.
- Clementi, E. & Roetti, C. (1974). *Atom. Data Nucl. Data Tables*, **14**, 177–478.
- Coppens, P. (1998). *Acta Cryst.* **A54**, 779–788.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Dittrich, B., Hübschle, C. B., Messerschmidt, M., Kalinowski, R., Girtl, D. & Luger, P. (2005). *Acta Cryst.* **A61**, 314–320.
- Dittrich, B., Koritsánszky, T. & Luger, P. (2004). *Angew. Chem. Int. Ed.* **43**, 2718–2721.
- Dittrich, B., Munshi, P. & Spackman, M. A. (2007). *Acta Cryst.* **B63**, 505–509.
- Domagała, S., Fournier, B., Liebschner, D., Guillot, B. & Jelsch, C. (2012). *Acta Cryst.* **A68**, 337–351.
- Drissi, M., Benhalima, N., Megrouss, Y., Rachida, R., Chouaih, A. & Hamzaoui, F. (2015). *Molecules*, **20**, 4042–4054.
- Düsterberg, B. & Nishino, Y. (1982). *Maturitas*, **4**, 315–324.
- Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.
- Guillot, B. (2011). *Acta Cryst.* **A67**, C511–C512.
- Guillot, B., Viry, L., Guillot, R., Lecomte, C. & Jelsch, C. (2001). *J. Appl. Cryst.* **34**, 214–223.
- Hansen, N. K. & Coppens, P. (1978). *Acta Cryst.* **A34**, 909–921.

- Hegazy, M.-E. F., Mohamed, T. A., ElShamy, A. I., Mohamed, A.-E.-H. H., Mahalel, U. A., Reda, E. H., Shaheen, A. M., Tawfik, W. A., Shahat, A. A., Shams, K. A., Abdel-Azim, N. S. & Hammouda, F. M. (2015). *J. Adv. Res.* **6**, 17–33.
- Hussain, Z., Dastagir, N., Hussain, S., Jabeen, A., Zafar, S., Malik, R., Bano, S., Wajid, A. & Choudhary, M. I. (2016). *Steroids*, **112**, 68–73.
- Iriarte, J., Ringold, H. & Djerassi, C. (1958). *J. Am. Chem. Soc.* **80**, 6105–6110.
- Jayatilaka, D. (2012). *Modern Charge-Density Analysis*, edited by C. Gatti & P. Macchi, pp. 213–257. New York: Springer.
- Jelsch, C., Ejsmont, K. & Huder, L. (2014). *IUCrJ*, **1**, 119–128.
- Jelsch, C., Guillot, B., Lagoutte, A. & Lecomte, C. (2005). *J. Appl. Cryst.* **38**, 38–54.
- Jelsch, C., Pichon-Pesme, V., Lecomte, C. & Aubry, A. (1998). *Acta Cryst.* **D54**, 1306–1318.
- Jones, P. G. (1986). *Acta Cryst.* **A42**, 57.
- Kissel, L., Zhou, B., Roy, S. C., Sen Gupta, S. K. & Pratt, R. H. (1995). *Acta Cryst.* **A51**, 271–288.
- Krause, L., Herbst-Irmer, R., Sheldrick, G. M. & Stalke, D. (2015). *J. Appl. Cryst.* **48**, 3–10.
- Lilly, M. D. (1994). *Chem. Eng. Sci.* **49**, 151–159.
- Macrae, C. F., Bruno, I. J., Chisholm, J. A., Edgington, P. R., McCabe, P., Pidcock, E., Rodriguez-Monge, L., Taylor, R., van de Streek, J. & Wood, P. A. (2008). *J. Appl. Cryst.* **41**, 466–470.
- Madsen, A. Ø. (2006). *J. Appl. Cryst.* **39**, 757–758.
- Matta, C. F., Hernández-Trujillo, J., Tang, T. H. & Bader, R. F. (2003). *Chem. Eur. J.* **9**, 1940–1951.
- McKinnon, J. J., Jayatilaka, D. & Spackman, M. A. (2007). *Chem. Commun.* pp. 3814–3816.
- Nankai, H., Miyazawa, M. & Kameoka, H. (1997). *J. Nat. Prod.* **60**, 287–289.
- Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst.* **B69**, 249–259.
- Pichon-Pesme, V., Lecomte, C. & Lachezar, H. (1995). *J. Phys. Chem.* **99**, 6242–6250.
- Ruysink, A. F. J. & Vos, A. (1974). *Acta Cryst.* **A30**, 503–506.
- Shah, S. A. A., Sultan, S., Hassan, N. B., Muhammad, F. K. B., Faridz, M. A., Hussain, F. B., Hussain, M. & Adnan, H. S. (2013). *Steroids*, **78**, 1312–1324.
- Sheldrick, G. M. (2015). *Acta Cryst.* **C71**, 3–8.
- Spackman, M. A. & Byrom, P. G. (1997). *Chem. Phys. Lett.* **267**, 215–220.
- Spackman, M. A. & Jayatilaka, D. (2009). *CrystEngComm*, **11**, 19–32.
- Su, Z. & Coppens, P. (1992). *Acta Cryst.* **A48**, 188–197.
- Wang, Z., Xu, J.-H. & Chen, D. (2008). *J. Ind. Microbiol. Biotechnol.* **35**, 645–656.
- Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.
- Wolff, S. K., Grimwood, D. J., McKinnon, J. J., Turner, M. J., Jayatilaka, D. & Spackman, M. A. (2012). *CrystalExplorer*. The University of Western Australia.

supporting information

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Biotransformation, spectroscopic investigation, crystal structure and electrostatic properties of 3,7 α -dihydroxyestra-1,3,5(10)-trien-17-one monohydrate studied using transferred electron-density parameters

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Computing details

For all structures, data collection: Bruker D8 Venture PHOTON II Detector; cell refinement: *APEX2* (Bruker, 2014); data reduction: *SAINT* (Bruker, 2014). Program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993) in *WinGX* (Farrugia, 2012) for IAM_SHELXL; *SIR92* (Altomare *et al.*, 1993) for IAM_MoPro, ELMAM2_MoPro. Program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015) for IAM_SHELXL; *MoPro* (Jelsch *et al.*, 2005) for IAM_MoPro, ELMAM2_MoPro. Molecular graphics: *Mercury* (Macrae *et al.*, 2008) for IAM_SHELXL; *Mercury* (Macrae *et al.*, 2008) and *MoProViewer* (Guillot, 2011) for IAM_MoPro, ELMAM2_MoPro. Software used to prepare material for publication: *publCIF* (Westrip, 2010) for IAM_SHELXL, IAM_MoPro; *pubCIF* (Westrip, 2010) for ELMAM2_MoPro.

3,7 α -Dihydroxyestra-1,3,5(10)-trien-17-one monohydrate (IAM_SHELXL)

Crystal data

$C_{18}H_{22}O_3 \cdot H_2O$

$M_r = 304.37$

Monoclinic, $P2_1$

$a = 6.143$ (3) Å

$b = 8.4833$ (17) Å

$c = 14.767$ (3) Å

$\beta = 91.94$ (2)°

$V = 769.2$ (4) Å³

$Z = 2$

$F(000) = 328$

$D_x = 1.314$ Mg m⁻³

Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å

Cell parameters from 2931 reflections

$\theta = 3.0$ – 72.2 °

$\mu = 0.74$ mm⁻¹

$T = 100$ K

Block, colorless

$0.46 \times 0.22 \times 0.12$ mm

Data collection

Bruker D8 Venture PHOTON II Detector
diffractometer

Radiation source: Microfocus

ω and phi scan

Absorption correction: multi-scan
(SADABS; Krause *et al.*, 2015)

$T_{\min} = 0.727$, $T_{\max} = 0.916$

9196 measured reflections

2931 independent reflections

2905 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.043$

$\theta_{\text{max}} = 72.2$ °, $\theta_{\text{min}} = 3.0$ °

$h = -7 \rightarrow 7$

$k = -10 \rightarrow 10$

$l = -18 \rightarrow 18$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.040$

$wR(F^2) = 0.111$

$S = 1.10$

2931 reflections

216 parameters

1 restraint

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0682P)^2 + 0.209P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.34 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.27 \text{ e } \text{\AA}^{-3}$

Absolute structure: Flack x determined using

1292 quotients $[(I+)-(I-)]/[(I+)+(I-)]$ (Parsons *et al.*, 2013)

Absolute structure parameter: -0.01 (7)

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.6688 (3)	0.5239 (2)	0.69523 (11)	0.0141 (4)
H1A	0.774 (6)	0.490 (5)	0.730 (2)	0.030 (9)*
O2	0.6550 (3)	0.7883 (2)	0.27748 (12)	0.0148 (4)
H2A	0.574 (6)	0.870 (6)	0.289 (3)	0.033 (10)*
O1W	0.9626 (3)	0.3746 (3)	0.80166 (12)	0.0201 (4)
H1W	0.981 (6)	0.370 (5)	0.856 (3)	0.027 (9)*
H2W	1.078 (7)	0.343 (5)	0.783 (3)	0.028 (9)*
O3	1.0195 (3)	0.3311 (3)	-0.01042 (12)	0.0231 (5)
C1	0.9590 (4)	0.4364 (3)	0.48721 (16)	0.0124 (5)
H1	1.0902	0.3880	0.4693	0.015*
C2	0.9183 (4)	0.4486 (3)	0.57874 (16)	0.0136 (5)
H2	1.0214	0.4102	0.6228	0.016*
C3	0.7254 (4)	0.5174 (3)	0.60558 (16)	0.0125 (5)
C4	0.5790 (4)	0.5774 (3)	0.54083 (16)	0.0131 (5)
H4	0.4494	0.6271	0.5594	0.016*
C5	0.6200 (4)	0.5654 (3)	0.44851 (16)	0.0118 (5)
C6	0.4464 (4)	0.6267 (3)	0.38191 (16)	0.0128 (5)
H6A	0.3933	0.7294	0.4041	0.015*
H6B	0.3219	0.5526	0.3806	0.015*
C7	0.5227 (4)	0.6481 (3)	0.28548 (16)	0.0116 (5)
H7	0.3922	0.6576	0.2435	0.014*
C8	0.6552 (4)	0.5052 (3)	0.25817 (15)	0.0110 (5)
H8	0.5623	0.4096	0.2656	0.013*
C9	0.8621 (4)	0.4845 (3)	0.31968 (15)	0.0104 (5)
H9	0.9604	0.5752	0.3067	0.013*
C10	0.8115 (4)	0.4937 (3)	0.42027 (15)	0.0108 (5)
C11	0.9846 (4)	0.3337 (3)	0.29445 (15)	0.0129 (5)
H11A	0.8934	0.2411	0.3082	0.015*

H11B	1.1203	0.3263	0.3323	0.015*
C12	1.0424 (4)	0.3285 (3)	0.19371 (15)	0.0131 (5)
H12A	1.1505	0.4116	0.1813	0.016*
H12B	1.1081	0.2251	0.1797	0.016*
C13	0.8380 (4)	0.3538 (3)	0.13362 (15)	0.0128 (5)
C14	0.7266 (4)	0.5091 (3)	0.15995 (15)	0.0113 (5)
H14	0.8409	0.5927	0.1572	0.014*
C15	0.5634 (4)	0.5425 (3)	0.08079 (15)	0.0150 (5)
H15A	0.5223	0.6553	0.0783	0.018*
H15B	0.4302	0.4776	0.0854	0.018*
C16	0.6951 (4)	0.4945 (3)	-0.00233 (15)	0.0145 (5)
H16A	0.6002	0.4404	-0.0481	0.017*
H16B	0.7598	0.5886	-0.0306	0.017*
C17	0.8726 (4)	0.3840 (3)	0.03380 (16)	0.0144 (5)
C18	0.6847 (4)	0.2096 (3)	0.13510 (17)	0.0169 (5)
H18A	0.5525	0.2319	0.0983	0.025*
H18B	0.6455	0.1876	0.1976	0.025*
H18C	0.7588	0.1177	0.1103	0.025*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0172 (8)	0.0134 (9)	0.0116 (8)	-0.0012 (7)	-0.0026 (6)	-0.0006 (6)
O2	0.0149 (8)	0.0080 (9)	0.0215 (8)	0.0008 (7)	0.0007 (6)	0.0014 (7)
O1W	0.0199 (9)	0.0266 (11)	0.0137 (9)	0.0079 (8)	-0.0012 (7)	0.0011 (8)
O3	0.0279 (10)	0.0280 (11)	0.0134 (8)	0.0139 (8)	0.0013 (7)	0.0012 (8)
C1	0.0111 (10)	0.0088 (11)	0.0170 (11)	0.0002 (9)	-0.0033 (8)	-0.0004 (9)
C2	0.0145 (10)	0.0109 (11)	0.0151 (11)	-0.0012 (9)	-0.0049 (8)	0.0015 (9)
C3	0.0176 (11)	0.0062 (11)	0.0134 (10)	-0.0044 (9)	-0.0024 (8)	-0.0008 (9)
C4	0.0144 (11)	0.0085 (11)	0.0164 (11)	-0.0001 (9)	-0.0016 (8)	-0.0018 (9)
C5	0.0124 (10)	0.0066 (11)	0.0162 (11)	-0.0015 (9)	-0.0037 (8)	-0.0001 (9)
C6	0.0111 (10)	0.0126 (12)	0.0144 (11)	0.0022 (9)	-0.0017 (8)	0.0015 (9)
C7	0.0107 (10)	0.0093 (11)	0.0146 (11)	-0.0001 (9)	-0.0027 (8)	0.0017 (9)
C8	0.0111 (10)	0.0100 (11)	0.0116 (10)	0.0000 (9)	-0.0045 (8)	0.0006 (9)
C9	0.0108 (10)	0.0092 (11)	0.0112 (10)	0.0016 (9)	-0.0034 (8)	0.0011 (8)
C10	0.0129 (10)	0.0077 (10)	0.0116 (10)	-0.0010 (9)	-0.0021 (8)	-0.0006 (9)
C11	0.0157 (11)	0.0111 (11)	0.0117 (10)	0.0027 (9)	-0.0033 (8)	0.0003 (9)
C12	0.0163 (11)	0.0105 (12)	0.0124 (10)	0.0043 (9)	-0.0014 (8)	-0.0003 (9)
C13	0.0157 (11)	0.0110 (12)	0.0114 (10)	0.0009 (9)	-0.0038 (8)	-0.0008 (9)
C14	0.0121 (10)	0.0088 (11)	0.0125 (11)	0.0011 (9)	-0.0048 (8)	0.0003 (9)
C15	0.0163 (11)	0.0160 (12)	0.0125 (10)	0.0052 (9)	-0.0041 (9)	0.0024 (9)
C16	0.0166 (11)	0.0142 (11)	0.0123 (10)	0.0028 (10)	-0.0044 (8)	0.0010 (9)
C17	0.0194 (11)	0.0099 (11)	0.0134 (11)	0.0017 (10)	-0.0049 (8)	-0.0002 (9)
C18	0.0239 (13)	0.0100 (11)	0.0166 (11)	-0.0019 (10)	-0.0049 (9)	-0.0014 (9)

Geometric parameters (Å, °)

O1—C3	1.381 (3)	C8—H8	1.0000
O1—H1A	0.87 (4)	C9—C10	1.530 (3)
O2—C7	1.447 (3)	C9—C11	1.536 (3)
O2—H2A	0.87 (5)	C9—H9	1.0000
O1W—O1W	0.000 (6)	C11—C12	1.542 (3)
O1W—H1W	0.81 (4)	C11—H11A	0.9900
O1W—H2W	0.81 (4)	C11—H11B	0.9900
O3—C17	1.217 (3)	C12—C13	1.528 (3)
C1—C2	1.387 (3)	C12—H12A	0.9900
C1—C10	1.405 (3)	C12—H12B	0.9900
C1—H1	0.9500	C13—C17	1.518 (3)
C2—C3	1.391 (4)	C13—C14	1.540 (3)
C2—H2	0.9500	C13—C18	1.544 (3)
C3—C4	1.387 (3)	C14—C15	1.541 (3)
C4—C5	1.398 (3)	C14—H14	1.0000
C4—H4	0.9500	C15—C16	1.547 (3)
C5—C10	1.401 (3)	C15—H15A	0.9900
C5—C6	1.518 (3)	C15—H15B	0.9900
C6—C7	1.525 (3)	C16—C17	1.521 (3)
C6—H6A	0.9900	C16—H16A	0.9900
C6—H6B	0.9900	C16—H16B	0.9900
C7—C8	1.523 (3)	C18—H18A	0.9800
C7—H7	1.0000	C18—H18B	0.9800
C8—C14	1.530 (3)	C18—H18C	0.9800
C8—C9	1.547 (3)		
C3—O1—H1A	111 (2)	C1—C10—C9	121.2 (2)
C7—O2—H2A	108 (3)	C9—C11—C12	112.87 (18)
O1W—O1W—H1W	0 (10)	C9—C11—H11A	109.0
O1W—O1W—H2W	0 (10)	C12—C11—H11A	109.0
H1W—O1W—H2W	103 (4)	C9—C11—H11B	109.0
C2—C1—C10	121.8 (2)	C12—C11—H11B	109.0
C2—C1—H1	119.1	H11A—C11—H11B	107.8
C10—C1—H1	119.1	C13—C12—C11	110.15 (18)
C1—C2—C3	119.5 (2)	C13—C12—H12A	109.6
C1—C2—H2	120.2	C11—C12—H12A	109.6
C3—C2—H2	120.2	C13—C12—H12B	109.6
O1—C3—C4	117.9 (2)	C11—C12—H12B	109.6
O1—C3—C2	122.3 (2)	H12A—C12—H12B	108.1
C4—C3—C2	119.8 (2)	C17—C13—C12	116.61 (19)
C3—C4—C5	120.7 (2)	C17—C13—C14	100.30 (19)
C3—C4—H4	119.6	C12—C13—C14	109.68 (19)
C5—C4—H4	119.6	C17—C13—C18	104.66 (18)
C4—C5—C10	120.17 (19)	C12—C13—C18	111.7 (2)
C4—C5—C6	117.5 (2)	C14—C13—C18	113.43 (19)
C10—C5—C6	122.3 (2)	C8—C14—C13	111.41 (18)

C5—C6—C7	114.50 (19)	C8—C14—C15	121.54 (18)
C5—C6—H6A	108.6	C13—C14—C15	104.42 (19)
C7—C6—H6A	108.6	C8—C14—H14	106.2
C5—C6—H6B	108.6	C13—C14—H14	106.2
C7—C6—H6B	108.6	C15—C14—H14	106.2
H6A—C6—H6B	107.6	C14—C15—C16	102.07 (18)
O2—C7—C8	109.01 (18)	C14—C15—H15A	111.4
O2—C7—C6	111.41 (19)	C16—C15—H15A	111.4
C8—C7—C6	109.67 (19)	C14—C15—H15B	111.4
O2—C7—H7	108.9	C16—C15—H15B	111.4
C8—C7—H7	108.9	H15A—C15—H15B	109.2
C6—C7—H7	108.9	C17—C16—C15	105.76 (19)
C7—C8—C14	114.03 (18)	C17—C16—H16A	110.6
C7—C8—C9	111.77 (18)	C15—C16—H16A	110.6
C14—C8—C9	107.62 (17)	C17—C16—H16B	110.6
C7—C8—H8	107.7	C15—C16—H16B	110.6
C14—C8—H8	107.7	H16A—C16—H16B	108.7
C9—C8—H8	107.7	O3—C17—C13	126.1 (2)
C10—C9—C11	113.27 (17)	O3—C17—C16	125.1 (2)
C10—C9—C8	111.99 (18)	C13—C17—C16	108.8 (2)
C11—C9—C8	110.57 (18)	C13—C18—H18A	109.5
C10—C9—H9	106.9	C13—C18—H18B	109.5
C11—C9—H9	106.9	H18A—C18—H18B	109.5
C8—C9—H9	106.9	C13—C18—H18C	109.5
C5—C10—C1	118.0 (2)	H18A—C18—H18C	109.5
C5—C10—C9	120.76 (19)	H18B—C18—H18C	109.5
C10—C1—C2—C3	0.8 (4)	C8—C9—C10—C1	162.4 (2)
C1—C2—C3—O1	175.8 (2)	C10—C9—C11—C12	-177.84 (17)
C1—C2—C3—C4	-1.9 (4)	C8—C9—C11—C12	55.5 (2)
O1—C3—C4—C5	-175.9 (2)	C9—C11—C12—C13	-53.9 (3)
C2—C3—C4—C5	1.9 (4)	C11—C12—C13—C17	168.4 (2)
C3—C4—C5—C10	-0.7 (3)	C11—C12—C13—C14	55.3 (3)
C3—C4—C5—C6	177.1 (2)	C11—C12—C13—C18	-71.4 (3)
C4—C5—C6—C7	165.5 (2)	C7—C8—C14—C13	-173.83 (18)
C10—C5—C6—C7	-16.8 (3)	C9—C8—C14—C13	61.6 (2)
C5—C6—C7—O2	-76.3 (3)	C7—C8—C14—C15	-50.2 (3)
C5—C6—C7—C8	44.5 (3)	C9—C8—C14—C15	-174.7 (2)
O2—C7—C8—C14	-61.8 (2)	C17—C13—C14—C8	175.36 (17)
C6—C7—C8—C14	175.94 (18)	C12—C13—C14—C8	-61.4 (2)
O2—C7—C8—C9	60.5 (2)	C18—C13—C14—C8	64.3 (2)
C6—C7—C8—C9	-61.7 (2)	C17—C13—C14—C15	42.4 (2)
C7—C8—C9—C10	49.0 (3)	C12—C13—C14—C15	165.7 (2)
C14—C8—C9—C10	174.96 (19)	C18—C13—C14—C15	-68.6 (2)
C7—C8—C9—C11	176.37 (18)	C8—C14—C15—C16	-166.9 (2)
C14—C8—C9—C11	-57.7 (2)	C13—C14—C15—C16	-40.0 (2)
C4—C5—C10—C1	-0.5 (3)	C14—C15—C16—C17	21.3 (3)
C6—C5—C10—C1	-178.1 (2)	C12—C13—C17—O3	31.8 (4)

C4—C5—C10—C9	-178.0 (2)	C14—C13—C17—O3	150.0 (3)
C6—C5—C10—C9	4.4 (3)	C18—C13—C17—O3	-92.2 (3)
C2—C1—C10—C5	0.4 (3)	C12—C13—C17—C16	-147.2 (2)
C2—C1—C10—C9	177.9 (2)	C14—C13—C17—C16	-28.9 (2)
C11—C9—C10—C5	-146.1 (2)	C18—C13—C17—C16	88.8 (2)
C8—C9—C10—C5	-20.2 (3)	C15—C16—C17—O3	-174.0 (2)
C11—C9—C10—C1	36.5 (3)	C15—C16—C17—C13	4.9 (3)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O1—H1 <i>A</i> ...O1 <i>W</i>	0.87 (4)	1.82 (4)	2.672 (3)	167 (4)
O2—H2 <i>A</i> ...O1 ⁱ	0.87 (5)	2.00 (5)	2.858 (3)	166 (4)
O1 <i>W</i> —H1 <i>W</i> ...O3 ⁱⁱ	0.81 (4)	2.00 (4)	2.809 (3)	173 (4)
O1 <i>W</i> —H2 <i>W</i> ...O2 ⁱⁱⁱ	0.81 (4)	1.95 (4)	2.758 (3)	171 (4)
C16—H16 <i>B</i> ...O3 ^{iv}	0.99	2.53	3.353 (3)	141

Symmetry codes: (i) $-x+1, y+1/2, -z+1$; (ii) $x, y, z+1$; (iii) $-x+2, y-1/2, -z+1$; (iv) $-x+2, y+1/2, -z$.

3,7 α -Dihydroxyestra-1,3,5(10)-trien-17-one monohydrate (IAM_MoPro)

Crystal data

C₁₈H₂₂O₃·H₂O

M_r = 304.37

Monoclinic, *P*2₁

Hall symbol: P 2yb

a = 6.143 (3) Å

b = 8.4833 (17) Å

c = 14.767 (3) Å

β = 91.94 (2)°

V = 769.2 (4) Å³

Z = 2

F(000) = 328

D_x = 1.315 Mg m⁻³

Cu *K* α radiation, λ = 1.54178 Å

Cell parameters from 2931 reflections

θ = 3.0–72.2°

μ = 0.74 mm⁻¹

T = 100 K

Block, colorless

0.46 × 0.22 × 0.12 mm

Data collection

Bruker D8 Venture PHOTON II Detector
diffractometer

Radiation source: Microfocus

Graphite monochromator

ω and ϕ scan

Absorption correction: multi-scan
(SADABS; Krause *et al.*, 2015)

T_{min} = 0.727, *T_{max}* = 0.916

9196 measured reflections

2931 independent reflections

2905 reflections with $> 2.0\sigma(I)$

R_{int} = 0.043

θ_{\max} = 72.2°, θ_{\min} = 3.0°

h = 0→7

k = -10→10

l = -18→18

Refinement

Refinement on *F*²

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)]$ = 0.046

wR(*F*²) = 0.134

S = 1.70

2931 reflections

271 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: difference Fourier map

Only H-atom coordinates refined

$w = 1/[\sigma^2(F_o^2) + (0.06P)^2 + 0.05P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.48 \text{ e \AA}^{-3}$

$\Delta\rho_{\min} = -0.47 \text{ e \AA}^{-3}$

Special details

Refinement. Refinement of F^2 against reflections. The threshold expression of $F^2 > \sigma(F^2)$ is used for calculating R -factors(gt) 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 (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.6691 (2)	0.5303 (18)	0.69523 (9)	0.0145 (2)
H1A	0.771 (7)	0.497 (6)	0.729 (3)	0.02703
O2	0.6550 (2)	0.7949 (18)	0.27754 (9)	0.0150 (2)
H2A	0.569 (7)	0.878 (6)	0.287 (3)	0.02693
O1W	0.9627 (2)	0.3808 (18)	0.80172 (10)	0.0210 (3)
H1W	0.981 (7)	0.383 (7)	0.857 (3)	0.03779
H2W	1.089 (7)	0.352 (6)	0.778 (3)	0.03638
O3	1.0190 (3)	0.3374 (18)	-0.01060 (10)	0.0237 (3)
C1	0.9593 (3)	0.4431 (18)	0.48726 (13)	0.0131 (3)
H1	1.108 (17)	0.387 (5)	0.467 (2)	0.02779
C2	0.9186 (3)	0.4551 (18)	0.57883 (13)	0.0142 (3)
H2	1.036 (5)	0.411 (5)	0.629 (17)	0.02932
C3	0.7256 (3)	0.5237 (18)	0.60563 (13)	0.0126 (3)
C4	0.5789 (3)	0.5840 (18)	0.54091 (13)	0.0133 (3)
H4	0.431 (17)	0.640 (5)	0.562 (3)	0.02804
C5	0.6200 (3)	0.5721 (18)	0.44843 (13)	0.0122 (3)
C6	0.4462 (3)	0.6331 (18)	0.38198 (13)	0.0136 (3)
H6A	0.387 (6)	0.746 (17)	0.407 (2)	0.02937
H6B	0.309 (5)	0.551 (17)	0.381 (3)	0.02862
C7	0.5231 (3)	0.6547 (19)	0.28560 (13)	0.0120 (3)
H7	0.380 (4)	0.665 (6)	0.239 (17)	0.02545
C8	0.6548 (3)	0.5115 (18)	0.25829 (12)	0.0111 (3)
H8	0.553 (5)	0.406 (17)	0.266 (3)	0.02337
C9	0.8624 (3)	0.4910 (18)	0.31962 (12)	0.0108 (3)
H9	0.971 (5)	0.590 (17)	0.305 (3)	0.02281
C10	0.8115 (3)	0.5000 (19)	0.42027 (12)	0.0111 (3)
C11	0.9845 (3)	0.3399 (18)	0.29438 (12)	0.0135 (3)
H11A	0.884 (6)	0.238 (17)	0.310 (3)	0.02872
H11B	1.134 (3)	0.331 (6)	0.336 (17)	0.02925
C12	1.0428 (3)	0.3350 (18)	0.19373 (12)	0.0136 (3)
H12A	1.162 (5)	0.426 (17)	0.180 (3)	0.03017
H12B	1.115 (7)	0.221 (17)	0.178 (3)	0.03286
C13	0.8378 (3)	0.3600 (18)	0.13353 (12)	0.0136 (3)
C14	0.7264 (3)	0.5152 (19)	0.15996 (12)	0.0115 (3)
H14	0.852 (5)	0.607 (17)	0.157 (3)	0.02364
C15	0.5631 (3)	0.5489 (18)	0.08092 (12)	0.0155 (3)
H15A	0.518 (7)	0.673 (17)	0.078 (3)	0.03038
H15B	0.417 (17)	0.477 (5)	0.086 (3)	0.03153
C16	0.6949 (3)	0.5010 (18)	-0.00233 (12)	0.0153 (3)
H16A	0.591 (6)	0.441 (5)	-0.053 (17)	0.03449

H16B	0.767 (6)	0.604 (17)	-0.034 (3)	0.03202
C17	0.8725 (3)	0.3904 (18)	0.03395 (13)	0.0146 (3)
C18	0.6848 (3)	0.2162 (18)	0.13490 (13)	0.0177 (3)
H18A	0.539 (4)	0.240 (6)	0.094 (17)	0.03948
H18B	0.642 (8)	0.191 (6)	0.204 (17)	0.03737
H18C	0.766 (7)	0.115 (17)	0.108 (3)	0.04153

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0176 (6)	0.0141 (7)	0.0117 (6)	-0.0003 (5)	-0.0019 (5)	-0.0012 (5)
H1A	0.02706	0.03136	0.02233	0.00451	-0.00430	0.00016
O2	0.0144 (6)	0.0091 (7)	0.0216 (7)	0.0011 (5)	0.0009 (5)	0.0012 (5)
H2A	0.03105	0.01544	0.03446	0.00548	0.00326	0.00141
O1W	0.0208 (7)	0.0274 (9)	0.0147 (7)	0.0072 (6)	-0.0016 (5)	0.0022 (6)
H1W	0.04395	0.05082	0.01821	0.00667	-0.00468	0.00094
H2W	0.02978	0.04780	0.03155	0.01047	0.00111	-0.00082
O3	0.0293 (8)	0.0280 (9)	0.0137 (6)	0.0140 (7)	0.0012 (5)	0.0002 (6)
C1	0.0124 (8)	0.0096 (9)	0.0170 (9)	-0.0006 (7)	-0.0042 (6)	-0.0007 (7)
H1	0.02197	0.03414	0.02717	0.00888	-0.00037	-0.00007
C2	0.0153 (8)	0.0113 (9)	0.0156 (9)	-0.0012 (7)	-0.0043 (6)	0.0014 (7)
H2	0.02675	0.03748	0.02314	0.00692	-0.00765	0.00240
C3	0.0174 (8)	0.0058 (9)	0.0144 (8)	-0.0052 (7)	-0.0029 (6)	0.0000 (7)
C4	0.0151 (8)	0.0086 (8)	0.0161 (9)	-0.0005 (7)	-0.0023 (6)	-0.0020 (7)
H4	0.02474	0.03053	0.02896	0.00864	0.00237	-0.00087
C5	0.0126 (8)	0.0072 (9)	0.0167 (8)	-0.0010 (7)	-0.0031 (6)	0.0000 (7)
C6	0.0125 (8)	0.0142 (10)	0.0139 (8)	0.0020 (7)	-0.0016 (6)	0.0024 (7)
H6A	0.03667	0.02074	0.03065	0.00916	0.00047	-0.00151
H6B	0.02316	0.03043	0.03196	-0.00917	-0.00359	0.00363
C7	0.0115 (8)	0.0091 (9)	0.0151 (8)	0.0004 (7)	-0.0022 (6)	0.0021 (7)
H7	0.02021	0.02912	0.02652	0.00301	-0.00676	0.00291
C8	0.0109 (8)	0.0108 (8)	0.0114 (8)	0.0008 (7)	-0.0046 (6)	-0.0001 (7)
H8	0.02430	0.01689	0.02868	-0.00739	-0.00288	0.00072
C9	0.0103 (7)	0.0104 (9)	0.0115 (8)	0.0017 (7)	-0.0036 (6)	0.0003 (7)
H9	0.02167	0.01778	0.02886	-0.00632	-0.00097	0.00246
C10	0.0135 (8)	0.0085 (8)	0.0112 (8)	0.0001 (7)	-0.0024 (6)	-0.0007 (7)
C11	0.0167 (8)	0.0126 (9)	0.0110 (8)	0.0032 (7)	-0.0030 (6)	0.0000 (7)
H11A	0.03655	0.01767	0.03204	-0.00378	0.00287	-0.00013
H11B	0.02460	0.03568	0.02691	0.00779	-0.00750	-0.00081
C12	0.0175 (9)	0.0114 (9)	0.0119 (8)	0.0046 (7)	-0.0014 (6)	0.0003 (7)
H12A	0.02907	0.03178	0.02948	-0.00280	-0.00150	0.00574
H12B	0.04432	0.02512	0.02894	0.01663	-0.00201	-0.00150
C13	0.0163 (9)	0.0115 (10)	0.0127 (8)	0.0010 (7)	-0.0041 (6)	-0.0007 (7)
C14	0.0126 (8)	0.0094 (9)	0.0123 (8)	0.0016 (7)	-0.0047 (6)	0.0002 (7)
H14	0.02192	0.01980	0.02905	-0.00377	-0.00134	0.00257
C15	0.0166 (8)	0.0182 (10)	0.0113 (8)	0.0051 (7)	-0.0039 (6)	0.0027 (7)
H15A	0.03665	0.02393	0.03029	0.00882	-0.00279	0.00352
H15B	0.02636	0.03797	0.02990	-0.00855	-0.00436	0.00059

C16	0.0173 (8)	0.0152 (9)	0.0131 (8)	0.0030 (8)	-0.0038 (6)	0.0002 (8)
H16A	0.03392	0.04041	0.02838	0.00303	-0.00994	-0.00706
H16B	0.03317	0.02901	0.03405	0.00454	0.00353	0.00855
C17	0.0199 (9)	0.0099 (9)	0.0138 (9)	0.0011 (8)	-0.0050 (6)	0.0004 (7)
C18	0.0238 (10)	0.0115 (9)	0.0173 (9)	-0.0027 (8)	-0.0054 (7)	-0.0009 (7)
H18A	0.03997	0.03535	0.04182	-0.00483	-0.01769	0.00351
H18B	0.05575	0.03369	0.02263	-0.01254	0.00065	-0.00135
H18C	0.05443	0.02297	0.04739	0.00447	0.00474	-0.01130

Geometric parameters (Å, °)

O1—C3	1.3804 (9)	C8—H8	1.10 (5)
O1—H1A	0.84 (3)	C9—C10	1.5311 (8)
O2—C7	1.4463 (9)	C9—C11	1.5368 (10)
O2—H2A	0.89 (3)	C9—H9	1.10 (5)
O1W—H1W	0.83 (3)	C11—C12	1.5412 (8)
O1W—H2W	0.89 (3)	C11—H11B	1.09 (6)
O3—C17	1.2187 (12)	C11—H11A	1.09 (5)
C1—C10	1.4057 (11)	C12—C13	1.5317 (11)
C1—C2	1.3872 (10)	C12—H12B	1.09 (6)
C1—H1	1.08 (4)	C12—H12A	1.09 (5)
C2—C3	1.3900 (12)	C13—C17	1.5151 (8)
C2—H2	1.08 (8)	C13—C14	1.5404 (10)
C3—C4	1.3887 (11)	C13—C18	1.5409 (10)
C4—C5	1.4008 (9)	C14—C15	1.5398 (10)
C4—H4	1.08 (4)	C14—H14	1.10 (5)
C5—C10	1.4014 (11)	C15—C16	1.5492 (10)
C5—C6	1.5165 (10)	C15—H15A	1.09 (6)
C6—C7	1.5256 (9)	C15—H15B	1.09 (4)
C6—H6A	1.09 (6)	C16—C17	1.5224 (11)
C6—H6B	1.09 (4)	C16—H16A	1.09 (8)
C7—C8	1.5214 (10)	C16—H16B	1.09 (5)
C7—H7	1.10 (7)	C18—H18A	1.08 (6)
C8—C14	1.5317 (8)	C18—H18B	1.08 (11)
C8—C9	1.5491 (10)	C18—H18C	1.08 (5)
C3—O1—H1A	111 (12)	C11—C9—H9	107 (24)
C7—O2—H2A	108 (12)	C12—C11—H11B	109 (49)
H1W—O1W—H2W	108 (17)	C12—C11—H11A	109 (12)
C10—C1—C2	121.8 (7)	H11B—C11—H11A	107 (24)
C10—C1—H1	119 (16)	C13—C12—C11	110.0 (6)
C2—C1—H1	119 (12)	C13—C12—H12B	109 (12)
C3—C2—C1	119.5 (7)	C13—C12—H12A	110 (13)
C3—C2—H2	120 (34)	H12B—C12—H12A	108 (33)
C4—C3—C2	119.9 (7)	C17—C13—C14	100.3 (6)
C5—C4—H4	119 (13)	C17—C13—C12	116.5 (6)
C10—C5—C6	122.5 (7)	C17—C13—C18	104.7 (6)
C10—C5—C4	120.1 (7)	C14—C13—C12	109.6 (6)

C6—C5—C4	117.4 (6)	C14—C13—C18	113.4 (6)
C7—C6—C5	114.3 (6)	C15—C14—H14	106 (13)
C7—C6—H6A	109 (14)	C16—C15—H15A	111 (14)
C7—C6—H6B	109 (10)	C16—C15—H15B	111 (14)
H6A—C6—H6B	108 (31)	H15A—C15—H15B	110 (22)
C8—C7—C6	109.6 (6)	C17—C16—C15	105.7 (6)
C8—C7—H7	109 (24)	C17—C16—H16A	110 (19)
C14—C8—C9	107.4 (5)	C17—C16—H16B	110 (18)
C14—C8—H8	108 (11)	H16A—C16—H16B	109 (35)
C9—C8—H8	108 (12)	H18A—C18—H18B	109 (56)
C10—C9—C11	113.2 (6)	H18A—C18—H18C	109 (32)
C10—C9—H9	107 (11)	H18B—C18—H18C	109 (27)
O1—C3—C4—C5	-175.99 (13)	C8—C14—C15—H15B	-48 (3)
O1—C3—C4—H4	4 (2)	C8—C9—C11—C12	55.95 (13)
O1—C3—C2—C1	175.82 (13)	C8—C9—C11—H11B	177.2 (10)
O1—C3—C2—H2	-4 (9)	C8—C9—C11—H11A	-66 (3)
H1A—O1—C3—C4	-176.2 (9)	H8—C8—C14—C13	-54 (6)
H1A—O1—C3—C2	6 (3)	H8—C8—C14—C15	70 (3)
O2—C7—C8—C14	-61.66 (14)	H8—C8—C14—H14	-169 (6)
O2—C7—C8—C9	60.34 (14)	H8—C8—C9—C10	-69 (2)
O2—C7—C8—H8	178.7 (4)	H8—C8—C9—C11	58 (6)
O2—C7—C6—C5	-76.28 (14)	H8—C8—C9—H9	174 (5)
O2—C7—C6—H6A	45 (6)	C9—C8—C14—C13	61.61 (14)
O2—C7—C6—H6B	162 (5)	C9—C8—C14—C15	-174.55 (13)
H2A—O2—C7—C8	172.5 (8)	C9—C8—C14—H14	-53 (4)
H2A—O2—C7—C6	-66 (3)	C9—C11—C12—C13	-54.22 (15)
H2A—O2—C7—H7	54 (6)	C9—C11—C12—H12B	-175 (1)
O3—C17—C13—C14	150.3 (3)	C9—C11—C12—H12A	67 (6)
O3—C17—C13—C12	32.18 (16)	H9—C9—C8—C14	58 (3)
O3—C17—C13—C18	-91.98 (17)	H9—C9—C11—C12	-60 (3)
O3—C17—C16—C15	-174.23 (12)	H9—C9—C11—H11B	61 (6)
O3—C17—C16—H16A	66 (7)	H9—C9—C11—H11A	178 (6)
O3—C17—C16—H16B	-54 (4)	C10—C9—C8—C14	175.09 (13)
C1—C10—C9—C8	162.51 (14)	C10—C9—C11—C12	-177.79 (13)
C1—C10—C9—C11	36.89 (16)	C10—C9—C11—H11B	-57 (12)
C1—C10—C9—H9	-81 (3)	C10—C9—C11—H11A	61 (3)
C1—C10—C5—C6	-178.07 (11)	C11—C9—C8—C14	-57.82 (14)
C1—C10—C5—C4	-0.86 (13)	C11—C12—C13—C17	168.36 (15)
C1—C2—C3—C4	-2.10 (13)	C11—C12—C13—C14	55.42 (15)
H1—C1—C10—C9	-3 (2)	C11—C12—C13—C18	-71.24 (15)
H1—C1—C10—C5	-179.94 (19)	H11A—C11—C12—C13	67 (3)
H1—C1—C2—C3	-178.6 (3)	H11A—C11—C12—H12B	-53 (9)
H1—C1—C2—H2	1 (9)	H11A—C11—C12—H12A	-172 (7)
C2—C3—C4—C5	2.01 (13)	H11B—C11—C12—C13	-175.5 (10)
C2—C3—C4—H4	-178.4 (4)	H11B—C11—C12—H12B	64 (6)
C2—C1—C10—C9	177.83 (5)	H11B—C11—C12—H12A	-55 (7)
C2—C1—C10—C5	0.76 (13)	C12—C13—C17—C16	-147.1 (3)

H2—C2—C3—C4	178.4 (4)	C12—C13—C14—C15	165.61 (14)
H2—C2—C1—C10	-180 (1)	C12—C13—C14—H14	54 (4)
C3—C4—C5—C10	-0.51 (13)	C12—C13—C18—H18A	177 (1)
C3—C4—C5—C6	176.84 (10)	C12—C13—C18—H18B	57 (7)
C3—C2—C1—C10	0.71 (13)	C12—C13—C18—H18C	-62 (3)
C4—C5—C10—C9	-177.94 (5)	H12A—C12—C13—C17	47 (3)
C4—C5—C6—C7	165.44 (14)	H12A—C12—C13—C14	-66 (6)
C4—C5—C6—H6A	44 (4)	H12A—C12—C13—C18	168 (2)
C4—C5—C6—H6B	-73 (2)	H12B—C12—C13—C17	-71 (3)
H4—C4—C5—C10	179.86 (11)	H12B—C12—C13—C14	175.9 (9)
H4—C4—C5—C6	-3 (2)	H12B—C12—C13—C18	49 (6)
C5—C10—C9—C8	-20.50 (16)	C13—C17—C16—C15	5.03 (14)
C5—C10—C9—C11	-146.1 (3)	C13—C17—C16—H16A	-115 (13)
C5—C10—C9—H9	96 (4)	C13—C17—C16—H16B	125 (5)
C5—C6—C7—C8	44.91 (16)	C13—C14—C15—C16	-39.91 (19)
C5—C6—C7—H7	164 (3)	C13—C14—C15—H15A	-159 (18)
C6—C7—C8—C14	175.79 (15)	C13—C14—C15—H15B	79 (3)
C6—C7—C8—C9	-62.21 (13)	C14—C13—C17—C16	-28.9 (2)
C6—C7—C8—H8	56 (3)	C14—C13—C18—H18A	53 (6)
C6—C5—C10—C9	4.85 (12)	C14—C13—C18—H18B	-68 (4)
H6A—C6—C7—C8	166 (2)	C14—C13—C18—H18C	173 (2)
H6A—C6—C7—H7	-75 (6)	C14—C15—C16—C17	21.2 (2)
H6A—C6—C5—C10	-139 (7)	C14—C15—C16—H16A	141 (14)
H6B—C6—C7—C8	-77 (6)	C14—C15—C16—H16B	-98 (3)
H6B—C6—C7—H7	42 (7)	H14—C14—C13—C17	-69 (3)
H6B—C6—C5—C10	104 (5)	H14—C14—C13—C18	179 (2)
C7—C8—C14—C13	-174.06 (14)	H14—C14—C15—C16	72 (3)
C7—C8—C14—C15	-50.22 (15)	H14—C14—C15—H15A	-47 (9)
C7—C8—C14—H14	71 (6)	H14—C14—C15—H15B	-169 (6)
C7—C8—C9—C10	49.36 (15)	C15—C14—C13—C17	42.47 (17)
C7—C8—C9—C11	176.45 (14)	C15—C14—C13—C18	-68.59 (15)
C7—C8—C9—H9	-67 (6)	H15A—C15—C16—C17	140 (9)
C7—C6—C5—C10	-17.27 (12)	H15A—C15—C16—H16A	-100 (5)
H7—C7—C8—C14	57 (12)	H15A—C15—C16—H16B	20 (12)
H7—C7—C8—C9	179 (2)	H15B—C15—C16—C17	-97 (4)
H7—C7—C8—H8	-62 (5)	H15B—C15—C16—H16A	22 (10)
C8—C14—C13—C17	175.43 (14)	H15B—C15—C16—H16B	143 (11)
C8—C14—C13—C12	-61.43 (13)	C16—C17—C13—C18	88.77 (15)
C8—C14—C13—C18	64.37 (15)	C17—C13—C18—H18A	-56 (13)
C8—C14—C15—C16	-166.96 (14)	C17—C13—C18—H18B	-176 (2)
C8—C14—C15—H15A	74 (2)	C17—C13—C18—H18C	65 (4)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O1—H1A...O1 <i>W</i>	0.87	1.82	2.673 (2)	167
C2—H2...O1 <i>W</i>	1.08	2.62	3.354 (2)	125
C8—H8...C18	1.10	2.67	3.106 (3)	103

C18—H18A...C15	1.08	2.64	3.021 (3)	100
O1W—H1W...O3 ⁱ	0.85	1.97	2.805 (2)	167
O1W—H1W...C17 ⁱ	0.85	2.69	3.492 (2)	158
O2—H2A...O1 ⁱⁱ	0.91	1.96	2.857 (2)	169
O2—H2A...C3 ⁱⁱ	0.91	2.73	3.533 (3)	148
C6—H6A...C2 ⁱⁱ	1.09	2.60	3.594 (3)	151
C6—H6A...C3 ⁱⁱ	1.09	2.46	3.484 (3)	156
O1W—H2W...O2 ⁱⁱⁱ	0.91	1.85	2.758 (2)	176
C2—H2...O2 ⁱⁱⁱ	1.08	2.51	3.581 (3)	170
C16—H16B...O3 ^{iv}	1.09	2.45	3.354 (3)	139

Symmetry codes: (i) $x, y, z+1$; (ii) $-x+1, y+1/2, -z+1$; (iii) $-x+2, y-1/2, -z+1$; (iv) $-x+2, y+1/2, -z$.

3,7 α -Dihydroxyestra-1,3,5(10)-trien-17-one monohydrate (ELMAM2_MoPro)

Crystal data

$C_{18}H_{22}O_3 \cdot H_2O$

$M_r = 304.37$

Monoclinic, $P2_1$

Hall symbol: P 2yb

$a = 6.143$ (3) Å

$b = 8.4833$ (17) Å

$c = 14.767$ (3) Å

$\beta = 91.94$ (2)°

$V = 769.2$ (4) Å³

$Z = 2$

$F(000) = 328$

$D_x = 1.315$ Mg m⁻³

Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å

Cell parameters from 2931 reflections

$\theta = 3.0$ – 72.2 °

$\mu = 0.74$ mm⁻¹

$T = 100$ K

Block, colorless

$0.46 \times 0.22 \times 0.12$ mm

Data collection

Bruker D8 Venture PHOTON II Detector
diffractometer

Radiation source: Microfocus

Graphite monochromator

ω and phi scan

Absorption correction: multi-scan
(SADABS; Krause *et al.*, 2015)

$T_{\min} = 0.727$, $T_{\max} = 0.916$

9196 measured reflections

2931 independent reflections

2905 reflections with $> 2.0\sigma(I)$

$R_{\text{int}} = 0.043$

$\theta_{\max} = 72.2$ °, $\theta_{\min} = 3.0$ °

$h = 0 \rightarrow 7$

$k = -10 \rightarrow 10$

$l = -18 \rightarrow 18$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.032$

$wR(F^2) = 0.088$

$S = 1.10$

2931 reflections

199 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: difference Fourier map

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.06P)^2 + 0.05P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$

$\Delta\rho_{\max} = 0.28$ e Å⁻³

$\Delta\rho_{\min} = -0.26$ e Å⁻³

Special details

Refinement. Refinement of F^2 against reflections. The threshold expression of $F^2 > \sigma(F^2)$ is used for calculating R -factors(gt) 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 (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.66934 (14)	0.5271 (6)	0.69518 (5)	0.01249 (14)
H1A	0.78728	0.48787	0.73396	0.02703
O2	0.65437 (13)	0.7914 (6)	0.27769 (6)	0.01295 (14)
H2A	0.56171	0.88335	0.29040	0.02693
O1W	0.96343 (14)	0.3775 (6)	0.80181 (6)	0.01836 (16)
H1W	0.98485	0.37473	0.86647	0.03779
H2W	1.10074	0.34539	0.77855	0.03638
O3	1.01932 (17)	0.3342 (6)	-0.01049 (6)	0.02196 (18)
C1	0.95933 (19)	0.4396 (6)	0.48704 (8)	0.01045 (18)
H1	1.10790	0.38308	0.46660	0.02779
C2	0.91906 (19)	0.4515 (6)	0.57890 (8)	0.01165 (18)
H2	1.03592	0.40638	0.62899	0.02932
C3	0.72546 (19)	0.5206 (6)	0.60582 (8)	0.01016 (18)
C4	0.57842 (19)	0.5805 (6)	0.54090 (8)	0.01125 (18)
H4	0.42972	0.63616	0.56191	0.02804
C5	0.61985 (18)	0.5686 (6)	0.44846 (8)	0.00959 (18)
C6	0.44667 (18)	0.6297 (6)	0.38192 (8)	0.01110 (18)
H6A	0.38771	0.74265	0.40678	0.02937
H6B	0.31014	0.54726	0.38075	0.02862
C7	0.52304 (18)	0.6516 (6)	0.28552 (8)	0.00955 (18)
H7	0.37942	0.66095	0.23940	0.02545
C8	0.65512 (18)	0.5084 (6)	0.25817 (7)	0.00876 (17)
H8	0.55387	0.40286	0.26620	0.02337
C9	0.86237 (18)	0.4879 (6)	0.31961 (8)	0.00877 (17)
H9	0.97100	0.58709	0.30536	0.02281
C10	0.81158 (18)	0.4968 (6)	0.41997 (8)	0.00865 (17)
C11	0.98469 (19)	0.3368 (6)	0.29441 (8)	0.01118 (19)
H11A	0.88480	0.23425	0.30958	0.02872
H11B	1.13422	0.32752	0.33621	0.02925
C12	1.04240 (19)	0.3314 (6)	0.19371 (8)	0.01138 (19)
H12A	1.16232	0.42251	0.17980	0.03017
H12B	1.11403	0.21712	0.17828	0.03286
C13	0.83842 (19)	0.3569 (6)	0.13365 (8)	0.01037 (19)
C14	0.72626 (18)	0.5124 (6)	0.16002 (8)	0.00954 (18)
H14	0.85241	0.60391	0.15702	0.02364
C15	0.5634 (2)	0.5455 (6)	0.08096 (8)	0.01324 (19)
H15A	0.51819	0.66995	0.07825	0.03038
H15B	0.41742	0.47303	0.08606	0.03153
C16	0.69493 (19)	0.4977 (6)	-0.00228 (8)	0.01307 (19)
H16A	0.59085	0.43715	-0.05261	0.03449
H16B	0.76674	0.60091	-0.03380	0.03202
C17	0.8726 (2)	0.3874 (6)	0.03400 (8)	0.0127 (2)
C18	0.6848 (2)	0.2130 (6)	0.13507 (8)	0.0159 (2)
H18A	0.53899	0.23603	0.09467	0.03948
H18B	0.64203	0.18746	0.20368	0.03737

H18C 0.76569 0.11131 0.10834 0.04153

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0154 (4)	0.0115 (5)	0.0105 (4)	−0.0019 (3)	−0.0020 (3)	−0.0012 (3)
H1A	0.02706	0.03136	0.02233	0.00451	−0.00430	0.00016
O2	0.0129 (4)	0.0078 (4)	0.0182 (4)	0.0008 (3)	0.0005 (3)	0.0012 (3)
H2A	0.03105	0.01544	0.03446	0.00548	0.00326	0.00141
O1W	0.0189 (4)	0.0230 (5)	0.0131 (4)	0.0065 (4)	−0.0017 (3)	0.0018 (4)
H1W	0.04395	0.05082	0.01821	0.00667	−0.00468	0.00094
H2W	0.02978	0.04780	0.03155	0.01047	0.00111	−0.00082
O3	0.0273 (5)	0.0277 (6)	0.0109 (4)	0.0161 (4)	0.0013 (3)	0.0016 (4)
C1	0.0102 (5)	0.0108 (6)	0.0101 (5)	0.0025 (4)	−0.0034 (4)	0.0001 (4)
H1	0.02197	0.03414	0.02717	0.00888	−0.00037	−0.00007
C2	0.0113 (5)	0.0122 (6)	0.0112 (5)	0.0017 (4)	−0.0039 (4)	0.0006 (5)
H2	0.02675	0.03748	0.02314	0.00692	−0.00765	0.00240
C3	0.0129 (5)	0.0078 (6)	0.0096 (5)	−0.0008 (5)	−0.0022 (4)	−0.0005 (4)
C4	0.0124 (5)	0.0092 (5)	0.0120 (5)	0.0019 (5)	−0.0021 (4)	−0.0008 (5)
H4	0.02474	0.03053	0.02896	0.00864	0.00237	−0.00087
C5	0.0099 (5)	0.0069 (6)	0.0117 (5)	0.0016 (5)	−0.0029 (4)	0.0000 (4)
C6	0.0096 (5)	0.0109 (6)	0.0126 (5)	0.0029 (4)	−0.0017 (4)	0.0019 (4)
H6A	0.03667	0.02074	0.03065	0.00916	0.00047	−0.00151
H6B	0.02316	0.03043	0.03196	−0.00917	−0.00359	0.00363
C7	0.0090 (5)	0.0077 (6)	0.0117 (5)	0.0013 (5)	−0.0024 (4)	0.0014 (4)
H7	0.02021	0.02912	0.02652	0.00301	−0.00676	0.00291
C8	0.0088 (5)	0.0084 (5)	0.0088 (5)	0.0011 (5)	−0.0042 (4)	0.0001 (5)
H8	0.02430	0.01689	0.02868	−0.00739	−0.00288	0.00072
C9	0.0090 (5)	0.0075 (6)	0.0096 (5)	0.0023 (4)	−0.0033 (4)	0.0003 (4)
H9	0.02167	0.01778	0.02886	−0.00632	−0.00097	0.00246
C10	0.0085 (5)	0.0082 (5)	0.0091 (5)	0.0017 (4)	−0.0028 (4)	−0.0001 (5)
C11	0.0146 (5)	0.0089 (6)	0.0098 (5)	0.0039 (5)	−0.0038 (4)	0.0008 (4)
H11A	0.03655	0.01767	0.03204	−0.00378	0.00287	−0.00013
H11B	0.02460	0.03568	0.02691	0.00779	−0.00750	−0.00081
C12	0.0134 (5)	0.0102 (6)	0.0103 (5)	0.0041 (5)	−0.0027 (4)	−0.0003 (4)
H12A	0.02907	0.03178	0.02948	−0.00280	−0.00150	0.00574
H12B	0.04432	0.02512	0.02894	0.01663	−0.00201	−0.00150
C13	0.0130 (5)	0.0078 (6)	0.0100 (5)	0.0019 (5)	−0.0039 (4)	0.0005 (4)
C14	0.0108 (5)	0.0067 (6)	0.0109 (5)	0.0017 (4)	−0.0037 (4)	0.0005 (4)
H14	0.02192	0.01980	0.02905	−0.00377	−0.00134	0.00257
C15	0.0139 (5)	0.0149 (6)	0.0106 (5)	0.0050 (5)	−0.0040 (4)	0.0018 (4)
H15A	0.03665	0.02393	0.03029	0.00882	−0.00279	0.00352
H15B	0.02636	0.03797	0.02990	−0.00855	−0.00436	0.00059
C16	0.0156 (5)	0.0124 (6)	0.0109 (5)	0.0031 (5)	−0.0044 (4)	0.0015 (5)
H16A	0.03392	0.04041	0.02838	0.00303	−0.00994	−0.00706
H16B	0.03317	0.02901	0.03405	0.00454	0.00353	0.00855
C17	0.0174 (6)	0.0104 (6)	0.0101 (5)	0.0049 (5)	−0.0038 (4)	0.0013 (5)
C18	0.0229 (7)	0.0089 (6)	0.0154 (5)	−0.0025 (5)	−0.0049 (4)	−0.0017 (5)

H18A	0.03997	0.03535	0.04182	-0.00483	-0.01769	0.00351
H18B	0.05575	0.03369	0.02263	-0.01254	0.00065	-0.00135
H18C	0.05443	0.02297	0.04739	0.00447	0.00474	-0.01130

Geometric parameters (Å, °)

O1—C3	1.3762 (14)	C8—H8	1.0990
O1—H1A	0.9671	C9—C10	1.5266 (14)
O2—C7	1.4414 (15)	C9—C11	1.5379 (17)
O2—H2A	0.9873	C9—H9	1.0990
O1W—H1W	0.9597	C11—C12	1.5411 (15)
O1W—H2W	0.9609	C11—H11B	1.0920
O3—C17	1.2200 (18)	C11—H11A	1.0920
C1—C10	1.4067 (17)	C12—C13	1.5259 (17)
C1—C2	1.3907 (16)	C12—H12A	1.0920
C1—H1	1.0830	C12—H12B	1.0920
C2—C3	1.3960 (18)	C13—C17	1.5157 (15)
C2—H2	1.0830	C13—C14	1.5443 (17)
C3—C4	1.3910 (17)	C13—C18	1.5440 (18)
C4—C5	1.4007 (16)	C14—C15	1.5374 (16)
C4—H4	1.0830	C14—H14	1.0990
C5—C10	1.4032 (18)	C15—C16	1.5479 (17)
C5—C6	1.5152 (16)	C15—H15A	1.0920
C6—C7	1.5251 (16)	C15—H15B	1.0920
C6—H6A	1.0920	C16—C17	1.5207 (18)
C6—H6B	1.0920	C16—H16A	1.0920
C7—C8	1.5229 (17)	C16—H16B	1.0920
C7—H7	1.0990	C18—H18A	1.0770
C8—C14	1.5283 (14)	C18—H18B	1.0770
C8—C9	1.5480 (16)	C18—H18C	1.0770
C3—O1—H1A	110.298	C9—C11—C12	112.85 (9)
C7—O2—H2A	107.872	C9—C11—H11B	109.377
H1W—O1W—H2W	104.856	C9—C11—H11A	109.363
C10—C1—C2	122.00 (10)	C12—C11—H11B	109.058
C10—C1—H1	119.091	C12—C11—H11A	108.890
C2—C1—H1	118.906	H11B—C11—H11A	107.138
C3—C2—C1	119.32 (10)	C13—C12—C11	110.21 (9)
C3—C2—H2	120.357	C13—C12—H12A	109.660
C1—C2—H2	120.322	C13—C12—H12B	109.472
O1—C3—C4	117.93 (9)	C11—C12—H12A	109.839
O1—C3—C2	122.23 (9)	C11—C12—H12B	109.577
C4—C3—C2	119.79 (10)	H12A—C12—H12B	108.052
C3—C4—C5	120.67 (10)	C17—C13—C14	100.16 (9)
C3—C4—H4	119.743	C17—C13—C12	116.78 (8)
C5—C4—H4	119.590	C17—C13—C18	104.67 (9)
C10—C5—C6	122.16 (10)	C14—C13—C12	109.83 (9)
C10—C5—C4	120.38 (10)	C14—C13—C18	113.19 (10)

C6—C5—C4	117.41 (9)	C12—C13—C18	111.75 (10)
C7—C6—C5	114.55 (9)	C13—C14—C8	111.38 (9)
C7—C6—H6A	108.858	C13—C14—C15	104.43 (9)
C7—C6—H6B	108.875	C13—C14—H14	105.785
C5—C6—H6A	108.426	C8—C14—C15	121.63 (8)
C5—C6—H6B	108.230	C8—C14—H14	106.174
H6A—C6—H6B	107.698	C15—C14—H14	106.377
O2—C7—C8	109.29 (9)	C14—C15—C16	102.19 (9)
O2—C7—C6	111.45 (9)	C14—C15—H15A	111.263
O2—C7—H7	109.308	C14—C15—H15B	111.075
C8—C7—C6	109.52 (9)	C16—C15—H15A	111.309
C8—C7—H7	108.486	C16—C15—H15B	111.045
C6—C7—H7	108.737	H15A—C15—H15B	109.785
C7—C8—C14	113.95 (9)	C17—C16—C15	105.62 (10)
C7—C8—C9	111.68 (9)	C17—C16—H16A	110.326
C7—C8—H8	108.212	C17—C16—H16B	110.355
C14—C8—C9	107.60 (8)	C15—C16—H16A	110.752
C14—C8—H8	107.547	C15—C16—H16B	110.948
C9—C8—H8	107.599	H16A—C16—H16B	108.823
C8—C9—C10	111.86 (9)	O3—C17—C13	126.06 (10)
C8—C9—C11	110.54 (9)	O3—C17—C16	124.92 (10)
C8—C9—H9	107.113	C13—C17—C16	109.02 (9)
C10—C9—C11	113.19 (8)	C13—C18—H18A	110.242
C10—C9—H9	107.065	C13—C18—H18B	109.893
C11—C9—H9	106.688	C13—C18—H18C	109.759
C9—C10—C5	120.92 (9)	H18A—C18—H18B	109.445
C9—C10—C1	121.21 (9)	H18A—C18—H18C	109.152
C5—C10—C1	117.82 (10)	H18B—C18—H18C	108.316
O1—C3—C4—C5	-176.00 (16)	C8—C14—C15—H15B	-48.32
O1—C3—C4—H4	3.49	C8—C9—C11—C12	55.64 (17)
O1—C3—C2—C1	175.81 (17)	C8—C9—C11—H11B	177.23
O1—C3—C2—H2	-3.52	C8—C9—C11—H11A	-65.72
H1A—O1—C3—C4	-176.65	H8—C8—C14—C13	-54.18
H1A—O1—C3—C2	5.73	H8—C8—C14—C15	69.56
O2—C7—C8—C14	-61.83 (18)	H8—C8—C14—H14	-168.87
O2—C7—C8—C9	60.35 (18)	H8—C8—C9—C10	-69.34
O2—C7—C8—H8	178.60	H8—C8—C9—C11	57.77
O2—C7—C6—C5	-76.29 (17)	H8—C8—C9—H9	173.64
O2—C7—C6—H6A	45.25	C9—C8—C14—C13	61.48 (18)
O2—C7—C6—H6B	162.40	C9—C8—C14—C15	-174.78 (17)
H2A—O2—C7—C8	175.02	C9—C8—C14—H14	-53.21
H2A—O2—C7—C6	-63.79	C9—C11—C12—C13	-53.86 (19)
H2A—O2—C7—H7	56.43	C9—C11—C12—H12A	67.06
O3—C17—C13—C14	150.5 (3)	C9—C11—C12—H12B	-174.39
O3—C17—C13—C12	32.0 (2)	H9—C9—C8—C14	58.01
O3—C17—C13—C18	-92.1 (2)	H9—C9—C11—C12	-60.49
O3—C17—C16—C15	-174.29 (15)	H9—C9—C11—H11B	61.10

O3—C17—C16—H16A	65.98	H9—C9—C11—H11A	178.15
O3—C17—C16—H16B	-54.31	C10—C9—C8—C14	175.03 (17)
C1—C10—C9—C8	162.4 (5)	C10—C9—C11—C12	-177.98 (16)
C1—C10—C9—C11	36.8 (2)	C10—C9—C11—H11B	-56.39
C1—C10—C9—H9	-80.52	C10—C9—C11—H11A	60.65
C1—C10—C5—C6	-178.13 (14)	C11—C9—C8—C14	-57.85 (18)
C1—C10—C5—C4	-0.63 (16)	C11—C12—C13—C17	168.2 (6)
C1—C2—C3—C4	-1.77 (16)	C11—C12—C13—C14	55.12 (19)
H1—C1—C10—C9	-3.10	C11—C12—C13—C18	-71.36 (18)
H1—C1—C10—C5	179.61	H11A—C11—C12—C13	67.77
H1—C1—C2—C3	-178.41	H11A—C11—C12—H12A	-171.31
H1—C1—C2—H2	0.92	H11A—C11—C12—H12B	-52.75
C2—C3—C4—C5	1.68 (16)	H11B—C11—C12—C13	-175.63
C2—C3—C4—H4	-178.83	H11B—C11—C12—H12A	-54.71
C2—C1—C10—C9	177.82 (6)	H11B—C11—C12—H12B	63.84
C2—C1—C10—C5	0.52 (16)	C12—C13—C17—C16	-147.3 (3)
H2—C2—C3—C4	178.90	C12—C13—C14—C15	165.8 (7)
H2—C2—C1—C10	-180.00	C12—C13—C14—H14	53.76
C3—C4—C5—C10	-0.47 (16)	C12—C13—C18—H18A	177.40
C3—C4—C5—C6	177.15 (12)	C12—C13—C18—H18B	56.69
C3—C2—C1—C10	0.67 (16)	C12—C13—C18—H18C	-62.33
C4—C5—C10—C9	-177.93 (6)	H12A—C12—C13—C17	47.16
C4—C5—C6—C7	165.4 (7)	H12A—C12—C13—C14	-65.91
C4—C5—C6—H6A	43.59	H12A—C12—C13—C18	167.61
C4—C5—C6—H6B	-72.97	H12B—C12—C13—C17	-71.22
H4—C4—C5—C10	-179.96	H12B—C12—C13—C14	175.71
H4—C4—C5—C6	-2.34	H12B—C12—C13—C18	49.23
C5—C10—C9—C8	-20.4 (2)	C13—C17—C16—C15	5.06 (18)
C5—C10—C9—C11	-146.0 (4)	C13—C17—C16—H16A	-114.67
C5—C10—C9—H9	96.69	C13—C17—C16—H16B	125.04
C5—C6—C7—C8	44.8 (2)	C13—C14—C15—C16	-39.9 (2)
C5—C6—C7—H7	163.15	C13—C14—C15—H15A	-158.78
C6—C7—C8—C14	175.82 (19)	C13—C14—C15—H15B	78.59
C6—C7—C8—C9	-61.99 (16)	C14—C13—C17—C16	-28.9 (3)
C6—C7—C8—H8	56.25	C14—C13—C18—H18A	52.78
C6—C5—C10—C9	4.57 (14)	C14—C13—C18—H18B	-67.93
H6A—C6—C7—C8	166.31	C14—C13—C18—H18C	173.05
H6A—C6—C7—H7	-75.30	C14—C15—C16—C17	21.2 (3)
H6A—C6—C5—C10	-138.84	C14—C15—C16—H16A	140.67
H6B—C6—C7—C8	-76.55	C14—C15—C16—H16B	-98.37
H6B—C6—C7—H7	41.85	H14—C14—C13—C17	-69.68
H6B—C6—C5—C10	104.61	H14—C14—C13—C18	179.42
C7—C8—C14—C13	-174.12 (17)	H14—C14—C15—C16	71.72
C7—C8—C14—C15	-50.38 (19)	H14—C14—C15—H15A	-47.16
C7—C8—C14—H14	71.19	H14—C14—C15—H15B	-169.79
C7—C8—C9—C10	49.27 (19)	C15—C14—C13—C17	42.4 (2)
C7—C8—C9—C11	176.38 (17)	C15—C14—C13—C18	-68.54 (19)
C7—C8—C9—H9	-67.75	H15A—C15—C16—C17	140.07

C7—C6—C5—C10	-17.1 (2)	H15A—C15—C16—H16A	-100.48
H7—C7—C8—C14	57.27	H15A—C15—C16—H16B	20.48
H7—C7—C8—C9	179.46	H15B—C15—C16—C17	-97.29
H7—C7—C8—H8	-62.30	H15B—C15—C16—H16A	22.16
C8—C14—C13—C17	175.39 (17)	H15B—C15—C16—H16B	143.12
C8—C14—C13—C12	-61.17 (17)	C16—C17—C13—C18	88.54 (19)
C8—C14—C13—C18	64.49 (18)	C17—C13—C18—H18A	-55.31
C8—C14—C15—C16	-166.8 (4)	C17—C13—C18—H18B	-176.02
C8—C14—C15—H15A	74.31	C17—C13—C18—H18C	64.96

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
O1—H1A \cdots O1 <i>W</i>	0.97	1.73	2.6761 (17)	167
C2—H2 \cdots O1 <i>W</i>	1.08	2.62	3.3530 (16)	125
C8—H8 \cdots C18	1.10	2.66	3.1051 (19)	103
C18—H18A \cdots C15	1.08	2.64	3.019 (2)	100
O1 <i>W</i> —H1 <i>W</i> \cdots O3 ⁱ	0.96	1.85	2.8054 (14)	171
O1 <i>W</i> —H1 <i>W</i> \cdots C17 ⁱ	0.96	2.59	3.4934 (17)	156
O2—H2A \cdots O1 ⁱⁱ	0.99	1.89	2.8576 (17)	166
O2—H2A \cdots C3 ⁱⁱ	0.99	2.65	3.529 (2)	149
C6—H6A \cdots C2 ⁱⁱ	1.09	2.60	3.595 (2)	151
C6—H6A \cdots C3 ⁱⁱ	1.09	2.46	3.487 (2)	156
O1 <i>W</i> —H2 <i>W</i> \cdots O2 ⁱⁱⁱ	0.96	1.80	2.7589 (17)	173
C2—H2 \cdots O2 ⁱⁱⁱ	1.08	2.51	3.580 (2)	170
C16—H16B \cdots O3 ^{iv}	1.09	2.45	3.354 (2)	139

Symmetry codes: (i) $x, y, z+1$; (ii) $-x+1, y+1/2, -z+1$; (iii) $-x+2, y-1/2, -z+1$; (iv) $-x+2, y+1/2, -z$.