Acta Cryst C
STRUCTURAL CHEMISTRY
ISSN 2053-2296

Structural corroboration of two important building blocks of the anticancer drug eribulin mesylate through two-dimensional NMR and single-crystal X-ray diffraction studies

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Received 14 October 2015
Accepted 20 November 2015

Edited by P. Fanwick, Purdue University, USA

Keywords: Halichondrin B; eribulin mesylate; double stereodiffrentiation; asymmetric di-hydroxylation; crystal structure; Karplus equation; anticancer drug; two-dimensional NMR; NOESY; COSY.

CCDC references: 1438133; 1438132

Supporting information: this article has supporting information at journals.iucr.org/c

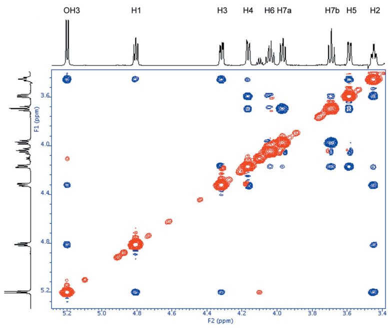
Eribulin mesylate, one of the most synthetically challenging drugs to date, possesses 19 stereocentres in its structure and ascertaining the absolute stereochemistry at every stage of the 64-stage synthesis is crucial. In our quest to synthesize eribulin, we identified two critical building blocks of this molecule, namely 3,4:6,7-di-*O*-cyclohexylidene-D-*glycero*-α-L-*talo*-heptopyranose methanol monosolvate, $C_{19}H_{30}O_7 \cdot CH_3OH$, and (2*R*,3*R*,4*R*,5*S*)-5-allyl-2-[(*S*)-2,3-dihydroxypropyl]-4-[(phenylsulfonyl)methyl]tetrahydrofuran-3-ol, $C_{17}H_{24}O_6S$, for which two-dimensional NMR (2D-NMR) data were not sufficient to prove the absolute configuration. To ensure structural integrity, single-crystal X-ray diffraction data were obtained to confirm the structures. This information provides useful insights into the structural framework of the large eribulin mesylate molecule.

1. Introduction

Eribulin mesylate is a structurally truncated synthetic analogue of Halichondrin B (Hirata & Uemura, 1986; Kishi *et al.*, 1994), the most bioactive natural product isolated from the marine sponge *Halichondria okadai* commonly found off the coasts of Japan and New Zealand. Eribulin mesylate (Halaven®) interferes with microtubule dynamics (Smith *et al.*, 2010) and was approved in November 2010 by the United States Food and Drug Administration (USFDA) for the treatment of metastatic breast cancer (Towle *et al.*, 2001). The structure of eribulin resembles a macrocyclic ketone showcasing a fully synthetic drug available on the market today. 19 of the 36 C atoms that constitute the skeleton of the molecule are stereogenic in nature.

The structural framework of eribulin is built up by assembling three key fragments: (i) the C1–C13 aldehyde fragment (I), (ii) the C14–C26 vinyl triflate fragment (II) and (iii) the C27–C35 phenyl sulfone fragment (III) (Fig. 1).

Several synthetic routes have been used for the preparation of eribulin, (V), each of which utilize the same strategy described by Kishi and co-workers, known for their pioneering work on the total synthesis of Halichondrins, and Halichondrin B in particular (Aicher *et al.*, 1992). Over the years, synthetic routes have evolved continuously, with scale-up and route refinement as the key areas of improvement (Yu *et al.*, 2013; Austad *et al.*, 2013).



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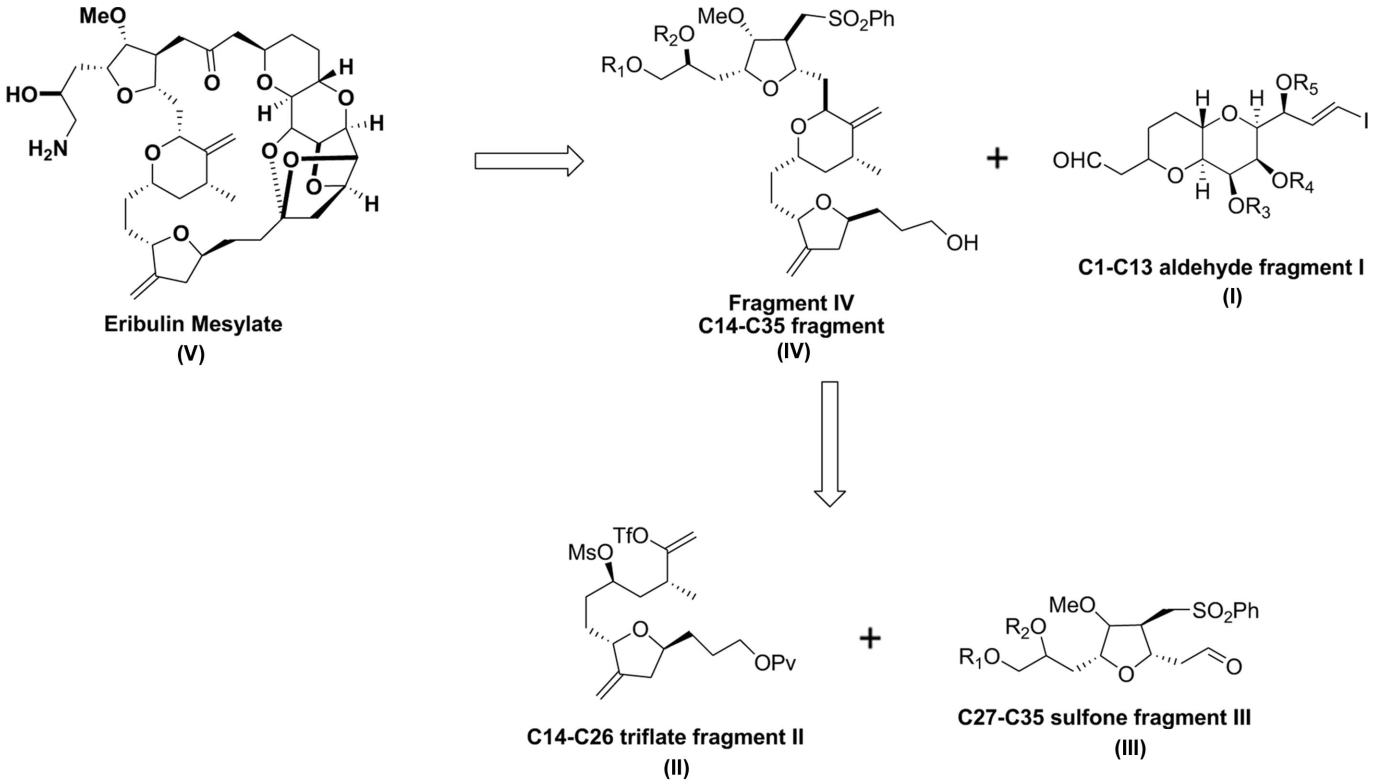


Figure 1
Retero-synthetic scheme for the coupling of fragments I and IV, and the construction of eribulin molecule (V).

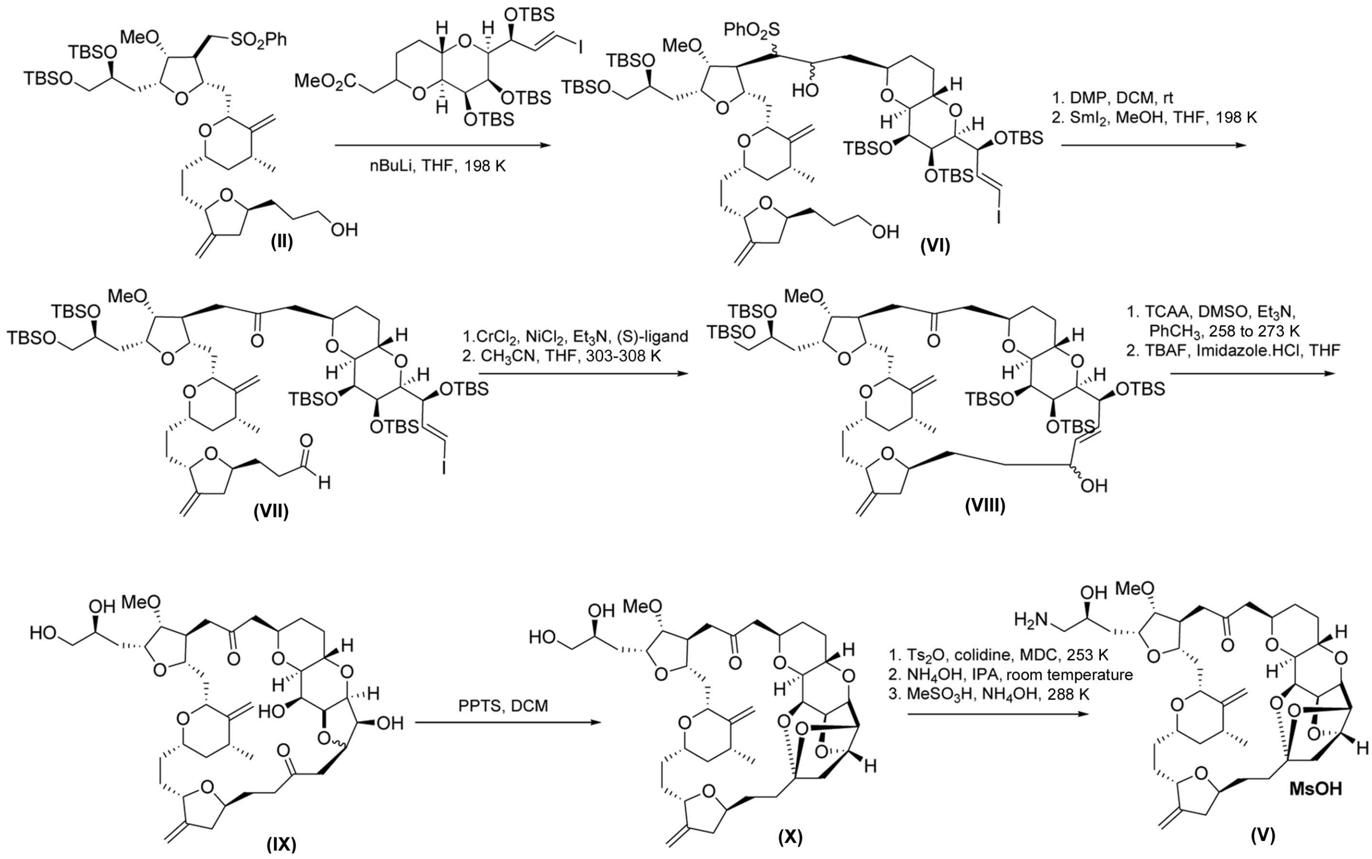


Figure 2
The final stages in the synthesis of eribulin mesylate, (V).

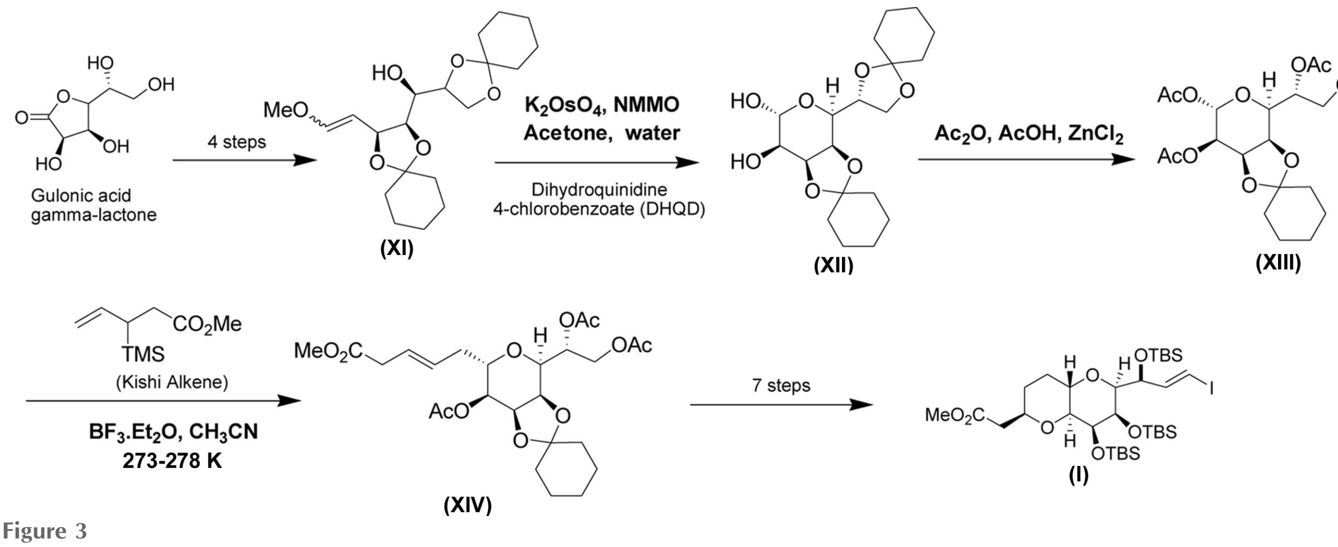
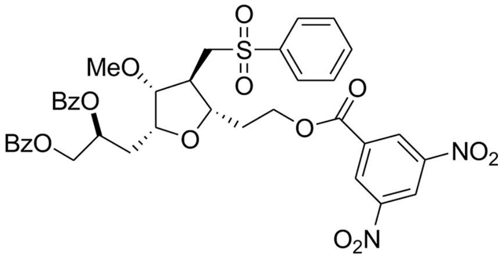


Figure 3
An overview of the synthetic scheme for the preparation of (I).

The three key fragments (I)–(III) (Fig. 1) are synthesized in 15–20 stages each and have been reported in detail. In the later stages, (II) and (III) are subjected to Nozaki–Hiyama–Kishi (NHK) coupling (Hiyama *et al.*, 1981; Jin *et al.*, 1986) to yield fragment (IV) (the C14–C35 fragment) (Fig. 1), which is then coupled with (I) under basic conditions. The final stages (Fig. 2) involve a macrocyclization achieved again through NHK coupling of (VIII), the formation of cyclic ketal (IX) and the conversion of terminal diol (X) to an *in situ* epoxide on which the primary amine is added to finally realize eribulin mesylate, (V).



(III*a*) (Yang *et al.*, 2009)
Scheme 1

The goal of our synthesis was to conduct feasibility studies and develop an optimized and scalable process for the preparation of (V). Owing to the presence of 19 stereocentres in this molecule, it was required to continuously ensure the correct stereoisomer at every stage of this extensive synthesis. The important check-point was to characterize newly formed stereocentres in selected molecules through two-dimensional NMR (2D-NMR) data. There were, however, instances where 2D-NMR data were not conclusive enough to prove the absolute stereochemistry or there was a need to prove the molecular geometry for subsequent reactions. Hence, single-crystal X-ray diffraction analysis was employed to identified intermediates of compounds (I)–(III) in order to conclusively establish the structures (Fig. 1).

The single-crystal X-ray structure of (IV) has been reported previously (Austad *et al.*, 2013). Also, a 3,5-dinitrophenyl ester derivative of the alcohol variant of (III) (Fig. 1) has been reported, denoted (III*a*) (Yang *et al.*, 2009) (Scheme 1).

We report here the single-crystal X-ray data for two relatively important intermediates of (I) and (III) which have an important bearing on the structural orchestration of the eribulin molecule.

The selected intermediate of (I) is 3,4:6,7-di-*O*-cyclohexylidene-D-glycero-α-L-talo-heptopyranose, (XII) (Scheme 2), whose stereochemistry has important implications for the C-allylation product (XIV) two stages later (Fig. 3). The synthesis of (I) starts with D-gulono-γ-lactone (Fig. 3) having two sets of vicinal diol groups, the stereochemistries of which are fixed. The D-gulono-γ-lactone is converted into its lactol which reacts with MeOCH$_2$PPh$_3$Cl under Wittig conditions to produce hydroxyalkene (XI). The Sharpless dihydroxylation protocol through which (XII) is finally obtained involves a

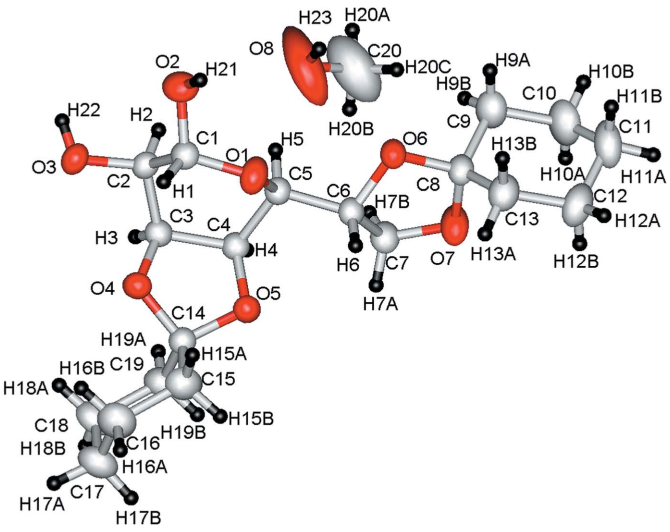
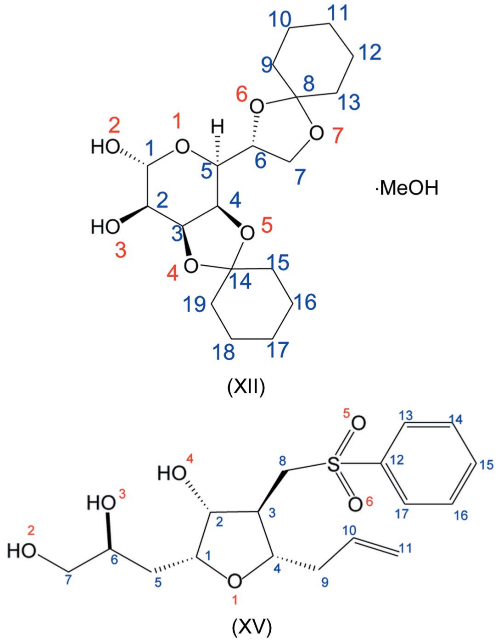


Figure 4
The molecular structure of (XII), showing atom H1 in a different plane to the other H atoms of the cyclohexylidene ring. Displacement ellipsoids are drawn at the 50% probability level.

catalytic osmylation (Kolb *et al.*, 1994) of (XI) using the double stereo-differentiation strategy (Masamme *et al.*, 1985). It provides a 4:1 mixture of diastereoisomers, which after purification delivers (XII) as a single diastereoisomer in the form of a white crystalline solid. This mechanism should force the H atom on C1 (*i.e.* H1) to lie on the opposite side of the tetrahydropyran ring plane in the desired diastereoisomer, compared with the other H atoms on atoms C2–C5 (Fig. 4). However, the nuclear Overhauser effect spectroscopy (NOESY) (Fig. 5) of this molecule unusually showed that atom H1 has an interaction with H2, which normally means that they are on the same side of the tetrahydropyran ring plane. Further insight into this molecule could be provided by using single-crystal X-ray diffraction to align the mechanistic rationale and determine the absolute configuration. Compound (XII) is then subjected to acetylation yielding tetraacetate (XIII). C-Allylation of (XIII) using methyl 3-(trimethylsilyl)pent-4-enoate (also known as the Kishi alkene) retains the configuration on C1 after displacement of the *O*-acetyl group to yield allylic ester (XIV) which exists as a 1:1 mixture of conformers (Stamos & Kishi, 1996).



(XII)

(XV)

Scheme 2

The second intermediate, (2*R*,3*R*,4*R*,5*S*)-5-allyl-2-[(*S*)-2,3-dihydroxypropyl]-4-[(phenylsulfonyl)methyl]tetrahydrofuran-3-ol, (XV) (Scheme 2), from the synthesis of (III) is obtained through a sequence of 15 chemical transformations (Fig. 6) starting from D-glucorono-6,3-lactone (Yang *et al.*, 2009). The correlation NMR spectra (COSY) of the tetrahydrofuran framework present in (V) and its intermediates show that the vicinal H atoms on C2 and C3 do not correlate. It became vital to understand the spatial orientation of these two H atoms along with the structural framework so as to deduce the relative configuration of this molecule. Further, the C6—C7 diol functionality is introduced through asymmetric dihydroxylation in a 3:1 diastereoisomeric ratio in (XX). The undesired isomer after two stages at (XXI) is removed through recrystallization. Our attempts to prepare single crystals of (XXI) were unsuccessful. We then went five stages further to triol (XV) (Fig. 4) which exists as a white crystalline solid and was successful crystallized.

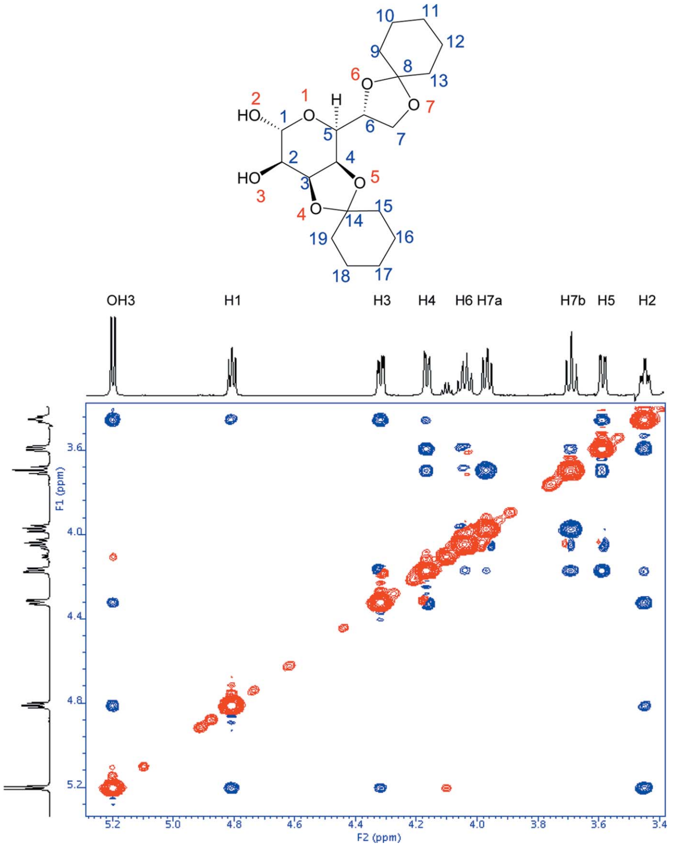


Figure 5
The 2D-NOESY spectrum of (XII).

2. Experimental

2.1. General considerations

Compounds (XII) and (XV) were prepared according to existing synthesis routes (Charles *et al.*, 2013; Brian *et al.*, 2013). NMR spectra were recorded at room temperature using an Agilent 500 MHz spectrometer. ^{1}H chemical shifts are reported in p.p.m. referenced to tetramethylsilane (TMS, 0.0 p.p.m.). ^{13}C chemical shifts are reported in p.p.m. referenced to the solvent resonance of 39.5 p.p.m. for DMSO-d_6.

2.2. NMR data

2.2.1. ^{1}H and ^{13}C NMR data for (XII). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.30–1.35 (*m*, 4H), 1.42–1.60 (*m*, 16H), 3.43–3.44 (*dd*, J = 3 Hz, 1.5 Hz, 1H), 3.56–3.58 (*dd*, J = 2, 1.5 Hz, 1H), 3.66–3.69 (*t*, 1H), 3.94–3.97 (*q*, 1H), 4.00–4.05 (*q*, 1H), 4.14–4.16 (*dd*, J = 2.5, 1.5 Hz, 1H), 4.29–4.32 (*dd*, J = 2.5, 3 Hz, 1H), 4.79–4.80 (*d*, J = 6 Hz, 1H), 5.23–5.24 (*d*, 1H), 6.34–6.35 (*d*, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 23.38 (–CH$_2$), 23.44 (–CH$_2$), 23.50 (–CH$_2$), 23.62 (–CH$_2$), 24.63 (–CH$_2$), 24.66 (–CH$_2$), 34.60 (–CH$_2$), 34.98 (–CH$_2$), 35.47 (–CH$_2$), 35.86 (–CH$_2$), 64.78 (–CH$_2$), 68.87 (–CH), 70.93 (–CH), 74.20 (–CH),

Table 1
Experimental details.

	(XII)	(XV)
Crystal data		
Chemical formula	$C_{19}H_{30}O_7{\cdot}CH_4O$	$C_{17}H_{24}O_6S$
M_r	402.48	356.43
Crystal system, space group	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$
Temperature (K)	293	200
a, b, c (Å)	7.2240 (18), 12.935 (3), 22.0691 (10)	7.593 (6), 8.542 (7), 26.70 (2)
V (Å^3)	2062.2 (7)	1732 (2)
Z	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.10	0.22
Crystal size (mm)	0.20 × 0.20 × 0.20	0.40 × 0.32 × 0.20
Data collection		
Diffractometer	Rigaku XtaLAB mini diffractometer	Rigaku XtaLAB mini diffractometer
Absorption correction	Numerical (*NUMABS*; Rigaku, 1999)	Numerical (*NUMABS*; Rigaku, 1999)
$T_{\min}$, $T_{\max}$	0.967, 0.980	0.887, 0.958
No. of measured, independent and observed [$F^2 > 2.0\sigma(F^2)$] reflections	20377, 4735, 4568	14279, 3942, 3733
R_{int}	0.027	0.034
$(\sin \theta/\lambda)_{\max}$ (Å^{-1})	0.649	0.650
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.037, 0.100, 1.08	0.033, 0.082, 1.05
No. of reflections	4735	3942
No. of parameters	256	220
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å^{-3})	0.29, −0.29	0.23, −0.24
Absolute structure	Flack x determined using 1853 quotients $[(I^+) - (I^-)]/[(I^+) + (I^-)]$ (Parsons *et al.*, 2013)	Flack x determined using 1453 quotients $[(I^+) - (I^-)]/[(I^+) + (I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.0 (3)	0.00 (3)

Computer programs: *CrystalClear-SM Expert* (Rigaku, 2014), *SIR92* (Altomare *et al.*, 1994), *SHELXL2014* (Sheldrick, 2015) and *CrystalStructure* (Rigaku, 2015).

74.85 (–CH), 75.65 (–CH), 93.59 (–CH), 108.84 (quaternary C), 109.48 (quaternary C). The NMR spectra are available in the *Supporting information*.

2.2.2. ^{1}H and ^{13}C NMR data for (XV). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.51–1.53 (*m*, 1H), 1.69–1.71 (*m*, 1H), 2.00–2.01 (*t*, 1H), 2.22–2.54 (*m*, 2H), 3.25–3.28 (*m*, 2H), 3.31–3.32 (*d*, 1H), 3.43–3.47 (*m*, 2H), 3.53–3.54 (*q*, 1H), 3.72–3.73 (*q*, 1H), 3.95–3.97 (*t*, 1H), 4.39–4.42 (*m*, 2H), 4.80–4.81 (*d*, J = 5 Hz, 1H), 4.87–4.90 (*t*, 2H), 5.61–5.69 (*m*, 1H), 7.64–7.67 (*t*, 2H), 7.73–7.76 (*t*, 1H), 7.92-7.93 (*d*, J = 8 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 32.53 (–CH$_2$), 38.75 (–CH$_2$), 47.49 (–CH), 56.52 (–CH$_2$), 65.80 (–CH$_2$), 68.89 (–CH), 75.75 (–CH), 78.64 (–CH), 81.20 (–CH), 116.67 (–CH$_2$), 127.78 (2-aryl-CH), 129.38 (2-aryl-CH), 133.83 (–CH), 135.06 (–CH), 139.31 (quaternary C). The NMR spectra are available in the *Supporting information*.

2.3. Crystallization

Compound (XII) was crystallized by slow evaporation from a solution in methanol, yielding crystals suitable for single-crystal X-ray diffraction analysis. Compound (XV) was recrystallized by slow evaporation from a solution in a mixture of toluene and *n*-butanol (7:1 *v*/*v*), yielding crystals in the form of colourless prisms ideal for single-crystal X-ray diffraction analysis.

2.4. Refinement

Crystal data, data collection and structure refinement details for (XII) and (XV) are summarized in Table 1. H atoms were placed in geometrically optimized positions and constrained to ride on their parent atoms, with C—H = 0.96 (methyl), 0.97 (methylene) or 0.98 Å (methine) and O—H = 0.82 Å for (XII), and C—H = 0.95 (aryl), 0.99 (methylene) or 1.00 Å (methine) and O—H = 0.84 Å for (XV). Displacement parameters for all H atoms were assigned as $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C,O})$. The orientation of the solvent methyl group in (XII) was allowed to rotate about the C—O bond to find the best fit to the observed electron-density peaks and the hydroxy groups in (XV) were similarly allowed to rotate. For (XII), the hydroxy groups at O3 and O9 were also treated this way, but the hydroxy group at O2 was oriented such that the H atom was in a staggered position with respect to the substituents on the parent C atom.

For compound (XII), the chosen absolute configuration of the model was based on known stereochemistry as discussed below, whereas for (XV), the absolute stereochemistry was deduced independently from Parson's z parameter [0.00 (3); Parsons *et al.*, 2013].

3. Results and discussion

The single-crystal X-ray structure of (XII) (Fig. 4) shows that the compound crystallizes in a 1:1 ratio with methanol solvent

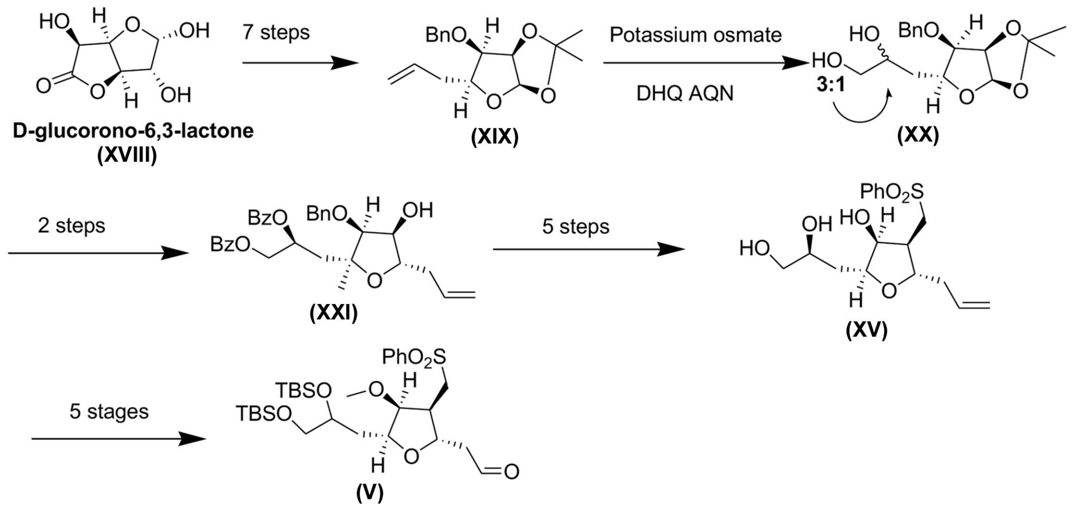


Figure 6
An overview of the synthetic scheme for the preparation of (V).

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

D—H···A	D—H	H···A	D···A	D—H···A
O2—H21···O8^{i}	0.82	1.98	2.653 (3)	139
O3—H22···O6^{ii}	0.82	2.02	2.829 (2)	171
O8—H23···O3^{i}	0.82	1.92	2.727 (3)	169

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

Table 3
Hydrogen-bond geometry (Å, °) for (XV).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H18···O1^{i}	0.84	2.05	2.859 (3)	161
O2—H18···O3	0.84	2.46	2.817 (3)	107
O3—H19···O4^{ii}	0.84	1.98	2.813 (3)	172
O4—H20···O2^{iii}	0.84	1.89	2.719 (3)	171

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

molecules. The cyclohexylidene rings assume chair conformations, whereas the five-membered rings have envelope conformations. The molecules pack together in the solid state with a few intermolecular hydrogen bonds. The O2 and O3 hydroxy groups form hydrogen-bonding interactions with methanol atom O8^{i} and with the O6^{ii} atom of another molecule, respectively (Table 2). These interactions link the constituents into extended chains which run parallel to the [100] direction.

The NOESY spectrum of (XII) (Fig. 5) shows that the H atom at C1 (H1, 4.8 p.p.m.) has an interaction with H2, which was unexpected from mechanistic considerations. The single-crystal X-ray diffraction data, however, confirm the mechanistic rationale wherein atom H1 lies on the opposite side of the ring plane from the other H atoms (those on on C2, C3, C4 and C5) of the tetrahydropyran ring. Furthermore, the H1···H2 distance of 2.83 Å supports a NOESY interaction between these atoms. The interatomic distance between atoms C1 and C2 is 1.523 (3) Å. Also, atoms H1 and H5 are on opposite sides of the C1—O1—C5 unit, with an H1···H5 interatomic distance of 3.55 Å. The interatomic distance between atoms C1 and H5 is 2.68 Å, and that between atoms C5 and H1 is 3.12 Å.

We further focused our attention on the starting material, *i.e.* D-gulono-γ-lactone, which has a specific optical rotation (SOR) of −55°. The stereochemistry at atoms C3 and C4 in this molecule are fixed and this is carried through onto atoms C3 and C4 in (XII). Because the known stereochemistry at atoms C3 and C4 remains fixed during the synthesis, the crystal structure allows the configuration of all stereocentres in (XII) to be established relative to those. We were thus able to establish the absolute configuration of (XII) in this manner with the aid of both the NOESY and the single-crystal X-ray data.

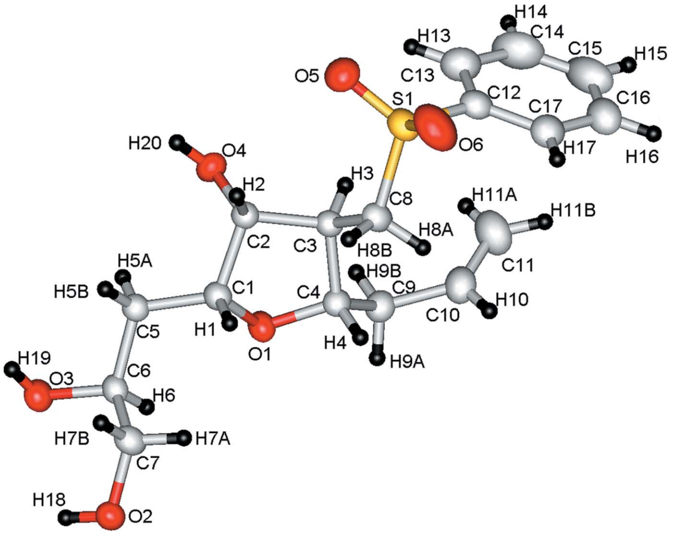


Figure 7
Single-crystal X-ray view of (XV), showing atoms H2 and H3 in a perpendicular orientation to each other. Displacement ellipsoids are drawn at the 50% probability level.

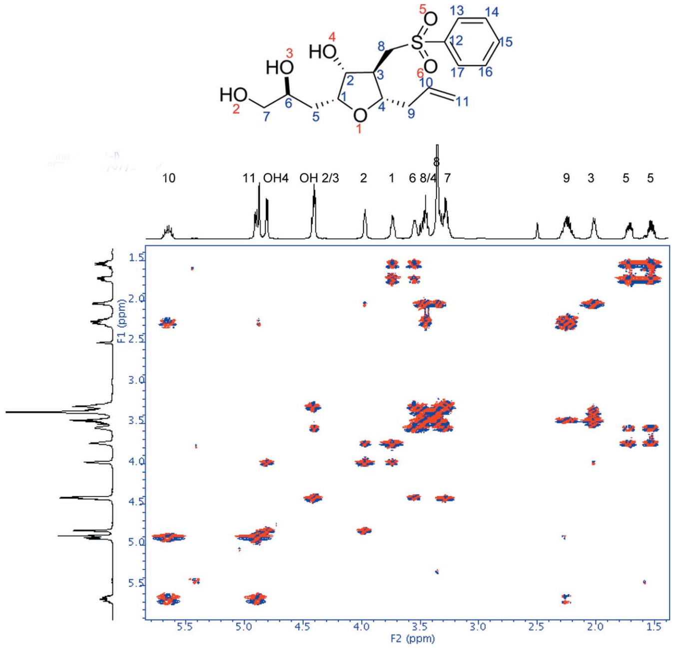


Figure 8
The 2D-COSY spectrum of (XV).

The single-crystal X-ray analysis of (XV) shows that the tetrahydrofuran ring has an envelope conformation (Fig. 7). Again the molecules pack together in the solid state with few inter- or intramolecular hydrogen bonds. The O2 and O3 hydroxy groups form an intramolecular hydrogen-bonding interaction, and also form intermolecular hydrogen-bonding interactions with atoms $O1^{i}$ and $O4^{ii}$ of other molecules (Table 3). Also, atom O4 forms an intermolecular hydrogen-bonding interaction with atom $O2^{iii}$ of another molecule. These interactions link the molecules into two-dimensional networks, which lie parallel to the (001) plane.

We were particularly interested to see the orientation of the vicinal H atoms on atoms C2 and C3 of the tetrahydrofuran ring, as these two H atoms show an unusually weak interaction in the COSY spectrum (Fig. 8; H2 at 4 p.p.m. and H3 at 2 p.p.m.). This can happen when the C—H bonds form a 90° dihedral angle. The Karplus relationship is based on the observation that vicinal H–H couplings will be at a maximum for H atoms with dihedral angles of 180 and 0° (an *anti* or eclipsed relationship results in optimal orbital overlap) and that coupling ($^{3}J_{HH}$) will be minimal (near 0°) for H atoms that are 90° from each other. Atoms H2 and H3 exhibit minimal J coupling, suggesting that their C—H bonds are nearly perpendicular to one another. The tetrahydrofuran ring with its envelope conformation facilitates this orientation of the vicinal H atoms. This conclusion is consistent with the molecular structure elucidated from the single-crystal X-ray diffraction data, which shows that the H2—C2—C3—H3 torsion angle is −110°. The H2⋯H3 interatomic distance is 2.71 Å.

In conclusion, we have synthesized two compounds, (XII) and (XV), which have important structural implications for the Eribulin framework. We deduced the relative molecular framework of both structures through 2D-NMR experiments and conclusively proved the absolute structure of both these structures using single-crystal X-ray diffraction techniques.

Acknowledgements

We wish to thank our integrated product development (IPD) leadership team comprising of Ms Geena Malhotra, Mr Dharmaraj Rao and Dr Manish Gangrade for their continual support and guidance to this project. We also extend our heartfelt thanks to Professor Vedavati Puranik from the National Chemical Laboratory (NCL), Pune, India, for providing important input during the drafting of this paper.

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supporting information

Acta Cryst. (2016). C**72**, 14-20 [doi:10.1107/S2053229615022305]

Structural corroboration of two important building blocks of the anticancer drug eribulin mesylate through two-dimensional NMR and single-crystal X-ray diffraction studies

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Computing details

For both compounds, data collection: *CrystalClear-SM Expert* (Rigaku, 2014); cell refinement: *CrystalClear-SM Expert* (Rigaku, 2014); data reduction: *CrystalClear-SM Expert* (Rigaku, 2014); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *CrystalStructure* (Rigaku, 2015); software used to prepare material for publication: *CrystalStructure* (Rigaku, 2015).

(Comp_XII) 3,4:6,7-Di-*O*-cyclohexylidene-*D*-glycero-*α*-*L*-talo-heptopyranose methanol monosolvate

Crystal data

$C_{19}H_{30}O_7 \cdot CH_4O$
$M_r = 402.48$
Orthorhombic, $P2_12_12_1$
$a = 7.2240\ (18)$ Å
$b = 12.935\ (3)$ Å
$c = 22.0691\ (10)$ Å
$V = 2062.2\ (7)$ Å^3
$Z = 4$
$F(000) = 872.00$
$D_x = 1.296$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71075$ Å
Cell parameters from 6335 reflections
$\theta = 3.2$–$27.5°$
$\mu = 0.10$ mm^{-1}
$T = 293$ K
Prism, colorless
0.20 × 0.20 × 0.20 mm

Data collection

Rigaku XtaLAB mini diffractometer
Detector resolution: 13.653 pixels mm^{-1}
ω scans
Absorption correction: numerical (*NUMABS*; Rigaku, 1999)
$T_{\min} = 0.967$, $T_{\max} = 0.980$
20377 measured reflections
4735 independent reflections
4568 reflections with $F^2 > 2.0\sigma(F^2)$
$R_{\text{int}} = 0.027$
$\theta_{\max} = 27.5°$, $\theta_{\min} = 3.2°$
$h = -9 \rightarrow 9$
$k = -16 \rightarrow 16$
$l = -28 \rightarrow 28$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.100$
$S = 1.08$
4735 reflections
256 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0514P)^2 + 0.2988P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

Absolute structure: Flack *x* determined using 1853 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)
Absolute structure parameter: 0.0 (3)

Special details

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

Refinement. Refinement was performed using all reflections. The weighted R-factor (wR) and goodness of fit (S) are based on F^2. R-factor (gt) are based on F. The threshold expression of F^2 > 2.0 sigma(F^2) is used only for calculating R-factor (gt).

Neutral-atom scattering factors were taken from international tables for crystallography, Vol. C, Table 6.1.1.4. Anomalous dispersion effects were included in Fcalc (Ibers & Hamilton, 1964); the values for ?f' and ?f" were extracted from international tables of crystallography (Creagh & McAuley, 1992). The values for the mass attenuation coefficients are those of Creagh and Hubbell.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.35295 (19)	0.58282 (12)	0.48548 (6)	0.0371 (3)
O2	0.3077 (2)	0.72969 (12)	0.42698 (7)	0.0421 (3)
H21	0.2018	0.7108	0.4194	0.050*
O3	0.6894 (2)	0.72168 (11)	0.39171 (6)	0.0384 (3)
H22	0.6789	0.7848	0.3911	0.046*
O4	0.75860 (19)	0.51822 (10)	0.42770 (6)	0.0311 (3)
O5	0.6597 (2)	0.43865 (10)	0.51248 (7)	0.0382 (3)
O6	0.19472 (19)	0.55968 (11)	0.60599 (6)	0.0336 (3)
O7	0.3195 (2)	0.46408 (14)	0.68318 (7)	0.0471 (4)
O8	0.5386 (3)	0.8094 (4)	0.65156 (10)	0.1275 (16)
H23	0.4296	0.8074	0.6412	0.153*
C1	0.4200 (3)	0.64349 (14)	0.43614 (8)	0.0294 (4)
H1	0.4191	0.6011	0.3993	0.035*
C2	0.6160 (3)	0.68268 (13)	0.44707 (8)	0.0283 (4)
H2	0.6111	0.7392	0.4766	0.034*
C3	0.7420 (2)	0.59962 (13)	0.47104 (8)	0.0273 (4)
H3	0.8640	0.6284	0.4806	0.033*
C4	0.6584 (3)	0.54600 (13)	0.52731 (8)	0.0280 (4)
H4	0.7365	0.5587	0.5629	0.034*
C5	0.4611 (3)	0.58198 (14)	0.53966 (8)	0.0279 (4)
H5	0.4647	0.6520	0.5565	0.033*
C6	0.3620 (2)	0.51148 (14)	0.58383 (8)	0.0287 (4)
H6	0.3316	0.4459	0.5639	0.034*
C7	0.4637 (3)	0.49056 (17)	0.64252 (9)	0.0351 (4)

H7A	0.5508	0.4340	0.6379	0.042*
H7B	0.5297	0.5515	0.6562	0.042*
C8	0.1523 (3)	0.51299 (15)	0.66350 (9)	0.0331 (4)
C9	0.0938 (4)	0.5960 (2)	0.70757 (11)	0.0524 (6)
H9A	−0.0106	0.6337	0.6909	0.063*
H9B	0.1948	0.6444	0.7133	0.063*
C10	0.0394 (5)	0.5495 (2)	0.76878 (12)	0.0625 (7)
H10A	0.1474	0.5182	0.7874	0.075*
H10B	−0.0039	0.6042	0.7953	0.075*
C11	−0.1116 (4)	0.4685 (3)	0.76198 (12)	0.0617 (7)
H11A	−0.1374	0.4377	0.8011	0.074*
H11B	−0.2241	0.5012	0.7476	0.074*
C12	−0.0527 (4)	0.3850 (2)	0.71778 (12)	0.0530 (6)
H12A	−0.1545	0.3372	0.7117	0.064*
H12B	0.0502	0.3466	0.7348	0.064*
C13	0.0050 (3)	0.43058 (18)	0.65660 (10)	0.0418 (5)
H13A	0.0519	0.3757	0.6309	0.050*
H13B	−0.1026	0.4603	0.6369	0.050*
C14	0.7801 (3)	0.42518 (14)	0.46154 (8)	0.0305 (4)
C15	0.7147 (3)	0.33586 (16)	0.42330 (11)	0.0423 (5)
H15A	0.5917	0.3507	0.4079	0.051*
H15B	0.7071	0.2742	0.4482	0.051*
C16	0.8454 (4)	0.31621 (18)	0.37032 (11)	0.0475 (5)
H16A	0.8046	0.2554	0.3484	0.057*
H16B	0.8408	0.3746	0.3428	0.057*
C17	1.0433 (4)	0.3003 (2)	0.39150 (13)	0.0526 (6)
H17A	1.1235	0.2917	0.3566	0.063*
H17B	1.0507	0.2379	0.4158	0.063*
C18	1.1088 (3)	0.3921 (2)	0.42881 (12)	0.0478 (5)
H18A	1.1127	0.4532	0.4034	0.057*
H18B	1.2330	0.3789	0.4436	0.057*
C19	0.9804 (3)	0.41131 (17)	0.48222 (10)	0.0384 (4)
H19A	1.0204	0.4728	0.5037	0.046*
H19B	0.9877	0.3534	0.5100	0.046*
C20	0.5497 (5)	0.8009 (5)	0.70985 (16)	0.1046 (17)
H20A	0.5570	0.8684	0.7277	0.126*
H20B	0.6583	0.7620	0.7203	0.126*
H20C	0.4419	0.7658	0.7249	0.126*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0301 (6)	0.0475 (8)	0.0337 (7)	−0.0081 (6)	−0.0046 (6)	0.0125 (6)
O2	0.0391 (8)	0.0433 (8)	0.0439 (8)	0.0115 (7)	−0.0042 (7)	0.0044 (6)
O3	0.0463 (8)	0.0315 (6)	0.0373 (7)	0.0007 (6)	0.0088 (7)	0.0103 (6)
O4	0.0377 (7)	0.0272 (6)	0.0283 (6)	0.0048 (5)	0.0037 (5)	−0.0007 (5)
O5	0.0444 (8)	0.0265 (6)	0.0436 (8)	0.0037 (6)	0.0168 (7)	0.0042 (5)
O6	0.0306 (6)	0.0381 (7)	0.0321 (7)	0.0063 (6)	0.0068 (6)	0.0102 (5)

O7	0.0331 (7)	0.0700 (11)	0.0382 (8)	0.0060 (7)	0.0031 (6)	0.0235 (8)
O8	0.0373 (10)	0.296 (5)	0.0495 (12)	0.015 (2)	0.0035 (10)	0.006 (2)
C1	0.0320 (9)	0.0305 (8)	0.0257 (8)	0.0019 (7)	−0.0004 (7)	0.0011 (7)
C2	0.0324 (9)	0.0241 (8)	0.0284 (8)	−0.0005 (7)	0.0029 (7)	0.0015 (6)
C3	0.0261 (8)	0.0267 (8)	0.0291 (8)	−0.0006 (7)	0.0005 (7)	−0.0013 (7)
C4	0.0295 (8)	0.0280 (8)	0.0266 (8)	0.0014 (7)	0.0000 (7)	0.0005 (6)
C5	0.0283 (8)	0.0279 (8)	0.0273 (8)	0.0002 (7)	0.0017 (7)	0.0012 (7)
C6	0.0271 (8)	0.0297 (8)	0.0292 (8)	−0.0003 (7)	0.0036 (7)	0.0022 (7)
C7	0.0291 (9)	0.0412 (10)	0.0352 (9)	0.0028 (8)	0.0016 (8)	0.0062 (8)
C8	0.0313 (9)	0.0379 (9)	0.0302 (9)	0.0032 (8)	0.0048 (7)	0.0088 (7)
C9	0.0696 (17)	0.0458 (12)	0.0418 (12)	−0.0032 (12)	0.0181 (12)	−0.0015 (10)
C10	0.0811 (19)	0.0695 (17)	0.0369 (12)	−0.0062 (15)	0.0208 (13)	−0.0041 (11)
C11	0.0542 (14)	0.088 (2)	0.0426 (12)	−0.0018 (14)	0.0173 (12)	0.0176 (13)
C12	0.0490 (13)	0.0579 (15)	0.0521 (13)	−0.0116 (11)	0.0022 (11)	0.0207 (11)
C13	0.0395 (11)	0.0465 (11)	0.0396 (11)	−0.0043 (9)	0.0002 (9)	0.0080 (9)
C14	0.0331 (9)	0.0267 (8)	0.0319 (9)	0.0023 (7)	0.0051 (7)	0.0025 (7)
C15	0.0408 (11)	0.0328 (10)	0.0534 (12)	−0.0055 (8)	0.0008 (10)	−0.0082 (9)
C16	0.0569 (14)	0.0408 (11)	0.0450 (12)	−0.0035 (11)	0.0005 (11)	−0.0151 (9)
C17	0.0536 (14)	0.0463 (13)	0.0581 (15)	0.0107 (11)	0.0114 (12)	−0.0125 (11)
C18	0.0335 (10)	0.0513 (13)	0.0585 (14)	0.0060 (9)	0.0055 (10)	−0.0108 (11)
C19	0.0373 (10)	0.0378 (10)	0.0401 (10)	0.0094 (8)	−0.0041 (9)	−0.0040 (8)
C20	0.0575 (19)	0.192 (5)	0.064 (2)	−0.003 (3)	−0.0071 (17)	−0.044 (3)

Geometric parameters (Å, º)

O1—C1	1.427 (2)	C9—H9A	0.9700
O1—C5	1.428 (2)	C9—H9B	0.9700
O2—C1	1.394 (2)	C10—C11	1.520 (4)
O2—H21	0.8200	C10—H10A	0.9700
O3—C2	1.424 (2)	C10—H10B	0.9700
O3—H22	0.8200	C11—C12	1.517 (4)
O4—C14	1.425 (2)	C11—H11A	0.9700
O4—C3	1.428 (2)	C11—H11B	0.9700
O5—C4	1.427 (2)	C12—C13	1.531 (3)
O5—C14	1.432 (2)	C12—H12A	0.9700
O6—C8	1.439 (2)	C12—H12B	0.9700
O6—C6	1.445 (2)	C13—H13A	0.9700
O7—C7	1.417 (2)	C13—H13B	0.9700
O7—C8	1.431 (2)	C14—C15	1.507 (3)
O8—C20	1.294 (4)	C14—C19	1.528 (3)
O8—H23	0.8200	C15—C16	1.524 (3)
C1—C2	1.523 (3)	C15—H15A	0.9700
C1—H1	0.9800	C15—H15B	0.9700
C2—C3	1.504 (2)	C16—C17	1.518 (4)
C2—H2	0.9800	C16—H16A	0.9700
C3—C4	1.545 (2)	C16—H16B	0.9700
C3—H3	0.9800	C17—C18	1.520 (3)
C4—C5	1.524 (3)	C17—H17A	0.9700

C4—H4	0.9800	C17—H17B	0.9700
C5—C6	1.515 (2)	C18—C19	1.520 (3)
C5—H5	0.9800	C18—H18A	0.9700
C6—C7	1.513 (3)	C18—H18B	0.9700
C6—H6	0.9800	C19—H19A	0.9700
C7—H7A	0.9700	C19—H19B	0.9700
C7—H7B	0.9700	C20—H20A	0.9600
C8—C9	1.509 (3)	C20—H20B	0.9600
C8—C13	1.514 (3)	C20—H20C	0.9600
C9—C10	1.530 (3)		

C1—O1—C5	117.22 (14)	C9—C10—H10A	109.3
C1—O2—H21	109.5	C11—C10—H10B	109.3
C2—O3—H22	109.5	C9—C10—H10B	109.3
C14—O4—C3	106.31 (13)	H10A—C10—H10B	108.0
C4—O5—C14	107.60 (14)	C12—C11—C10	110.7 (2)
C8—O6—C6	107.20 (13)	C12—C11—H11A	109.5
C7—O7—C8	108.75 (14)	C10—C11—H11A	109.5
C20—O8—H23	109.5	C12—C11—H11B	109.5
O2—C1—O1	110.68 (15)	C10—C11—H11B	109.5
O2—C1—C2	107.32 (16)	H11A—C11—H11B	108.1
O1—C1—C2	112.19 (15)	C11—C12—C13	111.6 (2)
O2—C1—H1	108.9	C11—C12—H12A	109.3
O1—C1—H1	108.9	C13—C12—H12A	109.3
C2—C1—H1	108.9	C11—C12—H12B	109.3
O3—C2—C3	109.24 (15)	C13—C12—H12B	109.3
O3—C2—C1	109.16 (15)	H12A—C12—H12B	108.0
C3—C2—C1	112.36 (15)	C8—C13—C12	111.97 (19)
O3—C2—H2	108.7	C8—C13—H13A	109.2
C3—C2—H2	108.7	C12—C13—H13A	109.2
C1—C2—H2	108.7	C8—C13—H13B	109.2
O4—C3—C2	110.01 (14)	C12—C13—H13B	109.2
O4—C3—C4	103.90 (13)	H13A—C13—H13B	107.9
C2—C3—C4	111.54 (15)	O4—C14—O5	104.05 (14)
O4—C3—H3	110.4	O4—C14—C15	108.65 (16)
C2—C3—H3	110.4	O5—C14—C15	110.03 (17)
C4—C3—H3	110.4	O4—C14—C19	111.03 (16)
O5—C4—C5	110.13 (15)	O5—C14—C19	110.79 (16)
O5—C4—C3	104.48 (14)	C15—C14—C19	111.98 (17)
C5—C4—C3	111.83 (14)	C14—C15—C16	111.30 (18)
O5—C4—H4	110.1	C14—C15—H15A	109.4
C5—C4—H4	110.1	C16—C15—H15A	109.4
C3—C4—H4	110.1	C14—C15—H15B	109.4
O1—C5—C6	106.55 (15)	C16—C15—H15B	109.4
O1—C5—C4	111.36 (14)	H15A—C15—H15B	108.0
C6—C5—C4	111.91 (15)	C17—C16—C15	111.7 (2)
O1—C5—H5	109.0	C17—C16—H16A	109.3
C6—C5—H5	109.0	C15—C16—H16A	109.3

C4—C5—H5	109.0	C17—C16—H16B	109.3
O6—C6—C7	101.16 (14)	C15—C16—H16B	109.3
O6—C6—C5	110.69 (14)	H16A—C16—H16B	107.9
C7—C6—C5	115.41 (16)	C16—C17—C18	110.74 (19)
O6—C6—H6	109.8	C16—C17—H17A	109.5
C7—C6—H6	109.8	C18—C17—H17A	109.5
C5—C6—H6	109.8	C16—C17—H17B	109.5
O7—C7—C6	103.20 (15)	C18—C17—H17B	109.5
O7—C7—H7A	111.1	H17A—C17—H17B	108.1
C6—C7—H7A	111.1	C17—C18—C19	111.0 (2)
O7—C7—H7B	111.1	C17—C18—H18A	109.4
C6—C7—H7B	111.1	C19—C18—H18A	109.4
H7A—C7—H7B	109.1	C17—C18—H18B	109.4
O7—C8—O6	105.87 (14)	C19—C18—H18B	109.4
O7—C8—C9	110.8 (2)	H18A—C18—H18B	108.0
O6—C8—C9	109.25 (17)	C18—C19—C14	111.43 (18)
O7—C8—C13	108.20 (17)	C18—C19—H19A	109.3
O6—C8—C13	110.89 (16)	C14—C19—H19A	109.3
C9—C8—C13	111.64 (18)	C18—C19—H19B	109.3
C8—C9—C10	111.2 (2)	C14—C19—H19B	109.3
C8—C9—H9A	109.4	H19A—C19—H19B	108.0
C10—C9—H9A	109.4	O8—C20—H20A	109.5
C8—C9—H9B	109.4	O8—C20—H20B	109.5
C10—C9—H9B	109.4	H20A—C20—H20B	109.5
H9A—C9—H9B	108.0	O8—C20—H20C	109.5
C11—C10—C9	111.6 (2)	H20A—C20—H20C	109.5
C11—C10—H10A	109.3	H20B—C20—H20C	109.5

C5—O1—C1—O2	−109.98 (18)	C7—O7—C8—O6	6.6 (2)
C5—O1—C1—C2	9.9 (2)	C7—O7—C8—C9	−111.7 (2)
O2—C1—C2—O3	−71.31 (18)	C7—O7—C8—C13	125.54 (17)
O1—C1—C2—O3	166.90 (15)	C6—O6—C8—O7	17.8 (2)
O2—C1—C2—C3	167.35 (14)	C6—O6—C8—C9	137.22 (19)
O1—C1—C2—C3	45.6 (2)	C6—O6—C8—C13	−99.31 (18)
C14—O4—C3—C2	−147.13 (15)	O7—C8—C9—C10	−66.1 (3)
C14—O4—C3—C4	−27.62 (17)	O6—C8—C9—C10	177.7 (2)
O3—C2—C3—O4	−58.95 (19)	C13—C8—C9—C10	54.6 (3)
C1—C2—C3—O4	62.34 (19)	C8—C9—C10—C11	−55.9 (3)
O3—C2—C3—C4	−173.70 (14)	C9—C10—C11—C12	55.7 (3)
C1—C2—C3—C4	−52.4 (2)	C10—C11—C12—C13	−54.5 (3)
C14—O5—C4—C5	135.78 (16)	O7—C8—C13—C12	68.4 (2)
C14—O5—C4—C3	15.54 (19)	O6—C8—C13—C12	−175.94 (19)
O4—C3—C4—O5	7.32 (18)	C9—C8—C13—C12	−53.9 (3)
C2—C3—C4—O5	125.79 (16)	C11—C12—C13—C8	53.9 (3)
O4—C3—C4—C5	−111.78 (16)	C3—O4—C14—O5	37.86 (18)
C2—C3—C4—C5	6.7 (2)	C3—O4—C14—C15	155.06 (16)
C1—O1—C5—C6	−179.18 (15)	C3—O4—C14—C19	−81.37 (18)
C1—O1—C5—C4	−56.9 (2)	C4—O5—C14—O4	−32.95 (19)

O5—C4—C5—O1	−69.48 (18)	C4—O5—C14—C15	−149.19 (17)
C3—C4—C5—O1	46.22 (19)	C4—O5—C14—C19	86.43 (18)
O5—C4—C5—C6	49.67 (19)	O4—C14—C15—C16	69.4 (2)
C3—C4—C5—C6	165.37 (15)	O5—C14—C15—C16	−177.24 (18)
C8—O6—C6—C7	−33.24 (18)	C19—C14—C15—C16	−53.6 (2)
C8—O6—C6—C5	−156.06 (16)	C14—C15—C16—C17	54.8 (3)
O1—C5—C6—O6	−71.94 (18)	C15—C16—C17—C18	−56.1 (3)
C4—C5—C6—O6	166.11 (14)	C16—C17—C18—C19	56.3 (3)
O1—C5—C6—C7	173.96 (15)	C17—C18—C19—C14	−55.2 (3)
C4—C5—C6—C7	52.0 (2)	O4—C14—C19—C18	−67.5 (2)
C8—O7—C7—C6	−26.9 (2)	O5—C14—C19—C18	177.44 (17)
O6—C6—C7—O7	36.38 (19)	C15—C14—C19—C18	54.2 (2)
C5—C6—C7—O7	155.87 (16)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H21···O8^{i}	0.82	1.98	2.653 (3)	139
O3—H22···O6^{ii}	0.82	2.02	2.829 (2)	171
O8—H23···O3^{i}	0.82	1.92	2.727 (3)	169

Symmetry codes: (i) $x-1/2, -y+3/2, -z+1$; (ii) $x+1/2, -y+3/2, -z+1$.

(Comp_XV) (2*R*,3*R*,4*R*,5*S*)-5-Allyl-2-[(*S*)-2,3-dihydroxypropyl]-4-[(phenylsulfonyl)methyl]tetrahydrofuran-3-ol

Crystal data

$C_{17}H_{24}O_6S$
M_r = 356.43
Orthorhombic, $P2_12_12_1$
a = 7.593 (6) Å
b = 8.542 (7) Å
c = 26.70 (2) Å
V = 1732 (2) Å^3
Z = 4
$F(000)$ = 760.00

D_x = 1.367 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71075 Å
Cell parameters from 4380 reflections
θ = 3.1–27.5°
μ = 0.22 mm^{-1}
T = 200 K
Prism, colorless
0.40 × 0.32 × 0.20 mm

Data collection

Rigaku XtaLAB mini diffractometer
Detector resolution: 13.653 pixels mm^{-1}
ω scans
Absorption correction: numerical (*NUMABS*; Rigaku, 1999)
T_{min} = 0.887, T_{max} = 0.958
14279 measured reflections

3942 independent reflections
3733 reflections with $F^2 > 2.0\sigma(F^2)$
R_{int} = 0.034
θ_{max} = 27.5°, θ_{min} = 3.1°
$h = -9\rightarrow 9$
$k = -11\rightarrow 11$
$l = -34\rightarrow 34$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.082
S = 1.05
3942 reflections
220 parameters

0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0405P)^2 + 0.1659P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$

$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.24$ e Å^{-3}
Absolute structure: Flack *x* determined using 1454 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)
Absolute structure parameter: 0.00 (3)

Special details

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

Refinement. Refinement was performed using all reflections. The weighted R-factor (wR) and goodness of fit (S) are based on F^2. R-factor (gt) are based on F. The threshold expression of F^2 > 2.0 sigma(F^2) is used only for calculating R-factor (gt).

Neutral-atom scattering factors were taken from international tables for crystallography, Vol. C, Table 6.1.1.4. Anomalous dispersion effects were included in Fcalc (Ibers & Hamilton, 1964); the values for ?f' and ?f" were extracted from international tables of crystallography (Creagh & McAuley, 1992). The values for the mass attenuation coefficients are those of Creagh and Hubbell.

Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

Creagh, D. C. & McAuley, W. J. (1992). International Tables for Crystallography, (A. J. C. Wilson, ed.), Kluwer Academic Publishers, Boston, Vol C, Table 4.2.6.8, 219-222.

Ibers, J. A. & Hamilton, W. C. (1964). Acta Cryst. 17, 781–782.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.75191 (7)	0.69616 (6)	0.55350 (2)	0.03182 (14)
O1	0.26736 (18)	0.69593 (16)	0.68646 (5)	0.0270 (3)
O2	−0.16817 (19)	0.34917 (19)	0.72260 (6)	0.0327 (4)
H18	−0.1726	0.3074	0.7511	0.039*
O3	0.1105 (2)	0.3635 (2)	0.79208 (5)	0.0328 (4)
H19	0.1752	0.2837	0.7923	0.039*
O4	0.64460 (18)	0.61630 (18)	0.70728 (5)	0.0284 (3)
H20	0.7053	0.5376	0.7149	0.034*
O5	0.8699 (2)	0.6311 (2)	0.58990 (7)	0.0467 (5)
O6	0.7510 (3)	0.6297 (2)	0.50392 (6)	0.0502 (5)
C1	0.3456 (3)	0.5447 (2)	0.68089 (7)	0.0241 (4)
H1	0.2854	0.4884	0.6528	0.029*
C2	0.5358 (2)	0.5797 (2)	0.66544 (7)	0.0221 (4)
H2	0.5864	0.4906	0.6458	0.027*
C3	0.5122 (2)	0.7255 (2)	0.63198 (7)	0.0228 (4)
H3	0.5996	0.8075	0.6418	0.027*
C4	0.3228 (3)	0.7839 (2)	0.64351 (7)	0.0251 (4)
H4	0.2441	0.7590	0.6145	0.030*
C5	0.3185 (3)	0.4530 (3)	0.72883 (8)	0.0277 (4)
H5A	0.3862	0.5039	0.7560	0.033*
H5B	0.3664	0.3462	0.7243	0.033*
C6	0.1256 (3)	0.4405 (2)	0.74488 (7)	0.0247 (4)
H6	0.0794	0.5494	0.7491	0.030*

C7	0.0107 (3)	0.3587 (3)	0.70659 (8)	0.0299 (4)
H7A	0.0164	0.4163	0.6745	0.036*
H7B	0.0565	0.2517	0.7008	0.036*
C8	0.5323 (3)	0.6877 (3)	0.57634 (7)	0.0280 (4)
H8A	0.4594	0.7621	0.5569	0.034*
H8B	0.4854	0.5813	0.5702	0.034*
C9	0.3069 (3)	0.9562 (2)	0.65609 (8)	0.0292 (4)
H9A	0.1841	0.9789	0.6662	0.035*
H9B	0.3842	0.9801	0.6850	0.035*
C10	0.3560 (3)	1.0602 (3)	0.61316 (9)	0.0350 (5)
H10	0.2976	1.0449	0.5821	0.042*
C11	0.4748 (4)	1.1710 (3)	0.61602 (10)	0.0475 (6)
H11A	0.5353	1.1889	0.6466	0.057*
H11B	0.5004	1.2334	0.5875	0.057*
C12	0.7918 (3)	0.8995 (3)	0.54793 (8)	0.0309 (5)
C13	0.8810 (3)	0.9767 (3)	0.58547 (10)	0.0416 (6)
H13	0.9228	0.9217	0.6140	0.050*
C14	0.9085 (4)	1.1358 (4)	0.58069 (13)	0.0564 (7)
H14	0.9690	1.1911	0.6063	0.068*
C15	0.8489 (4)	1.2146 (4)	0.53927 (14)	0.0605 (9)
H15	0.8698	1.3238	0.5362	0.073*
C16	0.7584 (4)	1.1360 (3)	0.50181 (12)	0.0529 (7)
H16	0.7167	1.1915	0.4733	0.064*
C17	0.7289 (3)	0.9771 (3)	0.50593 (9)	0.0386 (5)
H17	0.6669	0.9220	0.4805	0.046*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0310 (3)	0.0329 (3)	0.0315 (3)	0.0026 (2)	0.0104 (2)	0.0010 (2)
O1	0.0278 (7)	0.0240 (7)	0.0293 (6)	0.0051 (7)	0.0081 (6)	0.0045 (5)
O2	0.0242 (7)	0.0388 (9)	0.0351 (8)	−0.0017 (6)	0.0005 (6)	0.0113 (6)
O3	0.0306 (8)	0.0414 (9)	0.0263 (7)	0.0036 (7)	0.0059 (6)	0.0081 (6)
O4	0.0253 (7)	0.0307 (8)	0.0292 (7)	0.0008 (6)	−0.0051 (6)	0.0030 (6)
O5	0.0337 (9)	0.0484 (10)	0.0582 (11)	0.0123 (8)	0.0058 (8)	0.0165 (9)
O6	0.0644 (11)	0.0472 (10)	0.0389 (9)	−0.0066 (10)	0.0241 (10)	−0.0119 (7)
C1	0.0240 (9)	0.0223 (10)	0.0259 (9)	0.0003 (8)	0.0020 (7)	0.0009 (7)
C2	0.0217 (9)	0.0218 (10)	0.0228 (9)	0.0013 (7)	0.0018 (7)	−0.0001 (7)
C3	0.0211 (8)	0.0236 (10)	0.0238 (9)	−0.0001 (8)	0.0012 (7)	0.0011 (7)
C4	0.0225 (9)	0.0284 (11)	0.0244 (9)	0.0016 (8)	0.0015 (7)	0.0031 (8)
C5	0.0228 (9)	0.0301 (11)	0.0301 (10)	0.0014 (8)	0.0027 (8)	0.0074 (8)
C6	0.0255 (9)	0.0225 (10)	0.0261 (9)	0.0010 (8)	0.0037 (8)	0.0046 (8)
C7	0.0261 (9)	0.0348 (12)	0.0289 (10)	−0.0030 (9)	0.0041 (8)	0.0015 (8)
C8	0.0250 (9)	0.0356 (11)	0.0233 (9)	−0.0028 (9)	0.0017 (7)	0.0019 (9)
C9	0.0298 (10)	0.0264 (11)	0.0315 (10)	0.0042 (8)	0.0017 (8)	0.0019 (8)
C10	0.0398 (12)	0.0289 (12)	0.0364 (11)	0.0082 (10)	0.0049 (10)	0.0042 (9)
C11	0.0582 (16)	0.0312 (13)	0.0531 (15)	−0.0015 (12)	0.0139 (13)	0.0030 (11)
C12	0.0246 (9)	0.0372 (12)	0.0311 (10)	0.0003 (9)	0.0066 (8)	0.0015 (9)

C13	0.0338 (12)	0.0479 (15)	0.0432 (13)	−0.0022 (11)	−0.0006 (10)	−0.0030 (11)
C14	0.0419 (14)	0.0501 (17)	0.077 (2)	−0.0097 (14)	0.0021 (14)	−0.0164 (15)
C15	0.0414 (14)	0.0361 (15)	0.104 (3)	−0.0017 (13)	0.0187 (16)	0.0052 (16)
C16	0.0389 (13)	0.0508 (16)	0.0691 (17)	0.0089 (13)	0.0140 (14)	0.0251 (14)
C17	0.0317 (12)	0.0471 (14)	0.0370 (11)	0.0027 (11)	0.0055 (10)	0.0073 (10)

Geometric parameters (Å, º)

S1—O5	1.4339 (19)	C6—C7	1.515 (3)
S1—O6	1.4403 (19)	C6—H6	1.0000
S1—C12	1.769 (3)	C7—H7A	0.9900
S1—C8	1.777 (2)	C7—H7B	0.9900
O1—C1	1.430 (3)	C8—H8A	0.9900
O1—C4	1.434 (2)	C8—H8B	0.9900
O2—C7	1.426 (3)	C9—C10	1.497 (3)
O2—H18	0.8400	C9—H9A	0.9900
O3—C6	1.426 (2)	C9—H9B	0.9900
O3—H19	0.8400	C10—C11	1.310 (4)
O4—C2	1.424 (2)	C10—H10	0.9500
O4—H20	0.8400	C11—H11A	0.9500
C1—C5	1.514 (3)	C11—H11B	0.9500
C1—C2	1.531 (3)	C12—C13	1.378 (3)
C1—H1	1.0000	C12—C17	1.388 (3)
C2—C3	1.543 (3)	C13—C14	1.381 (4)
C2—H2	1.0000	C13—H13	0.9500
C3—C8	1.528 (3)	C14—C15	1.371 (5)
C3—C4	1.554 (3)	C14—H14	0.9500
C3—H3	1.0000	C15—C16	1.387 (5)
C4—C9	1.514 (3)	C15—H15	0.9500
C4—H4	1.0000	C16—C17	1.380 (4)
C5—C6	1.530 (3)	C16—H16	0.9500
C5—H5A	0.9900	C17—H17	0.9500
C5—H5B	0.9900		

O5—S1—O6	118.24 (13)	C7—C6—H6	107.6
O5—S1—C12	109.31 (11)	C5—C6—H6	107.6
O6—S1—C12	108.07 (11)	O2—C7—C6	111.86 (17)
O5—S1—C8	109.73 (11)	O2—C7—H7A	109.2
O6—S1—C8	107.17 (12)	C6—C7—H7A	109.2
C12—S1—C8	103.27 (10)	O2—C7—H7B	109.2
C1—O1—C4	105.59 (14)	C6—C7—H7B	109.2
C7—O2—H18	109.5	H7A—C7—H7B	107.9
C6—O3—H19	109.5	C3—C8—S1	114.77 (14)
C2—O4—H20	109.5	C3—C8—H8A	108.6
O1—C1—C5	108.84 (16)	S1—C8—H8A	108.6
O1—C1—C2	104.07 (16)	C3—C8—H8B	108.6
C5—C1—C2	117.17 (16)	S1—C8—H8B	108.6
O1—C1—H1	108.8	H8A—C8—H8B	107.5

C5—C1—H1	108.8	C10—C9—C4	112.76 (18)
C2—C1—H1	108.8	C10—C9—H9A	109.0
O4—C2—C1	112.26 (16)	C4—C9—H9A	109.0
O4—C2—C3	110.11 (16)	C10—C9—H9B	109.0
C1—C2—C3	101.79 (15)	C4—C9—H9B	109.0
O4—C2—H2	110.8	H9A—C9—H9B	107.8
C1—C2—H2	110.8	C11—C10—C9	123.7 (2)
C3—C2—H2	110.8	C11—C10—H10	118.1
C8—C3—C2	112.39 (17)	C9—C10—H10	118.1
C8—C3—C4	110.67 (16)	C10—C11—H11A	120.0
C2—C3—C4	104.60 (15)	C10—C11—H11B	120.0
C8—C3—H3	109.7	H11A—C11—H11B	120.0
C2—C3—H3	109.7	C13—C12—C17	121.9 (2)
C4—C3—H3	109.7	C13—C12—S1	119.54 (19)
O1—C4—C9	107.97 (16)	C17—C12—S1	118.57 (18)
O1—C4—C3	105.16 (15)	C12—C13—C14	118.6 (3)
C9—C4—C3	115.47 (17)	C12—C13—H13	120.7
O1—C4—H4	109.3	C14—C13—H13	120.7
C9—C4—H4	109.3	C15—C14—C13	120.5 (3)
C3—C4—H4	109.3	C15—C14—H14	119.7
C1—C5—C6	113.76 (16)	C13—C14—H14	119.7
C1—C5—H5A	108.8	C14—C15—C16	120.5 (3)
C6—C5—H5A	108.8	C14—C15—H15	119.7
C1—C5—H5B	108.8	C16—C15—H15	119.7
C6—C5—H5B	108.8	C17—C16—C15	119.9 (3)
H5A—C5—H5B	107.7	C17—C16—H16	120.0
O3—C6—C7	109.69 (17)	C15—C16—H16	120.0
O3—C6—C5	110.90 (15)	C16—C17—C12	118.6 (2)
C7—C6—C5	113.23 (17)	C16—C17—H17	120.7
O3—C6—H6	107.6	C12—C17—H17	120.7

C4—O1—C1—C5	170.74 (15)	C2—C3—C8—S1	−87.49 (19)
C4—O1—C1—C2	45.09 (18)	C4—C3—C8—S1	155.97 (15)
O1—C1—C2—O4	81.59 (18)	O5—S1—C8—C3	39.8 (2)
C5—C1—C2—O4	−38.6 (2)	O6—S1—C8—C3	169.40 (16)
O1—C1—C2—C3	−36.12 (18)	C12—S1—C8—C3	−76.62 (18)
C5—C1—C2—C3	−156.31 (17)	O1—C4—C9—C10	−178.13 (17)
O4—C2—C3—C8	135.57 (17)	C3—C4—C9—C10	64.6 (2)
C1—C2—C3—C8	−105.19 (17)	C4—C9—C10—C11	−125.5 (3)
O4—C2—C3—C4	−104.31 (17)	O5—S1—C12—C13	−18.8 (2)
C1—C2—C3—C4	14.93 (19)	O6—S1—C12—C13	−148.67 (19)
C1—O1—C4—C9	−158.33 (16)	C8—S1—C12—C13	98.00 (19)
C1—O1—C4—C3	−34.53 (19)	O5—S1—C12—C17	162.38 (17)
C8—C3—C4—O1	131.96 (18)	O6—S1—C12—C17	32.5 (2)
C2—C3—C4—O1	10.70 (19)	C8—S1—C12—C17	−80.87 (19)
C8—C3—C4—C9	−109.15 (19)	C17—C12—C13—C14	−0.2 (4)
C2—C3—C4—C9	129.58 (18)	S1—C12—C13—C14	−179.1 (2)
O1—C1—C5—C6	55.3 (2)	C12—C13—C14—C15	−0.4 (4)

C2—C1—C5—C6	172.89 (17)	C13—C14—C15—C16	0.8 (4)
C1—C5—C6—O3	−175.56 (17)	C14—C15—C16—C17	−0.5 (4)
C1—C5—C6—C7	60.6 (2)	C15—C16—C17—C12	−0.1 (4)
O3—C6—C7—O2	55.6 (2)	C13—C12—C17—C16	0.5 (3)
C5—C6—C7—O2	−179.89 (16)	S1—C12—C17—C16	179.33 (18)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H18···O1^{i}	0.84	2.05	2.859 (3)	161
O2—H18···O3	0.84	2.46	2.817 (3)	107
O3—H19···O4^{ii}	0.84	1.98	2.813 (3)	172
O4—H20···O2^{iii}	0.84	1.89	2.719 (3)	171

Symmetry codes: (i) −*x*, *y*−1/2, −*z*+3/2; (ii) −*x*+1, *y*−1/2, −*z*+3/2; (iii) *x*+1, *y*, *z*.