



Crystal structure of natural phaeosphaeride A

Victoria V. Abzianidze,^{a*} Ekaterina V. Poluektova,^b
Ksenia P. Bolshakova,^b Taras L. Panikorovskii,^c
Alexander S. Bogachenkov^d and Alexander O.
Berestetskiy^{b*}

^aChemical Modeling Laboratory, Research Institute of Hygiene, Occupational Pathology and Human Ecology, Medical Biological Agency, p/o Kuz'molovskiy, Saint Petersburg, 188663, Russian Federation, ^bAll-Russian Institute of Plant Protection, Russian Academy of Agricultural Sciences, Pushkin, Saint Petersburg, 196608, Russian Federation, ^cDepartment of Crystallography, Institute of Earth Sciences, Saint Petersburg State University, University Emb., 7/9, Saint Petersburg, 199034, Russian Federation, and ^dDepartment of Organic Chemistry, Institute of Chemistry, Saint Petersburg State University, University Emb., 26, Saint Petersburg, 198504, Russian Federation. *Correspondence e-mail: vvaavv@mail.ru, aberestetski@yahoo.com

Received 14 July 2015; accepted 22 July 2015

Edited by S. Parkin, University of Kentucky, USA

The asymmetric unit of the title compound, C₁₅H₂₃NO₅, contains two independent molecules. Phaeosphaeride A contains two primary sections, an alkyl chain consisting of five C atoms and a cyclic system consisting of fused five- and six-membered rings with attached substituents. In the crystal, the molecules form layered structures. Nearly planar sheets, parallel to the (001) plane, form bilayers of two-dimensional hydrogen-bonded networks with the hydroxy groups located on the interior of the bilayer sheets. The network is constructed primarily of four O—H...O hydrogen bonds, which form a zigzag pattern in the (001) plane. The butyl chains interdigitate with the butyl chains on adjacent sheets. The crystal was twinned by a twofold rotation about the *c* axis, with refined major–minor occupancy fractions of 0.718 (6):0.282 (6).

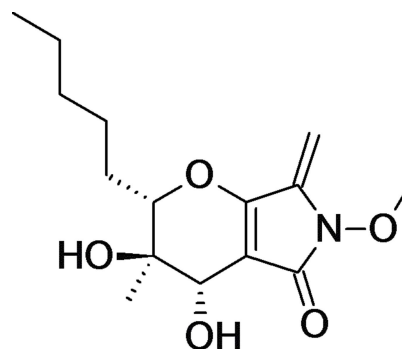
Keywords: crystal structure; natural phaeosphaeride A.

CCDC reference: 1412515

1. Related literature

For details of the extraction of natural phaeosphaeride A and a discussion of its biological activities, see: Maloney *et al.* (2006). For details of trials of the synthesis of natural phaeosphaeride A, see: Kobayashi *et al.* (2011); Chatzimpaloglou *et al.* (2012, 2014); Kobayashi *et al.* (2015). Ring-puckering

parameters are as defined by Cremer & Pople (1975). Hydrogen bonding is described in detail by Desiraju & Steiner (1999) and by Arunan *et al.* (2011). The twin law was identified using TwinRotMat in *PLATON* (Spek, 2009). Criteria for absolute configuration determination are described by Flack (1983) and Parsons *et al.* (2013).



2. Experimental

2.1. Crystal data

C₁₅H₂₃NO₅
M_r = 297.34
Monoclinic, *P*2₁
a = 10.14078 (18) Å
b = 9.10361 (14) Å
c = 17.5991 (3) Å
 β = 100.1847 (16)°
V = 1599.11 (5) Å³
Z = 4
Cu *K*α radiation
 μ = 0.77 mm⁻¹
T = 100 K
0.35 × 0.35 × 0.05 mm

2.2. Data collection

Agilent SuperNova Dual Source diffractometer with an Atlas detector
6054 measured reflections
6054 independent reflections
5940 reflections with *I* > 2σ(*I*)
Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2012)
*T*_{min} = 0.824, *T*_{max} = 1.000

2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.058$
 $wR(F^2) = 0.150$
S = 1.10
6054 reflections
389 parameters
1 restraint
H-atom parameters constrained
 $\Delta\rho_{\max} = 0.36$ e Å⁻³
 $\Delta\rho_{\min} = -0.30$ e Å⁻³
Absolute structure: Flack *x* determined using 2632 quotients $[(I^+) - (I^-)] / [(I^+) + (I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: 0.05 (8)

Table 1

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>
O2—H2...O2A	0.82	2.04	2.818 (5)	158
O3—H3...O4 ⁱ	0.82	2.03	2.836 (5)	168
O2A—H2A...O4 ⁱ	0.82	2.00	2.685 (5)	141
O3A—H3A...O4A ⁱⁱ	0.82	2.10	2.829 (5)	149

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

Data collection: *CrysAlis PRO* (Agilent, 2012); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to

solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2*.

Acknowledgements

XRD study was completed at the X-ray Diffraction Centre of St Petersburg State University. The research was financially supported by Russian Scientific Fund (project No. 14-26-00067).

Supporting information for this paper is available from the IUCr electronic archives (Reference: PK2560).

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supporting information

Acta Cryst. (2015). E71, o625–o626 [doi:10.1107/S205698901501395X]

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S1. Comment

In 2006, Clardy and colleagues isolated phaeosphaeride A from an endophytic fungus FA39 (Maloney *et al.*, 2006). Phaeosphaeride A turned out to be an inhibitor of signal transduction and an activator of transcription 3 (STAT3)-dependent signaling. It was reported to selectively inhibit STAT3/DNA binding with an IC₅₀ of 0.61 mM and to exhibit promising cell growth inhibition in STAT3-dependent U266 multiple myeloma cells with an IC₅₀ of 6.7 μM.

While the relative stereochemistry of phaeosphaeride A was deduced on the basis of NOE experiments, its absolute configuration remained undetermined (Maloney *et al.*, 2006). Moreover, the attempts of total synthesis of phaeosphaeride A showed considerable differences in ¹H and ¹³C NMR data between the synthetic and natural phaeosphaeride A (Kobayashi *et al.*, 2011; Chatzimpaloglou *et al.*, 2012, 2014). In 2015, Kobayashi and colleagues established the relative and absolute configurations of natural phaeosphaeride A by completing the first total synthesis of ent-phaeosphaeride A (Kobayashi *et al.*, 2015).

Our research group isolated phaeosphaeride A from a fungal strain belonging to the genus *Phoma*. Phaeosphaeride A was obtained as an optically active (-108.33 (c 0.06, CH₂Cl₂)) yellow glass. ¹H and ¹³C NMR data as well as mass spectra of our phaeosphaeride A match with the data reported for Clardy's natural phaeosphaeride A (Maloney *et al.*, 2006). Optical rotation of Clardy's product (-93.6 (c 2.0, CH₂Cl₂)) and our phaeosphaeride A have the same sign. In this work we describe the crystal structure of natural phaeosphaeride A.

S2. Experimental

NMR spectra were recorded on a Bruker AVANCE III 400 MHz spectrometer in DMSO-d₆. The same solvent was used as an internal standard. High-resolution mass spectra (HRMS) were recorded on a LTQ Orbitrap Velos spectrometer. Optical rotations were determined on an Optical Activity AA-55 polarimeter using a 20 cm cell with a Na 589 nm filter.

Phaeosphaeride A was isolated from solid culture of the fungus *Phoma* sp. N 19. The microorganism was obtained from leaves of *Cirsium arvense* (L.) Scop. and deposited in the culture collection of the All-Russian Institute of Plant Protection (Saint-Petersburg, Russian Federation). The metabolite was purified from the fungal extract with a combination of preparative column chromatography and TLC on silica gel to give phaeosphaeride A as a yellow precipitate. (-108.33 (c 0.06, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-d₆) δ 5.44 (d, J = 5.8 Hz, 1H), 4.97 (s, 2H), 4.92 (s, 1H), 4.07 (d, J = 11.3 Hz, 1H), 3.86 (d, J = 5.8 Hz, 1H), 3.79 (s, 3H), 1.82 (m, 1H), 1.58-1.22 (m, 7H), 1.19 (s, 3H), 0.86 (t, J = 6.4 Hz, 3H); ¹³C NMR (100.6 MHz, DMSO-d₆) δ 166.53, 155.30, 137.12, 104.80, 90.80, 86.25, 70.96, 64.36, 63.76, 30.90, 27.60, 26.11, 21.96, 20.40, 13.85; HRMS [M + H]⁺ calcd for C₁₅H₂₄NO₅ 298.16490, found 298.16493. Recrystallization from heptane yielded yellow crystals (-116.66; -108.33 (c 0.06, CH₂Cl₂)).

S3. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1.

H atoms bonded to C atoms were included in calculated positions and refined using a riding model, with $U_{iso}(H)$ set to $1.2U_{eq}(C)$ and $C-H = 0.97 \text{ \AA}$ for CH_2 groups, $U_{iso}(H)$ set to $1.5U_{eq}(N)$ and $C-H = 0.96 \text{ \AA}$ for CH_3 groups and $U_{iso}(H)$ set to $1.2U_{eq}(N)$ and $C-H = 0.93 \text{ \AA}$ for CH groups. All H atoms bonded to O atoms were located in a difference Fourier map and were refined with distance restraints and constrained displacement parameters $OH = 0.82 \text{ \AA}$ and $U_{iso}(H)$ set to $1.2U_{eq}(O)$. The large thermal ellipsoid on C13 is characteristic for the distal end of long alkyl chains.

The structure of phaeosphaeride A (Fig.1) was refined as rotational twin [by a two-fold rotation about (001)] with twin fractions of 0.718 (6) and 0.282 (6). The 'HKL F 5' format file for the final refinement was generated by the TwinRotMat facility in Platon (Spek, 2009). The ratio $(F_o^2 - F_c^2)/\text{esd}$ for the reflections with the highest error in final refinement model (as a rotational twin) has lower residuals than in the initial solution. We have used Bayesian Statistics for verifying absolute structure. Supplementary crystallographic data for this paper have been deposited at Cambridge Crystallographic Data Centre (CCDC 1412515) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

S4. Geometry

The asymmetric unit contains two independent molecules of phaeosphaeride A (I and II) (**fig. 1**). Each molecule of phaeosphaeride A (numbering of atoms of phaeosphaeride A is given according to Clardy (Maloney *et al.*, 2006)) contains two primary sections; an alkyl chain consisting of C(13)—C(12)—C(11)—C(10)—C(9) atoms and a cyclic system consisting of five and six membered rings with adjacent atoms.

For the five-membered ring C(1)—N(2)—C(3)—C(4)—C(5) of molecule I the Cremer-Pople (Cremer & Pople, 1975) parameters are $Q=0.0714 \text{ \AA}$, $\varphi=197.99^\circ$, revealing a slightly distorted half-chair (2T_1) conformation. Cremer-Pople parameters of $Q=0.501 \text{ \AA}$, $\theta=128.71^\circ$, $\varphi=88.01^\circ$ for the six-membered heterocycle of molecule I are consistent with a half-chair conformation (5H_4). The geometric parameters of the six-membered rings for both molecules are similar, but the five-membered rings have different conformations. The five-membered ring in molecule II exhibits an envelope (1E) conformation.

Torsion angles O(1)—C(4)—C(5)—C(1) and C(3)—C(4)—C(5)—C(6) are $-178.2 (4)^\circ$ and $-177.1 (4)^\circ$ respectively, corresponding to co-planar conformation between the five and six-membered rings. The geometry of the heterocyclic ring system of the molecule (base of the half chair and the five-membered ring) is close to planar.

The exocyclic alkyl chain of I and the back of the half-chair lie approximately in the same plane. The deviation between the plane of alkyl atoms C(8)—C(9)—C(10)—C(11)—C(12)—C(13) and the back of the chair is $9.7 (4)^\circ$.

The geometric parameters are similar for both molecules I and II forming the weak hydrogen-bonded dimer through $O2 \cdots H2 \cdots O2A$. But angles characterizing the methoxy groups N(2)—O(5)—C(16) are slightly different ($109.9 (3)^\circ$ for I and $110.4 (4)^\circ$ for II). The difference between angles O(4)—C(1)—C(5) is much greater with values of $129.4 (4)^\circ$ and $123.2 (4)^\circ$ for I and II respectively.

The molecules form layered structures. Nearly planar sheets, parallel with the (001) plane, form primary layers of two-dimensional hydrogen-bonded networks with the hydroxyl moieties located on the interior of the sheets. The network (Fig. 2) is dependent primarily on four hydrogen bonds (Table 1) $O2-H2 \cdots O2A$, $O3-H3 \cdots O4$, $O2A-H2A \cdots O4$, $O3A-H3A \cdots O4A$ (Desiraju *et al.*, 1999; Arunan *et al.*, 2011). In the (001) plane, two-dimensional hydrogen-bonded networks form a zig-zag pattern. The aliphatic butyl chains interdigitate with the butyl chains on the adjacent sheets.

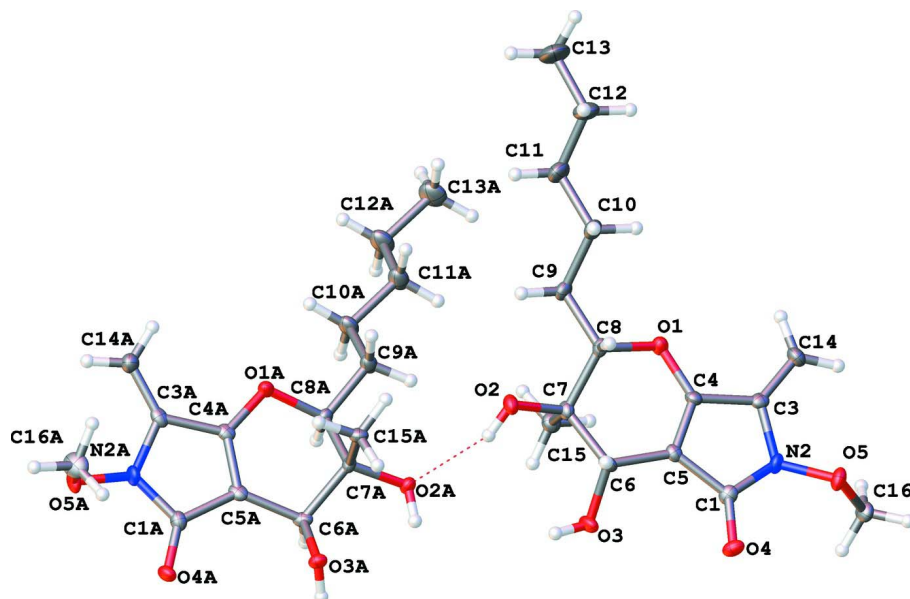


Figure 1

A view of molecules I (left) and II (right) of phaeosphaeride A. The atom numbering scheme is that of Maloney *et al.* (2006). Displacement ellipsoids are shown at the 50% probability level.

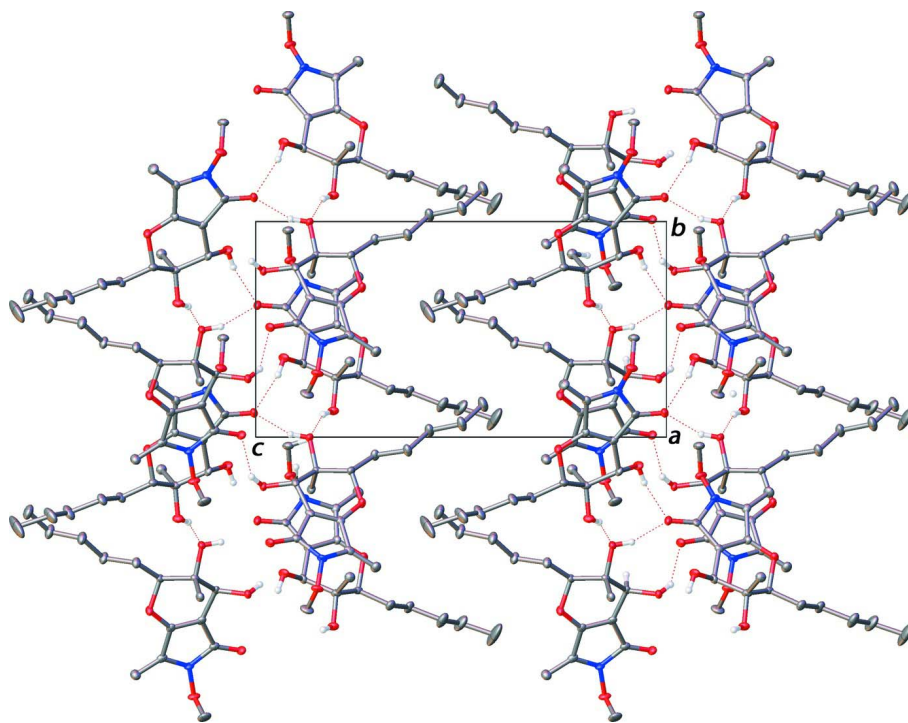


Figure 2

Projection of the layered crystal structure of phaeosphaeride A on the (100) plane. The dashed lines indicate the short contacts between molecules of phaeosphaeride A (only hydrogen atoms forming hydrogen bonds are shown).

3,4-Dihydroxy-6-methoxy-3-methyl-7-methylidene-2-pentyl-3,4-dihydro-2H,7H-pyrano[2,3-c]pyrrol-5(6H)-one*Crystal data*

$C_{15}H_{23}NO_5$	$F(000) = 640$
$M_r = 297.34$	$D_x = 1.235 \text{ Mg m}^{-3}$
Monoclinic, $P2_1$	Cu $K\alpha$ radiation, $\lambda = 1.54184 \text{ \AA}$
$a = 10.14078 (18) \text{ \AA}$	Cell parameters from 14376 reflections
$b = 9.10361 (14) \text{ \AA}$	$\theta = 4.4\text{--}75.9^\circ$
$c = 17.5991 (3) \text{ \AA}$	$\mu = 0.77 \text{ mm}^{-1}$
$\beta = 100.1847 (16)^\circ$	$T = 100 \text{ K}$
$V = 1599.11 (5) \text{ \AA}^3$	Tabular, colourless
$Z = 4$	$0.35 \times 0.35 \times 0.05 \text{ mm}$

Data collection

Agilent SuperNova Dual Source diffractometer with an Atlas detector	$T_{\min} = 0.824$, $T_{\max} = 1.000$
Radiation source: SuperNova (Cu) X-ray Source	6054 measured reflections
Mirror monochromator	6054 independent reflections
Detector resolution: $10.3829 \text{ pixels mm}^{-1}$	5940 reflections with $I > 2\sigma(I)$
ω scans	$\theta_{\max} = 70.0^\circ$, $\theta_{\min} = 4.4^\circ$
Absorption correction: multi-scan (<i>CrysAlis PRO</i> ; Agilent, 2012)	$h = -12 \rightarrow 12$
	$k = -11 \rightarrow 11$
	$l = -4 \rightarrow 21$

Refinement

Refinement on F^2	H-atom parameters constrained
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0289P)^2 + 2.9758P]$
$R[F^2 > 2\sigma(F^2)] = 0.058$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.150$	$(\Delta/\sigma)_{\max} < 0.001$
$S = 1.10$	$\Delta\rho_{\max} = 0.36 \text{ e \AA}^{-3}$
6054 reflections	$\Delta\rho_{\min} = -0.30 \text{ e \AA}^{-3}$
389 parameters	Absolute structure: Flack x determined using
1 restraint	2632 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons <i>et al.</i> , 2013)
Hydrogen site location: inferred from neighbouring sites	Absolute structure parameter: 0.05 (8)

Special details

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

Refinement. Refined as a 2-component twin.

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

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	1.1431 (5)	0.8972 (6)	0.9253 (3)	0.0153 (10)
N2	1.1842 (4)	0.7850 (5)	0.8817 (2)	0.0163 (9)
C3	1.1862 (5)	0.8314 (6)	0.8053 (3)	0.0149 (10)
C4	1.1266 (5)	0.9782 (6)	0.8025 (3)	0.0143 (10)
C5	1.0975 (5)	1.0166 (5)	0.8717 (3)	0.0135 (9)
C6	1.0311 (5)	1.1589 (6)	0.8845 (3)	0.0159 (10)
H6	1.0984	1.2269	0.9115	0.019*

C7	0.9703 (5)	1.2250 (6)	0.8039 (3)	0.0167 (10)
C8	1.0752 (5)	1.2122 (5)	0.7508 (3)	0.0144 (10)
H8	1.1580	1.2596	0.7765	0.017*
C9	1.0343 (5)	1.2809 (6)	0.6718 (3)	0.0194 (11)
H9A	1.0006	1.3791	0.6779	0.023*
H9B	0.9620	1.2237	0.6426	0.023*
C10	1.1482 (5)	1.2899 (7)	0.6264 (3)	0.0231 (11)
H10A	1.1855	1.1924	0.6231	0.028*
H10B	1.2183	1.3519	0.6543	0.028*
C11	1.1059 (7)	1.3504 (8)	0.5454 (4)	0.0349 (15)
H11A	1.0380	1.2864	0.5171	0.042*
H11B	1.0657	1.4463	0.5487	0.042*
C12	1.2195 (8)	1.3646 (9)	0.5007 (4)	0.0433 (19)
H12A	1.2627	1.2697	0.4998	0.052*
H12B	1.2852	1.4326	0.5278	0.052*
C13	1.1771 (12)	1.4175 (13)	0.4187 (5)	0.080 (4)
H13A	1.1119	1.3511	0.3913	0.120*
H13B	1.2538	1.4211	0.3936	0.120*
H13C	1.1387	1.5138	0.4189	0.120*
C14	1.2311 (5)	0.7567 (6)	0.7508 (3)	0.0213 (11)
H14A	1.2660	0.6629	0.7611	0.026*
H14B	1.2277	0.7979	0.7021	0.026*
C15	0.8381 (5)	1.1508 (6)	0.7705 (3)	0.0193 (10)
H15A	0.8540	1.0495	0.7600	0.029*
H15B	0.7986	1.1992	0.7235	0.029*
H15C	0.7782	1.1570	0.8070	0.029*
C16	1.2068 (6)	0.5407 (6)	0.9208 (3)	0.0203 (11)
H16A	1.1648	0.5103	0.8701	0.031*
H16B	1.1400	0.5521	0.9528	0.031*
H16C	1.2706	0.4678	0.9429	0.031*
O1	1.1050 (4)	1.0568 (4)	0.73717 (19)	0.0172 (7)
O2	0.9541 (4)	1.3789 (4)	0.8112 (2)	0.0183 (8)
H2	0.8942	1.3951	0.8359	0.027*
O3	0.9324 (4)	1.1327 (4)	0.9312 (2)	0.0213 (8)
H3	0.9060	1.2114	0.9456	0.032*
O4	1.1447 (4)	0.8881 (4)	0.99543 (19)	0.0183 (8)
O5	1.2747 (4)	0.6794 (4)	0.9159 (2)	0.0194 (8)
C1A	0.4815 (5)	1.9716 (6)	0.8996 (3)	0.0156 (10)
N2A	0.4361 (4)	2.0638 (5)	0.8379 (2)	0.0174 (9)
C3A	0.4890 (5)	2.0271 (6)	0.7717 (3)	0.0159 (10)
C4A	0.5564 (5)	1.8865 (6)	0.7938 (3)	0.0136 (9)
C5A	0.5529 (5)	1.8520 (5)	0.8678 (3)	0.0147 (10)
C6A	0.6116 (5)	1.7116 (5)	0.9032 (3)	0.0140 (10)
H6A	0.5393	1.6398	0.9020	0.017*
C7A	0.7097 (5)	1.6545 (5)	0.8525 (3)	0.0126 (9)
C8A	0.6355 (5)	1.6563 (5)	0.7676 (3)	0.0140 (10)
H8A	0.5498	1.6055	0.7656	0.017*
C9A	0.7086 (5)	1.5840 (6)	0.7096 (3)	0.0191 (11)

H9AA	0.7419	1.4891	0.7296	0.023*
H9AB	0.7853	1.6439	0.7038	0.023*
C10A	0.6212 (6)	1.5621 (7)	0.6302 (3)	0.0223 (11)
H10C	0.5384	1.5139	0.6364	0.027*
H10D	0.5986	1.6572	0.6066	0.027*
C11A	0.6921 (6)	1.4697 (7)	0.5771 (3)	0.0270 (13)
H11C	0.7732	1.5202	0.5699	0.032*
H11D	0.7183	1.3768	0.6023	0.032*
C12A	0.6074 (6)	1.4392 (8)	0.4983 (3)	0.0295 (14)
H12C	0.5805	1.5318	0.4730	0.035*
H12D	0.5269	1.3871	0.5051	0.035*
C13A	0.6823 (7)	1.3483 (8)	0.4466 (3)	0.0344 (15)
H13D	0.6244	1.3297	0.3982	0.052*
H13E	0.7096	1.2566	0.4715	0.052*
H13F	0.7599	1.4013	0.4377	0.052*
C14A	0.4806 (5)	2.1038 (6)	0.7075 (3)	0.0210 (11)
H14C	0.4356	2.1932	0.7026	0.025*
H14D	0.5198	2.0685	0.6671	0.025*
C15A	0.8399 (5)	1.7422 (6)	0.8646 (3)	0.0160 (10)
H15D	0.8201	1.8444	0.8550	0.024*
H15E	0.8958	1.7077	0.8296	0.024*
H15F	0.8858	1.7298	0.9168	0.024*
C16A	0.5035 (6)	2.3002 (6)	0.8752 (4)	0.0273 (12)
H16D	0.5616	2.2998	0.8376	0.041*
H16E	0.5520	2.2663	0.9238	0.041*
H16F	0.4719	2.3983	0.8809	0.041*
O1A	0.6069 (4)	1.8064 (4)	0.74144 (18)	0.0166 (7)
O2A	0.7369 (3)	1.5024 (4)	0.86892 (19)	0.0145 (7)
H2A	0.7410	1.4877	0.9152	0.022*
O3A	0.6775 (3)	1.7297 (4)	0.98091 (18)	0.0145 (7)
H3A	0.6363	1.6850	1.0097	0.022*
O4A	0.4586 (4)	1.9909 (4)	0.9650 (2)	0.0179 (7)
O5A	0.3911 (4)	2.2045 (4)	0.8499 (2)	0.0186 (8)

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.015 (2)	0.013 (2)	0.017 (2)	-0.004 (2)	-0.0009 (19)	-0.0023 (19)
N2	0.016 (2)	0.013 (2)	0.018 (2)	0.0036 (17)	-0.0009 (16)	0.0025 (17)
C3	0.011 (2)	0.018 (2)	0.016 (2)	-0.0028 (19)	0.0039 (18)	0.0019 (19)
C4	0.014 (2)	0.016 (2)	0.015 (2)	-0.0008 (19)	0.0064 (18)	-0.0002 (19)
C5	0.010 (2)	0.014 (2)	0.017 (2)	-0.0018 (19)	0.0024 (17)	-0.0027 (19)
C6	0.017 (2)	0.017 (2)	0.014 (2)	0.001 (2)	0.0063 (19)	-0.0035 (19)
C7	0.017 (2)	0.012 (2)	0.022 (3)	0.001 (2)	0.006 (2)	-0.0002 (19)
C8	0.013 (2)	0.012 (2)	0.017 (2)	0.0003 (18)	-0.0002 (18)	0.0007 (19)
C9	0.018 (2)	0.021 (3)	0.018 (2)	0.005 (2)	0.0005 (19)	0.006 (2)
C10	0.022 (3)	0.027 (3)	0.020 (3)	0.009 (2)	0.003 (2)	0.008 (2)
C11	0.037 (4)	0.041 (4)	0.027 (3)	0.016 (3)	0.009 (3)	0.017 (3)

C12	0.055 (5)	0.047 (4)	0.035 (3)	0.015 (4)	0.027 (3)	0.021 (3)
C13	0.113 (9)	0.095 (8)	0.046 (5)	0.054 (7)	0.049 (5)	0.046 (5)
C14	0.021 (3)	0.022 (3)	0.022 (3)	0.005 (2)	0.009 (2)	-0.002 (2)
C15	0.016 (2)	0.020 (3)	0.021 (2)	0.000 (2)	0.003 (2)	0.000 (2)
C16	0.024 (3)	0.012 (2)	0.026 (3)	0.000 (2)	0.007 (2)	0.000 (2)
O1	0.0200 (18)	0.0170 (18)	0.0144 (16)	0.0042 (15)	0.0022 (13)	-0.0008 (14)
O2	0.0174 (18)	0.0135 (17)	0.0253 (19)	0.0032 (14)	0.0075 (15)	0.0004 (14)
O3	0.030 (2)	0.0158 (18)	0.0222 (18)	0.0035 (16)	0.0158 (16)	-0.0017 (15)
O4	0.0252 (19)	0.0170 (17)	0.0123 (16)	-0.0038 (15)	0.0022 (14)	0.0014 (14)
O5	0.0177 (18)	0.0127 (18)	0.0263 (19)	0.0023 (14)	-0.0006 (15)	0.0034 (14)
C1A	0.013 (2)	0.013 (2)	0.021 (2)	-0.0010 (19)	0.0022 (19)	-0.0025 (19)
N2A	0.021 (2)	0.011 (2)	0.020 (2)	0.0053 (18)	0.0049 (17)	-0.0022 (17)
C3A	0.010 (2)	0.016 (2)	0.023 (2)	-0.0024 (19)	0.0038 (18)	-0.005 (2)
C4A	0.010 (2)	0.014 (2)	0.017 (2)	-0.0044 (19)	0.0032 (18)	-0.0027 (19)
C5A	0.013 (2)	0.014 (2)	0.019 (2)	-0.0059 (19)	0.0059 (19)	-0.0034 (19)
C6A	0.016 (2)	0.014 (2)	0.012 (2)	-0.0061 (19)	0.0038 (18)	-0.0016 (18)
C7A	0.012 (2)	0.011 (2)	0.015 (2)	0.0008 (19)	0.0008 (18)	0.0019 (18)
C8A	0.014 (2)	0.014 (2)	0.013 (2)	0.0007 (19)	-0.0007 (18)	0.0015 (18)
C9A	0.018 (3)	0.024 (3)	0.015 (2)	0.006 (2)	0.002 (2)	0.000 (2)
C10A	0.023 (3)	0.028 (3)	0.016 (2)	0.006 (2)	0.004 (2)	-0.005 (2)
C11A	0.031 (3)	0.032 (3)	0.018 (3)	0.010 (3)	0.003 (2)	-0.004 (2)
C12A	0.029 (3)	0.041 (4)	0.019 (3)	0.006 (3)	0.003 (2)	-0.008 (2)
C13A	0.040 (4)	0.043 (4)	0.020 (3)	0.003 (3)	0.005 (3)	-0.010 (3)
C14A	0.021 (3)	0.021 (3)	0.021 (3)	0.005 (2)	0.005 (2)	0.003 (2)
C15A	0.017 (2)	0.018 (2)	0.014 (2)	-0.002 (2)	0.0056 (18)	0.0015 (19)
C16A	0.029 (3)	0.017 (3)	0.036 (3)	-0.011 (2)	0.006 (2)	-0.008 (2)
O1A	0.0188 (17)	0.0195 (18)	0.0120 (15)	0.0060 (15)	0.0039 (13)	0.0011 (14)
O2A	0.0181 (17)	0.0128 (17)	0.0122 (15)	0.0024 (14)	0.0016 (13)	0.0016 (13)
O3A	0.0175 (17)	0.0154 (17)	0.0104 (15)	-0.0013 (14)	0.0022 (13)	0.0008 (13)
O4A	0.0234 (19)	0.0152 (18)	0.0175 (17)	0.0020 (15)	0.0105 (14)	-0.0016 (14)
O5A	0.0157 (18)	0.0102 (17)	0.0301 (19)	0.0022 (14)	0.0044 (15)	-0.0040 (15)

Geometric parameters (Å, °)

C1—N2	1.385 (7)	C1A—N2A	1.386 (7)
C1—C5	1.460 (7)	C1A—C5A	1.472 (7)
C1—O4	1.234 (6)	C1A—O4A	1.226 (6)
N2—C3	1.412 (6)	N2A—C3A	1.406 (7)
N2—O5	1.391 (5)	N2A—O5A	1.389 (5)
C3—C4	1.463 (7)	C3A—C4A	1.471 (7)
C3—C14	1.320 (7)	C3A—C14A	1.318 (7)
C4—C5	1.349 (7)	C4A—C5A	1.347 (7)
C4—O1	1.339 (6)	C4A—O1A	1.345 (6)
C5—C6	1.495 (7)	C5A—C6A	1.498 (7)
C6—H6	0.9800	C6A—H6A	0.9800
C6—C7	1.563 (7)	C6A—C7A	1.540 (7)
C6—O3	1.423 (6)	C6A—O3A	1.422 (6)
C7—C8	1.540 (7)	C7A—C8A	1.549 (6)

C7—C15	1.523 (7)	C7A—C15A	1.526 (7)
C7—O2	1.419 (6)	C7A—O2A	1.431 (6)
C8—H8	0.9800	C8A—H8A	0.9800
C8—C9	1.514 (7)	C8A—C9A	1.515 (7)
C8—O1	1.475 (6)	C8A—O1A	1.455 (6)
C9—H9A	0.9700	C9A—H9AA	0.9700
C9—H9B	0.9700	C9A—H9AB	0.9700
C9—C10	1.518 (7)	C9A—C10A	1.529 (7)
C10—H10A	0.9700	C10A—H10C	0.9700
C10—H10B	0.9700	C10A—H10D	0.9700
C10—C11	1.519 (7)	C10A—C11A	1.528 (7)
C11—H11A	0.9700	C11A—H11C	0.9700
C11—H11B	0.9700	C11A—H11D	0.9700
C11—C12	1.510 (9)	C11A—C12A	1.523 (8)
C12—H12A	0.9700	C12A—H12C	0.9700
C12—H12B	0.9700	C12A—H12D	0.9700
C12—C13	1.511 (10)	C12A—C13A	1.527 (8)
C13—H13A	0.9600	C13A—H13D	0.9600
C13—H13B	0.9600	C13A—H13E	0.9600
C13—H13C	0.9600	C13A—H13F	0.9600
C14—H14A	0.9300	C14A—H14C	0.9300
C14—H14B	0.9300	C14A—H14D	0.9300
C15—H15A	0.9600	C15A—H15D	0.9600
C15—H15B	0.9600	C15A—H15E	0.9600
C15—H15C	0.9600	C15A—H15F	0.9600
C16—H16A	0.9600	C16A—H16D	0.9600
C16—H16B	0.9600	C16A—H16E	0.9600
C16—H16C	0.9600	C16A—H16F	0.9600
C16—O5	1.448 (6)	C16A—O5A	1.442 (6)
O2—H2	0.8200	O2A—H2A	0.8200
O3—H3	0.8200	O3A—H3A	0.8200
N2—C1—C5	106.4 (4)	N2A—C1A—C5A	105.5 (4)
O4—C1—N2	123.6 (5)	O4A—C1A—N2A	123.9 (5)
O4—C1—C5	129.9 (5)	O4A—C1A—C5A	130.6 (5)
C1—N2—C3	111.3 (4)	C1A—N2A—C3A	112.5 (4)
C1—N2—O5	120.6 (4)	C1A—N2A—O5A	120.8 (4)
O5—N2—C3	120.0 (4)	O5A—N2A—C3A	122.0 (4)
N2—C3—C4	103.3 (4)	N2A—C3A—C4A	102.4 (4)
C14—C3—N2	127.0 (5)	C14A—C3A—N2A	127.4 (5)
C14—C3—C4	129.7 (5)	C14A—C3A—C4A	130.1 (5)
C5—C4—C3	111.2 (4)	C5A—C4A—C3A	111.6 (4)
O1—C4—C3	121.4 (4)	O1A—C4A—C3A	120.4 (4)
O1—C4—C5	127.4 (5)	O1A—C4A—C5A	127.9 (5)
C1—C5—C6	130.4 (4)	C1A—C5A—C6A	131.2 (4)
C4—C5—C1	107.1 (4)	C4A—C5A—C1A	107.1 (4)
C4—C5—C6	122.5 (5)	C4A—C5A—C6A	121.6 (4)
C5—C6—H6	109.0	C5A—C6A—H6A	108.7

C5—C6—C7	108.3 (4)	C5A—C6A—C7A	107.3 (4)
C7—C6—H6	109.0	C7A—C6A—H6A	108.7
O3—C6—C5	108.9 (4)	O3A—C6A—C5A	112.7 (4)
O3—C6—H6	109.0	O3A—C6A—H6A	108.7
O3—C6—C7	112.6 (4)	O3A—C6A—C7A	110.8 (4)
C8—C7—C6	108.5 (4)	C6A—C7A—C8A	107.6 (4)
C15—C7—C6	111.0 (4)	C15A—C7A—C6A	112.0 (4)
C15—C7—C8	112.8 (4)	C15A—C7A—C8A	113.0 (4)
O2—C7—C6	109.4 (4)	O2A—C7A—C6A	109.3 (4)
O2—C7—C8	103.5 (4)	O2A—C7A—C8A	104.4 (4)
O2—C7—C15	111.4 (4)	O2A—C7A—C15A	110.3 (4)
C7—C8—H8	108.3	C7A—C8A—H8A	107.8
C9—C8—C7	114.8 (4)	C9A—C8A—C7A	115.7 (4)
C9—C8—H8	108.3	C9A—C8A—H8A	107.8
O1—C8—C7	110.8 (4)	O1A—C8A—C7A	110.5 (4)
O1—C8—H8	108.3	O1A—C8A—H8A	107.8
O1—C8—C9	106.1 (4)	O1A—C8A—C9A	106.8 (4)
C8—C9—H9A	108.9	C8A—C9A—H9AA	108.9
C8—C9—H9B	108.9	C8A—C9A—H9AB	108.9
C8—C9—C10	113.3 (4)	C8A—C9A—C10A	113.5 (4)
H9A—C9—H9B	107.7	H9AA—C9A—H9AB	107.7
C10—C9—H9A	108.9	C10A—C9A—H9AA	108.9
C10—C9—H9B	108.9	C10A—C9A—H9AB	108.9
C9—C10—H10A	108.9	C9A—C10A—H10C	109.3
C9—C10—H10B	108.9	C9A—C10A—H10D	109.3
C9—C10—C11	113.5 (4)	H10C—C10A—H10D	107.9
H10A—C10—H10B	107.7	C11A—C10A—C9A	111.7 (5)
C11—C10—H10A	108.9	C11A—C10A—H10C	109.3
C11—C10—H10B	108.9	C11A—C10A—H10D	109.3
C10—C11—H11A	108.8	C10A—C11A—H11C	108.7
C10—C11—H11B	108.8	C10A—C11A—H11D	108.7
H11A—C11—H11B	107.7	H11C—C11A—H11D	107.6
C12—C11—C10	113.9 (5)	C12A—C11A—C10A	114.0 (5)
C12—C11—H11A	108.8	C12A—C11A—H11C	108.7
C12—C11—H11B	108.8	C12A—C11A—H11D	108.7
C11—C12—H12A	108.7	C11A—C12A—H12C	109.1
C11—C12—H12B	108.7	C11A—C12A—H12D	109.1
C11—C12—C13	114.2 (7)	C11A—C12A—C13A	112.4 (5)
H12A—C12—H12B	107.6	H12C—C12A—H12D	107.8
C13—C12—H12A	108.7	C13A—C12A—H12C	109.1
C13—C12—H12B	108.7	C13A—C12A—H12D	109.1
C12—C13—H13A	109.5	C12A—C13A—H13D	109.5
C12—C13—H13B	109.5	C12A—C13A—H13E	109.5
C12—C13—H13C	109.5	C12A—C13A—H13F	109.5
H13A—C13—H13B	109.5	H13D—C13A—H13E	109.5
H13A—C13—H13C	109.5	H13D—C13A—H13F	109.5
H13B—C13—H13C	109.5	H13E—C13A—H13F	109.5
C3—C14—H14A	120.0	C3A—C14A—H14C	120.0

C3—C14—H14B	120.0	C3A—C14A—H14D	120.0
H14A—C14—H14B	120.0	H14C—C14A—H14D	120.0
C7—C15—H15A	109.5	C7A—C15A—H15D	109.5
C7—C15—H15B	109.5	C7A—C15A—H15E	109.5
C7—C15—H15C	109.5	C7A—C15A—H15F	109.5
H15A—C15—H15B	109.5	H15D—C15A—H15E	109.5
H15A—C15—H15C	109.5	H15D—C15A—H15F	109.5
H15B—C15—H15C	109.5	H15E—C15A—H15F	109.5
H16A—C16—H16B	109.5	H16D—C16A—H16E	109.5
H16A—C16—H16C	109.5	H16D—C16A—H16F	109.5
H16B—C16—H16C	109.5	H16E—C16A—H16F	109.5
O5—C16—H16A	109.5	O5A—C16A—H16D	109.5
O5—C16—H16B	109.5	O5A—C16A—H16E	109.5
O5—C16—H16C	109.5	O5A—C16A—H16F	109.5
C4—O1—C8	112.3 (4)	C4A—O1A—C8A	111.8 (4)
C7—O2—H2	109.5	C7A—O2A—H2A	109.5
C6—O3—H3	109.5	C6A—O3A—H3A	109.5
N2—O5—C16	110.1 (4)	N2A—O5A—C16A	109.9 (4)
C1—N2—C3—C4	-6.7 (5)	C1A—N2A—C3A—C4A	8.7 (5)
C1—N2—C3—C14	173.8 (5)	C1A—N2A—C3A—C14A	-170.0 (5)
C1—N2—O5—C16	107.4 (5)	C1A—N2A—O5A—C16A	76.8 (6)
C1—C5—C6—C7	-165.0 (5)	C1A—C5A—C6A—C7A	-162.9 (5)
C1—C5—C6—O3	-42.4 (7)	C1A—C5A—C6A—O3A	-40.7 (7)
N2—C1—C5—C4	-6.6 (5)	N2A—C1A—C5A—C4A	5.5 (5)
N2—C1—C5—C6	173.7 (5)	N2A—C1A—C5A—C6A	-172.8 (5)
N2—C3—C4—C5	2.4 (5)	N2A—C3A—C4A—C5A	-5.0 (5)
N2—C3—C4—O1	-176.8 (4)	N2A—C3A—C4A—O1A	172.2 (4)
C3—N2—O5—C16	-106.7 (5)	C3A—N2A—O5A—C16A	-77.1 (6)
C3—C4—C5—C1	2.5 (6)	C3A—C4A—C5A—C1A	-0.2 (6)
C3—C4—C5—C6	-177.7 (4)	C3A—C4A—C5A—C6A	178.2 (4)
C3—C4—O1—C8	-166.3 (4)	C3A—C4A—O1A—C8A	-164.3 (4)
C4—C5—C6—C7	15.3 (7)	C4A—C5A—C6A—C7A	19.1 (6)
C4—C5—C6—O3	137.9 (5)	C4A—C5A—C6A—O3A	141.3 (4)
C5—C1—N2—C3	8.4 (6)	C5A—C1A—N2A—C3A	-9.1 (6)
C5—C1—N2—O5	157.1 (4)	C5A—C1A—N2A—O5A	-165.3 (4)
C5—C4—O1—C8	14.7 (7)	C5A—C4A—O1A—C8A	12.4 (7)
C5—C6—C7—C8	-45.3 (5)	C5A—C6A—C7A—C8A	-49.7 (5)
C5—C6—C7—C15	79.3 (5)	C5A—C6A—C7A—C15A	75.0 (5)
C5—C6—C7—O2	-157.4 (4)	C5A—C6A—C7A—O2A	-162.5 (4)
C6—C7—C8—C9	-176.2 (4)	C6A—C7A—C8A—C9A	-171.8 (4)
C6—C7—C8—O1	63.7 (5)	C6A—C7A—C8A—O1A	66.7 (5)
C7—C8—C9—C10	170.0 (5)	C7A—C8A—C9A—C10A	168.8 (4)
C7—C8—O1—C4	-47.0 (5)	C7A—C8A—O1A—C4A	-45.8 (5)
C8—C9—C10—C11	176.6 (5)	C8A—C9A—C10A—C11A	-171.9 (5)
C9—C8—O1—C4	-172.2 (4)	C9A—C8A—O1A—C4A	-172.5 (4)
C9—C10—C11—C12	178.0 (6)	C9A—C10A—C11A—C12A	177.7 (5)
C10—C11—C12—C13	177.0 (8)	C10A—C11A—C12A—C13A	179.3 (6)

C14—C3—C4—C5	-178.1 (5)	C14A—C3A—C4A—C5A	173.7 (5)
C14—C3—C4—O1	2.7 (8)	C14A—C3A—C4A—O1A	-9.1 (8)
C15—C7—C8—C9	60.4 (6)	C15A—C7A—C8A—C9A	64.2 (6)
C15—C7—C8—O1	-59.7 (5)	C15A—C7A—C8A—O1A	-57.4 (5)
O1—C4—C5—C1	-178.4 (5)	O1A—C4A—C5A—C1A	-177.1 (5)
O1—C4—C5—C6	1.4 (8)	O1A—C4A—C5A—C6A	1.3 (8)
O1—C8—C9—C10	-67.3 (6)	O1A—C8A—C9A—C10A	-67.7 (6)
O2—C7—C8—C9	-60.1 (5)	O2A—C7A—C8A—C9A	-55.7 (5)
O2—C7—C8—O1	179.8 (4)	O2A—C7A—C8A—O1A	-177.2 (4)
O3—C6—C7—C8	-165.6 (4)	O3A—C6A—C7A—C8A	-173.1 (4)
O3—C6—C7—C15	-41.1 (6)	O3A—C6A—C7A—C15A	-48.4 (5)
O3—C6—C7—O2	82.2 (5)	O3A—C6A—C7A—O2A	74.1 (5)
O4—C1—N2—C3	-173.2 (5)	O4A—C1A—N2A—C3A	173.0 (5)
O4—C1—N2—O5	-24.5 (7)	O4A—C1A—N2A—O5A	16.8 (8)
O4—C1—C5—C4	175.2 (5)	O4A—C1A—C5A—C4A	-176.8 (5)
O4—C1—C5—C6	-4.6 (9)	O4A—C1A—C5A—C6A	5.0 (9)
O5—N2—C3—C4	-155.6 (4)	O5A—N2A—C3A—C4A	164.6 (4)
O5—N2—C3—C14	24.9 (8)	O5A—N2A—C3A—C14A	-14.2 (8)

Hydrogen-bond geometry (\AA , $^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O2—H2 \cdots O2A	0.82	2.04	2.818 (5)	158
O3—H3 \cdots O4 ⁱ	0.82	2.03	2.836 (5)	168
O2A—H2A \cdots O4 ⁱ	0.82	2.00	2.685 (5)	141
O3A—H3A \cdots O4A ⁱⁱ	0.82	2.10	2.829 (5)	149

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