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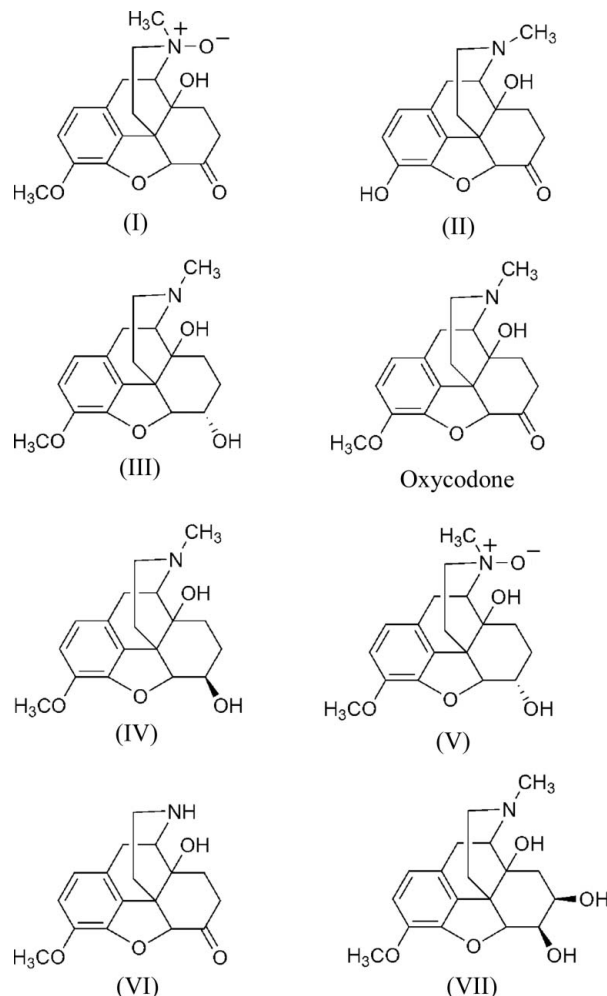
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The title compound, (5*R*,9*R*,13*S*,14*S*,17*R*)-14-hydroxy-3-methoxy-17-methyl-4,5-epoxymorphinan-6-one *N*-oxide, C₁₈H₂₁NO₅, has been prepared in a diastereomerically pure form by the reaction of oxycodone with 3-chloroperbenzoic acid and subsequent crystallization of the product from chloroform. The crystal packing shows that the molecule exhibits intramolecular O—H...O [*D*...*A* = 2.482 (2) Å] hydrogen bonding. In addition, there are weak intermolecular C—H...O interactions which, along with van der Waals forces, stabilize the structure. The new chiral center at the 17-position is demonstrated to be *R*.

Comment

Oxycodone is a semisynthetic codeine derivative that has been used as both an analgesic and an antitussive agent. In the mid-1990s, oxycontin was introduced as a slow-release formulation of oxycodone for use in patients with moderate to severe chronic pain associated with such ailments as arthritis, vertebral disc disease and cancer (Moore *et al.*, 2003). Oxycodone metabolites excreted in the urine and faeces of several mammalian species, including man, have been reported (Ishida *et al.*, 1982; Moore *et al.*, 2003). There are seven known metabolites of oxycodone: oxycodone *N*-oxide, (I), oxymorphone, (II), 6 α -oxycodol, (III), 6 β -oxycodol, (IV), 6 α -oxycodol *N*-oxide, (V), noroxycodone, (VI), and 7 β -hydroxy-6 β -oxycodol, (VII) (see Scheme). In order to confirm the absolute stereochemistry of oxycodone *N*-oxide at the N atom in the 17-position, we synthesized (I) by the reaction of oxycodone with 3-chloroperbenzoic acid, employing non-aqueous solvents, to afford a diastereomerically pure compound with subsequent crystallization of the product from chloroform. Depending on the orientation of the N—CH₃ group, two diastereoisomers of oxycodone *N*-oxide are possible. However, in the present study, we obtained exclusively a single diastereoisomer, according to NMR analysis of the product. To establish the orientation of the N—CH₃ group in this synthetic *N*-oxide derivative of oxycodone, and to study

the detailed conformation of this molecule, its X-ray structure determination was carried out and the results are presented here.



In an earlier study, a conformational analysis of several morphinan-6-one alkaloids was carried out using two-dimensional NMR techniques (Caldwell *et al.*, 1993). In support of these NMR studies, an X-ray crystallographic analysis of oxycodone *N*-oxide, (I), was also carried out. The present study of (I) and the Caldwell study are the same compound, but the X-ray analyses were undertaken at different temperatures, 90 and 293 K, respectively.

The numbering system of the non-H atoms and the overall configuration of the title compound are shown in Fig. 1, which shows that the absolute configuration of the chiral C centers in the molecule is identical to that of the starting material, oxycodone. The new chiral center at the 17-position is demonstrated to be *R*. The five-membered ring is distorted and the ethanamine ring has a typical chair conformation, with the newly formed N—O bond projected in an axial orientation. The conformation of the cyclohexanone ring is a twisted chair, caused by the presence of the 4,5-ether bridge, which is also responsible for the overall rigidity of the molecule. The observed C3—O19 [1.372 (2) Å] and O19—C20 [1.447 (2) Å] bond lengths are comparable with values found for methoxy O—CH₃ bonds. There is an asymmetry of the exocyclic angles

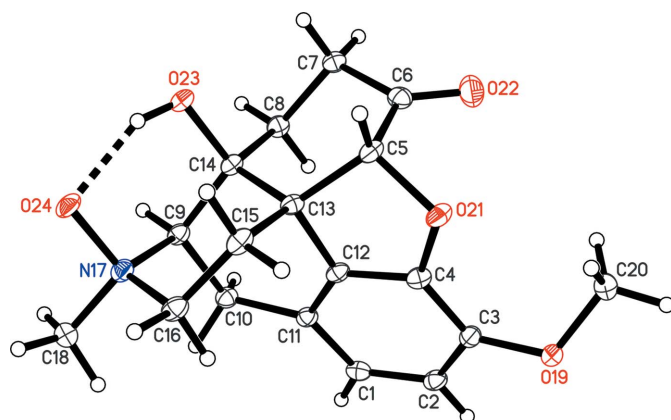


Figure 1
A view of the asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. The dashed line indicates the intramolecular hydrogen bond.

at C3 for (I) [$O19-C3-C4 = 126.72(19)^\circ$ and $O19-C3-C2 = 117.16(16)^\circ$], as is typical of anisoles (Seip & Seip, 1973). This asymmetry of the angles at C3 is caused by the tendency of the methoxy group to be coplanar with the benzene ring, due to conjugation of the O19 lone pair with the benzene ring of (I), which is in agreement with earlier observations of the 4-methoxybenzyl group (Domiano *et al.*, 1979). Most of the bond lengths and angles are in agreement with reported values (Caldwell *et al.*, 1993), although values for the torsion angles are not available for comparison.

The X-ray structure of protonated oxymorphone, (II) (amine salt), has already been reported (Darling *et al.*, 1982). We compared our results from (I) with these findings. Most of the bond lengths, bond angles and torsion angles for the non-H atoms of (I) are in agreement with the literature values for protonated (II). The C2–C3, C11–C12, C13–C5, C7–C8, C8–C14, C14–C9, C10–C11 and C15–C16 bonds are considerably longer (0.034–0.053 Å) in (I) compared with the values observed for protonated (II). Also, the N17–C9 bond is longer by 0.037 Å. Comparison of the bond angles for (I) and protonated (II) suggests that they are essentially very similar, except for C9–C14–O23, which is larger by nearly 8° . This may be the result of strong intramolecular hydrogen bonding, resulting in some stretching of the molecule. This accounts for the increases in the above-mentioned bond lengths and bond angle. Furthermore, the C8–C14–C13–C5, C14–C13–C5–C6, C14–C13–C15–C16 and C13–C15–C16–N17 torsion angles in (I) are slightly larger than the values reported for protonated (II). Changes in some of the bond lengths, bond angles and torsion angles away from the site of the newly formed N–O bond suggest long-range substituent effects. The positive charge on the N atom also has an effect, which can be transmitted throughout the molecule via long-range inductive and electrostatic field effects.

The H atom attached to atom O23 is involved in an intramolecular hydrogen bond with atom O24 (Table 1). In addition, there are weak intermolecular C–H...O interactions (Table 1) which, along with van der Waals forces, stabilize the structure.

Experimental

To a stirred solution of oxycodone (0.315 g, 1 mmol) [(5*R*,9*R*,13*S*,14*S*,17*R*)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one; Zalucky & Hite, 1961] in chloroform (30 ml), maintained at 273–278 K, was added 3-chloroperbenzoic acid (0.259 g, 1.5 mmol) in small portions. After complete addition of 3-chloroperbenzoic acid, stirring was continued at room temperature for 12 h. The solution was passed through basic alumina (110–200 mesh) and traces of unreacted oxycodone were removed by washing with chloroform. Elution with methanol–chloroform (1:3 v/v) afforded oxycodone *N*-oxide. The crude product was crystallized from chloroform as colorless crystals, which were suitable for X-ray analysis. $^1\text{H NMR}$ (CDCl_3): δ 1.56–1.74 (*m*, 2H), 1.94–2.01 (*m*, 1H), 2.20–2.27 (*m*, 1H), 3.08–3.30 (*m*, 6H), 3.31 (*s*, 3H), 3.60 (*d*, 1H), 3.90 (*s*, 3H), 4.77 (*s*, 1H), 6.65 (*d*, 1H), 6.75 (*d*, 1H), 12.34 (*s*, 1H); $^{13}\text{C NMR}$ (CDCl_3): δ 26.1, 29.0, 33.2, 35.2, 50.2, 57.1, 59.8, 62.0, 72.5, 76.0, 90.1, 116.0, 120.2, 120.4, 129.4, 144.1, 145.5, 207.8.

Crystal data

$\text{C}_{18}\text{H}_{21}\text{NO}_5$	$V = 1505.52(6) \text{ \AA}^3$
$M_r = 331.36$	$Z = 4$
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 7.2080(1) \text{ \AA}$	$\mu = 0.11 \text{ mm}^{-1}$
$b = 12.7611(3) \text{ \AA}$	$T = 90 \text{ K}$
$c = 16.3676(4) \text{ \AA}$	$0.22 \times 0.20 \times 0.15 \text{ mm}$

Data collection

Nonius KappaCCD area-detector diffractometer	3445 measured reflections
Absorption correction: multi-scan (<i>SCALEPACK</i> ; Otwinowski & Minor, 1997)	1988 independent reflections
$T_{\min} = 0.977$, $T_{\max} = 0.984$	1746 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.023$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.034$	220 parameters
$wR(F^2) = 0.081$	H-atom parameters constrained
$S = 1.07$	$\Delta\rho_{\max} = 0.24 \text{ e \AA}^{-3}$
1988 reflections	$\Delta\rho_{\min} = -0.21 \text{ e \AA}^{-3}$

H atoms were found in difference Fourier maps and subsequently placed in idealized positions, with constrained distances of 0.95 ($\text{C}_{\text{Ar}}-\text{H}$), 0.98 (RCH_3), 0.99 (R_2CH_2), 1.00 (R_3CH) and 0.84 Å (OH). $U_{\text{iso}}(\text{H})$ values were set at $1.2U_{\text{eq}}(\text{C}_{\text{Ar}}\text{H}$, R_2CH_2 and R_3CH) or $1.5U_{\text{eq}}(\text{RCH}_3$ and OH) of the parent atom.

Since there was no measurable anomalous signal, Friedel pairs were merged.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to

Table 1
Hydrogen-bond geometry (Å, $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$O23-H23\cdots O24$	0.84	1.72	2.483 (2)	151
$C5-H5\cdots O23^i$	1.00	2.60	3.536 (2)	157
$C9-H9\cdots O23^{ii}$	1.00	2.36	3.314 (2)	160
$C16-H16B\cdots O22^{iii}$	0.99	2.40	3.227 (3)	141
$C18-H18B\cdots O19^{iv}$	0.98	2.46	3.413 (2)	165

Symmetry codes: (i) $x + \frac{1}{2}, -y + \frac{3}{2}, -z$; (ii) $x - \frac{1}{2}, -y + \frac{3}{2}, -z$; (iii) $-x + \frac{3}{2}, -y + 2, z - \frac{1}{2}$; (iv) $x - \frac{1}{2}, -y + \frac{5}{2}, -z$.

refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELX97-2* (Sheldrick, 2008) and local procedures.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: UK3053). Services for accessing these data are described at the back of the journal.

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supplementary materials

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(5*R*,9*R*,13*S*,14*S*,17*R*)-14-hydroxy-3-methoxy-17-methyl-4,5-epoxymorphinan-6-one *N*-oxide

Crystal data

$C_{18}H_{21}NO_5$	$F(000) = 704$
$M_r = 331.36$	$D_x = 1.462 \text{ Mg m}^{-3}$
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
Hall symbol: P 2ac 2ab	Cell parameters from 2010 reflections
$a = 7.2080 (1) \text{ \AA}$	$\theta = 1.0\text{--}27.5^\circ$
$b = 12.7611 (3) \text{ \AA}$	$\mu = 0.11 \text{ mm}^{-1}$
$c = 16.3676 (4) \text{ \AA}$	$T = 90 \text{ K}$
$V = 1505.52 (6) \text{ \AA}^3$	Irregular block, colourless
$Z = 4$	$0.22 \times 0.20 \times 0.15 \text{ mm}$

Data collection

Nonius KappaCCD area-detector diffractometer	3445 measured reflections
Radiation source: fine-focus sealed tube	1988 independent reflections
Graphite monochromator	1746 reflections with $I > 2\sigma(I)$
Detector resolution: 18 pixels mm^{-1}	$R_{\text{int}} = 0.023$
ω scans at fixed $\chi = 55^\circ$	$\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 2.0^\circ$
Absorption correction: multi-scan (<i>SCALEPACK</i> ; Otwinowski & Minor, 1997)	$h = -9 \rightarrow 9$
$T_{\text{min}} = 0.977$, $T_{\text{max}} = 0.984$	$k = -16 \rightarrow 16$
	$l = -21 \rightarrow 21$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.034$	H-atom parameters constrained
$wR(F^2) = 0.081$	$w = 1/[\sigma^2(F_o^2) + (0.0417P)^2 + 0.3029P]$
$S = 1.07$	where $P = (F_o^2 + 2F_c^2)/3$
1988 reflections	$(\Delta/\sigma)_{\text{max}} < 0.001$
220 parameters	$\Delta\rho_{\text{max}} = 0.24 \text{ e \AA}^{-3}$
0 restraints	$\Delta\rho_{\text{min}} = -0.21 \text{ e \AA}^{-3}$
Primary atom site location: structure-invariant direct methods	

Special details

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

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

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.3016 (3)	1.20159 (15)	0.06279 (11)	0.0147 (4)
H1	0.1848	1.2343	0.0543	0.018*
C2	0.4411 (3)	1.25459 (15)	0.10378 (11)	0.0154 (4)
H2	0.4166	1.3236	0.1228	0.019*
C3	0.6170 (3)	1.21116 (15)	0.11858 (11)	0.0133 (4)
C4	0.6434 (3)	1.10873 (15)	0.09187 (12)	0.0132 (4)
C5	0.7225 (3)	0.93839 (15)	0.09201 (12)	0.0143 (4)
H5	0.8221	0.8893	0.0735	0.017*
C6	0.6397 (3)	0.90168 (15)	0.17395 (12)	0.0160 (4)
C7	0.4885 (3)	0.82149 (15)	0.16823 (12)	0.0160 (4)
H7A	0.4386	0.8069	0.2234	0.019*
H7B	0.5395	0.7554	0.1460	0.019*
C8	0.3317 (3)	0.86096 (16)	0.11264 (11)	0.0141 (4)
H8A	0.2279	0.8101	0.1126	0.017*
H8B	0.2844	0.9290	0.1330	0.017*
C9	0.2608 (3)	0.92092 (15)	-0.03283 (11)	0.0132 (4)
H9	0.1523	0.8721	-0.0332	0.016*
C10	0.1887 (3)	1.02933 (14)	-0.00568 (12)	0.0143 (4)
H10A	0.1375	1.0659	-0.0540	0.017*
H10B	0.0857	1.0189	0.0335	0.017*
C11	0.3327 (3)	1.09923 (14)	0.03368 (11)	0.0127 (4)
C12	0.5060 (3)	1.05840 (15)	0.04889 (11)	0.0122 (4)
C13	0.5729 (3)	0.95099 (15)	0.02522 (11)	0.0122 (4)
C14	0.4083 (3)	0.87383 (15)	0.02601 (12)	0.0129 (4)
C15	0.6570 (3)	0.95335 (16)	-0.06137 (11)	0.0148 (4)
H15A	0.7644	1.0017	-0.0622	0.018*
H15B	0.7021	0.8825	-0.0759	0.018*
C16	0.5150 (3)	0.98887 (15)	-0.12392 (12)	0.0157 (4)
H16A	0.4822	1.0630	-0.1136	0.019*
H16B	0.5695	0.9841	-0.1793	0.019*
N17	0.3418 (2)	0.92248 (13)	-0.12008 (10)	0.0144 (4)
C18	0.2051 (3)	0.96126 (16)	-0.18133 (12)	0.0191 (5)
H18A	0.2487	0.9442	-0.2365	0.029*
H18B	0.1920	1.0374	-0.1760	0.029*
H18C	0.0847	0.9277	-0.1718	0.029*
O19	0.7461 (2)	1.27432 (10)	0.15561 (8)	0.0158 (3)
C20	0.8802 (3)	1.22387 (16)	0.20839 (12)	0.0184 (4)
H20A	0.8156	1.1774	0.2466	0.028*
H20B	0.9487	1.2772	0.2391	0.028*
H20C	0.9670	1.1828	0.1752	0.028*

O21	0.7970 (2)	1.04401 (10)	0.10352 (8)	0.0153 (3)
O22	0.6926 (2)	0.93888 (12)	0.23779 (9)	0.0264 (4)
O23	0.4629 (2)	0.77234 (9)	0.00009 (9)	0.0149 (3)
H23	0.4567	0.7687	-0.0511	0.022*
O24	0.3857 (2)	0.81906 (10)	-0.14319 (8)	0.0169 (3)

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0159 (10)	0.0141 (9)	0.0142 (9)	0.0024 (8)	0.0026 (9)	0.0027 (8)
C2	0.0217 (11)	0.0115 (9)	0.0132 (9)	0.0006 (9)	0.0029 (9)	-0.0005 (8)
C3	0.0167 (10)	0.0124 (9)	0.0109 (8)	-0.0022 (8)	0.0020 (9)	-0.0005 (7)
C4	0.0117 (9)	0.0128 (9)	0.0152 (9)	-0.0006 (8)	0.0032 (9)	0.0015 (8)
C5	0.0133 (10)	0.0096 (9)	0.0199 (9)	-0.0005 (8)	0.0007 (9)	-0.0016 (8)
C6	0.0143 (10)	0.0147 (9)	0.0189 (10)	0.0026 (9)	-0.0018 (9)	0.0011 (8)
C7	0.0188 (11)	0.0123 (9)	0.0171 (9)	-0.0030 (9)	-0.0007 (9)	0.0025 (8)
C8	0.0127 (10)	0.0140 (9)	0.0156 (9)	-0.0020 (9)	0.0013 (8)	0.0008 (8)
C9	0.0139 (10)	0.0116 (9)	0.0140 (9)	-0.0021 (8)	0.0034 (8)	0.0000 (8)
C10	0.0130 (10)	0.0132 (9)	0.0168 (9)	0.0008 (9)	-0.0003 (9)	0.0000 (8)
C11	0.0144 (10)	0.0115 (9)	0.0122 (8)	-0.0011 (8)	0.0018 (8)	0.0009 (7)
C12	0.0136 (10)	0.0098 (9)	0.0130 (8)	-0.0012 (8)	0.0040 (9)	0.0005 (8)
C13	0.0104 (10)	0.0102 (9)	0.0158 (9)	0.0000 (8)	0.0010 (8)	0.0008 (8)
C14	0.0131 (10)	0.0104 (9)	0.0151 (9)	0.0004 (8)	0.0012 (8)	-0.0011 (7)
C15	0.0128 (10)	0.0129 (9)	0.0186 (9)	-0.0023 (9)	0.0050 (9)	-0.0019 (8)
C16	0.0165 (11)	0.0128 (9)	0.0177 (9)	-0.0022 (9)	0.0048 (9)	-0.0001 (8)
N17	0.0171 (9)	0.0114 (7)	0.0147 (8)	-0.0001 (7)	0.0020 (7)	-0.0016 (6)
C18	0.0240 (12)	0.0170 (10)	0.0161 (9)	-0.0008 (10)	-0.0037 (9)	0.0003 (8)
O19	0.0185 (7)	0.0118 (6)	0.0170 (6)	-0.0012 (6)	-0.0043 (6)	0.0002 (6)
C20	0.0185 (11)	0.0185 (10)	0.0182 (9)	-0.0005 (9)	-0.0040 (9)	-0.0011 (8)
O21	0.0122 (7)	0.0103 (6)	0.0234 (7)	0.0001 (6)	0.0001 (6)	-0.0016 (6)
O22	0.0305 (9)	0.0282 (8)	0.0206 (7)	-0.0091 (8)	-0.0067 (7)	0.0017 (7)
O23	0.0176 (7)	0.0094 (7)	0.0177 (6)	-0.0001 (6)	0.0006 (6)	-0.0018 (6)
O24	0.0226 (8)	0.0094 (6)	0.0188 (7)	0.0022 (6)	0.0019 (7)	-0.0041 (6)

Geometric parameters (\AA , $^\circ$)

C1—C2	1.385 (3)	C10—C11	1.512 (3)
C1—C11	1.408 (3)	C10—H10A	0.9900
C1—H1	0.9500	C10—H10B	0.9900
C2—C3	1.405 (3)	C11—C12	1.376 (3)
C2—H2	0.9500	C12—C13	1.504 (3)
C3—O19	1.372 (2)	C13—C15	1.542 (3)
C3—C4	1.391 (3)	C13—C14	1.542 (3)
C4—C12	1.374 (3)	C14—O23	1.419 (2)
C4—O21	1.394 (2)	C15—C16	1.517 (3)
C5—O21	1.463 (2)	C15—H15A	0.9900
C5—C6	1.541 (3)	C15—H15B	0.9900
C5—C13	1.544 (3)	C16—N17	1.510 (3)
C5—H5	1.0000	C16—H16A	0.9900
C6—O22	1.209 (2)	C16—H16B	0.9900

C6—C7	1.498 (3)	N17—O24	1.409 (2)
C7—C8	1.536 (3)	N17—C18	1.490 (3)
C7—H7A	0.9900	C18—H18A	0.9800
C7—H7B	0.9900	C18—H18B	0.9800
C8—C14	1.530 (3)	C18—H18C	0.9800
C8—H8A	0.9900	O19—C20	1.447 (2)
C8—H8B	0.9900	C20—H20A	0.9800
C9—N17	1.543 (2)	C20—H20B	0.9800
C9—C10	1.543 (3)	C20—H20C	0.9800
C9—C14	1.555 (3)	O23—H23	0.8400
C9—H9	1.0000		
C2—C1—C11	120.09 (19)	C4—C12—C11	124.74 (18)
C2—C1—H1	120.0	C4—C12—C13	109.08 (17)
C11—C1—H1	120.0	C11—C12—C13	126.12 (18)
C1—C2—C3	123.10 (18)	C12—C13—C15	110.19 (16)
C1—C2—H2	118.5	C12—C13—C14	109.46 (16)
C3—C2—H2	118.5	C15—C13—C14	108.84 (15)
O19—C3—C4	126.72 (19)	C12—C13—C5	97.84 (15)
O19—C3—C2	117.16 (16)	C15—C13—C5	112.22 (16)
C4—C3—C2	116.10 (18)	C14—C13—C5	117.71 (15)
C12—C4—C3	120.08 (19)	O23—C14—C8	106.21 (15)
C12—C4—O21	111.44 (16)	O23—C14—C13	111.53 (16)
C3—C4—O21	128.47 (18)	C8—C14—C13	110.73 (15)
O21—C5—C6	108.07 (15)	O23—C14—C9	110.93 (15)
O21—C5—C13	104.58 (14)	C8—C14—C9	111.64 (16)
C6—C5—C13	112.17 (17)	C13—C14—C9	105.90 (15)
O21—C5—H5	110.6	C16—C15—C13	111.16 (16)
C6—C5—H5	110.6	C16—C15—H15A	109.4
C13—C5—H5	110.6	C13—C15—H15A	109.4
O22—C6—C7	123.48 (19)	C16—C15—H15B	109.4
O22—C6—C5	120.70 (18)	C13—C15—H15B	109.4
C7—C6—C5	115.79 (16)	H15A—C15—H15B	108.0
C6—C7—C8	110.39 (15)	N17—C16—C15	111.23 (15)
C6—C7—H7A	109.6	N17—C16—H16A	109.4
C8—C7—H7A	109.6	C15—C16—H16A	109.4
C6—C7—H7B	109.6	N17—C16—H16B	109.4
C8—C7—H7B	109.6	C15—C16—H16B	109.4
H7A—C7—H7B	108.1	H16A—C16—H16B	108.0
C14—C8—C7	108.57 (16)	O24—N17—C18	106.20 (15)
C14—C8—H8A	110.0	O24—N17—C16	109.18 (15)
C7—C8—H8A	110.0	C18—N17—C16	109.40 (14)
C14—C8—H8B	110.0	O24—N17—C9	108.75 (14)
C7—C8—H8B	110.0	C18—N17—C9	112.15 (16)
H8A—C8—H8B	108.4	C16—N17—C9	111.00 (14)
N17—C9—C10	112.48 (15)	N17—C18—H18A	109.5
N17—C9—C14	108.64 (15)	N17—C18—H18B	109.5
C10—C9—C14	113.47 (16)	H18A—C18—H18B	109.5
N17—C9—H9	107.3	N17—C18—H18C	109.5

C10—C9—H9	107.3	H18A—C18—H18C	109.5
C14—C9—H9	107.3	H18B—C18—H18C	109.5
C11—C10—C9	114.86 (17)	C3—O19—C20	117.07 (15)
C11—C10—H10A	108.6	O19—C20—H20A	109.5
C9—C10—H10A	108.6	O19—C20—H20B	109.5
C11—C10—H10B	108.6	H20A—C20—H20B	109.5
C9—C10—H10B	108.6	O19—C20—H20C	109.5
H10A—C10—H10B	107.5	H20A—C20—H20C	109.5
C12—C11—C1	115.75 (18)	H20B—C20—H20C	109.5
C12—C11—C10	118.46 (17)	C4—O21—C5	103.67 (14)
C1—C11—C10	125.59 (19)	C14—O23—H23	109.5
C11—C1—C2—C3	0.0 (3)	C6—C5—C13—C14	-34.6 (2)
C1—C2—C3—O19	176.25 (17)	C7—C8—C14—O23	62.85 (19)
C1—C2—C3—C4	-2.1 (3)	C7—C8—C14—C13	-58.4 (2)
O19—C3—C4—C12	-173.94 (18)	C7—C8—C14—C9	-176.12 (15)
C2—C3—C4—C12	4.2 (3)	C12—C13—C14—O23	177.08 (15)
O19—C3—C4—O21	7.0 (3)	C15—C13—C14—O23	56.6 (2)
C2—C3—C4—O21	-174.82 (17)	C5—C13—C14—O23	-72.5 (2)
O21—C5—C6—O22	-24.0 (3)	C12—C13—C14—C8	-64.9 (2)
C13—C5—C6—O22	-138.7 (2)	C15—C13—C14—C8	174.65 (16)
O21—C5—C6—C7	154.04 (16)	C5—C13—C14—C8	45.6 (2)
C13—C5—C6—C7	39.3 (2)	C12—C13—C14—C9	56.31 (19)
O22—C6—C7—C8	122.7 (2)	C15—C13—C14—C9	-64.18 (19)
C5—C6—C7—C8	-55.2 (2)	C5—C13—C14—C9	166.73 (16)
C6—C7—C8—C14	64.1 (2)	N17—C9—C14—O23	-56.82 (19)
N17—C9—C10—C11	-87.7 (2)	C10—C9—C14—O23	177.27 (16)
C14—C9—C10—C11	36.1 (2)	N17—C9—C14—C8	-175.07 (15)
C2—C1—C11—C12	0.0 (3)	C10—C9—C14—C8	59.0 (2)
C2—C1—C11—C10	174.67 (18)	N17—C9—C14—C13	64.34 (18)
C9—C10—C11—C12	-6.0 (2)	C10—C9—C14—C13	-61.6 (2)
C9—C10—C11—C1	179.44 (17)	C12—C13—C15—C16	-59.9 (2)
C3—C4—C12—C11	-4.6 (3)	C14—C13—C15—C16	60.2 (2)
O21—C4—C12—C11	174.58 (16)	C5—C13—C15—C16	-167.76 (15)
C3—C4—C12—C13	178.05 (17)	C13—C15—C16—N17	-54.5 (2)
O21—C4—C12—C13	-2.8 (2)	C15—C16—N17—O24	-65.20 (19)
C1—C11—C12—C4	2.3 (3)	C15—C16—N17—C18	178.96 (16)
C10—C11—C12—C4	-172.74 (18)	C15—C16—N17—C9	54.7 (2)
C1—C11—C12—C13	179.22 (17)	C10—C9—N17—O24	-173.78 (16)
C10—C11—C12—C13	4.2 (3)	C14—C9—N17—O24	59.75 (18)
C4—C12—C13—C15	-94.21 (19)	C10—C9—N17—C18	-56.6 (2)
C11—C12—C13—C15	88.5 (2)	C14—C9—N17—C18	176.89 (15)
C4—C12—C13—C14	146.13 (16)	C10—C9—N17—C16	66.1 (2)
C11—C12—C13—C14	-31.2 (3)	C14—C9—N17—C16	-60.39 (18)
C4—C12—C13—C5	23.01 (19)	C4—C3—O19—C20	-33.7 (3)
C11—C12—C13—C5	-154.31 (18)	C2—C3—O19—C20	148.20 (17)
O21—C5—C13—C12	-34.57 (17)	C12—C4—O21—C5	-20.43 (19)
C6—C5—C13—C12	82.31 (18)	C3—C4—O21—C5	158.66 (19)
O21—C5—C13—C15	81.06 (18)	C6—C5—O21—C4	-84.92 (17)

C6—C5—C13—C15	-162.06 (16)	C13—C5—O21—C4	34.76 (18)
O21—C5—C13—C14	-151.46 (16)		

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O23—H23 \cdots O24	0.84	1.72	2.483 (2)	151
C5—H5 \cdots O23 ⁱ	1.00	2.60	3.536 (2)	157
C9—H9 \cdots O23 ⁱⁱ	1.00	2.36	3.314 (2)	160
C16—H16B \cdots O22 ⁱⁱⁱ	0.99	2.40	3.227 (3)	141
C18—H18B \cdots O19 ^{iv}	0.98	2.46	3.413 (2)	165

Symmetry codes: (i) $x+1/2, -y+3/2, -z$; (ii) $x-1/2, -y+3/2, -z$; (iii) $-x+3/2, -y+2, z-1/2$; (iv) $x-1/2, -y+5/2, -z$.