

Crystal structure of 7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)heptanoate 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium monohydrate: a new solid form of seratrodist

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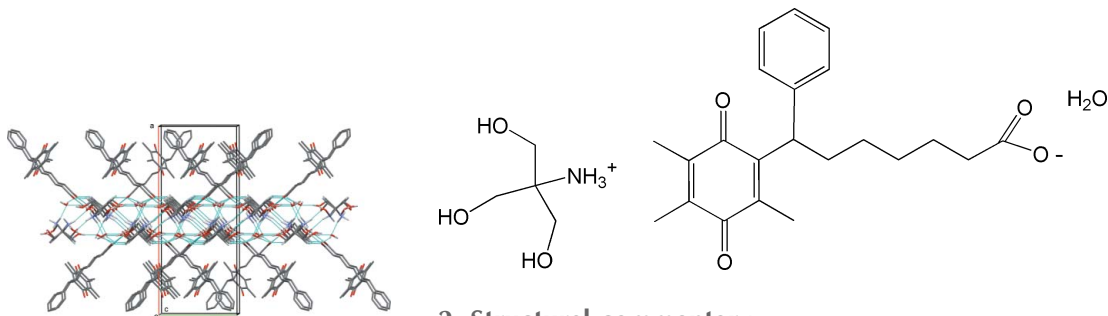
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In the title hydrated salt, $C_4H_{12}NO_3^+ \cdot C_{22}H_{25}O_4^- \cdot H_2O$, seratrodist [systematic name: 7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)heptanoic acid] crystallized with trometamol [systematic name: 2-amino-2-(hydroxymethyl)propane-1,3-diol] to form a monohydrated salt form of seratrodist. The carboxylic acid group of seratrodist has transferred its proton to the amino N atom of trometamol. In the crystal, the trometamol cations are linked to the water molecules and to each other by $N-H \cdots O$ and $O-H \cdots O$ hydrogen bonds forming sheets parallel to (100). The seratrodist anions are linked to both sides of these sheets by $O-H \cdots O$ and $C-H \cdots O$ hydrogen bonds, forming a three-layer two-dimensional structure. After forming the title salt, the solubility of seratrodist was found to be greatly improved.

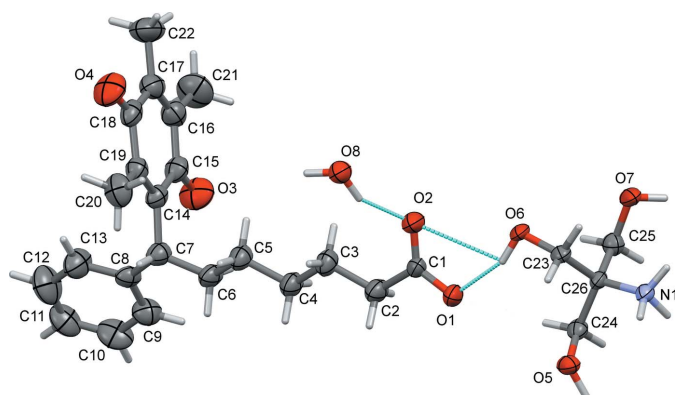
1. Chemical context

Seratrodist is the first thromboxane A₂ receptor antagonist to have been developed as an anti-asthmatic drug (Samara, 1996). This drug molecule with a carboxylic group is practically insoluble in water. Its new solid forms have been scarcely exploited and only a polymorphic transition was ever investigated (Urakami & Beezer, 2003). Tris(hydroxymethyl)amino methane, commonly called trometamol, is often used as a buffer in biochemical studies. It has been successfully exploited for improving properties of APIs such as ketoprofen (Zippel & Wagenitz, 2006). In this study, trometamol was employed to co-crystallize with seratrodist to give rise to a hydrated salt. To the best of our knowledge, the title salt is the first multi-component crystalline form of seratrodist to be reported.



2. Structural commentary

The molecular structure of the title salt is illustrated in Fig. 1. It was clear from a difference Fourier map that the carboxylic group of seratrodist had transferred its proton to the amino N atom of trometamol. The bond distances C1—O1 and C1—O2

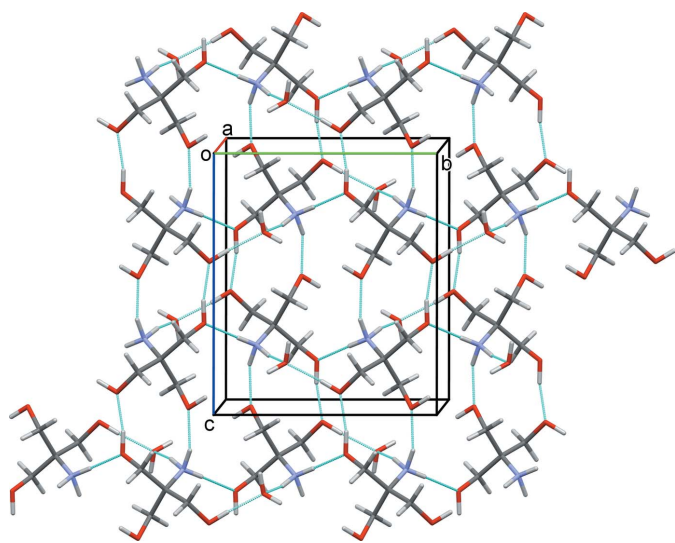

Figure 1

A view of the molecular structure of the title salt, with atom labelling. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen bonds are shown as dashed lines (see Table 1 for details).

of the carboxylate group of the seratrodast anion are 1.258 (4) and 1.232 (4) Å, respectively. The phenyl ring is normal to the dioxocyclohexadiene ring, with a dihedral angle of 89.95 (19)°, and the alkyl chain has an extended conformation.

3. Supramolecular features

In the crystal, the trometamol cations are linked to the water molecules and to each other by N—H···O and O—H···O hydrogen bonds, forming sheets parallel to (100); see Table 1 and Fig. 2. The seratrodast anions are linked to both sides of these sheets by O—H···O and C—H···O hydrogen bonds, forming a three-layer two-dimensional structure (Fig. 3 and Table 1). Further details of the hydrogen bonding are given below and in Table 1. The carboxylate anion interacts with one hydroxyl group of trometamol through strong hydrogen


Figure 2

A view along the *a* axis of the two-dimensional hydrogen-bonded structure of the trometamol cations and the water molecules (hydrogen bonds are shown as dashed lines; see Table 1 for details).

Table 1

Hydrogen-bond geometry (Å, °).

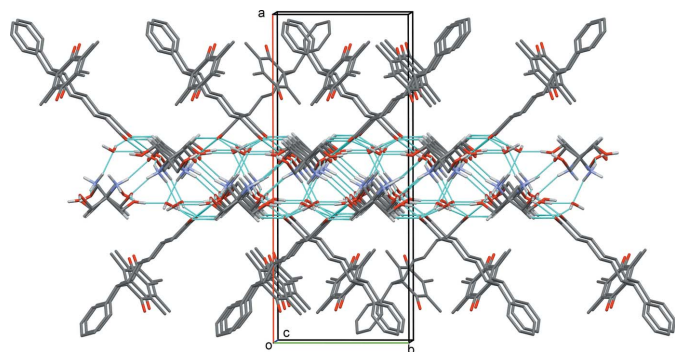
<i>D</i> —H··· <i>A</i>	<i>D</i> —H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> —H··· <i>A</i>
N1—H1C···O8 ⁱ	0.99	1.85	2.800 (4)	160
N1—H1B···O5 ⁱⁱ	0.91	2.04	2.935 (3)	166
N1—H1A···O6 ⁱⁱⁱ	0.97	1.88	2.779 (3)	153
O5—H5···O7 ⁱⁱⁱ	0.97	1.76	2.714 (3)	170
O6—H6···O1	0.91	1.81	2.662 (3)	154
O7—H7A···O8 ⁱⁱⁱ	0.92	1.77	2.686 (3)	173
O8—H8B···O2	0.92	1.76	2.617 (3)	152.3
O8—H8A···O1 ^{iv}	0.91	1.76	2.667 (3)	173
C24—H24A···O1	0.99	2.55	3.410 (4)	146
C25—H25A···O2 ⁱⁱⁱ	0.99	2.44	3.326 (4)	149

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

bonding [O6···O1 = 2.662 (3) Å]. There also exist hydrogen-bonding interactions between carboxylate anion and water molecule [O8···O2 = 2.617 (3) Å, O8···O1ⁱ = 2.667 (3) Å]. The protonated trometamol cation interacts with each other through three kinds of hydrogen-bonding interactions. An $R_2^2(11)$ heterosynthon is formed through hydrogen-bonding interactions between the hydroxyl groups [O5···O7ⁱⁱⁱ = 2.714 (3) Å] and between the hydroxyl group and the amino group [N1···O6ⁱⁱⁱ = 2.779 (3) Å]. Along the *c* axis, the $R_2^2(11)$ heterosynthon gives rise to a hydrogen-bonded chain of trometamol cations, which is further linked into a two-dimensional structure by hydrogen-bonding interactions between the amino and the hydroxyl groups [N1···O5ⁱⁱ = 2.935 (3) Å]. There also exist hydrogen-bonding interactions between water and trometamol [N1···O8ⁱ = 2.800 (4) Å; O7···O8ⁱⁱⁱ = 2.686 (3) Å]. The various hydrogen-bonding interactions result in a two-dimensional layer structure in which the seratrodast anions are spread around two sides of the layer in an orderly manner (Table 1 and Fig. 3).

4. Database survey

To the best of our knowledge, the title salt is the first multi-component crystalline form of seratrodast to be reported.


Figure 3

A view along the *c* axis of the crystal packing of the title compound (hydrogen bonds are shown as dashed lines; see Table 1 for details). H atoms not involved in hydrogen bonding have been omitted for clarity.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_4H_{12}NO_3^+ \cdot C_{22}H_{25}O_4^- \cdot H_2O$
M_r	493.58
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	293
a, b, c (Å)	23.506 (9), 9.665 (4), 11.344 (5)
β (°)	94.223 (7)
V (Å ³)	2570.0 (17)
Z	4
Radiation type	Mo $K\alpha$
μ (mm ⁻¹)	0.09
Crystal size (mm)	0.20 × 0.20 × 0.20
Data collection	
Diffractometer	Rigaku Mercury CCD
Absorption correction	Multi-scan (<i>CrystalClear</i> ; Rigaku, 2000)
T_{\min} , T_{\max}	0.549, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	20028, 5762, 3564
R_{int}	0.062
$(\sin \theta/\lambda)_{\text{max}}$ (Å ⁻¹)	0.649
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.074, 0.288, 1.10
No. of reflections	5762
No. of parameters	319
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å ⁻³)	0.55, -0.42

Computer programs: *CrystalClear* (Rigaku, 2000), *SHELXS97* and *SHELXL97* (Sheldrick, 2008), *Mercury* (Macrae *et al.*, 2008), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

5. Synthesis and crystallization

Seratrodast (354 mg, 1 mmol) and trometamol (121 mg, 1 mmol) were dissolved in methanol (15 ml). The resulting solution was kept in air and after several days yellow block-like crystals of the title salt were obtained.

6. Solubility Studies

Excess amounts of seratrodast and the title salt were suspended in 10 ml of water in screw-capped glass vials, respectively. These vials were kept at 310 K and were stirred at

100 r.p.m. using a magnetic stirrer. After 72 h, the suspensions were filtered through a 0.2 µm syringe filter. The filtered aliquots were sufficiently diluted, and the absorbances were measured at 268 nm in triplicate. Finally, the concentration of seratrodast after 72 h in each sample was determined from the previously made standard graph. A standard graph was made by measuring the absorbance of varied concentrations of seratrodast (2–16 mg/L) in water/methanol (9:1) solution using a UV-2500 spectrophotometer at 268 nm. The calibrated plot showed a good correlation coefficient ($y = 0.04997x + 0.00459$, $R^2 = 0.9991$). After forming the title salt, the solubility of seratrodast was found to be greatly improved.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The C-bound H atoms were positioned geometrically and refined as riding atoms: C–H = 0.95–1.00 Å with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. The OH and NH_3^+ H atoms were located in difference Fourier maps and refined as riding atoms with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{O}, \text{N})$.

Acknowledgements

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Crystal structure of 7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)heptanoate 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium monohydrate: a new solid form of seratrodist

Benyong Lou

Computing details

Data collection: *CrystalClear* (Rigaku, 2000); cell refinement: *CrystalClear* (Rigaku, 2000); data reduction: *CrystalClear* (Rigaku, 2000); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *SHELXL97* (Sheldrick, 2008), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

7-Phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)heptanoate 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium monohydrate

Crystal data

$C_4H_{12}NO_3^+ \cdot C_{22}H_{25}O_4^- \cdot H_2O$

$M_r = 493.58$

Monoclinic, $P2_1/c$

Hall symbol: -P 2ybc

$a = 23.506$ (9) Å

$b = 9.665$ (4) Å

$c = 11.344$ (5) Å

$\beta = 94.223$ (7)°

$V = 2570.0$ (17) Å³

$Z = 4$

$F(000) = 1064$

$D_x = 1.276$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 6295 reflections

$\theta = 2.1$ – 27.5 °

$\mu = 0.09$ mm⁻¹

$T = 293$ K

Prism, yellow

$0.20 \times 0.20 \times 0.20$ mm

Data collection

Rigaku Mercury CCD
diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

Detector resolution: 28.5714 pixels mm⁻¹

CCD_Profile_fitting scans

Absorption correction: multi-scan
(*CrystalClear*; Rigaku, 2000)

$T_{\min} = 0.549$, $T_{\max} = 1.000$

20028 measured reflections

5762 independent reflections

3564 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.062$

$\theta_{\max} = 27.5$ °, $\theta_{\min} = 2.6$ °

$h = -30 \rightarrow 30$

$k = -12 \rightarrow 12$

$l = -12 \rightarrow 14$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.074$

$wR(F^2) = 0.288$

$S = 1.10$

5762 reflections

319 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

$$w = 1/[\sigma^2(F_o^2) + (0.1567P)^2]$$

where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.55 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.42 \text{ e } \text{\AA}^{-3}$

Special details

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

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

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.38025 (10)	0.4145 (2)	0.4397 (2)	0.0447 (6)
O2	0.38047 (12)	0.4204 (3)	0.6328 (2)	0.0537 (7)
O3	0.09684 (12)	0.0531 (3)	0.8988 (3)	0.0749 (9)
O4	0.25430 (13)	-0.0713 (4)	1.2339 (3)	0.0789 (10)
O5	0.44774 (10)	0.5677 (2)	0.17616 (18)	0.0408 (6)
O6	0.44283 (9)	0.6368 (2)	0.49902 (17)	0.0389 (6)
O7	0.42596 (11)	0.9565 (2)	0.43874 (19)	0.0482 (6)
O8	0.42283 (9)	0.2989 (2)	0.8260 (2)	0.0440 (6)
H8B	0.4079	0.3136	0.7498	0.053*
H1C	0.5077	0.7821	0.1992	0.053*
H7A	0.4222	1.0380	0.3969	0.053*
H1B	0.4962	0.9171	0.2650	0.053*
H1A	0.4590	0.8684	0.1637	0.053*
H8A	0.4059	0.2252	0.8599	0.053*
H5	0.4389	0.5703	0.0917	0.053*
H6	0.4274	0.5623	0.4592	0.053*
N1	0.47892 (10)	0.8382 (3)	0.2369 (2)	0.0333 (6)
C1	0.36324 (13)	0.3727 (3)	0.5360 (3)	0.0339 (7)
C2	0.31629 (15)	0.2633 (4)	0.5285 (3)	0.0469 (8)
H2A	0.2801	0.3087	0.5001	0.056*
H2B	0.3254	0.1944	0.4681	0.056*
C3	0.30659 (14)	0.1871 (4)	0.6411 (3)	0.0470 (8)
H3A	0.3018	0.2554	0.7047	0.056*
H3B	0.3408	0.1309	0.6644	0.056*
C4	0.25457 (15)	0.0926 (4)	0.6304 (3)	0.0465 (8)
H4A	0.2204	0.1495	0.6080	0.056*
H4B	0.2592	0.0259	0.5656	0.056*
C5	0.24405 (15)	0.0123 (4)	0.7421 (3)	0.0502 (9)
H5A	0.2750	-0.0560	0.7580	0.060*
H5B	0.2448	0.0769	0.8099	0.060*

C6	0.18728 (15)	-0.0623 (4)	0.7312 (3)	0.0475 (9)
H6A	0.1567	0.0078	0.7184	0.057*
H6B	0.1861	-0.1212	0.6597	0.057*
C7	0.17374 (14)	-0.1507 (4)	0.8334 (3)	0.0452 (8)
H7	0.2046	-0.2222	0.8397	0.054*
C8	0.11810 (13)	-0.2336 (4)	0.8148 (3)	0.0412 (8)
C9	0.08118 (15)	-0.2237 (4)	0.7166 (4)	0.0566 (10)
H9	0.0876	-0.1562	0.6581	0.068*
C10	0.03397 (16)	-0.3118 (5)	0.7012 (5)	0.0725 (13)
H10	0.0092	-0.3051	0.6314	0.087*
C13	0.10716 (18)	-0.3320 (5)	0.8987 (4)	0.0670 (12)
H13	0.1327	-0.3426	0.9670	0.080*
C12	0.0590 (2)	-0.4157 (5)	0.8836 (5)	0.0860 (16)
H12	0.0512	-0.4800	0.9437	0.103*
C11	0.02316 (17)	-0.4075 (5)	0.7856 (5)	0.0689 (12)
H11	-0.0090	-0.4671	0.7752	0.083*
C14	0.17815 (13)	-0.0778 (3)	0.9519 (3)	0.0397 (8)
C15	0.13375 (14)	0.0248 (4)	0.9771 (3)	0.0463 (9)
C16	0.13441 (16)	0.0942 (4)	1.0924 (4)	0.0531 (9)
C19	0.22057 (13)	-0.1042 (4)	1.0361 (3)	0.0426 (8)
C18	0.21906 (15)	-0.0386 (4)	1.1559 (3)	0.0494 (9)
C17	0.17570 (17)	0.0652 (4)	1.1788 (4)	0.0555 (10)
C20	0.27017 (17)	-0.1961 (4)	1.0232 (4)	0.0655 (11)
H20A	0.2645	-0.2481	0.9491	0.098*
H20B	0.2740	-0.2607	1.0898	0.098*
H20C	0.3049	-0.1401	1.0220	0.098*
C21	0.0871 (2)	0.1955 (6)	1.1065 (5)	0.0896 (16)
H21A	0.0928	0.2408	1.1838	0.134*
H21B	0.0505	0.1466	1.1011	0.134*
H21C	0.0871	0.2653	1.0439	0.134*
C22	0.1798 (2)	0.1297 (6)	1.2988 (4)	0.0891 (17)
H22A	0.2194	0.1556	1.3207	0.134*
H22B	0.1669	0.0634	1.3565	0.134*
H22C	0.1556	0.2125	1.2979	0.134*
C23	0.47623 (12)	0.6918 (3)	0.4125 (2)	0.0319 (6)
H23A	0.4992	0.6168	0.3801	0.038*
H23B	0.5029	0.7612	0.4494	0.038*
C24	0.40803 (12)	0.6541 (3)	0.2309 (3)	0.0346 (7)
H24A	0.3833	0.5965	0.2781	0.042*
H24B	0.3834	0.7023	0.1693	0.042*
C25	0.39738 (13)	0.8612 (3)	0.3592 (3)	0.0392 (7)
H25A	0.3773	0.9124	0.2930	0.047*
H25B	0.3686	0.8093	0.4008	0.047*
C26	0.43939 (11)	0.7603 (3)	0.3108 (2)	0.0296 (6)

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0627 (15)	0.0412 (12)	0.0308 (13)	-0.0161 (10)	0.0075 (10)	0.0027 (10)
O2	0.0810 (18)	0.0487 (14)	0.0311 (13)	-0.0191 (12)	0.0032 (12)	-0.0005 (11)
O3	0.0648 (18)	0.090 (2)	0.067 (2)	0.0198 (16)	-0.0195 (15)	0.0060 (17)
O4	0.0712 (19)	0.099 (3)	0.062 (2)	-0.0058 (17)	-0.0235 (15)	0.0159 (18)
O5	0.0564 (13)	0.0365 (11)	0.0280 (12)	0.0050 (10)	-0.0064 (10)	-0.0036 (9)
O6	0.0626 (14)	0.0380 (12)	0.0156 (10)	-0.0120 (10)	-0.0012 (9)	0.0025 (9)
O7	0.0854 (18)	0.0351 (12)	0.0226 (12)	0.0038 (11)	-0.0057 (11)	0.0000 (9)
O8	0.0505 (13)	0.0447 (13)	0.0368 (13)	-0.0080 (10)	0.0037 (10)	-0.0006 (10)
N1	0.0433 (14)	0.0333 (12)	0.0227 (13)	-0.0094 (10)	-0.0014 (10)	0.0024 (10)
C1	0.0450 (17)	0.0294 (14)	0.0279 (17)	0.0010 (12)	0.0072 (13)	0.0024 (12)
C2	0.052 (2)	0.053 (2)	0.0360 (19)	-0.0131 (16)	0.0066 (15)	0.0017 (16)
C3	0.0459 (18)	0.052 (2)	0.044 (2)	-0.0116 (15)	0.0043 (15)	0.0099 (16)
C4	0.0498 (19)	0.052 (2)	0.038 (2)	-0.0124 (15)	0.0065 (15)	0.0046 (16)
C5	0.053 (2)	0.057 (2)	0.040 (2)	-0.0163 (16)	0.0010 (16)	0.0065 (17)
C6	0.052 (2)	0.056 (2)	0.0357 (19)	-0.0158 (16)	0.0109 (15)	-0.0008 (16)
C7	0.0446 (18)	0.053 (2)	0.0377 (19)	-0.0103 (15)	0.0033 (14)	-0.0009 (16)
C8	0.0364 (16)	0.0511 (19)	0.0372 (18)	-0.0077 (14)	0.0110 (13)	-0.0085 (15)
C9	0.045 (2)	0.066 (2)	0.059 (2)	-0.0098 (17)	0.0019 (17)	-0.006 (2)
C10	0.043 (2)	0.083 (3)	0.089 (3)	-0.010 (2)	-0.015 (2)	-0.017 (3)
C13	0.061 (2)	0.081 (3)	0.059 (3)	-0.031 (2)	0.0041 (19)	0.004 (2)
C12	0.067 (3)	0.073 (3)	0.119 (5)	-0.032 (2)	0.011 (3)	0.008 (3)
C11	0.044 (2)	0.064 (3)	0.099 (4)	-0.0171 (19)	0.003 (2)	-0.012 (3)
C14	0.0358 (16)	0.0472 (18)	0.0365 (18)	-0.0106 (13)	0.0043 (13)	0.0026 (15)
C15	0.0420 (18)	0.053 (2)	0.043 (2)	-0.0035 (15)	-0.0028 (15)	0.0080 (16)
C16	0.056 (2)	0.048 (2)	0.057 (2)	-0.0016 (16)	0.0137 (18)	-0.0014 (18)
C19	0.0399 (17)	0.0440 (17)	0.044 (2)	-0.0069 (13)	0.0005 (14)	0.0041 (15)
C18	0.0477 (19)	0.055 (2)	0.044 (2)	-0.0183 (16)	-0.0044 (16)	0.0112 (17)
C17	0.064 (2)	0.054 (2)	0.049 (2)	-0.0185 (18)	0.0087 (18)	-0.0054 (18)
C20	0.053 (2)	0.060 (2)	0.082 (3)	0.0060 (18)	-0.003 (2)	0.009 (2)
C21	0.087 (3)	0.082 (4)	0.101 (4)	0.029 (3)	0.021 (3)	-0.009 (3)
C22	0.120 (4)	0.092 (4)	0.058 (3)	-0.029 (3)	0.025 (3)	-0.026 (3)
C23	0.0401 (15)	0.0323 (14)	0.0224 (15)	-0.0022 (12)	-0.0033 (12)	0.0006 (12)
C24	0.0361 (15)	0.0371 (15)	0.0297 (16)	-0.0072 (12)	-0.0043 (12)	0.0038 (13)
C25	0.0427 (17)	0.0362 (16)	0.0385 (18)	0.0011 (13)	0.0009 (13)	0.0006 (14)
C26	0.0362 (15)	0.0316 (14)	0.0210 (14)	-0.0061 (11)	0.0009 (11)	0.0043 (12)

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

O1—C1	1.258 (4)	C9—C10	1.400 (5)
O2—C1	1.232 (4)	C9—H9	0.9500
O3—C15	1.226 (4)	C10—C11	1.369 (7)
O4—C18	1.209 (4)	C10—H10	0.9500
O5—C24	1.428 (4)	C13—C12	1.392 (5)
O5—H5	0.9657	C13—H13	0.9500
O6—C23	1.406 (4)	C12—C11	1.347 (7)

O6—H6	0.9109	C12—H12	0.9500
O7—C25	1.423 (4)	C11—H11	0.9500
O7—H7A	0.9202	C14—C19	1.353 (4)
O8—H8B	0.9191	C14—C15	1.483 (5)
O8—H8A	0.9142	C15—C16	1.469 (5)
N1—C26	1.499 (4)	C16—C17	1.357 (6)
N1—H1C	0.9892	C16—C21	1.499 (6)
N1—H1B	0.9100	C19—C20	1.482 (5)
N1—H1A	0.9682	C19—C18	1.502 (5)
C1—C2	1.526 (4)	C18—C17	1.467 (6)
C2—C3	1.507 (5)	C17—C22	1.493 (6)
C2—H2A	0.9900	C20—H20A	0.9800
C2—H2B	0.9900	C20—H20B	0.9800
C3—C4	1.523 (4)	C20—H20C	0.9800
C3—H3A	0.9900	C21—H21A	0.9800
C3—H3B	0.9900	C21—H21B	0.9800
C4—C5	1.522 (5)	C21—H21C	0.9800
C4—H4A	0.9900	C22—H22A	0.9800
C4—H4B	0.9900	C22—H22B	0.9800
C5—C6	1.514 (5)	C22—H22C	0.9800
C5—H5A	0.9900	C23—C26	1.540 (4)
C5—H5B	0.9900	C23—H23A	0.9900
C6—C7	1.493 (5)	C23—H23B	0.9900
C6—H6A	0.9900	C24—C26	1.524 (4)
C6—H6B	0.9900	C24—H24A	0.9900
C7—C14	1.515 (5)	C24—H24B	0.9900
C7—C8	1.535 (4)	C25—C26	1.519 (4)
C7—H7	1.0000	C25—H25A	0.9900
C8—C9	1.364 (5)	C25—H25B	0.9900
C8—C13	1.383 (5)		
C24—O5—H5	108.4	C12—C11—C10	118.7 (4)
C23—O6—H6	100.0	C12—C11—H11	120.6
C25—O7—H7A	101.8	C10—C11—H11	120.6
H8B—O8—H8A	111.6	C19—C14—C15	118.8 (3)
C26—N1—H1C	116.1	C19—C14—C7	122.5 (3)
C26—N1—H1B	120.2	C15—C14—C7	118.7 (3)
H1C—N1—H1B	108.0	O3—C15—C16	120.2 (4)
C26—N1—H1A	110.6	O3—C15—C14	118.7 (3)
H1C—N1—H1A	95.6	C16—C15—C14	121.1 (3)
H1B—N1—H1A	102.8	C17—C16—C15	120.6 (4)
O2—C1—O1	123.3 (3)	C17—C16—C21	123.7 (4)
O2—C1—C2	119.9 (3)	C15—C16—C21	115.7 (4)
O1—C1—C2	116.7 (3)	C14—C19—C20	126.0 (3)
C3—C2—C1	116.4 (3)	C14—C19—C18	119.6 (3)
C3—C2—H2A	108.2	C20—C19—C18	114.4 (3)
C1—C2—H2A	108.2	O4—C18—C17	119.8 (4)
C3—C2—H2B	108.2	O4—C18—C19	119.4 (4)

C1—C2—H2B	108.2	C17—C18—C19	120.8 (3)
H2A—C2—H2B	107.3	C16—C17—C18	118.8 (4)
C2—C3—C4	113.3 (3)	C16—C17—C22	124.5 (4)
C2—C3—H3A	108.9	C18—C17—C22	116.7 (4)
C4—C3—H3A	108.9	C19—C20—H20A	109.5
C2—C3—H3B	108.9	C19—C20—H20B	109.5
C4—C3—H3B	108.9	H20A—C20—H20B	109.5
H3A—C3—H3B	107.7	C19—C20—H20C	109.5
C5—C4—C3	114.7 (3)	H20A—C20—H20C	109.5
C5—C4—H4A	108.6	H20B—C20—H20C	109.5
C3—C4—H4A	108.6	C16—C21—H21A	109.5
C5—C4—H4B	108.6	C16—C21—H21B	109.5
C3—C4—H4B	108.6	H21A—C21—H21B	109.5
H4A—C4—H4B	107.6	C16—C21—H21C	109.5
C6—C5—C4	111.8 (3)	H21A—C21—H21C	109.5
C6—C5—H5A	109.3	H21B—C21—H21C	109.5
C4—C5—H5A	109.3	C17—C22—H22A	109.5
C6—C5—H5B	109.3	C17—C22—H22B	109.5
C4—C5—H5B	109.3	H22A—C22—H22B	109.5
H5A—C5—H5B	107.9	C17—C22—H22C	109.5
C7—C6—C5	116.5 (3)	H22A—C22—H22C	109.5
C7—C6—H6A	108.2	H22B—C22—H22C	109.5
C5—C6—H6A	108.2	O6—C23—C26	111.9 (2)
C7—C6—H6B	108.2	O6—C23—H23A	109.2
C5—C6—H6B	108.2	C26—C23—H23A	109.2
H6A—C6—H6B	107.3	O6—C23—H23B	109.2
C6—C7—C14	114.7 (3)	C26—C23—H23B	109.2
C6—C7—C8	114.9 (3)	H23A—C23—H23B	107.9
C14—C7—C8	111.5 (3)	O5—C24—C26	110.5 (2)
C6—C7—H7	104.8	O5—C24—H24A	109.6
C14—C7—H7	104.8	C26—C24—H24A	109.6
C8—C7—H7	104.8	O5—C24—H24B	109.6
C9—C8—C13	118.1 (3)	C26—C24—H24B	109.6
C9—C8—C7	124.0 (3)	H24A—C24—H24B	108.1
C13—C8—C7	117.7 (3)	O7—C25—C26	110.8 (2)
C8—C9—C10	120.7 (4)	O7—C25—H25A	109.5
C8—C9—H9	119.7	C26—C25—H25A	109.5
C10—C9—H9	119.7	O7—C25—H25B	109.5
C11—C10—C9	120.7 (4)	C26—C25—H25B	109.5
C13—C10—H10	119.7	H25A—C25—H25B	108.1
C9—C10—H10	119.7	N1—C26—C25	109.1 (2)
C8—C13—C12	120.4 (4)	N1—C26—C24	107.3 (2)
C8—C13—H13	119.8	C25—C26—C24	110.4 (2)
C12—C13—H13	119.8	N1—C26—C23	107.3 (2)
C11—C12—C13	121.4 (5)	C25—C26—C23	110.5 (2)
C11—C12—H12	119.3	C24—C26—C23	112.1 (2)
C13—C12—H12	119.3		

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
N1—H1C \cdots O8 ⁱ	0.99	1.85	2.800 (4)	160
N1—H1B \cdots O5 ⁱⁱ	0.91	2.04	2.935 (3)	166
N1—H1A \cdots O6 ⁱⁱⁱ	0.97	1.88	2.779 (3)	153
O5—H5 \cdots O7 ⁱⁱⁱ	0.97	1.76	2.714 (3)	170
O6—H6 \cdots O1	0.91	1.81	2.662 (3)	154
O7—H7A \cdots O8 ⁱⁱⁱ	0.92	1.77	2.686 (3)	173
O8—H8B \cdots O2	0.92	1.76	2.617 (3)	1523
O8—H8A \cdots O1 ^{iv}	0.91	1.76	2.667 (3)	173
C24—H24A \cdots O1	0.99	2.55	3.410 (4)	146
C25—H25A \cdots O2 ⁱⁱⁱ	0.99	2.44	3.326 (4)	149

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