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Iclaprim mesylate displaying a hydrogen-bonded molecular tape

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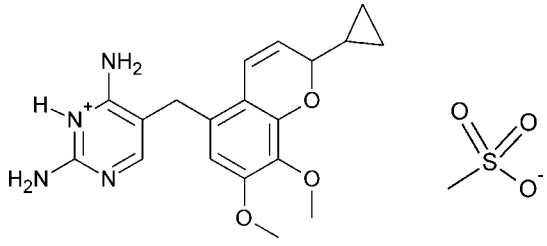
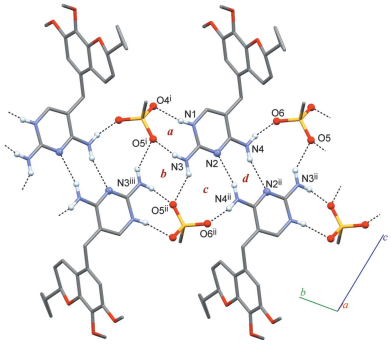
The title compound, 2,6-diamino-5-[(2-cyclopropyl-7,8-dimethoxy-*2H*-1-benzopyran-5-yl)methyl]pyrimidin-1-ium methanesulfonate, $C_{19}H_{23}N_4O_3^+\cdot CH_3O_3S^-$, is a salt made up from a protonated iclaprim molecule and a mesylate anion. The pyrimidine and chromene units of the iclaprim molecule form an orthogonal arrangement [interplanar angle of 89.67 (6)°], and the 3-nitrogen position of the pyrimidine ring is protonated. Four distinct N—H···O interactions and an additional N—H···N hydrogen bond connect iclaprim and mesylate molecules to one another, resulting in an infinite hydrogen-bonded molecular tape structure. The central section of the tape is formed by a sequence of fused hydrogen-bonded rings involving four distinct ring types.

1. Chemical context

Iclaprim is a dihydrofolate reductase (DHFR) inhibiting antibiotic containing a 2*H*-chromene structure that targets Gram-positive bacteria (Masciadri, 1997). The current study is part of an investigation aimed at improving the synthetic route to iclaprim and accessing its salts (Nerdinger *et al.*, 2020).



Iclaprim was synthesized according to the original route described by Jaeger *et al.* (2005), using 3-hydroxy-4,5-dimethoxybenzaldehyde (Cervi *et al.*, 2013), which was further purified by recrystallization from ethanol/*n*-hexane. We achieved a much better purity by trituration in hot ethanol and subsequent recrystallization from boiling acetonitrile. The title compound, (I), is the corresponding mesylate salt, and it was produced in a subsequent step.



2. Structural commentary

The asymmetric unit of (I) consists of one formula unit, composed of an $CH_3SO_3^-$ anion and an iclaprim cation in which the 3-nitrogen atom of the pyrimidine ring is protonated, *i.e.* N1 (Fig. 1). The molecular conformation of the iclaprim molecule is largely defined by the relative arrange-

ment of the essentially planar pyrimidine and chromene units. The CH_2 carbon atom C5 links the pyrimidine ring (C1, N1, C2, N2, C3, C4) with the fused benzene ring of the chromene unit (C6, C7, C8, C9, C10, C11). With regard to the two bridging bonds, the torsion angles C3—C4—C5—C6 [–160.8 (2)°] and C4—C5—C6—C7 [–96.5 (3)°] indicate that the C5—C6 bond is twisted slightly out of the pyrimidine plane, whilst the C4—C5 bond is oriented approximately perpendicular to the benzene ring. Accordingly, the two six-membered rings linked *via* C5 form an orthogonal arrangement with an interplanar angle of 89.67 (6)°. In the chromene moiety, the 7-methoxy substituent is significantly twisted out of the ring plane [C10—C9—O3—C19 = −70.3 (3)°], whilst the 8-methoxy substituent is almost coplanar with the plane of the fused benzene ring [C9—C8—O2—C18 = 167.6 (2)°]. The 2*H*-pyran ring displays the expected bond lengths [C12—C13 = 1.323 (4) Å]. The program *PLATON* (Spek, 2020) was used to calculate puckering parameters (Cremer & Pople, 1975) for the 2*H*-pyran ring. The obtained values, θ = 65.5 (7)°, φ = 328.4 (7)° and q = 0.253 (3) Å, are consistent with the presence of a skew-boat conformation (Boeyens, 1978).

3. Supramolecular features

The iclaprim molecule displays two NH_2 groups attached to the pyrimidine ring (N3, N4) and the protonated N1 atom of the pyrimidine ring as potential hydrogen-bond donor groups.

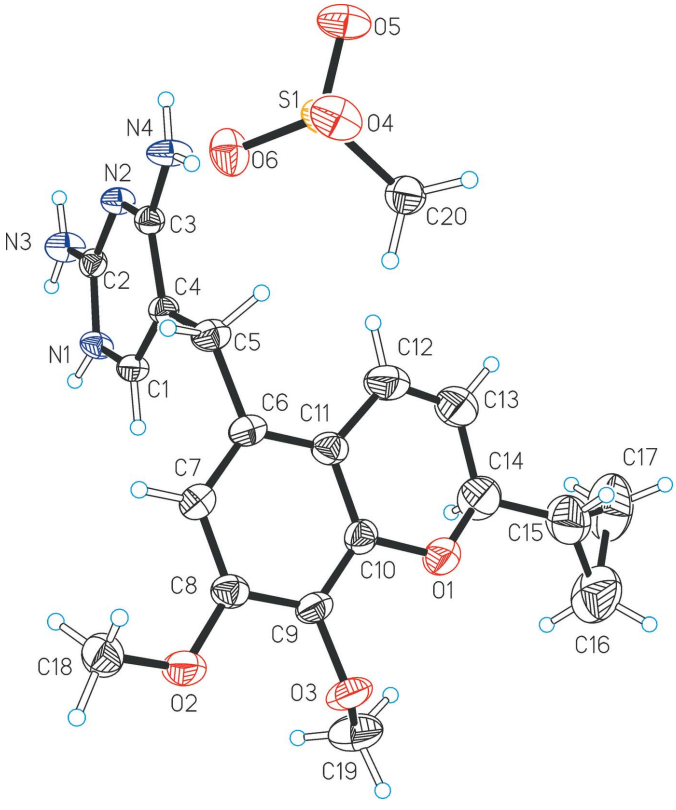


Figure 1
The structures of the molecular entities with displacement ellipsoids drawn at the 50% probability level and hydrogen atoms drawn as spheres of arbitrary size.

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*N*···O4^{i}	0.85 (3)	1.99 (3)	2.827 (2)	168 (3)
N3—H3*A*···O5^{i}	0.86 (2)	2.06 (2)	2.896 (3)	166 (2)
N3—H3*B*···O5^{ii}	0.87 (2)	2.15 (2)	2.871 (3)	140 (2)
N4—H4*A*···N2^{ii}	0.87 (2)	2.27 (2)	3.107 (3)	163 (2)
N4—H4*B*···O6	0.86 (2)	2.11 (2)	2.948 (3)	163 (2)

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

These hydrogen-bond donor functions are engaged in five distinct intermolecular N—H···*A* interactions (Table 1). N1 and N3 are linked to two O sites, each belonging to the same mesylate anion, *i.e.* N1—H1*N*···O4^{i} and N3—H3*A*···O5^{i}. In Fig. 2, the resulting ring motif is denoted as *a*, and it has the graph-set symbol $R_2^2(8)$ (Etter *et al.*, 1990; Bernstein *et al.*, 1995). N3 is additionally linked, *via* an N3—H3*B*···O5^{ii} interaction, to a second mesylate unit. The resulting centrosymmetric ring *b* (Fig. 2) comprises two iclaprim and two mesylate units (with O5 accepting two hydrogen bonds) and is described by the symbol $R_4^2(8)$. The second NH_2 group forms an N4—H4*B*···O6 interaction with a mesylate anion, and it is also hydrogen-bonded to the unprotonated pyrimidine N atom of a second iclaprim molecule *via* N4—H4*A*···N2^{ii}. The latter two interactions generate two additional ring motifs, namely the $R_3^3(10)$ ring *c* linking two pyrimidine molecules with one anion and the centrosymmetric $R_2^2(8)$ ring *d*. The diagram in Fig. 2 illustrates that certain hydrogen-bonded rings are fused together because of shared N—H···*A* interactions, *i.e.* *a* + *b*, *b* + *c* and *c* + *d*. Altogether, the five distinct interactions listed in Table 1 result in a one-dimensional extended molecular tape structure of hydrogen-bonded iclaprim and mesylate units propagating parallel to [$\bar{1}$10]. The

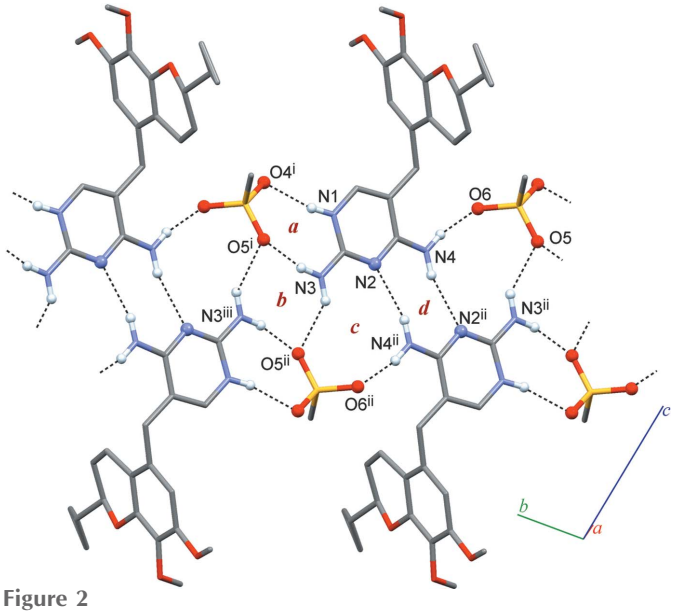


Figure 2
Tape structure composed of N—H···O and N—H···N-bonded iclaprim and mesylate molecules, based on four essential ring motifs (*a*–*d*). [Symmetry codes: (i) $x-1, y+1, z$; (ii) $-x, -y+1, -z$; (iii) $-x-1, y+2, z$.]

iclaprim molecule is bonded to two different mesylate anions, one is a two-point and the other a one-point connection. It is also two-point connected to a neighbouring iclaprim molecule. In turn, the mesylate anion accepts four hydrogen-bonds from three iclaprim molecules, and all of its O atoms participate in hydrogen bonding.

4. Database survey

The Cambridge Structural Database (version 5.43, September 2022; Groom *et al.*, 2016) contains two other examples of molecules displaying the 7,8-dimethoxy-2*H*-chromene fragment, namely methylripariochromene A (Guerin *et al.*, 1989; CSD refcode JAZLIF) and 6,7,8-trimethoxycoumarin (Saidi *et al.*, 2007; CSD refcode KIKDOY). In each case, the 7- and 8-methoxy substituents are significantly twisted out of the ring plane as shown by the corresponding torsion angles, *i.e.* molecule *A* of JAZLIF: 63.4°,–66.2°; molecule *B* of JAZLIF: −140.2°, 89.4°; KIKDOY: 88.0, −110.9°.

5. Synthesis and crystallization

Iclaprim mesylate was prepared according to a modified procedure based on the original synthesis by Jaeger *et al.* (2005) shown in Fig. 3. The iclaprim free base (500 mg, 1.41 mmol) was suspended in 75 ml of acetonitrile and heated to reflux. The resulting clear solution was slowly cooled to room temperature overnight and then kept at 253 K to complete the crystallization process. The resulting white solid was isolated by filtration and dried under high vacuum at room temperature. The obtained iclaprim free base (1.00 g, 2.82 mmol) was recrystallized in acetonitrile and was suspended in 35 ml of ethanol and heated to reflux. Heating was interrupted and a solution of 183 ml methylsulfonic acid (2.82 mmol) in 5 ml of ethanol was added in a dropwise manner. Refluxing was resumed and a further 10 ml of ethanol were added to obtain a clear solution. The solution was concentrated and allowed to cool slowly to room temperature, at which point aggregates of colourless columnar crystals started to form. The crystals were isolated *via* filtration and dried under high vacuum overnight; yield: 900 mg (71%).

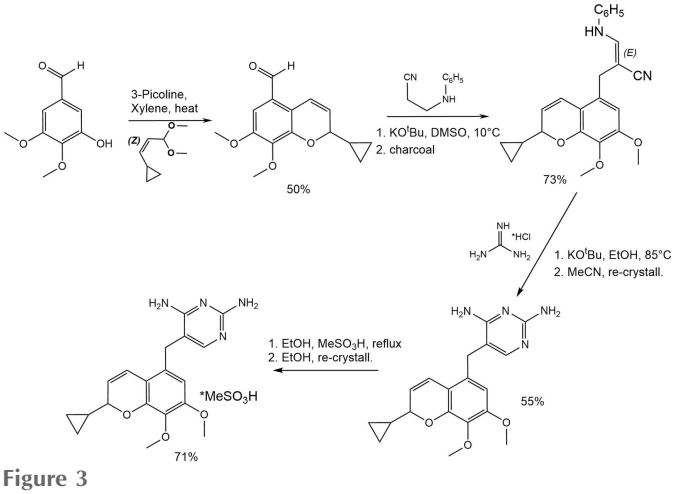


Figure 3
Synthesis scheme to prepare iclaprim.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{19}H_{23}N_4O_3^+\cdot CH_3O_3S^-$
M_r	450.51
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	223
a, b, c (Å)	5.4726 (3), 8.8450 (4), 22.1395 (11)
α, β, γ (°)	98.094 (2), 93.754 (2), 98.919 (2)
V (Å^3)	1043.98 (9)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.20
Crystal size (mm)	0.21 × 0.18 × 0.03
Data collection	
Diffractometer	Bruker D8 QUEST PHOTON 100
Absorption correction	Multi-scan (*TWINABS*; Bruker, 2013)
T_{min}, T_{max}	0.910, 0.971
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3851, 3851, 3507
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.604
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.043, 0.104, 1.08
No. of reflections	3851
No. of parameters	320
No. of restraints	10
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.57, −0.31

Computer programs: *APEX3* and *SAINT* (Bruker, 2013), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*), *XP* in *SHELXTL* (Sheldrick, 2008), *Mercury* (Macrae *et al.*, 2020), *PLATON* (Spek, 2020) and *publCIF* (Westrip, 2010).

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The structure was refined as a two-component twin with the components being related by a 179.9° rotation about the *a* axis. The refined value of the minor twin component fraction was 0.260 (1). All H atoms were identified in difference-Fourier maps and those of NH and NH_2 groups were refined with a restrained N—H distance of 0.88 (2) Å and their U_{iso} parameters refined freely. The H atoms at the cyclopropyl ring (C15, C16, C17) were refined with a restrained C—H distance of 0.96 (2) Å and with U_{iso}(H) = 1.2U_{eq}(C). Other H atoms bonded to secondary CH_2 (C—H = 0.98 Å) or aromatic CH (C—H = 0.94 Å) carbon atoms were positioned geometrically. Their U_{iso} parameters were set to 1.2U_{eq}(C). Methyl H atoms were idealized and included as rigid groups allowed to rotate but not tip (C—H = 0.97 Å) and their U_{iso} parameters were set to 1.5 U_{eq}(C) of the parent carbon atom.

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supporting information

Acta Cryst. (2023). E**79**, 24-27 [https://doi.org/10.1107/S2056989022011689]

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Computing details

Data collection: *APEX3* (Bruker, 2013); cell refinement: *SAINT* (Bruker, 2013); data reduction: *SAINT* (Bruker, 2013); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015b); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 2008), *Mercury* (Macrae *et al.*, 2020); software used to prepare material for publication: *PLATON* (Spek, 2020) and *publCIF* (Westrip, 2010).

2,6-Diamino-5-[(2-cyclopropyl-7,8-dimethoxy-*2H*-1-benzopyran-5-yl)methyl]pyrimidin-1-ium methanesulfonate

Crystal data

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b = 8.8450 (4) Å
c = 22.1395 (11) Å
α = 98.094 (2)°
β = 93.754 (2)°
γ = 98.919 (2)°
V = 1043.98 (9) Å^3
Z = 2
$F(000)$ = 476
D_x = 1.433 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9886 reflections
θ = 2.3–25.3°
μ = 0.20 mm^{-1}
T = 223 K
Prism, colourless
0.21 × 0.18 × 0.03 mm

Data collection

Bruker D8 QUEST PHOTON 100 diffractometer
Radiation source: Incoatec Microfocus
Multi layered optics monochromator
Detector resolution: 10.4 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan (*TWINABS*; Bruker, 2013)
T_{min} = 0.910, T_{max} = 0.971
3851 measured reflections
3851 independent reflections
3507 reflections with $I > 2\sigma(I)$
θ_{max} = 25.4°, θ_{min} = 2.4°
h = −6→6
k = −10→10
l = −26→10

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.104
S = 1.08
3851 reflections
320 parameters
10 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0406P)^2 + 0.7995P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.57 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

Extinction correction: SHELXL, $Fc^{*}=kFc[1+0.001xFc^{2}\lambda^{3}/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.026 (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.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.3058 (4)	0.7951 (2)	0.38547 (8)	0.0428 (5)
O2	0.9479 (4)	1.1480 (2)	0.33158 (8)	0.0413 (5)
O3	0.6716 (4)	1.0418 (2)	0.41560 (7)	0.0418 (5)
N1	0.0557 (4)	0.9523 (2)	0.10508 (8)	0.0239 (4)
H1N	0.015 (5)	1.042 (3)	0.1116 (12)	0.035 (7)*
N2	0.0189 (3)	0.7157 (2)	0.03914 (8)	0.0240 (4)
N3	−0.2450 (4)	0.8895 (2)	0.02407 (10)	0.0314 (5)
H3A	−0.292 (5)	0.976 (2)	0.0359 (11)	0.030 (7)*
H3B	−0.318 (5)	0.831 (3)	−0.0091 (10)	0.041 (8)*
N4	0.2945 (4)	0.5524 (2)	0.05307 (9)	0.0296 (4)
H4A	0.215 (5)	0.491 (3)	0.0214 (10)	0.042 (8)*
H4B	0.416 (4)	0.528 (3)	0.0742 (11)	0.034 (7)*
C1	0.2336 (4)	0.9125 (2)	0.14129 (10)	0.0230 (5)
H1	0.3024	0.9821	0.1765	0.028*
C2	−0.0565 (4)	0.8502 (2)	0.05556 (9)	0.0219 (4)
C3	0.2094 (4)	0.6806 (2)	0.07298 (9)	0.0216 (4)
C4	0.3182 (4)	0.7772 (2)	0.12931 (9)	0.0210 (4)
C5	0.5138 (5)	0.7290 (3)	0.17050 (10)	0.0287 (5)
H5A	0.4704	0.6177	0.1715	0.034*
H5B	0.6731	0.7464	0.1527	0.034*
C6	0.5457 (4)	0.8135 (3)	0.23546 (10)	0.0263 (5)
C7	0.7329 (4)	0.9416 (3)	0.25216 (10)	0.0280 (5)
H7	0.8359	0.9748	0.2226	0.034*
C8	0.7705 (4)	1.0212 (3)	0.31165 (10)	0.0291 (5)
C9	0.6184 (5)	0.9716 (3)	0.35590 (10)	0.0292 (5)
C10	0.4339 (5)	0.8453 (3)	0.33923 (10)	0.0289 (5)
C11	0.3909 (5)	0.7643 (3)	0.27896 (10)	0.0297 (5)
C12	0.1991 (6)	0.6280 (3)	0.26835 (13)	0.0480 (7)
H12	0.1796	0.5622	0.2305	0.058*
C13	0.0514 (6)	0.5956 (3)	0.31140 (14)	0.0506 (8)
H13	−0.0684	0.5052	0.3038	0.061*
C14	0.0691 (5)	0.6975 (4)	0.37117 (13)	0.0477 (7)
H14	−0.0506	0.7688	0.3658	0.057*
C15	0.0006 (7)	0.6284 (4)	0.42415 (16)	0.0603 (9)
H15	0.088 (6)	0.537 (3)	0.4274 (16)	0.072*
C16	−0.0784 (9)	0.7122 (6)	0.47930 (19)	0.0775 (11)

H16A	−0.051 (8)	0.687 (5)	0.5200 (11)	0.093*
H16B	−0.082 (9)	0.821 (3)	0.4736 (19)	0.093*
C17	−0.2553 (8)	0.5873 (6)	0.4384 (2)	0.0800 (12)
H17A	−0.310 (8)	0.490 (3)	0.4518 (19)	0.096*
H17B	−0.369 (7)	0.614 (5)	0.4075 (15)	0.096*
C18	1.1370 (5)	1.1840 (3)	0.29246 (12)	0.0407 (6)
H18A	1.2567	1.2718	0.3128	0.061*
H18B	1.0637	1.2093	0.2549	0.061*
H18C	1.2199	1.0953	0.2830	0.061*
C19	0.4888 (7)	1.1252 (4)	0.44003 (14)	0.0568 (8)
H19A	0.5389	1.1668	0.4827	0.085*
H19B	0.3308	1.0562	0.4368	0.085*
H19C	0.4719	1.2095	0.4172	0.085*
S1	0.73446 (11)	0.29318 (6)	0.12358 (2)	0.02483 (16)
O4	0.9826 (3)	0.26069 (18)	0.14030 (8)	0.0348 (4)
O5	0.5834 (3)	0.16098 (19)	0.08426 (8)	0.0381 (4)
O6	0.7365 (3)	0.43739 (19)	0.09992 (8)	0.0362 (4)
C20	0.5874 (5)	0.3152 (3)	0.19206 (11)	0.0339 (6)
H20A	0.5974	0.2263	0.2127	0.051*
H20B	0.4145	0.3227	0.1827	0.051*
H20C	0.6694	0.4086	0.2185	0.051*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0498 (11)	0.0446 (10)	0.0295 (9)	−0.0066 (9)	0.0072 (8)	0.0039 (8)
O2	0.0414 (11)	0.0421 (10)	0.0327 (9)	−0.0078 (8)	0.0035 (8)	−0.0043 (8)
O3	0.0470 (12)	0.0497 (11)	0.0230 (8)	0.0026 (9)	0.0004 (8)	−0.0070 (7)
N1	0.0272 (10)	0.0169 (9)	0.0275 (10)	0.0082 (8)	−0.0012 (8)	0.0003 (7)
N2	0.0252 (10)	0.0222 (9)	0.0236 (9)	0.0068 (8)	−0.0005 (8)	−0.0014 (7)
N3	0.0311 (11)	0.0299 (11)	0.0323 (11)	0.0133 (9)	−0.0084 (9)	−0.0021 (9)
N4	0.0301 (11)	0.0273 (10)	0.0288 (10)	0.0134 (9)	−0.0077 (9)	−0.0094 (8)
C1	0.0248 (11)	0.0207 (10)	0.0221 (10)	0.0037 (9)	−0.0009 (9)	−0.0002 (8)
C2	0.0227 (11)	0.0224 (10)	0.0214 (10)	0.0048 (9)	0.0037 (9)	0.0041 (8)
C3	0.0221 (11)	0.0206 (10)	0.0217 (10)	0.0036 (9)	0.0026 (9)	0.0018 (8)
C4	0.0222 (11)	0.0204 (10)	0.0201 (10)	0.0041 (9)	0.0025 (9)	0.0013 (8)
C5	0.0334 (13)	0.0278 (11)	0.0256 (11)	0.0133 (10)	−0.0025 (10)	−0.0002 (9)
C6	0.0306 (12)	0.0270 (11)	0.0226 (11)	0.0145 (10)	−0.0033 (9)	0.0003 (9)
C7	0.0283 (12)	0.0320 (12)	0.0247 (11)	0.0085 (10)	0.0025 (9)	0.0040 (9)
C8	0.0291 (13)	0.0280 (11)	0.0288 (12)	0.0052 (10)	−0.0027 (10)	0.0017 (9)
C9	0.0342 (13)	0.0318 (12)	0.0205 (11)	0.0071 (10)	−0.0019 (9)	0.0005 (9)
C10	0.0348 (13)	0.0284 (11)	0.0251 (11)	0.0090 (10)	0.0017 (10)	0.0059 (9)
C11	0.0321 (13)	0.0267 (11)	0.0291 (11)	0.0064 (10)	−0.0038 (11)	0.0020 (9)
C12	0.0526 (18)	0.0426 (15)	0.0401 (15)	−0.0066 (14)	0.0002 (14)	−0.0057 (12)
C13	0.0493 (18)	0.0459 (16)	0.0488 (17)	−0.0112 (14)	0.0013 (14)	0.0034 (13)
C14	0.0366 (15)	0.0582 (18)	0.0450 (16)	−0.0016 (13)	0.0020 (13)	0.0079 (13)
C15	0.061 (2)	0.0572 (19)	0.062 (2)	−0.0019 (17)	0.0203 (17)	0.0109 (16)
C16	0.072 (3)	0.097 (3)	0.064 (2)	0.002 (3)	0.026 (2)	0.019 (2)

C17	0.046 (2)	0.112 (3)	0.089 (3)	0.002 (2)	0.014 (2)	0.048 (3)
C18	0.0365 (15)	0.0428 (14)	0.0404 (14)	−0.0013 (12)	0.0012 (12)	0.0081 (12)
C19	0.069 (2)	0.0547 (18)	0.0415 (16)	0.0133 (17)	0.0076 (15)	−0.0144 (13)
S1	0.0219 (3)	0.0225 (3)	0.0302 (3)	0.0083 (2)	−0.0031 (2)	0.0019 (2)
O4	0.0245 (9)	0.0312 (8)	0.0486 (10)	0.0121 (7)	−0.0063 (8)	0.0022 (7)
O5	0.0330 (9)	0.0345 (9)	0.0417 (10)	0.0086 (8)	−0.0085 (8)	−0.0093 (7)
O6	0.0366 (10)	0.0325 (9)	0.0468 (10)	0.0173 (8)	0.0103 (8)	0.0150 (7)
C20	0.0357 (14)	0.0319 (12)	0.0333 (13)	0.0051 (11)	0.0015 (11)	0.0034 (10)

Geometric parameters (Å, º)

O1—C10	1.365 (3)	C10—C11	1.410 (3)
O1—C14	1.431 (3)	C11—C12	1.451 (4)
O2—C8	1.364 (3)	C12—C13	1.323 (4)
O2—C18	1.420 (3)	C12—H12	0.9400
O3—C9	1.371 (3)	C13—C14	1.481 (4)
O3—C19	1.423 (4)	C13—H13	0.9400
N1—C1	1.341 (3)	C14—C15	1.441 (4)
N1—C2	1.362 (3)	C14—H14	0.9900
N1—H1N	0.85 (3)	C15—C17	1.458 (5)
N2—C2	1.330 (3)	C15—C16	1.463 (5)
N2—C3	1.345 (3)	C15—H15	1.007 (18)
N3—C2	1.325 (3)	C16—C17	1.500 (6)
N3—H3A	0.857 (17)	C16—H16A	0.965 (19)
N3—H3B	0.869 (17)	C16—H16B	0.988 (19)
N4—C3	1.322 (3)	C17—H17A	0.958 (19)
N4—H4A	0.871 (17)	C17—H17B	0.971 (19)
N4—H4B	0.863 (17)	C18—H18A	0.9700
C1—C4	1.347 (3)	C18—H18B	0.9700
C1—H1	0.9400	C18—H18C	0.9700
C3—C4	1.444 (3)	C19—H19A	0.9700
C4—C5	1.510 (3)	C19—H19B	0.9700
C5—C6	1.510 (3)	C19—H19C	0.9700
C5—H5A	0.9800	S1—O6	1.4442 (16)
C5—H5B	0.9800	S1—O5	1.4588 (17)
C6—C7	1.394 (3)	S1—O4	1.4658 (17)
C6—C11	1.395 (3)	S1—C20	1.763 (2)
C7—C8	1.390 (3)	C20—H20A	0.9700
C7—H7	0.9400	C20—H20B	0.9700
C8—C9	1.400 (3)	C20—H20C	0.9700
C9—C10	1.375 (3)		
C10—O1—C14	119.5 (2)	C12—C13—C14	122.0 (3)
C8—O2—C18	117.48 (19)	C12—C13—H13	119.0
C9—O3—C19	115.4 (2)	C14—C13—H13	119.0
C1—N1—C2	119.79 (18)	O1—C14—C15	109.1 (2)
C1—N1—H1N	121.2 (18)	O1—C14—C13	112.5 (2)
C2—N1—H1N	118.9 (18)	C15—C14—C13	118.4 (3)

C2—N2—C3	118.52 (18)	O1—C14—H14	105.2
C2—N3—H3A	119.3 (18)	C15—C14—H14	105.2
C2—N3—H3B	121.4 (19)	C13—C14—H14	105.2
H3A—N3—H3B	119 (3)	C14—C15—C17	123.6 (4)
C3—N4—H4A	118.4 (19)	C14—C15—C16	124.3 (3)
C3—N4—H4B	119.0 (18)	C17—C15—C16	61.8 (3)
H4A—N4—H4B	122 (3)	C14—C15—H15	110 (2)
N1—C1—C4	122.8 (2)	C17—C15—H15	108 (2)
N1—C1—H1	118.6	C16—C15—H15	120 (2)
C4—C1—H1	118.6	C15—C16—C17	58.9 (3)
N3—C2—N2	120.8 (2)	C15—C16—H16A	124 (3)
N3—C2—N1	117.59 (19)	C17—C16—H16A	112 (3)
N2—C2—N1	121.6 (2)	C15—C16—H16B	109 (3)
N4—C3—N2	117.50 (19)	C17—C16—H16B	118 (3)
N4—C3—C4	120.4 (2)	H16A—C16—H16B	120 (4)
N2—C3—C4	122.07 (19)	C15—C17—C16	59.3 (3)
C1—C4—C3	114.73 (19)	C15—C17—H17A	120 (3)
C1—C4—C5	123.42 (19)	C16—C17—H17A	120 (3)
C3—C4—C5	121.84 (18)	C15—C17—H17B	110 (3)
C6—C5—C4	114.54 (18)	C16—C17—H17B	120 (3)
C6—C5—H5A	108.6	H17A—C17—H17B	114 (4)
C4—C5—H5A	108.6	O2—C18—H18A	109.5
C6—C5—H5B	108.6	O2—C18—H18B	109.5
C4—C5—H5B	108.6	H18A—C18—H18B	109.5
H5A—C5—H5B	107.6	O2—C18—H18C	109.5
C7—C6—C11	119.7 (2)	H18A—C18—H18C	109.5
C7—C6—C5	119.6 (2)	H18B—C18—H18C	109.5
C11—C6—C5	120.8 (2)	O3—C19—H19A	109.5
C8—C7—C6	121.3 (2)	O3—C19—H19B	109.5
C8—C7—H7	119.3	H19A—C19—H19B	109.5
C6—C7—H7	119.3	O3—C19—H19C	109.5
O2—C8—C7	125.0 (2)	H19A—C19—H19C	109.5
O2—C8—C9	115.5 (2)	H19B—C19—H19C	109.5
C7—C8—C9	119.5 (2)	O6—S1—O5	113.41 (11)
O3—C9—C10	121.8 (2)	O6—S1—O4	113.82 (11)
O3—C9—C8	119.0 (2)	O5—S1—O4	111.29 (10)
C10—C9—C8	119.0 (2)	O6—S1—C20	105.55 (11)
O1—C10—C9	116.1 (2)	O5—S1—C20	105.63 (12)
O1—C10—C11	121.4 (2)	O4—S1—C20	106.36 (11)
C9—C10—C11	122.4 (2)	S1—C20—H20A	109.5
C6—C11—C10	118.2 (2)	S1—C20—H20B	109.5
C6—C11—C12	125.0 (2)	H20A—C20—H20B	109.5
C10—C11—C12	116.7 (2)	S1—C20—H20C	109.5
C13—C12—C11	120.6 (3)	H20A—C20—H20C	109.5
C13—C12—H12	119.7	H20B—C20—H20C	109.5
C11—C12—H12	119.7		
C2—N1—C1—C4	3.6 (3)	C7—C8—C9—C10	−0.3 (3)

C3—N2—C2—N3	−179.3 (2)	C14—O1—C10—C9	161.4 (2)
C3—N2—C2—N1	0.5 (3)	C14—O1—C10—C11	−23.3 (4)
C1—N1—C2—N3	174.6 (2)	O3—C9—C10—O1	0.6 (3)
C1—N1—C2—N2	−5.3 (3)	C8—C9—C10—O1	174.7 (2)
C2—N2—C3—N4	−174.6 (2)	O3—C9—C10—C11	−174.6 (2)
C2—N2—C3—C4	5.9 (3)	C8—C9—C10—C11	−0.5 (4)
N1—C1—C4—C3	2.4 (3)	C7—C6—C11—C10	−1.3 (3)
N1—C1—C4—C5	−178.4 (2)	C5—C6—C11—C10	178.4 (2)
N4—C3—C4—C1	173.2 (2)	C7—C6—C11—C12	−176.3 (2)
N2—C3—C4—C1	−7.3 (3)	C5—C6—C11—C12	3.4 (4)
N4—C3—C4—C5	−6.0 (3)	O1—C10—C11—C6	−173.7 (2)
N2—C3—C4—C5	173.5 (2)	C9—C10—C11—C6	1.3 (4)
C1—C4—C5—C6	20.0 (3)	O1—C10—C11—C12	1.8 (4)
C3—C4—C5—C6	−160.8 (2)	C9—C10—C11—C12	176.7 (2)
C4—C5—C6—C7	−96.5 (3)	C6—C11—C12—C13	−176.0 (3)
C4—C5—C6—C11	83.8 (3)	C10—C11—C12—C13	8.9 (4)
C11—C6—C7—C8	0.5 (3)	C11—C12—C13—C14	1.7 (5)
C5—C6—C7—C8	−179.1 (2)	C10—O1—C14—C15	165.4 (3)
C18—O2—C8—C7	−12.6 (3)	C10—O1—C14—C13	31.8 (4)
C18—O2—C8—C9	167.6 (2)	C12—C13—C14—O1	−21.4 (4)
C6—C7—C8—O2	−179.5 (2)	C12—C13—C14—C15	−150.4 (3)
C6—C7—C8—C9	0.3 (3)	O1—C14—C15—C17	149.3 (4)
C19—O3—C9—C10	−70.3 (3)	C13—C14—C15—C17	−80.3 (5)
C19—O3—C9—C8	115.5 (3)	O1—C14—C15—C16	72.7 (5)
O2—C8—C9—O3	−6.2 (3)	C13—C14—C15—C16	−156.8 (4)
C7—C8—C9—O3	174.0 (2)	C14—C15—C16—C17	113.3 (4)
O2—C8—C9—C10	179.5 (2)	C14—C15—C17—C16	−114.3 (4)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O4^{i}	0.85 (3)	1.99 (3)	2.827 (2)	168 (3)
N3—H3*A*···O5^{i}	0.86 (2)	2.06 (2)	2.896 (3)	166 (2)
N3—H3*B*···O5^{ii}	0.87 (2)	2.15 (2)	2.871 (3)	140 (2)
N4—H4*A*···N2^{ii}	0.87 (2)	2.27 (2)	3.107 (3)	163 (2)
N4—H4*B*···O6	0.86 (2)	2.11 (2)	2.948 (3)	163 (2)

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