IUCrData

ISSN 2414-3146

Meloxicam hydrochloride

Fermin Flores Manuel,[a] Martha Sosa Rivadeneyra[a] and Sylvain Bernès[b]*

[a]Facultad de Ciencias Químicas, Benemérita Universidad Autónoma de Puebla, 72570 Puebla, Pue., Mexico, and [b]Instituto de Física, Benemérita Universidad Autónoma de Puebla, 72570 Puebla, Pue., Mexico. *Correspondence e-mail: sylvain_bernes@hotmail.com

Received 27 February 2023
Accepted 2 March 2023

Edited by I. Brito, University of Antofagasta, Chile

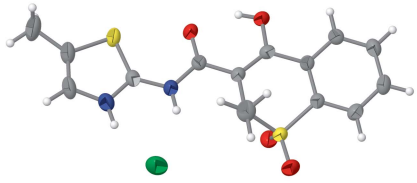
Keywords: crystal structure; meloxicam; thiazole; benzothiazine; polymorphism.

CCDC reference: 2246003

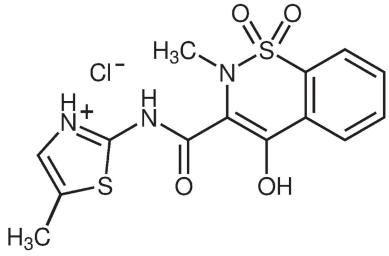
Structural data: full structural data are available from iucrdata.iucr.org

The title salt, $C_{14}H_{14}N_3O_4S_2^+\cdot Cl^-$ [systematic name: 2-(4-hydroxy-2-methyl-1,1-dioxo-1,2-benzothiazine-3-amido)-5-methyl-1,3-thiazol-3-ium chloride] is the hydrochloride derivative of meloxicam, a drug used to treat pain and inflammation in rheumatic disorders and osteoarthritis. Although its molecular structure is similar to that previously reported for the hydrobromide analogue, both salts are not isomorphous. Different crystal structures originate from a conformational modification, arising from a degree of rotational freedom for the thiazolium ring in the cations. By taking as a reference the conformation of meloxicam, the thiazolium ring is twisted by 10.96 and −16.70° in the hydrochloride and hydrobromide salts, while the 1,2-benzothiazine core is a rigid scaffold. This behaviour could explain why meloxicam is a polymorphous compound.

3D view



Chemical scheme



Structure description

Meloxicam [abbreviated hereafter as MX; systematic name: 4-hydroxy-2-methyl-*N*-(5-methyl-1,3-thiazol-2-yl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide] is an achiral benzothiazine drug, practically insoluble in water at physiological pH (Luger *et al.*, 1996). This molecule was patented in 1977, and is currently classified as an antipyretic and non-steroidal anti-inflammatory medication, used for the management of pain and inflammation associated with rheumatoid arthritis and osteoarthritis, in adults and children. In some countries, it has also been approved for use in veterinary medicine. The crystallization of meloxicam is a 'difficult art' (Śniechowska *et al.*, 2021), since four neat polymorphic forms are known, along with one hydrated form (Coppi *et al.*, 2003; Freitas *et al.*, 2017). So far, only the triclinic form I and the hydrated form were structurally characterized by X-ray diffraction (Luger *et al.*, 1996; Fabiola *et al.*, 1998; Fedorov *et al.*, 2019). Actually, the formula of MX·H_2O is not well defined: for the reported structure, the water

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1O···O2	0.84 (2)	1.85 (2)	2.5921 (18)	148 (2)
N1—H1N···Cl1	0.89 (2)	2.16 (2)	2.992 (2)	155.5 (19)
N2—H2N···Cl1	0.87 (2)	2.35 (2)	3.1185 (18)	147.8 (18)
C1—H1D···O4^{i}	0.96	2.62	3.286 (3)	127
C14—H14C···O2^{ii}	0.96	2.52	3.380 (3)	150

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

molecule is disordered over two general positions, with occupancies reported as 0.53 (3) and 0.63 (3).

Among the many meloxicam salts characterized by X-ray diffraction, the hydrobromide was deposited as a CSD communication (Tumanov *et al.*, 2011; CSD refcode: XATJAF). MX·HBr crystallizes in space group $P2_1/c$. The thiazole group is protonated, in such a way that a double-acceptor hydrogen bond is formed with the bromide ion accepting links from the thiazolium and amide NH groups, to form a common $R_2^1(6)$ ring motif with the thiazolium and amide NH groups as donors. The conformation for HMX^+ is close to that observed for neutral MX, owing to an intramolecular hydrogen bond between the enol group in the 1,2-benzothiazine core and the carbonyl group of the amide functionality, which gives the common $S(6)$ motif. We have now determined the structure of the hydrochloride salt, MX·HCl, which also crystallizes in space group $P2_1/c$, although with different unit-cell parameters. The molecular structure of MX·HCl is similar to that of MX·HBr, including the same intramolecular O—H···O and intermolecular N—H···Cl hydrogen bonds (Fig. 1; Table 1, entries 1–3). Molecules are however packed in different ways in both salts, as corroborated by their simulated powder diffraction patterns, which are clearly different (Fig. 2). If the nature of the anion, Cl^- or Br^-, is not taken into account, MX·HBr and MX·HCl can thus be described as polymorphic forms crystallizing in a single space group.

A close examination of the conformation of the cations, and a comparison with the neutral molecule MX (Fabiola *et al.*, 1998; CSD refcode: SEDZOQ) rationalizes this behaviour.

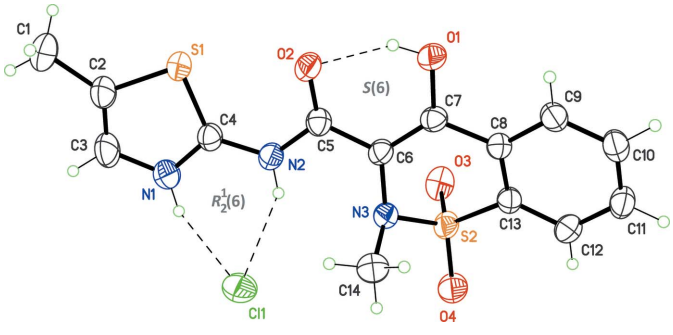


Figure 1
Molecular structure of the title compound, with displacement ellipsoids at the 50% probability level for non-H atoms. Dashed lines represent intramolecular hydrogen bonds (Table 1, entries 1–3). The labelling scheme is that adopted for MX·HBr (Tumanov *et al.*, 2011).

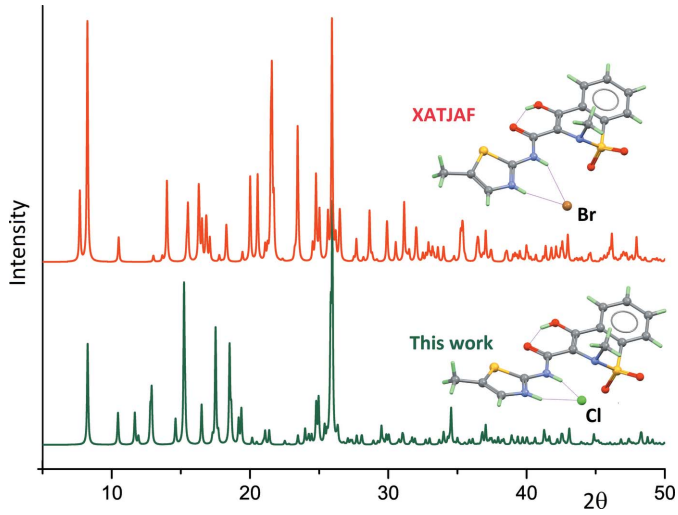


Figure 2
Simulated powder X-ray diffraction patterns for MX·HBr (top, pattern calculated using the deposited Cif file for XATJAF; Tumanov *et al.*, 2011) and MX·HCl (bottom). Patterns were calculated with *Mercury* (Macrae *et al.*, 2020), assuming the Cu Kα radiation. Molecular structures are represented along with their patterns.

Assuming that the 1,2-benzothiazine core is a rigid moiety, an overlay between HMX^+ in both salts and MX shows that the thiazolium ring has some degree of rotational freedom. Taking MX as reference, the HMX^+ cation has its thiazolium ring twisted by 10.96° in MX·HCl and by −16.70° in MX·HBr (Fig. 3). This rotation over a range of *ca* 25° is sufficient to enable the formation of distinct secondary intermolecular contacts (Table 1, entries 4 and 5), which, in turn, alter the packing of the cations in the crystal. By widening this behaviour to meloxicam, for which the rotation of the thiazole group is less restrained, since no $R_2^1(6)$ ring motif involving an halide ion is present, one would assume that the rich poly-

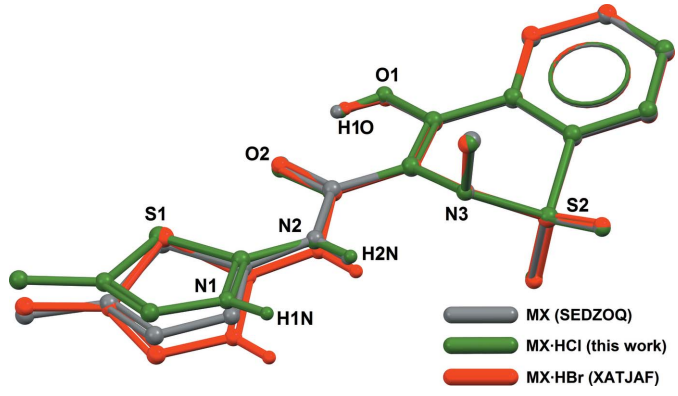


Figure 3
Overlay between meloxicam (grey), MX·HBr (red) and MX·HCl (green), calculated with *Mercury* (Macrae *et al.*, 2020). The fits were carried out using atoms belonging to the 1,2-benzothiazine core (14 atoms), while the amide and thiazole groups were kept free. The r.m.s. deviations for the fits are better than 0.04 Å. For the structure of the neutral molecule MX, which has been reported three times, refcode SEDZOQ was retained (Fabiola *et al.*, 1998), in order to have all models at room temperature. For clarity, halide anions are omitted, as well as H atoms bonded to C atoms. Note that in MX, the thiazole ring is not protonated.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{14}H_{14}N_3O_4S_2^+\cdot Cl^-$
M_r	387.85
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	295
a, b, c (Å)	11.3380 (6), 10.7346 (5), 14.5503 (10)
β (°)	109.430 (5)
V (Å^3)	1670.05 (17)
Z	4
Radiation type	Ag $K\alpha$, λ = 0.56083 Å
μ (mm^{-1})	0.26
Crystal size (mm)	0.23 × 0.09 × 0.07
Data collection	
Diffractometer	Stoe Stadivari
Absorption correction	Multi-scan *X-AREA* 1.88 (Stoe & Cie, 2019)
T_{min}, T_{max}	0.407, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	40949, 3902, 2285
R_{int}	0.088
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.653
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.032, 0.074, 0.83
No. of reflections	3902
No. of parameters	234
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.26, −0.24

Computer programs: *X-AREA* 1.88 (Stoe & Cie, 2019), *SHELXT2018/2* (Sheldrick, 2015*a*), *SHELXL2018/3* (Sheldrick, 2015*b*), *XP* in *SHELXTL-Plus* (Sheldrick, 2008), *Mercury* (Macrae *et al.*, 2020) and *publCIF* (Westrip, 2010).

morphism observed for this drug is also associated to similar conformational modifications.

Synthesis and crystallization

Meloxicam hydrochloride was unintentionally crystallized while screening slurry co-crystallizations using derivatives of (*S*)-α-methylbenzylamine or L-proline as coformers. In some experiments, an amount of a 0.02 *N* HCl solution was added to the slurry, for the purpose of modifying the pH of the medium. Single crystals of the MX·HCl salt were recovered from these slurries.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Funding information

Funding for this research was provided by: Consejo Nacional de Ciencia y Tecnología (grant No. 268178).

References

Coppi, L., Bartra Sanmartí, M. & Closa Clavo, M. (2003). US patent 2003/0109701 A1.

Fabiola, G. F., Pattabhi, V., Manjunatha, S. G., Rao, G. V. & Nagarajan, K. (1998). *Acta Cryst.* C**54**, 2001–2003.

Fedorov, A. Y., Drebushchak, T. N. & Tantardini, C. (2019). *Comput. Theor. Chem.* **1157**, 47–53.

Jacon Freitas, J. T., Santos Viana, O. M. M., Bonfilio, R., Doriguetto, A. C. & de Araújo, M. B. (2017). *Eur. J. Pharm. Sci.* **109**, 347–358.

Luger, P., Daneck, K., Engel, W., Trummlitz, G. & Wagner, K. (1996). *Eur. J. Pharm. Sci.* **4**, 175–187.

Macrae, C. F., Sovago, I., Cottrell, S. J., Galek, P. T. A., McCabe, P., Pidcock, E., Platings, M., Shields, G. P., Stevens, J. S., Towler, M. & Wood, P. A. (2020). *J. Appl. Cryst.* **53**, 226–235.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.

Śniechowska, J., Paluch, P. & Dudek, M. K. (2021). *Acta Cryst.* A**77**, C897.

Stoe & Cie (2019). *X-AREA* and *X-RED32*, Stoe & Cie, Darmstadt, Germany.

Tumanov, N., Dyakonova, M., Pankrushina, N. & Shahtshneider, T. P. (2011). CSD Communication (refcode XATJAF, CCDC 832082). CCDC, Cambridge, England.

Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.

full crystallographic data

IUCrData (2023). **8**, x230202 [https://doi.org/10.1107/S2414314623002020X]

Meloxicam hydrochloride

Fermin Flores Manuel, Martha Sosa Rivadeneyra and Sylvain Bernès

2-(4-Hydroxy-2-methyl-1,1-dioxo-1,2-benzothiazine-3-amido)-5-methyl-1,3-thiazol-3-ium chloride

Crystal data

$C_{14}H_{14}N_3O_4S_2^+\cdot Cl^-$
M_r = 387.85
Monoclinic, $P2_1/c$
a = 11.3380 (6) Å
b = 10.7346 (5) Å
c = 14.5503 (10) Å
β = 109.430 (5)°
V = 1670.05 (17) Å^3
Z = 4
$F(000)$ = 800
D_x = 1.543 Mg m^{-3}
Ag $K\alpha$ radiation, λ = 0.56083 Å
Cell parameters from 19546 reflections
θ = 2.2–26.5°
μ = 0.26 mm^{-1}
T = 295 K
Block, yellow
0.23 × 0.09 × 0.07 mm

Data collection

Stoe Stadivari diffractometer
Radiation source: Sealed X-ray tube, Axo Astix-f Microfocus source
Graded multilayer mirror monochromator
Detector resolution: 5.81 pixels mm^{-1}
ω scans
Absorption correction: multi-scan X-AREA 1.88 (Stoe & Cie, 2019)
T_{min} = 0.407, T_{max} = 1.000
40949 measured reflections
3902 independent reflections
2285 reflections with $I > 2\sigma(I)$
R_{int} = 0.088
θ_{max} = 21.5°, θ_{min} = 2.2°
h = −14→14
k = −14→14
l = −19→19

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.032
$wR(F^2)$ = 0.074
S = 0.83
3902 reflections
234 parameters
0 restraints
0 constraints
Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0329P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Special details

Refinement. All H atoms bonded to heteroatoms (H1O, H1N and H2N) were refined with free coordinates, and remaining H atoms were placed in idealized positions, with C—H bond lengths constrained to 0.96 (methyl groups) or 0.93 Å (aromatic CH). All H atoms were refined with calculated isotropic displacement parameters.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.97139 (5)	0.37304 (6)	0.36101 (5)	0.05872 (19)
S1	0.78018 (5)	0.80065 (5)	0.39329 (4)	0.04065 (15)
S2	0.63352 (4)	0.19526 (5)	0.43965 (4)	0.03731 (14)
O1	0.39766 (12)	0.51274 (13)	0.39149 (12)	0.0416 (4)
H1O	0.441 (2)	0.576 (2)	0.3941 (18)	0.062*
O2	0.59216 (11)	0.64257 (12)	0.39574 (11)	0.0402 (4)
O3	0.67314 (12)	0.23387 (14)	0.53969 (11)	0.0463 (4)
O4	0.68678 (13)	0.08624 (14)	0.41315 (13)	0.0544 (5)
N1	0.94397 (15)	0.64715 (18)	0.38545 (14)	0.0421 (5)
H1N	0.9763 (19)	0.572 (2)	0.3827 (16)	0.050*
N2	0.76883 (14)	0.54411 (16)	0.39712 (14)	0.0355 (4)
H2N	0.8075 (18)	0.4746 (19)	0.3955 (16)	0.043*
N3	0.65464 (13)	0.31354 (15)	0.37489 (13)	0.0338 (4)
C1	0.9370 (2)	0.9923 (2)	0.3668 (2)	0.0715 (9)
H1B	0.886168	1.017468	0.302491	0.107*
H1C	1.023451	1.007147	0.375131	0.107*
H1D	0.913849	1.039311	0.414236	0.107*
C2	0.91763 (19)	0.8566 (2)	0.37994 (18)	0.0474 (6)
C3	0.9929 (2)	0.7626 (2)	0.37786 (18)	0.0503 (6)
H3	1.071320	0.773685	0.371823	0.060*
C4	0.83125 (16)	0.65175 (18)	0.39320 (15)	0.0336 (5)
C5	0.64622 (16)	0.54299 (19)	0.39282 (15)	0.0329 (5)
C6	0.58544 (16)	0.42257 (18)	0.38367 (15)	0.0314 (5)
C7	0.46600 (16)	0.41332 (18)	0.38478 (15)	0.0315 (5)
C8	0.40231 (15)	0.29411 (18)	0.38082 (14)	0.0304 (4)
C9	0.27306 (16)	0.28810 (19)	0.35974 (15)	0.0362 (5)
H9	0.226126	0.360935	0.350480	0.043*
C10	0.21526 (17)	0.1742 (2)	0.35270 (16)	0.0399 (5)
H10	0.129213	0.170995	0.339433	0.048*
C11	0.28195 (18)	0.0647 (2)	0.36485 (17)	0.0420 (5)
H11	0.240667	−0.011404	0.357289	0.050*
C12	0.41100 (18)	0.06833 (19)	0.38842 (16)	0.0384 (5)
H12	0.457202	−0.004976	0.397669	0.046*
C13	0.46958 (16)	0.18279 (18)	0.39791 (15)	0.0314 (4)
C14	0.6498 (2)	0.2839 (2)	0.27407 (17)	0.0482 (6)
H14A	0.699323	0.211130	0.274864	0.072*
H14B	0.682318	0.352942	0.247956	0.072*
H14C	0.564780	0.268629	0.234186	0.072*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0481 (3)	0.0530 (4)	0.0799 (5)	0.0108 (3)	0.0278 (3)	−0.0043 (4)
S1	0.0437 (3)	0.0326 (3)	0.0513 (4)	−0.0087 (2)	0.0233 (3)	−0.0037 (3)
S2	0.0316 (2)	0.0271 (3)	0.0530 (4)	0.0024 (2)	0.0138 (2)	0.0052 (3)

O1	0.0363 (7)	0.0272 (8)	0.0634 (11)	0.0046 (6)	0.0194 (7)	0.0013 (8)
O2	0.0383 (7)	0.0267 (8)	0.0571 (11)	−0.0007 (6)	0.0179 (7)	0.0027 (7)
O3	0.0430 (7)	0.0456 (9)	0.0426 (10)	−0.0028 (7)	0.0039 (7)	0.0088 (8)
O4	0.0467 (8)	0.0310 (8)	0.0918 (14)	0.0089 (7)	0.0316 (9)	0.0046 (9)
N1	0.0338 (9)	0.0423 (11)	0.0521 (13)	−0.0032 (8)	0.0169 (8)	−0.0026 (10)
N2	0.0326 (8)	0.0290 (9)	0.0457 (12)	−0.0017 (7)	0.0141 (8)	0.0003 (9)
N3	0.0342 (8)	0.0279 (9)	0.0428 (11)	0.0000 (7)	0.0173 (8)	0.0012 (8)
C1	0.0752 (17)	0.0440 (16)	0.110 (3)	−0.0216 (13)	0.0501 (18)	−0.0070 (16)
C2	0.0467 (11)	0.0437 (14)	0.0579 (17)	−0.0157 (11)	0.0254 (12)	−0.0081 (12)
C3	0.0397 (11)	0.0536 (15)	0.0611 (17)	−0.0186 (11)	0.0215 (11)	−0.0060 (13)
C4	0.0311 (9)	0.0348 (12)	0.0344 (13)	−0.0046 (8)	0.0101 (9)	−0.0015 (10)
C5	0.0323 (9)	0.0318 (11)	0.0341 (13)	−0.0008 (9)	0.0104 (9)	0.0034 (10)
C6	0.0315 (9)	0.0251 (10)	0.0378 (13)	0.0008 (8)	0.0116 (9)	0.0023 (9)
C7	0.0341 (9)	0.0270 (10)	0.0333 (13)	0.0031 (8)	0.0111 (9)	0.0021 (9)
C8	0.0316 (9)	0.0291 (11)	0.0320 (12)	−0.0015 (8)	0.0125 (8)	0.0000 (9)
C9	0.0330 (9)	0.0365 (12)	0.0414 (13)	0.0008 (9)	0.0156 (9)	0.0027 (10)
C10	0.0321 (9)	0.0445 (13)	0.0448 (14)	−0.0055 (9)	0.0152 (10)	−0.0001 (11)
C11	0.0443 (11)	0.0367 (13)	0.0475 (15)	−0.0123 (10)	0.0186 (11)	−0.0026 (11)
C12	0.0431 (10)	0.0294 (12)	0.0437 (14)	−0.0011 (9)	0.0156 (10)	0.0015 (10)
C13	0.0305 (8)	0.0298 (11)	0.0350 (12)	−0.0012 (8)	0.0123 (8)	0.0013 (9)
C14	0.0536 (12)	0.0463 (14)	0.0492 (15)	−0.0053 (11)	0.0232 (11)	−0.0096 (12)

Geometric parameters (Å, º)

S1—C4	1.700 (2)	C1—H1D	0.9600
S1—C2	1.740 (2)	C2—C3	1.328 (3)
S2—O4	1.4275 (15)	C3—H3	0.9300
S2—O3	1.4343 (16)	C5—C6	1.450 (3)
S2—N3	1.6455 (17)	C6—C7	1.363 (2)
S2—C13	1.7580 (17)	C7—C8	1.461 (3)
O1—C7	1.341 (2)	C8—C13	1.395 (3)
O1—H1O	0.84 (2)	C8—C9	1.395 (2)
O2—C5	1.240 (2)	C9—C10	1.375 (3)
N1—C4	1.321 (2)	C9—H9	0.9300
N1—C3	1.377 (3)	C10—C11	1.376 (3)
N1—H1N	0.89 (2)	C10—H10	0.9300
N2—C4	1.366 (2)	C11—C12	1.388 (3)
N2—C5	1.371 (2)	C11—H11	0.9300
N2—H2N	0.87 (2)	C12—C13	1.382 (3)
N3—C6	1.438 (2)	C12—H12	0.9300
N3—C14	1.484 (3)	C14—H14A	0.9600
C1—C2	1.495 (3)	C14—H14B	0.9600
C1—H1B	0.9600	C14—H14C	0.9600
C1—H1C	0.9600		
C4—S1—C2	90.37 (10)	O2—C5—C6	123.12 (16)
O4—S2—O3	119.55 (10)	N2—C5—C6	117.12 (17)
O4—S2—N3	108.82 (10)	C7—C6—N3	121.01 (17)

O3—S2—N3	107.58 (9)	C7—C6—C5	120.50 (17)
O4—S2—C13	109.75 (9)	N3—C6—C5	118.49 (15)
O3—S2—C13	108.11 (9)	O1—C7—C6	122.89 (18)
N3—S2—C13	101.50 (9)	O1—C7—C8	114.19 (16)
C7—O1—H1O	107.9 (16)	C6—C7—C8	122.91 (17)
C4—N1—C3	113.59 (19)	C13—C8—C9	118.14 (18)
C4—N1—H1N	117.6 (14)	C13—C8—C7	120.63 (15)
C3—N1—H1N	128.8 (14)	C9—C8—C7	121.23 (17)
C4—N2—C5	122.49 (17)	C10—C9—C8	119.81 (19)
C4—N2—H2N	116.9 (13)	C10—C9—H9	120.1
C5—N2—H2N	120.3 (13)	C8—C9—H9	120.1
C6—N3—C14	114.85 (17)	C9—C10—C11	121.45 (17)
C6—N3—S2	112.92 (13)	C9—C10—H10	119.3
C14—N3—S2	115.87 (14)	C11—C10—H10	119.3
C2—C1—H1B	109.5	C10—C11—C12	119.80 (19)
C2—C1—H1C	109.5	C10—C11—H11	120.1
H1B—C1—H1C	109.5	C12—C11—H11	120.1
C2—C1—H1D	109.5	C13—C12—C11	118.80 (19)
H1B—C1—H1D	109.5	C13—C12—H12	120.6
H1C—C1—H1D	109.5	C11—C12—H12	120.6
C3—C2—C1	127.9 (2)	C12—C13—C8	121.86 (16)
C3—C2—S1	110.25 (17)	C12—C13—S2	121.34 (15)
C1—C2—S1	121.73 (18)	C8—C13—S2	116.68 (14)
C2—C3—N1	113.77 (19)	N3—C14—H14A	109.5
C2—C3—H3	123.1	N3—C14—H14B	109.5
N1—C3—H3	123.1	H14A—C14—H14B	109.5
N1—C4—N2	120.09 (18)	N3—C14—H14C	109.5
N1—C4—S1	112.01 (15)	H14A—C14—H14C	109.5
N2—C4—S1	127.88 (14)	H14B—C14—H14C	109.5
O2—C5—N2	119.75 (18)		

O4—S2—N3—C6	169.71 (13)	N2—C5—C6—N3	−3.0 (3)
O3—S2—N3—C6	−59.40 (14)	N3—C6—C7—O1	−179.05 (19)
C13—S2—N3—C6	54.01 (15)	C5—C6—C7—O1	1.9 (3)
O4—S2—N3—C14	34.30 (16)	N3—C6—C7—C8	2.3 (3)
O3—S2—N3—C14	165.18 (13)	C5—C6—C7—C8	−176.80 (19)
C13—S2—N3—C14	−81.41 (15)	O1—C7—C8—C13	−164.08 (19)
C4—S1—C2—C3	−1.0 (2)	C6—C7—C8—C13	14.7 (3)
C4—S1—C2—C1	175.5 (2)	O1—C7—C8—C9	16.1 (3)
C1—C2—C3—N1	−175.5 (2)	C6—C7—C8—C9	−165.1 (2)
S1—C2—C3—N1	0.7 (3)	C13—C8—C9—C10	−2.5 (3)
C4—N1—C3—C2	0.1 (3)	C7—C8—C9—C10	177.4 (2)
C3—N1—C4—N2	177.2 (2)	C8—C9—C10—C11	−0.8 (3)
C3—N1—C4—S1	−0.9 (2)	C9—C10—C11—C12	2.5 (4)
C5—N2—C4—N1	−171.6 (2)	C10—C11—C12—C13	−0.9 (3)
C5—N2—C4—S1	6.2 (3)	C11—C12—C13—C8	−2.5 (3)
C2—S1—C4—N1	1.08 (18)	C11—C12—C13—S2	173.43 (17)
C2—S1—C4—N2	−176.9 (2)	C9—C8—C13—C12	4.2 (3)

C4—N2—C5—O2	−7.8 (3)	C7—C8—C13—C12	−175.7 (2)
C4—N2—C5—C6	171.4 (2)	C9—C8—C13—S2	−171.96 (16)
C14—N3—C6—C7	95.1 (2)	C7—C8—C13—S2	8.2 (3)
S2—N3—C6—C7	−40.8 (2)	O4—S2—C13—C12	29.6 (2)
C14—N3—C6—C5	−85.8 (2)	O3—S2—C13—C12	−102.42 (19)
S2—N3—C6—C5	138.34 (16)	N3—S2—C13—C12	144.58 (18)
O2—C5—C6—C7	−4.7 (3)	O4—S2—C13—C8	−154.31 (16)
N2—C5—C6—C7	176.1 (2)	O3—S2—C13—C8	73.71 (18)
O2—C5—C6—N3	176.19 (19)	N3—S2—C13—C8	−39.29 (18)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*O*···O2	0.84 (2)	1.85 (2)	2.5921 (18)	148 (2)
N1—H1*N*···Cl1	0.89 (2)	2.16 (2)	2.992 (2)	155.5 (19)
N2—H2*N*···Cl1	0.87 (2)	2.35 (2)	3.1185 (18)	147.8 (18)
C1—H1*D*···O4^{i}	0.96	2.62	3.286 (3)	127
C14—H14*C*···O2^{ii}	0.96	2.52	3.380 (3)	150

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