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Crystal structure of 4,6-diamino-2,2-dimethyl-3-[3-(2,4,5-trichlorophenoxy)-propoxy]-2,3-dihydro-1,3,5-triazin-1-ium chloride methanol monosolvate

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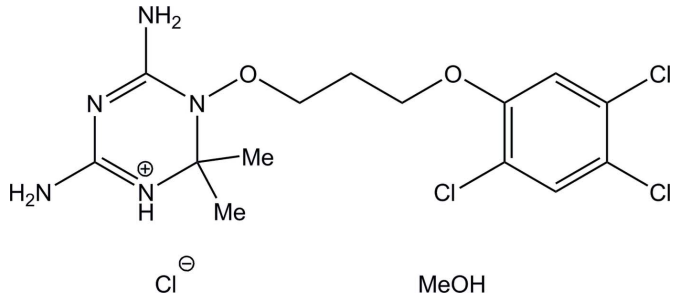
In the title methanol-solvated salt, $C_{14}H_{19}Cl_3N_5O_2^+\cdot Cl^-\cdot CH_3OH$, the triazine molecule is protonated at one of the triazine N atoms. In the crystal, the triazine cations are linked through a pair of N—H···N hydrogen bonds, with graph-set $R_2^2(8)$, forming an inversion dimer. The protonated N atom and the 2- and 4-amino groups of the triazine cation interact with the chloride anion through N—H···Cl hydrogen bonds, leading to the formation of a tape structure running along the *b*-axis direction. A short Cl···Cl contact [3.2937 (9) Å] is observed in the tape. The methanol molecule is linked to the chloride anion and the triazine cation, respectively, by an O—H···Cl hydrogen bond and a C—H···O interaction.

Keywords: crystal structure; triazine; antifolate drug; antimalarial; hydrogen bonding.

CCDC reference: 1414045

1. Related literature

For antifolate antimalarial drugs, see: Toyoda *et al.* (1997); Yuthavong (2002). For antifolate drug resistance, see: Nzila (2006); Rieckmann *et al.* (1996). For our previous work on the protein crystallographic analysis of dihydrofolate reductase, see: Yuvaniyama *et al.* (2003); Kongsaeree *et al.* (2005).



2. Experimental

2.1. Crystal data

$C_{14}H_{19}Cl_3N_5O_2^+\cdot Cl^-\cdot CH_4O$
M_r = 463.18
Triclinic, $P\overline{1}$
a = 8.5930 (4) Å
b = 9.3510 (3) Å
c = 14.6970 (7) Å
α = 75.422 (3)°
β = 78.2260 (19)°
γ = 70.194 (3)°
V = 1066.13 (8) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.58 mm^{-1}
T = 298 K
0.32 × 0.20 × 0.18 mm

2.2. Data collection

Nonius KappaCCD diffractometer
5032 measured reflections
2935 independent reflections
2681 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 23.3°

2.3. Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.087
S = 1.06
2935 reflections
268 parameters
6 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···Cl4^{i}	0.87 (1)	2.27 (1)	3.1236 (17)	167 (2)
N2—H2A···Cl4^{ii}	0.87 (1)	2.64 (2)	3.3285 (17)	137 (2)
N2—H2B···N3^{iii}	0.87 (1)	2.26 (1)	3.122 (2)	170 (2)
N4—H4A···Cl4^{iv}	0.88 (1)	2.31 (1)	3.1419 (19)	158 (2)
O3—H3···Cl4	0.82	2.35	3.166 (2)	176
C14—H14···O3^{v}	0.93	2.53	3.423 (3)	161

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

Data collection: *KappaCCD Software* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2015); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *publCIF* (Westrip, 2010).

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Supporting information for this paper is available from the IUCr electronic archives (Reference: IS5407).

References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.

Kongsaeree, P., Khongsuk, P., Leartsakulpanich, U., Chitnumsub, P., Tarnchompoo, B., Walkinshaw, M. D. & Yuthavong, Y. (2005). *Proc. Natl Acad. Sci. USA*, **102**, 13046–13051.

Nonius (1999). *KappaCCD software*. Nonius BV, Delft, The Netherlands.

Nzila, A. (2006). *J. Antimicrob. Chemother.* **57**, 1043–1054.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.

Rieckmann, K. H., Yeo, A. E. & Edstein, M. D. (1996). *Trans. R. Soc. Trop. Med. Hyg.* **90**, 568–571.

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

Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.

Toyoda, T., Brobey, R. K. B., Sano, G.-I., Horii, T., Tomioka, N. & Itai, A. (1997). *Biochem. Biophys. Res. Commun.* **235**, 515–519.

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

Yuthavong, Y. (2002). *Microbes Infect.* **4**, 175–182.

Yuvaniyama, J., Chitnumsub, P., Kamchonwongpaisan, S., Vanichtanankul, J., Sirawaraporn, W., Taylor, P., Walkinshaw, M. D. & Yuthavong, Y. (2003). *Nat. Struct. Biol.* **10**, 357–365.

supporting information

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Crystal structure of 4,6-diamino-2,2-dimethyl-3-[3-(2,4,5-trichlorophenoxy)-propoxy]-2,3-dihydro-1,3,5-triazin-1-ium chloride methanol monosolvate

Pattarapol Khongsuk, Samran Prabpai and Palangpon Kongsaeree

S1. Comment

The structure of the methanol-solvated salt compound, $C_{14}H_{19}Cl_3N_5O_2^+.Cl^-.CH_3OH$, was determined as part of a structural study of our dihydrofolate reductase (DHFR) in complex with its antifolate inhibitors. WR99210 {systematic name: 6,6-dimethyl-1-[3-(2,4,5-trichlorophenoxy)propoxy]-1,6-dihydro-1,3,5-triazine-2,4-diamine} is a potent inhibitor of dihydrofolate reductase enzyme (DHFR). With a structural resemblance with cycloguanil (Cyc), a metabolite of the antimalarial drug proguanil (Toyoda *et al.*, 1997), WR99210 has a flexible propoxy linker and a phenyl group with three chlorine atoms (Yuthavong, 2002; Nzila, 2006). Studies in animal models demonstrated a low bioavailability of WR99210, preventing its further development as an antimalarial agent (Rieckmann *et al.*, 1996). The crystal structures of the bifunctional *Plasmodium falciparum* DHFR-TS and the monofunctional *P. vivax* DHFR have been reported in complex with WR99210, and with pyrimethamines, respectively (Yuvaniyama *et al.*, 2003; Kongsaeree *et al.*, 2005). The protein structures complexed with WR99210 have provided valuable insight into interdomain interactions and also opened a new dimension in the design of new drugs to fight against malaria. Herein, we report a single crystal X-ray structure of 4,6-diamino-2,2-dimethyl-3-[3-(2,4,5-trichlorophenoxy)propoxy]-2,3-dihydro-1,3,5-triazin-1-ium chloride methanol solvate, (I).

In the title compound, the WR99210 molecule is protonated at one of the nitrogen atoms of the triazine moiety. This is evident from the increase in the internal angle at protonated N1 [C1—N1—C3 = 122.30 (16) Å] compared with that of the unprotanated atoms N3 [C2—N3—C1 = 116.03 (16) Å] and N5 [C2—N5—C3 = 117.77 (15) Å]. The triazine ring adopts the conformation described as an intermediate between a flatten screw-boat and a half-chair with C3 atom. The angle between the geminal flagpole and bowsprit methyl groups is 112.31 (18)°. In addition, the propoxy linker between the triazine and the trichlorophenyl group allowed free rotations of sp^3-hybridized C6, C7 and C8 atoms (Fig. 1).

In the crystal, the triazine moiety is centrosymmetrically paired through N—H···N hydrogen bonds involving the 2-amino group and the N3 atom of the triazine, leading to a hydrogen-bonding pattern with a graph-set $R_2^2(8)$ (Fig. 2). The pairs further interact with the chloride anion through N—H···Cl hydrogen bonds. The chloride anion connects 2-amino and 4-amino groups on either side of the paired triazine, forming an eight-membered hydrogen bonded ring motif with a graph-set $R_3^2(8)$. The protonated N1 and 2-amino groups of the cationic triazine also interacted with two chloride anions to form a ring motif with a graph-set $R_4^2(12)$. In addition, we found a graph-set $R_3^2(15)$ ring motif through an O—H···Cl hydrogen bond between the methanol molecule and the chloride anion as well as a C—H···O hydrogen bond between the benzene ring (C14) and the methanol molecule (Table 1).

S2. Experimental

WR99210 was a kind gift from Dr. Bongkoch Tarnchompoo, BIOTEC, National Science and Technology Development Agency, Thailand. Single crystals of the title compound were prepared from a methanolic solution by slow evaporation at 298 K. The colorless crystals suitable for X-ray diffraction were obtained after a few days.

S3. Refinement

The N-bound H atoms were located in a difference Fourier map and were refined with restraint of N—H = 0.88 (1) Å. All other H atoms were placed in idealized positions and refined as riding atoms, with C—H = 0.93–0.97 Å and O—H = 0.82 Å, and with U_{iso}(H) = 1.5U_{eq}(O, C_{methyl}) and 1.2U_{eq}(C) for other H atoms.

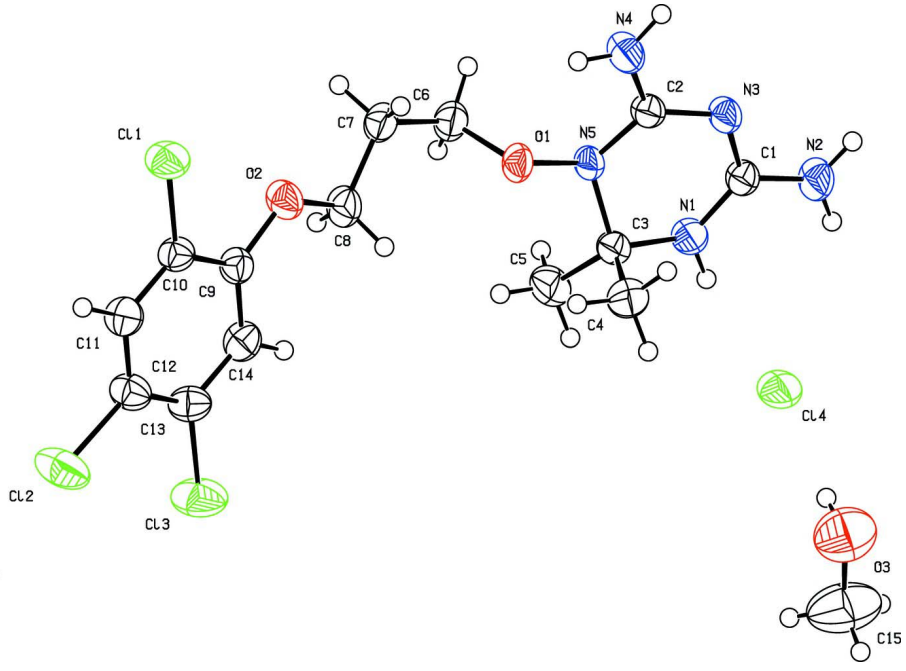

Figure 1

View of the molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level.

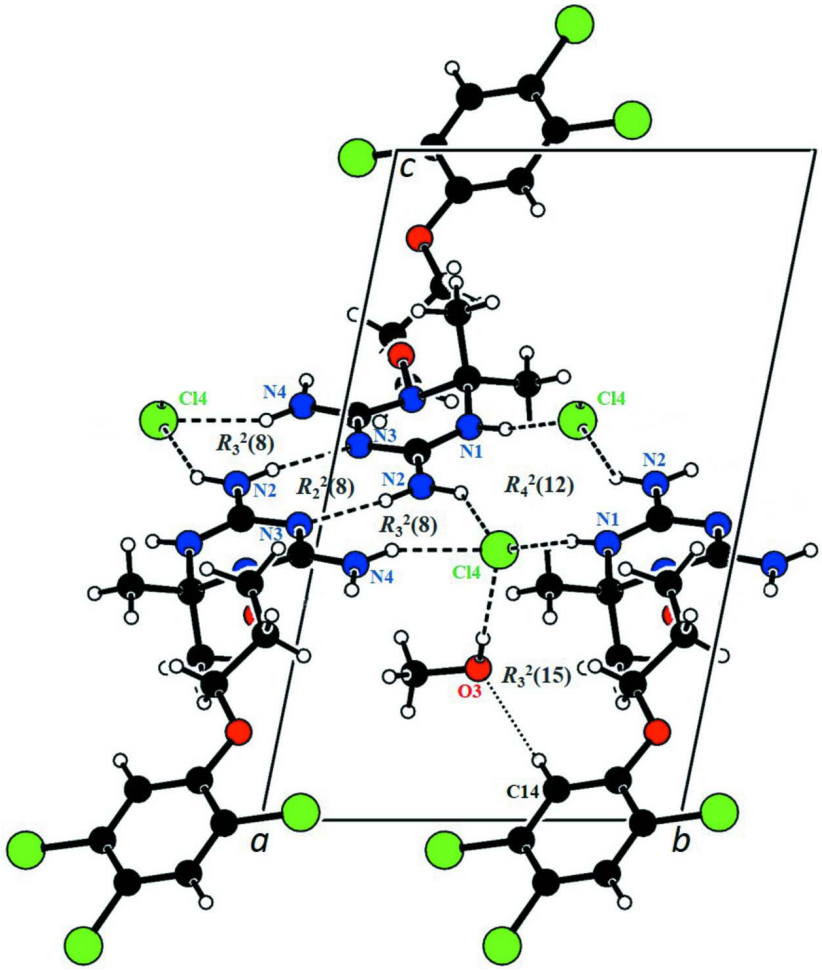

Figure 2

Hydrogen bonding interactions, showing molecules linked through N—H···N, N—H···Cl and O—H···Cl (dashed lines), and C—H···O (dotted line) hydrogen bonds.

4,6-Diamino-2,2-dimethyl-3-[3-(2,4,5-trichlorophenoxy)propoxy]-2,3-dihydro-1,3,5-triazin-1-ium chloride methanol monosolvate

Crystal data

$C_{14}H_{19}Cl_3N_5O_2^+ \cdot Cl^- \cdot CH_4O$
$M_r = 463.18$
Triclinic, $P\overline{1}$
$a = 8.5930$ (4) Å
$b = 9.3510$ (3) Å
$c = 14.6970$ (7) Å
$\alpha = 75.422$ (3)°
$\beta = 78.2260$ (19)°
$\gamma = 70.194$ (3)°
$V = 1066.13$ (8) Å^3
$Z = 2$
$F(000) = 480$
$D_x = 1.443$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2724 reflections
$\theta = 2.9$–23.3°
$\mu = 0.58$ mm^{-1}
$T = 298$ K
Rod, colourless
0.32 × 0.20 × 0.18 mm

Data collection

Nonius KappaCCD diffractometer
Radiation source: fine-focus sealed tube
Detector resolution: 9 pixels mm^{-1}
CCD scans
5032 measured reflections
2935 independent reflections
2681 reflections with $I > 2\sigma(I)$
$R_{int} = 0.017$
$\theta_{max} = 23.3°$, $\theta_{min} = 3.1°$
$h = -9 \rightarrow 9$
$k = -10 \rightarrow 9$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.087$
$S = 1.06$
2935 reflections
268 parameters
6 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
$w = 1/[\sigma^2(F_o^2) + (0.0351P)^2 + 0.5001P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
Cl1	−0.26674 (7)	−0.09037 (6)	0.98859 (4)	0.05048 (18)
Cl2	−0.50317 (9)	0.36361 (7)	1.18779 (4)	0.0669 (2)
Cl3	−0.27290 (9)	0.54749 (7)	1.04479 (5)	0.0658 (2)
Cl4	0.17598 (7)	0.43814 (6)	0.40327 (4)	0.05568 (19)
O1	0.36692 (15)	0.10928 (15)	0.69350 (9)	0.0364 (3)
O2	−0.07327 (17)	0.09663 (16)	0.86849 (10)	0.0423 (3)
O3	0.0138 (3)	0.4448 (3)	0.22657 (17)	0.0928 (7)
H3	0.0601	0.4417	0.2709	0.139*
N1	0.6726 (2)	0.30658 (19)	0.58733 (12)	0.0404 (4)
N2	0.9243 (2)	0.2208 (2)	0.49858 (14)	0.0459 (4)
N3	0.77155 (19)	0.05192 (18)	0.56004 (11)	0.0369 (4)
N4	0.5995 (2)	−0.1015 (2)	0.61841 (14)	0.0491 (5)
N5	0.49520 (18)	0.15639 (17)	0.62848 (11)	0.0327 (4)
C1	0.7877 (2)	0.1939 (2)	0.54981 (13)	0.0338 (4)
C2	0.6256 (2)	0.0339 (2)	0.60370 (13)	0.0334 (4)
C3	0.5346 (2)	0.2785 (2)	0.65866 (14)	0.0356 (4)
C4	0.5862 (3)	0.2234 (3)	0.75760 (15)	0.0501 (5)

H4C	0.4938	0.2043	0.8026	0.060*
H4D	0.6195	0.3015	0.7732	0.060*
H4E	0.6779	0.1294	0.7596	0.060*
C5	0.3872 (3)	0.4247 (2)	0.65107 (18)	0.0509 (6)
H5A	0.2982	0.4096	0.7001	0.061*
H5B	0.3498	0.4478	0.5903	0.061*
H5C	0.4200	0.5094	0.6580	0.061*
C6	0.2207 (2)	0.1419 (3)	0.64724 (14)	0.0422 (5)
H6A	0.2490	0.0902	0.5939	0.051*
H6B	0.1740	0.2525	0.6248	0.051*
C7	0.0993 (2)	0.0797 (3)	0.72291 (15)	0.0421 (5)
H7A	0.0103	0.0749	0.6935	0.051*
H7B	0.1564	−0.0249	0.7532	0.051*
C8	0.0247 (3)	0.1781 (2)	0.79714 (14)	0.0418 (5)
H8A	0.1119	0.1912	0.8241	0.050*
H8B	−0.0448	0.2796	0.7698	0.050*
C9	−0.1674 (2)	0.1672 (2)	0.94055 (13)	0.0348 (4)
C10	−0.2683 (2)	0.0871 (2)	1.00452 (13)	0.0349 (4)
C11	−0.3698 (3)	0.1481 (2)	1.07983 (14)	0.0405 (5)
H11	−0.4368	0.0939	1.1217	0.049*
C12	−0.3719 (3)	0.2895 (2)	1.09306 (14)	0.0419 (5)
C13	−0.2726 (3)	0.3696 (2)	1.02998 (14)	0.0418 (5)
C14	−0.1711 (3)	0.3094 (2)	0.95396 (14)	0.0407 (5)
H14	−0.1053	0.3647	0.9118	0.049*
C15	0.0334 (5)	0.2948 (4)	0.2183 (3)	0.1067 (12)
H15A	−0.0107	0.2981	0.1625	0.160*
H15B	−0.0254	0.2456	0.2732	0.160*
H15C	0.1498	0.2369	0.2133	0.160*
H1	0.700 (3)	0.3881 (18)	0.5866 (17)	0.053 (7)*
H2A	0.944 (3)	0.3083 (16)	0.4926 (16)	0.045 (6)*
H2B	1.002 (2)	0.144 (2)	0.4770 (16)	0.052 (7)*
H4A	0.680 (2)	−0.181 (2)	0.6007 (17)	0.057 (7)*
H4B	0.507 (2)	−0.108 (3)	0.6546 (16)	0.067 (8)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0612 (4)	0.0386 (3)	0.0568 (3)	−0.0254 (3)	0.0059 (3)	−0.0153 (2)
Cl2	0.0924 (5)	0.0554 (4)	0.0519 (4)	−0.0290 (3)	0.0215 (3)	−0.0243 (3)
Cl3	0.0963 (5)	0.0422 (3)	0.0678 (4)	−0.0344 (3)	0.0018 (3)	−0.0180 (3)
Cl4	0.0613 (4)	0.0410 (3)	0.0719 (4)	−0.0260 (3)	0.0097 (3)	−0.0241 (3)
O1	0.0292 (7)	0.0467 (8)	0.0340 (7)	−0.0173 (6)	0.0032 (5)	−0.0070 (6)
O2	0.0422 (8)	0.0407 (8)	0.0426 (8)	−0.0178 (6)	0.0095 (6)	−0.0107 (6)
O3	0.1093 (18)	0.0790 (15)	0.0964 (17)	−0.0336 (13)	−0.0224 (13)	−0.0144 (12)
N1	0.0407 (9)	0.0317 (9)	0.0515 (10)	−0.0178 (8)	0.0047 (8)	−0.0123 (8)
N2	0.0406 (10)	0.0400 (11)	0.0577 (11)	−0.0220 (9)	0.0091 (8)	−0.0093 (9)
N3	0.0341 (9)	0.0332 (9)	0.0432 (9)	−0.0151 (7)	0.0078 (7)	−0.0109 (7)
N4	0.0443 (11)	0.0340 (10)	0.0682 (13)	−0.0196 (9)	0.0168 (9)	−0.0172 (9)

N5	0.0283 (8)	0.0344 (9)	0.0365 (8)	−0.0138 (7)	0.0058 (6)	−0.0111 (7)
C1	0.0334 (10)	0.0335 (11)	0.0346 (10)	−0.0140 (9)	0.0008 (8)	−0.0060 (8)
C2	0.0354 (10)	0.0323 (10)	0.0335 (10)	−0.0135 (8)	0.0018 (8)	−0.0086 (8)
C3	0.0337 (10)	0.0342 (10)	0.0408 (11)	−0.0117 (8)	0.0014 (8)	−0.0138 (8)
C4	0.0487 (13)	0.0593 (14)	0.0474 (13)	−0.0177 (11)	−0.0071 (10)	−0.0173 (11)
C5	0.0450 (12)	0.0382 (12)	0.0661 (15)	−0.0051 (10)	−0.0028 (11)	−0.0183 (10)
C6	0.0342 (11)	0.0594 (13)	0.0372 (11)	−0.0190 (10)	−0.0018 (8)	−0.0124 (9)
C7	0.0345 (11)	0.0544 (13)	0.0433 (11)	−0.0211 (9)	−0.0007 (9)	−0.0130 (10)
C8	0.0373 (11)	0.0454 (12)	0.0425 (11)	−0.0194 (9)	0.0047 (9)	−0.0068 (9)
C9	0.0326 (10)	0.0356 (11)	0.0358 (10)	−0.0116 (8)	−0.0022 (8)	−0.0065 (8)
C10	0.0379 (11)	0.0301 (10)	0.0379 (11)	−0.0124 (8)	−0.0048 (8)	−0.0061 (8)
C11	0.0458 (12)	0.0398 (12)	0.0368 (11)	−0.0210 (9)	0.0022 (9)	−0.0039 (9)
C12	0.0503 (12)	0.0394 (12)	0.0356 (11)	−0.0151 (10)	−0.0002 (9)	−0.0091 (9)
C13	0.0526 (12)	0.0325 (11)	0.0431 (12)	−0.0162 (9)	−0.0068 (10)	−0.0073 (9)
C14	0.0428 (11)	0.0379 (11)	0.0425 (11)	−0.0202 (9)	−0.0007 (9)	−0.0030 (9)
C15	0.152 (4)	0.064 (2)	0.120 (3)	−0.035 (2)	−0.050 (3)	−0.0171 (19)

Geometric parameters (Å, º)

Cl1—C10	1.7290 (19)	C4—H4D	0.9600
Cl2—C12	1.734 (2)	C4—H4E	0.9600
Cl3—C13	1.730 (2)	C5—H5A	0.9600
O1—N5	1.4177 (19)	C5—H5B	0.9600
O1—C6	1.455 (2)	C5—H5C	0.9600
O2—C9	1.361 (2)	C6—C7	1.509 (3)
O2—C8	1.436 (2)	C6—H6A	0.9700
O3—C15	1.389 (4)	C6—H6B	0.9700
O3—H3	0.8200	C7—C8	1.506 (3)
N1—C1	1.325 (3)	C7—H7A	0.9700
N1—C3	1.462 (2)	C7—H7B	0.9700
N1—H1	0.866 (10)	C8—H8A	0.9700
N2—C1	1.324 (2)	C8—H8B	0.9700
N2—H2A	0.868 (10)	C9—C14	1.382 (3)
N2—H2B	0.874 (10)	C9—C10	1.396 (3)
N3—C2	1.332 (2)	C10—C11	1.377 (3)
N3—C1	1.349 (2)	C11—C12	1.378 (3)
N4—C2	1.317 (3)	C11—H11	0.9300
N4—H4A	0.883 (10)	C12—C13	1.381 (3)
N4—H4B	0.873 (10)	C13—C14	1.383 (3)
N5—C2	1.369 (2)	C14—H14	0.9300
N5—C3	1.481 (2)	C15—H15A	0.9600
C3—C5	1.514 (3)	C15—H15B	0.9600
C3—C4	1.519 (3)	C15—H15C	0.9600
C4—H4C	0.9600		

N5—O1—C6	110.75 (13)	O1—C6—H6A	110.8
C9—O2—C8	118.27 (15)	C7—C6—H6A	110.8
C15—O3—H3	109.5	O1—C6—H6B	110.8

C1—N1—C3	122.30 (16)	C7—C6—H6B	110.8
C1—N1—H1	117.3 (16)	H6A—C6—H6B	108.9
C3—N1—H1	116.2 (16)	C8—C7—C6	112.46 (17)
C1—N2—H2A	121.4 (15)	C8—C7—H7A	109.1
C1—N2—H2B	118.5 (16)	C6—C7—H7A	109.1
H2A—N2—H2B	120 (2)	C8—C7—H7B	109.1
C2—N3—C1	116.03 (16)	C6—C7—H7B	109.1
C2—N4—H4A	119.9 (16)	H7A—C7—H7B	107.8
C2—N4—H4B	114.9 (18)	O2—C8—C7	105.97 (16)
H4A—N4—H4B	124 (2)	O2—C8—H8A	110.5
C2—N5—O1	112.83 (14)	C7—C8—H8A	110.5
C2—N5—C3	117.77 (15)	O2—C8—H8B	110.5
O1—N5—C3	110.56 (13)	C7—C8—H8B	110.5
N2—C1—N1	119.24 (17)	H8A—C8—H8B	108.7
N2—C1—N3	117.74 (17)	O2—C9—C14	125.37 (17)
N1—C1—N3	123.01 (16)	O2—C9—C10	115.84 (17)
N4—C2—N3	120.33 (17)	C14—C9—C10	118.79 (18)
N4—C2—N5	118.00 (17)	C11—C10—C9	120.85 (18)
N3—C2—N5	121.51 (16)	C11—C10—Cl1	119.59 (14)
N1—C3—N5	103.00 (14)	C9—C10—Cl1	119.56 (15)
N1—C3—C5	108.81 (16)	C10—C11—C12	120.00 (18)
N5—C3—C5	109.49 (16)	C10—C11—H11	120.0
N1—C3—C4	111.45 (16)	C12—C11—H11	120.0
N5—C3—C4	111.35 (16)	C11—C12—C13	119.49 (18)
C5—C3—C4	112.31 (18)	C11—C12—Cl2	118.64 (15)
C3—C4—H4C	109.5	C13—C12—Cl2	121.85 (16)
C3—C4—H4D	109.5	C12—C13—C14	120.82 (18)
H4C—C4—H4D	109.5	C12—C13—Cl3	120.49 (16)
C3—C4—H4E	109.5	C14—C13—Cl3	118.68 (15)
H4C—C4—H4E	109.5	C9—C14—C13	120.05 (18)
H4D—C4—H4E	109.5	C9—C14—H14	120.0
C3—C5—H5A	109.5	C13—C14—H14	120.0
C3—C5—H5B	109.5	O3—C15—H15A	109.5
H5A—C5—H5B	109.5	O3—C15—H15B	109.5
C3—C5—H5C	109.5	H15A—C15—H15B	109.5
H5A—C5—H5C	109.5	O3—C15—H15C	109.5
H5B—C5—H5C	109.5	H15A—C15—H15C	109.5
O1—C6—C7	104.82 (15)	H15B—C15—H15C	109.5

C6—O1—N5—C2	−107.86 (18)	O1—C6—C7—C8	72.4 (2)
C6—O1—N5—C3	117.90 (17)	C9—O2—C8—C7	−174.20 (16)
C3—N1—C1—N2	−168.24 (18)	C6—C7—C8—O2	−174.17 (16)
C3—N1—C1—N3	12.8 (3)	C8—O2—C9—C14	−3.3 (3)
C2—N3—C1—N2	−173.42 (18)	C8—O2—C9—C10	176.05 (17)
C2—N3—C1—N1	5.6 (3)	O2—C9—C10—C11	−179.53 (18)
C1—N3—C2—N4	−178.78 (19)	C14—C9—C10—C11	−0.1 (3)
C1—N3—C2—N5	5.9 (3)	O2—C9—C10—Cl1	0.1 (2)
O1—N5—C2—N4	19.0 (2)	C14—C9—C10—Cl1	179.54 (15)

C3—N5—C2—N4	149.69 (18)	C9—C10—C11—C12	−0.3 (3)
O1—N5—C2—N3	−165.59 (16)	Cl1—C10—C11—C12	−179.98 (16)
C3—N5—C2—N3	−34.9 (3)	C10—C11—C12—C13	0.5 (3)
C1—N1—C3—N5	−35.7 (2)	C10—C11—C12—Cl2	179.18 (16)
C1—N1—C3—C5	−151.85 (19)	C11—C12—C13—C14	−0.1 (3)
C1—N1—C3—C4	83.8 (2)	Cl2—C12—C13—C14	−178.82 (17)
C2—N5—C3—N1	45.5 (2)	C11—C12—C13—Cl3	179.94 (17)
O1—N5—C3—N1	177.24 (14)	Cl2—C12—C13—Cl3	1.3 (3)
C2—N5—C3—C5	161.15 (17)	O2—C9—C14—C13	179.80 (18)
O1—N5—C3—C5	−67.12 (19)	C10—C9—C14—C13	0.4 (3)
C2—N5—C3—C4	−74.1 (2)	C12—C13—C14—C9	−0.3 (3)
O1—N5—C3—C4	57.68 (19)	Cl3—C13—C14—C9	179.62 (16)
N5—O1—C6—C7	177.50 (15)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···Cl4^{i}	0.87 (1)	2.27 (1)	3.1236 (17)	167 (2)
N2—H2*A*···Cl4^{ii}	0.87 (1)	2.64 (2)	3.3285 (17)	137 (2)
N2—H2*B*···N3^{iii}	0.87 (1)	2.26 (1)	3.122 (2)	170 (2)
N4—H4*A*···Cl4^{iv}	0.88 (1)	2.31 (1)	3.1419 (19)	158 (2)
O3—H3···Cl4	0.82	2.35	3.166 (2)	176
C14—H14···O3^{v}	0.93	2.53	3.423 (3)	161

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