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Crystal structure and Hirshfeld surface analysis of 2-methylquinazolin-4(3*H*)-one hydrochloride

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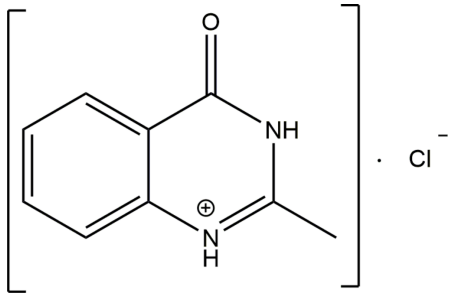
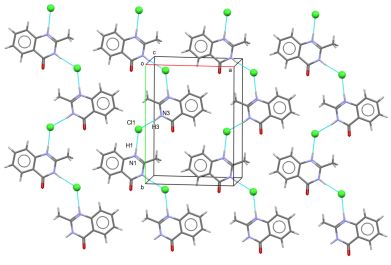
The title salt (systematic name: 2-methyl-4-oxo-3,4-dihydroquinazolin-1-ium chloride), $C_9H_9N_2O^+\cdot Cl^-$, has orthorhombic (*Pbcm*) symmetry. Except for two methyl H atoms, all atoms of the molecular cation are located about a mirror plane, making the quinazolinium moiety exactly planar. Individual molecules are arranged in (001) layers in the crystal. Supramolecular features include N—H···Cl hydrogen-bonding interactions, leading to zigzag chains along [010] with $D_1^1(2)$ and $C_1^2(6)$ graph-set motifs. Additionally, weak π–π stacking interactions occur between benzene rings in adjacent layers. Hirshfeld surface analysis revealed that the most important contributions to the surface contacts are from H···H (36.1%), H···C/C···H (25.8%), and H···O/O···H (17.7%) interactions.

1. Chemical context

Syntheses based on pyrimidines (quinazolines) condensed with a benzene ring are widely used in agricultural and medical practice (Zayed, 2023). In particular, drugs based on compounds of this class are used against viruses, microbes, colds and cancer (Li *et al.*, 2021; Arachchige & Yi, 2019) as well as stimulants and pesticides (Alsibaee *et al.*, 2023). Examples of such types of drugs that have been used successfully against various types of cancer in recent years are *imatinib*, *erlotinib*, *lapatinib* and *afatinib*. Therefore, targeted syntheses of biologically active compounds containing this pharmacophore (*i.e.* the quinazoline ring), are important to determine their physical, chemical and biological properties. In this context, we report here the molecular and crystal structures of 2-methyl quinazolin-4(3*H*)-one hydrochloride (**I**) and its Hirshfeld surface analysis.





2. Structural commentary

The asymmetric unit of (**I**) consists of a quinazolinium cation and a Cl^- anion (Fig. 1). Except for methyl H atom H11*b* and

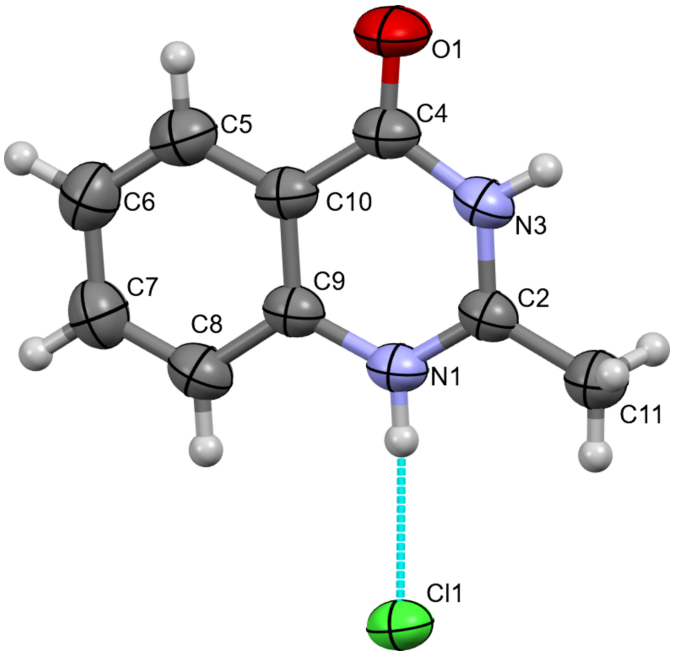


Figure 1
The asymmetric unit of (**I**) with displacement ellipsoids drawn at the 50% probability level. The dotted turquoise line represents an N—H···Cl hydrogen bond.

its symmetry-related counterpart, all atoms are located on a mirror plane, making the benzene and pyrimidine rings in the cation exactly planar (Fig. 2). The basic heteroatom N1 of the pyrimidine ring is protonated, and the resulting positive charge is delocalized within the –N—C—N– moiety in the ring, making the C2—N1 and C2—N3 bonds shorter than the C4—N3 and C9—N1 bonds. Similar differences were observed in related compounds reported in the literature (Sharma *et al.*, 1993; Turgunov *et al.*, 2003; Tozhiboev *et al.*, 2005, Tojiboev *et al.*, 2021).

3. Supramolecular features

In the crystal of (**I**), the cationic molecules are arranged in flat (001) layers. Individual molecules are linked to Cl^- anions through N—H···Cl hydrogen-bonding interactions (Table 1) into zigzag chains extending parallel to [010] (Fig. 3), generating $D_1^1(2)$ and $C_2^1(6)$ graph-set motifs (Bernstein *et al.*, 1995). In addition, weak highly slipped π–π stacking interactions (Fig. 2) occur between benzene (centroid *Cg*2) rings in adjacent layers and involve contact distances *Cg*2···*Cg*2(1 − *x*, 1 − *y*, 1 − *z*) of 4.987 (14) Å (slippage 3.280 Å).

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···Cl1	0.86	2.19	3.052 (2)	176
N3—H3···Cl1^{i}	0.86	2.25	3.108 (3)	175

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

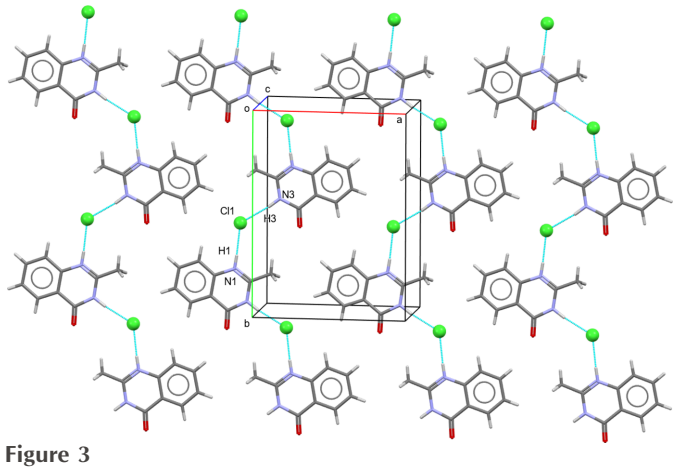


Figure 3
Packing of (**I**) along the *c* axis. Hydrogen bonding between N1—H1···Cl and N3—H3···Cl is shown as blue dotted lines.

4. Hirshfeld surface analysis

A Hirshfeld surface analysis (Hirshfeld, 1977) was carried out using *CrystalExplorer* (Spackman *et al.*, 2021) to visualize non-covalent interactions in the crystal packing of (**I**). The Hirshfeld surface mapped over d_{norm} is represented in Fig. 4. The white surface indicates contacts with distances equal to the sum of van der Waals radii, and the red and blue colours indicate distances shorter or longer than the van der Waals radii, respectively. The bright-red spot near N1 indicates its role as a hydrogen-bond donor towards Cl1.

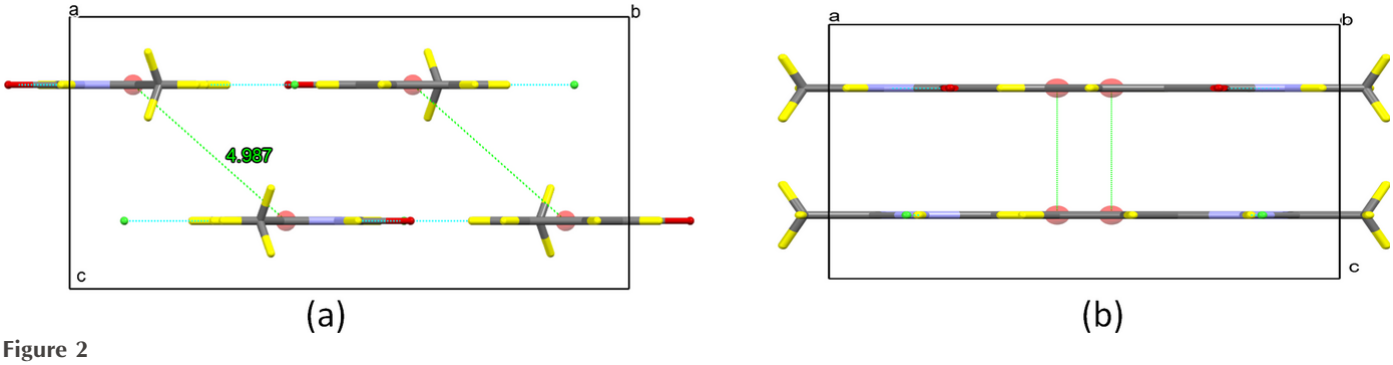


Figure 2
Packing of (**I**) (*a*) along the *a* axis and (*b*) along the *b* axis, showing the π–π interactions.

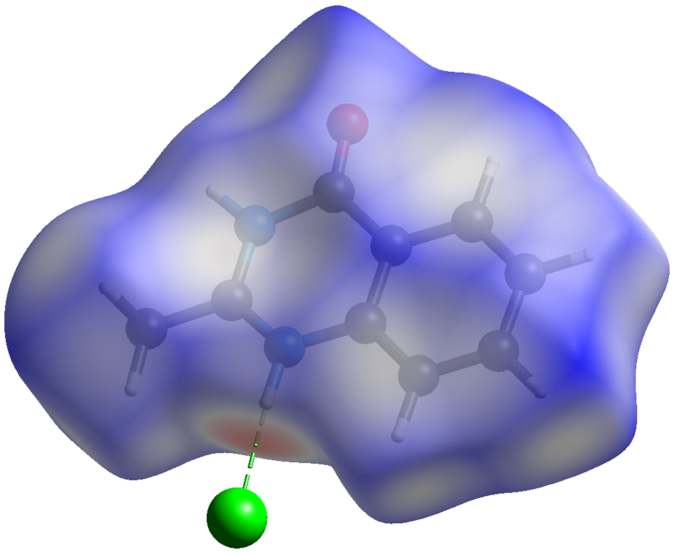


Figure 4
Three-dimensional Hirshfeld surface of (**I**) mapped over d_{norm}.

The most important contributions to the Hirshfeld surface arise from H···H contacts at 36.1% (Fig. 5*b*). C···H/H···C and O···H/H···O interactions follow with contributions of 25.8% and 17.7%, respectively (Fig. 5*c*,*d*). The classical N—H···Cl hydrogen bonds correspond to H···Cl/Cl···H contacts (10.3% contribution) and show up as a spike (Fig. 5*e*). Minor contributors are due to C···Cl/Cl···C (3.3%), N···H/H···N (2.4%), N···Cl/Cl···N (2.2%) and C···C (1.8%) interactions.

5. Database survey

A search of the Cambridge Structural Database (CSD, Version 5.43, last update November 2022; Groom *et al.*, 2016) for the 2-methylquinazolin-4(3H)-one moiety resulted in twelve hits with a similar planar conformation: ACANLC10 (Etter *et al.*, 1983), AWIYIR (Kalogirou *et al.*, 2021*a*), BIHJUA and BIHKAH (Liao *et al.*, 2018), BOLGAK (Etter *et al.*, 1983) and BOYMAD (Chadwick & Easton, 1983), DILFEL (Rybarczyk-Pirek *et al.*, 2013), RUGTEV (Kalogirou *et al.*, 2020), UQOGAL (Kalogirou *et al.*, 2021*b*) and YILLEM (Moghimi *et al.*, 2013). The main difference with respect to the molecular structures of these compounds is that the C2—N1 bond in the pyrimidine ring of (**I**) is slightly longer due to the protonation of the N atom.

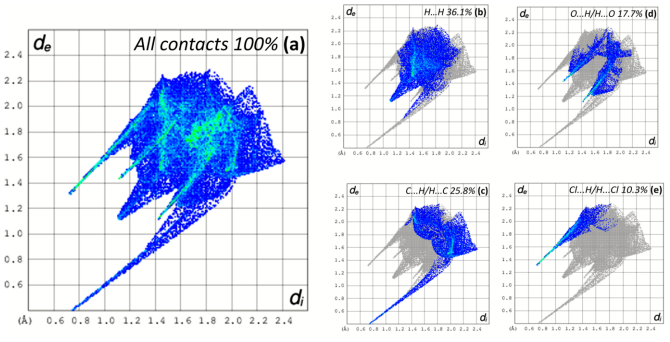


Figure 5
Two-dimensional fingerprint plots for the title compound, showing (*a*) all interactions, and decomposed into (*b*) H···H, (*c*) C···H/H···C, (*d*) O···H/H···O, (*e*) Cl···H/H···Cl interactions. Values for d_i and d_e represent the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_9H_9N_2O^+\cdot Cl^-$
M_r	196.64
Crystal system, space group	Orthorhombic, *Pbcm*
Temperature (K)	295
a, *b*, *c* (Å)	10.1221 (5), 13.6533 (4), 6.6248 (3)
V (Å^3)	915.55 (7)
Z	4
Radiation type	Cu *Kα*
μ (mm^{-1})	3.37
Crystal size (mm)	0.20 × 0.15 × 0.05
Data collection	
Diffractometer	PhotonJet (Cu) X-ray Source
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2020)
T_{min}, T_{max}	0.600, 1.000
No. of measured, independent and observed [$I \geq 2u(I)$] reflections	7833, 977, 824
R_{int}	0.086
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.616
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.043, 0.133, 1.01
No. of reflections	977
No. of parameters	84
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.35

Computer programs: *CrysAlis PRO* (Rigaku OD, 2020), *SHELXT* (Sheldrick, 2015), *OLEX2-refine* (Bourhis *et al.*, 2015) and *OLEX2* (Dolomanov *et al.*, 2009).

6. Synthesis and crystallization

30 g (0.2 mol) of *N*-acetylanthranilic acid and 76.53 g (1.4 mol) of ammonium chloride were placed in a 250 ml round-bottom flask. The mixture was heated in a sand bath at 498–503 K for 4 h. Then the reaction mixture was cooled and treated with boiling water. The mixture was filtered and brought to pH 7–9, and then was left at room temperature. The precipitate was filtered off, washed with distilled water and dried. Recrystallization from ethanol yielded 20.4 g (76%) of 2-methylquinazolin-4(3*H*)-one; m.p. 511–513 K, R_f = 0.28. In order to get 2-methylquinazolin-4(3*H*)-one hydrochloride crystals, the latter was dissolved in a mixture of ethanol and methanol (9:1 *v*:*v*) to which 10 drops of 30%$_{wt}$ HCl solution were added and stirred on a magnetic stirrer for 2 h. Crystal growth was carried out in a drying oven at 303 K. Colourless single crystals suitable for X-ray diffraction analysis were obtained after 5 d.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. H atoms were positioned geome-

trically (aromatic C—H = 0.93 Å, N—H = 0.86 Å and methyl C—H = 0.96 Å) and treated as riding atoms, with U_{iso}(H) = 1.2U_{eq}(aromatic C, N) or 1.5U_{eq}(methyl C).

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Computing details

2-Methyl-4-oxo-3,4-dihydroquinazolin-1-ium chloride

Crystal data

$C_9H_9N_2O^+\cdot Cl^-$
M_r = 196.64
Orthorhombic, *Pbcm*
a = 10.1221 (5) Å
b = 13.6533 (4) Å
c = 6.6248 (3) Å
V = 915.55 (7) Å^3
Z = 4
F(000) = 410.692
D_x = 1.427 Mg m^{-3}
Cu *Kα* radiation, *λ* = 1.54184 Å
Cell parameters from 2575 reflections
θ = 4.4–70.9°
μ = 3.37 mm^{-1}
T = 295 K
Prizm, colourless
0.20 × 0.15 × 0.05 mm

Data collection

PhotonJet (Cu) X-ray Source diffractometer
Detector resolution: 10.0000 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2020)
T_{min} = 0.600, T_{max} = 1.000
7833 measured reflections
977 independent reflections
824 reflections with $I \geq 2u(I)$
R_{int} = 0.086
θ_{max} = 71.7°, θ_{min} = 4.4°
h = −12→12
k = −16→16
l = −8→5

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.133
S = 1.01
977 reflections
84 parameters
0 restraints
14 constraints
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0787P)^2 + 0.2674P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = −0.0005
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}

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

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.15171 (8)	0.09775 (5)	0.75	0.0549 (3)

O1	0.2374 (3)	0.60927 (16)	0.75	0.0819 (9)
N1	0.1883 (2)	0.31959 (17)	0.75	0.0472 (6)
H1	0.1741 (2)	0.25748 (17)	0.75	0.0708 (9)*
C2	0.0870 (3)	0.3786 (2)	0.75	0.0463 (7)
N3	0.1070 (3)	0.47530 (17)	0.75	0.0502 (6)
H3	0.0384 (3)	0.51250 (17)	0.75	0.0753 (10)*
C4	0.2314 (3)	0.5209 (2)	0.75	0.0558 (8)
C5	0.4723 (3)	0.4864 (3)	0.75	0.0622 (9)
H5	0.4897 (3)	0.5532 (3)	0.75	0.0746 (10)*
C6	0.5757 (4)	0.4204 (3)	0.75	0.0679 (9)
H6	0.6625 (4)	0.4428 (3)	0.75	0.0814 (11)*
C7	0.5498 (4)	0.3204 (3)	0.75	0.0659 (9)
H7	0.6197 (4)	0.2762 (3)	0.75	0.0791 (11)*
C8	0.4220 (3)	0.2862 (2)	0.75	0.0584 (8)
H8	0.4052 (3)	0.2192 (2)	0.75	0.0701 (10)*
C9	0.3187 (3)	0.3528 (2)	0.75	0.0469 (7)
C10	0.3423 (3)	0.4534 (2)	0.75	0.0491 (7)
C11	−0.0492 (4)	0.3396 (3)	0.75	0.0610 (9)
H11a	−0.058 (4)	0.274 (4)	0.75	0.0914 (13)*
H11b	−0.090 (3)	0.360 (2)	0.869 (5)	0.0914 (13)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0623 (5)	0.0370 (4)	0.0655 (5)	−0.0071 (3)	−0.000000	0.000000
O1	0.0805 (18)	0.0339 (12)	0.131 (3)	−0.0025 (11)	−0.000000	0.000000
N1	0.0543 (14)	0.0323 (11)	0.0551 (14)	−0.0005 (10)	−0.000000	0.000000
C2	0.0531 (16)	0.0375 (13)	0.0483 (15)	0.0031 (12)	−0.000000	0.000000
N3	0.0558 (15)	0.0351 (12)	0.0597 (14)	0.0064 (11)	−0.000000	0.000000
C4	0.0652 (19)	0.0372 (15)	0.0651 (18)	−0.0022 (13)	−0.000000	0.000000
C5	0.065 (2)	0.0510 (18)	0.070 (2)	−0.0085 (16)	−0.000000	0.000000
C6	0.0526 (19)	0.071 (2)	0.080 (2)	−0.0055 (17)	−0.000000	0.000000
C7	0.0546 (19)	0.067 (2)	0.076 (2)	0.0093 (17)	−0.000000	0.000000
C8	0.0633 (19)	0.0425 (16)	0.069 (2)	0.0071 (14)	−0.000000	0.000000
C9	0.0555 (17)	0.0378 (14)	0.0474 (15)	0.0000 (13)	−0.000000	0.000000
C10	0.0566 (17)	0.0390 (14)	0.0518 (16)	−0.0038 (13)	−0.000000	0.000000
C11	0.0562 (19)	0.0480 (17)	0.079 (2)	0.0000 (15)	−0.000000	0.000000

Geometric parameters (Å, º)

O1—C4	1.208 (3)	C5—C10	1.391 (5)
N1—H1	0.8600	C6—H6	0.9300
N1—C2	1.304 (4)	C6—C7	1.389 (5)
N1—C9	1.396 (4)	C7—H7	0.9300
C2—N3	1.335 (4)	C7—C8	1.375 (5)
C2—C11	1.478 (5)	C8—H8	0.9300
N3—H3	0.8600	C8—C9	1.386 (4)
N3—C4	1.404 (4)	C9—C10	1.394 (4)

C4—C10	1.452 (5)	C11—H11a	0.91 (5)
C5—H5	0.9300	C11—H11b^{i}	0.93 (3)
C5—C6	1.381 (5)	C11—H11b	0.93 (3)
C2—N1—H1	118.56 (17)	H7—C7—C6	119.6 (2)
C9—N1—H1	118.56 (15)	C8—C7—C6	120.8 (3)
C9—N1—C2	122.9 (2)	C8—C7—H7	119.6 (2)
N3—C2—N1	119.5 (3)	H8—C8—C7	120.4 (2)
C11—C2—N1	120.7 (3)	C9—C8—C7	119.1 (3)
C11—C2—N3	119.9 (3)	C9—C8—H8	120.43 (19)
H3—N3—C2	117.49 (17)	C8—C9—N1	120.1 (3)
C4—N3—C2	125.0 (3)	C10—C9—N1	118.8 (3)
C4—N3—H3	117.49 (16)	C10—C9—C8	121.1 (3)
N3—C4—O1	119.2 (3)	C5—C10—C4	121.7 (3)
C10—C4—O1	126.5 (3)	C9—C10—C4	119.5 (3)
C10—C4—N3	114.3 (2)	C9—C10—C5	118.7 (3)
C6—C5—H5	119.8 (2)	H11a—C11—C2	117 (3)
C10—C5—H5	119.8 (2)	H11b—C11—C2	107.9 (19)
C10—C5—C6	120.4 (3)	H11b^{i}—C11—C2	107.9 (19)
H6—C6—C5	120.1 (2)	H11b^{i}—C11—H11a	105 (2)
C7—C6—C5	119.8 (3)	H11b—C11—H11a	105 (2)
C7—C6—H6	120.1 (2)	H11b—C11—H11b^{i}	116 (4)
O1—C4—N3—C2	180.0	N3—C4—C10—C5	180.0
O1—C4—C10—C5	0.0	N3—C4—C10—C9	0.0
O1—C4—C10—C9	180.0	C4—C10—C5—C6	180.0
N1—C2—N3—C4	0.0	C4—C10—C9—C8	180.0
N1—C9—C8—C7	180.0	C5—C6—C7—C8	0.0
N1—C9—C10—C4	0.0	C5—C10—C9—C8	0.0
N1—C9—C10—C5	180.0	C6—C7—C8—C9	0.0
C2—N3—C4—C10	0.0	C7—C8—C9—C10	0.0

Symmetry code: (i) x, y, $-z+3/2$.

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···Cl1	0.86	2.19	3.052 (2)	176
N3—H3···Cl1^{ii}	0.86	2.25	3.108 (3)	175

Symmetry code: (ii) $-x$, $-y$, $z+1/2$.