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Synthesis, crystal structure and Hirshfeld surface analysis of *N*-(4-chlorophenyl)-5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxamide

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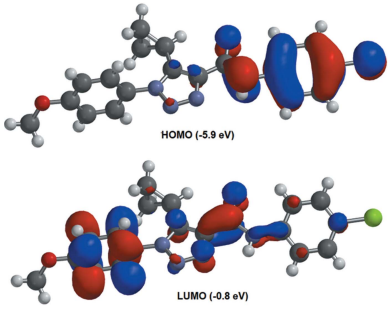
The title compound, $C_{19}H_{17}ClN_4O_2$, was obtained *via* a two-step synthesis involving the enol-mediated click Dimroth reaction of 4-azidoanisole with methyl 3-cyclopropyl-3-oxopropanoate leading to the 5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid and subsequent acid amidation with 4-chloroaniline by 1,1′-carbonyldiimidazole (CDI). It crystallizes in space group $P2_1/n$, with one molecule in the asymmetric unit. In the extended structure, two molecules arranged in a near coplanar fashion relative to the triazole ring planes are interconnected by N—H···N and C—H···N hydrogen bonds into a homodimer. The formation of dimers is a consequence of the above interaction and the edge-to-face stacking of aromatic rings, which are turned by 58.0 (3)° relative to each other. The dimers are linked by C—H···O interactions into ribbons. DFT calculations demonstrate that the frontier molecular orbitals are well separated in energy and the HOMO is largely localized on the 4-chlorophenyl amide motif while the LUMO is associated with aryltriazole grouping. A Hirshfeld surface analysis was performed to further analyse the intermolecular interactions.

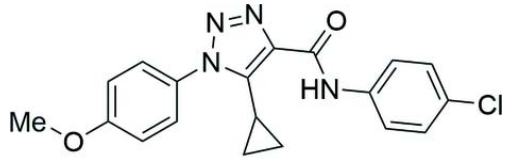
1. Chemical context

The number of compounds containing a 1,2,3-triazolyl-4-carboxamide motif that are known to exhibit biological activity is increasing rapidly. At present, there are two approved drugs and a number of compounds are undergoing preclinical studies. For instance, rufinamide is a well-known drug among those currently marketed, which is used to treat Lennox–Gastaut syndrome (childhood-onset epilepsy) (Wheless & Vazquez, 2010). Carboxyamidotriazole is a calcium channel blocker (Figg *et al.*, 1995) and is currently being actively investigated as an anticancer drug *in vitro* (Bonnefond *et al.*, 2018). As an example of preclinical anticancer studies, the cytotoxic activity at nanomolar levels of asymmetric 1-*R*-*N*-[(1-*R*-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-1,2,3-triazole-4-carboxamides in B16 melanoma cells have been estimated (Elamari *et al.*, 2013).

In our previous studies on the anticancer screening of various 1,2,3-triazoles, compounds based on 1,2,3-triazolyl-4-carboxamide scaffolds possessed the highest antiproliferative activity (Shyyka *et al.*, 2019; Pokhodylo *et al.*, 2013, 2014). Furthermore, a series of 6,7-disubstituted-4-(2-fluorophenoxy)quinoline derivatives possessing the 1,2,3-triazole-4-carboxamide moiety have been evaluated against *c*-Met kinase and five typical cancer cell lines (A549, H460, HT-29, MKN-45 and U87MG) and exhibited moderate to excellent



antiproliferative activity (Zhou *et al.*, 2014). A library of 1-benzyl-*N*-(2-(phenylamino)pyridin-3-yl)-1*H*-1,2,3-triazole-4-carboxamides was screened for their antiproliferative activity and showed promising cytotoxicity against lung cancer cell line A549 (Prasad *et al.*, 2019). In addition to the anti-tumor studies, 1*H*-1,2,3-triazole-4-carboxamides exhibit other biological activities such as fungicidal (Wang *et al.*, 2014), antiviral (Krajczyk *et al.*, 2014) and antimicrobial (Jadhav *et al.*, 2017) activities and were found to be inhibitors of the Wnt/β-catenin signalling pathway (Obianom *et al.*, 2019). It should be noted that the diversity of such compounds can be obtained by amidation of 1*H*-1,2,3-triazole-4-carboxylic acids prepared by convenient Dimroth synthesis and further modifications (Pokhodylo *et al.*, 2009, 2017, 2018; Pokhodylo, Matiychuk *et al.*, 2010; Pokhodylo, Savka *et al.*, 2010; Pokhodylo & Obushak, 2019). Given the considerable interest in such scaffolds for drug discovery, a detailed study of their structural features is relevant and the crystal structure of the title compound, $C_{19}H_{17}ClN_4O_2$, is described herein.



2. Structural commentary

The title compound crystallizes in the monoclinic centrosymmetric space group $P2_1/n$, with one molecule in the asymmetric unit. As shown in Fig. 1, the 4-methoxyphenyl and 1,2,3-triazole rings are turned relative to each other by 87.77 (7)° because of a significant steric hindrance of the cyclopropyl ring relative to the 4-methoxyphenyl substituent [the N1—C9—C11—C13 and N1—C9—C11—C12 torsion angles are 41.2 (4) and −31.6 (4)°, respectively]. The above angle between the planes is comparable with that for the bulky 5-(2-phenylhydrazineylidene)methyl analogue [73.3 (2)°; Pokhodylo *et al.*, 2018] but is considerably larger than in the structure of 5-cyclopropyl-1-(3-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid [39.1 (2)°] in which the cyclopropyl ring is oriented to the triazole ring (Pokhodylo *et al.*, 2017) or in 5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-ylphosphonate [45.36 (6)°; Pokhodylo *et al.*, 2020]. In selected 5-free triazoles, 1-(3-bromo- or 4-fluorophenyl)-1*H*-1,2,3-triazol-4-yl)methyl methylphosphonates, this angle is 22.9 (3) and 15.7 (2)°, respectively (Pokhodylo, Shyyka *et al.*, 2019). Within the cyclopropyl ring in the title compound, the three C—C bond lengths differ by an insignificant amount [C11—C12 = 1.491 (3), C11—C13 = 1.475 (3), C12—C13 = 1.457 (3) Å]. The amide group is turned slightly by 7.5 (3)° relative to the triazole ring while the proton of the amide group is involved in an intramolecular hydrogen bond with the heterocyclic N3 atom (Table 1). The angle between the 4-chlorophenyl and 1,2,3-triazole planes is 29.8 (1)°.

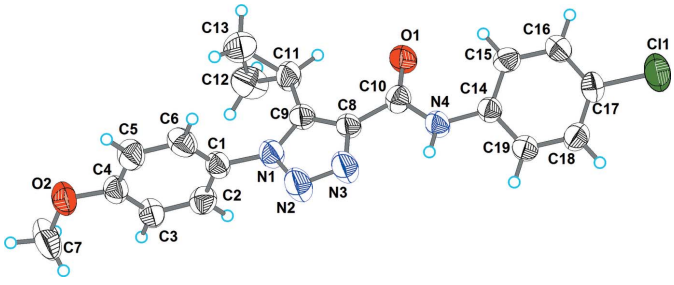


Figure 1
The molecular structure of the title compound with displacement ellipsoids drawn at the 50% probability level.

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4···N3	0.86	2.24	2.680 (3)	112
N4—H4···N2^{i}	0.86	2.68	3.491 (2)	157
C15—H15···O1	0.93	2.39	2.936 (2)	117
C19—H19···N2^{i}	0.93	2.68	3.475 (3)	144
C2—H2···O1^{ii}	0.93	2.53	3.439 (3)	167
C11—H11···O1	0.98	2.47	3.124 (2)	124

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

3. Supramolecular features

As shown in Fig. 2 and Table 2, the extended structure of the title compound is consolidated by a number of intermolecular interactions. Two molecules arranged in a near coplanar manner relative to the triazole ring planes are interconnected by N4—H4···N2^{i} and C19—H19···N2^{i} hydrogen bonds into a homodimer. Within the dimer, the edge-to-face stacked aromatic rings are tilted by 58.0 (3)°. Atom O1 of the amide group accepts both an intramolecular C—H···O link (with the 4-chlorophenyl and cyclopropyl H atoms) and an intermolecular C2—H2···O1 interaction with the 4-methoxyphenyl H atom. The last of these links neighbouring dimers

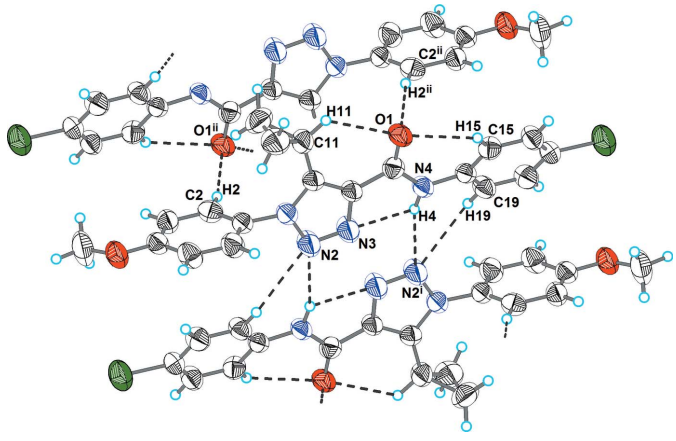


Figure 2
The hydrogen bonding of molecules in the title compound. Hydrogen bonds are shown as dashed lines. The symmetry codes are as in Table 1.

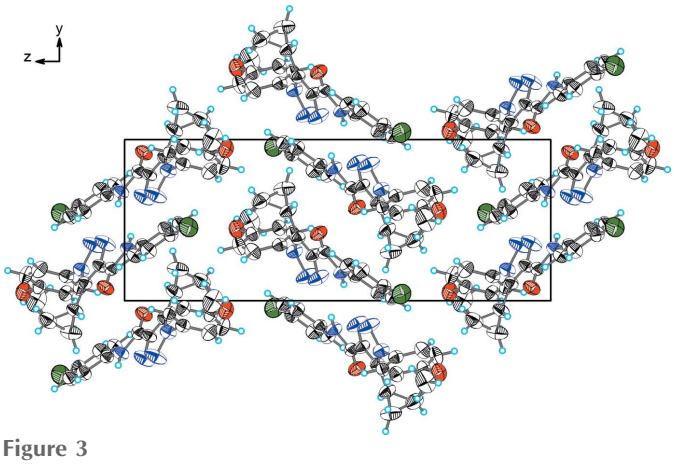


Figure 3
A view along the *a* axis of the crystal packing of the title compound.

into hydrogen-bonded ribbons parallel to the [010] direction (Fig. 3).

4. Hirshfeld surface analysis and computational study

Hirshfeld surface analysis was used to analyse the various intermolecular interactions in the title compound, through mapping the normalized contact distance (d_{norm}) using *CrystalExplorer* (Turner *et al.*, 2017; Spackman & Jayatilaka, 2009). Hirshfeld surfaces enable the visualization of intermolecular interactions by using different colours and colour intensity to represent short or long contacts and indicate the relative strength of the interactions. The most prominent interactions (the *ortho*-proton of the aryltriazole moiety and the carbonyl group as well as bifurcated interactions among protons of the amide group and the *ortho*-proton of the aryl group with the triazole ring nitrogen (N2) atoms of neighbouring molecules) can be seen in the Hirshfeld surface plot as red areas (Fig. 4). Fingerprint plots were produced to show the intermolecular surface bond distances with the regions highlighted for (C)H···O and (C, N)H···N interactions (Fig. 4). The contribution to the surface area for such contacts are 11.6% and 10.8%, respectively.

The frontier molecular orbitals HOMO and LUMO were analysed to better understand the electronic charge transfer within the molecule and its electron donating and accepting

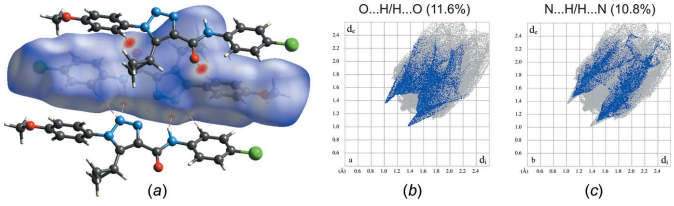


Figure 4
(*a*) Hirshfeld surface for the title molecule mapped with d_{norm} over the range −0.171 to 1.473 a.u. showing N—H···N, C—H···N and C—H···O hydrogen-bonded contacts. Fingerprint plots resolved into (*b*) N···H/H···N and (*c*) O···H/H···O contacts. Neighbouring molecules associated with close contacts are also shown.

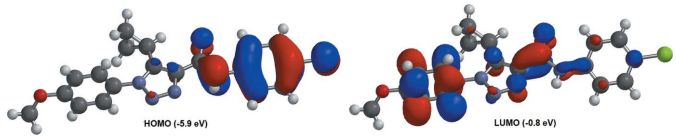


Figure 5
Frontier molecular orbital energies.

ability. The molecular orbital energies were calculated using the B3LYP functional level with the 6-31+G* basis set in a vacuum with *GAMESS* software (Schmidt *et al.*, 1993). The HOMO and LUMO orbitals were found to be well separated in energy and largely localized on the 4-chlorophenyl amide or aryltriazole motifs, respectively (Fig. 5). Their respective energy values were estimated to be −5.9 eV and −0.8 eV.

5. Database survey

The closest related compounds containing a similar 1-aryl-1*H*-1,2,3-triazole-4-carboxamide skeleton to the title compound but with different substituents on the amide are: (*S*)-1-(4-chlorophenyl)-*N*-(−1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (I) (CCDC refcode: ZIPSEY; Shen *et al.*, 2013), 1-(4-chlorophenyl)-5-methyl-*N*-[(3-phenyl-1,2-oxazol-5-yl)methyl]-1*H*-1,2,3-triazole-4-carboxamide (II) (LELHOB; Niu *et al.*, 2013), (5-methyl-1-(8-[trifluoromethyl)quinolin-4-yl]-1*H*-1,2,3-triazol-4-yl)morpholino)methanone (III) (LOHWIP; Anuradha *et al.*, 2008) and 1-(3-amino-5-(3-hydroxy-3-methylbut-1-yn-1-yl)phenyl)-*N*-butyl-1*H*-1,2,3-triazole-4-carboxamide (IV) (BEBJEZ; Li *et al.*, 2012).

Compounds (I) and (II) crystallize in the monoclinic crystal system [non-centrosymmetric space group $P2_1$ in (I) and centrosymmetric $P2_1/c$ in (II)], while compounds (III) and (IV) crystallize in the triclinic space group $P\overline{1}$. Structure (I) contains two crystallographically independent molecules, the hydroxyl groups of which participate in intermolecular O—H···O hydrogen bonds. In contrast to the structure of title compound, the dihedral angles between the phenyl rings and triazole rings in (I) are −45.2 (6)° (C5—C6—N1—N2) and 39.9 (6)° (C1′—C6′—N1′—N2′). The analogous angle in (II) is 19.2 (2)°. In structure (II), the carboxamide groups connect neighbouring molecules into infinite hydrogen-bonded chains by means of N—H···O hydrogen bonds: these are linked by N—H···O (oxazole) contacts into a three-dimensional framework. Similarly to (I) and (II), structure (III) contains a 5-methyl substituent at the triazole ring and, because of significant steric hindrance of the 8-(trifluoromethyl)quinoline group, the dihedral angle between the rings is 54.7°. The phenyl and triazole rings in (IV) are close to coplanar (7.5°), while the hydroxyl, carboxamide and amino groups participate in O—H···O and N—H···O hydrogen bonds. Finally, two copper(I) π-complexes with compositions $[Cu(C_{12}H_{13}N_5O)(NO_3)]\cdot 0.5H_2O$ and $[Cu(C_{12}H_{13}N_5O)(CF_3COO)]$ ($C_{12}H_{13}N_5O$ is *N*-allyl-5-amino-1-phenyl-1*H*-1,2,3-triazole-4-carboxamide) were obtained by electrochemical synthesis (ZEQTOG and ZEQTUM; Slyvka *et al.*, 2012). Crystals of both compounds

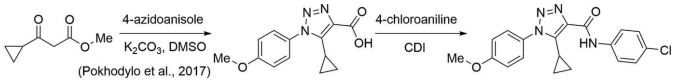


Figure 6
Synthesis of *N*-(4-chlorophenyl)-5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxamide.

are monoclinic, space group *C*2/*c*. In both structures, the *N*-allyl-1*H*-1,2,3-triazole-4-carboxamide moiety acts as a bridging chelating ligand and forms, with the copper(I) atoms, infinite chains containing [CuC_4NO] seven-membered rings.

6. Synthesis and crystallization

The title compound was synthesized from 5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid (Pokhodylo *et al.*, 2017) by the following procedure (Fig. 6). 5-Cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid **1** (1.3 g, 5.0 mmol) was added to a solution of 1,1′-carbonyldiimidazole (0.81 g, 5.0 mmol) in dry acetonitrile (25 ml) and the mixture was kept for 30 min at 323 K. Then 4-chloroaniline **2** (0.64 g, 5.0 mmol) was added, and the mixture was heated at 343 K for 1 h. After cooling to room temperature, water (30 ml) was added. The precipitate was filtered off, washed with water on a filter, recrystallized from ethanol solution, and dried in air to give the title compound as colourless prismatic crystals, m.p. 422–423 K; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.56 (*s*, 1H, NH), 7.89 (*d*, *J* = 8.6 Hz, 2H, H_{Ar}), 7.58 (*d*, *J* = 8.6 Hz, 2H, H_{Ar}), 7.39 (*d*, *J* = 8.6 Hz, 2H, H_{Ar}), 7.16 (*d*, *J* = 8.6 Hz, 2H, H_{Ar}), 3.86 (*s*, 3H, MeO), 2.10–1.99 (*m*, 1H, $_{cPr}$CH), 0.95–0.80 (*m*, 4H, $_{cPr}CH_2$); ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.62 (C═O or C_{Ar}—O), 159.60 (C═O or C_{Ar}—O), 142.26 ($C_{Triazole}$-4), 138.87 ($C_{Triazole}$-5), 138.21 (C^{ClAr}-1), 129.08 (C_{Ar}-1), 128.91 (2 × C_{ClAr}-3,5), 127.77 (2 × C_{Ar}-2,6), 127.70 (C_{ClAr}-4), 122.25 (2 × C_{ClAr}-2,6), 115.00 (2 × C_{Ar}-3,5), 56.06 (MeO), 8.09 (2 × CH_2^{cPr}), 5.75 (CH^{cPr}); MS *m*/*z* = 369 (M^++1); Analysis calculated for $C_{19}H_{17}ClN_4O_2$ (M_r = 368.82), (%): C 61.88, H 4.65, N 15.19; found (%): C 61.91, H 4.74, N 15.21.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All H atoms were positioned geometrically with N—H = 0.86 Å and C—H = 0.93–0.98 Å and refined as riding atoms. The constraint U_{iso}(H) = 1.2U_{eq}(carrier) or 1.5U_{eq}(C-methyl carrier) was applied in all cases.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{19}H_{17}ClN_4O_2$
M_r	368.82
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	293
a, *b*, *c* (Å)	10.5673 (4), 8.0182 (3), 21.2318 (10)
β (°)	95.282 (4)
V (Å^3)	1791.35 (13)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.24
Crystal size (mm)	0.5 × 0.08 × 0.07
Data collection	
Diffractometer	Oxford Diffraction Xcalibur3 CCD
Absorption correction	Multi-scan (*CrysAlis RED*; Oxford Diffraction, 2005)
T_{min}, T_{max}	0.890, 0.982
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10913, 3475, 1534
R_{int}	0.046
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.040, 0.053, 1.05
No. of reflections	3475
No. of parameters	236
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.14, −0.19

Computer programs: *CrysAlis PRO* (Oxford Diffraction, 2005), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*) and *OLEX2* (Dolomanov *et al.*, 2009).

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supporting information

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Synthesis, crystal structure and Hirshfeld surface analysis of *N*-(4-chlorophenyl)-5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxamide

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Computing details

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2005); cell refinement: *CrysAlis PRO* (Oxford Diffraction, 2005); data reduction: *CrysAlis PRO* (Oxford Diffraction, 2005); program(s) used to solve structure: ShelXT (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015b); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

N-(4-Chlorophenyl)-5-cyclopropyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxamide

Crystal data

$C_{19}H_{17}ClN_4O_2$
$M_r = 368.82$
Monoclinic, $P2_1/n$
$a = 10.5673$ (4) Å
$b = 8.0182$ (3) Å
$c = 21.2318$ (10) Å
$\beta = 95.282$ (4)°
$V = 1791.35$ (13) Å^3
$Z = 4$
$F(000) = 768$
$D_x = 1.368$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1540 reflections
$\theta = 0.9$–$1.0°$
$\mu = 0.24$ mm^{-1}
$T = 293$ K
Prism, colourless
0.5 × 0.08 × 0.07 mm

Data collection

Oxford Diffraction Xcalibur3 CCD diffractometer
ω scans
Absorption correction: multi-scan (CrysAlis RED; Oxford Diffraction, 2005)
$T_{min} = 0.890$, $T_{max} = 0.982$
10913 measured reflections
3475 independent reflections
1534 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$
$\theta_{max} = 26.0°$, $\theta_{min} = 2.7°$
$h = -12 \rightarrow 12$
$k = -5 \rightarrow 9$
$l = -25 \rightarrow 26$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.053$
$S = 1.05$
3475 reflections
236 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0071P)^2 + 0.050P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	1.19945 (6)	0.04278 (8)	0.35044 (3)	0.0860 (2)
O1	0.80102 (13)	0.41861 (18)	0.54511 (7)	0.0627 (5)
O2	0.01792 (15)	0.44313 (19)	0.73741 (7)	0.0686 (5)
N4	0.75389 (15)	0.1763 (2)	0.49150 (8)	0.0524 (5)
H4	0.695819	0.101374	0.485272	0.063*
N1	0.43143 (16)	0.3069 (2)	0.60195 (9)	0.0556 (5)
C14	0.8626 (2)	0.1540 (2)	0.45845 (11)	0.0443 (6)
C1	0.3243 (2)	0.3477 (2)	0.63661 (12)	0.0492 (6)
C9	0.5403 (2)	0.3903 (2)	0.59331 (10)	0.0479 (6)
C4	0.1154 (2)	0.4142 (3)	0.70082 (12)	0.0512 (6)
C10	0.7294 (2)	0.3016 (3)	0.53206 (11)	0.0505 (6)
N3	0.53626 (18)	0.1428 (2)	0.54590 (10)	0.0763 (7)
C15	0.9796 (2)	0.2218 (2)	0.47738 (10)	0.0520 (6)
H15	0.989197	0.290445	0.512804	0.062*
C8	0.6050 (2)	0.2842 (3)	0.55768 (11)	0.0486 (6)
C3	0.11310 (19)	0.4532 (2)	0.63777 (11)	0.0546 (6)
H3	0.041147	0.501519	0.616770	0.066*
N2	0.43009 (18)	0.1551 (2)	0.57229 (11)	0.0831 (7)
C19	0.84942 (19)	0.0551 (3)	0.40452 (10)	0.0539 (6)
H19	0.770296	0.011077	0.390662	0.065*
C2	0.2188 (2)	0.4199 (3)	0.60555 (10)	0.0546 (6)
H2	0.218048	0.446667	0.562890	0.066*
C16	1.0831 (2)	0.1881 (3)	0.44386 (11)	0.0573 (7)
H16	1.162198	0.233351	0.456901	0.069*
C11	0.57821 (19)	0.5584 (3)	0.61661 (11)	0.0596 (6)
H11	0.658079	0.596910	0.601492	0.072*
C18	0.9525 (2)	0.0218 (2)	0.37150 (10)	0.0585 (7)
H18	0.943421	−0.045418	0.335686	0.070*
C17	1.0685 (2)	0.0881 (3)	0.39158 (11)	0.0533 (6)
C5	0.2213 (2)	0.3398 (3)	0.73129 (11)	0.0635 (7)
H5	0.222148	0.312257	0.773873	0.076*
C6	0.3263 (2)	0.3056 (3)	0.69943 (12)	0.0623 (7)
H6	0.397430	0.254642	0.720160	0.075*
C13	0.5580 (2)	0.6216 (3)	0.68014 (12)	0.0782 (8)
H13A	0.511849	0.550992	0.707204	0.094*
H13B	0.625552	0.687084	0.702118	0.094*
C12	0.4869 (2)	0.6965 (3)	0.62524 (13)	0.0809 (8)
H12A	0.510672	0.808059	0.613084	0.097*
H12B	0.396882	0.671863	0.618174	0.097*

C7	−0.0993 (2)	0.4984 (3)	0.70643 (12)	0.0970 (9)
H7A	−0.128382	0.419658	0.674241	0.146*
H7B	−0.087613	0.605304	0.687433	0.146*
H7C	−0.161144	0.507674	0.736641	0.146*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0723 (5)	0.0988 (5)	0.0925 (5)	0.0004 (4)	0.0379 (4)	−0.0087 (4)
O1	0.0573 (10)	0.0568 (10)	0.0765 (12)	−0.0187 (8)	0.0189 (9)	−0.0171 (9)
O2	0.0585 (11)	0.0879 (12)	0.0627 (12)	0.0026 (9)	0.0231 (10)	0.0082 (9)
N4	0.0475 (12)	0.0478 (12)	0.0639 (14)	−0.0110 (9)	0.0167 (11)	−0.0108 (10)
N1	0.0512 (13)	0.0499 (12)	0.0682 (15)	−0.0072 (11)	0.0186 (12)	−0.0094 (11)
C14	0.0454 (15)	0.0413 (14)	0.0468 (15)	−0.0044 (11)	0.0087 (14)	−0.0008 (12)
C1	0.0468 (16)	0.0458 (14)	0.0565 (18)	−0.0048 (12)	0.0130 (15)	−0.0036 (13)
C9	0.0480 (15)	0.0428 (14)	0.0534 (16)	−0.0059 (12)	0.0067 (14)	−0.0038 (12)
C4	0.0516 (17)	0.0527 (15)	0.0507 (17)	−0.0039 (12)	0.0127 (15)	0.0017 (13)
C10	0.0562 (17)	0.0463 (15)	0.0501 (16)	0.0002 (13)	0.0103 (15)	−0.0024 (13)
N3	0.0591 (14)	0.0633 (15)	0.1115 (19)	−0.0171 (11)	0.0347 (14)	−0.0363 (12)
C15	0.0512 (15)	0.0488 (15)	0.0553 (18)	−0.0033 (12)	0.0013 (15)	−0.0112 (12)
C8	0.0436 (15)	0.0443 (15)	0.0589 (17)	−0.0099 (12)	0.0110 (14)	−0.0123 (12)
C3	0.0493 (15)	0.0617 (15)	0.0540 (17)	0.0043 (12)	0.0109 (14)	0.0055 (13)
N2	0.0665 (16)	0.0618 (14)	0.127 (2)	−0.0215 (11)	0.0420 (15)	−0.0392 (13)
C19	0.0503 (15)	0.0561 (14)	0.0564 (16)	−0.0130 (12)	0.0109 (14)	−0.0093 (13)
C2	0.0619 (17)	0.0589 (15)	0.0434 (15)	−0.0041 (14)	0.0065 (15)	0.0055 (12)
C16	0.0456 (16)	0.0629 (16)	0.0644 (19)	−0.0073 (13)	0.0105 (15)	−0.0063 (14)
C11	0.0580 (16)	0.0533 (15)	0.0704 (18)	−0.0040 (13)	0.0210 (14)	−0.0185 (14)
C18	0.0657 (17)	0.0595 (16)	0.0520 (16)	−0.0095 (14)	0.0143 (15)	−0.0114 (12)
C17	0.0523 (16)	0.0561 (15)	0.0542 (17)	0.0004 (13)	0.0198 (14)	0.0034 (13)
C5	0.0602 (18)	0.0838 (18)	0.0474 (17)	−0.0001 (14)	0.0095 (16)	0.0168 (14)
C6	0.0478 (17)	0.0717 (17)	0.067 (2)	0.0024 (13)	0.0025 (16)	0.0143 (15)
C13	0.083 (2)	0.0669 (18)	0.085 (2)	−0.0152 (15)	0.0110 (19)	−0.0197 (16)
C12	0.073 (2)	0.0489 (16)	0.119 (2)	0.0045 (14)	−0.0003 (19)	−0.0099 (17)
C7	0.0580 (18)	0.136 (3)	0.102 (2)	0.0258 (17)	0.0314 (17)	0.0219 (19)

Geometric parameters (Å, º)

Cl1—C17	1.742 (2)	C3—H3	0.9300
O1—C10	1.221 (2)	C3—C2	1.389 (3)
O2—C4	1.366 (2)	C19—H19	0.9300
O2—C7	1.419 (2)	C19—C18	1.375 (3)
N4—H4	0.8600	C2—H2	0.9300
N4—C14	1.412 (2)	C16—H16	0.9300
N4—C10	1.364 (2)	C16—C17	1.367 (3)
N1—C1	1.443 (2)	C11—H11	0.9800
N1—C9	1.358 (2)	C11—C13	1.475 (3)
N1—N2	1.370 (2)	C11—C12	1.491 (3)
C14—C15	1.376 (3)	C18—H18	0.9300

C14—C19	1.389 (2)	C18—C17	1.367 (3)
C1—C2	1.370 (3)	C5—H5	0.9300
C1—C6	1.374 (3)	C5—C6	1.379 (3)
C9—C8	1.363 (2)	C6—H6	0.9300
C9—C11	1.478 (3)	C13—H13A	0.9700
C4—C3	1.373 (3)	C13—H13B	0.9700
C4—C5	1.376 (3)	C13—C12	1.457 (3)
C10—C8	1.476 (3)	C12—H12A	0.9700
N3—C8	1.357 (2)	C12—H12B	0.9700
N3—N2	1.303 (2)	C7—H7A	0.9600
C15—H15	0.9300	C7—H7B	0.9600
C15—C16	1.385 (3)	C7—H7C	0.9600

C4—O2—C7	117.47 (18)	C15—C16—H16	120.1
C14—N4—H4	115.9	C17—C16—C15	119.8 (2)
C10—N4—H4	115.9	C17—C16—H16	120.1
C10—N4—C14	128.10 (18)	C9—C11—H11	113.1
C9—N1—C1	132.18 (19)	C9—C11—C12	124.1 (2)
C9—N1—N2	110.40 (17)	C13—C11—C9	124.2 (2)
N2—N1—C1	117.40 (17)	C13—C11—H11	113.1
C15—C14—N4	123.7 (2)	C13—C11—C12	58.84 (14)
C15—C14—C19	119.1 (2)	C12—C11—H11	113.1
C19—C14—N4	117.2 (2)	C19—C18—H18	120.2
C2—C1—N1	119.5 (2)	C17—C18—C19	119.7 (2)
C2—C1—C6	120.7 (2)	C17—C18—H18	120.2
C6—C1—N1	119.8 (2)	C16—C17—Cl1	119.63 (19)
N1—C9—C8	103.98 (17)	C16—C17—C18	120.8 (2)
N1—C9—C11	127.6 (2)	C18—C17—Cl1	119.56 (18)
C8—C9—C11	128.4 (2)	C4—C5—H5	119.6
O2—C4—C3	124.7 (2)	C4—C5—C6	120.8 (2)
O2—C4—C5	115.5 (2)	C6—C5—H5	119.6
C3—C4—C5	119.9 (2)	C1—C6—C5	119.1 (2)
O1—C10—N4	124.08 (19)	C1—C6—H6	120.5
O1—C10—C8	122.9 (2)	C5—C6—H6	120.5
N4—C10—C8	113.0 (2)	C11—C13—H13A	117.7
N2—N3—C8	108.94 (17)	C11—C13—H13B	117.7
C14—C15—H15	119.9	H13A—C13—H13B	114.8
C14—C15—C16	120.2 (2)	C12—C13—C11	61.14 (16)
C16—C15—H15	119.9	C12—C13—H13A	117.7
C9—C8—C10	130.9 (2)	C12—C13—H13B	117.7
N3—C8—C9	109.70 (18)	C11—C12—H12A	117.8
N3—C8—C10	119.4 (2)	C11—C12—H12B	117.8
C4—C3—H3	120.2	C13—C12—C11	60.02 (15)
C4—C3—C2	119.6 (2)	C13—C12—H12A	117.8
C2—C3—H3	120.2	C13—C12—H12B	117.8
N3—N2—N1	106.97 (17)	H12A—C12—H12B	114.9
C14—C19—H19	119.8	O2—C7—H7A	109.5
C18—C19—C14	120.4 (2)	O2—C7—H7B	109.5

C18—C19—H19	119.8	O2—C7—H7C	109.5
C1—C2—C3	120.0 (2)	H7A—C7—H7B	109.5
C1—C2—H2	120.0	H7A—C7—H7C	109.5
C3—C2—H2	120.0	H7B—C7—H7C	109.5
O1—C10—C8—C9	6.7 (4)	C4—C5—C6—C1	0.4 (3)
O1—C10—C8—N3	−173.6 (2)	C10—N4—C14—C15	23.3 (4)
O2—C4—C3—C2	179.10 (19)	C10—N4—C14—C19	−158.0 (2)
O2—C4—C5—C6	−179.5 (2)	C15—C14—C19—C18	1.7 (3)
N4—C14—C15—C16	177.1 (2)	C15—C16—C17—Cl1	−178.77 (17)
N4—C14—C19—C18	−177.10 (19)	C15—C16—C17—C18	0.6 (3)
N4—C10—C8—C9	−171.8 (2)	C8—C9—C11—C13	−139.8 (3)
N4—C10—C8—N3	7.9 (3)	C8—C9—C11—C12	147.4 (3)
N1—C1—C2—C3	177.23 (19)	C8—N3—N2—N1	−0.5 (3)
N1—C1—C6—C5	−177.6 (2)	C3—C4—C5—C6	0.8 (3)
N1—C9—C8—C10	179.6 (2)	N2—N1—C1—C2	−86.6 (2)
N1—C9—C8—N3	−0.1 (3)	N2—N1—C1—C6	89.8 (3)
N1—C9—C11—C13	41.2 (4)	N2—N1—C9—C8	−0.2 (2)
N1—C9—C11—C12	−31.6 (4)	N2—N1—C9—C11	179.1 (2)
C14—N4—C10—O1	1.2 (4)	N2—N3—C8—C9	0.4 (3)
C14—N4—C10—C8	179.7 (2)	N2—N3—C8—C10	−179.4 (2)
C14—C15—C16—C17	0.5 (3)	C19—C14—C15—C16	−1.6 (3)
C14—C19—C18—C17	−0.7 (3)	C19—C18—C17—Cl1	178.88 (17)
C1—N1—C9—C8	178.1 (2)	C19—C18—C17—C16	−0.5 (3)
C1—N1—C9—C11	−2.7 (4)	C2—C1—C6—C5	−1.2 (3)
C1—N1—N2—N3	−178.2 (2)	C11—C9—C8—C10	0.4 (4)
C9—N1—C1—C2	95.2 (3)	C11—C9—C8—N3	−179.3 (2)
C9—N1—C1—C6	−88.4 (3)	C5—C4—C3—C2	−1.2 (3)
C9—N1—N2—N3	0.4 (3)	C6—C1—C2—C3	0.8 (3)
C9—C11—C13—C12	−112.4 (3)	C7—O2—C4—C3	8.1 (3)
C9—C11—C12—C13	112.6 (3)	C7—O2—C4—C5	−171.63 (19)
C4—C3—C2—C1	0.4 (3)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4···N3	0.86	2.24	2.680 (3)	112
N4—H4···N2^{i}	0.86	2.68	3.491 (2)	157
C15—H15···O1	0.93	2.39	2.936 (2)	117
C19—H19···N2^{i}	0.93	2.68	3.475 (3)	144
C2—H2···O1^{ii}	0.93	2.53	3.439 (3)	167
C11—H11···O1	0.98	2.47	3.124 (2)	124

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