IUCrData

ISSN 2414-3146

5-Aminolevulinic acid hydrochloride

Jean guillaume Ducreux,[a] James A. Kaduk,[a]* Anja Dosen[b] and Thomas N. Blanton[b]

[a]North Central College, Department of Chemistry, 131 S. Loomis St, Naperville, IL 60540, USA, and [b]ICDD, 12 Campus Blvd, Newtown Square, PA 19073, USA. *Correspondence e-mail: kaduk@polycrystallography.com

Received 26 March 2026
Accepted 17 April 2026

Edited by M. Zeller, Purdue University, USA

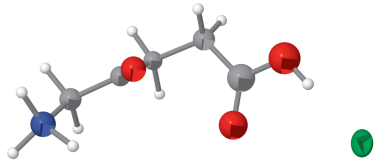
Keywords: powder diffraction; aminolevulinic acid; Rietveld refinement; density functional theory.

CCDC reference: 2548850

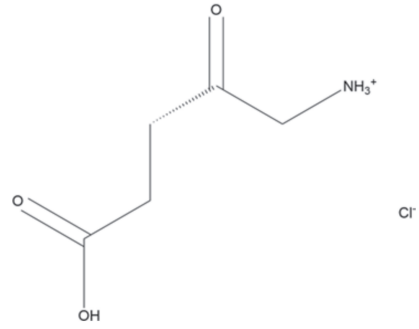
Structural data: full structural data are available from iucrdata.iucr.org

The crystal structure of 5-aminolevulinic acid hydrochloride (systematic name: 4-carboxy-2-oxobutan-1-aminium chloride), $C_5H_{10}NO_3^+\cdot Cl^-$, has been solved and refined using synchrotron X-ray powder diffraction data, and optimized using density functional theory (DFT) techniques. The structure is compared to a recent single-crystal determination [Wang *et al.* (2025). *Z. Kristallogr. New Cryst. Struct.* **240**, 413–414]. 5-Aminolevulinic acid hydrochloride crystallizes in the space group *Pbca* (No. 61), with a = 8.20862 (9), b = 11.22253 (10), c = 16.8595 (2) Å, V = 1553.12 (4) Å^3, and Z = 8 at 298 K. The crystal structure consists of layers parallel to the *ab* plane. The center of the layers contains hydrophilic NH_3, Cl, and CO_2H groups, and the outer surface of the layers is composed of hydrophobic CH_2 groups. Hydrogen bonds are prominent in the crystal structure. The ammonium group acts as a donor to three chloride anions, and one hydrogen bond is bifurcated to the carbonyl group. Each Cl^- anion is an acceptor in three N—H···Cl hydrogen bonds, plus one from the carboxylic acid group. These hydrogen bonds connect the cations and anions into the layers parallel to the *ab* plane. The powder pattern has been submitted to the International Centre for Diffraction Data (ICDD) for inclusion in the Powder Diffraction File (PDF)

3D view



Chemical scheme



Structure description

5-Aminolevulinic acid hydrochloride is a porphyrin precursor and a photosensitizing agent. It finds application in the treatment of skin problems, including actinic keratosis and early-stage carcinomas. The systematic name (CAS Registry Number 5451-09-2) is 4-carboxy-2-oxobutan-1-aminium chloride. X-ray powder diffraction data for 5-aminolevulinic acid hydrochloride has been reported in Chinese Patent CN113149854A (Gu *et al.*, 2021). The single-crystal structure of 5-aminolevulinic acid hydrochloride has been determined very recently [Wang *et al.*, 2025; Cambridge Structural Database (CSD; Groom *et al.*, 2016) refcode MUPYOP]. This work is part of a project (Kaduk *et al.*, 2014)

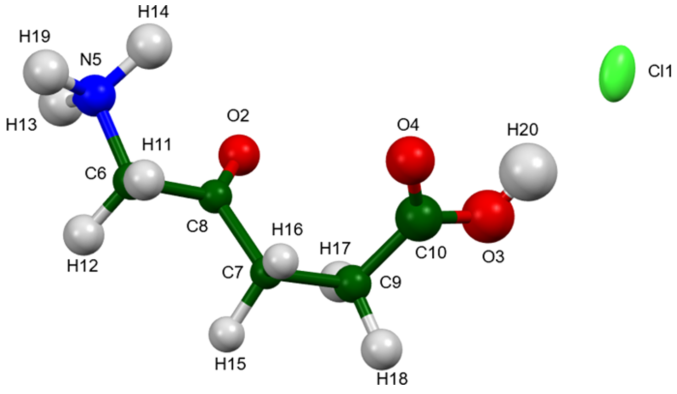


Figure 1
The asymmetric unit of 5-aminolevulinic acid hydrochloride, with the atom numbering. The atoms are represented by 50% probability spheroids/ellipsoids. Image generated using *Mercury* (Macrae *et al.*, 2020).

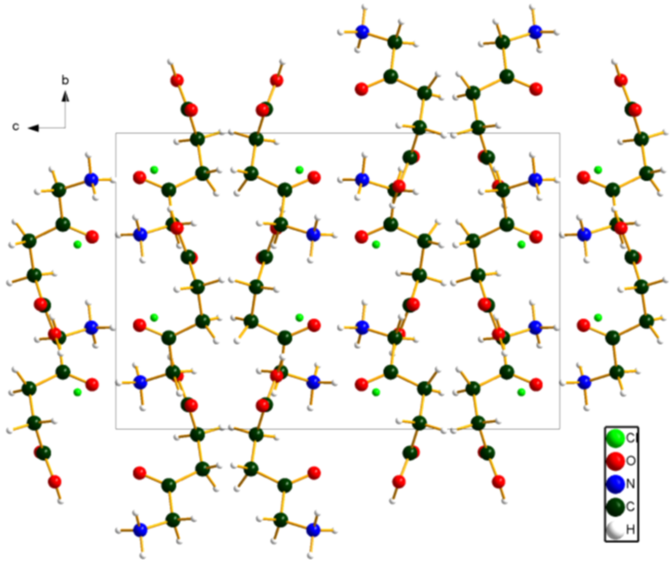


Figure 2
The crystal structure of 5-aminolevulinic acid hydrochloride, viewed down the *a* axis. Image generated using *DIAMOND* (Putz & Brandenburg, 2025).

to determine commercial pharmaceutical crystal structures and add high-quality powder diffraction data to the Powder Diffraction File (Kabekkodu *et al.*, 2024).

The r.m.s. Cartesian displacement of the single-crystal (Wang *et al.*, 2025) and Rietveld-refined structures is 0.159 Å. The r.m.s. agreement of the Rietveld-refined and *VASP*-optimized structures is 0.172 Å. The agreement of the single-crystal, Rietveld, and *VASP* structures is very good. The agreements are all well within the normal range for correct structures (van de Streek & Neumann, 2014). The isotropic displacement coefficients from the Rietveld refinement correlate very well to the isotropic equivalents calculated form the anisotropic displacement coefficients from the single-crystal refinement, providing another measure of the accuracy of the powder structure. The standard uncertainties on the fractional coordinates from the Rietveld refinement average about 3.5 times larger than those from the single-crystal structure. The powder structure is accurate, but less precise, than the single-crystal structure. The asymmetric unit with the atom numbering is presented in Fig. 1.

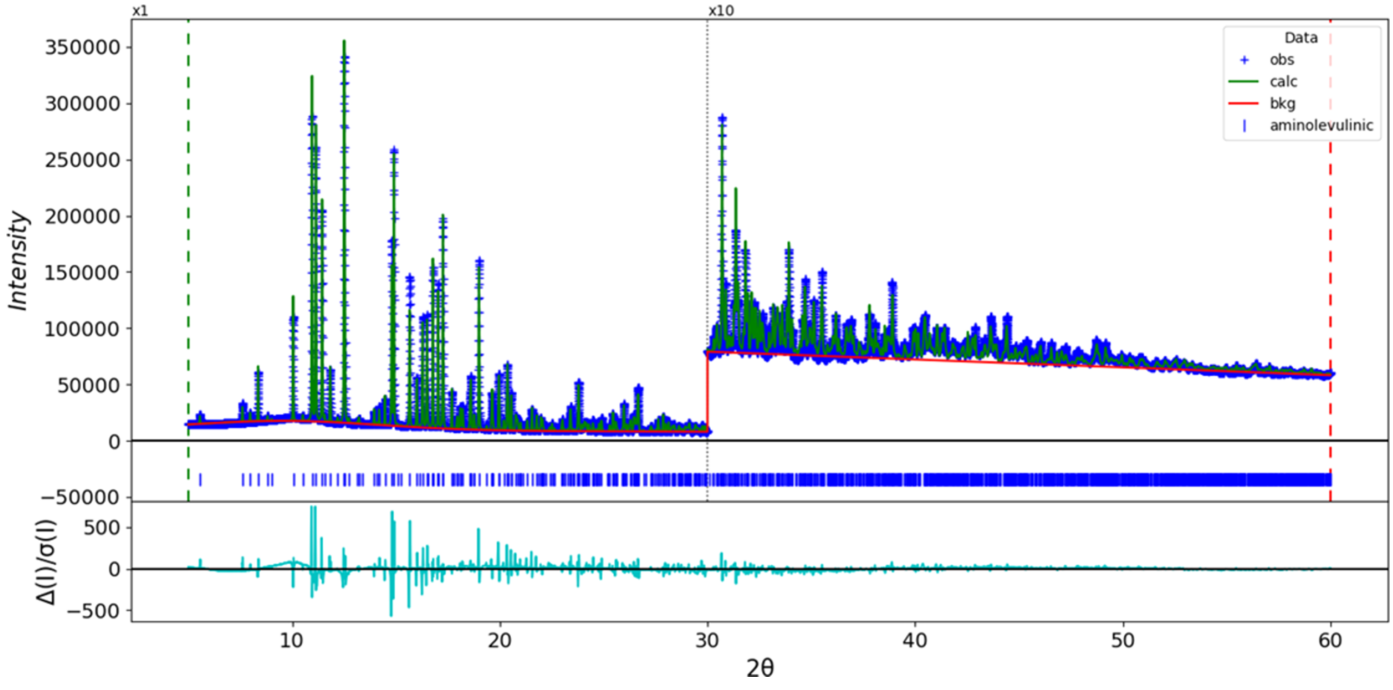


Figure 3
The Rietveld plot for 5-aminolevulinic acid hydrochloride. The blue crosses represent the observed data points and the green line is the calculated pattern. The cyan curve is the normalized error plot and the red line is the background curve. The blue tick marks indicate the peak positions. The vertical scale has been multiplied by a factor of ×10 for $2\theta > 30.0°$.

All of the bond distances, bond angles, and torsion angles fall within the normal ranges indicated by a *Mercury Mogul* Geometry check (Macrae *et al.*, 2020). Quantum chemical geometry optimization of the isolated cation (DFT/B3LYP/6-31G*/water) using *Spartan '24* (Wavefunction, 2023) indicated that it is 3.1 kcal mol^{-1} higher in energy than the local minimum, which has a similar conformation (r.m.s. displacement = 0.087 Å). The global minimum-energy conformation has the same energy, but a slightly different conformation (r.m.s. difference = 0.917 Å), mainly at the periphery of the cation. The cation is apparently flexible, and intermolecular interactions determine the solid-state conformation.

The crystal structure (Fig. 2) consists of layers parallel to the *ab* plane. The center of layers contains hydrophilic NH_3, Cl, and CO_2H groups, and the outer surface of the layers is composed of hydrophobic CH_2 groups.

Analysis of the contributions to the total crystal energy of the structure using the Forcite module of *Materials Studio* (Dassault Systèmes, 2024) suggests that the intramolecular deformation energy is dominated by angle distortion terms, while van der Waals attractions (which in this force field-based analysis include hydrogen bonds) dominate the intermolecular energy.

Hydrogen bonds are prominent in the crystal structure. The ammonium group acts as a donor to three chloride anions, and one hydrogen bond is bifurcated to the O2 carbonyl group. Each chloride anion is an acceptor in three N—H···Cl hydrogen bonds, plus one from the carboxylic acid group. These hydrogen bonds connect the cations and anions into layers parallel to the *ab* plane. The energies of the N—H···O hydrogen bonds were calculated using the correlation of Wheatley & Kaduk (2019), and the energy of the O—H···Cl hydrogen bond was calculated using the correlation of Kaduk (2002). Three C—H···O/Cl hydrogen bonds also contribute to the lattice energy.

The Bravais–Friedel–Donnay–Harker (Bravais, 1866; Friedel, 1907; Donnay & Harker, 1937) morphology suggests that we might expect isotropic morphology for 5-aminolevulinic acid hydrochloride. A second-order spherical harmonic model was included in the refinement. The texture index was 1.010 (0), indicating that preferred orientation was not significant in this rotated capillary specimen.

Synthesis and crystallization

5-Aminolevulinic acid hydrochloride was a white powder purchased from TargetMol (Batch No. 146376), and was used as-received.

Refinement

The powder sample was analyzed at 298 K at the Wiggler Low Energy Beamline (Leontowich *et al.*, 2021) of the Brockhouse X-ray Diffraction and Scattering Sector of the Canadian Light Source using a wavelength of 0.819325 (2) Å (15.1 keV). The pattern was indexed using *JADE Pro* (MDI, 2025) and the crystal structure was solved independently using direct methods, as implemented in *EXPO2014* (Altomare *et al.*, 2013). The original structure solution yielded the carboxylic acid group rotated ∼180° from the single-crystal structure. The single-crystal structure was 26.7 kcal/mol/cell lower in energy, and that conformation was adopted for the refinement.

Rietveld refinement (Fig. 3) was carried out using *GSAS-II* (Toby & Von Dreele, 2013). All non-H bond distances and angles were restrained according to a *Mercury/Mogul Geometry Check* (Sykes *et al.*, 2011; Bruno *et al.*, 2004). H atoms were included in calculated positions and recalculated during the refinement using the *Mercury* (Macrae *et al.*, 2020) 'Auto Edit' feature and the 'Adjust Hydrogen' feature of *Materials Studio* (Dassault Systèmes, 2024). The Cl atom was refined anisotropically. the U_{iso} values of the C, N, and O atoms were refined individually, while the U_{iso} values for the H atoms were fixed at 1.2 times the U_{iso} of the C, N, and O atoms to which they are attached. The final refinement yielded R_{wp} = 0.10874. The largest features in the normalized error plot are in the positions of many of the strong low-angle peaks, and may indicate that the specimen changed during the measurement. The largest peak (0.55 Å from Cl1) and hole (1.86 Å from Cl1) in the difference Fourier map were 0.87 (18) and −0.81 (18) e Å^{-3}, respectively.

The crystal structure of 5-aminolevulinic acid hydrochloride was optimized (fixed unit cell) with density functional theory (DFT) techniques using *VASP* (Version 6.0; Kresse & Furthmüller, 1996) through the *MedeA* graphical interface (Materials Design, 2024). Single-point density functional theory calculations (fixed experimental cell) and population

Table 1
Experimental details.

Crystal data	
Chemical formula	$C_5H_{10}NO_3^+\cdot Cl^-$
M_r	167.59
Crystal system, space group	Orthorhombic, *Pbca*
Temperature (K)	298
a, *b*, *c* (Å)	8.20862 (9), 11.22253 (10), 16.8595 (2)
V (Å^3)	1553.12 (4)
Z	8
Radiation type	Synchrotron, λ = 0.81933 Å
μ (mm^{-1})	0.29
Specimen shape, size (mm)	Cylinder, 0.45 × 0.15
Data collection	
Diffractometer	Wiggler Low Energy Beamline, Brockhouse X-ray Diffraction and Scattering Sector, Canadian Light Source
Specimen mounting	Kapton capillary
Data collection mode	Transmission
Scan method	Step
2θ values (°)	$2\theta_{min}$ = −9.008 $2\theta_{max}$ = 75.047 $2\theta_{step}$ = 0.003
Refinement	
R factors and goodness of fit	R_p = 0.071, R_{wp} = 0.109, R_{exp} = 0.002, $R(F^2)$ = 0.09084, χ^2 = 2566.942
No. of parameters	64
No. of restraints	34
$(\Delta/\sigma)_{max}$	7.079

Computer programs: *GSAS*-II (Toby & Von Dreele, 2013).

analysis were carried out using *CRYSTAL23* (Erba *et al.*, 2023) using H, C, N, and O basis sets defined by Gatti *et al.* (1994) and the Cl basis set of Peintinger *et al.* (2013).

Experimental details are given in Table 1.

Acknowledgements

Part of the research described in this article was performed at the Canadian Light Source, a national research facility of the University of Saskatchewan, which is supported by the Canada Foundation for Innovation (CFI), the Natural Sciences and Engineering Research Council (NSERC), the Canadian Institute of Health Research (CIHR), the Government of Saskatchewan, and the University of Saskatchewan. This work was partially supported by the International Centre for Diffraction Data. We thank Adam Leontowich for his assistance in the data collection. We also thank the ICDD team – Megan Rost, Steve Trimble, and Dave Bohnenberger – for their contribution to research, sample preparation, and in-house XRD data collection and verification.

Funding information

Funding for this research was provided by: International Centre for Diffraction Data (grant No. 09-03).

References

Altomare, A., Cuocci, C., Giacovazzo, C., Moliterni, A., Rizzi, R., Corriero, N. & Falcicchio, A. (2013). *J. Appl. Cryst.* **46**, 1231–1235.

Bravais, A. (1866). In *Etudes Cristallographiques*. Paris: Gauthier Villars.

Bruno, I. J., Cole, J. C., Kessler, M., Luo, J., Motherwell, W. D. S., Purkis, L. H., Smith, B. R., Taylor, R., Cooper, R. I., Harris, S. E. & Orpen, A. G. (2004). *J. Chem. Inf. Comput. Sci.* **44**, 2133–2144.

Dassault Systèmes (2024). *BIOVIA Materials Studio 2025*. BIOVIA, San Diego, CA, USA.

Donnay, J. D. H. & Harker, D. (1937). *Am. Mineral.* **22**, 446–467.

Erba, A., Desmarais, J. K., Casassa, S., Civalleri, B., Donà, L., Bush, I. J., Searle, B., Maschio, L., Edith-Daga, L., Cossard, A., Ribaldone, C., Ascrizzi, E., Marana, N. L., Flament, J.-P. & Kirtman, B. (2023). *J. Chem. Theory Comput.* **19**, 6891–6932.

Friedel, G. (1907). *Bull. Soc. Fr. Mineral.* **30**, 326–455.

Gatti, C., Saunders, V. R. & Roetti, C. (1994). *J. Chem. Phys.* **101**, 10686–10696.

Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.

Gu, H., Li, B. & Chen, C. (2021). Chinese Patent CN113149854A.

Kabekkodu, S., Dosen, A. & Blanton, T. N. (2024). *Powder Diffr.* **39**, 47–59.

Kaduk, J. A. (2002). *Acta Cryst.* B**58**, 370–379.

Kaduk, J. A., Crowder, C. E., Zhong, K., Fawcett, T. G. & Suchomel, M. R. (2014). *Powder Diffr.* **29**, 269–273.

Kresse, G. & Furthmüller, J. (1996). *Comput. Mater. Sci.* **6**, 15–50.

Leontowich, A. F. G., Gomez, A., Diaz Moreno, B., Muir, D., Spasyuk, D., King, G., Reid, J. W., Kim, C.-Y. & Kycia, S. (2021). *J. Synchrotron Rad.* **28**, 961–969.

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.

Materials Design (2024). *MedeA*. Version 3.7.2. Materials Design Inc., San Diego, CA, USA.

MDI (2025). *JADE Pro*. Version 9.3. Materials Data, Livermore, USA.

Peintinger, M. F., Oliveira, D. V. & Bredow, T. (2013). *J. Comput. Chem.* **34**, 451–459.

Putz, H. & Brandenburg, K. (2025). *DIAMOND*. Crystal Impact, Bonn, Germany.

Streek, J. van de & Neumann, M. A. (2014). *Acta Cryst.* B**70**, 1020–1032.

Sykes, R. A., McCabe, P., Allen, F. H., Battle, G. M., Bruno, I. J. & Wood, P. A. (2011). *J. Appl. Cryst.* **44**, 882–886.

Toby, B. H. & Von Dreele, R. B. (2013). *J. Appl. Cryst.* **46**, 544–549.

Wang, F., Zhang, C., Wang, Y., Luan, L., Hu, X. & Liu, Y. (2025). *Z. Kristallogr. New Cryst. Struct.* **240**, 413–414.

Wavefunction (2023). *Spartan '24*. Wavefunction Inc., Irvine, CA , USA.

Wheatley, A. M. & Kaduk, J. A. (2019). *Powder Diffr.* **34**, 35–43.

full crystallographic data

IUCrData (2026). **11**, x260404 [https://doi.org/10.1107/S2414314626004049]

5-Aminolevulinic acid hydrochloride

Jean guillaume Ducreux, James A. Kaduk, Anja Dosen and Thomas N. Blanton

4-Carboxy-2-oxobutan-1-aminium chloride

Crystal data

$C_5H_{10}NO_3^+ \cdot Cl^-$
M_r = 167.59
Orthorhombic, *Pbca*
a = 8.20862 (9) Å
b = 11.22253 (10) Å
c = 16.8595 (2) Å
V = 1553.12 (4) Å^3
Z = 8
D_x = 1.434 Mg m^{-3}
Synchrotron radiation, λ = 0.81933 Å
μ = 0.29 mm^{-1}
T = 298 K
cylinder, 0.45 × 0.15 mm

Data collection

Wiggler Low Energy Beamline, Brockhouse X-ray Diffraction and Scattering Sector, Canadian Light Source diffractometer
Specimen mounting: Kapton capillary
Data collection mode: transmission
Scan method: step
$2\theta_{min}$ = −9.008°, $2\theta_{max}$ = 75.047°, $2\theta_{step}$ = 0.003°

Refinement

Least-squares matrix: full
R_p = 0.071
R_{wp} = 0.109
R_{exp} = 0.002
$R(F^2)$ = 0.09084
33623 data points
Profile function: Finger-Cox-Jephcoat function parameters U, V, W, X, Y, SH/L: peak variance(Gauss) = Utan(Th)^2+Vtan(Th)+W: peak HW(Lorentz) = X/cos(Th)+Ytan(Th); SH/L = S/L+H/L U, V, W in (centideg)^2, X & Y in centideg 6.157, -1.198, 1.258, 0.000, 0.667, 0.002,
64 parameters
34 restraints
0 constraints
Weighting scheme based on measured s.u.'s
$(\Delta/\sigma)_{max}$ = 7.079
Background function: Background function: "chebyschev-1" function with 3 terms: 7.73(3)e3, -1.90(5)e3, -8(3), Background peak parameters: pos, int, sig, gam: 9.68(4), 9.22(18)e6, 1.98(5)e5, 0.100,
Preferred orientation correction: Simple spherical harmonic correction Order = 2 Coefficients: 0:0:C(2,0) = -0.185(6); 0:0:C(2,2) = -0.092(8)

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

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	−0.08722 (19)	−0.38073 (14)	0.41224 (10)	0.0481
O2	0.0446 (6)	0.1463 (3)	0.4452 (3)	0.0436 (19)*
O3	0.1421 (6)	−0.1790 (3)	0.3666 (3)	0.072 (2)*
O4	−0.0889 (6)	−0.0777 (4)	0.3361 (2)	0.061 (2)*
N5	−0.1619 (6)	0.3359 (4)	0.4450 (3)	0.045 (2)*
C6	−0.0760 (7)	0.3045 (5)	0.3692 (4)	0.036 (3)*

C7	0.0829 (8)	0.1383 (5)	0.3041 (4)	0.028 (2)*
C8	0.0181 (8)	0.1909 (6)	0.3815 (5)	0.029 (2)*
C9	0.1717 (9)	0.0206 (6)	0.3188 (4)	0.037 (3)*
C10	0.0637 (10)	−0.0816 (7)	0.3375 (4)	0.057 (3)*
H11	−0.16952	0.29163	0.31995	0.0432*
H12	0.01136	0.37928	0.35232	0.0432*
H13	−0.07194	0.37918	0.48770	0.0535*
H14	−0.21369	0.25158	0.47304	0.0535*
H15	0.17071	0.20435	0.27562	0.0332*
H16	−0.02297	0.12117	0.26185	0.0332*
H17	0.26049	0.03343	0.37008	0.0438*
H18	0.24389	−0.00500	0.26360	0.0438*
H19	−0.26527	0.40077	0.43180	0.0535*
H20	0.07050	−0.24190	0.38070	0.0865*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0527 (18)	0.0384 (15)	0.053 (2)	0.006 (3)	−0.026 (3)	−0.018 (3)

Geometric parameters (Å, º)

O2—C8	1.205 (8)	C8—C7	1.528 (8)
O3—C10	1.360 (7)	C9—C7	1.529 (7)
O3—H20	0.949 (4)	C9—C10	1.483 (8)
O4—C10	1.254 (8)	C9—H17	1.140 (6)
N5—C6	1.502 (8)	C9—H18	1.141 (7)
N5—H13	1.139 (5)	C10—O3	1.360 (7)
N5—H14	1.140 (5)	C10—O4	1.254 (8)
N5—H19	1.140 (5)	C10—C9	1.483 (8)
C6—N5	1.502 (8)	H11—C6	1.140 (6)
C6—C8	1.505 (6)	H12—C6	1.140 (6)
C6—H11	1.140 (6)	H13—N5	1.139 (5)
C6—H12	1.140 (6)	H14—N5	1.140 (5)
C7—C8	1.528 (8)	H15—C7	1.140 (6)
C7—C9	1.529 (7)	H16—C7	1.140 (6)
C7—H15	1.140 (6)	H17—C9	1.140 (6)
C7—H16	1.140 (6)	H18—C9	1.141 (7)
C8—O2	1.205 (8)	H19—N5	1.140 (5)
C8—C6	1.505 (6)	H20—O3	0.957 (4)
C10—O3—H20	113.3 (5)	C8—C7—H16	109.5 (6)
C6—N5—H13	109.5 (5)	C9—C7—H16	108.6 (5)
C6—N5—H14	109.4 (4)	H15—C7—H16	109.2 (5)
H13—N5—H14	109.5 (5)	O2—C8—C6	124.5 (8)
C6—N5—H19	109.4 (5)	O2—C8—C7	122.6 (7)
H13—N5—H19	109.5 (4)	C6—C8—C7	112.9 (7)
H14—N5—H19	109.5 (4)	C7—C9—C10	114.7 (6)

N5—C6—C8	108.8 (6)	C7—C9—H17	108.6 (5)
N5—C6—H11	109.5 (5)	C10—C9—H17	108.7 (6)
C8—C6—H11	109.8 (5)	C7—C9—H18	109.4 (6)
N5—C6—H12	109.5 (6)	C10—C9—H18	106.8 (5)
C8—C6—H12	109.6 (5)	H17—C9—H18	108.6 (6)
H11—C6—H12	109.6 (6)	O3—C10—O4	120.5 (8)
C8—C7—C9	111.1 (6)	O3—C10—C9	114.5 (7)
C8—C7—H15	109.1 (5)	O4—C10—C9	124.5 (7)
C9—C7—H15	109.2 (6)		