ISSN 1070-3284, Russian Journal of Coordination Chemistry, 2018, Vol. 44, No. 1, pp. 52–58. © Pleiades Publishing, Ltd., 2018.

Syntheses and Crystal Structures of Quinidinum-Zinc(II)-Trichloride and Quinidinum Iron(III) Tetrachloride Hydrogen Chloride Hydrate[1]

J. Gu, A. Q. Jia*, and Q. F. Zhang

Institute of Molecular Engineering and Applied Chemistry, and Anhui Province Key Laboratory of Metallurgy Engineering and Resources Recycling, Anhui University of Technology, Ma'anshan, Anhui, 243002 P.R. China

**e-mail: jaiquan@ahut.edu.cn*

Received April 7, 2017

Abstract—A mononuclear coordination complex, quinidinum-zinc(II)-trichloride (**I**), and a *multi*-component ionic complex, quinidinum iron(III) tetrachloride hydrogen chloride hydrate (**II**), have been synthesized and characterized by elemental analyses, IR spectra, and single crystal X-ray diffraction (CIF files nos. 1497628 (**I**) and 1497629 (**II**)). The weak hydrogen-bonding interactions exist in both complexes **I** and **II**. Both complexes crystallize in the chiral space groups with the absolute configuration. Complex **I** crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 7.6651(6)$, $b = 11.4923(9)$, $c = 24.653(2)$ Å, and $Z = 4$. Complex **II** crystallizes in the monoclinic space group $P2_1$ with $a = 6.6425(15)$, $b = 18.660(4)$, $c = 10.958(3)$ Å, $\beta = 104.973(3)$, and $Z = 2$.

Keywords: quinine, zinc complex, iron complex, crystal structure, hydrogen bonds

DOI: 10.1134/S1070328418010049

INTRODUCTION

The modification of existing anti-malarial drugs by coordination to a metal center has attracted considerable attention in past decades. Obviously, the synthetic strategy involves modification of the activity of the anti-malarial drugs through the incorporation of a transition metal into the molecular structure, which may enhance anti-malarial activities of such complexes [1]. Despite the fact that various metal complexes of anti-malarial drugs, such as amodiaquine and chloroquine, and ferrocenic complexes of quinine have been reported, their according mode of coordination and geometry still remain a matter of discussion [2, 3]. Up to date, quite few reports on the preparation and coordination chemistry of quinine have appeared in several papers [4–10]. As well-known, quinine has four potential donor sites which are the hydroxyl group, quinuclidinic nitrogen, quinolinic nitrogen and the olefinic carbon–carbon double bonds. Accordingly, coordination of transition metals using the four potential donor sites of quinine was also reported in [5]. It has thus noted that the pharmacological action of quinine seems to be associated with its ability to form metal complexes. First-row transition metal such as Cu(II), Co(II), Cr(II), and Zn(II) coordination complexes and second-row transition metal such as Pt(II) and Pd(II) organometallic complexes with quinine as a ligand have been synthesized and structurally characterized [5]. In our approach to the synthesis of the quinine-metal complexes, we tried to devise a typical process that could use zinc(II) chloride and iron(III) chloride to react with quinine, respectively, and a mononuclear complex, quinidinum-zinc(II)-trichloride (**I**), and a multi-component complex, quinidinum iron(III) tetrachloride hydrogen chloride hydrate (**II**), were accordingly isolated and structurally characterized in this paper.

EXPERIMENTAL

Materials and methods. All syntheses were carried out under a nitrogen atmosphere. Quinine was pharmaceutical grade from Sigma Pharmaceutical. All other commercial solvents and reagents were of high purity (Aldrich and Sigma) and were used without further purification. $ZnCl_2$ and $FeCl_3$ were used as metal ion source. Infrared spectra (KBr) were recorded on a Perkin-Elmer 16 PC FT-IR spectrophotometer with the use of pressed KBr pellets. Elemental analyses were carried out using a Perkin-Elmer 2400 CHN analyzer.

Synthesis of complex I. To a solution of quinine (78.2 mg, 0.2 mmol) in methanol (10 mL), a solution of $ZnCl_2$ (27.2 mg, 0.2 mmol) in methanol (10 mL) was added. The mixture was stirred and heated at 50°C for 2 h, and cooled to room temperature. The resulting solution was treated with aqueous HCl and filtered to remove staring materials. By slow evaporation of the

---

[1] The article is published in the original.

filtrate at room temperature, white single crystals suitable for X-ray diffraction were obtained after two weeks. The complex was identified as [(Quin)$ZnCl_3$] (**I**). The yield was 78.8 mg (79.3%).

IR (ν, cm^{-1}): 3356 ν(OH), 3074 ν(CH_{ar}), 2971 ν(CH_{aliph}).

For $C_{20}H_{25}N_2O_2Cl_3Zn$

anal. calcd., %	C, 48.32	H, 5.07	N, 5.63
Found, %	C, 48.24	H, 5.02	N, 5.59

Synthesis of complex II. To a solution of quinine (78.2 mg, 0.2 mmol) in methanol (10 mL), a solution of $FeCl_3$ (32.4 mg, 0.2 mmol) in methanol (10 mL) was added. The mixture was stirred and heated at 70°C for 4 h, and cooled to room temperature. The resulting brown solution was treated with aqueous HCl and filtered to remove staring materials. By slow evaporation of the filtrate at room temperature, dark red single crystals suitable for X-ray diffraction were obtained after three weeks. The complex was identified as [(Quin)][$FeCl_4$] · HCl · H_2O (**II**). The yield was 83.8 mg, 72.6%.

IR (cm^{-1}): 3362 ν(OH), 3070 ν(CH_{ar}), 2974 ν(CH_{aliph}).

For $C_{20}H_{28}N_2O_3Cl_5Fe$

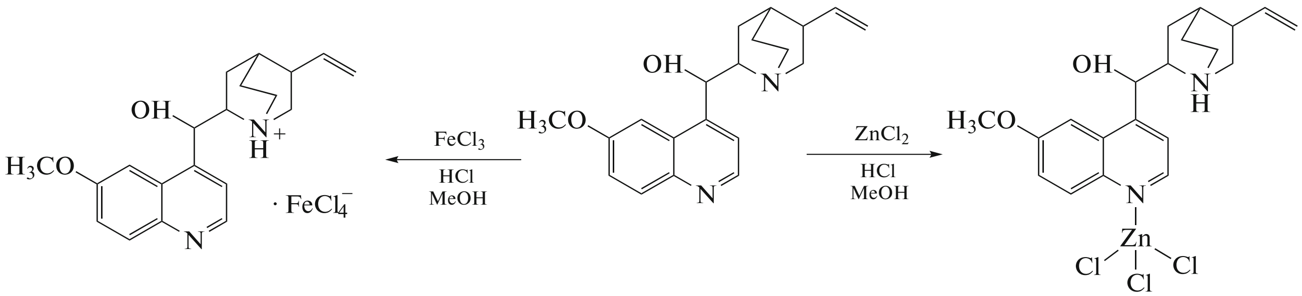
anal. calcd., %	C, 41.59	H, 4.89	N, 4.85
Found, %	C, 41.52	H, 4.94	N, 4.91

X-ray crystallography. Intensity data were collected on a Bruker SMART APEX 2 CCD diffractometer using graphite-monochromated MoK_α radiation (λ = 0.71073 Å) at 296(2) K. The collected frames were processed with the software SAINT [11]. The data was corrected for absorption using the program SADABS [12]. Structures were solved by the direct methods and refined by full-matrix least-squares on F^2 using the SHELXTL software package [13, 14]. All non-hydrogen atoms were refined anisotropically. The positions of all hydrogen atoms were generated geometrically (C_{sp3}–H = 0.96, C_{sp2}–H = 0.93 and N–H = 0.86–0.93 Å), assigned isotropic thermal parameters, and allowed to ride on their respective parent carbon atoms before the final cycle of least-squares refinement. The Flack parameter values of 0.010(7) and 0.04(2) indicate that the correct enantiomorphs have been selected in the structures of complexes **I** and **II**, respectively. A summary of crystallographic data and experimental details for **I** and **II** are summarized in Table 1. Selected bond lengths and angles for **I** and **II** are given in Table 2. The hydrogen-bond characteristics for complexes **I** and **II** are listed in Table 3.

Crystallographic data for **I** and **II** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication (CCDC nos. 1497628 and 1497629, respectively; deposit@ccdc.cam.ac.uk).

RESULTS AND DISCUSSION

As shown in Scheme 1, reaction of zinc(II) chloride or iron(III) chloride with quinine in methanol followed by treatment of aqueous HCl afforded corresponding complexes **I** and **II** in good yields. Previously, an ionic quininium tetrachloridozinc(II) complex was synthesized by reaction of quinine, $ZnCl_2$ and 10% HCl in water [15].



Scheme 1.

Additionally, a polymeric zinc(II) complex of quinine was prepared by reactions of quinine hemisulfate and $ZnCl_2$ in methanol [16]. In zwitterionic complex **I**, the zinc atom coordinated to the quinolinic nitrogen. A *multi*-component ionic complex, 2-[(R)-hydroxy(6-methoxyquinolinium-4-yl)me-thyl]-8-vinyl-1-azoniabicyclo-[2.2.2]octane tetrachloridoferrate(III) chloride monohydrate, in which the two nitrogen atoms are both protonated [17], while in complex **II**, the quinuclidinic nitrogen is protonated only. The infrared spectra of complexes **I** and **II** showed OH stretching vibration at around 3360 cm^{-1} as a broad band. The absorption band of 2660 and 2661 cm^{-1} due to N–H^+ stretching is observed in complexes **I** and **II**, respectively [16]. The band at 1510 cm^{-1} in **II** corresponding to ν(C=N) is shifted to higher frequency (1513 cm^{-1} in **I**) upon complexation [16].

Table 1. Crystallographic data and experimental details for complexes **I** and **II**

Parameter	Value	
	I	**II**
Formula weight	497.14	577.54
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
a, Å	7.6651(6)	6.6425(15)
b, Å	11.4923(9)	18.660(4)
c, Å	24.653(2)	10.958(3)
β, deg	90	104.973(3)
V, Å^3	2171.7(3)	1312.1(5)
Z	4	2
ρ_{calcd}, g cm^{-3}	1.521	1.462
F(000)	1024	594
μ(MoK_α), mm^{-1}	1.518	1.462
Total reflections	13398	8155
Independent reflections	4924	4771
R_{int}	0.0260	0.0226
Parameters	259	296
R_1, wR_2 ($I > 2\sigma(I)$)*	0.0264, 0.0488	0.0434, 0.1085
R_1, wR_2 (all data)	0.0347, 0.0513	0.0569, 0.1185
GOOF**	0.957	1.020
Largest diff. peak and hole, e Å^{-3}	0.199/−0.156	0.406/−0.504
Flank parameters	0.010(7)	0.04(2)

* $R(F) = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma w|F_o^2|^2]^{1/2}$.

** GOOF $= S = [\Sigma w(|F_o| - |F_c|)^2/(N_{\text{obs}} - N_{\text{param}})]^{1/2}$.

Molecular structures of complexes **I** and **II** were further confirmed by single-crystal X-ray diffraction analysis (Figs. 1 and 2). The Zn(II) atom in **I** is tetrahedrally coordinated to three chlorine atoms with average Zn–Cl bond length of 2.2519(6) Å and one quinolinic nitrogen. The Zn–N distance of 2.0865(16) Å is near to related zinc-nitrogen bond length observed in the zwitterionic structure of the product between $ZnCl_2$ and quinine hemisulfate (2.053(4) Å) [16]. The packing view of complex **I** along with *xz* plane is shown in Fig. 1b. The crystal packing in **I** molecules are governed by the weak intermolecular O–H···Cl and N–H···Cl hydrogen-bonding interactions. In the crystal structure of **I**, the molecules are thus arranged in discrete two-dimensional layers that lie parallel to the crystallographic *xz* plane. The chloride ions act as the hydrogen-bond bridges, providing further stability to the crystal lattice. The separation of H(2N)···Cl(3) is 2.36 Å and the angle of N(2)–H(2N)···Cl(3) is 158°, which are compared with those in the molecule of **I**-isomer [4].

The Fe(III) atom in ionic complex **II** is tetrahedrally coordinated to four chlorine atoms with the average Fe–Cl bond length of 2.1894(17) Å, which is slightly shorter than that in similar complex 2-[(R)-hydroxy(6-methoxyquinolinium-4-yl)methyl]-8-vinyl-1-azoniabicyclo-[2.2.2]octane tetrachloride-ferrate(III) chloride monohydrate (2.1908(14) Å) [17]. The packing view of complex **II** along with *xy* plane is shown in Fig. 2b. The crystal structure of II contains one independent molecular quin cation, one $[FeCl_4]^-$ anion, one free hydrogen chloride molecule and one water solvato molecule which are involved in the formation of hydrogen-bonded three-dimensional network via N–H···Cl, O–H···Cl, and O–H···O hydrogen bonds, as seen in Table 3 and Fig. 2b. Obviously, the $[FeCl_4]^-$ ion, the free hydrogen chloride

Table 2. Selected bond lengths (Å) and angles (deg) for complex **I** and **II**

Bond	*d*, Å	Bond	*d*, Å
		I	
Zn(1)–N(1)	2.0865(16)	Zn(1)–Cl(1)	2.2424(6)
Zn(1)–Cl(2)	2.2463(6)	Zn(1)–Cl(3)	2.2670(6)
O(1)–C(7)	1.355(3)	O(1)–C(9)	1.426(3)
O(2)–C(10)	1.419(2)	N(1)–C(1)	1.317(3)
N(1)–C(5)	1.372(3)	N(2)–C(15)	1.494(3)
N(2)–C(11)	1.510(3)	N(2)–C(16)	1.512(3)
		II	
Fe(1)–Cl(1)	2.2086(13)	Fe(1)–Cl(2)	2.1726(16)
Fe(1)–Cl(3)	2.1914(19)	Fe(1)–Cl(4)	2.1852(18)
Cl(5)–H(1S)	1.104(10)	O(1)–C(1)	1.351(6)
O(1)–C(10)	1.406(8)	O(2)–C(11)	1.410(5)
N(1)–C(5)	1.330(6)	N(1)–C(4)	1.353(6)
N(2)–C(12)	1.509(5)	N(2)–C(16)	1.500(6)
N(2)–C(18)	1.512(6)		
Angle	**ω, deg**	**Angle**	**ω, deg**
		I	
N(1)Zn(1)Cl(1)	112.09(5)	N(1)Zn(1)Cl(2)	108.83(5)
Cl(1)Zn(1)Cl(2)	111.66(2)	N(1)Zn(1)Cl(3)	100.04(5)
Cl(1)Zn(1)Cl(3)	113.32(2)	Cl(2)Zn(1)Cl(3)	110.28(2)
C(7)O(1)C(9)	118.77(18)	C(1)N(1)C(5)	118.34(17)
C(15)N(2)C(11)	113.26(18)	C(15)N(2)C(16)	109.52(18)
C(11)N(2)C(16)	108.9(2)		
		II	
Cl(2)Fe(1)Cl(1)	109.66(6)	Cl(2)Fe(1)Cl(4)	109.96(9)
Cl(2)Fe(1)Cl(3)	107.80(9)	Cl(4)Fe(1)Cl(3)	109.57(8)
Cl(4)Fe(1)Cl(1)	108.87(6)	Cl(3)Fe(1)Cl(1)	110.97(7)
C(1)O(1)C(10)	118.0(4)	C(5)N(1)C(4)	121.1(4)
C(16)N(2)C(12)	109.0(3)	C(16)N(2)C(18)	108.9(3)
C(12)N(2)C(18)	113.2(3)		

Table 3. Geometric parameters of hydrogen-bonds for complexes **I** and **II**

D–H···A	Distance, Å			Angle DHA, deg
	D–H	H···A	D···A	
O(2)–H(2A)···Cl(2)	0.82	2.52	3.254(2)	150
N(2)–H(2N)···Cl(3)	0.90	2.36	3.211(2)	158
O(2)–H(2)···O(1*w*)	0.82	2.10	2.857(10)	154
O(2)–H(2)···Cl(5)	0.82	2.77	3.398(4)	135
N(2)–H(2N)···Cl(5)	0.97	2.10	3.031(4)	162
O(1*w*)–H(1*w*)···O(2)	0.88	2.29	2.857(10)	122

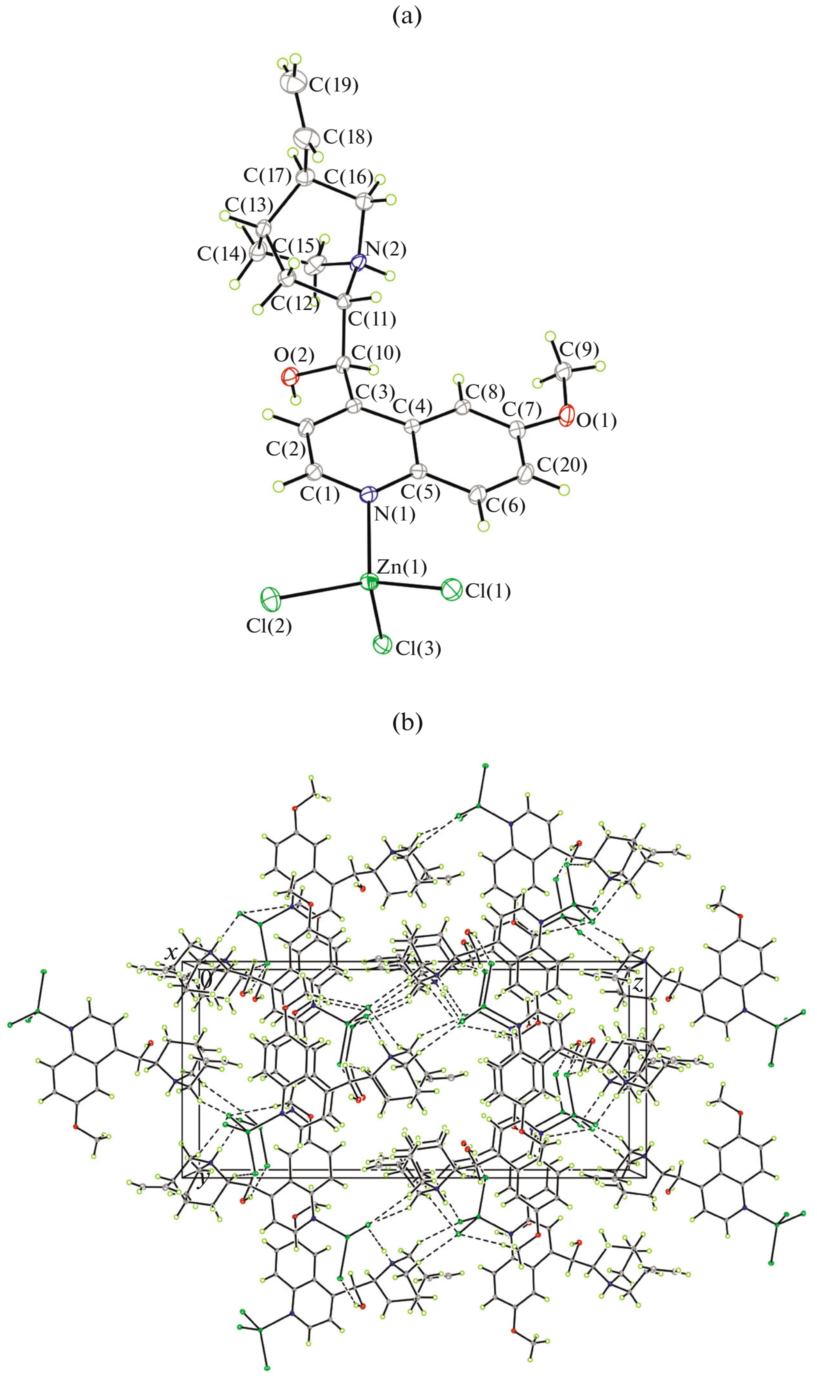


Fig. 1. The content of asymmetric unit in **I**, showing the atom-labelling scheme (displacement ellipsoids are drawn at the 40% probability level) (a); a packing diagram of **I**, projected along with *xz* plane (hydrogen bonds are shown as dashed lines) (b).

molecule and the water molecules act as hydrogen-bond bridges which may provide further stability to the crystal lattice.

Thus, two quinidinum Zn/Fe complexes are synthesized and characterized by single-crystal X-ray diffraction along with spectroscopic methods, of which they were obtained from reaction of quinine and $ZnCl_2$ or $FeCl_3$ in methanol solution. In the crystal structure of **I**, the molecules are arranged in discrete two-dimensional layers formed by the weak intermolecular O–H···Cl and N–H···Cl hydrogen-bonding interactions, whereas the crystal packing in **II** displays

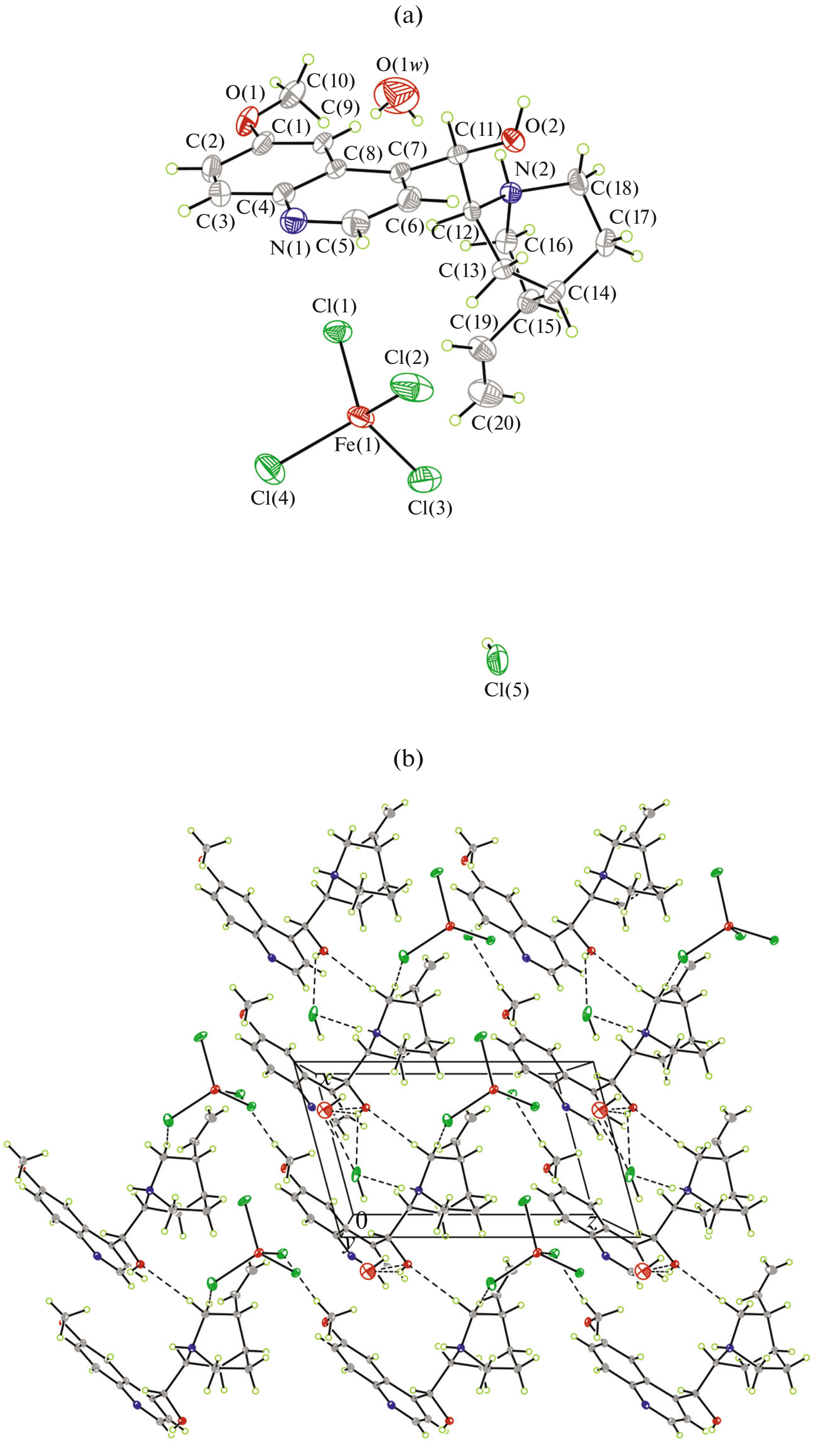


Fig. 2. The content of asymmetric unit in **II** · HCl · $2H_2O$, showing the atom-labelling scheme (displacement ellipsoids are drawn at the 40% probability level) (a); a packing diagram of **II** · HCl · $2H_2O$, projected along with *xy* plane (hydrogen bonds are shown as dashed lines) (b).

the hydrogen-bonded three-dimensional framework involved in different types of N–H···Cl, O–H···Cl, and O–H···O hydrogen bonds.

ACKNOWLEDGMENTS

This project was supported by the Natural Science Foundation of China (no. 21372007).

REFERENCES

1. Corey, E.J., Mark, C.N., and Sepehr, S., *J. Am. Chem. Soc.*, 1993, vol. 115, p. 3828.
2. Zhao, H., Qu, Z.R., Ye, Q., et al., *Chem. Mater.*, 2003, vol. 15, p. 4166.
3. Muñiz, K. and Nieger, M., *Organometallics*, 2003, vol. 22, p. 4616.
4. Skórska, A., Stadnicka, K., and Oleksyn, B.J., *Chirality*, 2005, vol. 17, p. 73.
5. Hubel, R., Polborn, K., and Beck, W., *Eur. J. Inorg. Chem.*, 1999, p. 471.
6. Qu, Z.R., Chen, Z.F., Zhang, J., et al., *Organometallics*, 2003, vol. 22, p. 2814.
7. Fu, D.W., Ye, H.Y., Ye, Q., Pan, K.J., and Xiong, R.G., *Dalton Trans.*, 2008, p. 874.
8. Prochowicz, D., Justyniak, I., Kornowicz, A., et al., *Chem. Eur. J.*, 2012, vol. 18, p. 7367.
9. Tesarowicz, I., Oleksyn, B.J., and Nitek, W., *Chirality*, 2007, vol. 19, no. 2, p. 152.
10. Pytel, P., Oleksyn, B.J., and Sliwinski, J., *Enantiomer*, 2001, vol. 6, p. 201.
11. *SMART and SAINT+ for Windows NT* (*version 6.02a*), Madison: Bruker Analytical X-ray Instruments Inc., 1998.
12. Sheldrick, G.M., *SADABS*, Göttingen: Univ. of Göttingen, 1996.
13. Sheldrick, G.M., *SHELXTL* (*version 5.1*), *Software Reference Manual*, Madison: Bruker AXS Inc., 1997.
14. Betz, R., Gerber, T., and Schalekamp, H., *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2011, vol. 67, p. 01577.
15. Chen, L.Z., *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2009, vol. 65, p. m1172.
16. Obaleye, J.A., Caira, M.R., and Tella, A.C., *J. Chem. Crystallogr.*, 2007, vol. 37, p. 707.
17. Chen, L.Z. and Huang, M.N., *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2010, vol. 66, p. m377.