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Crystal and Molecular Structures of Fenethazine Hydrochloride and Its Cation Radical-Copper(II) Complex Salt

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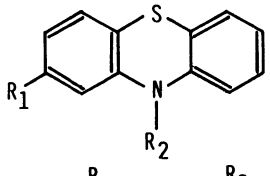
The crystal structures of fenethazine hydrochloride hydrate (FTZ·HCl) and $[FTZ\,H]^{2+}\cdot[CuCl_4]^{2-}$ (FTZ-Cu) were determined. FTZ·HCl crystallized in the monoclinic space group $P2_1/a$ with $a=8.686(1)$, $b=31.660(2)$, $c=6.140(1)$ Å, $\beta=100.44(1)°$, $V=1660.5(3)$ Å^3, and $Z=4$. FTZ-Cu crystallized in the triclinic space group $P\bar{1}$ with $a=20.433(5)$, $b=12.721(4)$, $c=7.526(2)$ Å, $\alpha=91.31(3)$, $\beta=94.56(3)$, $\gamma=99.69(2)°$, $V=1920.9(1)$ Å^3, and $Z=4$. The structures were solved using the heavy-atom method and were refined by the block-diagonal least-squares method. The final R values were determined to be 0.052 for FTZ·HCl and 0.050 for FTZ-Cu. The formation of a cation radical causes the phenothiazine ring of the FTZ molecule to be flattened; the dihedral angle between benzene rings is increased from 140.3° for FTZ·HCl to 174.7 or 167.5° for FTZ-Cu. The 2-aminoethyl chain holds a trans conformation in FTZ-Cu and a near gauche form in FTZ·HCl. In FTZ·HCl crystals, the FTZ molecules form a layer along a in which the molecules array the phenothiazine ring as faced with the ring in the neighboring layer. In FTZ-Cu, two FTZ molecules form a pair with a close overlap of the phenothiazine rings, directed approximately perpendicular to a. The $CuCl_4^{2-}$ is located so as to counterbalance both the positive charge of the ring and the protonated amino group of the side chain.

It is well known that phenothiazine drugs have many therapeutical uses and that variations of substituents at the 2- and 10-positions in the tricyclic ring system are responsible for the diversity of pharmacological activities. Conformational studies on drugs with a 3-aminopropyl chain at the 10-position, which are mainly employed as tranquilizers, have been reported in connection with the structure-activity relationship.[1,2] However, no structural analysis has been described yet on drugs bearing a 2-aminoethyl substituent at the same position, showing the efficacy of antihistaminics. These types of drugs are easily converted into one-electron-oxidation products under relatively mild conditions owing to the low ionization potential of the phenothiazine ring.[3] Horse-radish peroxidase catalyzes 2-chloro-10-(3-dimethylaminopropyl)phenothiazine (chlorpromazine, CPZ) *in vitro* in the presence of hydrogen peroxide to the cation radical species.[4] Thus, it is expected that such cation radicals of the drugs may be generated *in vivo* and may play some kind of pharmacological role.[5]



	R_1	R_2
CPZ :	Cl	$(CH_2)_3N(CH_3)_2$
PMZ:	H	$(CH_2)_3N(CH_3)_2$
FTZ :	H	$(CH_2)_2N(CH_3)_2$

In the course of our study regarding the interaction between neuroleptics and copper ions, we prepared stable complex salts of CPZ[6] and 10-(3-dimethylaminopropyl)phenothiazine (promazine, PMZ)[7] cation radicals with $[CuCl_4]^{2-}$ and determined their structures. So far, only the perchlorate salt of the CPZ cation radical has been obtained in crystal form among this type of drug,[8-10] though the structure has not been clarified. An application of a similar synthetic method[6] to 10-(2-dimethylaminoethyl)phenothiazine (fenethazine, FTZ) afforded stable crystals of the cation radical salt composed of $[FTZ\,H]^{2+}\cdot[CuCl_4]^{2-}$ (FTZ-Cu). In this paper we describe the crystal and molecular structures of FTZ·HCl and FTZ-Cu and discuss the structural differences between them.

Experimental

The FTZ·HCl was prepared by coupling *N,N*-dimethyl-2-chloroethylamine with phenothiazine[11] and crystallizing with water to yield white needles with the composition FTZ·HCl·H_2O. The FTZ-Cu was obtained as black plates according to a previously reported method.[7] Found: C, 40.06; H, 3.60; N, 5.57%. Calcd for $[FTZ\,H]^{2+}\cdot[CuCl_4]^{2-}$ ($C_{16}H_{19}N_2SCuCl_4$): C, 40.31; H, 4.02; N, 5.88%. The crystals were stable in air for several months when dried, although they decomposed slowly in aqueous solutions.

The X-ray diffraction data were measured on a Rigaku AFC-5 automatic four-circle diffractometer using graphite-monochromated Cu $K\alpha$ radiation ($\lambda=1.5418$ Å). The unit-cell parameters were refined from least-squares fits of 24 2θ values ($48<2\theta<52°$) for FTZ·HCl and 50 ($48<2\theta<53°$) for FTZ-Cu. The crystal data and a part of the experimental details are tabulated in Table 1. Intensities were measured by the θ–2θ scan technique and the counting time was 1 s. Each background was measured for 10 s at the begining and end of the scan range. During data collection, three standard reflections were monitored every 100 or 50 reflections and showed no significant variation in their intensities. For FTZ·HCl, 3226 reflections with $2\theta\leq130°$ were measured and 2297 independent reflections with $|F_o|>3\sigma(|F_o|)$ were used for the structure determination. For FTZ-Cu, 5557 reflections with $2\theta\leq120°$ were collected and 4478 reflections with $|F_o|>12\sigma(|F_o|)$ were used in the subsequent analysis. Each data set was corrected for Lorentz and polarization effects, but not for absorption.

The structures were solved using the heavy-atom and Fourier methods and were refined by the block-diagonal least-squares method. The minimized function was $\sum w(|F|-|F_c|)^2$,

where $w=1/[\sigma^2+(0.02F_o)^2]$. All the positional parameters and anisotropic thermal parameters for non-hydrogen atoms, and isotropic thermal parameters for hydrogen atoms were refined. All the parameter shifts in the final cycle of the refinement were less than 0.2σ for both compounds. The final R values were 0.052 for FTZ·HCl and 0.050 for FTZ-Cu.

The neutral atomic-scattering factors were taken from the International Tables for X-ray Crystallography.[12] All the calculations were carried out on a FACOM M-160F computer at Josai University using the UNICS III[13] and ORTEP[14] programs. The final positional and thermal parameters (with standard deviations) are given in Tables 2 and 3. Data regarding structure factors, anisotropic thermal parameters, and hydrogen-atom coordinates have been deposited in the office of the Chemical Society of Japan (Document No. 8507).

TABLE 1. CRYSTAL DATA AND EXPERIMENTAL DETAILS

	FTZ·HCl	FTZ-Cu
Formula	$C_{16}H_{18}N_2S$ HCl H_2O	$C_{16}H_{19}N_2S$ $CuCl_4$
F.W.	324.85	476.76
Crystal size/mm³	0.16×0.77×0.11	0.38×0.30×0.08
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/a$	$P\bar{1}$
a/Å	8.686(1)	20.433(5)
b/Å	31.660(2)	12.721(4)
c/Å	6.140(1)	7.526(2)
α/°	—	91.31(3)
β/°	100.44(1)	94.56(3)
γ/°	—	99.69(2)
V/Å³	1660.5(3)	1920.9(1)
Z	4	4
F(000)	688	968
Dm/Mg m^{-3}	1.307	1.636
Dc/Mg m^{-3}	1.300	1.649
μ(Cu *Kα*)/mm^{-1}	3.21	7.87
Scan rate/° min^{-1}	3	4
Scan width/°	1.0	1.0
$2\theta_{max}$/°	130	120
R	0.052	0.050
Rw	0.053	0.057

TABLE 2. ATOMIC COORDINATES (×10⁴) AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS FOR FTZ·HCl

	x	*y*	*z*	B_{eq}/Å²
Cl	−4094(1)	7923.3(3)	3938(1)	4.16(3)
O	2087(3)	7991(1)	5400(4)	5.9(1)
C(1)	2844(4)	8756(1)	10856(5)	3.8(1)
C(2)	4427(4)	8788(1)	9966(7)	5.1(1)
C(3)	4907(4)	8977(1)	7929(7)	5.7(1)
C(4)	3815(4)	9137(1)	6774(6)	4.7(1)
S(5)	813(1)	9284.5(3)	6145(1)	3.85(3)
C(6)	−1536(4)	9807(1)	8129(6)	4.3(1)
C(7)	−2717(4)	9930(1)	9827(7)	5.0(1)
C(8)	−2945(4)	9714(1)	11788(7)	4.9(1)
C(9)	−2014(4)	9371(1)	12081(6)	3.9(1)
N(10)	95(3)	8878(1)	10525(4)	3.0(1)
C(11)	1726(3)	8909(1)	9691(5)	2.9(1)
C(12)	2223(4)	9102(1)	7650(5)	3.3(1)
C(13)	−622(4)	9462(1)	8381(5)	3.2(1)
C(14)	−852(3)	9235(1)	10363(5)	2.9(1)
C(15)	−449(4)	8547(1)	12142(5)	3.2(1)
C(16)	−89(3)	8109(1)	11176(5)	2.8(1)
N(17)	−1366(3)	7942(1)	10056(4)	2.9(1)
C(18)	−1038(4)	7495(1)	9388(6)	4.2(1)
C(19)	−1627(4)	8204(1)	8132(5)	4.4(1)

TABLE 3. ATOMIC COORDINATES (×10⁴) AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS FOR FTZ-Cu

	x	*y*	*z*	B_{eq}/Å²
Cu(A)	−3748.2(4)	−3257(1)	−2048(1)	2.91(3)
Cu(B)	1158.3(4)	−3093(1)	−3659(1)	2.61(3)
Cl(1)(A)	−2766(1)	−2629(1)	−597(2)	4.2(1)
Cl(2)(A)	−4388(1)	−2427(1)	−414(2)	3.8(1)
Cl(3)(A)	−4302(1)	−3120(2)	−4683(2)	5.1(1)
Cl(4)(A)	−3618(1)	−5015(1)	−2505(2)	4.1(1)
Cl(1)(B)	843(1)	−3012(1)	−858(2)	3.4(1)
Cl(2)(B)	1711(1)	−4487(1)	−3135(2)	3.21(4)
Cl(3)(B)	1883(1)	−2112(1)	−5287(2)	3.7(1)
Cl(4)(B)	198(1)	−2935(1)	−5170(2)	4.2(1)
C(1)(A)	5817(3)	1918(5)	6300(8)	3.7(2)
C(2)(A)	5494(3)	1351(6)	7601(9)	4.4(2)
C(3)(A)	5456(3)	250(6)	7667(9)	4.5(2)
C(4)(A)	5717(3)	−274(5)	6366(9)	4.1(2)
S(5)(A)	6305(1)	−507(1)	3441(2)	4.0(1)
C(6)(A)	6901(3)	−29(5)	515(9)	3.8(2)
C(7)(A)	7206(3)	612(6)	−702(9)	4.6(2)
C(8)(A)	7261(3)	1716(6)	−474(9)	4.6(2)
C(9)(A)	7020(3)	2156(5)	965(9)	4.0(2)
N(10)(A)	6463(2)	1978(3)	3699(6)	2.7(1)
C(11)(A)	6114(3)	1402(4)	4975(8)	2.8(2)
C(12)(A)	6038(3)	282(5)	5017(8)	3.1(2)
C(13)(A)	6650(3)	411(4)	1999(8)	2.9(2)
C(14)(A)	6706(3)	1523(4)	2246(7)	2.8(2)
C(15)(A)	6585(3)	3157(4)	3913(8)	2.9(2)
C(16)(A)	6021(3)	3575(4)	2855(8)	3.3(2)
N(17)(A)	6053(2)	4758(3)	3109(6)	2.5(1)
C(18)(A)	5475(3)	5058(5)	1978(9)	4.2(2)
C(19)(A)	6686(3)	5391(5)	2647(9)	3.9(2)
C(1)(B)	586(3)	1541(5)	1801(8)	3.0(2)
C(2)(B)	457(3)	798(5)	3078(8)	3.8(2)
C(3)(B)	598(3)	−219(5)	2884(9)	4.2(2)
C(4)(B)	864(3)	−509(5)	1392(8)	3.6(2)
S(5)(B)	1313(1)	−252(1)	−1793(2)	3.8(1)
C(6)(B)	1942(3)	760(5)	−4339(8)	3.7(2)
C(7)(B)	2180(3)	1609(5)	−5312(8)	4.0(2)
C(8)(B)	2014(3)	2599(5)	−4881(8)	3.9(2)
C(9)(B)	1630(3)	2741(5)	−3539(8)	3.3(2)
N(10)(B)	1023(2)	2046(3)	−1057(6)	2.6(1)
C(11)(B)	870(3)	1280(4)	252(7)	2.7(2)
C(12)(B)	1002(3)	229(4)	64(8)	3.1(2)
C(13)(B)	1563(3)	891(4)	−2908(7)	2.9(2)
C(14)(B)	1398(3)	1897(4)	−2475(7)	2.6(2)
C(15)(B)	835(3)	3110(5)	−745(8)	3.1(2)
C(16)(B)	1401(3)	3790(4)	440(8)	3.2(2)
N(17)(B)	1270(2)	4881(3)	911(6)	2.9(1)
C(18)(B)	702(4)	4860(5)	2061(9)	4.7(2)
C(19)(B)	1896(3)	5526(5)	1828(9)	4.6(2)

Results and Discussion

The FTZ-Cu displays a maximum (electronic spectrum) at 513 nm (ε 9500) in aqueous solution and at 560—580 nm (broad band) in the solid state. These appear also for the CPZ-Cu and PMZ-Cu complex salt and are ascribable to the cation radical species of the phenothiazine ring in agreement with the maximum wavelengths reported for the cation radicals of the same ring.[15]

The molecular structures and atom-numbering are given in Figs. 1 and 2, and the bond lengths and angles are listed in Table 4. As the difference Fourier maps revealed the hydrogen atom attached to the N(17) atom

Table 4. Bond lengths (l/Å) and angles (ϕ/°)

	FTZ-Cu		FTZ·HCl
	A	B	
C(1)-C(2)	1.375(9)	1.373(9)	1.388(4)
C(2)-C(3)	1.393(10)	1.380(10)	1.382(6)
C(3)-C(4)	1.365(10)	1.356(10)	1.379(6)
C(4)-C(12)	1.394(9)	1.400(8)	1.394(4)
C(11)-C(12)	1.409(8)	1.415(8)	1.391(4)
C(1)-C(11)	1.412(9)	1.399(8)	1.394(5)
C(6)-C(7)	1.360(9)	1.363(9)	1.380(5)
C(7)-C(8)	1.397(10)	1.397(10)	1.367(6)
C(8)-C(9)	1.372(10)	1.355(9)	1.385(5)
C(9)-C(14)	1.396(9)	1.396(8)	1.390(4)
C(13)-C(14)	1.408(8)	1.415(8)	1.397(4)
C(6)-C(13)	1.409(9)	1.399(9)	1.376(5)
S(5)-C(12)	1.718(6)	1.722(6)	1.760(3)
S(5)-C(13)	1.715(6)	1.719(6)	1.770(3)
N(10)-C(11)	1.391(7)	1.418(7)	1.420(4)
N(10)-C(14)	1.390(8)	1.391(7)	1.413(4)
N(10)-C(15)	1.483(7)	1.489(8)	1.461(4)
C(15)-C(16)	1.528(8)	1.533(8)	1.518(4)
C(16)-N(17)	1.504(7)	1.498(8)	1.503(4)
N(17)-C(18)	1.505(8)	1.500(9)	1.486(4)
N(17)-C(19)	1.476(7)	1.506(8)	1.494(4)
Cu-Cl(1)	2.221(2)	2.258(2)	
Cu-Cl(2)	2.235(2)	2.284(2)	
Cu-Cl(3)	2.230(2)	2.234(2)	
Cu-Cl(4)	2.319(2)	2.229(2)	
C(11)-C(1)-C(2)	121.2(6)	120.2(6)	120.3(3)
C(1)-C(2)-C(3)	121.0(7)	121.7(6)	120.2(4)
C(2)-C(3)-C(4)	119.1(6)	119.9(6)	120.1(3)
C(3)-C(4)-C(12)	120.8(6)	119.9(6)	120.0(3)
C(4)-C(12)-C(11)	121.2(6)	121.0(6)	120.4(3)
C(1)-C(11)-C(12)	116.6(5)	117.3(5)	119.0(3)
C(7)-C(6)-C(13)	120.6(6)	120.4(6)	120.3(3)
C(6)-C(7)-C(8)	119.2(7)	118.3(6)	119.6(3)
C(7)-C(8)-C(9)	120.9(6)	122.3(6)	120.8(3)
C(8)-C(9)-C(14)	121.6(6)	120.8(6)	120.3(3)
C(9)-C(14)-C(13)	117.1(6)	117.0(5)	118.1(3)
C(6)-C(13)-C(14)	120.7(5)	121.0(5)	120.9(3)
C(11)-N(10)-C(14)	124.5(5)	123.9(5)	118.3(2)
N(10)-C(11)-C(12)	122.1(5)	121.7(5)	118.9(3)
C(11)-C(12)-S(5)	124.2(5)	123.8(4)	119.0(2)
C(12)-S(5)-C(13)	102.4(3)	102.4(3)	99.0(2)
S(5)-C(13)-C(14)	124.6(5)	124.2(5)	118.8(2)
C(13)-C(14)-N(10)	121.8(5)	121.9(5)	118.7(2)
C(1)-C(11)-N(10)	121.3(5)	121.0(5)	122.2(3)
C(4)-C(12)-S(5)	114.7(5)	115.3(5)	120.5(3)
C(6)-C(13)-S(5)	114.6(4)	114.8(5)	120.3(3)
C(9)-C(14)-N(10)	121.1(5)	121.1(5)	123.2(3)
C(11)-N(10)-C(15)	117.6(5)	116.7(5)	118.3(2)
C(14)-N(10)-C(15)	117.9(4)	119.0(4)	120.0(2)
N(10)-C(15)-C(16)	108.1(4)	107.9(5)	111.7(2)
C(15)-C(16)-N(17)	113.1(4)	113.8(5)	112.6(2)
C(16)-N(17)-C(18)	107.5(4)	112.9(4)	110.0(2)
C(16)-N(17)-C(19)	113.6(5)	108.9(5)	113.3(2)
C(18)-N(17)-C(19)	110.5(5)	110.3(5)	111.1(2)
Cl(1)-Cu-Cl(2)	98.7(1)	94.2(1)	
Cl(1)-Cu-Cl(3)	139.4(1)	136.6(1)	
Cl(1)-Cu-Cl(4)	99.1(1)	99.1(1)	
Cl(2)-Cu-Cl(3)	96.8(1)	99.2(1)	
Cl(2)-Cu-Cl(4)	135.0(1)	133.9(1)	
Cl(3)-Cu-Cl(4)	95.9(1)	100.6(1)	

in both compounds, a positive charge in FTZ·HCl is located on the amino group of the side chain, and the same group together with the tricyclic ring in FTZ-Cu

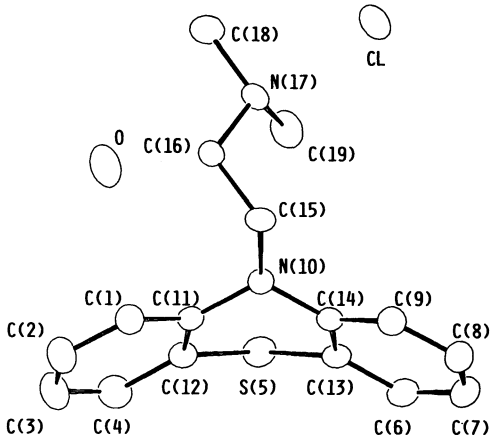


Fig. 1. Perspective view of FTZ·HCl·H_2O with 50% probability ellipsoids.

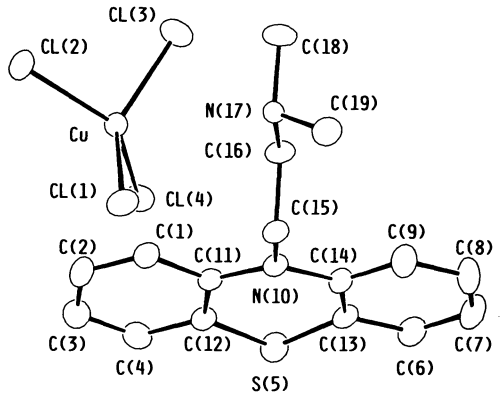


Fig. 2. Perspective view of $[FTZ\ H]^{2+}\cdot[CuCl_4]^{2-}$ (A) with 50% probability ellipsoids.

bears a positive charge. In the FTZ-Cu crystals there are two crystallographically independent FTZ molecules and two independent $[CuCl_4]^{2-}$ ions with different bond lengths and angles (hereafter discriminated by the notation A and B, respectively).

The conversion into the cation radical salt causes the almost planar geometry of the phenothiazine ring in the FTZ molecule as is obvious by a comparison of Figs. 1 and 2. The dihedral angle between the lateral benzene rings is 174.7° in FTZ-Cu (A) and 167.5° in FTZ-Cu (B). All the component atoms in the ring lie on a near plane, while the angle in FTZ·HCl is 140.3° owing to the folding of the ring around the S-N axis. This results in a bent boat-form. The C-N and C-S bond lengths in the thiazine ring of FTZ·HCl are approximately the same as those of *N*-methylphenothiazine (the C-N and C-S bond lengths are 1.402 and 1.764 Å, respectively).[16] The C-N-C and C-S-C angles in the ring are also in accordance with the 118° of the C-N-C angle and the 97° of the C-S-C in *N*-methylphenothiazine. These facts indicate that the positive charge on the protonated amino group of the side chain causes no significant perturbation in the structure of the phenothiazine moiety. On the other hand, the geometry of the thiazine ring in FTZ-Cu reveals a clear difference in comparison with that in

FTZ·HCl. The C–N and C–S bonds are shortened by the ranges of 0—0.03 and 0.04—0.05 Å, respectively. The C–N–C and C–S–C angles are spread by 5.4 (A) and 4.8 (B), and 3.3°, respectively, implying an increase of the double-bond characteristics of both bonds. In particular, the C–S bond lengths become shorter than the value of 1.740 Å reported regarding an aromatic molecule, dibenzothiophene.[17] The sums of the three bond angles around the N(10) atom amount to 359.6(9) (A) and 360.0(9)° (B). This indicates that the N(10) atom sustains a substantial sp^2 hybridization in contrast to the large sp^3 character of the corresponding N atom in the phenothiazine molecule.[18] These geometrical features signify that the π-electrons are delocalized over the tricyclic ring system by forming a cation radical salt. This situation is similar to the cases of the CPZ–Cu and PMZ–Cu complex salt.

The 2-aminoethyl chains of both compounds elongate into the direction approximately bisecting the external angle of C(11)–N(10)–C(14). The N(10)–C(15)–C(16)–N(17) torsion angles of 174.7° in FTZ–Cu (A) and of 181.7° in FTZ–Cu (B), holding trans conformations, are much greater than that of 89.0° in FTZ·HCl, being in a near gauche conformation. On the assumption that the cationic charge on the phenothiazine ring localizes in the center of the ring, tentative calculations demonstrate that the distances from the middle point between the S(5) and N(10) atoms in the ring to the N(17) atom in the side chain attain 4.002 Å in FTZ·HCl, and 4.650 (A) and 4.724 Å (B) in FTZ–Cu. This difference suggests that the two positive charges in the FTZ molecule of FTZ–Cu keep each other apart to make the electrostatic repulsion between them as small as possible.

Figures 3 and 4 show the crystal packing diagrams of both compounds. In the FTZ·HCl crystals, the FTZ molecules arrange themselves in layers along the a axis. Along the b axis, the phenothiazine moieties of the two FTZ molecules are coupled with the insertion of one of the lateral benzene rings into the void volume of the bent plane to one another. This packing fashion resembles that of 10H-phenothiazine-10-propionic acid as reported by S. M. C. Malmstrom *et al.*[19] It is interesting that the different substituents with an opposite polarity, such as a carboxyl and amino group, afford similar packing arrangements. The closest in-

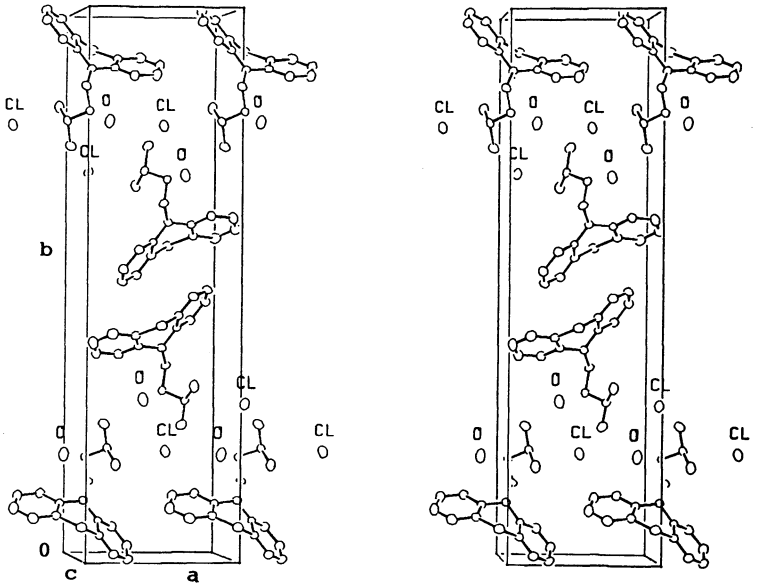


Fig. 3. Stereoscopic diagram of the crystal structure of FTZ·HCl·H_2O viewed down c.

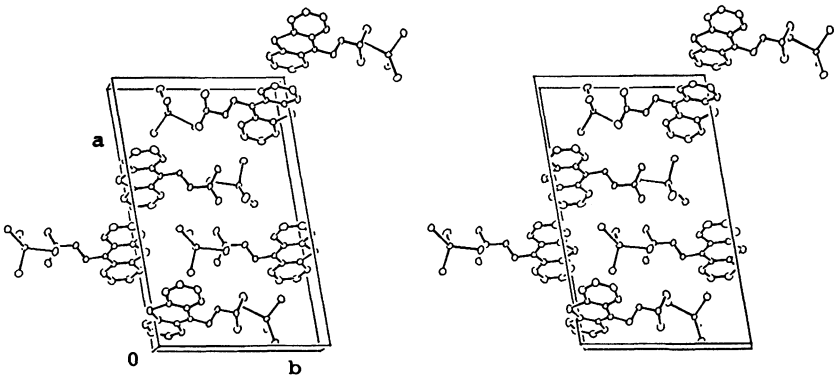


Fig. 4. Stereoscopic diagram of the crystal structure of $[FTZ\ H]^{2+\cdot}$-$[CuCl_4]^{2-}$ viewed down c.

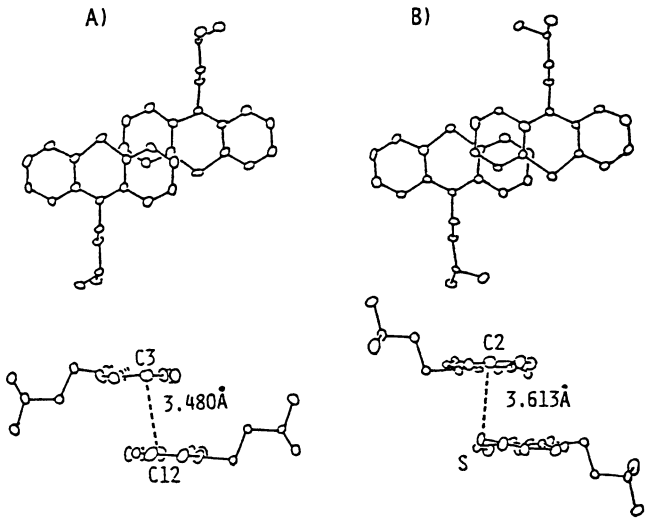


Fig. 5. Intermolecular overlap of the FTZ molecular pair in the $[FTZ\ H]^{2+\cdot}$ $[CuCl_4]^{2-}$ crystals.

termolecular contact is observed for C(7)–C(12^{ii}) [symmetry code: ii) $-x$, $-y$, $-z$] as 3.495(5) Å and all the other nonbonded contacts are greater than the sum of the van der Waals radii of the atoms. The chloride ions and the water molecules of crystallization are located in the vicinity of the ammonium groups of the side chains. The close contacts between these groups reveal the existence of a bridge structure linked with the hydrogen bonds (two hydrogen atoms of water are expressed as H(O1) and H(O2)): N(17)–Cl 3.042(2), H(17)–Cl 2.08(3), Cl–H(O2) 2.55(4), and H(O1)–Cl^{ii} 2.19(5) Å. In the case of the FTZ–Cu crystals, two crystallographically equivalent FTZ molecules form a pair with each other with the inversion centers to give a parallel overlap of the flattened phenothiazine rings. The side chains of the different pairs are stretched out in alternative directions as shown in Fig. 5; inside the faced planes (A) and outside the faced planes (B). The shortest intermolecular contact between the faced planes is seen for C(3)–C(12^{ii}) as 3.480(8) Å in an A pair, and for C(2)–S(5^{ii}) as 3.613(6) Å in a B pair. These values are within the van der Waals distances of the atoms, sufficiently indicating the intermolecular interaction between the faced rings. This type of dimer-like structure is widely seen in many organic radicals[20] and may contribute to the stabilization of the compounds in crystals. However, in the present case the degree of the ring overlap is relatively small.

The tetrachlorocuprate(2-) ions in which the copper atom has a pseudotetrahedral coordination sphere are positioned so as to neutralize the cationic charges of the phenothiazine ring and the protonated amino group in one pair and that of the ring in another pair. Among the coordinating chlorine atoms, the close nonbonded contacts occur around the Cl(4) (A) and Cl(1) (B) atom: Cl(4)(A)–N(17) 3.312(4), Cl(4)(A)–H(17) 2.56(5), Cl(1)(B)–N(17) 3.238(5), and Cl(1)(B)–H(17) 2.49(7) Å. These Cl–H distances are within the accepted hydrogen-bond range[21] and the Cl–N distances are considerably shorter than the van der Waals distances. This fact suggests that the electrostatic bonds that stand between N(17) and Cl(4)(A) or Cl(1)(B) are mediated through the hydrogen bonds.

In conclusion, FTZ–Cu differs largely from FTZ·HCl not only in its molecular structure but also in its crystal-packing mode. This differenece arises from the cation radical formation of the FTZ molecule. This fact might provide a clue to the explication of the pharmacological effect of the drug from a structural point of view, though it remains uncertain at the present stage.

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