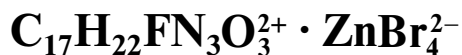


PHYSICAL METHODS
OF INVESTIGATION

Crystal Structure of Pefloxancindium Tetrabromidozinkate



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Abstract—A new compound, namely pefloxancindium tetrabromidozincate $\text{C}_{17}\text{H}_{22}\text{FN}_3\text{O}_3^{2+} \cdot \text{ZnBr}_4^{2-}$, where $\text{C}_{17}\text{H}_{20}\text{FN}_3\text{O}_3$ is 1-ethyl-N-methyl-6-fluoro-1,4-dihydro-4-oxo-7-(4-methyl-1-piperazinyl)-3-quinoline carboxylic acid (PefH, pefloxacin), has been synthesized and its crystal and molecular structure has been solved. It contains PefH_3^{2+} and ZnBr_4^{2-} ions. The latter is a slightly distorted tetrahedron. The supramolecular architecture of a crystal has been analyzed.

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Fluoroquinolones (FxH) are one of the best groups of synthetic antibiotics. The wide medical applications of pefloxacin (PefH, $\text{C}_{17}\text{H}_{20}\text{FN}_3\text{O}_3$, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(4-methyl-1-piperazinyl)-3-quinoline carboxylic acid) [1] are responsible for its comprehensive study. The synthesis of PefH metal-containing compounds and the study of their physico-chemical characteristics may lead to the obtaining of more efficient medicinal forms and the development of new methods for the purification of a substance. On the whole, the analysis of different interactions in the fluoroquinolone-derived compounds is important for the understanding of their effect on an organism. The insertion of hydrophilic species into their channels is supposed to be of great biomedical importance [2].

The structures of ionic compounds containing the FxH_3^{2+} cation are studied relatively poorly, and only those with chloride metal complexes as counterions [3–5]. With the purpose of systematically studying the influence of the nature of a halide ligand on the lattice packing type and its structural motifs, a new compound $\text{C}_{17}\text{H}_{22}\text{Br}_4\text{FN}_3\text{O}_3\text{Zn}$ ($\text{PefH}_3[\text{ZnBr}_4]$, pefloxancindium tetrabromidozincate) was synthesized and its crystal and molecular structure was solved.

EXPERIMENTAL

PefH was synthesized as follows. Pefloxacin methanesulfonate dihydrate $\text{PefHCH}_3\text{SO}_3\text{H} \cdot 2\text{H}_2\text{O}$ (2 g, Nakoda Chemicals Ltd., India) was dissolved in 20% aqueous ammonia (50 mL, pH 11–12) under short-time heating. The resulting solution was heated and allowed to stand in air to pH 8 to remove ammonia. The white crystalline PefH precipitate obtained in this

way was filtered out, washed with abundant water, and dried in air to constant weight.

Synthesis of $\text{C}_{17}\text{H}_{22}\text{FN}_3\text{O}_3^{2+} \cdot \text{ZnBr}_4^{2-}$ (I). Pefloxacin (30 g) was dissolved in 6 M HBr (3 mL, chemically pure grade), and to the resulting solution, ZnO (chemically pure grade) was slowly added to a molar ratio Zn : PefH = 2 : 1. Crystals of I were separated out by evaporating the solution; the yield was 83%.

The results of chemical analysis were as follows:

For $\text{C}_{17}\text{H}_{22}\text{Br}_4\text{FN}_3\text{O}_3\text{Zn}$, anal. calcd. (%): C, 28.34; H, 3.08; N, 5.48; Zn, 9.08.

Found (%): C, 28.03, H, 2.87, N, 5.66; Zn, 8.89.

For structural study, we selected a colorless $0.45 \times 0.30 \times 0.22$ -mm crystal. The reflection intensities were measured on a SMART APEX II single-crystal X-ray diffractometer with a CCD-detector (Bruker AXS) using MoK_α radiation. Experimental corrections for absorption were applied for 8281 reflections measured more than once. The structural model was solved by direct methods (SHELXS [6]) and refined with the SHELXTL software suite [7]. The positions of hydrogen atoms were determined from difference electron density syntheses and then idealized and refined as bound to the basal atoms. The characteristics of X-ray diffraction experiments and structure refinement details are given in Table 1.

The crystallographic data were deposited with the Cambridge Crystallographic Data Centre, CCDC no. 775005.

RESULTS AND DISCUSSION

Crystal **I** contains PefH_3^{2+} and ZnBr_4^{2-} ions. Their structure, as well as the numeration of atoms, is shown in Fig. 1. The C–O, C–N, C–F, and C–C bond lengths and the corresponding bond angles in compound **I** are close to those found for $(\text{PefH}_2^+)_2\text{PtCl}_4^{2-} \cdot 2\text{H}_2\text{O}$, $(\text{PefH}_2^+)\text{CH}_3\text{SO}_3^- \cdot 2\text{H}_2\text{O}$, $(\text{PefH}_2^+)\text{CH}_3\text{SO}_3^- \cdot 0.1\text{H}_2\text{O}$, $\text{Ag}(\text{H}_2\text{O})\text{Pef} \cdot 3\text{H}_2\text{O}$ [3] and $(\text{PefH}_3^+)\text{CuCl}_4^{2-}$ [4]. When comparing **I** and the last structure, we can see that similar lattice packing types and structural motifs are typical for them.

The Zn–Br distances (Table 2) slightly exceed the average value of 2.35(15) Å for 17 compounds having this bond [8], and the BrZnBr bond angles range from 106.74(2)° to 113.18(2)°.

The $\text{C}_{17}\text{H}_{22}\text{FN}_3\text{O}_3^{2+}$ molecular ion (Fig. 1) represents a planar group of two hexacycles bound by a common C(9)–C(10) edge; F, N(2), C(11), C(12), C(1), O(1), O(2), and O(3) atoms (maximum and mean square deviations from the plane are 0.097(3) and 0.041(3) Å, respectively), the N(2)–C(14)–C(15)–N(3)–C(16)–C(17) hexacycle with a chair conformation ($Q = 0.572(4)$ Å, $\theta = 5.8(4)^\circ$, and $\varphi = 21(4)^\circ$); and two methyl groups with the C(12) and C(13) atoms. The O1 atom of the hydroxyl group forms an intramolecular hydrogen bond with the O(2) carbonyl atom. The second weaker intramolecular bond (C–H...F), as well as the first one, forms a six-membered ring. The crystal also contains intermolecular N(3)–H...Br and O(3)–H...Br hydrogen bonds, which serve as the basis for the formation of zigzag chains (Fig. 2) oriented in the [2, 0, –1] direction. The planes of zigzags are perpendicular to the *ac* unit cell plane. The parameters of hydrogen bonds are listed in Table 3. The structure also incorporates five shortened C–H...Br intermolecular contacts, which are geometrically similar to hydrogen bonds and have C–Br and H...Br distances of from 3.634 to 3.814 Å and of from 2.77 to 2.88 Å, respectively, and CHBr angles of from 143 to 175°.

Owing to the head–tail π – π interaction of aromatic six-membered rings, the supramolecular coupling of PefH_3^{2+} ions occurs in the structure of the crystal. The projection of the structure parallel to the planes of ions is shown in Fig. 3, from which it can be seen that the ions are grouped pairwise in parallel arrangement. The numerical characteristics calculated for this interaction in compliance with [9] are given in Table 4. Interplanar distances of 3.4–3.5 Å between plane-parallel aromatic moieties are optimal for such contacts [2]. In compound **I**, they are about 0.04 Å larger than those in $(\text{PefH}_3^+)\text{CuCl}_4^{2-}$ [4], and

Table 1. Crystallographic data and structure refinement parameters for compound **I**

Gross formula	$\text{C}_{17}\text{H}_{22}\text{Br}_4\text{FN}_3\text{O}_3\text{Zn}$
<i>T</i> , K	298
Space group	$P2_1/c$
<i>Z</i>	4
$2\theta_{\text{max}}$, deg	52
<i>a</i> , <i>b</i> , <i>c</i> , Å	14.261(2), 12.354(2), 13.495(2)
β , deg	90.230(2)
<i>V</i> , Å ³	2377.6(6)
ρ , g/cm ³	2.013
μ , mm ^{–1}	7.79
Total number of measured reflections	18548
Independent reflections	4678
Number of reflections with $F > 4\sigma(F)$	3218
Ranges of <i>h</i> , <i>k</i> , <i>l</i>	$-17 \leq h \leq 17$; $-15 \leq k \leq 15$; $-16 \leq l \leq 16$
Refinement over F^2	$w = [\sigma^2(F_o^2) + (0.0238P)^2 + 0.12P]^{-1}$, where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$
Number of refined parameters	268
<i>R</i> 1 [$F_o > 4\sigma(F_o)$]	0.0336
<i>wR</i> 2	0.0663
GOOF	1.012
$(\Delta\rho)_{\text{max}}$, e/Å ³	0.47
$(\Delta\rho)_{\text{min}}$, e/Å ³	–0.42
$(\Delta/s)_{\text{max}}$	0.001

Table 2. Selected bond lengths (*d*) and bond angles (ω) in the structure of compound **I**

Bond	<i>d</i> , Å	Bond	<i>d</i> , Å
C(1)–O(2)	1.210(5)	C(4)–O(1)	1.316(4)
C(1)–O(3)	1.307(5)	F–C(6)	1.360(4)
Zn–Br(1)	2.4522(7)	Zn–Br(2)	2.4058(7)
Zn–Br(3)	2.4221(7)	Zn–Br(4)	2.3779(7)
Angle	ω , deg	Angle	ω , deg
O(2)C(1)O(3)	124.9(4)	O(2)C(1)C(3)	122.2(4)
O(3)C(1)C(3)	112.8(4)	C(10)C(4)O(1)	117.1(4)
C(3)C(4)O(1)	123.2(4)	FC(6)C(5)	119.3(4)
FC(6)C(7)	117.4(3)	C(17)N(2)C(14)	110.3(3)

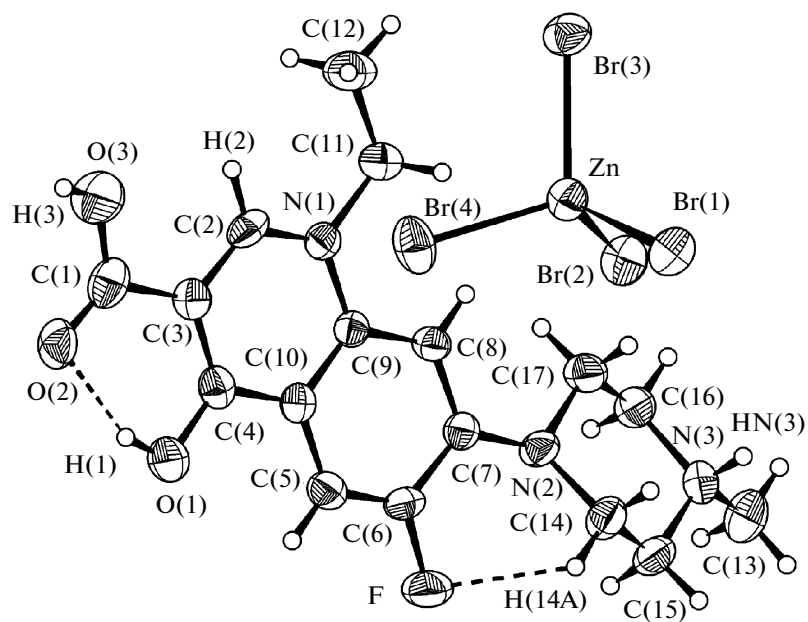


Fig. 1. PefH_3^{2+} and ZnBr_4^{2-} ions with numbered atoms. Dashed lines denote intramolecular hydrogen bonds. The sizes of thermal vibration ellipsoids correspond to a 50-% probability.

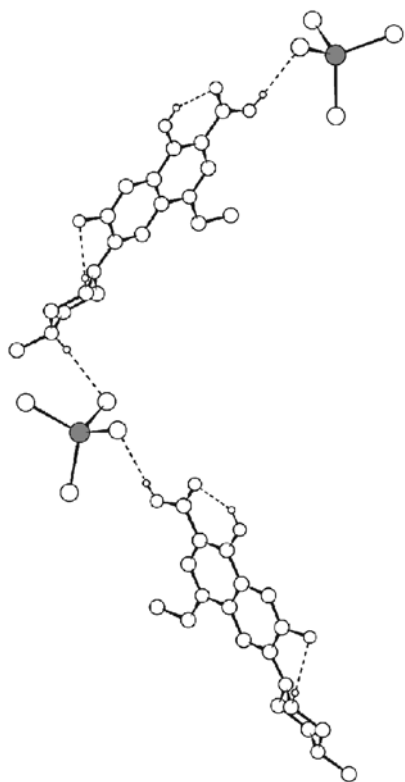


Fig. 2. Chain of PefH_3^{2+} and $[\text{ZnBr}_4]^{2-}$ molecular ions in the crystal of compound I. Hydrogen bonds are denoted with dotted lines. Hydrogen atoms, which do not participate in hydrogen bonds, are omitted.

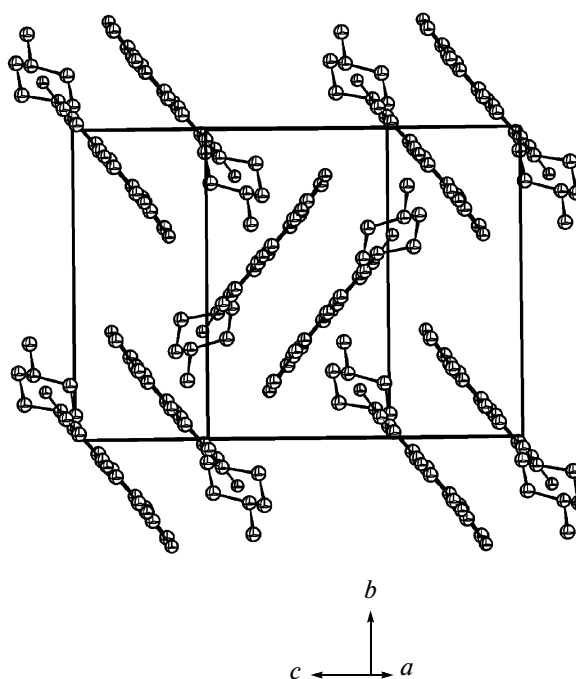


Fig. 3. PefH_3^{2+} molecular ion pairs bound by the π - π interaction in the crystal of compound I. $[\text{ZnBr}_4]^{2-}$ ions and hydrogen atoms are omitted.

Table 3. Geometric characteristics of D–H...A hydrogen bonds (bond lengths d , Å; bond angles, deg) in the structure of compound **I**

D–H	$d(\text{D–H})$	$d(\text{H}\cdots\text{A})$	$\angle\text{DHA}$	$d(\text{D}\cdots\text{A})$	A	Symmetry codes for the A atom
O(1)–H(1)	0.82	1.88	144	2.593(4)	O(2)	
C(14)–H(14B)	0.97	2.21	122	2.850(5)	F	
O(3)–H(3)	0.82	2.38	179	3.200(3)	Br(3)	$1 - x, -y, 1 - z$
N(3)–H(N(3))	0.87	2.53	175	3.395(3)	Br(1)	$2 - x, 0.5 + y, 0.5 - z$

Table 4. Parameters of the π – π interaction in a crystal of compound **I**

Cg_i – Cg_j	d , Å	α , deg	β , deg	Cg_i – p , Å	Shift Å
Cg_1 – Cg_1	3.983(2)	0	30.1	3.446(2)	1.998
Cg_1 – Cg_2	3.615(2)	1.39(2)	15.9	3.460(2)	–
Cg_2 – Cg_1	3.616(2)	1.39(2)	16.9	3.477(2)	–

Note: Interacting ions are bound via the symmetry center. Cg_1 is the N(1)–C(2)–C(3)–C(4)–C(10)–C(9) hexacycle, Cg_2 is the C(5)–C(6)–C(7)–C(8)–C(9)–C(10) hexacycle, d is the distance between the cycle centroids, Cg_i – p is the interplanar distance between the Cg_i and Cg_j cycles, shift is the distance between the Cg_i centroid and the Cg_j centroid's perpendicular projection onto the Cg_i plane.

this fact, with consideration for the close van der Waals radii of the Zn^{2+} and Cu^{2+} ions, may be explained by greater sizes of the bromide ion. The compounds under comparison have similar lattice packing types and structural motifs and consist of layers formed by PefH_3^{2+} ions spaced with tetrahalometalate anions.

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