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SYNTHESIS AND HIRSCHFELD SURFACE ANALYSIS OF THE ORGANIC SALT OF NORFLOXACIN WITH ACETATE ANION

Abdusamat A. Rasulov
Institute of Bioorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan, Junior Researcher of Laboratory of Complex Compounds
https://orcid.org/0009-0005-3905-5556

Kholmuhammad A. Aralov
1st general secondary school, Termiz district, Surkhandarya region, chemistry teacher

Jabbor R. Suyunov
Termiz State University, Senior Lecturer, Department of Analytical Chemistry, Ph.D.
https://orcid.org/0000-0003-0321-3274

Jamshid M. Ashurov
Institute of Bioorganic Chemistry named after O.S. Sodikov of the Academy of Sciences of the Republic of Uzbekistan, Head of the Laboratory of Complex Compounds, Professor, Doctor of Chemical Sciences
https://orcid.org/0000-0002-4441-2803

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Norfloxacin, organic salt, acetic acid, acetate anion, Hirschfeld

Abstract

In this article, the synthesis, composition, molecular and crystal structures of the new organic salt complex compound $C_{36}H_{50}F_2N_6O_{13}$ formed by norfloxacin (HL) with acetic acid anion were studied using X-ray structural analysis (RSA). It was determined by the RSA method that the molecular mass of the organic salt compound is 812.8 g/mol, the syngonia is triclinic, and the spatial form is P-1. Hirschfeld surface analysis of the complex was performed based on the data obtained in the RS analysis of the synthesized organic salt and the intermolecular interaction energies were calculated. According to the results of the Hirshfeld surface analysis, it was found that H...H (46.5%), H...O/O...H (30.0%) bonds make up the main part of the effects.

How to Cite

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Introduction. Various diseases are on the rise worldwide as a result of the creation of strains of hazardous germs that are resistant to current medications and their activity. These circumstances throw a critical burden on the shoulders of chemists, biologists, pharmaceuticals, and medical representatives: developing new treatments that can successfully combat hazardous germs. As we all know, developing a new drug requires a significant amount of time. As a result, it is critical to minimize the amount of active material in existing medicines while increasing their range of impact. Because the antibacterial ingredient employed in medication has a very poor solubility in water, it is present in significant quantities in the formulation of medicines. As a result, it is critical to create their soluble compounds: organic salts and complexes containing physiologically active metals.

Literature review on the subject. It has been discovered that particular medicines' organic salts containing inorganic or organic molecules often boost their effectiveness against the free ligand [1]. Among the fluoroquinolones with the highest efficacy is norfloxacin (HL) [2]. In terms of medicine, it is useful against skin, lung, prostate, and other infectious disorders, as well as digestive and urinary tract infections [3, 4]. Since HL is poorly soluble in water, it is critical to synthesise its constituents with high water solubility and biological activity [5–6]. World-class scientists have synthesised and analysed compounds of HL in the form of organic salts [7, 8]. Given the aforementioned conditions, our goal was to create HL complex compounds in the form of organic salts that would dissolve well in a range of different organic and inorganic substances. We also wanted to investigate the physicochemical characteristics of the resulting complex. The RSA method was used in this study to analyse the crystal and molecular structure of the complex containing the acetate anion of HL in the state of an organic salt. Hirshfeld surface area analyses and intermolecular interaction energies were also carried out.

Research methodology. The primary research method employed was x-ray crystallography, which was carried out at room temperature using an automated Xcalibur R Oxford Diffraction diffractometer. The Mercury 2021.3.0 [9] program's UNI force fields [10] approach was utilized to ascertain the intermolecular interaction energies in the produced organic salt's crystal structure. Additionally, the Crystal Explorer 17.5 [11] program was used to analyze the Hirschfeld surface.

Experimental part. This work synthesized a complex HL molecule with an acetate anion in the form of an organic salt having $C_{36}H_{50}F_2N_6O_{13}$, keeping in mind the need of creating HL compounds with strong water solubility for use in medicine and pharmaceuticals. By combining 12 milliliters of glacial acetic acid with 50 milliliters of water, a pH=5 solution was created, utilizing the low water solubility of HL. In this solution, Ligand HL dissolved. A 2:1 mol ratio of HL to CH_3COOH was found in the solution. Clear, colorless single crystals formed after 6 to 9 days of evaporation at room temperature in the resultant clear solution. Among the formed crystals, a crystal with a size of 0.2-0.4 mm, suitable for X-ray diffraction analysis (RSA), was selected and studied.. Upon selecting and analyzing the crystal, a novel complex compound with the formula $C_{36}H_{50}F_2N_6O_{13}$ was discovered. 90% of the reaction was yielded. Fig. 1 shows the complex compound's synthesis process plan.

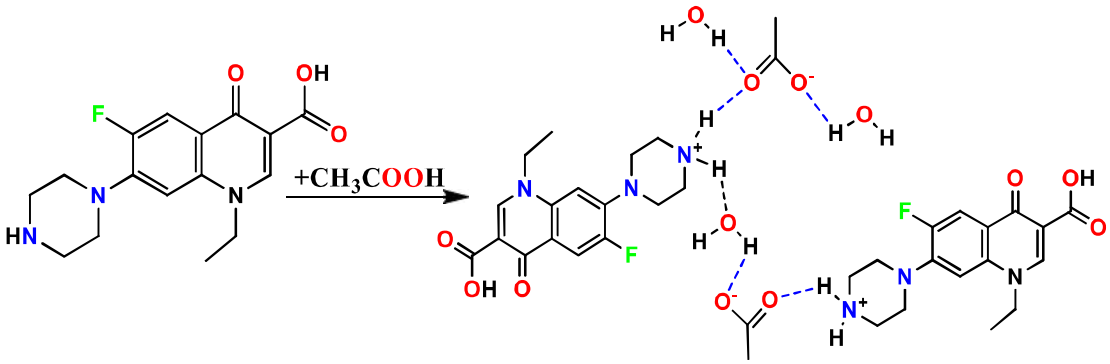


Figure 1. Synthesis scheme of the $C_{36}H_{50}F_2N_6O_{13}$ complex

Analyzing the obtained results. The formation reaction equation and structural formula for the synthesized metallocomplex compound were examined. In addition, Hirshfeld surface analysis of the produced complex chemical was performed.

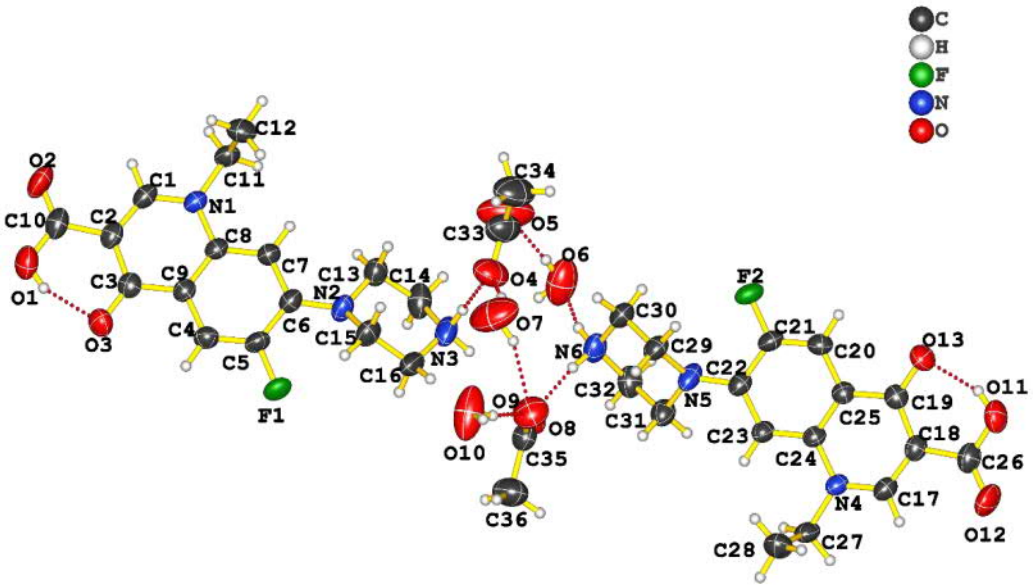


Figure 2. Molecular structure of the complex compound $C_{36}H_{50}F_2N_6O_{13}$. Internal hydrogen bonds are indicated by red dotted lines

The intermolecular interaction energy in the crystal structure of the synthesized organic salt with the composition $C_{36}H_{50}F_2N_6O_{13}$ were measured using the UNI force field method in the Mercury 2023.3.0 program (Fig. 3; Table 1).

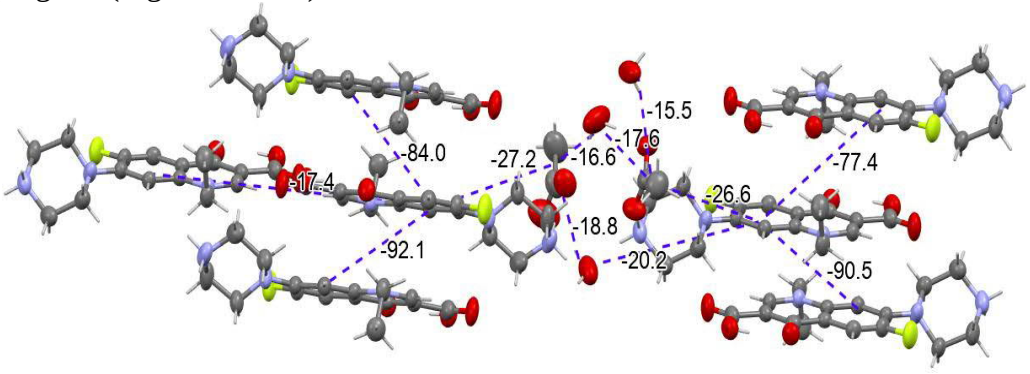


Figure 3 shows the intermolecular interaction energies of molecules in the $C_{36}H_{50}F_2N_6O_{13}$ complex as calculated by the UNI force field method, in kJ/mol.

Table 1

The $C_{36}H_{50}F_2N_6O_{13}$ complex's intermolecular distances (Å) and interaction energy (kJ/mol) were measured using the UNI force field approach.

№	Affected molecules	Distance Å	Energy kJ/mol
1	$[HL]^+$……$[HL]^+$	6.0264	-92.0897
2	$[HL]^+$……$[HL]^+$	6.26256	-90.5015
3	$[HL]^+$……$[HL]^+$	6.6092	-84.0022
4	$[HL]^+$……$[HL]^+$	7.16896	-77.3561
5	$[HL]^+$……$[CH_3COO]^-$	6.91969	-27.2325
6	$[HL]^+$……$[CH_3COO]^-$	6.67421	-26.5713
7	$[HL]^+$……$[H_2O]$	7.5034	-20.2005
8	$[CH_3COO]^-$……$[H_2O]$	3.70095	-18.7909
9	$[CH_3COO]^-$…… $[H_2O]$	4.01798	-17.6118

10	$[HL]^+$……$[HL]^+$	12.0243	-17.4381
11	$[CH_3COO]^-$……$[H_2O]$	3.41886	-16.612
12	$[CH_3COO]^-$……$[H_2O]$	3.7314	-15.5395

The findings in Table 1 show that when the distance between the same molecules grows, the interaction energy drop. At the same time, the number of atoms in a molecule influences the energy of intermolecular interactions. The total dissolving energy of the organic salt complex produced by HL and acetate anion is -628.4 kJ/mol.

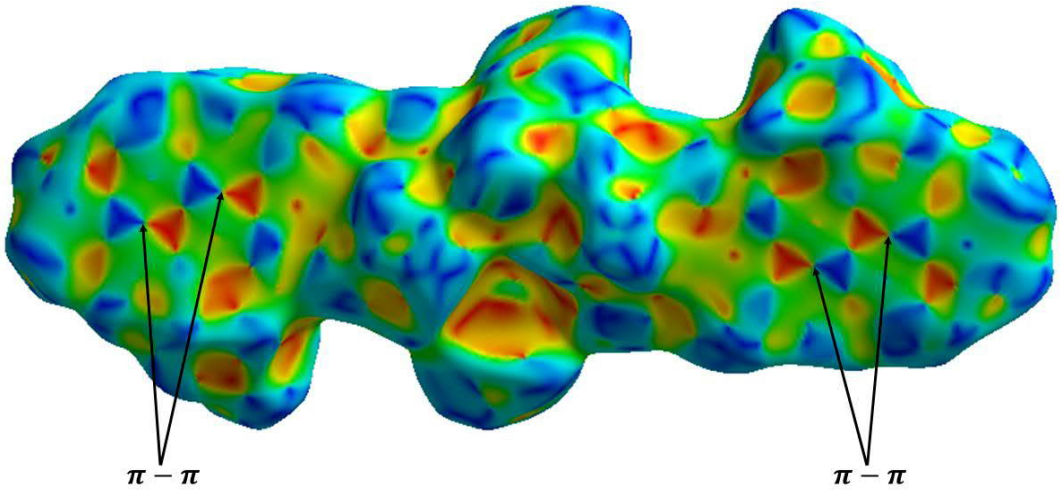


Figure 4 depicts -1.0000 to 1.0000 a.m.b. in the $C_{36}H_{50}F_2N_6O_{13}$ complex. Effects of π-π stacking on a three-dimensional Hirschfeld surface with Shape Index mapping between

If there is an aromatic ring in the molecule of a complex compound, the π-π interaction of the rings occurs. These π-π effects increase the stability of the crystal system.

Hirschfeld surface analysis can provide a wealth of information on a molecule's contact surface with other molecules in the crystal, including size and distances (Fig. 5), as well as extra functions placed into the program. The standard field volume is 392.65 Å^3, the surface is 341.55 Å^2, and the dimensions are -0.6269 (red) and 1.6815 a.m.b. (blue). The distances to the nearest nucleus are calculated as outer (de) and inner (di). On the Hirschfeld surface, points with a low effect contribution are blue, while those with a large impact contribution are red (Fig. 5).

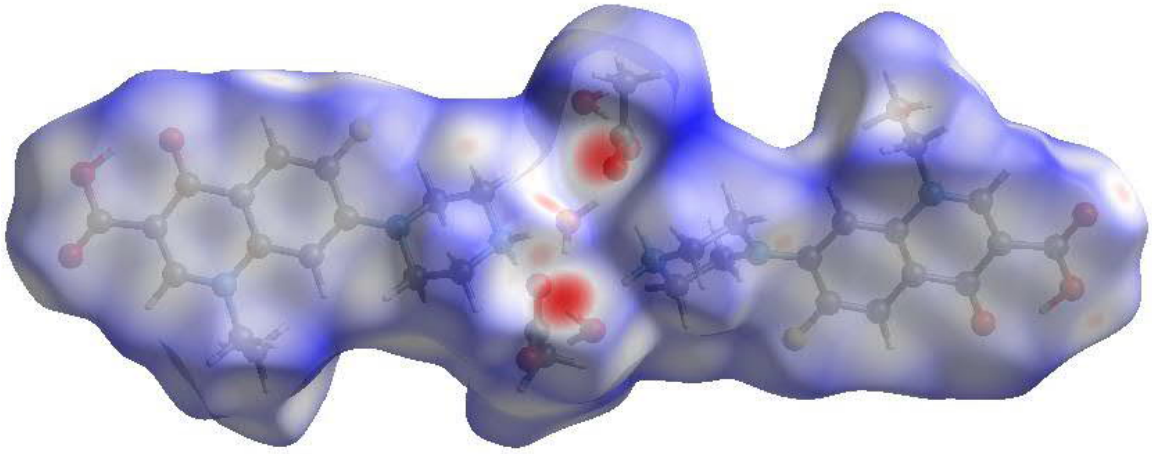


Figure 5. -0.6269 to 1.6815 a.m.b. in the $C_{36}H_{50}F_2N_6O_{13}$ complex. is a three-dimensional Hirshfeld surface mapped by d_{norm} between

Analysis of the two-dimensional fingerprint domain plots revealed that H…H and H…O/O…H interactions contribute the most to the Hirschfeld surface. In the organic salt, H…H is

46.5%, H…O/O…H is 30.0%, which is expected for molecules dominated by oxygen atoms (Figure 6).

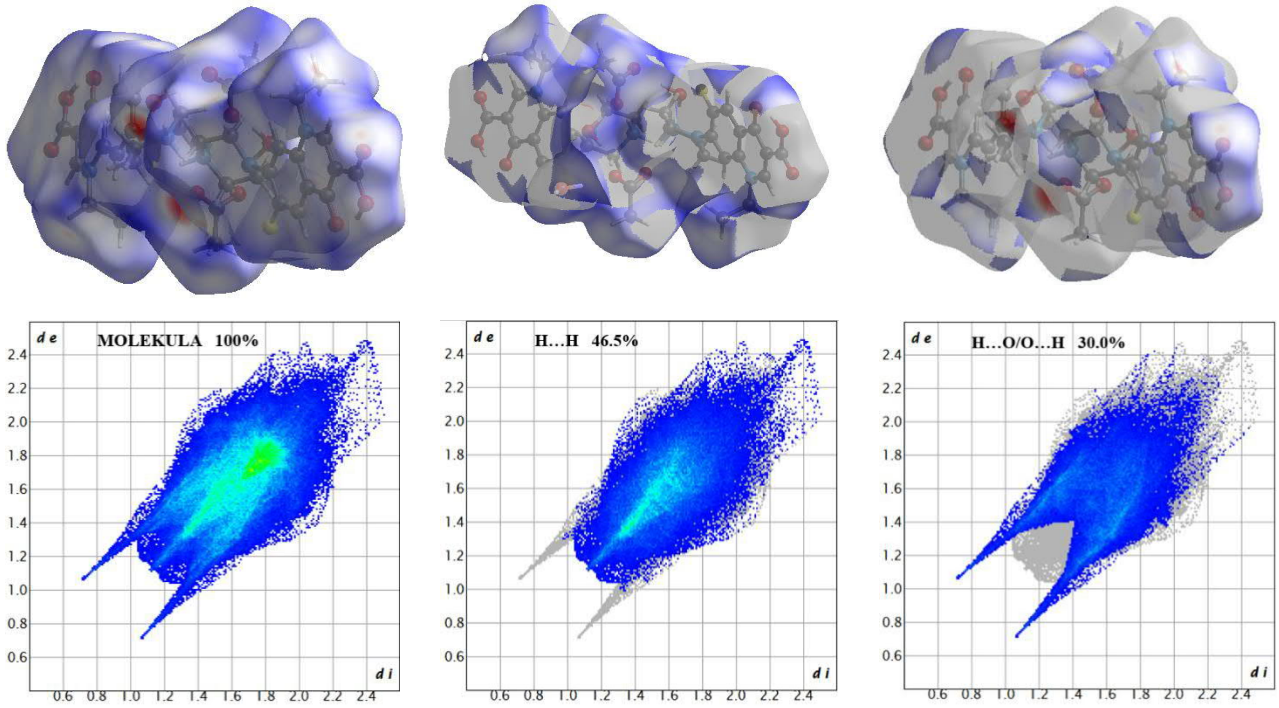


Figure 6. A d_{norm}-mapped Hirschfeld surface and two-dimensional fingerprint area representing H…H and H…O/O…H interactions in an organic salt crystal

The remaining reactions in the organic salt are C…C (7.8%), H…F/F…H (5.9%), H…C/C…H (3.7%), O…C/C…O (2.6%) while the effects are significant, F...O/O...F(1.3%), N...O/O...N(0.8%), N...C/C...N(0.6%), H...N/N...H (0.3%), F...F(0.3%), O...O(0.1%) have a smaller contribution (Fig. 7).

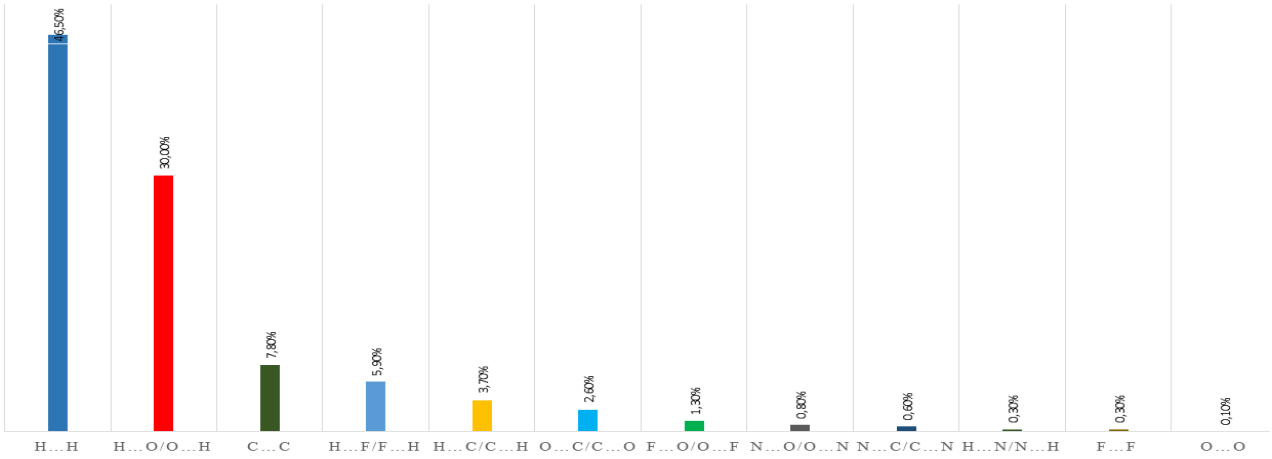


Figure 7. Hirschfeld fingerprint diagram of the $C_{36}H_{50}F_2N_6O_{13}$ complex

Conclusion: The conducted research resulted in the synthesis of an organic salt complex containing norfloxacin's acetate ion. The chemical, molecular, and crystal structures of the newly synthesized organic salt were characterized by X-ray structural analysis (RSA). The total energy of the mutual, intermolecular interaction of selected organic salt molecules in the crystal cell was

determined to be -628.4 kJ/mol. Hirschfeld surface analysis identified H…H (46.5%), H…O/O…H (30.0%), C…C (7.8%), and H…F/F…H (5.9%) as the primary interactions between molecules

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