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Synthesis, Crystal Structure and Hirshfeld Surface Studies of 8-Hydroxyquinoline Copper(II) Complex

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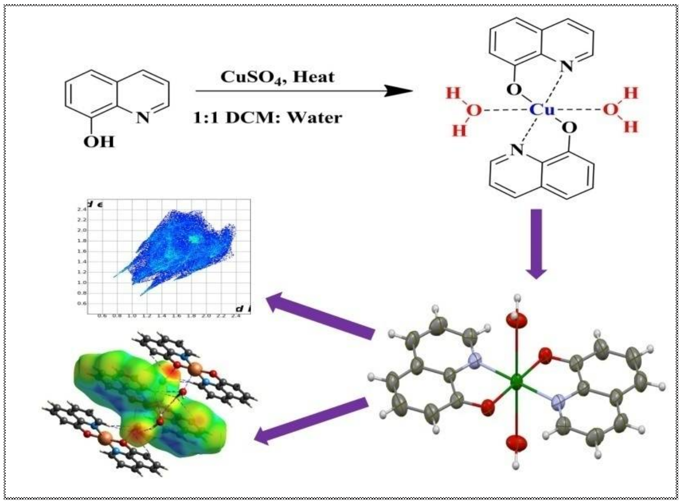
ABSTRACT

A copper salt of 8-hydroxyquinoline $[Cu(C_9H_6NO)_2(H_2O)_2]$ *has been synthesized and crystallized by slow evaporation method. The X-ray structural analysis of this copper complex revealed that, coordination environment around the central metal atom is slightly distorted octahedral geometry with trans-isomer favored structure. Further, crystal structure is stabilized by intermolecular hydrogen bond interaction of type O-H…O, which forms supramolecular* R_2^2 *(8) ring motif along c-axis and π- π interaction between pyridine and benzene rings of the adjacent complexes. Hirshfeld surface analysis identified H…H (43.7 %) and C…H (25 %) interactions are dominant and responsible for crystal packing and stability.*

Graphical Abstract



Keywords: 8-hydroxyquinoline acid, Antimicrobial agents, Hirshfeld surface.

INTRODUCTION

Quinoline, benzene ring is fused with pyridine and their derivatives are versatile organic compound. Many natural products have quinoline moiety and the versatility of quinoline are found to be bioactive and its derivatives have attracted great attention in the field of drug development of quinoline derivatives exhibits varies activities such as fungicide, insecticide, pesticide in agricultural field, antibacterial, anticancer, anti HIV activity in medicinal field and preservatives in textile, paper industries[1-3]. 8-hydroxyquinoline gained much attention due to its vast multifunctional applications. Apart from the bioactivities, it exhibit florescence and luminous property which helps in detection of essential metals like Zn, Cu, Co, Ni, etc., [4] and also in the field of OLEDs [5]. Among hydroxyl quinoline derivatives, 8-hydroxy quinoline has the divalent metal chelating ability [6]. Metal ions play a vital role in biological systems by controlling many biological processes. Sometimes metal ion can interact with proteins in our body, which can changes the functionality of the protein. Therefore, to restore the metal ion imbalance in the body metal chelation therapy is needed by chelators.

Copper (II) complexes are widely used in many pharmacological studies due to their biocompatibility. They are extensively used in medicinal field as anti bacterial [7], antioxidant [8], anticancer [9] and anti-inflammatory [10]. The redox property of copper complexes generates toxicity and they can directly interact and damage nucleic acids make them potential antimicrobial agents [11-12].

We present herein the synthesis and crystal structure of 8-hydroxyquinoline copper complex (8HqCc) for the first time, which reveals the geometrical environment around the central copper(II) metal atom. Hirshfeld surface analysis was carried out to understand the various intermolecular interactions present in the molecular crystal.

MATERIALS AND METHODS

All the reagents and solvents were procured from Sigma-Aldrich & Merck.Pvt.Ltd. Elemental analyses were recorded on VarioMICRO superuser V1.3.2 Elementar.

Synthesis of 8HqCc: Aqueous solution of copper sulphate was added slowly to the methanolic solution of 8-hydroxyquinoline in a 1:2 molar ratio. The sodium acetate was added to the resultant mixture and warmed this mixture on a water bath for 15 min followed by cooling in an ice bath. Light green precipitate was formed. The filtered precipitate was washed with distilled water and dried in an oven.The complex is crystallized using 1:1 dichloromethane: water as a solvent. After a week bluish green rod shaped crystals were obtained.

X-ray structure determination: Good quality crystal of 8HqCc was selected for X-ray intensity data collection. X-ray diffraction data were collected by RigakuXta LAB mini CCD diffractometer with X-ray generator operating at 45 kV and 10 mA, using Mo-Kα (λ = 0.71073 Å) radiation source, keeping the scan width of 0.5°, exposure time of 3sec, the sample to detector distance of 50 mm. A complete data set was processed using *CRYSTAL CLEAR* [13]. The structure was solved using *SHELXS-97*structure solution program using direct methods and refined with the *SHELXL-97* [14]. The geometrical calculations were carried out using *PLATON* [15] and the packing diagrams were generated using *MERCURY* [16]. The crystal data and the structure refinement details are given in table 1.

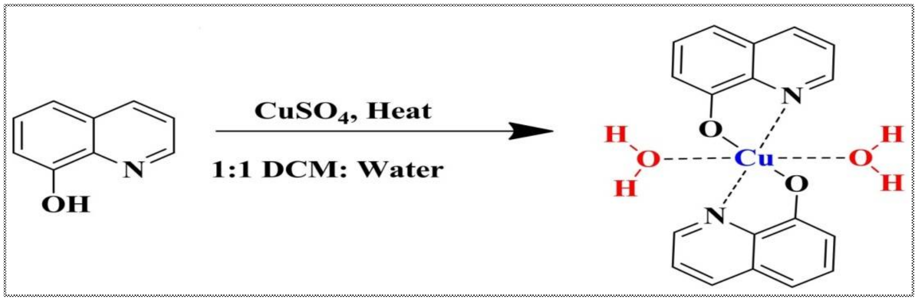
Hirshfeld surface analysis: Analysis of Hirshfeld surfaces and their associated two dimensional fingerprint plots of this copper complex compound were calculated using Crystal Explorer 3.1 [17]. The Hirshfeld surfaces mapped with different properties d_{norm}, curvedness, d_i and d_e. The d_{norm} is normalized contact distance, defined in terms of $d_{i,}$ d_e (where d_i is the closest internal distance from a given point on the Hirshfeld surface and d_e is the closest external contacts) and the vdW radii of the atoms.

Table 1. Crystal data and structure refinement details.

CCDC Number	1835510	Absorption coefficient	1.402 mm^{-1}
Empirical formula	$C_{18}H_{16}CuN_2O_4$	F_{000}	398
Formula weight	387.88		
Temperature	293 K	Index ranges	$-14 \le h \le 14$ $-7 \le k \le 4$ $-16 \le l \le 12$
Wavelength	0.71073 Å	θ range for data collection	3.28° to 27.57°
Crystal system	Monoclinic	Reflections collected	3771
Space group	$P\,2_1/a$	Independent reflections	1788 [R_{int} = 0.0781]
Cell dimensions	A = 11.50(3) Å b = 5.557(1) Å c = 12.95(3) Å β = 106.36(2)°	Refinement method Data / restraints / parameters Goodness-of-fit on F^2	Full matrix least-squares on F^2 1788 / 0 / 118 1.108
Volume	794(3) $Å^3$	Final [$I > 2\sigma(I)$]	$R1$ = 0.0723, $wR2$ = 0.2064
Z	2	R indices (all data)	$R1$ = 0.0813, $wR2$ = 0.2134
Density(calculated)	1.622 Mg m^{-3}	Largest diff. peak and hole	1.375 and −1.072 $eÅ^{-3}$

RESULTS AND DISCUSSION

Synthesis of 8HqCc: The desired copper(II) 8-hydroxyquinoline complex was synthesized by mixing $CuSO_4$ with the 8-hydroxyquinolinecomplex in [1:2] molar ratio, as shown in Scheme 1. Synthesis of such complexes was sensitive to the counter ion as well as the solvents used. The purity of the metal complex was determined by elemental analysis.



Scheme 1. Synthetic route of 8HqCc.

Crystal structure of 8HqCc: Single crystal structural analysis of the grown crystal shows the symmetry dependent mononuclear complex $[Cu(C_9H_6NO)_2(H_2O)_2]$ having metal-ligand stochiometry of 1:2 ratio. The structural studies reveal that central Cu^{2+} ion is surrounded by 8-hydroxyquinoline (8Hq) and water molecules to form coordination complex. Symmetrically dependent 8Hq ligand adopts coplanar conformation with N-C-C-O torsion angle of 1.3^o which shows slightly distorted structure with a dihedral angle of 83.93^o between their planes. A nitrogen and an oxygen atom from each 8Hq ligand and two oxygen atoms from each water molecule form moderately distorted octahedral stereochemistry of the Cu(II) centre (Fig 1). The OH group connected to the benzoid ring of8Hq shows lesser Cu-O bond distance of 8Hq ligand(1.966 Å)compared to the coordinated water molecule (2.459 Å),whereas Cu-N distance is 2.014 Å (Table 2). The average O-Cu-O and O-Cu-N bond angles are 113(6) Å and 89.5(2) Å respectively (Table 3).

Interestingly, a hydrogen atom of chelating water molecule connected to the O(1) of 8Hq ligand through O-H...O hydrogen bond. These hydrogen bonds form $R_2^2(8)$ ring motif sustaining the stability of the crystal structure, which are favorable to form supramolecular architecture of 8HqCc along the *a*-axis (Fig 2).

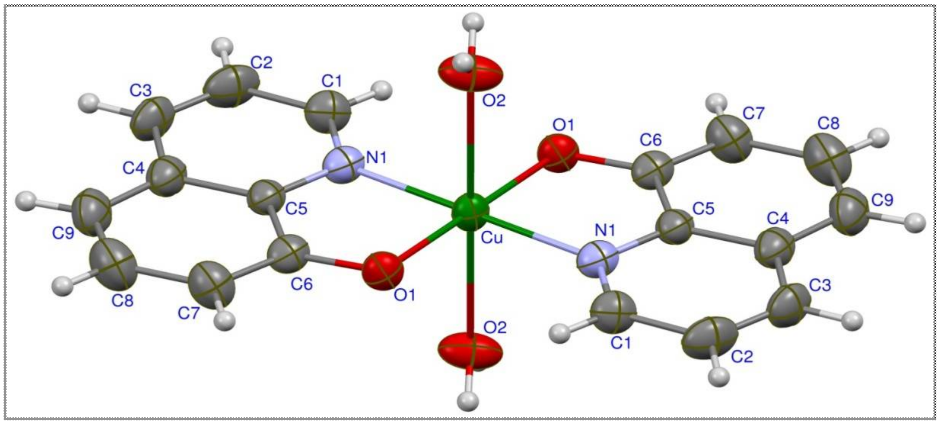


Figure 1. ORTEP diagram of the 8HqCcwith displacement ellipsoids are drawn at 50% probability level.

The crystal packing of 8HqCc is stabilized by amalgamation of intra-molecular and inter-molecular hydrogen bond interactions and π···π stacking. Figure 3 emphasize the molecular packing mode in a unit cell and various weak interactions lead to 2-D zig-zag molecular arrangement along *b*-axis. The π-π stacking interactions (green dashed lines) between pyridine and benzene ring with centre-to-centre distance (d_{c-c}) of 4.022 Å, perpendicular distance ($d_{\pi-\pi}$) of 5.284 Å, α=0° β = 4.5°and γ= 74.1° (α is the dihedral angle between the two quinoline planes, β and γ are the angle of the centroid-centroid distance vector and its alternate interior angle, respectively) is depicted in figure 4.

Table 2: bond lengths (Å) of 8HqCc

Atoms	Length	Atoms	Length
Cu-O1	1.966(6)	C1-C2	1.416(10)
Cu-O2	2.459(7)	C2-C3	1.352(9)
Cu-N1	2.014(7)	C3-C4	1.416(9)
Cu-O1	1.966(6)	C4-C9	1.399(9)
Cu-O2	2.459(7)	C4-C5	1.427(9)
Cu-N1	2.014(7)	C5-C6	1.444(9)
O1-C6	1.325(7)	C6-C7	1.364(9)
N1-C1	1.311(8)	C7-C8	1.401(10)
N1-C5	1.350(8)	C8-C9	1.375(10)

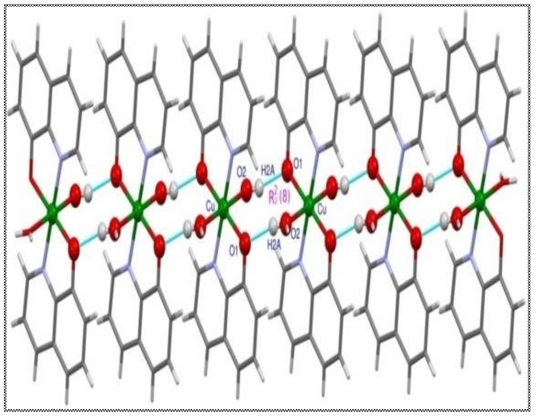


Figure 2. Supramolecular architecture of 8HqCc formed along the *a*-axis.

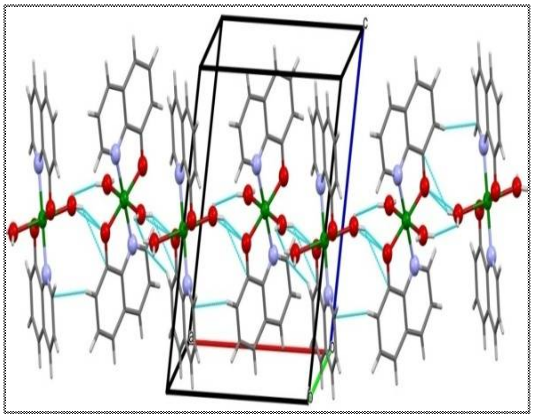


Figure 3. Packing of the molecules when viewed down along the *b*-axis. The blue dotted lines represent the intermolecular interaction bonds.

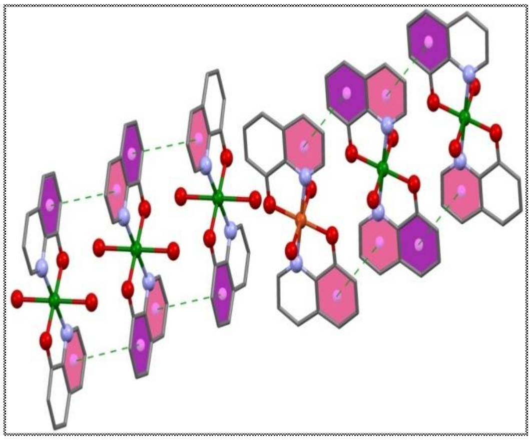


Figure 4. $\pi \ldots \pi$ stacking contacts along [001] direction in the crystal structure of 8HqCc.

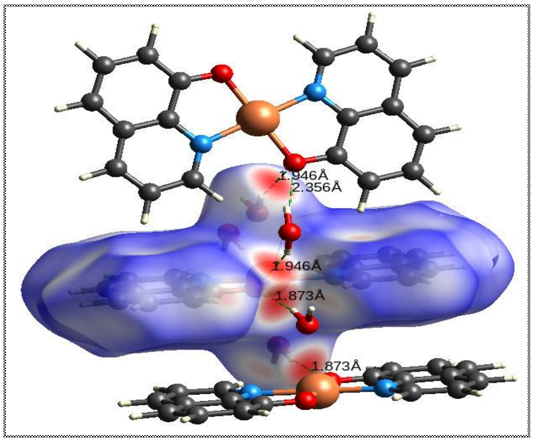


Figure 5. The d_{norm}mapped on Hirshfeld surface for visualizing the intermolecular contacts of the 8HqCc.

Hirshfeld surface analysis: Various molecular interactions in the crystal were visualized using Hirshfeld surface analysis [**18**]. The two-dimensional fingerprint plots represent the percentage of contacts contributed towards the crystal packing. The Hirshfeld surfaces of $[Cu(C_9H_6NO)_2(H_2O)_2]$ were examined to elucidate type and nature of intermolecular interactions. Figure 5 shows d_{norm} surfaces of the complex molecule and is shown as transparent to allow visualization of coordination environment around the central copper atom and electron donating water molecules. Fig. 5 revealed the close contacts of hydrogen bond donors and acceptors. Although, O…H interactions are less and most likely strongest, they contribute 14% of the Hirshfeld surface of the molecules. On the other hand H…H interactions dominating the total Hirshfeld surface (43.7%), C…H interactions cover one-fourth of the Hirshfeld surface are observed as spikes in the lower and upper middle of the fingerprint plots (Fig. 6). Apart from these, C…C (5.2%), Cu…O (4.3%), H…N (2.4%) and Cu…N (2.3%) interactions (Fig 7) were observed. The large flat region which is outlined by a blue color on curvedness of the complex reveals $\pi \ldots \pi$ stacking interaction between adjacent molecules (Fig. 8). Figure 9 displays d_i and d_e Hirshfeld surfaces of the complex surrounded by two neighboring molecule associated with close contacts, whereas orange spots indicate the strong hydrogen bond interactions.

Table 3. Bond angles (°) of 8HqCc.

Atoms	Angle	Atoms	Angle
O1-Cu-O2	89.30(1)	Cu-N1-C5	109.7(4)
O1-Cu-N1	83.93(2)	C1-N1-C5	119.7(5)
O1-Cu-O1	180.00(1)	N1-C1-C2	122.0(6)
O1-Cu-O2	90.70(1)	C1-C2-C3	119.6(6)
O1-Cu-N1	96.07(2)	C2-C3-C4	120.1(6)
O2-Cu-N1	86.45(2)	C3-C4-C9	125.9(6)
O1-Cu-O2	90.70(1)	C3-C4-C5	116.4(5)
O2-Cu-O2	180.00(1)	C5-C4-C9	117.8(5)
O2-Cu-N1	93.56(2)	N1-C5-C4	122.2(5)
O1-Cu-N1	96.07(2)	N1-C5-C6	117.1(5)
O2-Cu-N1	93.56(2)	C4-C5-C6	120.7(5)
N1-Cu-N1	180.00(1)	C5-C6-C7	118.1(5)
O1-Cu-O2	89.30(1)	O1-C6-C5	117.0(4)
O1-Cu-N1	83.93(2)	O1-C6-C7	124.8(5)
O2-Cu-N1	86.45(2)	C6-C7-C8	121.5(6)
Cu-O1-C6	112.2(3)	C7-C8-C9	120.7(6)
Cu-N1-C1	130.6(4)	C4-C9-C8	121.2(6)

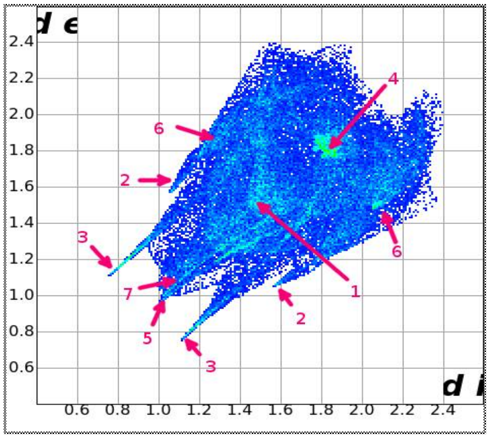


Figure 6. Two-dimensional fingerprint plots of 8HqCccontacts involved in the crystal packing of 8HqCc. Close contacts are divided into seven regions; H…H (1), C…H (2), O…H (3), C...C (4), Cu…O (5), H…N (6) and Cu…N (7).

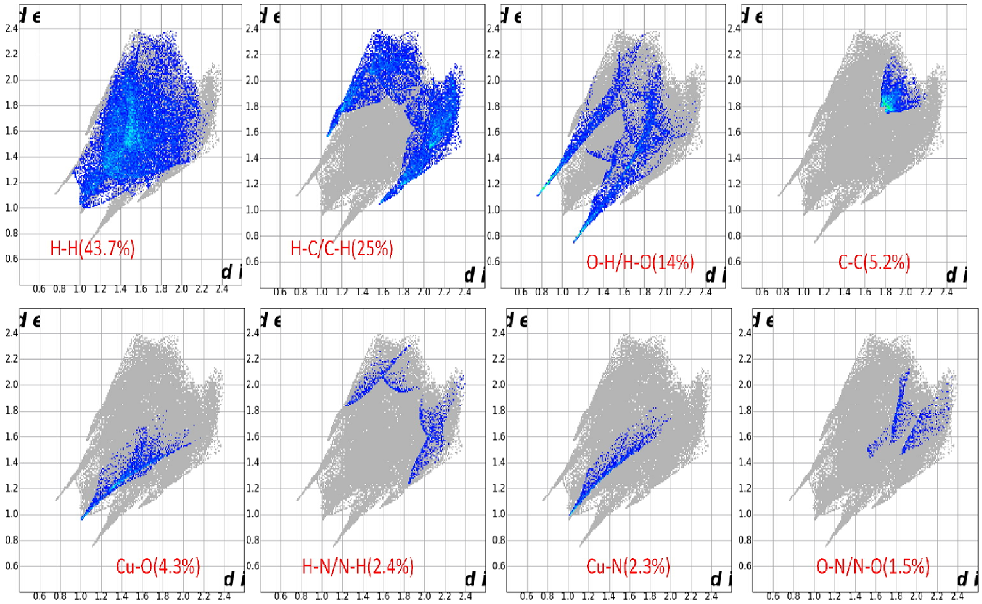


Figure 7. Two-dimensional fingerprint plots indicate the major contributions of intermolecular interactions in 8HqCc.

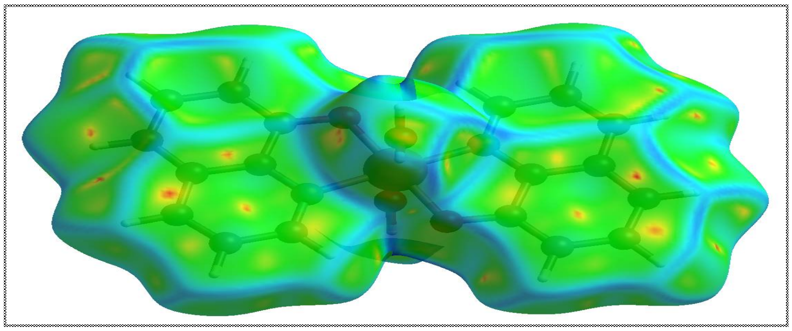


Figure 8. Curvedness mapped on Hirshfeld surface for 8HqCc.

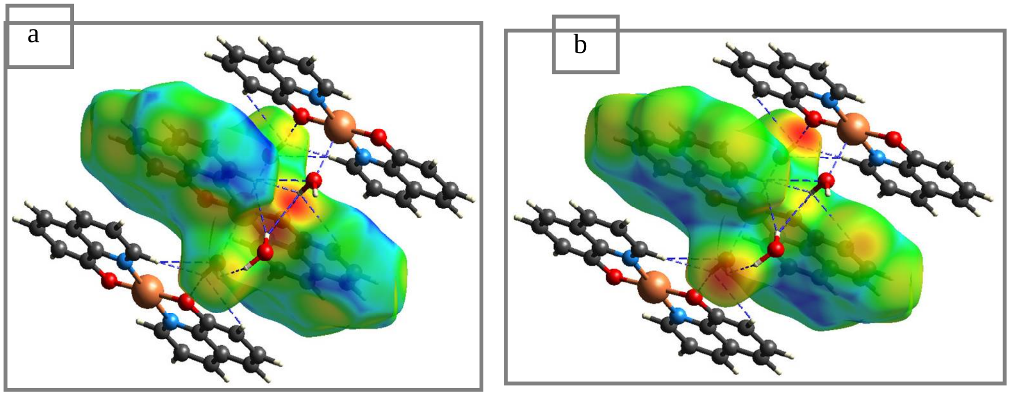


Figure 9. d_i(a) and d_e(b) mapped on Hirshfeld surface for visualizing the intermolecular contacts of the 8HqCc.

APPLICATIONS

The diverse intermolecular interactions demonstrate, this copper (II) complex compound can be used for various pharmacological applications.

CONCLUSIONS

Novel 8-hydroxyquinoline copper(II) complex was synthesized. The crystal structure studies show that the complex is crystallized in monoclinic crystal system, with $P2_1/a$ space group and central copper atom adopts slightly distorted octahedral coordination geometry. Intermolecular hydrogen bond interactions of type O-H...O form two-dimensional supramolecular architecture of 8HqCc along the a-axis. Hirshfeld surface and fingerprint plot analysis provides rapid quantitative insight into the intermolecular interactions. H...H and C...H interactions dominate the Hirshfeld surfaces of 8HqCc and other relatively weak interactions have clear signature in the fingerprint plots.

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