www.dergipark.gov.tr
ISSN:2148-3736
El-Cezerî Fen ve Mühendislik Dergisi
Cilt: 9, No: 2, 2022 (695-707)

El-Cezerî Journal of Science and Engineering
Vol: 8\9, No: 2, 2022 (695-707)
DOI : 10.31202/ecjse.995055

ECJSE

Research Paper / Makale

Synthesis, Crystallographic Structure, Spectral (FT-IR, UV) Properties, Hirshfeld Surface Analysis and Molecular Docking Studies of a New Cobalt-(II) Complex with Diclofenac Including Nitrogen Donor Ligands

Serap UZUN[1a]

[a]Basic Sciences Department, Samsun University, Samsun, Türkiye
serap.uzun@samsun.edu.tr

Received/Geliş: 14.09.2021 **Accepted/Kabul:** 28.10.2021

Abstract: The new diclofenac-based cobalt (II) complex, namely bis {2- [2-(2,6-dichloro anilino) phenyl] acetato-$\kappa'O, O'$} bis (2-methyl-1*H*-imidazole-κN^3cobalt (II) has been synthesized and characterized by FT–IR, UV spectroscopies and single crystal X-ray diffraction techniques. The title complex crystallizes in the monoclinic space group I2/a with a = 19.0546(8) Å, b = 13.7167(8) Å, c = 14.7165(7) Å, α = 90˚, b = 13.7167(8) Å and γ = 90˚ and Z=4. According to the X-ray diffraction technique results, the cobalt ion is coordinated to diclofenac and methyl imidazole ligands and the title complex adopts a distorted tetrahedral geometry with τ'_4 = 0.75. The monomer is linked by conventional C–H···O and C–H···N intermolecular hydrogen bonds as well as C–H···π interactions to form sheet structures in 3D space. Additionally, the intermolecular interactions in the title complex have examined using Hirshfeld surface analysis technique. The major interactions of the complex are H···H (46%), H···Cl (21%), C···H (17.2%) and O···H (7.6%). Finally, molecular docking studies with different two receptors (5U9D and 4XTA) have been performed to show whether the title molecule has anti-tumor and anti-inflammatory activity, respectively.

Keywords: cobalt (II), diclofenac, crystal structure, Hirshfeld surface analysis, molecular docking.

Nitrojen Donör Ligantları İçeren Diklofenaklı yeni bir Kobalt-(II) Kompleksinin Sentez, Kristalografik Yapı, Spektral (FT-IR, UV) Özellikleri, Hirshfeld Yüzey Analizi ve Moleküler Kenetlenme Çalışmaları

Öz: Yeni diklofenak bazlı cobalt (II) kompleksi, bis {2- [2-(2,6-dikloro anilino) fenil] asetato-$\kappa'O, O'$} bis (2-metil-1*H*-imidazol-κN^3cobalt (II) sentezlenmiş ve FT-IR, UV spektroskopileri ve tek kristal X-ışını kırınımı ile karakterize edilmiştir. Başlık kompleksi I2/a momoklinik uzay grubunda a = 19.0546(8) Å, b = 13.7167(8) Å, c = 14.7165(7) Å, α = 90˚, b = 13.7167(8) Å ve γ = 90˚ ve Z=4 ile kristalleşir. X-ışını kırınım tekniğine göre, kobalt iyonu diklofenak ve metil imidazol ligandlarına koordinedir ve başlık kompleksi $\boldsymbol{\tau'_4}$ = 0.75 ile çarpık bir tetrahedral formu benimsemektedir. Monomer, 3-boyutlu uzayda tabaka yapıları oluşturmak için C–H···π etkileşimlerinin yanı sıra moleküller arası geleneksel C–H···O ve C–H···N hidrojen bağları yoluyla bağlanır. Ek olarak başlık kompleksindeki moleküller arası etkileşimler Hirshfeld yüzey analizi tekniği kullanılarak incelenmiştir. Kompleksin başlıca etkileşimleri, H···H (%46), H···Cl (%21), C···H (%17,2) ve O···H (%7,6) dır. Son olarak başlık molekülünün sırasıyla, anti-tümör ve anti-inflamatuar aktiviteye sahip olup olmadığını göstermek için iki farklı reseptör (5U9D ve 4XTA) ile moleküler kenetlenme çalışmaları yapılmıştır.

Anahtar Kelimeler: kobalt (II), diklofenak, kristal yapı, Hirshfeld yüzey analizi, moleküler kenetlenme.

How to cite this article
Uzun, S., "*Synthesis, crystallographic structure, spectral (FT-IR, UV-vis) properties, hirshfeld surface analysis and molecular docking studies of a new cobalt-(II) complex with diclofenac including nitrogen*" El-Cezerî Journal of Science and Engineering, 2022, 9 (2); 695-707.

Bu makaleye atıf yapmak için
Uzun, S., " Nitrojen Donör Ligantları İçeren Diklofenaklı yeni bir Kobalt-(II) Kompleksinin Sentez, Kristalografik Yapı, Spektral (FT-IR, UV) Özellikleri, Hirshfeld Yüzey Analizi ve Moleküler Kenetlenme Çalışmaları " El-Cezerî Fen ve Mühendislik Dergisi 2022, 9 (2); 695-707.
ORCID ID: [a]0000-0002-2982-8376

1. Introduction

Cobalt ion that is less toxic than other metal ions like platinum [1,2] is used in coordination chemistry and pharmacology for different therapeutic drugs development, due to its different geometries and coordination numbers [3]. Many cobalt complexes have been reported to date that is showing antitumor, antiproliferative [4,5], antimicrobial [6,7], antifungal [8], antiviral [9] and antioxidant [10] activity. Achieving the desired or needed structural and chemical properties can only be possible with appropriate ligand selection [11]. The diclofenac is an important ligand group because it is active molecule as biological and so is used in the treatment of many diseases. In addition, it is used as an analgesic, anti-inflammatory and antipyretic drug for injuries, pains, rheumatic inflammations and osteoarthritis [12–15]. On the other hand, imidazole ligands are nitrogen-based ligands and these ligands can be useful in coordination chemistry and are important for pharmacologic investigations [16,17]. Molecular docking can provide information to the researcher about the realizability of biochemical reactions before experimental researchs. Therefore molecular docking study of the title complex has been performed to analysis its antitumor and anti-inflammatory aspects against the target 5U9D and 4XTA proteins, respectively. Furthermore, a new cobalt complex with diclofenac including nitrogen donor ligands has been characterized by single-crystal X-ray diffraction, FT-IR and UV spectroscopic techniques. Additionally, Hirshfeld surface analysis technique has also used for understanding the intermolecular interactions of the crystal structure in this paper.

2. Experimental Methods

2.1. Synthesis

$CoNO_3·6H_2O$ (0.15 g, 0.5 mmol) and Nadicl (sodium diclofenac) (0.32 g, 1 mmol) were dissolved in methanol (15cm^3), separately. These solutions were mixed with continuous stirring at 50°C. Then, 2-methylimidazole (0.08 g, 1 mmol) was added to the mixture. The resulting solution was allowed to evaporate slowly at 25°C. A few days later, purple crystallization occurred, suitable for X-ray experimentation. Yield: 95%; Analytical data for [$C_{36}H_{32}N_6O_4Cl_4Co$]: Found: C, 53.21; H, 4.02; N, 10.28%; Calcd: C, 53.16; H, 3.96; N, 10.33%.

2.2. Instrumentation

The FT-IR spectrum of the title complex was recorded by using a Bruker Vertex 80 V FT-IR spectrophotometer (450–4000 cm^{-1}). The ultraviolet absorption measurement of the title complex was examined using a Unicam UV2 in 200–900 nm range in methanol (MeOH).

2.3. X-Ray Crystallography

The X-ray diffraction data of $C_{36}H_{32}CoN_6Cl_4O_4$ were illuminated by the same procedure as previous publication [18], using the relevant programs [19–22]. The X-ray experiment details and parameters of the refinement process were showed in Table 1.

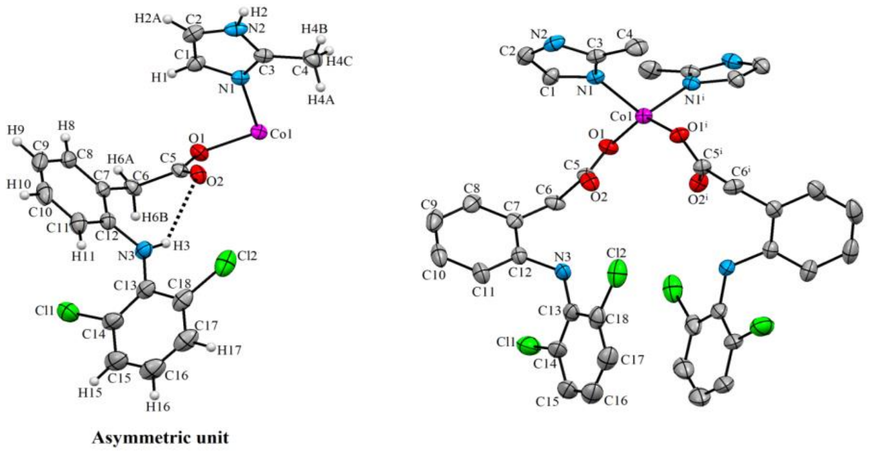
3. Results and Discussion

3.1. Crystal Structure

The Ortep diagram of $C_{36}H_{32}CoN_6Cl_4O_4$ is shown in Fig. 1. Selected bond distances and bond angles are tabulated in Table 2. Detailed structure parameters are listed in Table 1. The complex crystallizes in monoclinic space group I2/a. The Co (II) ion is coordinated by two oxygen atoms from diclofenac ligands and two nitrogen atoms from the methyl imidazole parts of the complex. The structural distortion indexes tau (**τ_4**) [23] and (**τ'_4**) [24] are calculated as 0.81, 0.75 for the title molecule and the Co (II) centre has a distorted tetrahedral geometry with two monodentate methylimidazole ligand and two monodentate diclofenac ligands, in this way forming a CoN_2O_2 chromophore. While the Co1–N1 bond length [2.030 (2) Å] is compatible with the literature [25], Co1–O1 bond length [1.987(1) Å] is slightly shorter than the value in the literature [26,27]. The reason for this may be that the studied complex adopted a distorted tetrahedral geometry.

Table 1. Crystal data and structure refinement parameters for the title compound.

Chemical formula	**$C_{36}H_{32}CoN_6Cl_4O_4$**
Color/shape	Violet/Plate
Formula weight	813.42
Temperature	293 K
Crystal system	Monoclinic
Space group	I2/a
Unit cell parameters	a = 19.0546(8) Å
	b = 13.7167(8) Å
	c = 14.7165(7) Å
	α =90°
	β = 90.948(4)°
	γ = 90°
Volume	3845.9(3)Å^3
Z	4
Density	1.405 g/cm^3
Absorption cefficient	0.77 mm^{-1}
T_{min}, T_{max}	0.639, 0.945
θ range for data collection	1.76° to 28°
Unique reflections measured	22933
Independent/observed reflections	3074/3749
Data/restraints/parameters	3074/13/232
Goodness of fit on F^2	1.056
R [I>2σ(I)], wR	0.0436, 0.1052
CCDC Number	19775551



Asymmetric unit

Figure 1. ORTEP 3 diagram for bis {2- [2-(2,6-dichloro anilino) phenyl] acetato-*κ'O, O'*} bis (2-methyl-1*H*-imidazole-*κN*^{3}cobalt (II).

Table 2. Some selected bond lengths and angles of $C_{36}H_{32}CoN_6Cl_4O_4$ (Å, °)

Parameters		**Parameters**	
Co1– N1	2.030(2)	C18– Cl2	1.728 (5)
Co1– O1	1.987(1)	O1– Co1– N1	101.10 (9)
N1– C1	1.383 (4)	C1– N1– C3	106.0 (2)
N1– C3	1.320 (3)	O2 –C5– O1	122.5 (2)
C5 –O2	1.237 (3)	C12– N3– C13	123.7 (2)
C5– C6	1.509 (3)	C1– N1– Co1– O1	–139.2 (2)
C12– N3	1.410 (4)	C6– C5– O1– Co1	178.0 (2)
C14–Cl1	1.716 (5)	C11– C12– N3– C13	18.8 (5)

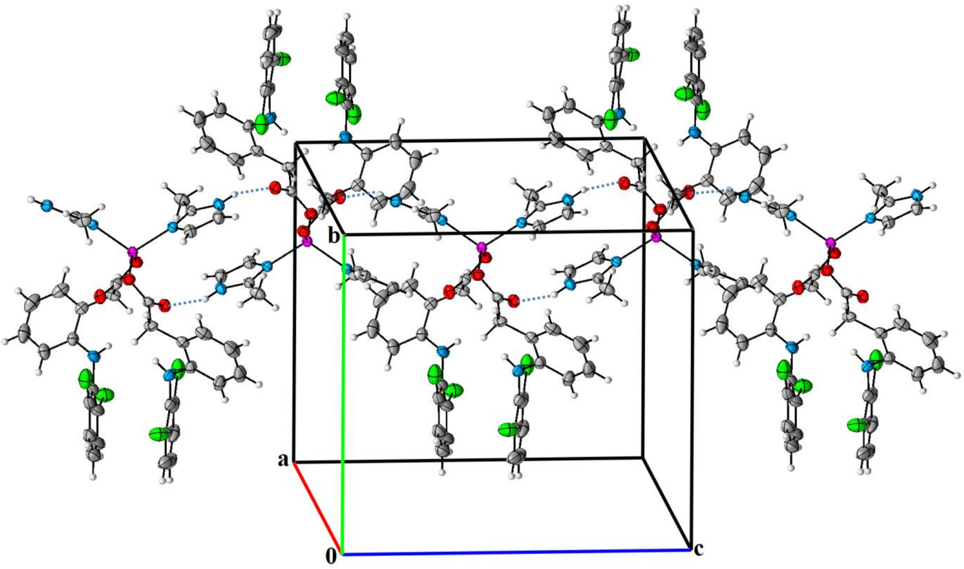


Fig. 2. A partial packing diagram of $C_{36}H_{32}CoN_6Cl_4O_4$. N2—H2···O2 interactions are indicated by dashed lines.

Table 3. Hydrogen-bond geometry (Å, º).

D—H···A	**D—H**	**H···A**	**D···A**	**D—H···A**
N3–H3···O2	0.86	2.37	2.951(3)	125
N2–H2···O2$^{(i)}$	0.86	1.93	2.750(3)	158
C4–H4a···O1$^{(ii)}$	0.96	2.54	3.251(5)	131
C6–H6a···Cl1$^{(iii)}$	0.97	2.93	3.872(3)	164
C4–H4B···π$^{(i)}$	0.96	2.88	3.757(4)	153
C16–H16···π$^{(iv)}$	0.93	2.71	3.545(5)	149

(i) –x+3/2, –y+3/2, –z+3/2; (ii) –x+3/2, y, –z+1; (iii) –x+1, –y+1, –z+1; (iv) x+1, y, z+1

The dihedral angles of 71.48 (10)°, 80.83(10)° and 66.86 (11)° are between the (C13–C18) and (C7–C12), (C7–C12) and the imidazole ring (C1/C2/N2/C3/N1), (C13–C18) and (C1/C2/N2/C3/N1), respectively. In the crystal, there is N3–H3···$O2_{carboxyl}$ intramolecular hydrogen bond which generates S (7) ring motif [D···A= 2.951 Å]. This intramolecular interaction affects the conformation of the ligand (Table 3).

The atoms C4, N2 and C6 in the title complex at (x, y, z) are hydrogen-bond donor, by atom H4a, H2 and H6a, to atoms O1 at (3/2–x, y, –z+1), O2 at (3/2–x,3/2–y,3/2–z) and Cl1 at (–x+1, –y+1, –z+1), respectively. These interactions, which are also tabulated in Table 3 and shown in Fig. 2, play major role for the 3D supramolecular structure of the complex as well as C–H$\cdots\pi$ interactions.

3.2. Hirshfeld Surface (HS) Analysis

The HS analysis is a very successful technique in describing the intermolecular interactions and contributions from atoms in the crystal structure. [28–31]. The fingerprint plots are represented as a 2D image of the HSs. d_{norm} represent the normalized contact distance that is the function of d_i, d_e and van der Waals (VdW) radii of the atoms in the molecule and is expressed by the equation [32,33].

$$d_{norm} = \frac{d_i - r_i^{VdW}}{r_i^{VdW}} + \frac{d_e - r_e^{VdW}}{r_e^{VdW}} \tag{1}$$

In here, d_i and d_e are the distances from the HS to the nearest atoms inside and outside the surface, respectively, r_e^{VdW} and r_i^{VdW} is Van der Waals radii of atoms. For the title complex, the the Crystal Explorer program [34] was used for HS analysis. There are three colours on the d_{norm} surface where the red and blue regions represent shorter and longer intercontacts, respectively. Also, white regions show the contacts are equal to the sum of the van der Waals radii [35,36].

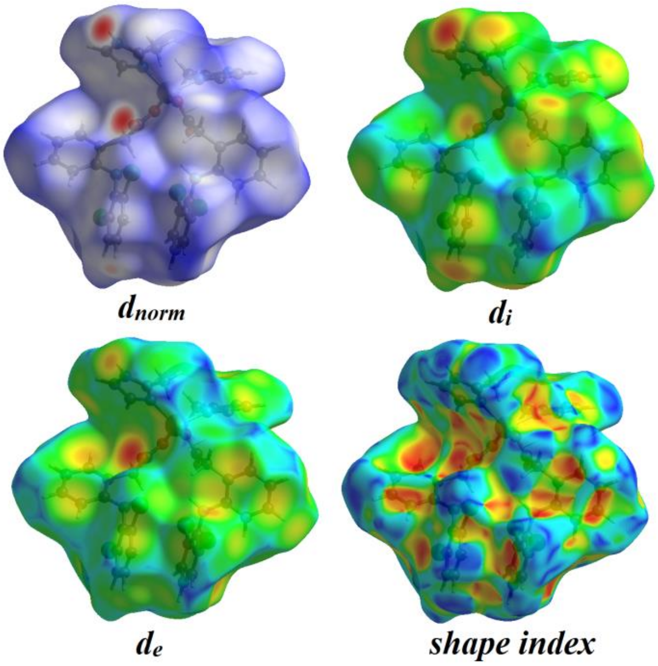


Fig. 3. The Hirshfeld surface of $C_{36}H_{32}CoN_6Cl_4O_4$ mapped with d_{norm}, d_i, d_e and shape index.

For $C_{36}H_{32}CoN_6Cl_4O_4$, d_{norm}, d_i and d_e shape indices are –0.6302 to 1.7680, 0.7232 to 2.8591 and 0.7256 to 2.7349 Å, respectively and are illustrated in Fig. 3. The red regions on the surface are the regions where the molecular interaction tends to be strongest. (Fig. 4). The N2–H2$\cdots$O2^{i} and C4–H4a$\cdots$O1^{ii} intermolecular hydrogen bonds are shown on the d_{norm}, d_i and d_e surfaces as red spots for title complex (Fig. 3). Also, Figure 5 is illustrated the 2D fingerprint plots for the title complex. The major interactions of the complex are H$\cdots$H (or van der Waals) with 46%, H$\cdots$Cl (or H$\cdots\pi$) with 21%, C$\cdots$H with 17.2%, O$\cdots$H with 7.6%. The other important interactions are Cl–C, C–C, C–N, Cl–O and N–H with 2.7%, 1.2%, 0.7%, 0.4% and 2.8%, respectively.

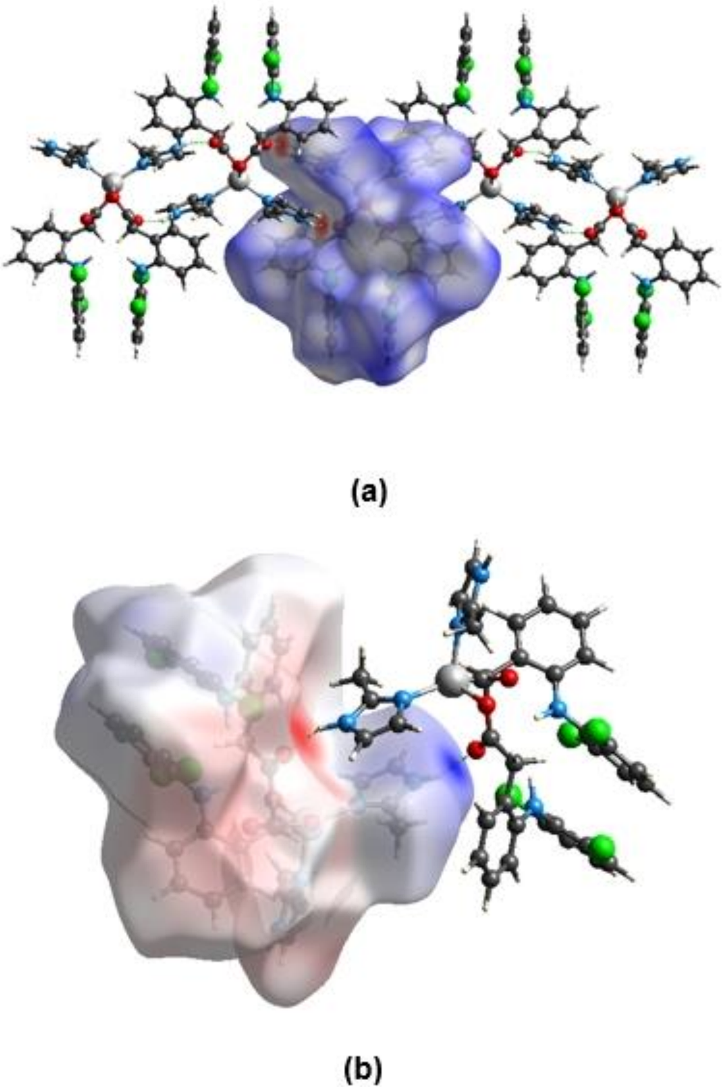


Fig. 4. The Hirshfeld surface for the intercontacts of $C_{36}H_{32}CoN_6Cl_4O_4$ **(a)** mapped with d_{norm} and **(b)** electrostatic potential surface

3.3. FT-IR and UV Spectroscopy

For the title complex, Fig. 6 shows FT-IR spectrum and the most important bands are illustrated in Table 4. The N–H stretching mode which is comparatively broad absorption band due to hydrogen bonding is centred at 3180 cm^{-1} which as reported for the ligand [37]. While the aromatic C–H stretching mode is observed at 3111 cm^{-1} as a weak band the C–Cl stretching mode has appeared at 768 cm^{-1} as a strong band. It is known that the asymmetric and symmetric vibration modes of the carboxylate group are important characteristic vibrations in the FT-IR spectra of the diclofenac complexes [38]. For the title complex, these modes are observed at 1594 and 1383 cm^{-1}, respectively. The calculated value of the difference between the ν_{as} (OCO) and ν_s(OCO) stretching vibrations is 211 cm^{-1}. The Δ(OCO) value is consistent with a monodentate ligand [39].

The electronic absorption spectrum of the complex was recorded at room temperature in methanol (Fig. 7). No transitions above 450 nm were observed in the absorption spectrum of complex. In the UV spectrum of the Co (II) complex, the intense band in 448 nm is due to charge transfer transition. A *d–d* transition belonging to the Co (II) is not observed.

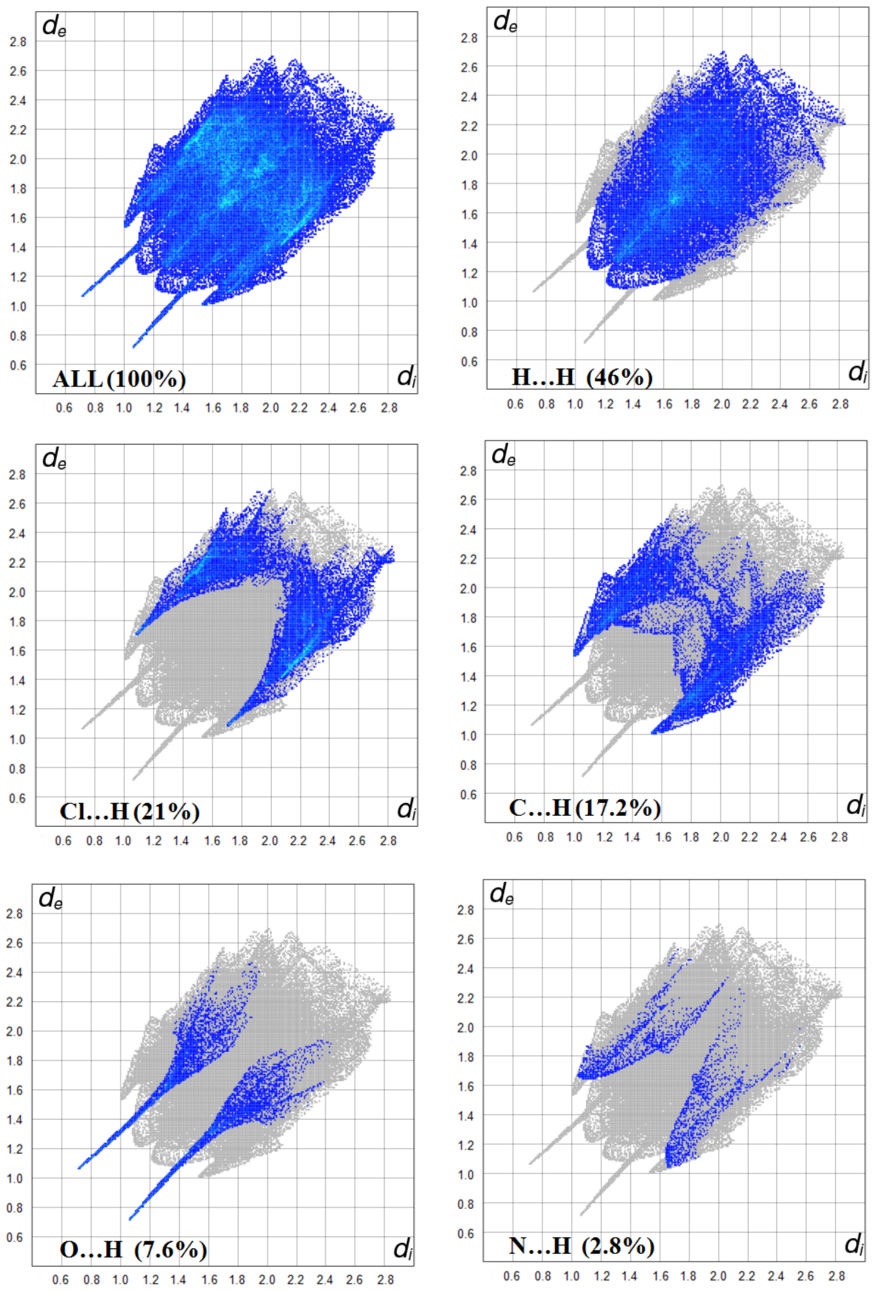


Fig. 5. Fingerprint plots (d_e vs d_i) of the title compound.

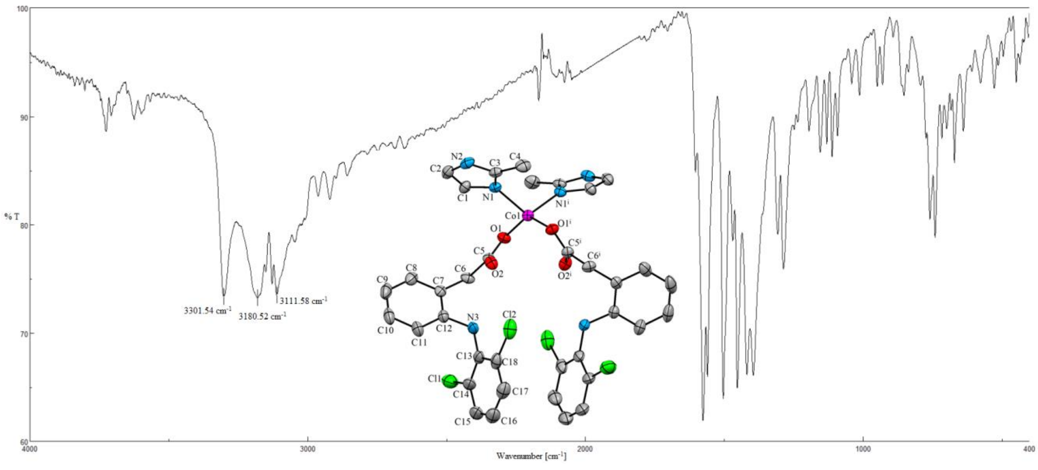


Fig. 6. The experimental FT-IR spectrum of $C_{36}H_{32}CoN_6Cl_4O_4$

Table 4. Selected IR spectral data for $C_{36}H_{32}CoN_6Cl_4O_4$

Assignment	**(cm^{-1})**
v (N–H) *str.*	3301
v(N–H) *str.*	3180
v_{ar}(C–H) *str.*	3111
v_{as}(OCO) *str.*	1594
v_s(OCO) *str.*	1383
v(C–Cl) *str.*	740

str.: stretching, ar.: aromatic, s.: symmetric, as.: asymmetric

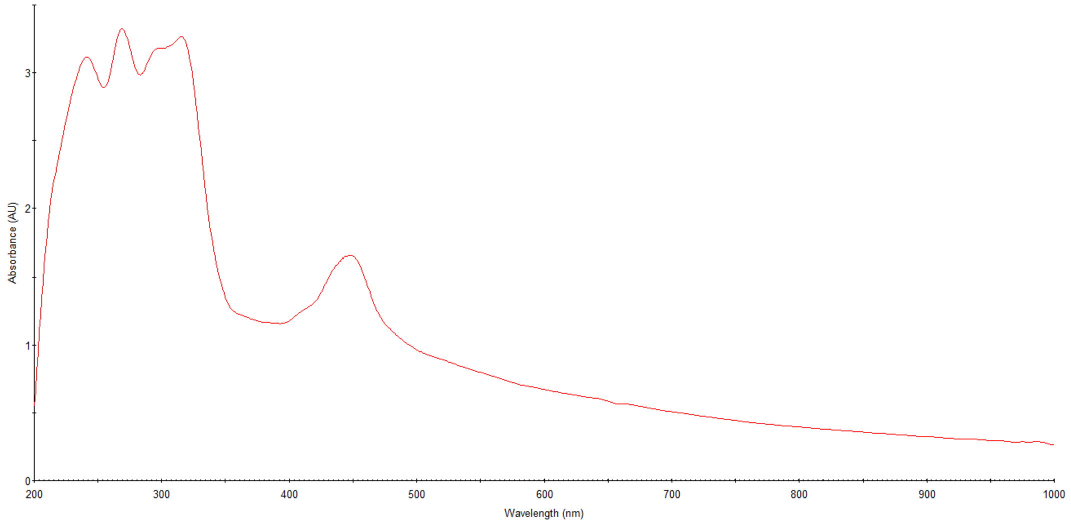


Fig. 7. The experimental UV spectrum of $C_{36}H_{32}CoN_6Cl_4O_4$

3.4. Molecular Docking

The title molecule was tested to be docked into the active sites of the protein PDB ID: 5U9D which belongs to the protein classification as antitumor and PDB ID: 4XTA which belongs to the protein class interacts with non-steroidal anti-inflammatory drugs. All docking calculations were done using AutoAock 4.2 software along with the graphical interface AutoDockTools (ADT) version 1.5.6 [40]. The water molecules in the proteins were removed and polar hydrogens were added.

Table 5. Binding affinity number of hydrogen bond residues and hydrogen bond distances of 5U9D and 4XTA proteins

Protein [PDB ID]	**Bond distances (Å)**	**Bonded residues**	**Binding energy (kcal/mol)**
5U9D	2.6 / 2.3	GLN 412 / TYR 551	-7.0
4XTA	2.7, 2.6 / 2.9	ARG 443 / ASP 441	-7.0

The protein binding sites were restricted to a grid box size of 40 × 40 × 40 Å^3 with 0.375 Å^3 grid spacing. The other docking parameters were obtained using standart protocols in previous study [41]. The Discovery Studio 4.0 (BIOVIA Discovery Studio 2016) [42] was used for visualized to obtained results. Fig. 8 created using the PyMol software shows the protein-complex interactions [43]. The title compound exhibits same binding energy (-7 kcal/mol) at the position where it makes hydrogen bonds with amino acid residues (GLN 412, TYR 551) of 5U9D protein and (ARG 443, ASP 441) of 4XTA protein. Table 5 illustrated to binding energy, bonded distance and bonded residuies of the protein-ligand interactions of two diferent protein.

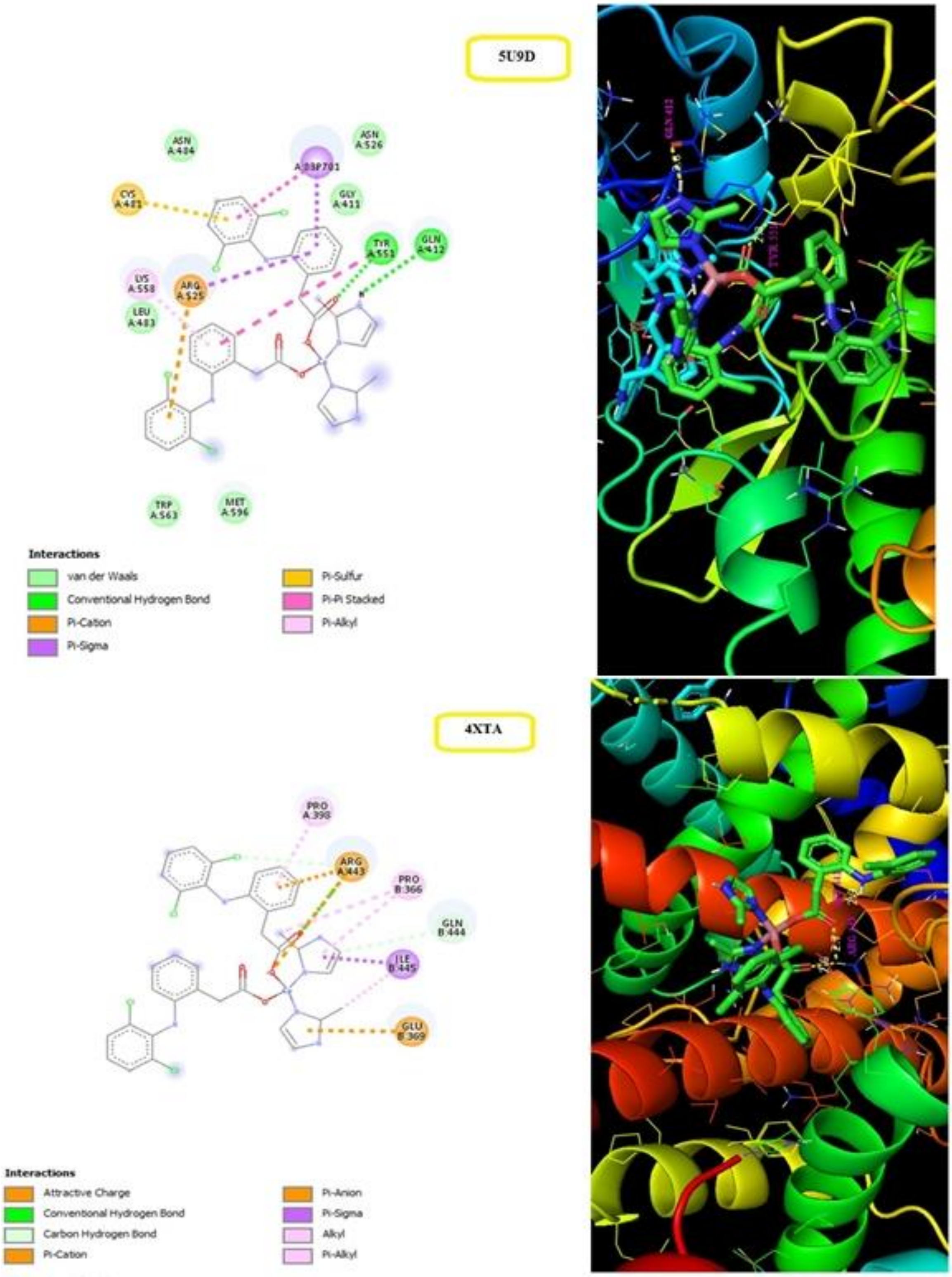


Figure 8. 2D surfaces (left) and the hydrogen bond interactions (right) between the title molecule and protein 5U9D, 4XTA.

4. Conclusions

In the present work, the molecular and structural properties of newly synthesized $C_{36}H_{32}CoN_6Cl_4O_4$ complex determined by FT-IR, UV and single-crystal X-ray diffraction techniques. According to the results of the X-ray experiment, the title complex contains the cobalt ion coordinated with the ligands of diclofenac and methyl imidazole and has a distorted tetrahedral geometry. C–H···O and N–H···O intermolecular hydrogen bonds and C–H···π interactions play a major role in the stability of the crystal structure in 3D space. From FT- IR results, the difference of the asymmetric and symmetric vibration modes of the carboxylate group indicates that the ligand coordinates to Co (II) ion as monodentate. Additionally, the HS and fingerprint plots of the complex specifies that the major contributions for the crystal packing are from H···H (46%), H···Cl (21%), C···H (17.2%), O···H (7.6%). As a result of the molecular docking study of the title compound, it has established good inhibitory nature against 5U9D and 4XTA with -7 kcal/mol binding energies for both proteins. This work may help to researchers for development of new anti-tumor and anti-inflammatory agents.

Acknowledgement

I gratefully acknowledge Associate Professor Sevim Hamamcı Alışır, Department of Metallurgical & Materials Engineering, Faculty of Engineering, Ondokuz Mayıs University for her sincere help in the synthesis of Co (II) complex. I'm greatly thankful Professor Dr. Orhan Büyükgüngör, Department of Physics, Faculty of Arts and Sciences, Ondokuz Mayıs University for single-crystal XRD measurement of the title complex.

Authors' Contributions

All studies of the article were done by SU.
Author read and approved the final manuscript.

Competing Interests

The author declares that I have no competing interests.

Refereneces

[1]. Fan, X., Dong, J., Min, R., Chen, Y., Yi, X., Zhou, J., & Zhang, S, "Cobalt (II) complexes with thiosemicarbazone as potential antitumor agents: synthesis, crystal structures, DNA interactions, and cytotoxicity", Journal of Coordination Chemistry, 2013, 66(24): 4268–4279.

[2]. Ali, H. A., Shamma, A. A., & Kamel, S, "New mixed ligand cobalt (II/III) complexes based on the drug sodium valproate and bioactive nitrogen-donor ligands. Synthesis, structure and biological properties", Journal of Molecular Structure, 2017, 1142: 40–47.

[3]. Heffern, M. C., Velasco, P. T., Matosziuk, L. M., Coomes, J. L., Karras, C., Ratner, M. A., ... & Meade, T. J, "Modulation of amyloid-β aggregation by histidine-coordinating Cobalt (III) Schiff base complexes", Chembiochem: a European Journal of Chemical Biology, 2014, 15(11): 1584.

[4]. Lopez-Sandoval, H., Londono-Lemos, M. E., Garza-Velasco, R., Poblano-Meléndez, I., Granada-Macías, P., Gracia-Mora, I., & Barba-Behrens, N, "Synthesis, structure and biological activities of cobalt (II) and zinc (II) coordination compounds with 2-benzimidazole derivatives" , Journal of Inorganic Biochemistry, 2008, 102(5-6): 1267–1276.

[5]. Ott, I., Abraham, A., Schumacher, P., Shorafa, H., Gastl, G., Gust, R., & Kircher, B, "Synergistic and additive antiproliferative effects on human leukemia cell lines induced by

combining acetylenehexacarbonyldicobalt complexes with the tyrosine kinase inhibitor imatinib" , Journal of Inorganic Biochemistry, 2006, 100(11): 1903–1906.

[6]. Miodragović, D. U., Bogdanović, G. A., Miodragović, Z. M., Radulović, M. Đ., Novaković, S. B., Kaluđerović, G. N., & Kozłowski, H, "Interesting coordination abilities of antiulcer drug famotidine and antimicrobial activity of drug and its cobalt (III) complex" , Journal of Inorganic Biochemistry, 2006, 100(9): 1568–1574.

[7]. Nomiya, K., Yoshizawa, A., Tsukagoshi, K., Kasuga, N. C., Hirakawa, S., & Watanabe, J, " Synthesis and structural characterization of silver (I), aluminium (III) and cobalt (II) complexes with 4-isopropyltropolone (hinokitiol) showing noteworthy biological activities. Action of silver (I)-oxygen bonding complexes on the antimicrobial activities" , Journal of inorganic biochemistry, 2004, 98(1): 46–60.

[8]. Lv, J., Liu, T., Cai, S., Wang, X., Liu, L., & Wang, Y, "Synthesis, structure and biological activity of cobalt (II) and copper (II) complexes of valine-derived schiff bases", Journal of Inorganic Biochemistry, 2006, 100(11): 1888–1896.

[9]. Böttcher, A., Takeuchi, T., Hardcastle, K. I., Meade, T. J., Gray, H. B., Cwikel, D., ... & Dori, Z, " Spectroscopy and electrochemistry of cobalt (III) Schiff base complexes", Inorganic Chemistry, 1997, 36(12): 2498–2504.

[10]. Dimiza, F., Papadopoulos, A. N., Tangoulis, V., Psycharis, V., Raptopoulou, C. P., Kessissoglou, D. P., & Psomas, G, " Biological evaluation of non-steroidal anti-inflammatory drugs-cobalt (II) complexes", Dalton Transactions, 2010, 39(19): 4517–4528.

[11]. Ashouri, F., Faraji, A. R., Molaeian, S., Fall, M. A., & Butcher, R. J, "The novel cobalt and manganese polymeric complex with the non-steroidal anti-inflammatory drug diclofenac: Synthesis, characterization and antibacterial studies", Journal of Molecular Structure, 2020, 1204: 127483.

[12]. Aguilar-Lira, G. Y., Álvarez-Romero, G. A., Zamora-Suárez, A., Palomar-Pardavé, M., Rojas-Hernández, A., Rodríguez-Ávila, J. A., & Páez-Hernández, M. E, "New insights on diclofenac electrochemistry using graphite as working electrode" , Journal of Electroanalytical Chemistry, 2017, 794: 182–188.

[13]. Moreno, M. M., Garidel, P., Suwalsky, M., Howe, J., & Brandenburg, K, "The membrane-activity of Ibuprofen, Diclofenac, and Naproxen: A physico-chemical study with lecithin phospholipids", Biochimica et Biophysica Acta (BBA)-Biomembranes, 2009, 1788(6): 1296–1303.

[14]. Yang, X., Wang, F., & Hu, S, "Enhanced oxidation of diclofenac sodium at a nano-structured electrochemical sensing film constructed by multi-wall carbon nanotubes–surfactant composite", Materials Science and Engineering: C, 2008, 28(1): 188–194.

[15]. Khoobi, A., Soltani, N., & Aghaei, M, "Computational design and multivariate statistical analysis for electrochemical sensing platform of iron oxide nanoparticles in sensitive detection of anti-inflammatory drug diclofenac in biological fluids", Journal of Alloys and Compounds, 2020, 831: 154715.

[16]. Tong, S. L., Tian, Z. Y., Wu, Y. H., Yan, Y., Hu, S., & Yu, J, " Crystal assembly based on 3, 5-bis (2′-benzimidazole) pyridine and its complexes" , Solid State Sciences, 2013, 17: 6–13.

[17]. Zhan, S. J., Sun, Y., Li, S. P., Tang, G. M., Wang, Y. T., & Cui, Y. Z, " Syntheses, crystal structures and luminescent properties of three metal coordination polymers based on aromatic carboxylic acids and 2-(pyridine-4-yl)-(1H)-benzoimidazole", Polyhedron, 2017, 121: 252–263.

[18]. Uzun, S., Demircioğlu, Z., Taşdoğan, M., Ağar, E., "Quantum chemical and X-ray diffraction studies of (E)-3-(((3,4-dimethoxybenzyl)imino)methyl)benzene-1,2-diol", Journal of Molecular Structure, 2020, 1206: 127749.

[19]. Sheldrick, G. M, "SHELXS-97. Program for the Solution of Crystal Structures", 1997, Univ. of Gottingen.

[20]. Sheldrick, 3. 3. G, "SHELXL-97. Program for crystal-structure refinement", 1997.

[21]. Farrugia, L. J, “ WinGX (Version 1.64. 05)” , Journal of Applied. Crystallography ,1999, 32: 837–838.

[22]. Farrugia, L. J, “ORTEP-3 for Windows-a version of ORTEP-III with a Graphical User Interface (GUI)”, Journal of Applied. Crystallography, 1997, 30: 565.

[23]. Yang, L., Powell, D. R., & Houser, R. P, “Structural variation in copper (I) complexes with pyridylmethylamide ligands: structural analysis with a new four-coordinate geometry index, τ 4”, Dalton Transactions, 2007, 9: 955–964.

[24]. Okuniewski, A., Rosiak, D., Chojnacki, J., & Becker, B, “Coordination polymers and molecular structures among complexes of mercury (II) halides with selected 1-benzoylthioureas” , Polyhedron, 2015, 90: 47–57.

[25]. Huang, X. C., Xu, R., Chen, Y. Z., Zhang, Y. Q., & Shao, D, “Two Four-Coordinate and Seven-Coordinate CoII Complexes Based on the Bidentate Ligand 1, 8-Naphthyridine Showing Slow Magnetic Relaxation Behavior”, Chemistry–An Asian Journal, 2020, 15(2): 279–286.

[26]. Hamamci, S., Yilmaz, V. T., & Harrison, W. T, “Synthesis, spectra, thermal analysis and crystal structure of Trans-Bis (2-Pyridinepropanol) Bis (Saccharinato) Cobalt (II)” , Journal of Coordination Chemistry, 2003, 56(12): 1033–1039.

[27]. Perontsis, S., Dimitriou, A., Fotiadou, P., Hatzidimitriou, A. G., Papadopoulos, A. N., & Psomas, G, “ Cobalt (II) complexes with the non-steroidal anti-inflammatory drug diclofenac and nitrogen-donor ligands”, Journal of Inorganic Biochemistry, 2019, 196: 110688.

[28]. Ramalingam, A., Kansız, S., Dege, N., & Sambandam, S, “Synthesis, Crystal Structure, DFT Calculations and Hirshfeld Surface Analysis of 3-Chloro-2, 6-Bis (4-Chlorophenyl)-3-Methylpiperidin-4-One”, Journal of Chemical Crystallography, 2021, 51(2): 273–287.

[29]. Ilmi, R., Kansız, S., Al-Rasbi, N. K., Dege, N., Raithby, P. R., & Khan, M. S, “Towards white light emission from a hybrid thin film of a self-assembled ternary samarium (III) complex” , New Journal of Chemistry, 2020, 44(15): 5673–5683.

[30]. Albayati, M. R., Kansız, S., Lgaz, H., Kaya, S., Dege, N., Ali, I. H., ... & Chung, I. M, “Synthesis, experimental and theoretical characterization of (E)-2-((2, 3-dimethylphenyl) amino)-N’-(furan-2-ylmethylene) benzohydrazide”, Journal of Molecular Structure, 2020, 1219: 128518.

[31]. Kansız, S., Qadir, A. M., Dege, N., & Faizi, S. H, “ Two new copper (II) carboxylate complexes based on N, N, N', N'-tetramethylethyleneamine: Synthesis, crystal structures, spectral properties, dft studies and hirshfeld surface analysis”, Journal of Molecular Structure, 2021, 1230: 129916.

[32]. McKinnon, J. J., Spackman, M. A., & Mitchell, A. S, “ Novel tools for visualizing and exploring intermolecular interactions in molecular crystals”, Acta Crystallographica Section B: Structural Science, 2004, 60(6): 627–668.

[33]. Wood, P. A., McKinnon, J. J., Parsons, S., Pidcock, E., & Spackman, M. A, “Analysis of the compression of molecular crystal structures using Hirshfeld surfaces” ,CrystEngComm, 2008, 10(4): 368–376.

[34]. Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Spackman, P. R., Jayatilaka, D., & Spackman, M. A, CrystalExplorer17, 2017.

[35]. Hirshfeld, F. L, “Bonded-atom fragments for describing molecular charge densities”, Theoretica Chimica Acta, 1997,44(2): 129–138.

[36]. Spackman, M. A., & Jayatilaka, D, ” Hirshfeld surface analysis”, CrystEngComm, 2009, 11(1): 19–32.

[37]. Sağlam, E. G., Dal, H., Mougang-Soumé, B., & Hökelek, T, “ Syntheses and structural characterization of new trans-bis-[n-butyl-(p-methoxyphenyl) dithiophosphinato] nickel (II), the pyridine derivative thereof, and bis-{bis-[n-butyl-(p-methoxyphenyl) dithiophosphinato] cobalt (II)} complexes”, Journal of Molecular Structure, 2020, 1202: 127222.

[38]. Hamamci Alisir, S., Dege, N., & Tapramaz, R, “Synthesis, crystal structures and characterizations of three new copper (II) complexes including anti-inflammatory diclofenac”, Acta Crystallographica Section C: Structural Chemistry, 2019, 75(4): 388–397.

[39]. Nakamoto, K, “Infrared and Raman spectra of inorganic and coordination compounds”, Wiley Online Library, 1986.

[40]. Sanner, M. F, “Python: a programming language for software integration and development”, J Mol Graph Model, 1999, 17(1): 57–61.

[41]. Dimić, D., Milanović, Ž., Jovanović, G., Sretenović, D., Milenković, D., Marković, Z., & Marković, J. D, “Comparative antiradical activity and molecular Docking/Dynamics analysis of octopamine and norepinephrine: the role of OH groups”, Computational Biology and Chemistry, 2020, 84: 107170.

[42]. BIOvIA, D. S., & Dsme, R, “Dassault Systèmes BIOVIA”, Discovery Studio Modeling Environment, 2017.

[43]. DeLano, W. L., & Bromberg, S, “PyMOL user’s guide”, DeLano Scientific LLC, 629, 2004.