IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Quantitative And Qualitative Analysis Of Reported Manganese(II) Complexes With The Non-Steroidal Anti-Inflammatory Drug (NSAID) Tolfenamic Acid With Secondary Ligand Bipyam: Hirshfeld Surface And 2D Fingerprint Analysis

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Abstract

This study investigates the intermolecular interactions in a Reported[i] Manganese(II) Complexes with the (NSAID) Tolfenamic Acid with secondary ligand bipyam [bis(μ2-Tolfenamato-O,O')-bis(tolfenamato-O,O')-bis(bis(2-pyridyl)amine-N,N')-di-manganese(ii)] using Hirshfeld surface analysis and 2D fingerprint plots. The Hirshfeld surface[ii] provides a qualitative understanding of molecular packing[iii] and non-covalent interactions, while 2D fingerprint plots[iv] enable a quantitative breakdown of interaction contributions, revealing key features such as hydrogen bonding, van der Waals interactions, and π–π stacking. In addition, dnorm, shape index, curvedness, and fragment patch analysis are discussed to highlight the molecular environment[vviviiviii].

Keywords: Reported Manganese(II) Complexes with the (NSAID) Tolfenamic Acid with secondary ligand bipyam, Hirshfeld Surface Analysis , 2D Fingerprint Analysis

1. Introduction

NSAIDs are widely used as antipyretic, analgesic, and anti-inflammatory drugs, primarily by inhibiting prostaglandin production via cyclooxygenase (COX). While their side effects are well-known, NSAIDs also show potential anticancer activity through COX-independent mechanisms, caspase-mediated apoptosis, and free radical involvement. Studying their antioxidant properties and interactions with DNA is crucial to understanding their anti-inflammatory and anticancer potential, but more research is needed due to limited existing data.

Manganese is an essential bimetal found in many enzymes and used in medicine, such as the anticancer agent SC-52608 and MRI contrast agent Teslascan. Manganese complexes also show bactericidal, antifungal, and anti-proliferative properties, making the study of new Mn complexes increasingly important. The secondary ligand bipyam (bipyridylamine) enhances the stability, reactivity, and geometry of metal complexes by binding to the metal ion. It also improves solubility, making it useful for applications in catalysis, imaging, and medicine.

Our objective is to Studying Mn-tolfenamic acid-bipyam using Hirshfeld surface analysis and 2D fingerprint plots provides a detailed understanding of intermolecular interactions, crystal stability, and structure-function relationships. These insights are crucial for advancing coordination chemistry, designing functional materials, and exploring potential applications in pharmaceuticals and catalysis. By combining qualitative visualization with quantitative metrics, such analyses deepen our understanding of the molecular environment and its broader implications.

2. Experimental Details

2.1 Synthesis of Reported Structure

A methanolic solution (10 mL) of KOH (0.4 mmol, 22 mg) and tolfenamic acid (0.4 mmol, 105 mg) was added, after 1 h of stirring, slowly and simultaneously with a methanolic solution (5 mL) of bipyam (0.2 mmol, 34 mg), to a methanolic solution (10 mL) of MnCl2·4H2O (0.2 mmol, 40 mg). Colorless crystals of [Mn2(tolf)4(bipyam)2], 3 (105 mg, 70%), suitable for X-ray structure determination, were deposited in a couple of days. Anal. Calcd for [Mn2(tolf)4(bipyam)2] (C76H62Cl4Mn2N10O8) (MW = 1495.04): C, 61.06; H, 4.18; N, 9.37.

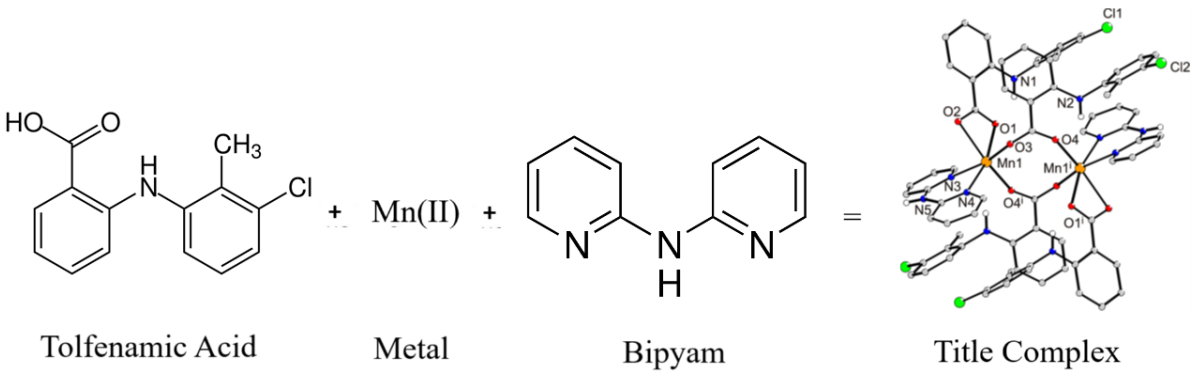

Figure 1: Synthesis of Reported title compound

2.2 Computational Methods

Hirshfeld surface and their related 2D fingerprint plots are created using the crystal explorer 3.1. Hirshfeld surfaces in the crystal structure are constructed based on the electron Distribution calculated as the sum of spherical atom electron densities. The normalized Contact distance (dnorm) is based on both de (distance from the point to the nearest nucleus External to the surface) and di (distance to the nearest nucleus internal to the surface). The Combination of de and di in the form of 2D fingerprint plot provides a summary of intermolecular contacts in the crystal. Two colored properties (shape-index and curvedness) based on the local curvature of the surface are also specified.

3. Results and Discussion

3.1 Hirshfeld Surface Analysis

Dnorm Analysis: Highlight key interaction regions using dnorm (negative values for close contacts and positive for longer contacts). Discuss regions of high significance, such as O-H hydrogen bonding and Cl-H interactions. Shape Index and Curvedness: Explain how these tools visualize π–π stacking interactions (if any) and the topology of molecular packing. Discuss the regions of concave and convex curvature, indicating complementary interactions. Fragment Patch Analysis: Present a fragment-based approach to understand molecular contacts and emphasize any directional intermolecular interactions, such as H-H, C-H, or Cl-H. Visual representation include color-coded dnorm maps to show regions of close intermolecular interactions. Shape index and curvedness plots to identify π–π stacking and surface curvature. Annotate the 2D fingerprint plot to highlight interaction "wings" for Cl-H, C-H, and O-H contacts.

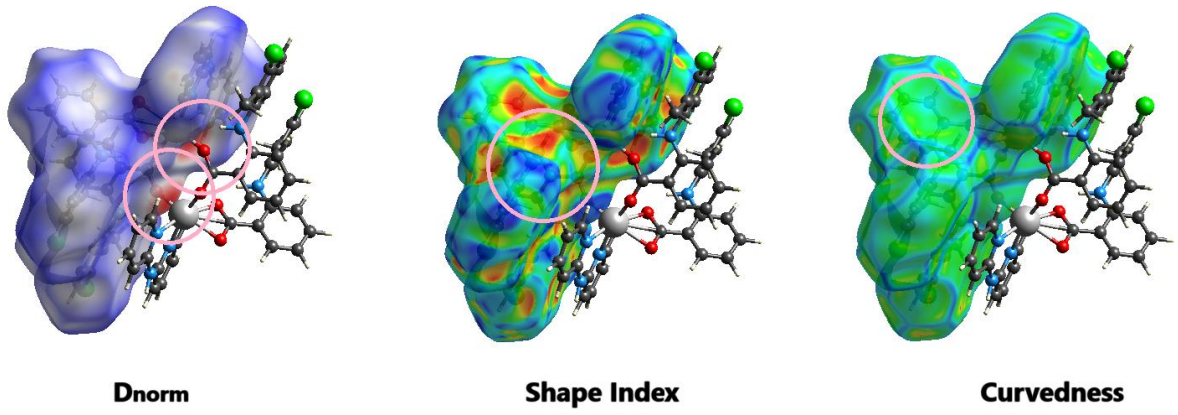

Figure 2: Dnorm, Shape index and curvedness indicating Title complex

3.2 2D Fingerprint Plot

The 2D fingerprint plot provides a visual representation of the relative contributions of various intermolecular interactions. Table 1 summarizes the percentage contributions for each type of interaction in the Mn-Tolfenamic acid-bipyam complex. H-H Contacts: These dominate the fingerprint plot, reflecting van der Waals forces due to the high proportion of hydrogen atoms on Tolfenamic acid and bipyam. C-H Contacts: Represent hydrophobic interactions and π–H interactions, significant for stabilizing the crystal structure. Cl-H and O-H Interactions: These indicate moderate hydrogen bonding, with Cl-H interactions being notable due to the presence of chlorophenyl rings in Tolfenamic acid. C-C Contacts: Reflect weak π–π stacking

interactions among aromatic rings. N-H Interactions: Evidence of weak hydrogen bonding involving the bipyam nitrogen.

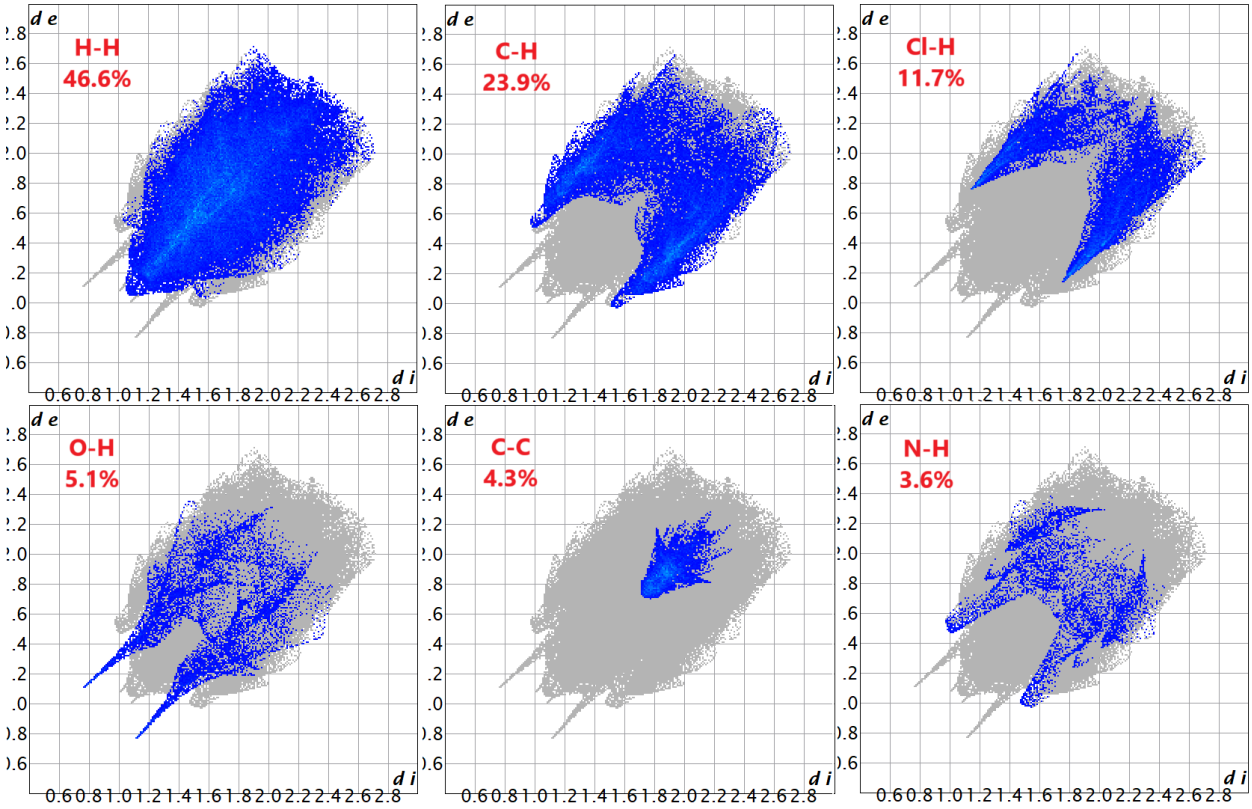

Figure 3: 2D Fingerprint plot of Title complex

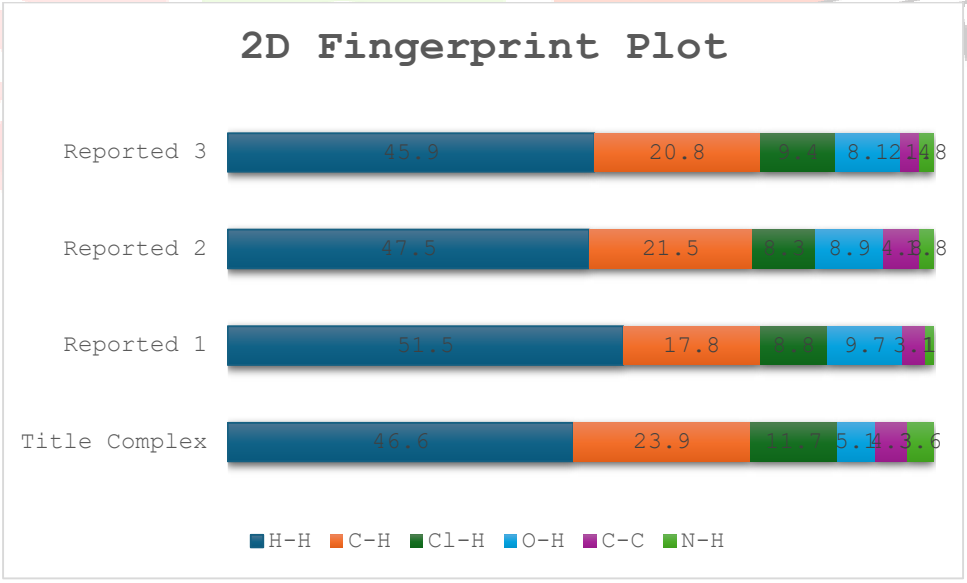

Figure 4: Percentage chart of Title complex with Reported data

4. Conclusion

The Hirshfeld surface analysis qualitatively identified key intermolecular interactions, with dnorm highlighting hydrogen bonding and weak van der Waals forces. The 2D fingerprint plot quantitatively confirmed the dominance of H-H contacts (46.6%), followed by significant C-H (23.9%) and Cl-H (11.7%) contributions. These results underline the critical role of weak interactions in the stabilization of the Mn-

tolfenamic acid-bipyam crystal lattice. Discuss the broader implications for molecular design in coordination chemistry and potential applications in materials science.

Supplementary information

CCDC-947342 contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgement

Authors are thankful to Department of Physics, Maharaja Krishnakumarsinhji Bhavnagar University, Bhavnagar -364001, Gujarat, India

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