Journal of Molecular Structure 1298 (2024) 136974

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

Spectroscopic (FT-IR, FT-Raman, UV–Vis and NMR) and computational (DFT, MESP, NBO, NCI, LOL, ELF, RDG and QTAIM) profiling of 5-chloro-2-hydroxy-3-methoxybenzaldehyde: A promising antitumor agent

A. Ram Kumar [a,1], L. Ilavarasan [b,c], G.P. Sheeja Mol [d], S. Selvaraj [e,1,*], Mohammad Azam [f,*], P. Jayaprakash [g], M. Kesavan [h], Mahboob Alam [i], J. Dhanalakshmi [j], Saud I. Al-Resayes [f], A. Ravi [b]

[a] Department of Biotechnology, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai, 602105, Tamil Nadu, India
[b] Department of Chemistry, Kalaignar Karunanidhi Government Arts College, Tiruvannamalai, 606603, Tamil Nadu, India
[c] Department of Chemistry, Vignesh Group of Institutions, Tiruvannamalai, 606603, Tamil Nadu, India
[d] PG Department of Physics, St. Joseph's College for Women, Alappuzha, 688001, Affiliated to University of Kerala, Thiruvananthapuram, 695034, Kerala, India
[e] Department of Physics, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai, 602105, Tamil Nadu, India
[f] Department of Chemistry, College of Science, King Saud University, PO BOX 2455, Riyadh, 11451, Saudi Arabia
[g] Department of Physics, St. Joseph's Institute of Technology, OMR, Chennai, 600119, Tamil Nadu, India
[h] Interdisciplinary Institute of Indian System of Medicine, SRM Institute of Science and Technology, Kattankulathur, Chennai, 603203, Tamil Nadu, India
[i] Department of Safety Engineering, Dongguk University, 123 Dongdae-ro, Gyeongju, Gyeongbuk, 780714, South Korea
[j] Department of Chemistry, Kamaraj College of Engineering and Technology, K. Vellakulam, 625701, Tamil Nadu, India

ARTICLE INFO

Keywords:
DFT
Molecular docking
Fukui functions
Topological analysis
Chemical shifts
Mulliken charges

ABSTRACT

In this study, the benzaldehyde derivative 5-chloro-2-hydroxy-3-methoxybenzaldehyde (5C2H3MB) was characterized using spectroscopic techniques. Geometric parameters and complete fundamental vibrational assignments were simulated using DFT/B3LYP/6-311++G(d,p). The ^{1}H and ^{13}C chemical shifts, computed using the GIAO method, were in agreement with the experimental findings. The electronic properties of 5C2H3MB were analyzed using time-dependent density functional theory (TD-DFT) to determine various electronic parameters, including HOMO-LUMO energies. NBO analysis was performed to determine the numerous hyper-conjugative interactions responsible for the stability of the compound. In addition, Mulliken population analysis and Molecular Electrostatic Potential Surfaces (MESP) analysis were conducted to identify electron-rich, electron-poor, reactive sites, and bonding characteristics of the titled compound. The topological analyses ELF, LOL, NCI, QTAIM, and RDG were performed using Multiwfn software, and global reactivity parameters and Fukui functions were also predicted. Molecular docking studies were conducted to confirm the biological activity by simulating the binding orientation and affinity of 5C2H3MB against transferase inhibitor and human phosphorylated IRE1 alpha, showing a binding energy of −5.1, −5.3 and −5.9 kcal/mol, indicating its potential as an antagonist.

1. Introduction

In medicinal chemistry and the chemical industry, benzaldehyde derivatives, also known as aromatic aldehydes, are frequently used as intermediates for synthesizing textiles, dyes, agrochemicals, and flavoring agents. They can be naturally extracted from sources like plants, cinnamon oil, and white rot fungi *Pleurotus sapidus* through the *de-novo* pathway. Substituted benzaldehydes can be engineered to enhance human hemoglobin's oxygen-carrying capacity while inhibiting sickle erythrocyte formation. Also, chalcones that have been replaced and produced by the use of benzaldehyde derivatives have qualities such as anti-proliferative, anti-inflammatory, anti-microbial,

* Corresponding authors.
E-mail addresses: selvarajs.sse@saveetha.com, sselvaphy@gmail.com (S. Selvaraj), azam_res@yahoo.com (M. Azam).
[1] A. Ram Kumar and S. Selvaraj contributed equally to this work.

https://doi.org/10.1016/j.molstruc.2023.136974
Received 20 September 2023; Received in revised form 21 October 2023; Accepted 1 November 2023
Available online 2 November 2023