2nd International Conference on Scientific and Academic Research
March 14-16, 2023 : Konya, Turkey
All Sciences Proceedings
http://as-proceeding.com/

Structural Investigation of a Hydrazide Derivate Compound Including Pyridine Ring

Sevgi Kansız*[1]

[1]Department of Fundamental Sciences, Samsun University, Turkey

*(sevgi.kansiz@samsun.edu.tr) Email of the corresponding author

Abstract – Hydrazides have a variety of applications in different fields, including pharmaceuticals, agrochemicals, and materials science. In the pharmaceutical industry, hydrazides are widely used as intermediates in the synthesis of various drugs. They exhibit a range of biological activities, such as anticancer, antibacterial, antiviral, and anti-inflammatory properties. Theoretical calculations provide predictions about the molecular groups to be synthesized by determining the chemical activities of the molecules and by predetermining the electrophilic and nucleophilic regions. For this reason, Density Functional Theory (DFT), which is the most preferred chemical calculation method in the literature, was preferred in this study. (*E*)-N'-(4-methylbenzylidene)isonicotinohydrazide compound was optimized using the B3LYP model and the 6-311G(d,p) base set to obtain the most stable state of the molecule. In addition, the stability of the optimized structure with frontier orbitals (HOMO and LUMO) and its susceptibility to chemical activity were investigated. With chemical activity parameters, kinetic stability, and chemical stability were determined. In addition to these, electron-rich and electron-poor regions were determined by molecular electrostatic potential (MEP) analysis. The popularity of Hirshfeld surface analysis has grown within the fields of materials science, crystal engineering, and computational chemistry, as it provides a robust tool for comprehending the intermolecular interactions and packaging in molecular crystals, as well as predicting material properties. In this study, the Hirshfeld surface was analyzed to investigate the intermolecular interactions that control the supramolecular structure. The results indicate that H···H (42%) contacts are the most significant interactions, whereas C···H (29%), O···H (13%), and N···H (12%) interactions are less notable.

Keywords – Hydrazide, Pyridine, DFT, MEP, HOMO-LUMO, Hirshfeld Surface Analysis

I. INTRODUCTION

Hydrazides are organic compounds that contain the hydrazide functional group (-CONHNH2). They are derived from the reaction of hydrazine with carboxylic acids or their derivatives. Hydrazides are commonly used as intermediates in the synthesis of various pharmaceuticals, agrochemicals, and dyes. They also exhibit a range of biological activities, such as antitumor, antibacterial, and antiviral properties [1-3]. Some examples of hydrazides include isonicotinyl hydrazide (INH), a drug used to treat tuberculosis, and nicotinic acid hydrazide (isoniazid), an antitubercular medication. Hydrazides have a variety of applications in different fields, including pharmaceuticals, agrochemicals, and materials science. In the pharmaceutical industry, hydrazides are widely used as intermediates in the synthesis of various drugs. They exhibit a range of biological activities, such as anticancer, antibacterial, antiviral, and anti-inflammatory properties [4,5]. For example, isoniazid (INH), which is a hydrazide derivative, is an important drug used to treat tuberculosis. In the agrochemical industry, hydrazides are used as intermediates in the synthesis of herbicides and

pesticides. For example, the herbicide isoxaflutole is produced by the reaction of 5-chloro-3-isoxazolyl hydrazide with acetic anhydride. In materials science, hydrazides are used in the synthesis of polymers, resins, and coatings. For example, hydrazides can be used to modify epoxy resins to improve their mechanical properties and adhesion to surfaces. Furthermore, hydrazides have potential applications in fields such as energy storage, catalysis, and fluorescence sensing.

Theoretical calculations provide predictions about the molecular groups to be synthesized by determining the chemical activities of the molecules and by predetermining the electrophilic and nucleophilic regions. Density Functional Theory (DFT) is a computational method used to calculate the electronic structure and properties of molecules. It is a quantum mechanical approach that solves the Schrödinger equation for the electronic density of a system and provides a theoretical understanding of molecular properties and reactivity.

Overall, the combination of DFT calculations with various parameters and analyses provides a detailed understanding of the electronic properties, reactivity, and stability of a molecule, and can be used to guide the synthesis and design of new compounds with desired properties. In this study, DFT was used to optimize the molecular structure of the compound using the B3LYP functional and the 6 311G(d,p) basis set. The B3LYP functional is a hybrid functional that combines the Becke three-parameter exchange functional and the Lee-Yang-Parr correlation functional. The stability of the optimized structure with frontier orbitals (HOMO and LUMO) and its susceptibility to chemical activity were investigated. With chemical activity parameters, kinetic stability, chemical stability, and intramolecular charge transfer were determined. In addition, electron-rich and poor regions were determined by molecular electrostatic potential (MEP) analysis.

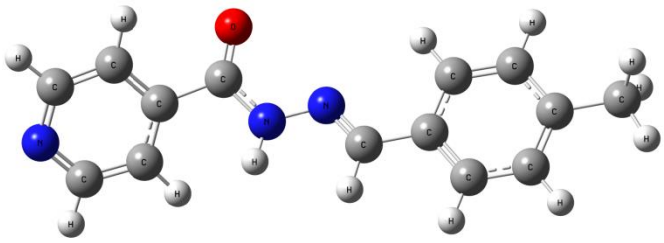

Fig. 1 The optimized geometry of the title compound.

II. Materials and Method

In this study, the DFT method was used to calculate geometric parameters of the compounds in the gas phase using the B3LYP functional and the 6-311G(d,p) basis set. The Gaussian03 program was used to obtain molecular electrostatic potentials (MEP) and other calculations to determine intermolecular hydrogen bond interactions [6]. The optimized geometry of the compound given in Fig. 1, MEP maps, and HOMO-LUMO energy gaps were visualized using GaussView software [7]. To investigate intermolecular interactions in the solid phase, Hirshfeld surface analysis was performed. Hirshfeld surfaces are three-dimensional maps that provide information about the intermolecular contacts within a crystal [8]. The 2D fingerprint graph is a summary of the intermolecular contacts on the Hirshfeld surface. The CrystalExplorer21 program was used to create Hirshfeld surfaces and 2D fingerprint graphs using d_{norm} [9].

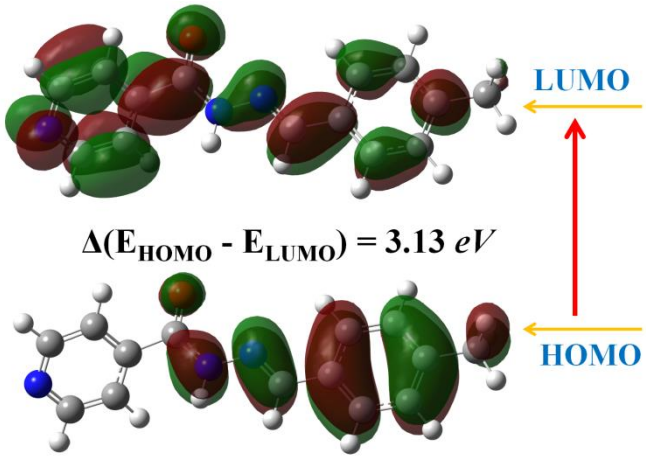

Fig. 2 The energy gap of the compound.

III. RESULTS AND DISCUSSION

A. *The Frontier Orbitals*

The HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) are boundary orbitals that provide information about the electronic properties and reactivity of a molecule. The HOMO represents the electron-donating ability of a molecule, while the LUMO represents the electron-accepting ability. The energy difference between the HOMO and LUMO, known as the HOMO-LUMO gap, is an important indicator of the chemical reactivity and stability of the molecule. Chemical activity parameters, such as chemical potential, electronegativity, and hardness, were calculated to assess the kinetic and chemical

stability of the molecule. Chemical stability refers to the ability of the molecule to resist chemical reactions, while kinetic stability refers to the speed of a chemical reaction. Hardness is a measure of the resistance of the molecule to electron transfer, while electronegativity is a measure of the tendency of an atom to attract electrons. The intramolecular charge transfer refers to the transfer of electrons within a molecule from one part to another. This phenomenon can affect the reactivity and stability of the molecule and can be analyzed by calculating the dipole moment and the charge distribution of the molecule.

The HOMO and LUMO molecular orbital surfaces of the studied molecule are given in Fig. 2. The HOMO energy was calculated as -8.52 eV and the LUMO energy as 5.39 eV. The energy range was found to be ΔE=3.13 eV as an indicator of the stability of the structure. If the chemical hardness value is high, the intramolecular charge transfer of the molecules may occur less or not at all. The softness parameter is the opposite of hardness. While the hardness value for the studied molecule was 1.565 eV, the softness parameter was measured as 0.319 $(eV)^{-1}$. Calculated chemical activity parameters and high energy range, high hardness and low softness data values indicate that the studied molecule is a stable and hard molecule with low chemical activity and high kinetic stability.

B. *The Molecular Electrostatic Potentials*

Molecular electrostatic potential (MEP) analysis is a method used to determine the electron-rich and electron-poor regions of a molecule. The MEP is a three-dimensional map that shows the electrostatic potential of a molecule and provides information about the molecular shape and reactivity. Color coding is used to determine electrophilic and nucleophilic behaviors in molecular electrostatic potential maps. While the blue color is observed predominantly in the regions with low electron density, the localizations with high electron density are coded with red. In the molecule under study, the most negative regions were localized on the oxygen atom, while the most positive regions were located on the hydrogen atoms. A blue shift was observed on the regions where hydrogen atoms are concentrated and on the nitrogen atom. Electrophilic regions define the area where oxygen and nitrogen atoms are located, while nucleophilic regions represent regions where hydrogen atoms are concentrated (Fig. 3).

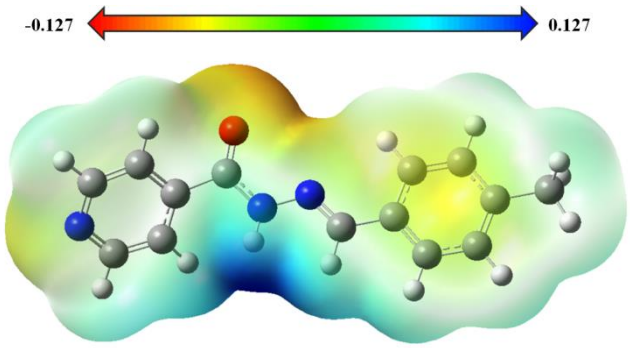

Fig. 3 The MEP surface of the compound.

C. *Hirshfeld Surface Analysis*

The red spots observed on the Hirshfeld surface (d_{norm}) provide information about the strength of intermolecular interactions within a crystal. The intensity of the color concentration in the red regions indicates the strength of the hydrogen bonds, with darker red spots indicating stronger bonds than lighter red spots.

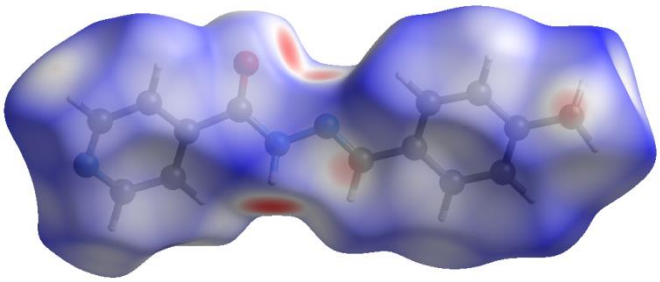

Fig. 4 Hirshfeld surface of the compound.

In the case of the compound shown in Fig. 4, the red regions in the dnorm map are concentrated around the oxygen, nitrogen and hydrogen atoms involved in the N–H···O and N–H···N contacts. The most significant interaction is estimated to be H···H (42%), C···H (29%), O···H (13%) and N···H (12%) interactions, which are characterized by the presence of deep red color and its association with the N–H···O and N–H···N interaction. The interaction energy calculations also provide similar evidence as the crystal analysis, indicating the presence of N–H···O and N–H···N interactions in the molecular structure. Overall, Hirshfeld surface analysis, combined with other computational methods, provides a detailed understanding of intermolecular interactions and the strength of hydrogen bonds within crystals. These insights can be used to design new materials and optimize their

properties, as well as to gain insights into the mechanisms of chemical reactions.

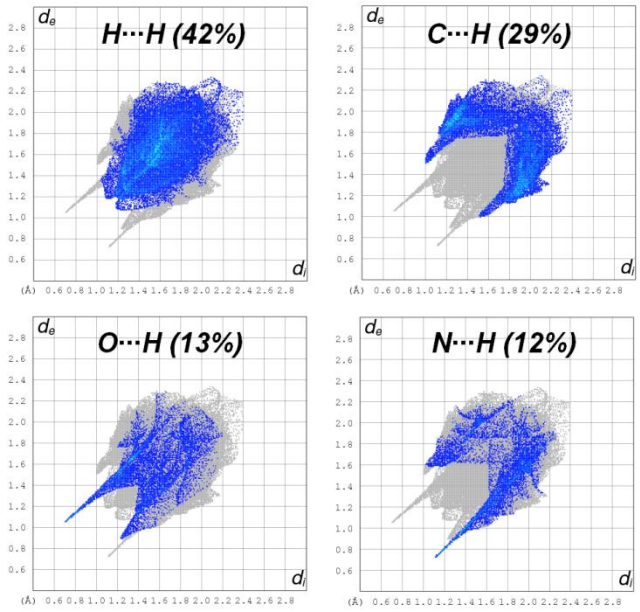

Fig. 5 2D fingerprint plots of the compound.

IV. CONCLUSION

All theoretical calculations of the (*E*)-N'-(4-methylbenzylidene)isonicotinohydrazide molecule were performed with DFT/B3LYP/6-311G(d,p). Low chemical activity with ΔE=3.13 eV energy range of optimized structure, hardness 1.565 eV and low softness 0.319 $(eV)^{-1}$ data was found to be quite stable. By MEP and Hirshfeld surface analysis, it was predicted that the electrophilic nature of the optimized structure is an indication that these regions, which are more dominant and localized on oxygen atoms, are effective in hydrogen bonding. Overall, the combination of DFT calculations and Hirshfeld surface analysis provides a comprehensive understanding of the electronic and structural properties of compounds in the gas and solid phases. These calculations can be used to predict and optimize the properties of new compounds, guide the design of materials, and provide insights into the mechanisms of chemical reactions.

REFERENCES

[1] P. De, M. Baltas, D. Lamoral-Theys, C. Bruyère, R. Kiss, F. Bedos-Belval, and N. Saffon, "Synthesis and anticancer activity evaluation of 2 (4-alkoxyphenyl) cyclopropyl hydrazides and triazolo phthalazines," *Bioorg. Med. Chem.*, vol. 18(7), pp. 2537-2548, 2010.

[2] M. Wolter, A. Klapars, and S. L. Buchwald, "Synthesis of N-aryl hydrazides by copper-catalyzed coupling of hydrazides with aryl iodides," *Org. Lett.*, vol. 3(23), pp. 3803-3805, 2001.

[3] R. Narang, B. Narasimhan, and S. Sharma, "A review on biological activities and chemical synthesis of hydrazide derivatives," *Curr. Med. Chem.*, vol. 19(4), pp. 569-612, 2012.

[4] Y. C. Huang, G. M. Fang, and L. Liu, "Chemical synthesis of proteins using hydrazide intermediates," *Natl. Sci. Rev.*, vol. 3(1), pp. 107-116, 2016.

[5] K. K. Bedia, O. Elçin, U. Seda, K. Fatma, S. Nathaly, R. Sevim, and A. Dimoglo, "Synthesis and characterization of novel hydrazide–hydrazones and the study of their structure–antituberculosis activity," *Eur. J. Med. Chem.*, vol. 41(11), pp. 1253-1261, 2006.

[6] M. J. Frisch, G. Trucks, H. Schlegel, G. Scuseria, M. Robb, J. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. Petersson, Gaussian 09, Revision D. 01, Gaussian, Inc.: Wallingford, CT (2009).

[7] R. Dennington, T. Keith, J. Millam, GaussView, version 5, Semichem Inc.: Shawnee Mission, KS (2009).

[8] M. A. Spackman, and P. G. Byrom, "A Novel Definition of a Molecule in a Crystal," *Chem. Phys. Lett.* vol. 267 (3−4), pp. 215–220, 1997.

[9] M. J. Turner, J .J. MacKinnon, S. K. Wolff, D. J. Grimwood, P. R. Spackman, D. Jayatilaka, and M. A. Spackman, Crystal Explorer Ver. 17.5. University of Western Australia, 2017. http://hirshfeldsurface.net.