MINOR RESEARCH PROJECT

Research and Development Scheme, Higher Education Department, U.P. Government, Lucknow

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Title of Project : Molecular Structure and Spectroscopic Studies of Morpholine Derivatives and their Interpretation Using DFT Calculation

SUMMARY OF THE MINOR PROJECT WORK

The present minor research project entitled **"MOLECULAR STRUCTURE AND SPECTROSCOPIC STUDIES OF MORPHOLINE DERIVATIVES AND THEIR INTERPRETATION USING DFT CALCULATION"** sanctioned by the Director, Higher Education, Uttar Pradesh, Prayagraj vide letter no. Degree Vikas/225–232/2021-22 dated 01.04.2021 embodies the result of investigations carried out in the Molecular Spectroscopy and Biophysics Laboratory, Department of Physics, D.N. College, Meerut during the period May 2021 to May 2023.

The present work is on the field of spectroscopy in general and molecular spectroscopy in particular. The title of the project reveals that the work is based on the vibrational and electronic spectral studies of some substituted morpholines. The morpholine derivatives were chosen for analysis since they have many applications in various fields.

Morpholine and its derivatives are six–membered rings having amine and ether groups. Morpholine derivatives are therapeutic agents and have various natural and artificial products with many applications as corrosion inhibitors, textile solvents, bleaching agents and fruit and vegetable preservation. Morpholine derivatives also act as antidepressants, antitumor agents, antifungals, antioxidants, antibiotics, and treatments in dementia and nervous system disorders. Morpholine with pyrazolopyrimidine acts as the target for cancer and Type 2 diabetes treatment. Some 4-[5-(4-phenoxyphenyl)-2H-pyrazole-3-yl]morpholine derivative act as anti-parasitic agents. Chen Chang et al. synthesized a morpholine derivative that can be used in reverse flotation carnallite ore to produce potash fertilizer. Ah Ram Jeon et al. use diisobutyl(morpholino)aluminum for the synthesis and conversion of aldehydes and ketones from esters. K. Fabitha et al. analyzed a morpholine derivative for its

anti-bacterial activity. Xiao-Man Chen et al. evaluated morpholine derivative for its antitumor and DNA targeting agent.

Due to large applications of morpholine derivatives, they are subject to computational studies such as Density Functional Theory (DFT). Chaimaa El Haimer et al. studied chemical reactivity of morpholine derivative by DFT studies. V. Balachandran et al. studied vibrational spectra and NBO analysis of 4-Methylmorpholine molecule by DFT analysis. R. Bhuvaneswari et al. analysed molecular structure, vibrational spectra and NBO of morpholinium oxalate by density functional theory. V.S. Jeba Reeda et al. studied morpholine derivative for its vibrational spectral study, reactivity (ELF, LOL and Fukui) and molecular docking studies by DFT. The vibrational study of morpholine derivatives along with DFT studies have been analyzed by many researchers.

In recent times, drug discovery efforts have motivated researchers to synthesize numerous morpholine-based compounds. There is still a lot to be explored when it comes to the synthesis of drugs and intermediates. With the advancement in technology, morpholine will find more applications in various industries.

The compounds under investigation are given below and no computational works on these compounds have been reported so far.

1. 2-Benzyl-2-(dimethylamino)-4-morpholinobutyrophenone
2. Benzyl (3-Fluoro-4-morpholinophenyl)carbamate
3. 3-Fluoro-4-morpholinoaniline

In this work, the molecules under study are studied both experimentally and theoretically. The computational calculations are performed by Density Functional Theory (DFT) using Gaussian 09 and Gaussview softwares. The other software programs used are chemcraft, origin and VEDA.

A comparative study is done between the experimental data and theoretical data. Comparing theoretical and experimental calculations is of utmost importance in various fields of science and engineering. Here are some key reasons why this comparison is essential as follow. Theoretical calculations are based on assumptions, mathematical models, and theoretical frameworks. By comparing these theoretical predictions with experimental results, scientists and researchers can validate the accuracy and reliability of their models. If the experimental results closely match the theoretical calculations, it provides confidence in the underlying assumptions and models used. On the other hand, significant discrepancies between theory and experiment may indicate the need for refining or revising the theoretical model. Another aspect of these comparisons is that it helps identify systematic errors that may arise from various sources such as experimental apparatus, measurement techniques, or data analysis methods. Systematic errors, unlike random errors, consistently affect the results in a particular direction, leading to discrepancies between theory and experiment. By analyzing these discrepancies, researchers can uncover the sources of systematic errors and take steps to minimize or eliminate them, thus improving the accuracy and reliability of future calculations. In addition, discrepancies between theoretical and experimental calculations can be valuable indicators of areas where theoretical models need improvement. If the theoretical predictions consistently deviate from experimental results, it may suggest limitations or inaccuracies in the underlying theories or assumptions. Researchers can then refine the theoretical models by incorporating additional factors or developing more sophisticated mathematical frameworks that better capture the complexities of the system under investigation. The process of comparing theoretical and experimental calculations plays a crucial role in advancing scientific knowledge. It helps identify gaps in our understanding and drives further research to address these gaps. The iterative cycle of refining theoretical models based on experimental data and using improved theoretical models to guide further

experiments leads to a deeper understanding of natural phenomena and allows for the development of more accurate predictive models. Practical Applications: Theoretical and experimental calculations are often used in tandem to guide practical applications and technological advancements. By comparing theoretical predictions with experimental results, engineers and technologists can assess the feasibility and effectiveness of proposed designs, optimize performance, and identify potential issues before implementation. This iterative feedback loop between theory and experiment ensures that scientific knowledge translates into practical solutions that benefit society.

The structural parameters (bond lengths and bond angles) of the studied molecules are calculated by DFT computations using the B3LYP method with 6-311++G(d,p) and cc-pVDZ basis sets. The thermodynamic parameters (Heat capacity, Entropy and Enthalpy) are calculated in the temperature range between 100 to 1000 Kelvin. The hybridization and covalent effects are investigated using Natural Bond Orbital (NBO) calculations with the help of the charge delocalization energies and hyperconjugative interactions. The Non-linear optical (NLO) properties of the molecules such as first order hyperpolarizability β_{total} along with dipole moment μ, mean polarizability $<\alpha>$, anisotropy of the polarizability $\Delta\alpha$ are calculated. The Fukui function is used as a local density functional descriptor to model chemical reactivity and site selectivity.

Based on the research work done in this project the following two research papers have been published which are attached to the project report.

1. B. S. Yadav, A. Singh, J. Teotia, V. Kumar, R. Saran, D. Teotia, Vinita, R. K. Uppadhayay, Structural Parameters, NLO Properties, Thermodynamic Functions, NBO Analysis And Fukui Functions Of Benzyl(3-Fluoro-4-Morpholinophenyl)Carbamate By Density Functional Theory, Journal of Pharmaceutical Negative Results, 14(1), 2023, pp.1-9, DOI:10.47750/pnr.2023.14.S01.175

2. B. S. Yadav, A. Singh, J. Teotia, R. Saran, D. Teotia, Vinita, R. K. Uppadhayay, V. Kumar, Computational DFT Study of 3-fluro-4-morpholinoaniline: Structural Parameters, NLO Properties, Thermodynamic Functions, NBO Analysis and Fukui, Eur. Chem. Bull. 2023, 12(5), pp. 195 – 205. DOI: 10.31838/ecb/2023.12.si5.025