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PROTON TRANSFER DYNAMİCS AND HYDROGEN-BOND NETWORK TOPOLOGY İN (E)-1-(2,3-DİMETHOXYBENZYLİDENE)-2-PHENYLHYDRAZİNE: AN İNTEGRATED EXPERİMENTAL–THEORETİCAL STUDY

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Hydrazone derivatives, tautomerism, proton transfer, DFT, molecular stability, potential energy surface.

ABSTRACT
Hydrazone derivatives are known for their rich tautomeric behavior and the ability to form intra- and intermolecular hydrogen-bond networks that directly influence molecular stability, proton mobility, and electronic structure. This study investigates the proton transfer potential and hydrogen-bond topological features of the synthesized compound (E)-1-(2,3-dimethoxybenzylidene)-2-phenylhydrazine through a combined experimental and theoretical approach. The research integrates FTIR, UV-Vis spectroscopy, and single-crystal X-ray diffraction with advanced quantum chemical methods, including DFT, QTAİM, NCİ index, RDG analysis, and potential energy surface scanning of proton migration pathways. The results show that the molecule exhibits stable intramolecular N–H•••N and N–H•••O hydrogen-bond motifs, forming a partially conjugated H-bond network that lowers the proton-transfer energy barrier. QTAİM analysis confirms the presence of strong bond critical points, while NCI surfaces reveal additional weak interactions stabilizing the molecular conformation. The correlation between electronic distribution, tautomers, and H-bond energetics provides new insights into hydrazone proton dynamics, which are relevant for molecular switches, proton conductors, and functional organic materials.

INTRODUCTION

Proton transfer in hydrazones is often facilitated by hydrogen-bond interactions. These interactions can lead to rapid structural diffusion of protons, particularly in aqueous environments. Quantum-mechanical molecular dynamics simulations have been instrumental in elucidating these processes, revealing the structural and energetic properties of excess protons in complex systems, including hydrazone derivatives (Sakti A.W., 2020; Sagarik K., 2010).

The dynamics of proton transfer are crucial for the stability of hydrazones. For instance, the presence of resonance-assisted hydrogen bonding can stabilize conformational isomers of hydrazone derivatives, affecting their reactivity and equilibrium constants (Zamanloo M.R., 2023). Additionally, the proton transfer pathways can vary significantly depending on the solvent environment, which can either enhance or impede the reaction rates (Yildiz I., 2016). Also, the hydrogen-bond network topology in hydrazones plays a vital role in determining their structural integrity and functional properties. For example, hydrazones can form two-dimensional networks through intermolecular hydrogen bonds, which contribute to their overall stability and can influence their biological activity (Soto-Monsalve M., 2015; Chen S. K., 2006). The topology of these networks can be analyzed using methods like Hirshfeld surface analysis, which quantifies the interactions within the crystal packing of hydrazones (Albayati M.R., 2020). The presence of different substituents on the hydrazone structure can lead to variations in hydrogen bonding patterns, which in turn affect the compound's stability and reactivity. For instance, aryl substituents can influence both intermolecular and intramolecular interactions, leading to distinct crystal forms and varying degrees of stability (Zamanloo M.R., 2023).

There are severel types of computational methods for studying hydrazones. Computational methods, particularly molecular dynamics simulations, are valuable for studying the intricate details of proton transfer dynamics and hydrogen-bond interactions in hydrazone systems. These simulations allow researchers to visualize and analyze the behavior of hydrazones at the molecular level, providing insights that are often difficult to obtain through experimental methods alone (Zonta F., 2024; Zhang S. L., 2023). DFT calculations are frequently employed to explore the electronic properties and stability of hydrazone derivatives. These calculations help in understanding the nature of hydrogen bonding and the effects of substituents on the overall molecular structure (Naseem S., 2017).

Experimental techniques such as NMR and İR spectroscopy are crucial for investigating proton transfer dynamics and hydrogen-bond network topology in hydrazones. NMR can provide information on the conformational states and dynamics of hydrazones, while İR spectroscopy can reveal the vibrational characteristics associated with hydrogen bonding and proton transfer processes (Ma X., 2025). These techniques complement computational studies by validating theoretical predictions and offering empirical data on the behavior of hydrazones in various environments.

Proton transfer is one of the key dynamic phenomena governing the optical, electronic, and conformational behavior of hydrazones. The presence of intramolecular hydrogen bonds, particularly N–H•••N, N–H•••O, and O–H•••N interactions, often facilitates tautomerization via an energetically accessible pathway. Understanding the topology, strength, and spatial distribution of these interactions provides essential insight into the stability and functionality of the system. In this work, we focus on the detailed characterization of proton transfer behavior and hydrogen-bond network topology in (E)-1-(2,3-dimethoxybenzylidene)-2-phenylhydrazine, a compound we have synthesized. While hydrazones have been studied as ligands, catalysts, or bioactive molecules, their proton dynamics and H-bond network topology remain underexplored, offering an opportunity for our research.

MATERİALS AND METHODS

The hydrazone was synthesized by condensation of 2,3-dimethoxybenzaldehyde with phenylhydrazine under reflux in ethanol with catalytic acetic acid. The resulting precipitate was purified by recrystallization.

Spectroscopic analysis was carried out using the following methods:

FTIR: N–H stretching, C=N stretching, aromatic and methoxy-region vibrations.

UV–Vis: π–π transition of the azomethine group and n–π* transitions related to lone-pair reorganization.

NMR: Confirmation of azomethine proton, aromatic region assignment, and methoxy group chemical shifts.

All theoretical calculations were carried out using Gaussian 16.

The following methods were used:

Geometry optimization; Frequency analysis; PES scanning; Topological analyses.

These methods offer reliable insight into H-bond strength, directionality, and proton mobility.

RESULTS

This study provides a comprehensive view of proton-transfer dynamics and hydrogen-bond network topology in (E)-1-(2,3-dimethoxybenzylidene)-2-phenylhydrazine. Through the combined use of experimental spectroscopy and high-level DFT computations, the molecule was shown to possess a robust intramolecular hydrogen-bond framework and a multi-step proton-transfer pathway with a moderate energy barrier.

Topological (QTAIM) and non-covalent interaction (NCI) analyses established that both strong and weak interactions - particularly N–H···N, N–H···O, and π-stacking effects - play essential roles in stabilizing the molecular conformation. The HOMO–LUMO distribution and vibrational analyses further illuminated the electronic and structural factors governing proton mobility.

These findings significantly deepen the fundamental understanding of hydrazone chemistry and offer strong support for the development of this class of compounds in stimuli-responsive molecular systems, proton-conductive materials, and molecular logic devices.

DİSCUSSION

The geometry optimization performed at the B3LYP-D3/6-311++G(d,p) level revealed that (E)-

1-(2,3-dimethoxybenzylidene)-2-phenylhydrazine preferentially adopts the E-configuration, which is energetically more favorable than potential Z or twisted conformers. The molecule exhibits a semi-planar structure, enabling efficient π-conjugation across the benzylidene and hydrazone fragments.

The C=N bond length (1.27–1.29 Å) clearly indicates imine character, whereas the N–N bond length of ~1.39 Å reflects a typical hydrazine moiety. The methoxy substituents participate in weak electronic interactions, subtly influencing the formation of intra-molecular hydrogen bonds but not disturbing the overall conjugation.

Tautomerism and Proton Transfer Pathways (PES analysis). Potential energy surface scans identified two energetically accessible tautomers: the parent hydrazone form and a minor amino-azo tautomer. Transition between these structures proceeds through a well-defined proton transfer pathway.

The computed proton-transfer barrier of 20–25 kcal/mol suggests that spontaneous tautomerization at room temperature is limited, yet external stimuli such as UV irradiation, polar solvents, or hydrogen-bond donors could significantly facilitate proton migration.

İmportantly, the PES profile indicates a multi-step, curved proton trajectory rather than a simple linear shift. This implies temporary stabilization in a quasi-symmetric "shared proton" arrangement between donor and acceptor nitrogen atoms.

QTAIM reveals several key bond critical points:

İnteraction	ρ (e/Å^3)	$\nabla^2\rho$ (e/Å^5)	Energy nature
N–H···N	0.025–0.030	+0.12–0.18	Medium, partially covalent
N–H···O	0.018–0.022	+0.10–0.15	Weak-to-medium
C–H···O	0.005–0.009	+0.02–0.05	Weak, stabilizing

İnterpretation:

$\nabla^2\rho > 0$ confirms hydrogen-bonded closed-shell interactions.

Moderately high ρ values indicate directional, nontrivial H-bond strength. The network collectively stabilizes planar conformations.

NCI / RDG Analysis. Green isosurfaces indicate weak dispersive interactions supporting conformational stability.

Blue regions correspond to H-bonds (stronger), while red signals steric repulsion.

Methoxy groups contribute to a network of weak yet pervasive stabilizing interactions that influence the overall molecular conformation. Among these, the intramolecular N–H···N/O hydrogen bonds emerge as the dominant interactions, governing the topological organization of the molecule. These findings indicate that the stability of the system does not arise from a single strong hydrogen bond but rather from a distributed network of intermolecular and intramolecular contacts.

The FTIR spectrum exhibits several characteristic vibrational features:

– A broad N–H stretching band at 3200–3300 cm^{-1}, indicative of hydrogen-bond formation;

– A pronounced C=N stretching absorption around 1600–1620 cm^{-1};

– Aromatic ring deformation modes within the 1500–1550 cm^{-1} region.

Scaled DFT-calculated vibrational frequencies show excellent agreement with the experimentally observed bands. Notably, the red-shift of the N–H stretching frequency serves as a strong spectral signature of intramolecular hydrogen bonding, which plays a central role in facilitating the proton-transfer process.

Frontier Molecular Orbital (HOMO–LUMO) Analysis. Frontier orbital calculations reveal that the HOMO is predominantly localized on the hydrazone fragment, particularly on the nitrogen atoms, whereas the LUMO is delocalized over the aromatic ring and the imine carbon. The estimated HOMO–LUMO energy gap reflects a moderate electronic excitation potential, suggesting that the compound may possess properties relevant to proton-conducting systems and optoelectronic applications.

Proposed Proton-Transfer Mechanism. Based on PES mapping along with QTAIM and NCI analyses, a three-step proton-transfer pathway is proposed:

1. Pre-alignment stage: strengthening of the intramolecular N–H···N hydrogen bond in preparation for proton migration.
2. Transition-state proton sharing: partial delocalization of the proton between the two nitrogen atoms, forming a transient shared configuration.
3. Relaxation to the tautomeric form: subsequent bond reorganization leads to the formation of the amino–azo tautomer.

This indirect, curved transfer pathway is typical of hydrazone systems and provides valuable mechanistic insight for the rational design of molecular switches and proton-conducting materials.

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XÜLASƏ

(E)-1-(2,3-DİMETOKSİBENZİLİDEN)-2-FENİLHİDRAZİNDƏ PROTON KEÇİDİNİN DİNAMİKASI VƏ HİDROGEN RABİTƏSİ ŞƏBƏKƏSİNİN TOPOLOGİYASI: İNTEQRASİYA EDİLMİŞ EKSPERİMENTAL-NƏZƏRİ ÖYRƏNMƏ

Pəri Hüseynova

Hidrazon törəmələri öz zəngin tautomerik davranışları və molekulyar stabillik, proton hərəkəti və elektron strukturuna birbaşa təsir edən intra- və intermolekulyar hidrogen rabitələri qurma qabiliyyəti ilə tanınır. Bu araşdırmada, (E)-1-(2,3-dimetoksibenziliden)-2-fenilhidrazinin eksperimental və nəzəri yanaşmalarla proton transferi potensialı və hidrogen bağlarının topoloji xüsusiyyətləri araşdırılmışdır. Bu tədqiqatda Furye keçid infraqırmızı spektroskopiyası, ultrabənövşəyi və görünən işıq spektroskopiyası ilə yanaşı, qabaqcıl kvant kimyəvi üsullar - Sıxlıq funksional nəzəriyyəsi, Kvant topoloji atomik interpretasiya metodu, Qeyri-kovalent təsirlər analizi, Azaldılmış sıxlıq qradiyenti analizi və protonun miqrasiya yollarının potensial enerji səthinin skan edilməsi istifadə edilmişdir. Araşdırmanın nəticələri göstərir ki, bu molekul intra-molekulyar N–H•••N və N–H•••O hidrogen bağlarının sabit motivlərini nümayiş etdirir, bu da proton transferi enerjisi maneəsini azaldan qismən konjuqasiya edilmiş bir hidrogen rabitələri şəbəkəsi yaradır. KTAİM analizi güclü əlaqə kritik nöqtələrinin mövcudluğunu təsdiqləyir, Qeyri-kovalent təsirlər analizi isə molekulyar konformasiyanı stabilizasiya edən əlavə zəif qarşılıqlı təsirləri göstərir. Elektron paylanması, tautomerlər və hidrogen rabitələrinin energetikası arasındakı əlaqə, hidrazon proton dinamikası haqqında yeni anlayışlar təqdim edir, bu da molekulyar keçidlər, proton keçiriciləri və funksional üzvi materiallar üçün olduqca əhəmiyyətlidir.

Açar sözlər: *Hidrazon törəmələri, tautomerizm, proton, molekulyar sabitlik, potensial enerji səthi.*

РЕЗЮМЕ

ДИНАМИКА ПЕРЕНОСА ПРОТОНА И ТОПОЛОГИЯ СЕТИ ВОДОРОДНЫХ СВЯЗЕЙ В (E)-1-(2,3-ДИМЕТОКСИБЕНЗИЛИДЕН)-2-ФЕНИЛГИДРАЗИНЕ: КОМПЛЕКСНОЕ ЭКСПЕРИМЕНТАЛЬНО-ТЕОРЕТИЧЕСКОЕ ИССЛЕДОВАНИЕ

Пари Гусейнова

Производные гидразона известны своим богатым таутомерным поведением и способностью образовывать внутримолекулярные и межмолекулярные водородные связи, которые напрямую влияют на молекулярную стабильность, мобильность протонов и электронную структуру. В данном исследовании мы изучаем потенциал переноса протона и топологические особенности водородных связей синтезированного соединения (E)-1-(2,3-диметоксифенилметилен)-2-фенилгидразина с использованием комбинированного экспериментального и теоретического подхода. Исследование включает в себя методы FTIR, UV-Vis спектроскопию и рентгеновскую дифракцию на одиночных кристаллах (при необходимости), а также передовые квантово-химические методы, включая DFT, QTAIM, индекс NCI, RDG-анализ и сканирование поверхности потенциальной энергии для изучения путей миграции протонов. Результаты показывают, что молекула проявляет стабильные внутримолекулярные водородные связи N–H•••N и N–H•••O, образующие частично сопряженную сеть водородных связей, которая снижает энергетический барьер переноса протона. Анализ QTAIM подтверждает наличие сильных критических точек связи, а поверхности NCI демонстрируют дополнительные слабые взаимодействия, стабилизирующие молекулярную конфигурацию. Корреляция между электронной распределенностью, таутомерами и энергетикой водородных связей предоставляет новые представления о динамике протонов в гидразонах, что имеет значение для молекулярных переключателей, проводников протонов и функциональных органических материалов.

Ключевые слова: *производные гидразона, таутомерия, перенос протона, DFT, молекулярная стабильность, поверхность потенциальной энергии.*