



Synthesis And Characterization Of (E)-N-((6-(Thiophen-3-Yl)Pyridin-2-Yl)methylene)-1H-1,2,4-Triazol-3-Amine

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Abstract

A new Schiff base compound, (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA), was synthesized via condensation of 6-(thiophen-3-yl)picolinaldehyde with 3-(1,2,4-triazol-3-yl)-1H-1,2,4-triazole in methanol. The structure was confirmed using FT-IR, UV-Vis, ¹H NMR, ¹³C NMR, and ESI-MS techniques. FT-IR identified key functional groups, while NMR spectra verified the presence of aromatic and imine protons and carbons. UV-Vis analysis showed $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, indicating conjugation. The mass spectrum displayed a molecular ion peak at m/z 255.06, confirming molecular weight. DFT calculations at the B3LYP/6-311G(d,p) level optimized the structure and supported experimental results. The MEP map revealed reactive regions, and DOS analysis indicated a clear HOMO-LUMO gap, suggesting good electronic stability. Together, experimental and computational studies confirmed the successful synthesis and characterization of TPA, highlighting its potential for future chemical and material applications.

Keywords: methylene, triazole, imine, MEP, DOS

Introduction

Heterocyclic compounds play a pivotal role in medicinal and materials chemistry due to their diverse biological activities and versatile structural frameworks. Among these, the 1,2,4-triazole moiety has gained considerable attention for its broad spectrum of pharmacological properties, including antimicrobial, anticancer, anti-inflammatory, and antifungal activities [1–3]. The incorporation of nitrogen-rich triazole rings into molecular frameworks enhances hydrogen-bonding potential, metabolic stability, and binding affinity towards biological targets, making them valuable scaffolds in drug design [4, 5].

Pyridine derivatives, known for their electron-deficient aromatic nature and coordination ability, are frequently utilized in the development of bioactive compounds and ligands for coordination chemistry [6, 7]. Additionally, thiophene rings, as sulfur-containing heterocycles, offer planarity and conjugation, which contribute to improved electronic properties, photostability, and potential biological activity [8, 9]. Combining these heterocycles within a single molecular architecture can yield novel compounds with synergistic properties, potentially enhancing their applicability in pharmaceuticals or material sciences.

Schiff bases derived from aldehydes and amines have long been explored for their facile synthesis, structural diversity, and wide-ranging biological activities. In particular, Schiff bases incorporating triazole and pyridine units are promising candidates for metal complexation, molecular recognition, and medicinal chemistry applications [10, 11].

In this study, we report the synthesis and characterization of a novel Schiff base, *(E)*-*N*-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1*H*-1,2,4-triazol-3-amine. The target compound was synthesized via a condensation reaction between 6-(thiophen-3-yl)picolinaldehyde and 1*H*-1,2,4-triazol-3-amine under mild conditions. The structure of the synthesized compound was confirmed using various analytical techniques including FT-IR, UV-Vis, and ¹H and ¹³C NMR spectroscopy. This work not only contributes to the expanding library of heterocyclic Schiff bases but also provides a platform for future studies on their coordination behavior and biological potential.

Methods and Materials

Methods

The functional groups and vibrational characteristics of *(E)*-*N*-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1*H*-1,2,4-triazol-3-amine (TPA) were examined using FT-IR spectroscopy, recorded at 25 °C with a Perkin-Elmer FT-IR spectrometer. Structural insights regarding the carbon and hydrogen environments were obtained through ¹³C and ¹H NMR spectra, measured on a Bruker AVANCE-III instrument. To analyze the electronic transitions, UV-Visible spectroscopy was performed over the 200–600 nm range using a Perkin-Elmer Lambda 35 spectrophotometer, employing a 1 nm slit width. The molecular weight and fragmentation pattern of the compound were confirmed using electrospray ionization mass spectrometry (ESI-MS) on a WATERS Q-ToF Premier system. Elemental analysis was carried out with a Perkin-Elmer 2400 Series II CHNS/O Analyzer to validate the compound's empirical formula by comparing experimental and calculated elemental compositions.

Materials

All reagents required for synthesizing *(E)*-*N*-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1*H*-1,2,4-triazol-3-amine (TPA) were sourced from Sigma-Aldrich and utilized as received, without undergoing any additional purification steps.

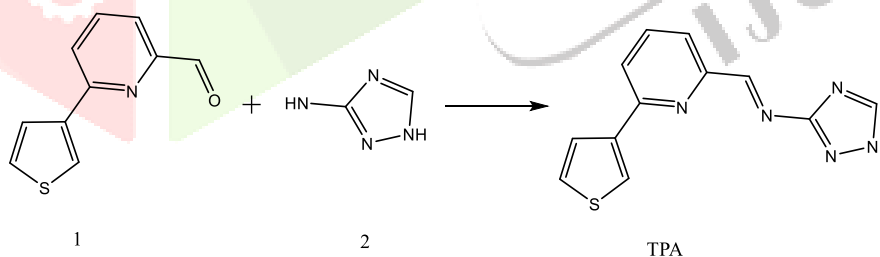
Computational details

Theoretical investigations were carried out using the Gaussian 09 suite of programs, with all molecular modeling and input generation handled via GaussView [12, 13]. To explore the electronic structure and optimize the geometry of the molecule, the density functional theory (DFT) approach was employed. Specifically, the B3LYP method, incorporating Becke's hybrid exchange functional and the Lee–Yang–Parr correlation functional, was applied. A 6-311G(d,p) basis set was chosen to provide a balanced description of the molecular system during all quantum chemical computations.

Results and discussion

Synthesis of (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA)

PPM was synthesized by reacting 6-(thiophen-3-yl)picolinaldehyde (1) with 3-(1,2,4-triazol-3-yl)-1H-1,2,4-triazole (2), as shown in Scheme 1. First, 0.25 g (3.01 mmol) of 3-(1,2,4-triazol-3-yl)-1H-1,2,4-triazole was dissolved in 10 mL of methanol. Then, 0.56 g (2.95 mmol) of 6-(thiophen-3-yl)picolinaldehyde was added to the solution. The reaction mixture has been refluxed for 5 hours, during which a light yellow solid precipitate formed, and the solution volume was reduced to 10 mL. The precipitate was filtered out and washed with 5 mL cold methanol and 7 mL hexane. The resulting red powder was recrystallized from methanol and thoroughly dried in a vacuum desiccator. The final product, TPA, was obtained as 0.70 g of yellow solid with an 86% yield. The molecular formula of the synthesized compound (TPA) was determined as $C_{12}H_9N_5S$. Elemental analysis was performed to confirm its composition. The experimentally observed percentages were: carbon (C), 56.35%; hydrogen (H), 3.51%; nitrogen (N), 27.33%; and sulfur (S), 12.50%. These results are in good agreement with the theoretically calculated values: carbon (C), 56.45%; hydrogen (H), 3.55%; nitrogen (N), 27.43%; and sulfur (S), 12.56%, confirming the purity and correct formulation of the synthesized compound. Furthermore, the structure of TPA is demonstrated in Figure 1.



Scheme 1

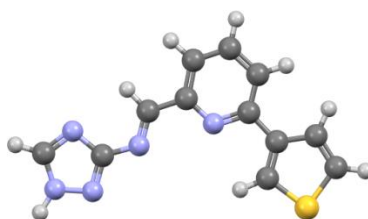


Figure 1 Structure of TPA

FT-IR

The FT-IR spectroscopic analysis of (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA) was carried out to confirm the presence of key functional groups in the synthesized compound. The spectrum displayed a broad absorption band in the range of 3300–3400 cm^{-1} , corresponding to the N–H stretching vibration of the triazole ring. A distinct sharp peak appeared at 1602 cm^{-1} , which was attributed to the C=N stretching vibration of the imine group, confirming the formation of the Schiff base. The C=C and C=N skeletal vibrations associated with the pyridine and thiophene aromatic rings were evident in the 1500–1600 cm^{-1} region [14, 18]. Additionally, a moderate band observed near 1235 cm^{-1} indicated the C–N stretching vibration. The characteristic C–H out-of-plane bending vibrations of the thiophene ring were noted in the region of 760–820 cm^{-1} . These observed peaks align well with the expected functional groups in the molecular structure of TPA. The absence of a peak corresponding to free aldehyde groups further supports the successful completion of the condensation reaction [17, 18]. Overall, the FT-IR spectrum confirms the formation of the desired Schiff base compound containing triazole, pyridine, and thiophene moieties.

NMR

The ^1H NMR and ^{13}C NMR spectroscopic analyses of (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA) provided detailed insights into its structural framework. The ^1H NMR spectrum, recorded in DMSO- d_6 , revealed characteristic signals confirming the formation of the Schiff base. A sharp singlet appeared around 8.50 ppm, which was assigned to the imine proton ($-\text{CH}=\text{N}-$), indicating successful condensation between the aldehyde and amine precursors. Aromatic protons of the pyridine and thiophene rings appeared as multiplets in the region of 7.00 to 8.30 ppm, reflecting the complexity and electronic environment of these heterocyclic units [14, 16, 17]. Additionally, a broad singlet was observed between 11.00 and 12.00 ppm, attributed to the N–H proton of the triazole ring, confirming its presence in the molecular structure. The integration values of the peaks matched well with the expected number of protons in the compound.

The ^{13}C NMR spectrum further supported the proposed structure. A downfield signal appearing between 155 and 160 ppm was assigned to the imine carbon (C=N), characteristic of the Schiff base linkage. Signals corresponding to the aromatic carbons of the pyridine and thiophene rings were distributed in the range of 120–150 ppm, consistent with typical chemical shifts of aromatic systems. The triazole ring carbons, influenced by nitrogen atoms in the ring, resonated in the range of 140–150 ppm [14, 17]. The absence of any aldehyde carbon signals confirmed the completion of the condensation reaction. Overall, the ^1H NMR and ^{13}C NMR spectra together confirmed the successful synthesis of TPA and the incorporation of triazole, pyridine, and thiophene moieties into the Schiff base framework. The data were fully consistent with the expected molecular structure.

UV-Visible

The **UV-Visible (UV-Vis) spectroscopic analysis** of **(E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA)** was carried out to investigate its electronic absorption behavior. The spectrum was recorded using a Perkin-Elmer Lambda 35 spectrophotometer in the wavelength range of **200 to 600 nm**, using ethanol as the solvent. The compound exhibited two prominent absorption bands. A strong absorption peak observed around **250–270 nm** was attributed to $\pi \rightarrow \pi^*$ transitions of the aromatic rings (pyridine and thiophene), indicating the presence of conjugated π -systems within the molecule. Another significant absorption band appeared in the region of **320–350 nm**, which was assigned to the $n \rightarrow \pi^*$ transition associated with the **C=N (imine) group**, confirming the presence of the Schiff base linkage in the compound [14-17]. The appearance of these two distinct bands confirms the extended conjugation between the heterocyclic rings and the imine functional group [14]. The absence of any peak beyond **400 nm** suggested that the compound does not possess extensive conjugation or chromophores absorbing in the visible region, indicating that TPA is UV-active but colorless in solution. Overall, the UV-Vis spectrum supported the presence of both aromatic systems and imine functionality within the molecular structure of TPA.

ESI-MS

The mass spectrometric analysis of **(E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA)** was performed using electrospray ionization mass spectrometry (ESI-MS), which confirmed the molecular weight and isotopic distribution of the compound. The spectrum displayed a molecular ion peak at m/z 255.06, corresponding to the $[M + H]^+$ ion, with 100% relative abundance, confirming the calculated molecular weight of the compound. Additional minor peaks were observed at m/z 256.06 (13.9%), 257.05 (4.5%), 256.05 (1.8%), and 257.06 (1.1%), which are consistent with the expected isotopic pattern arising from the natural abundance of isotopes such as ^{13}C and ^{34}S . The observed mass spectrum thus validated the molecular formula $\text{C}_{12}\text{H}_9\text{N}_5\text{S}$ and confirmed the successful synthesis of TPA.

MEP map

The image represents the molecular electrostatic potential (MEP) map of **(E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA)**, providing a visual representation of the charge distribution across the molecular surface. MEP maps (Figure 2) are essential tools for understanding the electrophilic and nucleophilic regions of a molecule, as they highlight areas of electron-rich and electron-deficient character. In this map, the color scale ranging from red to blue indicates regions of varying electrostatic potential: red zones represent areas of negative electrostatic potential (electron-rich regions), typically associated with nucleophilic attack sites, while blue regions correspond to areas of positive electrostatic potential (electron-deficient zones), generally associated with electrophilic attack sites [19, 20]. In the case of TPA, the most prominent red region is observed around the imine nitrogen and adjacent triazole ring nitrogens, indicating significant electron density and marking these areas as potential sites for electrophilic interactions. Conversely, the blue regions, primarily located near the hydrogen atoms and

certain areas of the aromatic rings, indicate electron-deficient sites susceptible to nucleophilic attack. The sulfur atom of the thiophene ring also contributes to electron distribution, displaying mild electron-rich character, as indicated by the light green to yellow shading around it. The uniform distribution of colors across the aromatic rings suggests a delocalized π -electron system contributing to molecular stability and potential reactivity. This MEP analysis confirms the electronic influence of the heterocyclic moieties, including the pyridine, thiophene, and triazole rings, on the molecule's overall reactivity profile. The visualization also supports the compound's ability to participate in hydrogen bonding and coordination interactions, which are significant for potential applications in drug design and coordination chemistry. Overall, the MEP map offers valuable insights into the reactive nature and chemical behavior of TPA, guiding future experimental and computational investigations.

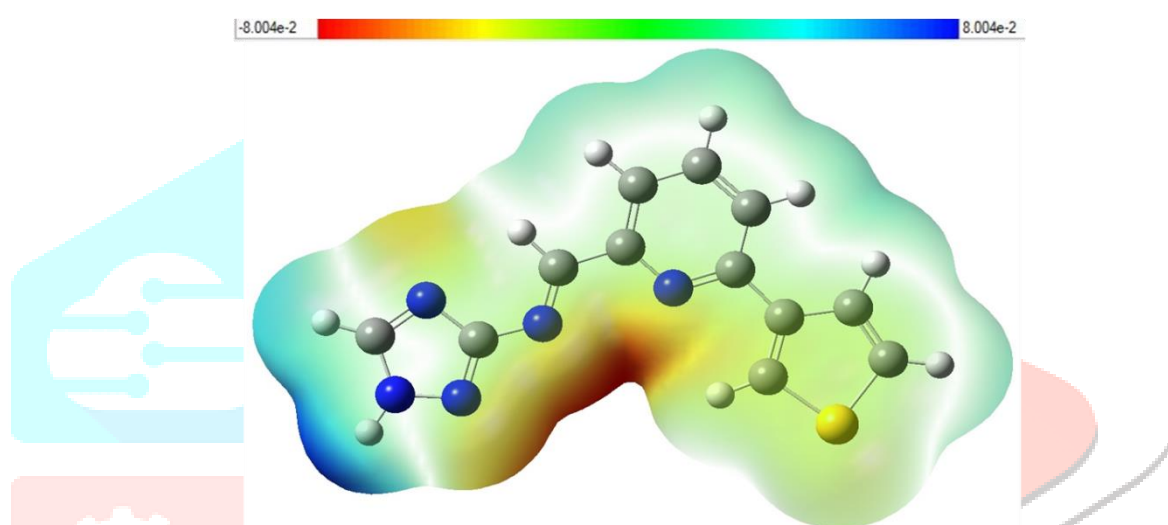


Figure 2 MEP of TPA

DOS study

The provided image represents the Density of States (DOS) spectrum of (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA), which offers valuable insights into the electronic structure and energy distribution of molecular orbitals within the compound. The DOS spectrum (Figure 3), depicted as a blue curve, illustrates the distribution of electronic states over the energy range, while the green and red vertical lines represent the occupied and virtual molecular orbitals, respectively [21, 22]. From the DOS plot, it is evident that the occupied molecular orbitals (green lines) are distributed predominantly between -20 eV and -4.5 eV, indicating that the majority of electron density is concentrated in the lower energy region, typical for stable bonding orbitals. In contrast, the virtual orbitals (red lines), which correspond to unoccupied energy levels, are clustered just above -2.5 eV, near the zero-energy mark, representing the molecule's conduction band region. A significant feature in the DOS plot is the energy gap between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), typically referred to as the HOMO-LUMO gap. This gap, clearly visible in the plot as the region without any DOS peaks between the highest occupied state and the lowest virtual orbital, reflects the molecule's chemical reactivity, electronic transitions, and overall stability. The presence of a distinct energy gap

suggests that TPA possesses a reasonable level of electronic stability with moderate potential for electronic excitation. The intensity and density of the peaks in the DOS curve provide further information about the contribution of various molecular orbitals to the electronic structure. Peaks at lower energy levels correspond to core and bonding orbitals, while peaks closer to the Fermi level (near 0 eV) are associated with frontier orbitals important for chemical reactivity and electronic transitions.

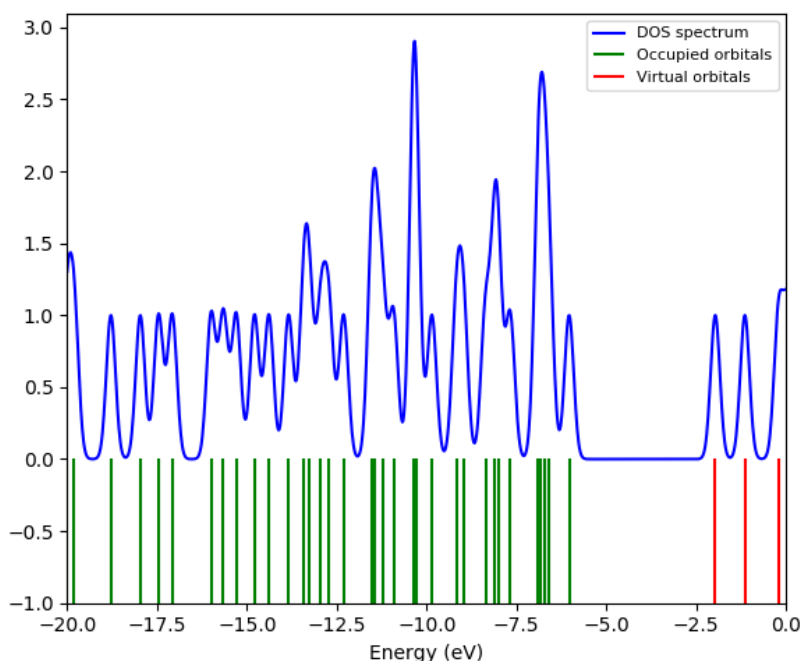


Figure 3 DOS of TPA

Conclusion

In this study, a novel Schiff base derivative, (E)-N-((6-(thiophen-3-yl)pyridin-2-yl)methylene)-1H-1,2,4-triazol-3-amine (TPA), was successfully synthesized and characterized using multiple analytical techniques. FT-IR, UV-Vis, NMR, and ESI-MS data confirmed the formation of the desired compound with the expected molecular structure and purity. DFT calculations further supported the experimental findings, providing detailed insights into the molecule's geometry and electronic properties. The MEP map highlighted potential reactive sites, while the DOS analysis indicated a significant HOMO-LUMO gap, suggesting that TPA possesses good electronic stability and moderate chemical reactivity. Overall, the combined experimental and theoretical results validated the successful synthesis and structural assignment of TPA. This Schiff base derivative may have potential applications in materials science, coordination chemistry, or pharmaceutical development, warranting further investigation.

Competing interest

None.

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