

NITROGEN HETEROCYCLES IN MEDICINAL AND FUNCTIONAL APPLICATIONS: SYNTHESIS, CHARACTERIZATION AND DEVELOPMENT OF A TRIAMTERENE DERIVATIVE

Anjali¹, Shraddha Upadhyay^{2*}

^{1,2}Department of Chemistry, Keral Verma Subharti College of Science, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India - 250005

ABSTRACT

Nitrogen-containing heterocycles are an important class of organic compounds with broad applications in medicinal chemistry, pharmaceuticals, and materials science. Fused nitrogen-rich heterocyclic systems are of particular interest due to their diverse biological activities and favorable physicochemical properties. This study reports the synthesis of a novel triamterene-derived heterocycle, 2-phenylbenzopyrazino[2,3-g][1,8]naphthyridin-3,12-diamine, via a straightforward and cost-effective multistep process involving nitrosation, cyclization, and mild catalytic transformation. Reaction progress was monitored by thin-layer chromatography. The target compound was isolated as a pale-yellow crystalline solid in 78% yield, with a melting point of 115–118 °C. Structural characterization by FTIR, ¹H NMR, ¹³C NMR, and ESI-MS confirmed the fused nitrogen-containing heterocyclic framework, including N–H, C=N, and C–N functionalities, and the expected molecular ion peak. The methodology offers excellent reproducibility and scalability, with minimal side product formation. These findings provide an efficient approach to structurally complex triamterene-based heterocycles with potential pharmaceutical applications.

KEYWORDS: Nitrogen heterocycles; medicinal chemistry; functional materials; triamterene derivative; heterocyclic synthesis; spectral characterization; pharmacological applications.

INTRODUCTION

Heterocyclic compounds are a significant and diverse class of organic molecules, widely present in biologically active systems and advanced materials [1]. Defined by cyclic structures containing at least one heteroatom, usually nitrogen, oxygen, or sulfur, these compounds exhibit unique chemical reactivity, electronic properties, and biological activity. Nitrogen-containing heterocycles (N-heterocycles) are especially important due to their prevalence in pharmaceuticals, natural products, nucleic acids, vitamins, antibiotics, hormones, agrochemicals, dyes, and polymeric materials [2,3]. Incorporating nitrogen into these rings changes electron distribution, molecular polarity, and intermolecular interactions, which enhances binding to biological receptors through hydrogen bonding, dipole–dipole interactions, van der Waals forces, hydrophobic effects, and π – π stacking [4–6]. As a result, nitrogen heterocycles are essential in medicinal chemistry, materials science, organic electronics, semiconductors, photovoltaic systems, liquid crystals, and light-harvesting applications [7–9].

Pyrrole-based heterocycles demonstrate significant antibacterial, anticancer, and anti-inflammatory properties, and their synthesis has become more efficient and environmentally friendly through green methods such as β -cyclodextrin and polyethylene glycol [10]. Pyrazole derivatives, which exhibit strong antimicrobial, antioxidant, anti-inflammatory, and anticancer activities, have benefited from increasingly accessible catalytic and multicomponent synthetic strategies [11,12]. Imidazole-containing compounds not only serve pharmaceutical purposes, as antifungal, antibacterial, and enzyme-modulating agents, but also play crucial roles in electroactive polymers and functional materials [13]. Meanwhile, triazole derivatives are valued as pharmacophores for their pharmacological activity and chemical stability, which supports their widespread use in medicinal and click-chemistry-based synthesis [14]. The significance of nitrogen heterocycles extends beyond therapeutic uses, as they are pivotal in polymer science, fluorescent dyes, corrosion inhibition, agrochemicals, organic semiconductors, and energy-related materials due to their favorable optical, thermal, and electrochemical properties [15]. As a result, these developments underscore the central role of nitrogen heterocycles in the design of medicinal and functional materials.

Although significant advancements have been made in the synthesis and application of nitrogen-containing heterocycles, the structural modification and development of triamterene-derived heterocyclic systems have not been extensively investigated. Triamterene is a clinically important potassium-sparing diuretic with a pyrazine-based framework, used to manage hypertension and edema by selectively inhibiting epithelial sodium channels (ENaC) [16]. There is significant potential to create new triamterene-based heterocyclic derivatives with greater structural diversity and pharmacological activity using cost-effective, scalable methods. This study provides an overview of the medicinal and functional importance of nitrogen heterocycles, focusing on the synthesis, characterization, and development of a triamterene-derived

heterocyclic compound. The derivative was synthesized via a multistep process involving nitrosation and cyclization and characterized by thin-layer chromatography (TLC), melting-point analysis, Fourier-transform infrared spectroscopy (FTIR), ^1H NMR, ^{13}C NMR, and mass spectrometry. The study also aims to establish a practical and economically viable synthetic method for preparing pharmaceutically relevant nitrogen-containing heterocyclic derivatives.

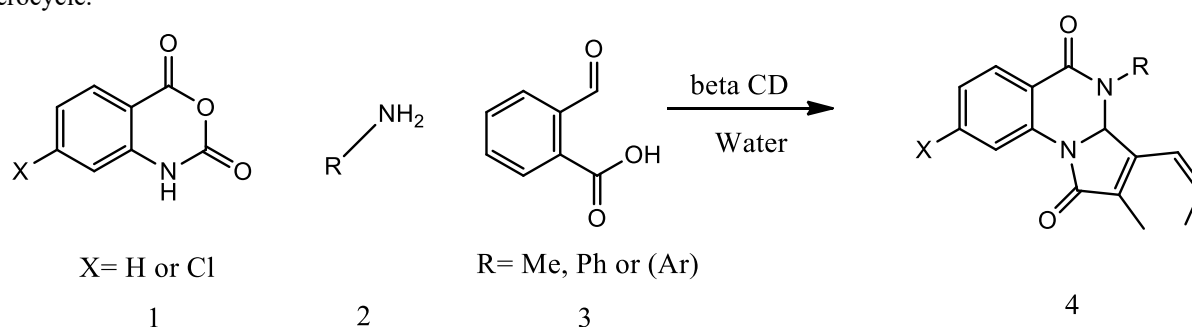
2. LITERATURE BACKGROUND ON NITROGEN HETEROCYCLES

2.1 Synthetic Approaches to Nitrogen Heterocycles

Nitrogen-containing heterocycles are of significant interest due to their broad applications in medicinal chemistry, pharmaceuticals, materials science, and agrochemicals. Recent advances in synthetic organic chemistry emphasize environmentally sustainable, catalyst-assisted, and high-yield methods for producing these frameworks. Pyrrole, pyrazole, imidazole, and triazole derivatives are especially notable for their chemical versatility and biological relevance [17]. The use of green solvents, recyclable catalysts, multicomponent reactions, and aqueous-phase synthesis has improved reaction efficiency, selectivity, and scalability.

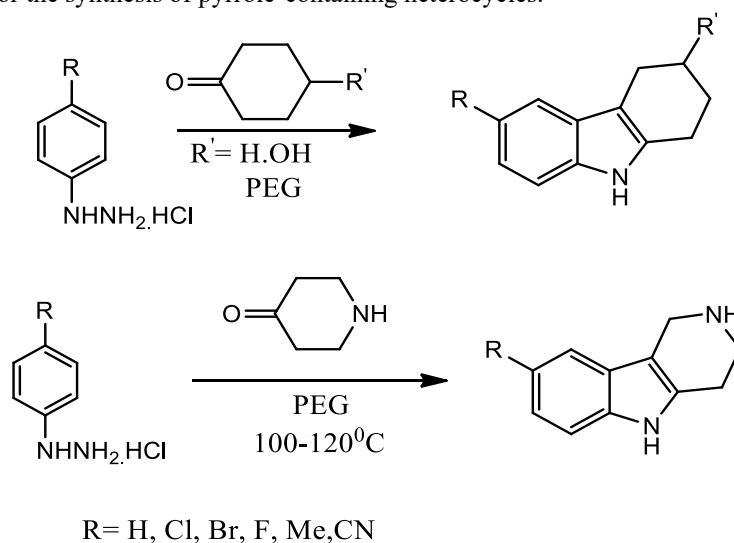
2.1.1 Synthesis of Pyrrole Derivatives

Pyrrole-based heterocycles are important nitrogen-containing compounds with broad pharmaceutical and biological activities. Recent strategies focus on efficient, environmentally sustainable methods for constructing pyrrole rings. Reddy et al. developed a one-pot, three-component synthesis of 6-substituted-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-diones from isatoic anhydride, amines, and 2-formylbenzoic acid, using β -cyclodextrin as a catalyst [18]. This catalyst activates carbonyl groups and improves reactant solubility in water, increasing reaction efficiency and yield. The mechanism involves nucleophilic attack, intermediate formation, and intramolecular cyclization to produce the target heterocycle.



Scheme 1: β -Cyclodextrin mediated synthesis of isoindoloquinazoline derivatives

Yedukondalu et al. [19] synthesized substituted tetrahydrocarbazoles by reacting substituted cyclohexanones or piperidone derivatives with phenylhydrazine hydrochloride in a polyethylene glycol (PEG) medium. This synthetic strategy demonstrated operational simplicity, high reaction efficiency, and improved product yields under relatively mild reaction conditions. The use of polyethylene glycol as a green solvent further enhanced the sustainability and environmental compatibility of the process. These findings collectively highlight the growing emphasis on eco-friendly, scalable methodologies for the synthesis of pyrrole-containing heterocycles.



Scheme 2. Synthesis of substituted tetrahydrocarbazoles in polyethylene glycol.

2.1.2 Synthesis of Pyrazole Derivatives

Pyrazole derivatives are of significant interest for their broad pharmacological activities, including antimicrobial, anti-inflammatory, anticancer, antioxidant, and antihypertensive effects. This has driven efforts to develop efficient catalytic systems for pyrazole ring synthesis. Reddy and Jeong [20] developed an InCl_3 -catalyzed, solvent-free, one-pot three-

component cyclocondensation strategy for the synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones. The protocol afforded excellent product yields, shortened reaction times, and facile purification, highlighting its efficiency and sustainability. Furthermore, the atom-economical methodology provides a practical route to pharmaceutically relevant N-fused heterocyclic frameworks

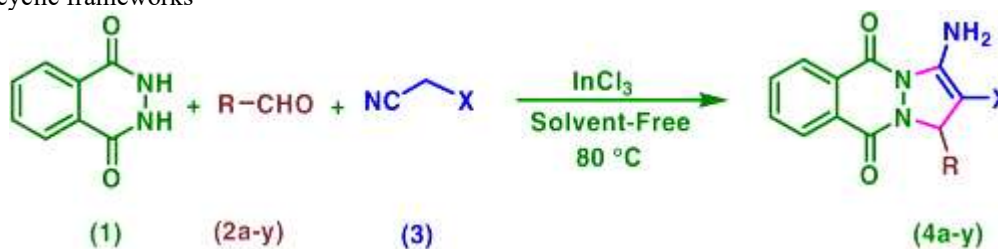
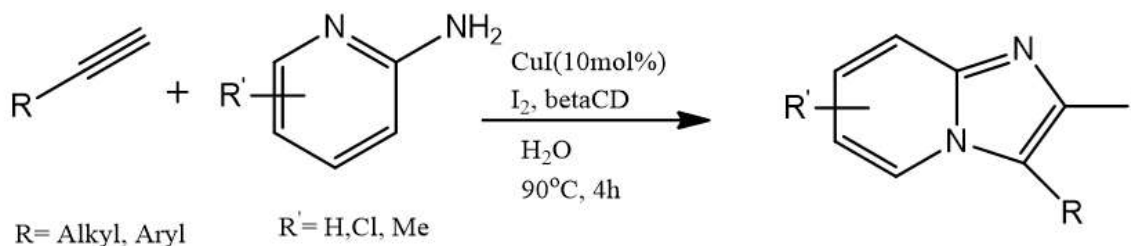


Figure X. Synthetic route for the preparation of 1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivatives via InCl_3 -catalyzed solvent-free multicomponent cyclocondensation.

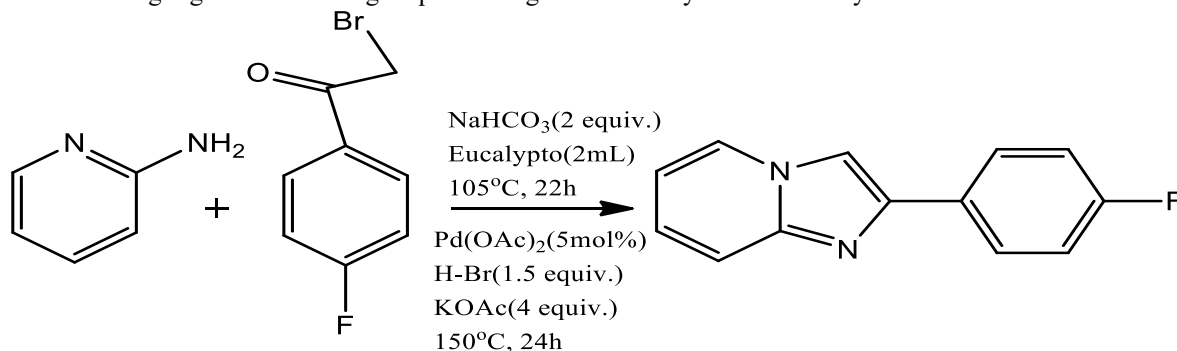
2.1.3 Synthesis of Imidazole Derivatives

Imidazole-containing heterocycles are important in medicinal chemistry due to their antifungal, antibacterial, anti-inflammatory, and enzyme-modulating properties. Their electronic characteristics also make them valuable in electroactive polymers and functional materials. Tran et al. [21] developed a green, solvent-free synthesis of 1,2,4,5-tetrasubstituted imidazoles using a recyclable deep eutectic solvent, affording high yields and operational simplicity. Dheer et al. [22] reported the regioselective synthesis of 2-iodo-imidazo[1,2-a]pyridines and 2-iodobenzoimidazo[2,1-b]thiazoles using a CuI/β -cyclodextrin catalytic system in water [12–20]. This method achieved excellent regioselectivity and good yields while using water as an environmentally friendly solvent, supporting greener synthetic practices.



Scheme 5: CuI/β -cyclodextrin mediated synthesis of imidazole derivatives

El Qami et al. [23] developed a sustainable Groebke–Blackburn–Bienaymé reaction in eucalyptol, efficiently synthesizing 32 imidazo-fused heterocycles with potential central nervous system activity under green conditions. Campos et al. [24] introduced eucalyptol, a recyclable, biomass-derived solvent, for the one-pot synthesis of 2,3-diaryl-imidazo[1,2-a]pyridines. This process uses condensation of 2-aminopyridine with bromoacetophenones, followed by C–H activation at the C-3 position. The method is efficient, environmentally sustainable, and reduces reliance on toxic organic solvents. These advances highlight the increasing emphasis on green chemistry in imidazole synthesis.

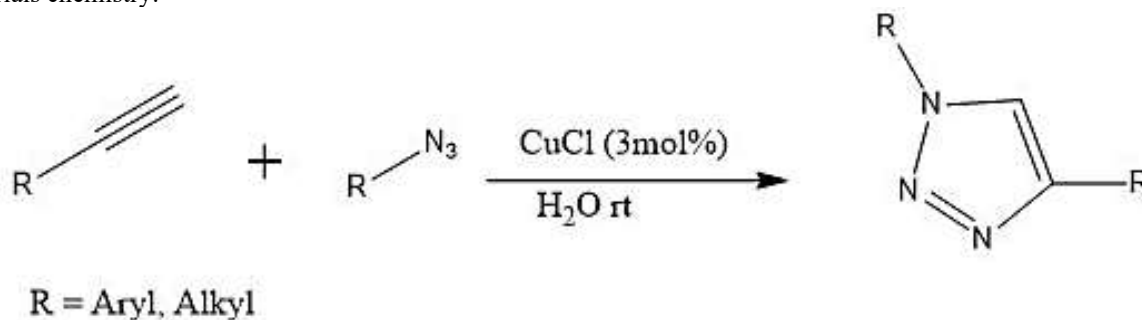


Scheme 6: Eucalyptol-assisted synthesis of diarylimidazo[1,2-a]pyridines

2.1.4 Synthesis of Triazole Derivatives

Triazole derivatives constitute a significant class of nitrogen heterocycles owing to their exceptional biological stability, pharmacological diversity, and ease of synthesis. Akyıldırım et al. [25] successfully synthesized and characterized novel 1,2,4-triazole naphthalene-2-sulfonate derivatives. The compounds demonstrated potent inhibition of α -Gly, α -Amy, AChE, and GST enzymes, significant anticancer activity against HepG2 and U87 cell lines, and strong binding affinities confirmed through molecular docking studies. Karakoyun et al. [26] efficiently synthesized novel mono- and bis-1,2,3-triazole–quinoline derivatives via one-pot azide–alkyne cycloaddition. DFT/TD-DFT studies revealed strong ligand-to-metal charge transfer, significant bathochromic shifts upon metal coordination, and enhanced electronic delocalization, highlighting their potential for tunable optoelectronic applications. Hiroki et al. [27] developed a method to synthesize 1,4-disubstituted 1,2,3-triazoles using copper(I) chloride and 2-ethynylpyridine as a catalyst system. The azide–alkyne cycloaddition proceeds efficiently at room temperature, producing triazole derivatives in high yields. This approach

highlights the versatility of copper-catalyzed click chemistry for triazole synthesis and its importance in medicinal and materials chemistry.



Scheme 8: Copper(I)-catalyzed synthesis of 1,4-disubstituted 1,2,3-triazoles

2.2 Applications of Nitrogen-Containing Heterocycles

Nitrogen-containing heterocycles are essential organic compounds with diverse structures and broad applications in medicine, industry, and materials science. Incorporating nitrogen atoms into cyclic frameworks modifies electronic distribution, polarity, hydrogen-bonding capacity, and biological affinity, enabling interactions with various molecular targets. These properties support their widespread use in pharmaceuticals, polymers, agrochemicals, dyes, corrosion inhibitors, and functional materials. Their structural flexibility and ease of modification make them valuable for developing advanced compounds with significant biological and technological relevance.

2.2.1 Medicinal and Functional Applications of Nitrogen Heterocycles

Nitrogen heterocycles are key pharmacophores in drug discovery, with about 59% of FDA-approved small-molecule drugs containing nitrogen-based heterocyclic frameworks. Structural types such as pyrroles, pyrazoles, imidazoles, triazoles, and pyrazines display diverse biological activities, including antibacterial, antifungal, anti-inflammatory, antihypertensive, anticancer, and neuroprotective effects [28]. Their therapeutic value arises from favorable interactions with biological targets through hydrogen bonding, π - π stacking, and electrostatic forces. Beyond medicine, nitrogen heterocycles are crucial in advanced functional materials. Pyrrole, imidazole, and azine derivatives are used in conductive polymers, electrochemical sensors, fuel cells, batteries, and organic semiconductors due to their excellent electronic and thermal properties [29]. These compounds are also important in agrochemicals, where pyridine, pyrazole, and triazole derivatives provide enhanced fungicidal, herbicidal, and insecticidal activity. Additionally, nitrogen heterocycles are used in dyes, fluorescent probes, and optoelectronic devices for their favorable photophysical properties, and their strong adsorption on metal surfaces makes them effective corrosion inhibitors [30]. The broad biological and functional significance of nitrogen heterocycles highlights the need to develop new nitrogen-rich fused-ring systems with improved physicochemical and pharmacological properties, which is the focus of this study.

Structure	Name	Activity
	Fleroxacin	Antibacterial
	Fenquizone	Antihypertensive
	Piroxicam	Anti-inflammatory

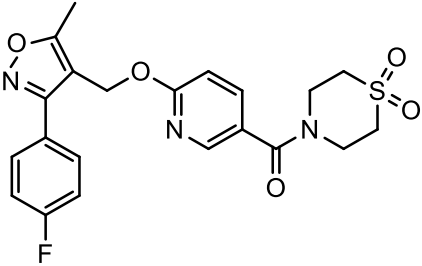
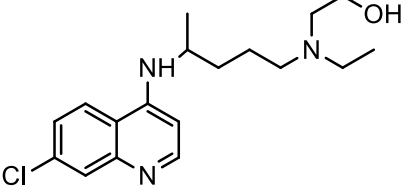
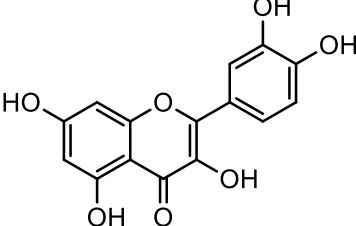
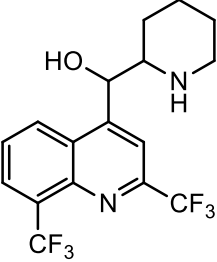
	Basmisanil	Central nervous activity
	Hydroxychloroquine	Antirheumatic
	Quercetin	Antioxidant
	Mefloquine	Antimalarial

Figure 1: Selected medicinal applications of nitrogen-containing heterocycles

3. Pharmacological Significance and Development of a Triamterene Derivative

Triamterene is a potassium-sparing diuretic commonly used to treat hypertension, edema, congestive heart failure, and renal disorders [31]. As a nitrogen-rich pyrazine-based heterocycle, it increases sodium and water excretion while minimizing potassium loss, which lowers the risk of hypokalemia, a frequent side effect of other diuretics. Due to its mild antihypertensive effect, triamterene is often prescribed alone or with thiazide diuretics, especially hydrochlorothiazide, to improve efficacy and maintain electrolyte balance [32].

This study develops a triamterene-derived heterocyclic compound using a multistep synthetic strategy involving nitrosation and cyclization. The synthesis was designed to be simple, economical, and scalable. The resulting derivative was purified and characterized by thin-layer chromatography (TLC), melting point determination, Fourier-transform infrared spectroscopy (FTIR), ¹H nuclear magnetic resonance (¹H NMR), ¹³C nuclear magnetic resonance (¹³C NMR), and mass spectrometry to confirm its structure and successful synthesis.

4. MATERIALS AND METHODS

4.1 Materials

All chemicals and reagents used in the present investigation were of analytical grade and employed without further purification. Aniline, benzyl cyanide (PhCH₂CN), copper (II) chloride (CuCl₂), nitric acid (HNO₃), sulfuric acid (H₂SO₄), sodium bicarbonate (NaHCO₃), sodium methoxide (CH₃ONa), ethanol, petroleum ether, and ethyl acetate. Aniline and other required reagents were procured from the Sigma-Aldrich and used as received. All solvents utilized during synthesis and purification were distilled prior to use to ensure purity and reproducibility of the experimental procedures. Standard laboratory-grade chemicals and glassware were employed throughout the experimental work to ensure reaction consistency and purity under controlled experimental conditions.

4.2 Instrumentation

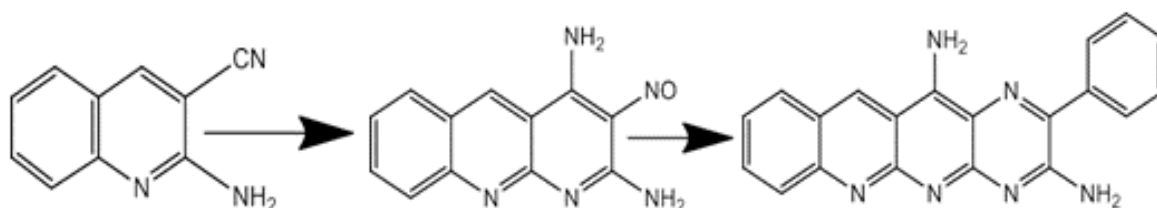
The progress of the reaction was monitored using thin-layer chromatography (TLC) performed on silica gel plates (0.25 mm, 60G F254) with ethyl acetate and petroleum ether as the mobile phase. Melting point determination was carried out using an open capillary digital melting point apparatus and was recorded without correction. Fourier-transform infrared (FTIR) spectra were recorded using KBr pellets in the range of 4000–400 cm⁻¹. ¹H nuclear magnetic resonance (¹H NMR) and ¹³C nuclear magnetic resonance (¹³C NMR) spectra were recorded in DMSO-d₆ using tetramethylsilane (TMS) as the internal standard. Mass spectral analysis was performed using electrospray ionization mass spectrometry (ESI-MS).

4.3 Synthesis of the Triamterene Derivative

4.3.1: Synthesis of 2-Phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine

Precursor 1 was treated with an excess amount of nitrous acid (HNO_2) in ethanol under controlled reaction conditions to generate the corresponding nitroso intermediate. Following completion of nitrosation, the reaction mixture was subjected to intramolecular cyclization using benzyl cyanide (PhCH_2CN) in ethanolic sodium methoxide (CH_3ONa), facilitating the formation of a fused nitrogen-containing heterocyclic framework. The cyclization reaction proceeded efficiently to afford 2-phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine as the desired product.

The progress of the reaction was monitored by thin-layer chromatography (TLC) using silica gel plates (0.25 mm, 60G F254) as the stationary phase, while a mixture of ethyl acetate and petroleum ether served as the mobile phase. Upon completion, the product was isolated and purified according to standard laboratory procedures. The melting point of the synthesized compound was determined using an open-capillary digital melting point apparatus and recorded without correction. Structural characterization of the synthesized derivative was performed using Fourier-transform infrared spectroscopy (FTIR), proton nuclear magnetic resonance (^1H NMR), carbon-13 nuclear magnetic resonance (^{13}C NMR), and mass spectrometry (MS) to confirm the successful formation and molecular integrity of the target heterocyclic compound



Scheme 9. Proposed Synthetic Route for the Preparation of 2-Phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine

4.3.2 Catalytic Transformation and Product Isolation

Following completion of the cyclization step, the reaction mixture was allowed to cool to room temperature prior to catalytic transformation. Subsequently, CuCl_2 (0.5 mmol), HNO_3 (0.5 mL), and H_2SO_4 (0.2 mL) were added directly to the reaction medium under ambient conditions. The resulting mixture was gently stirred at room temperature for 2 h to facilitate the catalytic conversion and promote completion of the reaction. After the reaction period, the mixture was quenched with ice-cold water and carefully neutralized using sodium bicarbonate (NaHCO_3) solution until neutral pH was attained. Formation of a yellow-green precipitate was observed, indicating successful product formation. The crude solid product was subsequently collected by filtration, washed thoroughly to remove residual impurities, and dried overnight at room temperature prior to further purification and characterization. This refined protocol ensured efficient isolation of the synthesized triamterene derivative and improved product recovery for subsequent physicochemical and spectroscopic analyses.

4.4 Characterization of the Synthesized Compound

The synthesized compound was evaluated based on physicochemical properties, reaction yield, melting point, and spectral analyses. The purified derivative was obtained in 78% yield with a melting point range of 115–118 °C. Structural confirmation was performed using FTIR, ^1H NMR, ^{13}C NMR, and mass spectrometry.

Table 1. Physicochemical and spectral characteristics of the synthesized triamterene derivative.

Parameter	Data
Physical appearance	Pale yellow crystalline solid
Melting point	115-118 degrees Celsius
Yield	78%
IR (KBr, cm^{-1})	3395 (N-H), 1815 (N=O), 1612 (C=N), 1254 (C-N)
^1H NMR (400 MHz, DMSO-d_6)	δ 9.85 (s, 1H), 8.47-7.36 (m, 5H, Ar-H), 5.12 (s, 2H, NH_2)
^{13}C NMR (100 MHz, DMSO-d_6)	δ 173.6, 155.3, 144.7, 139.1, 126.9, 114.5, 112.6, 111.4
MS (ESI)	m/z $[\text{M}+\text{H}]^+ = 190.2$ ($\text{C}_{20}\text{H}_{14}\text{N}_6$)

IR (KBr, cm^{-1}): 3395 (N-H), 1815 (N=O), 1612 (C=N), and 1254 (C-N). ^1H NMR (400 MHz, DMSO-d_6): δ 9.85 (s, 1H), 8.47-7.36 (m, 5H, Ar-H), and 5.12 (s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.6, 155.3, 144.7, 139.1, 126.9, 114.5, 112.6, and 111.4.

MS (ESI): m/z $[\text{M}+\text{H}]^+ = 190.2$ ($\text{C}_{20}\text{H}_{14}\text{N}_6$).

5. RESULTS AND DISCUSSION

A triamterene derivative, 2-phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine, was synthesized via a multistep process comprising nitrosation, cyclization, and catalytic transformation under mild conditions. This methodology enabled efficient conversion of the nitrile group while preserving the amine moiety, thereby maintaining the

nitrogen-rich heterocyclic framework. Nitrosation with HNO_2 in ethanol proceeded rapidly, suggesting favorable kinetics and efficient intermediate formation [33]. Subsequent treatment with benzyl cyanide (PhCH_2CN) in ethanolic sodium methoxide (CH_3ONa) facilitated intramolecular cyclization and formation of the fused heterocycle. The use of mild conditions minimized side reactions and contributed to a satisfactory product yield.

The proposed reaction mechanism consists of a three-step transformation, with in situ generation of a cyclized intermediate during the second stage. Formation of 2-phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine is believed to proceed via nucleophilic activation, ring closure, and stabilization of the condensed heterocycle. The methodology demonstrated reproducibility on a 1–10 mmol scale, indicating synthetic robustness and scalability. Thin-layer chromatography (TLC) monitoring confirmed efficient reaction progress and minimal side-product formation.

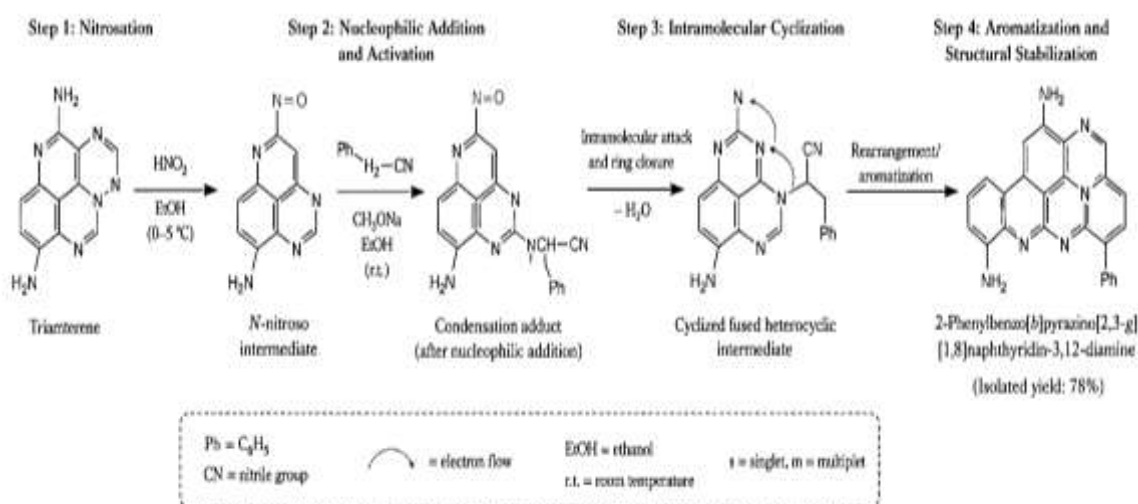
The product was isolated as a pale yellow crystalline solid in 78% yield, with a melting point of 115–118 °C, indicating high purity and crystallinity. The high recovery rate reflects efficient conversion during cyclization and catalytic transformation. Recrystallization from ethanol further enhanced purity and facilitated isolation. Physicochemical characteristics and spectral data are presented in Table 1.

Structural confirmation was achieved using FTIR, ^1H NMR, ^{13}C NMR, and mass spectrometry. FTIR analysis revealed a band at 3395 cm^{-1} , corresponding to N–H stretching and confirming the presence of amino groups. The 1612 cm^{-1} band is consistent with $\text{C}=\text{N}$ stretching, supporting heterocycle formation, while the 1254 cm^{-1} peak is attributed to $\text{C}-\text{N}$ vibrations, confirming nitrogen incorporation. The absence of impurity bands indicates successful purification.

The ^1H NMR spectrum exhibited a singlet at δ 9.85 ppm corresponding to nitrogen-associated protons and aromatic signals at δ 8.47–7.36 ppm, confirming the presence of phenyl groups. The singlet at δ 5.12 ppm was assigned to amino protons (NH_2), indicating retention of amine groups. The ^{13}C NMR spectrum displayed resonances between δ 111.4–173.6 ppm, consistent with aromatic and heterocyclic carbons. Mass spectrometry (ESI-MS) revealed the expected protonated molecular ion peak ($[\text{M}+\text{H}]^+$), confirming successful synthesis.

Table 1. Physicochemical and Spectral Characterization Data of 2-Phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine

Parameter	Observation
Compound Name	2-Phenylbenzo[b]pyrazino[2,3-g][1,8]naphthyridin-3,12-diamine
Appearance	Pale yellow crystalline solid
Isolated Yield (%)	78
Melting Point (°C)	115–118
FTIR (cm^{-1})	3395 (N–H stretching), 1612 ($\text{C}=\text{N}$ stretching), 1254 ($\text{C}-\text{N}$ stretching)
^1H NMR (δ , ppm)	9.85 (s, N-containing proton environment), 8.47–7.36 (m, aromatic protons), 5.12 (s, NH_2)
^{13}C NMR (δ , ppm)	111.4–173.6 (aromatic and heterocyclic carbons)
ESI-MS	Molecular ion peak corresponding to $[\text{M}+\text{H}]^+$ observed
Purification Method	Recrystallization from ethanol
Reaction Scale Tested	1–10 mmol
TLC Monitoring	Single major product spot with minimal side products



Scheme 10: Proposed reaction mechanism of triamterene derivative synthesis

6. CONCLUSION

The present study demonstrates the importance of nitrogen-containing heterocycles in medicinal and functional applications, due to their diverse biological activities and structural versatility. A triamterene-derived heterocycle was synthesized via a simple, cost-effective multistep process involving mild nitrosation and cyclization. The method yielded 78% and proved reproducible and scalable. Structural integrity was confirmed by FTIR, ^1H NMR, ^{13}C NMR, mass

spectrometry, and physicochemical analyses, verifying successful synthesis. Identification of key functional groups and heterocyclic carbon environments confirmed the product's purity. This work offers an efficient approach for synthesizing triamterene-based heterocycles with potential pharmaceutical value. Further biological and molecular studies are recommended to assess the therapeutic potential of the synthesized compound.

Declarations

Acknowledgments

The authors are thankful to the Department of Chemistry, Swami Vivekanand Subharti University, Meerut, India, for providing laboratory and research facilities to carry out this research work.

Funding: The authors received no specific financial support for the research, authorship, and/or publication of this work.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Ethical Approval: This study did not involve human participants, animals, or clinical samples; therefore, ethical approval was not required.

Consent to Participate: Not applicable.

Consent for Publication: All authors have reviewed and approved the manuscript for publication.

Data Availability Statement: The data supporting the findings of this study are available within the article. Additional data may be provided by the corresponding author upon reasonable request.

Author Contributions:

- Conceptualization, Investigation, Writing – Original Draft: Anjali
- Methodology, Data Curation, Review & Editing, Supervision: Shraddha Upadhyay

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