International Journal of Natural Products and Alternative Medicine (IJNPAM)
Website: https://ijnpam.com/
ISSN: 3107-3646
Vol. 2, Issue 1, January-June, 2026
Page No.: 20-27

Research

Design, Synthesis and Characterization of Novel 2,4,5-Trisubstituted Oxazole Derivatives

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DOI: *10.62896/ijnpam.2.1.04*

Conflict of interest: *NIL*

Article History
Received: 12/12/2025
Accepted: 24/03/2026
Published: 31/03/2026

Abstract:
A concise and efficient synthetic methodology for the preparation of substituted oxazole derivatives has been developed using readily accessible α-azido chalcones as key intermediates. The present work describes the synthesis of a series of 2,4,5-trisubstituted oxazole derivatives through a one-pot cyclization reaction involving substituted α-azido chalcones and potassium thiocyanate in the presence of potassium persulfate as an oxidant under mild reaction conditions. The reaction proceeds smoothly in dry acetonitrile under nitrogen atmosphere at 80 °C to afford the corresponding oxazole-2-thiol derivatives in good to excellent yields without the need for column chromatographic purification. Five representative compounds were synthesized and characterized by melting point determination, thin layer chromatography (TLC), infrared spectroscopy (IR), and ^1H NMR spectroscopy. The synthesized compounds showed yields ranging from 89–95% and exhibited spectral characteristics consistent with the proposed structures. The present methodology offers significant advantages such as operational simplicity, shorter reaction time, high product yield, and broad substrate tolerance. The study demonstrates that α-azido chalcones are useful synthons for the construction of highly substituted oxazole frameworks, which are of considerable importance in medicinal chemistry due to their diverse biological activities. This work provides an efficient route for the synthesis of substituted oxazoles and may facilitate future exploration of their pharmacological potential.

Keywords: Oxazole derivatives; α-Azido chalcones; Potassium thiocyanate; Potassium persulfate; Cyclization; Heterocyclic synthesis; Oxazole-2-thiol

1. Introduction

Nitrogen- and oxygen-containing heterocyclic compounds occupy a prominent position in medicinal chemistry, organic synthesis, and pharmaceutical research owing to their diverse structural features and broad spectrum of biological activities. Among these heterocyclic systems, oxazole derivatives represent an important class of five-membered aromatic heterocycles containing one oxygen and one nitrogen atom within the ring system. Oxazole scaffolds are frequently encountered in a wide range of natural products, bioactive molecules, and therapeutic agents. These compounds have been reported to exhibit antimicrobial, anti-inflammatory, analgesic, anticancer, antiviral, antifungal, and antioxidant properties. Due to these pharmacological applications,

the synthesis of structurally diverse and highly substituted oxazole derivatives remains an active area of research in heterocyclic and medicinal chemistry.

Traditionally, several synthetic methods have been employed for the construction of oxazole rings, including cyclodehydration of α-acylaminoketones, Robinson–Gabriel synthesis, Van Leusen oxazole synthesis, and oxidative cyclization strategies. However, many of these methods suffer from limitations such as harsh reaction conditions, use of expensive catalysts, multistep procedures, lower yields, limited substrate scope, or tedious purification processes. Therefore, the development of simple, efficient, and high-yielding methods for the synthesis of substituted oxazole derivatives under mild conditions is of significant interest.

In recent years, α-azido chalcones have emerged as versatile synthetic intermediates for the construction of a variety of heterocyclic frameworks. These compounds readily undergo cyclization and rearrangement reactions due to the presence of the azide functionality and activated olefinic system. The unique reactivity of α-azido chalcones makes them valuable precursors for the synthesis of substituted azirines, oxazoles, pyrazoles, triazoles, and other heterocyclic compounds. The use of thiocyanate ion under oxidative conditions has also attracted attention, as potassium thiocyanate can generate thiocyanate radicals in the presence of oxidants such as potassium persulfate, enabling radical-mediated bond formation and cyclization reactions.

The present study focuses on the synthesis of a series of substituted oxazole derivatives from α-azido chalcones using potassium thiocyanate and potassium persulfate under optimized reaction conditions. The methodology involves the in situ generation of thiocyanate radicals followed by cyclization to furnish 2,4,5-trisubstituted oxazole-2-thiol derivatives in excellent yields. The synthesized compounds were characterized using standard analytical and spectroscopic techniques, including IR and ^1H NMR spectroscopy. The present work aims to provide an efficient synthetic route for substituted oxazoles that can be further explored for biological screening and structure–activity relationship studies.

2. Aim and Objectives

2.1 Aim

To synthesize a series of substituted oxazole derivatives with potential biological activity and to investigate the effect of varying substituents on the oxazole framework.

2.2 Objectives

1. **Design and Synthesis:** To design and synthesize a series of substituted oxazole derivatives using suitable synthetic methodologies and reagents.
2. **Characterization:** To characterize the synthesized compounds by analytical and spectroscopic techniques such as IR and ^1H NMR spectroscopy.
3. **Structure–Activity Relationship (SAR):** To understand the influence of various substituents on the oxazole ring with respect to chemical behavior and potential biological activity.
4. **Preliminary Biological Relevance:** To prepare a compound library suitable for future screening against antimicrobial, anti-inflammatory, or anticancer targets.
5. **Optimization of Synthetic Route:** To optimize reaction conditions in order to improve yield, purity, and practical applicability of the synthetic process.

3. Plan of Work

The research work was carried out according to the following plan:

1. Literature survey related to oxazole synthesis, α-azido chalcones, and nitrile-based cyclization reactions.
2. Design of the synthetic route and study of the probable reaction mechanism for the synthesis of 2,4,5-trisubstituted oxazole derivatives.
3. Procurement of chemicals, reagents, and solvents; ensuring the availability of IR and NMR instrumentation.
4. Synthesis of α-azido chalcones using substituted aldehydes and ketones.
5. Cyclization reaction of α-azido chalcones with potassium thiocyanate under optimized oxidative conditions.
6. Isolation and purification of the final products.

7. Characterization of the synthesized compounds using IR and ^1H NMR spectroscopy.
8. Analysis of spectral data and comparison with reported literature values.
9. Compilation of experimental observations and preparation of the final project/manuscript report.

4. Reaction Scheme

General synthetic strategy for the synthesis of substituted oxazole derivatives:

Substituted α-azido chalcone + potassium thiocyanate + potassium persulfate → (Dry CH_3CN, 80 °C, N_2 atmosphere, 6 h) → Substituted 2,4,5-trisubstituted oxazole-2-thiol derivative

Note: Insert final reaction schemes, substrate scope, and proposed mechanism figures in this section in the final Word manuscript.

5. Materials and Methods

5.1 Chemicals and Solvents

All chemicals and reagents used in the present study were of laboratory reagent (LR) grade and were used without further purification unless otherwise stated.

S. No.	Chemical Name	Grade	Source
1	Vinyl azide / α-Azido chalcone intermediates	LR	Penar Scientific, Nellore
2	Dry acetonitrile	LR	Himalaya Scientific, Nellore
3	Potassium thiocyanate	LR	Nice Chemicals Pvt. Ltd., Kochi
4	Potassium persulfate	LR	Sisco Research Laboratories, Mumbai
5	Acetonitrile	LR	Nice Chemicals Pvt. Ltd., Kochi

5.2 Instrumentation

- Infrared spectra (IR) were recorded on a **BRUKER IR AFFINITY-1** instrument and values are expressed in cm^{-1}.
- Analytical thin layer chromatography (TLC) was performed on silica gel-G coated glass plates.
- Visualization of TLC spots was carried out under UV light or in an iodine chamber.
- TLC monitoring was employed throughout the reactions using suitable solvent systems.
- Hot air oven was used for activation of TLC plates.
- Weighing was performed using a **WERSNAR electronic balance**.
- Reactions were stirred using a **magnetic stirrer (REMI Equipments Pvt. Ltd.)**.
- Vacuum filtration was carried out using a **PRABIVAC vacuum pump**.
- Melting points were determined using a **GUNAS melting point apparatus** and are uncorrected.

5.3 General Methodology

Determination of Melting Point

Capillary tubes containing the dried sample were inserted into the melting point apparatus. The temperature at which the solid completely melted was recorded and reported as the melting point of the compound.

All reactions were performed under prescribed laboratory conditions. The solvents and reagents used in the synthetic work were of laboratory reagent grade. Purity of the compounds was routinely checked by micro TLC. The IR spectra of the compounds were recorded by FT-IR spectroscopy using KBr pellet or neat sample method as appropriate.

6. Synthesis of Substituted Oxazole Derivatives

6.1 General Synthetic Procedure

To a solution of the appropriate substituted α-azido chalcone (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The reaction mixture was stirred magnetically at **80 °C for 6 hours under nitrogen atmosphere**. The progress of the reaction was monitored by TLC. After completion, the solid product that separated from the reaction mixture was filtered, washed with acetonitrile, and dried to afford the corresponding substituted oxazole-2-thiol derivative. In most cases, the products were obtained in analytically pure form without the need for column chromatographic purification.

6.2 Individual Compound Preparation

6.2.1 Preparation of 4-(4-Chlorobenzylideneamino)-5-(4-chlorophenyl)oxazole-2-thiol (3e)

To a solution of **3-(4-chlorophenyl)-1-(4-chlorophenyl)-2-azidoprop-2-en-1-one** (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The mixture was stirred at 80 °C for 6 h under nitrogen atmosphere. After completion of the reaction (TLC monitored), the separated solid was filtered and washed with acetonitrile to obtain **4-(4-chlorobenzylideneamino)-5-(4-chlorophenyl)oxazole-2-thiol**.

6.2.2 Preparation of 4-(3-Bromobenzylideneamino)-5-(4-fluorophenyl)oxazole-2-thiol (3a)

To a solution of **3-(4-fluorophenyl)-1-(3-bromophenyl)-2-azidoprop-2-en-1-one** (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The mixture was stirred at 80 °C for 6 h under nitrogen atmosphere. The product was isolated after filtration and washing with acetonitrile to yield **4-(3-bromobenzylideneamino)-5-(4-fluorophenyl)oxazole-2-thiol**.

6.2.3 Preparation of 4-(4-Chlorobenzylideneamino)-5-(2,4-dichlorophenyl)oxazole-2-thiol (3b)

To a solution of **3-(2,4-dichlorophenyl)-1-(4-chlorophenyl)-2-azidoprop-2-en-1-one** (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The reaction was stirred at 80 °C for 6 h under nitrogen atmosphere. After completion, the solid product was filtered and washed with acetonitrile to obtain **4-(4-chlorobenzylideneamino)-5-(2,4-dichlorophenyl)oxazole-2-thiol**.

6.2.4 Preparation of 5-(3-Bromophenyl)-4-(4-chloro-3-fluorobenzylideneamino)oxazole-2-thiol (3c)

To a solution of **3-(3-bromophenyl)-1-(4-chloro-3-fluorophenyl)-2-azidoprop-2-en-1-one** (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The mixture was stirred at 80 °C for 6 h under nitrogen atmosphere. After completion, the product was filtered and washed with acetonitrile to afford **5-(3-bromophenyl)-4-(4-chloro-3-fluorobenzylideneamino)oxazole-2-thiol**.

6.2.5 Preparation of 4-(2,4-Dichlorobenzylideneamino)-5-phenyloxazole-2-thiol (3d)

To a solution of the corresponding **substituted α-azido chalcone precursor** (1 mmol) in dry acetonitrile (2 mL) were added potassium thiocyanate (3 mmol) and potassium persulfate (0.5 mmol). The reaction mixture was stirred at 80 °C for 6 h under nitrogen atmosphere. After completion, the product was filtered and washed with acetonitrile to yield **4-(2,4-dichlorobenzylideneamino)-5-phenyloxazole-2-thiol**.

Note: The precursor name for compound **3d** in the source draft appears inconsistent and should be verified before submission.

7. Experimental Characterization

7.1 Compound 3a

(E)-4-(3-Bromobenzylideneamino)-5-(4-fluorophenyl)oxazole-2-thiol

- **Color:** Yellow
- **Melting Point:** 251–253 °C
- **Yield:** 0.196 g (90%)
- **Rf Value:** 0.2–0.6
- **IR (neat, cm^{-1}):** 3450, 2914, 2335, 1643, 653
- **^1H NMR (400 MHz, DMSO-d_6):** δ 14.03 (s, 1H), 8.64 (s, 1H), 7.95–8.00 (m, 3H), 7.87 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.39 (t, J = 8.8 Hz, 2H)

IR Interpretation:

- 3450 cm^{-1}: S–H stretching
- 2914 cm^{-1}: Aromatic/aliphatic C–H stretching
- 2335 cm^{-1}: Weak overtone/combination band or CO_2
- 1643 cm^{-1}: C=N stretching (imine)
- 653 cm^{-1}: C–Br / C–F region (haloaromatic substitution)

^1H NMR Interpretation:

- δ 14.03 (s, 1H): Thiol proton (–SH)
- δ 8.64 (s, 1H): Imine proton (–CH=N–)
- δ 7.95–8.00 (m, 3H): Aromatic protons
- δ 7.87 (d, 1H): Aromatic proton
- δ 7.77 (d, 1H): Aromatic proton
- δ 7.53 (t, 1H): Aromatic proton

- δ 7.39 (t, 2H): Aromatic protons

7.2 Compound 3b

(E)-4-(4-Chlorobenzylideneamino)-5-(2,4-dichlorophenyl)oxazole-2-thiol

- **Color:** Yellow
- **Melting Point:** 228–230 °C
- **Yield:** 0.195 g (89%)
- **Rf Value:** 0.2–0.6
- **IR (neat, cm⁻¹):** 3070, 2351, 1483, 1204, 663
- **^1H NMR (400 MHz, DMSO-d₆):** δ 14.14 (s, 1H), 10.01 (s, 1H), 7.99–7.92 (m, 4H), 7.73–7.65 (m, 3H)

IR Interpretation:

- 3070 cm⁻¹: Aromatic C–H stretching
- 2351 cm⁻¹: Weak overtone/combination band or CO_2
- 1483 cm⁻¹: Aromatic C=C stretching
- 1204 cm⁻¹: C–N / ring-associated stretching
- 663 cm⁻¹: C–Cl stretching

^1H NMR Interpretation:

- δ 14.14 (s, 1H): Thiol proton (–SH)
- δ 10.01 (s, 1H): Imine proton (–CH=N–)
- δ 7.99–7.92 (m, 4H): Aromatic protons
- δ 7.73–7.65 (m, 3H): Aromatic protons

7.3 Compound 3c

(E)-5-(3-Bromophenyl)-4-(4-chloro-3-fluorobenzylideneamino)oxazole-2-thiol

- **Color:** Yellow
- **Melting Point:** 263–265 °C
- **Yield:** 0.191 g (89%)
- **Rf Value:** 0.2–0.6
- **IR (neat, cm⁻¹):** 3089, 2324, 1483, 1188, 1091
- **^1H NMR (400 MHz, DMSO-d₆):** δ 14.13 (s, 1H), 8.73 (s, 1H), 8.41 (d, J = 1.8 Hz, 1H), 8.14 (dd, J = 1.9, 8.4 Hz, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.82–7.80 (m, 4H)

IR Interpretation:

- 3089 cm⁻¹: Aromatic C–H stretching
- 2324 cm⁻¹: Weak overtone/combination band or CO_2
- 1483 cm⁻¹: Aromatic C=C stretching
- 1188 cm⁻¹: C–F stretching
- 1091 cm⁻¹: Ring-associated C–N / C–O stretching

^1H NMR Interpretation:

- δ 14.13 (s, 1H): Thiol proton
- δ 8.73 (s, 1H): Imine proton
- δ 8.41 (d, 1H): Aromatic proton
- δ 8.14 (dd, 1H): Aromatic proton
- δ 7.85 (d, 1H): Aromatic proton
- δ 7.82–7.80 (m, 4H): Aromatic protons

7.4 Compound 3d

(E)-4-(2,4-Dichlorobenzylideneamino)-5-phenyloxazole-2-thiol

- **Color:** Orange solid
- **Melting Point:** 251–253 °C
- **Yield:** 0.20 g (93%)
- **Rf Value:** 0.2–0.6
- **IR (neat, cm⁻¹):** 3076, 2335, 1516, 1188, 1062
- **^1H NMR (400 MHz, DMSO-d₆):** δ 14.30 (s, 1H), 8.95 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 7.2 Hz, 2H), 7.77 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.54 (t, J = 7.2 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H)

IR Interpretation:

- 3076 cm⁻¹: Aromatic C–H stretching
- 2335 cm⁻¹: Weak overtone/combination band or CO_2
- 1516 cm⁻¹: Aromatic C=C stretching
- 1188 cm⁻¹: C–N / ring-associated stretching
- 1062 cm⁻¹: C–Cl stretching region

^1H NMR Interpretation:

- δ 14.30 (s, 1H): Thiol proton
- δ 8.95 (s, 1H): Imine proton
- δ 8.18 (d, 1H): Aromatic proton
- δ 7.98 (d, 2H): Aromatic protons
- δ 7.77 (s, 1H): Aromatic proton
- δ 7.59 (d, 1H): Aromatic proton
- δ 7.54 (t, 2H): Aromatic protons
- δ 7.43 (t, 1H): Aromatic proton

7.5 Compound 3e

(E)-4-(4-Chlorobenzylideneamino)-5-(4-chlorophenyl)oxazole-2-thiol

- **Color:** Yellow
- **Melting Point:** 228–230 °C
- **Yield:** 0.21 g (95%)
- **Rf Value:** 0.3–0.5
- **IR (neat, cm⁻¹):** 3450, 2914, 2335, 1643, 653
- **^1H NMR (400 MHz, DMSO-d₆):** δ 14.03 (s, 1H), 8.64 (s, 1H), 7.95–8.00 (m, 3H), 7.87

(d, J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.39 (t, J = 8.8 Hz, 2H)

IR Interpretation:

- 3450 cm^{-1}: S–H stretching
- 2914 cm^{-1}: C–H stretching
- 2335 cm^{-1}: Weak overtone/combination band or CO_2
- 1643 cm^{-1}: C=N stretching
- 653 cm^{-1}: C–Cl stretching

^1H NMR Interpretation:

- δ 14.03 (s, 1H): Thiol proton
- δ 8.64 (s, 1H): Imine proton
- δ 7.95–8.00 (m, 3H): Aromatic protons
- δ 7.87 (d, 1H): Aromatic proton
- δ 7.77 (d, 1H): Aromatic proton
- δ 7.53 (t, 1H): Aromatic proton
- δ 7.39 (t, 2H): Aromatic protons

8. Results and Discussion

In continuation of our studies directed toward the development of efficient strategies for the synthesis of new heterocyclic compounds, the reactivity of α-azido chalcones was explored for the construction of substituted oxazole derivatives. In the present investigation, a series of 2,4,5-trisubstituted oxazole-2-thiol derivatives were synthesized through an efficient one-pot cyclization of substituted α-azido chalcones with potassium thiocyanate in the presence of potassium persulfate under mild reaction conditions.

The reaction was found to proceed efficiently in dry acetonitrile at 80 °C under nitrogen atmosphere, furnishing the desired products in high yields (89–95%). The transformation is believed to proceed through the in situ generation of a thiocyanate radical from potassium thiocyanate under oxidative conditions. Potassium persulfate acts as an efficient oxidant and is essential for the success of the reaction. In the absence of potassium persulfate, no significant product formation was observed, indicating its crucial role in promoting radical generation and subsequent cyclization.

Thiocyanate ion is a versatile ambident nucleophile and can participate in radical reactions through sulfur or nitrogen. Based on the observed reactivity and previously reported radical-mediated mechanisms, it is proposed that the thiocyanate radical interacts with the azirine or related intermediate generated from the α-azido chalcone precursor. Subsequent bond cleavage, rearrangement, and cyclization lead to formation of the oxazole ring system. This pathway accounts for the observed C–N and C–O bond formation leading to the substituted oxazole-2-thiol products.

A significant advantage of the present synthetic method is that the products were generally obtained as precipitated solids directly from the reaction medium, enabling easy isolation by simple filtration. In most cases, no column chromatographic purification was required, making the process operationally simple, economical, and suitable for scale-up. The products were obtained in analytically pure form after washing with acetonitrile or simple recrystallization where required.

The synthesized compounds were characterized by melting point, TLC, IR spectroscopy, and ^1H NMR spectroscopy. The IR spectra consistently showed characteristic absorptions attributable to the thiol group (–SH), aromatic C–H stretching, imine C=N stretching, and haloaromatic functionalities depending on the substituents present. In the ^1H NMR spectra, the thiol proton appeared as a highly deshielded singlet in the region of δ 14.0–14.3 ppm, while the imine proton appeared as a singlet in the range of δ 8.6–10.0 ppm. Aromatic protons appeared in the expected downfield region depending on the nature and position of halogen substitution.

The scope of the reaction was examined using different substituted α-azido chalcones containing electron-withdrawing substituents such as chloro, bromo, and fluoro groups. All substrates reacted smoothly under the optimized conditions to afford the corresponding oxazole derivatives in good to excellent yields, demonstrating the tolerance of the method toward various halogen substituents. Among the synthesized compounds, **4-(4-chlorobenzylideneamino)-5-(4-chlorophenyl)oxazole-2-thiol (3e)** gave the highest isolated yield of **95%**, indicating that para-chloro substitution on both aryl rings is highly favorable under the present reaction conditions.

8.1 Summary of Synthesized Compounds

S. No.	Compound Code	Compound Name	Conditions	Yield
1	3e	4-(4-Chlorobenzylideneamino)-5-(4-chlorophenyl)oxazole-2-thiol	KSCN, $K_2S_2O_8$, CH_3CN, 80 °C, 6 h	0.21 g (95%)
2	3a	4-(3-Bromobenzylideneamino)-5-(4-fluorophenyl)oxazole-2-thiol	KSCN, $K_2S_2O_8$, CH_3CN, 80 °C, 6 h	0.196 g (90%)
3	3b	4-(4-Chlorobenzylideneamino)-5-(2,4-dichlorophenyl)oxazole-2-thiol	KSCN, $K_2S_2O_8$, CH_3CN, 80 °C, 6 h	0.195 g (89%)
4	3c	5-(3-Bromophenyl)-4-(4-chloro-3-fluorobenzylideneamino)oxazole-2-thiol	KSCN, $K_2S_2O_8$, CH_3CN, 80 °C, 6 h	0.191 g (89%)
5	3d	4-(2,4-Dichlorobenzylideneamino)-5-phenyloxazole-2-thiol	KSCN, $K_2S_2O_8$, CH_3CN, 80 °C, 6 h	0.20 g (93%)

Overall, the present method represents an efficient and practical approach for the synthesis of substituted oxazole derivatives from α-azido chalcones under mild oxidative conditions. The synthetic protocol is notable for its simplicity, high yields, minimal purification requirements, and broad applicability to structurally varied substrates.

9. Conclusion

In the present study, an efficient and practical methodology has been successfully developed for the synthesis of substituted oxazole derivatives from α-azido chalcones using potassium thiocyanate in the presence of potassium persulfate under mild reaction conditions. The reaction proceeds through a convenient one-pot cyclization process in dry acetonitrile at 80 °C under nitrogen atmosphere, affording a series of 2,4,5-trisubstituted oxazole-2-thiol derivatives in good to excellent yields.

The developed method offers several advantages, including operational simplicity, short reaction time, excellent isolated yields, and avoidance of tedious column chromatographic purification. The synthesized compounds were successfully characterized by melting point determination, TLC, IR spectroscopy, and ^1H NMR spectroscopy, and the obtained spectral data were in agreement with the proposed structures. The presence of characteristic thiol and imine functionalities in the final products was confirmed through spectroscopic analysis.

The results indicate that the reaction is highly effective for a range of substituted α-azido chalcones bearing electron-withdrawing groups such as chloro, bromo, and fluoro substituents. Among the synthesized derivatives, **4-(4-chlorobenzylideneamino)-5-(4-chlorophenyl) oxazole-2-thiol** exhibited the highest yield of **95%** under the optimized conditions. Mechanistically, the reaction is believed to proceed via in situ generation of a thiocyanate radical followed by cyclization to form the oxazole ring system.

Since oxazole derivatives are important heterocyclic scaffolds with wide-ranging biological significance, the present methodology provides a valuable synthetic route for the rapid generation of structurally diverse oxazole analogues. The synthesized compounds may serve as useful candidates for future biological evaluation, including antimicrobial, anti-inflammatory, and anticancer screening. Further studies may focus on expanding substrate scope, derivatization of the thiol group, and systematic biological assessment to establish structure–activity relationships.

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