

RESEARCH PAPER

Multicomponent Synthesis of 4H-pyrimido[2,1-b]benzothiazoles Using Ionic Liquid-Functionalized Graphene Oxide Catalyst and Their Antibacterial Evaluation

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ABSTRACT

A green and efficient multicomponent strategy has been developed for the synthesis of 4H-pyrimido[2,1-b]benzothiazole derivatives employing graphene oxide nanosheets functionalized with an acidic ionic liquid (GO-Si-Pr-Creatinine-SO₃H) as a reusable heterogeneous catalyst. The catalyst was synthesized through surface modification of graphene oxide with 3-chloropropyltrimethoxysilane, subsequent immobilization of creatinine, and sulfonation. Its structure and morphology were confirmed by FT-IR, XRD, SEM, and EDX analyses. The condensation of 2-aminobenzothiazole, aromatic aldehydes, and β -ketoesters under solvent-free conditions afforded the target products in excellent yields (92–98%) within 20–40 min at 80–90 °C, requiring only moderate catalyst loading (30–40 mg). The reaction mechanism proceeds through in-situ Knoevenagel condensation, Michael addition, and intramolecular cyclization, in which the catalyst acts as a Lewis acid to activate carbonyl groups. The catalyst demonstrated outstanding reusability for at least seven consecutive cycles with minimal loss of activity. The synthesized derivatives were fully characterized by FT-IR, ¹H-NMR, and ¹³C-NMR spectroscopy. Biological evaluation against representative Gram-positive and Gram-negative bacterial strains revealed notable antibacterial activity, comparable to standard pharmaceutical agents, underscoring the potential of this methodology in sustainable heterocyclic synthesis and biomedical applications.

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INTRODUCTION

Graphene oxide (GO), composed of two carbon layers with a closed lattice structure, has attracted growing interest in the field of catalysis, both as a catalyst and as a catalytic support. This is primarily due to the presence of active functional groups on its surface, its large surface

area, and its excellent thermal and mechanical properties. The high catalytic performance of GO is mainly attributed to the presence of hydroxyl, carboxyl, and epoxy groups, which provide strong acidity and outstanding oxidative capability.[1-3] Functionalization of graphene oxide (GO) with acidic ionic liquids (AILs) generates hybrid catalysts

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characterized by the presence of strong Brønsted acid sites on a highly dispersed nanostructured surface, while retaining the mechanical and thermal properties of the carbon framework.[4] This modification enhances the catalytic activity in cyclocondensation reactions and fused heterocyclic ring-forming processes, while improving stability and enabling reusability over multiple reaction cycles without significant loss of performance, thereby aligning this approach with the principles of green chemistry.[5] Multicomponent reactions (MCRs) represent one of the fundamental pillars of modern synthetic organic chemistry, owing to their ability to combine three or more starting materials in a single reaction medium to produce products with complex molecular architectures, while achieving high atom economy, excellent selectivity, and minimizing secondary synthetic steps. [6] This synthetic strategy offers an efficient approach for the rapid construction of heterocyclic compounds, which constitute one of the most important research areas in the design of pharmaceutical agents and biologically active materials[7] Pyrimido[2,1-b]benzothiazole derivatives have attracted considerable research interest due to their broad spectrum of biological activities, encompassing anti-tumor[8-10] anti-viral[11] anti-fungal[12] anti-bacterial[13] anti-allergic[14] and anti-inflammatory[15-18] properties, as well as their potential to inhibit lung cancer [19] Based on the above, this study aims to develop a multicomponent synthetic pathway for the preparation of 4H-pyrimido[2,1-b]benzothiazole derivatives via a condensation reaction between 2-aminobenzothiazole, aromatic aldehydes, and β -ketoesters,[20] employing acidic ionic liquid-functionalized graphene oxide (GO) as a heterogeneous catalytic medium. The work will also investigate the factors influencing the yield and selectivity of the reaction, characterize both the catalyst[21] and the synthesized compounds using various spectroscopic and analytical techniques, and evaluate the antibacterial activity of the resulting series against Gram-positive and Gram-negative bacterial strains, with the objective of identifying molecules with promising pharmaceutical potential [22].

MATERIALS AND METHODS

General remarks

The samples were analyzed by X-ray diffraction (XRD) using a PANalytical X'Pert PRO instrument

(Cu K α , $\lambda = 1.5406 \text{ \AA}$) with a scan range of 20° to 80° at a rate of 1°/min. Morphology and structure were examined by scanning electron microscopy (SEM), and chemical composition was determined by EDX attached to SEM. Fourier-transform infrared (FT-IR) spectra were recorded using a Shimadzu ATR-FTIR spectrometer, while ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained on a Bruker 500 MHz instrument using DMSO-d₆ as the solvent. All chemicals were used without further purification.

Providing of graphene Oxide (GO) nanosheets [23]

Using the optimized Hummer's method, graphene oxide (GO) nanosheets were synthesized from graphite powder. In a typical procedure, 10.0 g of graphite powder and 5.0 g of NaNO₃ were mixed with 230 mL of concentrated H₂SO₄ (98%) in a 2500 mL flask equipped with a condenser and magnetic stirrer, and placed in an ice bath. The resulting mixture was stirred, and 30.0 g of KMnO₄ was slowly added. The mixture was then stirred for 2 h. Afterwards, the flask was transferred to a water bath at 35 °C and stirred for an additional 30 min. Subsequently, 460 mL of deionized water was gradually added while maintaining the temperature at approximately 98 °C, followed by stirring for 15 min. To terminate the oxidation reaction, 1400 mL of deionized water and 100 mL of hydrogen peroxide (30%) were added sequentially. The resulting mixture was purified by washing with hydrochloric acid (5 v/v%) and then with deionized water several times. Filtration was carried out under reduced pressure using a sintered-glass funnel (G4) connected to a vacuum pump. The obtained graphite oxide was dried in a vacuum oven at 60 °C for 12 h. Finally, the graphite oxide was dispersed in water to prepare a 0.5 mg mL⁻¹ suspension, which was subjected to ultrasonic irradiation (45 W) for 30 min to exfoliate the layers into graphene oxide nanosheets. The suspension was then centrifuged at 3500 rpm for 30 min to remove any unexfoliated graphite oxide.

Synthesis of the GO-Si-Pr-Cl [24]

The synthesis process involved dispersing graphene oxide (GO) nanosheets in a two-neck round-bottom flask equipped with a condenser and magnetic stirrer, maintained under a nitrogen atmosphere. A mixture of 2.0 g GO nanosheets and 10.0 mL of 3-chloropropyltrimethoxysilane was added to 50 mL of anhydrous toluene as the

solvent, and the reaction mixture was refluxed for 6 hours. Upon completion, the mixture was gradually cooled to room temperature, followed by filtration through a sintered glass funnel and washing with dry toluene. The obtained functionalized graphene oxide, designated as GO-Si-Pr-Cl, was subsequently stored in a desiccator under nitrogen atmosphere until further use.

Synthesis of the GO-Si-Pr-Creatinne-SO₃H [25]

In a 200 mL flask equipped with a magnetic stirrer and condenser, under a continuous nitrogen atmosphere, lysine monohydrochloride (6.0 mmol), GO-Si-Pr-Cl (1.0 g), and triethylamine (Et₃N, 0.4 mL) were added to 50 mL of dry ethanol. The reaction mixture was stirred at 60 °C for 8 hours. Upon completion, the solid was washed and filtered sequentially with 10% aqueous sodium bicarbonate (NaHCO₃), warm water, and ethanol (4 portions of 5 mL each). The resulting GO-Si-Pr-Creatine-Cl was obtained as a dark solid after drying overnight in a vacuum oven at 60 °C. Subsequently, the dried GO-Si-Pr- Creatine -Cl was transferred to a 200 mL flask equipped with a magnetic stirrer and condenser, purged with nitrogen gas, and treated with chlorosulfonic acid (ClSO₃H, 2.0 mmol) and absolute ethanol (25 mL) at 40 °C for 24 hours under stirring. Afterward, 1.0 mL of concentrated sulfuric acid (H₂SO₄) was added, and the mixture was stirred for an additional 3 hours. The solid GO-Si-Pr- Creatine -SO₃H catalyst was then washed thoroughly with water and ethanol, followed by drying at 100 °C for 12 hours.

*General method for the preparation of 4H-Pyrimido[2,1-*b*]benzothiazole using GO-Si-Pr-Creatine-SO₃H [26]*

A mixture of 2-aminobenzothiazole (1 mmol), an aldehyde (1 mmol), ethyl acetoacetate (1 mmol), and GO-Si-Pr-Creatine-SO₃H catalyst (0.02 g) was stirred under solvent-free conditions at 90 °C. The progress of the reaction was monitored by thin-layer chromatography (TLC) using n-hexane:ethyl acetate (7:3) as the eluent. Upon completion, the reaction mixture was dissolved in 5 mL of ethanol, and the catalyst was separated using centrifuge. Subsequently, water (1 mL) was added dropwise to the solution, resulting in the precipitation of the pure product as a solid in high yield. The recovered catalyst was washed three times with chloroform, dried, and reused in subsequent reaction cycles

under identical conditions.

Synthesis of Hydrazide Compounds (2) [27]

A mixture of the esters (1) (0.1 mol) and hydrazine hydrate (80%, 0.05 mol) was refluxed in absolute ethanol (100 mL) for 10 h. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion, the reaction mixture was cooled to room temperature and concentrated under reduced pressure to approximately one-third of its original volume. The precipitate formed was filtered, washed thoroughly, and dried at room temperature. The crude product was recrystallized from ethanol to afford the pure hydrazide derivatives. The melting point was found to be 165-167 °C. The Yield obtaind was 81 %, Color Yellow.

Synthesis of Hydrazones Compounds(3) [28]

An equimolar mixture of hydrazides (2) (0.005 mol) and dialdehyde (2-chloro-3-formyl quinoline) (0.005 mol) was refluxed in absolute ethanol (20 mL) in the presence of a few drops of glacial acetic acid for 3 h. Upon completion, the solvent was evaporated under reduced pressure, and the resulting residue was poured onto crushed ice and allowed to stand to ensure complete precipitation. The solid product was filtered, washed thoroughly, and recrystallized from ethanol to afford the corresponding Schiff base derivatives in pure form. The melting point was found to be 211-113 °C. The Yield obtaind was 70 %, Color Orange.

Synthesis of Thiazolidines Compounds(4) [29]

An equimolar mixture of hydrazones (3) (8 mmol) and glycolic acid (8 mmol) was dissolved in absolute ethanol (20 mL). To this solution, anhydrous zinc chloride (8 mmol) was added, and the reaction mixture was refluxed for 8 h with the progress monitored by thin-layer chromatography (TLC). After completion, the solvent was evaporated under reduced pressure, and the resulting precipitate was filtered, washed with water, and recrystallized from ethanol to afford the cyclized heterocyclic derivatives in pure form. The melting point was found to be gum. The Yield obtaind was 56 %, Color Brown.

Synthesis of Tetrazole Compounds(5) [30]

The reaction mixture was prepared by combining equimolar amounts (6 mmol) of hydrazone (3) and sodium azide in 15 mL of

tetrahydrofuran (THF) and heated in a water bath for 12 hours. Upon completion of the reaction, the solvent was removed using a rotary evaporator, the resulting precipitate was washed with water, and the product was recrystallized from ethanol to obtain the pure compound. The melting point was found to be 277-279 °C. The Yield obtained was 53 %, Color Brown.

Antibacterial Activity of the Synthesized compounds [31-33]

The antibacterial activity of the newly synthesized compounds (3,4) was evaluated against two Gram-positive bacteria, in addition to the Gram-negative bacteria *Escherichia coli*

and *Pseudomonas aeruginosa*, at two different concentrations (10 and 1 mg) using the disc diffusion method. Ciprofloxacin was employed as a reference standard by measuring the diameter of the inhibition zone after 24 hours of incubation at 37 °C. This study aimed to assess the effectiveness of the synthesized compounds against both Gram-positive and Gram-negative bacterial strains at the selected concentrations.

General method for the reusability of the catalyst [34]

The recovery and reuse of catalysts hold significant importance from both economic and industrial standpoints. The reusability of GO-Si-

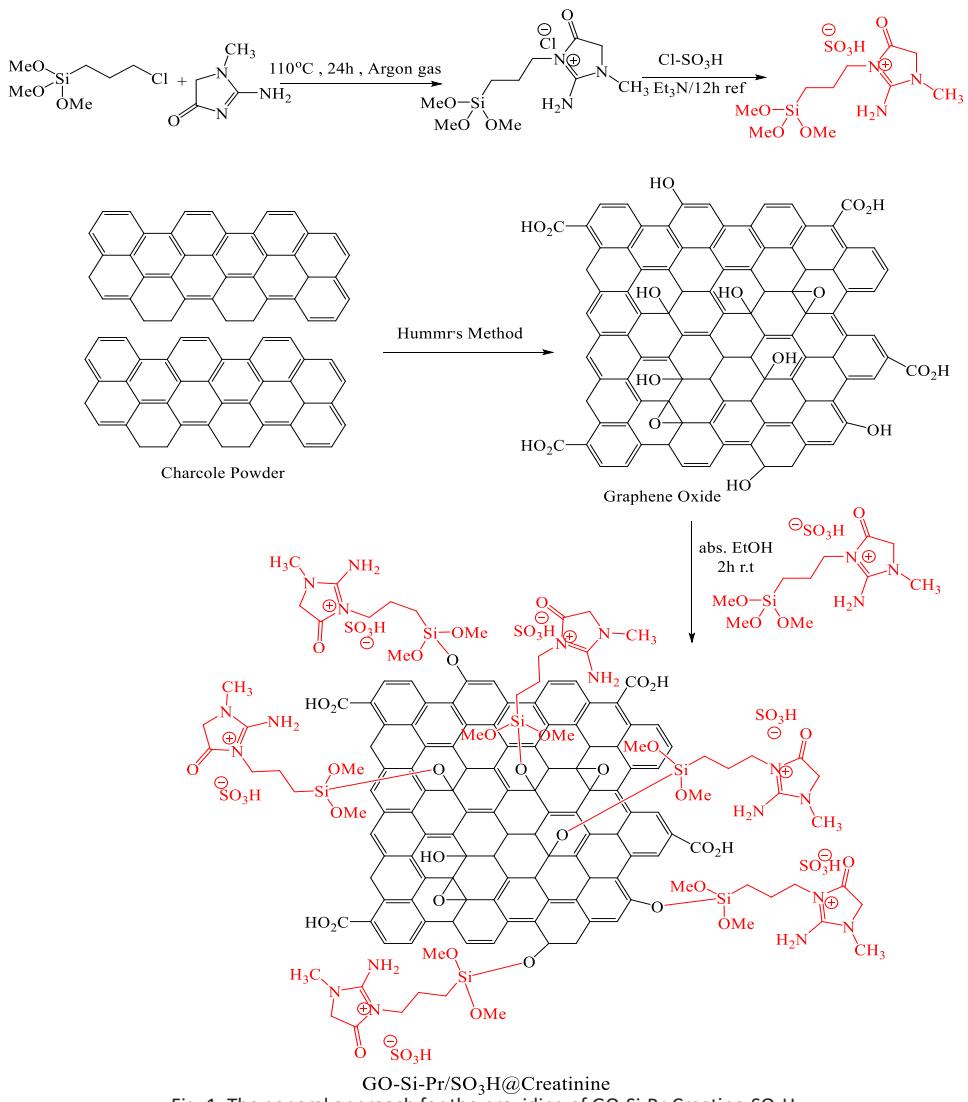


Fig. 1. The general approach for the providing of GO-Si-Pr-Creatinine-SO₃H.

Pr-Creatine-SO₃H was evaluated in the reaction involving 2-aminobenzothiazole, dimedone (2), and 2,4-dichlorobenzaldehyde, using 30 mg of GO-Si-Pr-Creatine-SO₃H as the catalyst. Upon completion of each catalytic cycle, 30 mL of hot ethyl acetate was added, and the catalyst along with any unreacted starting materials was separated by filtration. For regeneration, the recovered GO-Si-Pr-Creatine-SO₃H was thoroughly washed with ethanol and water, followed by drying at 80 °C overnight.

RESULTS AND DISCUSSION

Preparation of GO-Si-Pr-Creatine-SO₃H

Initially, GO-Si-Pr-Creatine-SO₃H was developed and introduced as an efficient heterogeneous catalyst for the synthesis of 4H-Pyrimido[2,1-b]

benzothiazole derivatives (Fig. 1). The preparation began with graphene oxide nanosheets, synthesized according to the procedure reported in the literature[23]. Subsequently, 3-chloropropyltrimethoxysilane was covalently anchored onto the surface of the nanosheets. Thereafter, Creatine monohydrochloride was immobilized onto GO-Si-Pr-Cl, followed by a two-step sulfonation process (step I: treatment with ClSO₃H; step II: treatment with H₂SO₄), which afforded the desired GO-Si-Pr-Creatine-SO₃H catalyst. The complete experimental details for the preparation of this catalyst are provided in the experimental section.

Characterization of the GO-Si-Pr-Creatine-SO₃H

The FT-IR spectrum of graphene oxide (GO)

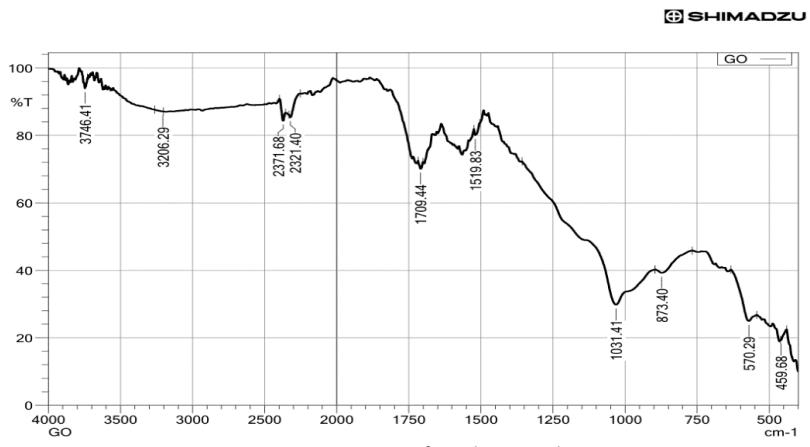


Fig. 2. FT-IR spectra of graphene Oxide.

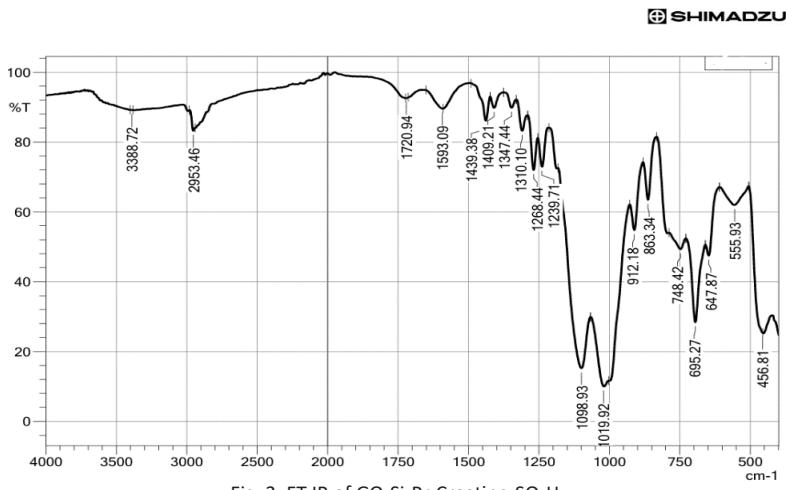


Fig. 3. FT-IR of GO-Si-Pr-Creatine-SO₃H.

exhibited a distinct band corresponding to the hydroxyl group (O–H) at 3206.64 cm^{−1}, in addition to a broad band in the range of 3206.6–2500 cm^{−1} assigned to carboxylic hydroxyl groups. Two additional bands appeared within 1709–1031 cm^{−1}, attributed to the stretching vibrations of C=O and C–O groups of the carboxylic carbonyl, respectively. Moreover, bands in the range of 1519–1031 cm^{−1} were assigned to the C=C stretching vibration, which indicates the typical carbon framework of graphene oxide. In the case of silanized graphene oxide (functionalized GO), new absorption peaks confirmed the successful immobilization. The bands at 3388.7–1593 cm^{−1} were associated with N–H and C–N vibrations, confirming the attachment of the amino acid to the GO surface. Additionally, absorption peaks at 2953–2873 cm^{−1} were attributed to the methylene groups (−CH₂−) of the CPTMS moiety. Furthermore, the absorption bands observed at 1098 cm^{−1} and 1019–912 cm^{−1} corresponded to the stretching vibrations of Si–O–Si and Si–O–C

bonds, respectively, providing clear evidence for the successful anchoring of silane units onto the GO surface (Figs 2 and 3).

The X-ray diffraction (XRD) patterns of both graphene oxide (GO) powder and silylated graphene oxide are presented in Figs. 4 and 5, respectively. For GO, a sharp diffraction peak was observed at $2\theta = 10^\circ$, which is attributed to the presence of oxygen-containing functional groups such as –COOH and –OH, indicating effective oxidation and the formation of active functional sites on the surface. The absence of other sharp peaks suggests that the sample may contain amorphous regions or that the crystalline phase is irregular. In the case of silylated graphene oxide, after functionalization with 3-chloropropyltrimethoxysilane, a significant decrease in the intensity of the original peak at $2\theta = 10^\circ$ was observed [35], along with the appearance of a new broad and weak peak at $2\theta = 21.43^\circ$, which is close to the crystalline pattern of reduced graphene oxide. This change indicates that most of the oxygen-containing functional

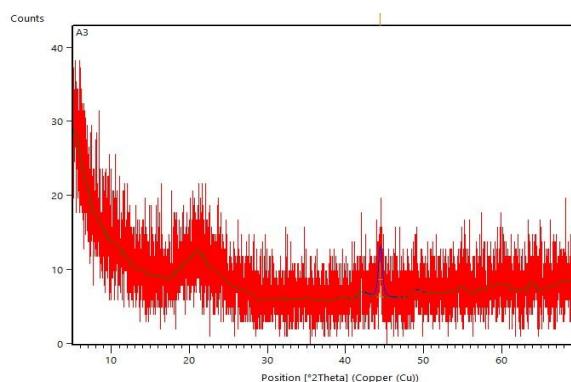


Fig. 4. XRD pattern of GO nanosheets.

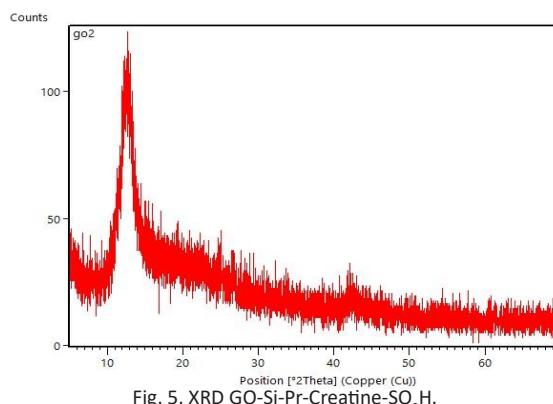


Fig. 5. XRD GO-Si-Pr-Creatine-SO₃H.

groups in GO were successfully anchored during the silylation process.

The scanning electron microscopy (SEM) analysis of graphene oxide (GO) and the catalyst (GO-Si-Pr-Creatinine-SO₃H) revealed distinct morphological features. The GO sample displayed irregular, flaky, and layered structures with pronounced multilayered stacking, which is characteristic of materials possessing a sheet-like architecture. The surface irregularities and distortions observed provide clear evidence of the chemical modifications induced by the oxidation process, leading to the incorporation of oxygen-containing functional groups. In contrast, the morphology of (GO-Si-Pr-Creatinine-SO₃H) exhibited a significant structural transformation

compared to pristine GO. The attachment of silane-linked organic units caused the disruption of the regular layered arrangement, resulting in a more heterogeneous surface with enhanced textural properties [36]. This morphological modification is highly beneficial for catalytic applications, as it increases the available surface area, enhances accessibility of active sites, and provides a more favorable environment for interactions with reactant molecules.

Energy-dispersive X-ray spectroscopy (EDX) analysis was performed to determine the elemental composition of the sample. The results revealed the presence of carbon, oxygen, silicon, chlorine, nitrogen, and sulfur. Carbon exhibited the highest weight percentage (35.67%), followed by oxygen

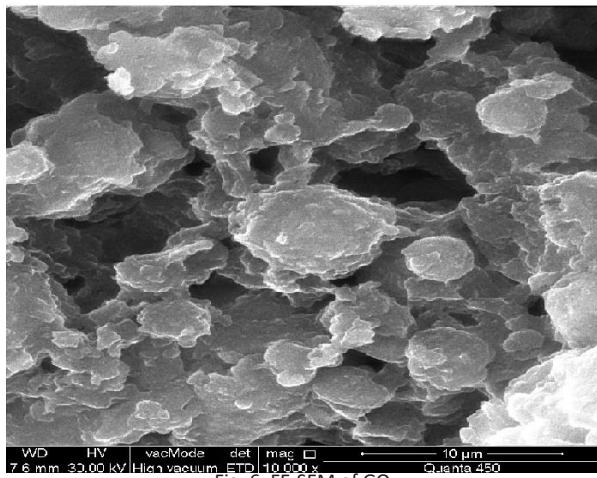


Fig. 6. FE-SEM of GO.

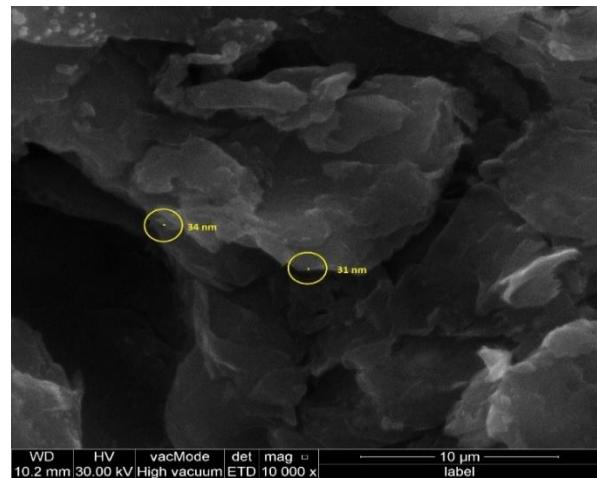


Fig. 7. SEM of GO-Si-Pr-Creatinine-SO₃H.

(27.14%), silicon (19.30%), and chlorine (15.02%), whereas lower percentages were recorded for nitrogen (4.19%) and sulfur (0.45%). These findings indicate that the sample possesses a hybrid organic–inorganic nature, with the organic fraction being rich in carbon and oxygen, while silicon and chlorine represent the inorganic components. The detection of nitrogen suggests the incorporation of

nitrogen-containing functional groups within the structure, although its relatively low percentage may be attributed to its limited concentration or heterogeneous distribution in the material. The trace amount of sulfur implies that it is a minor constituent, possibly associated with residual reagents or impurities from the synthesis process as shown in reference [37].

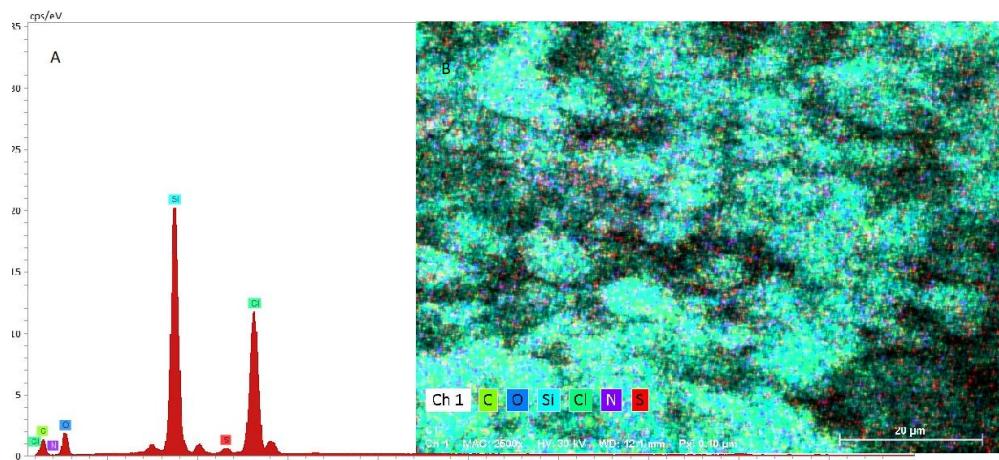


Fig. 8. EDX spectra of GO-Si-Pr-Creatine-SO₃H.

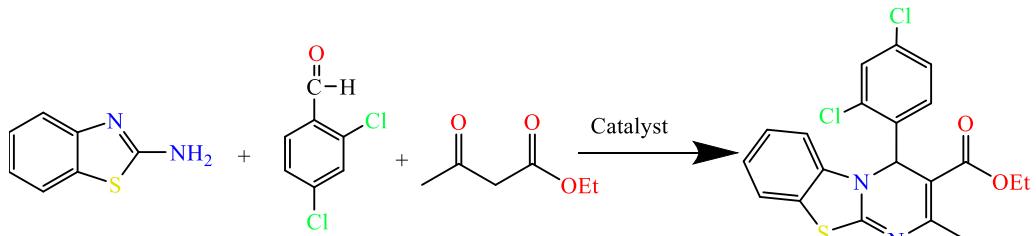


Fig. 9. The reaction of 2,4-dichlorobenzaldehyde (1 mmole), 2-aminobenzothiazole (1 mmol) and ethyl acetoacetate (1 mmol) under various condition.

Table 1. The obtained yields for reaction of 2,4-dichlorobenzaldehyde (1 mmole), 2-aminobenzothiazole (1 mmol) and ethyl acetoacetate (1 mmol) under various condition

Entry	Catalyst	Solvent	Catalyst (mg)	Temp (°C)	Time (min)	Yield (%)
1	-	EtOH	-	-	120	17
2	GO	EtOH	30	90	30	35
3	GO-Si-Pr-Cl	EtOH	30	90	30	35
4	GO-Si-Pr-Creatinine-SO ₃ H	EtOH	30	90	30	92
5	GO-Si-Pr-Creatinine-SO ₃ H	H ₂ O	30	Reflux	30	55
6	GO-Si-Pr-Creatinine-SO ₃ H	EtOH	30	Reflux	30	83
7	GO-Si-Pr-Creatinine-SO ₃ H	Solvent free	30	90	30	95
8	GO-Si-Pr-Creatinine-SO ₃ H	Solvent free	30	80	30	96
9	GO-Si-Pr-Creatinine-SO ₃ H	Solvent free	40	80	40	98
10	GO-Si-Pr-Creatinine-SO ₃ H	Solvent free	20	80	20	90

Catalytic application of GO-Si-Pr-Creatine- SO_3H

The target compound was synthesized via a one-pot multicomponent condensation reaction (MCR) using the catalyst GO-Si-Pr-Creatinine- SO_3H . The reaction was performed with equimolar amounts of 2-aminobenzothiazole, 4,2-dichlorobenzaldehyde, and ethyl acetoacetate, according to the following reaction Fig. 9

The results demonstrate that GO-Si-Pr-Creatinine- SO_3H is the most efficient catalyst for the synthesis of pyrimido[2,1-b]benzothiazole derivatives. In the absence of a catalyst, the reaction in ethanol yielded only 17%, highlighting the reaction's dependency on catalytic activation. Using unmodified GO or GO-Si-Pr-Cl slightly

improved the yield (35%), indicating that mere surface functionalities are insufficient to promote the condensation effectively. The functionalized catalyst, containing acidic SO_3H groups and immobilized creatinine, significantly enhanced the reaction efficiency, achieving excellent yields (92–98%) under solvent-free conditions at 80–90 °C within 20–40 minutes. Optimization studies revealed that moderate catalyst loading (30–40 mg) is sufficient to maintain high yields, while reducing the amount to 20 mg slightly decreased the yield (90%), confirming the importance of active sites. Temperature variation within the 80–90 °C range had minimal effect, suggesting the reaction is not highly temperature-sensitive. The solvent-free

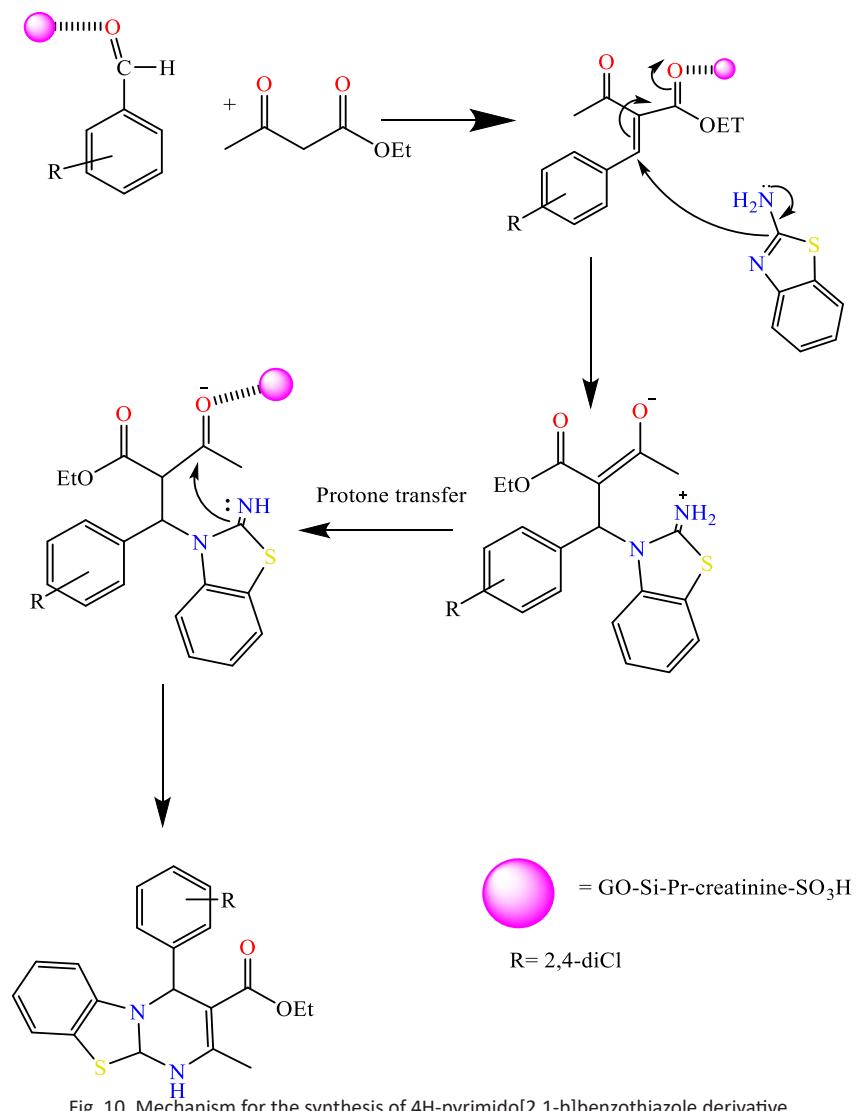


Fig. 10. Mechanism for the synthesis of 4H-pyrimido[2,1-b]benzothiazole derivative.

protocol not only improved the reaction efficiency but also reduced environmental impact, in line with green chemistry principles. Additionally, the catalyst was easily recovered using a magnet and showed excellent reusability over multiple cycles without significant loss in activity, highlighting its practical applicability for sustainable synthesis.

Fig. 10 illustrates the proposed mechanism for the synthesis of 4H-pyrimido[2,1-b]benzothiazole derivatives (4). The reaction begins with benzaldehyde acting as an electrophile and β -ketoester serving as an active methylene compound in an in-situ Knoevenagel condensation[38], leading to the formation of an α,β -unsaturated intermediate. Subsequently,

2-aminobenzothiazole, acting as a nucleophilic Michael donor, attacks this intermediate during the Michael addition, forming an iminium ion. This is followed by internal proton transfer and intramolecular cyclization with elimination of a water molecule, yielding the final 4H-pyrimido[2,1-b]benzothiazole derivative (4). In this process, the catalyst functions as a Lewis acid, activating the carbonyl groups[39], thereby accelerating the reaction and enhancing the efficiency of the cyclization under mild and sustainable conditions Fig. 11.

Antibacterial Activity

The results indicate that compounds 3 and 4

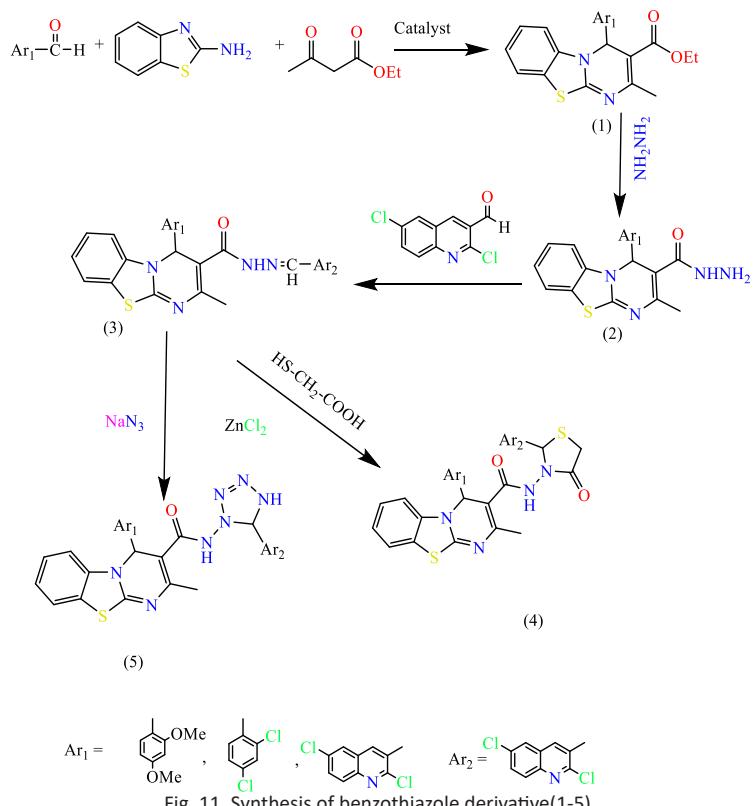


Table 2. Antibacterial activity data for compounds (3,4).

Comp No.	<i>Pseudomonas aeruginosa</i>		<i>Escherichia Coli</i>	
	10 (mg/ml)	1 (mg/ml)	10 (mg/ml)	1 (mg/ml)
3	24	13	11	8
4	20	18	13	9
Control (DMSO)	-	-	-	-
Ciprofloxacin	30		30	

exhibit variable activity against *Escherichia coli* and *Pseudomonas aeruginosa*. Compound 3 showed inhibition zones of 8 and 11 mm against *E. coli* at 1 and 10 mg/ml, and 13 and 24 mm against *P. aeruginosa* at the same concentrations. Compound 4 demonstrated higher activity against *E. coli* (9 and 13 mm) and *P. aeruginosa* (18 and 20 mm). In comparison, Ciprofloxacin showed maximum activity with inhibition zones of 30 mm against both strains. The antibacterial activity of the synthesized compounds generally increased with concentration, indicating a dose-dependent effect. Although the activity of these compounds does not reach the level of Ciprofloxacin, they represent promising candidates for further structural optimization to enhance their efficacy against both Gram-positive and Gram-negative bacteria [40,41].

Reusability of the Catalyst

The reusability of GO-Si-Pr-Creatine-HSO₄H was evaluated by isolating the catalyst from the

reaction mixture, followed by thorough washing with hot ethanol and subsequent drying at 60 °C overnight. The recovered material was then reused in successive runs of the model reaction, and the performance results are illustrated in Fig. 12.

The comparison of catalytic performance clearly demonstrates the high efficiency of GO-Si-Pr-Creatine-HSO₄H. Achieving a 98% yield under mild conditions (80 °C, 40 min, solvent-free), this catalyst matches the best-reported system (Fe₃O₄@NCS/Sb(V)) while offering the advantages of shorter reaction time and milder temperature. Moreover, the excellent reusability of GO-Si-Pr-Creatine-HSO₄H, as evidenced by successive reaction cycles without significant loss of activity, highlights its potential as a sustainable and practical heterogeneous catalyst. These findings underscore the dual benefits of high catalytic efficiency and recyclability, making GO-Si-Pr-Creatine-HSO₄H a promising candidate for green and efficient synthetic applications.

RECYCLES CATALYST

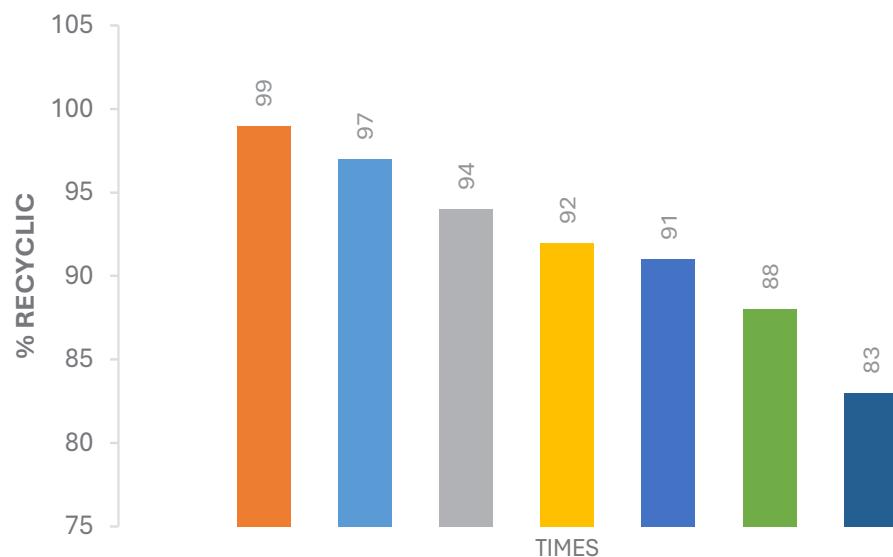


Fig. 12. The reusability of GO-Si-Pr-Creatine-HSO₄H.

Table 3. Comparison of the GO-Si-Pr-Creatine-HSO₄H with other catalyst in the synthesis of 4H-pyrimido[2,1-b]benzothiazole.

Entry	Catalyst/Tem/Time/Solvent	Yield(%)	Refs
1	Fe ₃ O ₄ @NCS/Sb(v)/90°C/0.5h/Solvent-free	98	[26]
2	TBAHS/120°C/2h/Ethylene glycol	72	[42]
3	FeF ₃ /80°C/2h/Solvent-free	85	[43]
4	GO-Si-Pr-Creatine-HSO ₄ H/80°C/40min/Solvent-Free	98	This work

CONCLUSION

In summary, an efficient and environmentally friendly protocol was developed for the multicomponent synthesis of 4H-pyrimido[2,1-b]benzothiazole derivatives using acidic ionic liquid-functionalized graphene oxide (GO-Si-Pr-Creatinine-SO₃H) as a reusable heterogeneous catalyst. The catalyst demonstrated remarkable activity, affording excellent yields (92–98%) under solvent-free conditions at moderate temperatures with short reaction times. Structural characterization confirmed the successful functionalization of graphene oxide, while catalytic studies revealed outstanding reusability and stability across multiple reaction cycles, in alignment with the principles of green chemistry. Moreover, preliminary antibacterial screening of the synthesized compounds showed promising inhibitory effects against Gram-positive and Gram-negative bacterial strains, highlighting their potential as lead scaffolds for further pharmaceutical development. Overall, the combination of high efficiency, sustainability, and biological activity underscores the significance of this catalytic system for the synthesis of biologically relevant heterocycles.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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