

RESEARCH PAPER

Recyclable Bio-Functionalized Graphene Oxide Nanocatalyst for Sustainable and High-Yield Synthesis of Arylimine-Substituted Benzo[b]pyridonaphthyridin-7-one Derivatives in Water

Amer Younis Othman ¹, Mohanad Y. Saleh ^{2*}, Khalid Ahmed Owaid ²

¹ Department of Biology, College of Education, Akre University for Applied Science, Duhok, Iraq

² Department of Chemistry, College of Education for Pure Science, University of Mosul, Mosul, Iraq

ARTICLE INFO

Article History:

Received 17 April 2025

Accepted 23 June 2025

Published 01 July 2025

Keywords:

Graphene oxide nanocatalyst

Green synthesis

Heterocyclic compounds

Multicomponent reaction

Recyclable catalyst

ABSTRACT

In this study, a novel and recyclable heterogeneous nanocatalyst based on creatinine-functionalized graphene oxide (GO-Si-Pr-Creatinine-SO₃H) was successfully synthesized and characterized for use in multicomponent condensation reactions. The preparation involved a stepwise functionalization of graphene oxide nanosheets synthesized via the improved Hummers' method, followed by grafting with 3-chloropropyltrimethoxysilane, creatinine, and sulfonic acid moieties to generate the final acidic nanocatalyst. The catalytic activity of GO-Si-Pr-Creatinine-SO₃H was evaluated in the green synthesis of 3-chloro-9,9-dimethyl-9,10-dihydrobenzo[b]pyrido[3,2-g] [1,8] naphthyridin-7(8H)-one derivatives via a one-pot three-component reaction of 2-amino-3-formylquinolines and dimedone in water. The process proceeded efficiently under mild conditions at 50 °C, yielding highly pure products after simple work-up and recrystallization. The use of water as an eco-friendly solvent further underscores the method's sustainability. Moreover, the catalyst demonstrated excellent recyclability over multiple runs with minimal loss in activity, confirming its potential as a cost-effective and environmentally benign catalyst for use in organic transformations. This work underlines the promising role of bio-functionalized graphene-based materials in sustainable catalysis and heterocyclic compound synthesis.

How to cite this article

Othman A., Saleh M., Owaid K. Recyclable Bio-Functionalized Graphene Oxide Nanocatalyst for Sustainable and High-Yield Synthesis of Arylimine-Substituted Benzo[b]pyridonaphthyridin-7-one Derivatives in Water. J Nanostruct, 2025; 15(3):1463-1474. DOI: 10.22052/JNS.2025.03.060

INTRODUCTION

Organocatalysts have attracted many researchers due to their catalytic properties. They can be successfully implemented as a strategy for greener synthesis of various chemical and pharmaceutical compounds [1-3]. These catalysts have the advantages of cheapness, availability, efficiency, and sufficient stability for

reuse. Absence of metals in their structures and, therefore, elimination of their contamination and high economic benefits are the other considerable advantages of organocatalysts [2, 4, 5]. Being easily recovered and reused in organic reactions makes these catalysts also economically and environmentally advantageous, as they minimize waste, reduce production costs, and comply

* Corresponding Author Email: mohanadalallaf@uomosul.edu.iq



with the principles of green chemistry [4]. environmentally desirable [6, 7]. Graphene oxide (GO) has garnered significant attention in recent years due to its exceptional physicochemical properties, including its high surface area, mechanical strength, and rich surface functionality, which make it a promising material for various applications, such as catalysis, energy storage, environmental remediation, and biomedical fields. storage, and environmental remediation [8]. GO is a highly oxidized form of graphene, containing oxygenated functional groups such as hydroxyl, epoxy, and carboxyl groups. These functional groups provide GO with excellent potential for further surface modifications, enabling the creation of hybrid materials with tailored properties [9, 10]. A promising approach to enhancing the catalytic activity of GO is its modification with ionic liquids (ILs), particularly acidic ionic liquids (AILs). ILs are known for their unique properties, such as low volatility, high thermal stability, and tunable acidity, making them suitable candidates for catalysis [11]. Beyond ionic liquids, decorating nanomaterial surfaces with biomolecules can deliberately tune colloidal stability and interfacial reactivity in water, showing how bioconjugation improves function in aqueous systems. This rationale aligns with our creatinine-modified GO, where a bio-inspired shell offers hydrogen-bonding and Brønsted-acid sites that organize substrates at the interface and support catalysis in water [15]. Heterocyclic compounds are the most important branches of organic chemistry, which are widely distributed in nature and are essential to life fund as potential anticancer agent [16,17] and antimalarial agent [18] 1,8-naphthyridine derivatives possessing a wide spectrum of biological activities such as antibacterial [19-21] antibiotic of group is being widely used for the diagnostics and chemotherapy of infection disease of human including aids [22] HIV inhibitor antibacterial activities (gemifloxacin,), antitumor activity (vosaroxin), etc. The 1,8-naphthyridine derivatives can also act as monodentate, bidentate, or binucleating bridging ligands. They also exhibit excellent thermally activated delayed fluorescence (TADF) and high photoluminescence quantum yield [23-25]. Recent reports also highlight greener ways to access functional nanostructures and why surface chemistry matters in realistic media [26]. Furthermore, a focused review on nanoparticle biofilm interactions emphasizes that ligand

choice governs adhesion, diffusion, and activity within complex matrices. These insights support coupling GO with biocompatible, acid-bearing moieties, as done here with creatinine/sulfonate, to marry activity with aqueous compatibility [27]. Alongside empirical screening, recent work shows that data-driven tools can mine structure property datasets to guide nanomaterial design. In particular, artificial intelligence frameworks indicate practical routes to correlate surface-ligand identity, acid loading, and hydration shell features with catalytic rate and selectivity. Such models could accelerate optimization of GO-based acidic IL catalysts in water by prioritizing the most informative experiments [28]. This study aims to develop and characterize a recyclable, bio-functionalized graphene oxide nanocatalyst (GO-Si-Pr-Creatinine-SO₃H) and assess its efficiency in the green, water-mediated synthesis of arylimine-substituted benzo[b]pyridonaphthyridin-7-one derivatives under mild and sustainable conditions.

MATERIALS AND METHODS

General remarks

The samples were analyzed by X-ray diffraction (XRD) using a PANalytical X'Pert PRO instrument (Cu K α , λ = 1.5406 Å) 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 ¹³C 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 graphene oxide (GO) nanosheets

The GO was synthesized by Hummer's method through the oxidation of graphite powder [29]. In a typical synthesis, the starting material, slowly (4 g) of graphite powder, was added to the concentrated sulfuric acid (200 mL) in a cleaned 2000 mL beaker kept under (0-5 °C) at an ice bath with continuous stirring. Then, potassium permanganate (16 g) was added gradually to the reaction mixture. The rate of addition was carefully controlled to keep the reaction temperature between (0-10 °C) for 2 hours, and it was transferred to a preheated oil bath at (35 °C) for 1 hour. Then, 200 mL of deionized water was added gradually to it. The

rate of addition was carefully controlled to keep the reaction temperature between 40–60 °C for 50 min. Later, the reaction mixture was allowed to stir continuously on the oil bath at 35 °C temperature for 1 hour, followed by increasing the temperature of the oil bath to 95–98 °C, and the reaction mixture was allowed to stir continuously until the mixture changed to brown color. Further, the reaction mixture was diluted by adding 600 mL of deionized water and stirred continuously. Finally, the suspension was treated with 40 mL of H₂O₂ to terminate the reaction. Then, for purification, the mixture was decanted and washed by rinsing and centrifugation with a mixture consisting of (1520:80 mL) of deionized H₂O, HCl, and then deionized water several times.

Synthesis of the GO-Si-Pr-Cl

The process involved introducing graphene

oxide nanosheets into a two-neck flask equipped with a condenser and magnetic stirrer, all under a nitrogen gas environment. A mixture of 2.0 g graphene oxide nanosheets and 10.0 mL 3-chloropropyltrimethoxysilane was then added to 50 mL of dry toluene as the solvent, and the mixture was refluxed for 6 hours. Upon finishing the reaction, the mixture underwent a gradual cooling process until it reached room temperature. Subsequently, it was filtered through sinter glass and then washed using dry toluene. The resulting functionalized graphene oxide with three chloropropyltrimethoxysilane (GO-Si-Pr-Cl) was then loaded into a desiccator system under N₂ surroundings [30].

Preparation of the GO-Si-Pr- Creatinine-SO₃H Nano catalyst

Using a flask (200 mL) equipped with a magnet

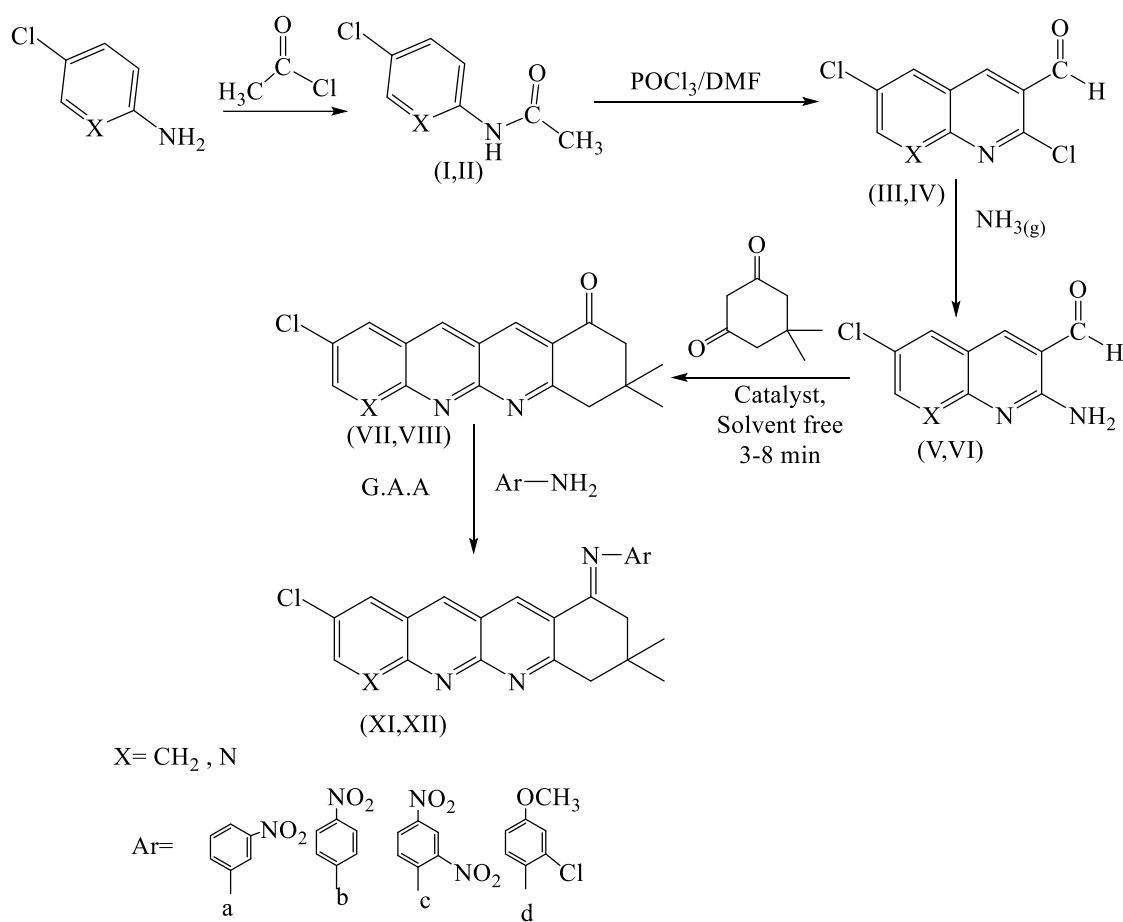


Fig. 1. Synthesis of compounds 1-12.

and condenser, the nitrogen atmosphere was maintained while lysine monohydrochloride (6.0 mmol), GO-Si-Pr-Cl (1.0 g), and Et_3N (0.4 mL) were added to dry ethanol (50 mL). The mixture was subjected to stirring for 8 hours at 60°C , followed by washing and filtration with NaHCO_3 (aq) at 10%, warm water, and ethanol (4 times of 5 mL each). The GO-Si-Pr- Creatinine -Cl was obtained as a dark solid after being dried in a vacuum oven at 60°C overnight. Then, it was added to a flask (200 mL) equipped with a magnet and condenser and

purged with nitrogen gas, along with ClSO_3H (2.0 mmol) and absolute ethanol (25 mL), at 40°C for 24 hours while stirring. Then, 1.0 mL of H_2SO_4 was added and stirred for an additional 3 h. After the suitable time, the solid GO-Si-Pr- Creatinine - SO_3H catalyst was washed and filtered with H_2O and $\text{C}_2\text{H}_5\text{OH}$ and dried at 100°C for 12 h [31].

N-(5-chloropyridin-2-yl) acetamid (3,4)

A mixture of the substrate 1 (0.93 g, 10 mmol), K_2CO_3 (2.07 g, 15mmol), a catalytic amount of PTC

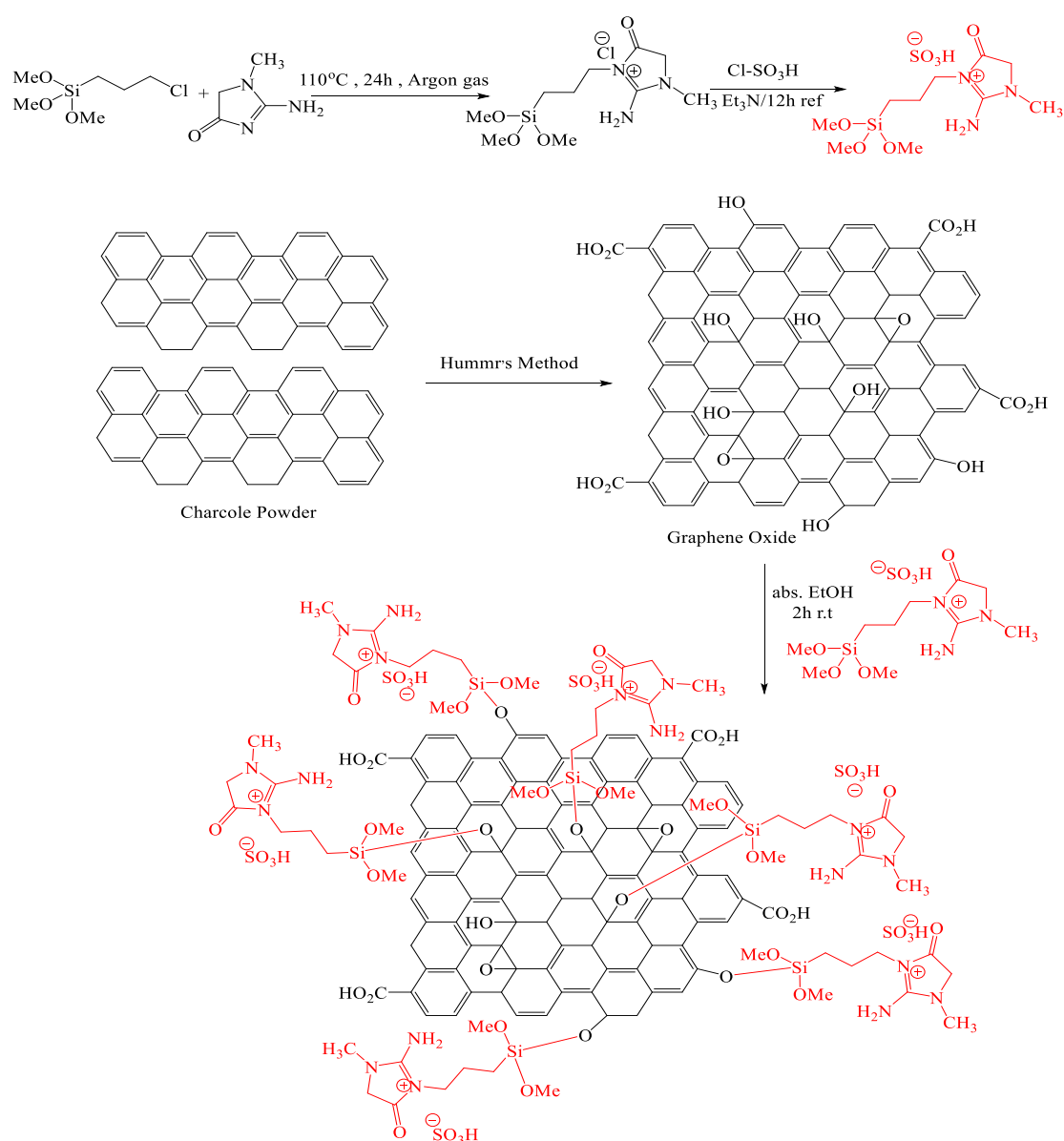


Fig. 2. Synthesis of GO-Si-Pr/SO₃H@Creatinine.

(0.32g, 1mmol), and acetyl chloride (0.71 ml, 10 mmol) in a solvent (20ml) was stirred at room temperature for 10-15 min. After the completion of the reaction (as indicated by the disappearance of the starting material on TLC), the mixture was poured into crushed ice (20gms). The separated solid was filtered, washed with water (2x 10 ml), and dried. The crude product on recrystallization from aq. methanol gave pure[32]: yield 96% white solid m.p.122-1225 ;F.T IR(V,Cm⁻¹) 3448(N-H),1685 (C=O),1571 (C-N),747.1(C-Cl).

Synthesis of 2-chloro-1,8-naphthyridine-3-carboaldehyde (5,6)

N-(pyridine -2-yl) acetamide (1 mol) equivalent was taken in around bottom flask (250 ml) to this add (3 mol) equivalent of dimethyl formamide (DMF) the round bottom flask in then equipped with a dropping funnel filled with (7 mol) equivalent POCl₃ (phosphoryl chloride), the whole assembly was placed on an ice bath and (0-5 °C) temperature was maintained. then drop wise adding of POCl₃, was done with continuous stirring after the drop-wise addition, dropping funnel was

removed and immediately the contents of reaction mixture in round bottom flask were equipped with a reflux condenser and then the mixture was stirred at (80-90 °C) for (15 hrs) then the reaction mixture was immediately poured in ice cold water and stirred for half an hour. the reaction mixture was filtered on Buchner funnel; the crystals [22]. The obtained were washed with cold water and dried. the recrystallization was done by ethanol to give compound (5,6), yield 63%. Yellow solid.m.p.149-151 F.T IR(V,Cm⁻¹) 3018(Ar-H),1665 (C=O),1578 (C=N),747.1(C-Cl) ¹H NMR (500 MHz, Chloroform-d) δ 8.57 (d, *J* = 2.1 Hz, 1H), 7.98 – 7.91 (m, 2H), 7.63 (dd, *J* = 8.3, 2.1 Hz, 1H), 2.75 (s, 3H).

Synthesis of 2-amino-3-formylquinolines (7,8)

Typical Procedure, 2-Amino-3-formylquinolines4 (2a-g): To a stirred solution of 2-chloro-3-formylbenzo[7,8-h] quinoline 1g (1.5 mole) in 40 mL ethanol was passed dry ammonia gas was passed for 3-4 h at 0-20°C. It was left aside for 12 h. The product separated was filtered and purified using column chromatography over silica gel (60-120 mesh, 50g) using pet. ether-ethyl

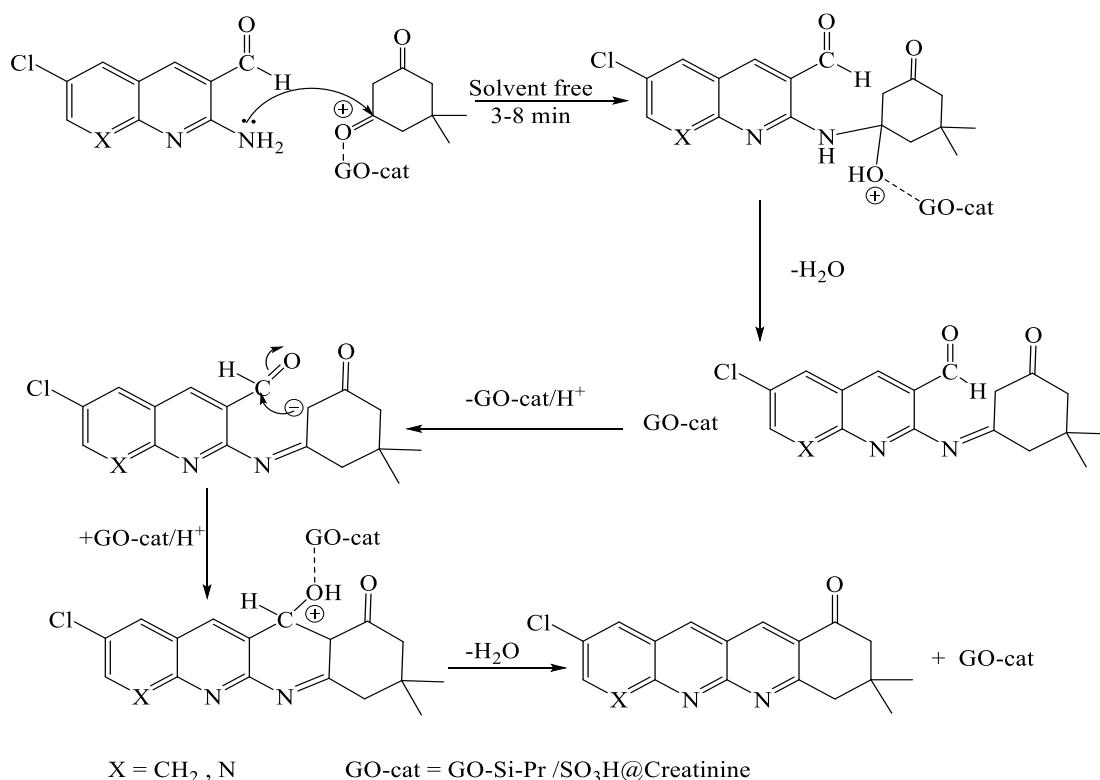


Fig. 3. Mechanism of catalyst reaction.

acetate mixture (98: 2 v/v) as eluant. The product was recrystallised from pet. ether- ethyl acetate (50: 50 v/v) mixture [33] to give compounds (7,8) yield 54%. Brown solid.m.p.175-177°C ¹H NMR (500 MHz, DMSO) δ 8.13 (s, 1H), 7.32 (s, 2H), 3.17 (s, 1H), 3.04 (s, 3H). ¹³C NMR (125 MHz,DMSO-d₆) δ(ppm) 192.17, 159.25, 150.37, 135.14, 129.87, 129.34, 127.98, 126.17, 123.12, 114.49.

Synthesis of 3-chloro-9,9-dimethyl-9,10-dihydrobenzo[b]pyrido[3,2-g][1,8] naphthyridin-7(8H)-one (9,10)

To a mixture of 2-amino-3-formylquinolines (2 mmol) and dimedone (3 mmol) in a 10 mL ethanol round-bottomed flask connected to a reflux condenser was added the catalyst (0.4 g). The resulting mixture was stirred in an oil bath (80 °C) for the appropriate time. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature, and EtOAc (40 mL) was added to it, stirred for 3 min, and filtered. The solvent was evaporated, and the crude product was purified by column chromatography on silica gel eluted with EtOAc-n-hexane [34] yield 67%. Brown solid.m.p.233-235°C ¹H NMR (400 MHz, DMSO) δ 10.35 (s, 2H), 8.92 (s, 2H), 8.39 (s, 2H), 3.29 (s, 1H), 3.05 (s, 1H), 2.51 (d, *J* = 7.9 Hz, 6H), 1.19 (s, 1H). ¹³C NMR (125 MHz,DMSO-d₆) δ(ppm) 196.76, 166.71, 157.85, 155.77, 151.62, 132.81, 132.23, 131.97, 127.87, 124.35, 122.37, 120.77, 48.76, 48.00, 32.92, 28.33.

General method for the preparation of 3-chloro-9,9-dimethyl-9,10-dihydrobenzo[b]pyrido[3,2-g][1,8] naphthyridin-7(8H)-one

Using GO-Si-Pr- Creatinine-SO₃H

In a round-bottom flask (25.0 mL), a mixture of 2-amino-3-formylquinolines (2 mmol) and dimedone (3 mmol), and 30 mg of GO-Si-Pr Creatinine-SO₃H was stirred completely at 50 °C in water as a green and environmentally friendly solvent. After completion of the reaction (monitoring by TLC), the mixture of reaction mixture was slowly cooled to room temperature. Then, 30 mL of EtOAc (Hot) was added, and the catalyst was separated by centrifugation. The remaining EtOAc was slowly evaporated to obtain crude products. To provide pure products, the crude products were recrystallized from ethanol or water: ethanol (1:1) to obtain highly pure products.

General method for the reusability of the catalyst

The recovery and reuse of catalysts are crucial from both an economic and industrial perspective in actual practice. Reusability of the GO-Si-Pr-Creatinine-SO₃H was investigated in 2-amino-3-formylquinolines (1), dimedone (2), and 30 mg of GO-Si-Pr-Creatinine-SO₃H. At the end of each catalytic cycle, 30 mL of ethyl acetate (Hot) was added, and the catalyst and remaining starting materials were filtered. For regeneration of the GO-Si-Pr-Creatinine-SO₃H, the catalyst was

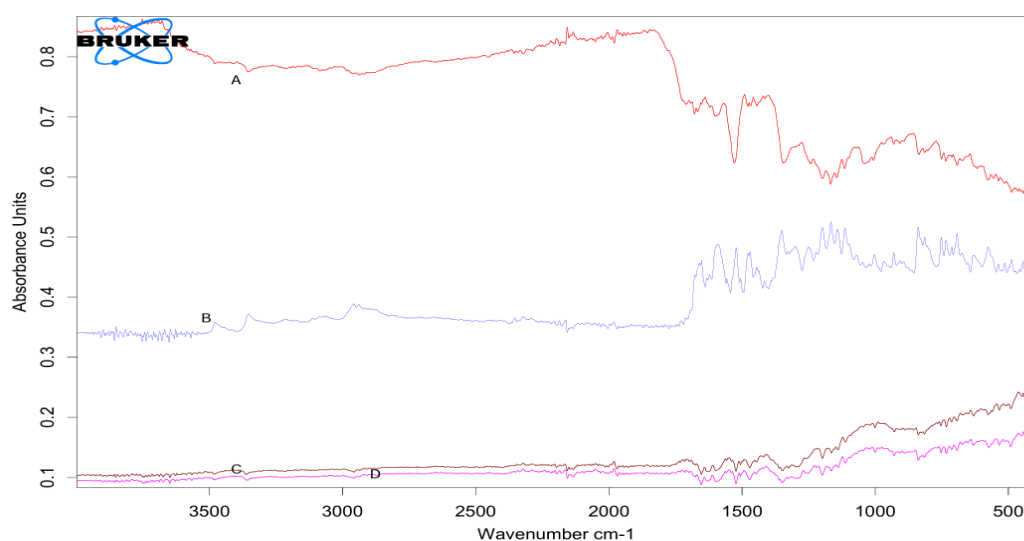


Fig. 4. FT-IR spectra a) graphene oxide b) GO-Si-Pr-Creatine-Cl

exhaustively washed using C_2H_5OH and water and dried at $80\text{ }^{\circ}C$ overnight. The synthesis of compounds 1-12 shown in Fig. 1.

RESULTS AND DISCUSSION

Preparation of the GO-Si-Pr-Creatinine- SO_3H

Initially, we provided GO-Si-Pr-Creatinine- SO_3H as a powerful catalyst for the application in the synthesis of 3-chloro-9,9-dimethyl-9,10-dihydrobenzo[b]pyrido[3,2-g][1,8] naphthyridin-7(8H)-one as shown in Fig. 2. Literature routes to related nitrogen-rich rings often rely on microwave assistance or multicomponent condensations to accelerate bond formation and library build-up [35,36]. Our aqueous Brønsted-acid surface provides a complementary path: the sulfonated-creatinine layer organizes partners via hydrogen-bonding while supplying localized acidity, enabling high conversions without specialized equipment and aligning with green-chemistry constraints.

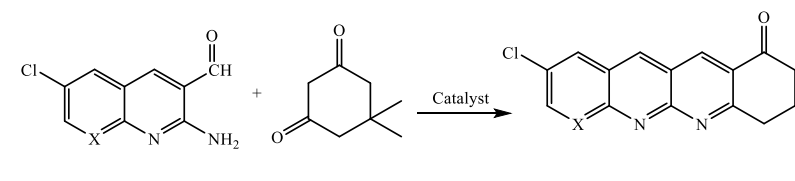
At first, the graphene oxide nanosheets were prepared according to the reported literature

[37]. Then, 3-chloropropyltrimethoxysilane was anchored on the surface of graphene oxide nanosheets. In this step, using Mohr's method, the total density of chlorine atoms was approximately measured as 1.25 mmol.g^{-1} . Then, the amino acid lysine monohydrochloride was supported on the GO-Si-Pr-Cl. Finally, through the two sequential steps (I: addition of $ClSO_3H$, II: addition of H_2SO_4), the GO-Si-Pr-Creatinine- SO_3H was successfully obtained. The details of the experimental preparation of the catalyst were described in the experimental part. The mechanism of the catalyst (Pathway of the catalyst reaction) shown in Fig. 3.

Characterization of the GO-Si-Pr-Creatinine- SO_3H

The FT-IR technique was used for the analysis of GO, Creatine-GO, and GO-Si-Pr-Creatinine- SO_3H (Fig. 4). As can be seen in Fig. 4, the transmittance peak at about 1519.8 cm^{-1} is related to $C=C$. A result of the asymmetry of GO is that the pointed peak is even sharper than graphite powder. The spectrum depicted in Fig. 4A exhibits peaks at

Table 1. Optimization of the reaction conditions.



X=CH, N

Entry	Catalyst	Solvent	Temp $^{\circ}C$	Time (min)	Weight (mg)	Yield (%)
1	-	-	Reflux	60	20	39
2	GO	EtOH	Reflux	60	20	64
3	GO	EtOH:H ₂ O (1:1)	Reflux	60	20	70
4	GO-Si-Pr-Creatinine- HSO_4H	EtOH	Reflux	60	20	70
5	GO-Si-Pr-Creatinine- HSO_4H	EtOH	90	60	20	72
6	GO-Si-Pr-Creatinine- HSO_4H	H ₂ O	90	60	20	77
7	GO-Si-Pr-Creatinine- HSO_4H	Solvent -free	Rt	20	20	86
8	GO-Si-Pr-Creatinine- HSO_4H	EtOH:H ₂ O (1:1)	80	60	20	92
9	GO-Si-Pr-Creatinine- HSO_4H	MeOH	90	60	20	75
10	GO-Si-Pr-Creatinine- HSO_4H	EtOH	50	60	25	80
11	GO-Si-Pr-Creatinine- HSO_4H	H ₂ O	50	60	30	92
12	GO	Solvent -free	R.T	20	50	25
13	GO-Si-Pr-Creatinine- HSO_4H	Solvent -free	R.T	20	30	45
14	GO-Si-Pr-Creatinine- HSO_4H	Solvent -free	R.T	25	30	45

1064, 1709, 1031, 874, 459, and 3206 cm^{-1} , which could be associated with the stretching modes of various groups attached to GO, such as C-O, C=O (carbonyl), and O-H (hydroxyl). The detection confirmed that the nitrogen-hydrogen bond bending and stretching frequencies of Creatine

monohydrochloride amino acid are located at $\sim 3310 \text{ cm}^{-1}$ and 960 cm^{-1} [38]. The bands at 1709 cm^{-1} were related to C=O of carboxylic acid. In addition, it could be well observed that the lysine monohydrochloride was successfully supported on the surface of GO through a covalent bond.

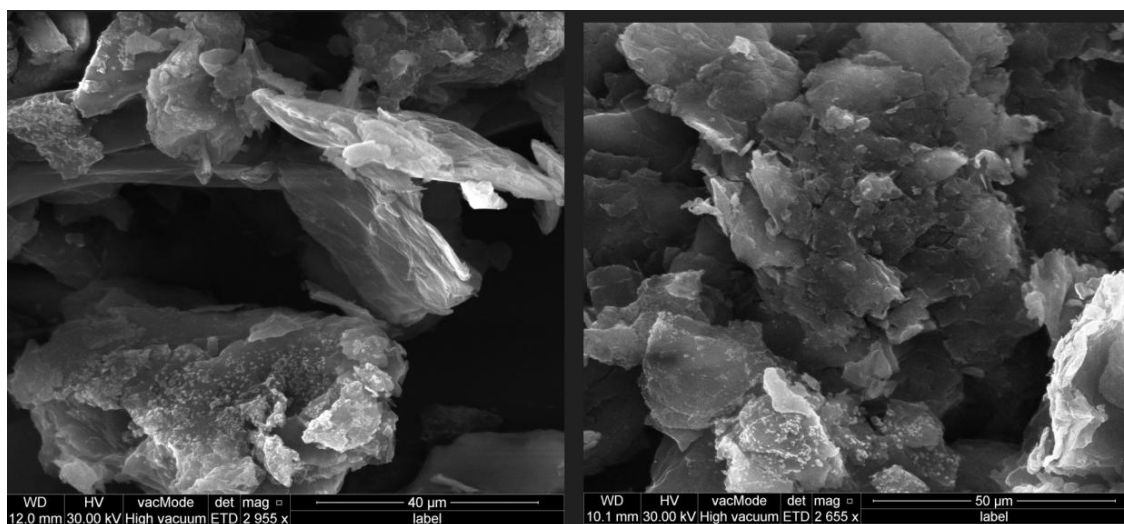


Fig. 5. SEM image of a) GO, b) GO-Si-Pr-Creatine-SO₃H.

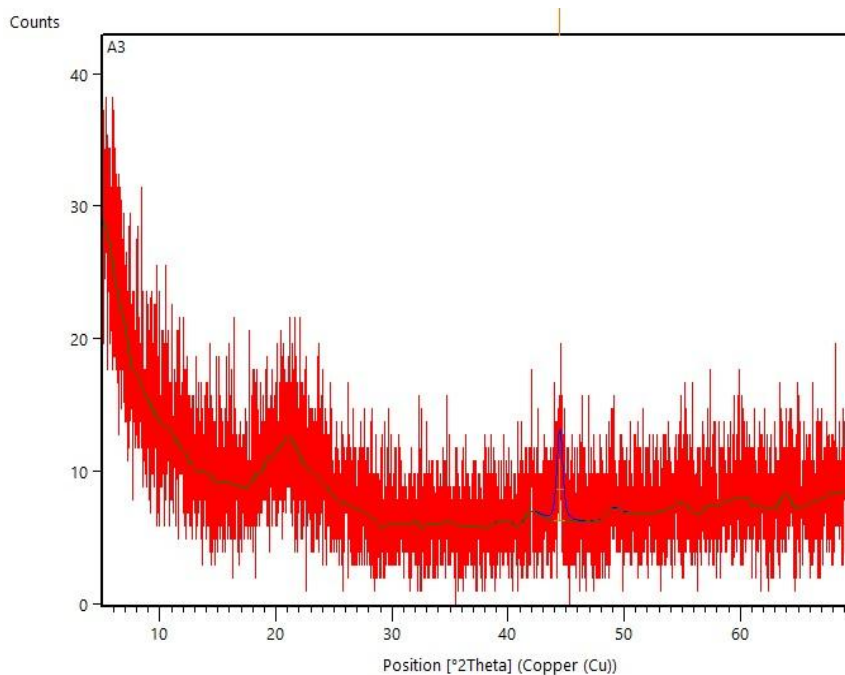


Fig. 6. XRD-GO.

Fig. 5 displays SEM images of graphene oxide and the GO Si-Pr-Creatine-SO₃H catalyst. The FE-SEM image of GO shows the exfoliated and layered graphene oxide sheets. The morphology of GO-Si-Pr-Creatine-SO₃H was converted relative to pristine GO.

The powder X-ray diffraction patterns of GO and GO@Si-Pr-Cl materials are given in Figs. 6 and 7), respectively. The X-ray diffraction pattern of GO shows the original sharp diffraction peak at $2\theta = 10.51$ due to the presence of oxygen-containing functional groups like carboxylic acid and hydroxyl on the basal plane of the graphite moiety. For the alkylated graphene nanosheets upon grafting with 3-CPTMS, the intensity of the former peak weakens immensely, and a new weak and broad peak at around $2\theta = 21.43$ is seen, which is closer to reduced graphene, indicating that the major oxygen-containing groups of GO have been successfully functionalized [39].

In this part of the study, the catalytic performance of the nanocatalyst GO-Si-Pr-Creatine-HSO₄H was evaluated and compared with unmodified graphene oxide (GO) under various conditions, including solvent type, temperature, catalyst amount, and reaction time. As shown in Table 1, the reaction in the absence of any catalyst

(Entry 1) resulted in a low yield of 39%, indicating the inefficiency of the process without a catalytic agent. When GO was used as a catalyst in ethanol, the yield improved to 64%, while the use of an ethanol/water mixture (1:1) further increased the yield to 70%, suggesting that water plays a role in enhancing the reaction efficiency.

Upon employing the modified catalyst GO-Si-Pr-Creatine-HSO₄H, a significant improvement in yield was observed under most conditions. For instance, a yield of 77% was obtained when water was used as the solvent at 90°C (Entry 6), and an even higher yield of 86% was achieved under solvent-free conditions at room temperature (Entry 7), highlighting the catalyst's ability to perform efficiently in green, solvent-free systems. The highest yield (92%) was achieved using an ethanol/water mixture (1:1) at 80°C with 20 mg of the catalyst (Entry 8). Furthermore, increasing the catalyst amount to 30 mg in water at 50°C (Entry 11) also produced an excellent yield of 92%, underscoring the significance of both the catalyst amount and solvent selection in enhancing the reaction outcome. The gain relative to pristine GO aligns with reports that the interfacial chemistry of GO dictates performance: surface functional groups and π -rich domains govern adsorption, local

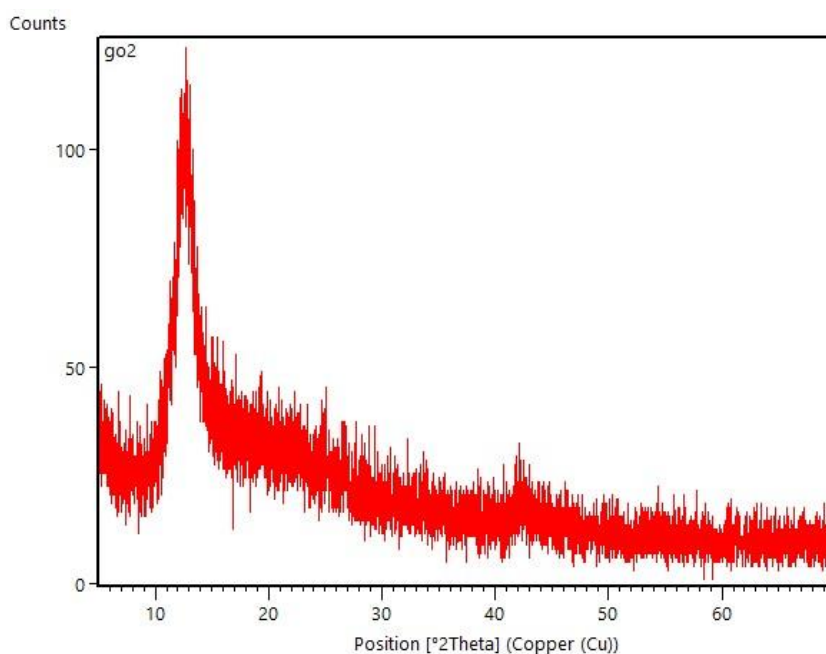


Fig. 7. XRD-GO-Si-Pr/SO₃H@Creatinine.

concentration, and orientation of organic partners in water. Studies on GO drug systems likewise show that tailored functionalization strengthens specific interactions and improves efficacy [40]. In our case, the sulfonated-creatinine layer likely combines Brønsted acidity with hydrogen-bond/ π - π contacts to pre-organize the components, rationalizing the higher yields under mild aqueous conditions. The performance gain relative to bare GO is consistent with reports where iron-oxide based nanostructures show stronger activity once paired with organic acids or plant-derived ligands, which create local acidic microenvironments and improve substrate partitioning at the surface [41]. By analogy, the sulfonated-creatinine layer likely offers both Brønsted acidity and directional hydrogen bonding that pre-organize the condensation partners in water, rationalizing the higher yields observed under mild conditions.

It is noteworthy that the use of unmodified GO under solvent-free conditions (Entry 12) produced negligible yield, whereas the use of the modified catalyst under the same conditions (Entries 13–14) yielded a moderate 45%, supporting the hypothesis that functionalizing GO with acidic groups (HSO_4H) and bio-based molecules such as creatine increases the number of active sites and significantly enhances the catalytic performance.

Beyond the catalytic efficiency, this work reflects a broader movement toward sustainable material utilization, where naturally abundant or waste-derived resources are repurposed for high-value applications. Comparable strategies have been reported in the valorization of diatomaceous earth as a sustainable eco-coagulant for wastewater treatment, where optimization by response surface methodology underscores the synergy between performance and environmental

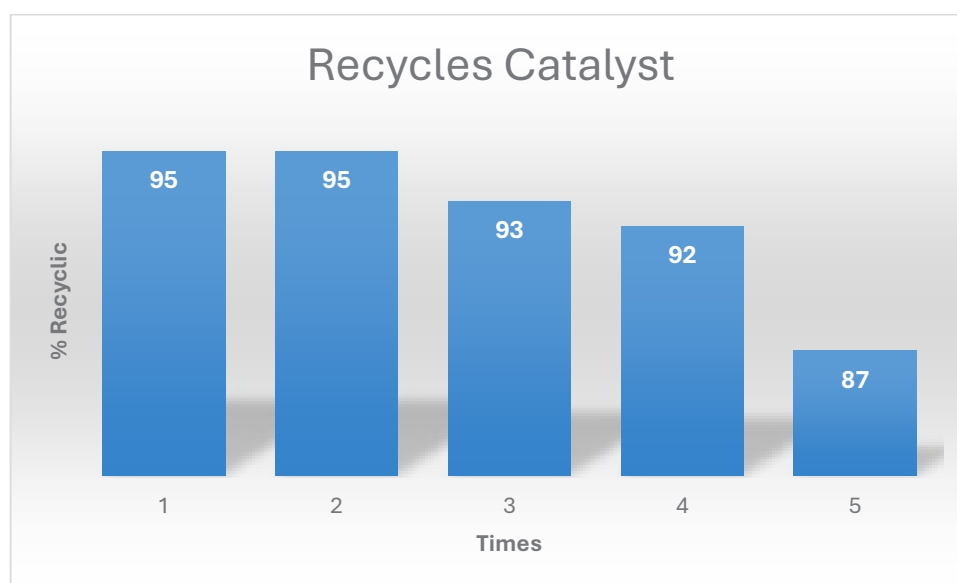


Fig. 8. Reusability of the catalyst.

Table 2. Comparison of the GO-Si-Pr-Creatine- HSO_4H with other catalysts in the synthesis of VII.

Entry	Catalyst/Tem/Time/Solvent	Yield (%)	Refs
1	ChOH/50°C/6h/ H_2O	99	[16]
2	$\text{P}_2\text{O}_5/\text{SiO}_2/80^\circ\text{C}/15\text{min}/\text{Solvent-free}$	93	[20]
3	DSIMHS/70°C/25min/Solvent-free	89	[43]
4	GO-Si-Pr-Creatine- $\text{HSO}_4\text{H}/50^\circ\text{C}/1\text{h}/\text{H}_2\text{O}$	92	This work

responsibility [42].

Reusability of the Catalyst

The reusability of GO-Si-Pr-Creatine- HSO_4H was assessed by recovering the catalyst from the reaction medium, thoroughly washing it with hot ethanol, and drying it at 60 °C overnight. The regenerated catalyst was subsequently applied in multiple consecutive cycles of the model reaction (Table 2), with the corresponding results presented in Fig. 8.

CONFLICT OF INTEREST

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

CONCLUSION

a novel, efficient, and recyclable heterogeneous nanocatalyst (GO-Si-Pr-Creatinine- SO_3H) was successfully synthesized via covalent functionalization of graphene oxide nanosheets and demonstrated excellent performance in promoting the green, water-mediated synthesis of 3-chloro-9,9-dimethyl-9,10-dihydrobenzo[b]pyrido[3,2-g][1,8]naphthyridin-7(8H)-one derivatives; key advantages include high catalytic activity under mild conditions (50 °C in water), use of a sustainable, metal-free, and non-toxic reaction medium, excellent product yields with high purity following simple work-up, and reusability for several cycles without significant loss of activity, underscoring the potential of GO-based biofunctionalized nanomaterials in sustainable catalysis and heterocyclic compound synthesis as valuable tools in modern green chemistry. If extended, these attributes, together with operational simplicity, suggest promising scalability and broader substrate scope in aqueous media.

REFERENCE

- Zafar A, Iqbal MA, Iram G, Shoukat US, Jamil F, Saleem M, et al. Advances in organocatalyzed synthesis of organic compounds. *RSC Advances*. 2024;14(28):20365-20389.
- Han B, He X-H, Liu Y-Q, He G, Peng C, Li J-L. Asymmetric organocatalysis: an enabling technology for medicinal chemistry. *Chem Soc Rev*. 2021;50(3):1522-1586.
- Martelli LSR, Machado IV, dos Santos JRN, Corrêa AG. Recent Advances in Greener Asymmetric Organocatalysis Using Bio-Based Solvents. *Catalysts*. 2023;13(3):553.
- Jia J, Shan S, Jia P, Song H. Chemical reaction process and dynamic characteristics of urea pyrolysis products in inhibiting gas explosion. *Arabian Journal of Chemistry*. 2024;17(6):105813.
- Dutta AK, Gogoi P, Saikia S, Borah R. N,N-disulfo-1,1,3,3-tetramethylguanidinium carboxylate ionic liquids as reusable homogeneous catalysts for multicomponent synthesis of tetrahydrobenzo[*a*]xanthene and tetrahydrobenzo[*a*]acridine derivatives. *J Mol Liq*. 2017;225:585-591.
- Sahoo BM, Banik BK. Organocatalysis: Trends of Drug Synthesis in Medicinal Chemistry. *Current Organocatalysis*. 2019;6(2):92-105.
- Khabnadideh S, Khorshidi K, Amiri-Zirtol L. A novel heterogeneous acid-base nano-catalyst designed based on graphene oxide for synthesis of spiro-indoline-pyranochromene derivatives. *BMC Chemistry*. 2023;17(1).
- Th. Sadeek G, Faiyq Saeed Z, Yakdhan Saleh M. Synthesis and Pharmacological Profile of Hydrazone Compounds. *Research Journal of Pharmacy and Technology*. 2023:975-982.
- An F, Maji B, Min E, Ofial AR, Mayr H. Basicities and Nucleophilicities of Pyrrolidines and Imidazolidinones Used as Organocatalysts. *Journal of the American Chemical Society*. 2020;142(3):1526-1547.
- Yokwana K, Ntsendwana B, Nxumalo EN, Mhlanga SD. Recent advances in nitrogen-doped graphene oxide nanomaterials: Synthesis and applications in energy storage, sensor electrochemical applications and water treatment. *J Mater Res*. 2023;38(13):3239-3263.
- Hamdoon A, Al-Iraqi M, Saleh M. Synthesis of Some Multi-cyclic Sulfhydryl Donor Compounds Containing 1,2-dithiol-3-thione moiety. *Egyptian Journal of Chemistry*. 2021;0(0):0-0.
- Dreyer DR, Park S, Bielawski CW, Ruoff RS. The chemistry of graphene oxide. *Chem Soc Rev*. 2010;39(1):228-240.
- Badoni A, Thakur S, Vijayan N, Swart HC, Bechelany M, Chen Z, et al. Recent progress in understanding the role of graphene oxide, TiO_2 and graphene oxide- TiO_2 nanocomposites as multidisciplinary photocatalysts in energy and environmental applications. *Catalysis Science and Technology*. 2025;15(6):1702-1770.
- Kalel R. Silica Immobilized Brønsted-Lewis Acidic Ionic Liquid : Heterogeneous catalyst for Condensation-Aromatization in the Synthesis of 2-(4-nitrophenyl)-1H-benzimidazole by cooperative catalysis. *Peeref*; 2023 2023/03/21.
- Al-Abboodi A, Albukhaty S, Sulaiman GM, Al-Saady MAAJ, Jabir MS, Abomughaid MM. Protein Conjugated Superparamagnetic Iron Oxide Nanoparticles for Efficient Vaccine Delivery Systems. *Plasmonics*. 2023;19(1):379-388.
- Al-Jumaili MHA, Bakr EA, Huessien MA, Hamed AS, Muhaidi MJ. Development of heterocyclic-based anticancer agents: A comprehensive review. *Heterocycl Commun*. 2025;31(1).
- Kumar S, Singh RK, Patial B, Goyal S, Bhardwaj TR. Recent advances in novel heterocyclic scaffolds for the treatment of drug-resistant malaria. *Journal of Enzyme Inhibition and Medicinal Chemistry*. 2015;31(2):173-186.
- Gurjar VK, Pal D. Recent Developments and Multiple Biological Activities Available with 1, 8-Naphthyridine Derivatives: A Review. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2019:17-37.
- Yakdhan Saleh M, Obaid Aldulaimi AK, Mahmood Saeed S, Hussein Adhab A. $\text{TiFe}_2\text{O}_4/\text{SiO}_2-\text{SO}_3\text{H}$: A novel and effective catalyst for esterification reaction. *Heliyon*. 2024;10(4):e26286.
- Saleh A, Saleh M, Chemistry C. Synthesis of heterocyclic compounds by cyclization of Schiff bases prepared from capric acid hydrazide and study of biological activity. *Egyptian Journal of Chemistry*. 2022;0(0):
- Saleh MY, Aldulaimi AKO, Saeed SM, Adhab AH. Palladium fabricated on Fe_3O_4 as an organic-inorganic hybrid

- nanocatalyst for the Suzuki and Stille coupling reactions. *J Mol Struct.* 2025;1321:139597.
22. Saleh M Y., Al-barwari A S., and Ayoob A. Synthesis of Some Novel 1, 8-Naphthyridine Chalcones as Antibacterial Agents. *Journal of Nanostructures*, 2022;12(3):598-606.
23. Ali AH, Saleh MY, Yaqoob QA, Saied SM, Hasan MS, Owaid KA, et al. Comprehensive evaluation of antibacterial and anticancer activities from indole butanoic acid. *Journal of Genetic Engineering and Biotechnology*. 2025;23(1):100452.
24. Assad H, Fatma I, Kumar A. Ionic Liquid in Phase Transfer Catalysis. *Ionic Liquids: Eco-friendly Substitutes for Surface and Interface Applications: BENTHAM SCIENCE PUBLISHERS*; 2023. p. 302-325.
25. Choudhury SS, Jena S, Sahoo DK, Shekh S, Kar RK, Dhakad A, et al. Gram-Scale Synthesis of 1,8-Naphthyridines in Water: The Friedlander Reaction Revisited. *ACS Omega*. 2021;6(29):19304-19313.
26. Ali, Z. H., Al-Saady, M. A. A. J., Aldujaili, N. H., Rabeea Banoon, S., & Abboodi, A. Evaluation of the antibacterial inhibitory activity of chitosan nanoparticles biosynthesized by streptococcus thermophilus. *Journal of Nanostructures*. 2022;12(3), 675-685.
27. Hassan EM, Saleh MY, Saied SM, Kazemi M. Magnetic-MOF Zinc nanocatalyst in DESs Solvent: a sustainable route for 2,4-Disubstituted Quinoline synthesis. *J Organomet Chem*. 2025;1040:123812.
28. Mohammed Saleh Al-Jubori H, Saddam Fandi Al-Mathkuri T, Rabeea Banoon Z, Yakhdan Saleh M. Synthesis of novel benzo[d] imidazole bearing α -aminophosphonate and their antimicrobial evaluation. *Results in Chemistry*. 2024;8:101586.
29. Zaaba NI, Foo KL, Hashim U, Tan SJ, Liu W-W, Voon CH. Synthesis of Graphene Oxide using Modified Hummers Method: Solvent Influence. *Procedia Engineering*. 2017;184:469-477.
30. Mahmood ZM, Saied SM, Saleh MY. Deep Eutectic Solvent (Reline) As Catalytic System in Synthesis of Schiff Bases Derived from Glucose and Different Amines. *Chemical Problems*. 2024;22(3):281-289.
31. Synthesis, Characterization, and Water Oxidation Activity of Isomeric Ru Complexes. *American Chemical Society (ACS)*.
32. Hashimoto I, Higashi T. *ChemInform Abstract: Phase-Transfer-Catalyzed O-Acetylation of Phenol with Acetyl Chloride in the Presence of Aqueous Sodium Hydroxide.* *ChemInform*. 1993;24(44).
33. Sheet SHM. Theoretical Study for Comparison of Pka of a Number of Schiff Bases by Employing Parameters Derived from Dft and Mp2 Method. *New Materials, Compounds and Applications*. 2024;8(1):94-108.
34. Benouis K, khane Y, Ahmed T, Albukhaty S, Banoon S. Valorization of diatomaceous earth as a sustainable eco-coagulant for wastewater treatment: optimization by response surface methodology. *Egyptian Journal of Chemistry*. 2022;0(0):0-0.
35. Hassan S. A. D. H., Almaliki M. N. S., Hussein Z. A., Albehadili H. M., Rabeea Banoon S., Abboodi A., Al-Saady M. Development of nanotechnology by artificial intelligence: a comprehensive review. *Journal of Nanostructures*. 2023;13(4):915-932.
36. Palakshi Reddy B, Iniyavan P, Sarveswari S, Vijayakumar V. *ChemInform Abstract: Nickel Oxide Nanoparticles Catalyzed Synthesis of Poly-Substituted Quinolines via Friedlander Hetero-Annulation Reaction.* *ChemInform*. 2015;46(19).
37. Prendergast K, Spiro TG. Core expansion, ruffling, and doming effects on metalloporphyrin vibrational frequencies. *Journal of the American Chemical Society*. 1992;114(10):3793-3801.
38. Mashkina AV. Catalytic Synthesis of Some Sulfur-containing Heterocyclic Compounds. (Review). *Chemistry of Heterocyclic Compounds*. 2002;38(5):503-523.
39. Long D, Li W, Ling L, Miyawaki J, Mochida I, Yoon S-H. Preparation of Nitrogen-Doped Graphene Sheets by a Combined Chemical and Hydrothermal Reduction of Graphene Oxide. *Langmuir*. 2010;26(20):16096-16102.
40. Shirini F, Yahyazadeh A, Mohammadi K, Khaligh NG. Solvent-free synthesis of quinoline derivatives via the Friedländer reaction using 1,3-disulfonic acid imidazolium hydrogen sulfate as an efficient and recyclable ionic liquid catalyst. *Comptes Rendus Chimie*. 2014;17(4):370-376.
41. Banoon SR, Ghasemian A. The Characters of Graphene Oxide Nanoparticles and Doxorubicin Against HCT-116 Colorectal Cancer Cells In Vitro. *J Gastrointest Cancer*. 2021;53(2):410-414.
42. Banoon ZR, Mahmood RS, Hamad AR, Hussein ZA. Design, microwave synthesis, characterization and antimicrobial activity of imidazolone derivatives. *J Mol Struct*. 2025;1322:140701.
43. Akkad DMHE, El-Gebaly NSM, Yousof H-ASA, Ismail MAM. Electron Microscopic Alterations in Pediculus humanus capitis Exposed to Some Pediculicidal Plant Extracts. *The Korean Journal of Parasitology*. 2016;54(4):527-532.