chemistry proceedings

MDPI

Proceeding Paper

Graphitic Carbon Nitride-supported L-arginine: Synthesis, Charachterization, and Catalytic Activity in Multi-component Reactions †

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† Presented at the 26th International Electronic Conference on Synthetic Organic Chemistry; Available online: https://ecsoc-26.sciforum.net.

Abstract: Graphitic carbon nitride-supported L-arginine (g-C_3N_4@L-arginine) has been prepared as a heterogeneous catalyst for synthesizing heterocyclic compounds such as pyranopyrazole and acridinedione derivatives. High efficiency, short reaction time, and easy separation are significant features for using g-C_3N_4@L-arginine as a catalyst in one-pot multicomponent reactions. Synthesized nanocatalyst was detected by numerous analyses, such as FE-SEM (Field Emission Scanning Electron Microscopy), EDX (Energy Dispersive X-ray spectroscopy), XRD (X-Ray Diffraction analysis), TGA (Thermo Gravimetric Analysis), and FT-IR (Fourier Transform Infrared Spectroscopy). G-C_3N_4@L-arginine nanocatalyst was reused five times in the reaction with no apparent decrease in reaction yield, which shows acceptable recyclability.

Keywords: g-C_3N_4–pyranopyrazole; acridinedione; multi-component; L-arginine

Citation: Bijari, F.; Talebi, M.; Ghafuri, H.; Tajik, Z.; Hanifehnejad, P. Graphitic carbon nitride-supported L-arginine: synthesis, charachterization, and catalytic activity in multi-component reactions. **2022**, *4*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s):

Published: 15 November 2022

1. Introduction

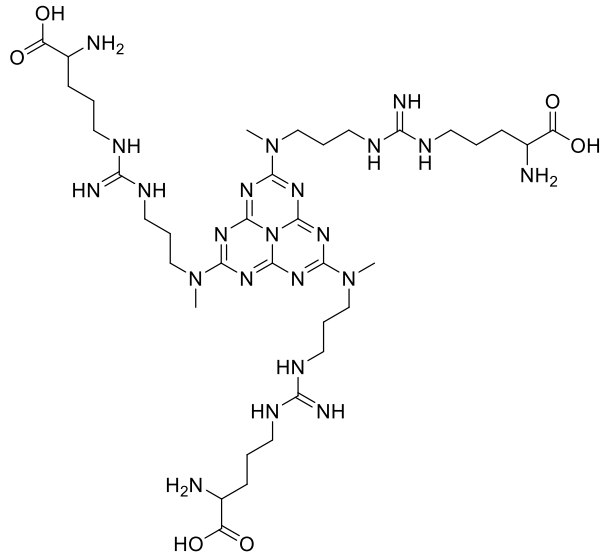
In the last decades, heterogeneous catalysts have been noticed because of large-scale production and selective product formation [1,2]. G-C_3N_4 is a widely used support for catalytic entities due to high physical and thermal stability, low density, versatile performance, and the ability to recyclability. Moreover, the preparation of g-C_3N_4 mostly perform by Cyanamid, urea, dicyanamide, melamine, and thiourea [3]. For increasing the efficiency of catalytic performance of g-C_3N_4 in organic reactions, it is suggested to modify this catalyst–supported by organic compounds [4–8]. For increasing the efficiency of catalytic performance of g-C_3N_4 in organic reactions, it is suggested to modify this catalyst–supported by organic compounds.

Significantly, L-arginine is a semi-essential amino acid in living organisms [9]. While the guanidine group in L-arginine is the precursor for synthesizing nitrogen derivatives. Using L-arginine with g-C_3N_4 as a catalyst- support can decrease the cost and toxicity. Among other benefits of composite productions with L-arginine, it should be mentioned that making composite with this amino acid can increase thermal stability and molar heat capacities. Although, on the other hand, it can reduce the thermal expansion coefficient. Moreover, the utilization of composites is one of the best ways for synthesizing heterocyclic compounds [10–13], while heterocyclic compounds have been considered essential groups of organic materials. Also, They have biological activities which could be effective in the treatment of different diseases. What makes these compounds more important than others is their application in various fields such as medicines, veterinary products, disinfectants, and antioxidants. There are several ways of synthesizing heterocyclic compounds including the multi-stages and one-pot multicomponent reactions. Lately projects

indicate that multicomponent reactions would be the best way for preparing heterocyclic compounds.

Multicomponent reactions have been mostly used for producing heterocyclic compounds because of their advantages including atom economic, efficiency, and convergent [14–18]. Pyranopyrazoles are nitrogen-containing heterocyclic compounds with various properties such as anti-cancer, anti-inflammatory, anti-bacterial, antioxidant, and antihypertensive. Knoevenagel condensation, Micheal addition, and cyclization are the main procedures for making pyranopyrazoles derivatives. Various catalysts can be utilized to prepare pyranopyrazole and its derivatives by multicomponent reactions such as cetyltrimethylammonium chloride (CTACl), montmorillonite K10, agave leaf ash, cytosine@MCM-41, Et_3N, and PTSA [19–24].

Other heterocyclic compounds with biological activities that can be produced with multicomponent reactions are Acridinedione derivatives [25]. They are nitrogen–mediated heterocyclic compounds with a vast spectrum of pharmaceutical and biological activities namely anti-tumor, SIRT1 inhibitors, anticancer, and antimicrobial agents [26–29]. There are different precursors as heterogeneous catalysts for preparing acridinedione including f-MWCNT, Amberlyst -15, CTAB, and Proline [30–33]. Usually, recent methods can cover problems of the latest projects such as harsh conditions, long reaction time, and using toxic solvents. So, new methods for synthesizing pyranopyrazole and acridinedione derivatives are a critical challenge in chemistry society. Therefore, in this research, we have synthesized g-C_3N_4@L-arginine nanocomposite and applied as a catalyst in the synthesizing pyranopyrazole and acridinedione derivatives in a high yield. The schematic of g-C_3N_4@L-arginine is shown in Scheme 1.



Scheme 1. Schematic of g-C_3N_4@L-arginine.

2. Experimental

2.1. Materials

All chemicals were prepared from sigma–Aldrich and Merck companies. Many analyses have been performed, including Fourier Transform Infrared Spectroscopy (FT-IR), which was recorded by Tensor27 for detecting functional groups of products, Thermal Gravimetric Analysis (TGA) under argon atmosphere was taken by STA 504, which displayed the thermal stability of nanocatalyst, Nuclear Magnetic Resonance (NMR) with Varian-Inova 500MHz, X-Ray Powder Diffraction (XRD) was performed by Dron-8, Energy-Dispersive X-ray (EDX) Numerix DXP–X10P for indicating the existence of elements of synthesized nanocatalyst, and Field Emission Scanning Electron Microscopy (FE-SEM) with TESCAN-MIRA lll for displaying the morphology of synthesized nanocatalyst.

2.2. Preparation of Bulk C_3N_4 and g-C_3N_4

Melamine is precursor for preparing bulk carbon nitride, which was heated to 550 °C temperature by the ramp of 2.5 °C.min^{-1} in a furnace for 4 h. Eventually, a yellow powder was formed. Then, for preparing g-C_3N_4, 1.0 g bulk C_3N_4 was stirred with 20mL H_2SO_4 at 90 °C for 5 h. Afterward, the mixture was diluted with 200 mL ethanol and stirred at room temperature for 2 h. Then, the mixture was dispersed in 100 mL water/isopropanol (1:1), sonicated for 6 h, and centrifuged to obtain g-C_3N_4.

2.3. Preparation of g-C_3N_4@L-arginine

(1.0 g) g-C_3N_4 with (20.0 mL) dry toluene was dispersed. Then, (2.0 mL) 1,3-dibromopropane was poured into the final mixture and refluxed for 24 h under an N_2 atmosphere. After filtration and washing with ethyl acetate, the product was dried at room temperature. The final product was dissolved in a mixture of water and methanol (1:1). Then, each of the following ingredients was added respectively, L-arginine (1mmol), K_2CO_3 (1.0 mmol), and NaI (1.0 mmol)). Afterward, it was stirred for 24 h at room temperature, washed with water and methanol, then dried at 80 °C.

2.4. Synthesizing Acridinedione Derivatives

A mixture of dimedone (2mmol), ammonium acetate (1mmol), aromatic aldehyde (1mmol), ethanol (5mL), and catalyst (0.18 mol %) was poured into a flask and refluxed for the appropriate time. The reaction progress monitored by TLC. After completion the reaction, the mixture was cooled to room temperature, the catalyst was filtered, and by crystallization the intended product was obtained.

2.5. Synthesizing Pyranopyrazole Derivatives

A mixture of aldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1.0 mmol), malononitrile (1.0mmol), catalyst (0.18 mol %), and ethanol (2.0 mL) was poured into a 25 mL round bottom flask and refluxed for the appropriate time. The reaction progress monitored by TLC. After completion the reaction, the mixture was cooled to room temperature, the catalyst was filtered, and by crystallization the intended product was obtained.

3. Results and Discussion

FT-IR spectra of a) g-C_3N_4, b) modified g-C_3N_4, and c) g-C_3N_4@L-arginine are shown in Fig 1. In Fig 1a, there is a broad peak around 3000 − 3300 cm^{-1} for N-H group stretching vibrations and is related to H- bonding or actually the existence of the OH group of water adsorption by g-C_3N_4 nanosheets. Fig 1(b) demonstrates the modified g-C_3N_4 nanosheets around 3000 − 2800 cm^{-1} which is related to C-H stretching vibrations. In Fig1(c), stretching vibrations of C=O and C-O were shown at (1705 cm^{-1}) and (1320 − 1210 cm^{-1}) respectively. A peak around 1602 cm^{-1} indicates carbon double bond nitrogen and its stretching vibrations. 1303 and 1082 cm^{-1} are related to the C-N bond stretching vibrations which are formed from triazine and N-H groups. The C-N stretching vibrations in the ring is significantly revealed at 1448 and 1379 cm^{-1}. 786 cm^{-1} was shown because of tri-s-triazine vibrations. According to the mentioned peaks, g-C_3N_4@L-arginine was synthesized [3,4].

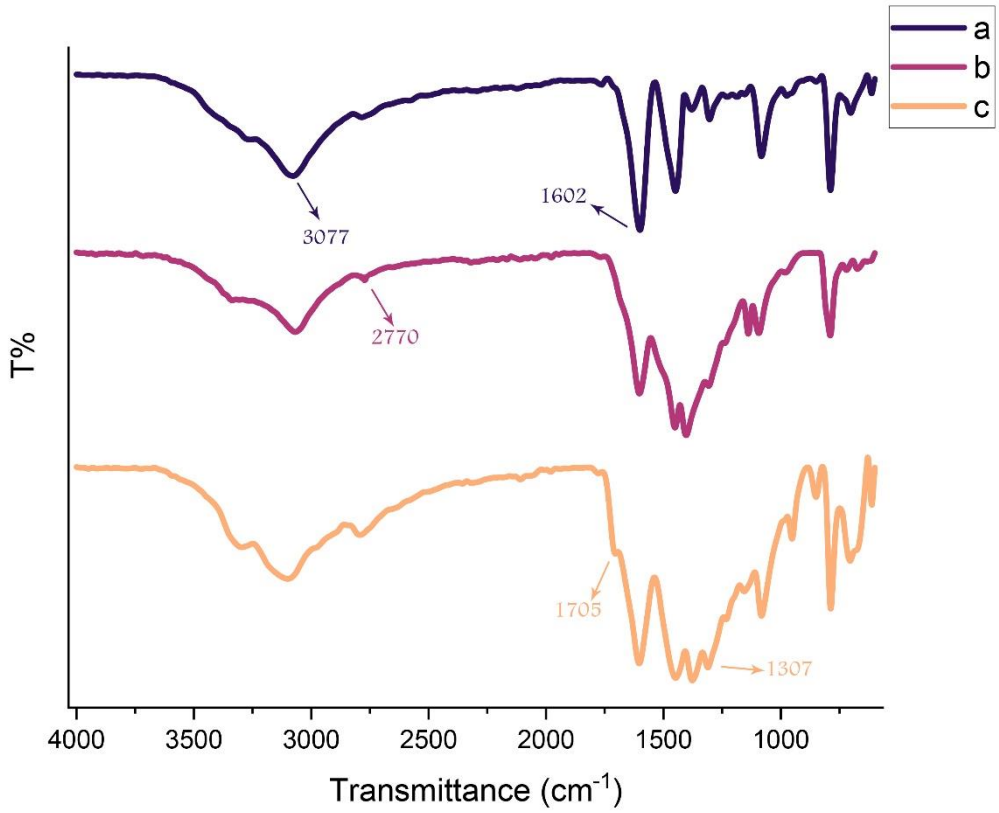
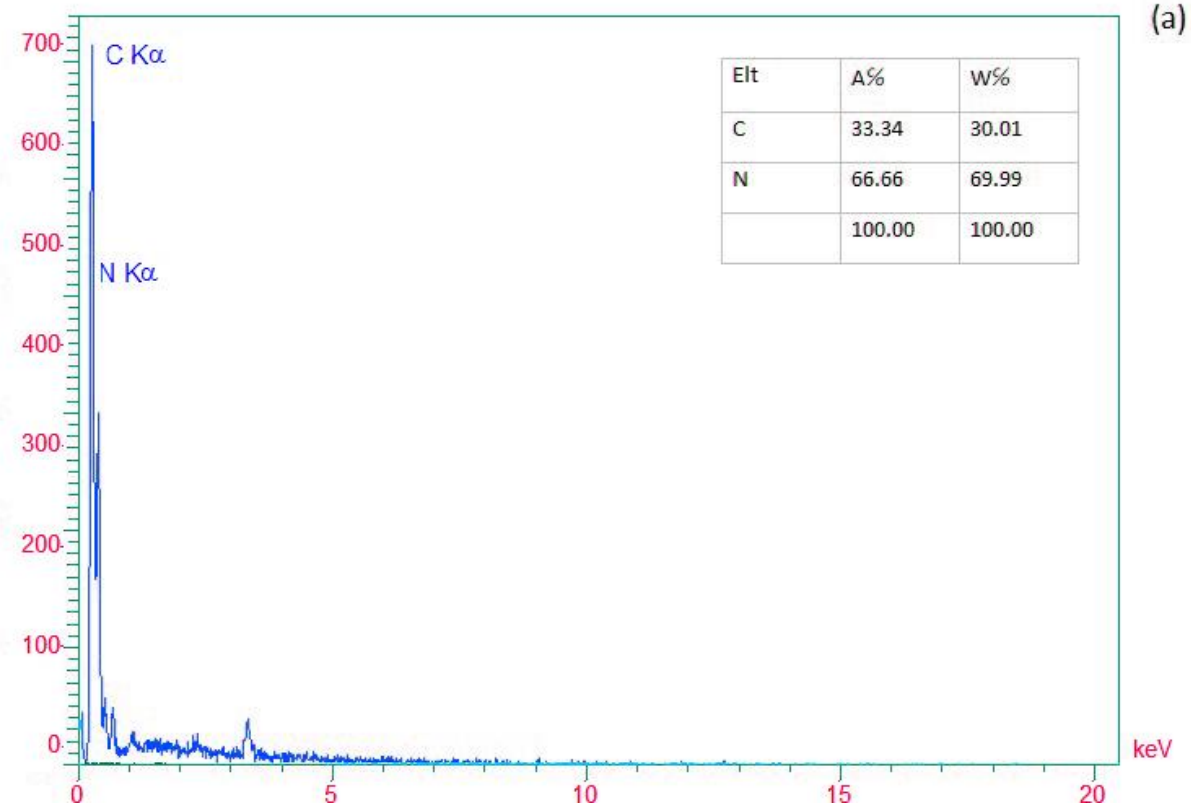


Figure 1. FT-IR spectra of a) g-C_3N_4, b) modified g-C_3N_4, and c) g-C_3N_4@L-arginine.

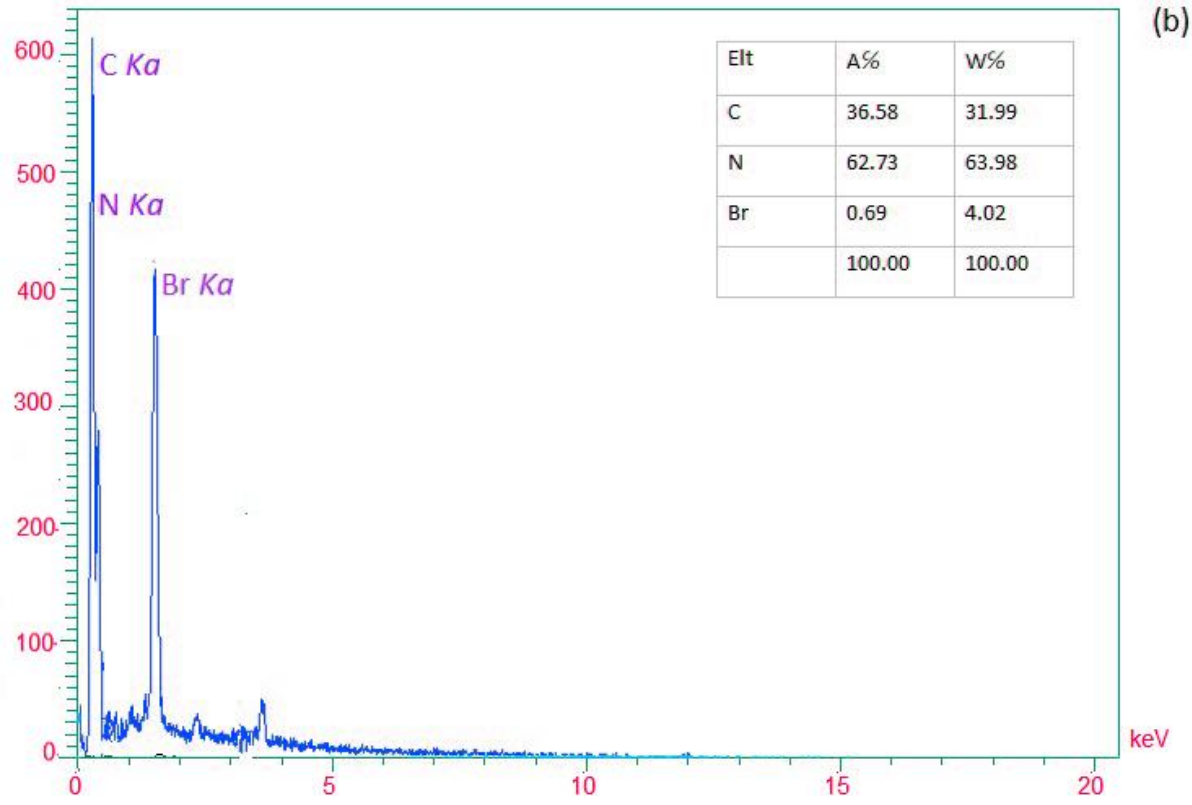
EDX analysis determined the presence of elements in a) g-C_3N_4 nanosheets, b) modified g-C_3N_4, and (c) g-C_3N_4@L-arginine. Nitrogen and Carbon elements in nanosheet g-C_3N_4 are visible in Fig2(a). In Fig2(b), the existence of the Br element would confirm the modification of g-C_3N_4 nanosheets. Moreover, Fig2(c) revealed the presence of carbon, nitrogen, and oxygen, which confirm the synthesizing of g-C_3N_4@L-arginine.

(a)



Elt	A%	W%
C	33.34	30.01
N	66.66	69.99
	100.00	100.00

(b)



Elt	A%	W%
C	36.58	31.99
N	62.73	63.98
Br	0.69	4.02
	100.00	100.00

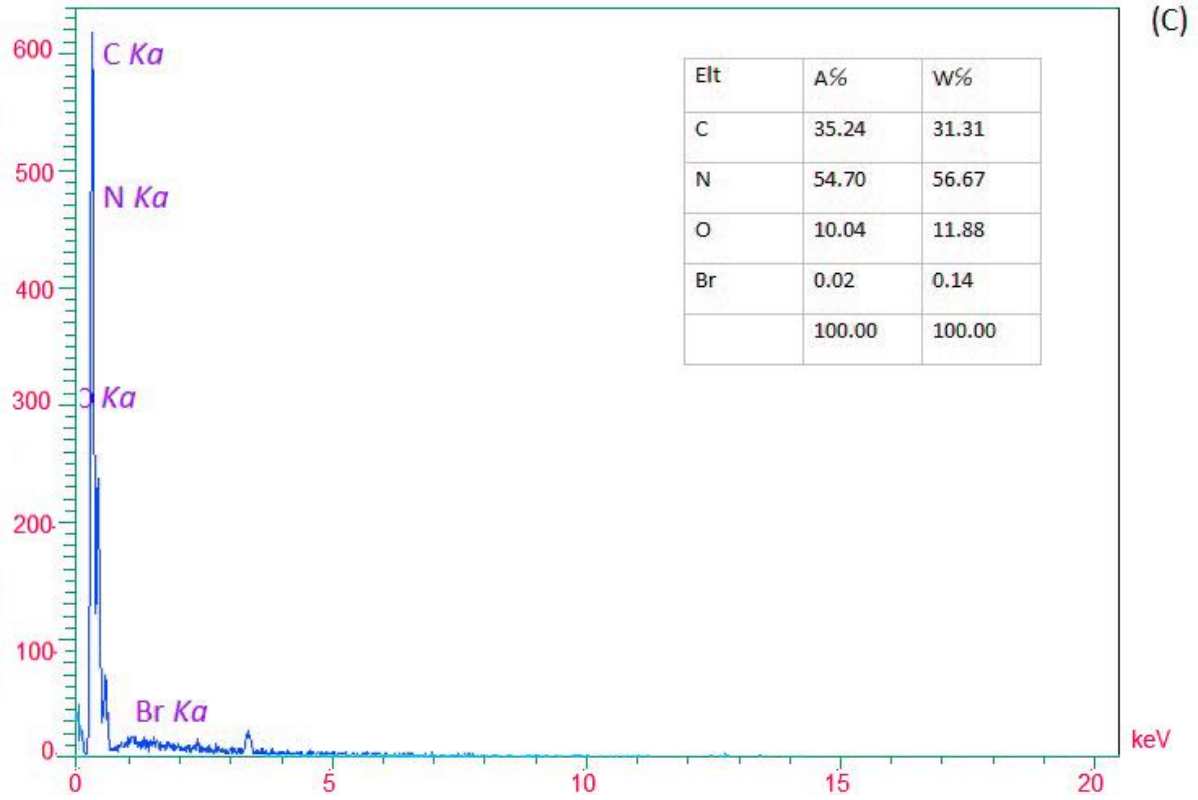


Figure 2. EDX spectra of a) g-C_3N_4 nanosheets, b) modified g-C_3N_4, and (c) g-C_3N_4@L-arginine.

The morphology of g-C_3N_4@L-arginine nanocatalyst was studied by FE-SEM analysis in two scales (200 nm and 1 μm). C_3N_4's graphitic and nanosheet properties are apparent based on Fig 3. It can be concluded that the g-C_3N_4@L-arginine nanocatalyst synthesizing has been successfully performed by observing the roughness of g-C_3N_4's surface.

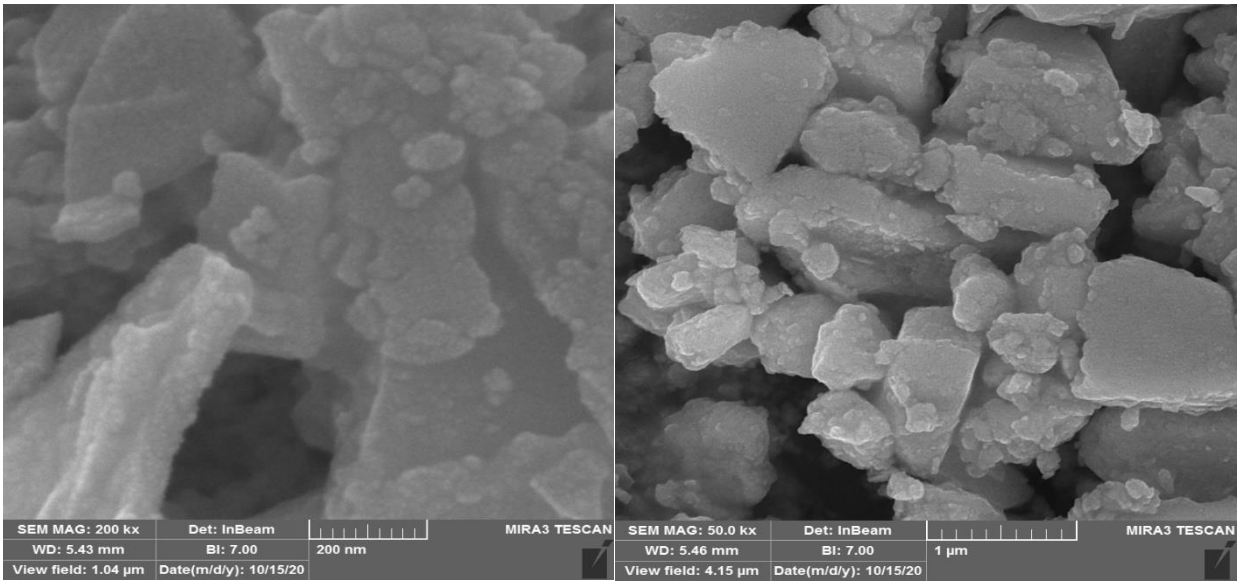


Figure 3. FE-SEM images of g-C_3N_4@L-arginine.

The XRD of g-C_3N_4 nanosheets and g-C_3N_4@L-arginine have been shown in Fig 4a-b. XRD pattern of nanosheet g-C_3N_4 in part (a) indicates the diffraction angles of $2\theta = 15.96°$ and $2\theta = 27.69°$, which approve the synthesizing of g-C_3N_4 [34]. Diffraction angles of $2\theta =$

30.97°, 23.60°, 12.21°, 10.85°, 6.07° in XRD pasttern part (b) indicate the L-arginine on the surface of g-C_3N_4@L-arginine (JCPDS card no. 00–004-0180).

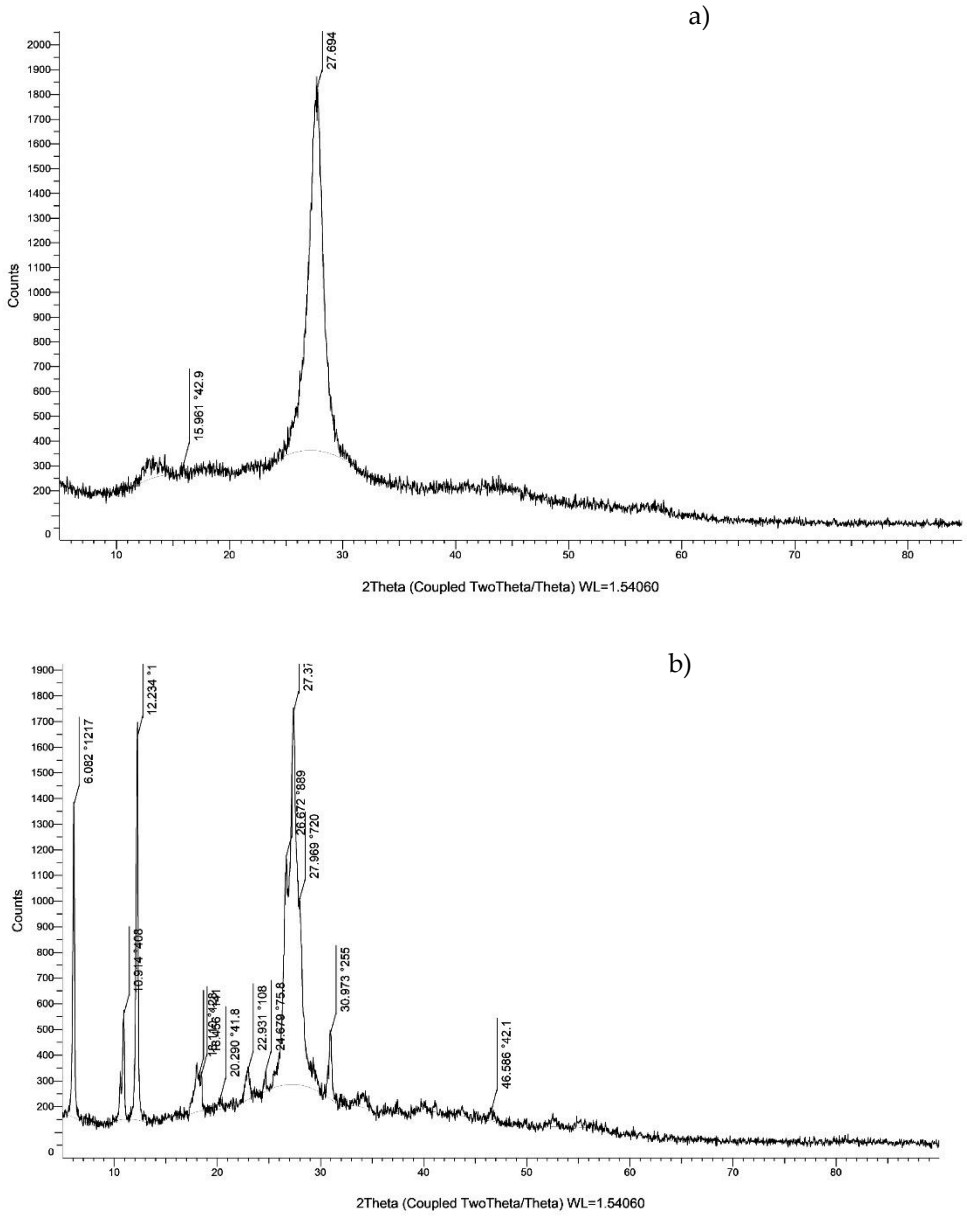


Figure 4. XRD spectra of a) g-C_3N_4 nanosheets and b) g-C_3N_4@L-arginine.

In Fig 5, g-C_3N_4@L-arginine thermal stability was shown at the range of 50 to 800 ℃. The weight ratio has decreased gradually from 100 to 200 °C because of the removal of absorbed water from g-C_3N_4@L-arginine. L-arginine's separation was observed from 200 to 400 °C. There is a dramatic decrease from 400 to 700 °C which is related to g-C_3N_4 nanosheets decomposition.

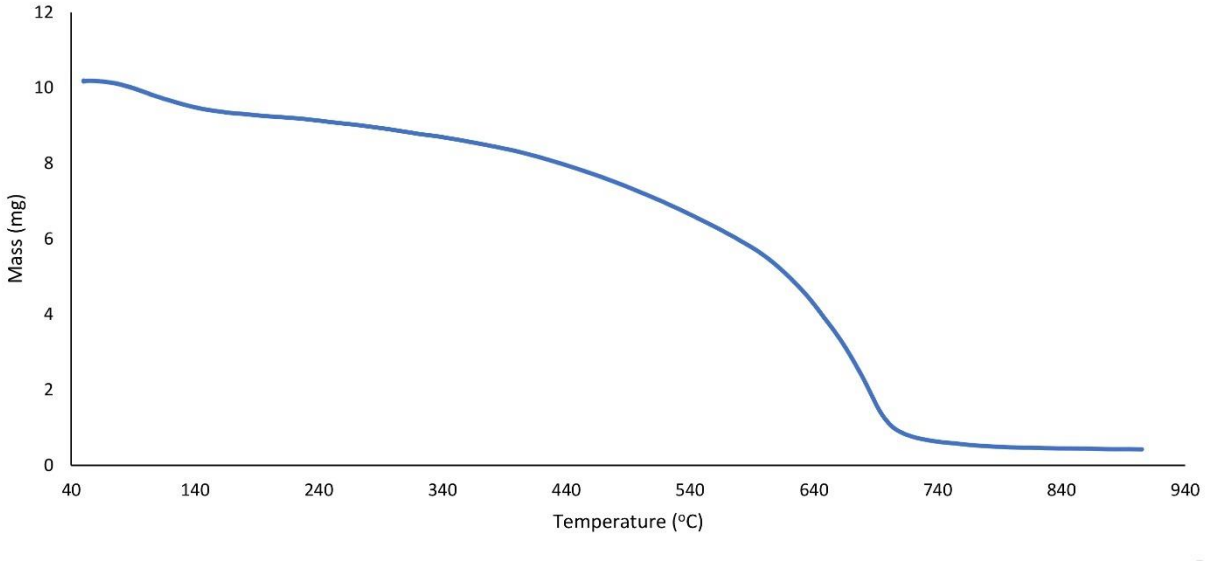


Figure 5. TGA spectrum of g-C_3N_4@L-arginine.

3.1. Application

The catalytic activity of produced heterogeneous nanocatalyst g-C_3N_4@L-arginine was studied for multi-component reactions. The optimum reaction conditions for synthesizing acridinedione and pyranopyrazole derivatives were evaluated. Synthesizing acridinedione derivatives have been performed by using dimedone (2mmol), 4-chloro benzaldehyde (1mmol), ammonium acetate (1mmol), ethanol (5mL), and catalyst (0.18 mol %) as model reaction1. In addition. pyranopyrazole derivatives were produced by malononitrile (1.0mmol), 4-chloro benzaldehyde (1.0 mmol), hydrazine hydrate (1.0 mmol), ethyl acetoacetate (1.0 mmol), ethanol (2.0 mL), and catalyst (0.18 mol %) as model reaction 2. The possibility of aldol reaction in aliphatic aldehydes would be the significant reason for using aromatic aldehydes compared to aliphatic aldehydes. Moreover, the reaction has been monitored by thin-layer chromatography (TLC). The model reactions have been investigated under different and convertible conditions. Initially, the reaction was performed with no catalyst at two different temperatures and the same reaction time (20 min). There was no acceptable efficiency as expected for both reactions (Table 1, entries 1-2). After using the catalyst (Table 1, entries 3-4), the desired products were produced in very small quantities at two different temperatures with the same environmental solvent. By using the catalyst at 80 °C for 20 min, there was a significant yield and efficiency up to 92% for the first reaction and 91% for the second one (Table 1, entry 5). Moreover, by increasing the reaction time up to 30 min, there are no noteworthy changes in the efficiency (Table 1, entry 6).

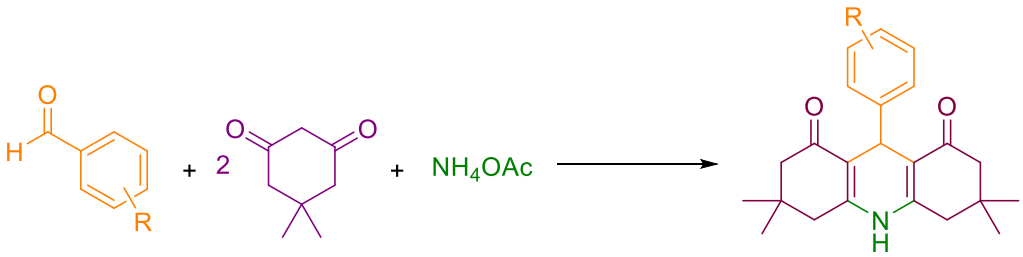
Also, changing the used solvent to water with the same condition as Table 1- entry 5 can decrease the efficiency of reactions 1 and 2 to 65% and 68 %, respectively (Table 1, entry 7). If the solvent of the reactions changed to methanol and acetonitrile (Table 1, entries 8 and 9), the reaction yield, in comparison with entry 5, will be increased and decreased, respectively. Likewise, the model reactions were performed by g-C_3N_4 (0.18 mol %) and L- arginine (0.18 mol %) with the same conditions, while the yield of the final products was decreased.

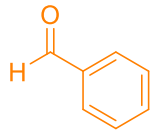
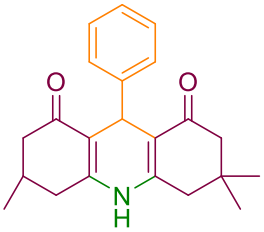
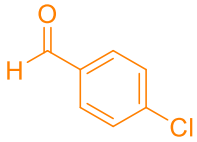
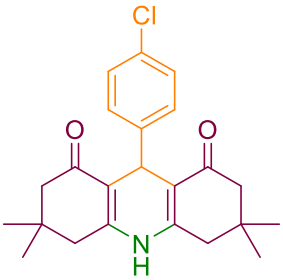
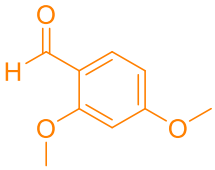
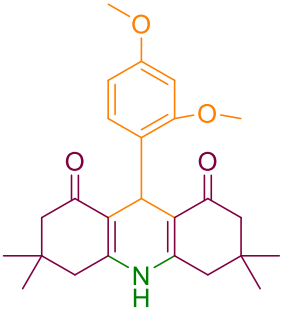
After optimization, different aromatic aldehydes were used to show the merits of g-C_3N_4@L-arginine catalytic activity and different pyranopyrazole and acridinedione derivatives were synthesized (Table 2 and 3).

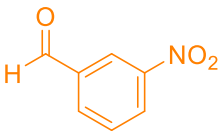
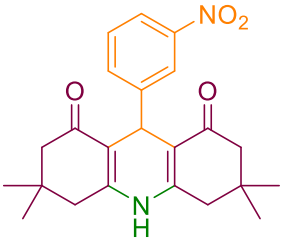
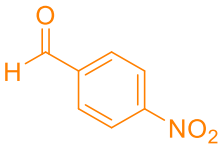
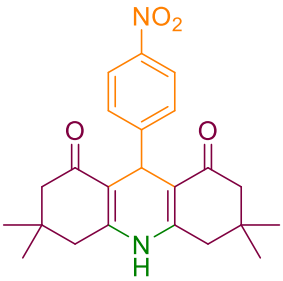
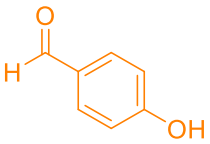
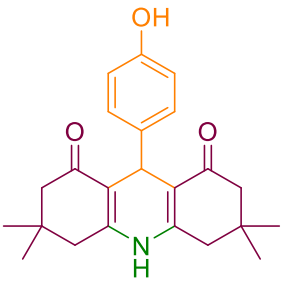
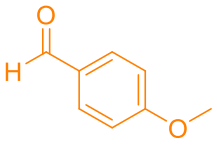
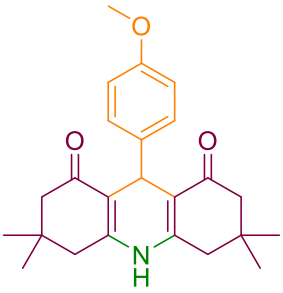
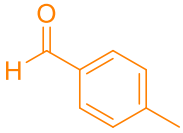
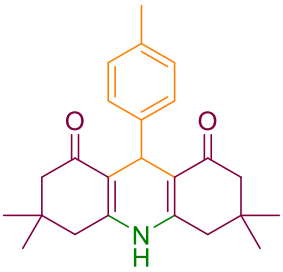
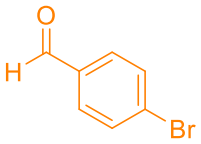
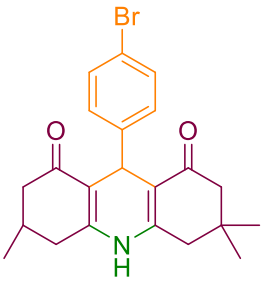
Table 1. Optimization of g-C_3N_4@L-arginine for reaction 1 and 2.

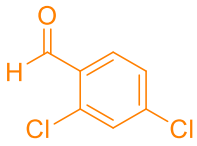
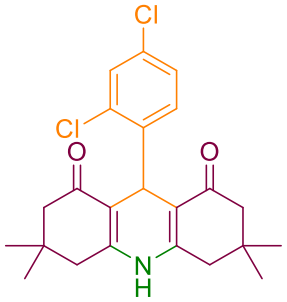
Entry	Catalyst	Temprature (℃)	Time (min)	Solvent	Yield (%) (Reaction 1)	Yield (%) (Reaction 2)
1	-	80	20	EtOH	-	-
2	-	80	20	EtOH	-	-
3	g-C_3N_4@L-arginine	RT	20	EtOH	12	14
4	g-C_3N_4@L-arginine	40	20	EtOH	53	48
5	g-C_3N_4@L-arginine	80	20	EtOH	92	91
6	g-C_3N_4@L-arginine	80	30	EtOH	90	87
7	g-C_3N_4@L-arginine	80	20	Water	65	68
8	g-C_3N_4@L-arginine	80	20	MeOH	86	73
9	g-C_3N_4@L-arginine	80	20	Acetonitrile	65	61
10	g-C_3N_4	80	30	EtOH	Trace	Trace
11	L-arginine	80	30	EtOH	32	30

Table 2. Synthesis acridinedione derivatives by g-C_3N_4@L-arginine[a,b].



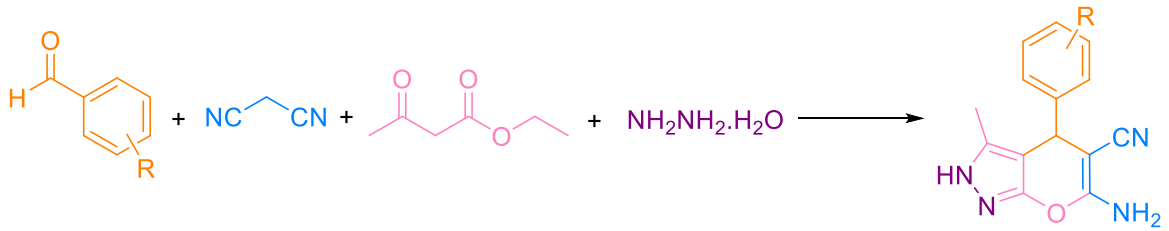
Entry	R	Amine	Product	Mp (℃, [Ref])	Yield (%)
1a		NH_4OAc		280–282 [35]	88
2a		NH_4OAc		302–304 [36]	92
3a		NH_4OAc		244–245 [37]	80

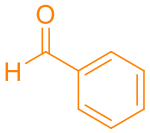
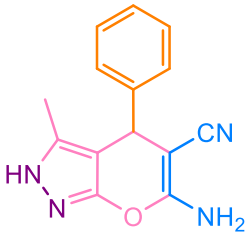
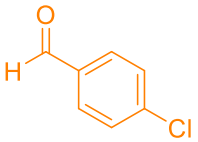
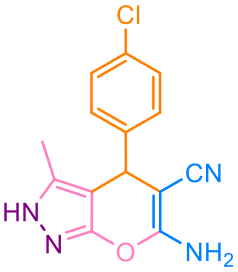
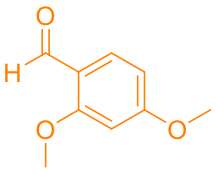
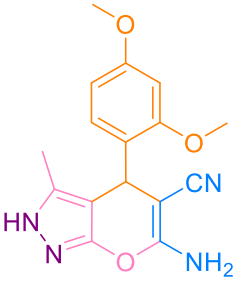
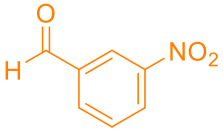
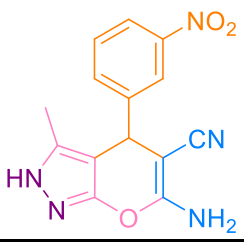
4a		NH_4OAc		291–293 [38]	83
5a		NH_4OAc		299–300 [39]	85
6a		NH_4OAc		283–285 [40]	79
7a		NH_4OAc		271–273 [41]	87
8a		NH_4OAc		330–333 [42]	78
9a		NH_4OAc		240–242 [43]	88

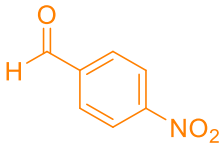
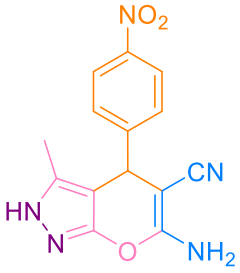
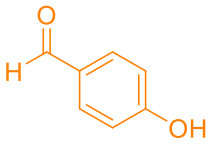
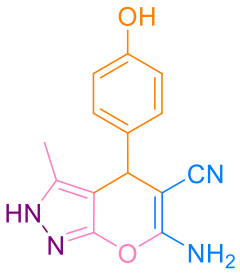
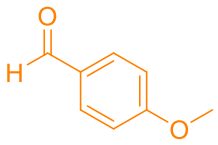
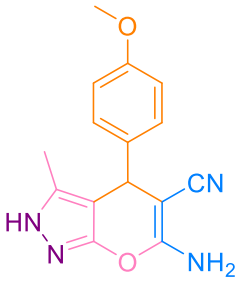
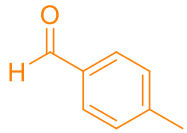
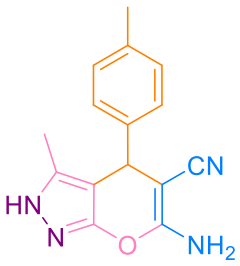
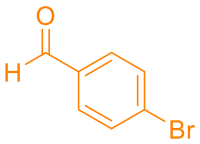
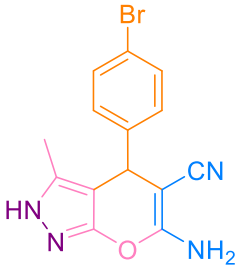
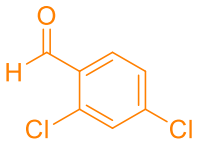
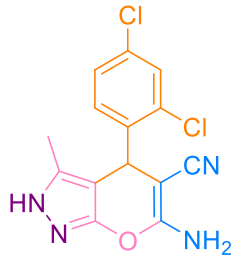
10a		NH_4OAc		319–321 [35]	90

[a] Reaction conditions: aromatic aldehyde (1mmol), dimedone (2mmol), ammonium acetate(1mmol), catalyst (20 mg), and ethanol (5mL) refluxed in 80 ℃. [b] Yields referred to pure products.

Table 3. Synthesis pyranopyrazole derivatives by g-C_3N_4@L-arginine[a,b].



Entry	R	Product	Mp (℃, [Ref])	Yield (%)
1b			244–245[44]	87
2b			227–229[45]	91
3b			185–187[46]	78
4b			237–238[47]	83

5b			250–251[48]	87
6b			225–227[49]	76
7b			211–213[19]	80
8b			208–210[49]	77
9b			184–186[45]	84
10b			197–198[50]	89

[a] Reaction conditions: aromatic aldehyde (1mmol), hydrazine hydrate (1mmol), ethyl acetoacetate (1mmol), malononitrile (1mmol) catalyst (20 mg), and ethanol (5mL) refluxed in 80 °C. [b] Yields referred to pure products.

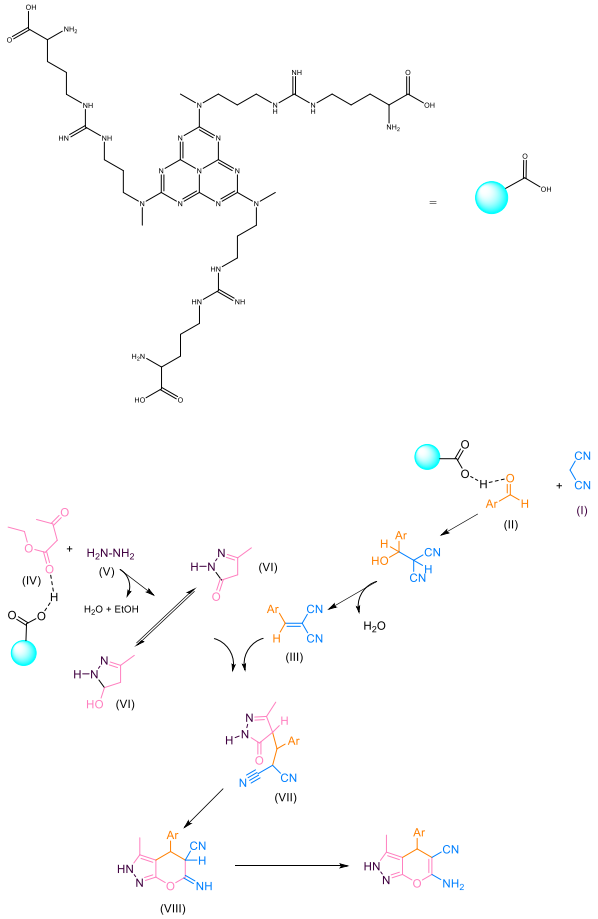
3.2. Mechanism of Using Nanocatalyst for Synthesizing Pyranopyrazole and Acridinedione Derivatives

3.2.1. Pyranopyrazoles

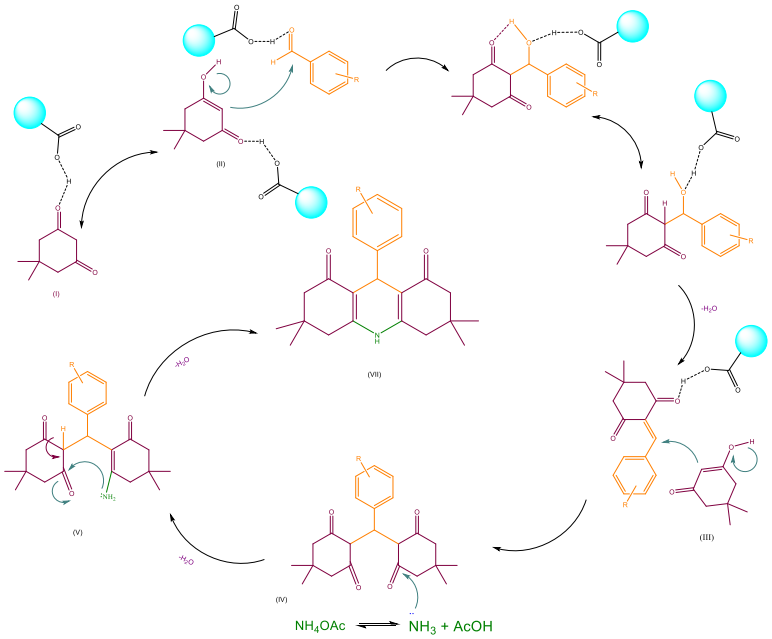
The study of the mechanism for pyranopyrazole derivatives and the proposed mechanism is shown in Scheme 2. Also, it needs g-C_3N_4@L-arginine for activating different intermediates and reactants. Malononitrile (I) and aromatic aldehyde (II) would react with each other by the carbon as a nucleophile. The carbon nucleophile reacts with the carbonyl group by releasing water, the intermediate (III) would produce. Simultaneously, ethyl acetoacetate (IV) and hydrazine hydrate (V) react with each other and form the intermediate (VI). Afterward, the amine group's non-bonding electron pair reacts with the ethyl acetoacetate's carbonyl group. In the following step, the 5-member ring was closed by removing the water molecule. In the last step, two produced intermediates, ((III) and (VI)), reacted with each, and the pryranopyrazole derivative has synthesized.

3.2.2. Acridinediones

The study of the mechanism for acridinedione derivatives synthesis and the proposed mechanism is exhibited in Scheme 3. For activating the carbonyl group of aldehyde, the existence of g-C_3N_4 @L-arginine is essential. After activating the carbonyl group with nanocatalyst (I) and producing the hydroxyl group on dimedone (II), the carbon nucleophile would react with activated aromatic aldehyde. Then the other dimedone reacts the double bond for donating electrons (III) and after a water molecule removal, the ring was closed by an intramolcular reaction (IV, V and VI). Eventually, the intended product has obtained (VII).



Scheme 2. Proposed mechanism for synthesizing pyranopyrazole derivatives.



Scheme 3. Proposed mechanism for synthesizing acridinedione derivatives.

3.3. Reusability

The recovery and recyclability of the catalyst are the essential principles of green chemistry. So, g-C_3N_4@L-arginine's reusability was studied for synthesizing pyranopyrazole and acridindione derivatives. G-C_3N_4@L-arginine was extracted from the reaction, washed with water and ethanol, then dried at 70 °C. It has been repeated five times in the same conditions. After each reaction, the yield decreased gradually, but it was acceptable (Fig 6).

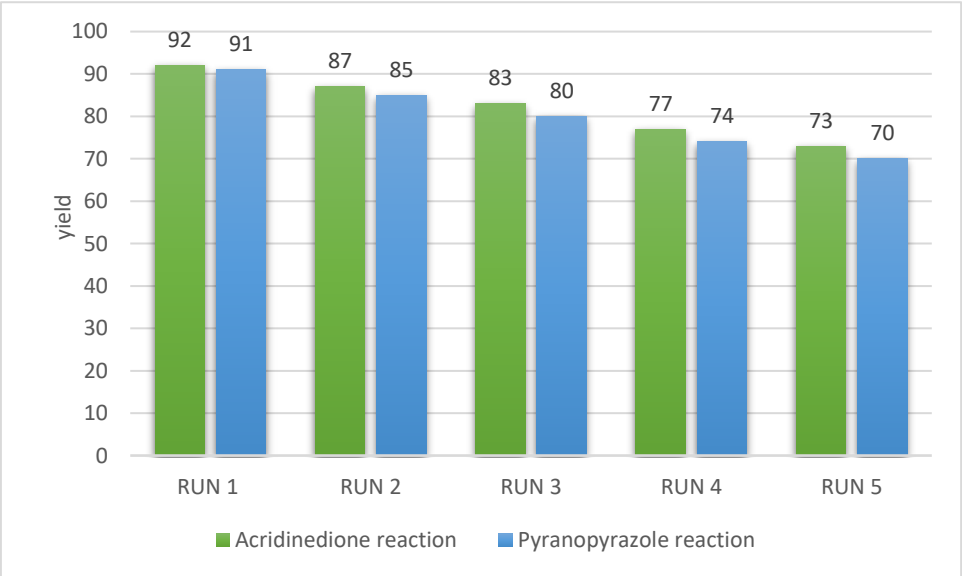


Figure 6. Reusability of g-C_3N_4@L-arginine in acridindione and pyranopyrazole derivatives.

4. Conclusion

In conclusion, in this project we utilized easy and convenient method for preparing g-C_3N_4@L-arginine nanocatalyst and applied for producing pyranopyrazole and acridindione derivatives. G-C_3N_4@L-arginine nanocatlayst has remarkable advantages such

as reusability, easy separation, high efficiency, and short reaction time. According to the results, produced nanocatalyst is the superiority over other reported catalysts.

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