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1,4-Butane-Sultone Functionalized Graphitic Carbon Nitride as a Highly Efficient Heterogeneous Catalyst for the Synthesis of 2,3-Dihydroquinazolines Derivatives †

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Abstract: 1,4-Butane-sultone functionalized graphitic carbon nitride nanosheets (g-C_3N_4@Bu-SO_3H) was prepared and applied as an efficient heterogeneous catalyst for the synthesis of various quinazolines derivatives with high yield. In next step, the structure and morphology of catalyst was characterized by different analyses such as, FT-IR, EDS, XRD and FE-SEM. On the other side, considering the noticeable features of g-C_3N_4@Bu- SO_3H such as high stability, easy to synthesize, non-toxicity, excellent reusability, and so on, the synthesis of 2,3-dihydroquinazolines derivatives with numerous advantages such as short reaction time reaction condition, easy separation and etc were realized.

Keywords: 1,4-Butane-sultone; graphitic carbon nitride; 2,3-dihydroquinazolines derivatives; heterogeneous catalyst

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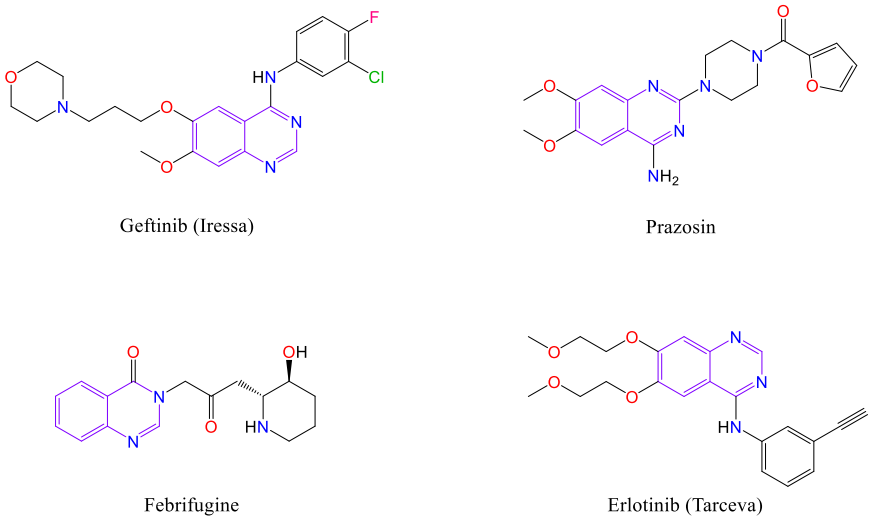
1. Introduction

Quinazolines and their derivatives are as a significant class of nitrogen-containing heterocyclic scaffolds that the structure of these compounds have been formed from six-membered fused rings [1]. Accordingly, these quinazolines derivatives have numerous biological activities, including anticancer, antimalaria, antimicrobial, antiviral, anti-HIV, anti-inflammatory, antifungal, acaricidal, weedicide, antidepressant, anticonvulsant, muscle relaxant, and so on [2,3]. On the other side, because of various biological values, they are utilized for synthesis of considerable drugs such as prazosin (treatment of benign prostatic obstruction) [4], geftinib (antitumor therapeutic agents) [5,6], erlotinib (EGFR inhibitor) [7], lapatinib (tyrosine kinase inhibitor) [8], alfuzosin (anticancer) [9], febrifugine (antimalaria) [10], and etc. (Scheme 1).

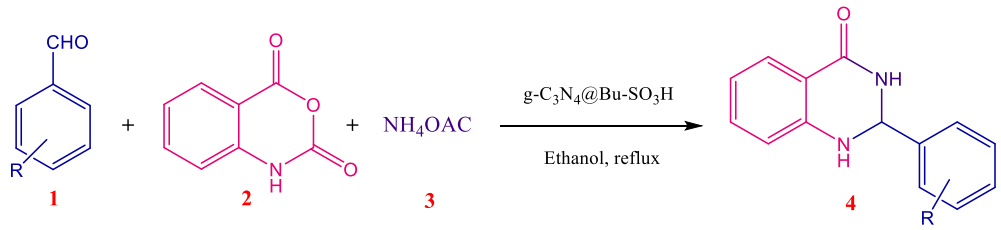
Recently, the preparation of 2,3-dihydroquinazolines derivatives has been heeded as the basic structure of the most bioactive medicines [11]. Therefore, to apply an effective and excellent catalyst is a noticeable approach to develop the synthesis of them with high yield. Because of various advantages such as, photocatalytic activity, wastewater treatment, organic transformation, disinfection, healthcare, environmental, electrochemical biosensor, CO_2 reduction, and H_2 generation [12,13]. Graphitic carbon nitride (g-C_3N_4) is considered as catalytic support for synthesis of different heterogeneous catalyst. In addition, Among the various catalytic methods, the use of metal-free heterogeneous catalysts is one of the best methods due to its green nature, easy synthesis and separation [14]. Although, there are different types of metal and metal-free catalysts such as PBDS-SCMNPs ionic liquid [15], Wang-OSO_3H [16], Silica sulfuric acid [17], titanium silicon oxide [18], montmorillonite-KSF [19], $SrCl_2.6H_2O$ [20], and $Y(NO_3)_3.6H_2O$ [21] that have been used for the synthesis of these heterocyclic derivatives but These catalysts have disadvantages and limitations

such as difficult and long synthesis steps, expensive reagents, high reaction temperature, and low stability that lead to importance of the synthesis and characterization of suitable metal-free catalyst that can be beneficial for eliminating these disadvantages.



Scheme 1. Some of the pharmaceutical active compounds containing quinazoline structures.

In this work, a high efficient metal-free heterogeneous catalyst (g-C_3N_4@Bu-SO_3H) was prepared and applied for synthesis of 2,3-dihydroquinazoline and its derivatives with excellent advantages consisting of short reaction time, inexpensive and available raw materials, no oxidant, and high selectivity (Scheme 2 and Table 1).



Scheme 2. Multi-component reaction for the synthesis of 2,3-dihydroquinazolines derivatives.

Table 1. Synthesis of 2,3-dihydroquinazoline derivatives using g-C_3N_4@Bu-SO_3H metal-free catalyst.

Entry	R	Product	Time (min)	Mp (°C)	Yield
1	H	4a	15	207–210	90
2	4-Cl	4b	15	203–206	96
3	2-Cl	4c	15	205–206	95
4	4-NO_2	4d	20	201–202	90
5	3-OH	4e	30	212–216	89

Reaction conditions: benzaldehyde (1 mmol), isotonic anhydride (1 mmol), and ammonium acetate (1 mmol), g-C_3N_4@Bu-SO_3H (20 mg) and ethanol (7 mL) under reflux conditions.

2. Experimental

2.1. Material

All chemicals were purchased from the Merck (NJ, USA) and Sigma-Aldrich (Burlington, MA, USA) Co. Fourier Transform Infrared (FT-IR) spectra were recorded on Tensor 27. Nuclear Magnetic Resonance (NMR) data were acquired on a Varian-Inova 500 MHz. X-Ray Diffraction (XRD) patterns were obtained using Dron-8 diffractometer. Energy-dispersive X-ray (EDX) spectrum was recorded on Numerix DXP-X10P. Field Emission Scanning Electron Microscopy (FE-SEM) images were recorder with TESCAN-MIRA III.

2.2. Preparation of Bulk g-C_3N_4 and Nanosheets

First, the melamine powder was heated at 550 °C in furnace in air atmosphere at the heating rate 2.5 °C/min for 4 h. Then, the obtained yellow powder was well ground with a mortar to obtain a blended solid powder. In next step, for the synthesis of g-C_3N_4 nanosheets, bulk g-C_3N_4 (1.0 g) was stirred with H_2SO_4 (20.0 mL) at 90 °C for 5 h. The resulting mixture was stirred by (200 mL) ethanol in room temperature at 2 h and it remained constant until all the material was settled. After 2 days, the resulting mixture was dispersed by ultrasonic probe at 300 W for 1.5 h. Eventually, the formed suspension was washed three times by ethanol and seven times by distilled water. After that, white product was dried in oven at 60 °C.

2.3. Preparation of Graphitic Carbon Nitride Nanosheets Functionalized with 1,4-Butane-Sultone (g-C_3N_4@Bu-SO_3H)

First, the g-C_3N_4 nanosheets (1.0 g) were dispersed in toluene (25 mL), after that 1,4-butane-sultone (3.0 g) was added the reaction mixture and was refluxed under nitrogen atmosphere for 6 h. Finally, the resulting product got cold in room temperature, then it was centrifuged and washed with chloroform and ethyl ether solvents, and dried in oven at 60 °C.

2.4. Selected Spectral Data

2-phenyl-2, 3-dihydro-4(1*H*)-quinazolinone (4a)

FT-IR (KBr, cm^{-1}): 3300, 3176, 2981, 1651, 1610, 1507, 1440, 1385, 745 cm^{-1}. ^{1}H NMR (500 MHz, DMSO): δ H (ppm) = 5.75 (s, 1H, CH), 6.67 (t, 1H, Ar-H), 6.74 (d, 1H, Ar-H), 7.1 (s, 1H, NH), 7.23 (t, 1H, Ar-H), 7.34 (t, 1H, Ar-H), 7.38 (t, 1H, Ar-H), 7.49 (d, 1H, Ar-H), 7.60 (d, 1H, Ar-H), 8.27 (s, 1H, CONH) (Figures 1 and 2).

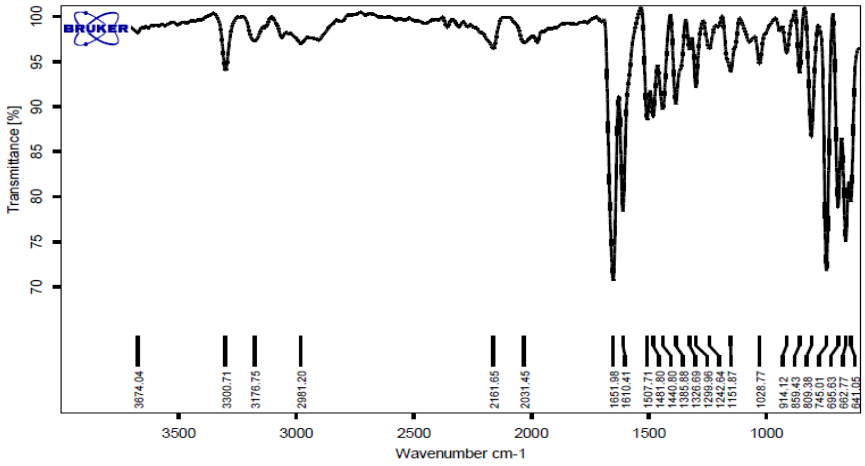


Figure 1. FT-IR spectrum of the 2-phenyl-2,3-dihydro-4(1H)-quinazolinone.

2-(4-chloro-phenyl)-2, 3-dihydro-1*H*-quinazoline-4-one (4b)

FT-IR (KBr, cm^{-1}): 3305, 3184, 3062, 1654, 1606, 1431, 1090, 749 cm^{-1}. ^{1}H NMR (500 MHz, DMSO): δ H (ppm) = 5.77 (s, 1H, CH), 6.68 (t, 1H, Ar-H), 6.74 (d, 1H, Ar-H), 7.1 (s, 1H, NH), 7.24 (t, 1H, Ar-H), 7.45 (d, 1H, Ar-H), 7.50 (d, 1H, Ar-H), 7.61 (d, 1H, Ar-H), 8.27 (s, 1H, CONH) (Figures 3 and 4).

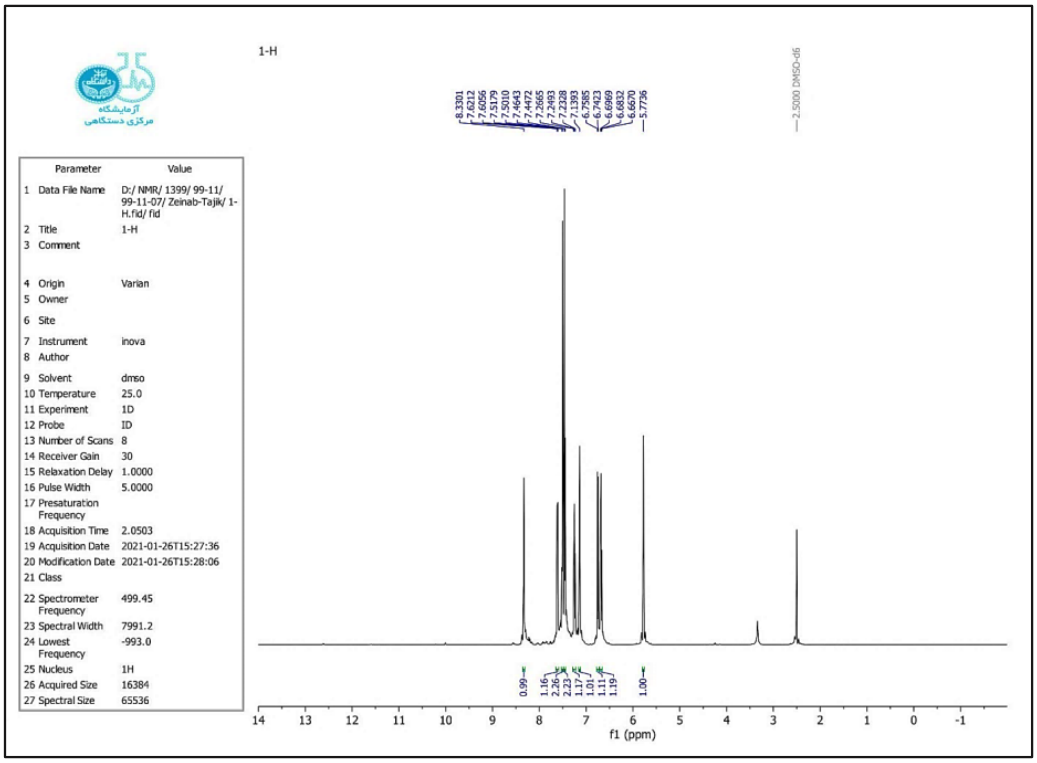


Figure 2. ^{1}H NMR spectrum of the 2-phenyl-2,3-dihydro-4(1H)-quinazolinone.

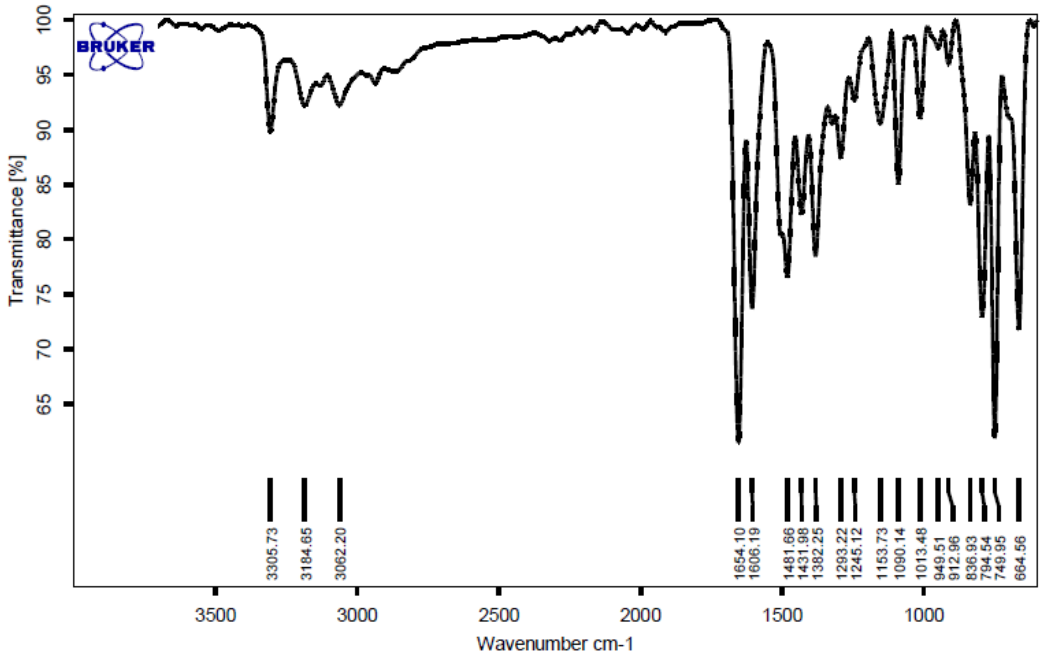


Figure 3. FT-IR spectrum of the 2-(4-chloro-phenyl)-2,3-dihydro-1H-quinazoline-4-one.

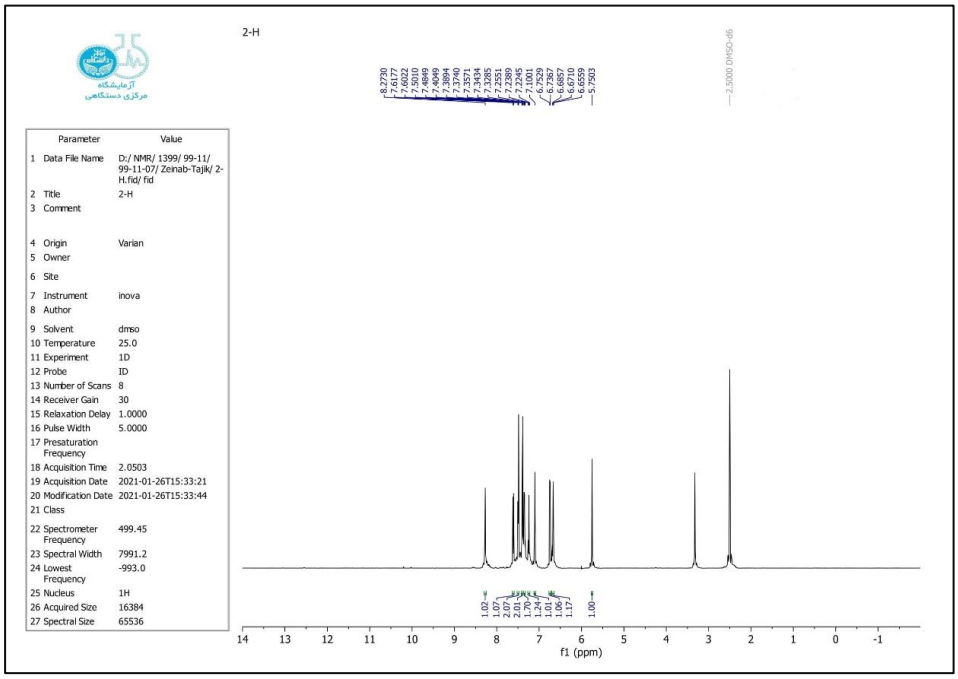


Figure 4. ^{1}H NMR spectrum of the 2-(4-chloro-phenyl)-2,3-dihydro-1H-quinazoline-4-one.

3. Results and Discussion

The g-C_3N_4@Bu-SO_3H heterogeneous catalyst was synthesized in just three steps (Scheme 3). In the first step, bulk g-C_3N_4 was prepared by polymerization of melamine. In the second step, the morphology of bulk g-C_3N_4 was changed to g-C_3N_4 nanoparticle. Finally, g-C_3N_4 nanoparticle was functionalized with 1,4-butane-sultone. This catalyst was proved by different analyses such as Fourier Transform Infrared (FT-IR) Spectroscopy, Energy Dispersive Spectrometer (EDS), Field Emission Scanning Electron Microscopy (FE-SEM), and X-ray diffraction analysis (XRD) [22].

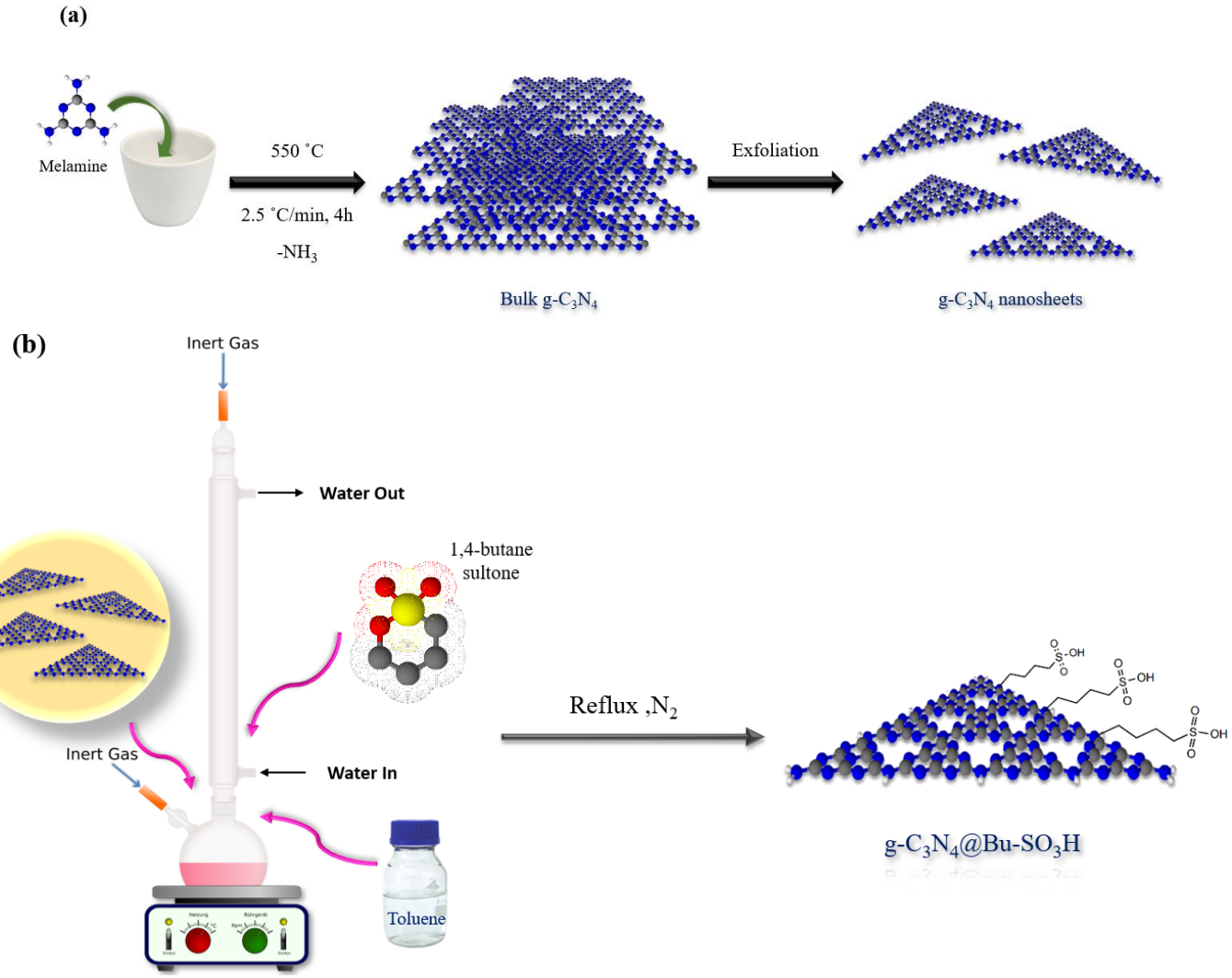
The FT-IR spectra of g-C_3N_4 nanosheets (a) and g-C_3N_4@Bu-SO_3H (b) have been showed in Figure 5. A relatively strong peak in the range of 3000 to 3300 cm^{-1} is related to stretching vibration of N–H bonds, the 1602 cm^{-1} peak is related to C=N stretching vibration modes. The absorption peak of C–N bonds observed in rang of 1303 and 1082 cm^{-1} that can be attributed to C–N bonds between triazine and N–H groups. On the other hand, the characteristic peaks at 1448 and 1379 cm^{-1} are related to C–N ring bonds and finally, the peak at 784 cm^{-1} may be related to tri-s-triazine units (Figure 5a).

In the spectrum of g-C_3N_4@Bu-SO_3H, which is shown in Figure 5b, the two peaks 2781 and 2758 cm^{-1} are related to C–H groups in 1,4-butane-sultone. The symmetric and asymmetric stretching vibration modes of SO_2 have appeared in the regions 1220 and 1348 cm^{-1}, the characteristic peaks at 1176 and 1207 cm^{-1} are related to S–OH bonds.

In the Figure 6a, the presence of carbon and nitrogen atoms in structure of g-C_3N_4 nanosheets was confirmed by the EDS analysis. As shown in the Figure 6b, the presence of oxygen and sulfur elements proves synthesis of desired catalyst (g-C_3N_4-Bu-SO_3H).

The morphology of g-C_3N_4 nanosheets and g-C_3N_4@Bu-SO_3H were shown by the FE-SEM images. In the Figure 7a, the g-C_3N_4 nanosheets have a relatively flat surface, while in the Figure 7b, image of g-C_3N_4@Bu-SO_3H is partly different and irregular. Therefore, this variance can verified the deposition of sultone on the g-C_3N_4 nanosheets.

The XRD pattern of g-C_3N_4 nanosheets and g-C_3N_4@Bu-SO_3H can be seen in Figure 8. Diffraction peaks at 2θ: 27.35° (002) and 13.04° (100) are related g-C_3N_4 nanosheets (Figure 8a). Also diffraction peaks at 2θ: 27.4° (002), 2θ = 17.9°, and 14.8° (100) are related to the g-C_3N_4@Bu-SO_3H that approve synthesis of this catalyst (Figure 8b).



Scheme 3. Synthesis of g-C_3N_4 nanosheets (**a**), g-C_3N_4@Bu-SO_3H (**b**).

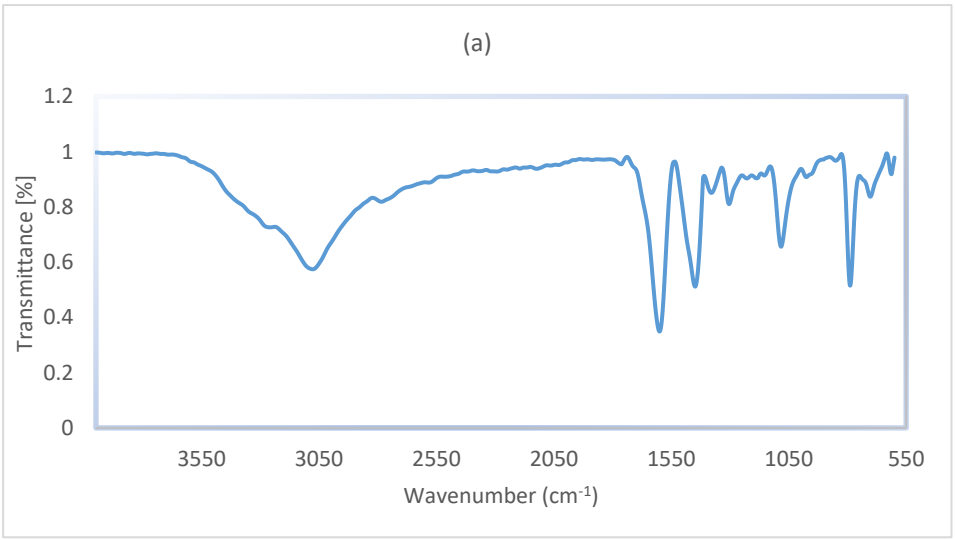


Figure 5. *Cont.*

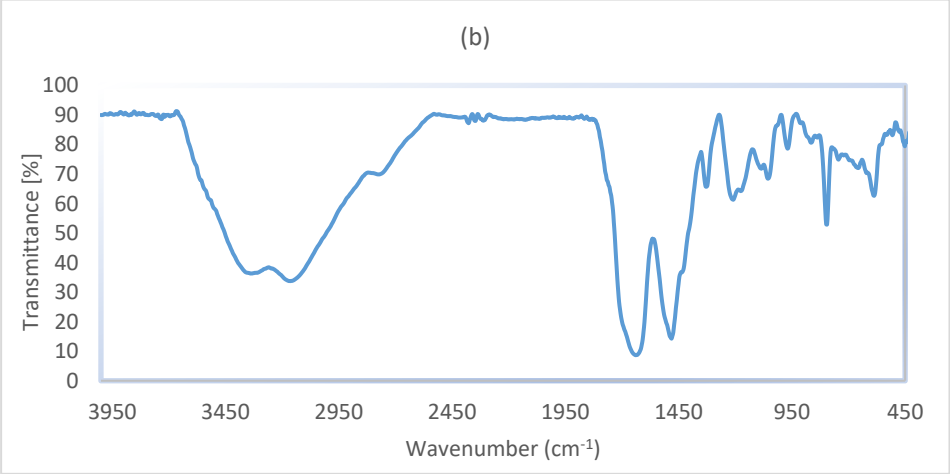


Figure 5. The FT-IR spectra of g-C_3N_4 nanosheets (**a**), g-C_3N_4@Bu-SO_3H catalyst (**b**).

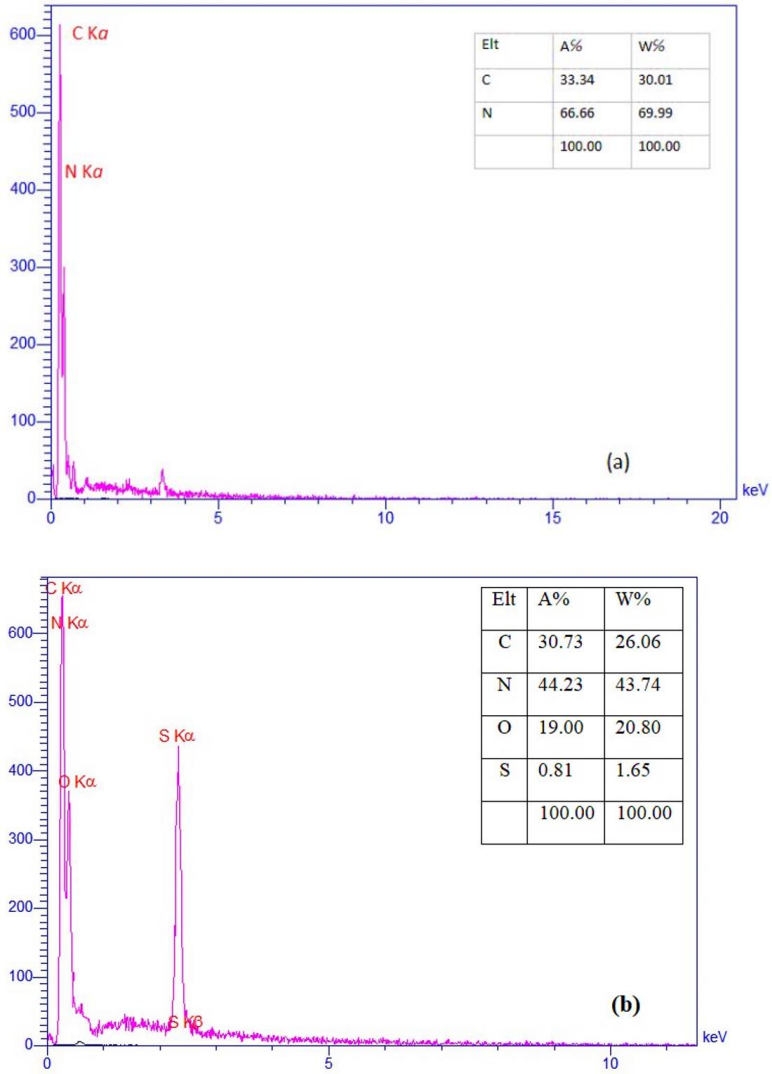


Figure 6. EDS spectra of g-C_3N_4 nanosheets (**a**), g-C_3N_4@Bu-SO_3H (**b**).

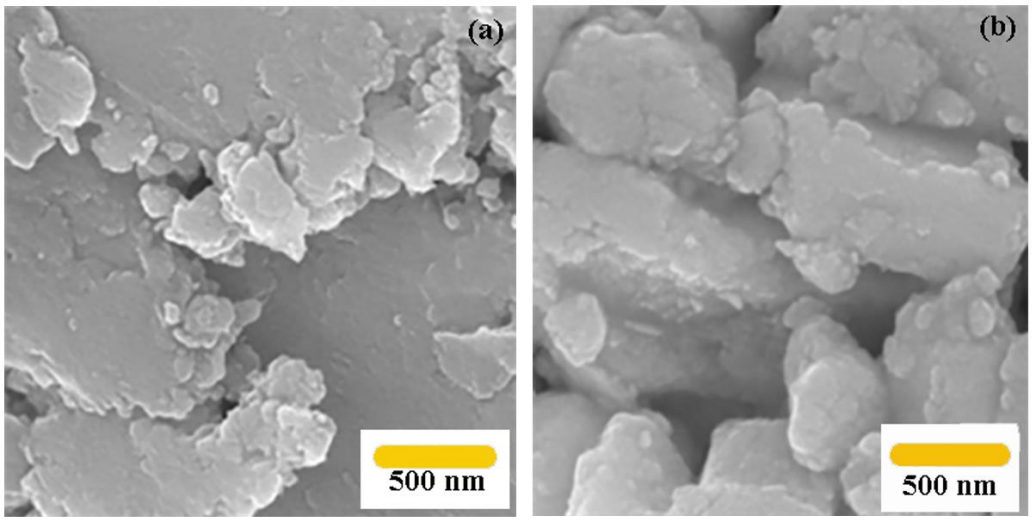


Figure 7. FE-SEM image of g-C_3N_4 nanosheets (**a**), g-C_3N_4@Bu-SO_3H (**b**).

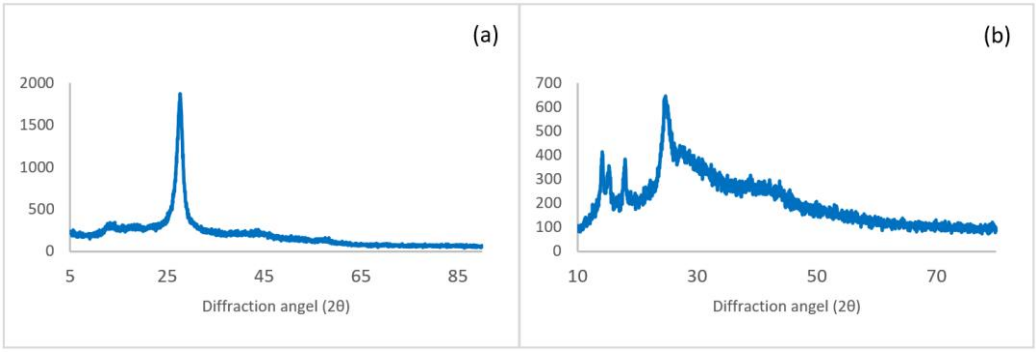


Figure 8. XRD spectra of g-C_3N_4 nanosheets (**a**), g-C_3N_4@Bu-SO_3H (**b**).

4. Reusability

Reusability of g-C_3N_4@Bu-SO_3H catalyst was examined for synthesis of 2,3-dihydroquinazolines derivatives in four runs, the considering Figure 9, reaction yield was decreased considerably after third run.

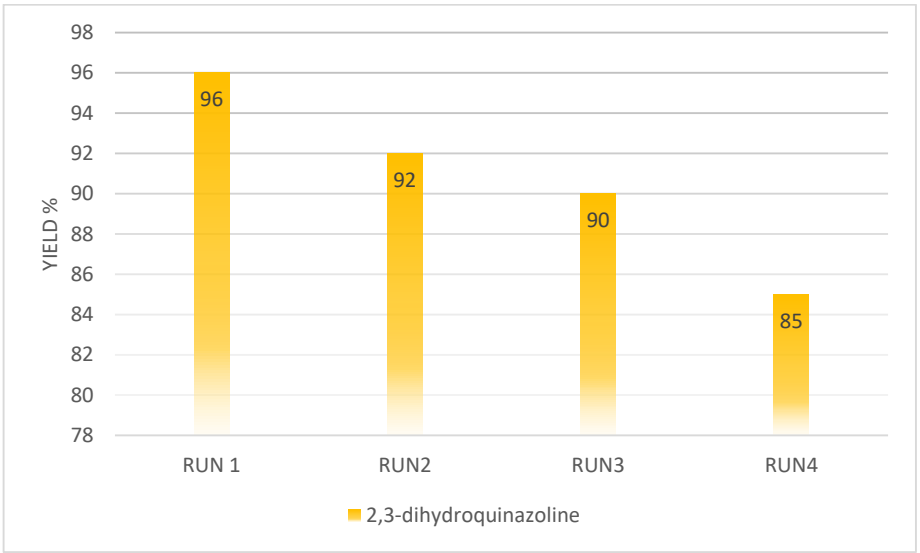


Figure 9. Reusability of g-C_3N_4@Bu-SO_3H catalyst for synthesis of 2,3-dihydroquinazolines derivatives.

5. Conclusions

In summary, an efficient heterogeneous catalyst (g-C_3N_4@Bu-SO_3H) was synthesized and utilized for production of 2,3-dihydroquinazolines derivatives with highly advantages such as short reaction time, mild condition, and easy separation. On the other side, this catalyst can be used and recycled for five times with high yield.

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