Facile Fabrication and Characterization of Sb(III)-Impregnated Magnetic Carbon Nitride Nanosheets: Evaluation of Its Catalytic Activity for Greener Synthesis of Biologically Relevant Imidazo[1,2-a]pyridines

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Research Article

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Abstract

The magnetic nanoparticle (Fe_3O_4) and catalytic antimony trichloride (SbCl_3) were co-immobilized in the graphitic carbon nitride nanosheets ($\text{SbCl}_3@ \text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$) using a straightforward solvent evaporation process. The designed catalysts showed excellent catalytic activity for the Groebke–Blackburn–Bienaymé multicomponent reaction for the preparation of substituted imidazo[1, 2-a]pyridines at room temperature. This convergent synthetic protocol enabled molecular diversity synthesis under appealingly mild conditions with operational simplicity in a selective, time, and cost-effective manner. X-ray diffraction (XRD), infrared spectroscopies (FTIR), thermogravimetry (TG), Scanning electron microscopy (SEM), indicate the structural integrity of all components. The combination of environmentally benign reaction conditions, effortless composite recyclability offers magnetic carbon nitride economically viable for industrial processes.

Running Head

Isocyanide-Based Multicomponent Reaction Enabled Carbon Nitride Nanosheets

1. Introduction

Carbon-based materials include carbon black, graphite, graphene nanosheets, carbon nanotubes, and graphitic carbon nitrides with diverse structures and outstanding physicochemical properties have attracted considerable interest [1–3]. Graphitic carbon nitride ($\text{g-C}_3\text{N}_4$), a low-cost carbon source material, has a unique electronic structure, and excellent chemical, physical, and thermal stability has gained extensive attention [4]. The system of $\text{g-C}_3\text{N}_4$ is similar to that of graphite sheets, by introducing nitrogen to produce the two-dimensional conjugated polymer in tri-s-triazine pattern in photocatalytic fields [5–8]. Thus, $\text{g-C}_3\text{N}_4$ can create one-step polymerization of various and easily accessible nitrogen-rich and carbon-rich precursors, such as cyanamide, melamine, and urea [9–11]. All of these have provided $\text{g-C}_3\text{N}_4$ as favorable and adoptable carbon-based support and catalyst for industries and academicians [12]. In general, the bulk $\text{g-C}_3\text{N}_4$ shows some severe drawbacks, such as small specific areas and low photocatalytic activity, which significantly limit its practical industrial applications [13–15]. Thus, it is desirable to improve the performance of $\text{g-C}_3\text{N}_4$ by hybridizing with other components to address these problems.

Passerini or Ugi isocyanide-based multicomponent reactions have been significant in many synthetically useful transformations [16–18]. Isocyanide derivatives are one of the simplest and abundant starting materials for synthesizing a broad array of pharmaceutically relevant scaffolds and materials science [19–20]. Therefore, one-pot, multicomponent isocyanide-based reactions are regarded as robust tools in combinatorial chemistry over the decades. Among the nitrogen derivatives, heterocyclic scaffolds derived from imidazole-fused heterocycles are of paramount interest in medicinal chemistry due to their antiviral, antibacterial, fungicidal, and antimicrobial activity [21]. Imidazo-fused heterocycles are the precursor of

some natural products and as well as in colored materials with unusual physical and chemical properties [22]. Due to their great importance, countless reports of their preparation and properties of these biologically critical heterocyclic compounds have appeared in the literature [23–25]. In 1998, an exciting isocyanide based multicomponent reaction was discovered by Groebke, Bienaymé, and Blackburn to prepare imidazopyridines [26–28]. This isocyanide-based multicomponent reaction was reported to be milder than the conventional methods with high yields in all cases [29–32]. The one-pot result became extremely popular in the last decade due to the advantages of simple operations, multicomponent, and environmentally benign nature of the procedure. Numerous reports have appeared covering a broad scope of the reaction [33]. A range of diversified catalysts, including Bronsted acids, Lewis acids like and metal catalysts for the one-pot, the three-component reaction of 2-aminopyridine, various aldehyde, and isocyanide to afford imidazo[1, 2-a] pyridines have been reported [34–41]. However, several of these approaches are hampered by several inherent drawbacks, namely long reaction time, the requirement for an inert atmosphere, moderate yield, boring work-up with innumerable toxic wastes. Thus, significant efforts have been made to improve the mild and environmentally benign catalytic system and reaction media (supercritical fluids, ionic liquids, water, deep eutectic solvent, and solvent-free) for Groebke reaction in recent years [42–46].

2. Experimental

2.1 General

All chemicals such as aldehydes, isocyanide, 2-aminopyridine, FeCl_2 , FeCl_3 , and melamine were commercially available. All reagents and starting materials were of analytical pure and used without any purification. Buchi melting point B-535 apparatus was used for the melting point. The samples' morphologies were taken by scanning electron microscopy (SEM Merlin, Zeiss) at an accelerating voltage of 300 kV.

2.2 Synthesis of $\text{g-C}_3\text{N}_4$

Bulk $\text{g-C}_3\text{N}_4$ sheets prepared from melamine source in a muffle furnace following our previously reported procedure [12]. Briefly, 10 g of melamine powder was put into an alumina crucible and heated to 500 °C with a rate of 10 °C/min and then kept at this temperature for 4 h under air conditions. After cooling down naturally, the yellow powder ground to powders in a mortar and washed several times with ethanol, and dried. The exfoliation process, where bulk $\text{g-C}_3\text{N}_4$ exfoliated into monolayered $\text{g-C}_3\text{N}_4$ nanosheets carried out in concentrated H_2SO_4 according to the Wang methods [47].

2.2.Preparation of $\text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$

15 mmol $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 5 mmol $\text{FeCl}_2 \cdot 2\text{H}_2\text{O}$, and the 4 g of $\text{g-C}_3\text{N}_4$ dissolved into 50 mL of H_2O /deep eutectic solvent oxalic acid-choline chloride (weight ratio water/ deep eutectic solvent = 1:2 v/v) under magnetic stirring for 40 min at rt. Next, 5.0 g sodium hydroxide was slowly added into the above mixture

and magnetically stirred for another 30 min. This mixture was transferred to a 100 mL Teflon-lined stainless steel autoclave and heated at 180 °C for 60 h. The sample was then washed with double-distilled water and ethanol in the presence of an external magnet and was dried.

2.3. Preparation of $\text{SbCl}_3@ \text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$ nanocomposites

1 g of SbCl_3 and 4 g of $\text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$ were dispersed in 200 mL of THF under sonication and continually stirred at 50 °C for 24 h. The reaction mixture was centrifuged, washed with methanol, and dried under vacuum at 60 °C to provide a dark yellow solid (Scheme 1).

Scheme 1. Schematic illustration of nanocomposite

2.4 General procedure:

The appropriate aldehyde (0.5 mmol), 2-aminopyridine (0.5 mmol), cyclohexyl isocyanide (0.5 mmol), ethylene glycol (2.0 mL) and $\text{SbCl}_3@ \text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$ (25 mg) was taken in a round bottom flask with a magnetic stir bar. The reaction mixture was stirred vigorously at room temperature for 2-5 h. After completion of the reaction (as monitored visually or by TLC), the product was precipitated out and extracted with hot ethyl acetate (15 mL) and recrystallized. The related products were formed with high purity and characterized by melting point and spectroscopic methods.

3. Results And Discussion

In connection with our research to develop the essential heterocyclic compounds in a greener way to improve the economic and environmental aspects, [48-51], we designed antimony decorated magnetic carbon nitride nanosheets as novel and highly efficient catalyst for Groebke–Blackburn–Bienayme reaction at room temperature.

Magnetic $\text{SbCl}_3@ \text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$ was fabricated for the first time through facile one-step synthesis using antimony trichloride, Fe_3O_4 melamine as precursors following our previous work [40]. The morphology, chemical states, and functional groups of the resultant nanocomposite have been thoroughly investigated. Figure 1 shows the SEM images for the composite catalyst. From Fig. 1, it can be seen that $\text{g-C}_3\text{N}_4$ displays a layered, flat, sheet-like structure with irregular morphology, and some of the particles agglomerate together. Whereas the morphology of Fe_3O_4 nanoparticles is grown on the $\text{g-C}_3\text{N}_4$ surface, have rough spheres with agglomeration.

EDS surface mapping analysis is used to identify the chemical composition of the catalyst displayed in Fig. 2. All elemental constituents of the composite (Sb, Cl, Fe, O, N and C) are found in the EDS spectra. The EDS mapping findings indicated that Fe_3O_4 and SbCl_3 uniformly located on the surface of the $\text{g-C}_3\text{N}_4$ is the evidence for successful modification.

FTIR spectra in Fig. 3 reveal that the incorporation of magnetic nanoparticles and SbCl_3 did little change to the basic C-N network and has the nearby pattern as pure $\text{g-C}_3\text{N}_4$. The broad peaks between 3490 and 2985 cm^{-1} are assigned to the typical N-H and O-H stretching vibrations. As indicated in Fig. 3, a series of peaks ranging between 1114 and 1635 cm^{-1} which can be assigned to stretching modes of N-containing aromatic rings (N-C=N) while the sharp peak placed at 806 cm^{-1} is attributed to the bending vibration of heptazine rings, clearly showing that the $\text{g-C}_3\text{N}_4$ is fabricated of heptazine units. The peak at 649 cm^{-1} is attributed to the Fe-O band's vibrations and suggests that Fe_3O_4 is chemically grafted onto the $\text{g-C}_3\text{N}_4$ rather than by physical adsorption. The peak at 743 cm^{-1} indicates the presence of antimony as Sb^{3+} caused by the formation of physical bonds between $\text{g-C}_3\text{N}_4$ and SbCl_3 in the composite. In addition, from the composite's FTIR spectra, the characteristic peaks of both SbCl_3 and Fe_3O_4 can be noticed, and composites contained both of them drawn.

The catalytic performance of the $\text{SbCl}_3@\text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$ composites was investigated using the three-component one-pot reaction of benzaldehyde (**1a**), 2-aminopyridine (**2**), and cyclohexyl isocyanide (**3**) in ethanol (2.0 mL) as a model reaction to identify suitable reaction conditions (Table 1). Initial attempts of the model reaction under catalyst-free conditions gave no desired product (Table 1, entry 1). An element of the catalyst used to determine the influence of each partner of composite on the yield of the reaction, it was found that SbCl_3 as Lewis acids play an essential catalytic role, and other components gave only traces of the desired product (Table 1, entries 2-5). For the sake of comparison, other Lewis acids supported magnetic carbon nitride such as BiCl_3 , SnCl_2 , ZnCl_2 , CeCl_3 , CuCl_2 , and FeCl_3 were used as catalysts for the same reaction (Table 1, entries 7-11). Among various examined Lewis acids, ZnCl_2 and SbCl_3 were found to be the most effective catalysts for this multicomponent reaction. Various protic and aprotic solvents, including dichloromethane, ethanol, methanol, water, ethyl acetate, acetonitrile, tetrahydrofuran, glycerole, and ethylene glycol, were explored (Table 1, entries 11-19). Antimony trichloride in ethylene glycol was found to be the most impressive media both in terms of reaction time and yield. The optimum amount of the nanocomposite was explored, and it identified that on increasing the amount of composite from 10 mg to 25 mg, the yield of the reaction increases progressively. Furthermore, no considerable improvement in the rate and the yield of the reaction, observed when more than 25 mg of catalyst used. Notably, the reaction proceeds smoothly at room temperature, and the progress of the reaction was followed visually by the appearance of reddish-yellow color solids.

Encouraged by these results, to evaluate this methodology's scope and generality, one-pot multicomponent reaction of a wide variety of aromatic aldehydes that contained electronically and sterically diverse substituents, 2-amino pyridine, and cyclohexyl isocyanide were examined (Table 2). The broader applicability of the catalytic effect of nanocomposite on Ugi-based multicomponent reactions is supported by a generation of a library of imidazo [1,2-a] pyridines derivatives under remarkably mild conditions. The aromatic aldehyde bearing a diverse range of functional groups, namely nitro, bromo and chloro ether, ester, alkyl, and methoxy, were identified to be compatible under the current system. The reaction performed well regardless of the position of functional groups on aromatic aldehydes. Acid-

sensitive heteroaryl aldehydes like 2-furaldehyde and thiophene-2-carboxaldehyde gave multicomponent products in good yield without any side reactions, which are usually found under acidic conditions.

The model reaction carried out a gram scale to demonstrate the potential and the practicality of our novel catalyst, which is essential from an industrial perspective. The model reaction with 10 mmol scales of starting materials in ethylene glycol (100 mL) in the presence of catalyst composite (0.2 g), proceeded smoothly at room temperature to give the desired product **4a** in 92 % yield.

The stability and the reusability of nanocomposite and its activity were studied by recycling experiments for the preparation of imidazo [1,2-a] pyridines **4a**, and the results are shown in Figure 4. Upon completion of the reaction, water and ethyl acetate added, and the catalyst separated by an external magnet and was washed with ethyl acetate, and dried under a vacuum. Investigations in the model multicomponent reaction showed that the recovered nanocomposite could be efficiently reused a minimum five times without noticeable loss of activity and yields.

Conclusion

In summary, unique, highly active, and talented, magnetic nanocomposite synthesized from economical precursors using a straightforward procedure. The nanocomposite was found to be a safe, non-toxic, and reusable, and inexpensive catalyst in the synthesis of fused imidazoles bridgehead heterocyclic nitrogen compounds from the Ugi-type isocyanide-based multicomponent reaction with a broad range of substrates in high yields. The mild reaction conditions, short reaction times, greener solvents, and recyclability of the catalyst are the outstanding features of the current work.

Declarations

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Tables

Due to technical limitations, table 1 and 2 is only available as a download in the Supplemental Files section.

Figures

Figure 1

SEM images of the prepared nanocomposite

Figure 2

EDX image of nanocomposite

Figure 3

FTIR spectra of nanocomposite

Figure 4

The recyclability test of $\text{SbCl}_3/\text{Fe}_3\text{O}_4/\text{g-C}_3\text{N}_4$

Supplementary Files

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