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p-Aminobenzenesulfonic Acid-Functionalized Periodic Mesoporous Organosilica: A Highly Efficient and Recyclable Nanoreactor for Sustainable Imidazopyrimidine Synthesis †

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Abstract

The innovative PABSA-Pr-PMO catalyst represents a significant advancement in nanomaterial design for sustainable catalysis. By combining periodic mesoporous organosilica (PMO) with *p*-aminobenzenesulfonic acid (PABSA) via a co-condensation process followed by sequential integration, the material achieves a hierarchical structure with exceptional thermal stability, a high surface area, and uniform mesopores. These features create abundant, accessible active sites while ensuring robustness for repeated use. The precise engineering of Brønsted acidic sites from PABSA enhances proton-transfer efficiency, critical for activating C–H acids in multicomponent reactions. In the Traube–Schwarz reaction, PABSA-Pr-PMO catalyzes the synthesis of imidazopyrimidine derivatives—compounds with pharmaceutical relevance, including anticancer and antimicrobial properties—by efficiently coupling 2-aminobenzoimidazole, C–H acids, and aromatic aldehydes under mild conditions. The catalyst's performance excels with ultralow loading, driving reactions to completion within 5–15 min versus hours with conventional acids. Yields reach 90–99% emphasizing precision in product formation. Its recyclability, maintaining >90% activity after five cycles, underscores economic and environmental benefits, aligning with green chemistry principles. The absence of toxic solvents or excessive energy input further reduces the process footprint. This protocol not only streamlines synthesis but also demonstrates scalable potential for industrial applications, offering a reusable, efficient alternative to homogeneous catalysts. By merging advanced nanomaterial design with sustainable reaction engineering, PABSA-Pr-PMO exemplifies a transformative approach to green chemical manufacturing, bridging molecular innovation with practical scalability.

Keywords: periodic mesoporous organosilica; imidazopyrimidine derivatives; multicomponent reactions (MCRs)

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1. Introduction

Imidazopyrimidines are bicyclic heterocyclic organic compounds that contain a five-membered imidazole ring fused to a six-membered pyrimidine ring [1]. This core structure, a fused ring system found in many biologically active molecules (like

pharmaceuticals and agrochemicals), can be described as a scaffolding or framework that is central to the chemical architecture of a large number of medicines and pesticides [2]. The location of the nitrogen atoms within the ring structures dictates the compound's characteristics and its potential to interact biologically [3]. Imidazopyrimidine synthesis can be achieved through multicomponent reactions (MCRs), which are single-pot organic transformations where three or more starting materials react to form a product that incorporates substantial portions of all the components [4,5]. This approach is highly prized in contemporary organic and medicinal chemistry because it offers excellent efficiency, superior atom economy, and the capacity to construct a wide variety of intricate molecular frameworks [6]. The broad utility of imidazole compounds demands efficient protocols for synthesizing their highly substituted derivatives [7].

A class of porous, structured hybrid solids that organically link silicate frameworks, resulting in materials with both a highly ordered, repeating internal pore system (periodic mesoporous) and chemically functional organic components integrated directly within the silica walls (organosilica) [8]. They are characterized by three-dimensional porous framework where organic groups are an integral part of the silica pore walls, forming "bridges" between silicon atoms [9]. This is a key distinction from other mesoporous silicas, where organic groups are often just attached to the surface [10]. PMOs combine the desirable properties of both organic and inorganic materials, making them versatile for a wide range of applications [11]. They serve as supports for catalysts, offering a large, accessible surface area for chemical reactions [12]. PMOs are typically synthesized using a sol-gel process involving the hydrolysis and co-condensation of bridged organosiloxane precursors in the presence of a structure-directing agent, such as a surfactant [13]. The surfactant acts as a template, guiding the formation of the ordered pores, which are then retained after the surfactant is removed [14].

This work describes the creation of a new, highly effective, and reusable solid catalyst called PABSA-Pr-PMO (**1**). This catalyst is specifically designed for the synthesis of imidazopyrimidine derivatives.

2. Materials and Methods

2.1. Materials

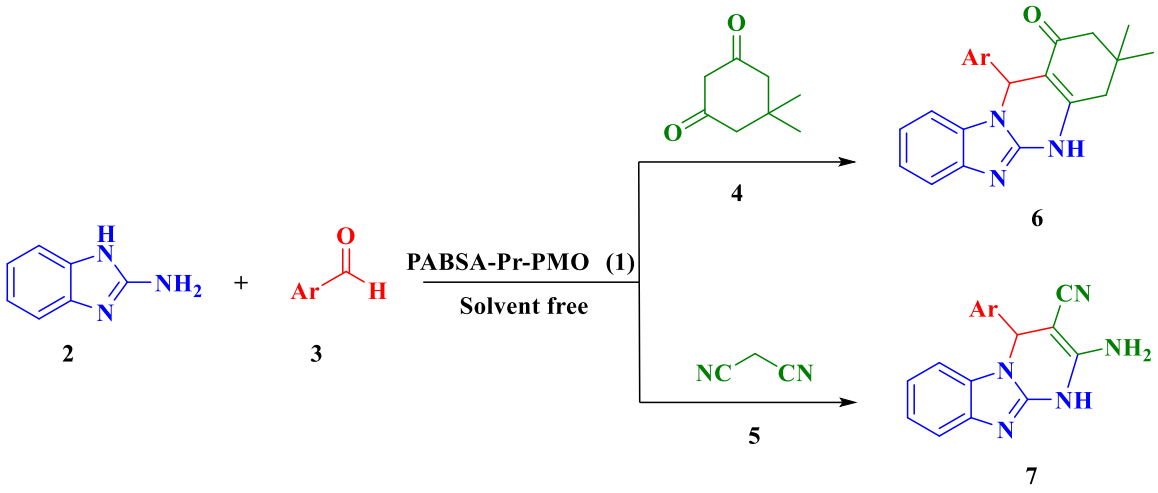
All chemical reagent were purchased from Merck. Thin-layer chromatography (TLC) was employed to track both the purity of the chemicals compounds and the completion of the reactions using ethyl acetate and n-hexane. Melting points were recorded by using an Electrothermal IA 9000 apparatus.

2.2. Methods

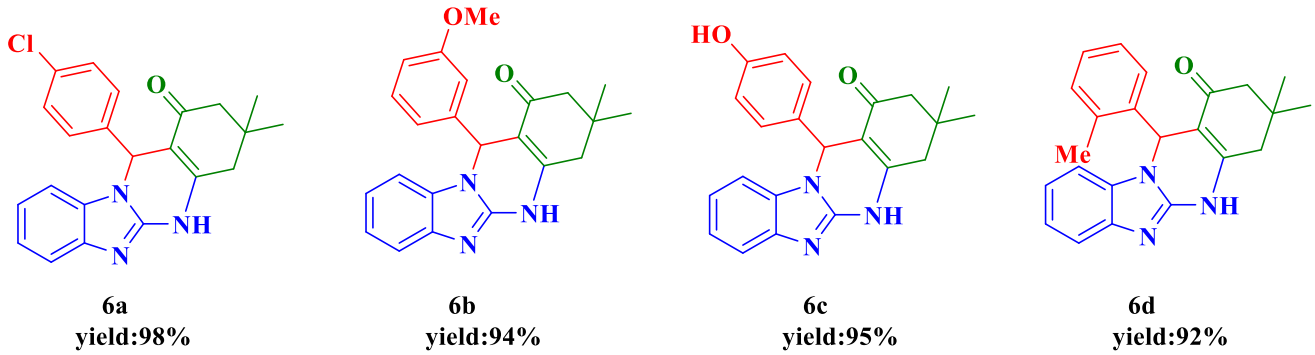
10 mg of the catalyst PABSA-Pr-PMO (**1**) was introduced to a reaction vessel containing a 2-aminobenzoimidazole (**2**, 1 mmol, 0.133 mg), aromatic aldehyde (**3**, 1 mmol), and either dimedone or malononitrile (**4**–**5**, 1 mmol). The reaction mixture obtained was mechanically agitated without the addition of a solvent. The development of reaction was tracked via TLC using a 1:3 mixture of ethyl acetate and n-hexane as the mobile phase. Once the reaction was complete, 2 mL of DMF was introduced, and the solution was heated to ensure all organic solids dissolvedFollowing filtration, the separated nanocatalyst 1 was retrieved and applied to the next set of reactions. Purification of the products was achieved through crystallization using ethanol as the solvent. The isolated powder was subjected to oven drying at 80 °C for 1 h.

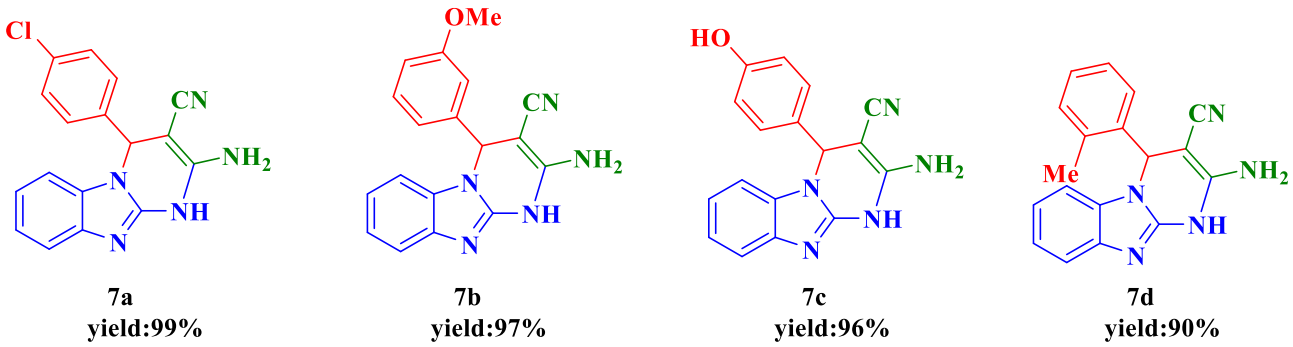
3. Results and Discussion

The overall strategy for making imidazopyrimidine derivatives via a multicomponent synthesis is depicted in Scheme 1. The model reaction involved the use of 2-aminobenzoimidazole (**2**), 4-cholorobenzaldehyde (**3**), and dimedone or malononitrile (**4**–**5**). The results indicate that the PABSA-Pr-PMO (**1**) green catalyst significantly shortens the reaction time for synthesizing imidazopyrimidine derivatives via multicomponent reactions, presenting an improvement over previous methods. The reaction successfully generated the corresponding product, resulting in high to excellent yields.



Scheme 1. The chemical process for making imidazopyrimidine is carried out with the assistance of the PMO-Pr-PABSA nanocatalyst (**1**).





Scheme 2. Synthesis of imidazopyrimidine derivatives (**6a–d**) and (**7a–d**) catalyzed by PABSA-Pr-PMO (**1**) nanocatalyt.

4. Conclusions

This work describes an efficient, green, environmentally friendly, and fast method for synthesizing highly-substituted imidazopyrimidine. The PABSA-Pr-PMO (**1**) as a new catalyst enabled the efficient synthesis of highly-substituted imidazopyrimidine compounds, which have great biological and pharmacological importance. This was achieved through the three-component condensation of 2-aminobenzoimidazole (**2**), aromatic aldehyde (**3**), and dimedone or malononitrile (**4**–**5**). Furthermore, conducting the reaction in the absence of a solvent resulted in the maximization of the desired product's yield.

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Conflicts of Interest:

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