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An Efficient and Reusable Succinimide-*N*-Sulfonic Acid Catalyst for the Synthesis of Benzimidazole at Room Temperature

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ABSTRACT

A facile an efficient protocol has been developed for the synthesis of benzimidazole from condensation reactions of o-phenylenediamines with aromatic aldehyde in presence of Succinimide - N - sulfonic acid (SuSA) as an efficient, cheap and reusable catalyst under mild reaction conditions.

Keywords: SuSA, o-phenylenediamines, aromatic aldehyde, recyclable

I. INTRODUCTION

The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. A number of heterocyclic derivatives containing nitrogen and sulphur atom serve as a unique and versatile scaffolds for experimental drug design [1]. The benzimidazole moieties are usually present in a large number of natural products in addition to pharmacologically active compounds [2]. It shows a wide range of biological and pharmacological properties such as antifungal [3], antimicrobial [4], anthelmintic [5, 6], antiviral [7, 8], topoisomerase inhibition [9] and anticancer activities [10]. A number of their derivatives are marketed as antifungal drug (Carbendazim) [11], anthelmintic drug (MebendazoleandThiabendazole) [12], antipsychotic drug (Pimozide) [13] and antiulcer agent (Omeprazole) [14]. Due to their attractive pharmacological properties, huge attention has been paid to the synthesis of benzimidazoles.

Because of their wide range of synthetic, industrial and pharmacological application, many methods for the preparation of benzimidazole are reported in the literature.The most common method is direct condensation of 1,2-phenylenediamine and carboxylic acids [15, 16] or their derivatives [17], that

require strong acidic conditions and sometimes need high temperature or the use of microwave [18].In recent years, solvent-free synthesis of benzimidazoles under microwave irradiation using $Yb(OTf)_3$ [19], KSF clay[20], PPA[21], Na_2SO_4 [22], K-10 clay[23], metal halide supported alumina[24] and solid support[25] have been reported.

However, a variety of catalysts have been reported for the synthesis of 2-aryl benzimidazole most of them suffer from disadvantages such as long reaction times, forceful conditions, low yields, low selectivity, tedious workup, and use of toxic or expensive reagents. Consequently, a new procedure that avoids these drawbacks is desirable.We report herein an efficient, low cost and environmentally benign protocol for the synthesis of benzimidazole using reusable SuSA catalyst under mild reaction condition.

II. METHODS AND MATERIAL

All purchased chemicals were of analytical grade and used without further purification. Silica gel coated aluminum sheets (Merck made) were used for thin layer chromatography (TLC) to monitor progress of reactions. Melting points were determined in an open capillary tube and are uncorrected. ^{1}H NMR spectra were recorded using DMSOas solvent and TMS as internal standard at 300 MHz on BruckerAvance spectrophotometer. All the products were characterized by IR spectral data and comparison of their melting points with those reported in literature and found to be identical. Also, the some products were confirmed by ^{1}H NMR spectral data.

Preparation Succinimide-N-sulfonic acid:

SuSA was easily prepared by addition of an equivalent amount of cholorosulfonic acid to succinimide (Su) [26].

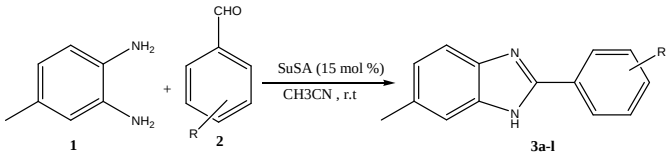
General procedure for the Synthesis of 2-aryl benzimidazole:

SuSA (15 mol %) was added to a stirred solution of the aldehyde (1 mmol) and o-phenylenediamines (1 mmol) in acetonirile (3 ml), and the mixture was stirred at room temperature for appropriate time (Table 1). After completion of the reaction monitored by TLC, the solvent was removed under reduced pressure and ethyl acetate (5 ml) was added, and the catalyst was recovered by filtration and washed with ethyl acetate (5 ml). The filtrate was washed with water and then dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure gave the highly pure product obtained. Further recrystalization was done in ethyl alcohol.

Selected spectral data:

5-methyl-2-(4-nitrophenyl)-1H-benzimidazole (Table 2, entry 3c)

IR(KBr pallets):Vmax3109, 1605, 1511, 1463, 1354, 1176, 739, 701 and 657 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d6):δ 8.39 (s, 4H+1H, overlapped Ar-H and N-H), 7.54 (d, J = 8.0 Hz, 1H, Ar-H), 7.43 (s, 1H, Ar-H), 7.09 (d, J =8.3 Hz, 1H, Ar-H) and 2.44 (s, 3H, $-CH_3$); ^{13}C NMR (75 MHz, DMSO-d_6):δ 159.0, 153.6, 143.2, 136.3, 131.0, 129.3, 127.9,119.4, 114.7, 114.6, 111.5 and 31.1. Mass (EI, m/z): 254 [M^+].



Scheme 1: Synthesis of benzimidazoles

III. RESULTS AND DISCUSSION

To explore the use of SuSA as a catalyst for the reaction of benzaldehyde and o-phenylenediamines for the preparation of 2-arylbenzimidazole compound **3a** was considered as a standard model reaction (**Table 2**). Model reaction in the absence of catalyst did not led to desired product formation. It means interference of catalyst was must for initiation of the reaction. To determine exact requirement of catalyst for the reaction, we used model reaction at different

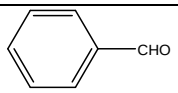
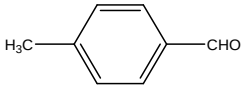
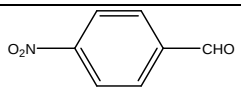
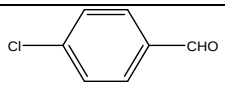
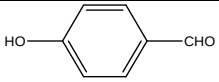
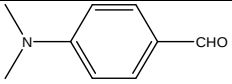
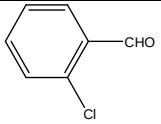
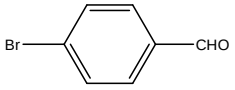
concentrations of SuSA (**Table 1**). During this study, we observed that, 15 mol% catalysts proved to be an efficient catalyst to carry out the reaction smoothly.

Encouraged by this result, in further set of experiments, in order to build the generality of the reaction, variety of aromatic aldehydes with either electron-donating or electron-withdrawing groups were converted to 2-arylbenzimidazoles derivatives in good to excellent yields. All the results are summarized in **Table 2.**

Table 1 Optimization of the catalyst

Entry	Catalyst (mol %)	Isolated Yield %
1	---	Trace
2	5	55
3	10	80
4	15	92
5	20	92

Table 2 Synthesis of 2-arylbenzimidazole in the presence of SuSA[a]

Entry	Aldehydes	Time (min.)	Yield[b] (%)
3a		65	91
3b		55	90
3c		52	92
3d		55	92
3e		75	85
3f		75	88
3g		60	88
3h		60	90

[a]Reaction conditions: Aromatic aldehydes (1 mmol), o-phenylenediamines (1 mmol), SuSA (15 mol%) at room temperature.[b] Isolated yield

IV. CONCLUSION

The Bronsted acid SuSA is a catalyst that has high efficiency in the synthesis of benzimidazoles. The reaction of the condensation of aromatic aldehyde with o-diphenylamines in acetonitrile as a solvent at room temperature gave maximum yields. The present protocol has numerous advantages such as high reaction rates and excellent yield, ease of preparation and handling of catalyst, inexpensive with lower loading and a simple experimental procedure.

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