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Synthesis of benzimidazole derivatives catalyzed by Cu NPs/ stilbite zeolite

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Abstract:

In this article benzimidazole derivatives prepared by condensation of o-phenylenediamine and aromatic aldehyde in the presence of catalytic amount of Cu NPs/stilbite zeolite. The reaction procedure is simple and cost effective, gives higher yield in short reaction time.

Keywords: Cu NPs/Stilbite zeolite, benzimidazole.

Introduction:

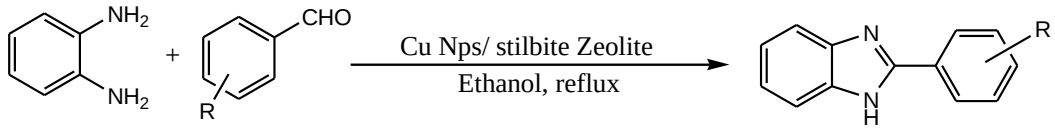
Benzimidazole is a heterocyclic aromatic organic compound composed of a benzene ring fused with an imidazole ring. The chemical structure of benzimidazole consists of a six-membered benzene ring fused to a five-membered imidazole ring. Various derivatives of benzimidazole exist, each with its own properties and applications. These derivatives are often used in medicinal chemistry, as benzimidazole-containing compounds have been found to exhibit biological activity. Benzimidazole and its derivatives have received much interest in the field of pharmaceutical chemistry [1,2]. Benzimidazole group of substances has found many practical applications in a number of fields. Recently the interest in benzimidazole and imidazole chemistry has been revived by the discovery that the 5,6- dimethyl benzimidazole moiety is part of the chemical structure of vitamin B_{12} [3]. Derivatives of Benzimidazoles display a broad spectrum of potential pharmacological and chemical activities and are present in a number of pharmacologically active molecules such as albendazole/mebendazole/thiabendazole (antihelmentic), omeprazole (anti-ulcer), etc. It is having a variety of medicinal, biological and chemical applications. Substituted benzimidazole derivatives are evaluated by their ability to inhibit gastric H^+/K^+ ATPase and by blocking the gastric acid secretion [4]. Recently, benzimidazoles have also been used as ligands for asymmetric catalysis [5]. Many methods have been reported for the synthesis of these benzimidazole derivatives. The condensation of 1,2-phenylenediamines with carboxylic acids or their derivatives is a common method, but it needs harsh conditions like polyphosphoric acid [6] at 170˚C - 180˚C. Another alternative approach is the condensation of aromatic aldehyde with 1,2-diaminobenzene in presence of different catalysts like Indion 190 resin [7], $BF_3.OEt_2$ [8], Ceric ammonium nitrate [9], iodine, [10] Silica sulfuric acid [11], $In(OTf)_3$ [12],

$SiO_2/ZnCl_2$ [13], silica supported sodium hydrogen sulphate [14], PEG [15], H_2O_2/ $Fe(NO_3)_3$ [16]. In recent years, Solvent-free synthesis of benzimidazoles under microwave irradiation using $Yb(OTf)_3$ [17], KSF clay [18], metal halide supported alumina [19] and solid support [20,21] has been reported.

However, many of these methods suffer from one or more drawbacks such as requirement of strong acidic conditions, long reaction times, low yields, tedious workup procedures, requirement of excess amounts of reagents, and use of toxic reagents, catalysts or solvents.

The development of simple, efficient and general synthetic method for biological active compounds from easily available catalyst is one of the major challenges in organic synthesis.

As part of our research program in developing various synthetic methodologies, we report the synthesis of benzimidazoles using Cu NPs/ stilbite zeolite as an efficient catalyst (Scheme 1). The same catalyst shows good results in the synthesis of azlactones [22].



1 2(a-l) 3(a-l)

Scheme 1

Experimental

All ^1H NMR spectra were recorded on 400 MHz Varian FT-NMR spectrometers. All chemical shifts are given as δ value with reference to tetra methyl silane (TMS) as an internal standard. The chemicals and solvents were purchased from commercial suppliers either from Aldrich, sd fine chemical, Spectrochem and they were used without purification prior to use. Melting points of the synthesized compounds were determined in open glass capillaries on Melting Point Apparatus (Metler).

Cu NPs/ stilbite zeolite catalyzed synthesis of substituted benzimidazole derivatives

A mixture of o-phenylenediamine (1 mmol), aromatic aldehyde (1 mmol) and Cu NPs/ stilbite zeolite (10 mol%) in Ethanol (5 ml) was placed in a 50 ml round bottom flask and stirred at reflux for appropriate time. The progress of the reaction was monitored by TLC (n-hexane: EtOAc (8:2)). After completion of the reaction, the reaction mixture was cooled and treated by dilution with EtOAc (20 mL). Total organic layer was washed with water, brine solution and dried over Na_2SO_4 and evaporated under vacuum. Obtained crude residue was purified by column chromatography to give substituted benzimidazoles.

Spectral Data

2-(3-chlorophenyl)-1*H*-benzimidazole (3g):

^1H NMR (DMSO, δ in ppm): 7.18-7.22 (m, 2H, Ar), 7.52-7.59 (m, 4H), 8.11 (dd, 1H), 8.20 (s, 1H, Ar), 13.01 (s, 1H).

IR (KBr): 3458, 2917, 2850, 2659, 1698, 1573, 1470, 1393, 1317, 1212, 832, 746 cm^{-1}.

2-(4-methylphenyl)-1*H*-benzimidazole (3k):

^{1}H NMR (DMSO, δ in ppm): 7.61 (m, 2H), 7.22 (dd, 2H), 7.19 (m, 2H), 6.95 (dd, 2H), 3.96 (brs, 1H), 2.37 (s, 3H).

IR (KBr): 3144, 2946, 1661. 1571, 1466, 1396, 1310, 1213, 833, 748 cm^{-1}.

Results and Discussion:

In order to establish the optimum reaction condition for this reaction, different solvents and various mole ratios of Cu NPs/ stilbite zeolite were examined. In our preliminarily, investigation was carried out on the model reaction of condensation of o-phenylenediamine and 4-chlorobenzaldehyde and 10 mol% of Cu NPs/ stilbite zeolite as shown in Table 1, different solvents can result in different yields. It was found that ethanol is the best solvent among dichloromethane, methanol, tetrahydrofuran, and acetonitrile for the condensation reaction, with its fast conversion, high yield and low toxicity. Cu NPs/ stilbite zeolite was varied by mole ratios in ethanol at reflux as shown in Table 2 to know the exact mol% required for the reaction but the best yields were obtained with 10 mol% of Cu NPs/ stilbite zeolite. The electronic effects of the different substituted aldehydes have been investigated in Table 3 and it was observed that aldehydes bearing both electron donating and electron with drawing substituents gave the desired benzimidazoles in good yields. Products were confirmed by comparing data with authentic sample (^{1}H-NMR, IR and Mass spectroscopy).

Table 1. Effect of Solvent in the synthesis of 2-(4-chlorophenyl)benzimidazole at reflux condition.

Entry	Solvent	Time (min)	Yield(%)[a]
1	CH_2Cl_2	120	48
2	CH_3OH	90	70
3	CH_3CH_2OH	60	95
4	THF	110	64
5	CH_3CN	90	81

a -All are isolated yields

Table 2. Various mole ratios of Cu NPs/ stilbite zeolite for the synthesis of 2-(4-chlorophenyl)benzimidazole.

Entry	Cu NPs/ stilbite zeolite (mol%)	Time (min)	Yield (%)
1	0	60	27
2	5	60	66
3	10	60	95
4	15	60	95
5	20	60	94

a - All are isolated yields.

Table 3. Synthesis of benzimidazoles from O-Phenylenediamine and aromatic aldehydes using Cu NPs/ stilbite zeolite as catalyst in ethanol at reflux condition.

Compound	Aldehyde	Time (min)	Yield (%)[a]	M.P. (°C)
3a	C_6H_5CHO	45	92	292-294
3b	3-NO_2 C_6H_5CHO	60	88	203-204
3c	4-Cl C_6H_5CHO	60	95	288-290
3d	4-NO_2 C_6H_5CHO	65	93	>300
3e	2-NO_2 C_6H_5CHO	55	94	265-266
3f	2-Cl C_6H_5CHO	60	92	233
3g	3-Cl C_6H_5CHO	45	89	237
3h	2-OCH_3 C_6H_5CHO	50	93	178-180
3i	3-OCH_3 C_6H_5CHO	45	88	204-205
3j	2-BrC_6H_5CHO	55	89	245
3k	4-$CH_3C_6H_5CHO$	65	88	263-264
3l	2-OHC_6H_5CHO	65	85	240-241

[a]Yields refer to isolated products.

Conclusion

In conclusion, Cu NPs/ stilbite zeolite was found to be an efficient catalyst for the formation of benzimidazole derivatives from aromatic aldehydes and o-phenylenediamine. The use of this inexpensive and easily available catalyst makes this protocol practical, environment friendly and economically attractive. The simple work-up procedure, high yields of products and nontoxic nature of the catalyst are other advantages of the present method.

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