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Synthesis of benzimidazole derivatives catalyzed by in/AlMCM-41as a heterogeneous catalyst

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ABSTRACT

An extremely efficient catalytic protocol for the synthesis of a series of benzimidazole derivatives developed in a one-pot two-component approach in the presence of indium modified mesoporous zeolite AlMCM-41 as heterogeneous catalyst using solvent free microwave irradiation is reported. The In/AlMCM-41exhibited excellent catalytic activity and the proposed methodology is capable of providing the desired products in good yield (74–93%) and short reaction time. After reaction course, In/AlMCM-41can be recycled and reused without any apparent loss of activity which makes this process cost effective. All the synthesized compounds have been characterized on the basis of elemental analysis, IR, ^{1}H NMR, and ^{13}C NMR spectral studies.

KEYWORDS

Benzimidazole;
Mesoporous zeolite In/AlMCM-41;
Heterogeneous catalyst.

INTRODUCTION

Solvent-free reaction is an advantage of this clean methodology, therefore the search of new and efficient catalysts able to promote organic reactions under solvent-free conditions is an area of continuous interest. The application of microwave irradiation (MWI) as a non-conventional energy source for activation of reactions, in general and under solvent-free conditions in particular, has now gained popularity over the usual homogeneous and heterogeneous reactions[1-4], because it provides enhanced reaction rates and improved product yields along with several eco-friendly advantages in the context of green chemistry which have been extended to modern drug discovery processes[5,6].

Benzimidazole derivatives have wide variety of biologically activities and they play very important role in development of heterocyclic compounds[7]. Benzimidazole derivatives exhibit significant activity against several viruses, such as HIV, human cytomegalovirus (HCMV)[8], herpes (HSV-1)[9], RNA[10] and influenza[11]. Substituted benzimidazoles have commercial applications in veterinarian medicine as anithelmintic agents and in diverse human therapeutic areas such as treatment of ulcers and as antihistaminic[12]. Recently, it has been found that two groups of benzimidazoles, namely the 5,6-dinitro and 2-trifiuoromethyl derivatives to be promising candidates for antimicrobial drugs[13]. Benzimidazoles

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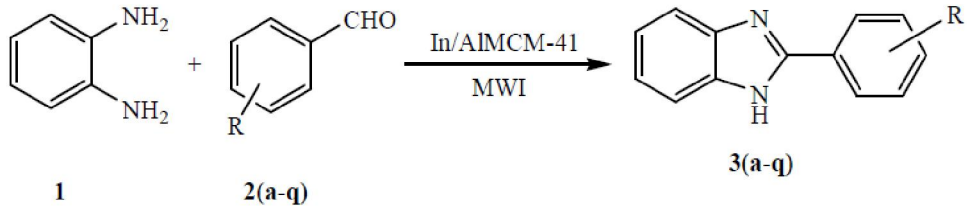
have crucial structures, which are contained in agrochemicals, dyestuffs, and high temperature polymer products[14], and also have interesting biological and pharmacological activities[15, 16], including inhibition of phosphodiesterase IV[17], neuropeptide Y binding[18] and anti-arrythmic and antiviral indications[19,20].

The applications of zeolites in the field of catalysis are growing continuously. Zeolites possess unique properties such as Bronsted and Lewis acidity, possibility to modify their acid:base and redox properties by changing their chemical composition by using different metals, ability to accept and release electrons, high proton mobility, easy work-up procedures, easy filtration, and minimization of cost and waste generation due to reuse and recycling of these catalysts. Because of their stronger acidity, they generally exhibit higher catalytic activity than conventional catalysts such as mineral acids, ion exchange resins, and mixed oxides. In the context of green chemistry, the substitution of harmful liquid acids by solid reusable zeolites or mesoporous materials as catalysts in organic synthesis is the most promising application. Recently the benzimidazole derivatives synthesized by using homogeneous and heterogeneous catalysts such as zeolite E4[21], NaY-zeolite[22], ceric ammonium nitrate[23], ionic liquid[24], H-ZSM-5 zeolite and heulandite zeolite[25], alumina and methyl sulphonic acid[26], $BF_3.OEt_2$[27] and transition metal/zeolite[28]. However, some of these methods have not been entirely satisfactory, associating with disadvantages such as longer reaction time, using volatile and toxic organic solvent, using catalyst that cannot be recycled.

In continuation of our ongoing research on zeolite as a solid as a solid catalyst for organic transformations[29-33], herein we report, the efficient method for the synthesis of various benzimidazole derivatives using heterogeneous catalyst indium modified mesoporous zeolite AlMCM-41.

RESULT AND DISCUSSION

Effect of quantity of catalyst



1 2(a-q) 3(a-q)

Scheme 1 : Synthesis of benzimidazole derivatives using In/AlMCM-41 under microwave irradiation

TABLE 1 : Effect of catalyst amount in the reaction of *o*-phenylenediamine and benzaldehyde

Entry	Catalyst amount (gm)	Time (min)	Yield (%)[a]
1	No catalyst	10	-
2	0.01	5	71
3	0.05	4	82
4	0.10	3	93
5	0.15	3	93
6	0.20	3	93

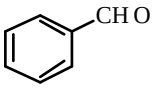
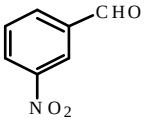
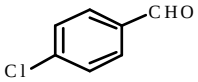
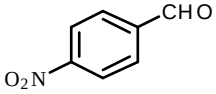
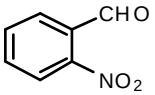
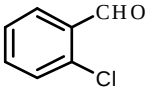
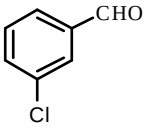
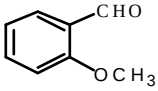
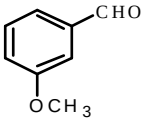
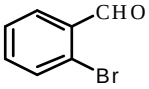
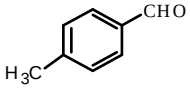
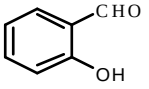
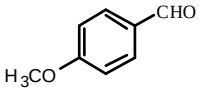
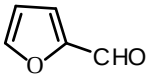
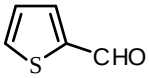
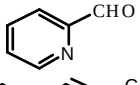
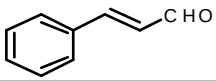
[a]Refers to isolated yields.

TABLE 2 : Effect of power input temperature in the reaction of *o*-phenylenediamine and benzaldehyde.[a]

Entry	Power (w)	Time (min)	Yields (%)[b]
1	150	5	42
2	300	4.5	57
3	450	3	93
4	600	2.5	86

[a] All reaction carried out using 0.1 gm In/AlMCM-41, [b]Isolated yields.

TABLE 3 : Synthesis of benzimidazole derivatives using In/AlMCM-41 under microwave irradiation

Compound	Aldehyde	Time (min)	Yield (%)[a]	M. P. (°C)
3a		3	93	292-293
3b		5	74	204-205
3c		3	91	288-289
3d		4	85	>300
3e		5	78	264-265
3f		3	92	234
3g		3	87	238
3h		4	82	179-180
3i		6	81	205-206
3j		3	86	246
3k		4	87	264-265
3l		5	81	239-240
3m		3	82	224-225
3n		6	81	284-285
3o		5	79	>300
3p		6	82	214-216
3q		2	89	199-201

[a]Yields refer to isolated products.

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The catalyst indium modified mesoporous zeolite AlMCM-41 was prepared by using our reported method[34]. In order to get best experimental conditions, initially we have studied the effect of catalyst loading, benzaldehyde (10 mmol) and *o*-phenylenediamine (10 mmol) was chosen as a model substrate (Scheme 1). 0.01 gm and 0.05 gm of catalyst loading gave low product yields (71% and 82%) after 5 min and 4 min. respectively (TABLE 1, entries 2, and 3). The use of 0.1 gm of catalyst delivers excellent yield within 3 min. (TABLE 1, entry 3). When we increase the amount of catalyst concentration no any significant changes observed with respective time and yield of product. A quantitative yield (93%) of desired product was obtained in the presence of 0.1 gm of In/AlMCM-41 within short spam indicating that the 0.1 gm of catalyst is very active catalytic system for this reaction. It is noteworthy to mention that in the absence of catalyst, reaction did not give any product after 10 min.

Next we have investigated the effect of microwave power for the same model reaction. The results in TABLE 2 shows the reaction carried out at 450 W gives good results (TABLE 2 entry 3) as compared to power input from 150>300 W (TABLE 2, entries 1 and 2).

With optimized reaction condition in hand, we have synthesized various benzimidazoles from substituted aldehydes with 1,2-diaminobenzene in the presence of In/AlMCM-41 under influence of microwave irradiation. The successful synthesis of benzimidazoles in shorter reaction times (3-6 min.) with excellent yields (74-93%) and avoids the use of hazardous solvent, requires only catalytic amount of the In/AlMCM-41 to promote the reaction.

Recovery and reusability of catalyst

TABLE 4 : Recovery and reusability studies of In/AlMCM-41 in the reaction of *o*-phenylenediamine and benzaldehyde

Entry	Cycle	Yield (%)[a]
1	Fresh	93
2	First	93
3	Second	92
4	Third	91

[a]Yield refers to isolated product.

The recovery and reusability of the catalyst was tested by performing same model reaction using recovered catalyst and observed that the percentage yield remains almost same as depicted in the TABLE 4. This indicates that the catalyst could be recycled without much loss of catalytic activity.

EXPERIMENTAL

All chemicals are purchased from Aldrich and Rankem chemical suppliers and used as received. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. 1H NMR spectra were recorded on an 300 MHz FT-NMR spectrometer in CDCl3 as a solvent and chemical shifts values are recorded in δ (ppm) relative to tetramethylsilane (Me4Si) as an internal standard.

General procedure for synthesis of benzimidazoles

Aldehyde (10 mmol) and 1,2-diaminobenzene (10 mmol) were thoroughly mixed in a 10 mL beaker at room temperature and then irradiated at 450W for 3-6 minutes in microwave oven. The progress of reaction monitored by TLC. After completion of the reaction, the reaction mixture poured on ice, filtered, washed with cold water to remove excess of impurities. The crude product obtained was crystallized from ethanol to afford high purity of the product.

Spectral data of representative compound (3g)

^{1}H 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}.

CONCLUSION

The In/AlMCM-41 catalyst is highly efficient for the synthesis of benzimidazole derivatives. Aldehydes bearing electron-donating and electron withdrawing groups did not affect on yield of products. The catalyst is easily recycled and reuse for several times without much loss in activity.

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