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Synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives using nano montmorillonite clay as an efficient catalyst

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Abstract

Benzimidazoles are among the most important nitrogen-containing heterocyclic compounds that have many pharmaceutical applications; including, antitumor, anticancer, anticorrosive, antibacterial, irritant and enzymatic interceptors. In this research, the synthesis of benzimidazoles using *o*-phenylenediamine and aldehyde derivatives in the presence of the nano montemurillonite in solvent-free and room temperature conditions has been investigated. All products with relatively good yields were identified by spectral and physical methods.

Keywords: Nano montemurillonite clay; benzimidazoles; solvent-free conditions; heterocyclic compounds.

Introduction

Nano montmorillonite clay is an important compounded availability in nature of micron sized particles. These micro particles are constructed of thickness ~1 nm and width 100-200 nm [1]. The chemical structure of Nano montmorillonite clay particle is generally perceivable in sheets and layers as the theoretical formula is $M_y^+(Al_{2-y}\ Mg_y)(Si_4)O_{10}(OH)_2.nH_2O$ [2] (Figure 1).

Nano montmorillonite clay has been used in vast areas such as catalysis [3], food additive [4], polymer [5], antibacterial activity [6], Sorbent [6], etc. "Nano montmorillonite clay is an efficient solid catalyst that has several advantages, such as high surface area, low cost, solid acid of moderate acid strength, ease of handling, non-corrosiveness, synthetic potential, Brønsted and Lewis acidities in both their natural and ion-exchanged forms and regeneration [7].

Benzimidazole derivatives are reported to possess a number of interesting biological activities such as anticancer [8], anthelmintic [9], antitubercular [10], antiallergic [11], antihistamines [12], antimicrobial [13], anti-HIV [14], antiulcer [15], antihypertensive [16], cardiotonic [17] and neuroleptic [18]. Thus, considering the application of benzimidazole moieties tremendous interest in developing efficient routes for the synthesis of this compound. Although, various routes have been developed for the synthesis of benzimidazole derivatives [8].

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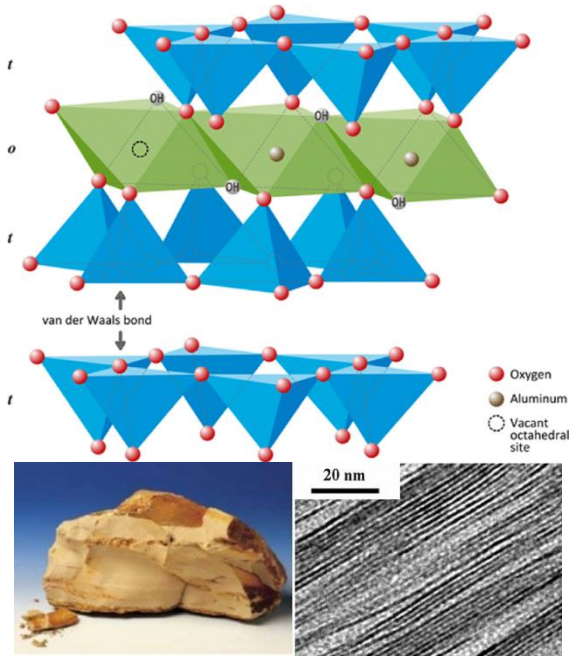


Figure 1. Structure of nano montmorillonite clay

The common method for the synthesis of benzimidazole involved condensation reaction between *o*-phenylenediamine and carboxylic acid acidic at high temperature or aldehydes. Though, most of these methods have significant drawbacks such as expansive reagent, the use of drastic reaction conditions, tedious work-up, low yields, a special oxidation process and a long reaction time were required. Thus, due to the availability of many aldehydes, synthesis of benzimidazole with different aldehydes have been extensively used. In this regards, many routs have been reported for the synthesis of benzimidazole derivatives in literatures.

In this work, we have reported nano montmorillonite as an efficient heterogeneous catalyst for the heterocyclic condensation between *o*-phenylenediamine and different aromatic aldehydes to give 2-aryl-1*H*-benzo[*d*]imidazole under mild reaction conditions.

Experimental

Materials and method

All chemical and solvents used in this work were obtained from Merck and were used without further purification. Analytical thin layer chromatography was performed using Merck silica gel GF254 plates. Plate chromatography was performed using silica gel 60 $PF_{254+366}$. All products are known and were characterized by comparison of their spectral (^{1}H NMR, ^{13}C NMR) and physical data with those of authentic samples. The ^{1}H-NMR spectra were recorded at 400 MHz and the ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ or DMSO-d_6 with TMS as the internal standard. All shifts are given in ppm and all coupling constants (J values) are reported in Hertz (Hz).

Synthesis of 2-aryl-1H-benzo[d]imidazole

A mixture of aldehyde (1.1 mmol) was added to *o*-phenylenediamine (1.0 mmol) in the presence of nano montmorillonite clay (0.1 g) at room temperature in the solvent-free condition until the reaction has gone to completion. Completion of the reaction was monitored by TLC. Then, ice water was added to the mixture reaction and the residue was filtered. The crude

products were purified by crystallization in ethanol.

*2-phenyl-1H-benzo[d]imidazole (**3a**)*
^{1}HNMR (400 MHz, $CDCl_3$) δ= 7.48-7.58 (4 H, m, Ar), 7.66 (1 H, m, Ar), 8.17-8.19 (2 H, m, Ar), 12.91 (s, NH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) = 117.0, 124.0, 127.7, 130.3, 131.1, 131.9, 140.3, 153.4.

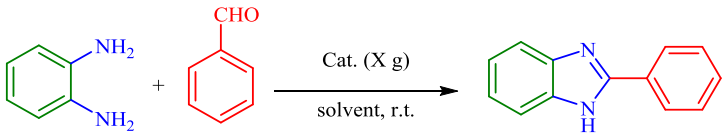
*2-(p-tolyl)-1H-benzo[d]imidazole (**3b**)*
^{1}H NMR (400 MHz, DMSO-d_6) δ= 2.37 (3H, s, CH_3), 7.17-7.19 (2 H, m, Ar), 7.35 (2 H, d, Ar), 7.58-7.60 (2 H, m, Ar), 8.10 (2 H, d, Ar), 13.13 (s, NH) ppm.

IR spectroscopy for nano montmorillonite clay
FT-IR: v= 3000 (OH stretch), 2933 (C-H stretch), 1640 (C=C stretch), 1100 (C-O stretch), 1050 (Si-O stretch) cm^{-1}.

Results and discussion

Initially, we attempted optimized reaction condition of the condensation of *o*-phenylenediamine and benzaldehyde using nano montmorillonite clay at room temperature for the synthesis of 2-phenyl-1*H*-benzo[*d*]imidazole (**3a**). Many solvents and different amounts of nano montmorillonite clay were tested. In the first step, the kind of solvent (Ethanol, THF, $CHCl_3$, DMF) was tested; in the solvent-free condition, significant yield (90%) was also observed (Table 1, Entry 5). In the next step, the influence of amount of nano montmorillonite clay was also examined. The results shown, the yield of production **3a** was depended on amount of nano montmorillonite clay. Similar results were observed in the presence of 0.15 g nano montmorillonite clay (Table 1, Entry 7). When the amount of nano montmorillonite clay was decreased to 0.05 g, the reaction was yielded 60% (Table 1, Entry 6). Significant proceed of the reaction was also observed in the presence of 0.1 g of nano montmorillonite clay as the product was yielded 90%.

Table 1. Optimization of reaction conditions[a]



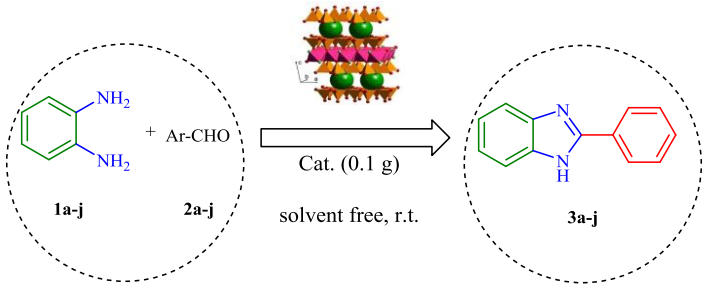
1a **2a** **3a**

Entry	Amount of catalyst (g)	Solvent	Time (min)	Yield (%)[b]
1	0.1	Ethanol	20	50
2	0.1	THF	20	40
3	0.1	$CHCl_3$	20	30
4	0.1	DMF	20	20
5	0.1	solvent-free	10	90
6	0.05	solvent-free	10	60
7	0.15	solvent-free	10	90

[a]Reaction conditions: *o*-phenylendiamine (1.0 mmol) and benzaldehyde (1.1 mmol) in the presence of nano montmorillonite clay, solvent (2.0 mL) and room temperature.
[b]Isolated yield.

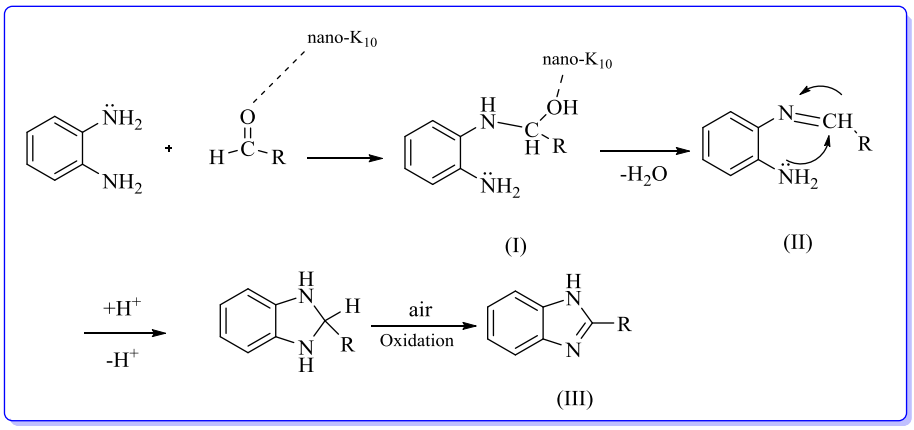
In order to test the generality and scope of this protocol, we used various aromatic aldehydes in the presence of nano montmorillonite clay and the obtained results are summarized in Table 2. In this condensation reaction, the yields were highly dependent on the substrate bearing an electron-withdrawing groups or electron-donating group. For instance, the substrate bearing a strong electron-withdrawing group gave lower yields (Table 2). The proposed mechanism of the reaction supported by previous research [23] probably involve the interaction of nano montmorillonite clay with the aldehyde by acting as an acid and also playing a complex role as shown in Scheme 1.

Table 2. Synthesis of 2-aryl-1*H*-benzo[*d*]imidazole in solvent-free condition at room temperature[a]



Entry	R	Product	Time (min)	Yield (%)[b]	M.p. (°C)
1	H	**3a**	10	90	288-290 [20]
2	4-Me	**3b**	10	92	275-278 [21]
3	4-Cl	**3c**	15	88	284-286 [22]
4	3-Cl	**3d**	15	83	284-286 [22]
5	4-NO_2	**3e**	20	85	307-309 [21]
6	2-NO_2	**3f**	20	82	209-211 [21]
7	4-OMe	**3g**	15	90	225-228 [21]
8	3-NO_2	**3h**	20	84	207-208 [21]
9	4- OH	**3i**	20	85	270-275 [21]
10	2-Cl	**3j**	20	81	258-262 [21]

[a]Reaction conditions: aldehyde (1.1 mmol), *o*-phenylenediamine (1.0 mmol) in the presence of nano montmorillonite clay at room temperature.
[b]Isolated yield.



Scheme 1. The plausible mechanism of 2-aryl-1*H*-benzo[*d*]imidazole synthesis

Generally to show the efficiency of the catalytic potentiality, the results obtained for the synthesis of products are compared with those of previously reported procedures (Table 3). The present protocol is aligned to some of the previously reported procedures in terms of product yield, reaction time and reaction conditions.

Table 3. Comparison of activity of various catalysts in the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole

Entry	Catalyst	Conditions	Time (h)	Yield (%)[a]	Ref
1	$Zn_3(BTC)_2$	EtOH, r.t.	10-60 min	91-97	[22]
2	$NaHSO_4$-SiO_2	EtOH, reflux	8	87-95	[24]
3	$Zn(OAc)_2.H_2O$	DMF, 120 °C	18	75-95	[25]
4	H_2O_2/SiO_2-$FeCl_3$ (0.1 gr)	Solvent-free, 150 °C	30 min	25	[26]
5	$Cu(OAc)_2.H_2O$ (7 gr)	MeOH / H_2O, reflux	3	72	[27]
6	*p*-TsOH (10 mol%)	DMF, 80 °C	10-60 min	trace-85	[28]
7	Fe_3O_4 magnetic nanoparticles	EtOH, reflux	120-300 min	83-98	[29]
8	H_2O_2 (30% in H_2O)/HCl (37% in H_2O)	CH_3CN, r.t.	30-50 min	96-99	[30]
9	$PhI(OAc)_2$	Dioxane, r.t.	3-5 min	86-90	[31]
10	$Yb(OTf)_3$ (0.5 mol%)	Solvent-free, 90 °C	1-6	40-92	[32]
11	$LaCl_3$ (10 mol%)	CH_3CN, r.t.	2-4	85-95	[33]
12	Fe_3O_4-IL	H_2O or Solvent-free, 80 °C	20-75 min	84-92	[34]
13	melamine-Br_3	EtOH, r.t.	1-2.5	82-96	[35]
14	SBSA	H_2O(10 mL), r.t.	-	trace-98	[36]
15	[MOEI]-BSA	H_2O, r.t.	15-40 min	80-95	[37-39]
16	nano montmorillonite clay	Solvent-free, r.t.	10-20 min	81-92	This work

Conclusion

In summary, we have reported a straightforward rout for the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives from different aromatic aldehydes and *o*-phenylenediamines in the presence of nano montmorillonite clay in solvent-free condition at room temperature. This work has several advantages such as higher yields, mild reaction conditions, high catalytic activity, fast reaction times (10–20 min), and commercially available catalyst. The reactions can be carried out in solvent-free conditions instead of the usually used organic solvents.

Acknowledgments

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