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Short communication

n-Propyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride-SBA-15 (SBA-DABCO) as basic mesoporous catalyst for the synthesis of 1,4-dihydropyridine hetrocyclic compounds

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ABSTRACT

Regarding the green chemistry's goals, the development of mesoporous silica materials as attractive candidates in the search for supporting of catalysts is currently a subject of increasing interest. Therefore, in the present research n-propyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride-SBA-15 (SBA-DABCO) was used as a basic catalyst for the synthesis of 1,4-dihydropyridine (DHP) derivatives from one pot, three-component condensation of aromatic aldehydes, ammonium acetate and ethylacetoacetate under solvent-free at 80 °C. This method offers several advantages, including high yield, short reaction time, simple work-up procedure, ease of separation and recyclability of the catalyst, as well as the ability to tolerate a wide variety of substitutions in the reagents. © 2015 Elsevier B.V. All rights reserved.

1. Introduction

Taking into account the basic principles of green synthesis, the use of catalysis is a major tool in green synthesis and engineering [1]. 1,4-Diazabicyclo[2.2.2]octane (DABCO) is an inexpensive commercially organic base which has been used as catalyst in different organic reactions [2–6]. However, in many of the reactions, DABCO has not been recovered. Thus, search for finding a heterogeneous, recoverable and reusable derivative of DABCO is very desirable.

Moreover, the DABCO-base ionic liquids are used for metal adsorbents from aqueous solutions, stationary phase for chromatography, ionophores in polymeric membrane ion-selective electrode, optical and electronic devices field [7–9]. This kind of ionic quaternary ammoniums, as well as, other resemblances can be used as highly efficient and environmentally friendly catalysts in organic synthesis.

High cost and difficulty in recycling limited ionic liquid (IL) applications to the industrial scale. Furthermore, it has been reported that supporting or immobilization became a general concept to heterogenized ILs, which led to more improvements in efficiency compared to homogenous ionic liquids [10,11].

In contrast to the solid acid catalysts, the solid base catalysts are much less frequently used in heterogeneous catalysts [12–15]. Herein, supported ionic liquid catalysts (SILCs) are an attractive research area

* Corresponding author. *E-mail address:* jamaldavarpanah@gmail.com (J. Davarpanah). of constant growth due to their applications in catalysis for a variety of reactions.

In recent year, silica has attracted significant attention of chemists as a good support for immobilization of homogeneous catalysts [16]. Perhaps no class of inorganic support has been more widely studied for catalytic applications than silica. Among these kinds of materials, mesoporous silica materials such as SBA-15, have attracted much attention, due to their interesting properties that include tunable pore sizes, stabilities and shape selectivity. SBA-15 is typically synthesized under mild conditions, allowing for the incorporation of constituent building blocks with desired functionalities, leading to numerous functional SBA-15 that has shown promise for a number of applications [17–20].

On the other hand, dihydropyridines and their derivatives (DHPs) are very well known for their wide range of biological activities including antihypertensive, vasodilator, antimutagenic, antitumor, anticonvulsant, antidiabatic, antianxiety, antidepressive, analgesic, seditative, bronchodilator, hypnotic and anti-inflammatory [21]. Consequently, several methods have been reported for the promoting preparation DHP derivatives [22]. Although most of these processes offer distinct advantages, they suffer from some drawbacks such as low yields, extended reaction times, harsh reaction conditions, tedious work-up procedures, toxic solvents and application of expensive or unavailability catalysts. Moreover, in most of the reported methods, catalysts are not recyclable. Therefore, to overcome these drawbacks a great deal of efforts is directed to develop an efficient catalytic system for synthesis of these compounds.







Scheme 1. Application of SBA–DABCO as basic mesoporous catalyst for the synthesis of DHP derivatives.

However, a supported DABCO as the catalyst for the synthesis of DHPs has not been studied yet. Thus, we envisioned that supported DABCO ionic liquid may act as base catalyst in the synthesis of DHPs. By considering all the above-mentioned points, we turned our attention towards the synthesis of 1,4-dihydropyridine (DHP) derivatives by inorganic–organic hybrid basic nanocatalyst by supporting DABCO, SBA–DABCO, as a proficient, mild, harmless to the environment, recyclable, non-toxic solid base catalyst with good stability towards humidity.

2. Experimental

2.1. General

For the direct synthesis of chloro-functionalized SBA-15, tetraethylorthosilicate (TEOS) was used as a silica source, 3-chloropropyltrimethoxysilane (CPTMS) was used as a chloropropyl group source and Pluronic P-123 triblock copolymer (EO₂₀PO₇₀EO₂₀, MW. 5800) was used as a structure-directing agent, were supplied by Aldrich. Other chemical materials were purchased from Fluka and Merck companies and used without further purification. Products were characterized by comparison of their physical data, IR and ¹H-NMR and ¹³C-NMR spectra with known samples. NMR spectra were recorded on a Bruker Advance DPX 400 MHz instrument spectrometer using TMS as internal standard. IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectrometer.

The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel PolyGram SILG/UV 254 plates. The particle morphology was examined by SEM (Philips XL30 scanning electron microscope) and TEM (Zeiss – EM10C - 80 KV). Nitrogen adsorption measurements were conducted at 77.4 K on a Micrometrics ASAP-2020 sorptionmeter. The specific surface area and the pore size



Fig. 1. The FT-IR spectra of SBA-DABCO.

distribution were calculated by Brunauer–Emmett–Teller (BET) method and Barrett–Joyner–Halenda (BJH) model, respectively.

2.2. Synthesis of 1,4-diazabicyclo[2.2.2]octane-SBA (SBA-DABCO)

First, chloropropyl-grafted SBA-15 (SBA-Cl) was prepared by the direct incorporation of chloropropyl groups through co-condensation of TEOS and CPTMS, according to the reported method [23]. Then, SBA-Cl (10.0 g) was added to a flask containing 100 mL of anhydrous toluene and an excess of DABCO (1 g, 9 mmol). The reaction mixture was refluxed with stirring for 24 h. Then, the reaction mixture was cooled to room temperature, transferred to a vacuum glass filter, and washed with toluene. The SBA chemically bonded with DABCO (SBA–DABCO) was dried at 50 °C for 8 h.

2.3. Typical procedure for the preparation of 1,4-DHPs

A mixture of aromatic aldehyde (1 mmol), ethylacetoacetate (2 mmol) and ammonium acetate (1.5 mmol), and SBA–DABCO (0.05 g) was heated at 80 °C for appropriate time. After satisfactory completion of the reaction and cooling, the crude product was extracted by CH_2Cl_2 . The organic solvent was removed by simple evaporation and finally crude product recrystallized from EtOH/H₂O to afford pure corresponding 1,4-dihydropyridine derivatives in high yields.

3. Results and discussion

In continuation to our study about application of heterogeneous catalysts as green catalyst in the synthesis of biologically relevant



Fig. 2. TEM image of SBA-DABCO.



Fig. 3. Thermal gravimetric analysis-derivative thermogravimetric analysis (TGA-DTG) of SBA-DABCO.

heterocyclic compounds, herein we report catalytic application of n-propyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride-SBA-15 (SBA-DABCO) as basic mesoporous catalyst for the synthesis of 1,4dihydropyridine (DHP) derivatives from one pot, three-component condensation of aromatic aldehydes, ammonium acetate and ethylacetoacetate under solvent-free conditions at 80 °C (Scheme 1).

Recently, we have obtained a new charged hybrid organic–inorganic mesoporous silica, n-propyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride-SBA-15 (SBA–DABCO). The catalyst (SBA–DABCO) was prepared according to the recently reported method [24] with some modifications by the direct incorporation of chloropropyl groups through co-condensation of TEOS and CPTMS and then grafting of DABCO onto the surface of the mesoporous silica by the simple nucleophilic substitution reaction. The catalyst has been characterized by a scanning electron microscope (SEM), Brunauer Emmett Teller (BET), X-ray powder diffraction (XRD) and elemental analysis (CHN) (see the Supplemental Materials for Figs. S_1 – S_3 and Table S_1), Fourier transform infrared spectroscopy (FT-IR) (Fig. 1), transmission electron microscopy (TEM) (Fig. 2), thermogravimetric analysis (TGA) and differential thermal

 Table 1

 Solvent-free reaction of benzaldehyde, ethylacetoacetate, and ammonium acetate under different conditions.

Entry	Solvent	T (°C)	Catalyst (g)	Time (min)	Yield ^a (%)
1	Ethanol	Reflux	0.05	30	42
2	Acetonitrile	Reflux	0.05	30	41
3	Water	Reflux	0.05	30	44
4	Toluene	Reflux	0.05	30	34
5	Ethanol-water	130	0.05	30	50
6	Solvent-free	120	0.05	7	86
7	Solvent-free	100	0.05	7	92
8	Solvent-free	25	0.05	60	Trace
9	Solvent-free	80	0.1	7	88
10	Solvent-free	80	0.05	7	96
11	Solvent-free	80	0.02	10	86
12	Solvent-free	80	-	60	Trace

^a Isolated yield.

analysis (DTA) (Fig. 3), and by their comparisons with that of authentic sample.

Fig. 1 shows the FT-IR spectra of SBA–DABCO in the 400–3800 cm⁻¹. The presence of peaks at 473, 801 and 1070 to 1200 cm⁻¹ was most probably due to the symmetric and asymmetric stretching vibrations of framework and terminal Si–O groups. The C–H stretching peaks at 1200 to 1250 and 2950 to 2830 cm⁻¹ indicate that the surface of silica is successfully modified by double-charged diazoniabicyclo[2.2.2]octane chloride. A band at 1465 cm⁻¹ is characteristic of the tertiary amine group. The bands around 1635 and 3400 cm⁻¹ are also due to the bending vibration of water molecules which were adsorbed on the surface.

The morphological characterization and the particle size distribution of SBA–DABCO were performed by measuring TEM (Fig. 2). From the TEM image, the pore structure and orderly pore arrangement could be clearly observed and confirmed the long-range, three dimensional and mesoporous ordering in this organocatalyst.

The TGA–DTG of SBA–DABCO is shown in Fig. 3. It can be observed from the thermogram that the sample shows a three-stage degradation pattern over the range of 50–600 °C. The onset of degradation occurred around 81 °C, which can be attributed completely to the loss of adsorbed water molecules. The second and third weight losses at about 320 and 480 °C associated to the thermal decomposition of Pr-DABCO. Thus, the TGA and DTG curves also convey the obvious information that the surface of silica is successfully modified by double-charged diazoniabicyclo[2.2.2]octane chloride. Figure S₃ shows the XRD diffractrogram of SBA–DABCO. The peak positions in the sample remained constant after the functionalization process compare to the SBA-15. It can be observed the intense peak corresponding to the pore family and the two additional weak reflections assigned to the family planes, which are indicative of high hexagonal mesoscopic order [25,26].

After characterization, the catalytic performance of this basic organocatalyst has been systematically studied in the rapid and efficient preparation of 1,4-dihydropyridine (DHP) heterocyclic compounds through a multicomponent reaction. A model four-component coupling reaction of benzaldehyde, ethylacetoacetate and ammonium acetate



Scheme 2. Synthesis of 1,4-dihydropyridines.

was examined to determine whether the use of SBA–DABCO was efficient and to investigate the optimized conditions (Table 1).

After some experiments (Table 1), it was found that the use of benzaldehyde (1 mmol), ethyl acetoacetate (2 mmol) and ammonium acetate (2 mmol) in the presence of SBA–DABCO (0.05 g) under solvent-free conditions at 80 °C were the best condition.

In order to elucidate the role of catalyst, a control reaction was set up in the absence of catalyst. It was found that in the absence of catalyst only trace amounts of the desired product was observed on the TLC plate even after 1 h of heating. When the reaction was performed in the presence of SBA–DABCO, it proceeded rapidly to give the desired product.

Under the optimized reaction conditions, different substituted 1,4dihydropyridine (DHP) heterocyclic compounds were prepared changing the aromatic aldehyde substituents (Scheme 2). Generally, the reactions that employed aromatic aldehydes bearing electron-withdrawing or electron-donating functional groups at different positions produced the corresponding products in good to excellent yields. Both of the aromatic aldehydes with electron-withdrawing and electrondonating functionalities were found to be compatible under the optimized reaction condition (Scheme 2) (Table 2), because the desired products were obtained in high yields in relatively short reaction times.

The structures of products were determined from their analytical and spectral (IR, ${}^{1}H \otimes {}^{13}C NMR$) data and by direct comparison with authentic samples. Formation of the products was also confirmed by the comparison of their melting points with the products prepared by reporting methods.

The reusability of the catalyst in the reaction of benzaldehyde, ethylacetoacetate and ammonium acetate under solvent-free conditions at 80 °C was evaluated. In this procedure, after completion of each reaction, hot ethanol was added and the catalyst was filtered. The recovered catalyst was washed with ethanol, dried and reused for five times. The average chemical yield for six consecutive runs was 94.8% (96, 96, 95, 94, 94 and 94%) which clearly demonstrates the practical recyclability of this catalyst.

 Table 2
 Solvent-free synthesis of 1,4-dihydropyridines heterocyclic compounds.

Entry	R	Time (min)	Yield (%)
1	Н	7	96
2	4-Cl	7	95
3	4-NO2	5	96
4	4-CH ₃	7	95
5	4-OCH ₃	10	93
6	4-CN	5	95
7	2-NO ₂	7	94
8	2-0H	10	93
9	2-Cl	7	93
10	3-CH ₃	10	93
11	3-NO ₂	7	95

4. Conclusion

In the present work, the performance of n-propyl-4-aza-1azoniabicyclo[2.2.2]octane chloride-SBA-15 (SBA-DABCO) as basic mesoporous catalyst for the synthesis of 1,4-dihydropyridine (DHP) derivatives under solvent-free conditions at 80 °C was investigated. The catalytic system can combine the advantages of homogeneous and heterogeneous catalysts and therefore they can be selective, reactive and recyclable. The attractive features of this method are high yield and clean reaction, simple procedure, short reaction time, ease of separation and recyclability of the solid catalyst and performing multicomponent reaction under solvent-free conditions.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx. doi.org/10.1016/j.catcom.2015.06.019.

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