

Highly Efficient Three-Component Strecker-Type Reaction of Aldehydes and Ketones Using TMSCN Catalyzed by Recyclable and Heterogeneous Mesoporous B-MCM-41

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Abstract: Mesoporous Borosilicate (B-MCM-41) efficiently catalyzed the three-component Strecker-type reaction of different amines and aldehydes or ketones with trimethylsilyl cyanide (TMSCN) in CH₂Cl₂ at room temperature to afford the corresponding α -aminonitriles in excellent yields. The catalyst can be recovered and reuse for at least 5 reaction cycles without significant lose of its reactivity.

Keywords: Carbonyl Compounds; Amine; Trimethylsilyl Cyanide (TMSCN); α -Aminonitriles; Mesoporous Materials.

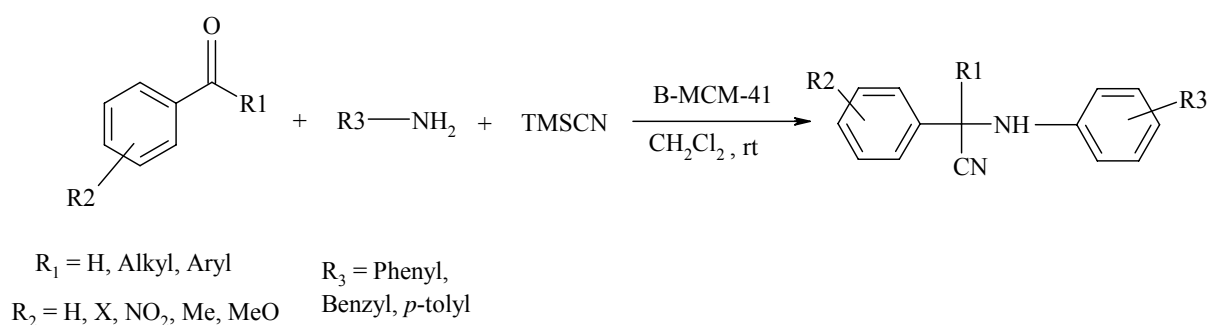
Introduction

The Strecker reaction, as the first multicomponent reaction [1], provides valuable α -aminonitriles synthons, which are important intermediates for the synthesis of amino acids and nitrogen-containing heterocycles such as thiadiazoles, imidazoles and other biologically-active molecules [2]. The Strecker reaction is generally carried out by addition of cyanide anion to imines [3]. Among various cyanide sources such as HCN, KCN, Et₂AlCN and Bu₃SnCN [4] which are toxic and require harsh reaction conditions, TMSCN is safer and more efficient. The efficiency of the reaction has been increased by the use of catalyst. Lewis acids such as Cu(OTf)₂, BiCl₃, NiCl₂, InCl₃, RuCl₃, Sc(OTf)₃, La(NO₃)₃·6H₂O or GdCl₃·6H₂O [5] have been used to catalyze homogeneously the Strecker reaction. Furthermore, several heterogeneous catalysts, which are more valuable in terms of catalyst/product separation and continuous production, have been proposed for the reaction. The examples include Solid catalysts such as, heteropoly acids [6], Montmorillonite KSF clay [7], and guanidine hydrochloride [8].

On the other hand, ordered mesoporous materials are very attractive as heterogeneous solid catalysts for fine chemicals synthesis. Mesoporous materials provide high surface areas which a high concentration of active sites often by incorporating metal ions into the siliceous framework can be produced. Herein, we wish to report mesoporous borosilicate (B-MCM-41) as an efficient nano-ordered solid acid catalyst for the three-component Strecker-type reaction of carbonyl compounds and amines with TMSCN in CH₂Cl₂ at room temperature to afford the corresponding α -aminonitriles in excellent yields (up to 97%) [9].

Results and Discussion

We initially used 4-chlorobenzaldehyde (1 equiv) and aniline (1 equiv) as model substrates to investigate the effect of different catalyst loading on the three-component Strecker-type reaction with TMSCN (1.2 equiv) in CH₂Cl₂ at room temperature (**Scheme 1**).

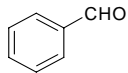
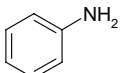
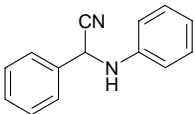
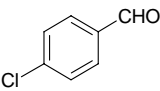
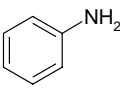
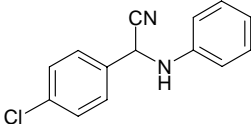
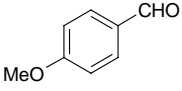
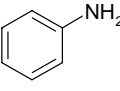
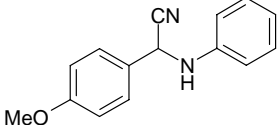
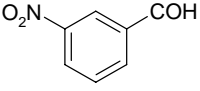
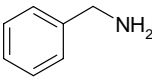
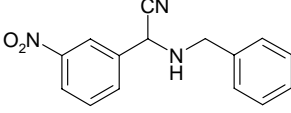
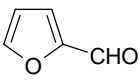
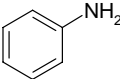
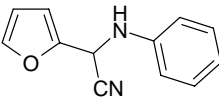
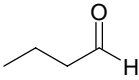
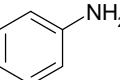
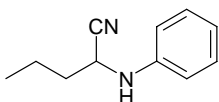


Scheme 1. Strecker-type reaction of carbonyl compounds and amines with TMSCN in the presence of B-MCM-41

It was found that the best result can be obtained by using 50 mg of B-MCM-41 per mmol of model substrates. The optimal conditions were developed to other carbonyl compounds and amines. The results of some representative carbonyl compounds and amines have been summarized in **Table 1**. It is noteworthy that the reaction hardly proceeded in the absence of catalyst. Aromatic, heterocyclic and aliphatic aldehyde or ketones were involved in the optimal reaction conditions very well to afford the corresponding α -aminonitriles in

excellent yields. For instance, heterocyclic furfural and aliphatic butanal gave 96% and 92% yield of the desired products on reacting with aniline and TMSCN, respectively (Entries 5,6). Furthermore, the reusability of B-MCM-41 for Strecker-type reaction was investigated with model substrates. It was found that the catalyst can be recovered and reuse for at least 5 reaction cycles without significant loss of its reactivity.

Table 1. Strecker Synthesis of α -Aminonitriles from Various Aldehydes and Ketones Catalyzed by B-MCM-41 at Room Temperature

Entry	Aldehyde	Amine	Product	Time (h)	Yield (%)	M.P ($^{\circ}$ C)
1				5	95	oil
2				5	98	114-116
3				7	85	93-94
4				4	91	oil
5				5	96	67-69
6				6	92	oil

Conclusion

In summary, we have prepared heterogeneous B-MCM-41 catalyst and explored it as an efficient, mild and safe catalyst for the one pot three component Strecker-type reaction of carbonyl compounds, amines and TMSCN to synthesize the corresponding α -aminonitriles in excellent yields and high purity. The important features of our method are: short reaction time, very simple work-up and reusability of catalyst for at least 5 reaction cycles without significant loss of its reactivity.

Experimental Procedure

General

All chemicals were purchased from Merck and Aldrich and used without further purification. All yields refer to the isolated products after purification. The products were characterized by IR and melting points. IR spectra were recorded on a Shimadzu FT IR-8400S spectrometer and performed using KBr pellets. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained using a Bruker DRX-500 AVANCE spectrometer. All NMR spectra were determined in CDCl_3 at ambient temperature. All melting points were compared with those of known samples [4-6].

General Procedure for Preparation of B-MCM-41

Hydrothermal synthesis of B-MCM-41 was carried out following the procedure described by Yuan et al. [10] with some variations, using gels with the following molar composition $\text{SiO}_2:0.05\text{B}_2\text{O}_3:0.10 \text{ CTAB}:0.33\text{NaOH}:70\text{H}_2\text{O}$. Typically, 2.8 g of cetyltrimethylammonium bromide (CTAB) was added to 100 mL of deionized water containing 0.8 g of NaOH and 0.5 g of H_3BO_3 . The mixture was constantly stirred with magnetic stirring at 50 °C until CTAB was completely dissolved. Then 17.36 mL of tetraethyl orthosilicate (TEOS, >98%) was added drop wise to the mixture with stirring at 50 °C for 2 h. The solid product was filtered, washed with deionized water, and dried in air at 45 °C for 12 h. The organic cations in the channels were removed by calcination of samples at 550 °C.

Typical Procedure for the Synthesis of α -Aminonitriles

A mixture of carbonyl compound (1 mmol), amine (1 mmol), TMSCN (1.2 mmol) and B-MCM-41 (50 mg) in CH_2Cl_2 (2 mL) was stirred at room temperature for an appropriate time (**Table 1**). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with ethyl acetate. Then organic solvent was evaporated under reduced pressure and the product was recrystallized from EtOH.

Acknowledgement

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