

# A Unique Heterogeneous Nucleophilic Catalyst Comprising Methylated Nitrogen-Substituted Porous Silica Provides High Product Selectivity for the Morita–Baylis–Hillman Reaction

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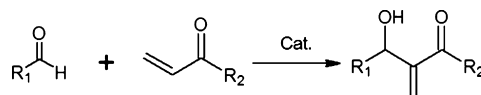
**ABSTRACT:** Methylated nitrogen-substituted microporous and mesoporous silica exhibited almost the same catalytic performance as that of a conventional homogeneous base catalyst. They also demonstrated unexpectedly high product selectivity for the Morita–Baylis–Hillman reaction of formaldehyde with methyl acrylate at high temperatures.

Solid base catalysts such as alkali and alkaline-earth metal oxides have been developed for use in industrially important chemical and biochemical processes, for example, isomerization, dehydration, and transesterification.<sup>1</sup> However, prior to use in base-catalyzed reactions, the aforesaid materials must be subjected to high-temperature pretreatment (~873 K) for the removal of inhibitors such as carbon dioxide and water; unfortunately, such high temperatures may lead to sintering and reduction in the catalytic performance.<sup>1</sup>

Nitrogen-substituted mesoporous silicas such as MCM-41 or SBA-15 have been shown to exhibit basic characteristics on the same magnitude as those of conventional base catalysts.<sup>2,3</sup> Our previous studies revealed that nitrogen-substituted mesoporous silica and microporous zeolites such as silicalite-1 showed high catalytic activity and product selectivity for the Knoevenagel condensation of benzaldehyde with malononitrile or ethyl cyanoacetate without any pretreatment, because they were hydrophobic.<sup>4</sup> Furthermore, it is interesting to note that nitrogen-containing silica facilitated only the targeted reaction, while a conventional base catalyst such as cesium oxide-loaded mesoporous silica catalyzed an additional reaction. This indicates that the basicity of these materials is similar, but the product selectivity of the former is much superior. Hence, nitrogen-containing mesoporous silica is a better candidate for use in industrial processes.<sup>4</sup> We recently reported that methylated nitrogen-substituted mesoporous silica SBA-15 (MeNSBA-15) demonstrated the unique catalytic performance for the Knoevenagel condensation of benzaldehyde with diethylmalonate, whose  $pK_a$  value is much higher than those of malononitrile and ethyl cyanoacetate.<sup>5</sup> To the best of our knowledge, this is the first report of such a reaction being catalyzed by a silica-based heterogeneous catalyst. MeNSBA-15 has stronger basicity than do the nitrogen-containing catalysts reported to date, which were shown to be ineffective for the catalysis of this reaction.

The Morita–Baylis–Hillman (MBH) reaction (Scheme 1) can be used to produce important aldol-type intermediates as a result of an organocatalyzed reaction at the  $\alpha$ -carbon of

Scheme 1. Morita–Baylis–Hillman reaction



unsaturated esters and ketones.<sup>6</sup> The conventional catalyst for this reaction is a homogeneous Lewis base such as a tertiary amine or alkylphosphine, both of which have high nucleophilicity. However, there are a number of problems associated with this reaction, including oligomerization of the reactants, low reaction rate, and relatively low product selectivity. Many researchers have tried to overcome these problems, in particular, by attempting to increase the reaction rate employing high-pressure conditions, a microwave technique, the addition of a Lewis acid, or by the use of other catalysts such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP).<sup>7</sup> Herein, we report that MeNSBA-15 can work as a heterogeneous nucleophilic catalyst, showing higher product selectivity than that of a homogeneous base catalyst for the MBH reaction of formaldehyde with methyl acrylate.

Nitridation of SBA-15, microporous zeolite beta (Si/2Al = 39, Tosoh Corp., Japan), and nonporous silica (fumed, Sigma-Aldrich, Japan) was carried out in a quartz tube surrounded by an electric furnace.<sup>4</sup> Pure ammonia gas at a flow rate of 1.0 L/min was used for nitridation. The typical temperature for the nitridation was set at 1173 K for 12 h. Before ramping the temperature, the tube was purged with N<sub>2</sub> and then ammonia for 30 min. The nitrogen-doped silica was subsequently methylated using methyl iodide and potassium carbonate (molar ratio of N-silica/MeI/K<sub>2</sub>CO<sub>3</sub> = 1:15:3), as described in our previous work.<sup>5</sup> Methylation for NSBA-15 and N-beta was conducted in a glass flask equipped with a reflux condenser under argon atmosphere. Adequate amounts of methyl iodide and dehydrated ethanol (solvent) were added. Then, the flask was heated in an oil bath typically at 350 K for 24 h with stirring.

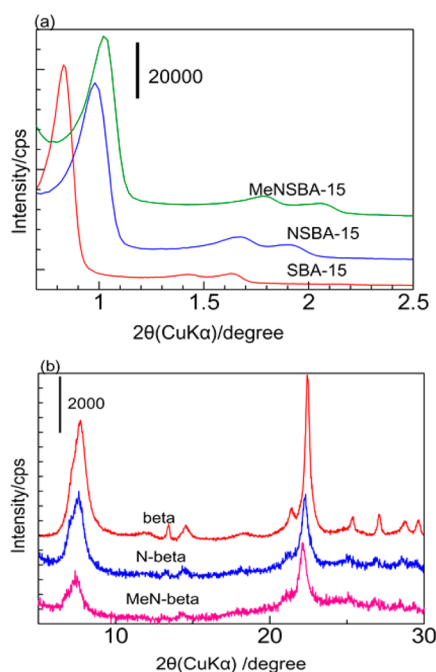
For the MBH reaction, 4.0 mmol of formaldehyde, 2.0 mmol of methyl acrylate, 2.0 mL of 1,4-dioxane, and 20 mg of catalyst were mixed in a 30 mL batch reactor, which was then heated in an oil bath to a predefined temperature. The reaction temperature was typically set at 423 K. 1,4-Diazabicyclo[2.2.2]octane (DABCO) was used as a conventional, homogeneous base catalyst for comparison. Cesium-loaded SBA-15 (Cs/SBA-

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15) was prepared by immersing the SBA-15 in an aqueous solution of cesium nitrate. Prior to the reaction, the silica material was pretreated by heating at 573 K for 2 h. To determine the effect of the silamino group (Si–NH–Si) on the solid surface, hexamethyl silazane was adopted as a homogeneous, silamino group-containing catalyst.

Figure 1a shows the powder X-ray diffraction (XRD) patterns of the SBA-15-based samples. All of the materials



**Figure 1.** XRD patterns of (a) SBA-15-based and (b) beta-based silamino or methylsilamino catalysts.

gave peaks corresponding to the 100, 110, and 200 planes, indicating that the samples retained the 2D hexagonal periodic mesostructure of SBA-15. Figure 1b shows the patterns collected for the beta-based samples, which demonstrate that these materials retained the original microcrystalline zeolite structure after nitridation, followed by methylation. The microporous structure was partially ruptured by the nitridation but was almost unaffected by its methylation.

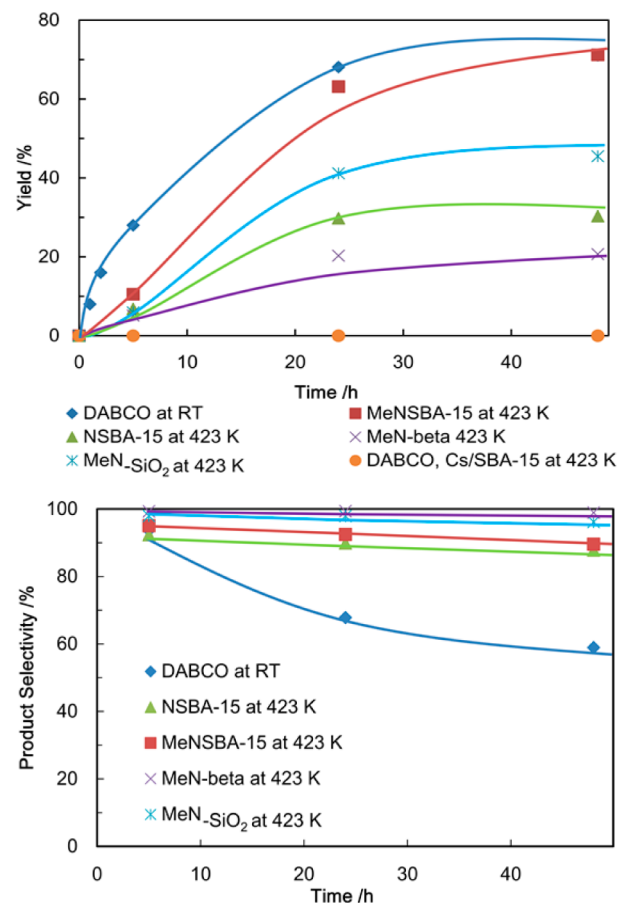
The amounts of nitrogen and carbon in the silica samples are listed in Table 1, wherein it can be seen that the amount of nitrogen in the beta samples was lower than that in the SBA-15 samples. The carbon was confirmed to derive from the methyl group on the silica surface; however, the amount of carbon relative to nitrogen (C/N) was lower than expected. As previously reported, in comparison with MCM-41, methylation of the silamino groups in the micropores by methyl iodide

**Table 1. Elemental Analysis of Each Catalyst**

sample	N mmol/g	C mmol/g	C/N
NSBA-15	17.0	–	–
MeNSBA-15	14.9	2.65	0.18
N-beta	11.5	–	–
MeN-beta	7.43	0.95	0.13
N-SiO <sub>2</sub>	13.7	–	–
MeN-SiO <sub>2</sub>	11.0	1.13	0.10
DABCO	17.8	53.4	3.0

seems to be inhibited.<sup>5</sup> On methylation, the amount of nitrogen decreased because of the susceptibility of the silamino species to hydrolysis, even though an anhydrous solvent was used for the methylation.

Figure 2a shows the catalytic performance of the materials for the MBH reaction of formaldehyde with methyl acrylate.



**Figure 2.** Catalytic performance of the MeN materials and other basic materials for the MBH reaction of formaldehyde with methylacrylate.

MeNSBA-15 showed high catalytic performance at 423 K, which was comparable to the activity of DABCO at room temperature. The conventional basic catalyst, Cs/SBA-15, showed very little activity for the MBH reaction but was effective for the Knoevenagel condensation of benzaldehyde with ethyl cyanoacetate. This implies that the MeN-substituted materials had a nucleophilic property derived from the lone-pair of electrons on the nitrogen atom. The function of the methyl silamino catalyst was not only to act as a Brønsted base for abstracting a proton from active methylene compounds<sup>4,5</sup> but also to initiate the reaction via nucleophilic attack. The nucleophilicity of MeNSBA-15 appears to be similar to that of DABCO; however, the rate of the reaction using DABCO was much higher than that using MeNSBA-15. The catalytic performance of DABCO gradually decreased with increasing reaction temperature, which was attributed to collapse of its molecular structure. NSBA-15 showed moderate catalytic activity, but the addition of the methyl group to the silamine enhanced it further. This was due to the increased nucleophilicity of the lone pair of electrons on the nitrogen atom, which was caused by the electron-donating ability of the methyl group. The MeN-beta zeolite-based material also

catalyzed this reaction, but diffusion limitations may have occurred because of the micropores, which resulted in poorer performance of the methyl silamine within the structure. The turnover numbers of the reactions involving the different catalysts were evaluated by calculating the molar ratio of the reacted benzaldehyde with the carbon number in the catalyst. The turnover number of MeN in the silicate structure was much higher than that of DABCO, even though the reaction temperatures were different. It is important to note that the selectivity for the primary product was ~60% in the case of DABCO, while MeNSBA-15 gave a value of almost 90%. The MeN-beta showed higher product selectivity than MeNSBA-15. A positive effect of the environment surrounding methyl silamino group is expected, and the crystalline structure of the MeN-beta might play an important role. A small amount of nitrogen was lost during the reaction, but the reaction was never catalyzed in the filtrate. Interestingly, this phenomenon could be seen only on the methylated samples; the silamino group is not resistant to hydration, but methylation prevents the leaching of the nitrogen species attached. This is another feature of methylation of the nitrated silica catalyst. At low temperatures, formaldehyde was observed to undergo oligomerization because of its high reactivity, with higher temperatures stabilizing the monomer. The advantages of the methyl silamino nucleophilic group on the heterogeneous silica catalyst lie not only in the improved efficiency resulting from the capability of easy separation of the products but also on the possibility of using high temperatures.

N-SiO<sub>2</sub> and MeN-SiO<sub>2</sub> were prepared from nonporous silica obtained using a flame decomposition method (fumed silica) to use as simple comparisons. According to Figure 2b, both silica materials showed almost the same product selectivity as MeNSBA-15, indicating that the catalytic activity was not altered by the porous structure. Further knowledge was gained by use of hexamethyl silazane, a homogeneous base catalyst containing of methyl silamino groups. Interestingly this compound catalyzed the same MBH reaction but gave product selectivity below ~20%, with decomposed products of the catalyst material and its derivatives, along with the reactant, found in the resulting reaction mixture. This implies that silamino and methyl silamino groups need to be located within a silica framework for highly selective product formation to be achieved.

In conclusion, a nucleophilic MBH reaction was successfully catalyzed by MeN-substituted silica materials. They showed excellent catalytic performance and significant selectivity compared to conventional base catalysts effective for the Knoevenagel condensation and MBH reaction. Furthermore, the methyl group helped to activate the silamino group, enhancing its nucleophilicity. Overall, the study demonstrates that MeN-silica materials are suitable for use as heterogeneous, nucleophilic catalysts for processes such as the MBH reaction, and have distinct advantages over conventional, homogeneous, nucleophilic catalysts such as DABCO.

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### Notes

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