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Ordered Hexagonal Mesoporous Aluminosilicates and their Application in Ligand-Free Synthesis of Secondary Amines

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A new facile synthesis of ordered mesoporous aluminosilicates has been developed and applied for the efficient catalytic synthesis of N-benzyl secondary amines under ligand and base-free conditions. The MAS(38) catalyst with a well-ordered mesoporous structure and strong acidic sites was used for acid-catalyzed organic transformations and its operational simplicity and ease of its isolation procedure make it an attractive alternative to current methodologies.

N-alkyl secondary amine derivatives linked to herbicides and pharmaceuticals have been demonstrated as numerous biologically active compounds for drug discovery.[1] N-benzyl secondary amines, in particular, have attracted considerable attention from both biological and organic chemists. This is because they appear as carboxamide derivatives, which are the most prevalent structural moieties in medicinal chemistry.[2] However, despite widespread interest, the most common strategies for the production of secondary amines such as electrophilic alkylation, reductive alkylation, and amination of aryl halides, often exhibit limitations such as low selectivity toward desired secondary amines, harsh reaction conditions, and stoichiometric amounts of wasteful salts.[3,4] In addition, various expensive [$Ru_3(CO)_7$] cluster, [Ir(COD)Cl] dimer, rhodium, and platinum transition metal complexes have been used as homogeneous catalysts for synthesizing secondary amines in the presence of base additives, which retard the commercialization of the process because of high cost and environmental concerns.[5–7]

The use of heterogeneous catalysts[8–12] offers several advantages over homogeneous catalysts, including ease of separating reactants, minimal trace metal in the products, ease of handling, process control, and reusability of catalysts. These advantages can thus improve reaction processes. Therefore, developing an environmentally friendly and recyclable heterogeneous catalytic system for synthesizing secondary amines is of considerable interest. Heterogeneous catalysts such as Fe/amino acids, Fe_3O_4, and Fe_3O_4/tBuO$^-$ have been used for the synthesis of secondary amines,[12,13] however, these systems suffer from complicated synthesis procedures and low activity compared with precious metal complexes.

In recent years, mesoporous materials have demonstrated their potential in solar cells, fuel cells, and drug delivery systems.[14–21] In addition, mesoporous materials have been increasingly applied as heterogeneous catalysts in various organic transformations because of their unique structural and textural properties such as controllable pore size, uniform pore-size distribution, high thermal stability, and ultrahigh specific surface area.[22,23] Among various heterogeneous catalysts, aluminosilicates have been considered useful solid catalysts because of their usage as effective catalysts in aldol, Friedel–Crafts, and Diels–Alder reactions.[24,25] However, based on our knowledge, no studies have synthesized secondary amines by using mesoporous aluminosilicate catalysts.

We present a facile synthesis of mesoporous aluminosilicate materials with highly ordered two-dimensional (2D) hexagonal structures (denoted as MAS) through direct hydrothermal synthesis. The synthesized MAS were further used as solid catalysts for efficiently catalyzing the synthesis of secondary amines through C–N bond formation between benzyl alcohol and aniline (Scheme 1). The MAS catalyst showed an excellent yield of secondary amines with high reusability of the catalyst for several cycles.

The MAS samples were prepared using a triblock copolymer (Pluronic P123, $EO_{20}PO_{70}EO_{20}$, molecular weight = 5800 g mol^{-1}) as a structure-directing agent.[26,27] Tetraethoxysilane (TEOS) and aluminum isopropoxide (AlIP) were used as silicon and aluminum sources, respectively. Typically, P123 (2.0 g) was dissolved in a hydrochloric acid solution (72.0 g) and stirred at room temperature for 10 h. The AlIP in the hydrochloric acid solution and TEOS were added to the mixture. The resulting

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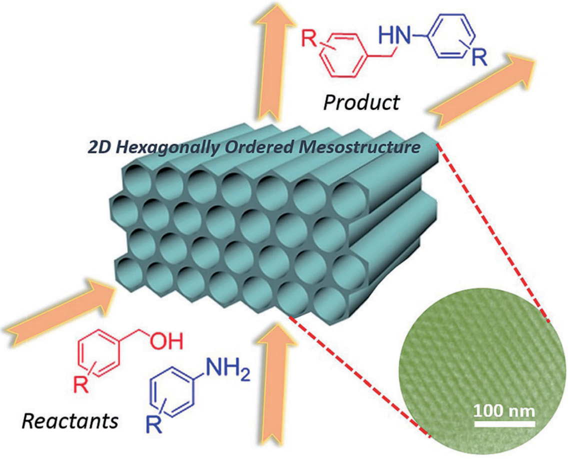


Scheme 1. Schematic representation of MAS-catalyzed synthesis of secondary amine in this study.

mixture was stirred at 35 °C for 20 h. Subsequently, the reaction mixture was heated for 48 h at 100 °C under static conditions for the hydrothermal treatment. The solid product was filtered, washed, and then dried at 80 °C. The obtained product after calcination at 550 °C is denoted as MAS(x), where x represents the Si/Al mole ratio. The Si/Al mole ratio was determined from an inductively coupled plasma analysis.

The structural characteristics of the MAS materials exhibited typical X-ray diffraction (XRD) patterns, which were indexed to the (10), (11), and (20) reflections of the hexagonal 2D pore ordering in the *p6mm* symmetry (data not shown). The nitrogen sorption measurement results of the MAS materials indicated type-IV curves with a sharp capillary condensation step and H1-type hysteresis loop, which indicates large uniform pores (Figure 1 a). The sharp capillary condensation step of the isotherm indicates the nitrogen condensation within mesopores, and the structural ordering of the mesopores remains well even after the incorporation of Al. Table 1 summarizes the textural properties such as the d_{10} value, mesopore diameter, BET specific surface area, and total pore volume of the MAS materials. The d_{10} value calculated from the XRD data of mesoporous silica (no Al incorporation) prepared under similar experimental conditions is 9.16 nm, which increases up to 10.86 nm for the MAS(38) material upon incorporating Al in the mesoporous framework. Notably, the capillary condensation step shifts to a higher relative pressure with increasing Al content in the mesoporous network, indicating that the mesopore diameter significantly increases from 8.3 to 9.2 nm (Figure 1 b). The plausible reason for the increase in the mesopore diameter with the Al-content increase is that the [AlO_4] tetrahedron is slightly larger than the [SiO_4] tetrahedron because the Al–O bond is longer compared with that of the Si–O bond.[28] Furthermore, the specific surface area and pore volume decreased from 826 $m^2 g^{-1}$ and 1.2 $cm^3 g^{-1}$, respectively, for MAS(93) to 672 $m^2 g^{-1}$ and 0.89 $cm^3 g^{-1}$ for MAS(38), as shown in Table 1.

Table 1. Summary of d_{10}-spacing, surface area, pore volume and pore size of MAS materials with different Si/Al mole ratios (MAS(93), MAS(54), and MAS(38) materials).

Sample	d_{10}-spacing [nm]	Pore size [nm]	Surface area [$m^1 g^{-1}$]	Pore volume [$cm^3 g^{-1}$]
MAS(38)	10.9	9.2	672	0.89
MAS(54)	10.5	8.8	734	0.96
MAS(93)	9.2	8.3	826	1.20

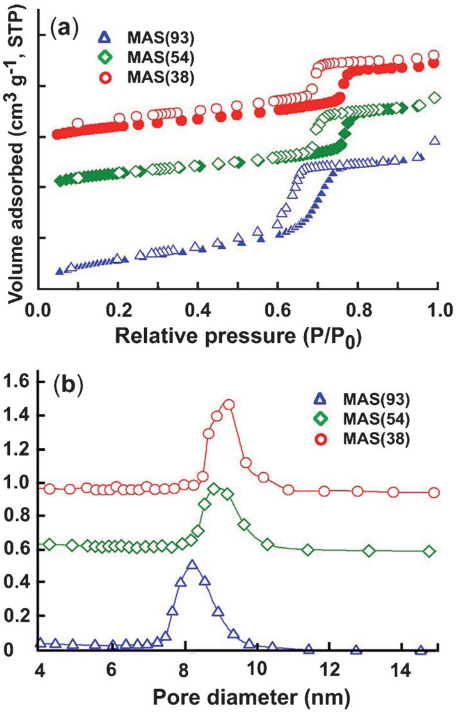


Figure 1. a) Nitrogen adsorption-desorption isotherms of MAS materials with different Si/Al mole ratios, MAS(93), MAS(54), and MAS(38), b) the corresponding pore size distributions.

To evaluate the strength and type of acidic sites on the MAS materials, IR spectra of adsorbed pyridine were studied (data not shown). The Fourier transform infrared spectra of the MAS(38) material show the coordinatively bounded pyridine band at 1445 and 1610 cm^{-1} that is characteristic of pyridine adsorbed on Lewis acid sites. In addition, the band at 1540 cm^{-1}, which is characteristic of pyridine adsorbed on Brønsted acid sites, exists in both MAS(54) and MAS(38) samples.[29] The presented results indicate that the MAS(38) material contains both Lewis and Brønsted acidic sites, whereas the other MAS materials (i.e., MAS(54) and MAS(93)) contain only Brønsted acidic sites. Notably, the acidity of the MAS materials can be tuned by adjusting the Al content in the mesoporous network.

The transmission electron microscopy images of the MAS(38) material with high Al content clearly show that the material comprised 2D ordered porous structures with honeycomb pores and linear pores, as shown in Figures 2 a-1 and a-2, respectively. Moreover, to assess the structure and coordination of Al species in MAS(38), the material was examined by using ^{27}Al magic-angle-spinning nuclear magnetic resonance

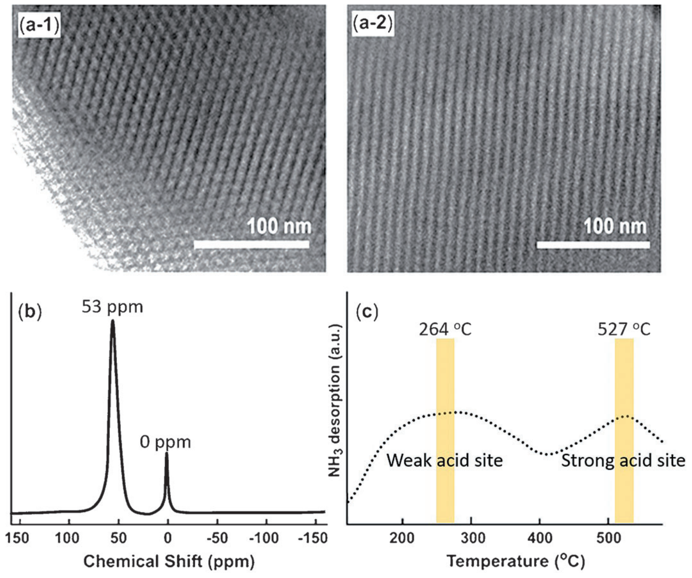


Figure 2. a) TEM images, b) ^{27}Al MAS-NMR spectra, and c) NH$_3$-TPD profile of the MAS(38) material.

(MAS-NMR). The spectrum of the calcined MAS(38) in Figure 2b shows two resonance peaks at 0 and 53 ppm. These peaks are attributed to extra-framework aluminum species in octahedral coordination and framework Al species in tetrahedral coordination, respectively.[30] These results clearly indicate that higher numbers of Al species are in the tetrahedral environment compared with the octahedral Al species. These results are also strongly reflected in the MAS(38) acidity data. In general, the mesoporous siliceous materials possess extremely low acidic sites. The surface acidity, which plays a vital role in the coupling reaction of aniline and 4-methoxybenzyl alcohol and its product selectivity of N-alkyl secondary amines, increases when Al is incorporated into the mesoporous siliceous materials. In this respect, MAS(38) demonstrated acid characteristics (Figure 2c), presenting a profile of the distribution acidic sites of the MAS(38) catalyst. The profile primarily shows a broad desorption temperature peak at approximately 260 °C, which is attributed to the NH$_3$ desorption from framework Al atoms of the weak adsorption site of the MAS(38) material. The high-temperature peak at approximately 520 °C is ascribed to the desorption of NH$_3$ from strong acidic sites on the extra-framework Al species; therefore, one can conclude that there is a strong interaction between ammonia and Al$_2$O$_3$ species.[31] These results are consistent with the ^{27}Al-MAS-NMR data.

To determine the optimal reaction conditions (i.e., solvent and temperature) to obtain maximum yield for the one-pot synthesis of N-benzyl secondary amines, coupling reactions of aniline (**1**) and 4-methoxybenzyl alcohol (**2**) were attempted using different solvents in the presence of the MAS(38) catalyst. In a typical procedure, a mixture of **1** (1.5 mmol) and **2** (1.0 mmol) as well as MAS(38) (50 mg) in toluene were stirred for 24 h; product **3** was formed in a yield of 51 and 68 % at 80 °C and reflux temperatures (i.e., around 110 °C), respectively, after column chromatography. The effect of different solvents on the yield of the final product was compared and shown in Figure 3a. The reaction did not proceed without a catalyst. Acetonitrile, isopropanol, dimethyl sulfoxide, and dimethyl formamide solvents generated a poor yield of the corresponding product. Unexpectedly, no product formation was observed when THF and DMA were used under similar reaction conditions. We concluded that at 110 °C toluene was the optimal solvent for the synthesis of N-benzyl secondary amines through C–N bond formation between benzyl alcohol and aniline when the synthesized MAS was used as a catalyst.

Furthermore, the reaction was attempted in the presence of different MAS catalysts with Si/Al mole ratios of 38, 54, and 93 to obtain excellent yields of the corresponding N-benzyl secondary amines (Figure 3b). Among the materials tested, MAS(38) demonstrated a high yield of secondary amines because of its large pore size and ordered mesoporous structure. These results demonstrate the significant catalytic activity of MAS catalysts with a high yield of benzyl secondary amines.

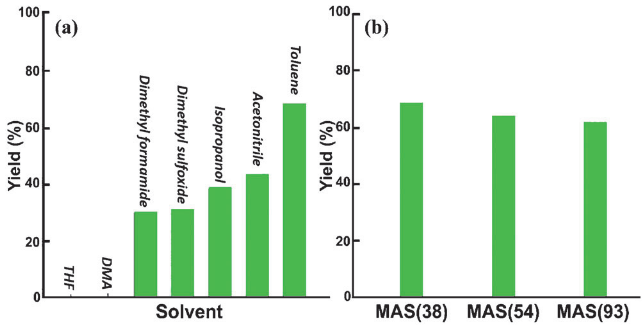
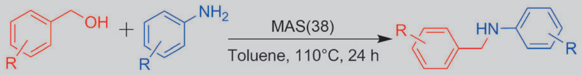


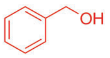
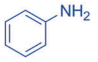
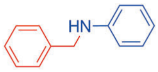
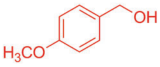
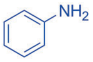
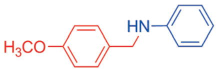
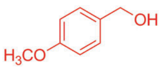
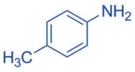
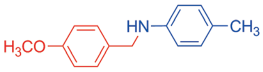
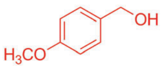
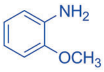
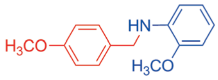
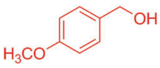
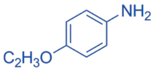
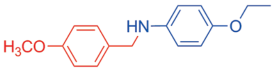
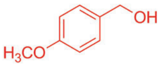
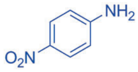
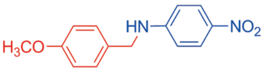
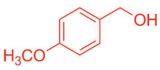
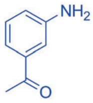
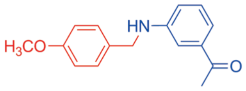
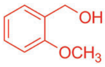
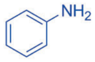
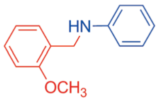
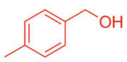
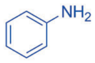
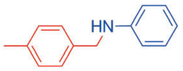
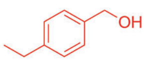
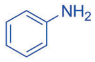
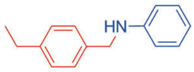
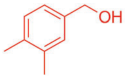
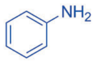
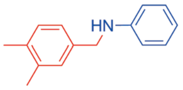
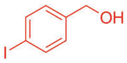
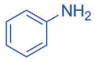
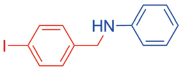
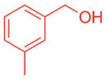
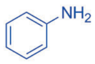
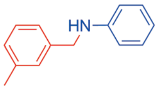
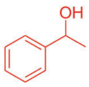
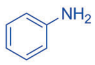
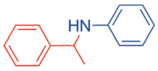
Figure 3. a) Optimization of the reaction for the synthesis of N-benzyl secondary amines over MAS(38), and b) effect of Si/Al mole ratios of MAS catalyst on the yield of N-benzyl secondary amines.

The scope of the reaction was further investigated using different amines and benzyl alcohols with toluene as the solvent at 110 °C and the MAS(38) as the catalyst under optimized conditions. As summarized in Table 2, the reaction between aniline with unsubstituted benzyl alcohol resulted in a 60 % yield of the corresponding product (Table 2, sample a). Notably, the reaction proceeded smoothly with electron-donating groups of benzyl alcohols with aniline (Table 2, samples b, h–k, m). In addition, other alkyl, alkoxy substituted anilines with methoxybenzyl alcohol produced excellent yields (Table 2, samples c–e). Electron-withdrawing groups on the aromatic ring of either benzyl alcohol or aniline influenced the reaction, and the corresponding N-benzyl secondary amines were obtained in 20–45 % yields (Table 2, samples f,g). The phenethanol and aniline reaction also proceeded smoothly, and the corresponding benzyl secondary amine product was obtained in a 55 % yield under the optimized conditions (Table 2, sample n). The pathway that we suggest for this process is that the acidic centers present in MAS(38) were active for dehydration of benzyl alco-

Table 2. One-pot synthesis of N-benzyl secondary amines with different substrates over MAS(38) catalyst (Reaction conditions: alcohol, amine, and MAS(38) at 110 °C in toluene). The purity of each reactant is shown in Table S1.



1 2 3

	Alcohol (1)	Amine (2)	Product (3)	Yield [%]
a				60.0
b				68.0
c				71.0
d				70.0
e				72.0
f				20.0
g				45.0
h				68.0
i				66.0
j				65.0
k				63.0
l				50.0
m				61.0
n				55.0

hol through the formation of hydrogen bonds, thereby generating the corresponding N-benzyl secondary amine and water.

The reusability of the MAS(38) catalyst was studied to determine the most suitable approach for recycling the catalyst for the N-alkylation of aniline with 4-methoxybenzyl alcohol in toluene at 110 °C. The catalyst was removed through centrifugation after the reaction, washed with ethyl acetate 3 times (by sonication for 5 min) to remove organic substances from the surface, and then later activated. Fresh aliquots of reactants were added to the recovered catalyst to test the reusability. The reusability test results indicated that because of the robustness of the MAS(38) catalyst, the high yield of product **3** was maintained without much loss of activity up to four cycles.

In summary, we have developed a facile synthesis of ordered mesoporous aluminosilicate-catalyzed and efficient synthesis of N-benzyl secondary amines through a C–N bond formation between benzyl alcohol and aniline under ligand and base-free conditions. The MAS(38) catalyst with a well-ordered mesopore structure and strong acidic sites can be used to produce excellent catalysts for acid-catalyzed organic transformations. Our MAS catalysts are highly active and potentially reusable; its operational simplicity and ease of its isolation procedure make it an attractive alternative to current methodologies.

Experimental Section

Typical procedure for the synthesis of secondary amines: MAS catalyst (50 mg), 1.5 mmol of alcohol and 2.0 mL of toluene (with purity 99.8%) were placed in a 15 mL sealed tube. To this mixture, 1.0 mmol of amine was added and stirred at 110 °C for 24 h. After cooling to room temperature, the reaction mixture was filtered and washed with dichloromethane (with purity 99.8%). The catalyst was recollected after the reaction. The combined organic layers were concentrated under reduced pressure, and the resulting crude product was then subjected to column chromatography using mixture of hexane and ethyl acetate (9:1) as eluent to afford the pure product. The obtained secondary amines were characterized on Bruker 300 MHz NMR (^{1}H and ^{13}C) spectrometer using TMS as internal standard and chloroform-*d* (with purity 99.8%) as a solvent. The yield of each product was calculated based on the result of ^{1}H and ^{13}C NMR spectra. The calibration curve for each product was made previously before measuring samples. All the chemicals were purchased from Sigma Aldrich and used without further purification. In addition, all reagent grade solvents were purchased from Sigma Aldrich and used as received.

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Keywords: ligand-free synthesis · mesoporous aluminosilicate · mesoporous materials · secondary amines

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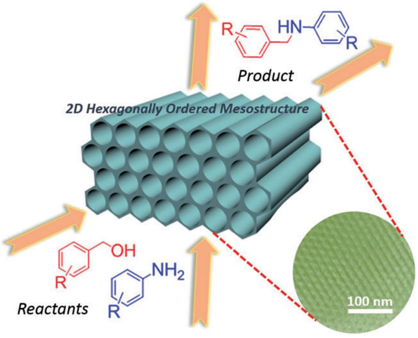
■■–■■

Ordered Hexagonal Mesoporous Aluminosilicates and their Application in Ligand-Free Synthesis of Secondary Amines



Get hexed! Mesoporous aluminosilicates were successfully synthesized and applied as ligand, base-free heterogeneous catalysts for C–N bond formation between benzyl alcohol and aniline for various N-benzyl secondary amines with excellent activity and selectivity.