

DOI: 10.1002/cctc.201200551

 **Efficient Tertiary Amine/Weak Acid Bifunctional Mesoporous Silica Catalysts for Michael Addition Reactions**Sayantani Das,^[a] Anandarup Goswami,^[a, b] Nagarajan Murali,^[a] and Tewodros Asefa^{*,[a, b, c]}

We describe the development and application of efficient bifunctional acid–base mesoporous silica catalysts, denoted hereafter as Ext-SBA-15-NMe₂, comprising tertiary amine and silanol (weak acid) groups for the Michael addition reaction. The catalysts were synthesized by grafting tertiary amine containing organosilane into the mesoporous channel pores of SBA-15 mesoporous silica in polar protic solvent (isopropyl alcohol) or nonpolar solvent (toluene). The resulting materials, Ext-SBA-15-NMe₂-IPA or Ext-SBA-15-NMe₂-Tol, respectively, were used as catalysts for the Michael addition reactions between *trans*- β -nitrostyrene(s) and active methylene compounds, such as malonitrile, acetylacetone, and diethylmalonate, at different temperatures. A variable-temperature NMR-array technique was used to monitor the reactant conversion and the reaction progress. Among the active methylene compounds tested with *trans*- β -nitrostyrene, malonitrile gave the highest conversion of 90% in 0.3 h at 0 °C if catalyzed by the catalyst Ext-

SBA-15-NMe₂-IPA, the silanol groups of which were not passivated by trimethylsilyl (–SiMe₃) groups. Compared with Ext-SBA-15-NMe₂-Tol, the Ext-SBA-15-NMe₂-IPA material (whose the amine groups were grafted in polar-protic solvents), in particular, demonstrated an effective cooperative bifunctional catalysis because of its optimized proportions of tertiary amine groups and a significant number of surface silanol groups that were judiciously left behind on the material with this optimized synthetic strategy. The catalytic activity of this material was found to be significantly higher than that of the corresponding material that was grafted in toluene and that contained less optimized proportions of these two catalytic groups (i.e., amine and silanol groups). The bifunctional catalysts also showed good recyclability upon washing with acetone, which offered an effective way of regenerating the catalyst free from any undesired product/substrate bound on the surface of the catalysts.

Introduction

The Michael reaction, which involves 1,4-addition of a nucleophile (preferably a C-nucleophile) to an α,β -unsaturated compound, offers a simple yet effective way of making C–C bonds, which makes it one of the most widely used reactions in both industry and academia. The reaction, as first reported by Arthur Michael in 1887,^[1] involves primarily the attack of a C-nucleophile, generated from compounds with active methylene groups, on the β position of unsaturated carbonyl compounds, giving the corresponding enol/enolate, followed by subsequent protonation and tautomerization of the enol to its keto form, yielding the so-called 1,4-addition product. Thus,


the customary steps in the reaction include the deprotonation of the parent active methylene compounds with basic reagents and the protonation of enolate with either the conjugate acid of that same base or the solvent. The ease of the reaction and the involvement of a base and the corresponding conjugate acid to catalyze the reaction have made the development of efficient acid or base catalysts, which can catalyze the reactions reversibly and effectively, the subject of intense research in catalysis. The concept has been applied to this reaction (in both stereoselective and non-stereoselective manner) by using metal-based Lewis acid catalysts^[2] and organocatalysts.^[3] Compared with organometallic catalytic systems, organocatalysts offer advantages because most of them are easy to handle, are stable under many different synthetic conditions, and have highly tunable synthetic skeletons.^[4]

In this particular context of Michael addition reaction, the most common organocatalytic systems are derived from organoamines because they have been found to be basic enough to take up the protons from the active methylene groups and generate carbanions, and their conjugate acids (ammonium ions) are proven to be capable of delivering the protons back to the enolate at the end of the catalytic cycle. Alternating modes of activation, that is, either activation of carbonyl using acid catalysts or use of highly reactive organometallic reagents to form the nucleophile,^[5] have also been used to make some of the most important synthetic skeletons.^[6] However, until re-

[a] S. Das, Dr. A. Goswami, Dr. N. Murali, Prof. T. Asefa
Department of Chemistry and Chemical Biology
Rutgers, The State University of New Jersey
610 Taylor Road, Piscataway, New Jersey 08854 (USA)
Fax: (+1) 848-445-2970
E-mail: tasefa@rci.rutgers.edu

[b] Dr. A. Goswami, Prof. T. Asefa
Department of Chemical and Biochemical Engineering
Rutgers, The State University of New Jersey
98 Brett Road, Piscataway, New Jersey 08854 (USA)

[c] Prof. T. Asefa
Institute for Advanced Materials, Devices and Nanotechnology (IAMDN)
Rutgers, The State University of New Jersey
607 Taylor Road, Piscataway, New Jersey 08854 (USA)

 Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/cctc.201200551>.

cently, the possibility of combining more than one catalytic system for the Michael reaction remained relatively unexplored owing to poor compatibility between a base and an acid catalytic group within the same system. This compatibility issue has lately been circumvented by the use of urea-based hydrogen-bonding homogeneous catalytic systems. The pioneering works by Rawal,^[7] Takemoto,^[8] Jacobsen,^[9] Macmillan,^[10] and others^[11] toward the development of these types of bifunctional catalysts (as well as their asymmetric variants) illustrated the importance of such a simple, but novel, idea of dual activation in this type of reaction. In addition to urea, silanols (Si–OH), in both homogeneous and heterogeneous forms, are attracting more attention as catalysts or co-catalytic species for a number of reactions. The recent work by Franz^[12] and Mattson^[13] showed that silanols could show paramount catalytic activities in reactions such as Michael, aldol, and Diels–Alder reactions. The group of homogeneous catalysts these two research groups reported have well-designed silanols with both sterically and electronically controlled substituents around the silicon atoms so that the silanols avoid potential self-condensation (the possible self-condensation of silanols is one of the main reasons for the difficulty in the synthesis of homogeneous silanol-based catalytic systems). This in turn enabled silanols to activate electrophiles without compromising their catalytic activity. The latest study by Franz even demonstrated that by carefully choosing the substituents on the silanol moiety, these types of catalysts can also be used as bifunctional catalysts for enantioselective aldol reactions.^[14] Intrigued by these results and our recent success in the field of heterogeneous catalysis,^[15] we investigated the possibility of using amine-functionalized mesoporous silica materials, which inherently contain silanol groups or can be judiciously made to contain more optimized density of silanol (weak acid) groups, as acid–base bifunctional organocatalysts for the Michael addition reaction.

Since the discovery in early 1990s, significant progress has been made in the field of the synthesis of various mesoporous silica materials and their potential applications as support materials for heterogeneous catalysts.^[16] This development can generally be attributed to the unique chemical and conducive physical properties of these types of materials as catalyst supports, among many other things. In addition to the common advantages of heterogeneous catalysts compared to their homogeneous counterparts (e.g., less waste generation, easy work-up methods, and recyclability), the resulting mesoporous silica-supported heterogeneous catalytic materials offer high surface areas, which provide large contact areas between reactants and catalytic sites and thus high catalytic activity. In addition, these catalysts can serve as shape-/size-selective catalysts as a result of their uniform yet con-

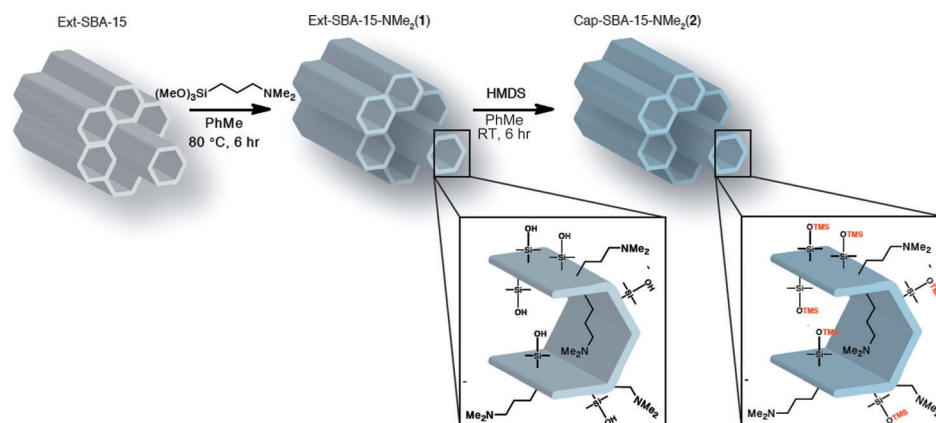
trollable nanometer pores, which allow controlled molecular diffusion of reactants. Moreover, besides their catalytically active groups, further functional groups can easily be introduced into these materials by either grafting or co-condensation synthetic methods. This in turn can result in surface modification and controllable physical and chemical properties, and thus efficient and tunable catalytic activities.^[17]

Among many types of organofunctionalized mesoporous materials, amino-functionalized hybrid mesoporous organosilica materials are well known for their catalytic activity in various carbon–carbon bond-forming reactions. Studies have shown that the presence of significant numbers of residual surface silanol groups can be beneficial for the catalytic performance of these materials, especially if an appropriate density of catalytic functional groups, such as organoamines, is present in their channel pores.^[18] This has encouraged us to develop a similar type of catalytic system that utilizes both silanol (as a hydrogen-bonding cocatalyst) and tertiary amine (as a base catalyst) as a mode of dual activation toward the Michael reaction. We herein report the synthesis of bifunctional mesoporous catalysts containing optimized density of tertiary amine and silanol groups and the use of the resulting materials as effective bifunctional catalysts for the Michael addition reactions between various nitroalkenes and active methylene compounds.

Results and Discussion

Synthesis of tertiary amine-functionalized SBA-15 mesoporous silica materials or bifunctional catalysts

The synthesis of the bifunctional catalyst Ext-SBA-15-NMe₂-Tol (1) or Ext-SBA-15-NMe₂-IPA (1') containing tertiary organoamine and silanol groups was achieved by stirring Ext-SBA-15 with an excess amount of 3-(*N,N*-dimethylaminopropyl)trimethoxysilane (DATS) in toluene or isopropyl alcohol, respectively, at 80 °C for 6 h. The corresponding control samples, labeled as Cap-SBA-15-NMe₂-Tol (or 2) and Cap-SBA-15-NMe₂-IPA (or 2'), respectively, were prepared by capping the external silanol (weak acid) groups of Ext-SBA-15-NMe₂-Tol or Ext-SBA-15-NMe₂-IPA with methyl groups by using hexamethyldisilazane



Scheme 1. Synthesis of Ext-SBA-15-NMe₂-Tol (1) and Cap-SBA-15-NMe₂-Tol (2).

(HMDS), as depicted in Scheme 1. The latter samples, Cap-SBA-15-NMe₂-Tol (2) and Cap-SBA-15-NMe₂-IPA (or 2'), respectively, were synthesized so that its accessible silanol groups would be protected by trimethylsilyl (–SiMe₃) groups and the resulting catalysts would have no accessible external silanol (active weak acid) groups, which could aid in hydrogen bonding during the Michael reaction. Thus, by using these materials (2 and 2') as reference, the effect of silanol groups as acid co-catalysts in the bifunctional catalysts (1 and 1') for the Michael reaction was investigated.

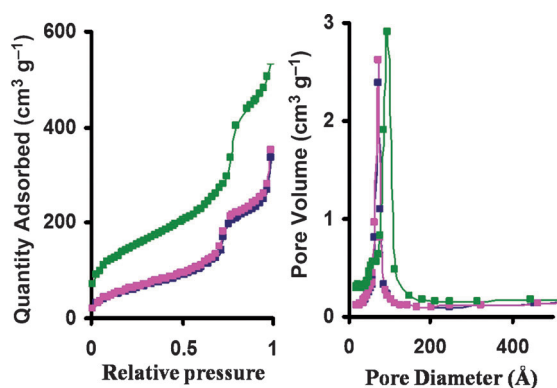


Figure 1. Nitrogen adsorption/desorption isotherm and pore size distribution of Ext-SBA-15 (■), Ext-SBA-15-NMe₂-Tol (●), and Cap-SBA-15-NMe₂-Tol (■).

The N₂ gas adsorption/desorption measurements were performed to characterize the mesoporous structure, surface area, and pore diameter of the catalysts and their parent materials. The N₂ gas adsorption measurements showed type IV isotherms, which were characteristic of mesoporous materials (Figure 1). The N₂ gas adsorption measurements also revealed that the BJH pore size distribution of the materials was monodisperse. The BET surface area and average pore diameter of the parent material (SBA-15) were 427 m² g^{−1} and 11.8 nm, respectively, whereas the surface area and pore diameter of Ext-SBA-15-NMe₂-Tol (1) were 235 m² g^{−1} and 8.4 nm, respectively, and those of Cap-SBA-15-NMe₂-Tol (2) were 225 m² g^{−1} and 8.4 nm, respectively. The decrease in surface area and pore diameter in the organo-functionalized materials compared with the parent material was expected because of the presence of

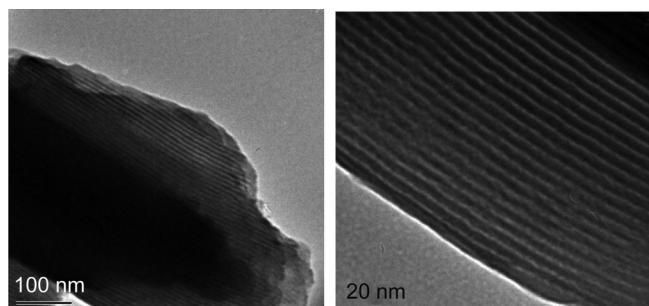


Figure 2. TEM images of Ext-SBA-15-NMe₂-Tol.

grafted organoamine (and trimethylsilyl) groups in the pores of these materials.

The materials, both before and after postgrafting with organosilanes, were also characterized by powder XRD (Figure S1) and TEM (Figure 2). The XRD pattern of all the samples showed a sharp peak corresponding to the (100) peak and very small peaks corresponding to the (110) and (200) peaks of hexagonally ordered mesostructured materials. The Bragg peaks remained intact after postgrafting of the materials with organoamine groups, which indicated that the mesostructures were stable after the postgrafting synthetic step. By indexing the (100) peak, the materials' unit cell sizes were found to be 11–12 nm. These and other physical properties of the materials are listed in Table S1. The TEM images of the samples confirmed the presence of ordered mesostructures in the materials (Figure 2).

The TGA traces of the organoamine- (and trimethylsilyl-) functionalized mesoporous silica materials (catalysts) (Figure 3) demonstrated a slight weight loss below 100 °C for all the sam-

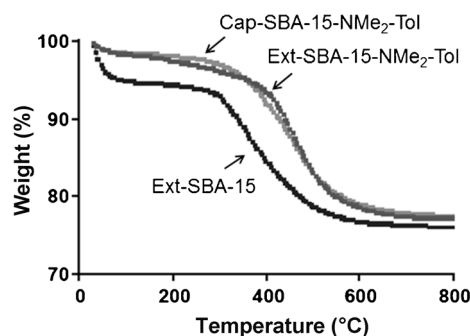


Figure 3. Thermogravimetric traces of Ext-SBA-15, Ext-SBA-15-NMe₂-Tol, and Cap-SBA-15-NMe₂-Tol.

ples because of the loss of water adsorbed on the materials. The weight loss in Ext-SBA-15 (extracted mesoporous silica) in between 100 and 600 °C was attributed mainly to residual templating agent and partly to water formed by condensation from the surface silanol groups of the material. The weight losses in the range between 100 and 600 °C from the catalysts were predominantly due to the loss of the organoamine (or –SiMe₃ trimethylsilyl) groups. The Ext-SBA-15-NMe₂-Tol and Cap-SBA-15-NMe₂-Tol samples showed a similar weight loss (≈21 %).

The catalysts Ext-SBA-15-NMe₂-Tol, Cap-SBA-15-NMe₂-Tol, and Cap-SBA-15-NMe₂-IPA were characterized by ¹³C cross-polarization magic angle spinning (CP-MAS), ²⁹Si CP-MAS, and ²⁹Si MAS (²⁹Si–¹H-decoupled) solid-state NMR spectroscopy (Figure S2). In the case of ¹³C CP-MAS NMR spectrum for Ext-SBA-15-NMe₂-Tol, the peaks at 10.2, 20.1, 43.2, and 61.6 ppm were designated as C4, C3, C1 (NMe₂), and C2 of alkylamine groups (Figure 4). The peaks marked with asterisks (*) correspond to the peaks from residual surfactants.^[19] A similar pattern (as well as a similar chemical shift) was observed in the case of Cap-SBA-15-NMe₂-Tol. However, the peaks corresponding to methyl groups that resulted from the capping of –Si–OH groups did

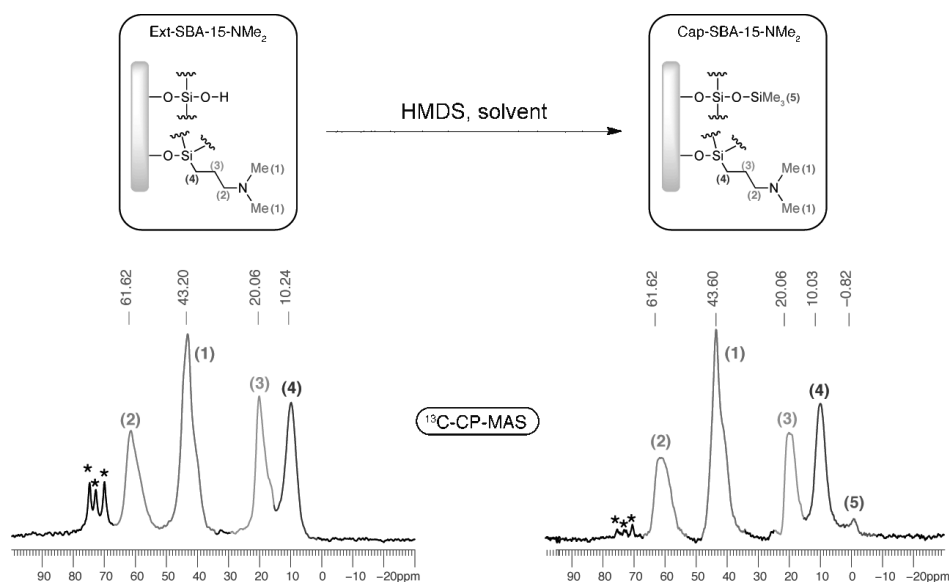


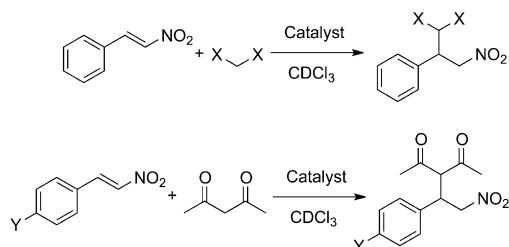
Figure 4. ^{13}C CP-MAS spectra and their peak assignments for Ext-SBA-15-NMe₂-IPA and Cap-SBA-15-NMe₂-IPA.

not show up in the spectra (at least under the same experimental conditions). Contrarily, in the case of Cap-SBA-15-NMe₂-IPA, the peak at 0.82 ppm indicating the presence of $-\text{O}-\text{SiMe}_3$ in the material was seen.^[20] Based on these observations, it seems likely that because of the higher degree of grafting in toluene,^[15] the number of free $-\text{Si}-\text{OH}$ groups reduces, which results in less number of free $-\text{Si}-\text{OH}$ groups for HMDS capping; however, in the case of grafting in isopropanol, the relative number of $-\text{Si}-\text{OH}$ sites remains significant owing to less grafting in the previous step.^[15b] As a result, the latter material reacts significantly upon treatment with HMDS and gives more $-\text{O}-\text{SiMe}_3$ groups that show up in its ^{13}C CP-MAS spectrum. Our effort to characterize this further by using ^{29}Si CP-MAS and $^{29}\text{Si}-^1\text{H}$ -decoupling experiments offered satisfactory information regarding the Q(s) and T(s) states of the material; however, the spectra failed to show the peaks for the M state corresponding to the silicon atoms in $-\text{OSiMe}_3$ in the Cap-SBA-15-NMe₂ sample under the same experimental conditions because of low signal-to-noise ratio as well as relatively lower number of possible $-\text{SiMe}_3$ capping sites in it.^[21] A comparative study of Ext-SBA-15-NMe₂ and Cap-SBA-15-NMe₂ (obtained from the same batch of SBA-15) revealed that the Ext-SBA-15-NMe₂ sample had a higher percentage of T(s) states (Figure S2). However, the apparent discrepancy in the percentage of T states between the two Cap-SBA-15-NMe₂ samples could presumably stem from the different batches of the SBA-15 precursor used during the experiments in addition to their low signal-to-noise ratios. The amount of amine groups present in both catalysts was obtained by using CHN elemental analysis (Table S2).

Catalytic activity of the catalysts in the Michael addition reaction

First, the catalytic activities of Ext-SBA-15-NMe₂-Tol and Cap-SBA-15-NMe₂-Tol were investigated in the Michael addition re-

action between *trans*- β -nitrostyrene and active methylene compounds at various temperatures (Scheme 2). Cap-SBA-15-NMe₂-Tol, which does not have active residual silanol (weak acid) groups in it, was used as the reference material to establish the combined effect of both the amine catalyst and the surface silanol groups of Ext-SBA-15-NMe₂-Tol on the reaction. Although the effect was less prominent at higher temperatures, the reaction was found to be faster with Ext-SBA-15-NMe₂-Tol than with Cap-SBA-15-NMe₂-Tol. This was presumably because the surface silanol groups in the former aided in the hydrogen



Scheme 2. The Michael addition reaction between nitrostyrene (or *p*-substituted nitrostyrenes) and various active methylene compounds.

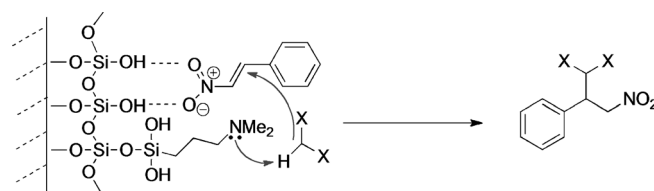


Figure 5. Proposed mechanism of dual activation involving hydrogen bonding by acid–base bifunctional mesoporous catalysts in the Michael addition reaction.

bonding of the substrate, which was absent in the latter catalyst. In other words, the $\text{Si}-\text{OH}$ groups in the former activated the nitro group of nitrostyrene, which makes it more electrophilic, and thus a facile addition of the nucleophile occurred (Figure 5).

The extent of dual activation by acid and base groups as well as how concerted such a process can be still remain to be areas of active research, although various models have been proposed in the case of some homogeneous versions. In most of the organocatalytic asymmetric Michael reactions, the activation of nucleophiles (in this case, active methylene compounds) by an amine-based catalytic system is well precedent and can certainly be extended to our case. However, the other

parallel activation mode, that is, the activation of hydrogen bonding, demands further discussion. Of the possible activation modes of an electrophile by an organocatalyst, two types of activation are commonly documented. In one case, an electrophile becomes activated by the formation of an iminium ion, which was generated through the reaction between the electrophile (in this case, Michael acceptor) and the catalyst. In the second case, hydrogen bonding between the catalyst and the Michael acceptor makes the electrophilicity of the acceptor molecule to increase. Although the first activation mode is historically important and offers some great advantages in the context of proline-catalyzed reactions, it is not applicable in the case of tertiary amine-catalyzed reactions. Contrarily, a relatively newer approach, that is, activation through hydrogen bonding, shows better resemblance with our catalytic system. On the basis of the X-ray structures of their alkaloid-based thiourea catalysts along with physical organic studies, Takemoto^[8] and Jacobsen^[9] proposed the concept of dual activation through two hydrogen bonds between the urea moiety and the electrophile. However, more recent theoretical study by Pápai and Soós^[22] showed an alternative approach, which uses the hydrogen bonding with amine as a plausible activation mode. The widely reported double hydrogen bond activation by urea or thiourea has also been challenged by Lu,^[23] who demonstrated that a single hydrogen bond activation of the urea N–H with the electrophile can also catalyze the reaction. In addition, the effects of additive, solvent, and temperature have been studied. However, till the studies by Franz^[12,14] and Mattson,^[13] silanol as a potential hydrogen-bonding source in homogeneous catalysis remained unexplored because of its propensity toward condensation, which leads to poor stability under normal reaction conditions. In this context, Franz's X-ray crystallographic study of the silanol-activated carbonyl groups along with the theoretical study of the pK_a of silanols are quite encouraging and the idea of similar hydrogen-bonding activation can easily be extended in case of our heterogeneous version, which thereby allows us to draw one of the possible mechanisms for the heterogeneous Michael reaction. In this case, in spite of the sharp advances in heterogeneous silica-supported catalysis, the investigation of the effect of the surface silanol group as a co-catalyst at molecular levels still poses significant challenges mainly due to the difficulty in comprehending the bonding pattern of these catalytic groups on the surface and the nanoscale pore channels of the materials. Furthermore, compared to homogeneous catalysis, obtaining crystal structures of intermediates in heterogeneous catalysis is difficult. Under these circumstances, the reaction mechanisms are often hypothesized on the basis of information from their homogeneous counterparts. As indicated previously, the detailed mechanistic investigation is beyond the scope of this current article; however, the catalytic results suggest that although activation of the nucleophile with basic groups is required for the reaction, a further rate acceleration can be achieved by the activation of the electrophile through hydrogen bonding using the silanol groups of the mesoporous silica support material. This hydrogen-bonding activation is not operative in the case of Cap-SBA-15-NMe₂-Tol, because this material

does not have many free or accessible Si–OH groups owing to its treatment with HMDS. The results of these experiments clearly showed that Ext-SBA-15-NMe₂-Tol, which was not treated with HMDS, could serve as an effective hydrogen-bond donor catalyst for the conjugate addition of various active methylene compounds to *trans*- β -nitrostyrene or substituted *trans*- β -nitrostyrenes.

The variable-temperature ¹H NMR-array technique experiment, which we used here, allowed us to study the catalytic reactions at different temperatures in real time and to obtain kinetic data. The results of the kinetic studies using the variable-temperature ¹H NMR-array technique matched closely with those of our bench-top experiments and eliminated the risk of potential rate difference between NMR and bench-top experimental conditions due to external influences (e.g., stirring), because of the smaller amount of the catalyst used in the former experiment. In addition, based on our current results, the results from this technique seem to be more reliable than those of (our) GC-based experimental catalytic studies for the bench-top reactions. Despite its apparent usefulness, such an experiment for monitoring heterogeneous catalysis is, however, rarely performed, and our work here is one of the first examples that demonstrates the use of such method for probing the catalytic activities of organoamine-functionalized mesoporous heterogeneous catalysts.^[24] The catalytic results are presented in Tables 1–3.

Under the reaction conditions, the catalyst with 34.3 μ mol of catalytic groups (calculated based on ≈ 3 wt% or ≈ 2.14 mmol g⁻¹ of the amine-functionalized material obtained by elemental analysis) was used for the reaction between 0.2 M nitrostyrene and 0.25 M active methylene compounds. The reaction between nitrostyrene and malononitrile was completed within 0.3 h at 0 °C in the presence of the catalyst Ext-SBA-15-NMe₂ (Figure 6), whereas the control experiment without the catalyst showed 80% conversion in 1.5 h at room temperature (Figure S3). The corresponding reactions involving acetylacetone and diethylmalonate as active methylene partners occurred only at a much higher temperature (50 °C), which yield-

Table 1. Catalytic activity of the supported catalyst used in the Michael addition reaction.^[a]

Entry ^[b]	Catalyst ^[c,d]	X ^[e]	T [°C]	t [h]	Conversion ^[f] [%]	TOF [h ⁻¹] ^[g]
1	1	CN	0	0.3	90	17 142
2	2	CN	0	0.3	80	15 238
3	1	COMe	50	3	85	1619
4	2	COMe	50	3	88	1676
5	1	CO ₂ Et	50	12	62	295
6	2 ^[h]	CO ₂ Et	50	–	–	–

[a] Refer to Scheme 2 for the reaction scheme and substituents in the reactants; [b] In each case, 0.2 M *trans*- β -nitrostyrene in CDCl₃ was used; [c] 16 mg of solid catalyst was used; [d] 1 = Ext-SBA-15-NMe₂-Tol and 2 = Cap-SBA-15-NMe₂-Tol (see also Scheme 1); [e] 0.25 M in CDCl₃; [f] Based on the disappearance of olefinic ¹H signal in ¹H NMR; [g] Obtained by using the number of catalytic (amine) groups in moles in the catalyst, which were determined by elemental analysis; [h] Reaction stalled after 4 h with 40% conversion.

Entry ^[b]	Catalyst ^[c,d]	X ^[e]	T [°C]	t [h]	Conversion ^[f] [%]
1	Ext-SBA-15	COMe	50	2	< 2
2	DATS	COMe	50	2	98
3	Ext-SBA-15 + TEA	COMe	50	2	90
4	1	COMe	50	3	85
5	2	COMe	50	3	88

[a] Refer to Scheme 2 for the reaction scheme and substituents in the reactants; [b] In each case, 0.2 M *trans*- β -nitrostyrene in CDCl₃ was used; [c] 16 mg of solid catalyst was used; [d] 1 = Ext-SBA-15-NMe₂-Tol and 2 = Cap-SBA-15-NMe₂-Tol (see also Scheme 1), the millimoles of triethylamine (TEA) and 3-(*N,N*-Dimethylaminopropyl)trimethoxysilane (DATS) were calculated on the basis of the nitrogen content of the catalyst 1; [e] 0.25 M in CDCl₃; [f] Based on the disappearance of olefinic ¹H signal in ¹H NMR.

Entry ^[b]	Catalyst ^[c,d]	Y ^[e]	T [°C]	t [h]	Conversion [%] ^[f]
1	1'	H	50	3	95
2	1'	Cl	50	3	75
3	1'	OMe	50	3	30

[a] Refer to Scheme 2b for the reaction scheme and substituents in the reactants; [b] In each case, 0.25 M acetylacetone in CDCl₃ was used; [c] 16 mg of solid catalyst was used; [d] 1' = Ext-SBA-15-NMe₂-IPA; [e] 0.2 M in CDCl₃; [f] Based on disappearance of olefinic ¹H signal in ¹H NMR.

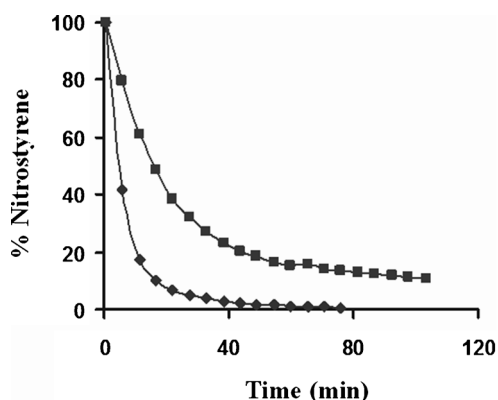


Figure 6. Percent conversion of nitrostyrene versus reaction time in the Michael addition reaction between malononitrile and nitrostyrene catalyzed with Ext-SBA-15-NMe₂-Tol (◆) and Cap-SBA-15-NMe₂-Tol (■).

ed the respective Michael addition products (Figure 7). The trend in reactivity corresponds closely to the pK_a values of the respective substrates and can be explained by the ease of formation of the carbanions from the substrates. The relative acidity of active methylene compounds in DMSO follows the trend: malononitrile (pK_a 11.1) > acetylacetone (pK_a 13.3) > diethylmalonate (pK_a 16.4).^[25] Hence, in the presence of the amine catalyst (base), the compound with lower pK_a showed

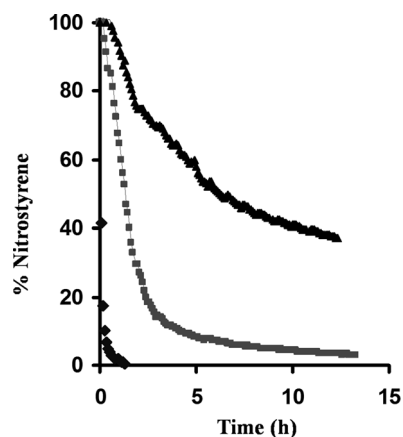


Figure 7. Percent conversion of nitrostyrene versus reaction time of Michael addition reaction between active methylene compounds and nitrostyrene catalyzed with Ext-SBA-15-NMe₂-Tol. Malonitrile (◆), acetylacetone (■), diethylmalonate (▲).

greater propensity to form the carbanion (also the nucleophile). Consequently, the reaction between malononitrile and nitrostyrene showed faster reactivity, followed by acetylacetone and finally diethylmalonate (Table 1).

We further investigated the reaction in more detail with the catalysts Ext-SBA-15-NMe₂-IPA and Cap-SBA-15-NMe₂-IPA, the tertiary amine catalytic groups of which were grafted in a more polar solvent, isopropyl alcohol. This choice of solvent was, however, not completely arbitrary. It was previously shown by our group that grafting aminosilanes on mesoporous silicas in polar solvents results in lesser amount of amine groups, which leaves behind more accessible silanol groups on the material compared with the one obtained using toluene—the more commonly used solvent for organosilane grafting.^[15,26] In the presence of Ext-SBA-15-NMe₂-IPA, the Michael addition between *trans*- β -nitrostyrene and malononitrile at 0 °C showed faster reactivity than its counterpart, which involved the catalyst Ext-SBA-15-NMe₂-Tol (Figure 8a). This diminishing catalytic efficiency in the case of Ext-SBA-15-NMe₂-Tol can be attributed to the fewer silanol (weak acid) sites this material has for dual activation; however, the possibility of aggregation of the catalytic groups or formation of densely populated organoamine groups within the mesopores cannot be ruled out.^[27] On comparing Ext-SBA-15-NMe₂-IPA with Cap-SBA-15-NMe₂-IPA, the latter showed lower catalytic activity, as expected, because of the lesser number of silanol groups present in it to activate nitrostyrene (Figure 8b). These experiments signify the importance of silanol groups, or conversely spatially isolated amine groups, for dual catalysis. This study was extended to other substrate and catalyst combinations. For instance, a comparative study of the catalytic activity of Ext-SBA-15-NMe₂-IPA and Ext-SBA-15-NMe₂-Tol was also performed for the substrate acetylacetone at 50 °C, and a similar trend was observed. The reaction was again faster with Ext-SBA-15-NMe₂-IPA than with Ext-SBA-15-NMe₂-Tol (Figure S4). Finally, the substrate scope was studied with the catalyst Ext-SBA-15-NMe₂-IPA, which also showed the same trend as Ext-SBA-15-NMe₂-Tol (Figure S5).

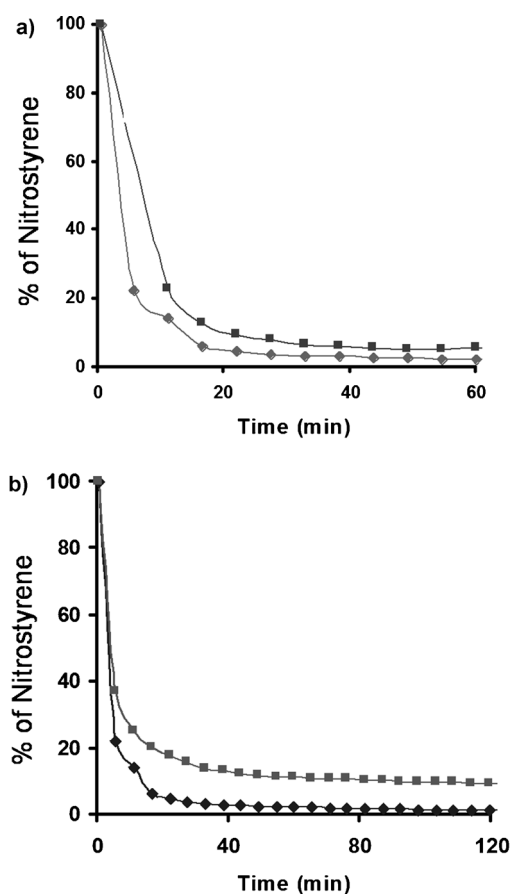


Figure 8. a) Kinetic plot of the Michael addition reaction between nitrostyrene and malononitrile at 0 °C catalyzed by Ext-SBA-15-NMe₂-IPA (◆) and Ext-SBA-15-NMe₂-Tol (■). b) Kinetic plot of the Michael addition reaction between nitrostyrene and malononitrile at 0 °C catalyzed by Ext-SBA-15-NMe₂-IPA (◆) and Cap-SBA-15-NMe₂-IPA (■).

To compare the catalytic activity of the bifunctional catalysts with their corresponding main individual components, we studied the catalytic activity of these different materials in the Michael addition reaction between *trans*- β -nitrostyrene and acetylacetone. Acetylacetone was chosen as an active methylene compound because of its slower reactivity, which also allows us to compare the conversion at a higher temperature with reasonable accuracy compared to malononitrile (which reacts at a faster rate even at a lower temperature). Ext-SBA-15 did not show appreciable conversion at 50 °C in 3 h (Table 2, entry 1), which suggests that the activation of nitrostyrene by the surface silanol group is not enough to drive the reaction forward. The homogeneous DATS reacted at a faster rate compared with either of the grafted catalysts (Table 2, entry 2). Our attempt to use a physical mixture of SBA-15 and DATS as the catalyst showed unexpected lower activity, presumably because at a higher temperature, grafting of aminosilane on SBA-15 competes with the actual catalysis method. To avoid this undesired reaction, Ext-SBA-15 was mixed with TEA (Table 2, entry 3) and the mixture showed catalytic activity comparable to that of its corresponding homogeneous organosilane catalyst (Table 2, entry 2). Although the homogeneous version is still slightly faster than the heterogeneous catalyst, these re-

sults indicate that dual activation by the grafted aminosilane and surface silanol groups is still important for better performance of the heterogeneous catalyst.

With the most active catalyst Ext-SBA-15-NMe₂-IPA (1'), we then investigated the substrate scope with different *para*-substituted nitrostyrenes (Table 3, entry 1). As discussed earlier, the yield of the reaction between nitrostyrene and acetylacetone was very good (95% conversion; see Figure S4) at 50 °C in 3 h. However, upon using substituted nitrostyrenes with the substituents at the *para*-position made the substrate demonstrate different reactivity with acetylacetone because of the change in its electronic properties. For instance, under the same reaction condition, 4-chloro-substituted nitrostyrene reacted at a slower rate compared with its unsubstituted counterpart, which yielded 70% conversion at 50 °C in 3 h (Table 3, entry 2). Although the electron-withdrawing halogen group is expected to increase the electrophilicity of the α carbon of nitrostyrene, the resonance effect (+R) of chlorine seems to be overriding the inductive effect (-I), which ultimately results in the diminished electrophilicity of the α carbon of nitrostyrene. This effect becomes more prominent if more electron-donating –OMe group was substituted at the *para*-position of nitrostyrene because this substrate gave only 30% conversion under the same reaction conditions.

Compared to the previous studies of heterogeneous catalysts for Michael addition reactions, the catalyst reported here is found to be more active. In previous studies using silica-based amino-functionalized catalysts, high temperatures and long reaction times were used to obtain comparable or much lower yields. For example, the Michael addition reaction between nitroalkane and α,β -unsaturated ketone in the presence of an MCM-41-based amine catalyst (with a loading of 50 mg) yielded 96% product at 90 °C in 20 h.^[28] In another study, using a high reaction temperature of 140 °C and reaction time of 8 h, a conversion of 92% was achieved in an intermolecular Michael addition reaction between benzaldehyde and 2'-hydroxyacetophenone catalyzed by an amine-functionalized SBA-type catalyst.^[29] The Michael addition of nitroalkane to α,β -unsaturated ketone, catalyzed by using the *N,N*-dimethyl-3-aminopropyl-derivatized hexagonal mesoporous silica catalyst, gave a yield of 70% in 3 h under reflux conditions.^[30] In our case, all the reactions were performed either at 0 °C or at 50 °C to achieve excellent conversion. For example, with the most reactive substrate malononitrile, Ext-SBA-15-NMe₂ (only 16 mg) catalyzed the reaction to completion at 0 °C in 0.3 h. These comparative results are listed in Table S2.

Recyclability studies using such a small amount of catalyst (16 mg) were challenging under NMR kinetic conditions mainly because of poor recovery of the catalyst at the end of the reaction after each cycle. To overcome these difficulties, a different approach was adopted. For the initial recyclability studies, the reaction between nitrostyrene and acetylacetone using the catalyst Ext-SBA-15-NMe₂-Tol at 50 °C for 2 h was performed on a larger scale (5 times than what was used in the catalytic studies above) on bench-top in parallel to the usual catalytic reaction under NMR condition. The catalyst for the bench-top reaction was isolated by centrifugation. At this moment, we

faced difficulty in removing the pale yellow color of the solid, which seemed to be coming from either the intermediate or final products adsorbed on the surface of the catalyst. At this stage, washing with CDCl_3 , chloroform, dichloromethane, dichloromethane + TEA (to remove the acid species generated during the reaction), ether, and water did not help much. The situation improved a little when we used alcohols, as they could remove most of the yellowish color from the catalyst. After several attempts with different solvents as well as their different combinations, acetone worked best, and after thorough washing with acetone (at least 5 times), the catalyst was dried and used for the next cycle. From this recovered catalyst, 16 mg was used for NMR kinetic studies, in which the reaction was performed under the original catalytic conditions and the rest of the catalyst was utilized for the same reaction but under bench-top reaction conditions. The same washing process was repeated for the subsequent cycles.

The reaction between nitrostyrene and acetylacetone at 50°C showed 70% conversion to the desired Michael product in 2 h. After second, third, and fourth cycles of reactions, the reaction with the recycled catalyst gave 62, 60, and 68% conversion of nitrostyrene, respectively (Figure 9). The TEM image

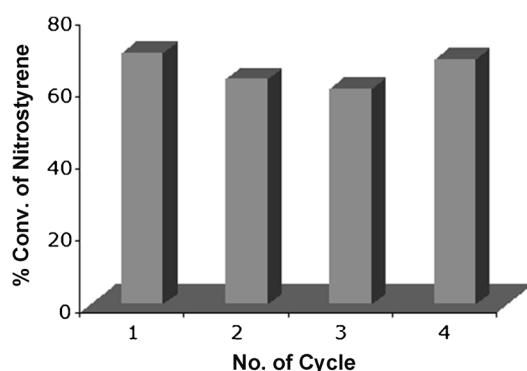


Figure 9. Recyclability results of the Michael addition reaction between nitrostyrene and acetylacetone at 50°C catalyzed by Ext-SBA-15- NMe_2 -Tol (1). Conversions of nitrostyrene were reported after 2 h based on the ^1H NMR integration of each array of experiment.

of the catalyst after the third cycle showed that the mesostructure of the recycled catalyst remained intact (Figure S6). The relatively lower catalytic activity with the recycled catalysts could stem from (1) the presence of catalyst-bound reactants/products (which was difficult even after several acetone wash) and/or (2) the incomplete removal of acid species generated during the reaction, which thereby decreased the active catalytic sites as well as the amount of the total catalyst. Although our recyclability studies did not reproduce the yield and conversion the way we wanted (possibly owing to the reasons stated above), our improved washing process with acetone can offer additional advantages for other heterogeneous catalysts, which often suffer from the complete lack of recyclability. However, during the washing process, the compatibility between acetone (the solvent) and the functional groups on the

catalytic surface has to be addressed very carefully (e.g., for our primary and secondary amine catalysts,^[15,26] acetone cannot be used as a solvent to wash the catalyst because it will react with amine groups and form imine/iminium species, which could be difficult to eliminate). We believe that further systematic investigation is possible to completely remove any undesired species bound on the catalysts effectively without decreasing the catalytic activity, as shown here.

Conclusions

In conclusion, we have described the synthesis of efficient mesoporous nanocatalysts for the Michael addition reaction by postgrafting of organoamine groups onto the surfaces of mesoporous silica. The synthesis of these nanocatalysts was achieved by reacting aminosilanes with mesoporous silica in either toluene or isopropyl alcohol. The catalysts with tertiary amine and enough silanol (weak acid) groups were found to demonstrate cooperative catalytic properties and thereby more efficient catalytic activities than the corresponding materials containing no active silanol groups. Furthermore, the catalysts were investigated with different active methylene compounds as nucleophiles to study the scope of the catalytic reaction and the versatility of the catalysts. The reactions were observed to be the fastest with malononitrile. In addition to their high catalytic activity, the catalysts reported here have many advantages, such as their ease of separation from reaction mixtures and greater shelf life as well good recyclability with insignificant loss of catalytic activity.

Experimental Section

Materials and reagents

Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol) copolymer (Pluronic 123, with an average molecular mass of ≈ 5800) was obtained from BASF. Tetraethylorthosilicate, hexamethyldisilazane (HMDS), malononitrile, acetylacetone, diethylmalonate, *trans*- β -nitrostyrene, triethylamine (TEA), dichloromethane, ethylacetate, hexane, acetone, isopropyl alcohol, and toluene were purchased from Sigma-Aldrich. Hydrochloric acid (36.5%) was obtained from Fischer Scientific. 3-(*N,N*-Dimethylaminopropyl)trimethoxysilane (DATS) was received from Gelest, Inc. Deuterated chloroform (CDCl_3) was obtained from Cambridge Isotope Laboratories.

Instrumentation

Analytical TLC was performed on EM Reagent 0.25 mm silica gel 60 F_{254} plates, which were obtained from VWR. Visualization was accomplished with UV light and freshly prepared KMnO_4 stain. ^1H NMR spectra were recorded on Varian VNMRS 400 MHz and Varian VNMRS 500 MHz instruments, and the spectra were reported and compared with the literature value (in ppm) by using solvent as an internal standard (CDCl_3 at 7.26 ppm). For kinetic studies at different temperatures, the "pad"-macro (pre-acquisition delay) command (built in vnmrj, version 2.1B) was used. The integration data for kinetic studies at different time points were processed by using vnmrj and plotted by using Microsoft Excel. Nitrogen gas adsorption-desorption measurements were performed on Micromer-

itics Tristar 3000 volumetric adsorption analyzer after degassing the samples at 160 °C for 12 h. The powder XRD patterns of the materials were measured by a Histar diffractometer at 295 K by using monochromatized $\text{CuK}\alpha$ radiation. Thermogravimetric analysis (TGA) or decomposition profiles of mesoporous materials were acquired with a Q50 thermogravimetric analyzer. The TGA data were collected under nitrogen atmosphere ($60 \text{ cm}^3 \text{ min}^{-1}$) in the temperature range of 25–700 °C (heating rate: $10 \text{ }^\circ\text{C min}^{-1}$). The solid-state ^{13}C (100.64 MHz) and ^{29}Si (79.51 MHz) NMR spectra were acquired by using a Bruker 400 MHz solid-state NMR spectrometer containing a 3.2 mm bore HXY Bruker probe operating in the HX mode at 298 K. For ^{13}C CP-MAS NMR experiments, 10.0 kHz spin rate, 3 s recycle delay, 2 ms contact time, $\pi/2$ pulse width of 5 μs (at 66 W), and at least 16 K scans using the SPINAL-64 ^1H decoupling method were used. For the ^{29}Si NMR experiments, 10.0 kHz spin rate, 10 s recycle delay, 5 ms contact time, $\pi/2$ pulse width of 5 μs (at 25.5 W), and at least 16 K scans using the SPINAL-64 ^1H decoupling method were used. The ^{13}C and ^{29}Si chemical shifts were referenced by using adamantane and standard silica sample, respectively, as external standards. The spectra were processed in Bruker's TopSpin (version 3.1) by using conventional techniques, and a 50 Hz of line broadening window function was applied to all the spectra. For future convenience, details of representative "acquisition" parameters have been included in the Supporting Information.

Synthesis of SBA-15 mesoporous silica material

SBA-15 was synthesized by using the templating agent Pluronic 123 in an acid solution, as reported previously by Zhao et al.^[16d] Typically, a solution of Pluronic 123/2 M HCl/tetraethylorthosilicate/ H_2O (2:12:4.3:26, mass ratio in grams) was prepared and stirred at 40 °C for 24 h. The solution was then aged at 65 °C for another 24 h. The resulting solution was filtered, and the solid material was washed with a large amount of water, which produced a material labeled as "as-synthesized mesostructured SBA-15". The as-synthesized mesostructured SBA-15 (4 g) was then dispersed in ethanol (400 mL) and diethyl ether (400 mL) and stirred at 50 °C for 5 h to remove the surfactant. After filtration and washing with ethanol, the final solid material was dried in oven, which gave SBA-15 mesoporous silica.

Synthesis of tertiary amine-functionalized SBA-15 mesoporous silica

The dried mesoporous SBA-15 sample (500 mg) was stirred with excess DATS (3.68 mmol, 1.5 mL) in anhydrous toluene (Tol; 250 mL) or anhydrous isopropyl alcohol (IPA) at 80 °C for 6 h. The solution was filtered, and the residue was washed with toluene (3 \times 20 mL) or isopropyl alcohol and then ethanol and finally air dried. The resulting dried samples, which contained tertiary amine catalytic groups and residual silanol groups in them, were labeled as Ext-SBA-15-NMe₂-Tol (**1**) and Ext-SBA-15-NMe₂-IPA (**1'**), respectively. Notably, the relative ratios of the two groups in the two materials were, however, different (i.e., the sample grafted in isopropyl alcohol will have more surface silanols than the one grafted in toluene^[15]; see the Discussion section for details).

Capping the silanol groups of tertiary amine-functionalized SBA-15 mesoporous silica

To prepare a control sample containing the tertiary amine catalytic groups but no active residual silanol groups in it, either Ext-SBA-15-NMe₂-Tol or Ext-SBA-15-NMe₂-IPA (200 mg) was suspended in toluene (11.5 mL) and HMDS (1.5 mL); the solution was then stirred at RT for 6 h to functionalize the external Si–OH groups of Ext-SBA-15-NMe₂ with –SiMe₃ groups. The solid samples were recovered by filtration, washed with toluene and ethanol, and finally air dried. The resulting samples, the accessible silanol groups of which were capped with methyl groups, were labeled as Cap-SBA-15-NMe₂-Tol (**2**) and Cap-SBA-15-NMe₂-IPA (**2'**), respectively.

Michael addition reaction

The Michael addition reaction was performed in both reaction flasks and NMR tubes. The latter allowed us to monitor the reaction progress and to reliably quantify the percentage conversion of the reaction directly in real time at different temperatures by using NMR spectroscopy. In a typical Michael addition experiment, an NMR tube was charged with either Ext-SBA-15-NMe₂ or Cap-SBA-15-NMe₂ (16 mg) and dried at 80 °C for 30 min. The NMR spectrometer was then set up at the desired temperature. Freshly prepared stock solution (in CDCl_3) of *trans*- β -nitrostyrene (1 equiv, 0.2 M in the NMR tube) and the corresponding active methylene compound (1.25 equiv, 0.25 M in the NMR tube) in CDCl_3 (total volume of 0.6 mL) were added to the NMR tube, capped (sealed with parafilm), and shaken well. For an experiment at 0 °C, this addition was performed in an ice bath and transferred quickly to the spectrometer. The tube was inserted into the spectrometer, and the reaction was monitored by following the disappearance of olefinic proton peaks of the starting materials in ^1H NMR.

Acknowledgements

T.A. gratefully acknowledges the financial assistance provided by the US National Science Foundation (grant numbers CAREER CHE-1004218 and NSF DMR-0968937), the NSF-American Competitiveness and Innovation Fellowships (NSF-ACIF), and the NSF Creativity Award. We thank Dr. Thomas J. Emge for powder XRD analysis.

Keywords: acid–base catalyst • bifunctional nanocatalyst • heterogeneous catalysis • mesoporous materials • Michael addition

- [1] a) A. Michael, *J. Prakt. Chem.* **1887**, 35, 349–356; b) A. Michael, *J. Prakt. Chem.* **1894**, 49, 20–29.
- [2] a) A. Alexakis, *Asymmetric Organocopper Chemistry: Cu-Catalyzed Conjugate Addition and Allylic Substitution* (Ch. 4), in *Methodologies in Asymmetric Catalysis*, (Ed.: S. V. Malhotra), American Chemical Society, Washington D.C., **2004**, pp. 43–59; b) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pàmies, M. Diéguez, *Chem. Rev.* **2008**, 108, 2796–2823; c) D. A. Evans, D. S. Johnson, *Org. Lett.* **1999**, 1, 595–598; d) D. A. Evans, T. Rovis, J. S. Johnson, *Pure Appl. Chem.* **1999**, 71, 1407–1415; e) D. A. Evans, T. Rovis, M. C. Kozłowski, J. S. Tedrow, *J. Am. Chem. Soc.* **1999**, 121, 1994–1995; f) D. A. Evans, M. C. Willis, J. N. Johnston, *Org. Lett.* **1999**, 1, 865–868; g) D. A. Evans, T. Rovis, M. C. Kozłowski, C. W. Downey, J. S. Tedrow, *J. Am. Chem. Soc.* **2000**, 122, 9134–9142; h) J. S. Johnson, D. A. Evans, *Acc. Chem. Res.* **2000**, 33, 325–335; i) D. A. Evans, K. A. Scheidt, J. N. Johnston, M. C. Willis, *J. Am. Chem. Soc.* **2001**, 123, 4480–4491.

- [3] For selected examples of organocatalyzed Michael reaction: a) J. M. Beancort, C. F. Barbas, III, *Org. Lett.* **2001**, *3*, 3737–3740; b) T. Bui, S. Syed, C. F. Barbas, III, *J. Am. Chem. Soc.* **2009**, *131*, 8758–8759; c) B. List, R. A. Lerner, C. F. Barbas, III, *J. Am. Chem. Soc.* **2000**, *122*, 2395–2396; d) D. B. Ramachary, N. S. Chowdari, C. F. Barbas, III, *Angew. Chem.* **2003**, *115*, 4365–4369; *Angew. Chem. Int. Ed.* **2003**, *42*, 4233–4237; e) K. Sakthivel, W. Notz, T. Bui, C. F. Barbas, III, *J. Am. Chem. Soc.* **2001**, *123*, 5260–5267; f) K. L. Jensen, G. Dickmeiss, H. Jiang, Ł. Albrecht, K. A. Jørgensen, *Acc. Chem. Res.* **2012**, *45*, 248–264; g) K. L. Jensen, P. H. Poulsen, B. S. Donslund, F. Morana, K. A. Jørgensen, *Org. Lett.* **2012**, *14*, 1516–1519.
- [4] Recent reviews on organocatalysis: a) D. W. C. MacMillan, *Nature* **2008**, *455*, 304–308; b) D. Enders, C. Grondal, M. R. M. Huttel, *Angew. Chem.* **2007**, *119*, 1590–1601; *Angew. Chem. Int. Ed.* **2007**, *46*, 1570–1581; c) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471–5569; d) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis: from Biomimetic Concepts to Applications in Asymmetric Synthesis*, Wiley-VCH, **2005**.
- [5] S. R. Harutyunyan, T. den Hartog, K. Geurts, A. J. Minnaard, B. L. Feringa, *Chem. Rev.* **2008**, *108*, 2824–2852.
- [6] Selective references in which asymmetric Michael additions were used to make natural products: a) B. Långström, G. Bergson, *Acta Chem. Scand.* **1973**, *27*, 3118–3119; b) W. Oppolzer, R. Pitteloud, G. Bernardinelli, K. Baettig, *Tetrahedron Lett.* **1983**, *24*, 4975–4978; c) D. F. Taber, J. F. Mack, A. L. Rheingold, S. J. Geib, *J. Org. Chem.* **1989**, *54*, 3831–3836; d) T. Arai, H. Sasai, K. Yamaguchi, M. Shibasaki, *J. Am. Chem. Soc.* **1998**, *120*, 441–442; e) B. M. Trost, E. Murayama, *J. Am. Chem. Soc.* **1981**, *103*, 6529–6530; f) M. Shibasaki, H. Sasai, Y. Arai, *Angew. Chem.* **1997**, *109*, 1290–1311; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1236–1256; g) E. J. Corey, F.-Y. Zhang, *Org. Lett.* **2000**, *2*, 1097–1100; h) F. Z. Peng, Z. H. Shao, B. M. Fan, H. Song, G. P. Li, H. B. Zhang, *J. Org. Chem.* **2008**, *73*, 5202–5205.
- [7] a) Y. Huang, A. K. Unni, A. N. Thadani, V. H. Rawal, *Nature* **2003**, *424*, 146–146; b) J. P. Malerich, K. Hagihara, V. H. Rawal, *J. Am. Chem. Soc.* **2008**, *130*, 14416–14417 (See also Supporting Information for control experiments); c) J. D. McGilvra, V. B. Gondi, V. H. Rawal, P. I. Dalko in *Enantioselective Organocatalysis* (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2007**, pp. 189–254; d) A. N. Thadani, A. R. Stankovic, V. H. Rawal, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5846–5850.
- [8] a) Y. Hoashi, T. Okino, Y. Takemoto, *Angew. Chem.* **2005**, *117*, 4100–4103; *Angew. Chem. Int. Ed.* **2005**, *44*, 4032–4035; b) T. Okino, Y. Hoashi, T. Furukawa, X. Xu, Y. Takemoto, *J. Am. Chem. Soc.* **2005**, *127*, 119–125; c) T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* **2003**, *125*, 12672–12673; d) Y. Yamaoka, H. Miyama, Y. J. Takemoto, *J. Am. Chem. Soc.* **2007**, *129*, 6686–6687.
- [9] a) A. G. Doyle, E. N. Jacobsen, *Chem. Rev.* **2007**, *107*, 5713–5743; b) H. Huang, E. N. Jacobsen, *J. Am. Chem. Soc.* **2006**, *128*, 7170–7171; c) I. T. Raheem, P. S. Thiara, E. A. Peterson, E. N. Jacobsen, *J. Am. Chem. Soc.* **2007**, *129*, 13404–13405; d) M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 4901–4902.
- [10] a) J. F. Austin, S. G. Kim, C. J. Sinz, W. J. Xiao, D. W. C. MacMillan, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5482–5487; b) S. P. Brown, N. C. Goodwin, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2003**, *125*, 1192–1194; c) C. J. Borths, D. E. Carrera, D. W. C. MacMillan, *Tetrahedron* **2009**, *65*, 6746–6753.
- [11] a) Z. Wang, G. Yin, J. Qin, M. Gao, L. Cao, A. Wu, *Synthesis* **2008**, 3565–3568; b) J. Zhou, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 7498–7499; c) Y. Chi, S. H. Gellman, *Org. Lett.* **2005**, *7*, 4253–4256; d) T. Ooi, D. Ohara, K. Fukumoto, K. Maruoka, *Org. Lett.* **2005**, *7*, 3195–3197; e) T. Okino, Y. Hoashi, T. Fukukawa, X. Xu, Y. Takemoto, *J. Am. Chem. Soc.* **2005**, *127*, 119–125; f) T. Hara, S. Kanai, K. Mori, T. Mizugaki, K. Ebitani, K. Jitsukawa, K. Kaneda, *J. Org. Chem.* **2006**, *71*, 7455–7462; g) S. Fioravanti, L. Pellacani, P. A. Tardella, M. C. Vergari, *Org. Lett.* **2008**, *10*, 1449–1451; h) K. Ebitani, K. Motokura, K. Mori, T. Mizugaki, K. Kaneda, *J. Org. Chem.* **2006**, *71*, 5440–5447; i) B. C. Ranu, R. Jana, *Eur. J. Org. Chem.* **2006**, 3767–3770; j) H. Li, B. Wang, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 732–733; k) T. Arai, M. Watanabe, A. Yanagisawa, *Org. Lett.* **2007**, *9*, 3595–3597; l) D. A. Evans, D. Seidel, M. Rueping, H. W. Lam, J. T. Shaw, C. W. Downey, *J. Am. Chem. Soc.* **2003**, *125*, 12692–12693; m) O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877–1894; n) A. K. Beck, D. Seebach, *Chem. Ber.* **1991**, *124*, 2897–2911.
- [12] a) N. T. Tran, S. O. Wilson, A. K. Franz, *Org. Lett.* **2012**, *14*, 186–189; b) N. T. Tran, T. Min, A. K. Franz, *Chem. Eur. J.* **2011**, *17*, 9897–9900; c) M. Liu, N. T. Tran, A. K. Franz, J. K. Lee, *J. Org. Chem.* **2011**, *76*, 7186–7194.
- [13] A. G. Schafer, J. M. Wieting, A. E. Mattson, *Org. Lett.* **2011**, *13*, 5228–5231.
- [14] T. Min, J. C. Fetting, A. K. Franz, *ACS Catal.* **2012**, *2*, 1661–1666.
- [15] a) K. K. Sharma, T. Asefa, *Angew. Chem.* **2007**, *119*, 2937–2940; *Angew. Chem. Int. Ed.* **2007**, *46*, 2879–2882; b) K. K. Sharma, A. Anan, R. P. Buckley, W. Quellet, T. Asefa, *J. Am. Chem. Soc.* **2008**, *130*, 218–228; c) A. Anan, K. K. Sharma, T. Asefa, *J. Mol. Catal. A* **2008**, *288*, 1–13.
- [16] a) C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli, J. S. Beck, *Nature* **1992**, *359*, 710–712; b) J. S. Beck, J. C. Vartuli, W. J. Roth, M. E. Leonowicz, C. T. Kresge, K. D. Schmitt, C. T.-W. Chu, D. H. Olson, E. W. Sheppard, S. B. McCullen, J. B. Higgins, J. L. Schlenker, *J. Am. Chem. Soc.* **1992**, *114*, 10834–10843; c) Q. S. Huo, D. I. Margolese, G. D. Stucky, *Chem. Mater.* **1996**, *8*, 1147–1160; d) Y. Zhao, J. L. Feng, Q. S. Huo, N. Melosh, G. H. Fredrickson, B. F. Chmelka, G. D. Stucky, *Science* **1998**, *279*, 548–552.
- [17] E. L. Margelefsky, R. K. Zeidan, M. E. Davis, *Chem. Soc. Rev.* **2008**, *37*, 1118–1126.
- [18] a) H. Hagiwara, S. Inotsume, M. Fukushima, T. Hoshi, T. Suzuki, *Chem. Lett.* **2006**, *35*, 926–927; b) S. Angloher, J. Kecht, T. Bein, *Microporous Mesoporous Mater.* **2008**, *115*, 629–633; c) R. Ballini, D. Fiorini, M. V. Gil, A. Palmieri, *Green Chem.* **2003**, *5*, 475–476; d) S. Luo, J. Li, L. Zhang, H. Xu, J.-P. Cheng, *Chem. Eur. J.* **2008**, *14*, 1273–1281; e) B. Das, K. Damodar, N. Chowdhury, *J. Mol. Catal. A* **2007**, *269*, 81–84.
- [19] O. H. Han, Y. K. Bae, *Bull. Korean Chem. Soc.* **2008**, *29*, 911–912.
- [20] Y. Xie, S. Quinlivan, T. Asefa, *J. Phys. Chem. C* **2008**, *112*, 9996–10003.
- [21] T. I. Suratwala, M. L. Hanna, E. L. Miller, P. K. Whitman, I. M. Thomas, P. R. Ehrmann, R. S. Maxwell, A. K. Burnham, *J. Non-Cryst. Solids* **2003**, *316*, 349–363.
- [22] A. Hamza, G. Schubert, T. Soós, I. Pápai, *J. Am. Chem. Soc.* **2006**, *128*, 13151–13160.
- [23] J. Luo, L.-W. Xu, R. A. S. Hay, Y. Lu, *Org. Lett.* **2009**, *11*, 437–440.
- [24] Selected examples of organocatalysis in which NMR were used as a tool to obtain kinetic information: a) F. López-Calahorra, R. Rubires, *Tetrahedron* **1995**, *51*, 9713–9728; b) F. Liu, X. Bugant, M. Schedler, R. Fröhlich, F. Glorius, *Angew. Chem.* **2011**, *123*, 12834–12839; *Angew. Chem. Int. Ed.* **2011**, *50*, 12626–12630; c) A. P. Dove, R. C. Pratt, B. G. G. Lohmeijer, R. M. Waymouth, J. L. Hedrick, *J. Am. Chem. Soc.* **2005**, *127*, 13798–13799; d) S. E. Denmark, B. M. Eklov, P. J. Yao, M. D. Eastgate, *J. Am. Chem. Soc.* **2009**, *131*, 11770–11787; e) G. Evans, T. J. K. Gibbs, R. L. Jenkins, S. J. Coles, Hursthouse, M. B. Platts, A. James, N. C. O. Tomkinson, *Angew. Chem.* **2008**, *120*, 2862–2865; *Angew. Chem. Int. Ed.* **2008**, *47*, 2820–2823.
- [25] a) W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum, N. R. Vanier, *J. Am. Chem. Soc.* **1975**, *97*, 7006–7014; b) W. N. Olmstead, F. G. Bordwell, *J. Org. Chem.* **1980**, *45*, 3299–3305.
- [26] Y. Xie, K. K. Sharma, A. Anan, G. Wang, A. V. Biradar, T. Asefa, *J. Catal.* **2009**, *265*, 131–140.
- [27] M. W. McKittrick, C. W. Jones, *J. Am. Chem. Soc.* **2004**, *126*, 3052–3053.
- [28] D. J. Macquarrie, R. Maggi, A. Mazzacani, G. Sartori, R. Sartorio, *Appl. Catal. A* **2003**, *246*, 183–188.
- [29] X. Wang, K. S. K. Lin, J. C. C. Chan, S. Cheng, *J. Phys. Chem. B* **2005**, *109*, 1763–1769.
- [30] J. E. G. Mdoe, J. H. Clark, D. J. Macquarrie, *Synlett* **1998**, 625–627.

Received: August 11, 2012

Revised: October 15, 2012

Published online on January 29, 2013