

## Dialkylaminopyridine-Functionalized Mesoporous Silica Nanosphere as an Efficient and Highly Stable Heterogeneous Nucleophilic Catalyst

Hung-Ting Chen,<sup>†,‡</sup> Seong Huh,<sup>†,‡</sup> Jerzy W. Wiench,<sup>‡</sup> Marek Pruski,<sup>‡</sup> and Victor S.-Y. Lin<sup>\*,†,‡</sup>

Contribution from the Department of Chemistry and United States Department of Energy Ames Laboratory, Iowa State University, Ames, Iowa 50011-3111

Received April 16, 2005; E-mail: vsylin@iastate.edu.

**Abstract:** A new nucleophilic catalytic system comprised of dialkylaminopyridine-functionalized mesoporous silica nanosphere (DMAP-MSN) has been synthesized and characterized. We have demonstrated that this material is an efficient heterogeneous catalyst for Baylis-Hillman, acylation, and silylation reactions with good reactivity, product selectivity, and recyclability. We envision that this DMAP-functionalized mesoporous silica material can also serve as an effective heterogeneous catalyst for many other catalytic nucleophilic reactions.

### 1. Introduction

Due to its high nucleophilicity, 4-(dimethylamino)pyridine (DMAP) has been widely utilized as an efficient catalyst for many important reactions,<sup>1–5</sup> such as acylation, silylation, tritylation, ester rearrangement, polymerization, Darkin-West reaction, and Baylis-Hillman reaction. Several approaches for immobilization of this remarkable homogeneous catalyst on various organic and inorganic solid supports, such as polymers<sup>6–16</sup> and sol–gel silica-based materials,<sup>17,18</sup> have been reported in the literature. However, the catalytic reactivities of most of these systems have been shown to be lower than that of the DMAP molecule in homogeneous solution reactions. The decrease in

catalytic reactivity has been attributed to the difficulty of controlling the degree of functionalization and the complication due to the mass transport of reactants and products in-and-out of the catalytic sites within the solid matrices. For example, the catalytic reactivity of DMAP-functionalized polymers has been shown to be solvent dependent due to the swelling and contraction of the polymer matrices in different solvent environments.<sup>19</sup>

The MCM- and SBA-type silicas, with their regular structural characteristics, high surface areas and tunable pore diameters, represent a promising support for DMAP immobilization. However, to the best of our knowledge, successful functionalization of DMAP on mesoporous silica surfaces has not yet been reported. This can be attributed to the undesired protonation of the pyridyl group of various trialkoxysilyl-derivatized dialkylamino pyridines by the surface silanol group during the conventional postsynthesis grafting reaction.

Recently, we have developed a co-condensation-based synthetic method that provides control of the degree of organic functionalization and particle morphology.<sup>20,21</sup> By utilizing this method, we report herein the synthesis, characterization, and catalytic reactivity study of a 4-(dialkylamino)pyridine-functionalized mesoporous silica nanosphere (DMAP-MSN) material. Our synthetic approach allows us to circumvent the undesired protonation of DMAP and produce a heterogeneous catalyst for Baylis-Hillman, acylation, and silylation reactions with superb reactivity, product selectivity, and recyclability.

### 2. Experimental Section

All reagents were purchased from commercial sources and used as received without further purification. Benzene was dried by calcium

<sup>†</sup> Department of Chemistry.

<sup>‡</sup> Ames Laboratory.

- (1) Hoeffle, G.; Steglich, W.; Vorbrueggen, H. *Angew. Chem.* **1978**, *90*, 602–615.
- (2) Heinrich, M. R.; Klisa, H. S.; Mayr, H.; Steglich, W.; Zipse, H. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 4826–4828.
- (3) Scriven, E. F. V. *Chem. Soc. Rev.* **1983**, *12*, 129–161.
- (4) Spivey, A. C.; Arseniyadis, S. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 5436–5441.
- (5) Murugan, R.; Scriven, E. F. V. *Aldrichim. Acta* **2003**, *36*, 21–27.
- (6) Hierl, M. A.; Gamson, E. P.; Klotz, I. M. *J. Am. Chem. Soc.* **1979**, *101*, 6020–6022.
- (7) Delaney, E. J.; Wood, L. E.; Klotz, I. M. *J. Am. Chem. Soc.* **1982**, *104*, 799–807.
- (8) Shinkai, S.; Tsuji, H.; Hara, Y.; Manabe, O. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 631–632.
- (9) Tomoi, M.; Akada, Y.; Kakiuchi, H. *Makromol. Chem., Rapid Commun.* **1982**, *3*, 537–542.
- (10) Menger, F. M.; McCann, D. J. *J. Org. Chem.* **1985**, *50*, 3928–3930.
- (11) Deratani, A.; Darling, G. D.; Frechet, J. M. J. *Polymer* **1987**, *28*, 825–830.
- (12) Deratani, A.; Darling, G. D.; Horak, D.; Frechet, J. M. J. *Macromolecules* **1987**, *20*, 767–772.
- (13) Guendouz, F.; Jacquier, R.; Verducci, J. *Tetrahedron* **1988**, *44*, 7095–7108.
- (14) Bergbreiter, D. E.; Li, C. *Org. Lett.* **2003**, *5*, 2445–2447.
- (15) Bergbreiter, D. E.; Osburn, P. L.; Li, C. *Org. Lett.* **2002**, *4*, 737–740.
- (16) Corra, A.; Garcia, H.; Leyva, A. *Chem. Commun.* **2003**, 2806–2807.
- (17) Rubinsztajn, S.; Zeldin, M.; Fife, W. K. *Macromolecules* **1990**, *23*, 4026–4027.
- (18) Rubinsztajn, S.; Zeldin, M.; Fife, W. K. *Macromolecules* **1991**, *24*, 2682–2688.

- (19) Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, *103*, 3401–3429.
- (20) Huh, S.; Wiench, J. W.; Trewyn, B. G.; Song, S.; Pruski, M.; Lin, V. S. Y. *Chem. Commun.* **2003**, 2364–2365.
- (21) Huh, S.; Wiench, J. W.; Yoo, J.-C.; Pruski, M.; Lin, V. S. Y. *Chem. Mater.* **2003**, *15*, 4247–4256.

hydride and used after distillation. Dichloromethane was dried by aluminum oxide column. All catalytic reactions were performed in a screw-capped vial.

**Preparation of 4-[N-[3-(Triethoxysilyl)propyl]-N-methyl-amino]-pyridine (DMAP-TES).** A solution of 4-(N-methylamino)pyridine (5.0 g, 46.2 mmol) in 70 mL of dry tetrahydrofuran (THF) was added dropwise to a suspension of sodium hydride (1.77 g, 73.9 mmol) in 30 mL of dry THF under N<sub>2</sub> atmosphere at 0 °C ice bath. The solution was stirred for additional 2 h at room temperature. A solution of chloropropyltriethoxysilane (11.1 mL, 46.2 mmol) in 10 mL of dry THF was introduced to the mixture at 0 °C ice bath via injection. After injection, the solution was stirred further for 15 h at 70 °C. The solution was filtered, evaporated in vacuo, and chromatographed on silica gel with eluent (MeOH/CHCl<sub>3</sub> = 1/9 with 5% NEt<sub>3</sub>), to give pure DMAP-TES as a liquid (8.85 g, yield = 61.3%). The <sup>1</sup>H and <sup>13</sup>C NMR spectra of the product were found identical with reported data.<sup>17,18</sup>

**Synthesis of Dialkylaminopyridine-Functionalized Mesoporous Silica Nanosphere Catalyst (DMAP-MSN).** The mixture of cetyltrimethylammonium bromide surfactant (CH<sub>3</sub>(CH<sub>2</sub>)<sub>15</sub>N(CH<sub>3</sub>)<sub>3</sub>Br, referred to as CTAB) (2.0 g, 5.49 mmol), 2.0 M of NaOH (aq) (7.0 mL, 14.0 mmol) and H<sub>2</sub>O (480 g, 26.67 mol) was heated to 80 °C for 30 min. To this clear solution, tetraethoxysilane (9.34 g, 44.8 mmol), DMAP-TES (1.80 mL, 5.74 mmol) was added sequentially and rapidly via injection. White solids were observed within 85 s upon mixing of the initial opaque emulsion. The reaction was stirred vigorously at 80 °C for 2 h followed by a hot filtration of the solution to yield the crude DMAP-MSN product (white solid). The as-made material was washed with copious amount of water and methanol and then dried under vacuum. An acid extraction was performed with a methanolic solution (100 mL) of concentrated hydrochloric acid (0.6 mL) and the as-made DMAP-MSN material (1.0 g) at 60 °C for 3 h. The resulting surfactant-removed DMAP-MSN was filtered, washed with water and methanol, and dried under vacuum. The neutralization was conducted in saturated sodium carbonate methanol solution (100 mL) of extracted DMAP-MSN (1.0 g) at room temperature for 3 h. The neutralized DMAP-MSN material was isolated by filtration, washed by water and methanol, and dried under vacuum.

**NMR Spectroscopy.** The <sup>1</sup>H and <sup>13</sup>C NMR spectra of products in solution were acquired on a Varian VRX 300 spectrometer. Solid-state <sup>13</sup>C and <sup>29</sup>Si NMR on DMAP-MSN utilized a Chemagnetics Infinity 400 MHz spectrometer equipped with 5 mm (Chemagnetics) and 1.8 mm (A. Samoson<sup>22</sup>) double tuned probes capable of MAS at 10 and 40 kHz, respectively. The fast MAS probe was used to carry out the two-dimensional (2D) heteronuclear <sup>1</sup>H–<sup>13</sup>C correlation (HETCOR) experiment, where a spinning rate of 40 kHz provided sufficient homonuclear <sup>1</sup>H–<sup>1</sup>H decoupling during proton evolution without any additional RF irradiation in the <sup>1</sup>H channel, as previously described.<sup>23</sup> In addition, a single  $\pi$  pulse at the <sup>13</sup>C spin frequency was introduced in the middle of the <sup>1</sup>H evolution period to refocus the J<sub>C–H</sub> coupling. One of the additional advantages of using the fast MAS is that low power decoupling could be efficiently used during the acquisition of <sup>13</sup>C signal.<sup>23,24</sup> Other experimental details are given in section 3 and in the figure captions, where  $\nu_R$  is the MAS rate and  $\nu_{RF}^X$  denotes the magnitude of radio frequency field applied to X nuclei (X = <sup>1</sup>H and <sup>13</sup>C). The <sup>1</sup>H, <sup>13</sup>C, and <sup>29</sup>Si chemical shifts are referenced to TMS at 0 ppm.

**General Procedure for DMAP-MSN-Catalyzed Baylis–Hillman Reactions.** An enone of choice (0.5 mmol), aldehyde of choice (0.25 mmol), and DMAP-MSN (50 mg, 30 mol%) were added to a mixture solution of tetrahydrofuran and water (2 mL, volume ratio = 3/1) in a

screw-capped vial at 50 °C for 24 h. After the reaction, the crude reaction mixture was filtered and washed by copious amount of acetone. The filtrate was concentrated under vacuum. The corresponding products were isolated by column chromatography with ethyl acetate/hexane as eluent.

**General Procedure for DMAP-MSN-Catalyzed Acylation Reactions.** The mixture of DMAP-MSN (50 mg, 7.5 mol%), an alcohol of choice (1 mmol), triethylamine (1.5 mmol), and dry benzene (2 mL) were charged to a screw-capped vial and heated to 60 °C for 20 min. Acetic anhydride (2 mmol) was added to the solution mixture via injection. After 2.5 to 24 h, the crude reaction mixture was filtered on a glass frit, and the catalyst was thoroughly washed with copious amount of chloroform. The resulting filtrate was evaporated under vacuum. The corresponding acetates were obtained by column chromatography with ethyl acetate/hexane as eluent.

**General Procedure for DMAP-MSN-Catalyzed Silylation Reactions.** An alcohol of choice (0.5 mmol), *tert*-butyldimethylsilyl chloride (0.55 mmol), DMAP-MSN (20 mg, 6 mol %), and triethylamine (0.55 mmol) were added to a dichloromethane solution (2 mL) in a screw-capped vial. The solution mixture was stirred at room temperature for 24 h. After the reaction, the reaction mixture was filtered and washed by copious amount of chloroform. The filtrate was concentrated under vacuum. The corresponding silyl ether products were isolated by column chromatography with ethyl acetate/hexane as eluent.

### 3. Results and Discussion

**Synthesis and Characterization of DMAP-MSN Catalyst.** We first synthesized an organosilane, 4-[N-[3-(triethoxysilyl)-propyl]-N-methyl-amino]pyridine (DMAP-TES), via a procedure described in the Experimental Section (Scheme 1). To prepare the DMAP-functionalized mesoporous silica nanosphere (DMAP-MSN) material, DMAP-TES and tetraethoxysilane (TEOS) were introduced to a sodium hydroxide aqueous solution with low concentration of cetyltrimethylammonium bromide (CTAB) under a reaction condition that we have reported previously.<sup>20,21</sup> After an acid extraction of the CTAB surfactant from the as-made material, the DMAP-MSN material was neutralized by submerging in a saturated sodium carbonate methanolic solution at room temperature for 3 h. The resulting solid was isolated by filtration, washed by water and methanol, and dried under vacuum.

The XRD measurement of DMAP-MSN showed a large (100) peak and a weak broad peak representing a higher-order diffraction (Figure 1a). The observed *d*<sub>100</sub> value was 32.2 Å. The observed low-intensity broad peak (2 $\theta$ ) at ~4.5° could be attributed to the overlapping (110) and (200) diffraction peaks, typical of a disordered pore structure as we investigated and reported previously.<sup>21</sup> The TEM micrograph of the material also confirmed its disordered pore structure (Figure 1b). The DMAP-MSN material exhibited a spherical particle shape with an average particle diameter of 400 nm as depicted in the SEM micrograph (Figure 1c). The N<sub>2</sub> surface sorption analysis of this mono-functionalized MSN exhibited a typical type IV isotherm without any significant hysteresis. The measured BET surface area of DMAP-MSN is 835 m<sup>2</sup>/g and the BJH average pore diameter is around 20 Å.

**Solid-State NMR Studies of DMAP-MSN Catalyst.** The structure of the organic functionality was detailed by comparing the <sup>13</sup>C liquid spectrum of DMAP-TES (Figure 2a) with the <sup>13</sup>C MAS spectrum of DMAP-MSN (Figure 2b) acquired using ramped-amplitude cross polarization (CP)<sup>25</sup> and with the <sup>1</sup>H–

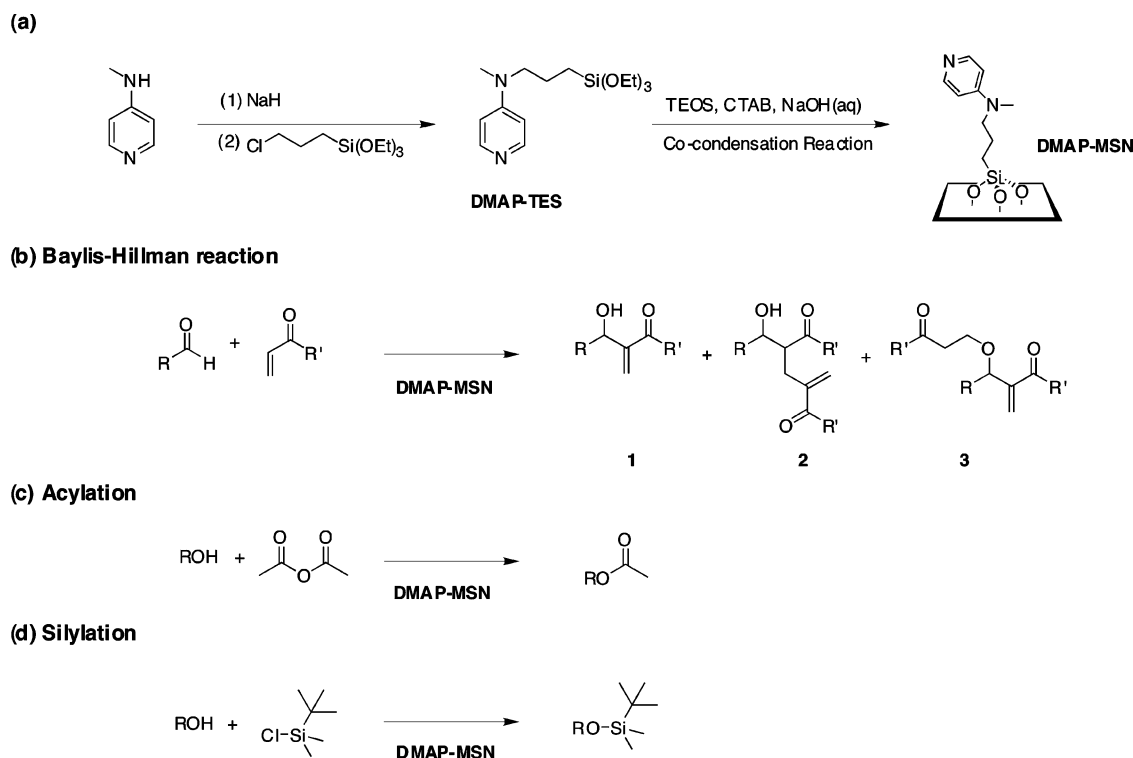
(22) Samoson, A. In *Encyclopedia of Nuclear Magnetic Resonance*; Grant, D. M., Harris, R. K., Ed.; John Wiley & Sons: Chichester, 2002; Vol. 9, pp 59–64.

(23) Trebosc, J.; Wiench, J. W.; Huh, S.; Lin, V. S. Y.; Pruski, M. *J. Am. Chem. Soc.* **2005**, *127*, 3057–3068.

(24) Ernst, M.; Samoson, A.; Meier, B. H. *Chem. Phys. Lett.* **2001**, *348*, 293–302.

(25) Metz, G.; Wu, X.; Smith, S. O. *J. Magn. Reson. Series A* **1994**, *110*, 219–227.

Scheme 1



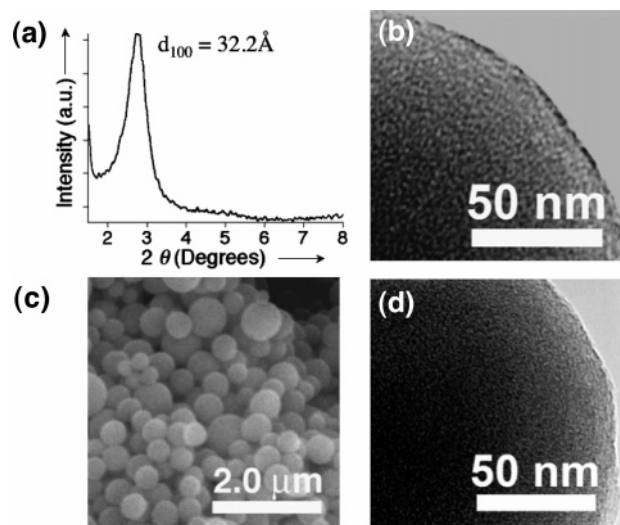
$^{13}\text{C}$  HETCOR spectrum of the same sample (Figure 3). The assignments of  $^{13}\text{C}$  resonances in solution DMAP-TES were based on the observed chemical shifts (see Table 1). The shifts obtained in solid-state NMR spectra of DMAP-MSN, which are also listed in Table 1, match well with the solution data, and thus confirm the presence of a DMAP ligand on the silica surface. The additional peak observed at around 48 ppm in Figure 2b most likely represents the methanol molecules adsorbed on the surface during the synthesis. The changes in peak intensities between solution and solid-state spectra reflect the differences in CP dynamics for individual carbon sites.

The concentration of functional groups in DMAP-MSN was measured from the relative intensities of  $T^n$  and  $Q^n$  silicon groups

observed by  $^{29}\text{Si}$  MAS NMR under direct polarization (DP), (Figure 2c).  $T^n$  and  $Q^n$  denote silicon sites  $(\equiv\text{SiO})_m\text{Si}(\text{OH})_{4-n-m}\text{R}_m$  with  $m = 1$  and  $m = 0$ , respectively. To improve the sensitivity, the  $^{29}\text{Si}$  DPMAS spectrum was acquired using the Carr–Purcell–Meiboom–Gill (CPMG) train of echoes during the acquisition period.<sup>23</sup> By co-adding 10 echoes to construct the enhanced spectrum, a sensitivity gain of approximately 3 was achieved without any distortions due to transverse relaxation. We first note that the presence of resonances representing  $T^2$  and  $T^3$  sites at around  $-60$  and  $-66$  ppm confirms that covalent bonds exist between DMAP and the surface in this sample. By deconvolution and integration of the  $^{29}\text{Si}$  spectrum, the following molecular formula was obtained for DMAP-MSN:  $(\text{SiO}_2)_{100}(\text{H}_2\text{O})_8(\text{C}_9\text{H}_{14}\text{N}_2)_{13}$ . From this formula, the amount of organic groups can be estimated at  $1.2 (\pm 0.1)$  per  $\text{nm}^2$  ( $1.6 \pm 0.15$   $\text{mmol}\cdot\text{g}^{-1}$ ) and the number of silanol groups at  $2.6 (\pm 0.2)$  per  $\text{nm}^2$ .

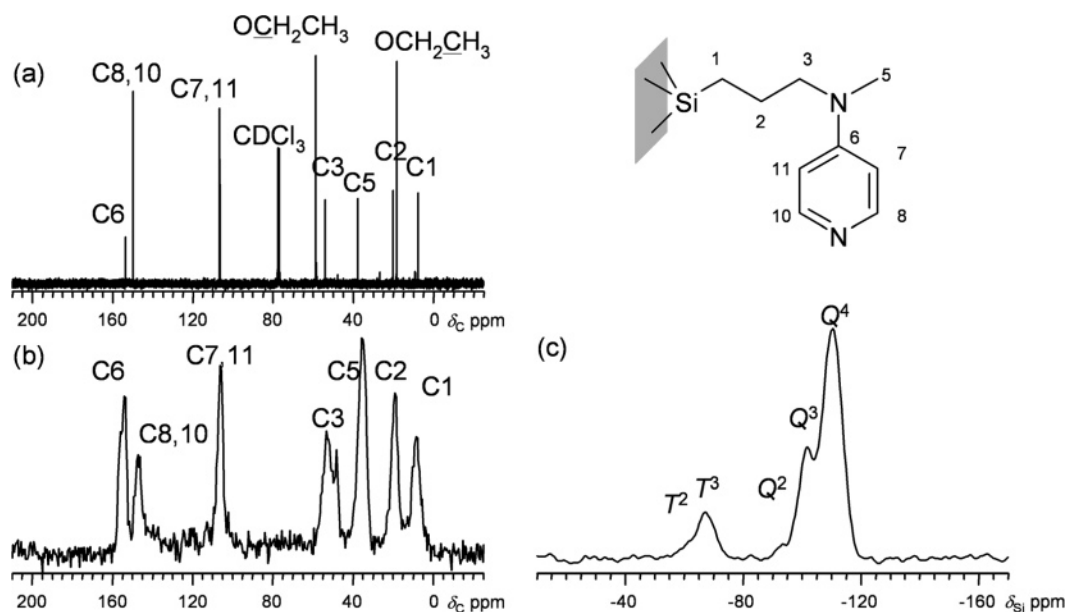
The NMR spectra also show that the pyridine and amine nitrogen atoms in DMAP-MSN are not protonated. In Table 1, we compare the chemical shifts of carbons of 4-(dimethylamino)pyridine in  $\text{CDCl}_3$  solution with the corresponding shifts observed in monoprotonated species (in the presence of trifluoroacetic acid) and diprotonated species (in the presence of trifluoromethanesulfonic acid).<sup>26</sup> After a prolonged exposure (3 weeks) of the DMAP-MSN sample to ambient humidity, an upfield shift of about 10 ppm was observed for C8 and C10 resonances in the 1D and 2D  $^{13}\text{C}$  spectra (not shown), which demonstrates that the pyridine nitrogen is susceptible to protonation under such conditions.

**DMAP-MSN Catalyzed Baylis–Hillman Reaction.** Baylis–Hillman reaction is one of the most useful synthetic ways for forming carbon–carbon bonds between aldehydes and  $\alpha,\beta$ -

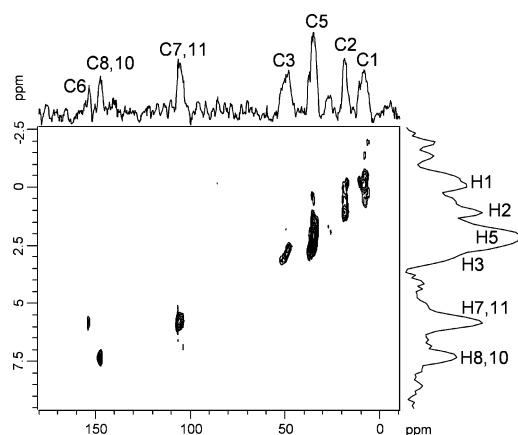


**Figure 1.** (a) XRD spectrum of DMAP-MSN. (b) TEM micrograph of DMAP-MSN, Scale bar = 50 nm, (c) SEM micrograph of DMAP-MSN, Scale bar = 2.0  $\mu\text{m}$ , (d) TEM micrograph of DMAP-MSN after 10 runs of acylations, Scale bar = 50 nm.

(26) Dega-Szafran, Z.; Kania, A.; Nowak-Wydra, B.; Szafran, M. *J. Mol. Struct.* **1994**, 322, 223–232.



**Figure 2.** (a)  $^{13}\text{C}$  NMR spectrum of DMAP-TES in  $\text{CDCl}_3$  solution. (b)  $^{13}\text{C}$  CPMAS spectrum of DMAP-MSN resulting from 12 000 scans acquired with a delay of 1 s in a 5 mm probe ( $\nu_{\text{R}} = 10$  kHz). During each CP period of 1.5 ms,  $\nu_{\text{RF}}^{\text{H}}$  was ramped between 16 and 40 kHz (in 11 steps), while  $\nu_{\text{RF}}^{\text{C}}$  was set to 36 kHz. The  $\nu_{\text{RF}}^{\text{H}}$  fields of 83 kHz and 65 kHz were applied to protons during initial excitation and high power decoupling, respectively. (c)  $^{29}\text{Si}$  DPMAS spectrum of DMAP-MSN obtained with the same probe using CPMG acquisition (10 echoes). A total of 600 scans were collected with a delay of 300 s to allow the complete relaxation of  $^{29}\text{Si}$  nuclei.



**Figure 3.**  $^1\text{H}$ - $^{13}\text{C}$  HETCOR spectrum of DMAP-MSN measured under MAS at 40 kHz. During the CP period of 1.5 ms, the  $\nu_{\text{RF}}^{\text{H}}$  field was ramped between 100 and 140 kHz (in 15 steps) and  $\nu_{\text{RF}}^{\text{C}}$  was set to 80 kHz. TPPM decoupling with  $\nu_{\text{RF}}^{\text{H}} = 10$  kHz was used during the detection of  $^{13}\text{C}$  signals, which were accumulated using a delay of 1 s between scans. The hypercomplex method was employed to discriminate the sine and cosine parts in the  $^1\text{H}$  dimension. The experiment was completed in approximately 80 h, using 10 mg of natural abundance sample.

**Table 1.**  $^{13}\text{C}$  Chemical Shifts Observed in DMAP-MSN and in the Reference Compounds (DMAP-TES and 4NMe<sub>2</sub>-Py)

| sample                             | solvent                          | C1  | C2   | C3   | C5   | C6    | C7,C11 | C8,C10 |
|------------------------------------|----------------------------------|-----|------|------|------|-------|--------|--------|
| DMAP-TES                           | $\text{CDCl}_3$                  | 7.8 | 20.1 | 54.0 | 37.5 | 153.5 | 106.6  | 149.8  |
| DMAP-MSN                           | Solid-state                      | 8.8 | 19.3 | 53.0 | 35.8 | 153.8 | 106.1  | 147.8  |
| 4NMe <sub>2</sub> -Py <sup>a</sup> | $\text{CDCl}_3$                  |     |      |      | 38.4 | 153.6 | 106.0  | 149.1  |
|                                    | $\text{CF}_3\text{COOH}$         |     |      |      | 40.1 | 153.6 | 105.6  | 139.9  |
|                                    | in $\text{CDCl}_3$               |     |      |      |      |       |        |        |
|                                    | $\text{CF}_3\text{SO}_3\text{H}$ |     |      |      | 47.3 | 157.8 | 120.6  | 145.6  |
|                                    | in $\text{CD}_3\text{NO}_2$      |     |      |      |      |       |        |        |

<sup>a</sup> Data taken from ref 26.

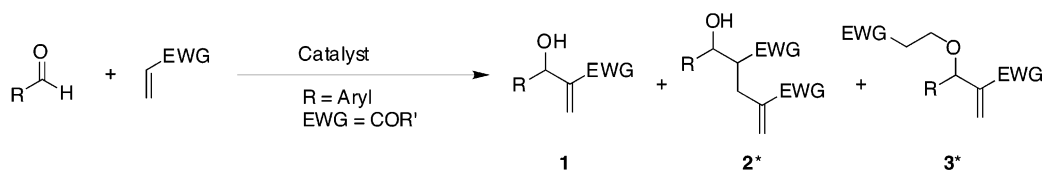
unsaturated ketones or esters. This reaction can be catalyzed by organic bases, such as amines, pyridines, and phosphines, without any assistance of metal.<sup>27,28</sup> It typically requires

stoichiometric or overstoichiometric amounts of catalysts and is usually performed in homogeneous solutions. Among various ketone substrates, cycloalkenones are known for their low reactivities for undergoing the Baylis–Hillman reaction catalyzed by nucleophilic molecules, such as DABCO (1,4-diazabicyclo [2,2,2]-octane).<sup>29</sup> Furthermore, in the homogeneous reaction of aryl aldehydes with methyl vinyl ketone (MVK) catalyzed by DABCO, the formation of undesired products, such as diadduct (compound 2 in Scheme 1) and Michael adduct (compound 3), have been reported in the literature.<sup>30</sup>

DMAP, on the other hand, is able to efficiently catalyze the Baylis–Hillman reaction of cycloalkenones in homogeneous solutions.<sup>31</sup> To construct a recyclable DMAP catalyst, Corma and co-workers<sup>16</sup> have recently reported on the synthesis of a DMAP-functionalized, Merrifield-type polystyrene resin that could serve as an active catalyst for the Baylis–Hillman reaction. However, this polymer-based DMAP catalyst showed a lower reactivity in protic solvents in comparison with those of DMAP-catalyzed homogeneous reactions.<sup>32,33</sup> The low reactivity was attributed to the contraction of polymer matrix in protic solvents.<sup>16</sup> Furthermore, a stoichiometric amount of the polymer-based DMAP catalyst was needed to obtain decent yields within reasonable reaction times. In some cases, the undesired diadduct and Michael adduct were also observed.

In contrast, our DMAP-MSN material showed an excellent catalytic performance (Table 2) for the Baylis–Hillman reaction of aryl aldehydes and various  $\alpha,\beta$ -unsaturated ketones. Only a

- (27) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–891.
- (28) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001–8062.
- (29) Rezgui, F.; El Gaid, M. M. *Tetrahedron Lett.* **1998**, *39*, 5965–5966.
- (30) Shi, M.; Li, C.-Q.; Jiang, J.-K. *Chem. Commun.* **2001**, 833–834.
- (31) Lee, K. Y.; Gong, J. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2002**, *23*, 659–660.
- (32) Aggarwal, V. K.; Dean, D. K.; Mereu, A.; Williams, R. J. *Org. Chem.* **2002**, *67*, 510–514.
- (33) Yu, C.; Liu, B.; Hu, L. *J. Org. Chem.* **2001**, *66*, 5413–5418.

**Table 2.** DMAP-MSN Catalyzed Baylis–Hillman Reaction<sup>a</sup>

\* Side products **2** and **3** are not observed in all reactions.

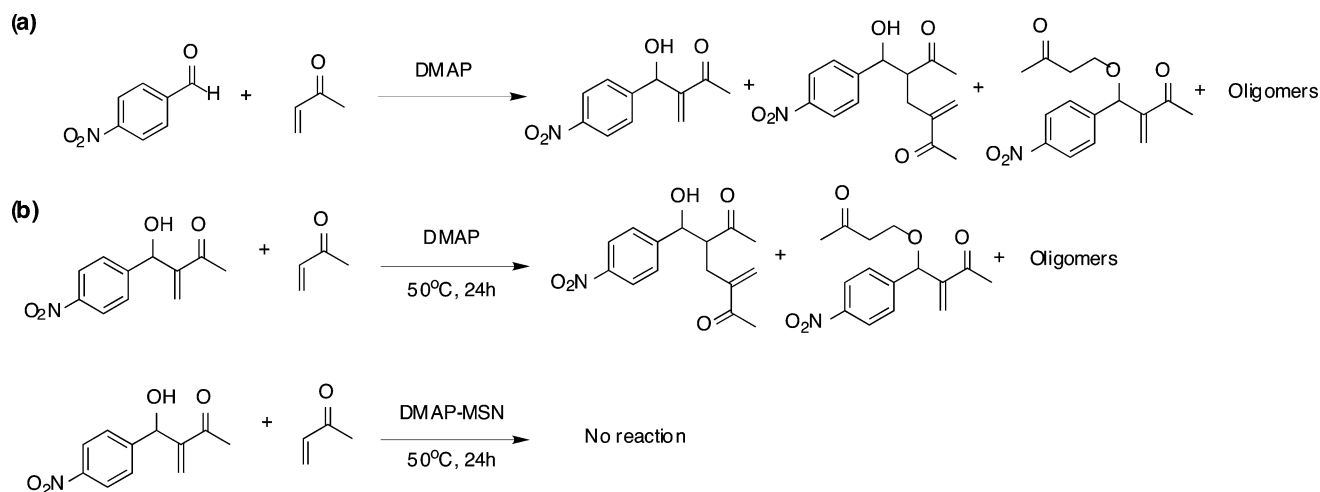
| Entry            | Aldehyde | Ketone | Catalyst                            | Product | Yield [%] <sup>[b]</sup> |
|------------------|----------|--------|-------------------------------------|---------|--------------------------|
| 1                |          |        | DMAP-MSN                            |         | 86                       |
| 2                |          |        | DMAP-MSN                            |         | 49                       |
| 3                |          |        | DMAP-MSN                            |         | 99                       |
| 4                |          |        | DMAP-MSN                            |         | 49                       |
| 5                |          |        | DMAP-MSN                            |         | 25                       |
| 6 <sup>[c]</sup> |          |        | DMAP-MSN                            |         | 50                       |
| 7 <sup>[c]</sup> |          |        | DMAP-MSN                            |         | 25                       |
| 8                |          |        | DMA-SiO <sub>2</sub> <sup>[d]</sup> |         | 20                       |
| 9                |          |        | MCM-41                              |         | NR <sup>[e]</sup>        |

\* Side products **2** and **3** are not observed in all reactions. <sup>a</sup> Reaction condition: aldehyde (0.25 mmol),  $\alpha,\beta$ -unsaturated ketone (0.5 mmol), and catalyst (50 mg, 30 mol %) in THF/H<sub>2</sub>O = 3:1 (2 mL) at 50 °C for 24 h. <sup>b</sup> Isolated yield. <sup>c</sup> Aldehyde/ketone = 1:4 at 50 °C for 3 d. <sup>d</sup> 3-(dimethylamino)propyl-functionalized silica gel. <sup>e</sup> No reaction.

catalytic amount (30 mol%) of DMAP-MSN was needed for the complete conversion of cyclic and aliphatic enones to the corresponding Baylis–Hillman products (entry 1–3 in Table 2). In the case of methyl vinyl ketone (MVK), the desired product was obtained in quantitative yield (entry 3 in Table 2) within 24 h. No undesired diadduct and Michael adduct were detected even at relatively high reaction temperature (50 °C). Conversely, the same reaction catalyzed by DMAP in homogeneous solution gave rise to a mixture of products under the same reaction condition (Scheme 2a). In addition to the diadduct

and Michael addition side products, the formation of insoluble brown precipitates was also observed, which could be attributed to products of the oligomerization of MVK and compound **1** catalyzed by DMAP at the elevated temperature. Using a physical mixture of DMAP and fumed silica gel as catalysts yielded a mixture of product as well. Based on these results, the high yield and good product selectivity of DMAP-MSN catalyzed reactions could not be due to the silanol groups on the silica surface. Given the fact that the DMAP catalytic groups are mainly located in the mesopores of MSN, we suspect that

Scheme 2



the observed product selectivity could be attributed to the difference in the rate of diffusion to the “active sites” located inside the pores between the aldehyde reactant and compound **1**, which would serve as the reactant for the undesired side reactions. To investigate this supposed “matrix effect”, we carried out two DMAP- and DMAP-MSN-catalyzed Baylis–Hillman reactions by using compound **1** (1.0 equiv) as reactant to interact with MVK (2.0 equiv) in the aforementioned THF/H<sub>2</sub>O solution at 50 °C for 24 h. Indeed, the reaction catalyzed by homogeneous DMAP catalyst gave rise to a mixture of products. On the contrary, no reaction was observed in the case of DMAP-MSN. The results support the hypothesis that the MSN matrix could regulate the reaction selectivity by preferentially allowing certain reactants to access the catalytic sites.

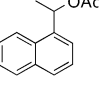
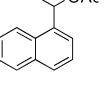
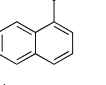
The intrinsic steric and electronic properties of the aldehyde reactants also strongly affect the product yields of the Baylis–Hillman reaction catalyzed by our DMAP-MSN. In the case of sterically hindered aryl aldehydes, e.g., *o*-nitrobenzaldehyde, a lower product yield of 49% was observed (entry 4 in Table 2). Compared to the case of *p*-nitrobenzaldehyde, the reactions of the less activated or nonactivated aldehydes, such as *p*-chlorobenzaldehyde and benzaldehyde, respectively, required more methyl vinyl ketones and extended reaction time to obtain the desired products (entry 6, 7 in Table 2). In contrast to the reactivities of other reported, surface-supported DMAP catalysts, the DMAP-MSN-catalyzed Baylis–Hillman reaction of a non-activated aryl aldehyde (benzaldehyde) with MVK gave rise to a high yield of the desired product with less catalyst loading (0.3 equiv vs 1.0 equiv) and shorter reaction time (4 days vs 10 days).<sup>16</sup> Therefore, our heterogeneous DMAP-MSN catalyst exhibits higher reactivity than polymer-based DMAP catalyst (entry 7 in Table 2). Among the examined substrates, the reactivity of  $\alpha,\beta$ -unsaturated ketones follows the order: methyl vinyl ketone > cyclopentenone > cyclohexenone. To further compare the catalytic performance of DMAP-MSN with other silica-immobilized tertiary amines, we have examined a Baylis–Hillman reaction catalyzed by 3-(dimethylamino)propyl-functionalized silica gel (DMA-SiO<sub>2</sub>). A 20% yield (entry 8 in Table 2) was observed, which indicated that the reactivity of DMAP-MSN (99% yield, entry 3 in Table 2) was indeed superior. Unlike DMAP-MSN, pure MCM-41 silica showed no reactivity in catalyzing the Baylis–Hillman reaction (entry 3, 9 in Table 2).

**DMAP-MSN Catalyzed Acylation Reaction.** Catalytic acylations of various alcohols by DMAP-MSN were investigated, and the results are outlined in Table 3. As shown in entry 1 and 2, the acylations of secondary alcohols proceeded rapidly and completed within 2.5 h under our reaction condition. In the absence of DMAP-MSN catalyst, however, only a small amount of product (33%) was obtained under the same reaction condition. As a control, pure inorganic MCM-41 silica, prepared by a similar procedure, was also used as a catalyst for the acylations. As shown in Table 3 (entry 3, 4), pure MCM-41 silica does not catalyze acylation. These results clearly indicated that DMAP-MSN could efficiently catalyze acylation reactions of various secondary alcohols. Contrary to the reactions with secondary alcohols, lower yields and longer reaction times were found in the cases of various tertiary alcohols (entry 5, 6 in Table 3). Such a pronounced difference could be attributed to the steric hindrance of carbinol as observed in homogeneous reactions.<sup>34</sup>

**Recyclability and Stability Studies of DMAP-MSN Catalyst.** To investigate the recyclability of DMAP-MSN catalyst, 1-(1-naphthyl)ethanol was chosen as a substrate because the chemical shift of the  $\alpha$ -proton of this molecule could be clearly resolved from other peaks in the <sup>1</sup>H NMR spectrum. After the reaction reached completion, the catalyst was reused in 10 consecutive cycles, which included recovery by decanting the aliquots after centrifuge and drying in air followed by the reaction. No change in reaction yield was observed. The TEM micrograph of the recovered DMAP-MSN catalyst (Figure 1d) showed the same clear structure as the freshly synthesized material. The result indicated that the mesopores of DMAP-MSN were not destroyed by chemical or thermal decompositions during the repeated use as a catalyst. To further evaluate the stability of DMAP-MSN, cyclohexanol (100.2 mmol) was introduced to a 200 mL benzene solution with acetic anhydride (200.4 mmol) and DMAP-MSN (20 mg). The reaction was stirred vigorously at 60 °C for 24 days. The resulting cyclohexyl acetate product was obtained in 100% yield based on the <sup>1</sup>H NMR spectrum, which gave rise to a turnover number (TON) of 3340 for 24 days. This result suggested that the catalytic reactivity of DMAP-MSN could be maintained for an extended period of time.

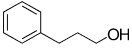
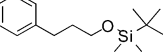
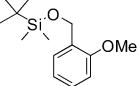
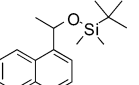
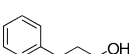
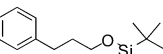
(34) Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069–2076.

**Table 3.** DMAP-MSN Catalyzed Acylation of Alcohols<sup>a</sup>

| $\text{ROH} \xrightarrow[\text{Catalyst}]{\text{Ac}_2\text{O, NEt}_3} \text{ROAc}$ |                                                                                   |                  |       |                                                                                    |                        |
|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------|-------|------------------------------------------------------------------------------------|------------------------|
| Entry                                                                              | Alcohol                                                                           | Catalyst         | t [h] | Product                                                                            | Yield [%] <sup>b</sup> |
| 1                                                                                  |  | DMAP-MSN         | 2.5   |   | 90                     |
| 2                                                                                  |  | DMAP-MSN         | 2.5   |  | 93                     |
| 3                                                                                  |  | MCM-41           | 2.5   |  | 32                     |
| 4                                                                                  |  | Without catalyst | 2.5   |  | 33                     |
| 5                                                                                  |  | DMAP-MSN         | 6     |   | 54                     |
| 6                                                                                  |  | DMAP-MSN         | 24    |   | 13                     |

<sup>a</sup> Reaction condition: alcohol (1 mmol), catalyst (50 mg, 7.5 mol %), Ac<sub>2</sub>O (2 mmol), and NEt<sub>3</sub> (1.5 mmol) in dry benzene (2 mL) at 60 °C. <sup>b</sup> Isolated yield.

**Table 4.** DMAP-MSN Catalyzed Silylation of Alcohols<sup>a</sup>

| $\text{ROH} \xrightarrow[\text{Catalyst}]{\text{TBDMSCl, NEt}_3} \text{ROTBDMS}$ |                                                                                     |          |                                                                                      |                        |
|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------|--------------------------------------------------------------------------------------|------------------------|
| Entry                                                                            | Alcohol                                                                             | Catalyst | Product                                                                              | Yield [%] <sup>b</sup> |
| 1                                                                                |  | DMAP-MSN |  | 96                     |
| 2                                                                                |  | DMAP-MSN |   | 52                     |
| 3                                                                                |  | DMAP-MSN |   | 35                     |
| 4                                                                                |  | MCM-41   |  | 64                     |

<sup>a</sup> Reaction condition: alcohol (0.5 mmol), catalyst (20 mg, 6 mol %), *t*-butyldimethylsilyl chloride (0.55 mmol), and NEt<sub>3</sub> (0.55 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at room temperature for 24 h. <sup>b</sup> Isolated yield.

**DMAP-MSN Catalyzed Silylation Reaction.** We also carried out several silylation reactions of alcohols by using DMAP-MSN as a catalyst (Table 4).<sup>35</sup> The reaction yield of these DMAP-MSN-catalyzed silylations appeared to be sensitive to the steric hindrance of the alcohols. In the case of sterically hindered alcohols, lower yields (entry 1–3 in Table 4) were observed in comparison with those of less sterically demanding alcohols. It is interesting to note that pure MCM-41 silica also catalyzed the silylation reactions and gave rise to certain amounts of silyl ethers. The result suggested that the acidic surface silanol groups of MCM-41 could be responsible for catalyzing the silylation reactions.

#### 4. Conclusion

We have successfully synthesized and characterized DMAP immobilized mesoporous silica catalyst, which showed high recyclability and high turnover number for Baylis–Hillman, acylation, and silylation reaction. We expect that this DMAP-functionalized mesoporous silica material also can serve as an efficient heterogeneous catalyst for many other catalytic nucleophilic reactions.

**Acknowledgment.** This research was supported at Ames Laboratory by the U.S. Department of Energy, Office of Basic Energy Sciences, through the Catalysis Science Grant No. AL-03-380-011 and under Contract W-7405-Eng-82.

JA0524898

(35) Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, 99–102.