

## Strong Organic Bases as Building Blocks of Mesoporous Hybrid Catalysts for C-C Forming Bond Reactions

Enrica Gianotti,<sup>[a,b]</sup> Urbano Diaz,<sup>[a]</sup> Alexandra Velty,<sup>[a]</sup> and Avelino Corma\*<sup>[a]</sup>

Keywords: Organic-inorganic hybrid composites / Proton sponges / Sol-gel processes / Basic catalysts / C-C coupling

1,8-Bis(tetramethylguanidino)naphthalene (TMGN), a neutral organic base that combines the properties of guanidine and the properties of proton sponges, was used as a building block to produce organic–inorganic silica-based mesoporous hybrids with strong basic properties. The TMGN-based mesoporous hybrids (TMGN/SiO<sub>2</sub>) were prepared by a solgel route working at a neutral pH and low temperatures, which avoided the use of SDAs. TMGN has been modified in order to have two terminal reactive silyl groups able to

### Introduction

The design of organic-inorganic hybrid mesoporous materials with strong basic functionalities has attracted great attention in the last decade because of their potential application in heterogeneous catalysis for the synthesis of fine chemicals.<sup>[1]</sup> The basic properties can be introduced into ordered or nonordered mesoporous supports by incorporating primary, secondary, or tertiary amines.<sup>[2,3]</sup> In this case, the resultant catalyst will have Lewis basic sites, while there are other cases in which catalytic Brønsted basic sites are preferred. Several examples of strong basic catalysts are reported in the literature by anchoring an organic ammonium quaternary salt<sup>[4,5]</sup> or guanidine<sup>[6]</sup> on different mesoporous silica supports. Recently, a proton sponge, 1,8-bis(dimethylamino)naphthalene, with strong basicity, was used as an organic building block to produce organic-inorganic hybrid mesoporous materials with good catalytic properties.<sup>[7]</sup> The proton sponges are diamines with neighboring atoms at short distances and aromatic frames, such as naphthalene,<sup>[8,9]</sup> fluorine,<sup>[10]</sup> heterofluorene,<sup>[11]</sup> phenanthrene,<sup>[12]</sup> and their analogues.<sup>[13]</sup> These molecules exhibit high unusual 1,8-bis(dimethylamino)naphthalene basicity, where (DMAN, Scheme 1) is the archetype of a proton sponge

 [a] Instituto de Tecnología Química (UPV-CSIC) Universidad Politécnica de Valencia, Consejo Superior de Investigaciones Científicas, Avenida de los Naranjos s/n., 46022 Valencia, Spain E-mail: acorma@itq.upv.es

Homepage: http://itq.upv-csic.es/

[b] Dipartimento di Scienze e Innovazione Tecnologica, Centro Interdisciplinare Nano-SiSTeMI, Università del Piemonte Orientale, V.T. Michel 11, 15100, Alegendria, Italy.

V. T. Michel 11, 15100 Alessandria, Italy

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejic.201200716.

perform co-condensation with a conventional organosilane (TMOS) used as a silicon source. This synthesis has allowed us to directly introduce the unmodified, functionalized TMGN as part of the walls of the mesoporous silica by a one-pot synthesis. TMGN/SiO<sub>2</sub> hybrid materials present excellent catalytic properties for C–C bond forming reactions: Knoevenagel, Henry (nitroaldol), and Claisen–Schmidt condensations. The activity of the hybrid materials is higher than that of the counterpart homogeneous catalyst.

with a  $pK_a$  of 12.1 in MeCN and PA(MP2)<sub>gas</sub> of 245.5 kcalmol<sup>-1</sup>. The proton sponges are a matter of interest in current research investigations and the design of more basic proton sponges has received great attention.<sup>[14–17]</sup> By combining the proton sponge skeleton with two peralkyl guanidine functions, known for their strong proton affinity and high basicity, a neutral organic base, named 1,8-bis-(tetramethylguanidino)naphthalene (TMGN, Scheme 1) was recently obtained with an experimental  $pK_a$  of 25 in MeCN and PA(MP2)<sub>gas</sub> of 257.5 kcalmol<sup>-1</sup>.<sup>[18]</sup>



Scheme 1. Scheme of 1,8-bis(dimethylamino)naphthalene (DMAN) and 1,8-bis(tetramethylguanidino)naphthalene (TMGN).

From theoretical studies, the relatively high proton affinity of TMGN is a consequence of the inherent basicity of the guanidine fragment and a relatively strong intramolecular hydrogen bond (IMHB) in [TMGN]H<sup>+</sup> (Scheme 2).<sup>[19–22]</sup>

Because of this strong basicity, the proton sponges have found applications in the field of synthetic organic chemistry as homogeneous catalysts for C–C forming bond reactions such as Knoevenagel or aldol condensations and Michael additions.<sup>[23]</sup> Moreover, different transition-metal complexes of proton sponges, such as Pd, Pt, Re, and Mn 4,9-dichloroquino[7,8-*h*]quinoline<sup>[24]</sup> and more recently,



Scheme 2. Intramolecular hydrogen bond (IMHB) formation in TMGN.

Pd–TMGN complexes<sup>[25]</sup> have been synthesized. The latter was tested in Heck reactions between phenyliodide and styrene to obtain *trans*-styrene.

1,8-Bis(tetramethylguanidino)naphthalene (TMGN), which combines the properties of guanidine and the properties of proton sponges, is an interesting organic molecule that could be used as building blocks to prepare organicinorganic silica-based hybrid materials with strong basic features. Organic-inorganic hybrid materials can be synthesised following several routes.<sup>[1]</sup> However, for introducing a base as a building block to form mesoporous organicinorganic hybrid materials, it is necessary to select and optimize the synthesis methodology in order to avoid degradation of the base either during the synthesis or during the removal of the template. In our case, we have used a procedure that allows us to carry out the synthesis at neutral pH, room temperature, and in the absence of structural directing agents. Using this method, it should be possible to achieve mesoporous hybrid organic-inorganic materials that, although will not have a long-range order, will have mesopores in a narrow pore-size distribution and be thermally stable.<sup>[26-29]</sup> In our case, TMGN is the organic builder of the hybrid and the inorganic part corresponds to silica tetrahedra. The organic moiety may be a part of the solid network if the organosilane contains more than one silicon center. Therefore, TMGN has been modified in order to have two terminal reactive silvl groups able to perform cocondensation with a conventional organosilane (TMOS), through sol-gel routes. This method has allowed the direct introduction of the functionalized TMGN builders into nonordered mesoporous silica by a one-pot synthesis. The synthesized TMGN hybrid materials present interesting properties as solid base catalysts and they have been used for catalyzing Knoevenagel and nitroaldol condensations and their activity has been compared with the DMANbased hybrids and the corresponding homogeneous catalysts. Moreover, these organic-inorganic hybrids were also used as catalysts in the Claisen-Schmidt condensation reactions that produce valuable chemicals of biological and pharmaceutical importance, such as chalcones.[30-33]

### **Results and Discussion**

### Synthesis and Characterization of the Hybrid Materials

To become part of the silica network of a mesoporous material, the organic bases have to be functionalized with two terminal reactive silyl groups that are able to perform co-condensation with a conventional organosilane (TMOS), through a sol–gel route. The level of functionalization of the organic bases was followed using liquid NMR spectroscopy (see Supporting Information, Figures S1–S4). More specifically, the <sup>1</sup>H NMR spectrum of the silylated TMGN and DMAN shows a signal at  $\delta = 6.11$  ppm assigned to NH groups attached to aromatic rings.<sup>[7]</sup> The incorporation of disilylated TMGN and disilylated DMAN in the silica mesoporous framework was carried out by a one-pot synthesis following a NH<sub>4</sub>F-catalyzed sol–gel route at neutral pH and room temperature, without the use of structure-directing agents.

These soft synthetic conditions allow covalent binding of the functionalized organic fragments within the walls of the nonordered inorganic silica, preserving the basic properties of the organic function in the resultant hybrid and avoiding the use of post-synthetic treatments to remove the SDAs.

The functionalized TMGN-Sil and DMAN-Sil have two terminal reactive silyl groups that are able to perform hydrolysis and co-condensation with a conventional organosilane (TMOS), used as a silicon source, as is represented in Scheme 3. Hybrids with low organic (TMGN or DMAN) loading have been synthesised to obtain isolated and welldispersed basic sites.



Scheme 3. Schematic representation of the synthesis of the TMGN/  $SiO_2$  hybrids.

The presence of the organic moieties in the hybrids was evidenced by means of elemental analysis. Then, to confirm that TMGN and DMAN are not just adsorbed but chemically stabilized and covalently bound into the silica framework, leaching tests were performed by washing the as-synthesized hybrids with ethanol at 298 K for 3 days and then performing a series of spectroscopic analyses, as will be described later.

In Table 1, the C, H, N content and the calculated percentage in weight of the organic species present in the assynthesized samples and in the hybrids after the leaching tests is reported. The efficiency of the covalent TMGN/ DMAN incorporation in the silica matrix, evaluated from the organic content of the as-synthesized and washed hybrids, is also reported in Table 1.

The C/N/H ratio, obtained by elemental analysis, confirms that the organic part corresponds to the TMGN or DMAN builders and that no decomposition of the organic content has occurred during the synthesis. However, it is



Table 1. Elemental analysis of the as-synthesized hybrids before and after the leaching tests and efficiency of TMGN/DMAN incorporation into the  $SiO_2$ .

Hybrids	As-synthesized hybrids		Washed hybrids			
	N, C, H [%]	Organic content (EA) [%]	N, C, H [%]	Organic content (EA) [%]	Organic loss [%]	Efficiency of TMGN/DMAN incorporation [%]
TMGN/SiO <sub>2</sub> -0.5	0.44, 2.6, 1.2	4.24	0.2, 2.5, 1.1	3.80	0.44	89
TMGN/SiO <sub>2</sub> -0.2	0.20, 1.7, 1.1	3.00	0.12, 1.6, 0.9	2.62	0.38	87
DMAN/SiO <sub>2</sub> -0.5	0.30, 1.8, 0.8	2.90	0.19, 1.6, 0.7	2.57	0.33	88
DMAN/SiO <sub>2</sub> -0.2	0.20, 1.4, 0.7	2.30	0.17, 1.2, 0.6	1.97	0.31	86

observed that the experimental C/N ratio is somewhat higher than the theoretical value, this is probably because of the entrapment of some methanol molecules that occurs during the formation of the hybrids.<sup>[7]</sup>

In the TMGN/SiO<sub>2</sub> hybrids, the organic content is larger than the organic content in DMAN/SiO<sub>2</sub> because of the higher molecular weight of the former organic superbase. In the washed hybrids, the loss of organic content goes from 0.4% for the TMGN/SiO<sub>2</sub> hybrids and from 0.3% for the DMAN/SiO<sub>2</sub> hybrids, confirming that in the hybrid materials most of the functionalized TMGN or DMAN is attached to silica, as the incorporation of the organic moiety is very efficient under our experimental conditions.



Figure 1. Section A: TGA and DTA curves of TMGN/SiO<sub>2</sub>-0.2 (curves a and c) TMGN/SiO<sub>2</sub>-0.5 (curves b and d). Section B: TGA and DTA curves of DMAN/SiO<sub>2</sub>-0.2 (curves a and c) and DMAN/SiO<sub>2</sub>-0.5 (curves b and d). DTA of pure TMGN (curve e) and DMAN (curve f) are also reported.

Thermogravimetric analysis was performed in order to gain insight, not only into the organic content of the solids, but also into the thermal stability of the inserted TMGN or DMAN units with respect to the pure TMGN and DMAN. The weight loss (TGA) and their respective derivatives (DTA) for the TMGN/SiO<sub>2</sub> and DMAN/SiO<sub>2</sub> hybrids and pure TMGN and DMAN molecules are reported in Figure 1. The first weight loss for the hybrids is observed at around 80-150 °C and can be associated with the removal of physisorbed water and methanol. At higher temperatures, the main weight loss is associated with the organic moieties (TMGN or DMAN). The DTA curves reveal that pure TMGN (Section A, curve e) decomposes at a higher temperature (350 °C) than DMAN (250 °C, Section B, curve f). The thermal stability of the organic bases incorporated into the silica network is very similar to the isolated bases. Indeed, the organic moieties in the hybrids start to decompose at around 280 °C. From the DTA curves it is possible to observe that DMAN/SiO<sub>2</sub> loses a higher quantity of water with respect to TMGN/SiO<sub>2</sub>, suggesting that DMAN hybrids are more hydrophilic than the TMGN ones, because of the lower organic content present in the silica (Table 1).

### Spectroscopic Characterization

To confirm that TMGN and DMAN are covalently inserted into the network of the mesoporous silicas, solidstate NMR spectroscopy was used. More specifically, the <sup>13</sup>C CP/MAS NMR spectra of the hybrids (Figure 2, curves a and b) present typical signals of methyl groups belonging to  $-N(CH_3)_2$  at 40–45 ppm, whilst in the range between 150-110 ppm, where the <sup>13</sup>C NMR signals from the naphthalene groups should appear,<sup>[14,18,22]</sup> very weak signals are detected because of the low loading of the organic bases inside the silica network. Nevertheless, the signals of the naphthalene groups are visible in the FTIR spectra of the hybrids (see Figure S5). In fact weak bands at 3045 and at 1530 cm<sup>-1</sup>, from the stretching mode of C–H and C=C of the aromatic rings, respectively, are present. These features indicate that the basic organic molecules are preserved in the mesoporous hybrids.

In addition to the <sup>13</sup>C CP/MAS NMR signals of the methyl groups, other signals at 158, 61, 22, and 10 ppm are observed that do not correspond to TMGN or DMAN molecules. In particular, the peak at  $\delta$  = 158 ppm is assigned to C=O groups and the other signals are from C1\* ( $\delta$  =



Figure 2. <sup>13</sup>C CP/MAS NMR of TMGN/SiO<sub>2</sub>-0.5 (curve a), DMAN/SiO<sub>2</sub>-0.5 (curve b).

10 ppm), C2\* ( $\delta$  = 22.7 ppm), and C3\* ( $\delta$  = 61.3 ppm) of the –CH<sub>2</sub> groups belonging to the terminal propyl-silyl fragments of the functionalized TMGN and DMAN (see the inset in Figure 2 for the labels of the C atoms).<sup>[34]</sup> In the case of the TMGN/SiO<sub>2</sub>-0.5 hybrid, a signal at  $\delta$  = 159 ppm is also visible that can be assigned to the carbon belonging to the guanidine functions.<sup>[18]</sup> The presence of all these signals also confirms that the TMGN and DMAN molecules were successfully functionalized.

To further confirm that the TMGN and DMAN fragments are not only intact after the synthesis of the hybrids but are also incorporated covalently into the nonordered porous network bound to the inorganic silica units, the hybrids were characterized by <sup>29</sup>Si BD/MAS NMR spectroscopy. The spectra of the hybrids (Figure 3) show three peaks at -92, -100, and -110 ppm, from the Q<sup>2</sup> [Si(OH)<sub>2</sub>-(OSi)<sub>2</sub>], Q<sup>3</sup> [Si(OH)(OSi)<sub>3</sub>], and Q<sup>4</sup> [Si(OSi)<sub>4</sub>] silicon units, respectively.<sup>[35]</sup>

The typical signals from -50 to -80 ppm, assigned to Ttype silicon species having a Si–C bond, are not visible in the TMGN/SiO<sub>2</sub>-0.5 and DMAN/SiO<sub>2</sub>-0.5 spectra, because of the low organic loading present in these hybrids, whilst they are well visible when the organic loading is higher (DMAN/SiO<sub>2</sub>-10, curve c). To identify better the T-type silicon species present in the hybrid materials, <sup>29</sup>Si CP/MAS NMR spectra have also been recorded (inset of Figure 3). There we can see two bands at -40 and -66 ppm, assigned to T-type silicon species having a Si–C bond for TMGN/ SiO<sub>2</sub>-0.5 (curve a') and DMAN-SiO<sub>2</sub>-0.5 (curve b'). The signal at -66 ppm confirms that the hydrolysis and polycondensation of silylated TMGN and DMAN has occurred through alkoxy terminal groups of the silylated moieties. Moreover, the as-synthesized hybrids also show a peak at



Figure 3.  $^{29}$ Si BD/MAS NMR of TMGN/SiO<sub>2</sub>-0.5 (curve a), DMAN/SiO<sub>2</sub>-0.5 (curve b), and DMAN/SiO<sub>2</sub>-10 (curve c). In the inset, the  $^{29}$ Si CP/MAS NMR of TMGN/SiO<sub>2</sub>-0.5 (curve a'), DMAN/SiO<sub>2</sub>-0.5 (curve b'), and TMGN/SiO<sub>2</sub>-0.5 after washing (curve c') with pure TMGN-Sil.

-40 ppm, which could be assigned to the pure TMGN-Sil or DMAN-Sil unreacted bis-silylated species, since this band disappears after washing the sample (curve c'). The incorporation of the disilylated organic bases into the framework of nonordered mesoporous silica is also confirmed by comparing the <sup>29</sup>Si NMR spectra of the hybrids and the pure disilylated TMGN (see inset of Figure 3). The TMGN-Sil exhibits one peak centered at -45 ppm typical of Si-C bonds. When the TMGN-Sil or DMAN-Sil builders are finally inserted into the silica framework, the signal from the silicon atoms bound to the carbon units shifts to the range -60 to -80 ppm, supporting the covalent incorporation of the disilylated organic species into the silica framework.

#### **Textural Properties of the Hybrid Materials**

The textural properties of the hybrids, measured by  $N_2$  adsorption, are reported in Table 2.

Table 2. Textural properties of the TMGN/SiO $_2$  and DMAN/SiO $_2$  hybrids.

Samples	SSA <sub>BET</sub> SSA [m <sup>2</sup> g <sup>-1</sup> ]	External SA [m <sup>2</sup> g <sup>-1</sup> ]	Pore size [Å]	Pore volume [cm <sup>3</sup> g <sup>-1</sup> ]
Pure SiO <sub>2</sub>	797	791	27	0.3
TMGN/SiO <sub>2</sub> -0.2	795	790	41	0.8
TMGN/SiO <sub>2</sub> -0.5	792	787	39	0.7
DMAN/SiO <sub>2</sub> -0.2	752	750	28	0.28
DMAN/SiO <sub>2</sub> -0.5	725	718	27	0.28

The BET specific surface area (SSA) of the TMGN/SiO<sub>2</sub> is around 800 m<sup>2</sup>g<sup>-1</sup>, whilst in the case of DMAN/SiO<sub>2</sub> it is ca 750 m<sup>2</sup>g<sup>-1</sup>. However, in all cases, the SSAs and pore volumes obtained are in the mesoporous range; the microporous contribution is practically negligible (Table 2). This

can also be deduced from the shape of the adsorption isotherms (Figure 4, A) that are typical of nonordered mesoporous systems. The pore distribution of the hybrid samples (Figure 4, B) are narrow and the mean pore diameters are centered at 40 Å for TMGN/SiO<sub>2</sub> hybrids, while DMAN/ SiO<sub>2</sub> shows a distribution centered around 30 Å. Hence, TMGN/SiO<sub>2</sub> also has a larger total pore volume. These features could be because of the larger molecular dimensions of TMGN in comparison with the DMAN proton sponge. The above conclusion is also supported by the presence of inflexion points in the adsorption isotherms. In the hybrid materials containing TMGN fragments, the inflexion point is close to p/p≈0.5, whilst in the case of DMAN builders inserted in the network, the inflexion point appears at lower relative pressures (p/p≈0.3).



Figure 4. Section A:  $N_2$  adsorption isotherms and Section B: Pore size distribution, calculated by the BJH method, of TMGN/SiO<sub>2</sub>, DMAN/SiO<sub>2</sub> hybrids, and pure SiO<sub>2</sub>.

In accordance with the nitrogen adsorption isotherms that are characteristic of nonordered conventional mesoporous materials synthesized through sol-gel routes catalyzed by fluoride ions, TEM micrographs show the formation of organosilica particles with inhomogeneous sizes (20– 60 nm). This makes it impossible to identify long-range order in the hybrid materials (Figure S6). The pore size distri-



bution is around 30–40 Å, estimated from textural property measurements, indicates that intracrystalline mesoporous cavities are present in the individual organosilica nanocrystals, although interparticle porosity is also observable in this range.

#### **Catalytic Activity**

In order to investigate the accessibility to the reactants and the activity of the organic strong base that has been inserted into the wall of the mesoporous silica, the catalytic performance of the hybrid materials was tested for base catalyzed C–C bond formation reactions such as Knoevenagel, Henry (nitroaldol), and Claisen–Schmidt condensations. The activity was then compared with that of DMAN/SiO<sub>2</sub> and with the activity of the molecular proton sponges TMGN and DMAN in the homogeneous phase.

### **Knoevenagel Condensation**

The Knoevenagel condensation of carbonyl compounds is widely used in organic synthesis to produce important intermediates and end products for perfumes, pharmaceuticals, and polymers.<sup>[5,37]</sup> The reaction can be catalyzed by strong and weak bases depending on the level of activation of the reactant containing methylenic activated groups. The kinetics of the Knoevenagel reaction is generally considered to be first order with respect to each reactant and the catalysts.<sup>[36–40]</sup> Here, the Knoevenagel reaction between benzaldehyde (1) and different methylene compounds (Scheme 4), with increasing  $pK_a$  values, was performed on TMGN/SiO<sub>2</sub> and DMAN/SiO<sub>2</sub> hybrids.



Scheme 4. Scheme of the Knoevenagel reaction of benzaldehyde and methylene compounds.

Ethyl cyanoacetate (**2a** ECA,  $pK_a \approx 9$ ), ethyl acetoacetate (**2b** EAA,  $pK_a \approx 10$ ), and diethyl malonate (**2c** DEM,  $pK_a \approx 13$ ) were used. In the case of ECA, one polar protic solvent, such as ethanol, was used as this is the most effective solvent for the formation of the *trans*- $\alpha$ -ethyl cyano-

cinnamate (product **3a**),<sup>[7,42]</sup> whilst toluene was used as a solvent when Knoevenagel condensation was performed using EAA and DEM.

In Figure 5, the yields for product **3a**, obtained with the TMGN/SiO<sub>2</sub> hybrids (Section A) and DMAN/SiO<sub>2</sub> hybrids (Section B), are reported, and compared to the yields of pure TMGN and DMAN. TMGN/SiO<sub>2</sub>-0.5 is the most active catalyst and reaches the yield of homogeneous TMGN in only 1 h with 100% selectivity. In the case of DMAN-containing hybrids, the yield observed is lower, and both the catalysts reach the yield of homogeneous DMAN after a 4 h reaction time. The turnover frequencies calculated after 30 min and the initial rate are reported in Table 3 (Figure S7). The TMGN/SiO<sub>2</sub>-0.5 hybrid shows the highest TOF, close to the one of the homogeneous base.



Figure 5. Knoevenagel condensation of benzaldeyde with ECA using TMGN/SiO<sub>2</sub> (Section A) and DMAN/SiO<sub>2</sub> (Section B) hybrids at 333 K with ethanol and using 1 mmol-% of proton sponges, in the silica, with respect to ECA. The yields of homogeneous TMGN and DMAN are also reported for comparison.

When more demanding reactants (EAA and DEM) were used and the Knoevenagel reactions were carried out at 353 K and 383 K, respectively, using toluene as the solvent, the TMGN/SiO<sub>2</sub>-0.5 hybrid displayed a higher yield towards the desired products (**3b** and **3c**) than the DMAN/

Table 3. Yields, turnover frequencies (TOF) calculated at 30 min, and initial rate.

Catalysts	Yield [%] (after 30 min)	TOF [min <sup>-1</sup> ]	$r_0 \ [min^{-1}]$
Pure TMGN	77	256	1.56
TMGN/SiO <sub>2</sub> -0.5	69	230	1.17
TMGN/SiO <sub>2</sub> -0.2	63	210	0.95
Pure DMAN	75	250	1.15
DMAN/SiO <sub>2</sub> -0.2	60	200	0.82
DMAN/SiO <sub>2</sub> -0.5	56	187	0.48

 $SiO_2$  hybrid material (Figure 6 A and B). In both hybrids, the selectivity towards the **3b** and **3c** products is 100%. The TOF and the initial rate, reported in Table 4, evidence the superior activity of the TMGN/SiO<sub>2</sub>-0.5 hybrid catalyst.



Figure 6. Knoevenagel condensation of benzaldehyde with EAA (A) and DEM (B) using TMGN/SiO<sub>2</sub>-0.5 and DMAN/SiO<sub>2</sub>-0.5 hybrids and homogeneous TMGN and DMAN at 353 K and 383 K, respectively.

The catalytic activity of the heterogeneous hybrids is higher than that observed using homogeneous TMGN and



Table 4. Yields, turnover frequencies (TOF), and initial rate for the Knoevenagel condensation of benzaldehyde with EAA and DEM.

Catalysts	EAA <sup>[a]</sup> Yield [%] of <b>3b</b>	TOF [min <sup>-1</sup> ]	$r_0$ [min <sup>-1</sup> ]	DEM <sup>[b]</sup> Yield [%] of <b>3c</b>	TOF [min <sup>-1</sup> ]	$r_0$ [min <sup>-1</sup> ]
TMGN/SiO <sub>2</sub> -0.5	81	13.5	0.68	28	1.6	0.16
DMAN/SiO <sub>2</sub> -0.5	51	8.5	0.35	18	1	0.1

[a] 1 h reaction time. [b] 3 h reaction time.

DMAN as organocatalysts that show very low yields. This behavior is due to the polarity of the solvent used that has a strong effect on the reaction rate. In fact, in the case of homogeneous proton sponges, the solvent influences the reaction mechanism and not the capacity of the organocatalysts for proton transfer. Thus, when polar solvents are used, the activation energy of the Knoevenagel reaction should be lower than when the reaction occurs in an apolar solvent (chlorobenzene, toluene).<sup>[37]</sup> In fact, the polar solvent polarizes the N-H+-N bond and the intramolecular hydrogen bond of the protonated proton sponge loses strength, facilitating the release of the proton. When proton sponges are introduced into the silica network to form organic-inorganic hybrid catalysts, the reaction rate is less affected by the solvent polarity and a role of the surface polarity of the silica support on the reaction rate has to be considered. Indeed, in heterogeneous catalysis, the reaction occurs on the surface and when polar reactants are involved (as in Knoevenagel condensation), the transition-state complex should be stabilized by polar surfaces, such as silica surfaces, which leads to an increase in the reaction rate. In this case, only a weak solvent effect is observed<sup>[41]</sup> and the reaction occurs both in polar and in apolar solvents.

### **Henry Reaction**

The TMGN- and DMAN-based hybrids were tested in the Henry reaction, i.e, a condensation reaction of nitroalkanes with carbonyl compounds to generate nitroalkenes (Scheme 5), which are of importance for the synthesis of pharmaceutical products.<sup>[42,43]</sup> However, the selective formation of a nitroalkene (product **2** in Scheme 5) using conventional strong bases is difficult to achieve since the conjugate addition of the nitroalkane to the C–C double bond of the nitrolkene gives bis-nitro compounds that results in poor yields because of their dimerization or polymerization (product **3**, Scheme 5).<sup>[44–47]</sup>



Scheme 5. Scheme of the Henry reaction of benzaldehyde and nitromethane.

The Henry reaction between benzaldehyde and nitromethane ( $pK_a = 10.2$ ) was performed with hybrids with higher organic loadings (TMGN/SiO<sub>2</sub>-0.5 and DMAN-SiO<sub>2</sub>-0.5) as they showed the highest activity for the Knoevenagel reaction. From the yields of nitrostyrene (product 2) reported in Figure 7, one can see that the TMGN/SiO<sub>2</sub>-0.5 material shows the best catalytic performance and reaches 100% conversion and 100% selectivity towards product 2 in 6 h, whilst DMAN/SiO<sub>2</sub>-0.5 reaches 80% conversion and 100% selectivity for the same reaction time. In the case of homogeneous TMGN and DMAN molecules, the conversions in the Henry reaction are lower than with the heterogeneous hybrid catalysts and, in addition, the formation of byproducts (1 and 3 in Scheme 5) are detected when working in the homogeneous phase (see Table 5, Figure S8 for the yields of byproducts and benzaldehyde conversion of the homogeneous bases). In particular, it is possible to observe that at the beginning of the reaction (up to 1 h), the homogeneous catalysts show conversions higher than heterogeneous hybrids and that after 1 h the conversion stops and remains almost the same until the end of the reaction. In the Henry reaction, the heterogeneous hybrid cata-



Figure 7. Henry condensation of benzaldeyde with nitromethane using TMGN/SiO-0.5 and DMAN/SiO<sub>2</sub>-0.5 hybrids at 363 K. The conversions of homogeneous TMGN and DMAN are also reported for comparison.

Table 5. Conversion and yields (%) of products 1, 2, and 3 of the heterogeneous hybrids and homogeneous bases calculated after 6 h.

Catalysts	% conv.	Yield 1	Yield 2	Yield 3	TOF <sup>[a]</sup> [min <sup>-1</sup> ]
Pure DMAN	28	11	4	13	2
Pure TMGN	36	13	7	16	2.6
DMAN/SiO <sub>2</sub> -0.5	80	0	80	0	2.3
TMGN/SiO <sub>2</sub> -0.5	100	0	100	0	4.4

[a] TOF calculated after 2 h of reaction time.

lysts, and in particular TMGN/SiO<sub>2</sub>, have evidenced a superior activity both in conversion and selectivity towards the desired product 2 compared with the homogeneous bases.

The superior catalytic activity shown by the heterogeneous hybrids with respect to the homogeneous ones can be inferred to the active role of surface silanol groups, which are weakly acidic, in performing a cooperative activation of the reactants producing a higher conversion towards the desired product.<sup>[48–51]</sup>

### **Claisen–Schmidt Condensation**

Claisen–Schmidt condensation between benzaldehyde (1) and acetophenone (2), produces *trans*-chalcones (Scheme 6), which are important compounds in many pharmaceutical applications. They are the main precursors for the biosynthesis of flavonoids and exhibit various biological activities, such as anticancer, anti-inflammatory, and anti-hyperglycemic agents.<sup>[30–33,52–55]</sup>



Scheme 6. Scheme of the Claisen–Schmidt reaction of benzaldehyde and acetophenone.

In Figure 8, the yields towards trans-chalcone of TMGN/ SiO<sub>2</sub> and DMAN/SiO<sub>2</sub> hybrids with reaction time are presented. TMGN/SiO<sub>2</sub>-0.5 reaches almost 100% conversion and selectivity in 10 h, while a 68% yield with 100% selectivity was observed using DMAN/SiO<sub>2</sub>-0.5. The TOF values are reported in Table 6. This result confirms that the high catalytic activity of TMGN/SiO2 is due to the particularly high basicity of this organic base ( $pK_a = 25$ ) that has been inserted into the network of mesoporous silica. In the case of the DMAN containing hybrid, the fact that the  $pK_a$ of acetophenone  $(pK_a = 20)^{[55]}$  is higher than that of DMAN ( $pK_a = 12.1$ ) suggests that not only the basic strength of the organic molecule is responsible for the catalytic activity. As has been reported,<sup>[41]</sup> the silanol groups of the inorganic support are able to interact with the carbonyl group of the acetophenone, polarizing the carbon-oxygen bond and increasing the density of the positive charge of the carbon. Thus, the acidity of the hydrogens in the  $\alpha$ position of the carbonyl group is enhanced and the abstraction by the catalyst becomes easier. The role of the silanols could then explain the catalytic activity observed when substrates with higher  $pK_a$  values than that of DMAN are used. In the case of the TMGN hybrid, the role of the silanols is less required since the  $pK_a$  of TMGN is very high.



Figure 8. Claisen–Schmidt condensation between benzaldehyde and acetophenone using the TMGN/SiO<sub>2</sub>-0.5 and DMAN/SiO<sub>2</sub>-0.5 hybrid materials at 403 K.

Table 6. Yields and turnover frequencies (TOF) calculated after 3 h.

Catalysts	Yield [%]	TOF [min <sup>-1</sup> ]
TMGN/SiO <sub>2</sub> -0.5	56	31
DMAN/SiO <sub>2</sub> -0.5	19	11

### Reusability

Catalyst deactivation and reusability was studied with TMGN/SiO<sub>2</sub>-0.5 and DMAN/SiO<sub>2</sub>-0.5 hybrids by recycling the used catalysts after each run, after being washed with  $CH_2Cl_2$ . The yields of the recycled catalysts in the Knoevenagel condensation and Henry reaction are reported in Figure 9 after 6 h of reaction. The yields are almost similar during three catalytic runs. After the third run, the yield slightly decreases for both types of hybrids, probably because of the deactivation of the basic moieties due to protonation that occurs during the reactions. No leaching of the organic bases was observed by performing elemental analysis on the used hybrids.



Figure 9. Knoevenagel condensation and Henry reaction recycling tests using TMGN/SiO<sub>2</sub>-0.5 and DMAN/SiO<sub>2</sub>-0.5 as catalysts. The yield (%) is reported after 6 h of reaction.

### Conclusions

The organic base 1,8-bis(tetramethylguanidino)naphthalene (TMGN) has been successfully inserted into the wall of nonordered mesoporous silica for the first time, to the best of our knowledge, to produce organic-inorganic hybrid materials. By using a fluoride-catalysed sol-gel process, at neutral pH and low temperatures, the use of SDAs was avoided. The characterization of the hybrids has revealed that this organic base is preserved inside the mesoporous silica network providing strong basic properties to the hybrid materials. These functional hybrid materials, which contain stable, isolated, and active basic sites, are able to carry out condensation processes to form carbon-carbon bonds. In particular, TMGN-based hybrids have shown higher conversions in the Knoevenagel, Henry (nitroaldol), and Claisen-Schmidt condensations with respect to DMANbased hybrids, because of the higher basicity of TMGN. In addition, the organic-inorganic hybrids have shown higher catalytic performances compared with the homogeneous organocatalysts because of the presence of silanol groups belonging to the silica support that are able to activate the reactants by cooperative effects. The role of silanols is particularly effective in the case of the DMAN hybrid in which, in some cases, the  $pK_a$  of the substrates is higher than that of DMAN. In this view, TMGN/SiO<sub>2</sub> hybrids represent promising organic-inorganic base catalysts and open up a route for the design and synthesis of multifunctional hybrids by combining acidic and basic sites or basic and redox functionalities within the mesoporous silica network.

## **Experimental Section**

### Synthesis of the Hybrid Materials

TMGN and DMAN were purchased by Sigma-Aldrich.

The 1,8-bis(tetramethylguanidino)naphthalene (TMGN) was functionalized according to the procedure described in ref.<sup>[7]</sup> All the steps required for TMGN and DMAN functionalization (see Supporting Information, Scheme S1) were followed by <sup>1</sup>H, <sup>13</sup>C, <sup>29</sup>Si liquid NMR (Figures S1–S4).

TMGN/SiO<sub>2</sub> and DMAN/SiO<sub>2</sub> hybrids were synthesized using a NH<sub>4</sub>F co-condensation route. Tetramethyl orthosilicate (TMOS) and disilylated TMGN or DMAN (TMGN-Sil or DMAN-Sil) were mixed in methanol at 298 K. After dissolution of precursors, a water solution of NH<sub>4</sub>F was added under vigorous stirring.

The final reaction mixture has the following molar composition:

(1 – x)SiO<sub>2</sub>/xDMAN-Sil/TMGN-Sil/4MeOH/4H<sub>2</sub>O/3.13 × 10<sup>-4</sup> NH<sub>4</sub>F

Hydrolysis and condensation of the silicon precursor was carried out under vigorous stirring at 298 K until gelation occurred. Then, the gel was aged at 36 °C for 24 h and finally dried at 60 °C for 24 h. Several hybrids with different TMGN/DMAN loadings, from x = 0.002 to x = 0.005, were synthesized (Table 7). Additionally, pure SiO<sub>2</sub> was also produced following the NH<sub>4</sub>F sol–gel route.



Table 7. Acronyms of the hybrid materials and TMGN/DMAN loadings.

Hybrid acronyms	TMGN/DMAN loading x <sup>[a]</sup>		
TMGN/SiO <sub>2</sub> -0.2	0.002		
TMGN/SiO <sub>2</sub> -0.5	0.005		
DMAN/SiO <sub>2</sub> -0.2	0.002		
DMAN/SiO <sub>2</sub> -0.5	0.005		

[a]  $x = \text{mol of the TMGN-Sil or DMAN-Sil with respect to the total mol of SiO<sub>2</sub>.$ 

To remove unreacted TMGN-Sil or DMAN-Sil molecules, the hybrids were washed for 3 d in ethanol at 298 K.

In Table 7, the acronyms for the synthesized hybrids and the loading of TMGN/DMAN are reported.

#### **Characterization of Hybrid Materials**

All the hybrids were characterized by  $N_2$  adsorption, thermogravimetric and elemental analyses, and solid-state MAS NMR (<sup>13</sup>C, <sup>29</sup>Si).

C, N, and H contents were determined with a Carlo–Erba 1106 elemental analyzer. Thermogravimetric and differential thermal analyses (TGA-DTA) were recorded in a nitrogen stream with a Metler–Toledo TGA/SDTA 851E instrument. Volumetric analyses were performed by nitrogen adsorption isotherms at 77 K with a Micromeritics ASAP2010. Before measurements were performed, the samples were outgassed for 12 h at 100 °C. The BET specific surface area<sup>[56]</sup> was calculated from the nitrogen adsorption data in a relative pressure range from 0.04 to 0.2. The total pore volume<sup>[57]</sup> was obtained from the amount of N<sub>2</sub> adsorbed at a relative pressure of about 0.99. The external surface area and micropore volume were estimated with the *t*-plot method in the *t* range 3.5 to 5. The pore diameter and the pore size distribution were obtained following the Barret–Joyner–Halenda (BJH) method<sup>[58]</sup> on the adsorption branch of the isotherms.

Solid-state MAS NMR spectra were recorded at room temperature under magic angle spinning (MAS) with a Bruker AV-400 spectrometer. The single pulse <sup>29</sup>Si spectra were acquired at 79.5 MHz with a 7-mm Bruker BL-7 probe using pulses of  $3.5 \,\mu$ s corresponding to a flip angle of 3/4 p radians, and a recycle delay of 240 s. For the <sup>13</sup>C NMR cross-polarization (CP) spectra, a 7-mm Bruker BL-7 probe was used at a sample spinning rate of 5 kHz. <sup>13</sup>C NMR and <sup>29</sup>Si NMR were referenced to adamantane and tetramethylsilane, respectively.

FTIR spectra were obtained with a Nicolet 710 spectrometer (4 cm<sup>-1</sup> resolution) using a conventional greaseless cell. Wafers of ca.  $10 \text{ mg cm}^{-2}$  were outgassed at room temperature, 100, and 200 °C overnight.

The morphology of the hybrid materials was studied by transmission electron microscopy (TEM). Samples were ultrasonically dispersed in a  $CH_2Cl_2$  solvent and transferred to carbon coated copper grids. TEM micrographs were collected with a Philips CM-10 microscope operating at 100 kV.

### **Catalytic Tests**

The hybrid materials were studied as catalysts for the Knoevenagel, Henry, and Claisen–Schmidt condensations. The catalysts used were washed for 3 d in ethanol to remove the unreacted TMGN-Sil or DMAN-Sil molecules. Before catalytic tests, all the catalysts were outgassed at 373 K for 12 h to remove physisorbed water. For Knoevenagel reactions, a mixture of benzaldehyde (8 mmol) and methylene compounds (7 mmol) was stirred at the desired tempera-

ture under a N<sub>2</sub> atmosphere. Then, 1 to 10 mmol-% of TMGN or DMAN, present in a silica network, with respect to the methylene compound was added and the reaction started. Ethyl cyanoacetate (ECA), ethyl acetoacetate (EAA), and diethyl malonate (DEM) have been used and the reaction temperatures were 333 K for ECA, 353 K for EAA, and 383 K for DEM. Ethanol and toluene were used as solvents.

For the Henry reaction, a solvent free mixture of benzaldehyde (5 mmol) and nitromethane (20 mmol) was stirred at 363 K under a  $N_2$  atmosphere. Then 10 mmol-% of TMGN or DMAN within the silica network, with respect to the benzaldehyde, was added and the reaction started. For the Claisen–Schmidt condensation, a mixture of benzaldehyde (12 mmol) and acetophenone (10 mmol) was stirred at 403 K under a  $N_2$  atmosphere, an excess of acetophenone (1 mL) was used as the solvent. Then 10 mmol-% of TMGN or DMAN with respect to the benzaldehyde was added and the reaction started.

Samples were taken periodically, and the evolution of the reaction was followed by GC and GC–MS, equipped with an Equity-5 column ( $30 \text{ m} \times 0.25 \times 0.25 \,\mu\text{m}$ ) and a FID as detector. For catalyst recycling studies, the solid was filtered and thoroughly washed with CH<sub>2</sub>Cl<sub>2</sub> after each run and then outgassed at 373 K for 12 h to remove the adsorbed species. In all experiments, nitrobenzene was used as the internal standard.

**Supporting Information** (see footnote on the first page of this article): Synthesis route followed to obtain silyl-TMGN derivative is shown in Scheme S1. Figures S1–S4 show <sup>1</sup>H, <sup>13</sup>C and <sup>29</sup>Si NMR spectra of pure and functionalized proton sponges. In Figure S5, FTIR spectra of the hybrids are shown. Morphology of TMGN/SiO<sub>2</sub> samples is detailed from TEM micrographs in Figure S6. Figure S7 shows the yields obtained for Knoevenagel condensation of benzaldeyde with ECA using 0.5 mmol-% of proton sponges in the silica, and Figure S8 shows the yields of byproducts and benzaldehyde conversions of the homogeneous TMGN and DMAN proton sponges for Henry reaction.

### Acknowledgments

The authors thank the Spanish Government by Consolider – Ingenio 2010 MULTICAT (number CSD2009-00050) and MAT2011 (number 29020-C02-01) projects. E. G. is grateful for the financial support from the Marie Curie Fellowship (grant number FP7-PEO-PLE-2009-IEF).

- [1] A. P. Wight, M. E. Davis, Chem. Rev. 2002, 102, 3589-3614.
- [2] F. Bigi, S. Carloni, R. Maggi, R. Mazzacani, G. Sartori, *Stud. Surf. Sci. Catal.* 2000, 130, 3501–3506.
- [3] S. Cheng, X. Wang, S.-Y. Chen, Top. Catal. 2009, 52, 681–687.
- [4] I. Rodriguez, S. Iborra, A. Corma, F. Rey, J. L. Jordá, Chem. Commun. 1999, 593–594.
- [5] I. Rodriguez, S. Iborra, F. Rey, A. Corma, *Appl. Catal. A* 2000, 194–195, 241–252.
- [6] A. C. Blanc, D. J. Macquarrie, S. Valle, G. Renard, C. R. Quinn, D. Brunel, *Green Chem.* 2000, 2, 283–288.
- [7] E. Gianotti, U. Diaz, S. Coluccia, A. Corma, *Phys. Chem. Chem. Phys.* 2011, 13, 11702–11709.
- [8] R. W. Alder, P. S. Bowman, W. R. Steele, D. R. Winterman, J. Chem. Soc., Chem. Commun. 1968, 723–724.
- [9] R. W. Alder, Chem. Rev. 1989, 89, 1215-1223.
- [10] H. A. Staab, T. Saupe, C. Krieger, Angew. Chem. 1983, 95, 748; Angew. Chem. Int. Ed. Engl. 1983, 22, 731–732.
- [11] H. A. Staab, M. Höne, C. Krieger, *Tetrahedron Lett.* 1988, 29, 1905–1908.

- [12] T. Saupe, C. Krieger, H. A. Staab, Angew. Chem. 1986, 98, 460; Angew. Chem. Int. Ed. Engl. 1986, 25, 451–453.
- [13] M. A. Zirnstein, H. A. Staab, Angew. Chem. 1987, 99, 460; Angew. Chem. Int. Ed. Engl. 1987, 26, 460–461.
- [14] A. F. Pozharskii, Russ. Chem. Rev. 1998, 67, 1-24.
- [15] V. Raab, E. Gauchenova, A. Merkoulov, K. Harms, J. Sundermeyer, B. Kovačević, Z. B. Maksić, J. Am. Chem. Soc. 2005, 127, 15738–15743.
- [16] S. A. Reiter, S. D. Nogai, K. Karaghiosoff, H. Schmidbaur, J. Am. Chem. Soc. 2004, 126, 15833–15843.
- [17] V. A. Ozeryanskii, A. F. Pozharskii, A. J. Bienko, W. Sawka-Dobrowolska, L. Sobczyk, J. Phys. Chem. A 2005, 109, 1637– 1642.
- [18] V. Raab, J. Kipke, R. M. Gschwind, J. Sundermeyer, *Chem. Eur. J.* 2002, 8, 1682–1693.
- [19] B. Kovačević, Z. B. Maksić, R. Vianello, M. Primorac, New J. Chem. 2002, 26, 1329–1334.
- [20] V. Raab, K. Harms, J. Sundermeyer, B. Kovačević, Z. B. Maksić, J. Org. Chem. 2003, 68, 8790–8797.
- [21] B. Kovačević, Z. B. Maksić, Chem. Eur. J. 2002, 8, 1694-1702.
- [22] P. Przybylski, B. Gierczyk, G. Schroeder, G. Zundel, B. Brzezinski, F. Bartl, J. Mol. Struct. 2007, 844–845, 157–165.
- [23] D. Margertic, in: Superbases for organic synthesis (Ed.: T. Ishikawa), Wiley-VCH, 2009, pp. 10–48.
- [24] H. U. Wüstefeld, W. C. Kaska, F. Schüth, G. D. Stucky, X. Bu,
  B. Krebs, Angew. Chem. 2001, 113, 3280; Angew. Chem. Int. Ed. 2001, 40, 3182–3184.
- [25] U. Wild, O. Hübner, A. Maronna, M. Enders, E. Kaifer, H. Wadepohl, H.-J. Himmel, *Eur. J. Inorg. Chem.* 2008, 4440– 4447.
- [26] E. J. A. Pope, J. D. Mackenzie, J. Non-Cryst. Solids 1986, 87, 185–198.
- [27] R. Winter, J. B. Chan, R. Frattini, J. Jonas, J. Non-Cryst. Solids 1988, 105, 214–222.
- [28] E. Reale, A. Leyva, A. Corma, C. Martinez, H. Garcia, F. Rey, J. Mater. Chem. 2005, 15, 1742–1754.
- [29] U. Diaz, T. Garcia, A. Velty, A. Corma, J. Mater. Chem. 2009, 19, 5970–5979.
- [30] Y. Xia, Z. Y. Yang, K. F. Bastow, Y. Nakanishi, K. H. Lee, *Bioorg. Med. Chem. Lett.* 2000, 10, 699–701.
- [31] H. K. Hsied, L. T. Tsao, J. P. Wang, C. N. Lin, J. Pharm. Pharmacol. 2000, 52, 163–171.
- [32] M. Satyanarayana, P. Tiwari, B. K. Tripathi, A. K. Srivastava, R. Pratap, *Bioorg. Med. Chem.* 2004, 12, 883–889.
- [33] H. Qian, D. Liu, C. Lv, Ind. Eng. Chem. Res. 2011, 50, 1146– 1149.
- [34] Y. Seo, S. Park, D. H. Park, J. Solid State Chem. 2006, 179, 1285–1288.
- [35] K. Kawahara, Y. Hagiwara, A. Shimojima, K. Kuroda, J. Mater. Chem. 2008, 18, 3193–3195.
- [36] M. J. Climent, A. Corma, S. Iborra, K. Epping, A. Velty, J. Catal. 2004, 225, 316–326.
- [37] I. Rodriguez, G. Sastre, A. Corma, S. Iborra, J. Catal. 1999, 183, 14–23.
- [38] F. S. Prout, U. D. Beaucaire, G. R. Dyrkarcz, W. M. Koppes, R. E. Kuznicki, T. A. Marlewski, J. A. Pienkowski, J. M. Puda, J. Org. Chem. 1973, 38, 1512–1517.
- [39] G. Jones, Org. React. 1967, 15, 204–599.
- [40] J. Guyot, A. Kergomard, Tetrahedron 1983, 39, 1161–1166.
- [41] A. Corma, S. Iborra, I. Rodriguez, F. Sanchez, J. Catal. 2002, 211, 208–215.
- [42] F. A. Luzzio, Tetrahedron 2001, 57, 915–945.
- [43] G. Sartori, F. Bigi, R. Maggi, R. Sartorio, D. J. Macquarrie, M. Leonardo, L. Storaro, S. Coluccia, G. Martra, J. Catal. 2004, 222, 410–418.
- [44] M. J. Climent, A. Corma, S. Iborra, Chem. Rev. 2011, 111, 1072–1133.
- [45] T. Hara, S. Kanai, K. Mori, T. Mizugaki, K. Ebitani, J. Jitsukawa, K. Kaneda, J. Org. Chem. 2006, 71, 7455–7462.



- [46] S. L. Poe, M. Kobaslija, D. T. McQuade, J. Am. Chem. Soc. 2006, 128, 15586–15587.
- [47] K. Motura, M. Tada, Y. Iwasawa, Angew. Chem. 2008, 120, 9370–9375; Angew. Chem. Int. Ed. 2008, 47, 9230–9235.
- [48] K. K. Sharma, T. Asefa, Angew. Chem. 2007, 119, 2937; Angew. Chem. Int. Ed. 2007, 46, 2879–2882.
- [49] Y. Xie, K. K. Sharma, A. Anan, G. Wang, A. V. Biradar, T. Asefa, J. Catal. 2009, 265, 131–140.
- [50] A. Anan, K. K. Sharma, T. Asefa, J. Mol. Catal. A 2008, 288, 1–13.
- [51] Q. Wang, D. F. Shantz, J. Catal. 2010, 271, 170–177.
- [52] J. F. Ballesteros, M. J. Sanz, A. Ubeda, M. A. Miranda, S. Iborra, M. Paya, M. J. Alcaraz, *J. Med. Chem.* **1995**, *38*, 2794– 2797.

- [53] L. W. Wattenberg, J. B. Coccia, A. R. Galhaith, *Cancer Lett.* **1994**, *83*, 165–169.
- [54] A. T. Dinkova-Kostova, C. Abeygunawardana, P. Talalay, J. Med. Chem. 1998, 41, 5287–5296.
- [55] M. Novak, G. M. Loudon, J. Org. Chem. 1977, 42, 2494–2498.
- [56] S. J. Gregg, K. S. W. Sing, Adsorption, Surface Area and Porosity, Academic Press, London, 1982.
- [57] K. S. W. Sing, D. H. Everett, R. A. W. Haul, L. Moscou, R. A. Pierotti, J. Rouquerol, T. Siemieniewska, *Pure Appl. Chem.* 1985, 57, 603–619.
- [58] E. P. Barrett, L. G. Joyner, P. P. Halenda, J. Am. Chem. Soc. 1951, 73, 373–380.

Received: June 29, 2012

Published Online: September 28, 2012