4.1 Final publishable summary report

- ***Executive summary***

Organic-inorganic hybrids are of great interest because they combine the advantage of inorganic solids (high mechanical, thermal and structural stability) and organic molecules (flexibility and functionality). The heterogeneous catalysts are limited in the nature of the active sites and thus the scope of reactions that they can accomplish, whilst the organic molecules can catalyse a larger variety of reactions but suffer from their inability to be recycled. The goal of the HYMUCAT project is to use the organic moiety as the active sites and the inorganic solid to provide a way to recover and to recycle the organic sites. The aim of this project is the synthesis and the characterisation of innovative organic-inorganic mesoporous hybrid materials to produce heterogeneous catalysts having basic and both basic and acid sites. These active sites can act in base reactions or in cascade reactions to provide catalytic activity and selectivity superior to what can be obtained from homogeneous catalysts. Co-condensation techniques have been used to produce organic-inorganic mesoporous hybrids that contain the organic moiety as part of the silica network. Diamines with neighboring atoms and aromatic frames, such as naphthalene, referred as proton sponges, have been used as organic part, in that they exhibit unusually high basicity constants. In particular, 1,8-bis(dimethylamino)naphthalene (DMAN), with a pK_a of 12.1 and the 1,8-bis(tetramethylguanidino) naphthalene (TMGN), recently obtained, with an experimental pK_a of 25, have been inserted in the silica mesoporous network to obtain hybrid materials with basic functionalities. Despite the interest in proton sponges as potential base catalysts and the fact that they are widely used for proton abstraction, reports dealing with their applications as catalysts for the preparation of fine chemicals are only few. To benefit from the catalytic properties of this organic base and to obtain solid recyclable catalysts, it is necessary to perform the heterogenisation of proton sponges producing hybrid systems. In the HYMUCAT project, sol-gel processes carried out by a co-condensation have been used to prepare organic-inorganic mesoporous hybrids that contain the organic moiety (the proton sponge) as part of the silica network. Different synthetic strategies to obtain hybrids porous materials have been followed, in particular innovative synthetic procedure performed in the absence of structural directing agent (SDA), at room temperature and neutral pH, to produce mesoporous materials has been explored. The hybrid catalysts have been tested and have showed excellent catalytic properties for C-C bond forming reactions: Knoevenagel and Henry (nitroaldol) condensations. Moreover, these organic-inorganic hybrids have also showed good catalytic performances in the Claisen-Schmidt condensation reactions that produce valuable chemicals of biological and pharmaceutical importance, such as chalcones. In addition, the activity of the hybrid materials was higher than the counterpart homogeneous catalysts.

The research activity was also devoted to the preparation of bifunctional mesoporous hybrid materials, containing concomitantly strong base and acid groups. These bifunctional hybrids have been prepared following different synthetic routes: co-condensation processes (sol-gel or micellar one-pot route) or post-synthetic grafting of the organic functionalities. DMAN was used as organic functional builder base and 3-

mercaptopropyltriethoxysilane (MPTES) as pending precursor of sulfonic acids. The bifunctional hybrid materials were extensively characterized and were investigated as heterogeneous catalysts for various one-pot C-C bond-forming cascade reactions such as deacetalization-Knoevenagel condensation or deacetalization-nitroaldol (Henry) reaction.

- ***A summary description of project context and objectives.***

The organic-inorganic hybrid porous materials have attracted great attention in the last decade due to their improved or unusual properties that open promising applications in different areas such as optics, electronics, energy, environment, biology, medicine and catalysis. In the field of heterogeneous catalysis, the organic-inorganic hybrids offer the advantage to merge the properties of inorganic materials (high mechanical, thermal and structural stability) and of organic moieties (flexibility and functionality). Since the type of the active sites that can be introduced in the inorganic catalysts is limited, whilst the organic molecules can be functionalized to catalyse a larger variety of reactions but suffer from their inability to be recycled, the production of new organic-inorganic hybrids may overcome these drawbacks. In fact, in the hybrid materials, specific catalytic functions are introduced by the structural insertion of the organic moieties, while the inorganic part allows heterogenizing the catalyst and increases the stability; in this way, multifunctional materials should be obtain. Different routes can be followed to synthesise organic-inorganic hybrid catalysts that include: adsorption of the organic species inside the pores of the inorganic host, inclusion of the organic within the pores of the support by “ship in a bottle” type procedure, grafting the desired organic moiety to the functional groups of the inorganic support, and one-pot synthesis of a composite material with the organic located into the walls of the pores. In the last approach, the use of bridged silsesquioxanes ($(R'O)_3SiRSi(OR')_3$) as precursors is decisive to incorporate organic builders into the framework of periodic mesoporous organosilicas (PMOs) following self-assembling routes. The presence of different active sites (acid, basic or redox) in the organic linkers contained in the silsesquioxane monomers generates specific multifunctional catalytic materials. For this purpose, surfactants or organic molecules, that are not always easily accessible, are used as structural directing agents (SDAs) to obtain ordered mesoporous hybrids. The possibility to avoid the use of SDAs could be of interest if the hybrids obtained present a high surface area within a narrow and controlled pore size distribution. In this sense, sol-gel processes can be used to synthesise materials due to the low temperature processing, high homogeneity of the solid synthesized and their ability to produce ordered and non-ordered porous materials with controlled textural properties. In particular, sol-gel methods based on a fluoride-catalysed route can be of interest when compared with the conventional basic or acid routes, since the former method allows performing the synthesis at nearly neutral pH and room temperature. The fluoride-catalysed route is simple and low cost and has been successfully used as a “one-pot” method to synthesise organic-inorganic non-ordered porous materials when functionalized silanes are used during the synthesis process.

The aim of the HYMUCAT project was the design and the synthesis of innovative organic-inorganic hybrid materials with a proton sponge as the organic building blocks using a fluoride-catalysed sol-gel process, at neutral pH and low temperatures, that avoids the use of SDAs. The proton sponges are diamines with neighbouring atoms at short distance and aromatic frames, such as naphthalene and phenanthrene. These molecules exhibit high unusual basicity, being 1,8-bis(dimethylamino)naphthalene (DMAN) with pK_a=12.1, the archetype of proton sponge.

It is accepted that the high basicity constants of the proton sponges are due to steric strains. In DMAN, for example, is not possible to bring even one of the dimethylamino groups into the plane of the rings, resulting in a very low resonance interaction between the nitrogen lone pairs and the aromatic rings. The extreme steric hindrance of DMAN and the destabilizing effect of the overlap of nitrogen lone pairs of the neutral diamines explain the formation of strong N-H-N hydrogen bonds upon monoprotonation, leading to a considerable relaxation of the steric strain. This strong basic molecule has been used as an effective organo-catalyst and as an heterogeneous catalyst, after a post-synthesis grafting of the DMAN on a MCM-41, for Knoevenagel condensation reactions. However, some problems with the mesoporous hybrid materials obtained by anchoring of organic moieties were observed, such as the inhomogeneous distribution of active functions into the channels or the partial blockage of the free path within the pores. To overcome these drawbacks, DMAN has been modified and two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS) through sol-gel routes have been introduced. This method has allowed to directly introduce the functionalized DMAN builders into the walls of mesoporous silica by one-pot synthesis. The synthesized hybrids were studied as base catalysts for Knoevenagel condensation of benzaldehyde with active compounds containing activated methylenic groups. Their reactivity has been compared with the homogeneous catalyst and several catalyst recycles were performed to evaluate catalyst deactivation and reusability.

Due to the scientific interest in the proton sponges in current research investigations, the design of more basic proton sponges have received great attention. 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) was recently obtained with an experimental pK_a of 25. 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 $[TMGN]H^+$. Due to the success in synthesizing the organic-inorganic hybrids using DMAN that have shown interesting application as heterogeneous basic catalysts, TMGN, that combines the properties of guanidine and the properties of proton sponges, was also used as building block to prepare organic-inorganic silica-based hybrid materials with stronger basic features. However, for introducing a base as a building block to form mesoporous organic-inorganic 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. To synthesize the TMGN containing hybrids, a procedure that allows carrying out the synthesis at neutral pH, room temperature and in absence of structural directing agents was employed. Using this method, it should be possible to achieve mesoporous hybrid organic-inorganic materials that, although they will not have long range order, they will have mesopores in a narrow pore size distribution and be thermally stable. TMGN has also been modified in order to have two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS), through sol-gel routes. This method has allowed introducing directly the functionalised TMGN builders into non-ordered mesoporous silica by 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 DMAN-based 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.

The good catalytic performances of the hybrids containing proton sponges have opened up a route for the design and the synthesis of multifunctional hybrids by combining acid and basic sites functionalities within the mesoporous silica network. The design of cooperative catalytic systems was one of the objectives of the HYMUCAT project. In fact, the inorganic porous supports can host different and often incompatible catalytic functionalities separated at suitable molecular distances, such as acid and basic groups, providing site isolation inside the inorganic network. The spatial isolation of incompatible active organic groups that cannot coexist in solution was the key to produce bifunctional acid-base heterogeneous hybrid catalysts.

Among the different synthetic strategies available to covalently incorporate organic groups into the silica network, post-synthetic grafting and co-condensation processes are the most suitable. The later approach, also referred as one-pot synthesis, has been the preferred route because of the easier single-pot synthetic protocol and better control of organosilane loading joined to a more homogeneous distribution of active sites; in fact, the grafting method presents several drawbacks such as the partial blockage of the pores and undesired site-site interactions due to the supramolecular association of the silylated organic precursors.

In the co-condensation method, the organic molecules can be integrated into the framework of ordered or non ordered mesoporous silica using bis-silylated precursors. In the synthesis of acid-base functionalized ordered mesoporous silicas, the presence of a surfactant, acting as structural directing agent (SDA), is necessary producing a ordered hybrid heterogeneous catalyst, the SDA being removed without altering the properties of the organic moieties incorporated into the framework. To avoid the use of sophisticated and expensive SDAs, a sol-gel procedure catalyzed by NH_4F using soft synthesis conditions, room temperature and neutral pH, can be used to synthesize hybrid materials. Using this method, it should be possible to achieve mesoporous hybrid organic-inorganic materials that, although they will not have long range order, will have accessible mesopores in a narrow pore size distribution and be thermally stable.

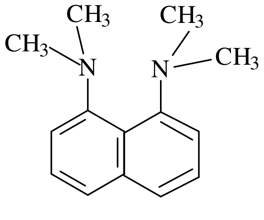
The synthesis of multifunctional hybrid materials containing both Brønsted acids and bases is not an easy task, due to the incompatible nature of these functional groups. Normally, the basic sites are represented by amines that can be easily protected using di-tert-butyl-dicarbonate (BOC). This strategy is commonly used for amino group protection during the acid treatment necessary to convert the organosiliceous precursor of acid groups, usually thiols or disulfide moieties, into the corresponding sulfonic acids. Then, a deprotection of the amine groups by thermal treatment is needed to restore the basic properties of the hybrid.

Ordered and non-ordered bifunctional mesoporous silica materials have been synthesized following grafting and co-condensation procedures, cohabiting in the final materials simultaneously proton sponge and sulfonic groups as organocatalytic builders. Remarkably, during the synthesis process, it was avoided the post-synthesis protection and deprotection procedure to preserve the basic functionality. Specifically, 1,8-bis(dimethylamino)naphthalene (DMAN), a proton sponge, was used as organic builder base and 3-mercaptopropyltriethoxysilane (MPTES) as pending precursor of sulfonic acids. The organic base may be a part of the solid network if the organosilane contains more than one silicon center, for this reason, DMAN has previously been modified in order to have two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS), through sol-gel or micellar one-pot routes. This

method has allowed introducing directly the functionalised DMAN builders into mesoporous silica by direct synthesis.
These bifunctional hybrid materials were extensively characterized and were investigated as reusable heterogeneous catalysts for various one-pot C-C bond-forming cascade reactions such as deacetalization-Knoevenagel condensation or deacetalization-nitroaldol (Henry) reactions.

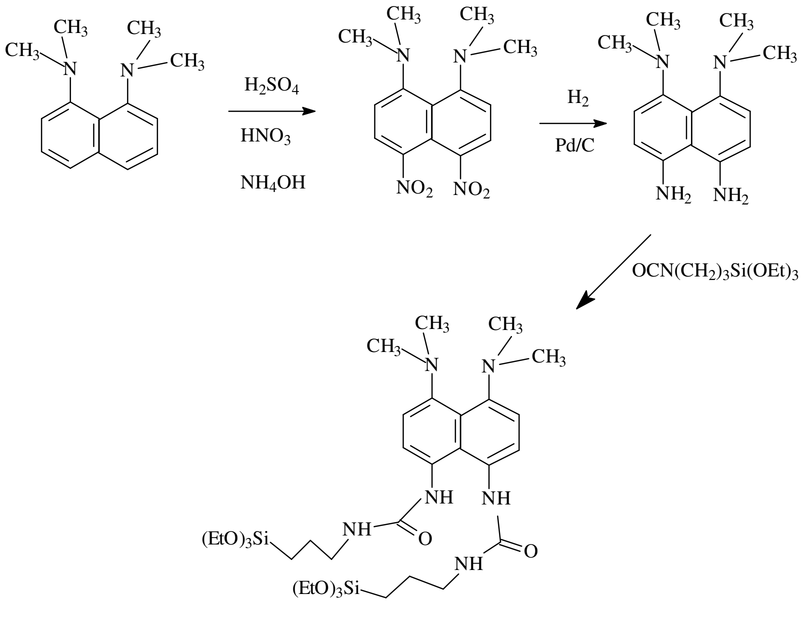
- ***A description of the main S&T results/foregrounds (not exceeding 25 pages)***

During the first year of the HYMUCAT project, the experimental work has been devoted to the synthesis and characterisation of organic-inorganic hybrid catalysts containing proton sponge, in particular 1,8-bis(dimethylamino)naphthalene (DMAN, scheme 1) into the network of mesoporous non-ordered silica. The work started with the preparation of basic hybrid catalyst to evidence if the proton sponges are suitable organic moieties to confer basic functionalities to a silica support.



Scheme 1 – Scheme of 1,8-bis(dimethylamino)naphthalene (DMAN)

The organic-inorganic hybrid materials with a proton sponge as the organic builder have been synthesized following a fluoride-catalysed sol-gel process, at neutral pH and low temperatures, that avoids the use of structure directing agents (SDAs). The fluoride-catalysed route is simple and low cost and has been successfully used as a "one-pot" method to synthesise organic-inorganic non-ordered porous materials when functionalized silanes are used during the synthesis process. To be a part of the inorganic network, the DMAN has been modified and two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS) through sol-gel routes have been introduced. The DMAN was functionalized by the insertion of nitro groups in the naphthalene molecule using a mixture of HNO_3 and H_2SO_4. The reaction mixture was neutralized with aqueous ammonium hydroxide. The nitro groups were reduced to the amino in H_2 using Pd/C as catalyst and, finally, the amino-DMAN was silylated using 3-(triethoxysilyl)propylisocyanate to obtain DMAN-Si. All the steps of DMAN functionalisation (Scheme 2) were followed by liquid (^1H, ^{13}C, ^{29}Si) NMR. The ^1H NMR spectrum of the silylated DMAN shows a signal at 6.11 ppm assigned to NH groups attached to aromatic rings.



Scheme 2 – Scheme of the DMAN functionalization

This method has allowed to directly introduce the functionalized DMAN builders into the walls of mesoporous silica by one-pot synthesis.

Tetramethyl orthosilicate (TMOS) and disilylated-DMAN (DMAN-Si) were mixed in methanol at 298K. After dissolution of precursors, a water solution of NH_4F was added under vigorous stirring. The final reaction mixture has the following molar composition:

$$1\text{-}x\ SiO_2 : x\ \text{DMAN-Si} : 4\ MeOH : 4\ H_2O : 0.00313\ NH_4F$$

Hydrolysis and condensation of the silicon precursor was carried out under vigorous stirring at 298K until gelation occurred. Then, the gel was aged at 36°C for 24h and finally dried at 60°C for 24 h. Several hybrids with different DMAN loadings, from x=0.001 to x= 0.1, were synthesized. Additionally, DMAN, without terminal silyl groups, was physically adsorbed during the NH_4F co-condensation route of the silica, and pure SiO_2 was also produced following the NH_4F sol-gel route. Leaching tests were also performed by washing the hybrids for 3 days in ethanol at 298K.

All the hybrids were characterized by N_2 adsorption at 77K, thermogravimetric and elemental analyses, solid state MAS-NMR (^{13}C, ^{29}Si) and FTIR spectroscopy.

The presence of the organic moieties in the resultant solids was evidenced by means of elemental analysis. The C/N/H ratio confirms that the organic corresponds to the proton sponge and no decomposition of the organic has occurred during the synthesis. The organic content in the hybrids varies from 1.57% for the low loading to 16.4% for the highest loading DMAN-hybrid, with a correlation between the amount of disilylated DMAN in the gel and the amount incorporated in the solid.

Thermogravimetric analysis was performed in order to gain insight, not only on the organic content presents in the solids, but also on the thermal stability of the inserted DMAN units with respect the pure DMAN or the simply adsorbed DMAN on SiO_2. Thus, the weight loss (TGA) and the DTA of the DMAN-hybrids, the adsorbed DMAN sample and pure DMAN molecule are reported in Figure 1. The first weight loss of the one-pot hybrid is observed at around 80-100°C and can be associated to the removal of physisorbed water. At higher temperature, the main weight loss is associated to the organic moieties (DMAN) and the organic content calculated between 150°C and 500°C, is similar to the results obtained by elemental analysis. The DTA curves reveal that when DMAN is simply adsorbed on silica (curve d), the decomposition of DMAN occurs at ca. 230°C, whilst the functionalized DMAN in the hybrid (curve c) decomposes at higher temperature, close to 300°C. From these data, it can be concluded that the DMAN incorporated in SiO_2 framework (curve c) is more stable than DMAN adsorbed on SiO_2 (curve d) and much more stable than pure DMAN (curve e), that decomposes at ca. 150°C.

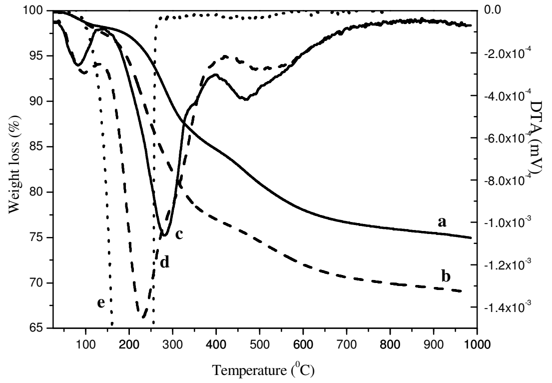


Fig.1 – TGA and DTA curves of DMAN-hybrid (curves a and c) and simply adsorbed DMAN on SiO_2 (curves b and d). Curve e: DTA of pure DMAN.

To confirm that DMAN is chemically stabilized and covalently bounded into the silica framework of the one-pot hybrid materials, leaching tests were performed both on the DMAN- hybrids and on the sample prepared by adsorbing DMAN on SiO_2. For doing that, the as-synthesized materials were washed with ethanol at 298K for 3 days to remove the un-reacted DMAN species. In Table 1, the organic content of the as-synthesized samples and after the leaching tests of the hybrids and of the sample with physically adsorbed DMAN is reported.

The organic content (EA%), after the washing treatment in ethanol, clearly shows that in the case of physically adsorbed DMAN sample, the loss is ca. 9% (i.e. ~ 60% of the total amount of organic), whilst in the case of the DMAN-hybrids, the loss of organic content goes from 0.3% to 2% for the low and highly loaded materials. This result confirms that in the hybrids most of the functionalized DMAN is attached covalently to silica and not simply adsorbed. The efficiency of the covalent DMAN incorporation in the silica matrix was evaluated from the N% content, measured by elemental analysis of the as-synthesized and washed hybrids (Table 1). The efficiency of organic incorporation decreases when increasing the DMAN loading. This means that a high loading in the synthesis gel does not ensure a higher level of organic incorporation into the silica network.

Samples with different DMAN loading	As-synthesized hybrids	Washed hybrids		

	N/%	C/%	H/%	Organic content (EA)/%	N/%	C/%	H/%	Organic content (EA)/%	Organic loss/%	Efficiency of DMAN incorporation/%
DMAN/SiO_2-0.1	0.07	0.7	0.8	1.57	0.067	0.5	0.7	1.267	0.30	96
DMAN/SiO_2-0.2	0.20	1.4	0.7	2.30	0.19	1.2	0.6	1.99	0.31	95
DMAN/SiO_2-0.5	0.30	1.8	0.8	2.90	0.27	1.6	0.7	2.57	0.33	90
DMAN/SiO_2-1	0.50	2.2	0.9	3.60	0.44	1.7	0.7	2.84	0.76	88
DMAN/SiO_2-5	2.20	8.5	1.9	12.6	1.50	7.4	1.9	10.7	1.9	68
DMAN/SiO_2-10	3.00	11.2	2.2	16.4	2.00	10.3	2.1	14.4	2.0	66
ADS-DMAN/SiO_2	3.40	18.0	2.9	24.3	2.10	10.7	2.4	15.2	9.10	-

Table 4. Elemental analysis after the leaching tests and efficiency of DMAN incorporation into the SiO_2 network.

These results confirm that DMAN is intact into the hybrid materials and that most of the organic is not physically but it is covalently attached. However, to reconfirm the integrity of the organic molecule in the final material, and specially the covalent insertion of the proton sponge into the network of the silica, NMR spectroscopy was used. Specifically, the ^{13}C CP/MAS NMR spectra of the hybrids (Fig. 2, curves a and b) present the typical signals of DMAN (curve c) confirming the integrity of the organic moiety after the synthesis process. In the range between 150-110 ppm should appear the ^{13}C signals due to naphthalene groups, while the peaks due to methyl groups belonging to $N(CH_3)_2$ should appear at 40-45 ppm. Indeed, the above signals are clearly seen in the ^{13}C spectra of the hybrid materials (curves a and b). However, in the hybrids, several other signals at 158.5, 61.3, 22.7 and 10 ppm also appear, that do not correspond to DMAN molecule. Then, the peak at 158.5 ppm is assigned to C=O groups and the other signals are due to C1 (10 ppm), C2 (22.7 ppm) C3 (61.3 ppm) of the $–CH_2$ groups belonging to the terminal silyl fragments of the functionalized DMAN (see the inset in Fig.2 for the labels of C atoms).
The presence of these signals also confirm that the DMAN molecules were successfully functionalized. The different intensity of the ^{13}C signals in the hybrids spectra reflects the different DMAN loadings.

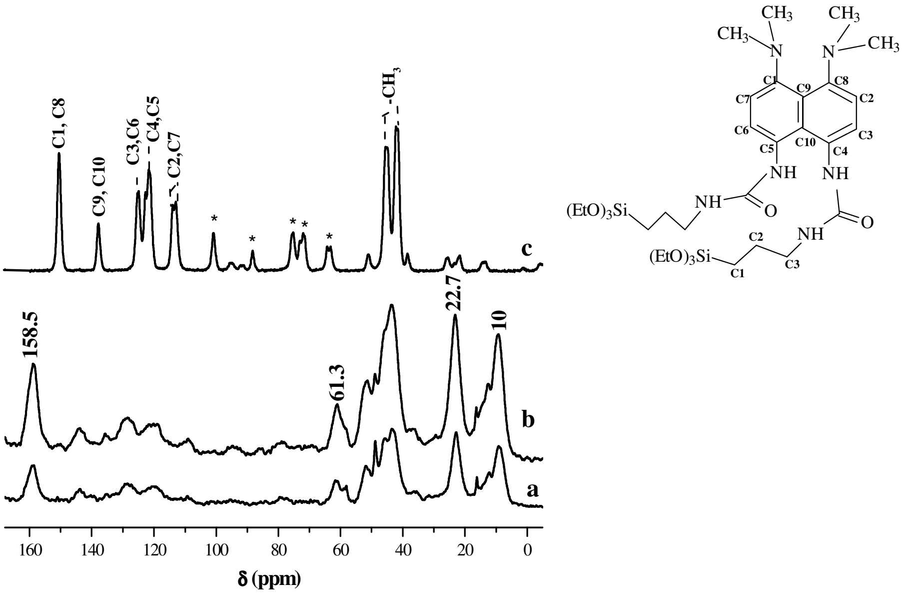


Fig. 2· ^{13}C-CP MAS NMR of DMAN/SiO$_2$-5 (curve a), DMAN/SiO$_2$-10 (curve b) and pure DMAN (curve c). * spinning bands.

^{29}Si MAS NMR spectra confirm that the DMAN fragments are not only intact after the synthesis of the hybrids but are also incorporated covalently into the non-ordered porous network bounded to inorganic silica units. In fact, the ^{29}Si MAS NMR spectra of the hybrids (Fig.3) exhibit bands from -50 ppm to -80 ppm assigned to T-type silicon species having a Si-C bond, being then confirmed that the hydrolysis and policondensation of silylated-DMAN occurs through alkoxy terminal groups of the silylated moieties. The intensity of the band corresponding to T-type silicon atoms is higher when the larger is the content of organic linkers into the hybrid frameworks. In addition, three peaks at -92, -100 and -110 ppm are also present, due to Q^2 ($Si(OH)_2(OSi)_2$), Q^3 ($Si(OH)(OSi)_3$) and Q^4 ($Si(OSi)_4$) silicon units respectively. The incorporation of the disilylated DMAN into the framework of non-ordered mesoporous silica is also confirmed by the comparison of ^{29}Si NMR spectra of the hybrids with the pure disilylated DMAN (see inset of Fig.3). The DMAN-Si exhibits one peak centered at -45.7 ppm typical of Si-C bonds. When the DMAN-Si builders are finally inserted into the silica framework, the signal due to silicon atoms bounded to carbon units shifted in the range -60 to -80 ppm, supporting the covalent incorporation of the disilylated organic species into the silica framework.

The integration of T and Q peaks in the ^{29}Si BD/MAS NMR spectra was performed to calculate the T/(Q+T) ratio and to evaluate the number of functionalized silicon atoms in the hybrids (Table 2). The Si_{func}/Si_{tot} ratio evidences that DMAN/SiO$_2$-10 has double Si atoms functionalized by organic linkers (~10%) than DMAN-SiO$_2$-5 (~5%), as expected considering the DMAN loading.

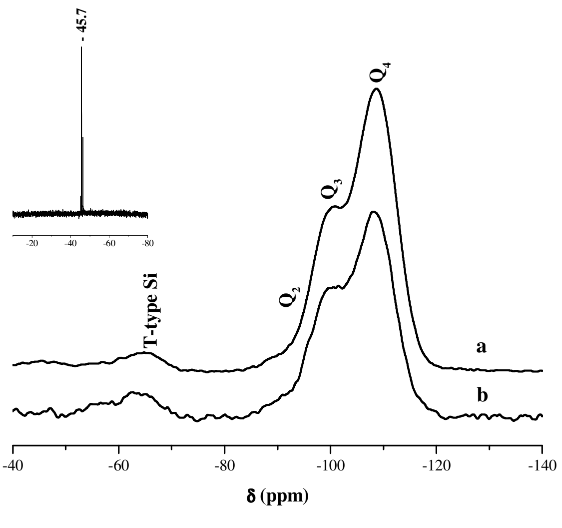


Fig. 3 ^{29}Si-BD MAS NMR of DMAN/SiO$_2$-5 (curve a) and DMAN/SiO$_2$-10 (curve b). In the inset, the ^{29}Si NMR spectrum of DMAN-Si is reported.

Table 2. Functionalized silicon atoms in the hybrids.

Samples	Si_{func}/Si_{tot} (NMR)
DMAN/SiO_2-5	0.048
DMAN/SiO_2-10	0.095

FTIR spectroscopy was used to investigate the surface vibration modes, confirming unambiguously the presence and integrity of organic DMAN builders in the network of the hybrid materials. In Fig. 4A, the FTIR spectra of DMAN/SiO_2-10 (curve a) and DMAN/SiO_2-5 (curve b), outgassed at 100ºC to remove the adsorbed water, are reported. The spectrum of pure DMAN (curve c) is also reported for comparison. The spectra of the hybrids differ on the intensity of the bands due to the organic moieties. In the FTIR spectra of DMAN/SiO_2 hybrids outgassed at 100°C (curves a and b), the band at 2945 cm^{-1}, assigned to the C-H stretching mode of the $–CH_3$ in $N(CH_3)_2$ groups, and the band at 3045 cm^{-1} (weak), due to the -C-H stretching mode of the aromatic ring, can be observed. The intense and broad absorption centered at 3370 cm^{-1} is due to the O-H stretching mode of Si-OH groups interacting with chemisorbed water or via H-bond. In the low frequency region, the bands at 1530 cm^{-1} and at lower wavenumber are associated to the stretching mode of the aromatic C=C, whilst the band at 1690 cm^{-1} is due to the stretching mode of the carbonyl group present in the functionalized DMAN. All these bands confirm the presence and the integrity of the functionalized DMAN into the hybrids. In Fig. 4B, the FTIR spectra of DMAN/SiO_2-5 upon thermal treatment are reported. When chemisorbed water is removed by outgassing at 200°C (curve b), a band at 3430 cm^{-1} is visible and can be assigned to the stretching mode of N-H groups present in the functionalized DMAN fragments, in addition the band due to free silanols (3745 cm^{-1}) becomes evident. Upon outgassing at 400°C (curves c), the bands due to the organic moieties are still present but with lower intensity. In fact, at 400°C there is still a fraction of undecomposed organic units that have also been detected by DTA analysis (Fig.1).

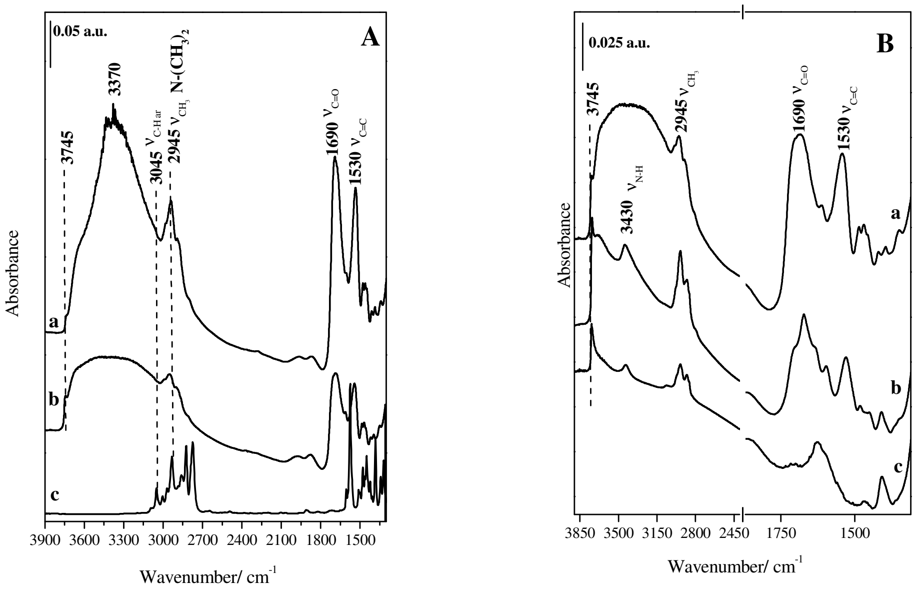


Fig. 4 Section A: FTIR spectra of DMAN/SiO_2-10 (curve a) and DMAN/SiO_2-5 (curve b) upon outgassing at 100°C. The spectrum of pure DMAN (curve c) is also reported.
Section B: FTIR spectra of DMAN/SiO_2-5 upon outgassing at 100°C (curve a), 200°C (curve b) and 400°C (curve c).

The textural properties measured by N_2 adsorption are reported in Table 3 and compared to a pure SiO_2 and to DMAN adsorbed on SiO_2 (ADS-DMAN/SiO_2) sample. The BET specific surface area (SSA) of the hybrids varies from 763 to 329 m^2 g^{-1} depending on the DMAN loading. A marked decrease in the SSA can be observed when the structural organic content is higher, probably due to the more difficult structuration of DMAN fragments into the porous framework. However, in all cases, the SSAs and pore volumes obtained are in the mesoporous range, being practically negligible the microporous contribution.

Table 3. Textural properties of the DMAN/SiO_2 hybrids.

Samples	SSA_{BET} SSA(m^2/g)	External SA (m^2/g)	Pore size Å	Pore volume cm^3/g
Pure SiO_2	797	791	27	0.3
DMAN/SiO_2-0.1	763	752	28	0.3
DMAN/SiO_2-0.2	752	750	28	0.28
DMAN/SiO_2-0.5	725	718	27	0.28
DMAN/SiO_2-1	600	592	26	0.23
DMAN/SiO_2-5	455	450	30	0.24
DMAN/SiO_2-10	329	320	30	0.17
ADS-DMAN/SiO_2	150	150	49	0.15

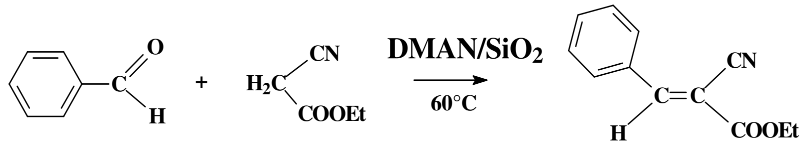
The pore distribution of the DMAN/SiO_2 samples are narrow and the mean pore diameters are centered at 30 Å, while the ADS-DMAN/SiO_2 sample shows a broader distribution. The physically adsorbed DMAN on silica has a low SSA and pore volume compared to the other hybrids and shows a broad distribution in the pore sizes, due probably to inhomogeneous distribution and a partial blockage of porous by the adsorbed DMAN.
All samples show an increase of the specific surface area upon the washing treatment with ethanol (Table 4). This observation indicates that after the one-pot synthesis there are some DMAN molecules that are simply adsorbed inside the mesopores, partially blocking the channels. The adsorbed molecules are removed after washing and consequently the specific surface area increases.

Table 3. Textural properties of the DMAN/SiO_2 hybrids after the leaching tests

Samples	SSA_{BET} (m^2/g)	Pore size Å	Pore volume cm^3/g
DMAN/SiO_2-5			
as-synthesized	455	30	0.24
washed	569	30	0.26
DMAN/SiO_2-10			
as-synthesized	329	30	0.17

washed	453	30	0.21
ADS-DMAN/SiO_2			
as-synthesized	150	49	0.15
washed	268	49	0.19

The basicity of the hybrid materials synthesized, containing proton sponges as catalytic organic builders, was tested for the Knoevenagel reaction of benzaldehyde (1) and ethyl cyanoacetate (2) ($pK_a = 9$) with ethanol at 333K (Scheme 3). A polar protic solvent, such as ethanol, is necessary for the formation of the trans-α-ethyl-cyanocinnamate (product 3). The Knoevenagel condensation of carbonyl compounds is widely used in organic synthesis to produce important intermediates and end products for perfumes, pharmaceutical and polymers.The reaction can be catalyzed by strong and weak basicities depending on the level of activation of the reactant containing methylenic activated groups, being therefore an adequate reaction for comparing catalysts with different basicities. The kinetics of the Knoevenagel reaction is generally considered to be a first order reaction with respect to each reactant and the catalysts.



1 **2** **3**

Scheme 3 – Scheme of the Knoevenagel reaction of benzaldehyde and ethyl cyanoacetate

The yields for product (3) obtained with the DMAN/SiO_2 hybrids are reported in Fig.5. The DMAN/SiO_2-0.5 and DMAN/SiO_2-0.2 hybrids show better catalytic performances than the hybrids with higher DMAN loadings. In fact, 100% conversion is achieved after 6h of reaction, with 100% of selectivity. Using DMAN/SiO_2-1, 98% yield was produced; whilst using DMAN/SiO_2-5 and DMAN/SiO_2-10, 93% and 78% conversion was respectively obtained at the same reaction time. This behavior suggests that a high concentration of basic sites has a detrimental effect on the catalytic activity. In fact, well isolated and separated basic sites are usually needed to have a good base catalyst. The activity of the very low loading hybrid (DMAN/SiO_2-0.1) lies between DMAN/SiO_2-5 and DMAN/SiO_2-10, meaning that, in this sample, the concentration of the basic sites is too low to perform a high catalytic activity. In addition, DMAN/SiO_2-0.5 shows a higher yield at low reaction time and reaches the yield of homogenous DMAN after 4h reaction. The Turnover frequencies calculated after 1h reaction, reported in Table 4, follow the trend observed in Fig.5, in fact the DMAN/SiO_2-0.5 hybrid shows the highest TOF that is close to the one of the homogeneous DMAN.

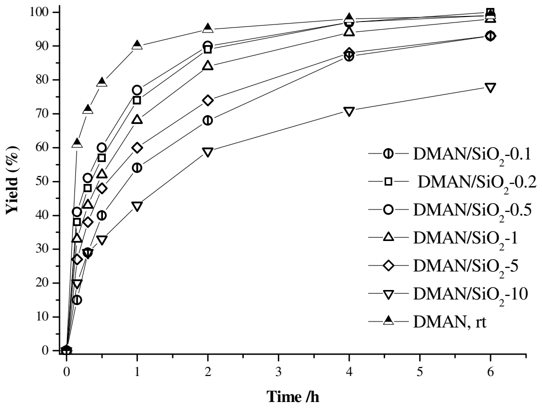


Fig. 5 - Knoevenagel condensation of benzaldeyde with ethyl cyanoacetate using heterogeneous hybrid catalysts at 333K with ethanol. The yield of homogeneous DMAN at room temperature is also reported for comparison.

Table 4. Initial kinetic constant calculated at 10 min and Turnover frequencies (TOF) calculated at 1h.

Catalysts	Yield (%) 2h	 6h	Initial kinetic constant/min	TOF/min
DMAN/SiO$_2$-0.1	54	93	0.7	90
DMAN/SiO$_2$-0.2	74	100	3.8	123
DMAN/SiO$_2$-0.5	77	100	4.1	128
DMAN/SiO$_2$-1	68	98	3.3	113
DMAN/SiO$_2$-5	60	93	2.7	100
DMAN/SiO$_2$-10	43	78	2	72
Pure DMAN	90	100	6.1	150

Catalyst deactivation and reusability was studied with DMAN/SiO$_2$-0.5. The yields after recycling the catalyst are reported in Fig. 6 after 2h and 6h of reaction. The yields calculated after 2h evidence that there is a slightly decrease after each catalytic runs, whilst after 6h, the yields are almost similar for the first three catalytic runs and then decreased. The elemental analysis performed on the used catalyst, after washing with CH_2Cl_2, reveals that no leaching has occurred from 1 to 3 runs whilst after the third run 0.2% of leaching, due to DMAN loss, has occurred explaining the decrease in the observed yield. The leaching observed after the third run, could be due to the temperature and solvent effect.

From the results obtained, it appears that the mesoporous hybrid materials, synthesized in absence of SDA by means of a simple procedure and containing DMAN as organic building block, offer possibilities for base catalysis.

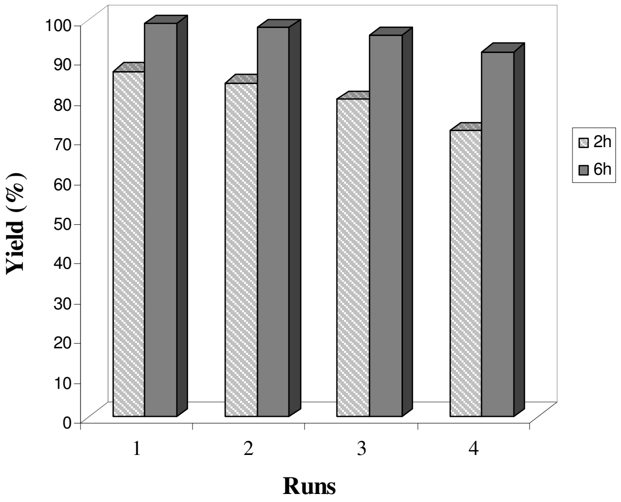
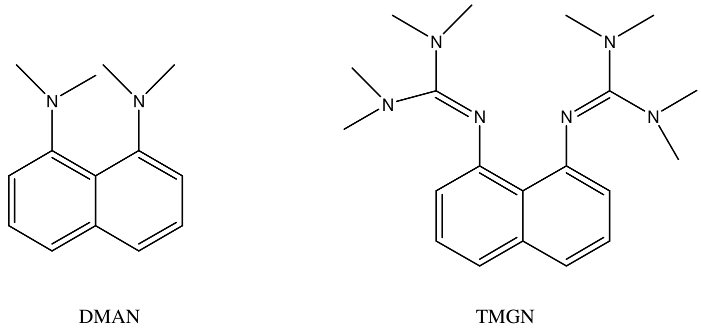


Fig. 6 – Recycling tests of Knoevenagel condensation of using DMAN/SiO_2-0.5 with ethanol at 333K. The yield (%) is reported after 2h and 6h of reaction.

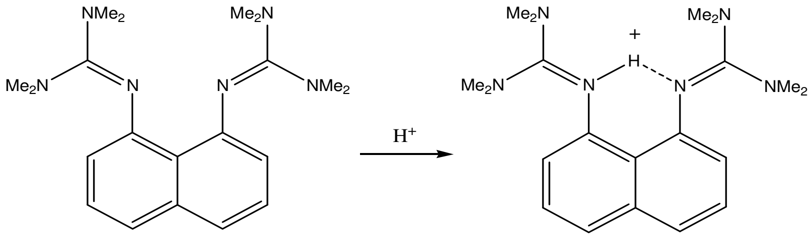
Due to the promising catalytic performances of DMAN-hybrids as basic heterogeneous catalysts, the research activity was also focused on the use of a novel proton sponge named 1,8-bis(tetramethylguanidino) naphthalene (TMGN, scheme 4), recently obtained with an experimental pK_a of 25, as building block to produce organic-inorganic silica-based mesoporous hybrid materials with strong basic properties.

TMGN, a neutral organic superbase, combines the properties of guanidine and the properties of proton sponges. The term superbase was introduced by Caubère: "*superbase does not mean a base is thermodynamically and/or kinetically stronger than another; instead it means that a basic reagent is created by combining the characteristic of several different bases*".



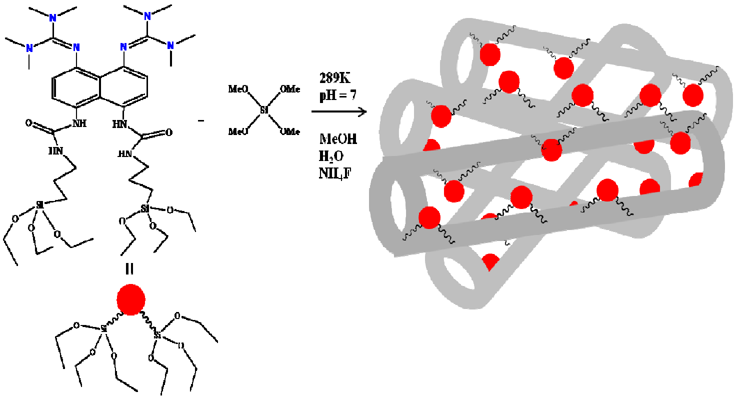
Scheme 4 - 1,8-bis(dimethylamino)naphthalene (DMAN) and 1,8-bis(tetramethylguanidino)naphthalene (TMGN).

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 $[TMGN]H^+$ (scheme 5).



Scheme 5 - Intramolecular hydrogen bond (IMHB) formation in TMGN.

To become part of the silica network of a mesoporous material, the organic bases have to be functionalized with two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS), through a sol-gel route. The level of functionalization of the TMGN was followed using liquid NMR. More specifically, the ^1H NMR spectrum of the silylated TMGN shows a signal at 6.11 ppm assigned to NH groups attached to aromatic rings. The incorporation of disilylated-TMGN in the silica mesoporous framework was carried out by one-pot synthesis following a NH_4F-catalyzed sol-gel route at neutral pH and room temperature, without the use of structure directing agents. These soft synthetic conditions allow binding covalently the functionalized organic fragments within the walls of non-ordered 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 has two terminal reactive silyl groups able to perform hydrolysis and co-condensation with a conventional organosilane (TMOS), used as silicon source, as it is represented in scheme 6. Hybrids with low organic loading have been synthesised to obtain isolated and well dispersed basic sites.



Scheme 6 - Schematic representation of the synthesis of the TMGN/SiO_2 hybrids

The properties and the catalytic performances of the TMGN-based hybrids were compared to the ones observed for DMAN-based hybrid materials. The presence of the organic moieties in the hybrids was evidenced by means of elemental analysis. Then, to confirm that TMGN is not just adsorbed but chemically stabilized and covalently bounded into the silica framework, leaching tests were performed by washing the as-synthesized hybrids with ethanol at 298K for 3 days and then performing a series of spectroscopic analysis. The C, H, N content and the calculated percentage in weight of the organic species present into the as-synthesized samples and in the hybrids after the leaching tests and the efficiency of the covalent TMGN/DMAN incorporation in the silica matrix, evaluated from the organic content of the as-synthesized and washed hybrids, are reported in Table 5.

The C/N/H ratio, obtained by elemental analysis, confirms that the organic corresponds to the TMGN or DMAN builders and that no decomposition of the organic has occurred during the synthesis. In the TMGN/SiO$_2$ hybrids, the organic content is larger than the organic content of DMAN/SiO$_2$, due to the higher molecular weight of the former organic superbase. In the washed hybrids, the loss of organic content goes from 0.4% for TMGN/SiO$_2$ hybrids and to 0.3% for DMAN/SiO$_2$ hybrids, confirming that in the hybrid materials most of the functionalized TMGN or DMAN is attached to silica, being the incorporation of the organic moiety very efficient under our experimental conditions.

Table 5. Elemental analysis of the as-synthesized hybrids 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$_2$-0.5	0.44	2.6	1.2	4.24	0.2	2.5	1.1	3.80	0.44	89
TMGN/SiO$_2$-0.2	0.20	1.7	1.1	3.00	0.12	1.6	0.9	2.62	0.38	87
DMAN/SiO$_2$-0.5	0.30	1.8	0.8	2.90	0.19	1.6	0.7	2.57	0.33	88
DMAN/SiO$_2$-0.2	0.20	1.4	0.7	2.30	0.17	1.2	0.6	1.97	0.31	86

Thermogravimetric analysis was performed to study 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 derivates (DTA) for the TMGN/SiO$_2$ and DMAN/SiO$_2$ hybrids and pure TMGN and DMAN molecules are reported in Figure 7.

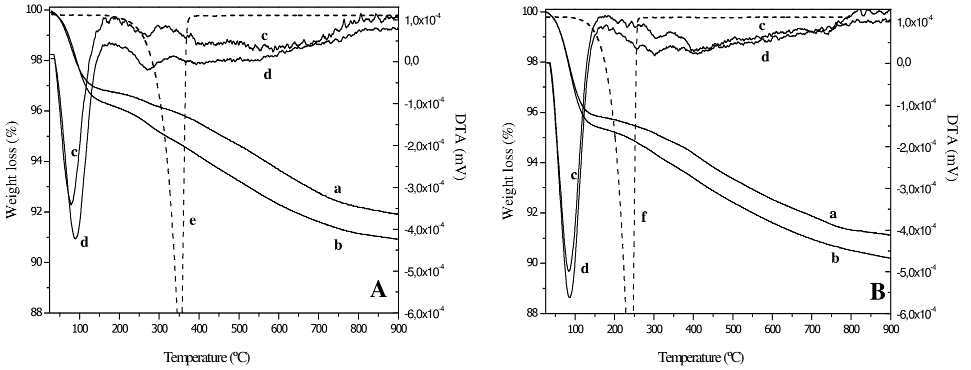


Fig. 7 - Section A: TGA and DTA curves of TMGN/SiO$_2$-0.2 (curves a and c) TMGN/SiO$_2$-0.5 (curves b and d). Section B: TGA and DTA curves of DMAN/SiO$_2$-0.2 (curves a and c) and DMAN/SiO$_2$-0.5 (curves b and d). DTA of pure TMGN (curve e) and DMAN (curve f) are also reported.

The first weight loss for the hybrids is observed at around 80-150°C and can be associated to the removal of physisorbed water and methanol. At higher temperature, the main weight loss is associated to the organic moieties (TMGN or DMAN). The DTA curves reveal that pure TMGN (Section A curve e) decomposes at higher temperature (350ºC) than DMAN (250ºC, 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 around 280ºC. From the DTA curves, it is possible to observe that DMAN/SiO_2 loses a higher quantity of water with respect to TMGN/SiO_2, suggesting that DMAN hybrids are more hydrophilic than the TMGN ones, due to the lower organic content present into the silica (Table 5).

To confirm that TMGN and DMAN are covalently inserted into the network of the mesoporous silicas, solid state NMR spectroscopy was used. More specifically, the ^{13}C CP/MAS NMR spectra of the hybrids (Fig. 8, curves a and b) present the 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 ^{13}C signals due to naphthalene groups should appear, very weak signals are detected due to 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 Fig. 9). In fact weak bands at 3045 and at 1530 cm^{-1}, due to the stretching mode of C-H and C=C of aromatic rings respectively, are present. These features indicate that the basic organic molecules are preserved in the mesoporous hybrids. In addition, to the ^{13}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 158 ppm is assigned to C=O groups and the other signals are due to C1* (10 ppm), C2* (22.7 ppm) and C3* (61.3 ppm) of the $-CH_2$ groups belonging to the terminal propyl-silyl fragments of the functionalized TMGN and DMAN (see the inset in Fig.8 for the labels of C atoms). In the case of TMGN/SiO_2-0.5 hybrid, a signal at 159 ppm is also visible that can be assigned to the carbon belonging to the guanidine functions. The presence of all these signals also confirms that the TMGN and DMAN molecules were successfully functionalized.

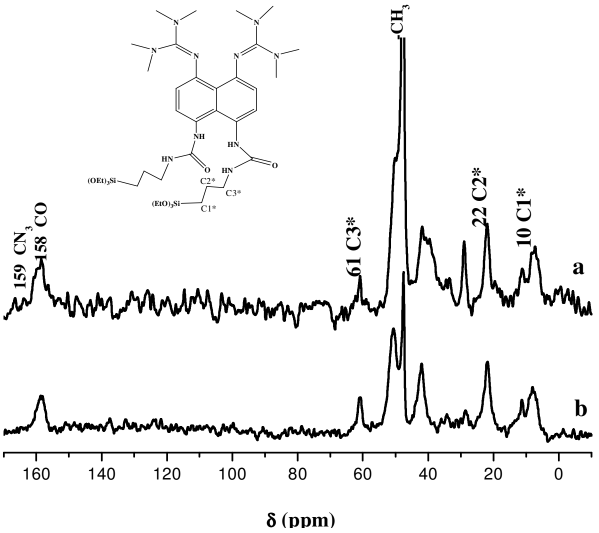


Fig. 8 - ^{13}C-CP MAS NMR of TMGN/SiO_2-0.5 (curve a), DMAN/SiO_2-0.5 (curve b).

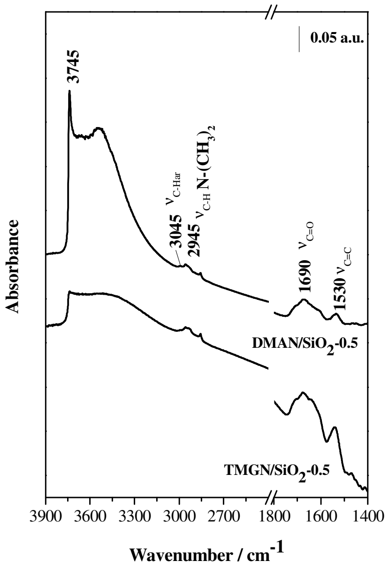


Fig. 9- FTIR spectra of TMGN/SiO_2-0.5 and DMAN/SiO_2-0.5 upon outgassing at 100°C.

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 non-ordered porous network bounded to inorganic silica units, the hybrids were characterized by ^{29}Si-BD MAS NMR spectroscopy. The spectra of the hybrids (Fig. 10) show three peaks at -92, -100 and -110 ppm, due to Q^2 ($Si(OH)_2(OSi)_2$), Q^3 ($Si(OH)(OSi)_3$) and Q^4 ($Si(OSi)_4$) silicon units respectively. The typical signals from -50 ppm to -80 ppm, assigned to T-type silicon species having a Si-C bond, are not visible in the TMGN/SiO_2-0.5 and DMAN/SiO_2-0.5, due to the low organic loading present in these hybrids, whilst they are well visible when the organic loading is higher (DMAN/SiO_2-10, curve c). To identify better the T-type silicon species present in the hybrid materials, ^{29}Si-CP MAS NMR spectra have also been recorded (inset of Fig. 10). There two bands at -40 and – 66 ppm, assigned to T-type silicon species having a Si-C bond for TMGN/SiO_2-0.5 (curve a') and DMAN-SiO_2-0.5 (curve b'), are present. The signal at -66 ppm confirms that the hydrolysis and policondensation of silylated-TMGN and DMAN has occurred through alkoxy terminal groups of the silylated moieties. Moreover, the as-synthesized hybrids show also a peak at -40 ppm, that 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 non-ordered mesoporous silica is also confirmed by comparing the ^{29}Si NMR spectra of the hybrids and the pure disilylated TMGN (see inset of Fig. 10). 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 due to silicon atoms bounded to carbon units shifted in the range -60 to -80 ppm, supporting the covalent incorporation of the disilylated organic species into the silica framework.

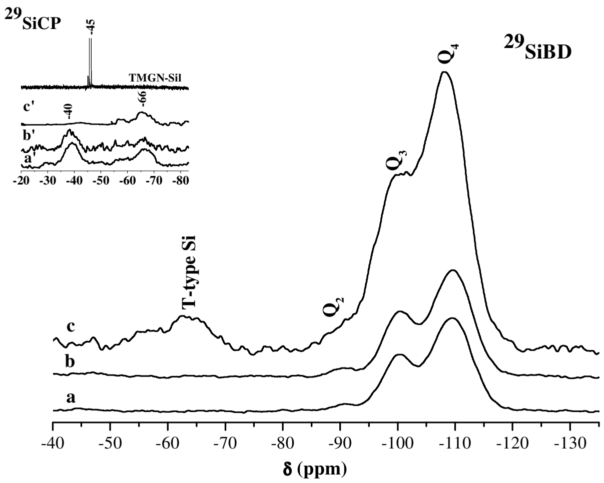


Fig. 10 - ^{29}Si-BD MAS NMR of TMGN/SiO$_2$-0.5 (curve a), DMAN/SiO$_2$-0.5 (curve b) and DMAN/SiO$_2$-10 (curve c). In the inset, the ^{29}Si-CP NMR of TMGN/SiO$_2$-0.5 (curve a'), DMAN/SiO$_2$-0.5 (curve b'), TMGN/SiO$_2$-0.5 after washing (curve c') together with pure TMGN-Sil are reported.

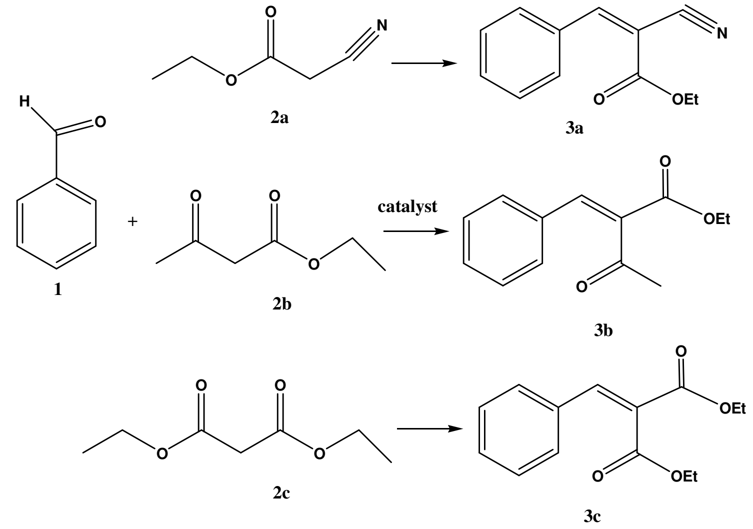
The textural properties of the hybrids, measured by N$_2$ adsorption at 77K, are reported in Table 6. The BET specific surface area (SSA) of the TMGN/SiO$_2$ is around 800 m^2 g^{-1}, whilst in the case of DMAN/SiO$_2$ is ca 750 m^2 g^{-1}. However, in all cases, the SSAs and pore volumes obtained are in the mesoporous range, being practically negligible the microporous contribution (Table 6). The pore distribution of the hybrid samples are narrow and the mean pore diameters are centered at 40 Å for TMGN/SiO$_2$ hybrids, while DMAN/SiO$_2$ shows a distribution centered around 30 Å, being also larger the total pore volume of TMGN/SiO$_2$. These features could be due to the larger molecular dimensions of TMGN respect to DMAN proton sponge.

Table 6. Textural properties of the TMGN/SiO$_2$ and DMAN/SiO$_2$ hybrids

Samples	SSA$_{BET}$ SSA(m^2/g)	External SA (m^2/g)	Pore size Å	Pore volume cm^3/g
Pure SiO$_2$	797	791	27	0.3
TMGN/SiO$_2$-0.2	795	790	41	0.8
TMGN/SiO$_2$-0.5	792	787	39	0.7
DMAN/SiO$_2$-0.2	752	750	28	0.28
DMAN/SiO$_2$-0.5	725	718	27	0.28

To investigate the accessibility to the reactants and the activity of the organic superbase that has been inserted into the wall of the mesoporous silica, the catalytic performance of the hybrid materials was tested for the 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$_2$ and with the activity of the molecular proton sponges TMGN and DMAN in homogeneous phase.

The Knoevenagel reaction between benzaldehyde (1) and different methylene compounds (scheme 7), with increasing pK_a values, was performed on TMGN/SiO_2 and DMAN/SiO_2 hybrids.



Scheme 7. Scheme of the Knoevenagel reaction of benzaldehyde and methylene compounds.

Ethyl cyanoacetate (2a ECA, pK_a ~ 9), ethyl acetoacetate (2b EAA, pK_a ~10) and diethyl malonate (2c DEM, pK_a ~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-α-ethyl-cyanocinnamate (product 3a), whilst toluene was used as solvent when Knoevenagel condensation was performed using EAA and DEM.

In Fig. 11, the yields for product (3a) obtained with the TMGN/SiO_2 hybrids (Section A) and DMAN/SiO_2 hybrids (Section B) are reported, compared to the yields of pure TMGN and DMAN. TMGN/SiO_2-0.5 is the most active catalyst and reaches the yield of homogeneous TMGN in only 1 h with 100% of selectivity. In the case of DMAN-containing hybrids, the yield observed is lower, and both the catalysts reach the yield of homogeneous DMAN after 4h reaction time. The Turnover frequencies calculated after 30 min and the initial rate are reported in Table 7. TMGN/SiO_2-0.5 hybrid shows the highest TOF, close to the one of the homogeneous base.

Fig. 11 - Knoevenagel condensation of benzaldeyde with ECA using TMGN/SiO$_2$ (Section A) and DMAN/SiO$_2$ (Section B) hybrids at 333K with ethanol and using 1 mmol% of proton sponges, in the silica, respect to ECA. The yields of homogeneous TMGN and DMAN are also reported for comparison.

Table 7. Yields, Turnover frequencies (TOF) calculated at 30 min and initial rate.

Catalysts	Yield (%) 30 min	TOF (min^{-1})	r_0 (min^{-1})
Pure TMGN	77	256	1.56
TMGN/SiO$_2$-0.5	69	230	1.17
TMGN/SiO$_2$-0.2	63	210	0.95
Pure DMAN	75	250	1.15
DMAN/SiO$_2$-0.2	60	200	0.82
DMAN/SiO$_2$-0.5	56	187	0.48

When more demanding reactants (EAA and DEM) were used and the Knoevenagel reactions were carried out at 353K and 383K respectively using toluene as solvent, TMGN/SiO$_2$-0.5 hybrid displays higher yield towards the desired products (3b and 3c) that the DMAN/SiO$_2$ hybrid material (Fig 12 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 8, evidence the superior activity of the TMGN/SiO$_2$-0.5 hybrid catalyst.

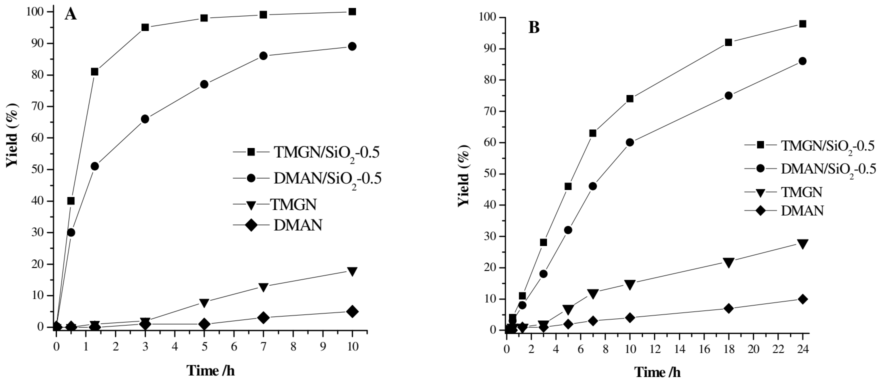


Fig. 12 - Knoevenagel condensation of benzaldehyde with EAA (A) and DEM (B) using TMGN/SiO$_2$-0.5 and DMAN/SiO$_2$-0.5 hybrids and homogeneous TMGN and DMAN at 353K and 383K respectively.

Table 8. Yields, Turnover frequencies (TOF) and initial rate for the Knoevenagel condensation of benzaldehyde with EAA and DEM.

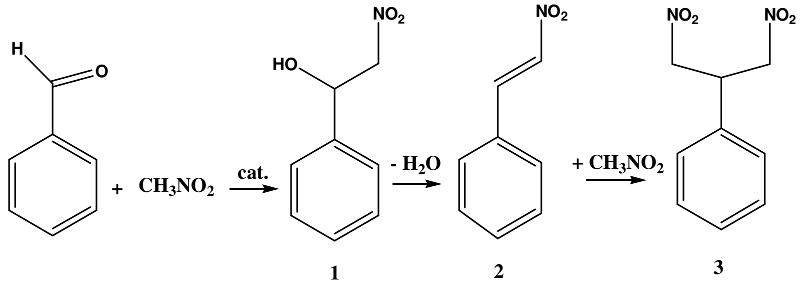
Catalysts	EAA[a]			DEM[b]		
	Yield (%) of 3b	TOF (min^{-1})	r_0 (min^{-1})	Yeld (%) of 3c	TOF (min^{-1})	r_0 (min^{-1})

TMGN/SiO_2-0.5	81	13.5	0.68	28	1.6	0.16
DMAN/SiO_2-0.5	51	8.5	0.35	18	1	0.1

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

The catalytic activity of the heterogeneous hybrids is higher than that observed using homogeneous TMGN and 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 Knoevenagel reaction should be lower than when the reaction occurs in apolar solvent (chlorobenzene, toluene). 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 transiton-state complex should be stabilized by polar surfaces, such as silica surfaces, which lead to an increase in the reaction rate. In this case, only a weak solvent effect is observed and the reaction occurs both in polar and in apolar solvents.

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 8), which are of importance for the synthesis of pharmaceutical products. However, the selective formation of a nitroalkene (product 2 in scheme 8) 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 due to their dimerisation or polymerization (product 3, scheme 8).



Scheme 8. 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_2-0.5 and DMAN-SiO_2-0.5) as they showed the highest activity for the Knoevenagel reaction. From the yields of nitrostyrene (product 2) reported in Fig.13, one can see that the TMGN/SiO_2-0.5 material shows the best catalytic performance and reaches 100% conversion and 100% selectivity towards product 2 in 6h, whilst DMAN/SiO_2-0.5 reaches 80% conversion and 100% selectivity at 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 by-products (1 and 3 in scheme 8) are detected when working in homogeneous phase (see Table 9). In particular, it is possible to observe that at the beginning of the reaction (up to 1h), the homogeneous catalysts show conversions higher than heterogeneous hybrids and that after 1h, the conversions stops and remains almost the same until the end of the reaction. In the Henry reaction, the heterogeneous hybrids catalysts, and in particular TMGN/SiO_2, have evidenced a superior activity both in conversion and selectivity towards the desired product (2) with respect to the homogeneous bases.

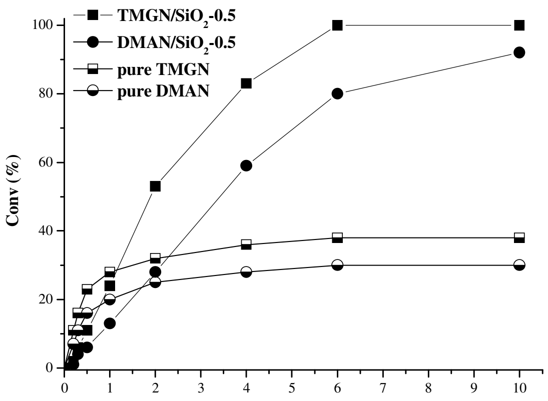


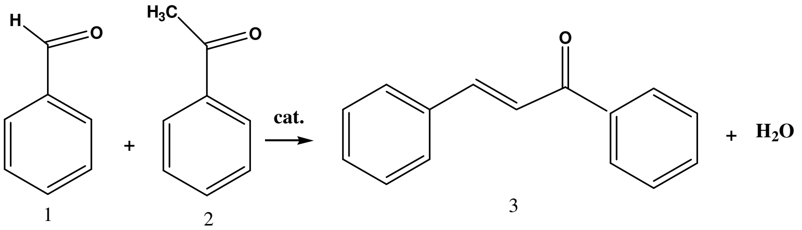
Fig. 13 - Henry condensation of benzaldeyde with nitromethane using TMGN/SiO-0.5 and DMAN/SiO_2-0.5 hybrids at 363K. The conversions of homogeneous TMGN and DMAN are also reported for comparison.

Table 9. Conversion and Yields of products 1, 2 and 3 of the heterogeneous hybrids and homogeneous bases calculated at 6h.

Catalysts	Conv. (%)	Yield (%) 1	Yield (%) 2	Yield (%) 3	TOF (min^{-1})
Pure DMAN	28	11	4	13	2
Pure TMGN	36	13	7	16	2.6
DMAN/SiO_2-0.5	80	0	80	0	2.3
TMGN/SiO_2-0.5	100	0	100	0	4.4

The superior catalytic activity shown by the heterogeneous hybrids respect to the homogeneous ones can be inferred to the active role of surface silanol groups, that are weakly acidic, in performing a cooperative activation of the reactants producing a higher conversion towards the desired product.

Claisen-Schmidt condensation between benzaldehyde (1) and acetophenone (2), produces *trans*-chalcones (Scheme 9), 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 antihyperglycemic agents.



Scheme 9. Scheme of the Claisen-Schmidt reaction of benzaldehyde and acetophenone.

In Fig.14, the yields towards *trans*-chalcone of TMGN/SiO_2 and DMAN/SiO_2 hybrids with reaction time are presented. TMGN/SiO_2-0.5 reaches almost 100% conversion and selectivity in 10h, while 68% yield with 100% selectivity was observed using DMAN/SiO_2-0.5. The TOF values are reported in Table 10. This result confirms that the high catalytic activity of TMGN/SiO_2 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 DMAN containing hybrid, the fact that the pK_a of acetophenone (pK_a = 20) is higher than 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, 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 α-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 DMAN are used. In the case of TMGN hybrid, the role of the silanols is less required since the pK_a of TMGN is very high.

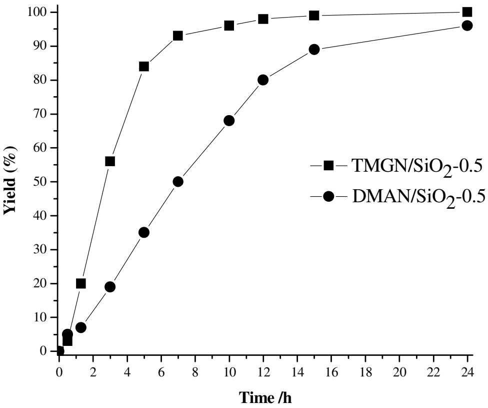


Fig. 14 - Claisen-Schmidt condensation between benzaldehyde and acetophenone using TMGN/SiO_2-0.5 and DMAN/SiO_2-0.5 hybrid materials at 403K.

Table 10. Yields, Turnover frequencies (TOF) calculated at 3h.

Catalysts	Yield (%) 3h	TOF (min^{-1})
TMGN/SiO_2-0.5	56	31
DMAN/SiO_2-0.5	19	11

Catalyst deactivation and reusability was studied with TMGN/SiO_2-0.5 and DMAN/SiO_2-0.5 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 Fig. 15 after 6h 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 due to 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

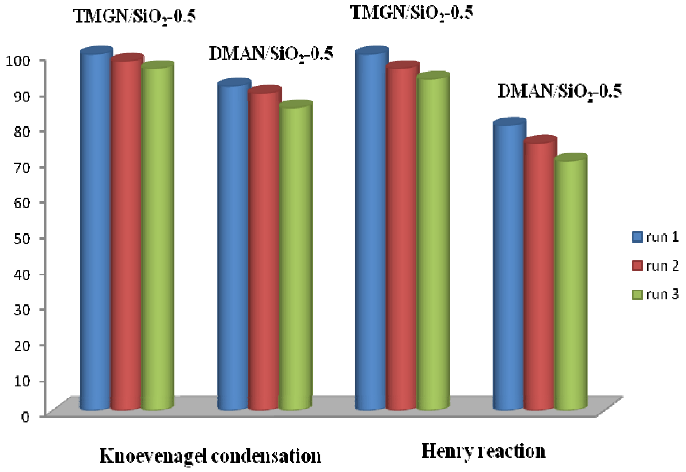


Fig. 15 - Knoevenagel condensation and Henry reaction recycling tests using TMGN/SiO_2-0.5 and DMAN/SiO_2-0.5 as catalysts. The yield (%) is reported after 6h of reaction

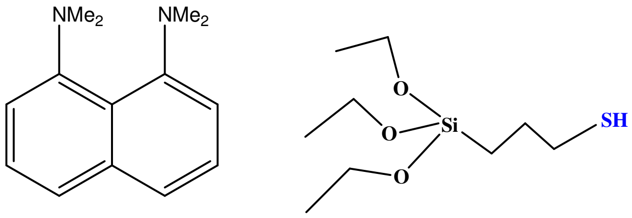
In the view of the good catalytic activities observed when proton sponges (TMGN or DMAN) based hybrid materials are used as heterogeneous catalysts in base reactions, the research activity was addressed also to the design, synthesis and characterisation of bifunctional hybrid materials containing concomitantly strong base and acid groups.

Nature has provided us with efficient catalysts, the enzymes that are able, through sophisticated strategies, achieving complex reactions or driving many biological processes. The highly efficient catalytic abilities of enzymes are due to cooperative interactions between accurately positioned functional groups present in their active sites. The mimicking of these abilities is one of the challenges in the heterogeneous catalysis and great efforts, in fact, have been focused on the stable immobilization of mutually incompatible functional groups, as in enzymes, that can be able to perform multistep or consecutive reactions. The design of cooperative catalytic systems can be achieved through a well-controlled multi functionalization of inorganic supports such as mesoporous silica. The inorganic porous supports can host different and often incompatible catalytic functionalities separated at suitable molecular distances, such as acid and basic groups, providing site isolation inside the inorganic network. The spatial isolation of incompatible active organic groups that cannot coexist in solution is the key to produce bifunctional acid-base heterogeneous hybrid catalysts. Recently, many examples of bifunctionalized mesoporous catalysts are reported, in which acid and base functional groups, with different strength, are hosted into the silica matrix such as amines together with silanols, amines with thiols, amines with ureas, amines with heteropolyacids or amines with Lewis and Brønsted acids. In most cases, the catalysts consist in bifunctionalized periodic mesoporous organosilica (PMO), modified SBA-15 and mesoporous silica nanoparticles (MSNs), having acidic groups within the framework walls and basic groups into the channel pores or viceversa. Bifunctional hybrid catalysts with PMO topology are also synthesized using bridged silsesquioxanes in which the organic linkers contain simultaneously acid and base active centres located in the same builder. This approach has been verified through the use of disilane organosilyl precursors which contain ionic liquids as functional building units. Among the different synthetic strategies available to covalently incorporate organic groups into the silica network, post-synthetic grafting and co-condensation processes are the most suitable. The later approach, also referred as one-pot synthesis, has been the preferred route because of the easier single-pot synthetic protocol and better control of organosilane loading joined to a more homogeneous distribution of active sites; in fact, the grafting method presents several drawbacks such as the partial blockage of the pores and undesired site-site interactions due to the supramolecular association of the silylated organic precursors. In the co-condensation method, the organic molecules can be integrated into the framework of ordered or non ordered mesoporous silica using bis-silylated precursors. In the synthesis of acid-base functionalized ordered mesoporous silicas (OMS), the presence of a surfactant, acting as structural directing agent (SDA), is necessary producing a ordered hybrid heterogeneous catalyst, the SDA being removed without altering the properties of the organic moieties incorporated into the framework. To avoid the use of sophisticated and expensive SDAs, a sol-gel procedure catalyzed by NH_4F using soft synthesis conditions, room temperature and neutral pH, can be used to synthesize hybrid materials. Using this method, it should be possible to achieve mesoporous hybrid organic-inorganic materials that, although they will not have long range order, will have accessible mesopores in a narrow pore size distribution and be thermally stable.

The synthesis of multifunctional hybrid materials containing both Brønsted acids and bases is not an easy task, due to the incompatible nature of these functional groups. Normally, the basic sites are represented by amines that can be easily protected using di-tert-butyl-dicarbonate (BOC). This strategy is commonly used for amino group protection during the acid treatment necessary to convert the organosiliceous precursor of acid groups, usually thiols or disulfide moieties, into the corresponding sulfonic acids. Then, a deprotection of the amine groups by thermal treatment is needed to restore the basic properties of the hybrid.

During the HYMUCAT project, ordered (OMS) and non-ordered bifunctional mesoporous silica materials have been synthesized following grafting and co-condensation procedures, cohabiting in the final materials simultaneously proton sponge and sulfonic groups as organocatalytic builders. Remarkably, during the synthesis process, it was avoided the post-synthesis protection and deprotection procedure to preserve the basic functionality. Specifically, 1,8-bis(dimethylamino)naphthalene (DMAN, scheme 10), a proton sponge, was used as organic builder base and 3-mercaptopropyltriethoxysilane (MPTES, scheme 10) as pending precursor of sulfonic acids. The organic base may be a part of the solid network if the organosilane contains more than one silicon center, for this reason, DMAN has previously been modified in order to have two terminal reactive silyl groups able to perform co-condensation with a conventional organosilane (TMOS), through sol-gel or micellar one-pot routes. This method has allowed introducing directly the functionalised DMAN builders into mesoporous silica by direct synthesis.

The bifunctional hybrid materials were extensively characterized and were investigated as reusable heterogeneous catalysts for various one-pot C-C bond-forming cascade reactions such as deacetalization-Knoevenagel condensation or deacetalization-nitroaldol (Henry) reaction.

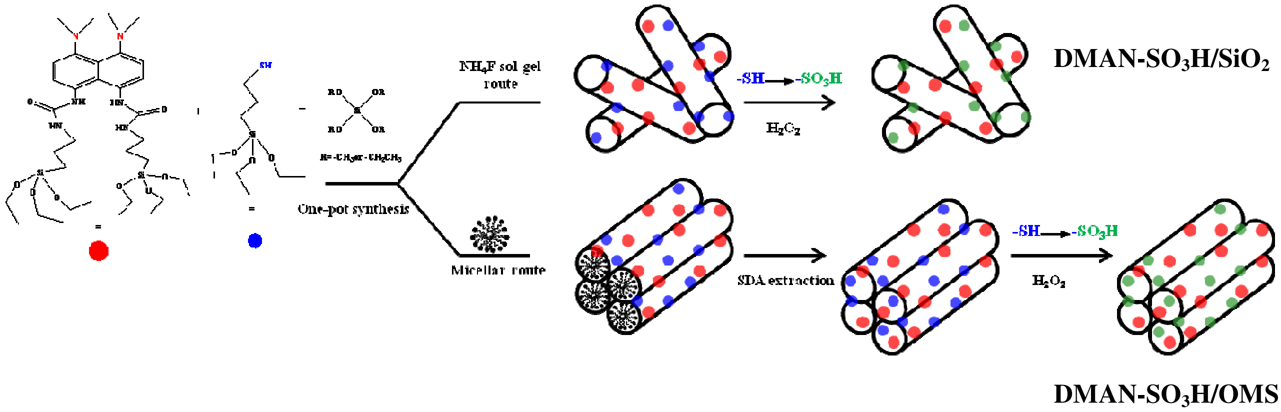


DMAN **MPTES**

Scheme 10

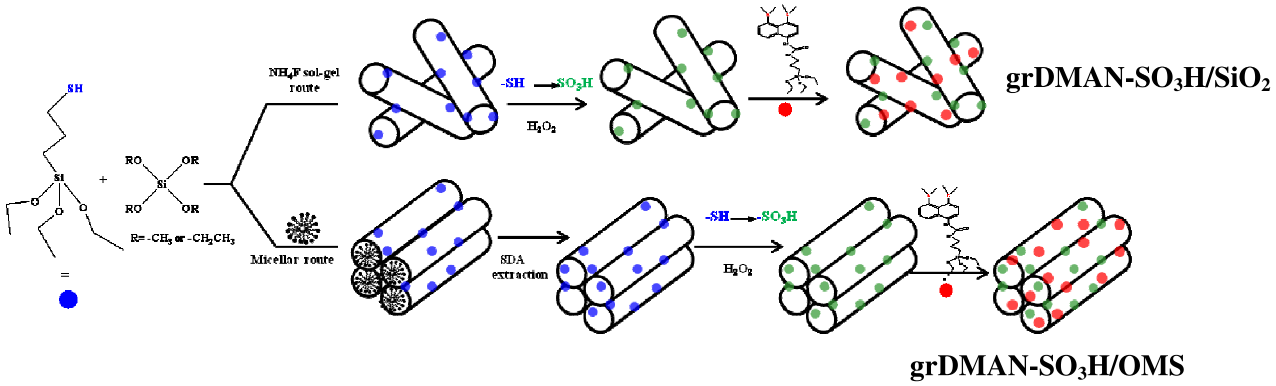
1,8-bis(dimethylamino)naphthalene (DMAN) was functionalized with terminal silyl-alcoxide reactive groups, obtaining mono and bi-silylated DMAN precursors. In fact, to graft DMAN onto the wall of mesoporous silica, a mono-silylated precursor (DMAN-1Sil) is necessary, whilst two terminal reactive silyl groups (DMAN-2Sil) are needed to integrate the basic organocatalysts into the framework of mesoporous material through one-pot synthesis with a conventional organosilane (TMOS or TEOS), used as additional silicon source, through sol-gel or micellar routes.

Different synthetic methodologies were followed to produce bifunctional mesoporous hybrid materials. Initially, thiols groups, the precursors of sulfonic acids, and DMAN basic moieties were simultaneously introduced into the network of ordered (OMS) and non-ordered mesoporous silicas through a one-pot synthesis. More specifically, a micellar self-assembling process, in the presence of surfactant molecules (HDA), and a sol-gel route, catalyzed by NH_4F as mineralizing agent in the absence of SDA, have been used to prepare ordered and non-ordered mesoporous hybrids, respectively, at room temperature. The soft synthetic conditions used allow binding covalently the functionalized organic fragments into the walls of ordered and non-ordered inorganic silicas preserving the basic properties of proton sponges in the resultant hybrids. In the case of ordered mesoporous silica synthesis, due to the instability of the strong basic DMAN molecules in acidic conditions, neutral long chains amine (HDA) has been choose as SDA for micellar self-assembly route, instead of triblock copolymers, such as P123, that requires strong acidic conditions during the synthesis. In addition, the extraction of the SDA molecules in ordered mesoporous hybrid materials has been carried out using neutral ethanol solutions to preserve the DMAN moieties. In scheme 11, a schematic representation of the two processes used to synthesize the bifunctional hybrids are reported, the last step for both processes being the oxidation of the thiol groups in strong sulfonic acid sites by using a H_2O_2 solution, without the use of strong acid solution that also would negatively affect the basic properties of DMAN.



Scheme 11- One-pot synthesis of bifunctional mesoporous hybrids

Additionally, DMAN basic molecules were grafted through a post-synthesis procedure, pending from the walls of ordered and non ordered mesoporous silicas, after the transformation of thiols into sulfonic acids, as reported in scheme 12. In this case, more post-synthesis steps are involved in the preparation of the bifunctional hybrid mesoporous materials.



Scheme 12- DMAN grafting on mesoporous silicas containing sulfon

The acronyms of the synthesized bifunctional hybrids are reported : with the DMAN and MPTES loadings.

Table 11. Acronyms of the bifunctional hybrid materials after the c(sulfonic groups. DMAN and MPTES loadings in the synthesis gel are

Sample Acronyms	DMAN-Sil loading x	MPTES loading y	Mesoporous silicas	Synthetic procedure
SO_3H/SiO_2-5	-	0.05	Non-ordered	NH_4F route,One-pot MPTES
gr$DMAN$-SO_3H/SiO_2-5	0.05	0.05	Non-ordered	NH_4F route, One-pot MPTES, Grafted DMAN-1Sil
DMAN-SO_3H/SiO_2-5-5	0.05	0.05	Non-ordered	NH_4F route, One-pot MPTS and DMAN-2Sil

SO_3H/OMS-5	-	0.05	Ordered	Micellar route, One-pot MPTES
grDMAN-SO_3H/OMS-5	0.05	0.05	Ordered	Micellar route, One-pot MPTES, Grafted DMAN-1Sil
DMAN-SO_3H/OMS-5	0.05	0.05	Ordered	Micellar route, One-pot MPTES and DMAN-2Sil

All the hybrids were characterized by XRD, TEM, N_2 adsorption at 77K, thermogravimetric and elemental analyses, solid state MAS-NMR (^{13}C, ^{29}Si) and FTIR spectroscopies.

The ordered mesoporous hybrid silicas (OMS) were characterized by XRD diffraction analysis (Fig. 16). The pattern of the hybrids mainly exhibit the (100) reflection peak at low diffraction angles which is typical of M41S mesoporous materials possessing short range hexagonal ordering. In the as-synthesized SO_3H/OMS-5 (curve a) and surfactant-extracted SO_3H/OMS-5 (curve b) are also visible the (110) peak due to the long-range order in the silica framework. Upon extraction of the HDA (curve b), the d_{100} peak increases in intensity due to a better ordering of the inorganic framework. The hexagonal order is maintained also after the post-synthetic grafting procedure (curve c) and after the oxidation of the thiol groups (curve d) in the bifunctional ordered OMS prepared with one-pot synthesis. The high intensity of the (100) peak confirms the homogeneous structural order of the hybrid materials prepared using self-assembly micellar route. Obviously, the non-ordered hybrid mesoporous materials, obtained by sol-gel process, do not show low-angle diffraction peak typical of M41S systems.

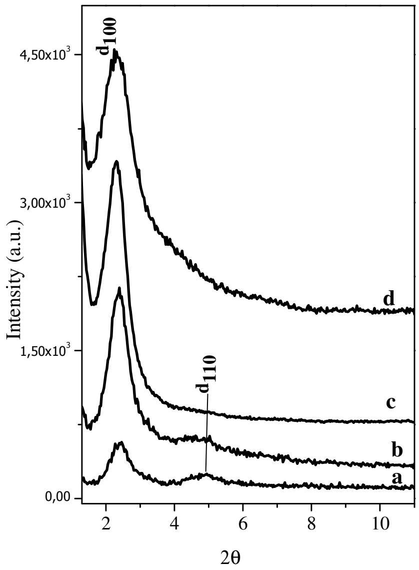


Fig. 16 – Powder XRD diffraction patterns of as synthesized SO_3H/OMS-5 (curve a), surfactant-extracted SO_3H/OMS-5 (curve b), grDMAN-SO_3H/OMS-5 (curve c) and surfactant-extracted bifunctional DMAN-SO_3H/OMS-5-5 (curve d) after the oxidation of thiol groups.

The ordered bifunctional OMS and the non-ordered bifunctional silicas show different morphology as evidenced by the TEM micrographs in Fig. 17. In particular, the ordered materials are formed by larger particles (a), whilst smaller organosilica particles are visible in the micrograph of the bifunctional non-ordered silica (b). In both hybrids it is possible to observe the presence of mesopores, being appreciated an important inter-particle mesoporous contribution in the hybrid obtained by sol-gel route. The homogeneous mesoporous distribution is clearly appreciated in the hybrid materials synthesized by template assisted methodology.

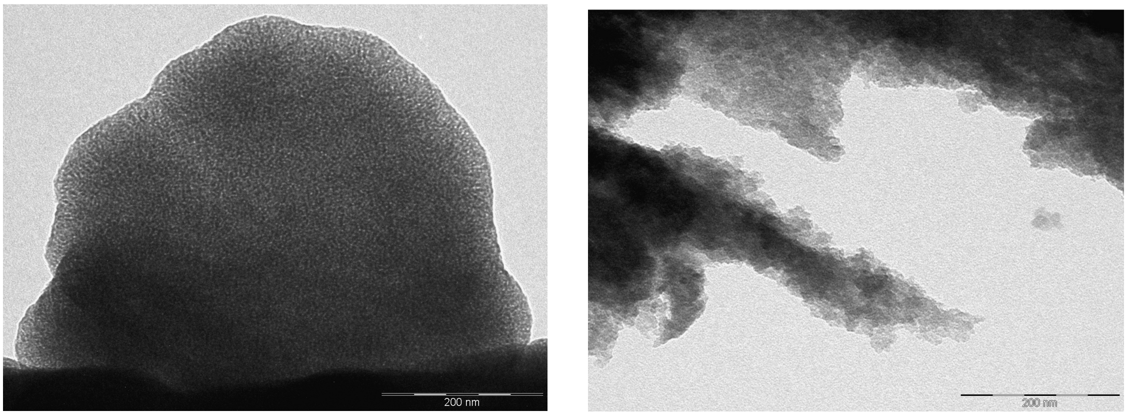


Fig. 17 – TEM micrographs: (a) DMAN-SO_3H/OMS-5-5 and (b) DMAN-SO_3H/SiO_2-5-5

The presence of the organic moieties in the synthesized hybrids was evidenced by means of elemental analysis. In Table 12, the C, H, N content and the calculated percentage in weight of the organic species present into the as-synthesized bifunctional hybrid materials are reported. The organic content of the OMS hybrids is higher respect the one of the hybrids prepared with the sol-gel process, moreover in both the grafted-DMAN hybrids the organic content is higher respect the hybrids produced with one–pot synthesis.

Table 12. Organic content in the mesoporous bifunctional hybrids estimated by Elemental Analysis.

Catalysts	N%	C%	H%	S%	Organic content (EA)/%
SO_3H/SiO_2-5	-	4.35	2.22	1.50	8.07
grDMAN-SO_3H/SiO_2-5	2.13	12.75	2.37	1.57	18.82
DMAN-SO_3H/SiO_2-5	1.44	9.2	2.4	1.51	14.55
SO_3H/OMS-5	0.2	5.20	2.04	1.36	8.8
grDMAN-SO_3H/OMS-5	2.68	15.41	2.67	1.64	22.4
DMAN-SO_3H/OMS-5-5	2.05	13.6	2.7	1.01	19.36

Thermogravimetric analysis was performed in order to gain insight on the organic content, on the thermal stability of the inserted DMAN and sulfonic groups and on the hydrophobic or hydrophilic character of the hybrid materials. The weight loss (TGA) and their respective derivates (DTA) for the one-pot non-ordered DMAN-SO_3H/SiO_2-5-5 and ordered DMAN-SO_3H/OMS-5-5 are reported in Figure 18 Section A. The first weight loss for the bifunctional hybrids is observed at around 80-150°C and can be associated to the removal of physisorbed water. The DTA curves reveal that the non-ordered DMAN-SO_3H/SiO_2-5-5 is more hydrophilic than ordered DMAN-SO_3H/OMS-5-5. At higher temperatures, flat weight loss profiles changed into a rapidly declining profile corresponding to the decomposition of the organic base (DMAN) and sulfonic acid groups. In particular, the DTA curves reveal that DMAN decomposes between 300-430ºC and sulfonic acids at ca. 500-550ºC. In fact, the DTA curves of SO_3H/SiO_2-5 and SO_3H/OMS-5 (Section C, curves c and d) have evidenced that the alkyl-sulfonic acid groups decompose at ca. 500-550ºC. The presence of a weight loss at this high temperature in the bifunctionalized hybrids confirms the complete oxidation of thiols into sulfonic groups. Moreover, in the case of SO_3H/OMS-5 (Section C, curve d), is also visible a weight loss at around 350ºC that can be associated with the decomposition of the residual of HDA molecules that were not completely removed after the surfactant extraction. The DTA curves of grafted-DMAN hybrids (Section B, curves c and d) showed a minor weight loss at around 80-150° suggesting a lower amount of physisorbed water with respect the one-pot bifunctional hybrids. In fact in the grafted hybrids the concentration of silanols should be lower due to the fact that the Si-OH groups are the locus on which the grafting of the basic DMAN occurs. The second weight loss at around 300-430ºC is due to the organic DMAN base and the third peak at ca. 500-550, due to the decomposition of alkyl-sulfonic acid groups, confirms that the acid properties are not altered by the post-synthetic grafting of the organic base.

The organic content, calculated from the weight loss in the 150-430ºC range, due to the decomposition of the DMAN base, and in the 430-900ºC range, where sulfonic groups decomposed, is in agreement with the results obtained by elemental analysis (Table 13). Moreover, the hybrids prepared with sol-gel synthesis that present a lower organic content, have an higher degree of hydrophilicity.

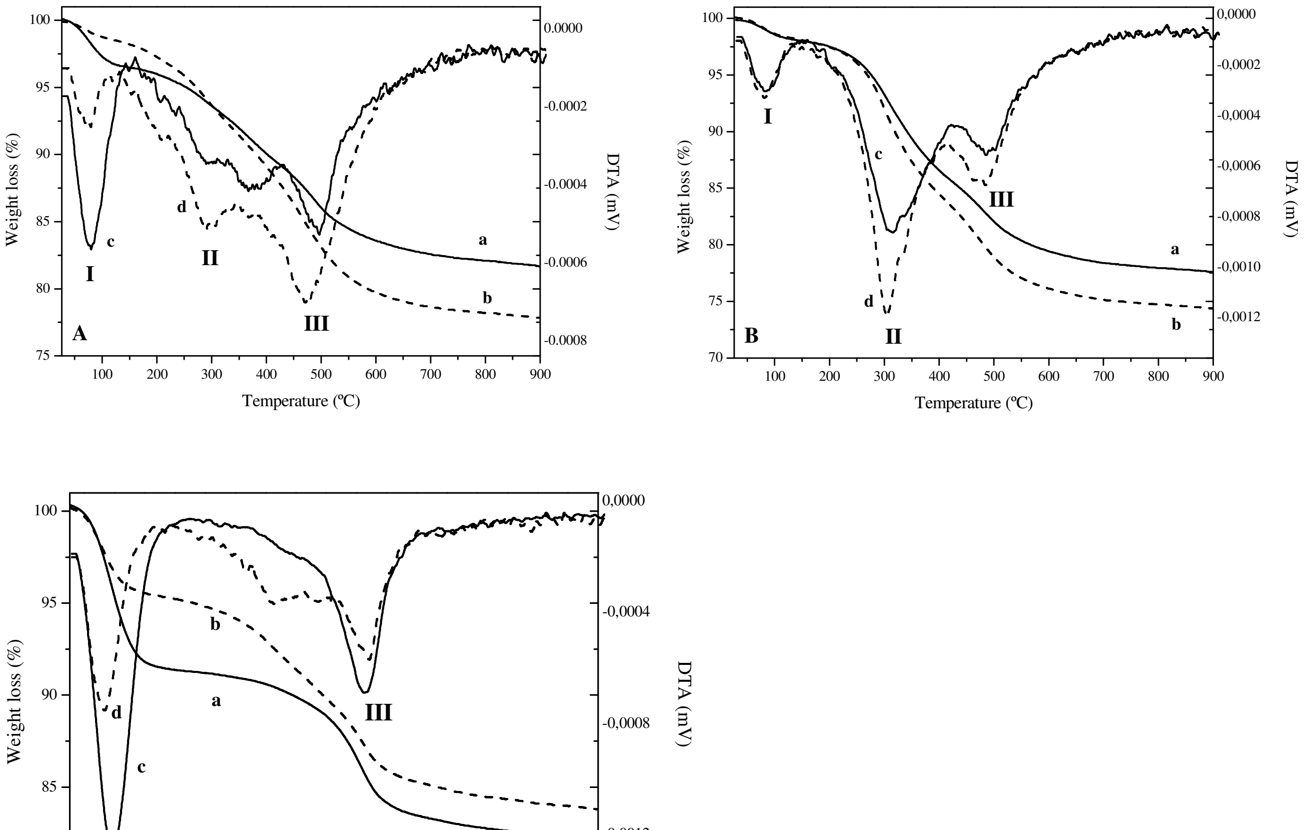


Fig.18 – Section A: TGA and DTA curves of DMAN-SO_3H/SiO_2-5-5 (a and c) and DMAN-SO_3H/OMS-5-5 (b and d). Section B: TGA and DTA curves of grDMAN-SO_3H/SiO_2 -5-5 (a and c) and grDMAN-SO_3H/OMS-5-5 (b and d). Section C: TGA and DTA curves of SO_3H/SiO_2-5 (a and c) and SO_3H/OMS-5 (b and d).

Table 13. Weight loss (%) due to organic content calculated from TGA analysis

Catalysts	Δwt% due to physisorbed H_2O^a (I)	Δwt% due to DMAN[b] (II)	Δwt% due to-SO_3H^c (III)	Δwt% due to organic content	Organic content (EA)/%
SO_3H/SiO_2-5	8.2	-	9.0	9.0	8.07
DMAN-SO_3H/SiO_2-5-5	3.6	8.9	5.2	14.1	14.5
grDMAN-SO_3H/SiO_2 -5-5	2	13	6.6	19.6	18.8
SO_3H/OMS-5	4.4	-	9.8	9.8	8.8
DMAN-SO_3H/OMS-5-5	1.8	9.2	10.4	19.6	19.4
grDMAN-SO_3H/OMS-5-5	2	15	7.9	22.9	22.4

[a]calculated from 25°C to 150°C; [b]calculated from 150°C to 430°C; [c]calculated from 430°C to 900°C.

The chemical nature of the organic moieties present into the ordered and non-ordered hybrid mesoporous silicas has been exploited by ^{13}C-CP MAS NMR technique (Fig. 19). The contribution of the DMAN, the organic base, and the MPTES, the precursor of sulfonic groups, was evidenced and also the oxidation of thiols into sulfonic groups upon the treatment with H_2O_2 was confirmed. Specifically, the ^{13}C CP/MAS NMR spectra of the bifunctional hybrids (Fig. 19, curves b-e) present the typical signals of DMAN confirming the integrity of the organic base after the synthesis process. In fact, in the range between 150-110 ppm, weak signals, due to naphthalene groups, are present, while the peaks due to methyl groups belonging to $N(CH_3)_2$ are visible at 40-45 ppm. In addition, the peak assigned to C=O groups (158 ppm), and the signals due to C1 (61 ppm), C2 (22 ppm) and C3 (10 ppm) of the $-CH_2$ groups belonging to the terminal silyl fragments of the functionalized DMAN are also present (see the inset in Fig.19 for the labels of C atoms). The presence of these signals also confirms that the DMAN molecules were successfully functionalized. Concerning MPTES, in the spectrum of DMAN-

MPTES/SiO$_2$-5-5 hybrid (curve b), a signal at 27 ppm, typical of C1 and C2 carbons adjacent to the -SH groups is evident, confirming the presence of mercaptopropyl groups; whilst the peak due to C3, that should appear at 11 ppm, is overlapped to the strong signal at 10 ppm due to the functionalized DMAN. Upon the oxidation with H_2O_2 necessary to convert thiols to suphonic groups, the peak at 27 ppm disappeared and contemporarily new signals at 54 ppm, due to C1, and at 18 ppm due to C2 adjacent to the –SO_3H groups, appeared (curves c-e), suggesting a complete oxidation of thiols in –SO_3H groups. The signal due to sulfonic acids is also present after the grafting of the DMAN organic base onto the mesoporous silica (curve e) and this confirms that the post-synthetic procedure used to graft the organic base does not affect the strong acid sites.

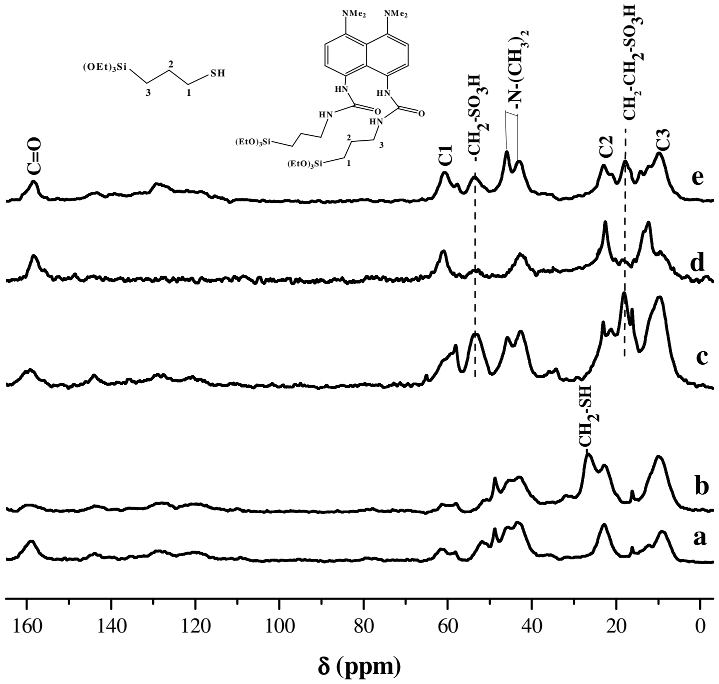


Fig. 19· ^{13}C-CP MAS NMR of DMAN/SiO$_2$-5 (curve a), DMAN-MPTES/SiO$_2$-5-5 (curve b), DMAN-SO$_3$H/SiO$_2$-5-5 (curve c), DMAN-SO$_3$H/OMS-5-5 (curve d) and grDMAN-SO$_3$H/SiO$_2$-5 (curve e).

Additionally, ^{29}Si MAS NMR spectra confirm that the DMAN fragments and MPTES are not only intact after the synthesis of the bifunctional hybrids but are also incorporated covalently into the ordered and non-ordered porous network bounded to inorganic silica units. In fact, the ^{29}Si MAS NMR spectra of the bifunctional hybrids (Fig. 20 curves b and c) exhibit bands from -50 ppm to -80 ppm assigned to T-type silicon (T^3, T^2 and T^1) species having a Si-C covalent bond, these signals are not present in the spectrum of siliceous material (curve a) synthesized for comparison, and then confirmed that the hydrolysis and policondensation of silylated-DMAN and MPTES occurs through reactive alkoxy terminal groups of the silylated moieties. In the spectrum of DMAN-SO$_3$H/SiO$_2$-5-5 (curve b) it is possible to identify the T-bands corresponding to the T^1 ($SiC(OH)_2(OSi)$), T^2 ($SiC(OH)(OSi)_2$) and T^3 ($SiC(OSi)_3$), whilst in the DMAN-SO$_3$H/OMS-5-5 spectrum (curve c), only the band due to T^3 is visible. In addition, three peaks at -92, -100 and -110 ppm are also present, due to Q^2 ($Si(OH)_2(OSi)_2$), Q^3 ($Si(OH)(OSi)_3$) and Q^4 ($Si(OSi)_4$)

silicon units respectively, which are typical of highly siliceous conventional mesoporous materials, associated to tetrahedrally coordinated silicon atoms conforming the solid network.

The incorporation of the disilylated DMAN into the framework of non-ordered mesoporous silica is also confirmed by the comparison of ^{29}Si NMR spectra of the hybrids with the pure disilylated DMAN (see inset of Fig. 20). The DMAN-2Sil exhibits one peak centered at -45 ppm typical of Si-C bonds. When the DMAN-2Sil builders are finally inserted into the silica framework, the signal due to silicon atoms bounded to carbon units shifted in the range -60 to -80 ppm, supporting the covalent incorporation of the disilylated organic species into the silica framework.

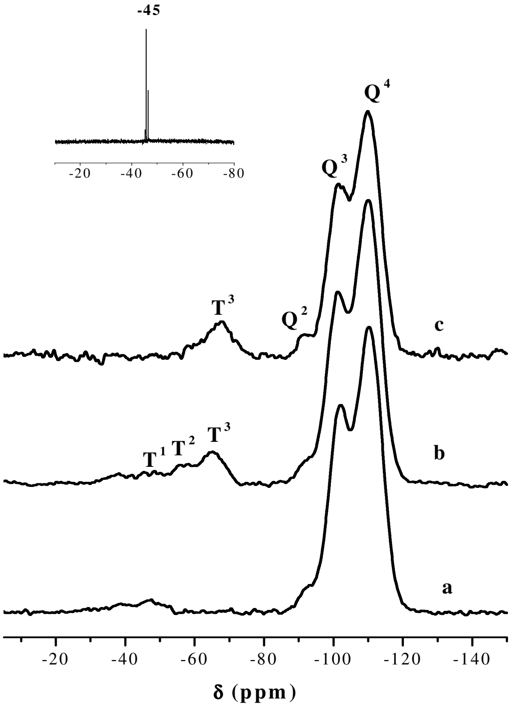


Fig. 20 - ^{29}Si-BD MAS NMR of pure SiO_2 (curve a), DMAN-SO_3H/SiO_2-5-5 (curve b) and DMAN-SO_3H/OMS-5-5 (curve c). In the inset, the ^{29}Si NMR spectrum of DMAN-2Sil is reported.

The textural properties of the hybrids, measured by N_2 adsorption at 77K, are reported in Table 14. In general, the BET specific surface area (SSA) of the non-ordered SiO_2 hybrids is lower than the orderd-OMS materials. However, in the ordered hybrid materials, important differences are observed when DMAN moieties are introduced by co-condensation or post-synthetic grafting routes. When DMAN bridged silsesquioxane and MPTES are incorporated one-pot during the synthesis, the isotherm obtained exhibits a shape more similar to the non-ordered silica with inflexion point close to p/p° 0.5, showing a reduction in the homogeneous porosity and in the SSA when the two silane precursors are simultaneously incorporated into the framework. This behavior is probably due to the difficulty in assembling the two types of silane precursors in a highly regular mesoporous structure. On the contrary, if the DMAN is grafted onto the mesopores of OMS or in absence of them, the hybrid materials show type IV isotherms clearly representative of standard M41S materials, with inflexion point a ca. p/p° 0.3. The non-ordered hybrid materials synthesized through fluoride-catalyzed sol-gel route, exhibit a more reduced porosity, associated to tortuous and irregular mesoporous channels, in fact the isotherms present a reduced slope and inflexion points at higher relative pressure (p/p°~0.5). It is important to remark that in all cases, the SSAs and pore volumes obtained are in the mesoporous range, being minority the microporous contribution (Table 14). The pore distribution of the hybrid samples are narrow and the mean pore diameters are centered at 28-30 Å.

Table 14. Textural properties of the bifunctional mesoporous hybrid materials

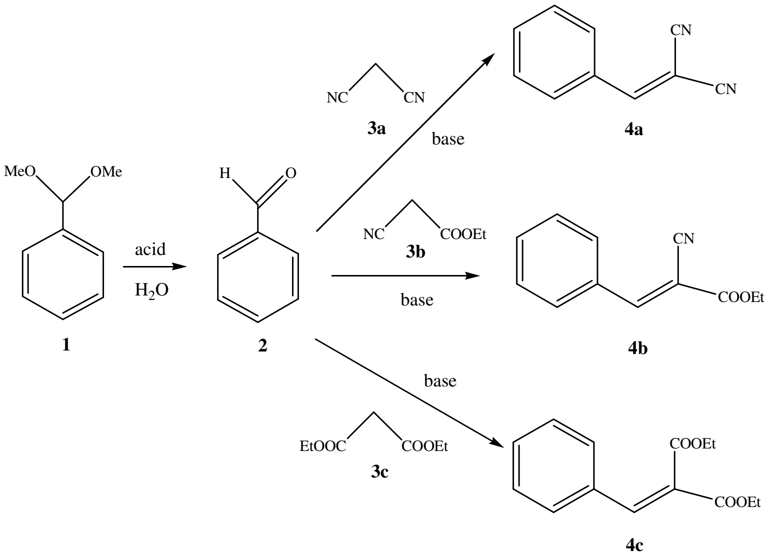
Catalysts	SSA_{BET} (m^2/g)	External SA (m^2/g)	Pore size Å	Pore volume cm^3/g
DMAN-SO_3H/SiO_2-5-5	481	472	31	0.25
SO_3H/SiO_2-5	599	422	27	0.22
grDMAN-SO_3H/SiO_2-5	436	393	26	0.21
DMAN-SO_3H/OMS-5-5	590	542	28	0.19
SO_3H/OMS-5	930	673	28	0.22
grDMAN-SO_3H/OMS-5	793	719	27	0.19

To investigate how the acid and base functionalities of the organic-inorganic hybrids cooperate synergistically, one-pot–two step processes that involved an acid-catalyzed acetal hydrolysis followed by a base-catalyzed Knoevenagel or nitroaldol (Henry) reactions were performed. The first step is the deacetalisation of the benzaldehyde dimethylacetal to benzaldehyde, that, in the second step, reacts with metylene compounds

(Knoevenagel condensation, scheme 13) or nitromethane (Henry reaction, scheme 14) to give the final product.

The condensation of carbonyl compounds (Knoevenagel condensation) and the condensation of nitroalkanes with carbonyl compounds (Henry reaction) are well-established and widely used in organic synthesis to produce important intermediates and end products for perfumes, pharmaceutical and polymers. However, in the case of Henry reaction, the selective formation of a nitroalkene (product 4 in scheme 14) 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 in a side reaction, therefore the synthesis of nitroalkenes often proceeds in poor yields due to their dimerisation or polymerization.

Different methylene compounds, malononitrile (MN, 3a), ethyl cyanoacetate (ECA, 3b) and diethylmalonate (DEM, 3c), with different pK_a, have been used in the second step Knoevenagel condensation (scheme 13).



Scheme 14- One-pot acetal hydrolysis- Knoevenagel condensation cascade reactions

In Fig. 21, the catalytic activity in the cascade reaction, using malononitrile as methylene compound, of the bifunctional non-ordered DMAN-SO_3H/SiO_2-5-5 hybrid catalyst is reported. It is possible to observe the conversion of benzaldehyde dimethylacetal (1) into benzaldehyde (2) that reacts through the consecutive Knoevenagel condensation with malononitrile (3a) to give the benzyilidene malononitrile (4a), the final product. The results showed that the tandem reaction was successfully performed; in fact 97% yield of the final product with 100% selectivity was achieved after 6h. Similar yields ($\geq$ 95%) of the final product with 100% selectivity were observed for the other one-pot and grafted-DMAN ordered and non-ordered bifunctional hybrid catalysts (Table 15) at the same reaction time. A blank experiment without the heterogeneous catalyst was also performed (entry 5, Table 15), and the results show that the cascade reaction does not occur in the absence of the hybrid catalyst. When MN is used as methylene compound, all the catalysts showed good and similar catalytic performances in the cascade reaction after 6h and no dependence of the synthesis procedure can be evidenced.

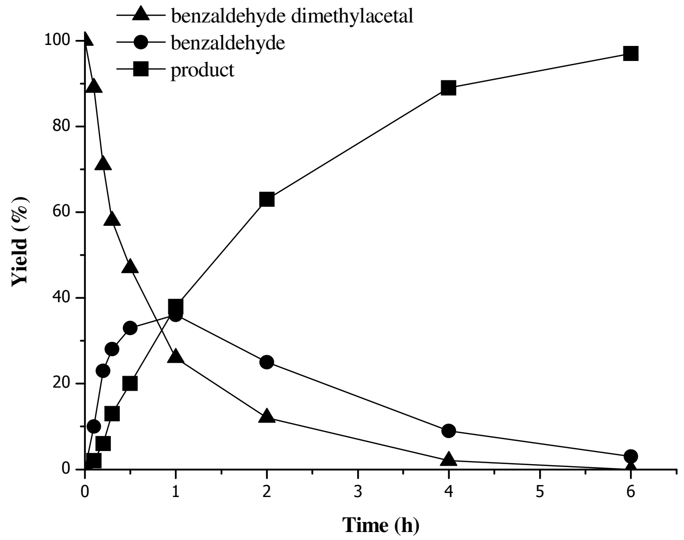


Fig. 21– Catalytic activity of the bifunctional DMAN-SO$_3$H/SiO$_2$-5-5 hybrid in the one-pot acetal hydrolysis-Knoevenagel condensation of malononitrile.

Table 15. One-pot acetal hydrolysis- Knoevenagel condensation cascade reactions using malononitrile (3a).

entry	Catalysts	Time (h)	Conv. of **1** (%)	Yield of **2** (%)	Yield of **4a** (%	TOF[b] (min^{-1})	r_0 (min^{-1})
1	DMAN-SO$_3$H/SiO$_2$-5-5	6	100	3	97	63	0.63
2	DMAN-SO$_3$H/OMS-5-5	6	100	2	98	66	0.68
3	grDMAN-SO$_3$H/SiO$_2$-5	6	97	2	95	56	0.56
4	grDMAN-SO$_3$H/OMS-5	6	99	3	96	58	0.59
5	[a]none	6	5	2	3	-	-

[a]cascade reaction without the heterogeneous catalyst: benzaldehyde dimethylacetal (5.45 mmol), malononitrile (5.24 mmol) and H$_2$O (30 µl) at 355K.
[b]TOF calculated at 60 min.

When ethyl cyanoacetate (3b) was used as methylene compound instead of malononitrile in the cascade reaction, the non-ordered DMAN-SO$_3$H/SiO$_2$-5-5 reaches 98% yields of the final product (4b) with 100% selectivity (Table 16, entry 1) after 7h, whilst 86% yield was obtained at the same reaction time using ordered DMAN-SO$_3$H/OMS-5-5 as catalysts (Table 16, entry 2). Lower yields of the final product were observed when grafted DMAN hybrids are used as catalysts (Table 16, entries 3 and 4).

Interestingly, it can be noted that if water is not added to the cascade reaction (Table 16, entries 5 and 6) and the catalysts is not outgassed at 100°C before the catalytic test, DMAN-SO$_3$H/SiO$_2$-5-5 hybrid shows superior catalytic activity respect to the ordered DMAN-SO$_3$H/OMS-5-5. In this condition, in fact, DMAN-SO$_3$H/SiO$_2$-5-5 hybrid catalyst can take advantage of the water absorbed in the mesopores due to its higher hydrophilic character respect to the ordered bifunctional OMS, as evidenced by TGA. Finally, when only acidic SO$_3$H/OMS-5 or SO$_3$H/SiO$_2$-5 are used as catalysts and therefore in the absence of any basic groups, benzaldehyede is the sole product (Table 16, entry 7).

Moreover, a physical mixture of acid SO_3H/SiO_2-5 and basic DMAN/SiO_2-5 was also tested in the tandem reaction and the result evidences that only 5% yield of the final product was achieved (entry 9). These results demonstrate that each catalyst (acid and base) on its own is unable to promote the one-pot cascade reaction, clearly indicating a cooperative behavior of the bifunctionalized hybrid catalysts, similar to biological systems.

Table 16. One-pot acetal hydrolysis- Knoevenagel condensation cascade reactions using ethyl cyanoacetate (3b).

entry	Catalysts	Time (h)	Conv of **1** (%)	Yield of **2** (%)	Yield of **4b** (%)	TOF^c (min^{-1})
1	DMAN-SO_3H/SiO_2-5-5	7	100	2	98	7.3
		10	100	0	100	
2	DMAN-SO_3H/OMS-5-5	7	100	14	86	6.1
		10	100	5	95	
3	grDMAN-SO_3H/SiO_2-5	7	90	21	79	2.0
		10	93	15	85	
4	grDMAN-SO_3H/OMS-5	7	95	19	81	2.4
		10	98	9	91	
5	^{a}DMAN-SO_3H/SiO_2-5-5	7	100	5	96	6.6
		10	100	2	98	
6	^{a}DMAN-SO_3H/OMS-5-5	7	100	76	24	1.1
		10	100	62	38	
7	SO_3H/PMO-5 or SO_3H/SiO_2-5	24	100	100	0	
8	DMAN/SiO_2-5	24	7	2	5	
9	SO_3H/SiO_2-5+ DMAN/SiO_2-5	24	100	95	5	
10	^{b}none	24	0	trace	trace	

[a] cascade reaction without the addition of water and without outgassing the hybrid catalysts at 100ºC before the catalytic test.

[b] cascade reaction without the heterogeneous catalyst: benzaldehyde dimethylacetal (5.45 mmol), ethyl cyanoacetate (5.24 mmol) and H_2O (30 μl) at 355K.

[c] TOF calculate at 90 min.

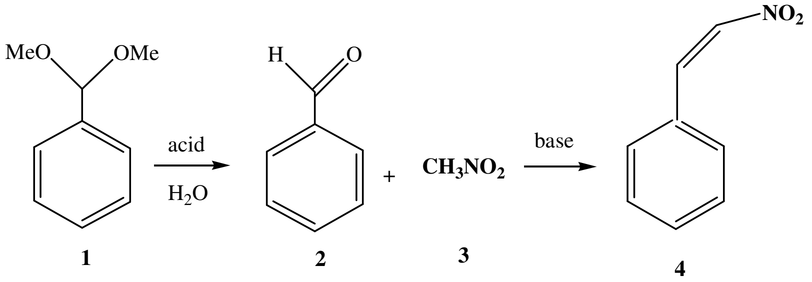
When more demanding reactant, such as diethylmalonate (scheme 14, 3c) was used as methylene compound in the second step Knoevenagel condensation, the bifunctionalized hybrids behave differently and the catalytic activity strictly depends on the synthesis procedure adopted in the production of the hybrid catalysts, as was also evidenced when ECA was used. In particular, non-ordered bifunctional DMAN-SO_3H/SiO_2-5-5 shows higher yields at different reaction time with 100% selectivity (Table 16, entry 1) respect to ordered DMAN-SO_3H/OMS-5-5 (Table 16, entry 2) and in the case of the grafted-DMAN bifunctional hybrid catalysts lower yields are obtained (Table 16, entries 3 and 4).

Table 16. One-pot acetal hydrolysis- Knoevenagel condensation cascade reactions using diethylmalonate (3c).

entry	Catalysts	Time (h)	Conv of **1** (%)	Yield of **2** (%)	Yield of **4c** (%)	TOF[a] (min^{-1})
1	DMAN-SO_3H/SiO_2-5-5	10	100	32	68	0.86
		15	100	25	75	
		24	100	4	96	
2	DMAN-SO_3H/OMS-5-5	10	100	56	44	0.41
		15	100	38	62	
		24	100	19	81	
3	grDMAN-SO_3H/SiO_2-5	10	100	87	13	0.11
		15	100	80	20	
		24	100	18	82	
4	grDMAN-SO_3H/OMS-5	10	100	86	14	0.14
		15	100	82	18	
		24	100	34	66	

[a] TOF calculate at 420 min

The catalytic activity of the synthesized bifunctional hybrids was also tested in the one–pot deacetalization-nitroaldol reaction (scheme 15). In this case, in the second step, benzaldehyde (2) reacts with nitromethane (3) giving the 2-nitrovinyl benzene (4), the final product. Similarly to the reaction that involved in the second step a Konevenagel condensation, the bifunctional non-ordered DMAN-SO_3H/SiO_2-5-5 hybrid catalyst (Table 17, entry 1) shows better catalytic conversions to yield the product respect to the other hybrid materials. In particular, grafted-DMAN hybrid materials show poor activities (Table 17, entries 3 and 4).



Scheme 15 - One-pot acetal hydrolysis- nitroaldol (Henry) cascade reaction.

Table 17. One-pot acetal hydrolysis- nitroaldol cascade reaction.

entry	Catalysts	Time (h)	Conv of **1** (%)	Yield of **2** (%)	Yield of **4** (%)	TOF[a] (min^{-1})
1	DMAN-SO_3H/SiO_2-5-5	15	100	40	60	0.33
		24	100	8	92	

2	DMAN-SO_3H/OMS-5-5	15	100	53	47	0.15
		24	100	14	86	
3	grDMAN-SO_3H/SiO_2-5	15	100	85	15	0.023
		24	100	72	28	
4	grDMAN-SO_3H/OMS-5	15	100	78	22	0.083
		24	100	69	31	
5	[a]none	24	5	trace	trace	-

[a]TOF calculate at 420 min

The catalytic performances of the different bifunctional hybrids in the one-pot cascade reactions have evidenced a superior activity of the non-ordered DMAN-SO_3H/SiO_2-5-5 with respect to the other hybrids expecially when, in the second step, a more demanding methylene compound, such as DEM, or nitrometane are involved. This superior activity could be inferred by the higher structural flexibility of the non-ordered silica network and by the higher amount of silanol groups that can perform a cooperative electrophilic activation. In the case of grafted-hybrids, the catalytic activity observed is lower with respect to the one-pot hybrid materials. It is, in fact, difficult to achieve a homogeneous distribution of the organic groups when post synthetic grafting is used and moreover, if the grafting reagents react preferentially at the pore openings during the initial stages of the synthesis process, the diffusion of further molecules into the centre of the pores can be hampered. In addition, also the densely packed organic basic moieties that greatly reduce the percentage of silanols (as evidence by TGA analysis) can affect negatively the catalytic activity of these hybrids. The probability of such aggregation effects is reduced in the one-pot synthesized hybrids and thus hybrid catalysts with spatially well isolated acid and base groups can be achieved.

Catalyst deactivation and reusability was studied by recycling the used hybrid catalysts after each run, after being washed with CH_2Cl_2. The yields of the recycled catalysts in the one-pot acetal hydrolysis-Knoevenagel condensation cascade reaction with ethyl cyanoacetate after 10h of reaction are presented in Fig. 22. It can be observed that the one-pot hybrid catalysts can be recycled with only slight loss in activity. A loss in activity after the 3rd run is obtained when grafted hybrids were used as catalysts. No leaching of the organic functionalities was observed by performing elemental analysis on the used one-pot hybrids, whilst a more evident loss in the N content is observed for the grafted-DMAN hybrids.

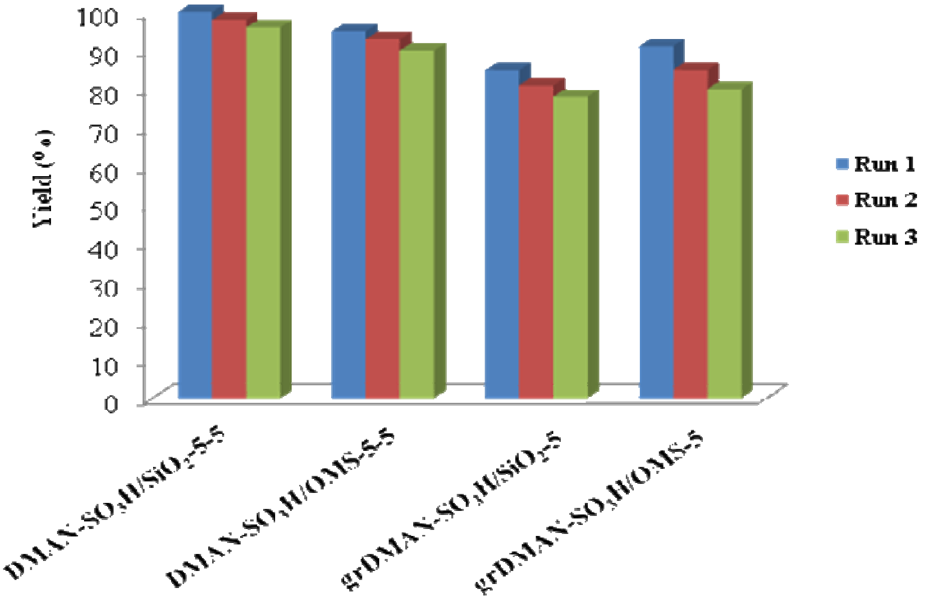


Fig.22 - Recycling tests of one-pot acetal hydrolysis-Knoevenagel condensation cascade reactions using ethyl cyanoacetate. The yield (%) is reported after 10h of reaction.

The research activity developed during the HYMUCAT project has evidenced that it is possible to synthesize organic-inorganic mesoporous hybrid materials using low cost preparation methods, in particular sol-gel processes. Hybrid catalysts with strong basic features have been obtained using DMAN or TMGN, an organic superbase, for the first time as the organic part of the hybrid materials. In addition, the synthesis of bifunctional acid-base hybrid catalysts have been successfully performed and these hybrids have shown excellent catalytic performances in cascade reactions, evidencing a synergistic role of the acid and basic centres inside the silica network.

The main results achieved during the HYMUCAT project have been published in International Journals and are listed below:

1) **E. Gianotti**, U. Diaz, S. Coluccia, A. Corma
"Hybrid organic-inorganic catalytic mesoporous materials with proton sponges as building blocks" *Phys. Chem. Chem. Phys.*, 2011, 13, 11702-11709.

2) **E. Gianotti**, U. Diaz, A. Velty, A. Corma
"Strong Organic Bases as Building Blocks of Mesoporous Hybrid Catalysts for C-C Forming Bond Reactions" *Eur.J. Inorg. Chem.*, **2012,** DOI:10.1002/ejic.201200716.

Another paper is in preparation:
E. Gianotti, U. Diaz, A. Velty, A. Corma
"Design of Bifunctional Acid-Base Mesoporous Hybrid Catalysts for Cascade Reactions"

Also several contributions have been presented at International Congress and are listed below:

1) Hybrid Materials 2011, Second International Conference on Multifunctional, Hybrid and Nanomaterials, march 6-10, 2011, Strasbourg, France.

Title of contribution:”*Organic-inorganic mesoporous hybrid materials based on structural diamines for base catalysis”*. Authors: **E. Gianotti**, U. Diaz, S. Coluccia, A. Corma.

2) 5th International FEZA Conference, july 3-7, 2011, Valencia Spain.
Title of contribution: ”*Proton sponges in hybrid mesoporous materials for base catalysis”*. Authors: **E. Gianotti**, U. Diaz, A. Corma, pag.199 ISBN 978-84-8363-722-7.

3) I Bilateral Spanish-Japanese Workshop on Nanotechnology and New Materials with Environmental Challenges, september 13-16, 2011, Toledo, Spain.
Title of contribution: ”*Functional Hybrids based on Organocatalytic builders into Mesoporous Framework*”. Authors: **E. Gianotti**, U. Díaz, A. Corma
4) V Workshop on Oxide Based Materials, September 23-26, 2012, Torino, Italy.
Title of contribution:” *Proton sponges in hybrid mesoporous materials for multifunctional catalysts”*. Authors: **E. Gianotti**, U. Diaz, A. Velty, S. Coluccia, A. Corma.