Mesoporous Materials

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Controlling and Imaging the Functional-Group Distribution on Mesoporous Silica**

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The control of the distribution of functional groups on mesoporous silica is essential for applications of these materials in various fields including catalysis,[1] drug delivery,[2] and sensing.[3] In order to define the interaction of the mesoporous silica particles with their surrounding medium, the selective modification of the external surface is of particular importance. Externally grafted functional groups can, for example, regulate the cellular uptake[4] or provide targeting ability[5] of mesoporous-silica-based drug-delivery systems.

The introduction of functional groups by grafting to a preformed mesoporous material (often referred to as post-synthetic functionalization) is a versatile modification method, as the desired pore-size distribution, pore system dimensionality, particle size, and particle morphology can be obtained in a straightforward manner. However, the control of the functional-group distribution poses a particular challenge. A recently reported concept employs fluorenylmethoxycarbonyl(Fmoc)-modified organosilanes which are grafted to the external and internal (pore) surfaces of mesoporous silica. Under certain reaction conditions, the external surface groups can be deprotected selectively and subsequently functionalized further, whereas the groups located on the pore surface remain protected by Fmoc.[6] A frequently used general method for modifying the external surface is based on the reaction of chloro-, methoxy-, or ethoxysilanes with as-synthesized mesoporous silica, in other words, mesoporous silica still containing the structure-directing agent (SDA). We show herein that considerable grafting to the pore surface can occur despite the presence of the SDA, and we describe a convenient postsynthetic functionalization method with a high selectivity for the external surface.

Confocal laser scanning microscopy (CLSM) has been used to visualize the spatial distribution of fluorescent guests in mesoporous and microporous host materials.[7] The distribution of functional groups covalently bound to mesoporous silica can be similarly imaged after coupling with appropriate fluorescent labels. Large particles of defined morphology are ideal for this purpose. We have been working with hexagonal particles, also known as arrays of silica nanochannels (ASNCs),[8] as well as with spherical particles of the SBA-15 type (SBA-s)[9] featuring a less ordered pore system and a larger average pore size than the ASNCs (Figure 1, Table 1). In both cases, functionalization reactions were carried out either before or after removal of the SDA.

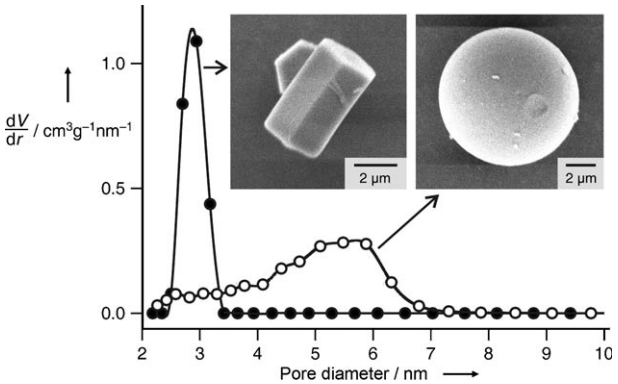

Figure 1. Pore-size distribution of ASNCs (●) and SBA-s (○). The morphology of the particles is evident in the corresponding electron micrographs. The image of the ASNCs shows two particles (one particle is standing on its hexagonal base).

Table 1: Structural properties of the parent ASNCs and SBA-s.

	ASNCs	SBA-s
average pore diameter [nm]	2.9	ca. 5.5
BET surface area [$m^2 g^{-1}$]	1120	795
external surface area [$m^2 g^{-1}$]	37	10
total pore volume [$cm^3 g^{-1}$]	0.62	0.74

Apart from the frequently employed 3-aminopropyltriethoxysilane (APTES), 3-aminopropyltris(methoxyethoxyethoxy)silane (APTMEES) and bis(triethoxysilylpropyl)-amine (BTESPA) were used as reactants (Figure 2). The surface-grafted amino groups were subsequently labeled with fluorescein isothiocyanate (FITC) or Texas Red sulfonyl chloride (TR). Deposition of the silanes from hexane at room temperature and curing at 80°C led to the remarkably different distributions shown in Figure 2. The following can be concluded: 1) As a result of the comparatively large pore diameter, reaction with calcined SBA-s leads to a high degree of pore-surface grafting for all investigated silanes. The uniformity of the functional-group distribution decreases in the series APTES > BTESPA > APTMEES. As a consequence of the narrower channels, this tendency is more pronounced when grafting to calcined ASNCs. In the case of APTMEES, excellent selectivity for the external surface is obtained. The observation that BTESPA produces a less uniform distribution than APTES is in agreement with results obtained from a systematic study of the pore-size distribu-

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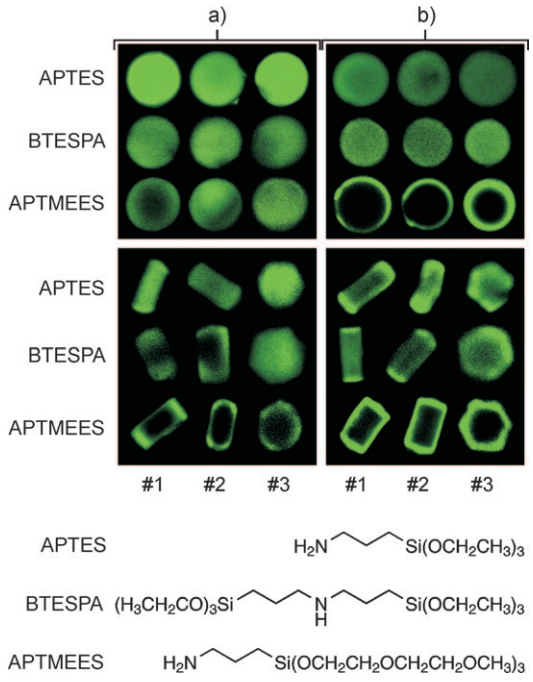

Figure 2. CLSM images (after FITC labeling) of SBA-s (top panels) and ASNCs (bottom panels) functionalized with APTES, BTESPA, or APTMEES. Three particles are shown for each silane/silica combination. In the case of the as-synthesized samples, the SDA was extracted after FITC labeling (b). The samples in (a) were calcined before the functionalization. Particles of ASNCs depicted in (a,#3) and (b,#3) are standing on their hexagonal base.

tions and luminescence intensities of respective FITC-coupled, MCM-41-based samples.[10] 2) Despite the presence of the SDA, grafting of APTES to as-synthesized SBA-s and ASNCs leads to significant pore-surface derivatization. The reaction of APTES with as-synthesized mesoporous materials of the MCM-41 (alkyltrimethylammonium ions as SDA) and SBA-15 type (poly(alkylene oxide) block copolymer as SDA) is a frequently used procedure for the functionalization of the external surface. Our results show, however, that this method is not ideal. A similar result is obtained with BTESPA, despite its larger size and higher reactivity. The ability of ethoxy-, methoxy-, and chlorosilanes to displace the SDA from MCM-41-type materials can, in fact, be exploited to functionalize the pore surface.[11] 3) High selectivity for the external surface is observed upon grafting of APTMEES to as-synthesized materials.

Analysis of the amount of surface-grafted amino groups by the fluorogenic derivatization reaction with fluorescamine[12] revealed quantitative adsorption of the respective silanes on calcined ASNCs and SBA-s. Exclusive grafting to the external surface would therefore give rise to an amino group density of 1.6 nm^{-2} for ASNCs and 6.0 nm^{-2} for SBA-s. As such high densities are unlikely, we assume that partial grafting to the pore surface occurs even in the case of APTMEES, although apparently predominantly at sites close to the pore entrances.

The question remains whether the pronounced tendency of APTMEES to graft to the external surface is a consequence of pore blocking. To exclude this possibility, we conducted the following experiment. As-synthesized SBA-s and ASNCs were functionalized with APTMEES as described above. After FITC labeling and extraction of the SDA, APTES was deposited from ethanol (3 h, RT), coupled to TR, and cured at 80 °C. The samples were washed repeatedly until the washing solution became colorless. Figure 3 shows that the bulky TR labels have entered the

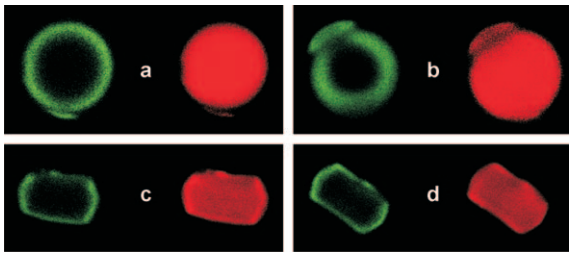

Figure 3. CLSM images of SBA-s (a and b) and ASNCs (c and d) after external-surface functionalization with APTMEES and labeling with FITC, followed by reaction with APTES in ethanol and labeling with TR. The left (green) images of each panel show the luminescence of the coupled FITC labels, whereas the right (red) images are obtained upon selective excitation of the TR labels.

channels despite the presence of FITC-labeled amino groups on the external surface. This indicates that the pores are indeed accessible after external surface functionalization with APTMEES.

Deposition of aminopropylalkoxysilanes on silica at room temperature results in the formation of hydrogen bonds between the amino groups and the surface silanols. There is evidence in the case of APTES that this adsorption step reaches an equilibrium within 1 min (in toluene).[13] Deprotonation of the silanol groups by the amines can lead to electrostatic interactions. The formation of siloxane bonds prior to the curing step has been observed in the APTES/silica system.[13] The distribution of a given aminosilane is determined by its mobility on the mesoporous silica surface, and, in the case of as-synthesized materials, its ability to penetrate the SDA-filled channels. Our results suggest that APTMEES is significantly less mobile than BTESPA and APTES.

It is reasonable to assume that polar solvents lead to increased mobility. This concept has been used previously to control the site isolation of amino groups on mesoporous silica.[10,14] The combination of APTMEES deposition and CLSM imaging can be used to directly visualize the effect of the solvent on the functional-group distribution. As can be seen in Figure 4, the uniformity of the functional-group distribution increases in the series toluene($\approx$hexane) < THF < acetone $\approx$ ethanol.

In summary, we have shown that the deposition of APTMEES from hexane leads to excellent selectivity for the external surface of mesoporous silica. In case of small mesopore sizes, a high degree of external surface modification is obtained even for calcined samples. In work with as-synthesized samples, APTMEES is superior to the frequently used APTES in terms of its tendency to graft to the external particle surface. The mesopores remain accessible after external surface functionalization with APTMEES.

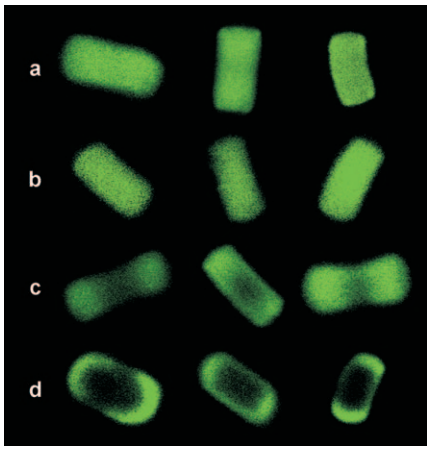

Figure 4. CLSM images of calcined ASNCs after functionalization with APTMEES in ethanol (a), acetone (b), THF (c), toluene (d), and subsequent FITC labeling. The amino content of the samples is close to 100 μmol g^{-1}.

Experimental Section

Spherical SBA-15 particles (SBA-s) were synthesized as follows:[9] A solution of hexadecyltrimethylammonium bromide (0.465 g; Fluka) in H_2O (20 mL) was added to a solution of Pluronic P123 (3.10 g; $EO_{20}PO_{70}EO_{20}$, $M_{av} = 5800$, Aldrich) in 1.5 M aqueous HCl (45.9 mL). After the addition of ethanol (7.8 mL), the mixture was stirred vigorously and tetraethoxysilane (10 mL; TEOS, Fluka) was added dropwise. Following further stirring for 2 h at RT, the mixture was transferred to a Teflon-lined autoclave and kept at 78 °C for 72 h. The product was obtained by filtration, washed with H_2O (50 mL), and dried at RT. Calcination was performed at 500 °C for 16 h with a heating rate of 1.2 K min^{-1}. As an alternative to calcination, the structure-directing agent (SDA) was removed by Soxhlet extraction with ethanol over 24 h.[15]

ASNCs were prepared by a procedure similar to the one reported by Kievsky and Sokolov.[8] Hexadecyltrimethylammonium chloride (4.85 g; Acros) was dissolved in a mixture of doubly distilled H_2O (76 mL) and 32 % aqueous HCl (60 mL) by stirring for 1 min at ca. 1000 rpm in a polypropylene beaker. The solution was subsequently cooled to 0 °C for 15 min without stirring, followed by the slow addition of cold TEOS (2 mL; Aldrich, 99.999 %) and further stirring for 30 s. The resulting mixture was kept at 0 °C under quiescent conditions for 3 h. The product was collected by filtration and washed with H_2O (250 mL). The SDA was removed by first heating at 300 °C for 2 h and calcining at 550 °C for 12 h. Heating rates of 2 K min^{-1} were applied. Alternatively, the SDA was extracted by dispersing 200 mg of the as-synthesized ASNCs in a solution of ammonium nitrate (90 mg) in ethanol (45 mL), and stirring the mixture at 60 °C for 15 min. For complete extraction, this step was repeated twice.[16] For both ASNCs and SBA-s, removal of the SDA by extraction was performed after aminosilane grafting and FITC coupling. Extraction of the SDA before FITC coupling led to the same results in terms of the distribution of the labels.

Amino groups were grafted to the mesoporous silica materials as follows: calcined or as-synthesized ASNCs or SBA-s (200 mg) was dispersed in hexane (10 mL), and APTES, APTMEES, or BTESPA (ABCR) (20 μmol) was added. After the mixture had been stirred for 10 min, the functionalized mesoporous silica was recovered by filtration and cured in an oven at 80 °C for 16 h.

The samples were labeled by stirring in ethanol containing three equivalents (relative to the amount of the respective silane) of FITC (fluorescein 5-isothiocyanate, isomer I, Fluka) or TR (Texas Red sulfonyl chloride, mixed isomers, Molecular Probes) for 16 h at RT. The labeled samples were washed repeatedly with ethanol until the washing solution became colorless.

Nitrogen sorption isotherms were collected at 77 K using a Quantachrome NOVA 2200. Samples were vacuum-degassed at 80 °C for 3 h. The total surface area was calculated by the BET method, whereas the external surface area was determined from the high-pressure linear part of the α_S plot ($\alpha_S > 1$).[17] Size distributions of the mesopores were evaluated by the NLDFT method developed for silica exhibiting cylindrical pore geometry (NOVAWin2 software, Version 2.2, Quantachrome Instruments).[18] The adsorption branch of the respective isotherm was used for the calculations. The total pore volume was determined by the amount of adsorbed nitrogen at a relative pressure of 0.95. Scanning electron microscopy images were acquired on a JEOL JSM-6060. The CLSM setup consisted of an Olympus BX 60 microscope equipped with a FluoView detector and lasers operating at 488 and 543.5 nm. Optical slices in the center of the particles were selected.

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[1] A. Taguchi, F. Schüth, *Microporous Mesoporous Mater.* **2005**, *77*, 1.
[2] M. Vallet-Regí, F. Balas, D. Arcos, *Angew. Chem.* **2007**, *119*, 7692; *Angew. Chem. Int. Ed.* **2007**, *46*, 7548.
[3] I. I. Slowing, B. G. Trewyn, S. Giri, V. S.-Y. Lin, *Adv. Funct. Mater.* **2007**, *17*, 1225.
[4] I. I. Slowing, B. G. Trewyn, V. S.-Y. Lin, *J. Am. Chem. Soc.* **2006**, *128*, 14792.
[5] M. Liong, J. Lu, M. Kovochich, T. Xia, S. G. Ruehm, A. E. Nel, F. Tamanoi, J. I. Zink, *ACS Nano* **2008**, *2*, 889.
[6] K. Cheng, C. C. Landry, *J. Am. Chem. Soc.* **2007**, *129*, 9674.
[7] a) S. Megelski, A. Lieb, M. Pauchard, A. Drechsler, S. Glaus, C. Debus, A. J. Meixner, G. Calzaferri, *J. Phys. Chem. B* **2001**, *105*, 25; b) M. Pauchard, S. Huber, R. Méallet-Renault, H. Maas, R. Pansu, G. Calzaferri, *Angew. Chem.* **2001**, *113*, 2921; *Angew. Chem. Int. Ed.* **2001**, *40*, 2839; c) C. Seebacher, J. Rau, F.-W. Deeg, C. Bräuchle, S. Altmaier, R. Jäger, P. Behrens, *Adv. Mater.* **2001**, *13*, 1374; d) G. Calzaferri, S. Huber, H. Maas, C. Minkowski, *Angew. Chem.* **2003**, *115*, 3860; *Angew. Chem. Int. Ed.* **2003**, *42*, 3732.
[8] Y. Kievsky, I. Sokolov, *IEEE Trans. Nanotechnol.* **2005**, *4*, 490.
[9] a) Y. Ma, L. Qi, J. Ma, Y. Wu, O. Liu, H. Cheng, *Colloids Surf. A* **2003**, *229*, 1; b) A. Katiyar, N. G. Pinto, *Small* **2006**, *2*, 644.
[10] H. Salmio, D. Brühwiler, *J. Phys. Chem. C* **2007**, *111*, 923.
[11] a) V. Antochshuk, M. Jaroniec, *Chem. Commun.* **1999**, 2373; b) V. Antochshuk, M. Jaroniec, *Chem. Mater.* **2000**, *12*, 2496.
[12] a) H. Ritter, M. Nieminen, M. Karppinen, D. Brühwiler, *Microporous Mesoporous Mater.* **2009**, *121*, 79; b) H. Ritter, D. Brühwiler, *J. Phys. Chem. C* **2009**, *113*, 10667.
[13] K. C. Vrancken, K. Possemiers, P. Van Der Voort, E. F. Vansant, *Colloids Surf. A* **1995**, *98*, 235.
[14] K. K. Sharma, A. Anan, R. P. Buckley, W. Ouellette, T. Asefa, *J. Am. Chem. Soc.* **2008**, *130*, 218.
[15] C. A. Melero, G. D. Stucky, R. van Grieken, G. Morales, *J. Mater. Chem.* **2002**, *12*, 1664.
[16] N. Lang, A. Tuel, *Chem. Mater.* **2004**, *16*, 1961.
[17] A. Sayari, P. Liu, M. Kruk, M. Jaroniec, *Chem. Mater.* **1997**, *9*, 2499.
[18] P. I. Ravikovitch, S. C. O. Domhnaill, A. V. Neimark, F. Schüth, K. K. Unger, *Langmuir* **1995**, *11*, 4765.

