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Functional Group Distributions on Mesoporous Silica

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Abstract: Most applications of mesoporous silica require some degree of functionalization. The surface of porous materials can be divided into external and internal (pore) surfaces, and in many cases, a selective functionalization of these surface subsections is desired. This short review outlines our recent work in this field and focuses on the postsynthetic functionalization of mesoporous silica with aminopropylalkoxysilanes and on the analysis of the respective functional group distributions by confocal laser scanning microscopy. Methods to obtain an amino-functionalized external surface and functional group gradients on the pore surface are reported. Arrays of silica nanochannels (ASNCs) serve as a model system for mesoporous silica.

Keywords: Amines · Confocal laser scanning microscopy · Functionalization · Nanochannels · Silica

1. Introduction

Since its discovery in the early 1990s,[1] mesoporous silica with ordered pores has quickly developed into an important class of materials with wide-spread applications in fields such as catalysis,[2] drug delivery,[3] sensing,[4] imaging,[5] and adsorption.[6] Most of these applications require functionalization of the mesoporous silica surface. Mesoporous silica particles for drug delivery are a particularly illustrative example for the need of modification techniques that enable a controlled placement of functional groups on specific parts of the very large surface of these materials. Functional groups on the external particle surface define the interaction with the surrounding medium, solving different tasks, such as targeting, avoiding detection by the immune system, or preventing particle aggregation. In addition to the modification of the external surface, the pore surface needs to be functionalized independently with moieties for the optimization of drug adsorption. An ideal drug delivery system should further be equipped with stimuli-responsive gates ensuring zero release before reaching the target. The concept of opening and closing mesoporous silica channels by a physical or chemical stimulus has recently gained substantial interest.[7]

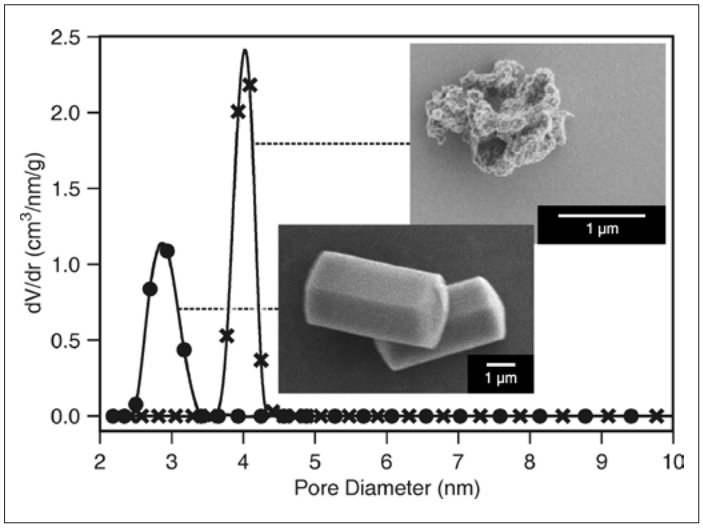

Fig. 1. Pore size distributions and scanning electron microscopy images of mesoporous silica MCM-41 (crosses) and arrays of silica nanochannels (ASNCs, dots).

A key issue in the characterization of functionalized mesoporous silica is the identification of the functional group distribution. Unfortunately, in many reports, particularly in the field of catalysis, this issue is not well addressed. As a result, conclusions regarding structure–activity relationships are often based on incomplete data and do not contribute to the understanding of the respective systems.

To investigate the parameters that affect the functional group distribution, we have been mainly focusing on amines, as they are among the most frequently employed groups for the modification of mesoporous silica surfaces. Once the amines are anchored, a further moiety can be coupled by means of amine-reactive derivatives such as isothiocyanates or sulfonyl chlorides. This concept is especially helpful for the analysis of the amino group distributions, because it allows the attachment of labels which amplify the presence of the amino groups in the pores by reducing the pore volume and, in certain cases, the pore diameter.[8,9] The use of fluorescent labels opens further possibilities for characterizing the functional group distributions by confocal laser scanning microscopy (CLSM).[10–12] However, CLSM requires relatively large mesoporous silica particles with defined morphology. Most procedures for the synthesis of mesoporous silica yield materials with irregular morphology but often extremely narrow pore size distributions (Fig. 1).

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Despite their slightly broader pore size distribution, arrays of silica nanochannels (ASNCs) are ideal for CLSM,[10] as the entrances of the hexagonally arranged channels are exclusively located on the base surfaces of the well-defined particles.[13] Selective external surface functionalization, accumulation at the pore entrances, or uniform distributions of functional groups can therefore immediately be identified.

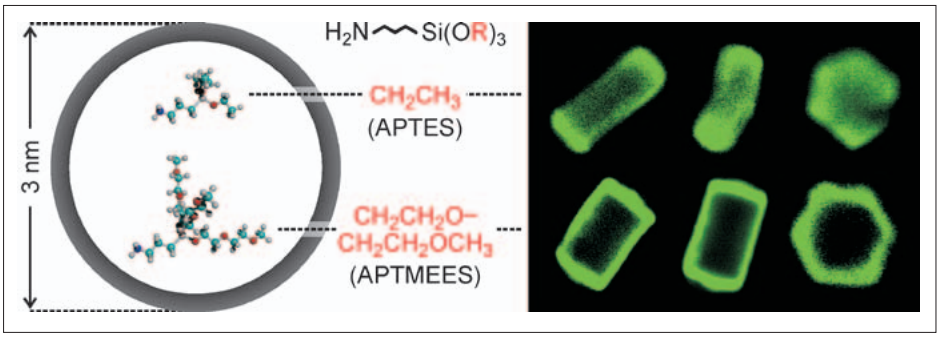

Fig. 2. Functionalization of as-synthesized mesoporous silica with a 3-aminopropyltrialkoxysilane. ASNCs were used to enable imaging of the functional group distribution by means of CLSM. The grafted amino groups were labeled with fluorescein isothiocyanate (FITC) and optical slices in the center of the particles were selected. Each row of CLSM images shows three particles, with the outermost right particle standing on its hexagonal base. The top row of the CLSM images indicates the distribution of the amino groups in the case of the frequently used precursor APTES (R = CH_2CH_3). Note that a significant amount of pore surface functionalization occurs. Selective functionalization of the external surface is obtained with APTMEES (R = $CH_2CH_2OCH_2CH_2OCH_3$), as apparent from the bottom row of CLSM images. The scheme on the left compares the size of the silanes with the pore size of the ASNCs.

2. Functionalization of the External Surface

The synthesis of mesoporous silica employs structure-directing agents (SDAs) to generate an ordered pore system.[14] Grafting of 3-aminopropyltrialkoxysilanes, typically 3-aminopropyltriethoxysilane (APTES), to mesoporous silica before removing the SDA is regarded as a straightforward method for external surface modification. Intuitively, one would assume that the SDA blocks the pores and thus prevents the silane molecules from reacting with silanol groups on the pore surface. Following this approach, we found that the degree of pore surface grafting strongly depends on the organosilane. In case of the frequently used APTES, significant derivatization of the pore surface was found despite the presence of the SDA in the pores, whereas 3-aminopropyltris(methoxyethoxyethoxy silane) (APTMEES), grafted preferentially to external surface sites, most likely as a consequence of the higher steric hindrance and lower surface mobility (Fig. 2). The mesopores remained fully accessible for further modification after functionalization of the external surface with APTMEES (Fig. 3). This method also works well for materials with pores larger than those of the ASNCs and has been tested for hexadecyltrimethylammonium and block copolymer SDAs.[10]

The technique of grafting to as-synthesized mesoporous silica (still containing the SDA) suffers from the disadvantage that the preferred method of SDA removal, *i.e.* calcination at temperatures around 500 °C, cannot be employed. The SDA needs to be extracted to conserve the functional groups, which often requires several steps to obtain a material that is free of residual SDA. We found that grafting of APTMEES from non-polar solvents produces a high degree of external surface functionalization even in the case of calcined materials with fully accessible pores. However, in contrast to grafting to as-synthesized mesoporous silica, the degree of external surface functionalization strongly depends on the pore diameter. Large pore diameters increase the degree of pore surface functionalization.[10]

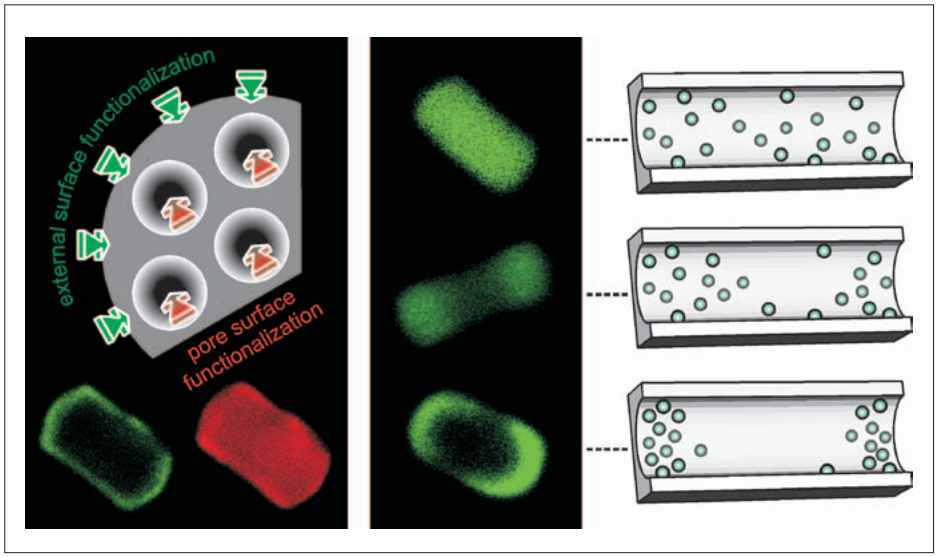

Fig. 3. Left: CLSM images of ASNCs after external surface functionalization with APTMEES and labeling with FITC, followed by reaction with APTES in ethanol and labeling with Texas red (TR). The green image shows the luminescence of the FITC labels, whereas the red image was obtained upon excitation of the TR labels, indicating the excellent accessibility of the channels after external surface functionalization. Right: CLSM images of calcined ASNCs after functionalization with APTMEES in acetone, THF, toluene (top to bottom, particles are FITC-labeled) and schematic representation of the corresponding functional group distribution in the silica nanochannels. Note that the channels are in fact much longer (*ca.* 5 μm) compared to the pore diameter (3 nm). One particle contains approximately 200'000 nanochannels.

3. Functionalization of the Pore Surface

Obtaining uniform distributions of functional groups by a postsynthetic approach is challenging. Co-condensation techniques are typically employed to achieve a homogeneous distribution over the entire mesoporous silica surface.[15] This requires a condensable precursor, often silanes of the type R'–$Si(OR)_3$, with the functionality R' being stable under the conditions of the mesoporous silica synthesis. The addition of organoalkoxysilanes to the synthesis mixture can have a pronounced effect on the pore structure and morphology of the resulting mesoporous material. High functionalization degrees lead to decreasing mesoscopic order. Postsynthetic functionalization, on the other hand, offers possibilities for functional group placement and high surface concentration without compromising the mesoscopic order.[16] A simple procedure for conducting postsynthetic functionalization is the reaction of an organotrialkoxysilane R'–$Si(OR)_3$ with the surface silanol groups of the calcined mesoporous silica. Such reactions are typically performed in an organic solvent, often at elevated tempera-

tures. Trace water needs to be avoided if a high uniformity of the functional group distribution is desired. We have observed that clustering of the silanes is promoted by the presence of water, leading to non-uniform distributions of the grafted amino groups with higher concentrations at the pore entrances. The accumulation of functional groups at the pore entrances in combination with cross-linking of the silanes eventually causes pore blocking. As a consequence, the central part of the channels (the pore body) becomes inaccessible.[11]

Particularly in the case of amino-functionalized silanes, it is reasonable to assume that polar solvents lead to increased mobility of the molecules on the mesoporous silica surface. This concept can for example be applied to control the site isolation of amino groups on mesoporous silica.[9,17] Using the deposition of APTMEES on ASNCs, we have investigated the influence of solvent polarity on the functional group distribution. The uniformity of the pore surface functionalization was found to increase with increasing solvent polarity. Interestingly, grafting of APTMEES from non-polar solvents led to external surface functionalization accompanied by an accumulation of functional groups on the pore surface close to the pore entrances. This feature is of particular interest for the installation of pore entrance gates.

4. Conclusions

For many applications of mesoporous silica, a controlled functional group placement is crucial. The functionalization of specific regions of the mesoporous silica surface (external surface, pore surface, pore entrances) forms an integral part of the concept of using these materials as drug delivery devices, sensors, or advanced adsorbents. CLSM is an ideal method to analyze the spatial distribution of functional groups on mesoporous silica and has allowed us to devise procedures for grafting to surface subsections or for producing functional group gradients. Considering the variety of pore and particle sizes in the mesopore range, it is obvious that the development of generally applicable methods for the selective functionalization of mesoporous silica surfaces remains a challenge. This is particularly true for mesoporous nanoparticles, where the differences in the accessibility of pore surface vs. external surface can become negligibly small.

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