Mesoporous silica nanomaterials for applications in catalysis, sensing, drug delivery and gene transfection

by

Daniela Rodica Radu

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Program of Study Committee:
Victor Shang-Yi Lin, Major Professor
William S. Jenks
Marc D. Porter
Nicola L. Pohl
Brent H. Shanks

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Graduate College

Iowa State University

This is to certify that the doctoral dissertation of

Daniela Rodica Radu

has met the dissertation requirements of Iowa State University

Major Professor

For the Major Program

DEDICATION

To my children

"Float straight ahead and if the land you are looking for does not exist yet, be sure that God will create it for rewarding your courage."

Isabella of Castile to Christopher Columbus

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ABSTRACT

Structurally well-defined mesoporous silica materials, such as MCM-type silicas with tunable pore size and narrow pore-size distribution have attracted much attention for their potential applications in adsorption, catalysis, separation, and sensing. Organofunctionalized MCM-41 silica pores could serve as synthetic scaffolds to mimic enzyme or antibody active sites for specific covalent and/or noncovalent interactions with target molecules. Herein, we designed and synthesized a fluorescence sensory system to study the molecular recognition events of biogenic molecules, such as dopamine and glucosamine, inside different functionalized mesoporous silica microenvironment.

We have also synthesized a poly(lactic acid) coated MCM-41-type mesoporous silica nanosphere (PLA-MSN) material that can serve as a fluorescence sensor system for the detection of amino-containing neurotransmitters in neutral aqueous buffer. Utilizing the PLA layer as a gatekeeper, we investigated the molecular recognition events between several structurally simple neurotransmitters, i.e., dopamine, tyrosine, and glutamic acid and a pore surface-anchored *o*-phthalic hemithioacetal (OPTA) groups. These OPTAs function as a fluorescence-sensing group that can react with the neurotransmitters with primary amine groups and form the corresponding fluorescent isoindole products. The poly(lactic acid) layer of the PLA-MSN sensor showed a unique "sieving" effect by regulating the rates of diffusion of the amino acid-based neurotransmitters into the sensor mesopores of the material.

An MCM-41 type mesoporous silica nanosphere-based (MSN) controlled-release delivery system has been synthesized and characterized using surface-derivatized cadmium sulfide (CdS) nanocrystals as *chemically removable caps* to encapsulate several

pharmaceutical drug molecules and neurotransmitters inside the organically functionalized MSN mesoporous framework. We studied the stimuli-responsive release profiles of vancomycin- and adenosine triphosphate (ATP)-loaded MSN delivery systems by using disulfide bond-reducing molecules, such as dithiothreitol (DTT) and mercaptoethanol (ME), as *release triggers*. The biocompatibility and delivery efficiency of the MSN system with neuroglial cells (astrocytes) in vitro were demonstrated. In contrast to many current delivery systems, the molecules of interest were encapsulated inside the porous framework of the MSN not by adsorption or sol-gel types of entrapment but by capping the openings of the mesoporous channels with size-defined CdS nanoparticles to physically block the drugs/neurotransmitters of certain sizes from leaching out. We envision that this new MSN system could play a significant role in developing new generations of site-selective, controlled-release delivery nanodevices.

For reaching and repairing a damaged cell or for killing a cancer cell, a drug molecule -- no matter how potent -- has to enter the particular cell. Several carriers have been imagined and designed to facilitate the membrane penetration – all suffering from laborious synthesis and the requirement of highly specific targeting. However, for many applications such as local cancer therapy or in vitro gene transfection, an ideal carrier will be able to penetrate any type of cell and deliver the encapsulated molecule inside the cell body.

We have recently developed a new mesoporous silica nanosphere-based (MSN) transmembrane carrier that demonstrates ability to effectively transport molecules of interest through various cell membranes via endocytosis. Our system took advantage of the ordered mesoporous structure of MSN, where the nanometer-sized pores are large enough to accommodate/encapsulate pharmaceutical drugs and neurotransmitters.[1] The drug-loaded

mesopores were covalently capped in situ with either surface derivatized CdS nanocrystals or polyamido amine (PAMAM) dendrimers through a chemically cleavable linkage. The removable caps prevented the mesopore-encapsulated molecules from leaching. As a proof of principle, we studied the transmembrane activity of MSNs loaded with membrane impermeable fluorescent dyes on HeLa human cancer cell line, rat neuronal cells, and CHO cell line. The confocal fluorescence images, TEM micrographs, and flow-cytometer measurements showed that the MSNs were successfully engulfed by the cells without exhibiting cytotoxicity or mitosis blockage.

In the same context, as the ability to penetrate the cell membrane was demonstrated, we tried our system as gene carrier. The plasmid DNA of choice was pEGFP – encoding Green Fluorescent Protein. We successfully achieved Green Fluorescent Protein (GFP) gene expression in HeLa human cancer cell line and rat neuronal cells. Attached we present a collection of images illustrating the engulfed fluorescent silica in the cell body (the nuclei of the cells were blue stained).

CHAPTER 1. GENERAL INTRODUCTION

Introduction and Dissertation Organization

The overall objective of this dissertation is to present the versatility of mesoporous silica nanomaterials for several applications described herein.

The dissertation is organized in eight chapters: the first chapter encloses a literature review, the chapters 2-8 consist of journal articles either published or submitted for publication and chapter 9 concludes this dissertation with summaries of the results and an outlook for future work.

Chapter 1 is an overview of nanostructured mesoporous sol-gel materials with emphasis on their application in catalysis, sensing and biology.

Chapter 2 presents a new method for fine tuning the amount of accessible functional groups on the internal surface of the mesopores in Mesoporous Silica Nanospheres (MSN) We developed a synthetic method that can fine tune the amount of chemically accessible organic functional groups on the pores surface of Mesoporous Silica Nanospheres (MSN). The principle of this method resides on exploiting electrostatic and size matching between the cationic alkylammonium head group of the CTAB surfactant with various anionic organoalkoxysilane precursors at the micelle-water interface in a base-catalyzed condensation reaction of silicate (a journal article accepted for publication). My personal contribution represents 55% of the presented research.

Chapter 3 describes the application of mesoporous silica nanomaterials in two catalysis applications. We demonstrated that a homogeneous coverage of mesopores with organic functional groups can be achieved through rational design/choice of organosilane

precursors. By employing an ethylenediamine functional group for chelating Cu^{2+}, a Cu-functionalized MSNs silica catalyst was used for the synthesis of polyalkynylene-based conducting polymer (molecular wire). My personal contribution represents 50% of the presented research.

Chapter 4 outlines the organically functionalized MSN for another catalytic application. Organosulfonic acid-functionalized mesoporous silicas were synthesized in a one-step approach of co-condensing inorganic-organic reagents in the presence of different surfactant templates with in situ oxidation of the thiol groups to the sulfonic acid groups. The resulting materials were tested for their catalytic performance in the esterification of fatty acid with methanol to produce methyl esters. The activity of the organosulfonic acid-functionalized silicas in the esterification was compared to that of standard acidic resins. (published journal articles). My personal contribution represents 30% of the presented research.

Chapter 5 presents a sensing application of Mesoporous Silica Nanospheres (MSNs). We have synthesized a poly(lactic acid) coated mesoporous silica nanosphere (PLA-MSN) material that can serve as a fluorescence sensor system for detection of amino-containing neurotransmitters in neutral aqueous buffer. We investigated the molecular recognition events between several structurally simple neurotransmitters, i.e., dopamine, tyrosine, and glutamic acid and a pore surface-anchored o-phthalic hemithioacetal (OPTA) group, which functions as a fluorescence-sensing group that can react with the neurotransmitters with primary amine groups and form the corresponding fluorescent isoindole products. The poly(lactic acid) layer of the PLA-MSN sensor showed a unique "sieving" effect that regulates the rates of diffusion of the amino acid-based neurotransmitters into the sensor

mesopores of the material (published journal article). My personal contribution represents 51% of the presented research.

Chapter 6 is focused on the application of MSNs in drug delivery. The mesoporosity of MSNs confer these materials properties of a sponge: they can soak impressive amounts of molecules in solution. However, the cannels being both-ends opened, the content is easily leaching. Consequently, we have developed a "capping" strategy. We examined bio-friendly molecules such as polyamidoamine dendrimers of generations G2.5 to G4.5 as the caps. The release profiles of the different capped MSNs were investigated. My personal contribution represents 20% of the presented research.

In Chapter 7 the drug delivery system employed MSNs loaded with Doxorubicin, an anticancer drug. The results demonstrated that these nano-Trojan horses have ability to deliver Doxorubicin to cancer cells and induce their apoptosis (submitted journal articles). My personal contribution represents 50% of the presented research.

Chapter 8 is devoted to the development of a gene transfection nanocarrier that has MSNs as a core of the nanocomposite. We exploited not only the mesopores but also the surface and the silica matrix of these beads for biological applications. A multi-functionalized, MSN-based transfection vector with G2-PAMAM dendrimers covalently attached to MSNs exterior surface was synthesized. The p-EGFP-C1 gene-coated MSN nanocomposite was able to transfect cancer cell lines, such as human HeLa and CHO cancer cell lines. The green fluorescent protein expression induced by the MSN system in these cells was monitored via fluorescent microscopy and confocal laser microscopy. The results indicated that the transfected cells exhibited less or none of the cytotoxicity commonly associated with the use other transfection methods. The gene carrier potential of MSNs by in

transfecting primary cells and cotransfecting of two different genes was also investigated. My personal contribution represents 49% of the presented research.

The results indicated the versatility of this novel gene carrier for rationally designed gene therapy (published and submitted journal articles).

Finally, Chapter 9 is a brief conclusion of the dissertation with a general assessment of the accomplished goals as well as an overview of potential future applications.

Literature Review

Several versatile surfactant templated sol-gel pathways have been developed to prepare nanostructured porous materials and composites with different morphologies (e.g., monoliths, nanospheres, nanoparticles, and thin films), structures, compositions and properties. The synthetic conditions were systematically studied and optimized. The template effects on pore structure as well as synthetic process, especially template removal steps as well as the systematic functionalization, have been investigated.[1-4]

In the early nineties,[1(a)] scientists from *Mobil Oil Corporation* synthesized ordered mesoporous materials of the M41S type, MCM-41 being one of the distinguished members of this family.

In M41S materials, a liquid crystal templating (LCT) mechanism is a process during which long chain surfactant molecules arrange themselves through micelle self-assembly to form liquid-crystalline phases, surrounded by inorganic oxides forming a framework to generate the formation of hexagonal, lamellar or cubic structures, as illustrated in Figure 1-1.

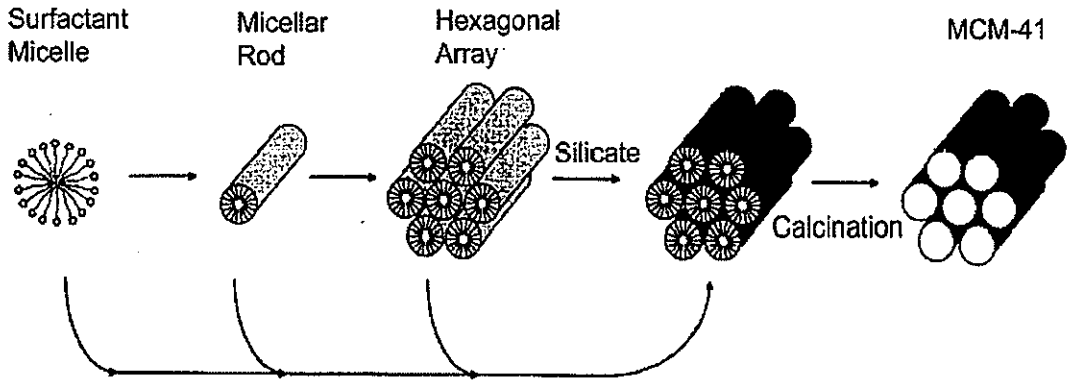

Figure 1-1. Schematics of MCM-41 type materials formation mechanism

This material possesses a porous system consisting of hexagonally arranged channels with diameters varying from 15 to 100 Å. MCM-41 has attracted the attention of scientists due to its elevated specific surface area, high thermal and hydrothermal stability, possibility of controlling its pore size and its hydrophobicity and acidity.

Also, recent advancements in utilizing organic surfactants or block copolymers as structure-directing templates for the syntheses of structurally well-defined mesoporous silica materials, such as MCM-48,[1(b)] SBA-15,[2] MSU,[3] and FSM-16,[4] has attracted much attention for their potential applications in sensing,[5] catalysis,[6] and drug delivery.[7] Obviously, the realization of these applications greatly depends on the ability of functionalization of the interior and exterior surfaces of the mesoporous silicas with various organic functional groups.

Although a wide variety of synthetic approaches have been pursued and some significant progresses have been made, few would argue that the current state-of-the-art methods, such as post synthesis grafting[8] and organosiloxane/siloxane co-condensation

methods,[9] need not to be improved in terms of controlling the amount and location of the incorporated functional groups on the surface of the mesoporous silica materials. For example, functional groups incorporated via the post synthesis grafting method typically congregate at the opening parts of porous channels resulting in an inhomogeneous surface coverage,[10] whereas the amount of functional groups introduced by the organosiloxane/siloxane co-condensation method is yet to reach above 25% surface coverage without reaching an uniform coverage.

The composition and pore structures were thoroughly studied with various spectroscopic and microscopic methods such as IR, TGA, SEM, TEM, BET (gas sorption measurements), XRD and solid state NMR.

As part of one of the most active research areas in science, nanoscience,[11] these materials has also raised great interest in the fields of microscale electronics,[12-14] electro-optics,[15] biosensors,[16-18] etc. One particularly interesting application is the development of novel nanomaterials-based drug delivery systems. Traditionally, responsive polymer systems have been employed in such devices. [19-20] For example, degradable polymers are synthesized in the presence of the drug molecule of interest.[21] The resulting polymer/drug composite materials usually exhibit slow rates of drug release under normal conditions. Upon stimulation, the degradation of polymer matrix is accelerated, and the release of drug molecules is thereby enhanced. Drug delivery polymers that are responsive toward several types of stimulants, such as temperature, pH, and magnetic/electric field, have been reported in the literature.[22-25]

In addition to polymer-based drug delivery systems, the organically functionalized MCM-type mesoporous silica materials[26-27] offer several attractive features, such as stable

mesoporous structures, large surface areas, tunable pore sizes and volumes, and well-defined surface properties, that are ideal for encapsulation of pharmaceutical drugs, proteins,[28-32] and other biogenic molecules.[33]

Few approaches reported in literature have utilized solid silica nanoparticles as gene transfection vectors or enhancers.[34-35] However, there are no precedent reports for utilization of mesoporous silica-based material in intracellular gene transfer. The two publications related to intracellular delivery: drug delivery and gene transfection have brought a new dimension to the applicability of MSNs. Virtually any drug within a size range compatible with the size of the meso-channels has potential to be encapsulated and further deliver intracellularly. In the same way, large polymeric molecules such as DNA and RNA that have ability to be electrostatically attached to the derivatized-MSN are delivered to cells.

In conclusion, mesoporous silica materials proved versatility in several applications, as will be showed in the current dissertation.

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CHAPTER 2. FINE-TUNING THE DEGREE OF ORGANIC FUNCTIONALIZATION OF MESOPOROUS SILICA NANOSPHERE MATERIALS VIA AN INTERFACIALLY DESIGNED CO-CONDENSATION METHOD

A paper accepted for publication in ***Chemical Communications***

Daniela R. Radu, Cheng-Yu Lai, Jianguo Huang, Xu Shu, Victor S.-Y. Lin

Department of Chemistry, Iowa State University, Ames, Iowa

Abstract

A synthetic method that enables the fine tuning of the amount of chemically accessible organic functional groups on the pore surface of MCM-41 type mesoporous silica nanosphere (MSN) materials has been developed by electrostatically matching various anionic organoalkoxysilanes with the cationic cetyltrimethylammonium bromide micelles in a base-catalyzed condensation reaction of tetraethoxysilane.

Introduction

Recent advancements in utilizing organic surfactants or block copolymers as structure-directing templates for the syntheses of structurally well-defined mesoporous silica materials, such as MCM-41/48,[1] SBA-15,[2] MSU-n,[3] and FSM-16,[4] has attracted much attention for their potential applications in sensing,[5] catalysis,[6] and drug delivery.[7] Obviously, the realization of these applications greatly depends on the ability of functionalization of the interior and exterior surfaces of the mesoporous silicas with various

organic functional groups. Although a wide variety of synthetic approaches have been pursued and some significant progresses have been made, few would argue that the current state-of-the-art methods, such as *post synthesis grafting*[8] and *organosiloxane/siloxane co-condensation*[9] methods, need to be improved in terms of controlling the amount and location of the incorporated functional groups on the surface of the mesoporous silica materials. For example, functional groups incorporated via the *post synthesis grafting* method typically congregate at the opening parts of porous channels resulting in an inhomogeneous surface coverage,[10] whereas the amount of functional groups introduced by the *organosiloxane/siloxane co-condensation* method is yet to reach above 25% surface coverage without destroying the structural integrity and the long-range periodicity of the synthesized materials.[9,10] Herein, we report on a new co-condensation method that could generate organically functionalized, MCM-41 type of mesoporous silica nanosphere materials while controlling the surface concentration of organic functional groups.

Materials and Methods

1. Materials

3-Mercaptopropionic acid (99+%), 2,2'-dipyridyl disulfide (98%), (3-mercaptopropyl)trimethoxysilane (MPTES) (95%), 2-mercaptoethanesulfonic acid sodium salt (98%), cetyltrimethylammonium bromide (CTAB), tetraethyl orthosilicate (TEOS, 96%) and dithiothreitol (DTT) were purchased from Aldrich Chemical Co. (Milwaukee, WI). Acetic acid (Glacial), hydrochloric acid (37.4%), sodium hydroxide, ethanol (anhydrous), methanol (HPLC grade), tetrahydrofuran (HPLC grade), hexanes (pesticide grade) and ethyl ether (anhydrous) were obtained from Fisher Scientific Co. (Pittsburgh, PA). Nanopure water

was deionized to 18.0 MΩ-cm in a Barnstead E-pure water purification system and used for the synthesis of MSN materials.

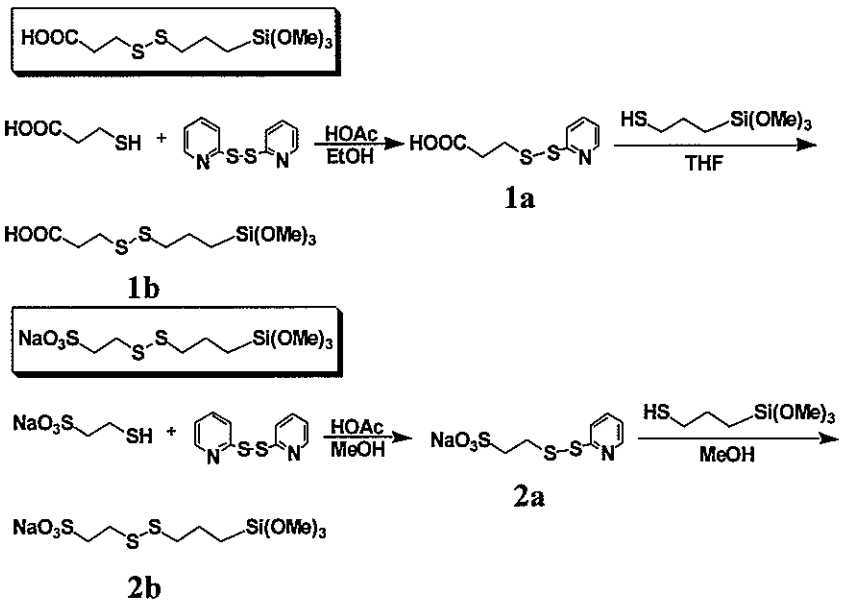


Figure 2-1. Schematic representation of the synthesis of organoalkoxysilane precursors

2. Synthesis of organoalkoxysilane precursors

2.1 Synthesis of 2-[3-(trimethoxysilyl)-propyldisulfanyl]-propionic acid (1b)

As depicted in Figure 2-1, 2-Carboxyethyl-2-pyridyl-disulfide, compound (1a), was prepared according to a procedure published by Carlsson.[14] In a typical synthesis, 3.75 g (17 mmol) of 2,2'-dipyridyl disulfide (Aldrithiol-2) was dissolved in 30 mL of ethanol and a solution of 0.87 mL of mercaptopropionic acid in 5 mL ethanol was injected dropwise. After 20 h of stirring at room temperature, the crude yellow oil product was isolated by rotary evaporation. The purified product (1.45 g, yield = 40%) was obtained from an alumina column chromatography (eluent = CH_2Cl_2/EtOH 3:2 v/v). The product 1.45 g (6.8 mmol) is

corresponding to 40% yield. The characterization of compound 1a is consistent with the literature reported data.[14]

2-[3-(trimethoxysilyl)-propyldisulfanyl]-propionic acid, compound (1b), was prepared by dissolving compound 1a (1.51 g, 7 mmol) in 30 mL THF, followed by a dropwise addition of MPTMS (1.1 g, 5.6 mmol). The resulting yellow solution was stirred under N2 atmosphere for 12 h. After flash evaporation of the solvent, the yellow product was purified by silicagel column chromatography using EA/ hexane in 1:2 ratio as eluent. The purified product (1 g) was isolated with a 60% yield. 1H-NMR ($CDCl_3$), δ 0.76 (t, 2H, CH_2(1)), 1.81 (q, 2H, CH_2(2)), 2.71 (t, 2H,CH_2(5)), 2.81 (*t*, 2H, CH_2(3)), 2.91 (*t*, 2H, CH_2(4)), 3.60 (*s*, 1H, OCH_3); ^{13}C-NMR (D_2O), δ 10.25, 13.69, 23.75, 34.83, 36.98, 42.26, 180.99.

2.2 Synthesis 2-[3-(trimethoxysilyl)-propyldisulfanyl]-ethanesulfonic acid, (2b)

As depicted in Fig. 2-1, 2,2'-dipyridyl disulfide (8.82 g, 40.0 mmol) was dissolved in 50.0 mL methanol, followed by an addition of 1.6 mL of glacial acetic acid as catalyst. To this mixture, 2-mercaptoethanesulfonic acid sodium salt (3.82 g, 20.0 mmol) in 30.0 mL methanol was added dropwise in 30 min with stirring. The reaction mixture was protected from light and stirred at room temperature overnight, followed by solvent evaporation under vacuum. The crude product was purified by dissolving in a small amount of methanol, followed by recrystallization in ethyl ether and dried under vacuum to yield compound 2a (5.14 g, yield = 94.0%). ^{1}H-NMR (300 MHz; DMSO-d6), δ 2.73 (*m*, 2H, CH_2), 3.02 (*m*, 2H, CH_2), 7.24 (*d*, 1H, ArH), 7.81 (*m*, 2H, ArH), 8.45 (*d*, 1H, ArH).

To synthesize 2-[3-(trimethoxysilyl)-propyldisulfanyl]-ethanesulfonic acid sodium salt (2b), compound **2a** (1.36 g, 5.0 mmol) was dissolved in 20.0 mL of methanol with 1.0 mL of glacial acetic acid. To this mixture, (3-mercaptopropyl) trimethoxysilane (0.95 mL,

5.0 mmol) in 10.0 mL of methanol was added dropwise. The mixture was protected from light and stirred under nitrogen at room temperature overnight. The reaction was quenched and the solvent was evaporated under vacuum. The solid product was dissolved in a small amount of methanol, followed by ethyl ether precipitation. The purified product (5.14 g, yield = 74.7%) was collected by filtration and dried under vacuum. 1H-NMR (300 MHz; D_2O) δ 0.79 (*t*, 2H, CH_2(1)), 1.83 (*q*, 2H, CH_2(2)), 2.81 (*t*, 2H, CH_2(3)), 3.03 (*t*, 2H, CH_2(5)), 3.27 (*t*, 2H, CH_2(4)), 3.60 (*s*, 7H, OCH_3).

3. Synthesis of MSN materials

Three organically functionalized mesoporous silica materials, MSN-COOH, MSN-SO3H, and MSN-SH, were prepared by adding an ethanolic solution (2 mL, 2.24 mmol) of CDSP-TMS, SDSP-TMS, and the commercially available MP-TMS, respectively, to an aqueous solution (480 mL) of CTAB (2.74 mmol), NaOH (7.00 mmol), and TEOS (22.40 mmol) at 80°C. The reaction mixture was stirred for 2 h. The solid products were isolated by filtration and washed thoroughly with methanol. The surfactant-removed materials were obtained by refluxing 1 g of the MSN material in 170 mL of methanolic solution of HCl (1 M) for 12 h. The resulting surfactant-removed material was isolated by filtration, washed extensively with methanol, and dried under vacuum. To obtain mesoporous silica material with free thiol groups, the surfactant extracted MSN material was added to 100.0 mL of 5% $NaHCO_3$ (aq) containing a disulfide reducing agent, dithiothreitol (DTT) (1.88 g, 12.2 mmol). The mixture was stirred at room temperature for 4 h. The white product was then filtered and washed with water and methanol, following by vacuum drying.

4. Characterization of the Organic Functionalization of the MSN Materials

4.1 Powder XRD

Powder XRD diffraction patterns of MSN-COOH, MSN-SO3H, and MSN-SH are summarized in Table 2-1. The data were collected on a Scintag XRD 2000 X-Ray diffractometer using Cu Kα radiation. Low angle diffraction with a 2θ range of 1 to 10° was used to investigate the long-range order of the materials.

4.2 Nitrogen Sorption Analysis

Surface area (SA) and Median Pore Diameter (MPD) were measured using a Micromeritics ASAP2000 sorptometer. Samples were degassed at 90 °C for 1 h and at 150 °C for 4 h. Nitrogen adsorption and desorption isotherms of the MSN materials were obtained at –196 °C. Specific surface areas and pore size distributions were calculated using the Brunauer-Emmett-Teller (BET) and Barrett-Joyner-Halenda (BJH) method, respectively.

4.3 Scanning Electron Microscopy

Particle morphology of these MSN materials was determined by scanning electron microscopy (SEM) using a JEOL 840A scanning electron microscope with 10 kV accelerating voltage and 0.005 nA of beam current for imaging. For obtaining the transmission electron microscopy (TEM) micrograph displayed in the main text, a small aliquot was taken from a suspension of MSN in methanol, and placed in a lacey carbon-coated TEM grid, which was pulled through the suspension and allowed to dry in air. The specimen was given no further treatment, as it appeared stable under beam bombardment.

4.4 Thermogravimetric Anaysis

TGA curves were recorded using a TA Instruments TGA 2950 thermogravimetric analyzer with a temperature ramp of 5 °C/min under continuous flow of nitrogen (100

mL/min). The percentage of weigh loss when heating the samples of MSNs in the range of 1-1000°C is concluded in Table 2-2. In general, three or four distinct weight loss TGA profiles were found, including methanol, organic functional groups, and a small weight loss due to the dehydration of the surface hydroxyl groups.

4.5 ^{13}C Solid State NMR

The ^{13}C spectra shown in the Figure. 2-5 confirm the presence of the three organic functional groups in the MSN materials before the disulfide bond reductions. Solid-state ^{13}C CP-MAS NMR spectra were obtained at 75.47 MHz on a Bruker MSL300 spectrometer equipped with Bruker 4 mm rotor MAS probe. Magic-angle sample spinning rate was maintained at 10 KHz. The NMR spectra consisted of between 2,000 and 6,000 acquisitions with cross polarization times of 3 ms and pulse repetition times of 15 s. All chemical shifts reported are referenced to liquid $SiMe_4$ (TMS).

5. Quantification of chemically accessible surface-functionalized thiol coverage.

All experiments were performed in triplicate, by reacting a predetermined amount of material (in the range of 20 to 25 mg) with a methanolic solution of excess 2, 2'-dipyridyl disulfide (44 mg, 0.2 mmol dissolved in 5 mL methanol)).

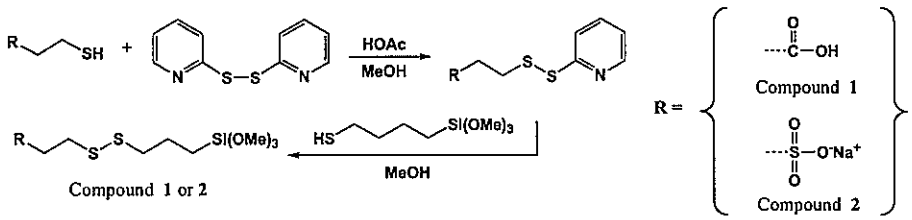
Results and Discussion

Our method involves the utilization of disulfide-containing organotrimethoxysilanes that have different anionic functional groups, such as 3-(3'-(trimethoxysilyl)-propyl-disulfanyl)-propionic acid (CDSP-TMS), 2-[3-(trimethoxy-silyl)-propyl-disulfanyl]-ethanesulfonic acid sodium salt (SDSP-TMS), and mercaptopropyl-trimethoxysilane (MP-

TMS), to electrostatically match with cationic cetyltrimethylammonium bromide (CTAB) surfactant micelles in a NaOH-catalyzed condensation reaction of tetraethoxysilane (TEOS) as shown in Figure 2-2. We were inspired by the recent reports by Larsen and Magid,[11] where they observed the anionic lyotropic series (citrate < CO_3^{2-} < SO_4^{2-} < $CH_3CO_2^-$ < F^- < OH^- < HCO_2^- < Cl^- < NO_3^- < Br^- < $CH_3C_6H_4SO_3^-$) for interaction with the CTAB surfactant micelle based on the enthalpy of transfer of the salt from water to solutions of 0.1 M CTAB. They concluded that anions less hydrated than Br^-, such as sulfonate, will be able to replace Br^- and bind tightly to the cetyltrimethylammonium head group of the CTAB molecule thereby effectively mitigating the repulsion between these cationic head groups and stabilizing the micelle structure. Also, several recent reports[12] have also revealed that the long-range structure ordering of CTAB-templated mesoporous silicas could be improved by the additions of various anions. The tightly bound (less hydrated) anions, such as acetate and BF_4^-, became incorporated in the silicate matrix due to their ability to compete with the silicate anions in displacing Br^- from the CTAB micelle.

In the present chapter, the different electrostatic matching effects of various anionic organoalkoxysilanes, such as thiolate-, carboxylate-, and sulfonate-containing organoalkoxysilanes, to CTAB micelles in governing the degree of organic functionalization of the MCM-41 type mesoporous silica materials are investigated.

Scheme 2-1.



First, two disulfide-containing organotrimethoxysilanes (CDSP-TMS and SDSP-TMS) with carboxylic and sulfonic acid groups, respectively, were synthesized via a synthetic approach outlined in Scheme 2-1. The two compounds were synthesized via a simple thiol activation of 3-mercaptopropionic acid and 2-mercaptoethanesulfonic acid sodium salt with 2,2'-dipyridyl disulfide followed by a disulfide exchange reaction with mercapto-propyltrimethoxysilane. Three organically functionalized mesoporous silica materials, MSN-COOH, MSN-SO3H, and MSN-SH, were prepared by adding an ethanolic solution (2 mL, 2.24 mmol) of CDSP-TMS, SDSP-TMS, and the commercially available MP-TMS, respectively, to an aqueous solution (480 mL, 80 °C) of CTAB (2.74 mmol), NaOH (7.00 mmol), and TEOS (22.40 mmol, added at 80 °C prior to the addition of organoalkoxysilanes). The reaction mixture was stirred for 2 h. The solid products were isolated by filtration and washed thoroughly with methanol. Surfactant-removed materials were obtained with an acid extraction. All three materials exhibited spherical particle shape with an average particle diameter of 200 nm (Figure 2-2).

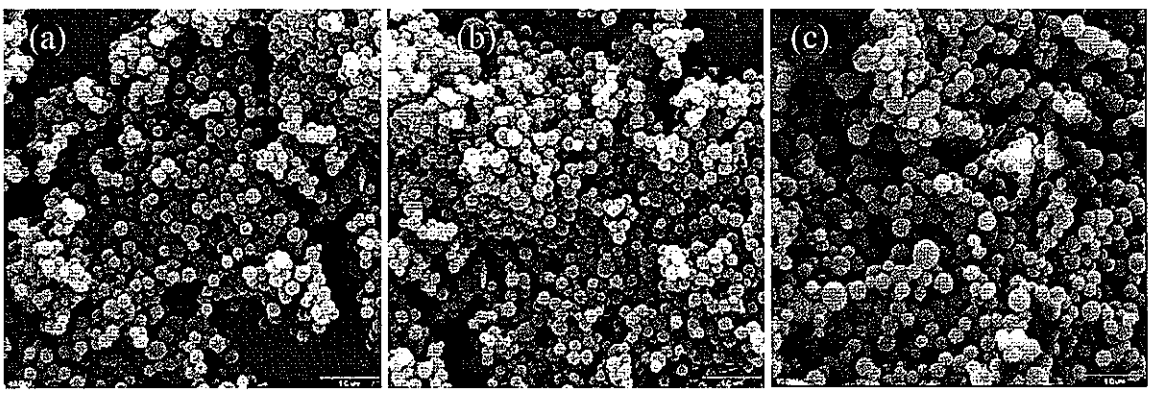


Figure 2-2. SEM images of MSN-SH (a), MSN-COOH (b) and MSN-SO3H (c). All three materials exhibited spherical particle morphology, with an average particle diameter of 200 nm. All images are presented using the same magnification (scale bar = 1 μm).

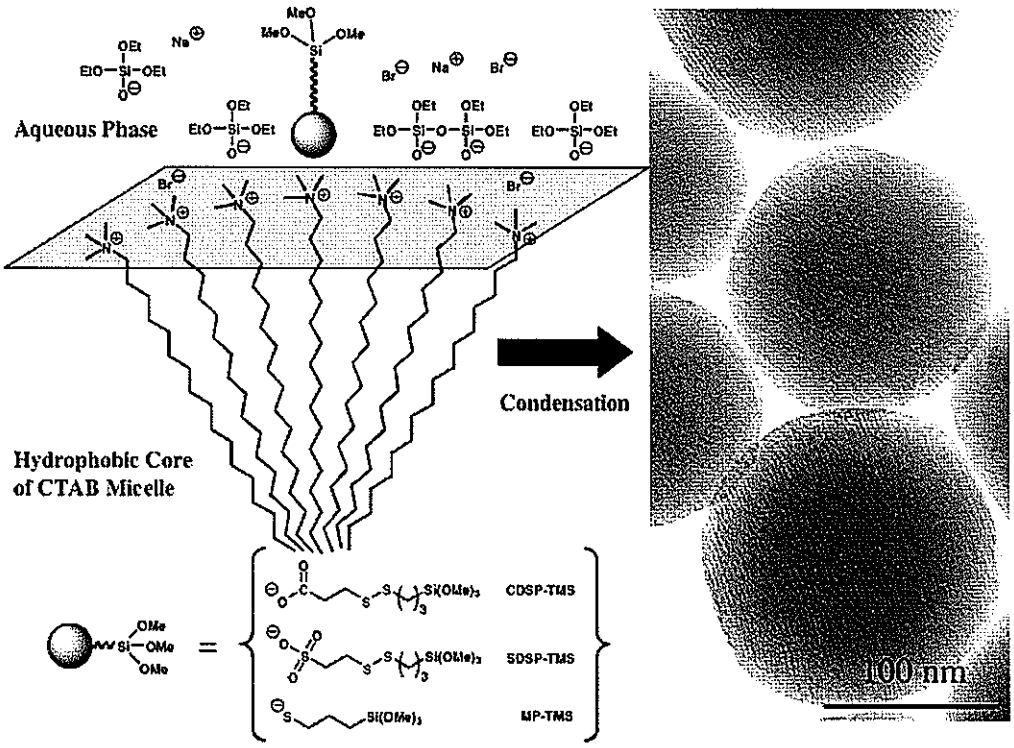


Figure 2-3. Schematic representation of the utilization of anionic organoalkoxysilane for controlling the functionalization of the MSN materials. The MCM-41 type mesoporous channels are illustrated by the parallel stripes shown in the TEM micrograph of the MSN-SH material.

The mesoporous structures of these organically functionalized MSN materials were determined by nitrogen adsorption-desorption surface analysis (BET isotherms and BJH pore size distributions), TEM, and powder X-ray diffraction (XRD) spectroscopy.

These materials exhibited diffraction patterns characteristic of hexagonal MCM-41 silicas, including (100), (110), and (200) peaks (Figure 2-3). In addition, all three MSN materials exhibited type IV BET isotherms with similar average BJH pore diameters (Figure 2-4 and Table 2-1). Hexagonally packed mesoporous channels were clearly observed in the TEM micrographs of these MSNs (Figure 2-1).

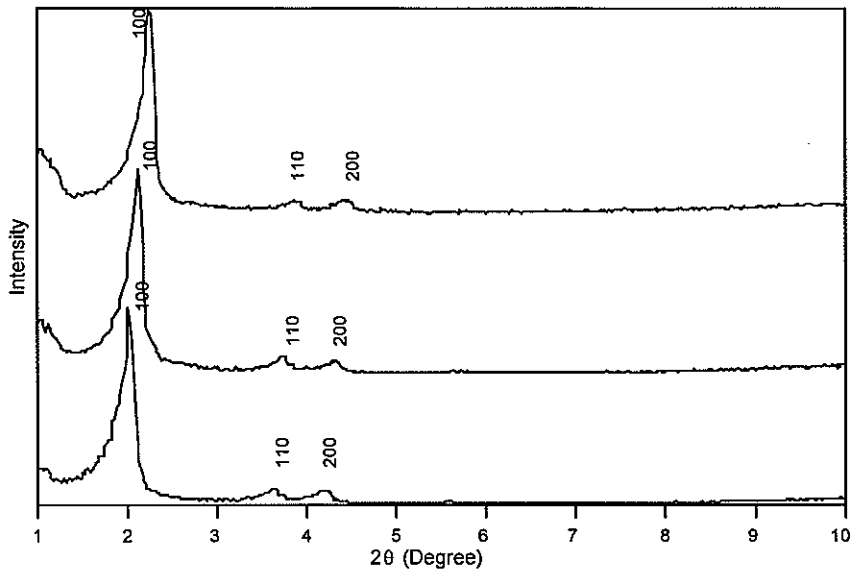


Figure 2-4. Powder XRD diffraction patterns of the MSN-SH (green), MSN-COOH (red) and MSN-SO3H (blue) materials after treatment with disulfide reducing agent (DTT).

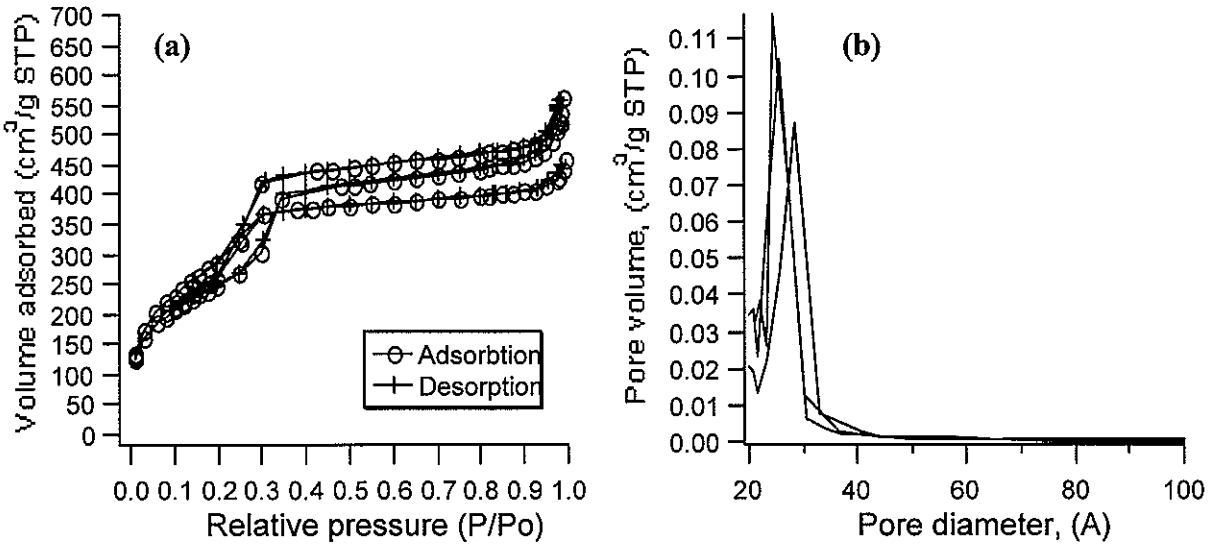


Figure 2-5. (a) Nitrogen sorption isotherms of the MSN-SH (green), MSN-COOH (red) and MSN-SO3H (blue) materials after treatment with disulfide reducing agent (DTT). (b) Pore size distributions of the MSN-SH, MSN-COOH and MSN-SO3H materials.

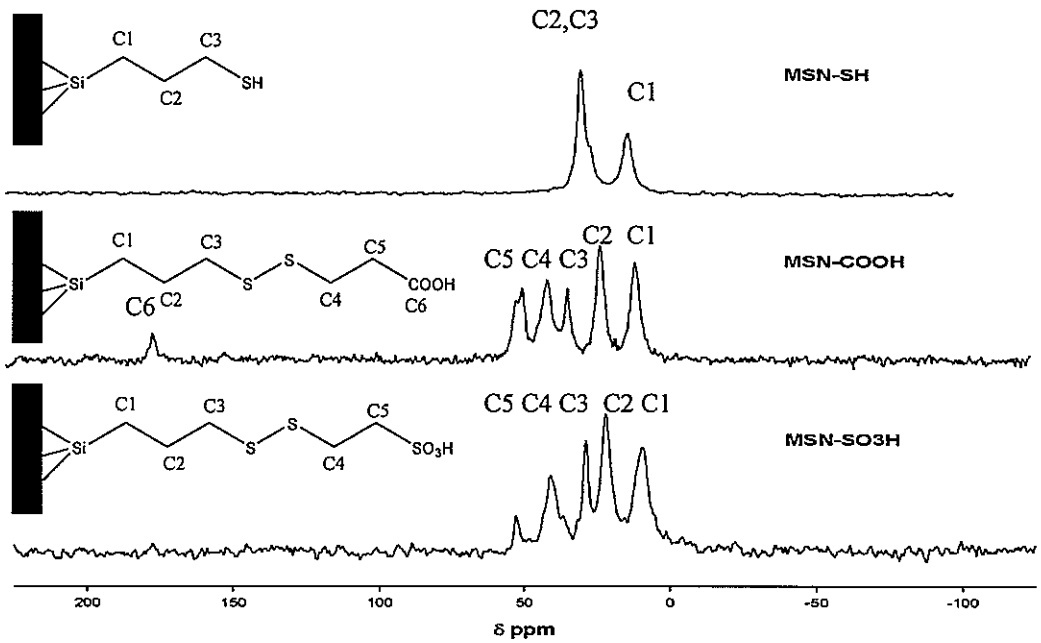


Figure 2-6. Solid state ^{13}C CP-MAS NMR spectra of the MSN-SH (up), MSN-COOH (middle) and MSN-SO3H (bottom).

The existence of the organic functional groups was confirmed by ^{13}C solid state NMR spectroscopy (Figure 2-6).

Table 2-1. Structural properties of the organically functionalized MSN materials.

	Powder XRD			Nitrogen Sorption Isotherms		
	Low angle (Silica) (Å)			BET surface area	BET pore volume	BJH pore diameter
	d_{100}	d_{110}	d_{200}	(m^2/g)	(mL/g)	(Å)
MSN-SH	39.8	22.9	19.9	999	0.793	25.8
MSN-COOH	40.5	22.8	20.1	920	0.657	27.3
MSN-SO3H	43.8	24.4	20.9	863	0.755	28.1

The nitrogen sorption isotherms of the three MSN materials exhibited a sharp step starting at ca. p/p_0 = 0.38, as shown in Figure 2-4a with reversible type IV isotherms. (The inflection

point is attributed to the commencement of pore filling from which the pore diameter can be roughly estimated).

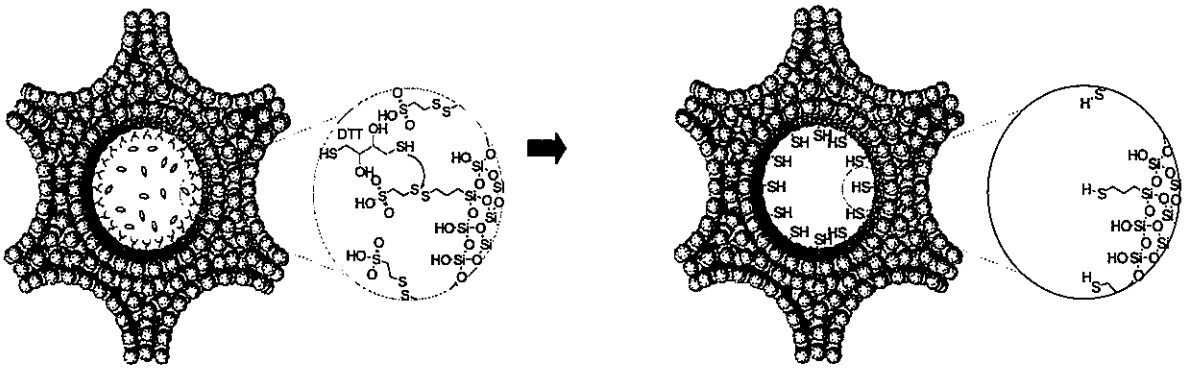


Figure 2-7. Schematic representation of the formation of thiol-functionalized mesoporous silica material (MSN-SO3H) via disulfide reduction with dithiothreitol (DTT).

To quantify the amount of chemically accessible functional groups that are incorporated and oriented properly on the mesopore surfaces, we chemically converted the surface bound organic groups of the MSN-COOH and MSN-SO3H materials to thiol (-SH) by treating them with a disulfide reducing agent, dithiothreitol (DTT) as depicted in Fig. 2-6.

As shown in Scheme 2-2, reactions of the resulting free thiol-functionalized materials with the 2,2'-dipyridyl disulfide gave rise to 2-pyidyldithio-derivatized surface functional groups along with a 2-pyridothione compound as the side product.

Scheme 2-2