

Well Ordered structure formation of organically modified silica particles using a self-assembly process

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Monodispersed, multi-functional organically modified silica (ORMOSIL) particles were prepared by simple one pot synthesis. The size and functionalities of the ORMOSIL particles were controlled by changing the reaction conditions such as the temperature, reaction time, and type of silane monomer. Using the surface modification reaction of glutaric anhydrides with amine groups on ORMOSIL particles, a new type of organic functional group, the carboxylic acid group, was introduced to provide additional functionalities for further modification. Well-ordered structures of ORMOSIL particles were constructed by either 3-dimensional self-assembly between two ORMOSIL particles with different sizes and functionalities or selective binding of ORMOSIL particles with multiple functional groups to a patterned surface.

Key words: Well-ordered structure, Multifunctional, ORMOSIL particles, Self-assembly, Surface modification.

Introduction

Multifunctional hybrid particles having monodispersity in size and morphology have been attracting much attention due to their wider applications in industrial fields, such as catalysts, electronics, and pigments [1-3] as well as biological technologies including bio-labeling, medical diagnostics, and drug delivery [4-6]. Several synthetic techniques have been developed for a variety of micron to submicron particles, including core-shell synthesis, layer-by-layer techniques, multi-block polymer emulsifications, and surface modifications. The particle structures can be engineered to perform multicolor imaging as well as multiplex tasking such as site-selective binding, detection, and separation [7-11]. Among multifunctional hybrid particles, colloidal silica particles with multiple functional groups have recently emerged with great promise because of their non-toxicity, comparable size to biomolecules, and ease of surface modification.

One of the most extensively studied particles is monodispersed colloidal silica as they can be easily synthesized with controlled size and shape [17-20]. Organically modified silica (ORMOSIL) particles are hybrid materials that can be prepared by the surface modification of silica particles from tetraethylorthosilicate (TEOS) or by using an organo-silane monomer as the starting material. However, these ORMOSIL particles usually contain only a single type of functional group [21-23]. In order to synthesize ORMOSIL particles

with more than two functional groups, a time-consuming multi-step preparation process needs to be employed. Therefore, the development of simple and efficient synthetic methods for multifunctional particles is important.

In this study, multifunctional ORMOSIL particles with uniform size and morphology were prepared using a modified sol-gel process [24]. The size and functionalities of the ORMOSIL particles were controlled by changing the reaction conditions such as the temperature, reaction time, and types of silane monomers. Monodisperse ORMOSIL particles, consisting of phenyl, aminopropyl, and 3-glycidoxypentyl (or 3-mercaptopentyl) silanes with a size of 300, 600, and 1300 nm, were prepared. Using the surface modification reaction of the glutaric anhydrides with amine groups on ORMOSIL particles, a new type of organic functional group, the carboxylic acid group, was also introduced. By using the chemical reactions between the amine groups and the carboxylic groups on different ORMOSIL particles, well-ordered structures of the ORMOSIL particles with two different sizes were obtained through 3-dimensional self-assembly. Finally, a patterned assembly of colloidal ORMOSIL particles was prepared by selective binding of the ORMOSIL particles with the carboxyl groups on a glass substrate, pretreated with aminosilanes.

Experimental

Materials

Phenyltrimethoxysilane [PTMS] (94%, Aldrich), 3-aminopropyltrimethoxysilane [AMPTMS] (99%, Aldrich), 3-glycidoxypentyltrimethoxysilane [GPTMS] (98%, Aldrich), Glutaric anhydride (95%, Aldrich), 3-

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mercaptopropyltrimethoxysilane [MPTMS] (97%, Fluka), Rhodamine B isothiocyanate (Fluka), and Fluorescamine (Sigma) were used without further purification. Ammonium hydroxide solution (30 wt% as NH_3) and Nitric acid (60%) were obtained from Sam-Chun Chemicals. De-ionized water and ethyl alcohol (EtOH, 95%, Sam-Chun Chemicals) were used as a solvent.

Characterization

The Fourier transform infrared spectrometer (FT-IR, AAB FTLA2000) and nuclear magnetic resonance spectrometer (NMR, Varian UnityInova 300 and Bruker Avance 400) were used for chemical characterization. The sizes and morphologies of the ORMOSIL particles and self-assembled products were examined with a field emission scanning electron microscope (FE-SEM, JEOL JEM-6340F) and a transmission electron microscope (TEM, JEOL EM-2000EXII). The Confocal Laser Scanning Microscope (Bio-Red, MRC-1204 and Radiance2000/MP) was used to obtain fluorescence images of the dye tagged ORMOSIL particles.

Preparation

Synthesis of tri-functional ORMOSIL particles consisting of phenyl, aminopropyl, and 3-glycidoxypropyl (or 3-mercaptopropyl) silanes

A 250 mL Erlenmeyer flask maintained at 40 °C was charged with 150 mL of deionized water, and 0.2 mL of nitric acid (2.67 mmol, 60 wt%) was added while stirring at 300 rpm. 5 ml of PTMS (24.89 mmole) was first injected into an acidic aqueous solution, followed by the addition of 0.5 mL APTMS (2.75 mmole) and 0.5 ml GPTMS (1.96 mmol) or MPTMS (2.57 mmol). The resulting solution was stirred for 90 seconds to assure hydrolysis and followed by the addition of 40 ml of ammonium hydroxide (305 mmole, 30 wt %) to induce condensation. The mixture became turbid and was stirred for an additional 4 hours. The resulting multifunctional ORMOSIL particles were filtered through a membrane and washed with 100 ml of deionized water three times. The filtered products were dried under vacuum and 2.8 g of phenyl-amine-epoxy based tri-functional particles were obtained. To adjust the size and functionalities of the particles, the temperature, concentration and type of monomers were modified, as shown in Table 1.

Table 1. Reaction condition of 1.3 μm , 600 nm, 300 nm particles.

Particle size	1.3 μm	600 nm	300 nm
PTMS : APTMS: GPTMS or MPTMS	5 ml : 0.5 ml : 0.5 ml	1 ml : 0.1 ml : 0.1 ml	1 ml : 0.1 ml : 0.1 ml
Temperature	40 °C	40 °C	40 °C
Hydrolysis time	90 sec	90 sec	90 sec
NH_4OH	40 ml	40 ml	40 ml
Reaction time	4 h	4 h	4 h

Surface modification reaction of aminopropyl silanes on ORMOSIL particles with glutaric anhydrides

To modify the amine groups to carboxylic acid groups on the surface of ORMOSIL particles, tri-functional ORMOSIL particles with phenyl, aminopropyl, and epoxy functional groups (0.2 g) were placed in a 250 ml three-neck round bottom flask, and the reaction vessel was heated to 85 °C. Glutaric anhydride (0.5 g, 4.16 mmole) was added to the ORMOSIL particles, and the resulting mixture was stirred for 3 hours. One hundred milliliters of de-ionized water and 100 ml of ethanol were poured into a reaction flask for dilution and removal of the unreacted glutaric anhydride. The suspension was stirred for 5 minutes and filtered through a membrane filter. The products were dried in air and 0.2 g of surface modified ORMOSIL particles was obtained.

Self-assembly of ORMOSIL particles to well-ordered structures

Surface modified, phenyl-based MHS particles with epoxy and carboxylic acid functional groups (0.03 g, average diameter of 1.4 μm) were dispersed in 8 mL of ethanol. Phenyl-based MHS particles with epoxy and amine functional groups (0.01 g, average diameter of 200 nm) were added to the dispersion, and the reaction mixture was sonicated for 2 hours. The suspension was filtered, and the product was washed with 20 ml of ethanol more than three times.

Results and Discussion

Synthesis of tri-functional ORMOSIL particles consisting of phenyl, aminopropyl, and 3-glycidoxypropyl (or 3-mercaptopropyl) silanes

The typical synthetic procedure for monodispersed multi-functional ORMOSIL particles was employed by two consecutive processes: In the first acidic condition, various silane monomers were hydrolyzed simultaneously and emulsion droplets with a homogeneous silane mixture were formed. In the second basic condition, a co-condensation reaction occurred among the hydrolyzed silane mixture. In order to produce different sizes of particles, silane concentrations, temperature, and reaction time need to be controlled, engendering that the sizes of the particles were fabricated from 300 nm to 1.3 μm . For instance, the size of the ORMOSIL particles decreased when the total concentration of the silane monomers and reaction time decreased, and the reaction temperature increased [25]. The major effect on controlling the size of the ORMOSIL particles was on the concentration of the monomers. We fabricated different sizes of ORMOSIL particles by controlling the concentration of the silane monomers and the reaction temperature, as shown in Table 1.

A chemical reaction of the surface functional groups on the ORMOSIL particles with organic molecules was

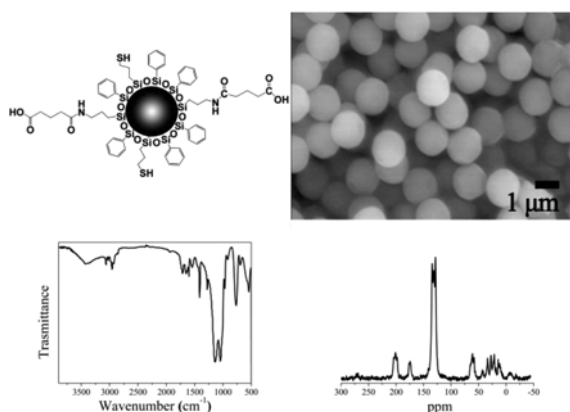
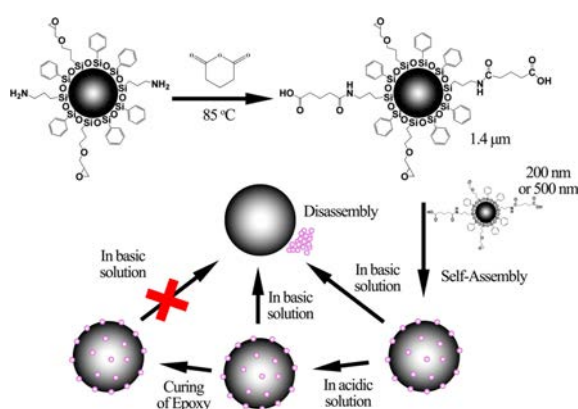


Fig. 1. Structures, SEM images, FT-IR, and NMR spectra of the tri-functional surface-modified ORMOSIL particles.



Scheme. 1. Self-assembly to a 3D structure.

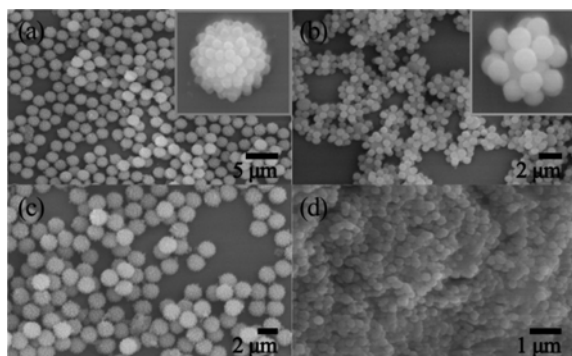


Fig. 2. Self-assemblies of the ORMOSIL particles with different sizes and functionalities.

initiated to endow additional or modified functionalities on the particle surfaces. Amine functional groups on the surface of the tri-functional ORMOSIL particles were converted to carboxyl groups by reaction with glutaric anhydrides [26, 27]. The IR spectra of the surface reacted ORMOSIL particles showed two $\nu(\text{C}=\text{O})$ stretching vibrational absorption peaks from the amide and carboxylic groups at 1685 and 1725 cm^{-1} , respectively. The CP-MAS ^{13}C NMR spectrum also exhibited an additional resonance peak from the $\text{C}=\text{O}$ functionality, as shown in Figure 1.

3-dimensional self-assembly of ORMOSIL particles

The ability of multifunctional ORMOSIL particles to act as potential building blocks was demonstrated by the 3-dimensional self-assembly of well-ordered structures constructed through chemical interactions between two ORMOSIL particles with different sizes and surface functional groups, as shown in Scheme 1. The phenyl-epoxy-carboxylic acid functionalized ORMOSIL particles of 1.3 μm in diameter and phenyl-epoxy-amine functionalized ORMOSIL particles of 300 nm or 600 nm in diameter were dispersed together in an aqueous solution. SEM images indicated that a well-ordered self-assembled structure was obtained, as shown in Fig. 2a and 2b. The formation of the self-assembled structures was probably due to the coulombic interaction between the negatively charged ORMOSIL particles with the carboxylate groups and the positively charged ORMOSIL particles with the ammonium functional groups, which were produced by the protonation and deprotonation of the corresponding functional groups on each ORMOSIL particle. In the presence of a strong base, the positively charged ammonium group transforms into a negatively charged amide group. This induces repulsion between the two types of ORMOSIL particles, eventually destroying the assembled structure, as shown in Fig. 2d. In an acidic condition, the negatively charged carboxylate groups are converted into neutral carboxylic acids, producing a mixture of neutral and positively charged ORMOSIL particles, resulting in no coulombic attraction/repulsion between the two types of particles. However, the hydrogen-bonding between the carboxylic acid and the ammonium functionalities may have prevented the disintegration of the assembled ORMOSIL particles, as can be seen in Fig. 2c. The formation of the self-assembled structures of the ORMOSIL particles and their stability in acid/base conditions indicate that these particles can be useful for the laboratory analysis of specific analytes, enabling detection, signal amplification, and separation as well as bio-labeling and intracellular or in vivo applications as they can achieve signal amplification consistently.

The instability of the self-assembled structures in specific conditions can be prevented by polymerization of the surface epoxy groups of the ORMOSIL particles. After the self-assembled particles were irradiated by UV light for about 1 hour, the self-assembled particles were maintained in either acidic or basic conditions, which were confirmed by SEM image.

As another example to show the self-assembly capability of ORMOSIL particles, selective binding of the ORMOSIL particles on the patterned glass surface was investigated. ORMOSIL particles with carboxylic acid functional groups were attached to the glass surface with patterned lines created by treating the glass surface with amino and octadecyl silanes, which were prepared with a slight modification of the method, described earlier [28]. The acid-base reaction between

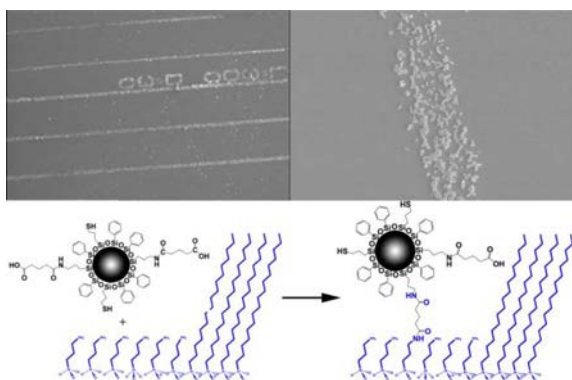


Fig. 3. Self-assembly of the ORMOSIL particles with a patterned substrate.

the amine groups on the glass surface and the carboxylic groups on the surface of the ORMOSIL particles led to the formation of the patterned assembly of ORMOSIL particles on the glass, as shown in Figure 3.

Conclusions

In conclusion, multi-functional ORMOSIL particles were prepared by facile one-pot synthesis. The types and numbers of the functional moieties on the particles can be controlled with great flexibility, and the size of the particles can also be controlled between 300 nm and 1.3 μm with a narrow size distribution. The surface can be further modified in order to introduce additional organic functional groups or to carry various dyes or molecules such as fluorescent image contrast agents or targeting ligands or drugs, making them useful for various biomedical applications such as multicolor imaging. The self-assembly behavior of ORMOSIL particles with other ORMOSIL particles of different sizes or on a patterned glass surface demonstrates the ability of ORMOSIL particles to act as potential building blocks for next generation multitasking nano-devices that can detect multiple analytes and amplify the signals.

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