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Light-Induced Transport of Water and Guest Molecules in Mesoporous Silica Nanocontainer Interface

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1. Introduction

Controlled mass transport in response to signals is critical for vital activity in nature.[1-3] Owing to such complex signaling system in nature, researchers have worked toward the development of precise nanocontainers in response to signals in physiological environment.[4-6] Inspired from nature, soft nanocontainers such as liposomes and micelles have been investigated for delivery systems. However, these materials are dynamic and they often release payloads under undesired conditions.[7,8] Mesoporous silica nanoparticles equipped with outer gatekeeper molecules have increasingly become popular for the controlled release of drug molecules in response to desired stimuli.[9-19] In many cases, such on-demand release characteristics were visibly compared to common soft drug carriers.

Here, we report a light-responsive release characteristic of guests entrapped in a mesoporous silica nanocontainer (MSN) caged with a photo-labile hydrophobic layer (Figure 1). The outer and channel surfaces of the MSN were decorated with a mixed layer of benzyl carbamate and nitrobenzyl carbamate moieties, thereby making it hydrophobic. The hydrophobic surface of MSN initially inhibits the transportation of outside water and inside guest molecules. Nitrobenzyl carbamate moiety, a photo-labile molecule, was selected as the gate molecule because its transformation to polar amine moiety upon UV irradiation at 365 nm can expose the entrapped guests to water media. Photolysis can induce the penetration of water molecules into the channels of MSNs owing to the change in their interfacial energy, which was supported by molecular dynamics (MD) simulations.

2. Experimental

2.1. Materials

Tetraethyl orthosilicate (TEOS), cetyltrimethylammonium bromide (CTAB), 3-(triethoxysilyl)propyl isocyanate, benzyl alcohol, 2-nitrobenzyl alcohol, and Rhodamine B (RB) were used as received without further purification. Unless otherwise noted, all other reagents were used as received.

2.2. Characterization

Surface analysis of the mesoporous silica nanoparticles was performed by nitrogen sorption isotherms at -196 °C using a BEL BELSORP-Max system. The surface area and pore size distributions were estimated using the Brunauer-Emmett-Teller (BET) equation and Barrett-Joyner-Halenda (BJH) method, respectively. All UV-visible absorption spectra were recorded in the range of 200 to 800 nm on a HP-8453A diode array spectrophotometer. The fluorescence spectra were obtained using a Cary Eclipse instrument (Varian). X-ray photoelectron spectroscopy (XPS) was conducted on a K-Alpha™+ X-ray photoelectron spectrometer system (thermo scientific).

2.3. Preparation of MSN-0

An aqueous solution (48 mL) of cetyltrimethylammonium bromide (CTAB, 0.107 g) was added to the NaOH solution (2M, 0.35 mL). After stirring at room temperature for 15 min, tetraethyl orthosilicate (TEOS, 0.5 mL) was added to the solution. The reaction mixture was vigorously stirred at 80 °C for 2 h. The resulting solid was filtered, washed thoroughly with methanol, and dried under vacuum for 20 h.

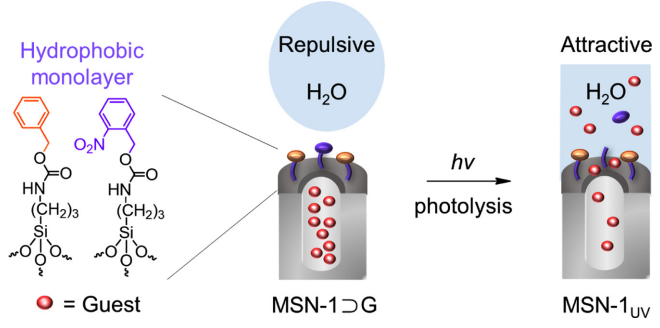

Figure 1. Schematic illustration of hydrophobic monolayer of MSN-1 and a photo-induced release of guest molecules from MSN-1.

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2.4. Preparation of MSN-1

The surface of MSN-0 was functionalized with 3-isocyanatopropyltriethoxysilane (ICPES) through a gas-phase reaction between MSN-0 and ICPES-toluene solution for 12 h under an inert atmosphere.[20] The resulting powder was washed with toluene and dried under reduced pressure. Then, the particle was refluxed in a dimethylformamide (DMF) solution of benzyl alcohol and 2-nitrobenzyl alcohol (3:1 molar ratio) for 10 h under an inert atmosphere afforded MSN-1.

2.5. Drug loading and release experiments

A fluorescence dye (Rhodamine B, 10 mg) was added to the DMF solution of MSN-1 (20 mg) while stirring at room temperature. After overnight stirring, the particle suspension was centrifuged and washed with water several times to remove excess guest molecules.

2.6. MD simulation

A computational MD simulation was conducted to provide insights into molecular deformation and evolution mechanisms in this study. Herein, the MD simulations were performed using a commercial software package Material Studio (BIOVIA, 2016) and a Forcite module, designed to perform calculations for a wide range of applications such as ensemble simulation and geometry optimization in the periodic system.

3. Results and discussion

To create a photo-responsive MSN, we first prepared a bare MSN (MSN-0) with hexagonally ordered pores by condensing the template of tetraethyl orthosilicate (TEOS) in the presence of a micellar solution of cetyltrimethylammonium bromide (CTAB). The obtained MSN-0 (diameter=53.2 nm estimated by dynamic light scattering) exhibited a lattice constant of 46.8 Å (by X-ray diffraction). The surface area (925. 7 m^2/g) and average pore diameter (2.35 nm) were estimated by the N_2 adsorption-desorption isotherm of MSN-0 after the removal of CTAB. Before the removal of CTAB, MSN-0 was further decorated with 3-(triethoxysilyl)propyl isocyanate to expose the NCO functional group on the outer surface of MSN-0. The successful functionalization was corroborated by Fourier infrared spectroscopy (FT-IR), showing a 2100 cm^{-1} indicative of NCO. Then, benzyl and nitrobenzyl alcohols (3:1 molar ratio) were introduced to react with the isocyanate groups on the outer surface of MSN-0 (1580-1650 cm^{-1}, Figure 2(a)). Transmission electron microscopy revealed the porous nanoparticles of MSN-0 and MSN-1, respectively (Figure 2(b)). XPS analysis also revealed the derivatization of MSN-0 (Figures 2(c) and (d)). The particle was extracted to remove CTAB micelles and the porous channels were then filled with guest molecules (Rhodamine B, RB) in a DMF solution. The resulting particle was thoroughly washed with water to remove excess RB molecules and the purified particles were denoted by MSN-1⊃G (Figure 1).

The MSN-1⊃G was stable without any payload leakage for the first 15 min in the absence of a light stimulus (Figure 3). The hydrophobic monolayer on the outer surface of MSN-1⊃G inhibited water transport to the mesoporous channel entrapping RB molecules, thereby suppressing the release. However, upon UV irradiation (λ=365 nm) to the aqueous solution of MSN-1⊃G,

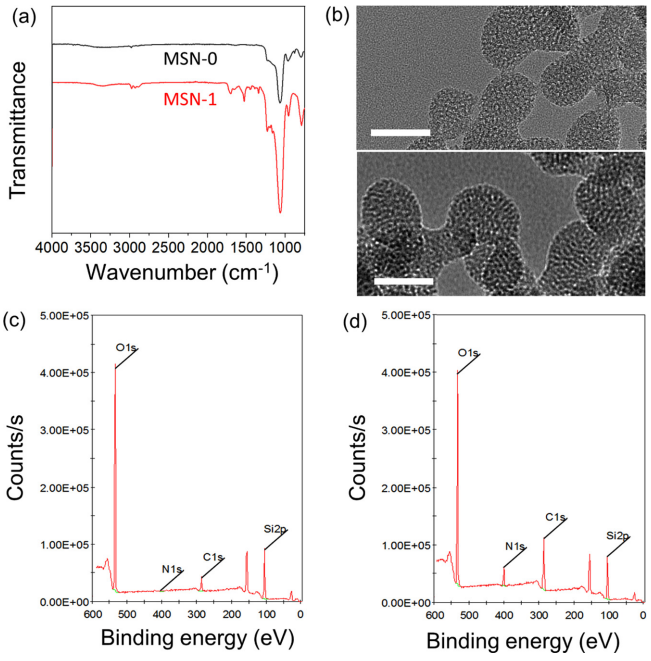

Figure 2. (a) FT-IR spectra of MSN-0 and MSN-1. (b) TEM images of MSN-0 (upper) and MSN-1 (lower), respectively (Scale bar=50 nm). XPS spectra of (c) MSN-0 and (d) MSN-1, respectively.

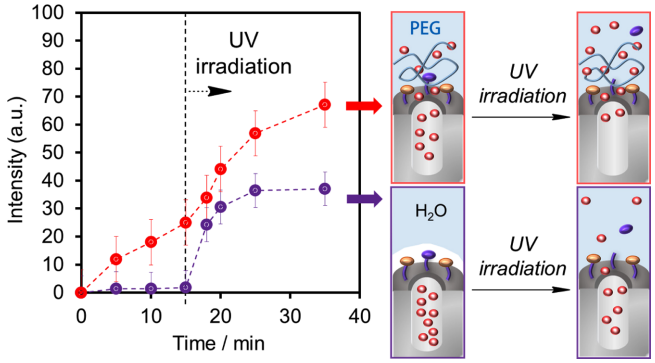

Figure 3. Photo-induced release profiles of guest molecules from MSN-1⊃G in the absence (purple) and presence (red) of PEG.

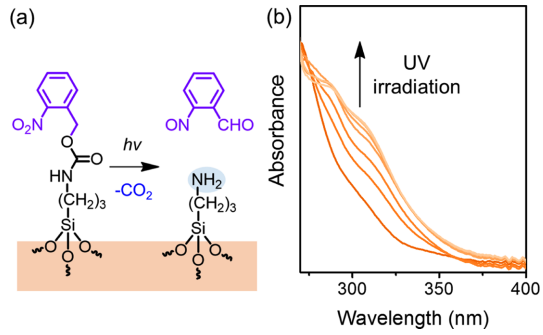

Figure 4. (a) Photo-induced cleavage of nitrobenzyl carbamate moiety from MSN-1. (b) Time course analysis of absorption spectra of MSN-1 upon UV irradiation.

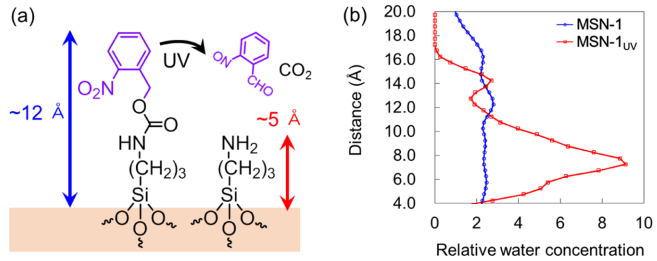

Figure 5. (a) Estimated dimension of photo-cleavable layer before and after UV irradiation. (b) MD simulation for water transport at the interface of MSN-1 and MSN-1_{UV}.

we observed a gradual release of entrapped RB molecules from MSN-1⊃G (Figure 3). The time course analysis of MSN-1 by UV/vis absorption spectroscopy under UV light irradiation (λ=365 nm) showed a gradual increase at 275-350 nm, indicating the photo-induced cleavage of nitrobenzyl carbamate moieties from the outer surface of MSN-1 (Figure 4). These results imply that the photo-responsive release of guests from MSN-1 is induced by a photo-cleavage of nitrobenzyl carbamate moieties from the hydrophobic monolayer. However, the residue (benzyl carbamate portions) of hydrophobic layers disturbed the efficient release of entrapped RB guest (Figures 1 and 3). On adding poly(ethylene glycol) (PEG, M_n=750) into MSN-1⊃G solution, we observed a continuous release of RB guests from MSN-1 due to the compatibility of PEG between the hydrophobic monolayer of MSN-1⊃G and aqueous phase. This might induce accelerated transport of water and RB molecules at the interface of MSN-1⊃G and aqueous phase.

We further investigated MD simulation to reveal water transport at the interface of silica surface covered with benzyl and nitrobenzyl carbamate moieties (3:1 molar ratio). As shown in Figure 5, the relative water concentration drastically increased in the case of MSN-1_{UV}. Owing to the increased thermodynamic instability at the interface, the photo-induced surface change can allow the access of water molecules on the surface, thereby inducing the release of guest molecules from the inner channel of MSN-1⊃G.

4. Conclusions

Hydrophobic monolayer spiked with photo-cleavable nitrobenzyl carbamate moieties was introduced in the outer surface of MSN. The nanoparticle system showed a stable entrapment of water-soluble guests in the aqueous solution. Upon UV irradiation (λ=365 nm), the nitrobenzyl carbamate moieties degraded, thereby exposing polar amine moieties. The time course analysis for guest release from MSN-1 upon UV irradiation revealed the photo-induced release characteristics. MD simulation supports the release characteristics induced by physical and chemical changes at the interface. Guest release from MSN-1 was disturbed by residual hydrophobic moieties. Based on our result and after adjusting a possible cytotoxicity form nitrobenzaldehyde and CO_2, we believe that an optimized design may be able to induce efficient release characteristics.

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