Nanodevices

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Installing Dynamic Molecular Photomechanics in Mesopores: A Multifunctional Controlled-Release Nanosystem**

*Yingchun Zhu and Masahiro Fujiwara**

There remains an ongoing interest in molecular nanotechnology.[1–10] The operational range of molecular motion is too restricted to create macroscopic phenomena. However, in the small spaces of mesopores, molecular movement on the nanometer level is sufficient to dominate the physical and chemical behaviors of guest molecules, for example, as shown by a molecular gating system on a mesopore outlet.[4] The release rates of guest molecules in pore voids are dominated by inactive diffusion in all reported gating systems,[4,7–12] and no acceleration of release has been claimed. Developing on from the primary gating system,[4] here we report a multifunctional, fully controlled storage and release system by installing two photomechanical units that behave as "stirrer" and "gate" functions into mesoporous silica. An enhancement of the release rate of the guest molecule in mesoporous silica is induced by reversible photoisomerization of azobenzene groups attached to the inner surface.

A sample of solvent-extracted mesoporous silica (**1A**) was modified with 5.6 wt% of *N*-(3-triethoxysilyl)-propyl-4-phenylazobenzamide inside the pores (**1B**), and this modified sample was then loaded with 35.1 wt% of cholesterol (**1C**; see Experimental Section). UV/Vis diffuse reflectance spectra were measured on the powdery azobenzene-modified (**1B**) and cholesterol-loaded samples (**1C**) under various photoirradiation conditions (Figure 1). As expected, both samples show similar variations in their UV/Vis diffuse reflectance spectra under photoirradiation (Figure 1), indicating that photoisomerization occurs even when a significant amount of cholesterol was loaded into the narrow pores. Irradiation with UV light ($\lambda \approx 360$ nm) induced a gradual decrease in the absorption at 340 nm (corresponding to the π–π* transition of the *trans* isomer) with an increase in the absorption at 430 nm (corresponding to the n–π* transition of the *cis* isomer). The *trans*-to-*cis* photoisomerization of the azobenzene group took place in the pore, and it reached a photostationary state after irradiation for 30 min. On the other hand, when UV/Vis light (UV: 80 mW, $\lambda \approx 360$ nm; Vis: 54 mW, $\lambda \approx 430$ nm) was used to irradiate samples **1B** and **1C** for 10 min, the isomerization reached another photostationary state.

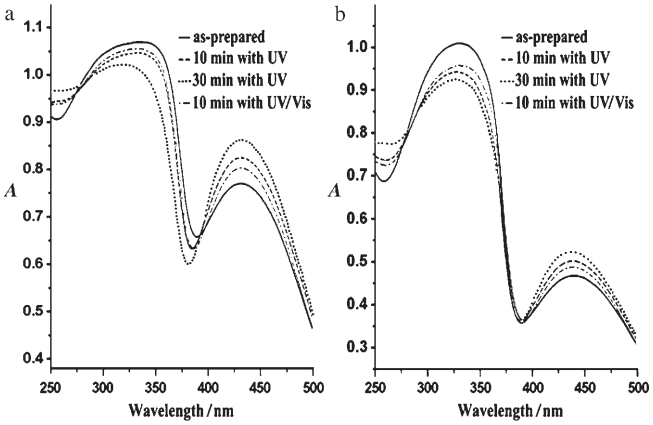

Figure 1. Changes in the UV/Vis spectra of modified mesoporous silica samples as-prepared and following irradiation with UV ($\lambda \approx 360$ nm, 58 mW) and UV/Vis (UV: 80 mW, $\lambda = \approx 360$ nm; Vis: 54 mW, $\lambda \approx 430$ nm) light. a) Sample **1B** (mesoporous silica grafted with 5.6 wt% azobenzene). b) Sample **1C** (as in part (b), but with 35.1 wt% cholesterol absorbed).

Azobenzene moieties are characterized by fast, stable, and reversible photoisomerization by a rotation–inversion mechanism,[13–15] which is exploited in various applications.[16–18] Here, we used the photoinduced molecular "motion" of azobenzene isomerization to accelerate the release of guest molecules from mesopores. When the *trans* isomer is irradiated with UV light, an excitation state is achieved and the benzene group rotates and/or inverts to form the *cis* isomer, while irradiation with visible light turns the *cis* isomer into the *trans* isomer. The reversible photoisomerization by UV and visible light creates a continuous rotation–inversion movement, accompanied with stretch–shrink motions. During this process, the azobenzene moiety acts as a molecular stirrer; this behavior is expected to propel the diffusion and the release of guest molecules from the pores of mesoporous silica.

Controlled-release experiments were carried out using sample **1C**, which contains cholesterol (length approximately 1.90 nm and diameter around 0.61 nm) as a model molecule (see the Supporting Information).[19] Cholesterol displays no UV absorption at wavelengths longer than 320 nm, thus its spectrum does not interfere with the UV/Vis spectra of azobenzene and certain other compounds. The amount of

[*] Dr. M. Fujiwara
Kansai Center
National Institute of Advanced Industrial Science and Technology (AIST)
1-8-31, Midorigaoka, Ikeda, Osaka, 563-8577 (Japan)
Fax: (+81) 72-751-9628
E-mail: m-fujiwara@aist.go.jp
Prof. Y. Zhu
Shanghai Institute of Ceramics, Chinese Academy of Sciences
Shanghai 200050 (P.R. China)

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cholesterol loaded into the pore of sample **1C** was 35.1 wt% (see the Experimental Section and Table 1). Figure 2 shows the release profiles of cholesterol from sample **1C** under various irradiation conditions. In the absence of irradiation, was carried out (UV: 80 mW, $\lambda = 360$ nm; Vis: 54 mW, $\lambda = 430$ nm) around 92% of the stored cholesterol was released in just 30 minutes and more than 98% was released after 90 minutes (Figure 2d) to yield sample **1D**.

Table 1: Properties of various modified mesoporous silica samples.

Sample[a]	Status	d_{100} [nm] [b]	S_{BET} [$m^2 g^{-1}$] [c]	V_p [$cm^3 g^{-1}$] [d]	APD [nm] [e]	PPD [nm] [f]	CS [wt%] [g]
1A	unmodified	4.12	1400	1.03	2.89	3.0	0.0
1B	modified	4.12	1296	0.90	2.91	2.8	0.0
1C	loaded	4.10	382	0.28	2.68	2.5	35.1
1D	released	4.12	1207	0.90	3.00	2.8	1.2
1E	released	4.12	787	0.58	3.07	2.8	7.0
2A	modified	4.12	1442	1.00	2.83	3.0	0.0
2B	modified	4.12	1160	0.75	2.82	2.8	0.0
2C	loaded	4.10	329	0.33	2.61	2.5	32.5
2D	released	4.12	1066	0.69	2.72	2.8	1.6
2E	released	4.12	675	0.57	2.91	2.8	9.1

[a] Sample **A**: without azobenzene derivative; Sample **B**: grafted with azobenzene derivative; Sample **C**: loaded with cholesterol; Sample **D**: released under UV/Vis irradiation; Sample **E**: released without irradiation. [b] X-ray diffraction (100) interplanar spacing. [c] BET specific surface area. [d] Primary mesopore volume. [e] Average pore diameter $= 4\ V_P/S_{BJH}$, where S_{BJH} = BJH specific surface area. [f] Peak pore diameter calculated from BJH pore size distribution curve using adsorption branches. [g] Weight percentage of cholesterol stored in the modified mesoporous silica.

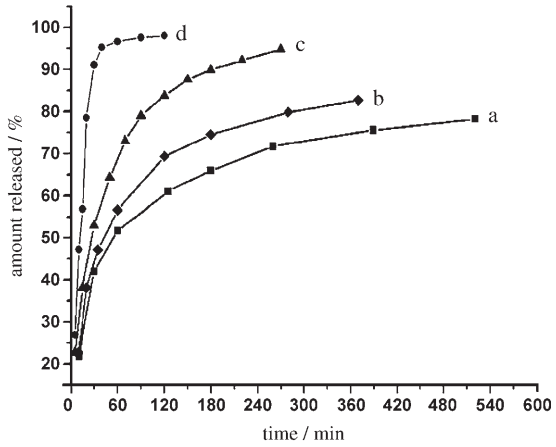

Figure 2. Release profiles of cholesterol for modified mesoporous silica sample **1C** (mesoporous silica grafted with 5.6 wt% azobenzene, with 35.1 wt% cholesterol absorbed). a) Without irradiation. b) After irradiation with visible light (Vis: 138 mW, $\lambda \approx 430$ nm). c) After irradiation with UV light (UV: 36 mW, $\lambda \approx 360$ nm). d) After irradiation with UV/Vis light (UV: 80 mW, $\lambda \approx 360$ nm; Vis: 54 mW, $\lambda \approx 430$ nm). The vertical axis corresponds to the amount of released guest molecules divided by the total amount of guest molecules stored in the mesopores.

cholesterol was released slowly from the pore (Figure 2a). This protracted diffusion of the molecule in the pore is attributed to the one-dimensional pore structure of the M41S-type mesoporous silica used.[11] In this case, approximately 87% of the cholesterol was released into hexane solution in over 48 h to yield sample **1E**. The release rate increased slightly upon irradiation of the sample with visible light (138 mW, $\lambda \approx 430$ nm; Figure 2b) and even more so with UV photoirradiation (36 mW, $\lambda \approx 360$ nm; Figure 2c). Furthermore, when simultaneous irradiation with UV and visible light

The results above indicate that the fastest release was achieved in the case of irradiation with both UV and visible light. The release of guest molecules from the mesopores involves the dissolution of the guest molecule in the solvent and its diffusion from the pore to the bulk solution. It is thought that the release rate, which exceeds that of natural diffusion by the concentration gradient of the guest molecule, is achieved here by acceleration through movement during photoisomerization of azobenzene groups. It is well known that the photostationary state of the *cis*–*trans* isomerization of azobenzene is dynamically balanced when the reversible isomerization between *trans* and *cis* isomers is ongoing. Under UV light *trans* isomers display a strong absorption and induce a photostationary-state motion of azobenzene from the *trans* to the *cis* form, whereas *cis* isomers reveal a strong absorption under irradiation with visible light and result in the photostationary-state motion of azobenzene from the *cis* to the *trans* form. In the case of irradiation with combined UV/Vis light, a fast reversible isomerization process is achieved.

Control experiments were carried out using samples with the azobenzene derivative attached only to the outlet of the pore and synthesized according to our previously reported procedure using mesoporous silica and templates.[4] In this case, the size of the pore outlet was regulated by the isomerization of azobenzene.[10] The release experiments showed that approximately 80% of the guest molecules were released after 8 h of photoirradiation to form the *cis* isomer (UV: 36 mW, $\lambda \approx 360$ nm), whereas it took 1.5 h to release 80% of the guest molecules from sample **1C** under the same conditions (Figure 2c). On the other hand, note that the most enhanced release was observed when not only UV light but also visible light was used (Figure 2d). In the present case, visible light was used concurrently to isomerize azobenzene from the *cis* to *trans* form. In addition, the effect of visible light irradiation on the release rate is quite limited comparing with UV/Vis light irradiation. About 69% of the guest molecules were released after 2 h of irradiation with visible light with a power of 138 mW ($\lambda \approx 430$ nm), while about 92% of the stored cholesterol was released in just 30 minutes under UV/Vis irradiation with a power of 134 mW (UV: 80 mW, $\lambda \approx 360$ nm; Vis: 54 mW, $\lambda \approx 430$ nm). Therefore, it is clear that the enhanced effect of release is dominantly attributed to movement of the azobenzene derivatives.

Control experiments using samples without azobenzene derivatives also showed that irradiation with UV or UV/Vis

light did not increase the release rate of the guest molecule in the mesopores. In short, the release rate is dominated by the reversible isomerization of the azobenzene moiety. This finding may add a new dimension to research on artificial light-driven active-transport systems.[20,21]

To verify the generality of the molecular "stirrers", other molecules were also explored on 3-(phenylazobenzoylthiopropyl)triethoxysilane and 4-(3-triethoxysilylpropylureido)-azobenzene, and all of them showed effective results. In the present study, the surface coverage of the mesopore is about 0.06 azobenzene ligands per square nanometer, with an average ligand-to-ligand spacing of around 4 nm in a mesopore with a diameter of approximately 3 nm. The proper spacing arrangement ensures that the movement of azobenzene is strong and efficient enough to propel the release of the guest molecule from the mesopores.

A multifunctional storage–release nanosystem was assembled by the combination of the azobenzene molecular stirring unit and the coumarin molecular gating system as illustrated in Figure 3. Mesoporous silica was modified with 1.0 wt% of 7-[(3-triethoxysilyl)propoxy]coumarin on the outlets (sample **2A**) using the as-synthesized material and a template. After the removal of the template by solvent extraction, sample **2A** was modified with 5.9 wt% of phenylazo-*N*-(3-triethoxysilyl)benzamide inside the mesopores to give sample **2B**, which was then loaded with 32.5 wt% of cholesterol (sample **2C**). This sample was then irradiated with UV light ($\lambda > 310$ nm). Even after thorough washing with *n*-hexane, a considerable amount of the guest molecule remained; that is, the guest was stored by photodimerization of the coumarin derivatives with UV irradiation. Figure 4 shows the release profiles of cholesterol from sample **2C** after photocleavage of the coumarin dimer with UV irradiation ($\lambda \approx 250$ nm). The release rates depended strikingly on the light exposure (Figure 4): Under the normal light of a room, only 35% of the stored cholesterol was released after 2 h. The release rate was slightly increased by UV irradiation (UV: 10 mW, $\lambda \approx 360$ nm), with 30% and 60% release after 30 min and 2 h, respectively. However, upon irradiation with UV/Vis light (UV: 22 mW, $\lambda \approx 360$ nm; Vis: 53 mW, $\lambda \approx 430$ nm) the discharge of the guest molecule was intensively accelerated, with release of 62% of cholesterol in 30 min and over 95% in 2 h. Moreover, under all the irradiation modes, the release rates were slower than the cases without coumarin substituents (e.g. sample **1C**, Figure 2). Thus, the presence of the coumarin substituent at the outlet of the mesopore modestly inhibits the release of cholesterol from the pore.

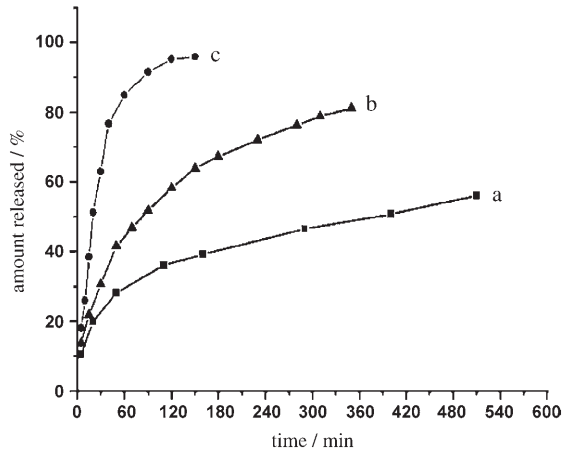

Figure 4. Release profiles of cholesterol from modified mesoporous silica sample **2C** (MCM-41 grafted with 1.0 wt% coumarin and 5.9 wt% azobenzene, with 32.5 wt% cholesterol absorbed). a) Without irradiation. b) Irradiated with UV light (UV: 10 mW, $\lambda \approx 360$ nm). c) Irradiated with UV/Vis light (UV: 22 mW, $\lambda \approx 360$ nm; Vis: 53 mW, $\lambda \approx 430$ nm).

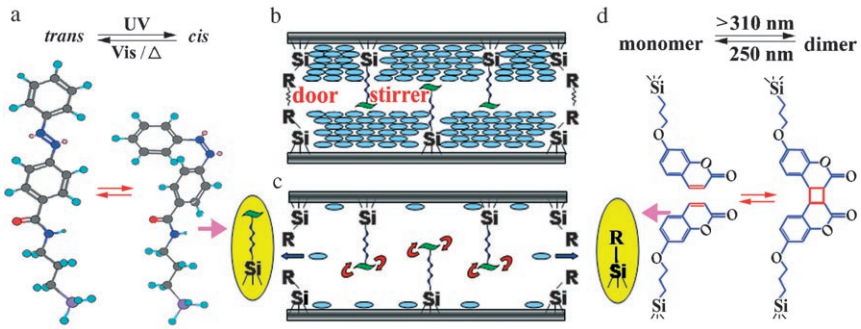

Figure 3. Multifunctional storage and release nanodevice comprised of mesoporous silica, a coumarin substituent, and an azobenzene substituent. a) Azobenzene substituents act as stirrers with their continuous rotation–inversion and stretch–shrink motions. b) Schematic of a mesopore with coumarin substituents as gates (R), azobenzene substituents as stirrers (green), and cholesterol as a guest molecule (blue). c) Cholesterol is released from the mesopore when the coumarin "gates" are opened with UV irradiation ($\lambda \approx 250$ nm); the release is enhanced by the stirring action of the azobenzene units powered by UV/Vis light. d) Coumarin substituents act as gates when reversibly dimerized with UV irradiation ($\lambda > 310$ nm); the dimers are cleaved with UV irradiation ($\lambda \approx 250$ nm).

In conclusion, our studies demonstrate the assembly of multifunctional nanodevices by integrating nanostructures with functional molecules through sequential chemical processes. The photomechanical nanodevice can be operated with combined UV/Vis light through a photochemical mechanism by sequential manipulation of the individual parts. These results may be a successful step toward practical photocontrolled storage–release nanosystems. Various substances can be stored and released into solution in ways that are controlled not only by diffusion but also by photoacceleration. This work takes us a step closer to multifunctional fully controlled release nanodevices. Together with previous important reports,[2–10] it is hoped that more molecular nanodevices with powerful functions will be created, such as autonomous, controlled storage–release implants or highly controllable tablets for drug-delivery applications. These nanodevices may find wide applications

in medical diagnostics, analytical chemistry, chemical detection, industrial process monitoring and control, combinatorial chemistry, and microbiology.

Experimental Section

Preparation of *N*-(3-triethoxysilyl)propyl-4-phenylazobenzamide and 7-[(3-triethoxysilyl)propoxy]coumarin. 3-Aminopropyltriethoxysilane (1.22 g, 5.5 mmol) and triethylamine (0.556 g, 5.5 mmol) were added to a solution of 4-phenylazobenzoyl chloride (1.22 g, 5 mmol) in dry toluene (50 mL) under a dry nitrogen atmosphere. The solution was stirred for 12 h at room temperature. After filtering off the solid, the solution was concentrated under reduced pressure and the solid was used directly to modify mesoporous silica. 7-[(3-triethoxysilyl)-propoxy]coumarin was prepared by using 7-allyloxycoumarin (3.24 g, 16 mmol), obtained from umbelliferone and allyl bromide, and triethoxysilane (2.94 g, 17.6 mmol) in toluene (100 mL) in the presence of platinum(0) 1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex (0.8 mL of a 2 mM solution in toluene). For details, see reference [4].

Preparation of azobenzene-modified mesoporous silica. Mesoporous silica material was prepared under hydrothermal conditions using a teflon-lined autoclave at 388 K for 24 h.[22] The molar composition was $1\,SiO_2$:0.25 NaOH:0.1 CTAB:20 H_2O (CTAB = cetyl trimethylammonium bromide). The obtained material was filtered off, washed, and dried at 373 K for 24 h. A sample of this as-synthesized material (2 g) was heated at reflux in ethanol (100 mL) containing 1M HCl (10 mL) at 353 K for 4 h. The solid was collected and washed with ethanol, and this process was carried out twice to ensure the complete removal of the surfactant. The obtained solid was filtered off, washed with ethanol, and finally dried at 353 K for 12 h (sample **1A**). Sample **1A** (1 g) was suspended in a solution containing toluene (10 mL) and *N*-(3-triethoxysilyl)propyl-4-phenylazobenzamide (0.08 g; see the Supporting Information), and the suspension was stirred at 353 K for 1 h. The volatiles were then removed by evaporation at 353 K for 2 h, and the solid was dried under vacuum at 363 K for 24 h, washed with toluene and ethanol, and finally dried at 353 K for 12 h (sample **1B**).

Preparation of coumarin-azobenzene-modified MCM-41. As-synthesized mesoporous silica (2 g) was suspended in a solution containing *n*-hexane (20 mL) and 7-[(3-triethoxysilyl)propoxy]coumarin[4] (0.05 g) with stirring at ambient temperature for 15 min. The volatiles were removed by evaporation at 353 K for 2 h, and the obtained solid was dried under vacuum at 423 K for 12 h and then washed with ethanol to completely remove the surfactant from the pores of MCM-41 (sample **2A**).[4] Sample **2A** (1 g) was suspended in a solution containing toluene (20 mL) and *N*-(3-triethoxysilyl)propyl-4-phenylazobenzamide (0.08 g) with stirring at 333 K for 6 h. The resulting material was concentrated using a rotary evaporator at 353 K for 1 h, and the residue was rinsed with toluene to remove the azobenzene adsorbed on the surface (outlets) of the particle. The suspension was concentrated again, and the residue was heated under vacuum at 363 K for 24 h. The obtained solid was washed with toluene and ethanol and finally dried at 353 K for 12 h (sample **2B**). The removal of surfactant and the amount of substituents in the mesoporous silica were assessed by gas chromatography, thermogravimetric analysis, and chemical analysis.

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