Molecular Recognition Inside of Multifunctionalized Mesoporous Silicas: Toward Selective Fluorescence Detection of Dopamine and Glucosamine

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Structurally well-defined mesoporous silica materials, such as MCM-type silicas,[1] 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.[2] Herein, we report the design and synthesis of a fluorescence sensory system to study the molecular recognition events of biogenic molecules, such as dopamine and glucosamine, inside different functionalized mesoporous silica microenvironments.

Our design strategy took advantage of the size-sieving ability of the mesoporous silica framework as the supporting matrix to first incorporate an amine-sensitive *o*-phthalic hemithioacetal (OPTA)[3] group on the pore-surface. Only small molecules with amino groups can diffuse into the pores and react with the OPTA group to give rise to highly fluorescent isoindole products as depicted in Figure 1. In contrast to the molecular imprinted micro- and/or mesoporous silica materials[4] where the selectivity was determined by the pore shape and the functional group density in each cavity, we prepared multifunctionalized pores to not only capture the target substrate molecules covalently but also provide different secondary noncovalent interactions. OPTA-derivatized mesoporous silica materials with various surface-bound functional groups allow modulation of our sensory system to enhance the substrate selectivity by tuning substrate accessibility and pore hydrophobicity.

To synthesize these multifunctionalized mesoporous silica materials, we first prepared a thiol-functionalized MCM-41 silica (**M1**) via a modified synthetic method of the well-developed surfactant templated co-condensation reaction.[5] The unoccupied silica pore surface of the **M1** was further functionalized with propyl, phenyl, and pentafluorophenyl groups via postsynthesis grafting procedures[6] using propyltrimethoxysilane, phenyltrimethoxysilane, and pentafluorophenyltriethoxysilane[7] to yield three other multifunctionalized organomesoporous silica materials, **M2**, **M3**, and **M4**, respectively.[8] The characterization of these materials is summarized in Table 1.

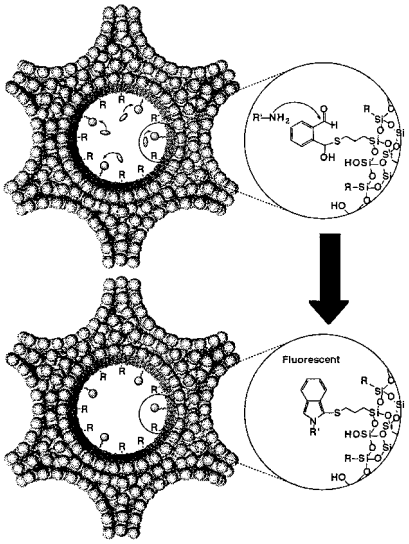

Figure 1. Schematic representation of the *o*-phthalic hemithioacetl (**OPTA**) functionalized mesoporous silica material and their fluorescent detection of amines. (R = siloxy, propyl, phenyl, or pentafluorophenyl groups; R′-NH_2 = dopamine or glucosamine).

Phthalic dicarboxaldehyde (*o*-phthalaldehyde, OPA) was introduced to suspensions of these thiol-containing multifunctionalized mesoporous silicas in a neutral buffer solution to form the amine-sensitive *o*-phthalic hemithioacetal-derivatized materials, **OPTA-MX** (**X** = 1 to 4). Incorporation of the OPTA groups was confirmed by ^{13}C CP-MAS NMR spectroscopy. The resulting OPTA-silica powder was dispersed in buffer for the fluorescence sensing experiments of dopamine or glucosamine. In contrast to the instantaneous completion of the homogeneous reaction of 2-mercaptoethanol, OPA, and dopamine to form a highly fluorescent isoindole,[10] the reactions of dopamine (30 μM) with all four of our OPTA-derivatized mesoporous silicas exhibited slower reaction rates (Figure 2a). For **OPTA-M1**, the increase of fluorescence intensity at the emission λ_{max} of isoindole (440 nm) reached a plateau indicating the completion of the reaction in about 10 min. In contrast to the dopamine experiment, **OPTA-M1** treated with 600 μM glucosamine took about 2 h for the reaction to proceed to completion (Figure 2b). The reaction rate of glucosamine is at least 1 order of magnitude slower than that of dopamine. Since dopamine and glucosamine are similar in their sizes and reactivities toward OPTA in homogeneous solutions,[10,11]

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Table 1. Characterization of Multifunctionalized Mesoporous Silicas

	BET surface area[a] (m^2/g)	BJH pore diameter[a] (Å)	chemically accessible thiol density[b] (mmol/g)	amount of the grafted group[c] (mmol/g)
M1	964	23.1	1.5	
M2	926	20.6	0.046	1.5
M3	936	20.6	0.042	1.0
M4	939	20.7	0.062	1.2

[a] See Supporting Information for the adsorption isotherms and pore-size distributions. [b] Chemically accessible thiol densities were determined by measuring the solution concentration of the side product (pyridine-2-thione) generated from the reaction of the pore-surface thiols with 2,2′-dipyridyl disulfide.[9] [c] Measured by CHNS elemental analyses.

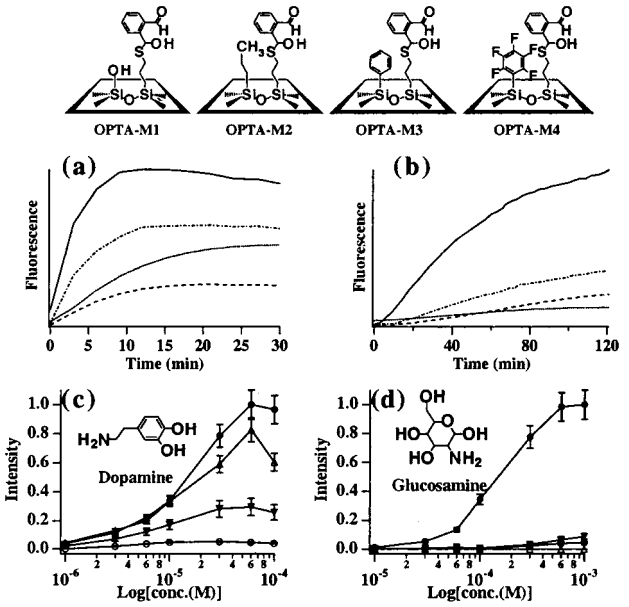

Figure 2. Kinetic measurements of the fluorescence detection of dopamine (a) and glucosamine (b) with OPTA-dervatized mesoporous silicas grafted with secondary functional groups, such as silanol (**M1**: solid line), propoyl (**M2**: dotted line), phenyl (**M3**: dashed line), and pentafluorophenyl (**M4**: dash−dotted line) groups. Fluorescence increase of **OPTA-MX** (**X** = **1** (●); **2** (○); **3** (▽); **4** (△) as a function of dopamine (c) and glucosamine (d) concentrations.

the large difference in reaction rates between dopamine and glucosamine could not be explained by the size-sieving effect of these functionalized mesoporous materials. Conceivably, the significantly slower reaction rates of glucosamine could be attributed to a strong dipolar interaction between the abundant hydroxy groups of glucosamine with the pore surface silicates leading to a slower diffusion process within the pores. In addition, as the silicate walls are functionalized with increasingly hydrophobic substituents (**OPTA-MX, X** = 2 to 4), the diffusion rates for both dopamine and glucosamine are slowed (Figure 2a,b).

The fluorescence intensity of these OPTA-derivatized mesoporous silicas treated with dopamine and glucosamine also varies dramatically depending on the pore environment (Figure 2c,d). In our study of dopamine binding, the measured fluorescence intensity of **OPTA-M1** increased with the increasing concentration of dopamine, but for the more hydrophobic **OPTA-MX** (**X** = 2 to 4) materials, the change of fluorescence intensity was smaller than that of **OPTA-M1**. The reaction rates of dopamine binding are clearly slower in these materials. Furthermore, the **OPTA-M4**/dopamine binding gives a significantly higher increase of fluorescence intensities at all concentrations in comparison with that of **OPTA-M3** and **OPTA-M4**. This observation strongly suggested that the pentafluorophenyl-functionalized mesopores of the **OPTA-M4** were more reactive and preferred by dopamine compared to the propyl- and phenyl-functionalized pores of the **OPTA-M2** and **OPTA-M3** materials. Since both the average pore sizes and the surface coverage of the thiol functionality of these materials (**MX**, **X** = 2 to 4) are very similar (Table 1), the large difference in binding behaviors is not likely due to the slight variation in the amount of chemically accessible thiol groups or the pore size of the functionalized mesopores of these materials. Compared with the phenyl-functionalized **OPTA-M3**, the better $\pi-\pi$ donor/acceptor type of stacking effect between the catechol rings of dopamine molecules and the pentafluorophenyl moieties of the **OPTA-M4** silica could induce a faster and more favorable diffusion of dopamine to enter their functionalized mesopores. The hydrophobic propyl-functionalized **OPTA-M2** material discourages the intercalation of dopamine.

The same fluorescence study for glucosamine binding to **OPTA-M1** at various concentrations showed similar large increases in fluorescence intensity (Figure 2d). In contrast to dopamine binding, the propyl-, phenyl-, and pentafluorophenyl-functionalized **OPTA-MX** (X = 2 to 4) materials showed only similar small increases of fluorescence intensities with increasing glucosamine concentrations. These data further support the possibility that the nonaromatic glucosamine molecules could not easily diffuse into either the propyl-, phenyl-, or pentafluorophenyl-functionalized mesopores to react with the OPTA groups due to the hydrophobic environment inside the pores.

In this study, we have demonstrated that selective molecular recognition of two multifunctional molecules with similar sizes and functionalities can be achieved not by shape recognition but by creating a multifunctionalized mesopore as the "active site" with combinations of covalent (isoindole formation) and noncovalent interactions (hydrophobic and $\pi-\pi$ interactions). The presented selectivity was not observed in the amorphous silica systems grafted with the same organofunctionalities, such as propyl and phenyl groups (see Supporting Information). Therefore, we envision that these multifunctionalized mesoporous silicas could serve as new materials for developing highly selective sensors and catalysts.

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Supporting Information Available: Experimental procedures and spectral data of the multifunctionalized mesoporous silicas (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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