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Surface patterned pH-sensitive fluorescence using β-cyclodextrin functionalized poly(ethylene glycol)

Sung Han Kim[a], Shazid Md. Sharker[b], Insik In[a,c], Sung Young Park[a,d,*]

[a] Department of IT Convergence, Korea National University of Transportation, Chungju 380-702, Republic of Korea
[b] Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 305-702, Republic of Korea
[c] Department of Polymer Science and Engineering, Korea National University of Transportation, Chungju 380-702, Republic of Korea
[d] Department of Chemical and Biological Engineering, Korea National University of Transportation, Chungju 380-702, Republic of Korea

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ABSTRACT

This paper reports the development of a pH-responsive molecular pattern that shows specific and selective affinity for particular host-guest interactions, and its use as a pH fluorescent sensor. The pH-responsive boronate ester is formed via interactions between the diol group of β-cyclodextrin (CD) and phenylboronic acid of poly(ethylene glycol), and is strategically designed to allow reversible formation of a molecular lining pattern. Printing on a versatile substrate provides a method to monitor the positioning of different molecules by using a pH-responsive boronate ester, allowing specific host-guest interactions on any surface. Confocal laser scanning microscopy, fluorescence spectroscopy, and ^{1}H NMR results indicate that the assembled CD monolayer can be removed by washing with an acidic pH buffer, demonstrating the presence of a boronate ester connective bridge, which is acid labile. Therefore, visualization of the pH-responsive fluorescence sensor using a rhodamine-CD complex allows straightforward discrimination between different molecules on any substrate, thus facilitating application of this sensor in clinical diagnostics and environmental monitoring.

1. Introduction

In the study of supramolecular interactions, the preparation of highly specific targets with controllable affinity and reversible immobilization is of great importance. Therefore, methods that facilitate the precise positioning of immobilized molecules are promising, allowing the development of molecular printed boards (Auletta et al., 2004; Mulder et al., 2005). Expansion of such printed boards has allowed versatile nanofabrication on substrates by molecular printing and patterning (Khalid, Wang, & Mirkin, 2007). In this new field of research, thermodynamically stable host-guest interactions allow the development of molecular print-boards by allowing the controllable, competitive dissociation of monovalent host or guest species (Crini & Morcellet, 2002; Crini et al., 1998; Crini, 2005; Gonzaílez-Campo et al., 2010). Additionally, stimulus responsive tools that control surface attachment and detachment may be used in multiple applications for immobilized patterns (Springsteen & Wang, 2002).

As pH-responsive functional groups, boronic acids have been widely used to bind compounds containing diol moieties with high affinity by reversible formation of esters (Springsteen & Wang, 2002). Such affinity allows boronic acids to be used as the recognition site in the construction of indicator for saccharides (Springsteen & Wang, 2002). However, the stability of boronate esters is dependent on the pH of the solution, which controls the attachment and detachment from the targeted carbohydrate surface (Chen, Wan, Ke & Xu, 2011). Among the different carbohydrate derivatives, cyclodextrin (CD) is considered to be an interesting surface target for boronic acids for supramolecular immobilization because of the dense hexagonal packing of the monolayers and its broad affinity for hydrophobic guest molecules that may be entrapped in the CD internal cavity (Böhm, Isenbgel, Ritter, Branscheid & Kolb, 2011; Sharker, Kim, Kim et al., 2015). Recently, it has been found that these CD monolayers can be used as molecular printed boards to draw supramolecular patterns (Auletta et al., 2004). To draw the desired pattern, a dopamine mimic, a low-molecular-weight catecholamine, is adhered, at alkaline pH, to a substrate. Furthermore, because catecholamines can adhere to a wide range of substrates, a 'universal platform' for the surface-anchoring of ligands can be formed (Kang et al., 2012).

* Corresponding author at: Department of IT Convergence, Korea National University of Transportation, Chungju 380-702, Republic of Korea.
E-mail address: parkchem@ut.ac.kr (S.Y. Park).

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The specific host-guest interactions of CD monolayer allow positioning of the guest molecules on the exposed host receiver (Aoki, Nishikawa & Hattori, 2003), forming a monolayer coating pattern. Under such conditions, the designed patterns must be stable towards rinsing with aqueous solvents; however, they can be removed through detachment of the CD host (Auletta et al., 2004; Mulder et al., 2005). Recently, much success has been made using fluorescence imaging techniques to visualize the formed patterns, and this is particular true in comparison to gold-substrate-based lithographic patterning, in which visualization is strongly hampered by fluorescence quenching (Auletta et al., 2004; Sharker, Kim, Lee et al., 2015). In contrast, bottom-up, micro-contact printing (μCP) nanotechnology, which involves specific recognition sites for the precise positioning of guest molecules have been less investigated despite their great promise (Biel et al., 2006; Wilbur, Kumar, Kim, & Whitesides, 1994).

In this study, we report a micro-contact patterning scheme prepared by using CD attached phenyl boronic acid (BA) and an adhesive surface coating, catechol (2-chloro-3′,4′-dihydroxyacetophenone, CCDP) quaternized polyethylene glycol grafted poly(*N,N*-dimethylaminoethyl methacrylate) [CCB-PgP]. In this system, the advantages of the host-guest interactions in the CD cavity include fluorescence across the surface, which can be used as the 'ink' in supramolecular printed boards. Additionally, attachment and detachment of CD located on BA diol moieties where the CCDP at the terminal end is attached under mild alkaline pH in any substrates can be triggered by pH control.

2. Experimental

2.1. Materials and methods

Polyethylene glycol (PEG, M_n 3500), 2-(dimethylamino)ethyl methacrylate (DMA), β-cyclodextrin(β-CD or CD), 2-chloro-3′,4′-dihydroxyacetophenone (CCDP), 4-chlorophenyl boronic acid (BA), dichloromethane (MC), diethyl ether, ethanol, toluene, hexane, Trizma base, Trizma HCl, and rhodamine B were purchased from Sigma Aldrich, Korea. PEG grafted poly(*N,N*-dimethylaminoethyl methacrylate) [PEG-*g*-PDMA, PgP] was synthesized following a previously published report (Sharker et al., 2014).

^{1}H NMR spectra were recorded using AVANCE 400 MHz (Bruker) spectrometer with deuterium oxide (D_2O) as the solvent. NMR proton peaks were calibrated by using D_2O solvent peaks in 4.8 ppm position. The number of scans was 32 and time domain size 65536. The UV–vis spectra were recorded using an Optizen 2020UV (Mecasys Co.). X-ray photoelectron spectroscopy (XPS) spectra were obtained using a PHI Quantera II (Japan) with 100 μm 100 W 20 kV_HP (High Power mode) and take off angle was 45°. The XPS scan area was 1000 μm × 1000 μm and number of survey scans 2 (55 eV) and narrow scans 7 (280 eV). The photoluminescence (PL) spectra were obtained on a L550B luminescence spectrometer (Perkin Elmer). Fluorescence microscopy was performed using an LSM510 confocal laser scanning microscope (Carl Zeiss, Germany). Static water contact angles were measured using a DO3210 (KRUSS Ltd., Germany), and 8 μL water drop was used to measure all apparent contact angle values. The identical contact angle recorded repeat-ably five times on similar type substrates and finally average value ware used to evaluate surface property. In this purpose, bare silicon wafer were cleaned using piranha solution, and modified with the treatment of coating/patterning solution.

The piranha solution was made from mixture of sulfuric acid (H_2SO_4) and hydrogen peroxide (H_2O_2) with%v/v (3–1). Silicon wafer was added to piranha solution then saturated for 10 min. In the end of time, the silicon wafer was removed from the piranha solution and washed with DDW twice to prepare Si wafer. The cleaned bare SiO_2 wafer has shown contact angle ~38° which might be due to contents of silicon and loss of oxide film during cleaning process. As the silicon dioxide (SiO_2) is more hydrophilic than silicon, the contact angle on oxide substrate can changed depending on cleaning process (Kim, Sung, Lee & Lim, 2010).

2.2. Synthesis of 4-chlorophenyl boronic acid quaternized PEG-g-PDMA (B-PgP)

To prepare the BA quaternized PgP, PgP (2.5 g) and 4-chlorophenyl boronic acid (0.245 g) were dissolved in anhydrous ethanol in a 150 mL flask. The mixture was stirred for 24 h at 70 °C under a nitrogen atmosphere. After stirring, the solvent was evaporated in a rotary evaporator, and hexane was added to the polymer to induce precipitation. The resulting B-PgP was dried in vacuum oven, and the product was analyzed. Using ^{1}H NMR, the aromatic protons of BA grafted PgP were identified at 7.4–7.5 ppm with a conjugation number of 12.

2.3. Synthesis of cyclodextrin grafted diols complexed B-PgP (CB-PgP)

B-PgP (1 g) and β-CD (0.655 g) were dissolved 10 mL of phosphate-buffered saline (PBS, pH 10.3) in a 150 mL flask. The mixture was stirred for 24 h at room temperature and after completion, the reaction solvent was dialyzed (MWCO: 3500) for 24 h after freeze drying. The aromatic groups of the β-CD grafted B-PgP were identified at 7.4–7.5 ppm with a conjugation number of 6 by ^{1}H NMR.

2.4. Synthesis of catechol quaternized CB-PgP (CCB-PgP)

To prepare catechol quaternized CB-PgP (CCB-PgP), CB-PgP (0.5 g) and CCDP (0.07 g) were dissolved in 20 mL of anhydrous ethanol in a 150-mL flask. The mixture was stirred for 24 h at 70 °C under a nitrogen atmosphere. After stirring, the solvent was evaporated in a rotary evaporator. Hexane was added to the polymer to induce precipitation. The resulting CCB-PgP was dried in vacuum oven and analyzed. The aromatic groups of CCDP grafted CB-PgP were found at 7.4–7.5 ppm with a conjugation number of 13 by ^{1}H NMR, and UV–visible spectroscopy investigation also showed the same number of grafted CCDP units.

2.5. Preparation of rhodamine complexed CCB-PgP

Rhodamine B was complexed to CCB-PgP following a widely used method for the formation of inclusion complexes. In detail, CCB-PgP and rhodamine B (100/1 ratio) were dissolved together in aqueous media to obtain rhodamine-complexed CCB-PgP. This solution was stirred for 12 h at room temperature (25 °C), before centrifugation and freeze drying. For surface application, the patterned surfaces were kept under rhodamine B solution, and this was then dialyzed (MWCO: 3500) for 24 h after freeze drying to remove unboundrhodamine B.

2.6. Preparation of coated substrates

The substrate was patterned using a polydimethylsiloxane (PDMS) imprinting technology and was carried out according to reported methods (Chien, Kuo, Wang, Tsai & Tsai, 2012). In brief, PDMS was prepared by casting a 10:1 (v/v) mixture of PDMS elastomer and its curing agent on a commercially available compact disk. The flexible PDMS was poured on the periodic side of the compact disk, and the temperature was maintained at 80 °C overnight. Then, the PDMS stamp was slowly peeled off from the compact disk, revealing the straight channeled structure formed on the PDMS