Tetrahedron Letters 49 (2008) 5593–5596

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis and lectin-binding activity of luminescent silica particles peripherally functionalized with lactose

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ARTICLE INFO

Article history:
Received 2 July 2008
Accepted 4 July 2008
Available online 9 July 2008

Keywords:
Carbohydrate
Glycocluster
Rubpy
Silica particles
Lectin-binding
Luminescent scaffold
Silane coupling agent

ABSTRACT

A novel O-protected lactose (Galβ1→4Glcβ1–) derivative bearing trimethoxysilyl group at the aglycon was developed as a silane coupling agent. Reaction of the coupling agent with tris(2,2′-bipyridine)ruthenium (II) dichloride (Rubpy) doped silica particle gave a Rubpy-doped silica particle peripherally functionalized with O-protected lactose derivative. De-O-protection of the particle with aqueous ammonia provided lactose-coating Rubpy-doped silica particles, combining luminophor encapsulated in silica matrix and carbohydrate having lectin-recognition ability. Specific adhesion of fluorescein isothiocyanate-labeled peanut agglutinin (FITC-PNA) to the lactose-coating Rubpy-doped silica particles was confirmed by fluorescence microscopic analysis.

Glycoconjugates, such as glycoprotein and glycolipids, are generally located on cell surfaces and play a key role in the process of cell adhesion with proteins of pathogens; that is, the early stage of cell adhesion involves carbohydrate-mediated specific recognition of pathogens. It is known that the clustering effect of carbohydrates enhances individual interaction between carbohydrates and proteins.[1] This effect has been applied for the molecular design of artificial inhibitors of pathogens such as toxins, bacteria and viruses, and several forms of glycoclusters have been developed.[2] We previously reported the syntheses of some glycoclusters[3] in which carbosilane dendrimers were employed as carbohydrate scaffolds, and we revealed the biological activities of some of these glycoclusters.[3e,g,h,4] We have been interested in the synthesis of luminescent glycoclusters because of their high potentiality for biomarkers of a variety of lectins and pathogens, and we recently reported the first synthesis and the unique optical properties of a luminescent glycocluster possessing a silole-core carbosilane dendrimer as a luminescent scaffold.[5]

On the other hand, silica particles are widely used in not only industrial applications but also fundamental research. Preparations and applications of monodisperse silica particles[6] and silica coating of other inorganic colloids[7] have been investigated in detail. Immobilizations of antibodies,[8] enzymes,[9] catalysts,[10] and magnetic substances[11] on a silica surface has attracted considerable attention in both clinical and chemical biology from the viewpoint of biocompatible silica particles. However, there have been few reports on the synthesis and application of carbohydrated silica particles.[12] In the course of our studies on glycoclusters, we became interested in a glycocluster in which luminescent silica particles are employed as a carbohydrate scaffold. Here, we report the synthesis of lactose-conjugated silica particles containing Rubpy as a luminophor and their lectin-binding activity.

Synthesis of Rubpy-doped silica particles **1** was carried out by the water-in-oil microemulsion method described previously.[13] The synthesized Rubpy-doped particles **1** were uniform in shape with an average diameter of about 500 nm (Fig. 1A).[14] The commonly used protocol for immobilization of functional compounds such as carbohydrate involves a surface modification of silica particles to combine the compound and silica particles. In this work, we used a new approach to carbohydrate-coating silica particles by means of a novel carbohydrated silane coupling agent. This procedure takes advantage of a simple approach to conjugate silica particles and carbohydrates.

The key intermediate **3a** was readily prepared in quantitative yield by hydrosilylation of a 1-*O*-pentenyl lactoside **2a** with trichlorosilane using $H_2PtCl_6{\cdot}6H_2O$ as a catalyst and subsequent methanolysis in the presence of a small amount of pyridine (Scheme 1). The ^{1}H NMR spectrum of **3a** showed a characteristic signal based on $Si(OCH_3)_3$ at 3.55 ppm.[15] However, the trimethoxysilyl derivative **3a** was slightly moisture-sensitive and slowly underwent intermolecular substitution leading to oligo- and

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doi:10.1016/j.tetlet.2008.07.034

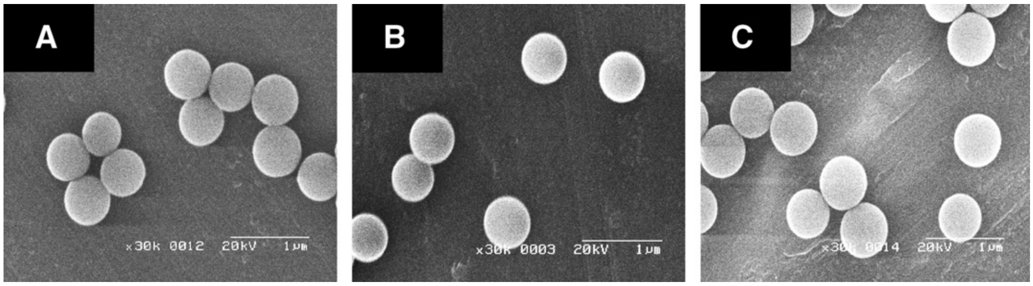
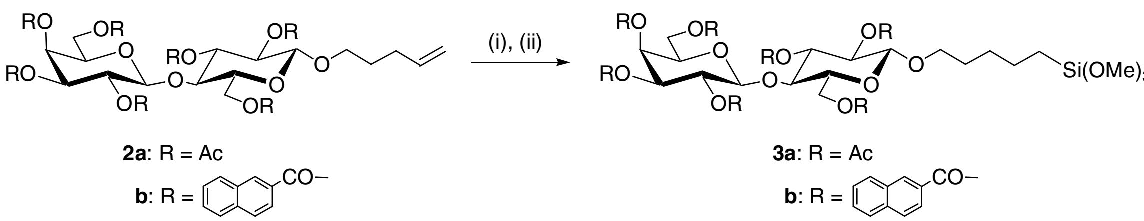


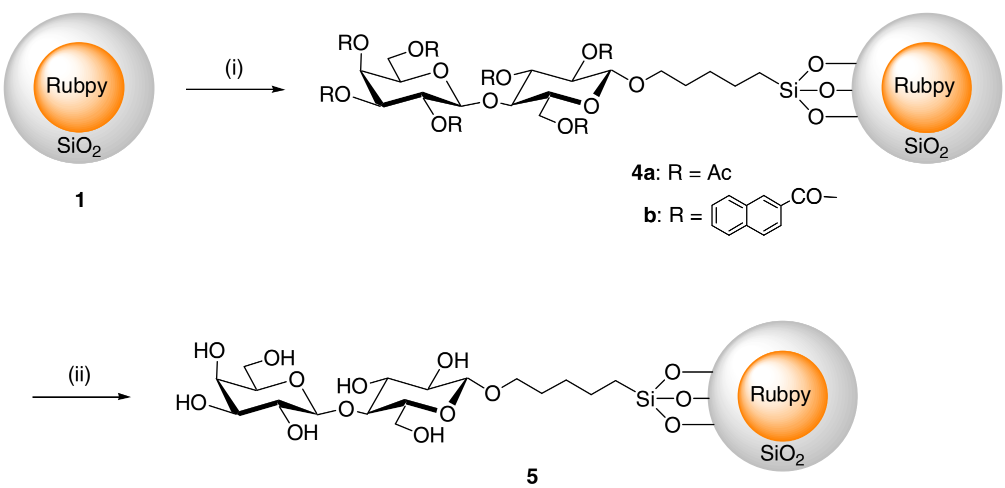
Figure 1. SEM mages of (A) Rubpy-doped silica particles **1**, (B) silica particles functionalized with acetyl-protected lactose derivative **4a** and (C) lactose-functionalized silica particles **5**.



Scheme 1. Reagents and conditions: (i) $HSiCl_3$, Speir cat., THF, rt→50 °C; (ii) MeOH, pyridine, THF.

polysiloxanes. Therefore, synthesized **3a** was immediately immobilized onto the Rubpy-doped silica particles **1** by a standard *sol–gel* process (see Scheme 2).

Reaction of **1** (1.000 g) with 10 wt% of the lactose derivative **3a** (0.12 mmol) in toluene at ambient temperature for 12 h followed by heating the reaction mixture at 80 °C for 3 h afforded 938 mg



Scheme 2. Reagents and conditions: (i) trimethoxysilylated lactose derivative **3**, toluene, rt→80 °C; (ii) NH_4OH, MeOH, rt.

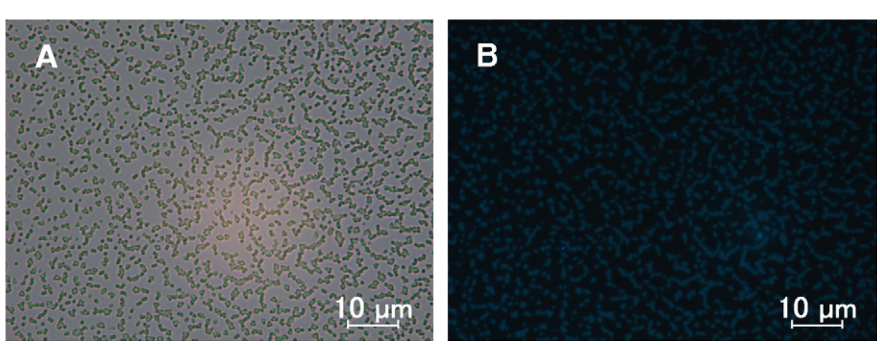


Figure 2. Fluorescence microscopy images of silica particles **4b** at 500 times magnification under transmitted light (A) and through a *Nikon* UV-2A filter set with 355/50-nm excitation and >420 nm emission (B).