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Switchable polymer-grafted mesoporous silica's: from polyesters to polyamides biosilica hybrid materials

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ABSTRACT

We report in this piece of work the synthesis of biosilica hybrid materials able to develop from hydrophobic polyesters to intermediate hydrophilic polyesters and then to polyamides through an O–N acyl transfer shift. After demonstration of the O–N acyl shift on a model depsipeptide anchored in the pores of ordered mesoporous silica (OMS), the preparation of three bio oligomer–silica hybrid materials is described. The oligomerisation of protected serine lactones was initiated in the pores of carboxylate functionalized OMS. Hybrid protected serine polyester–OMS were obtained and could be converted (i) into cationic polyesters, which could be switched (ii) into neutral polyamide–OMS in basic conditions through a multi O–N acyl shift.

1. Introduction

Silica hybrid based materials obtained by the sol–gel process have attracted considerable attention since a quarter of a century. They constitute a fascinating class of materials combining the properties of organic moieties and inorganic matrices.[1–4] Since the discovery of ordered mesoporous silicas,[5] their surface modification of inner pores with organic functional groups has been extensively investigated to render them suitable for a wide number of applications,[6] such as catalysis,[7] separation,[8] chemical sensors,[9,10] etc. Incorporation of several types of functional organic units into the channels of mesoporous silica has attracted many efforts for the design and organization of multi-functionalized mesoporous materials.[11]

Generally, organic functionalities can be incorporated into mesoporous materials, either by post synthesis[12] (grafting) or by direct synthesis (one-pot) method.[13] It was demonstrated that the direct synthesis method produces hybrid material with high content of organic groups (up to 25% molar) and more homogeneous surface coverage of the silica inner pores.[14] This approach consists in the co-hydrolysis and polymerization of tetraethylorthosilicate (TEOS: silica precursor) with an organotrialkoxysilane $RSi(OR')_3$ in the presence of a surfactant as a structure-directing agent. After elimination of the surfactant, ordered mesoporous silica (OMS) with high porosity, surface area, and tuneable pores of 2–30 nm diameter can be obtained.

Compared to other materials of undefined porosity, such as silica gels, the use of OMS greatly rationalizes the inclusion of organic compounds in a non-covalent or covalent way. Large protein, such as enzymes[15,16] and heme proteins[17] were covalently immobilized on hexagonal[18] and cubic[19] phases of OMS. Recently, hybrid peptide oligomer–silica OMS were prepared by amino acid *N*-carboxyanhydride (NCA)[20] polymerization, initiated by amino groups present in the pores of OMS.[21,22]

On the other hand, serine lactone has already been used to obtain polyesters.[23,24] In a general manner, esters formed on the side chain of serine, are known to easily undergo an O–N acyl shift.[25,26] This reaction is extensively used in the field of peptide science for the synthesis of difficult sequences,[27] cyclic peptides,[28] C-terminal peptide alcohols.[29] More recently, we take profit of this acyl transfer reaction to the synthesis of serine polyester oligomers in solution able to shift to serine polyamide oligomers.[30]

In this paper, we applied the same methodology to the preparation of bioorganic hybrid OMS whose pores contain switchable serine oligomers. Three different hybrid materials can be obtained sequentially (i.e., protected serine polyester, cationic polyester, and

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neutral polyamide silica hybrids) using a multi O–N acyl transfer that takes place within the pores of OMS. Such materials could find potential applications as controllable nanocontainers.

2. Results and discussion

2.1. Model depsipeptide grafted in OMS pores

As a proof of concept, we first studied the O–N acyl shift on a model depsipeptide Boc-Ser(Fmoc-Phe)-Lys-NH_2 **1** grafted on nonfunctionalized OMS. For that purpose, we used the methodology we recently set up[31] consisting in the synthesis of hybrid trialkoxysilyl protected peptides that were directly involved in hydrolysis and condensation on the surface of the OMS pores (Scheme 1, step f). The OMS used here was SBA-15 type, which was obtained by hydrolysis and polycondensation of TEOS in the presence of Pluronic P123 as surfactant.[32] The depsipeptide **1** reacted with trialkoxysilyl propyl isocyanate to yield the hybrid pseudo peptide **2**, which was isolated and characterized (Supplementary data S5–S6). Compound **2** was grafted into the pores of OMS by reaction between alkoxy groups and silanol (SiOH) of the surface. It is worth noting this new type of biomolecule grafting did not require any ligation chemistry between inorganic and bioorganic moieties. Briefly, SBA-15 suspended in a DMF solution containing the hybrid peptide blocks was stirred for 1 h at rt, then 24 h at 80 °C. This two-step procedure allowed the hybrid peptide block to penetrate into the pores. Hybrid material **3** was characterized by X-ray diffraction, elemental analysis, BET, and FTIR. N_2 adsorption–desorption measurements at 77 K showed type IV isotherms with a clear H1-type hysteresis loop at high relative pressure (Supplementary data S1), characteristic of mesoporous materials. XRD patterns exhibited three low-angle reflections, d_{100}, d_{110}, and d_{200}, characteristic of well-ordered SBA-15 type materials (Supplementary data S2). Transmission Electron Microscopy (TEM) provided further evidence of an ordered hexagonal structure (Supplementary data S2). Taken together, these results indicated that properties of OMS were conserved after chemical modification with depsipeptide units. The efficiency of depsipeptide loading of hybrid OMS **3** was determined by elemental analysis (0.11 mmol g^{-1}) (Table 1). Boc protecting groups were removed by neat TFA treatment yielding cationic material **4**. Boc removal and N–O acyl shift were monitored by the Kaiser test. It has to be underlined that the O–N acyl transfer could not take place till the amino group was free. This was achieved by treatment of hybrid silica **3** with 10% Et_3N in DCM. After 12 h, the hybrid silica **5** was obtained.

Table 1
Properties of OMS determined by N2 adsorption and elemental analysis

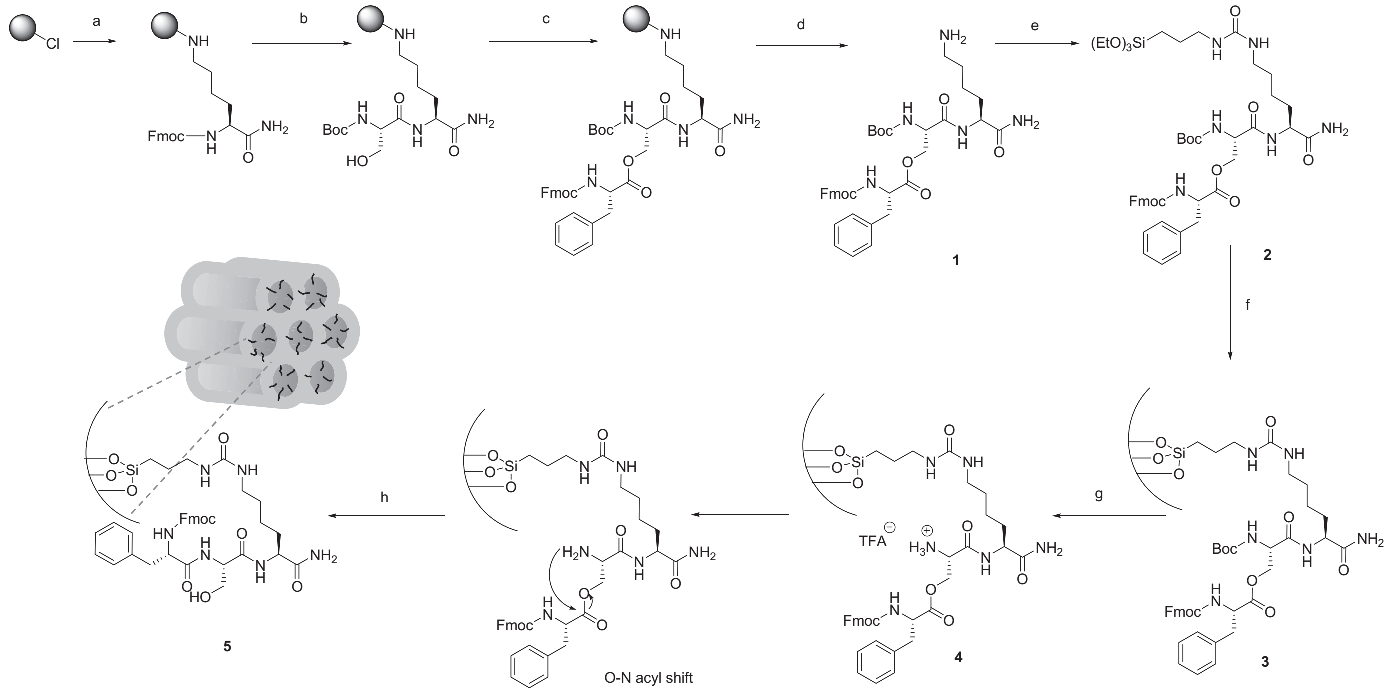
	Area surface[a] (m^2 g^{-1})	Pore volume[a] (cm^3 g^{-1})	%N[b]
SBA	674	1.18	—
3	337	0.63	0.85
4	520	0.91	/
5	457	0.86	/
6	643	1.22	1.02
7	540	0.83	—
9a–b	271–133	0.81–0.35	3.0–4.7
10a–b	389–323	0.89–0.65	/
11a–b	281–157	0.74–0.44	/

[a] Calculated by BET.
[b] Calculated by elemental analyses.

2.2. Hybrid biopolymer–silica material

The next step of the study was the use of the O–N acyl shift for the synthesis of a hybrid biopolymer–silica material. To obtain the starting polyester–silica hybrid material, we set up the polymerization of protected serine lactone. This ring opening polymerization (ROP)[33] could be initiated by the carboxylate salt prepared from cyano OMS **6**. Thus, a mesoporous material functionalized with CN groups with controlled loading (0.7 mmol g^{-1}) was prepared in one-pot by hydrolysis and co-condensation of tetraethylorthosilicate (TEOS) with the desired amount of cyanopropyltriethoxysilane in the presence of P123 as surfactant under acidic conditions. The obtained OMS **6** was well organized in a 2D-hexagonal structure as shown by the XRD pattern diffraction (Supplementary data S3).

Carboxylic functionalized mesoporous silicas (0.7 mmol g^{-1} loading) were prepared by oxidation of the nitrile **6** OMS following



Scheme 1. Synthesis of a hybrid trialkoxysylyl depsipeptide and preparation of switchable hybrid peptide-OMS. (a) Fmoc-Lys-NH_2, DIEA; (b) Fmoc deprotection: DMF/pip; coupling: Boc-Ser-OH, BOP, DIEA; (c) esterification: Fmoc-Phe-OH, DIC/DMAP; (d) TFE/DCM 3/7 v/v; (e) $Et_3OSi(CH_2)_3NCO$, DMF; (f) grafting on SBA-15 OMS in DMF; (g) Boc removal, TFA; (h) 10% Et_3N in DCM for 24 h, O–N acyl shift.