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Synthesis and chemical reactivity of semicarbazide-supported silicas

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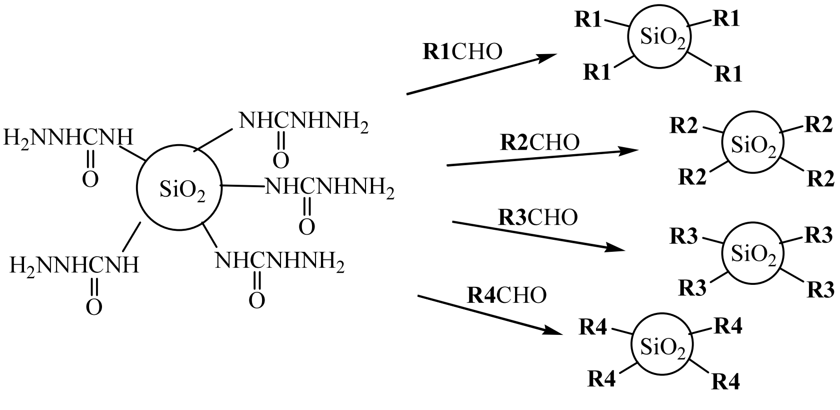
Abstract—The synthesis of xerogels possessing a Fmoc-protected semicarbazide group covalently linked to a silica matrix is described. BET and fluorescence analyses showed the homogeneity of the xerogels. The xerogels were deprotected and further reacted with aldehydes to give novel materials. © 2003 Elsevier Science Ltd. All rights reserved.

Developments over the last two decades in sol-gel processing have demonstrated unique advantages in the domain of materials sciences, for applications in optics, sensors, biomaterials and catalyst supports.[1] The discovery of materials possessing novel properties can be realized using a combinatorial strategy,[2] providing the possibility to synthesize libraries of materials that can enter the filter of a screening test. An appealing approach for the synthesis of such libraries consists upon the synthesis of a unique core material, which can be easily modified by reaction with a family of molecules allowing the introduction of a large diversity. The strategy described in Scheme 1 responds to these specifications and is based on the reaction of a semicarbazide supported silica with a variety of easily available aldehydes. We describe in this article the preparation and characterization of semicarbazide-based silicas using the sol–gel procedure, and their reaction with model aldehydes.

Triethoxysilylpropyl semicarbazide precursor **1** (Scheme 1) was synthesized by reacting commercially available triethoxysilylisocyanate with Fmoc-protected hydrazine. The alkoxysilane moiety was reacted with tetra-



Scheme 1. Synthesis of a library of materials.

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Table 1. BET of xerogels **X1**

Xerogel	Isotherm	Porous diameter (Å)	Microporous contribution (% volume)	Specific surface area (m^2 g^{-1})
X1–10	**IV**	45	None	457
X1–15	**I** and **IV**	40	18	422
X1–20	**I** and **IV**	37	25	511
X1–50	**I** and **IV**	38	11	533
X1–100	**I** and **IV**	40	16	912

ethoxysilane by using the NH_4F-catalyzed sol–gel method.[3] Gels were analysed by IR, ^{29}Si, ^{13}C NMR spectroscopy. The gels were well condensed since **T3**, **Q3 Q4** were the major signals by CPMAS ^{29}Si NMR (**Q1** and **T1** signals were not observed).

The organic part was not damaged (no cleavage of the Si–C bond). BET experiments[4] showed that the specific surface areas for **X1**–***x*** were high even at high content of the organic part inside the solid (Table 1). Mesoporous solids were obtained for $x = 10$–100. Xerogels **X1** presented a narrow distribution of mesopores (37–45 Å). Xerogel **X1–10** presented a type IV isotherm and no microporous contribution, whereas xerogels **X1** for x>10 presented a low distribution of micropores (11 to 25%). For **X1–15** and **X1–20**, the hysteresis did not close which suggest that some pores have an inkbottle shape with small pore openings, which do not facilitate N_2 desorption. The specific surface area increased by increasing x, up to 912 m^2 g^{-1} for **X1–100**, which is consistent with the specific surface area of pure silica. The behaviour of cogels **X1** is in agreement with the formation of solids controlled by kinetic factors,[1b] with ethoxy leaving groups at the silicon atom.[5]

The presence of the Fmoc group was detected by solid-state UV after transformation by the Kubelka–Munk procedure (Fig. 1). The Fmoc group absorbed between 200 and 300 nm, with a maximum at 300 nm. This absorption was close to the absorption of the Fmoc group in solution. Absorption was not dependant upon the content of the organic part inside the solid. The luminescence of the Fmoc group was then studied (Fig. 2). Excitation was performed at $\lambda_{ex} = 280$ nm, near the maximum of absorption. In every case, the fluorescence of the monomer in the excited state was observed with a maximum of emission at 315 nm (Fig. 2). Fluorescence did not depend upon the content of the organic part inside the solid for $x = 1$–100. This shows that the organic part was well dispersed in the silica matrix. To confirm that no aggregation occurred and that the solids were homogeneous, we performed a precipitation of precursor **1** with 5 equiv. of $Si(OEt)_4$ by adding 15% NH_4F 2M. Precipitation readily occurred just after addition of the catalyst. Fluorescence studies showed the presence of the monomer at 323 nm and now an excimer band at 450 nm (Fig. 2). During precipitation, phase segregation of $Si(OEt)_4$ and R-$Si(OEt)_3$ probably occured since the polymerisation of $Si(OEt)_4$ is known to be faster than that of R-$Si(OEt)_3$ derivatives. This gives rise to a distribution of aggregates and a slight red-shift of the monomer emission. The formation of excimers at 450 nm is probably the consequence of a face-to-face sandwich orientation of the Fmoc group in the R-$Si(OEt)_3$ aggregates. Solids **X1** were then treated in suspension with DMF-piperidine to give cogels **X2** (Scheme 2). Deprotection was about 60% as seen by solid-state ^{13}C NMR. A second treatment was necessary to achieve 85–90% deprotection of the gels. It seems that some Fmoc groups are inside the bulk material, where accessibility of piperidine is restricted. The reactivity of the supported semicarbazide group was studied by coupling **X2** with aldehydes **3** and **4** possessing functional groups easy to detect by IR and electrochemistry respectively (Scheme 3). Aldehyde **3** was prepared by complexation of hexyne-2-al with Co_2CO_8,[6] and aldehyde **4** was prepared by Heck reaction[7] of 4-bromobenzaldehyde with vinylferrocene. Materials **X3**, **X4** were washed with EtOH five times, acetone two times, Et_2O. Xerogels **X3**,

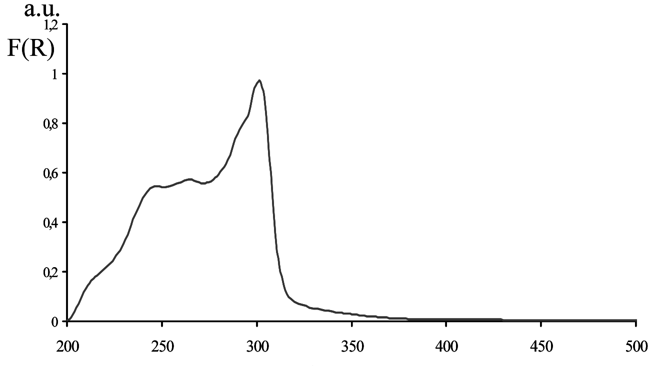


Figure 1. Solid-state UV of xerogel **X1**.

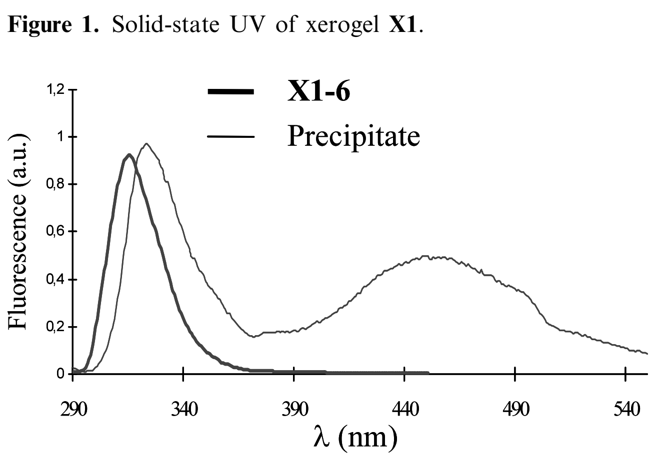
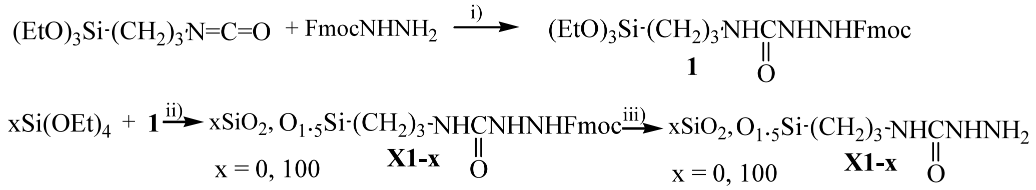
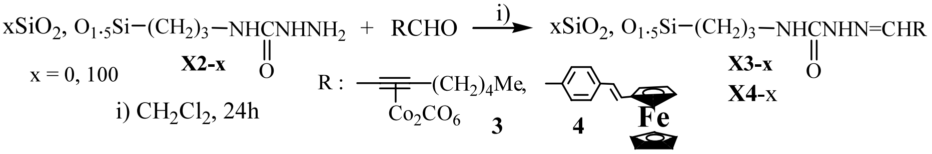


Figure 2. Fluorescence of **X1** and precipitate.



Scheme 2. Synthesis of cogels **X1**–*x*. *Reagents and conditions*: (i) CH_3CN, reflux; (ii) NH_4Fcat $(2x+1.5)H_2O$, EtOH; (iii) DMF piperidine.



Scheme 3. Reactivity of xerogels **X1**. *Condition*: (i) CH_2Cl_2, 24 h.

X4 were first analyzed by EDX. We observed a low coupling yield (about 15%) with xerogels **X2–3** to **X2–10**. The yield increased to 35% with **X2–20**, and **X2–100** gave the best result with 50% yield. Xerogels **X3** were analyzed by IR and characteristic bands of hexacarbonyldicobalt (2094, 2057, 2032 cm^{-1}) were observed. The intensity of the bands were higher with **X3–20** than **X3–3**, which confirm previous EDX analyses. To prove that aldehyde **3** was covalently bonded to **X3**, 1-hexyne hexacarbonyldicobalt complex was treated with **X2–20** in the same conditions. Carbonyl groups were not detected after washing. Reaction of aldehyde **3** with pure silica was performed using the same experimental conditions. Again the carbonyl groups were not detected after washing. These experiments confirm the reactivity of the supported semicarbazide group towards aldehydes. Note that the reaction with aldehyde **3** was reversible: when **X3–20** was treated in suspension under stirring with a solution of 90% EtOH, disappearance of the carbonyl groups was observed. Hexacarbonyl dicobalt is known to activate nucleophilic substitution at the α carbon, and thus the reversibility of the hydrazone formation.[8] Xerogels **X4** were analyzed by cyclic voltammetry after pressing the particles on a flat pad made on stainless steel.[9] A platinum electrode was used as the auxiliary electrode, and a saturated calomel electrode was the reference, 0.1M $LiClO_4$ was used as the electrolyte. The electrochemical analyses of **X4–20** and **X4–100** are presented in Figure 3. We observed the characteristic waves of the FeII/FeIII couple, which confirmed the presence of the ferrocene moiety. The non-reversibility of the system is shown, as diffusion and charge transfer processes in the solid are slower.[9] Thus, semicarbazide groups were partially accessible to functionalized aldehyde **3** and **4**.

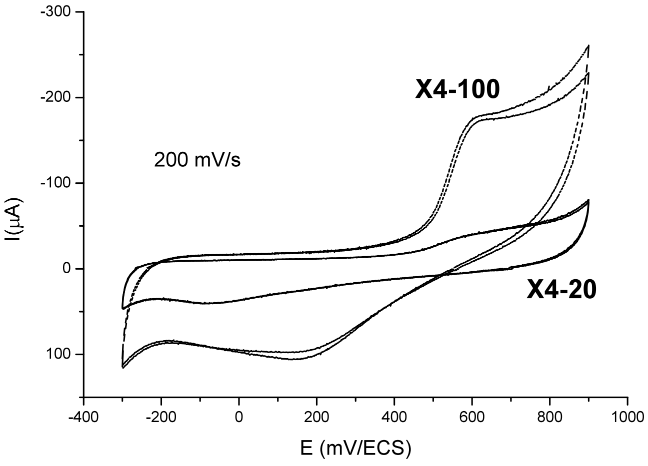


Fig. 3. Cyclic voltammetry of **X4–20** and **X4–100**.

In conclusion, we have prepared cogels possessing semicarbazide functions protected by Fmoc groups. BET and fluorescence spectroscopy showed that cogels were homogeneous and that aggregation did not occur. After deprotection, supported semicarbazide groups were found to react partially with model aldehydes **3** or **4**. Control experiments demonstrated the covalent immobilization of aldehydes **3** or **4** through a semicarbazone bond. Work is now in progress to apply this strategy for the preparation of organic–inorganic hybrid material libraries.

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