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Cucurbituril anchored silica gel

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Abstract—A cucurbit[6]uril anchored silica gel is synthesized via reaction of perallyloxycucurbit[6]uril and mercaptopropyl functionalized silica gel and fully characterized by various spectroscopic methods; the amount of accessible host molecules attached on silica surface is quantified by fluorescence spectroscopy using FITC-spermine as a guest molecule.

Cyclodextrins (CDs) and their derivatives, when immobilized on silica gel are widely used as a stationary phase in chromatographic methods, because of their ability to form inclusion complexes with a wide variety of guest molecules.[1] Cucurbit[*n*]uril (CB[*n*], $n = 5$–8) are a new family of molecular hosts comprising *n* glycoluril units, have a hydrophobic cavity that is accessible through two identical carbonyl-fringed portals.[2] Supramolecular chemistry of CB[*n*], including their host–guest chemistry and applications, has been studied extensively by Mock,[2a] us,[2b–e,3] and others.[4,5] Similar to CDs, the hydrophobic interior of CB[*n*] provides a potential site for inclusion of various small molecules including dyes, pharmaceuticals, insecticides and gases. Unlike CDs, however, the polar carbonyl groups at portals also allow CB[*n*] to bind ions and molecules through charge-dipole and hydrogen bonding interactions. Furthermore, CBs are both chemically and thermally robust in nature and thus CB[*n*] immobilized on silica gel or polymer beads would be useful in separation science but it had not been realized because no method to introduce reactive functional groups to CB[*n*] was available until recently. Our recent synthesis of perhydroxyCB[*n*] via direct functionalization,[6] which now allows us to synthesize a wide variety of CB[*n*] derivatives,[7] opened up new opportunities to explore many applications of CB[*n*] including their use in separation science. Our approach and preliminary results on the production of CB[*n*]-based stationary phase materials and their uses in chromatography have been disclosed in the patent literature.[8] While we are expanding this work, Liu et al. reported the preparation of a perhydroxyCB[6] bonded silica gel material and its use in HPLC as a stationary phase to separate alkaloids.[9] However, the paper lacks the detailed characterization of the perhydroxyCB[6] anchored silica gel. Furthermore, perhydroxyCB[6], synthesized by oxidation of CB[6] using potassium persulfate, usually contains a large amount of K_2SO_4, which originated from the decomposition of potassium persulfate, and the high salt contamination hinders the process of immobilization as we experienced. On the other hand, upon further functionalization of perhydroxyCB[6] to perallyloxyCB[6] via alkylation using allylbromide, we can eliminate the potassium salt by performing the column chromatography using chloroform:methanol mixture. Furthermore, perallyloxyCB[6] turned out to be a versatile precursor for many applications because of its good solubility in common organic solvents and the reactive functionality.[6,7] Here we wish to report a new immobilization method of CB[6] on silica gel using perallyloxyCB[6], and full characterization of the CB[6] anchored silica gel which may find important applications including HPLC stationary phase materials for the separation of various biogenic molecules.

HPLC grade silica gel (LiChrospher Si 100, pore size 100 Å, particle size 5 μm) was treated with 3-(mercaptopropyl)-trimethoxysilane in xylene under nitrogen atmosphere to afford mercaptopropyl functionalized

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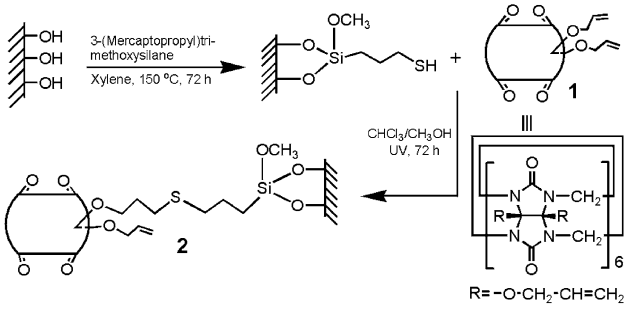
silica gel[10] which was characterized by elemental analysis and ^{13}C CP-MAS NMR spectroscopy. The three peaks at 51.9, 28.9 and 11.3 ppm in the ^{13}C CP-MAS NMR spectrum (Fig. S1, Supplementary data) confirmed the presence of methoxy and mercaptopropyl groups on silica gel. Elemental analysis (based on the carbon content) shows that 1.07 mmol of mercaptopropyl was attached per gram of the silica support. Irradiation of UV light on a mixture of perallyloxyCB[6] **1**,[6] and the mercaptopropyl functionalized silica gel in chloroform/methanol under nitrogen atmosphere for 72 h followed by removal of unreacted **1** by washing with solvents afforded perallyloxyCB[6] anchored silica gel **2** (Scheme 1).

The perallyloxyCB[6] anchored silica gel **2** has been characterized by IR and ^{13}C CP-MAS NMR spectroscopy and elemental analysis. The FT-IR spectrum (Fig. S2, Supplementary data) of **2** shows strong absorption bands at 1766 cm^{-1} and 1097 cm^{-1} attributed to the carbonyl groups of CB[6] and Si–O–Si units of silica gel, respectively. A broad band between 3680 and 3150 cm^{-1} is assigned to the OH groups of silica gel and adsorbed water. Furthermore, the peaks at 941 cm^{-1} and 1645 cm^{-1} are ascribed to the Si–O units and unreacted allyl groups, respectively. The immobilization of **1** on silica gel was further confirmed by ^{13}C CP-MAS NMR spectroscopy (Fig. 1). The peaks at



Scheme 1. Immobilization of perallyloxyCB[6] **1** on mercaptopropyl functionalized silica gel.

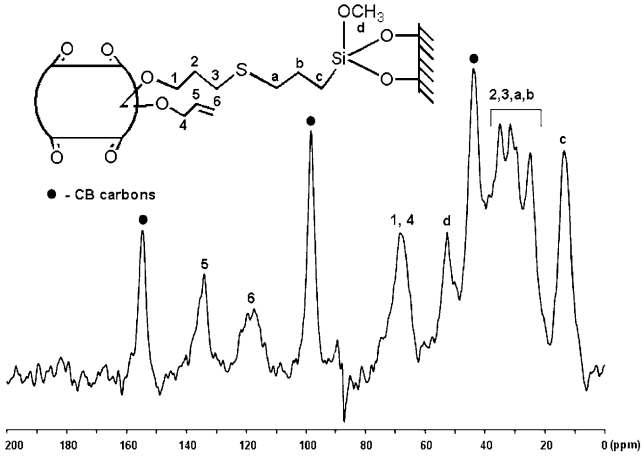
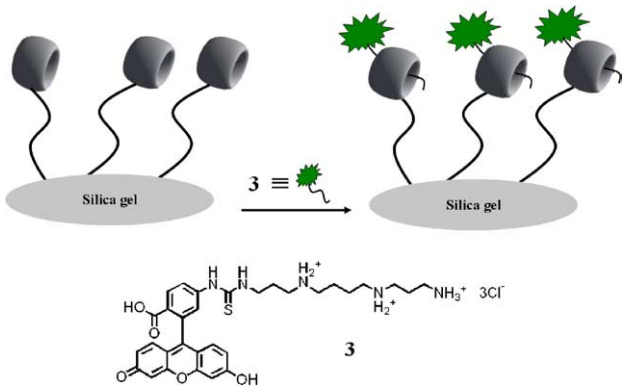


Figure 1. ^{13}C CP-MAS NMR spectrum of perallyloxyCB[6] anchored silica gel **2**.

154.7, 98.4, and 43.8 ppm correspond to the carbonyl, methine and methylene carbon atoms, respectively, of the CB[6] framework. The peaks at 35.0, 31.5, 24.8 and 13.5 ppm are due to the tether unit linking the CB[6] framework and silica gel as assigned in Figure 1. The peaks at 68.3 and 52.6 ppm correspond to the methylene carbon atoms (1 and 4 in Fig. 1) attached to the perallyloxyCB[6] framework, and the methoxy carbon (d in Fig. 1) attached to silane, respectively. The signals for the unreacted allyl groups attached to the CB[6] framework appear at 134.1, and 117.4 ppm. It should be noted that the relative intensity of these peaks with respect to that of the carbonyl carbon of CB[6] decreases upon immobilization of perallyloxyCB[6] (Fig. S1, Supplementary data), indicating that some of the allyl groups have reacted. The elemental analysis data (based on nitrogen content) indicate that 86 μmol of CB[6] units per gram of silica gel were immobilized in **2**.

By taking advantage of the fact that CB[6] forms a stable host–guest complex with spermine ($K > 10^7$),[2a] we quantified the amount of CB[6] anchored on silica surface in **2** that is accessible to a guest molecule using FITC (fluorescein isothiocyanate)-spermine conjugate **3** as a probe (Scheme 2). The amount of accessible CB[6] in **2** was measured by the decrease in the fluorescence intensity of a FITC-spermine solution of a known concentration upon addition of a given amount of **2**. The amount of accessible CB[6] in **2** was found to be 52 μmol/g, which is considerably smaller than that estimated by elemental analysis (86 μmol/g) indicating that not all the CB[6] units attached on the silica surface are accessible to the guest. A negligible amount of non-specific binding between an end-capped silica gel and FITC spermine was observed in control experiments. To the best of our knowledge, this is the first time that the amount of accessible host molecules attached on silica gel is quantified by host–guest chemistry.

In conclusion, perallyloxyCB[6] anchored silica gel was prepared and characterized by FT-IR, ^{13}C CP-MAS NMR spectroscopy and elemental analysis. The amount of accessible CB[6] units attached on silica surface was determined by fluorometry using FITC spermine as a guest molecule. Since CB[6] are known to interact with a wide variety of molecules and ions, the perallyloxyCB[6]



Scheme 2. Schematic representation of FITC spermine encapsulated in **2**.

anchored silica gel may be useful as a stationary phase in chromatographic methods. In fact, separation of several alkaloids has already been demonstrated using a CB[6]-anchored column material.[9] Separation of other biologically interesting molecules including amino acids using the new column material is under investigation. Anchoring of other members of the CB[*n*] family on silica gel and polymer beads is also being studied. Such materials may also find useful applications in other areas including extraction of metal ions and dye removal.

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Supplementary data

Experimental procedures, characterization data, ^{13}C CP-MAS NMR spectrum of **1**, FT-IR spectrum of **2**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.01.139.

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