



Modulating textural and chemical properties in mesoporous organosilicas via multifunctional dendrimers and self-assembly: Delivery of bactericides

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The combination of multifunctional organosilane precursors and self-assembly provides a range of synthetic strategies that offer exquisite control over the textural and surface properties of silsesquioxanes prepared via sol-gel processing, with a correspondingly wide range of potential applications. This presentation will explore and contrast two different approaches developed in our group which exploit multifunctional precursors for modulating textural, structural and chemical properties of silsesquioxanes-based materials.

The first approach exploits the unique properties of dendrimers, which are well-defined macromolecules that have been used for diverse applications, including controlled drug delivery, catalysis, etc. Although they have previously been incorporated into silica networks to create hybrid materials, their utilization as templates is still in its infancy. Here, we describe the synthesis of a new multifunctional dendrimer bearing a cleavable disulfide linker within each arm of the dendrimer and condensable trialkoxysilane sites on its periphery. A poly(amidoamine) (PAMAM, generation 0 or 3) core was modified with a linker bearing disulfide moieties and acetylenic peripheral groups. Silylated groups were subsequently introduced via a Huisgen CuAAC cycloaddition Click reaction. The PAMAM precursors, together with 1,4-bis(triethoxysilyl)benzene, were co-condensed to form mesoporous organosilica gels or periodic mesoporous organosilicas (PMOs).^[1] The controlled cleavage of the inner part of the dendrimer with dithiothreitol (with enzymatic approaches also envisaged) enabled pores located within the silsesquioxane network to be generated. These pores exhibited pendant thiol groups whose concentration was controlled by the generation of the dendrimer precursor. Gold salt impregnation of the powders followed by metal reduction led to the creation of polydisperse gold particles as well as well-defined gold/thiolate clusters (Au...S distances of 2.3 Å) within the pore networks of both the gels and the PMOs. The influence of the dendrimer generation on the textural and chemical properties of the organosilica, and on the formation of the gold particles, will be discussed.

In the second approach, we describe the synthesis of large-pore phenylene-bridged PMOs, mesostructured by polyion complex (PIC) micelles as structure-directing agents (SDAs).^[2] Here, the SDA consists of (1) a double-hydrophilic block copolymer, composed of poly(ethylene oxide) (PEO) (which interacts with the silanol functions of the hydrolyzed organosilane through H-bonds) and poly(acrylic acid) (PAA); and (2) an aminoglycoside-type micellizing agent (the neomycin B antibiotic, NMB) complexing the PAA functions to subsequently generate the PIC micelles. Self-assembly and micellization only occurs at pH values between the pKa of the polyacid and polybase, thus enabling the release of the antibiotic (NMB) to be triggered in a controlled manner outside of this well-defined pH range. A key feature of this approach is that the bioactive molecules are directly encapsulated within the PIC-PMOs during their formation. The engineered PIC-PMOs exhibit a well ordered hexagonal mesophase with a molecular-scale crystallinity and large mesopores (8 nm), which facilitates pH-triggered delivery of the drug. The antibacterial activity of the PIC-PMOs as a function of pH is explored with a pathogenic *Escherichia coli* strain, clearly demonstrating the potential of such PICPMOs for antibacterial applications.

- [1] M. Laird, N. Herrmann, C. Carcel, P. Trens, E. Oliviero, G. Toquer, R. Le Parc, J.-L. Bantignies, J. R. Bartlett, M. Wong Chi Man, *Nanoscale* **2022**, *14*, 15617-15634
- [2] A. Birault, E. Molina, G. Toquer, P. Lacroix-Desmazes, N. Marcotte, C. Carcel, M. Katouli, J.R. Bartlett, C. Gérardin, M. Wong Chi Man, *ACS Appl. Bio Mater.* **2018**, *1*, 1787-1792