

## Synthesis of new nanoscale MOFs for contrast agent applications

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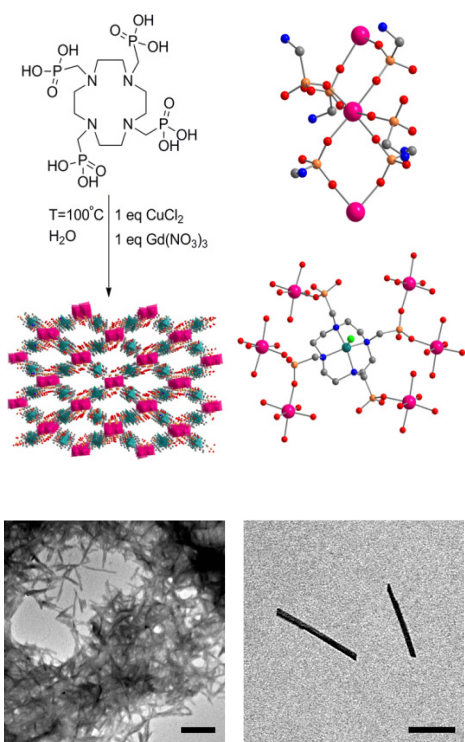
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Because of its noninvasive character and its sub-millimeter spatial resolution, Magnetic Resonance Imaging (MRI) is one of the most powerful diagnosis tools in medical science<sup>4</sup>. Based on the detection of nuclear spin reorientations under a magnetic field, MRI has demonstrated to be very effective not only for the assessment of anatomical changes but also for monitoring of organ functions. However, it was also found that in some cases (e.g. gastrointestinal tract or cerebral area) the sensitivity of MRI is not sufficient. In these cases, the use of a contrast agent (CA) to enhance the image contrast is necessary. Today, CAs are used in 35 % of MRI scans. They act shortening the T1 and or T2 relaxation times of water protons, enhancing contrast between the diseased and normal tissue. To date, the major family of CAs are chelates of the highly paramagnetic Gd(III) ion, which are extensively employed in the clinical setting. However, some limitations still persist due to the low sensitivity, lack of selectivity, and low retention time that make them effective only in areas of high accumulation. To

solve these problems, a common strategy consists on using nanostructures containing Gd(III) ions that provide increased *in vivo* circulation times and higher concentrations of Gd(III) ions per CA unit, which if targeted, yield superior MRI relaxativities. For example, Gd(III) chelates have been introduced in a variety of nanoparticle-based templates, such as nanoparticles, dendrimers, viral capsids, proteins, mesoporous silica, liposomes and zeolites.

Resulting from the combination of multitopic organic ligands with inorganic cores, Metal-Organic Frameworks (MOFs) can be also excellent candidates to incorporate Gd(III) ions into extended structures. For instance, Lin *et al.* have used this strategy to create three dimensional (3D) MOFs containing high concentration of Gd(III) ions, which in turn have shown exceptional relaxativities rates<sup>1</sup>. To create new Gd(III)-based MOFs that could be used for



**Figure 1.** (Above). Metal-organic structure resulting from the reaction of DOTP, Cu(II) and Gd(III) obtained by single crystal X-ray analysis. (Down). TEM images of the nanostructured version of this MOF. Scale bar 100 nm.

MRI, here we present a new supramolecular approach that consists on using cyclen-derivate ligands (commonly used as chelating agents to design molecular CAs) to create novel MOF-based structures with promising CA properties, controllable sizes and high stabilities. These ligands present two differentiated coordination sites: i) the nitrogenated core, and ii) the pendent arms that can be functionalized with carboxylate, phosphate or N-derivative groups. These two coordination sites can serve to create bimetallic structures that incorporates Gd(III) ions, and therefore, that can act as novel multimodal contrast agents. Following this approach, in this poster we show the first synthesized MOF made of Gd(III) and Cu(II) metal ions and the cyclen-derivative ligand DOTP (**Fig. 1**). The obtained MOF presents a 3-D porous structure in which the Cu(II) ions are placed in the center of DOTP, coordinated by the four nitrogen atoms and a chlorine, whereas Gd(III) ions expand the structure through phosphate coordination. Significantly, this new MOF can also be synthesized at the nanoscale in the form of nanowires of less than 100 nm in length and 10 nm in diameter. These nanowires present an exceptional stability and dispersability in physiological media. In addition, they show very low toxicity and promising CA properties, making them potential candidates for a future use in MRI.

### *References*

1. Della Rocca, J.; Liu, D.; Lin, W. *Acc. Chem. Res.* **2011**, *44*, 957-968.