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### COMMUNICATION

# Nano- and microcrystals of a Mn-based metal-oligomer framework showing size-dependent magnetic resonance behaviors<sup>†</sup>

Guozan Yuan, Chengfeng Zhu, Yan Liu and Yong Cui\*

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A robust 3D Mn-based metal-organic framework containing metallosalen hexamers is synthesized and its nano- and microcrystals are fabricated by using surfactant-mediated hydrothermal and solvent precipitation methods; the particles exhibit an inverse size-dependent effect of magnetic resonance relaxivity behaviors.

Metal-organic frameworks (MOFs) provide an interesting avenue to hybrid materials through fine-tuning their composition and structures by a judicious choice of metal ions and organic linkers,<sup>1</sup> and have promising applications in diverse areas including storage, catalysis and electro-optics.<sup>2</sup> All these possible applications could undergo remarkable development if bulk MOF materials were scaled down to micro- and nanometre regimes.<sup>3</sup> For example, nanoscaled MOFs have recently emerged as promising magnetic resonance imaging (MRI) agents and drug delivery agents.<sup>4</sup> Although several approaches have been developed to fabricate nano- and microscaled MOF particles including co-precipitation, solvothermal, reversed micelles and microwave-assisted methods,<sup>4–7</sup> there are no efficient synthetic routes to manipulate nano- and microcrystallite sizes and shapes of MOFs, prohibiting a detailed understanding of the systems at a molecular level.<sup>3,7</sup> Moreover, with few exceptions, research related to size/shape-dependent properties in MOFs has not yet been performed.8 In contrast, tuning of the chemical and physical properties of metal and inorganic particles through size and shape control is a well-known strategy.<sup>9</sup>

MRI is a powerful noninvasive tomographic technique that can detect differences between normal and diseased tissues based on their varied NMR water proton signals arising from different water densities and/or nuclear relaxation rates.<sup>10</sup> Most presently available MRI contrast agents are highly paramagnetic complexes, usually Gd<sup>3+</sup> and Mn<sup>2+</sup> chelates.<sup>11</sup> The metal-based contrast agents, however, exhibit modest longitudinal ( $R_1$ ) relaxivities and large quantities (several grams per patient) must be administered to get adequate MR contrast. Amongst them, complexes of Mn<sup>2+</sup> can exhibit very high *in vivo* longitudinal ( $R_1$ ) MR relaxivities by binding to intracellular proteins.<sup>11</sup> Metallosalen complexes have diverse potential applications in biological processes.<sup>12</sup> To prepare metal–metallosalen polymer particles for MRI, a dicarboxylate functionalized metalloligand H<sub>2</sub>[MnL] [H<sub>4</sub>L = (R,R)-(-)-N,N'-bis (3-*tert*-butyl-5-(carboxyl)salicylidene)-1,2diaminocyclohexane)] was chosen, as the linker to form stable MOFs and to carry a high payload of paramagnetic Mn ions for MRI. We report here the synthesis of a robust 3D Mn-based metal–metallosalen oligomer framework with controllable particle sizes and morphologies, which exhibits an inverse size-dependent effect of MR properties.

As outlined in Fig. 1, the enantiopure  $H_4L$  ligand was prepared in seven steps in an overall 33% yield from the readily available and cheap 2-*tert*-butyl-4-methylphenol. Heating a mixture of Mn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O and H<sub>4</sub>L (2 : 1 molar ratio) in DMF and water afforded brown crystals of [Mn<sup>II</sup><sub>3</sub>(Mn<sup>III</sup>L)<sub>6</sub>]·6DMF·6H<sub>2</sub>O (1) in 80% yield after three days. The product is stable in air and insoluble in water and common organic solvents and was formulated based on microanalysis and thermogravimetric analysis. The phase purity of the bulk sample was established by comparison of its observed and simulated powder X-ray diffraction (PXRD) patterns.

A single-crystal X-ray diffraction study on 1 exhibits a 3D metallosalen framework that crystallizes in the triclinic chiral space group P1 with one formula unit in the asymmetric unit.<sup>‡</sup> The basic building block is a linear trinuclear Mn unit with adjacent Mn–Mn distances of 3.4998(4) and 3.5245(4) Å and a



Fig. 1 Schematic showing the synthesis of the ligand  $H_4L$ .

School of Chemistry and Chemical Technology, Shanghai Jiao Tong University, Shanghai200240, China. E-mail: yongcui@sjtu.edu.cn; Fax: +86 21-5474-1297

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Mn–Mn–Mn angle of  $179.232(10)^{\circ}$ , which are bridged by six bidentate carboxylate groups of six MnL units. The central Mn ion is octahedrally coordinated by six oxygen atoms of six bidentate carboxylate groups from six MnL units, while each of the two terminal Mn ions are tetrahedrally coordinated by four oxygen atoms of three bidentate and one monodentate carboxylate groups from four MnL ligands. The Mn–O bonds of the central hexacoordinated Mn ion [2.128(7)–2.244(8) Å] are evidently longer than those of the terminal tetracoordinated Mn ions [2.011(9)–2.193(8) Å].

Of the six independent MnL ligands, four exhibit the exo-tridentate coordination mode including one monodentate and one bridging bidentate carboxylate group, and the other two exhibit the exo-tetradentate coordination mode with two bridging bidentate groups. In each MnL unit, the metal center adopts a square-pyramidal geometry with the equatorial plane occupied by the N<sub>2</sub>O<sub>2</sub> donors of one L ligand and the apical position by one carboxylate oxygen atom of another L ligand, with the Mn-N and Mn-O bond lengths ranging from 1.937(11) to 2.001(9) Å and from 1.825(9) to 2.219(9) Å, respectively. As a result, six MnL units self-assemble via complementary coordination of unsaturated metal centers of each unit to monodentate carboxylate oxygen atoms of other units into a  $Mn_6L_6$  hexamer (Fig. 2a). Each  $Mn_3$  core in 1 is thus linked by six Mn<sub>6</sub>L<sub>6</sub> assembles and each hexameric assemble is linked to six 6-connected Mn<sub>3</sub> cores to generate a chiral 3D hyperbranched framework (Fig. 2b,c). Oligomers are expected to display enhanced or novel electronic and magnetic behaviors and are widely studied substances in selfassembly of well-defined hybrid architectures, but no MOF derived from metal oligomers has thus far been reported.<sup>13</sup>

Calculations using PLATON show that 1 has about  $\sim 14.9\%$  of the total volume available for guest inclusion.<sup>14</sup> TGA revealed that the guest DMF and water molecules could be removed in the temperature range from 80 to 300 °C and the frameworks are stable up to 350 °C. Powder XRD experiments indicate that the framework and crystallinity of 1 remain intact upon complete removal of guest molecules (Fig. S6 in ESI†). CD spectra of 1 obtained from *R* and *S* enantiomers of the H<sub>4</sub>L ligand are mirror images of each other, indicative of their enantiomeric nature.

Micro- and nanoscale crystalline particles of **1** can be fabricated using surfactant-mediated hydrothermal and solvent precipitation methods. Microrods of **1a** were prepared by heating an optically transparent microemulsion of Mn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O and H<sub>4</sub>L (a 2 : 1 molar ratio) in the cationic cetyltrimethylammonium bromide (CTAB)/DMF/CHCl<sub>3</sub>/ water system with a water/surfactant molar ratio (*w*) of  $3.1 \times 10^3$  at 60 °C. After 12 h, the powders were isolated in 60% yield by centrifugation and washing with water and methanol. Scanning electron micrographic (SEM) images of **1a** revealed the morphological purity of microrods of 2–3 µm in length by 500–600 nm in diameter. Note that the shape and size of the particles were not greatly affected by the *w* value.

We have also carried out numerous experiments to obtain other morphologies and sizes of **1** (Fig. 3). For example, nanorods of **1b** of 600–700 nm in length by 200–300 nm in diameter could be readily obtained by heating  $Mn(ClO_4)_2 \cdot 6H_2O$ and  $H_4L$  (2 : 1 molar ratio) in tetrabutylammonium



Fig. 2 (a) The self-assembled  $Mn_6L_6$  hexamer; (b) the hyperbranched structure around the  $Mn_3$  building block; (c) a view of 3D structure of 1. The  $Mn_3$  units are shown in polyhedra.

bromide/DMF/toluene/H<sub>2</sub>O solution at 80 °C in 42% yield. After heating  $Mn(ClO_4)_2 \cdot 6H_2O$  and  $H_4L$  in DMF/THF/H<sub>2</sub>O at 80 °C for 24 h, the mixture was then cooled to room temperature and injected into distilled water with vigorous stirring, affording nanoparticles of 1c with diameters of 20–100 nm in 60% yield. PXRD studies showed that powders 1a-c were all highly crystalline and exhibited the same diffraction patterns as the bulk phase of 1 (Fig. S6 in ESI†).

Solid-state magnetic susceptibility ( $\chi_M$ ) data on 1 and 1a–c were collected in a 0.010 T field in the 2.0–300 K range (ESI<sup>†</sup>, Fig. S13). The 300 K  $\chi_M T$  values of 30.91 (1), 29.91 (1a), 29.31 (1b) and 29.69 (1c) cm<sup>3</sup> K mol<sup>-1</sup> are close to or slightly lower than the spin only (g = 2) value of 31.13 cm<sup>3</sup> K mol<sup>-1</sup> expected for three Mn<sup>II</sup> and six Mn<sup>III</sup> ions and decreases gradually to 11.13 (1), 10.03 (1a), 9.72 (1b) and 9.21 (1c) cm<sup>3</sup> K mol<sup>-1</sup> at 2 K, indicating the presence of dominant antiferromagnetic interactions.

The potential utility of particles 1a-c as contrast agents for MRI was examined. Relaxivity data were obtained on a 0.5 T scanner with suspensions of particles **1a–c** in water containing 0.2% xanthan gum. Microrods of **1a** have a longitudinal relaxivity ( $R_1$ ) of 41.44 and a transverse relaxivity ( $R_2$ ) of 94.64 mM<sup>-1</sup> s<sup>-1</sup> on a per formula basis, and nanorods of **1b** exhibited an  $R_1$  of 24.90 and an  $R_2$  of 49.80 mM<sup>-1</sup> s<sup>-1</sup>, whereas the smallest nanoparticles of **1c** had an  $R_1$  of 4.96 and an  $R_2$  of 6.14 mM<sup>-1</sup> s<sup>-1</sup>. Thus, an interesting sizedependent MR relaxivity behavior was observed for **1**: both  $R_1$ and  $R_2$  increase with the increase of particle sizes (Fig. 4a). This change trend was further confirmed by measurement of  $R_1$  values on a Mercury plus 400 spectrometer (Fig. S10 in the ESI†). The level of  $R_1$  relaxivities of **1a** and **1b** is comparable with those of Mn-based nanoparticles<sup>4a,15,16</sup> and may allow their potential use as  $T_1$  contrast agents depending on the MR pulse sequence employed.<sup>15</sup>

Indeed, as shown in Fig. 4b, the larger particles of 1a and 1b are much efficient in enhancing the water signals in  $T_1$ -weighted images, whereas significant signal reduction was

# Fig. 3 SEM images of particles 1a (a and b), 1b (c) and 1c (d).



**Fig. 4** (a)  $R_1$  relaxivity curves of **1a–c**; (b)  $T_1$ -weighted MR images of suspensions of **1a–c** in water containing 0.2% xanthan gum.

caused by the smallest nanoparticles of **1c** at the same Mn concentration. This size/shape-dependent behavior is thus consistent with the above relaxivity data. Note that the general reported trend of size dependent MR signals is that as particle size increases the  $T_1$ - or  $T_2$ -weighted (*e.g.*  $T_1$  for Mn or  $T_2$  for Gd ions) MR signal intensity continuously decreases which in turn appears as darker MR images.<sup>15</sup> Further works are in progress to investigate the inverse size effect of MRI properties and to evaluate the efficacy of **1** as MR contrast agents *in vitro*.

In conclusion, we have constructed a robust 3D Mn metaloligomer framework based on self-assembled metallosalen hexamers and developed an efficient route to control synthesis of its micro- and nanosized crystalline particles that exhibited size-dependent MR relaxivity behaviors. With a precise knowledge of their single crystal structures and facile tunability of their building blocks, the present research holds great promise in the development of novel MOF materials.

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#### Notes and references

‡ Crystal data for 1·6DMF·6H<sub>2</sub>O: triclinic, space group: *P*1, *a* = 13.663(2) Å, *b* = 18.329(3) Å, *c* = 22.173(4) Å,  $\alpha$  = 67.204(3)°,  $\beta$  = 88.260(4)°,  $\gamma$  = 86.712(3)°, *V* = 5110.5(15) Å<sup>3</sup>, *Z* = 1, *T* = 123 K, *F*(000) = 2181,  $\rho_{\text{calcd}}$  = 1.349 g cm<sup>-3</sup>,  $\mu$ (Mo K $\alpha$ ) = 0.617 mm<sup>-1</sup> ( $\lambda$  = 0.71073 Å), 72.357 measured reflections, 32.894 independent reflections (*R*<sub>int</sub> = 0.0685), 2291 refined parameters, *R*<sub>1</sub> = 0.0835, and *w*<sub>*R*<sub>2</sub></sub> = 0.2038 for *I* > 2 $\sigma$ (*I*), Flack parameter = 0.04(2), GOF = 1.051. CCDC 786168.

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