Programmable Permeability of Metal–Phenolic Network Microcapsules

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ABSTRACT: Developing materials with programmable permeability for cargo encapsulation and release is challenging but important in a number of fields including drug delivery and sensing. Metal–phenolic networks (MPNs) are an emerging class of hybrid coordination materials with pH-responsiveness and modularity that can be engineered into functional thin films for diverse applications. Herein, we engineer MPN-based microcapsules with a dynamic gating mechanism by adjusting the intermolecular interactions in the capsules. Altering the choice of building blocks and precursor ratio provides an intrinsic and modular means of tailoring capsule size and permeability. Alternatively, regulating the pH of the environment, and thereby the protonation states of MPNs, extrinsically enables capsules to switch between highly permeable (>90% of capsules permeable at pH 9) and near-impermeable (<20% at pH 3) states. These findings provide insights into the dynamic nature of MPNs and offer a route to engineer smart delivery systems and selective gating materials.

INTRODUCTION

Designing “programmable” thin films and membranes with selective and dynamic gating properties has received extensive attention in numerous fields, such as sensing and separations,^{1–3} molecular filtration,^{4–6} drug delivery,^{7,8} and nano/micro-reactors.⁹ State-of-the-art approaches for engineering thin films with selective permeability include multilayer assembly with specific polymer combinations,^{10–13} surface wettability modifications,¹⁴ host–guest interactions,^{15,16} and tuning of environmental conditions (e.g., light,¹⁷ temperature,^{18,19} and ionic strength⁷). However, it is challenging to engineer thin films where the permeability can be controlled both intrinsically (molecular composition changes) and extrinsically (environmental changes) in a modular approach in aqueous environments. Moreover, reversibly switching between highly permeable and impermeable states without requiring disassembly or degradation often necessitates covalent cross-linking of films.²⁰ For example, using thermal oxidative cross-linking and thiol-ene-based “click” chemistry can improve the selectivity of molecular sieving.^{21,22} Coordination chemistry involving organic ligands and metal ions enables dynamic manipulations of nano/microstructures through both the choice of building blocks and external environmental conditions,^{23–25} thereby offering a viable pathway to achieve tailorable cargo loading–release profiles.

Metal–phenolic networks (MPNs) are an emerging class of metal–organic materials that can be deposited as thin films on a broad range of substrates (e.g., colloidal particles, planar substrates, and bacteria/cells).^{25–28} Previously, we demonstrated the engineering of MPN microcapsules that were moderately permeable,²⁵ highly permeable,²⁹ or nearly impermeable,³⁰ by adopting distinct assembly kinetics (e.g., by controlling the reactive species). However, the ability of these systems to switch permeability and an understanding of the parameters that influence and enable tuning of MPN capsule permeability remains unexplored. Such information is important for the development of MPN materials for various applications including drug delivery and separations.

In the present study, we assemble a series of MPN capsules and investigate the effect of intrinsic (i.e., building blocks) and extrinsic (i.e., environmental pH) parameters on the selective gating of MPN microcapsules. MPN capsules are assembled from sacrificial polystyrene (PS) particle templates using naturally occurring phenolic ligands (e.g., tannic acid (TA), gallic acid (GA), and pyrogallol (PG); see Figure S1 in Supporting Information) and various metal ions (e.g., Fe^{III}, Al^{III}, and Cu^{II}). The complexation states of the coordinated ligands and metal ions involve mono, bis, or tris forms depending on the pH used to assemble the films (Figure 1a).²⁵ For MPN assembly, the coordination between catechol/galloyl groups and metal ions is the driving force, in conjunction with hydrogen bonding and π – π stacking interactions. Notably, intermolecular repulsion may also arise from the abundant phenolic groups present in the system when deprotonated (e.g., high pH). Therefore, the choice of phenolic and metal building blocks, precursor ratio, and pH conditions strongly influences the intermolecular dynamics after template removal, giving rise to different network microstructures and thereby capsule permeability (Figure 1b). For example, we herein demonstrate that constructing MPNs from metal ions with low binding affinities to the phenolic ligands (e.g., Al^{III} and Cu^{II}) can provide additional available sites for the other intermolecular attractions after template removal, leading to dense packing and reduced permeability. Alternatively, we show that MPNs prepared from high pH intrinsically have increased intermolecular repulsions (due to deprotonation), displaying a lower degree of molecular packing and thus increased permeability. Notably, our in situ analysis reveals that MPN capsules switch between “open” and “closed” states in response to pH changes, displaying programmable/dynamic cargo encapsulation and release profiles. These findings have implications for the design of future metal–organic materials.

RESULTS AND DISCUSSION

Figure 1. (a) Schematic of the assembly of phenolic ligands and metal ions to form an MPN film on a PS template particle (PS@MPN), followed by the formation of an MPN capsule after template removal. (b) Schematic diagram of programming the permeability of MPN capsules by adjusting intermolecular dynamics through both intrinsic and extrinsic modulations. (c) DIC microscopy image of TA/ Fe^{III} capsules assembled at pH 5. (d) AFM image and representative line profile of height measurement (indicated by the red arrow) of TA/ Fe^{III} capsules. Scale bar is 3 μm . (e) Percentage of permeable capsules as a function of the M_w of FITC-dextran. Inset pictures are representative confocal laser scanning microscopy (CLSM) images of the capsules; 100 capsules of each sample were measured. Capsules with dark interiors were considered to be impermeable, whereas those with interiors with the same fluorescence intensity as the outer FITC-dextran background were considered to be permeable. Scale bars are 5 μm .

As a proof-of-concept and experimental controls, TA/ Fe^{III} films were deposited on sacrificial PS particles ($3.6 \pm 0.2 \mu m$) via

coordination-driven assembly at pH 5 (using a Fe^{III} -to-TA molar ratio of 1.5:1 as per our protocol²⁵) to form PS@TA/ Fe^{III} core–

shell particles. Subsequent core (PS) removal yielded TA/Fe^{III} capsules. The monodisperse, spherical capsules observed from differential interference contrast (DIC) microscopy highlights the stability of the free-standing networks after template removal (Figure 1c). Atomic force microscopy (AFM) showed that the collapsed (air-dried) capsules had a shell (monolayer) thickness of ~10 nm (Figure 1d). The appearance of the characteristic ligand-to-metal charge transfer band with a peak around 570 nm wavelength suggests the existence of ligand–metal coordination chemistry (Figure S2). The permeability of TA/Fe^{III} capsules was investigated by incubating them with a series of fluorescein isothiocyanate-labeled dextran molecules (FITC-dextran) with different molecular weights (M_w). As shown in Figure 1e, the TA/Fe^{III} capsules displayed a M_w -dependent permeability, i.e., from permeable to near-impermeable as M_w increased. Specifically, more than 90% of the TA/Fe^{III} capsules were permeable when the M_w is low (<20 kDa), whereas ~80% capsules became near-impermeable when the M_w is high (i.e., 2000 kDa).

As MPNs have a high degree of modularity in terms of the choice of building blocks,^{26,27} we investigated the influence of different aspects of MPN assembly on the permeability of the corresponding capsules. Specifically, FITC-dextran with intermediate M_w (70 kDa) was used to investigate the effects of metal-to-ligand molar ratio, metal and ligand type, and environmental pH. The effect of varying the precursor molar ratio ($n(\text{Fe}^{\text{III}})$:

$n(\text{TA})$ of 0.5:1, 1.5:1 and 3:1) was examined while the amount of TA and the preparation pH were both fixed. Increasing the Fe^{III}/TA molar ratio did not significantly change the capsule size or shell thickness (Figure S3a). However, it significantly altered the permeability of the capsules. When the ratio was 0.5:1, only 20% of the capsules were permeable. As the molar ratio increased to 1.5:1, the permeability increased to ~75% and reached 100% as the molar ratio was increased further to 3:1 (Figure 2a, 2b). Coordinating TA with a larger proportion of Fe^{III} enlarged the size of the building blocks, which yielded capsules with more nanoscale defects (Figure S3b), as reflected by the root-mean-square roughness value, translating to higher permeability.

The effect of metal ion on capsule permeability was then examined. TA/Fe^{III}, TA/Al^{III}, and TA/Cu^{II} capsules were assembled at the same pH and metal-to-TA molar ratio of 1.5:1. Capsules assembled from Cu^{II} and Al^{III} were ~3 nm thinner than those assembled from Fe^{III} (Figure S4). Relative to the TA/Fe^{III} capsules, the TA/Al^{III} capsules were less permeable—only 20% of TA/Al^{III} capsules were permeable to FITC-dextran and the permeability decreased further to 2% when Cu^{II} metal ions were used (Figure 2c). This trend was attributed to capsule shrinkage (Figure 2d). The TA/Fe^{III} capsules had a diameter of $3.5 \pm 0.2 \mu\text{m}$, which was comparable to the size of the PS template ($3.6 \pm 0.2 \mu\text{m}$); the strong binding affinity between Fe^{III} and the catechol/galloyl groups of TA produced stable TA/Fe^{III} networks.

Figure 2. Effect of intrinsic factors of MPN capsules on (a, c, e) capsule permeability to FITC-dextran with a M_w of 70 kDa (inset pictures are corresponding CLSM images) and (b, d, f) capsule diameter after template removal (inset pictures are corresponding DIC images). Capsules are constructed from TA/Fe^{III} with different Fe^{III}-to-TA molar ratios (a, b), TA and different metals (c, d), or Fe^{III} and different phenolic ligands (e, f). For the analyses, 100 capsules of each sample were measured. Scale bars are 5 μm .

Figure 3. (a) Single wall thickness of TA/Fe^{III} capsules prepared at different pH (pH 3–9). (b) Heat map showing the percentage of TA/Fe^{III} capsules permeable to FITC-dextran (M_w = 4–2000 kDa) at different pH; 100 capsules of each sample were measured. (c) ζ -Potential of the TA/Fe^{III} capsules following dispersion at different pH. (d) Schematic of the effect of pH on capsule permeability.

In contrast, Al^{III} and Cu^{II} have a significantly lower binding affinity to TA,²⁶ which resulted in a lower cross-linking density of the network and reduced steric hindrance between TA molecules. Hence, more sites were available for intermolecular attraction on the TA molecules, which drove reorganization of the wall structure after template removal. This caused the TA/Al^{III} and TA/Cu^{II} capsules to shrink to $3.1 \pm 0.2 \mu\text{m}$ (11% shrinkage relative to TA/Fe^{III} capsules) and $2.8 \pm 0.2 \mu\text{m}$ (20% shrinkage relative to TA/Fe^{III} capsules), respectively, after PS removal (Figure 2d).

The effect of phenolic ligands on capsule permeability was also examined. Unlike TA, a dendrimer-like molecule, PG and GA are smaller phenolic ligands with fewer binding sites but with the same binding groups (i.e., galloyl groups) (Figure S1). TA/Fe^{III}, PG/Fe^{III}, and GA/Fe^{III} capsules were prepared with the same molar ratio of phenolic groups. Compared with TA/Fe^{III} and PG/Fe^{III} capsules with a single wall thickness of $\sim 12 \text{ nm}$ (12.9 ± 4.0 and $12.4 \pm 3.6 \text{ nm}$, respectively), GA/Fe^{III} capsules featured thinner walls ($6.8 \pm 1.6 \text{ nm}$) (Figure S5). Despite both PG and GA being simple phenolic ligands, the GA/Fe^{III} capsules

were less permeable ($\sim 0\%$) than the PG/Fe^{III} capsules (95%) (Figure 2e). Among all capsule types studied, GA/Fe^{III} capsules exhibited the lowest permeability. Interestingly, only the GA/Fe^{III} capsules shrank after template removal (to $2.2 \pm 0.4 \mu\text{m}$, i.e., 37% shrinkage relative to TA/Fe^{III} capsules) (Figure 2f). A comparable degree of metal–phenolic coordination is expected in the TA/Fe^{III}, PG/Fe^{III}, and GA/Fe^{III} capsules as the synthesis conditions were controlled so that the number of galloyl groups is the same. However, the carboxylic groups on GA could potentially provide additional driving forces (e.g., hydrogen bonding, salt bridging of carboxylate) for capsule shrinkage.

As pH-responsive multivalent coordination is a characteristic property of MPNs,²⁵ the effect of pH was explored, as an extrinsic factor influencing capsule permeability. TA/Fe^{III} capsules were prepared at varying solution pH, from 3 to 9. The thickness of the capsules prepared at pH 3 was $8.8 \pm 1.5 \text{ nm}$, which increased to $12.9 \pm 2.8 \text{ nm}$ at pH 6 and plateaued thereafter with a further increase in the pH (Figure 3a). A higher pH is likely to result in the formation of larger complexes when depositing on the template surface (Figure S6). The heat map in Figure 3b

Figure 4. (a) Schematic diagram of pH-regulated switchable permeability of TA/Fe^{III} capsules for cargo encapsulation and release. (b) Representative CLSM images of the encapsulation and release of FITC-dextran (M_w 250 kDa) from TA/Fe^{III} capsules at pH 4 and 9. Scale bars are 5 μm . (c) Time course plots of pH-dependent FITC-dextran release from TA/Fe^{III} over 90 min. (d) Recyclability of TA/Fe^{III} capsules represented by the ratio of the mean fluorescence intensity measured at the capsule center to that measured on the rim as a function of operating time; 100 capsules of each sample were measured.

shows the relationship between pH and permeability to FITC-dextran at varying M_w . Raising the pH increased capsule permeability. For instance, only ~35% of the TA/Fe^{III} capsules prepared at pH 3 were permeable to FITC-dextran of M_w of 250 kDa, whereas ~90% of the TA/Fe^{III} capsules prepared at pH 9 were permeable to FITC-dextran of M_w of 2000 kDa (Figures 3b, S7). The higher pH promoted deprotonation of TA, resulting in more negatively charged TA/Fe^{III} capsules (Figure 3c). The enhanced electrostatic repulsion between TA molecules and the increased propensity in the formation of tris-state TA/Fe^{III} complexes led to loosening of the internal molecular packing and enlargement of the pores in the film (Figure 3d).

The permeability differences arising from different pH suggest that the TA/Fe^{III} capsules can be engineered for programmable cargo encapsulation and release. In situ investigations were thus performed to examine the permeability states (i.e., "open" and "closed") of the TA/Fe^{III} capsules under different pH conditions

(Figure 4a). First, TA/Fe^{III} capsules were incubated with FITC-dextran at pH 9 to load the cargo (Figure 4b "Cargo loading (pH 9)"). While the loaded capsules remained in the "open" state, washing with water led to the escape of FITC-dextran from the capsules and fluorescence could not be detected (Figure S8a). However, reducing the pH to 4 after loading and subsequent washing with water led to most capsules being "closed", resulting in the encapsulation of FITC-dextran and a bright fluorescent ring (Figure 4b "Encapsulation (pH 4)"). To confirm that the fluorescence was from the inner rim rather than the outer rim of the capsules, PS@TA/Fe^{III} core-shell particles were prepared and treated under the same condition as a control. Fluorescence was not detected (Figure S8b), implying that the cargo was encapsulated and remained on the inner surface. Finally, loading of the cargo inside the capsules was examined at pH 4. As the capsules at pH 4 were significantly less permeable (compared with those under alkaline conditions), only dim fluorescence was detected

(Figure S8c, d). This further confirms the switchable “open–closed” state property of the capsules with pH regulation. The encapsulated cargo could be released by subsequently raising the pH (Figure 4b “Release (pH 9)”).

To further investigate the cargo release kinetics, FITC-dextran encapsulated in TA/Fe^{III} capsules was released in situ at different pH over a period of time, and the percentage of cargo release was evaluated as the ratio of the mean fluorescence intensity measured at the capsule center to that measured on the rim. At pH 5, the capsules exhibited low permeability, and only 10% of the cargo was released after 90 min (Figures 4c, S9). A more efficient release behavior was observed with increases in pH. For example, ~10% of the cargo was released after 10 min at pH 7, whereas 50% of the cargo was released after 10 min at pH 9. At pH 9, the percentage of cargo release increased in a sustained fashion, reaching 80% in 90 min (Figures 4c, S9). The recyclability of the “open–closed” states of the TA/Fe^{III} capsules was also examined. As shown in Figures 4d and S10, the cargo encapsulation–release profile could be repeated for at least 10 times. Moreover, the capsule permeability remained stable when exposed to a wide range of salt concentrations (0–1000 mM, Figure S11). Considering the physiological pH and salinity in the human body, we envisage that MPN capsules could provide an effective platform for delivering drugs to target sites in alkaline conditions such as oral cavities (pH 6.2–7.6),³¹ the duodenum (pH 4.8–8.2),³² and the colon (pH 7.0–8.0).³³ In addition, the recyclability and programmable permeability of MPN capsules could potentially be useful for catalysis and in smart anticorrosive coatings.³⁴

CONCLUSION

In summary, we systemically demonstrated that the permeability of MPN capsules can be programmed through both intrinsic (precursor ratio, choice of phenolic ligand and metal ion) and extrinsic (pH) parameters. Specifically, pairing Fe^{III} with GA or pairing Cu^{II} or Al^{III} with TA led to capsule shrinkage and reduced capsule permeability. pH could modulate TA/Fe^{III} complexation states and intermolecular repulsion, thereby resulting in increased permeability at increased pH. Importantly, the capsules showed reproducibly switchable “open” and “closed” states for programmable pH-responsive cargo encapsulation and release. This study provides valuable insight into metal–organic systems, which can improve our understanding and control over the design of smart hybrid materials. In addition, the previously reported inherent properties (e.g., endosomal escape³⁵), programmable permeability shown herein, coupled with controlled cargo release kinetics offer potential for the application of MPNs in numerous fields including drug delivery, catalysis, and smart anticorrosive coatings.

EXPERIMENTAL SECTION

Materials. TA, gallic acid monohydrate, PG, iron(III) chloride hexahydrate (FeCl₃·6H₂O), aluminum chloride hexahydrate (AlCl₃·6H₂O), copper chloride tetrahydrate (CuCl₂·4H₂O), sodium acetate (NaOAc), 3-(N-morpholino)propanesulfonic acid (MOPS), FITC, FITC-dextran of varying average molecular weights (4, 20, 70, 250, 500, and 2000 kDa), and (3-aminopropyl)triethoxysilane (APTES) were purchased from Sigma-Aldrich (USA). PS particles (*D* = 3.6 ± 0.2 μm) were purchased from microParticles GmbH. Tetrahydrofuran (THF) and ethanol were purchased from Chem-Supply. All chemicals were used as received without further purification. Milli-Q water with a

resistivity of greater than 18.2 MΩ cm was obtained from a three-stage Millipore Milli-Q plus 185 purification system (Millipore Corporation, USA).

Material Characterization. DIC images were taken with an inverted Olympus IX71 microscope (Olympus, Japan). Fluorescence imaging was performed via CLSM. AFM experiments were conducted using a JPK NanoWizard II BioAFM instrument. Capsule thickness and roughness were measured from 10 different areas on each sample, and the data are reported as the mean value ± standard deviation. UV–visible (UV–vis) absorption spectra were recorded on a Varian Cary 4000 UV–vis spectrophotometer. ζ-Potential measurements were performed using a Zetasizer Nano ZS instrument (Malvern Instrument, UK).

Modification of Microscopic Glass Substrates. Modified glass substrates were used for the capsule permeability studies. For the modification of glass substrates, a 0.5% APTES solution was first prepared by dissolving 400 μL of APTES in 80 mL of ethanol. Aminated microscopic glass substrates were obtained by immersing the substrates in 0.5% APTES solution for 24 h and subsequent thorough rinsing with ethanol and Milli-Q water. The cleaned substrates were then dried under a stream of air before use.

Preparation of TA/Fe^{III} Capsules at Different pH. All aqueous solutions were prepared freshly for immediate use. Before coating, 30 μL of 10% w/v PS dispersion was washed twice with Milli-Q water via centrifugation (2000 g, 1 min) and subsequently dispersed in 440 μL of Milli-Q water. Then, 5 μL of FeCl₃·6H₂O (37 mM) and 5 μL of TA (24 mM) were added successively to the PS dispersion at room temperature (25 °C) followed by brief vortexing and sonication. The pH of the mixed dispersion was adjusted by adding 500 μL of MOPS (100 mM, for pH 3, 6, 7, 8, and 9) or NaOAc (100 mM, for pH 4 and 5). The mixed dispersion was vortexed for 1 min and allowed to sit undisturbed for 5 min to achieve sufficient film formation and adherence. The coated particles were then washed three times with 10 mM buffer at the corresponding pH (MOPS for pH 3, 6, 7, 8, and 9; NaOAc for pH 4 and 5) by centrifugation (2000 g, 1 min). During each washing step, the supernatant was removed, and the suspension was briefly vortexed and sonicated to avoid particle aggregation. The pellet was redispersed in approximately 100 μL of Milli-Q water after the final wash for template removal. To obtain TA/Fe^{III} capsules, 800 μL of THF was added dropwise to the particle dispersion with a brief vortex. An additional 800 μL of THF was added to dilute the suspension and the particles were incubated with THF for at least 3 h to dissolve the template. Then, the capsules were washed twice with THF (2000 g, 3 min), and the remaining THF was removed by subsequent washing three times with buffer (10 mM, desired pH) (2000 g, 3 min).

Preparation of TA/Al^{III} and TA/Cu^{II} Capsules. The washed PS pellet was dispersed in 440 μL of Milli-Q water. Then, 5 μL of AlCl₃·6H₂O (37 mM) or CuCl₂·4H₂O (37 mM) and 5 μL of TA (24 mM) were added successively to the PS dispersion at room temperature (25 °C) followed by brief vortexing and sonication. The pH of the aforementioned dispersions was controlled to be the same by introducing 500 μL of NaOAc (100 mM, pH 5). Subsequent washing and template removal were performed as described for the preparation of TA/Fe^{III} capsules except that washing was performed with Milli-Q water instead of 10 mM buffer.

Preparation of GA/Fe^{III} and PG/Fe^{III} Capsules. For the synthesis of GA/Fe^{III} and PG/Fe^{III} capsules, the amount of GA and

PG added was controlled so that the number of moles of the phenolic groups was the same as that in 5 μL of TA (24 mM). To prepare GA/Fe^{III} coating: 5 μL FeCl₃·6H₂O (37 mM) and 50 μL of GA (4 mg mL⁻¹, 24 mM) were successively added followed by brief vortexing and sonication. To prepare PG/Fe^{III} coating: the precursors were changed to 5 μL FeCl₃·6H₂O (37 mM) and 5 μL of PG (29.6 mg mL⁻¹, 240 mM). Then, 500 μL of NaOAc (100 mM, pH 5) was added to the precursor solution to adjust the pH, followed by washing and template removal as per the same protocol described in *Preparation of TA/Al^{III} and TA/Cu^{II} Capsules*.

In Situ FITC-Dextran Permeability Study. To examine capsule permeability, 200 μL of an MPN-coated PS suspension was dropped onto the modified microscopic glass substrate, followed by standing for 5 min. The glass substrate was then immersed in THF for 1 h. The remaining THF was removed by immersing twice in 10 mM buffer (desired pH) or Milli-Q water (Scheme S1). Then, 200 μL of FITC-dextran (1 mg mL⁻¹ in solutions at the desired pH; M_w 4, 20, 70, 250, 500, and 2000 kDa) was added to the capsule area on the glass substrate and incubated for 10 min. The capsules ($n = 100$) were examined by CLSM. Capsules with dark interiors were regarded as impermeable, whereas those with interiors with the same fluorescence intensity as the outer environment were considered to be permeable.

In Situ Cargo Encapsulation and Release Study. For the cargo encapsulation and release studies, 400 μL of FITC-dextran (1 mg mL⁻¹, 250 kDa) dissolved in 10 μM NaOH (pH 9) was added to the capsule area on the glass substrate and incubated for 10 min. Then, FITC-dextran was encapsulated by rinsing and incubating with NaOAc (100 mM, pH 4) for at least 10 min. To release the cargo, the treated area was rinsed with Milli-Q water followed by incubation with 100 mM buffer of corresponding pH values. The capsules were imaged by CLSM after the desired period of time. The percentage of cargo release was calculated as the ratio of the mean fluorescence intensity measured at the capsule center to that measured on the rim. For the analysis, 100 capsules were measured for each sample, and the data are shown as the mean value $\pm$ standard deviation.

In Situ Recyclability Study. FITC-dextran (1 mg mL⁻¹, 250 kDa) was encapsulated and released using the same method as that described in *In Situ Cargo Encapsulation and Release Study*. CLSM images were captured, and the ratio of the mean fluorescent intensity measured at the capsule center to the mean fluorescent intensity detected on the rim was calculated after each encapsulation and release operation. The mean value was reported while the standard deviation is shown as error bars. The “open–closed” operation was repeated for 10 times.

ASSOCIATED CONTENT

Supporting Information. Experimental details, molecular structure of phenolic ligands, characterization data, and CLSM images. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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