Communication

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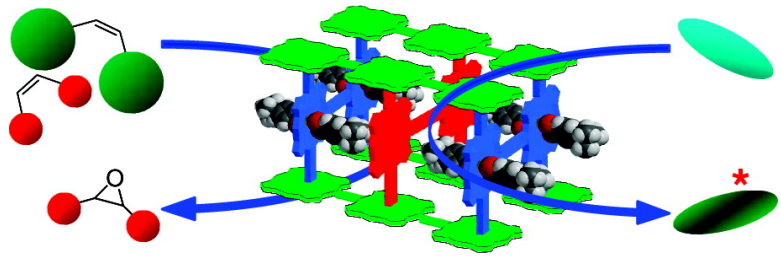

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# Cavity-Tailored, Self-Sorting Supramolecular Catalytic Boxes for Selective Oxidation

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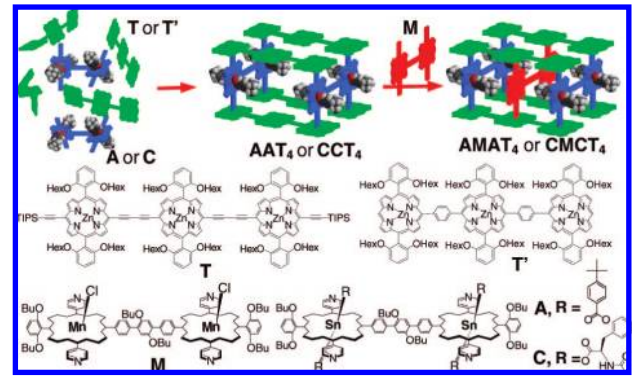
The field of metal-meditated functional assembly has seen tremendous growth,[1] with continuous emergence of exciting applications in catalysis,[2] chemical sensing,[3] and selective guest inclusion.[4] Although asymmetric catalysis has been demonstrated with abiotic supramolecular assemblies,[5] it has not yet been possible to achieve an enantioselective outcome via indirect through-space control of the chirality around the catalyst center. Such control should be feasible given the ability of a variety of enzymes to exploit environmental (e.g., polypeptide superstructure), rather than active site, chirality to achieve enantioselective catalysis. Specifically, if a remote chiral auxiliary could be incorporated into a supramolecular system to afford a well-defined enzyme-like chiral environment around an achiral catalyst center, asymmetric events could be controlled in through-space fashion. Previously, we have demonstrated the encapsulation of a manganese porphyrin catalyst within a large tetraporphyrin cavity structure (Figure 1), leading to a highly enhanced catalyst lifetime in epoxidation reactions as well as moderate size selectivity.[2e] While attempts to modify this catalytic cavity postsynthetically using pyridylbis(mentholate ester) lead to further improvements in size selectivity, enantioselectivity was not achieved. Subsequent modeling work[6] pointed to two factors that likely limited the selectivity of this supramolecular encapsulation system: (a) ligand binding on the outside of, rather than within, the cavity and (b) torsional freedom of the cavity walls and the encapsulated catalyst (Figure 1). Knowing these limitations, we set out to design porphyrin building blocks that can assemble into rigid, cavity-tailored, catalytic supramolecular boxes via a high-yielding self-sorting process.[7] With these highly stable assemblies, asymmetric catalysis via through-space control of cavity chirality should now be possible.


***Figure 1.*** Idealized vs more realistic representations of the chiral environment inside a pentaporphyrin catalyst assembly.

Herein, we demonstrate the use of steric self-sorting strategy to encapsulate catalytically active achiral manganese porphyrin dimers within rigid porphyrin boxes possessing cavities that can be tailored with carboxylate ligands. These assemblies readily effect size-selective olefin epoxidation and, when the cavity is modified with a chiral amino acid ligand, enantioselective sulfoxidation. To the best of our knowledge, this constitutes the first example of through-space control of chirality in abiotic supramolecular catalysis at a modularly assembled achiral site.[8]

***Scheme 1.*** Schematic Representation of the Steric-Self-Sorting Assembly of Supramolecular Catalytic Boxes, **AMAT4** and **CMCT4**




As described previously,[7] the free-base precursor to porphyrin dimer **A** was readily obtained in high yield via Suzuki coupling of 2,5-dibutoxy-1,4-phenyldiboronic acid and 5-(*p*-bromophenyl)-15-(2,6-dibutoxyphenyl)-10,20-dipyridyl-porphyrin (available through a one-pot synthesis in 18% yield; see Supporting Information (SI)). Subsequent treatment with $SnCl_2$ in air, followed by derivatization with *tert*-butylbenzoic acid, generates the (porphyrin)$Sn^{IV}$(carboxylate)$_2$ dimer **A** in high yield (Scheme SI-1 in SI). This highly efficient synthetic scheme facilitates the modification of dimer **A** with virtually any available carboxylic acid, allowing for the ready construction of a wide range of supramolecular environments (*vide infra*).

When 2 equiv of **A** are combined with 4 equiv of the diacetylene-linked (porphyrin)Zn trimer **T**, the rigid 16-porphyrin **AAT$_4$** "box" results.[7] The analogous combination of **A** with the phenylene-linked (porphyrin)Zn trimer **T′**, ~1.7 Å (Zn1 to Zn3) shorter than **T**, afforded the corresponding **AAT′$_4$** in good yield. These observations suggest that the self-assembly process responsible for formation of these boxes is reasonably tolerant to size variations among the partners, presumably due to cooperative binding between **A** and either **T** or **T′**.

Given the large axial steric bulk of the carboxylate ligand in **A**, the middle zinc porphyrins in the **T** components of **AAT$_4$** remain unbound, leaving an unoccupied cavity inside of the box.[7] We hypothesized that this space could be uniquely occupied by the manganese dimer **M** to generate a supramolecular catalyst box **AMAT$_4$** (Scheme 1). Indeed, **AMAT$_4$** can be obtained via the sequential addition of **M** to **AAT$_4$** or in a one-pot fashion where **A**, **T**, and **M** are added together in one step, illustrating the high selectivity and synthetic versatility of the self-sorting[9] process (Scheme 1).

Porphyrin box **AMAT$_4$** was characterized by UV−vis absorbance and fluorescence spectroscopy as well as solution-phase small-angle X-ray scattering (SAXS) (see SI). Fluorescence spectra of a

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solution of **AAT$_4$**, with increasing amounts of **M** (Figure S6), showed nearly complete quenching when 1 equiv of **M** was added. Data suggest the formation of a 1:1 **AAT$_4$** and **M** complex, which readily quenches the ns-time-scale emissions from the surrounding (porphyrin)Zn and, thus, is highly diagnostic of binding of **M** by the box.

***Table 1.*** Modeled and Experimentally Obtained $R_g$ Values for T and the Box Assemblies

| | model $R_g$ (Å) | expt $R_g$ (Å) |
|---|---|---|
| **T** | 14.8 | 15.1 ± 0.4 |
| **AAT$_4$** | 20.6 | 20.7 ± 0.3 |
| **AMAT$_4$** | 19.8 | 19.9 ± 0.3 |

While NMR characterization of **AMAT$_4$** was not possible (due to the paramagnetic nature of **M**), SAXS data (Table 1) proved particularly instructive in confirming its formation. We note that solution-phase X-ray scattering has become an increasingly powerful characterization strategy for supramolecular assemblies[10] whose structures cannot easily be determined by crystallographic and/or mass spectrometric methods. SAXS is well-suited for determining the overall sizes of large assemblies in solution as the electron-density-weighted radius of gyration ($R_g$) can be extracted from the scattering at very low angles by application of the Guinier analysis.[11] Formation of specific supramolecular assemblies can then be readily confirmed by comparing the experimental $R_g$ to the value extracted from the scattering of proposed model structures.[10] For **AMAT$_4$**, the experimental $R_g$ is 19.9 ± 0.3 Å, slightly smaller than that for the "empty" **AAT$_4$** box (20.7 ± 0.3 Å) and consistent with the increased electron density at the "center" of the box upon complexation of the Mn dimer. $R_g$ values for both **AAT$_4$** and **AMAT$_4$** are significantly larger than those for **T** alone, clearly indicating intact large assemblies in solution.

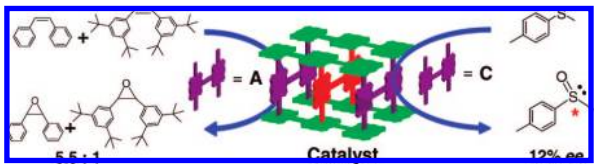


***Figure 2.*** Schematic representation of size-selective and enantioselective catalysis with torsionally rigid, self-assembling, porphyrin boxes.

As mentioned above, we anticipated that encapsulation of **M** by the rigid supramolecular boxes **AAT$_4$** and **AAT′$_4$** would impart both size selectivity and enantioselectivity if the boxes could be made chiral. To assess the ability of the resulting supramolecular boxes **AMAT$_4$** and **AMAT′$_4$** to effect size-selective catalysis, we first employed them in the epoxidation of *cis*-stilbene vs *cis*-3,3′,5,5′-tetra(*tert*-butyl)stilbene (Figure 2).[2e] Due to access inhibition of the larger olefin to the metal center by the cavity modifier, we anticipated that the smaller olefin would react preferentially. This is indeed the case: *cis*-stilbene is 5.5-fold more reactive with the catalytic boxes than the sterically bulky *cis*-3,3′,5,5′-tetra(*tert*-butyl)stilbene. Most gratifyingly, when **C$_D$MC$_D$T$_4$**, the chiral version of **AMAT$_4$**, was assembled and used in the catalytic sulfoxidation of methyl *p*-tolyl sulfide (Figure 2), methyl *p*-tolyl sulfoxide was obtained with 12% ee! (**C$_D$** is the (porphyrin)Sn$^{IV}$ dimer ligated with *N*-acetyl-(D)-phenylalanine.) The enantiomeric excess increased to 14% when the smaller catalytic box **C$_D$MC$_D$T′$_4$** was used. Importantly, the sense of the chiral excess was reversed when *N*-acetyl-(L)-phenylalanine was used and no enantioselectivity resulted when only free **M** was used, with or without **C$_D$**. To the best of our knowledge, these are the first instances where chiral environments surrounding active sites in abiotic supramolecular assemblies[8] have been shown to induce enantioselection by an achiral catalyst. That only modest chiral discrimination was observed can probably be attributed to the small size of *N*-acetyl-phenylalanine. Clearly, this strategy can be readily extended to other chiral ligands.

In conclusion, we have demonstrated the utility of the self-sorting strategy for the spontaneous assembly of highly ordered, rigid supramolecular boxes possessing catalytic properties. The formation of these assemblies, comprising up to 18 porphyrins, was readily confirmed by solution-phase X-ray scattering in conjunction with fluorescence spectroscopy. The resulting catalytically active boxes readily effect both size-selective and enantioselective oxidation catalysis. We anticipate that this powerful modular construction strategy will be of more general value for creating functional metallo-supramolecular assemblies. Current work in our laboratories with catalytic salen complexes and related porphyrin boxes is centered precisely on this notion.

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**Supporting Information Available:** Complete experimental details of syntheses, compound characterization, and X-ray experimental methods and data analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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