Supramolecular Assembly and Coordination-Assisted Deaggregation of Multimetallic Macrocycles**

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One of the most important objectives in supramolecular chemistry is the self-assembly of molecular building blocks into well-defined architectures.[1] The remarkable functions of self-assembled structures in biological systems has resulted in considerable effort being devoted to the development of new materials that employ this concept. Examples include catalysts,[2] organic nanotubes,[3] supramolecular polymers,[4] and chemical sensors.[5]

Aggregation of rigid, shape-persistent macrocycles has become a topic of growing interest.[6] Conjugated phenylacetylene macrocycles (PAMs), for example, show solvent- and concentration-dependent aggregation that is mediated by π–π interactions between the macrocycles and leads to nanotubular assemblies.[7] Such aggregation, however, is usually weak and depends strongly on the substituents of the macrocycles for organization.[8] Stronger forces, such as hydrogen-bonding interactions, have been used to aggregate cyclic D,L-peptides and urea macrocycles.[9] In these systems, solvents containing hydrogen-bond donors or acceptors may decrease aggregation.[10] The use of coordination chemistry to assemble shape-persistent macrocycles is an underdeveloped area.

We recently reported the synthesis of small macrocycles **1** containing Schiff bases with the intention of studying their self-assembly.[11] However, these macrocycles have only a very small cavity in the center and would not yield significant porosity if stacked. A larger, conjugated macrocycle **2a** containing Schiff bases (Scheme 1) is readily prepared in high yield without the use of a template.[12,13] This macrocycle may react with transition-metal salts to form trimetalated macrocycles, in which the metals are incorporated into the tetradentate (N_2O_2) binding sites. Herein, we report our findings on the surprising aggregation behavior of these large, shape-persistent metallomacrocycles in solution. The metal center plays an important role in mediating the assembly of the macrocycles. Furthermore, we demonstrate coordination-assisted deaggregation of the metallomacrocycles, a mechanism that may form the basis of new chemical sensors.

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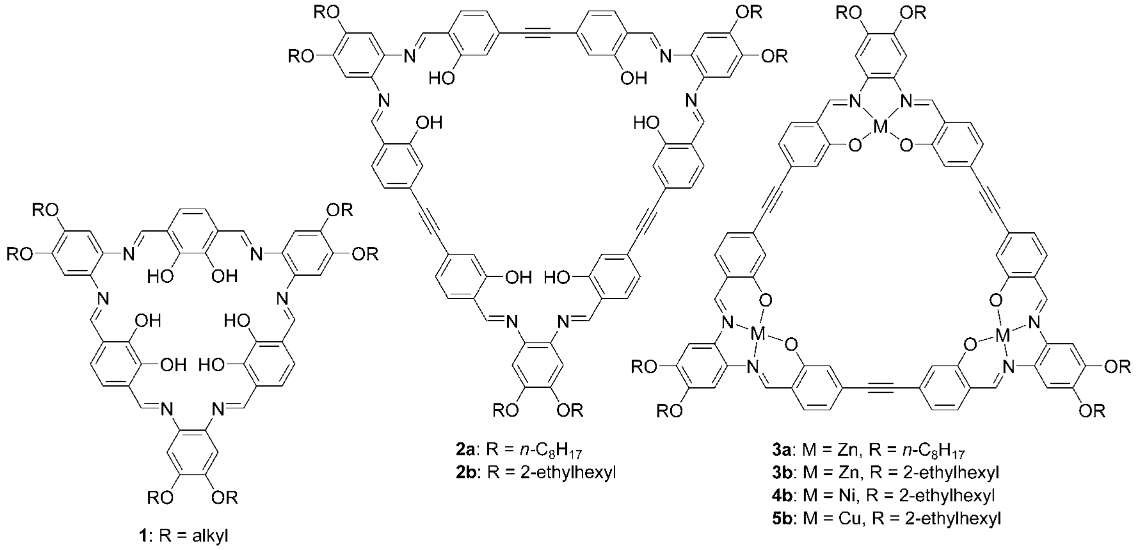


Scheme 1. Conjugated macrocycles **1**–**5**.

Metalation of **2a** with Zn^{II} salts afforded metallomacrocycle **3a**. Macrocycles with branched 2-ethylhexyloxy substituents **2b**–**5b** were also prepared to give enhanced solubility. MALDI-TOF mass-spectrometric analysis of metallomacrocycles **3**–**5** verified their composition. In addition to the molecular ion, signals corresponding to the protonated dimer were also observed. In the case of **3a**, significant aggregation was observed, as signals for ions of up to $[(\mathbf{3a})_9]^+$ were present in the spectrum (see the Supporting Information). The intensity of the signal that arose from the aggregates was very large only in the case of **3a**.

^1H NMR spectroscopic analysis of **3a** showed that it aggregates in solution. In $[D_8]$THF, sharp signals are displayed, all of which can be assigned to the macrocycle, including the imine resonance at $\delta = 8.85$ ppm. The resonances broaden as the ratio of $CD_2Cl_2/[D_8]$THF is increased such that the aromatic groups are no longer visible (Figure 1). This effect is attributed to a significant decrease in the T_2 relaxation time, caused by the formation of large aggregates.[14] Well-defined oligomeric structures (e.g., dimers) would be expected to give rise to sharp signals, but our results indicate that larger aggregates are present. The resonances associated with the macrocycle are completely diminished in CD_2Cl_2, whereas those for the alkoxy side groups are broad. Broadening has been observed in the aggregation of PAMs in highly polar solvents.[6c,15] For comparison, **2** and the monometalated compound **6** do not aggregate at similar concentrations in THF or CH_2Cl_2.

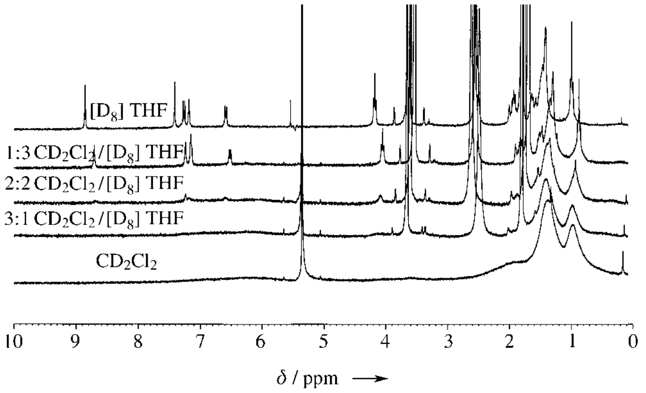
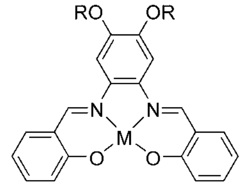


Figure 1. ^1H NMR spectra of **3a** in various mixtures of $CD_2Cl_2/[D_8]$THF ($[\mathbf{3a}] =$ ca. 6×10^{-4} M for all of the spectra).



6: M = Zn, R = C_6H_{13}

Self-association can have a large effect on the optical properties of macrocycles in solution. To investigate further the aggregation behavior of the macrocycles, we undertook UV/Vis and fluorescence spectroscopic studies of macrocycles **3**–**5** in mixtures of CH_2Cl_2/THF of different compositions at constant concentration (Figure 2a,b). Metallomacrocycles **4b** ($M = Ni^{II}$) and **5b** ($M = Cu^{II}$) both show UV/Vis spectra with several well-defined absorption features. Moreover, there is virtually no difference between the spectra recorded in THF and in CH_2Cl_2. The spectra of zinc macrocycles **3a** and **3b** in THF appear to be very similar to those of macrocycles **4b** and **5b**, with several distinct features observed. However, as the ratio of CH_2Cl_2/THF increases, the UV/Vis spectra for **3a** and **3b** undergo a dramatic change that leads to broad, featureless absorption spectra in CH_2Cl_2.

Metallomacrocycle **3a** is fluorescent in THF ($\phi = 0.86\,\%$), with signals at 558 and 596 nm (Figure 2b). The signals are red-shifted and diminish in intensity on changing the solvent from THF to CH_2Cl_2, thus leading to a broad emission for **3a** in CH_2Cl_2 that is similar to that arising from an excited-state complex (excimer) and that shows no vibrational fine structure. Metallomacrocycle **3b** with peripheral 2-ethylhexyloxy substituents behaves similarly to **3a**, which has unbranched alkyl substituents.

The optical properties for **3a** were examined in a range of solvents with varying dielectric constants (Figure 2c). In a coordinating solvent (e.g., THF, dimethyl sulfoxide (DMSO),

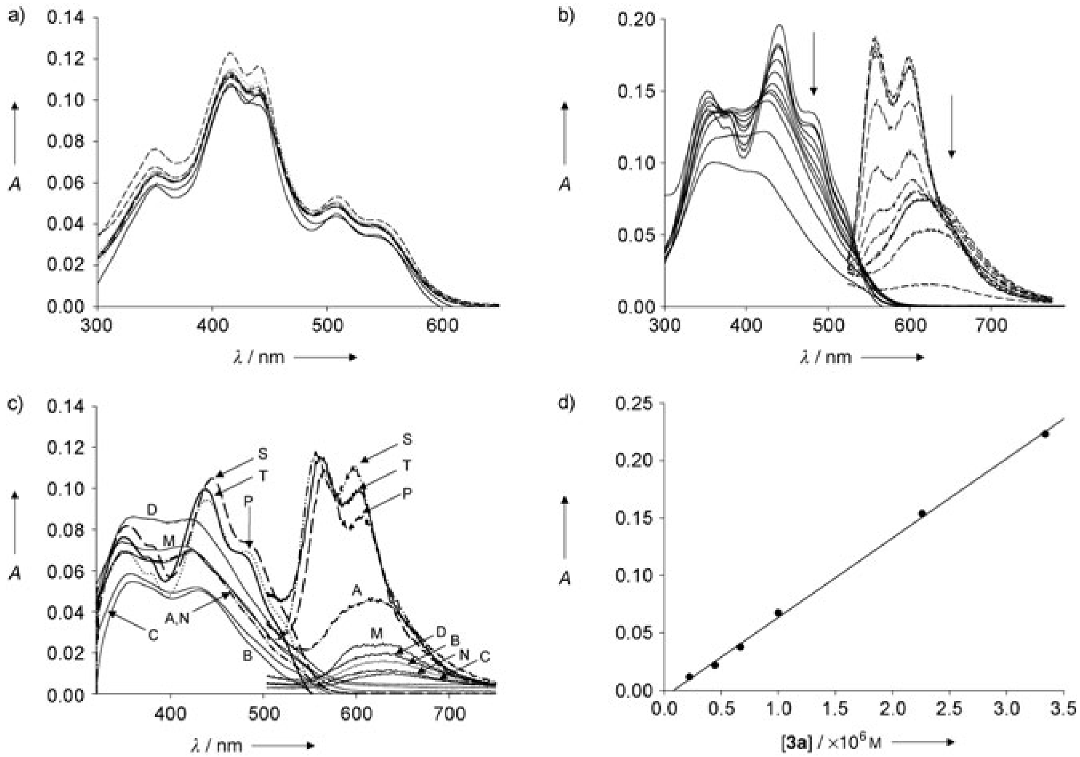


Figure 2. a) UV/Vis spectra of **4b** in various mixtures of CH_2Cl_2/THF (1:0–0:1 in 10% increments); [**4b**] = 9.0×10^{-7} M. b) UV/Vis and fluorescence spectra of **3a** in CH_2Cl_2/THF with the same solvent compositions; the arrows indicate the direction of the increasing CH_2Cl_2/THF ratio. c) UV/Vis and fluorescence spectra of **3a** in various solvents (T: THF, S: DMSO, P: pyridine, A: acetone, B: benzene, D: dichloromethane, M: methanol, C: cyclohexane, N: acetonitrile). d) Graph of absorbance (*A*) at 380 nm as a function of concentration (M) of **3a**.

and pyridine), the absorption spectrum shows well-defined features and the macrocycle fluoresces with two signals near to approximately 560 and 600 nm. In a weakly or noncoordinating solvent (e.g., acetone, methanol, dichloromethane, benzene, acetonitrile, and cyclohexane), the absorption spectrum is broad and nearly featureless and the emission spectrum is broad and red-shifted. The broad absorption spectra and the lack of any dependence on the dielectric constant corroborate the notion that the aggregation is a ground-state effect, and not because of excimers.

These results indicate that **3a** is aggregated at concentrations as low as 10^{-6} or 10^{-7} M in most noncoordinating solvents. Furthermore, a plot of absorbance versus concentration is linear with little concentration dependence on the aggregation (Figure 2d). A reliable equilibrium constant from the system could not be extracted, but it is estimated that K_{assoc} must be greater than 10^7.[16] Given that the macrocycle is electron rich, we were surprised that π–π interactions between the macrocycles would be significant at low concentration in a solvent such as CH_2Cl_2, in which **3a** is soluble.[8] Since **3a** aggregates in MeOH, it is unlikely that hydrogen-bonding interactions are an important factor for assembly. It is also surprising that **3a** aggregates in benzene, in which π–π interactions with the solvent are expected to compete with π–π interactions of the macrocycle, thus suppressing assembly. Moreover, if π–π interactions were solely responsible for the assembly, macrocycles containing Schiff bases and Cu^{II} and Ni^{II} centers are anticipated to be flat with square-planar geometry at the metal and would show a stronger tendency than Zn^{II} macrocycles to aggregate. These results suggest that the aggregation of the macrocycles involve a further interaction, namely, a Zn⋅⋅⋅O interaction between the macrocycles to maintain a coordination number of five at the Zn^{II} center. The fifth coordination site is occupied by a solvent molecule in coordinating solvents, but the coordination of phenolic oxygen atoms to the zinc centers is involved in the assembly. The coordination of phenolic oxygen atoms to metal centers in salen-type zinc complexes has been observed in the solid state.[17]

The addition of the paramagnetic Cu^{II} metallomacrocycle **5b** to a solution of the Zn^{II} metallomacrocycle **3b** in CH_2Cl_2 led to only a small degree of fluorescence quenching, but did not disrupt the aggregated state of **3b**, as observed by fluorescence and UV/Vis spectroscopies. This outcome indicates that **3b** prefers to interact with other macrocycles of the same type rather than forming dimers with **5b**, which further supports a Zn⋅⋅⋅O interaction between the macrocycles. If **5b** interacted with the aggregates of **3b**, the paramagnetic Cu^{II} centers would be expected to quench the fluorescence of the zinc metallomacrocycles.

In contrast to the negligible effects of nonpolar solvents on aggregation, coordinating solvents, such as THF and pyridine, readily interrupted the aggregation of **3a** and **3b**. To prove that coordination was the important interaction, **3a** was treated with pyridine and lutidine (Figure 3a,b). UV/Vis and fluorescence spectroscopic analysis showed that **3a** deaggre-

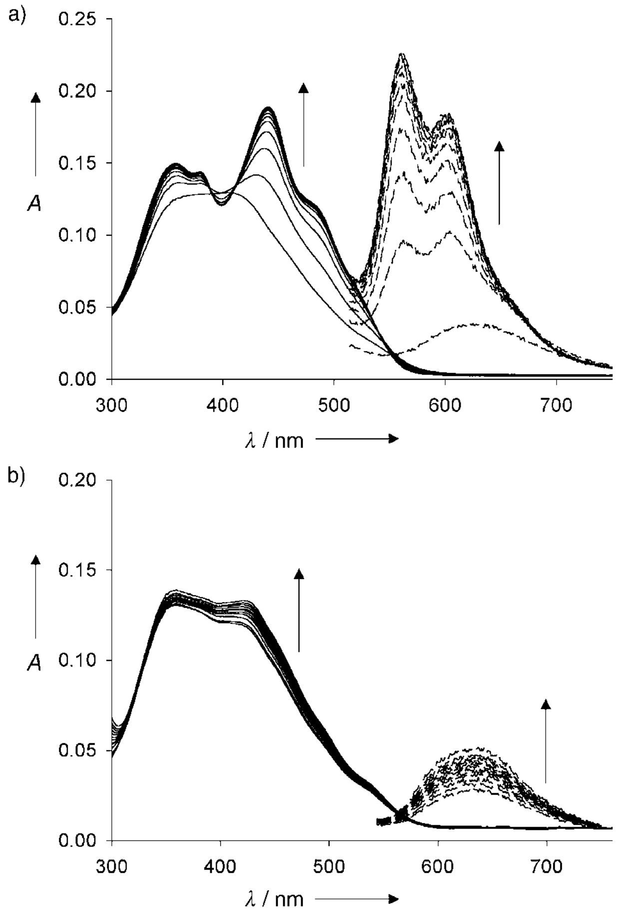


Figure 3. UV/Vis and fluorescence spectra of **3a** titrated with a) pyridine (3.6×10^{-3}–0.020 M; step size: 1.81×10^{-3} M) and b) lutidine (1.26×10^{-3}–0.014 M; step size: 1.26×10^{-3} M; [**3a**] = 1.8×10^{-6} M). The arrows indicate the direction of the increasing concentration of the base.

gates with the addition of pyridine. With lutidine, however, which is more basic but unable to coordinate to the metal centers, the macrocycle remained aggregated.[18] The absence of an isosbestic point in the titration of **3a** with pyridine is consistent with multiple metal centers being coordinated.

The aggregation behavior of **3a** and **3b** is illustrated in Figure 4. The molecules are not aggregated in THF but on changing the solvent to CH_2Cl_2 or benzene aggregate into supramolecular assemblies. We do not know for certain whether the assemblies are tubular, but it seems likely since the aggregation is dominant even at a concentration of 10^{-7} M. Although other possibilities cannot be ruled out, a tubular assembly would maximize interactions between the macrocycles. Addition of a molecule that can coordinate to the macrocycles results in deaggregation and replenished luminescence. These assemblies may serve as the basis of a new model for chemically sensing coordinating bases, in which the mechanism involves deaggregation of the supramolecular assembly.

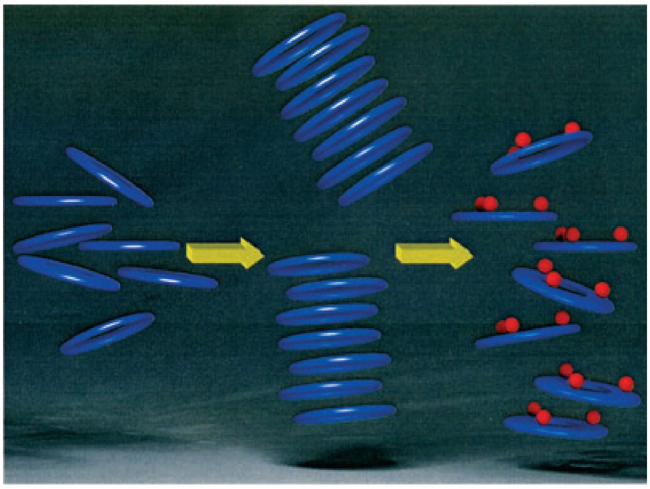


Figure 4. Illustration of aggregation and coordination-assisted deaggregation of multimetallic macrocycles. Left: macrocycles (blue) in THF. Middle: macrocycles aggregated when in CH_2Cl_2. Right: macrocyclic assemblies deaggregate after treatment with a coordinating ligand (red spheres).

To test this mechanism as the basis of a chemical sensor, we titrated the macrocycle assembly of **3a** in CH_2Cl_2 with quinuclidine. The fluorescence increased rapidly after 30 equivalents of quinuclidine were added, with a total fluorescence increase of 100% at 575 nm. The deaggregation was confirmed by ^{1}H NMR spectroscopic analysis. Although the ^{1}H NMR spectrum of **3a** in CD_2Cl_2 is broadened by aggregation, the spectrum displays the sharp signals expected for **3a** on addition of only three–six equivalents of quinuclidine. Thus, the deaggregation of the macrocyclic assemblies generates a turn-on signal for sensing coordinating bases, such as quinuclidine. This approach is a new method of chemical sensing that may be exploited for sensing molecules of biological relevance.

In summary, we have observed the strong aggregation of metallomacrocycles containing Schiff bases in solution that appears to be facilitated by Zn···O interactions between the macrocycles. The optical and fluorescent properties of the macrocyclic assemblies undergo significant changes when treated with coordinating bases that cause deaggregation of the supramolecular assemblies. These results suggest a new chemical method for control over the assembly of nanostructures from shape-persistent macrocycles. Future work will involve the use of bidentate ligands (e.g., 1,4-pyrazine) to form supramolecular nanotubes.

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