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Remarkable Stabilization of $M_{12}L_{24}$ Spherical Frameworks through the Cooperation of 48 Pd(II)−Pyridine Interactions

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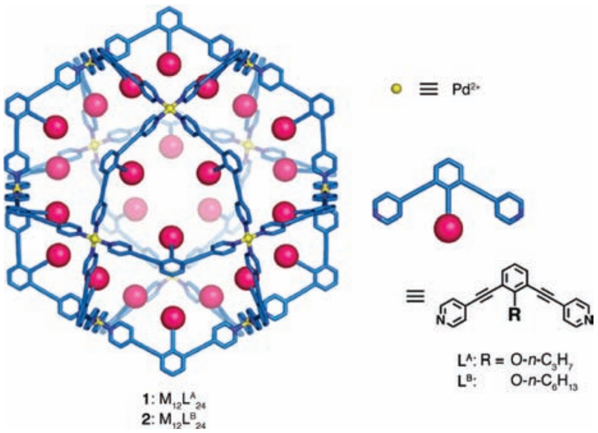
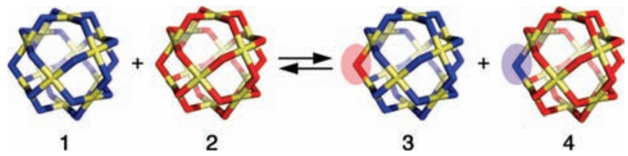
Even though the self-assembly process involves multiple weak interactions and reversible reactions, the final assembled products can show greater stability than would be expected from the simple sum of the weak interactions. For example, the highly stable, tertiary structures of proteins are sustained by many weak interactions that, when taken individually, are too weak to impose the necessary folded conformations of the peptide fragments constituting the final structure. Similar enhanced stability has been observed in relatively small, artificial self-assemblies, where the number of components (n) is less than 10, but larger assemblies, where $n = 10-50$, are less studied.[1] Recently, we reported the self-assembly of $M_{12}L_{24}$ spherical complexes held together by 48 Pd(II)−pyridine bonds.[2] Typically, monodentate Pd(II)−pyridine bonds are kinetically labile and easily dissociate under equilibrium conditions.[3] The combination and possible cooperativity of multiple labile, dative bonds in large, self-assembled structures is of fundamental importance for structural stability but has been rarely addressed.[1b,4] Thus, we measured the kinetics of ligand exchange rates to better understand their stability. We found that $M_{12}L_{24}$ complexes are remarkably stable and the half-lives are much longer than those for comparable monodentate Pd(II)−pyridine complexes by a factor of $\sim 10^5$. The results suggest that, once formed, the 36-component molecular spheres behave like covalent componds.



Scheme 1. Schematic Representation of Ligand Exchange between Spherical Complexes **1** and **2**



To evaluate the stability of $M_{12}L_{24}$ spherical complexes, a ligand exchange reaction between the nearly identical $M_{12}L^A_{24}$ (**1**) and $M_{12}L^B_{24}$ (**2**) was examined by cold-spray ionization mass spectrometry (CSI-MS)[5] (Scheme 1). Ligand components L^A and L^B have the same rigid framework with different pendant alkyl chains (n-C_3H_7 and n-C_6H_{13} for L^A and L^B, respectively). Both **1** and **2** efficiently self-assembled when the ligands were treated with $Pd(OTf)_2$ in acetonitrile at 50 °C for 5 h. The mass spectra displayed prominent peaks for $[M-(OTf)_n]^{n+}$ ($n = 7-12$) (Figure 1a−c) and the linear relationship between peak intensity and concentration was confirmed.[6] Molecular modeling confirmed that the pendant alkyl chains of both ligands are too short to interact within the sphere. Thus the stability of both spheres under MS conditions should be the same and the peak intensities independent of alkyl length. In fact, when a fresh 1:1 mixture of **1** and **2** was immediately subjected to MS analysis, the peak intensities were equivalent.

The remarkable stability of the $M_{12}L_{24}$ complexes was revealed by time dependent MS analysis. When a 1:1 mixture of **1** and **2** in acetonitrile was allowed to stand at 23 °C overnight, the formation of mixed products $M_{12}L^A_{23}L^B$ (**3**) and $M_{12}L^AL^B_{23}$ (**4**) was not observed (Figure 1d). Ligand exchange slowly occurs over 3 days at room temperature, and new peaks, corresponding to **3** and **4**, gradually appeared ($[M-(OTf)_{11}]^{11+}$: 1034.4 (calcd. 1034.4) for **3** and 1118.6 (calcd. 1118.6) for **4**) (Figure 1e,f). From t vs (1/[**1**]

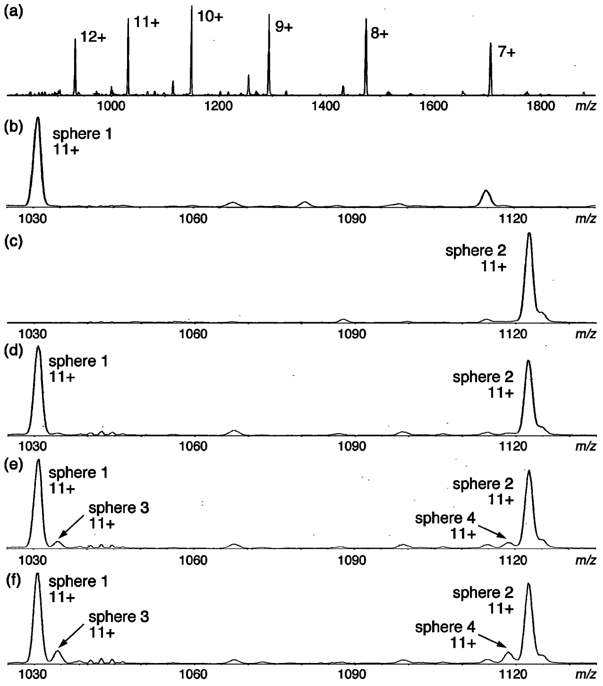


Figure 1. CSI−MS spectra (CH_3CN, OTf^- salt) showing the following: (a) the entire spectrum of sphere **1**; expanded regions showing the 11+ signal for (b) **1** and (c) **2**; time dependent spectra at (d) overnight, (e) 35 h, and (f) 70 h. The mixed species **3** and **4** only appeared after 35 h.

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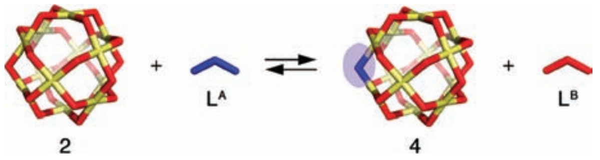
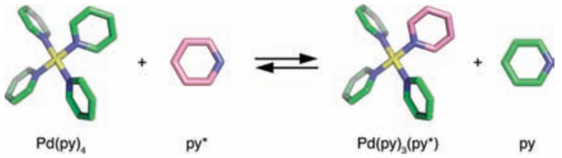
Scheme 2. Schematic Representation of Ligand Exchange between Spherical Complexes **2** and L^A



Scheme 3. Schematic Representation of Ligand Exchange between $[Pd(py)_4]^{2+}$ and Free Pyridine[a]



[a] Free pyridine (marked with pink color and an asterisk) is magnetically labeled.

$-$ 1/[**1**]$_0$) plots, the apparent exchange rate constant k_{obs} was estimated to be 2×10^{-2} M^{-1} s^{-1} with a half-life of 20 days.[6]

During the self-assembly process, the first $M_{12}L_{24}$ spheres to assemble coexist with free metal ions, free ligands, and intermediary $M_{(12-m)}L_{(24-n)}$ species. To model the stability of the $M_{12}L_{24}$ complexes during the intermediary stages of the assembly process, the rate of ligand exchange between $M_{12}L^B_{24}$ (**2**) and the free ligand L^A was examined (Scheme 2). Using continuous-flow techniques, solutions of **2** (0.031 mM) and L^A (1.7 mM) in acetonitrile were combined and instantly injected directly into the MS. The mixed species (**4** and free L^B) formed at a significantly faster rate; $k_{obs} = 5 \times 10^{-4}$ s^{-1} with $t_{1/2}$(**2**) = 23 min.[6] Thus, during the self-assembly process, rapid ligand exchange continues until the process reaches completion.

The stability of the $M_{12}L_{24}$ complexes arises from the cooperation of the 48 Pd(II)$-$pyridine interactions. To understand how effective the cooperativity works in stabilizing the $M_{12}L_{24}$ assembly, the ligand exchange rate of **1** was compared with that of a similar tetramonodentate model complex, $[Pd(py)_4](OTf)_2$ (py = pyridine),[7] for which the ligand exchange rate was previously unreported. Ligand exchange for $[Pd(py)_4](OTf)_2$ is very fast, and the kinetics was examined by NMR methods. The ^{1}H NMR signals of free and coodinated pyridine are sharp and independently observed. However, using saturation transfer NMR spectroscopy,[8] ligand equilibration can be observed (Scheme 3). The exchange rate, k_{obs}, was determined to be 1.9×10^{-2} s^{-1}, and the half-life was 36 s.[6] The half-life of the mononuclear complex is much smaller than that of the $M_{12}L_{24}$ complex by a factor of $\sim 10^5$.

In summary, the final 36-component $M_{12}L_{24}$ self-assembly gains remarkable stability in its framework through cooperation of 48 weak Pd(II)$-$pyridine interactions. The kinetic studies in this work demonstrate that multicomponent self-assembly roughly undergoes three stages. Initially, (i) there are very rapid equilibrations (ms^{-1}) among the many components; (ii) as more stable structures are formed, the system equilibrates quickly (s^{-1} to min^{-1}) among the completed and uncompleted self-assemblies; misassembled structures are presumably corrected at this stage; and finally (iii) very slow equilibration (hours to days) at the final stage after the self-assembly completes, producing the kinetic stability of the whole. So, unlike the simple mononuclear Pd$-$pyridine complexes, the $M_{12}L_{24}$ molecular spheres are remarkably stable and ligand exchange occurs only very slowly over weeks and months. Our system resembles self-assembly in nature (protein folding or DNA duplex formation) where initial structures subsequently experience three similar stages: very rapid trial-and-error to find the right pathways, moderate equilibration for error corrections, and the kinetic trap of the final complex structures.

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Supporting Information Available: Experimental details and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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