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Notes

Kinetically Trapped Receptor and its Thermodynamic Conversion During Metal-mediated Self-assembly

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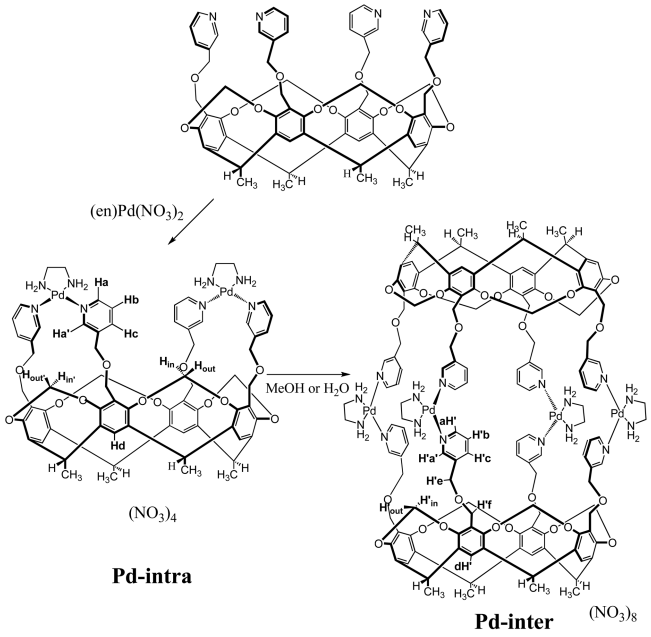
Metal-directed self assembly process provides the formation of unique discrete superstructures including molecular triangles, squares, helicates, catenanes, and cages[1] and some of as-assembled structures exist under dynamic equilibrium of coordination bond betweem metal ion and ligand. This reversibility is one of the interesting features in self assembly process, which not only allows spontaneous and selective formation of a distinct supramolecular structure,[2] but also affords facile routes for interconversion favoring formation of the thermodynamically more stable structures.[3] Thus, dynamic interconversion of assembled structures could be controlled by reaction conditions such as concentrations,[4] temperatures,[5] and solvents,[6] which are recently regarded as one of the interesting properties in developing functional materials. In this paper, we report the formation of a highly stable kinetic receptor in water solvent and its slow conversion into a thermodynamic product. Activation energy barrier in thermodynamic conversion of kinetic receptor is closely related to the solvent system stabilizing complex structure of the activated state and is remarkably high in D_2O solvent. We previously reported the structural properties of the resorcinarene-based receptor **Pd-intra**, which formed an intramolecular complex with (en)Pd$(NO_3)_2$, as shown in Scheme 1.[7]



Scheme 1. Proposed dynamic conversion of **Pd-intra** (kinetic product) into **Pd-inter** (thermodynamic product) by self assembly.

A solution of **Pd-intra** in D_2O was heated to 75 °C and maintained at this temperature for a considerable period of time; this was monitored at regular intervals of time by room-temperature ^{1}H-NMR. The time-dependent ^{1}H NMR spectra of **Pd-intra** in D_2O showed changes in peaks in the aromatic region; with time, the original peaks corresponding to **Pd-intra** gradually diminished, while signals attributable to a new component appeared (Figure 1). After approximately 152 h, **Pd-intra** was converted into a new com-

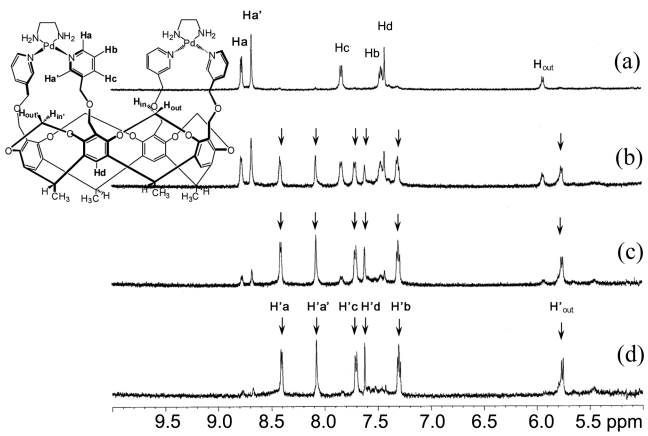


Figure 1. Partial ^{1}H NMR spectra (500 MHz, D_2O) of **Pd-intra** in D_2O after (a) 30 min, (b) 44 h, (c) 88 h, (d) 152 h at 75 °C. New components are indicated by arrows (↓) and see scheme 1 for proton labeling.

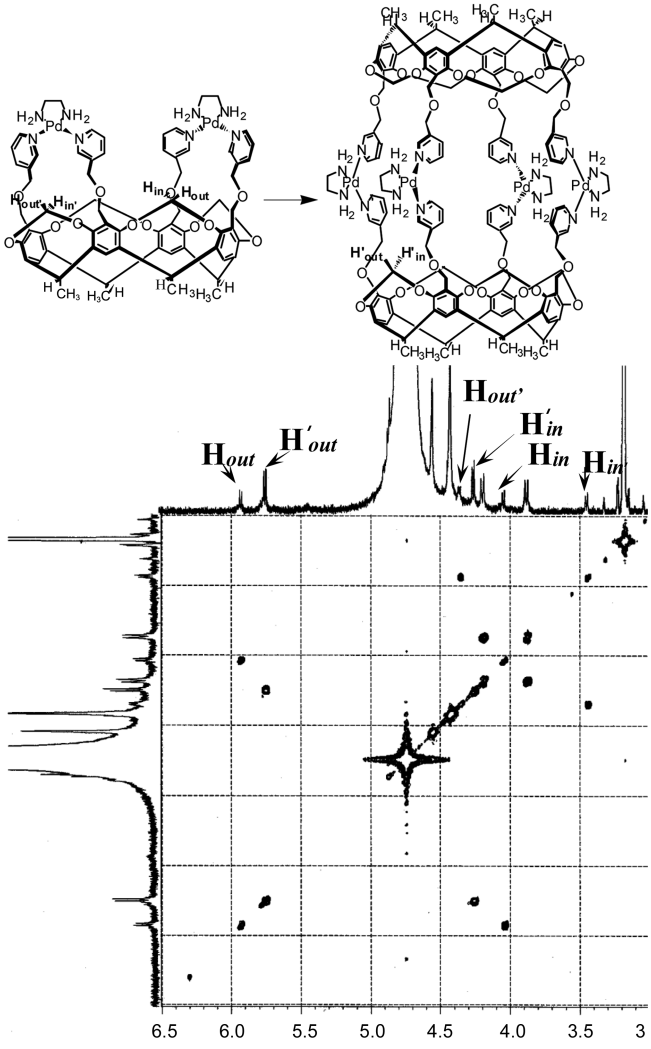


Figure 2. Partial HH COSY spectra (500 MHz, D_2O/MeOD-d_3, 1:5, v/v) of **Pd-intra** (H_{out}, H_{in}, $H_{out'}$, and $H_{in'}$) and **Pd-inter** (H'_{out} and H'_{in}) mixtures.

ponent that was obtained as the predominant species. While **Pd-intra** had a C_{2v} symmetric structure, the newly obtained component had D_{4h} symmetric structure, as was confirmed by NMR spectral analysis.

The D_{4h} symmetry, as suggested by the ^{1}H NMR signals corresponding to the new component (Figure 2), was confirmed by HH COSY analysis. On the basis of the symmetry indicated by the signals corresponding to the new component, we inferred that the component is an intermolecular self-assembled capsule, i.e., a thermodynamic product (**Pd-inter**), produced from the intramolecularly assembled receptor (**Pd-intra**), as shown in Figure 2. While the C_{2v} symmetry of **Pd-intra** resulted from the intramolecular complexation of Pd(II) with a ligand molecule, the D_{4h} symmetry of **Pd-inter** resulted from the intermolecular self-assembly of a ligand molecule and Pd(II) (Figure 2). The structural symmetry of **Pd-intra** and **Pd-inter** was deduced from the analysis of 1-D and 2-D ^{1}H NMR spectra; depending on the symmetry, the bridge protons, which were oriented toward or away from the cavity of a resorcinarene molecule could be indicative of a structural feature in NMR spectra. Upon intramolecular complexation of Pd(II) with a ligand molecule, the signals corresponding to the bridge protons on the upper rim of the resorcinarene skeleton split into two signals; One ($H_{out'}$, $H_{in'}$) of the bridge protons became surrounded by coordinations of the pyridyl groups with Pd(II). Because of the shielding effect of the two pyridyl groups, these signals ($H_{out'}$, $H_{in'}$) were shifted upfield as compared to the other (H_{out}, H_{in}) signals. However, when a self-assembled capsule was formed by intermolecular Pd(II)-ligand interactions, the outer and inner bridge protons on the upper rim became magnetically equivalent, thus giving rise to the D_{4h}-symmetric structure. In addition, whereas benzylic protons on the upper rim of **Pd-intra** became rigid upon intramolecular complexation with Pd(II), showing the diastereotopic pattern of a pair of doublet, benzylic protons of **Pd-inter** were homotopic and appeared as a singlet in H NMR spectra. (see Supplementary materials)

The structure of **Pd-inter** was confirmed by electrospray ionization mass spectrometry (ESI-MS) analysis of the precipitates obtained by anion exchange from NO_3^- to PF_6^- of **Pd-inter**. The signals observed at 1181, 846, and 649 m/z corresponded to the $[M\text{-}3(PF_6)]^{3+}$, $[M\text{-}4(PF_6)]^{4+}$, and $[M\text{-}5(PF_6)]^{5+}$ fragments of **Pd-inter** that underwent anion-exchange with PF_6^- (see Supplementary materials).

In the D_2O solution at room temperature (298 K), **Pd-intra** was not converted into **Pd-inter** (data not shown). This indicated that **Pd-intra** had high kinetic stability in D_2O and that the energy barrier required for its conversion into **Pd-inter** is high.

The solvent can influence the conversion rate by stabilizing the activation barrier in the transition state. **Pd-intra** was heated to 55 °C and maintained at this temperature for 12 h; D_2O:CD_3OD mixtures with various ratios (1:0.5, 1:1, 1:2, and 1:5, v/v) and the dynamic conversion of **Pd-intra**

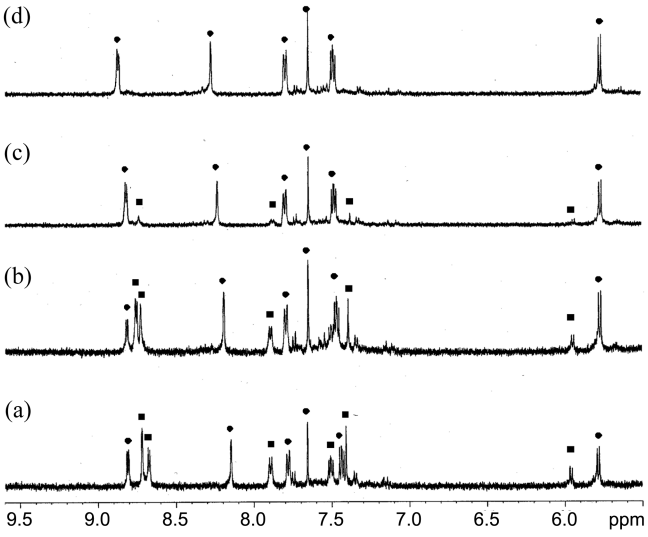


Figure 3. Partial ^{1}H NMR spectra showing the differences in the thermodynamic conversion of **Pd-intra** (■) into **Pd-inter** (●) for the following D_2O:MeOD-d_3 mixing ratios at 55 °C, 12 h: (a) 1:0.5, (b) 1:1, (c) 1:2, and 1:5 (v/v).

Table 1. Kinetic data pertaining to the conversion process at 298 K

	Rate constant (k)	Half life (τ)	Activation energy (ΔG^*)[a]
CD_3OD: D_2O (1:0)	0.842×10^{-5} s^{-1}	23 h	25.7 Kcal/mol
CD_3OD: D_2O (1:1)	0.302×10^{-6} s^{-1}	637 h	26.3 Kcal/mol

[a]$\Delta G^* = 4.57\ T\ (10.32 + \log(T) - \log(k))$. The equation was derived from the Eyring equation.

into **Pd-inter** was monitored in each solvent system by ^{1}H NMR spectroscopy. Figure 3 shows the aromatic region of the ^{1}H NMR spectrum for each solvent system. After heating at 55 °C for 12 h, **Pd-intra** was completely converted into **Pd-inter** in the solution in which the D_2O:CD_3OD ratio (v/v) was 1:5; however, when D_2O:CD_3OD ratio (v/v) was 1:0.5, only 50% of the **Pd-intra** was converted into **Pd-inter**. Thus, the rate of conversion of **Pd-intra** into **Pd-inter** was accelerated when the CD_3OD volume ratio in solvent was increased.

To evaluate the kinetic data for the conversion of **Pd-intra** into **Pd-inter**, we carried out time-dependent ^{1}H NMR experiments at 298 K using 100% CD_3OD and a mixed solvent system (CD_3OD/D_2O, 1:1) (see Supplementary materials). We observed that the conversion follows first-order kinetics; this unexpected behavior implied that the conversion process involves one single rate-determining step. **Pd-intra** is a kinetic intermediate and is stabilized by intramolecular Pd(II)-ligand coordination bonds; further, no anionic species (NO_3^-) would be involved in the conversion process. In a metal-mediated self-assembly, there could be several intermediates produced by dissociation as well as dynamic exchange of labile Pd-N bonds. On the basis of the first-order kinetic behavior of the conversion process, we suggest that the conversion might proceed sequentially and that the species initially formed by the dissociation of one of the labile Pd-N bonds in **Pd-intra** is the intermediate formed during the rate-determining step. Since intramolecular Pd(II)-ligand coordination bonds are very stable, the activation energy barrier for Pd(II)-ligand dissociation is relatively high, and thus, **Pd-inter** would be formed as a result of rapid ligand exchange between the labile Pd-N bonds after the intermolecular coordinations between the first dissociated Pd-N bonds of the intermediates.

Table 1 summarizes the kinetic parameters for the conversion process. Comparison of the kinetic data shows that the dissociation of the Pd-ligand bond in **Pd-intra** in the mixture of MeOD-d_3 and D_2O is almost 27 times slower than in MeOD-d_3; this implies that **Pd-intra** is highly stable in an aqueous solvent. The labile Pd-ligand coordination does not depend on the solvent system involved and does not have any significant influence on the activation energy barrier in the dissociation process. The solvation could be closely related to the activation energy barrier in the conversion of **Pd-intra** into the intermediate, which is formed by dissociation in the rate-determining step. In addition, generally, the smaller structure is entropically more stable. However, in our system, the both structures have the same number of Pd-pyridine linkage per Pd (II) ion and self assembly of **Pd-inter** is thermodynamically more favorable. Thus, the thermodynamic instability of **Pd-intra** would depend on the more sterically constrained structure around Pd (II) centers in **Pd-intra**, compared to the structure of **Pd-inter**, although it is necessary to study the detailed thermodynamic stabilities of both structures.

In summary, the kinetically trapped receptor is highly stable in an aqueous media and is converted into a thermodynamic product in the self assembly process. The metal-mediated self assembly of the complex superstructure can be kinetically or thermodynamically controlled. Kinetic data suggested that the initial dissociation of one of the labile Pd-N bonds in **Pd-intra** is the rate-determining step of the self-assembly pathway.

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