Pergamon

Tetrahedron Letters 40 (1999) 531–534

TETRAHEDRON LETTERS

Guest-Induced Binding Site Organization of Self-Assembled Pd(II) Complexes

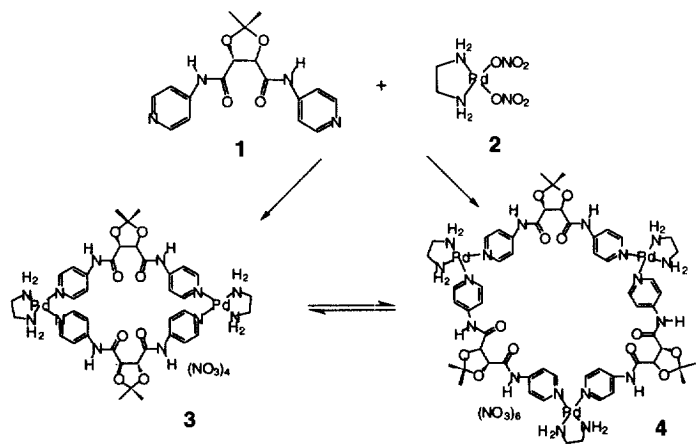
Gil Ma, You Sung Jung, Doo Soo Chung and Jong-In Hong*

Department of Chemistry, Seoul National University, Seoul 151-742, Korea

Received 29 August 1998; revised 9 November 1998; accepted 11 November 1998

Abstract: Self-assembled Pd(II) complexes derived from a chiral bidentate ligand **1** and (en)Pd(NO_3)$_2$ (**2**) in D_2O showed concentration dependent and guest-induced reorganization behaviour.

Proteins form their substrate binding sites by bringing together the component units in a process of self-assembly.[1] A range of different strategies can be envisioned for the receptor site self-assembly in the formation of artificial binding sites.[2] Hydrogen bonding has widely been used as the primary interaction to induce the binding site organization.[3] Metal-templated self-assembly has also been used for the construction of two-dimensional molecular boxes and three-dimensional molecular capsules.[4] However, there are only a few examples in the self-assembly of a macrocyclic Pd(II) complex controlled by guest inclusion in the hydrophobic binding cavity.[4b,5b] In our previous report, we have described concentration dependent and guest-induced reorganization of a self-assembled two-dimensional Pd(II) complex derived from a bidentate ligand *trans*-1,2-bis(4-pyridyl)ethylene and (en)Pd(NO_3)$_2$ (**2**) in D_2O.[5b] We find that treatment of a more flexible bidentate ligand **1** with **2** in D_2O gives macrocyclic complexes **3** and **4** depending on the concentration in dynamic equilibrium[5] and their hydrophobic interaction with guests in aqueous solution.[4b,4c,5b]



Scheme 1

The NMR spectra of a 1:1 mixture of **1** and **2**, obtained at various concentrations in D_2O, showed two different assemblies with highly symmetric structures.[6] Both products turned out to have macrocyclic structures because of the expected 1:1 stoichiometry of the components (**1**:(en)Pd^{2+} moiety) and the extremely simple

0040-4039/99/$ - see front matter
PII: S0040-4039(98)02431-9

spectra in the region of pyridine nuclei in each structure (PyH_α: 8.28, d, J=7.1Hz, PyH_β: 7.51, d, J=7.1Hz, for **3**; PyH_α: 8.39, d, J=7.1Hz, PyH_β: 7.62, d, J=7.1Hz, for **4**). Identification of the two structures as the dimeric assembly **3** and the trimeric assembly **4** follows from concentration dependent and guest-induced NMR behavior and electrospray ionization mass spectrometry (ESI-MS) (*vide infra*). ESI-MS showed a series of prominent peaks supporting the molecular masses of **3** and **4**, respectively: m/z 570 $[M\text{-}2NO_3]^{2+}$, 359 $[M\text{-}3NO_3]^{3+}$, 509 $[(M+2H)\text{-}4NO_3]^{2+}$ for **3**, 550 $[(M+2H)\text{-}4NO_3]^{2+}$ for **4**.[5c] The concentraion dependent equilibrium ratios (dimer/trimer 37:63, 47:53, 60:40, 64:36, 67:33 at 10.0, 4.8, 3.8, 1, and 0.2mM) strongly supported the major component at higher concentration as **4** and that at lower concentration as **3**. No oligomeric assemblies are observed despite using a more flexible ligand **1** compared to the previous guest-induced self-assembly, in which more rigid *trans*-1,2-bis(4-pyridyl)ethylene (BPE) was used as a bidentate ligand and oligomerization was inevitable even at low concentration.[5b]

In addition to the concentration-dependent self-assembly, a specific guest complementary to the cavity of a macrocyclic complex was shown to be able to control the size of the self-assembled macrocycle through hydrophobic interaction in water. For example, whereas *p*-toluic acid sodium salt complementary to the dimeric cavity turned out to induce the dimeric host **3**, the larger guest such as cholic acid sodium salt fitting the hydrophobic cavity of the trimeric host **4** favoured the formation of the larger host **4**. Fig. 1 showed increasing the amount of *p*-toluic acid sodium salt caused a gradual increase in the relative intensities of NMR signals corresponding to **3**. Addition of cholic acid sodium salt to the 1:1 mixture of **1** and **2** increased the relative NMR signals corresponding to **4**, as shown in Fig. 2. Remarkable is that almost one form of the energetically favourable self-assembled structures is generated upon the addition of complementrary guests. These guest-induced reorganization processes were complete within several seconds. This can be regarded as a model of "induced-fit" molecular recognition in which a specific substrate induces the organization of the recognition site of a receptor itself. Employing adamantane dicarboxylic acid sodium salt as a guest did not give any evidence for the effect of guest inclusion. The CPK molecular model showed that it was too large to be suitable for the dimer cavity and too small to be suitable for the trimer cavity.

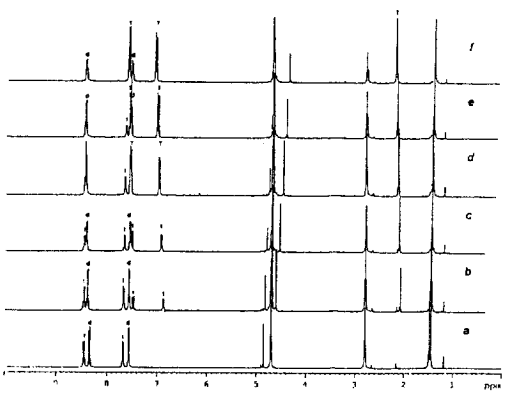


Figure 2. Guest-induced reorganization of the Pd(II) complexes for the dimer **3**: (a) 0 (b) 0.4 (c) 1.0 (d) 1.75 (e) 2.52 (f) 5.0 equiv. of *p*-toluic acid sodium salt + a 1:1 mixture of **1** and **2**, each in 3.2 mM (d=dimer, t=trimer, ▼=*p*-toluic acid sodium salt).

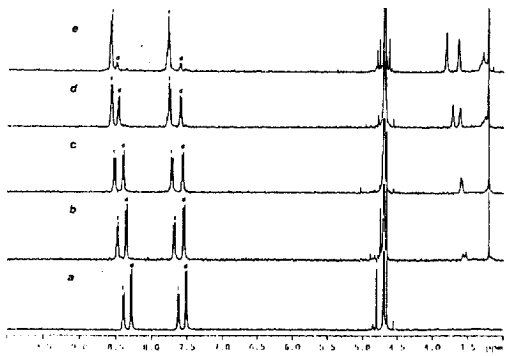
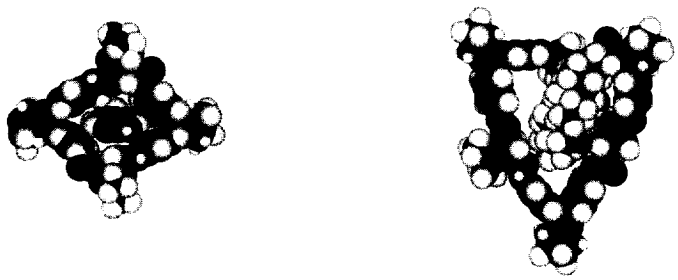


Figure 3. Guest-induced reorganization of the Pd(II) complexes for the trimer **4**: (a) 0 (b) 0.25 (c) 0.50 (d) 1.0 (e) 2.0 equiv. of cholic acid sodium salt + a 1:1 mixture of **1** and **2**, each in 3.2 mM.

In order to get some insight into the three-dimensional structures of the Pd(II) complexes, we carried out the geometry optimization of these macrocyclic dinuclear and trinuclear Pd(II) complexes and their guest-inclusion complexes. MacroModel V5.5 molecular modeling program (C. Still, Columbia University) with the MM2 forcefield was used. For the forcefield parameters regarding the Pd atoms, we used the same set as in refs. 4b and 7.[8] The Monte Carlo conformational search was performed for these systems,[9] with GB/SA solvation model[10] for water. The structures of supramolecular dimeric and trimeric complexes which were induced by toluate and cholate ions, respectively, are shown in Fig. 3. As expected, both **3**/toluate and **4**/cholate complexes showed good van der Waals contacts inside the binding cavity. Molecular modeling studies for these systems suggest that the binding cavity size could play a crucial role in self assembly and molecular recognition.



(a) **3**/*p*-toluic acid sodium salt complex (b) **4**/cholic acid sodium salt complex

Figure 3. Geometry-optimized structures of the dimer and the trimer complexes. Theses space-filling models were drawn to be 100% of van der Waals' volumes.

In fact, the macrocylic complexes **3** and **4** were designed to test the possibility of the chiral recognition for chiral guests. However, results with various amino acid sodium salts showed that these chiral hosts were not able to distinguish stereoisomers in aqueous solution.

In summary, self-assembled dimeric host **3** and trimeric host **4** were shown to exist in equilibrium in D_2O: **3** is favoured at lower concentration and in the presence of the guest complementary to the dimer cavity size, whereas **4** is more favoured at relatively higher concentration and in the presence of the guest complementary to the trimer cavity size.

Acknowledgments: This work was supported by the Ministry of Education (BSRI-97-3416).

References and Notes

* E-mail: jihong@plaza.snu.ac.kr

1. Wlodawer, A.; Miller, A.; Jaskolski, M.; Sathyanarayana, B.; Baldwin, E.; Weber, I.; Selk, L. ; Clawson, L.; Schneider, J.; Kent, S. *Science* **1989**, *245*, 616.
2. (a) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995. (b) Lindsey, J. S. *New J. Chem.* **1991**, *15*, 153. (c) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229. (c) Linton, B.; Hamilton, A. D. *Chem. Rev.* **1997**, *97*, 1669.
3. (a) Branda, N.; Wyler, R.; Rebek, J., Jr., *Science* **1994**, *263*, 1267. (b) Grotzfeld, R. M.; Branda, N.; Rebek, J., Jr. *Science*, **1996**, *271*, 487. (c) Meissner, R. S.; Rebek, J., Jr.; de Mendoza, J. *Science*,

1995, *270*, 1485. (d) Lee, S. B.; Hwang, S.; Chung, D. S.; Hong, J.-I. *Tetrahedron Lett.* **1997**, *38*, 8713.

4. (*a*) Fujita, M.; Yazaki, J.; Ogura, K. *J. Am. Chem. Soc.* **1990**, *112*, 5645. (b) Fujita, M.; Nagao, S.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 1649. (*c*) Fujita, M.; Nagao, S.; Iida, M.; Ogata, K.; . Ogura, K. *J. Am. Chem. Soc.* **1993**, *115*, 1574. (*d*) Jacopozzi, P.; Dalcanale, E. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 613. (*e*) Stang, P. J. *Chem. Eur. J.* **1998**, *4*, 19.
5. (*a*) Fujita, M.; Sasaki, O.; Mitsuhashi, T.; Fujita, T.; Yazaki, J.; Yamaguchi, K.; Ogura, K. *Chem. Commun.* **1996**, 1535. (*b*) Lee, S. B.; Hwang, S.; Chung, D. S.; Yun, H.; Hong, J.-I. *Tetrahedron Lett.* **1998**, *39*, 873. (*c*) Romero, F. M.; Ziessel, R.; Dupont-Gervais, A.; Dorsselaer, A. V. *Chem. Commun.* **1996**, 551.
6. Property of **1** : $[\alpha]_D^{21} = +114°$ (*c* 0.31, $CHCl_3$); mp 221 °C dec.; ^{1}H NMR (300 MHz, D_2O) δ 8.37 (d, J=6.3 Hz, 4H, PyH_α), 7.53 (d, J=6.3 Hz, 4H, PyH_β), 4.90 (s, 2H, -C*H*C*H*-), 1.48 (s, 6H, -C(CH_3)$_2$); FAB MS (NBA) m/z 343 ($M+H^+$).
7. Adam, K. R.; Antolovich, M.; Brigden, L. G.; Lindoy, L. F. *J. Am. Chem. Soc.* **1991**, *113*, 3346.
8. Stretching, bending, and torsion terms were taken from ref. 4b and out-of-plane bending term was taken from ref. 7. The additional torsion angle parameters in the form of N-Pd-N-X (where X=H and C) were set to zero as suggested in the ref. 7.
9. Chang, G.; Guida, W. C.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 4379.
10. Still, W. C.; Tempczyk, A.; Hawley, R. C.; Hendrickson, T. *J. Am. Chem. Soc.* **1990**, *112*, 6127.