*Self-Assembly*

# Kinetic Self-Assembly: Selective Cross-Catenation of Two Sterically Differentiated $Pd^{II}$-Coordination Rings**

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Like protein folding, self-assembly in biology is considered to be a kinetic process where the most favorable pathway to programmed structures is kinetically selected through metastable intermediary structures.[1–3] Although numerous reports have appeared on thermodynamically controlled self-assembly,[4–8] relatively few have discussed kinetic self-assembly in chemical systems.[9–13] Here we deal with kinetic self-assembly based on the dynamic behavior of coordination rings. We emphasize that designing not only structures but also pathways is an important yet unexplored task for controlling molecular self-assembly.

The kinetic self-assembly discussed here is demonstrated by the cross-catenation[14] of $Pd^{II}$-linked rings **1** and **2**, which

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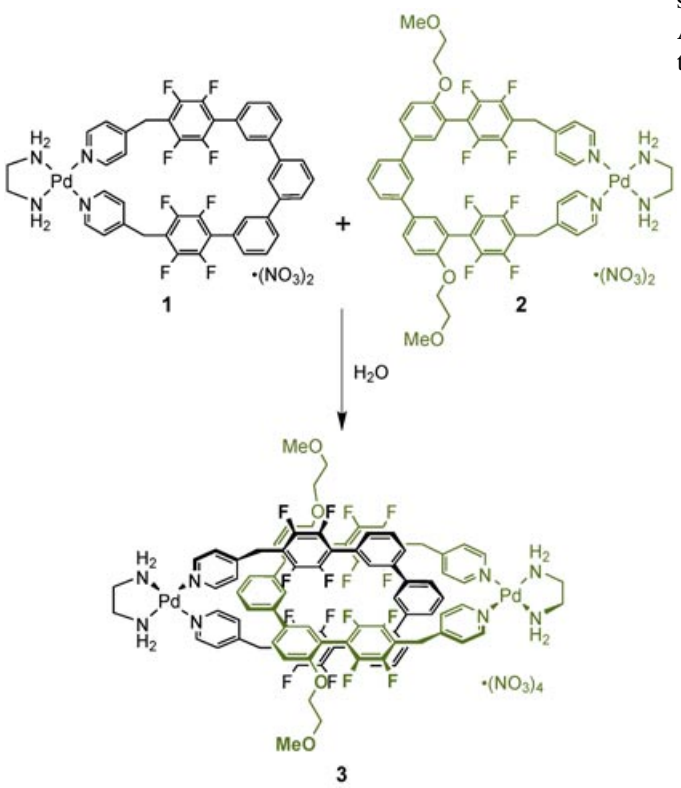
are differentiated by alkoxy side chains (Scheme 1). The homocatenation of **2** is kinetically unfavorable because of the steric demand of the alkoxy side chains.[15] Accordingly, ring **2** is only allowed to thread on less-hindered **1**, thus giving rise to the kinetic formation of cross-catenane **3**.




*Scheme 1.*

We first estimated the timescale of the homocatenation of **1** by 2D EXSY NMR spectroscopy.[16] This sterically less hindered ring rapidly forms catenanes,[17] and a clear correlation between **1** and its catenated dimer **4** was observed even after 30 ms mixing time, thus showing that the catenation takes place on a millisecond timescale. The rapid catenation should be retarded if a sterically demanding side chain is attached to the ligand of **1**. A bis(methoxyethoxy)-substituted ligand (the precursor of **2**) was synthesized and complexed with $[Pd(en)(NO_3)_2]$ (en = ethylenediamine) in DMSO to give **2** quantitatively. Since the catenation of $Pd^{II}$-linked rings is driven by aromatic-stacking interactions, which work efficiently in aqueous media,[17] water was added to the solution of **2** in DMSO to transform it into homocatenane **5**. As expected, the catenation was significantly retarded, and took 4–5 h to be completed (Figure 1).

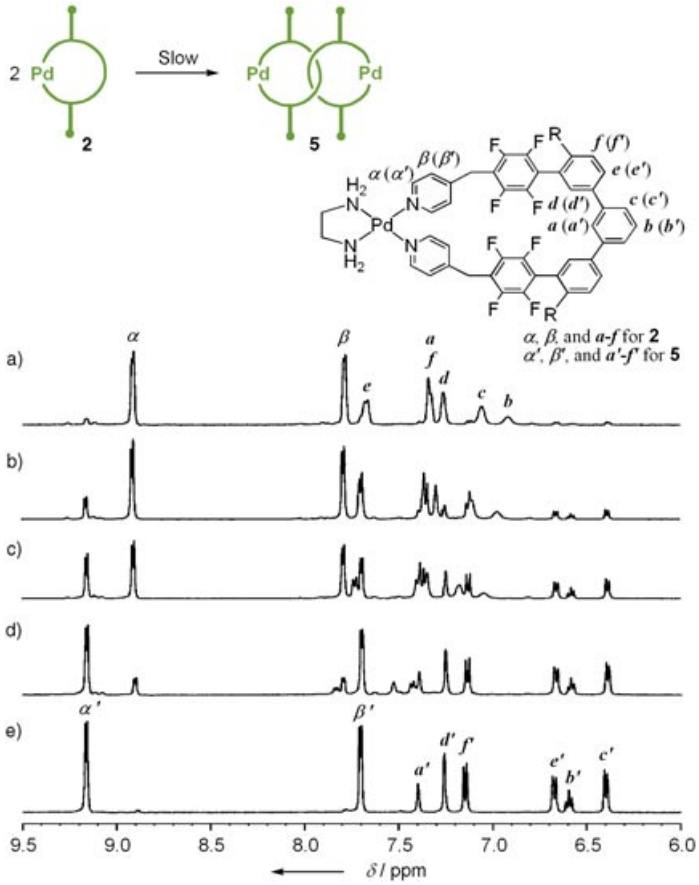
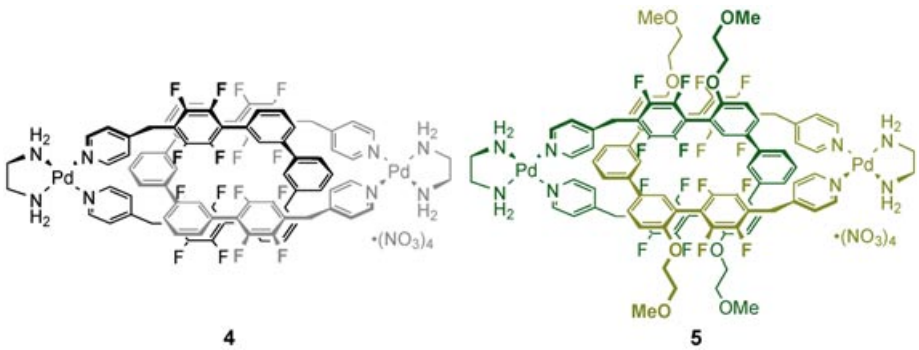



***Figure 1.*** NMR spectra indicating the transformation of **2** into catenane **5** (aromatic region, 500 MHz, 300 K, $[D_6]DMSO/D_2O$ (1:1.5), TMS as an external standard); after a) 3 min, b) 10 min, c) 20 min, d) 60 min, e) 240 min.

Accordingly, we examined the cross-catenation of **1** and **2** by utilizing the large difference in the catenation rate of **1** and **2**. Water (0.9 mL) was added to a solution of **1** (4.5 mg, 4.5 μmol) and **2** (5.2 mg, 4.5 μmol) in DMSO (0.6 mL) at ambient temperature. The two rings were immediately transformed into a single catenated product as indicated by NMR spectroscopic analysis (Figure 2). The large upfield shifts of the central aromatic protons are characteristic of interstrand stacking between the rings.[18] Since this spectrum was different from those of homocatenated compounds **4** and **5**, the selec-



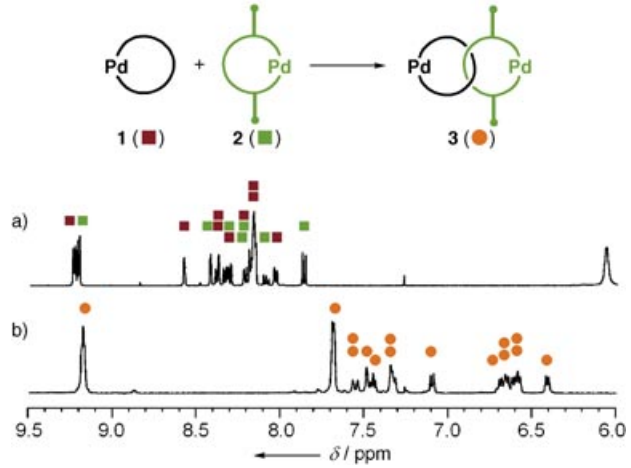



***Figure 2.*** Observation of cross-catenation by NMR spectroscopy (aromatic region, 500 MHz, 300 K, TMS as an external standard): a) The spectrum of a mixture of **1** and **2** in [$D_6$]DMSO, b) the spectrum after the addition of $D_2O$.

tive formation of cross-catenane **3** was strongly suggested. A coldspray ionization mass spectrometry (CSI-MS)[19] study confirmed the selective formation of cross-catenane **3** as evident from prominent signals that fully agreed with **3**: for example, *m*/*z* 572.0 $[\mathbf{3}-(NO_3)_4+(DMSO)_5]^{4+}$ (Figure 3). Signals indicating the presence of **4** or **5** were barely visible.

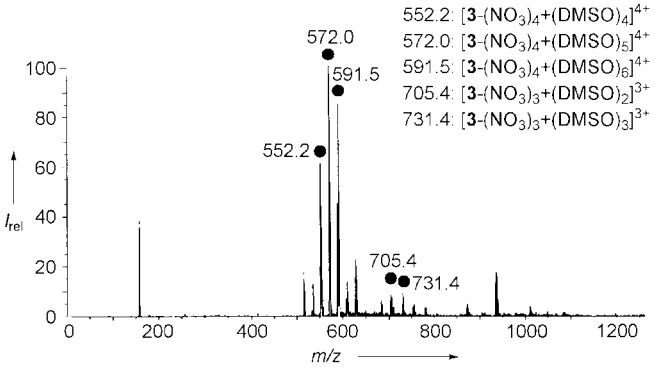



***Figure 3.*** CSI mass spectrum of cross-catenane **3** in DMSO/$H_2O$ (1:1.5) solution.

The selective formation of **3** is explained by the energy diagram shown in Figure 4. Although three possible catenanes **3**–**5** have similar thermodynamic stability, the formation of **5** is kinetically inhibited because ring **2** must thread on the bulky ligand of **2** itself. Thus, the states [I] and [II] will rapidly equilibrate and favor the formation of cross-catenane **3**.

This speculation suggests that cross-catenane **3** (state [I]) will be equilibrated with **4**+**5** (state [III]) if the reaction time is long (or temperature is high) enough to promote the formation of **5**. In fact, when the solution of **3** was allowed to stand at 25 °C for a week, new signals assigned to homocatenanes appeared in the NMR spectrum. The ratio of **3**:**4**:**5** was estimated to be 4.3:1:1 and 2.8:1:1 after 1 day and 2 days, respectively. The ratio finally became statistical (2:1:1) after

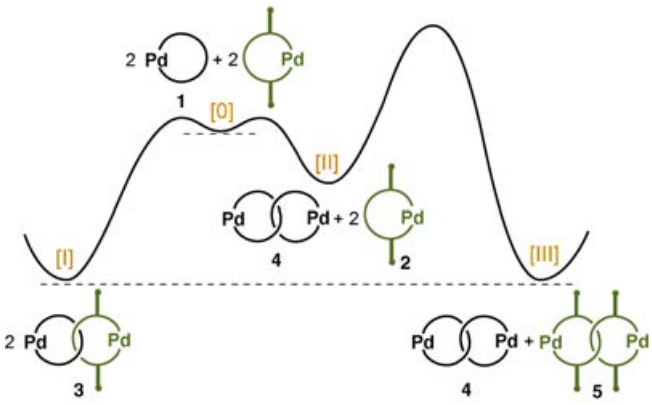



***Figure 4.*** The energy diagram for the homo- and cross-catenane of **1** and **2**.

8 days. The same statistical mixture was also obtained when presynthesized catenanes **4** and **5** were combined in a mixture of $H_2O$ and DMSO, and the solution was allowed to stand at 25 °C for 1 week. Clearly, the selective formation of cross-catenane over short times (minutes or hours) is kinetically controlled while the formation of a statistical mixture over longer times (days) is thermodynamically controlled. Of course, the equilibration became much slower at lower temperatures. The transformation of **3** into a statistical mixture took several months in a refrigerator (6 °C). Moreover, this transformation was completely suppressed in a freezer.

In summary, we have controlled the cross-catenation of two different rings by a kinetic method. Although still a preliminary study, the case detailed here demonstrates a new method of molecular self-assembly in which desired structures are generated by *programmed pathways*. Our results offer a good example of such kinetically controlled self-assembly and will, hopefully, be emulated by many other cases.

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[1] C. B. Anfinsen, *Science* **1973**, *181*, 223.
[2] P. A. Jennings, P. E. Wright, *Science* **1993**, *262*, 892.
[3] C. M. Dobson, A. Šali, M. Karplus, *Angew. Chem.* **1998**, *110*, 908; *Angew. Chem. Int. Ed.* **1998**, *37*, 868; A. R. Dinner, A. Šali, L. J. Smith, C. M. Dobson, M. Karplus, *Trends Biochem. Sci.* **2000**, *25*, 331.
[4] J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, **1995**.
[5] J. L. Atwood, J. E. D. Davies, D. D. Macnicol, F. Vögtle, *Comprehensive Supramolecular Chemistry*, *Vol. 9*, Pergamon, Oxford, **1996**.
[6] J.-M. Lehn, *Angew. Chem.* **1988**, *100*, 91; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89; J.-M. Lehn, *Angew. Chem.* **1990**, *102*, 1347; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1304.
[7] J. S. Lindsey, *New J. Chem.* **1991**, *15*, 153.
[8] D. Philp, J. F. Stoddart, *Synlett* **1991**, 445.

  

[9] M. Fujita, S. Nagao, K. Ogura, *J. Am. Chem. Soc.* **1995**, *117*, 1649; A. Hori, K. Kumazawa, T. Kusukawa, D. K. Chand, M. Fujita, S. Sakamoto, K. Yamaguchi, *Chem. Eur. J.* **2001**, *7*, 4142; S. Tashiro, M. Tominaga, T. Kusukawa, M. Kawano, S. Sakamoto, K. Yamaguchi, M. Fujita, *Angew. Chem.* **2003**, *115*, 3389; *Angew. Chem. Int. Ed.* **2003**, *42*, 3267.

[10] B. Hasenknopf, J.-M. Lehn, N. Boumediene, E. Leize, A. V. Dorsselaer, *Angew. Chem.* **1998**, *110*, 3458; *Angew. Chem. Int. Ed.* **1998**, *37*, 3265.

[11] L. J. Prins, E. E. Neuteboom, V. Paraschiv, M. Crego-Calama, P. Timmerman, D. N. Reinhoudt, *J. Org. Chem*, **2002**, *67*, 4808; V. Paraschiv, M. Crego-Calama, T. Ishi-i, C. J. Padberg, P. Timmerman, D. N. Reinhoudt, *J. Am. Chem. Soc.* **2002**, *124*, 7638.

[12] J. O. Jeppesen, J. Perkins, J. Becher, J. F. Stoddart, *Angew. Chem.* **2001**, *113*, 1256; *Angew. Chem. Int. Ed.* **2001**, *40*, 1216; J. O. Jeppesen, S. A. Vignon, J. F. Stoddart, *Chem. Eur. J.* **2003**, *9*, 4611; J. D. Badjie, S. J. Cantrill, J. F. Stoddart, *J. Am. Chem. Soc.* **2004**, *126*, 2288.

[13] B. J. Holliday, Y.-M. Jeon, C. A. Mirkin, C. L. Stern, C. D. Incarvito, L. N. Zakharov, R. D. Sommer, A. L. Rheingold, *Organometallics* **2002**, *21*, 5713; B. J. Holliday, C. A. Mirkin, *Angew. Chem.* **2001**, *113*, 2076; *Angew. Chem. Int. Ed.* **2001**, *40*, 2022.

[14] A. Hori, H. Kataoka, T. Okano, S. Sakamoto, K. Yamaguchi, M. Fujita, *Chem. Commun.* **2003**, 182; A. Hori, H. Kataoka, A. Akasaka, T. Okano, M. Fujita, *J. Polym. Sci. A* **2003**, *41*, 3478.

[15] Molecular modeling studies clearly show that a $Pd^{II}$-linked ring cannot thread on the dissociated form of **2** because of the steric bulk of the side chain.

[16] M. Fujita, F. Ibukuro, H. Seki, O. Kamo, M. Imanari, K. Ogura, *J. Am. Chem. Soc.* **1996**, *118*, 899.

[17] A. Hori, A. Akasaka, K. Biradha, S. Sakamoto, K. Yamaguchi, M. Fujita, *Angew. Chem.* **2002**, *114*, 3403; *Angew. Chem. Int. Ed.* **2002**, *41*, 3269.

[18] Selected data for **3**: $^1$H NMR (500 MHz, [D$_6$]DMSO/D$_2$O = 1:1.5, 280 K, TMS as an external standard): $\delta = 9.23$ (s, 8H, H$_\alpha$ and H$_{\alpha'}$), 7.74 (s, 8H, H$_\beta$ and H$_{\beta'}$), 7.61 (s, 1H, H$_a$), 7.59 (s, 1H, H$_{a'}$), 7.54 (s, 2H, H$_d$), 7.45 (t, $J = 6.2$ Hz, 2H, H$_f$), 7.39 (s, 2H, H$_{d'}$), 7.33 (d, $J = 6.2$ Hz, 2H, H$_g$), 7.11 (d, $J = 8.0$ Hz, 2H, H$_{f'}$), 6.72 (t, $J = 7.2$ Hz, 1H, H$_{b'}$), 6.69 (d, $J = 6.2$ Hz, 2H, H$_e$), 6.64–6.58 (m, 5H, H$_b$, H$_c$, H$_{e'}$), 6.45 (d, $J = 7.2$ Hz, 2H, H$_{c'}$), 4.25 (s, 4H, CH$_{g'}$), 4.17 (s, 8H, CH$_2$, CH$_2'$), 3.72 (s, 4H, CH$_{h'}$), 3.32 (s, 6H, CH$_{i'}$), 3.05 ppm (s, 8H, en, en′); $^{13}$C NMR (125 MHz, [D$_6$]DMSO/D$_2$O = 1:1.5, 280 K): $\delta = 155.4$ (Cq), 152.1 (Cq), 152.0 (CH$_\alpha$, CH$_{\alpha'}$, Cq), 145.5–142.0 (4 × CF), 139.2 (Cq), 138.9 (Cq), 138.4 (Cq), 132.2 (Cq), 129.7 (CH$_g$), 129.6 (CH$_f$), 129.3, 129.2, 129.0 (CH$_b$, CH$_{b'}$, CH$_{e'}$), 128.1 (CH$_\beta$, CH$_{\beta'}$), 127.8 (CH$_{d'}$), 127.4 (Cq), 127.0 (CH$_e$), 126.4 (CH$_d$), 125.1 (CH$_c$), 124.2 (CH$_{c'}$), 123.3 (CH$_a$), 122.9 (CH$_{a'}$), 118.4 (Cq), 116.4 (Cq), 115.4–115.2 (3 × Cq), 113.9 (CH$_{f'}$), 70.4 (CH$_{h'}$), 68.5 (CH$_{g'}$), 58.4 (CH$_{i'}$), 46.9 (en, en′), 27.7 ppm (CH$_2$ and CH$_2'$).

[19] S. Sakamoto, M. Fujita, K. Kim, K. Yamaguchi, *Tetrahedron* **2000**, *56*, 95.

  