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Self- and hetero-recognition in the guest-controlled assembly of Pd(II)-linked cages from two different ligands

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The equilibration of cage-like receptors, $M_3(L^1)_2$ + $M_3(L^2)_2$ ⇌ 2 $M_3(L^1)(L^2)$, was efficiently controlled by appropriate guest addition: large (spherical) or small (flat) guests stabilized the homoleptic cages ($M_3(L^1)_2$ or $M_3(L^2)_2$) while medium-sized guests preferred the heteroleptic cage ($M_3(L^1)(L^2)$).

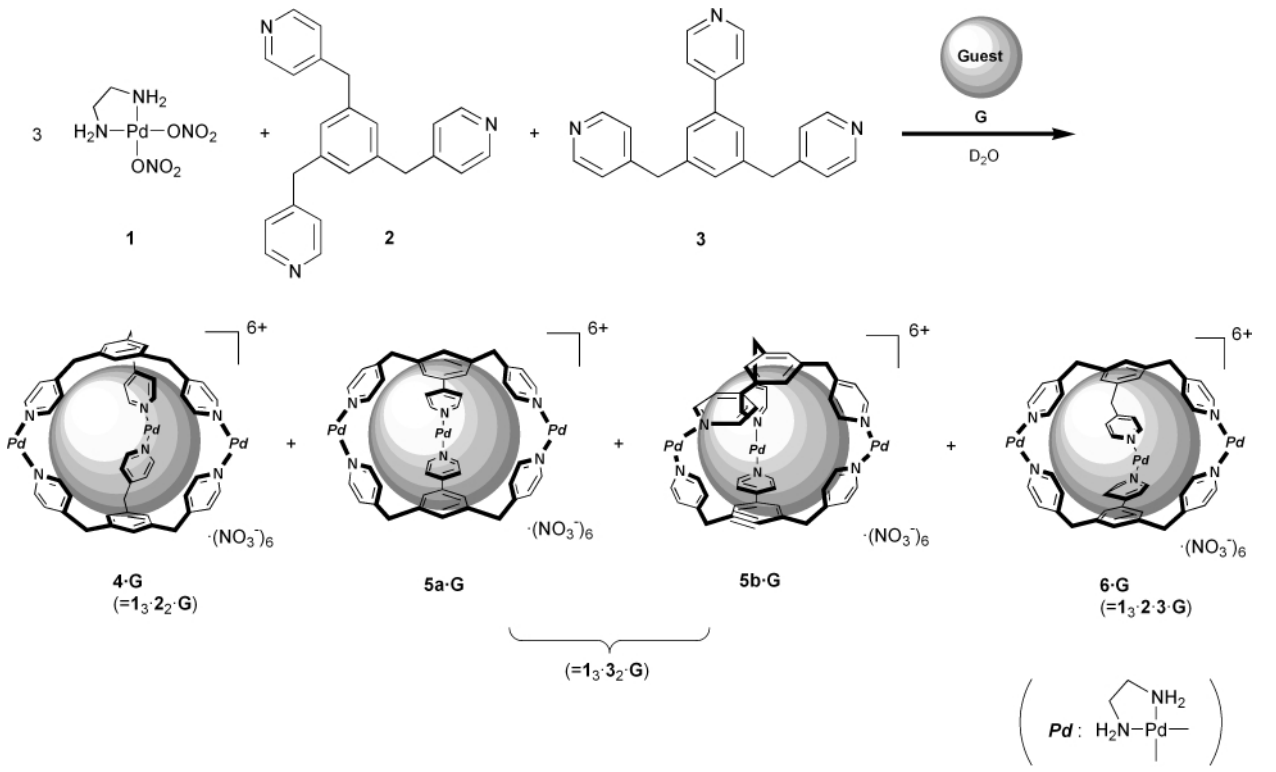
A dynamic receptor library is an equilibrium mixture of several receptors from which the appropriate one is selected by an optimal guest.[1–6] It is particularly important to study the dynamic features of guest-selected receptor formation from the library because the phenomenon is closely related to biological receptor systems.[7] Herein reported is the guest-controlled assembly of Pd(II)-linked cage-like receptors from a dynamic library generated from Pd(II) complex **1** and two different tridentate ligands **2** and **3**. As shown in Scheme 1, the library contains two classes of receptors: homoleptic (**4**, **5a** and **5b**) and heteroleptic (**6**). The homoleptic receptor contains two identical ligands and, hence, is termed a 'self-recognized' receptor while the heteroleptic receptor contains two different ligands and is termed 'hetero-recognized'.[8] We show that the equilibration between the receptors is very efficiently controlled by the addition of appropriate guests which selectively stabilize their optimal receptors.

The equilibration we deal with is represented by the following equation:

$$\underset{\text{'self - recognized'}}{\mathbf{4} + \mathbf{5}} \rightleftharpoons \underset{\text{'hetero - recognized'}}{2 \bullet \mathbf{6}}$$

Self-recognition should be dominant if only **4** and/or **5** are stabilized, while hetero-recognition is favored if **6** is selectively stabilized. Note that **5a** and **5b** are structural isomers with identical composition and the equilibration between these isomers is highly controlled by guest addition, as previously reported.[6]

When Pd(II) complex **1** (10 mM) was combined with tridentate ligands **2** and **3** (3.3 mM each) in D_2O, cages **4**–**6** and uncharacterized oligomeric products were formed with a very low self/hetero ratio‡ (**4**:**5**:**6**:oligomers = 15:35:30:20 corresponding to *ca.* 6:4 self/hetero ratio; see Table 1, run 1).[9] The product ratios were estimated by ^{1}H NMR (Fig. 1). Oligomer formation became predominant at higher concentrations and exclusive when $[\mathbf{1}]_0$ > 40 mM.



Scheme 1

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Table 1 Guest-selected formation of homo- and heteroleptic Pd(II)-linked receptors

Run	Guest[b]	Ratio[a] (%) **4**:**5a**:**5b**:**6**:Oligomers[c]	S/H[d]
1	None	15:0:35:30:20	6:4
2	PhCOOH	27:0:31:38:4	6:4
3	**7**	42:0:42:16:0	8:2
4	**8** + **9**	50:0:50:0:0	10:0
5	CCl_4	17:15:2:66:0	3:7
6	$CBrCl_3$	16:14:2:68:0	3:7
7	CBr_4	29:18:11:42:0	6:4
8	*c*-C_6H_{12}	19:6:13:62:0	4:6
9	*c*-C_7H_{14}	8:0:20:60:12	3:7
10	*c*-C_8H_{16}	15:0:33:34:18	6:4

[a] Determined by ^{1}H NMR ([**1**]$_0$ = 10 mM, 25 °C, D_2O). [b] Excess amounts of guests were used. [c] At 3.3 mM for each ligand, it was confirmed that only ligand **2** gives oligomeric components. Thus, the amount of the oligomers was estimated on the assumption that compound **3** does not contribute to the oligomeric fraction of complexes. [d] S/H = self/hetero ratio.

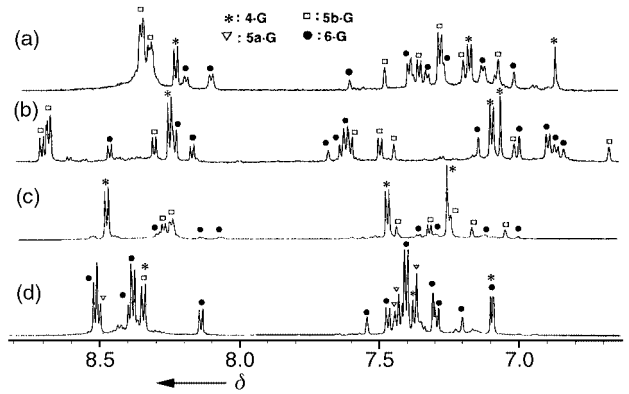

Fig. 1 ^{1}H NMR spectra (500 MHz, D_2O, aromatic region) of the mixture of complexes **4**–**6** obtained from a 3:1:1:1 mixture of **1** ([**1**]$_0$ = 10 mM), **2** ([**2**]$_0$ = 3.3 mM), **3** ([**3**]$_0$ = 3.3 mM) and various guests: (a) guest free; (b) guest = PhCOOH; (c) guest = **7**; (d) guest = $CBrCl_3$.

Upon the addition of adamantane-1-carboxylic acid (**7**), however, the oligomer formation was completely suppressed and the equilibration was significantly shifted toward the self-recognized products (**4** + **5** = 84%; run 3). The cavity size becomes larger and more spherical in the order of **5** < **6** < **4** because ligand **2** is larger than **3** by the length of a CH_2 unit. Thus the preference for the self-recognition can be ascribed to the efficient binding of the large and spherical guest by host **4**. In fact, only the signals of host **4** were downfield shifted while those of **5** and **6** were unchanged, suggesting the selective complexation of **7** and **4**.

Self-recognition should be most effective if **4** and **5** are stabilized simultaneously but not **6**. Thus, we attempted the use of two different guests adamantan-1-ol (**8**) and benzene-1,3,5-tricarboxylic acid (**9**) because the former was expected to be bound by bulky cage **4** and the latter by flat cage **5b**. When **8** and **9** were added, only self-recognized receptors **4** and **5b** were assembled exclusively as expected (**4** + **5b** = 100%; run 4). The signals of only **4** and **5b** were downfield shifted suggesting the selective formation of **4**•**8** and **5b**•**9** complexes.

In contrast, the equilibrium was markedly shifted toward hetero-recognition when $CBrCl_3$ was added as the guest: **6** was preferentially formed (68%) and the self/hetero ratio was *ca*. 3:7. This spherical and 'medium-sized' guest seems to best fit within the cavity of **6**. The formation of **6** was not exclusive because $CBrCl_3$ was also bound efficiently in the cavity of **5a**.[6] Similar spherical guests such as CCl_4 induced the preferential formation of **6** (66%) while the slightly larger CBr_4 was no longer a suitable guest for selective heteroleptic receptor formation (42%). Cyclohexane and cycloheptane were also favorable for hetero-recognition (self/hetero ratios 4:6 and 3:7, respectively), but cyclooctane, which seems too large, showed no stabilizing effects for any receptors.

Notes and references

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‡ Self-recognized receptors **4** and **5** have been obtained by two independent reactions: **1** + **2** → **4**;[9] **1** + **3** → **5**. Thus, from the NMR spectrum of a **4**–**6** mixture, **4** and **5** can be easily assigned. In the present reaction, the newly appeared signals, which contain the framework of both **2** and **3** in a 1:1 ratio, can be assigned as **6**. ^{1}H NMR data of **6** (from the reaction of run 6 in Table 1): ^{1}H NMR (500 MHz, D_2O, 25 °C) δ 8.51 (2H, d, *J* 6.6 Hz, PyH_α), 8.39 (4H, d, *J* 6.6 Hz, PyH_α), 8.38 (2H, d, *J* 6.6 Hz, PyH_α), 8.14 (4H, d, *J* 6.6 Hz, PyH_α), 7.54 (1H, s, Ar*H*), 7.47 (2H, d, *J* 6.8 Hz, PyH_β), 7.40 (8H, d, *J* 6.8 Hz, PyH_β), 7.31 (2H, s, Ar*H*), 7.29 (2H, d, *J* 6.8 Hz, PyH_β), 7.20 (1H, s, Ar*H*), 7.09 (2H, s, Ar*H*), 3.92–3.72 (10H, m, –CH_2–), 2.79–2.60 (12H, m, $NH_2CH_2CH_2NH_2$).

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