

Enantiomeric Self-Recognition of a Facial Amphiphile Triggered by $[\{\text{Pd}(\text{ONO}_2)(\text{en})\}_2]$ **

Lyle Isaacs* and Dariusz Witt

DNA, RNA, and proteins are composed of homochiral building blocks and undergo multiple levels of self-assembly to generate Nature's functional macromolecules. This hierarchical self-assembly process involves several types of non-covalent interactions and often results in the generation of additional elements of chirality at the supramolecular level. Supramolecular chemists have devised methods to prepare chiral molecular aggregates by the (self-)association of achiral molecules,^[1] by the use of enantiomerically pure molecules that induce further elements of chirality in polymers^[2] and molecular aggregates,^[3] and by the use of racemic mixtures of ligands that undergo enantiomeric self-recognition.^[4] Elucidation of the factors that dictate chirality in supramolecular systems may result in a better understanding of their natural counterparts, in the design of improved enantioselective catalysts, and in supramolecular materials with enhanced properties. We present a new model system for the study of enantiomeric self-recognition that is based on the hydrophobically driven self-association of facial amphiphile $(\pm)\text{-1}$ in the presence, but not in the absence, of **2** (Figure 1).

Amphiphilic molecular clips are known to undergo self-association to yield dimers.^{[5][6]} We have recently shown that methylene-bridged glycoluril dimers, with hydrophilic carboxylate solubilizing groups on their convex face, undergo hydrophobically driven self-association in water to yield tightly associated, discrete, dimeric assemblies.^[7] Towards the goal of creating structurally defined molecular aggregates of larger numbers of molecules, we designed **1**, which contains a hydrophobic cleft and a pyridyl ligand. We anticipated that **1** might undergo hydrophobic dimerization and coordination-driven self-assembly of the type pioneered by Fujita and co-workers.^[8] Herein, we report that the addition of **2** to an aqueous solution of racemic **1** triggers the formation of a single molecular aggregate $\text{1}_2 \cdot \text{2}_2$ (and $\text{ent-1}_2 \cdot \text{2}_2$) by an enantiomeric self-recognition process (Figure 1 a).

After synthesizing $(\pm)\text{-1}$, we investigated its self-association properties in the absence of **2**.^{[5][7b]} The ^1H NMR spectrum of **1** in buffered D_2O at 25°C showed two sets of resonance signals (Figure 2 a), which suggests that two diastereomeric aggregates were formed, namely, $\text{1} \cdot \text{ent-1}$ and the pair of enantiomers 1_2 and ent-1_2 . At 60°C , we observed a single set of resonances and measured the dissociation constant

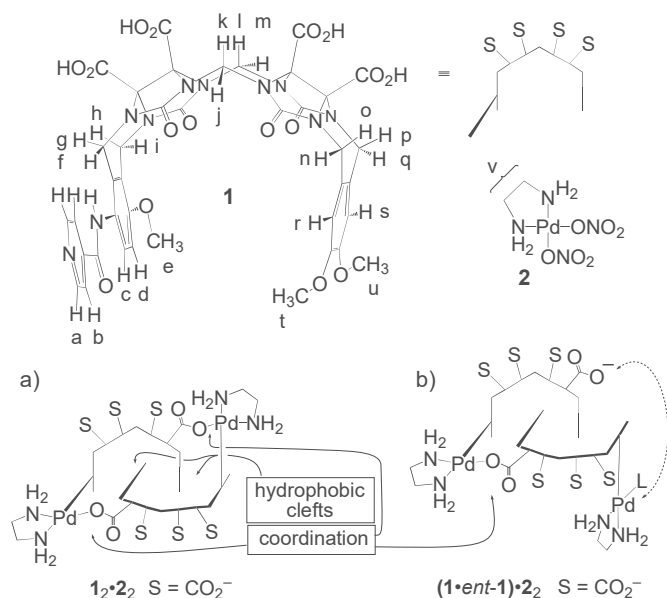


Figure 1. Schematic drawings of a) the observed aggregate $\text{1}_2 \cdot \text{2}_2$, and the undetected aggregate b) $(\text{1} \cdot \text{ent-1}) \cdot \text{2}_2$. The dashed arrow indicates the palladium-carboxylate interaction that cannot be formed in the heterochiral aggregate.

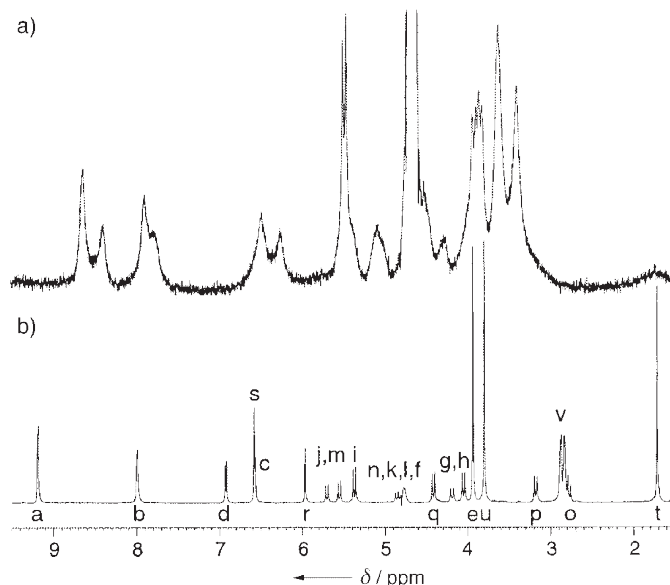


Figure 2. ^1H NMR spectra before and after the addition of **2**. a) $(\pm)\text{-1}$ (400 MHz, 5 mM, pD 7.4, 298 K), and b) $\text{1}_2 \cdot \text{2}_2$ (500 MHz, 2.5 mM, pD 7.4, 298 K). The broad resonance at 4.7 ppm is caused by incomplete suppression of residual HOD.

of the aggregate by ^1H NMR dilution experiments ($K_d = 337 \pm 40 \mu\text{M}$). The addition of **2** to a solution of $(\pm)\text{-1}$ resulted in dramatic changes in its ^1H NMR spectrum (Figure 2 b), indicative of a well-defined molecular aggregate of **1** and **2**.

To elucidate the structure of this aggregate, we determined the relative stoichiometry of **1:2** by ^1H NMR titration experiments, in which the **1:2** ratio was changed from 1:0 to 1:4 ($[\text{1}] = 4 \text{ mM}$). Based on the precedent of Fujita and co-workers,^[8] we expected to observe clean aggregate formation at a 2:1 ratio of **1:2**. In contrast, however, a single discrete aggregate (Figure 2 b) was only observed when the ratio of **1:2**

[*] Prof. L. Isaacs, Dr. D. Witt
Department of Chemistry and Biochemistry
University of Maryland
College Park, MD 20742 (USA)
Fax: (+1) 301-314-9121
E-mail: LI8@umail.umd.edu

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