Integrated Self-Sorting: Construction of A Cascade-Stoppered Hetero[3]Rotaxane

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I. Introduction

Natures functional architectures are complex and efficiently use the principles of self-assembly through non-covalent bonding. In addition, nature makes use of self-sorting phenomena in order to generate complex architectures from many *different*, correctly positioned building blocks that cooperate to fulfill the function. In contrast, most synthetic self-assembled architectures are highly symmetrical because of the repetitive use of *ever the same* building blocks. Self-sorting[1] is an elegant strategy to correctly position all subunits and a prerequisite for implementing function.

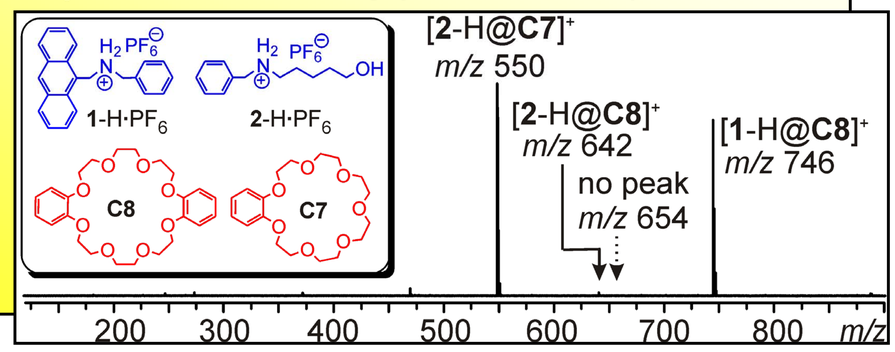
The more similar the building blocks become, the more difficult self-sorting is to achieve. Here, we report two social self-sorting systems based on two very similar crown ethers. When two binding sites are integrated in one axle component, self-sorting almost quantitatively generates a hetero[3]pseudorotaxane with a defined sequence of two different wheels. Stoppering gives rise to the corresponding "cascade-stoppered" hetero[3]rotaxane.

II. Self-Sorting

The association constants of [1-H@C8]·PF_6, [2-H@C7]·PF_6, and [2-H@C8]·PF_6 in acetone-d_6 are 496±18, 615±36, and 155±8 M^{-1}, respectively. Phenyl groups were reported to suffice as stoppers to trap C7 on the axle.[2]

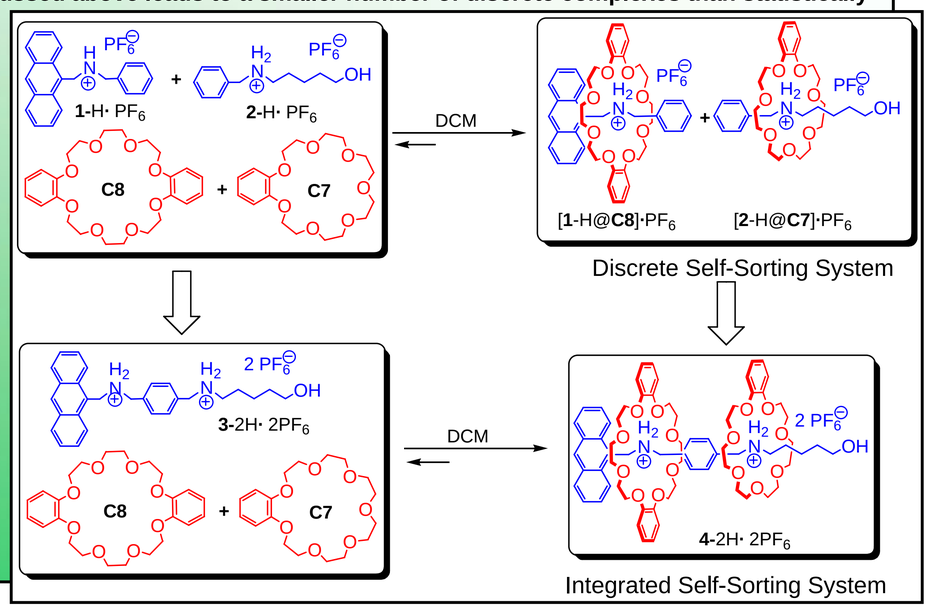
In the equimolar mixture of 1-H·PF_6, 2-H·PF_6, C7, and C8, C8 can form pseudorotaxane with 1-H·PF_6, but C7 can not because of the existence of a too high barrier at room temperature for C7 to slip over; C8 can also form pseudorotaxane with 2-H·PF_6, but C7 binds more strongly. Therefore, Thermodynamic properties thus control the preference of C8 for 1-H·PF_6, and C7 for 2-H·PF_6. This is a social self-sorting system based on competition.

The ESI-FTICR-MS experiment proved the high fidelity self-sorting feature of this equimolar mixture in DCM, which is also confirmed by ^{1}H NMR experiments.



III. Integrated Self-Sorting

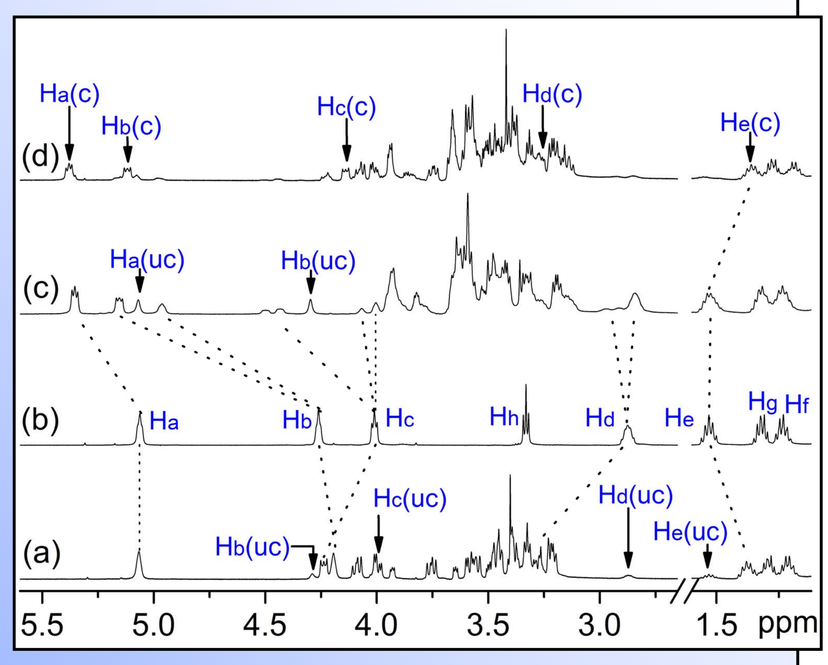
The self-sorting system discussed above leads to a smaller number of discrete complexes than statistically possible. We therefore use the term *discrete self-sorting* here. In contrast, we use the term *integrated self-sorting* to describe a system, in which the components are integrated through non-covalent interactions into one dominant complex.[3] As a prerequisite, two or more binding sites capable to self-sort must be integrated in at least one of the components. This strategy ensures programmability and correct positioning of all distinct subunits in the final complex.



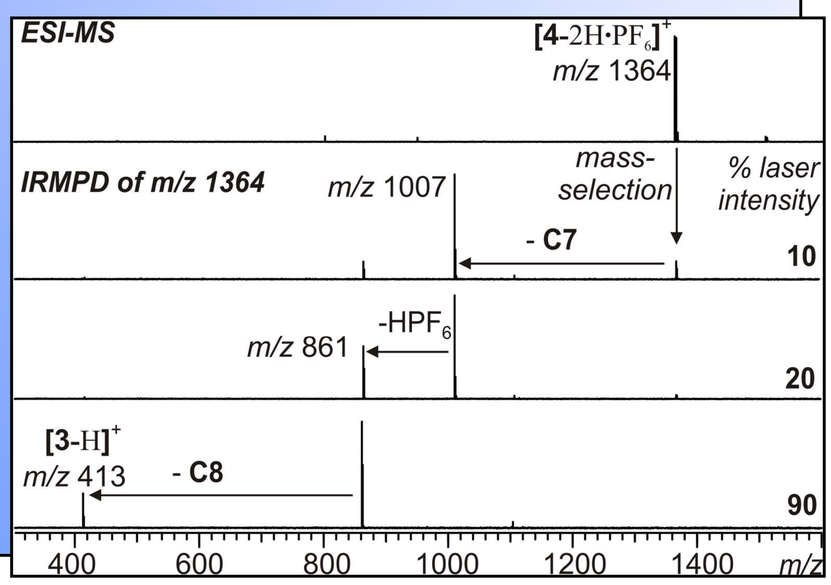
IV. Sequential Hetero[3]PseudoRotaxane

The ^{1}H NMR spectrum (Figure a) of a 1:1 mixture of 3-2H·$2PF_6$ and C7 confirmed C7 to bind exclusively at site B. While the signals for H_c, H_d, and H_e experience significant complexation-induced shifts, H_a and H_b remain almost unaffected with respect to the free axle (Figure b). Adding one equivalent of C8 to 3-2H·$2PF_6$ (Figure c) caused changes for all protons on both sites A and B, but the changes for the protons on site A are more obvious, indicating C8 to equilibrate between A and B with a clear preference for A in agreement with the binding constants discussed above.

In the equimolar mixture of 3-2H·$2PF_6$, C7, and C8, site B is occupied by C7 as most clearly seen from the shift of He to the same position observed in Figure 3a. Site A is bound to C8 as characterized by downfield shifts of H_a and H_b almost identical to those observed in Figure c. In line with expectation, C8 and C7 are thus bound almost quantitatively to A and B, respectively. Furthermore, irrespective of the mixing order of the three components, the ^{1}H NMR spectrum is always the same. This implies the equilibrium of all accessible complexes to be reached with 4-2H·$2PF_6$ being the only major component.

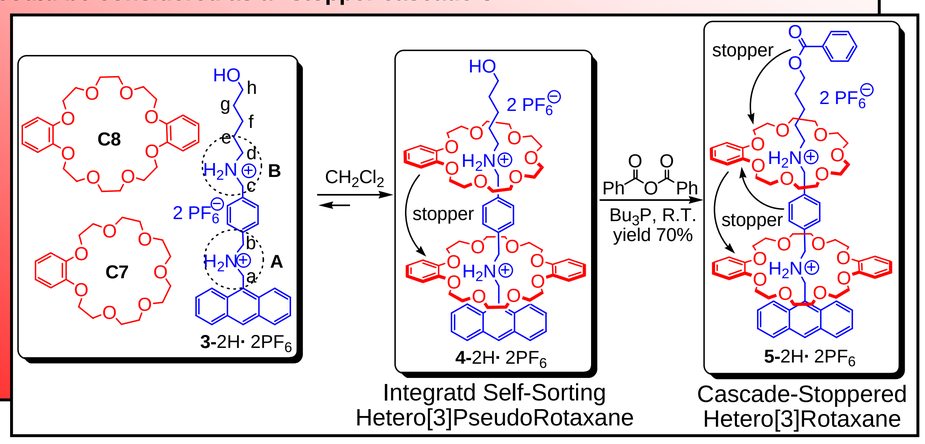


An ESI mass spectrum of the equimolar mixture of 3-2H·$2PF_6$, C7, and C8 in DCM confirmed the integrated self-sorting: In the clean spectrum, only one intense peak appears at *m/z* 1364 which corresponds to [4-2H·PF_6]$^+$. Moreover, the fragmentation reactions of mass-selected pseudo-rotaxane ions confirm the sequence of wheels: Infrared-multiphoton dissociation (IRMPD) experiments with [4-2H·PF_6]$^+$ reveal the loss of C8 to occur only at higher laser intensities as a consecutive fragment after losing C7 and HPF_6. This fragmentation pattern is only in agreement with C8 occupying site A and C7 site B. Thus, NMR and MS experiments agree that an integrated self-sorting system with a well-organized structure has successfully been constructed from the equimolar mixture of 3-2H·$2PF_6$, C7, and C8.



V. Synthesis of Cascade-Stoppered Hetero[3]Rotaxane

In the hetero-[3]rotaxane 5-2H·$2PF_6$, the phenyl groups at the end and middle of the axle trap C7. C8 can still slip over the central phenyl group, but certainly not over C7 so that it is also trapped by what could be considered as a "stopper cascade".

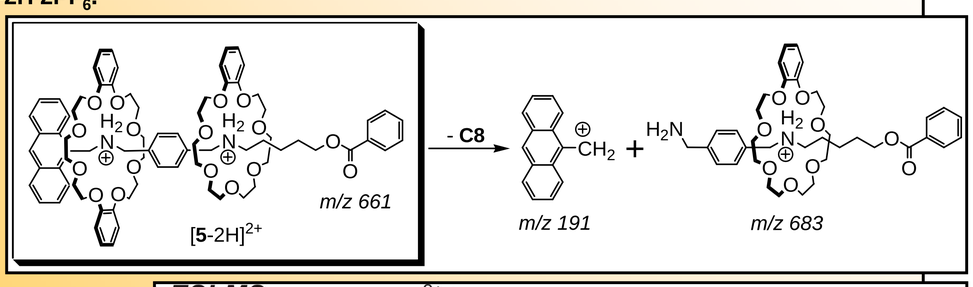


VI. Characterization of Cascade-Stoppered Hetero[3]Rotaxane

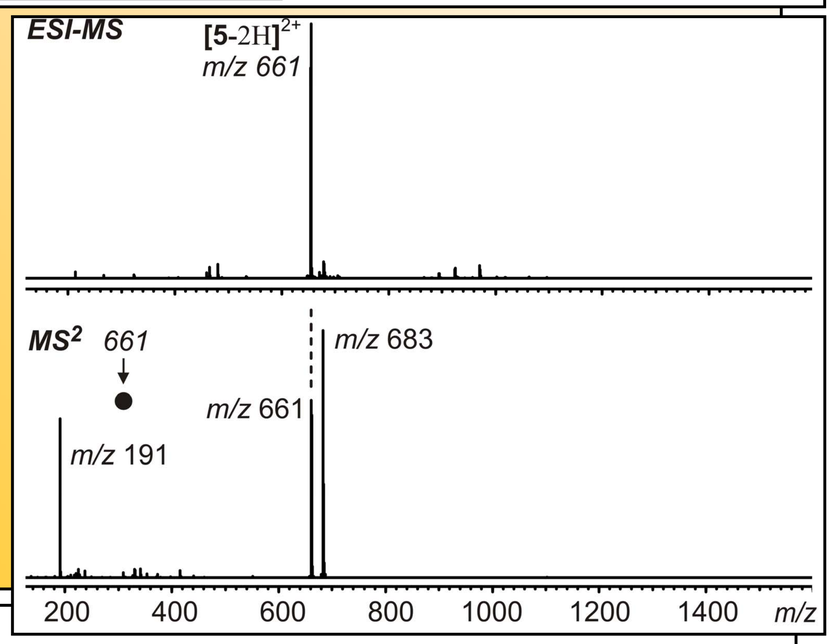
The cascade-stoppering strategy in 5-2H·$2PF_6$ has been tested by heating its DMSO-d_6 solution at 80 ° C for 2 days in the presence of excess Et_3N. Afterwards, no free components or deprotonated products have been detected by ^{1}H NMR experiments providing evidence for the rotaxane structure and quite a high stability of the [3]rotaxane against deslipping of one of the wheels.

The cascade-stoppered hetero[3]rotaxane 5-2H·2PF6 was also characterized intensely by ESI-FTICR-MS experiments.[4]

In IRMPD experiment of mass-selected [5-2H·PF_6]$^+$, no crown ether can leave the axle unless breaking the axle or crown ether, or deprotonating first, confirming the interlocked feature in 5-2H·$2PF_6$.



IRMPD experiment of mass-selected dication [5-2H]$^{2+}$ displays the simultaneous production of anthracenyl methylene cation (*m/z* 191), neutral C8 and another cation (*m/z* 683) with C7 still trapped on the remainder of the axle, confirming the location information of C8 and implicitly that of C7 in 5-2H·$2PF_6$ which is in line with the sequence of C7 and C8 in the sequential hetero-[3]pseudorotaxane 4-2H·$2PF_6$.



VII. Conclusion

We believe integrated self-sorting – as an important "programming language" in nature – will be highly useful in constructing complex supramolecular assemblies and various artificial smart materials with well-organized structure, distinct topology and function.

Reference:

[1] **(a) Wu, A.; Isaacs, L.** *J. Am. Chem. Soc.* **2003**, *125*, 4831-4835; **(b) Mukhopadhyay, P.; Wu, A.; Isaacs, L.** *J. Org. Chem.* **2004**, *69*, 6157-6164.

[2] **Zhang, C.-J.; Li, S.-J.; Zhang, J,-Q.; Zhu, K.-L.; Li, N.; Huang, F.-H.** *Org. Lett.* **2007**, 9, 5553-5556.

[3] **For two examples of integrated self-sorting, see: (a) Miyauchi, M.; Harada, A.** *J. Am. Chem. Soc.* **2004**, *126*, 11418-11419. **(b) Rudzevich, Y.; Rudzevich, V.; Moon, C.; Schnell, I.; Fischer, K.; Böhmer, V.** *J. Am. Chem. Soc.* **2005**, *127*, 14168-14169.

[4] **Reviews on the MS analysis of supramolecules: (a) Schalley, C. A.** *Mass Spectrom. Rev.* **2001**, *20*, 253-309; **(b) Baytekin, B.; Baytekin, H. T.; Schalley, C. A.** *Org. Biomol. Chem.* **2006**, *4*, 2825-2841.

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