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Control of Nanospaces with Molecular Devices

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Abstract

Cavitands and capsules define nanoliter spaces for recognition, isolation and reactions of small molecules. These systems are usually self-assembled and factors such as solvent size, stoichiometry, and packing factors determine what goes into the spaces. Here we examine two switching devices to control what and when guests get in and out of these hosts: bipyridyl-metal chelation and azobenzene photoisomerization. The effects are reversible by treatment with conventional chelating agents and brief heating, respectively. Accordingly, it is possible to trigger reactions that take place within a cylindrical capsule by light, even though the reaction process is not photochemical by nature. Likewise the presence of metals can regulate reactions without acting as direct catalysts.

Keywords

word; another word; lower case except names

1) Bipyridyl Rotors and Metals

Molecular devices reproduce on the nanoscale level notions and even real machines familiar on the macroscale.ⁱ Some time ago we introduced bipyridyl rotors as chemical models for the allosteric effects proteins,ⁱⁱ and even today biaryl rotors appear in many nanomachines.ⁱⁱⁱ Metal chelation of bipyridyls is accompanied by predictable changes in conformation, and in supramolecular systems this reliability has led to flapping motions^{iv} and controlled convergence of host on a guest.^v In molecular machinery, this rotor system is frequently used^{vi} as a switching device.^{vii} We describe here its application in the context of cavitand complexation.^{viii}

We outfitted a deep cavitand bearing a bipyridyl function and covalently tethered to it a cyclohexyl group^{ix} that allowed an intramolecular host/guest complex to form (Figure 1). Although cyclohexanes are generally poor guests for this cavitand, the case at hand enjoys a huge entropic advantage and it prevents entry of external guests. It may rightly be regarded as an introverted function^x but we called it a tail-eating arrangement - an “Ouroborand” - as suggested by the armadillo lizard and Ouroboros, an ancient symbol that represents a serpent swallowing its own tail.

An Ouroboros famously inspired Kekule’s formulation of benzene and was recently used to describe self-threading molecules.^{xi} In the resting state of the cavitand the cyclohexyl tail

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can reach the cavernous mouth (Figure 2 config. A) because the configuration of the bipyridine is anti. When a metal ion is chelated and forces a syn bipyridine conformation, the guest is jerked out of the host (config. B). This allows access of an external guest, in this case an adamantane derivative (config. C). Removal of the metal ion restores the initial configuration after the adamantane is released (config. D).

As a reflection of the entropic advantage enjoyed by the intramolecular host/guest complex, attempts to completely replace the tethered guest with various solvents, as external guests, were unsuccessful. Specifically, acetone showed no displacement of the cyclohexyl, dichloromethane displaced some 20% and tetrahydrofuran forced out only 80%, even though these solvents are present at ~10 molar concentration. The reversible cycle of events was realized in a solvent mixture that dissolved the metal complexes: 80% mesitylene- d_{12} and 20% acetonitrile- d_3 . The ^1H NMR spectra are shown during the switching cycle. They comprise the resting state with internalized cyclohexyl (Figure 3a); the addition of excess AdCN shows no changes (Figure 3b); but then addition of excess ZnBr_2 pulls the cyclohexyl tail out of the cavity with AdCN now inside almost half of the free cavities (Figure 3c); washing the NMR sample with water to remove the zinc ions returns the system to that seen after addition of AdCN (Figure 3d).

2) Photoisomerization of Azobenzenes

Shinkai and co-workers introduced the photoisomerization of azobenzenes to supramolecular chemistry in 1979,^{xii} and it continues to be applied in many of today's molecular devices.^{xiii,xiv} The isomerization of the long and narrow *trans*-**1** (Figure 1) causes its predictable folding to the shorter and wider *cis*-**1**. For the cylindrical capsule **2·2**,^{xv} only the *trans* form can be accommodated and it provides a good fit of guest in the host, as might be expected from its affinity for the nearly isosteric benzanilides,^{xvi} and stilbenes.^{xvii} We arranged a competition between *trans*-**1** and *n*-tridecane in deuterated mesitylene. Although *n*-alkanes are good guests^{xviii} only the azo compound is found inside the capsule, and a methyl singlet appears in the upfield region of the ^1H NMR spectrum (Fig. 4b). However, when this solution is irradiated at 365 nm for 1 hour, the *trans*-**1** is completely replaced by the encapsulated alkane.^{xix} On heating this sample to 160 °C for 2 minutes, the original complex reappears and the irradiation/heating cycle can be repeated many times.

Does the azobenzene “break out” of the capsule? We believe so. The exchange rate of encapsulated *trans*-**1** with *n*-tridecane without irradiation is very slow: replacement of encapsulated *trans*-**1** by added *n*-tridecane takes about one day to reach equilibrium. The isomerization of *trans*-**1** inside of the capsule forces the capsule walls outward, as occurs in the vase-to-kite conformational changes of cavitands.^{xx} This motion breaks some hydrogen bonds and facilitates guest exchange. For guest exchange in related cavitands, only 2 walls need to fold outward.^{xxi} The capsule halves do not need to separate; this would require the rupture of all 8 bifurcated hydrogen bonds and is a very slow process.^{xxii}

We performed parallel experiments on the extended capsule **2·3₄·2**. This system is assembled when suitable guests are present^{xxiii} and excess glycolurils such as dibutylaniline derivative **3** are in the solution with the original capsule **2·2**. We prepared a longer azobenzene, *trans*-4-methyl-4'-hexyl-azobenzene^{xxiv} (*trans*-**4**) as the light-responsive guest (Fig. 5a). In a solution containing 10 equiv. of *trans*-**4** and 2 equiv. of *p*-ethylbenzamide only the azo compound is encapsulated. But after irradiation with 365 nm light, the encapsulated homodimer *p*-ethylbenzamide has replaced the azo compound. This assembly is symmetric and the spectra are simplified accordingly. Heating the sample to 160 °C for 2 minutes restores the initial guest occupation (see Fig. 5b) and the cycle can be repeated many times.

The photoisomerization was also used to switch between the assemblies **2·2** and **2·5₄·2**. This took advantage of the low solubility of 4-dodecanophenyl glycoluril **5** in deuterated mesitylene. It shows good solubility only when it is incorporated into the capsular assembly. A mixture of **2**, glycoluril **5** and 3 equiv. of *trans*-**4** and 4,4'-dibromobenzil **6** gives exclusively the extended assembly **2·5₄·2** with only the azo compound as guest. On irradiation of the mixture, only the capsule assembly **2·2** is obtained with **6** as guest. The precipitation of **5** from solution is observed. On heating the turbid solution for 2 min to 160 °C, the original extended assembly **2·5₄·2** is restored with *trans*-**4** as the guest (Fig. 6).

We are currently working to apply photoisomerism to control chemical reactions not known to be photosensitive. This could be done for the reaction of carboxylic acids with isonitriles that take place under ambient conditions in the capsules^{xxv} but require microwave heating in free solution.^{xxvi}

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Figure 1.

An armadillo lizard and the ouroborand in various depictions: (a) planar formula and (b) energy minimized structures with the bipyridine ligand free or chelating a metal center; (c) perspective views.

Figure 2.
The reversible cycle of coordination-controlled guest exchange in the ouroboraand's cavity.

Figure 3.

NMR spectra of the coordination-triggered guest-exchange of the ouroborand; (a) pure ouroborand in mesitylene- d_{12} (80%) and CD_3CN (20%); (b) 10 eq. AdCN added in the NMR tube; (c) 10 eq. $ZnBr_2$ added in the NMR tube; (d) water added to the NMR tube, then extraction and drying on Na_2SO_4 .

Figure 4.

a) Light induced guest exchange of trans-**1** by n-tridecane in capsule **2'2**. **b)** Indicative regions of the ¹H NMR spectra (mesitylene-d₁₂, 20 °C) are shown before irradiation (trans-**1** is the only guest) and after irradiation at 365 nm wavelength for 50 min at 20 °C (n-tridecane is the only guest). After heating the sample to 160 °C for 2 min, the initial state is restored.

Figure 5.

a) Light induced guest exchange of *trans*-4 by the homodimer of 4-ethylbenzamide in the extended assembly $2 \cdot 3_4 \cdot 2$. **b)** Indicative regions of the ^1H NMR spectra (mesitylene- d_{12} , 20 °C) are shown before irradiation (*trans*-4 is the only guest) and after irradiation at 365 nm wavelength for 50 min at 20 °C (the homodimer of 4-ethylbenzamide is the only guest). After heating the sample to 160 °C for 2 min, the initial state is completely restored.

Figure 6. **a)** Light induced guest and capsule exchange. **b)** The ¹H NMR spectrum (mesitylene-d₁₂, 20 °C) is shown before irradiation (trans-4 is the guest in the extended assembly **2·5₄·2**) and after irradiation at 365 nm wavelength for 50 min at 20 °C (4,4'-dibromobenzil is the guest in the capsule **2·2**). After heating the sample to 160 °C for 2 min, the starting point is completely restored.