ORGANIC
LETTERS

2000
Vol. 2, No. 24
3817−3819

Molecular Assembly and Disassembly: Novel Photolabile Molecular Hosts

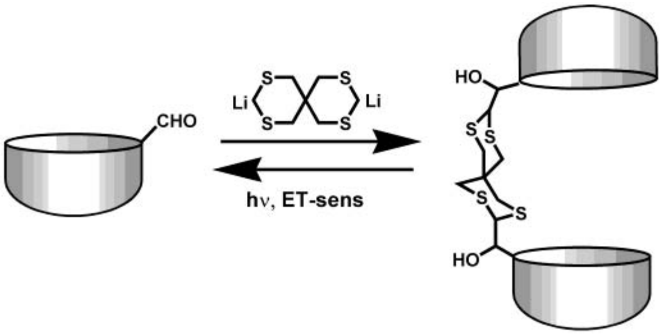
**Yongqin Wan, Oleg Mitkin, Loren Barnhurst, Alexei Kurchan, and
Andrei Kutateladze***

*Department of Chemistry and Biochemistry, University of Denver,
Denver, Colorado 80208-2436*

akutatel@du.edu

Received October 5, 2000

ABSTRACT

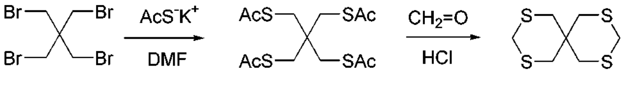


A new approach to the assembly and photochemical disassembly of molecular hosts is developed. It is based on photoinduced fragmentation in hydroxyalkyl dithianes and utilizes a novel spiro-bis-dithiane as a photolabile molecular tether to link two formylated macromolecular blocks, e.g., formyl calixarenes or formyl dibenzocrown ethers. A key feature of this molecular system is that after an assembly–disassembly cycle the starting macromolecular blocks are recovered intact and can be used again.

Basic and applied research targeting large molecules and supramolecular self-assembly has been on a steady rise over the past decade. We would argue that issues relevant to molecular *disassembly* should be an integral part of this development. In this context we have been searching for molecular latches that can be used to hold macromolecular building blocks together and, at the same time, can be selectively unfastened on demand.

Our specific approach is based on photoinduced fragmentation in hydroxyalkyl dithianes (Corey−Seebach dithiane−carbonyl adducts[1]) that we have recently developed.[2] This system possesses several features that make it appropriate for utilization as a molecular latch with a phototrigger: (i) the "assembly" step makes use of Corey−Seebach chemistry successfully implemented in numerous synthetic sequences; (ii) the nature of the newly formed carbon−carbon bond allows building robust molecular systems; (iii) the "disassembly" step is nearly quantitative—we have previously shown that the yields for release of aromatic aldehydes from their dithiane adducts upon ET sensitization are in the 95+% range.

In this paper we report the assembly of macromolecular hosts equipped with a photolabile latching module based on 2,4,8,10-tetrathiaspiro[5.5]undecane **1**, a novel spiro-bis-dithiane that we synthesized from pentaerythrityl tetrabromide.[3]



1

While other bis-dithianes (e.g., polymethylene-linked at position 5) may also be utilized, the spiro-bis-dithiane **1** has the advantage of being the shortest tether possible in the bis-dithiane family. It is also much easier to synthesize, as

---

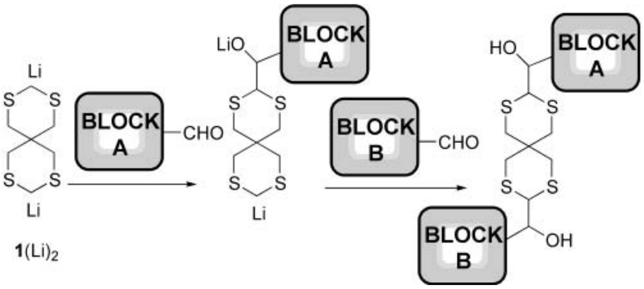
[1] For a review, see: Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.
[2] McHale, W. A.; Kutateladze, A. G. *J. Org. Chem.* **1998**, *63*, 9924.

10.1021/ol006692d CCC: $19.00

compared with the tedious multistep malonate-based approach.[4] This is important because of the sacrificial nature of the tether—due to partial degradation of the dithiane moiety in secondary photoprocesses it is not practical to recover the latch itself after the photodisassembly step.

We assemble the desired hosts by reacting dilithiated **1** with two macromolecular blocks bearing formyl groups (Scheme 1). This general strategy can be implemented for either the same or different Blocks A and B, thus providing access to both symmetric and "crossbreed" systems. A variety of compounds having a benzaldehyde fragment in their structure are suitable for such assembly.

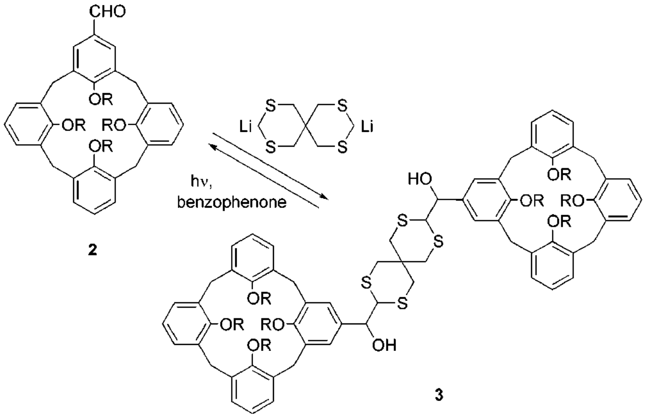
Scheme 1



Attempts to conjoin large macromolecular units with photolabile linkers are certainly not unprecedented in the literature. For example, McGrath recently utilized a classic *o*-nitrobenzyl alcohol-based tether to synthesize a photolabile dendrimer.[5] A critical distinction of our approach is that the latching mechanism is not permanently attached to either of the pieces it is holding together. It implies that such a molecular system can be photochemically *taken apart* in a fashion that allows for the recovery of larger (and implicitly more labor intensive) components at a sacrifice of smaller, less important pieces.

We first exemplify our approach utilizing monoformylated calix[4]arene **2**[6] as a building block (R = $CH_3CH_2OCH_2CH_2$). Its reaction with dilithiated **1** in THF furnishes biscalixarene **3** in a 71% yield[7] (Scheme 2).

Scheme 2



Irradiation of **3** (medium-pressure mercury lamp, Pyrex filter) in acetonitrile in the presence of benzophenone regenerates the formylcalixarene **2** nearly quantitatively (>95%). This is in keeping with our previous observations that electron-donating substituents in the aromatic moiety increase the quantum efficiency of the fragmentation.[2]

An interesting geometrical feature of bis-calixarenic hosts such as **3** is that they can assume a "pac-man" conformation with a clearly defined cavity (Figure 1).

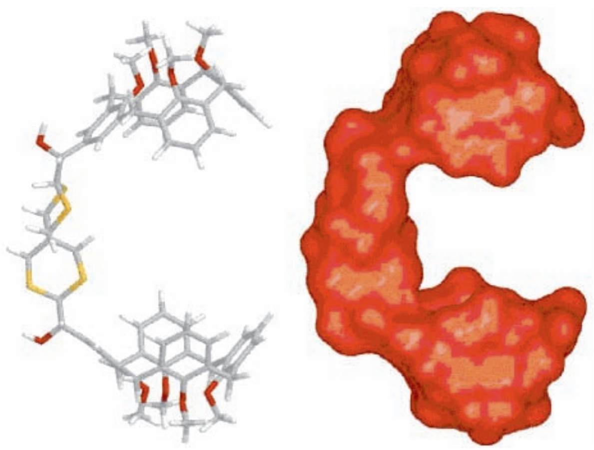


Figure 1. Force field geometry of the pac-man conformation of **3** (R = Me for computational simplicity). The solvent-excluded surface shows a 10 Å cavity (right).

Although **3** is suitable for hosting various guests, in this Letter we report our preliminary results on its complex with fullerene. Figure 2 reveals a nice computational fit. Experi-

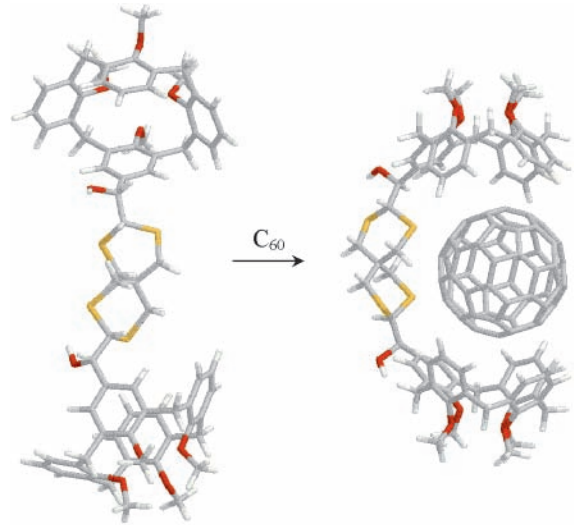


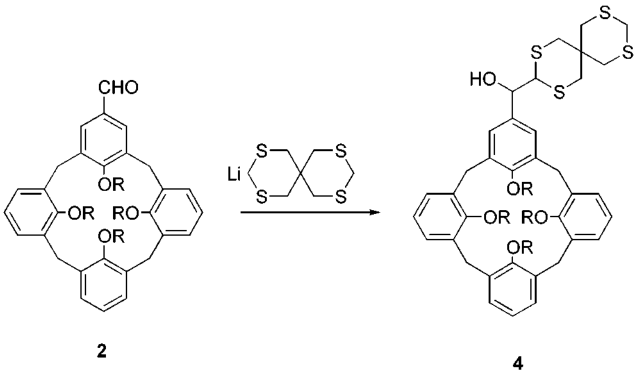
Figure 2. Force field geometries of an open conformation of **3** (left) and the pac-man conformation with entrapped C_{60} (R = Me for computational simplicity).

mentally, both ^{1}H and ^{13}C NMR of **3** showed considerable signal dispersion, especially in the aromatic part of the spectra, upon addition of fullerene in benzene-d_6. At the same time, NMR gives us no indication that the individual calix[4]arene **2** forms any complexes with fullerene. While complexes of fullerenes with bis-calix[*n*]arenes were reported for $n \geq 5$,[8] to the best of our knowledge such complexes with molecular hosts based on bis-calix[4]arenes have not yet been reported. Of "monomeric" calixarenes, only larger calix[8]arenes are known to form complexes with fullerenes, so it is not surprising that **2** itself is indifferent toward C_{60}.

We conducted a pulse field gradient LED NMR study[9] to determine translational diffusion coefficients of the free host and its complex with C_{60}. The diffusion coefficient (D_S) for the monocalixarene **2** was found to be 7.05×10^{-6} cm^2/s at 25 °C (interpolated to infinite dilution). Expectedly, D_S for the free host **3** is about half of that value, 3.13×10^{-6} cm^2/s. However, the diffusion coefficient for the complex with C_{60} is actually slightly higher than that: 3.45×10^{-6} cm^2/s. Our rationale is that by acquiring the fullerene molecule the bis-calixarene becomes more *compact* than the conformationally flexible free host, thus improving its mobility (Figure 2). More details on guest−host interactions in such complexes will be presented in the full paper.

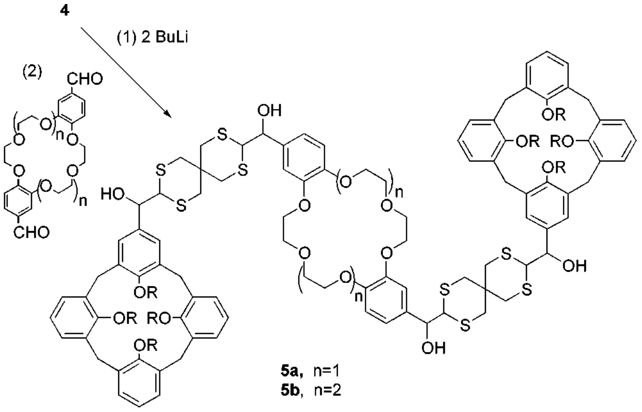
The "assembly" of the novel molecular hosts can also be carried out in a stepwise manner. Using 1 equiv of butyllithium we generate monolithio-**1,** which reacts with **2** to produce the monoadduct **4** (Scheme 3).

Scheme 3



Compound **4** proved to be a useful building block for assembling more complex systems. Treating **4** with 2 equiv of butyllithium and reacting it with bis-formyl dibenzo-18-crown-6 or -24-crown-8 furnishes hybrid hosts **5a**,**b** with the crown moiety at the core flanked by two calixarenes (18% and 26% yields, respectively) (Scheme 4).

Scheme 4



As in the case with bis-calixarene **3**, the hybrids **5a** and **5b** disassemble photochemically, regenerating the formylated calix[4]arene and respective dibenzocrown ethers. Work is underway to study complexation properties of the host molecules **3**, **5a**, and **5b** and other spiro-bis-dithiane hosts and to assess photophysical properties of their complexes.

Acknowledgment. Support of this research by the National Science Foundation (Career Award CHE-9876389) is gratefully acknowledged.

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

OL006692D

---

(3) For experimental details, see Supporting Information.

(4) Luk'yanenko, N. G.; Mel'nik, O. T. *Zh. Org. Khim.* **1989**, *25*, 2186.

(5) Smet, M.; Liao, L.-X.; Dehaen, W.; McGrath, D. V. *Org. Lett.* **2000**, *2*, 511.

(6) Arduini, A.; Fanni, S.; Manfredi, G.; Pochini, A.; Ungaro, R.; Sicuri, A. R.; Ugozzoli, F. *J. Org. Chem.* **1995**, *60*, 1448.

(7) The spiro-bis-dithiane−carbonyl adducts described in this work are isolated without separating the individual diastereomers.

(8) Wang, J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1998**, *120*, 12226.

(9) Altieri, A. S.; Hinton, D. P.; Byrd, R. A. *J. Am. Chem. Soc.* **1995**, *117*, 7566. For the original paper, see: Stejskal, E. O.; Tanner, J. E. *J. Chem. Phys.* **1965**, *42*, 288.