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Self-Assembling Bisurea Macrocycles Used as an Organic Zeolite for a Highly Stereoselective Photodimerization of 2-Cyclohexenone

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In nature, enzymes provide highly tailored microenvironments that promote reactions with high regio- and stereoselectivity. Chemists have long sought to design artificial cavities that can direct reactions with comparable levels of selectivity. A number of groups have designed and synthesized hollow host molecules,[1] while others have explored the use of inorganic materials with internal cavities, such as zeolites[2] and clays,[3] that provide well-defined microenvironments for reactions. Herein, we report the highly selective 2 + 2 cycloaddition of 2-cyclohexenone in the presence of self-assembled apohost **1** to yield the head-to-tail dimer (HT) **2a** in high conversion. This is in contrast to the photodimerization of 2-cyclohexenone within other confined environments that yield the head-to-head (HH) dimer **2b** and are limited to lower degrees of conversion to minimize secondary photorearrangements.[4] Another advantage to our method is that apohost **1** can be easily recovered and reused much like a zeolite.

Supramolecular chemistry offers great promise in reducing the size of the molecular building blocks that must be covalently synthesized while still directing the assembly of nanometer-sized cavities and channels with microenvironments designed to bind guest molecules[1,5] and regulate specific reactions.[2] One strategy is to use self-assembled macrocycles. We have reported the synthesis and self-assembly of macrocycle **1** to form apohost **1** that has columnar channels with an inner diameter of ~9−10 Å and can reversibly bind guests (Figure 1).[6] Macrocycle **1** self-assembles through strong, directional urea−urea hydrogen bonds and aromatic stacking interactions into columnar structures that pack together to form porous crystals (apohost **1**).

Apohost **1** can be readily loaded with guest 2-cyclohexenone.[7] First, macrocycle **1** was self-assembled in acetic acid.[6] The AcOH guest was removed by heating at 120 °C for 2 h to form apohost **1**, which is stable to UV irradiation for 48 h and shows no phase changes below 300 °C by DSC. The 2-cyclohexenone was introduced by vapor treatment (method a).[8] The loading of apohost **1** with the enone was measured by thermogravimetric analysis (Figure 2a) and ^{1}H NMR. The apohost **1**·2-cyclohexenone complex is highly ordered and gives a powder X-ray diffraction (PXRD) pattern distinct from that of the apohost (Figure 2b). ^{1}H NMR of the bound complex after PXRD showed no change in structure, and the material was stable in the dark at room temperature for weeks. Photodimerization of 2-cyclohexenone with apohost **1** was highly selective, yielding dimer **2a** (96%) after 24 h. The high degree of selectivity for **2a** is unusual. Zeolites, for example, typically favor **2b**, with Saponite giving the highest reported selectivity (82% of **2b**).[3] The apohost **1**·2-cyclohexenone complex was irradiated under UV light at room temperature with a Hanovia 450 W medium pressure mercury arc lamp. The reaction was monitored over 24 h. The disappearance of starting material corresponded with the appearance of **2a**. Analysis by ^{1}H NMR in DMSO-d_6 showed only peaks corresponding to macrocycle **1**, unreacted 2-cyclohexenone, and dimer **2a**. We measured 15.5% conversion to **2a** at 15 min and 44.5% conversion at 1 h. After 24 h, dimer **2a** was the major product and no enone was detectable by ^{1}H NMR or GC/MS.

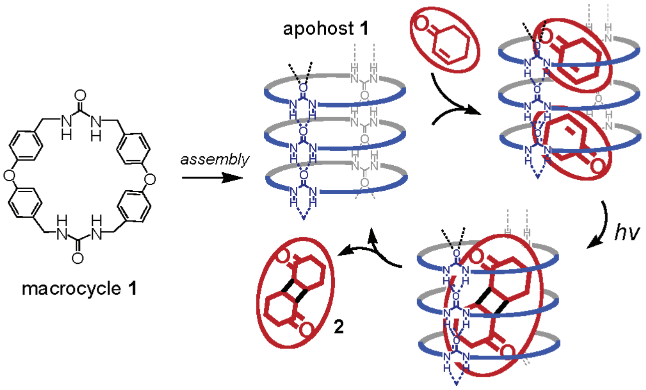


Figure 1. Bisurea macrocycle **1** self-assembles into tubular structures that can bind 2-cyclohexenone molecules. Irradiation of the enone in the confined environment selectively yields the head-to-tail photodimer.

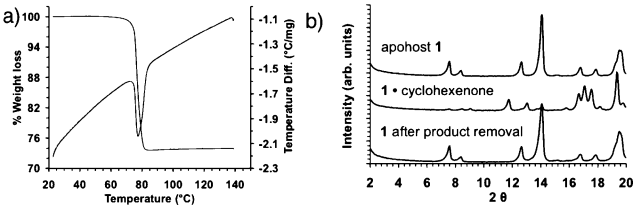
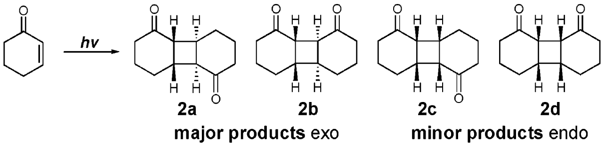


Figure 2. (a) Simultaneous TGA/DTA study of apohost **1**·2-cyclohexenone complex. (b) PXRD comparison of apohost **1** (top), apohost **1**·2-cyclohexenone complex (middle), and apohost **1** after the photoreaction (bottom).

Scheme 1. Photolysis of Neat 2-Cyclohexenone without Assembled **1** versus Photolysis of **1**·2-Cyclohexenone



	2a	2b	2c	2d
without apohost 1:	35%	49%	8%	8%
with apohost 1:	96%	3%	<1%	1%

The photoproducts can be separated from apohost **1** by washing with CH$_2$Cl$_2$, and apohost **1** was recovered. The ^{1}H NMR of the CH$_2$Cl$_2$ extract closely matched the product distribution that was observed by direct dissolution of the complex. Furthermore, ^{1}H NMR analysis of the recovered apohost showed peaks corresponding to macrocycle **1** and residual solvent, indicating that 2-cyclohexenone starting material and products were efficiently removed by the extraction process. The recovered apohost shows no change in structure by NMR and displays a PXRD pattern with peak positions and intensities nearly identical to those of the original apohost (Figure 2b, bottom). The ^{1}H NMR of the crude photolysis product extracted from apohost **1** (Figure 3) shows only the

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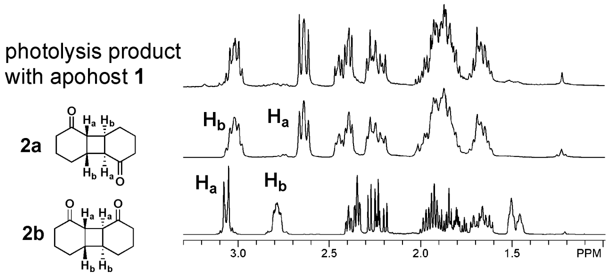

Figure 3. ^{1}H NMR (CDCl$_3$) comparison of crude photolysis product from apohost **1** (top) with standards for photodimer products **2a** and **2b**.

Table 1. Reaction Selectivity with Apohost **1**[8,10]

method	binding ratio **1**:enone	selectivity (%) 2a	2b	2c	2d
control		35	49	8	8
a	1:0.7	96	3	<1	1
b	1:1.4	94	3	2	1
c	1:2.0	90	7	2	1

chemical shifts of the head-to-tail dimer (**2a**), indicating a high degree of selectivity. ^{1}H NMR was not sensitive enough to detect **2b** or photorearrangement products **2c** and **2d**.

More careful analysis by GC/MS confirmed that the photodimerization reaction was highly selective for dimer **2a** (96%) versus **2b** (3%). In addition, the dimerization of 2-cyclohexenone in the presence of apohost **1** displayed decreased incidence of secondary photorearrangements (**2c** + **2d**, 1.2% versus 16% in the control). The high selectivity for the HT dimer **2a** and the reduced rate for secondary photorearrangement observed in the apohost **1** complexes suggest that a controlled photodimerization was occurring within a confined environment formed by apohost **1**.

We investigated the reaction selectivity of apohost complexes formed under different conditions. Crystalline apohost **1** was ground to a powder and equilibrated with 2-cyclohexenone vapor (method b) or immersed in liquid 2-cyclohexenone (method c).[10] The three guest loading methods gave different loading ratios by ^{1}H NMR (Table 1). Loading of enone vapor was kinetically slow (~5 days) and may be limited by accessibility as ground apohost **1** had higher loading than unground (methods b and a). Immersion of the ground apohost in neat enone (2 h, method c) gave higher loading values than equilibration with 2-cyclohexenone vapor (method b). The reasons for the dependence of the **1**:enone ratio on the loading method are under investigation.

Regardless of loading method, the photodimerization of the 2-cyclohexenone·apohost **1** complexes showed selectivity for the head-to-tail dimer **2a** (90−96%). The highest selectivity was observed with the lowest loading of enone. The selectivity observed with partial loading (method a) decreased a few percent when 2-cyclohexenone loading was increased 2- and 3-fold (methods b and c). Apohost **1** was efficient in templating the 2 + 2 reaction. In method c, the apohost **1**:enone ratio was 1:2, and yet high selectivity (90% **2a**) and conversion were observed. Multiple runs showed similar product selectivity. The recovered apohost can be reused multiple times by immersion in liquid 2-cyclohexenone (method c).

In summary, we report the application of porous apohost **1** as a confined environment for the selective 2 + 2 photoreaction of 2-cyclohexenone. The enone guest was readily loaded into these materials by vapor treatment or soaking in neat enone. Irradiation of the apohost **1**·enone complexes selectively yielded the head-to-tail dimer, which could be readily extracted from the crystalline apohost **1**. Furthermore, apohost **1** was easily recovered and reused after the reaction. We are currently investigating the use of our system as an organized environment to control the 2 + 2 photoadditions of other cyclic and acyclic enones.

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Supporting Information Available: Synthesis and characterization of key compounds are included. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Rebek, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 2068−2078. (b) Conn, M. M.; Rebek, J. *Chem. Rev.* **1997**, *97*, 1647−1668.

(2) (a) Turro, N. J. *J. Photochem. Photobiol., A* **1996**, *100*, 53−56. (b) Ramamurthy, V.; Eaton, D. F.; Caspar, J. V. *Acc. Chem. Res.* **1992**, *25*, 299−307. (c) Hashimoto, S. *J. Photochem. Photobiol., C* **2003**, *4*, 19−49. (d) Garcia, H.; Roth, H. D. *Chem. Rev.* **2002**, *102*, 3947−4007. (e) Tung, C. H.; Wu, L. Z.; Zhang, L. P.; Chen, B. *Acc. Chem. Res.* **2003**, *36*, 39−40. (f) Kaupp, G. *Top. Curr. Chem.* **2005**, *254*, 95−183. (g) MacGillivray, L. R.; Papaefstathious, G. S.; Friscic, T.; Varshney, D. B.; Hamilton, T. D. *Top. Curr. Chem.* **2004**, *248*, 201−221.

(3) (a) Madhavan, D.; Kasi, P. *Photochem. Photobiol. Sci.* **2002**, *1*, 991−995. (b) Usami, H.; Takagi, K.; Sawaki, Y. *Chem. Lett.* **1992**, *8*, 1405−1408.

(4) (a) Boyd, M. K.; Zopp, G. M. *Annu. Rep. Prog. Chem., Sect. B* **2003**, *99*, 396−419. (b) Tanaka, K.; Kakinoki, O.; Toda, F. *J. Chem. Soc., Perkin Trans. 1* **1992**, *3*, 307. (c) Tanaka, K.; Mochizuki, E.; Yasui, N.; Kai, Y.; Miyahara, I.; Hirotsu, K.; Toda, F. *Tetrahedron* **2000**, *56*, 6853−6865. (d) Yoshizawa, M.; Takeyama, Y.; Okano, T.; Fujita, M. *J. Am. Chem. Soc.* **2003**, *125*, 3243−3247. (e) Yoshizawa, M.; Fujita, M. *Pure Appl. Chem.* **2005**, *77*, 1107−1112.

(5) (a) Ohmori, O.; Kawano, M.; Fujita, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1962−1964. (b) Ghadiri, M. R.; Granja, J. R.; Buehler, L. K. *Nature* **1994**, *369*, 301. (c) Ranganathan, D.; Lakshmi, C.; Karle, I. L. *J. Am. Chem. Soc.* **1999**, *121*, 6103−6107. (d) Van Esch, J.; Schoonbeek, F.; De Loos, M.; Kooijman, H.; Spek, A. L.; Kellogg, R. M.; Feringa, B. L. *Chem.*−*Eur. J.* **1999**, *5*, 937−950. (e) Ranganathan, D.; Lakshmi, C.; Haridas, V.; Gopikumar, M. *Pure Appl. Chem.* **2000**, *72*, 365−372. (f) Semetey, V.; Didierjean, C.; Briand, J. P.; Aubry, A.; Guichard, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1895−1898. (g) Snellink-Ruel, B. H. M.; Antonisse, M. M. G.; Engbersen, J. F. J.; Timmerman, P.; Reinhoudt, D. N. *Eur. J. Org. Chem.* **2000**, *1*, 165−170. (h) Choi, K.; Hamilton, A. D. *Coord. Chem. Rev.* **2003**, *240*, 101−110.

(6) (a) Shimizu, L. S.; Hughes, A. D.; Smith, M. D.; Samuel, S. A.; Ciurtin-Smith, D. *Supramol. Chem.* **2005**, *17*, 27−30. (b) Shimizu, L. S.; Hughes, A. D.; Smith, M. D.; Davis, M. J.; Zhang, B. P.; Zur Loye, H. C.; Shimizu, K. D. *J. Am. Chem. Soc.* **2003**, *125*, 14972−14973.

(7) Crystals of apohost **1** show a type 1 isotherm by BET at 0 °C using CO$_2$. This behavior is consistent with a microporous material.

(8) Loading method a: Crystals of assembled **1** were heated at 120 °C for 2 h, cooled in a desiccator, and equilibrated with 2-cyclohexenone vapor in a sealed vessel for 12 h to 2 weeks. Loading of the enone vapor was time dependent and reached a maximum at 5−7 days.

(9) (a) Valentine, D.; Turro, N. J.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 5202−5208. (b) Lam, E. Y. Y.; Donald, V.; Hammond, G. S. *J. Am. Chem. Soc.* **1967**, *89*, 3482−3487. (c) Wagner, P. J.; David, J. B. *J. Am. Chem. Soc.* **1969**, *91*, 5090−5097. (d) Lem, G.; Nikolas, K. A.; Schuster, D. I.; Ghatlia, N. D.; Turro, N. J. *J. Am. Chem. Soc.* **1993**, *115*, 7009−7010. (e) Anklam, E. K.; Wilfried, A.; Margaretha, P. *Tetrahedron Lett.* **1983**, *24*, 5851−5854. (f) Schuster, D. I.; Lem, G.; Kaprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3−22. (g) Cecil, J. C.; Dyer, C. W.; Fleming, S. A.; Jessop, T. C. *Anal. Sci.* **1999**, *15*, 895−897.

(10) Guest loading methods: Assembled **1** was ground to a powder, heated at 120 °C for 2 h, and cooled in a desiccator. (method b) The apohost powder was equilibrated with 2-cyclohexenone vapor for 12 h to 2 weeks. (method c) The apohost powder was immersed in liquid cyclohexenone for 2 h. The complex was recovered by filtration.

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