ORGANIC LETTERS

2007
Vol. 9, No. 24
5059−5062

Controlling Photochemical Geometric Isomerization of a Stilbene and Dimerization of a Styrene Using a Confined Reaction Cavity in Water

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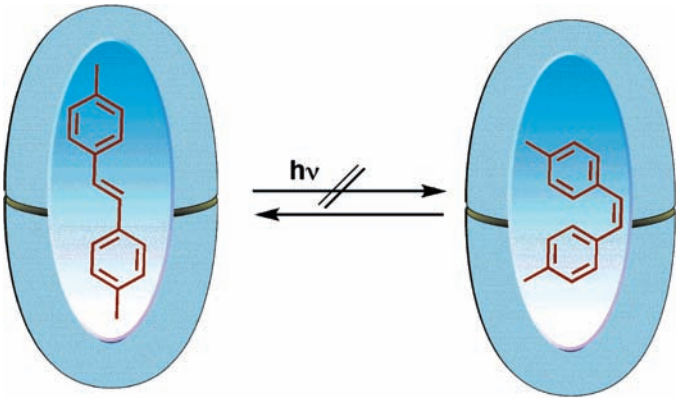
Received September 24, 2007

ABSTRACT



Utility of a water-soluble deep cavity cavitand, octa acid, as a reaction medium is illustrated by carrying out photochemical reactions of a stilbene and a styrene included within the octa acid in water. Geometric isomerization of *trans*-4,4′-dimethyl stilbene is restricted while dimerization of 4-methyl styrene is facilitated within the octa acid cavity. The excited-state chemistry of both systems is different in this medium from that in organic solvents. The change in chemistry is attributed to the supramolecular effects provided by the host cavity.

Two most common reactions of olefins are geometric isomerization and dimerization.[1] Geometric isomerization is utilized by proteins to trigger a number of biological events,[2] whereas dimerization is used by synthetic chemists to build complex molecules having cyclobutane rings.[3] Devising strategies to perform the above two reactions with high specificity in water is a worthwhile goal. We have been exploring with reasonable success the use of a synthetic water-soluble deep cavity cavitand known as octa acid (OA)[4] with dimensions shown in Figure 1 as a reaction cavity for photochemical reactions.[5] In this report we demonstrate that it forms supramolecular complexes with olefins such as

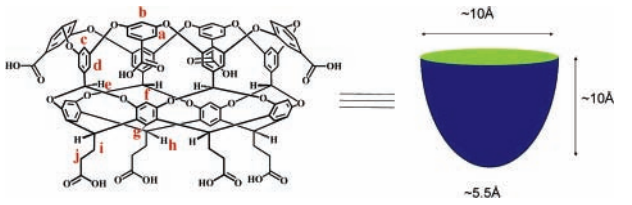


Figure 1. Pictorial representation of OA.

(1) Turro, N. J. *Modern Molecular Photochemistry*; University Science Books: Sausalito, CA, 1991.

(2) (a) Dugave, C., Ed. *cis-trans Isomerization in Biochemistry*; Wiley-VCH: Weinheim, Germany, 2006. (b) Dugave, C.; Demange, L. *Chem. Rev.* **2003**, *103*, 2475−2532. (c) van der Horst, M. A.; Helingwerf, K. J. *Acc. Chem. Res.* **2004**, *37*, 13−20. (d) Zimmer, M. *Chem. Rev.* **2002**, *102*, 759−781.

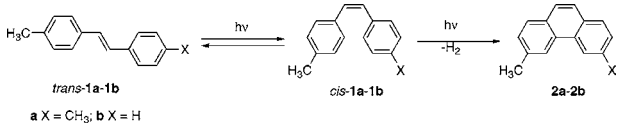
(3) Griesbeck, A. G., Mattay, J., Eds. *Synthetic Organic Photochemistry*; Marcel Dekker Inc.: New York, 2005.

10.1021/ol702322u CCC: $37.00
Published on Web 10/23/2007

stilbenes and styrenes in borate buffer at pH > 8.9 and controls the excited-state behavior of both 4,4′-dimethylstilbene and 4-methylstyrene.

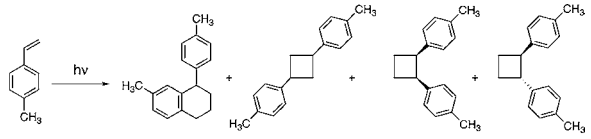
The emission from *trans*-4,4′-dimethylstilbene (**1a**; 2×10^{-5} M) in borate buffer was broad, characteristic of aggregates.[6] Remarkably, upon addition of OA (4×10^{-5} M) the turbid buffer solution containing **1a** became transparent, and the emission characteristic of monomer *trans*-**1a** appeared (Supporting Information, Figure S1). This observation opened up the possibility of investigating in detail host−guest complexation, photochemistry and photophysics of *trans* and *cis* isomers of **1a** and 4-methylstilbene (**1b**) and

Scheme 1. Photoisomerization of Stilbene



4-methylstyrene (**3**) placed within the OA capsule in water (Schemes 1 and 2).

Scheme 2. Photodimerization of 4-Methylstyrene



3	4	5	6	7
Acetonitrile / N_2 (ref. 10)	7	-	83	10
Benzene / Tetracyanobenzene (ref. 12)	54	-	20	26
Benzene / Benzophenone (ref. 10)	3	-	22	75
OA	45	55	-	-

Formation of 1:2 (guest:host) complexes in D_2O (pD ≈ 8.9; borate buffer) by *trans* and *cis* isomers of **1a** and **1b** with OA was established through ^{1}H NMR titration experiments (Figures S2 and S3 in Supporting Information). The identical nature of the top and bottom halves of the OA capsule in the case of **1a** was suggested by the single signal ($\delta = -2.3$ ppm) for both methyl groups of *trans*-**1a** molecule, reflecting symmetrical positioning within the OA capsule (Figure 2). This was reinforced by the single set of

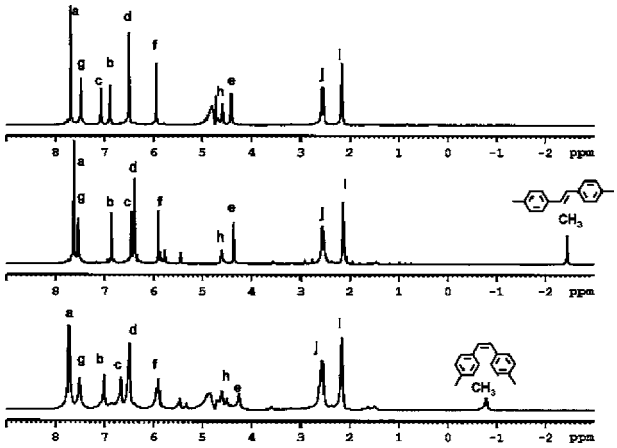


Figure 2. ^{1}H NMR (500 MHz, 20 mM borate buffer/D_2O) spectra of (i) OA (2 mM, top), (ii) 1:2 complex of *trans*-**1a** with OA (middle), and **(**iii**)** 1:2 complex of *cis*-**1a** with OA (bottom).

signals observed for the two OA molecules forming the top and bottom halves of the capsule. The large upfield shift in the signals due to methyl hydrogens of *trans*-**1a** ($\Delta\delta$ with respect to $CDCl_3 = -4.65$ ppm) suggested them to be located deeper within the tapering poles of the capsule where the aryl rings provide magnetic shielding. Pictorial representations of the NOESY data (Figure 3) reveal interactions

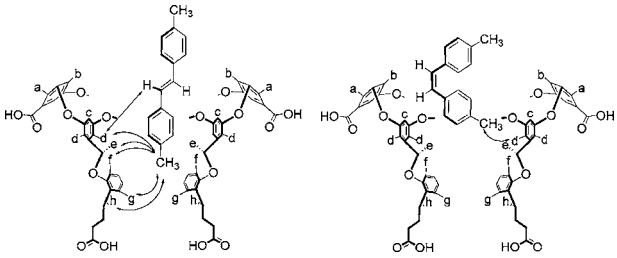


Figure 3. Pictorial representation of the NOESY correlations of *trans*-**1a** and *cis*-**1a** with one-half of OA.

between the methyl group of *trans*-**1a** and H_d, H_e, H_f, H_g, and H_h of OA (Figure 1 for lettering of hydrogens in OA) (Figure S4 for NOESY data in Suporting Information). Upfield shift for the methyl group of *trans*-**1b** ($\delta = -2.1$ ppm; $\Delta\delta = -4.45$ ppm) and NOESY data (Figure S5 in Supporting Information) suggested the methyl group to be positioned at the narrower ends of the capsule similar to that of *trans*-**1a**.

In contrast to the *trans* isomers, ^{1}H NMR and NOESY data (*cis*-**1a**: $\delta = -0.7$ ppm; *cis*-**1b**: $\delta = -1.2$ ppm; Figures S6 and S7 in Supporting Information) suggested the methyl groups of the *cis* isomers to be located near the spacious equatorial region of the capsule. Thus, NMR data clearly indicated *cis* and *trans* isomers of **1a** and **1b** to occupy different regions of the capsule having different amounts of

(4) Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2004**, *126*, 11408−11409.

(5) (a) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2004**, *126*, 14366. (b) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 3674−3675. (c) Kaanumalle, L. S.; Ramamurthy, V. *Chem. Commun.* **2007**, 1062−1064. (d) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C. *Org. Biomol. Chem.* **2007**, *5*, 236−238. (e) Natarajan, A.; Kaanumalle, L. S.; Jockusch, S.; Gibb, C. L. D.; Gibb, B. C.; Turro, N. J.; Ramamurthy, V. *J. Am. Chem. Soc.* **2007**, *129*, 4132−4133. (f) Sundaresan, A. K.; Ramamurthy, V. *Org. Lett.* **2007**, *9*, 3575−3578.

(6) Catalan, J.; Zimanyi, L.; Saltiel, J. *J. Am. Chem. Soc.* **2000**, *122*, 2377−2378.

free space around the C═C bond of the stilbenes. We envisioned that the differences in the available free space around the two isomers would have significant impact on their excited-state rotational dynamics. With this in mind we irradiated the OA encapsulated *trans* and *cis* isomers of **1a** and **1b** and analyzed the products by ^{1}H NMR (in situ) and by GC (following extraction with $CDCl_3$).

Within 15 min of irradiation ($\lambda > 310$ nm) *trans*-**1a** in hexane (5×10^{-3} M) established a pseudostationary state consisting of 18% *trans* and 76% *cis*. Upon continued irradiation phenanthrene was the final product.[7] Similar excitation of *trans*-**1a**@OA_2 capsule ([*trans*-**1a**]: 5×10^{-4} M and [OA]: 10^{-3} M) only led to slow isomerization and to establishment of a pseudostationary state in about an hour consisting of 85% *trans* and 15% *cis* isomers (Figure S8 in Supporting Information for absorption spectra of **1a** and OA).[8] Phenanthrene was formed in less that 5% yield even after 4 h of irradiation. Consistent with slow isomerization of *trans* to *cis* and enhanced fluorescence, the excited singlet state of *trans*-**1a** had a longer lifetime (τ: 1.51 ns) within OA capsule than in hexane ($\tau < 0.7$ ns) (Figure S9 in Supporting Information). The specific effect of the capsule on the *trans* isomer was confirmed by the fast isomerization obtained with *cis*-**1a**@OA_2 ([*cis*-**1a**]: 5×10^{-4} M and [OA]: 10^{-3} M) that showed 85% transformation to the *trans* isomer within 30 min. Above results unequivocally established the OA capsule to have a significant impact on the excited singlet state rotational dynamics of *trans*- but not of *cis*-**1a**. We believe the extraordinary influence of OA on the isomerization of **1a** to result from the "tighter fit" of *trans*-**1a** at the tapered ends of the capsule that provide a barrier for the relocation of the two methyl groups from the narrower bottom to broader middle region of the capsule (*trans* to *cis* conversion).

The above model suggested that removal of one methyl group from **1a** should allow isomerization by the flipping of the unsubstituted phenyl ring that has more free space around it. Investigations of the excited-state behavior of *trans*-4-methylstilbene (**1b**) that would clarify this speculation were pursued. Irradiation of *trans*-**1b** in hexane (5×10^{-4} M) and in water ([*trans*-**1b**]: 5×10^{-4} M and [OA]): 10^{-3} M; pH $\approx$ 8.9) as OA complexes gave identical mixtures of *cis* and *trans* isomers (85% and 15%).[8] Further, the lifetime of the excited singlet state of *trans*-**1b** ($\tau < 0.7$ ns in both OA and hexane) remained unaffected within the capsule. These studies unequivocally demonstrated that the excited-state geometric isomerization of **1b** is independent of the capsule, while that of **1a** is dependent. A comparison of the behavior of **1a** and **1b** suggested that the influence of OA on the excited-state behavior of guests is structure specific.

On the basis of the above results we visualized that two olefin molecules could be included within OA capsule, provided they are smaller in size than stilbenes **1a** and **1b**. With this in mind we explored the chemistry of 4-methylstyrene **3** (Scheme 2). ^{1}H NMR titration experiments revealed that, as expected, **3** formed 2:2 complexes with OA (Figure S10 in Supporting Information). Surprisingly, in the case of **3** two complexes with different arrangements of the olefin were identified by ^{1}H NMR. Two signals of unequal intensity (55:45) at -0.5 and -0.8 ppm (Figure 4) due to the 4-methyl

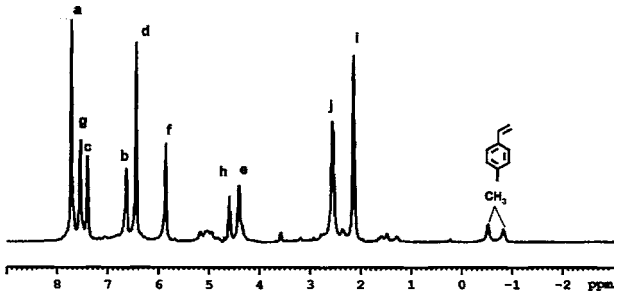


Figure 4. ^{1}H NMR (500 MHz, 20 mM borate buffer/D_2O) spectrum of 2:2 complex of **3** with OA.

group suggested the existence of two complexes with different structures. Had the signals been due to methyl group of two olefin molecules (arranged in an unsymmetrical fashion) of a single complex, the intensity of the two should have been equal. Observation of only one set of signals for the host protons (Figure 4) further suggested that the two olefin molecules are arranged in a symmetrical fashion within the capsule in each of these complexes. On the basis of NOESY data we speculate the two complexes to have structures **A** and **B** shown in Figure 5.

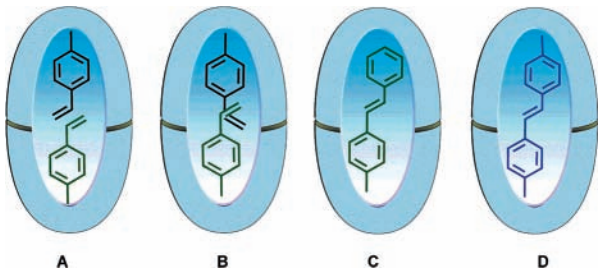


Figure 5. Cartoon representation of the encapsulated guest molecules in OA.

Irradiation (>290 nm) of **3** included within OA ([**3**]:[3] 10^{-3} M and [OA]: 10^{-3} M) gave two dimers **4** and **5** in the ratio 45:55 (Scheme 2), identical to the ratio of the two complexes present in solution (Figure S11 in Supporting Information for absorption spectra of **3** and OA).[9] This suggested that

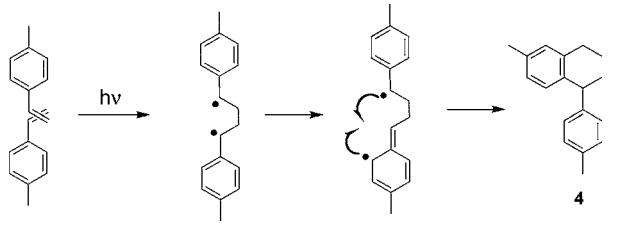
(7) (a) Mallory, F. B.; Mallory, C. W. In *Organic Reactions*; Dauben, W. G., Ed.; John Wiley & Sons, Inc.: New York, 1984; Vol. 30, pp 1−455. (b) Saltiel, J.; D'Agostino, J.; Megarity, E. D.; Metts, L.; Neuberger, K. R.; Wrighton, M.; Zafiriou, O. C. In *Organic Photochemistry*; Chapman, O. L., Ed.; Marcel Dekker, Inc.: New York, 1973; Vol. 3, pp 1−113.

(8) Stilbene absorbs at a slightly longer wavelength than OA. At the irradiation wavelength, stilbene alone absorbs the light, and we believe that the reaction occurs from the excited singlet state of stilbene.

(9) 4-Methylstyrene absorbs at a slightly shorter wavelength than OA. At the irradiation wavelength, OA alone absorbs the light.

the two complexes reacted independently and did not interconvert during the course of irradiation. It is important to note that the dimers formed within the OA capsule are different from the ones obtained in organic solvents by direct irradiation (**6**) and triplet sensitization (**7**).[10] On the basis of known singlet and triplet energies and electron donor−acceptor properties of **3** and OA we believe that the dimerization within the capsule was prompted by triplet sensitization of **3** by OA.[11] Formation of dimer **7** in solution from the triplet state has been rationalized on the basis of involvement of a most stable 1,4-dibenzylic diradical as an intermediate (Scheme 3).[10] Formation of dimer **4** instead of

Scheme 3. Proposed Mechanism for the Formation of **4**



7 within OA suggests that, within the restricted space of a capsule, stability of the diradical intermediate is not the controlling factor. Most likely, dimer **5** is formed from complex **A** (Figure 5) in which the olefins are pre-organized to form a 1,3-dimer. Dimer **4** that is formed as one of the products within OA is known to be a product of electron-transfer sensitization of **3** by 1,4-dicyanobenzene in acetonitrile.[12] Its formation within the capsule from the triplet state is surprising, and we believe that it resulted from complex **B** (Figure 5) via a previously unknown diradical rearrangement process (Scheme 2). Further work is underway to confirm this suggestion.

It is quite natural for the reader to wonder how OA capsule is different from other organized assemblies in which geometric isomerization and dimerization of olefins have been performed. Geometric isomerization of olefins have been investigated in a variety of solid matrices such as crystals, zeolites, solid host−guest complexes, and organic glasses.[13] As far as we are aware, no predictable model has emerged from these studies. However, it is common knowledge that exquisite control on the site of isomerization of retinal in rhodopsin and bacteriorhodopsin results from the restrictions placed on the guest (reacting molecule) by the host cavity.[2] Results reported here on two systems bear similarity to these protein-controlled isomerization processes and suggest that the observed specificity is system dependent and understandable on the basis of host−guest interactions and free space within the reaction cavity. During the last three decades photodimerization of olefins has been extensively investigated in various organized assemblies with the aim of orienting olefins toward a single dimer.[13c,14,15] The ability of the OA capsule to preorganize olefins toward dimers that are not formed in organic solvents adds a new dimension.[16]

The results presented above establish that a careful choice of the host−guest assembly based on host−guest interaction(s) and available free space could lead to a predictable photochemical outcome. Ability to generate dimeric products, within water-soluble hosts, that are not obtained in conventional solution medium opens up new opportunities in this area. We are currently exploring homo- and heterodimerization of olefins within the OA capsule. Further work needed for a greater comprehension of the observed selectivity and full exploitation of OA as a photochemical reaction cavity is underway in our laboratory.

Acknowledgment. We thank the National Science Foundation, U.S.A., for generous financial support (CHE-0213042 and CHE-0531802).

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

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(10) (a) Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8660−8664. (b) Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664−8670. (c) Nozaki, H.; Otani, I.; Noyori, R.; Kawanisi, M. *Tetrahedron* **1968**, *24*, 2183−2192. (d) Kojima, M.; Sakuragi, H.; Tokumaru, K. *Bull. Chem. Soc. Jpn.* **1989**, 3863−3868.

(11) On the basis of the ability of OA capsule to sensitize the di-π-methane rearrangement of benzonorbornadiene and dibenzobarralene, we believe that it has triplet energy close to that of acetophenone (∼73 kcal/mol).

(12) (a) Asanuma, T.; Gotoh, T.; Tsuchida, A.; Yamamoto, M.; Nishijima, Y. *J. Chem. Soc., Chem. Commun.* **1977**, 485−486. (b) Tojo, S.; Toki, S.; Takamuku, S. *J. Org. Chem.* **1991**, *56*, 6240−6243. (c) Schepp, N. P.; Johnston, L. J. *J. Am. Chem. Soc.* **1994**, *116*, 6895−6903. (d) Asanuma, T.; Yamamoto, M.; Nishijima, Y. *J. Chem. Soc., Chem. Commun.* **1975**, 608−609.

(13) (a) Zheng, S-L; Messerschimidt, M.; Coppens, P. *Chem. Commun.* **2007**, 2735−2737. (b) Arad-Yellin, R.; Brunie, S.; Green, B.; Knossow, M.; Tsoucaris, G. *J. Am. Chem. Soc.* **1979**, *101*, 7529−7537. (c) Ramamurthy, V., Ed. *Photochemistry in Organized and Constrained Media*; VCH: New York, 1991. (d) Duveneck, G. L.; Sitzmann, E. V.; Eisenthal, K. B.; Turro, N. J. *J. Phys. Chem.* **1989**, *93*, 7166−7170. (e) Natarajan, A.; Mague, J. T.; Venkatesan, K.; Arai, T.; Ramamurthy, V. *J. Org. Chem.* **2006**, *71*, 1055−1059. (f) Moorthy, J. N.; Venkatakrishnan, P.; Savitha, G.; Weiss, R. G. *Photochem. Photobiol. Sci.* **2006**, *5*, 903−913. (g) Yang, L-Y; Harigai, M.; Imamoto, Y.; Katoka, M.; Ho, T-I.; Federova, O.; Shevyakov, S.; Liu, R. S. H. *Photochem. Photobiol. Sci.* **2006**, *5*, 874−882.

(14) Bassani, D. M. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2003; pp 20-1−20-20.

(15) (a) Takaoka, K.; Kawano, M.; Ozeki, T.; Fujita, M. *Chem. Commun.* **2006**, 1625−1627. (b) Yoshizawa, M.; Takeyama, Y.; Okano, T.; Fujita, M. *J. Am. Chem. Soc.* **2003**, *125*, 3243−3247. (c) Yoshizawa, M.; Takeyama, Y.; Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1347−1349.

(16) Nishioka, Y.; Yamaguchi, T.; Yoshizawa, M.; Fujita, M. *J. Am. Chem. Soc.* **2007**, *129*, 7000−7001.