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A stable *cis*-stilbene derivative encapsulated in cucurbit[7]uril†

Soowhan Choi, Sang Hyun Park, Albina Y. Ziganshina, Young Ho Ko, Jae Wook Lee‡ and Kimoon Kim*

National Creative Research Initiative Center for Smart Supramolecules and Department of Chemistry, Division of Molecular and Life Sciences, Pohang University of Science and Technology (POSTECH), San 31 Hyojadong, Pohang 790-784, Republic of Korea. E-mail: kkim@postech.ac.kr; Fax: (+82)54-279-8129

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cis-Diaminostilbene dihydrochloride encapsulated in cucurbit[7]uril does not spontaneously isomerize to the _trans_ isomer at room temperature as a result of the strong host–guest interactions including strong hydrogen bonds between the two protonated amine termini of the C-shaped guest and the portal oxygen atoms of the host.

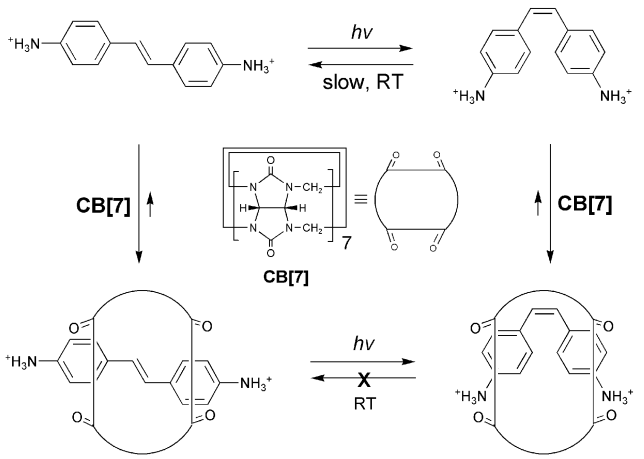
Stabilization of otherwise unstable molecules by encapsulation in molecular or supramolecular hosts has received much attention.[1–3] A classical example is cyclobutadiene stabilized in a hemicarcerand,[1] where it is protected from dimerization by its surrounding shell and from reactants too large to pass through the portal of the host. Recently, Fujita *et al.* reported a stable *cis*-azobenzene derivative enclathrated in a self-assembled coordination nanocage.[3] The remarkable stabilization of the *cis*-azobenzene derivative, which is well known to spontaneously isomerize to the more stable *trans* isomer under normal conditions, was attributed to the formation of a hydrophobic dimer of the "C-shaped" guest molecule that nicely fits the cavity of the supramolecular host.

Cucurbituril (CB[6]), a macrocycle comprising six glycoluril units, has a cavity and two identical carbonyl-laced portals, which allow it to form stable host–guest complexes with small molecules, particularly protonated diaminoalkanes (K > 10^5).[4,5] Recently synthesized cucurbituril homologues,[6] cucurbit[*n*]uril (CB[*n*]; n = 7 and 8) containing seven and eight glycoluril units, respectively, share characteristic features of CB[6], a hydrophobic cavity and polar carbonyl groups surrounding the portals. However, their larger cavity and portal sizes allow them to encapsulate guest molecules that are not included in CB[6].[7,8] For example, 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene, which is too large to be included in CB[6], forms a 1 : 1 host–guest complex with CB[7] and a 1 : 2 complex with CB[8]. We also discovered that *trans*-diaminostilbene dihydrochloride (*trans*-**1**) forms a stable 1 : 2 host–guest complex with CB[8] and furthermore undergoes a facile, stereoselective [2 + 2] photoreaction mediated by the host.[9] Extending this work, we decided to investigate the binding of *trans*- and *cis*-**1** to CB[7] and the effect of CB[7] on the *cis*–*trans* isomerization of diaminostilbene.[10,11] Surprisingly, *cis*-**1** encapsulated in CB[7] does not spontaneously isomerize to the *trans* isomer at room temperature (Scheme 1). Herein we report a remarkably stable *cis*-stilbene derivative that is stabilized by strong host–guest interactions.

trans-**1** forms a stable 1 : 1 host–guest complex with CB[7] as indicated by NMR spectroscopy.§ The signals for the phenyl and ethylene protons exhibit higher field shifts upon formation of the complex (Fig. 1a, c) indicating that they are located in the cavity of CB[7]. The formation constant of the 1 : 1 complex determined by UV-vis spectroscopic titration† is 1.2×10^5 M^{-1} (pH = 3).[12]

Irradiation with UV light (350 nm) of the aqueous solution of *trans*-**1**⊂CB[7] for 30 min causes isomerization of the guest leading to *cis*-**1**⊂CB[7] as evidenced by UV-vis and NMR spectroscopy.¶ Similar to *trans*-**1** itself,[10a] *trans*-**1**⊂CB[7] exhibits a large decrease in the absorption centered at ~300 nm (Fig. 2). There is a large up-field shift in the ^{1}H NMR signals for the guest as the photoisomerization to *cis*-**1**⊂CB[7] occurs (Fig. 1).

Surprisingly, *cis*-**1**⊂CB[7] is quite stable at room temp.; there is little change in its ^{1}H NMR spectrum even after 30 days. This is in sharp contrast to the fact that *cis*-**1** slowly isomerizes to *trans*-**1** at room temp. However, heating a solution of *cis*-**1**⊂CB[7] at 60 °C for 1 day causes its isomerization as indicated by ^{1}H NMR spectroscopy. Under the same conditions, the conversion of *cis*-**1** to *trans*-**1** is completed within 5 h. The apparent first order rate constants for the thermal isomerization of *cis*-**1** and *cis*-**1**⊂CB[7] to the corresponding *trans* isomers at 60 °C are 1.6×10^{-4} s^{-1} and 5.7×10^{-5} s^{-1}, respectively. The



Scheme 1

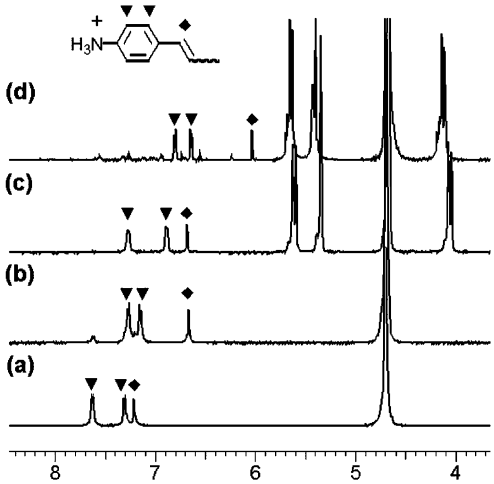


Fig. 1 ^{1}H-NMR spectra of (a) *trans*-**1** in D_2O (~1 mM), (b) *cis*-**1** after irradiation of solution (a) for 30 min, (c) *trans*-**1**⊂CB[7] in D_2O (~1 mM), and (d) *cis*-**1**⊂CB[7] after irradiation of solution (c) for 30 min.

† Electronic Supplementary Information (ESI) available: determination of binding constants. See http://www.rsc.org/suppdata/cc/b3/b306832c/

‡ Department of Chemistry, Dong-A University, 840 Hadandong, Busan 604-714, Republic of Korea.

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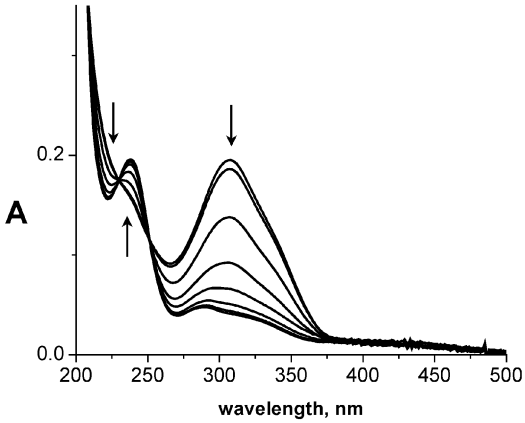

Fig. 2 UV spectral change during photoisomerization of *trans*-**1**⊂CB[7] to *cis*-**1**⊂CB[7] in water.

mechanism of the *cis–trans* isomerization of *cis*-**1**⊂CB[7] is not clear. Further studies are needed to clarify whether the guest molecule isomerizes while included in CB[7] or dissociates from the host first, isomerizes to the *trans* form and then forms *trans*-**1**⊂CB[7].

To understand the remarkable stabilization of *cis*-**1** achieved by forming a complex with CB[7] we carried out *ab initio* calculations on *trans*-**1**⊂CB[7] and *cis*-**1**⊂CB[7] in the gas phase.[13] Fig. 3 shows the energy-minimized structures of these inclusion complexes obtained by the calculations. In *cis*-**1**⊂CB[7], interestingly, the C-shaped guest fits well in the cavity of CB[7] with the two protonated amine termini of the guest interacting with the portal oxygen atoms of the host through hydrogen bonds as well as ion–dipole interactions. On the other hand, only a part of the guest in *trans*-**1**⊂CB[7] is included in the cavity of CB[7] such that only one protonated amine terminus of the guest interacts with the carbonyl O atoms of the host. Consequently, the binding energy of *cis*-**1** to CB[7] is much larger than that for *trans*-**1** to CB[7] (−159.2 *vs.* −126.8 kcal mol^{-1}) in the gas phase, according to the calculations. This result is at least qualitatively parallel with the observation that the complex formation constant of *cis*-**1**⊂CB[7] is ~3 times higher than that of *trans*-**1**⊂CB[7] measured by UV-vis spectroscopic titration (3.3×10^5 *vs.* 1.2×10^5 M^{-1}).

In conclusion, *cis*-**1** when encapsulated in CB[7] does not spontaneously isomerize to the *trans* isomer at room temp. The remarkable stability of *cis*-**1** is attributed to the strong host–guest interactions including strong hydrogen bonds between the two protonated amine termini of the C-shaped guest and the portal oxygen atoms of the host. This work not only demonstrates supramolecular control of molecular behavior but also provides an insight into designing molecular memory devices that are photochemically writable and readable, and thermally erasable.

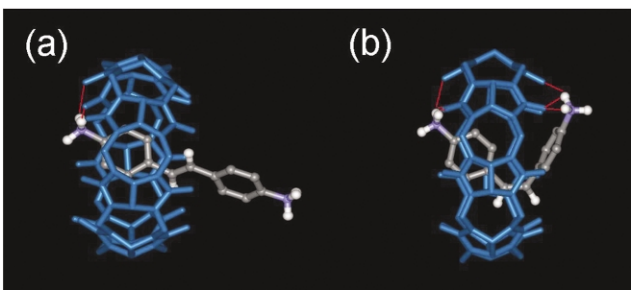

Fig. 3 Energy minimized structures of a) *trans*-**1**⊂CB[7] and b) *cis*-**1**⊂CB[7] in the gas phase by a HF/3-21G** calculation.

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Notes and references

§ *trans*-**1**⊂CB[7]. To a solution of diaminostilbene dihydroxychloride (Aldrich; 11.9 mg, 0.042 mmol) in 10 mL H_2O was added CB[7]·H_2SO_4·5H_2O (67.5 mg, 0.05 mmol) in small portions and stirred for 30 min at room temp. Excess CB[7] was filtered off to give a clear solution, which was concentrated to 2 mL. Addition of EtOH (10 mL) to the solution yields a precipitate which was isolated, washed with EtOH and dried (66.1 mg, 83%). ^{1}H NMR (500 MHz, D_2O): δ 4.19 (d, *J* 15 Hz, 14H), 5.48 (s, 14H), 5.76 (d, *J* 15 Hz, 14H), 6.79 (s, 2H), 6.93 (d, *J* 8 Hz, 4H), 7.36 (d, *J* 8 Hz, 4H); UV/Vis (H_2O): λ_{max} (log ε) = 307 nm (4.38); MS (ESI): *m*/*z* (%) 686.20 (100) [M^{2+}]; elemental analysis, calcd (%) for ($C_{14}H_{16}N_2^{2+}$)2Cl^-·($C_{42}H_{42}N_{28}O_{14}$)·H_2SO_4·2C_2H_5OH·14H_2O: C, 38.16; H, 5.34; N, 22.25; found: C, 38.06; H, 5.20; N, 22.44.

¶ *cis*-**1**⊂CB[7]. A solution of *trans*-**1**⊂CB[7] in D_2O (4×10^{-3} M) in a NMR tube was irradiated with UV light (350 nm) in a Rayonet photochemical reactor for 0.5 h to produce *cis*-**1**⊂CB[7]. ^{1}H NMR (500 MHz, D_2O): δ 4.22 (d, *J* 15 Hz, 14H), 5.50 (s, 14H), 5.74 (d, *J* 15 Hz, 14H), 6.14 (s, 2H), 6.77 (d, *J* 8 Hz, 4 H), 6.88 (d, *J* 8 Hz, 4H); UV/Vis (H_2O): λ_{max} (log ε) = 289 nm (3.79).

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