Template directed photodimerization of *trans*-1,2-bis(*n*-pyridyl)ethylenes and stilbazoles in water†

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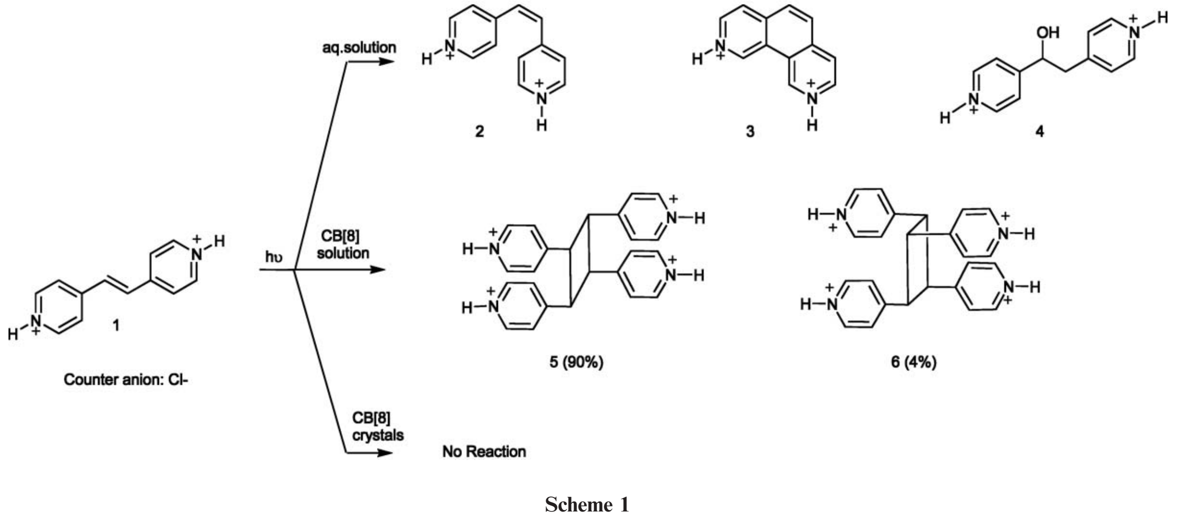
Template induced photodimerization of *trans*-1,2-bis(*n*-pyridyl)ethylene dihydrochlorides and *trans*-*n*-stilbazole hydrochlorides within cucurbit[8]uril in aqueous media leads to high yields of the *syn* dimer.

While control of unimolecular photoreactions in solution through the use of confined and organized media could be achieved, there is a paucity of general strategies to control bimolecular photoreactions in solution phase.[1] Most of the existing photodimerization strategies relate to crystalline solids.[2] Recognition of the facts that not all organic compounds are crystalline and the current need to devise methods to conduct selective photoreactions in water prompted us to explore methods to pre-orient olefins in aqueous media prior to excitation. Previously micelles,[3] cyclodextrins[4] and inorganic hosts[5] have been used with moderate success to template [2 + 2] and [4 + 4] photodimerizations in water. Recently, cucurbiturils, macrocycles composed of glycoluril units linked by methylene groups,[6] have been shown to template photodimerization of diaminostilbene dihydrochloride[7] and bimolecular thermal reactions.[8] Inspired by these reports we have explored the versatility of cucurbit[8]uril (CB[8]) having a cavity of inner diameter 8.8 Å and height 9.1 Å to template photodimerization of olefins in water. We have used *trans*-1,2-bis(*n*-pyridyl)ethylene dihydrochlorides and 2- and 4-stilbazole hydrochlorides, whose photochemistry has been investigated previously in solution[9] and organized media[10] as model compounds. In this report we show that CB[8] can pre-align a number of different olefins in water to yield a single dimer. The ability of CB[8] to template different olefins (cinnamic acids,[11] stilbazoles and bis(pyridyl)ethylenes) in aqueous solution is remarkable when one recognizes that in the solid state different templates are required to accomplish the same task.[2]

Irradiation of *trans*-1,2-bis(4-pyridyl)ethylene dihydrochloride (**4-BPE·2HCl** (**1**)) in water (5.4 × 10^{-3} M) produced predominantly the hydration product **4** as the major product (78%) and the corresponding *cis* isomer **2** and the cyclization product 2,9-phenanthroline **3** (17% and 5% respectively) as minor products (Scheme 1, Table 1). Olefin **1** forms an inclusion complex with half an equivalent of CB[8] in water. Inclusion of **1** into the CB[8] cavity was confirmed by upfield shifts in the guest ^{1}H NMR signals (Fig. 1).† Integration of the host and the guest proton signals suggested that the complex has 1 : 2 stoichiometry. The formation of the stable inclusion complex in water was also suggested by the observation of a peak corresponding to an *m*/*z* ratio of 1693 corresponding to the {**CB[8]·2BPE·H**}$^+$ species in MALDI-TOF MS experiments.† Confirmation of the inclusion complex formation came from X-ray structural studies of the crystals that resulted when the 1 : 2 complex in water was left alone for a few days. The crystal structure of the complex showed two



Scheme 1

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† Electronic supplementary information (ESI) available: Crystal structure coordinates and tables for positional and thermal parameters. Experimental protocol, ^{1}H NMR spectra and MALDI-TOF of guests included within CB[8], ^{1}H NMR data of dimers and MALDI-TOF of dimers included within CB[8]. See http://dx.doi.org/10.1039/b508458j

Table 1 Product distribution[a] (%) upon irradiation of *trans*-1,2-bis(*n*-pyridyl)ethylenes irradiated in various media[b,c]

Medium	2	3	4	5	6
4-BPE·2HCl (1)					
Water	17	5	78	—	—
CB[7]	67	12	21	—	—
CB[8]	2	2	2	90	4
	8	**9**		**10**	**11**
3-BPE·2HCl (7)					
Water	82	18	—	—	—
CB[7]	91	9	—	—	—
CB[8]	8	3	—	87	2
	13	**14**		**15**	**16**
2-BPE·2HCl (12)					
Water	86	14	—	—	—
CB[7]	89	11	—	—	—
CB[8]	4	2	—	88	6

[a] The % were calculated based on integration of ^{1}H NMR signals. [b] See Scheme 2 for structures of **2–16**. [c] Concentration of guest: 5.5×10^{-4} M.

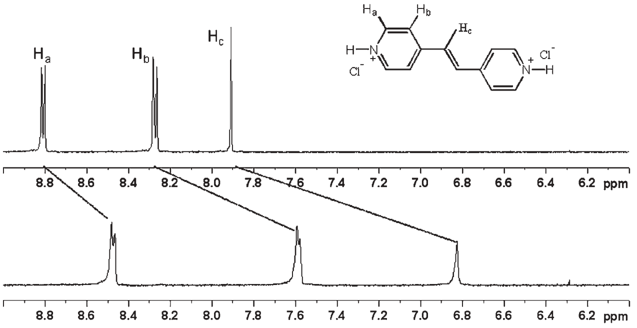


Fig. 1 ^{1}H NMR spectra of (top) **4-BPE·2HCl** in D_2O; (bottom) **4-BPE·2HCl** in the presence of 0.5 equivalent of CB[8] in D_2O.

olefins are accommodated within the cavity in a parallel and slipped fashion with the two olefinic bonds separated by 4.8 Å (Fig. 2).† Dissolution of the crystalline 1 : 2 complex in water and irradiation gave the *syn* dimer (**5**) as a single product. MALDI-TOF MS of the irradiated sample showed a peak at *m*/*z* of 1693 corresponding to the dimer trapped within the CB[8] cavity.

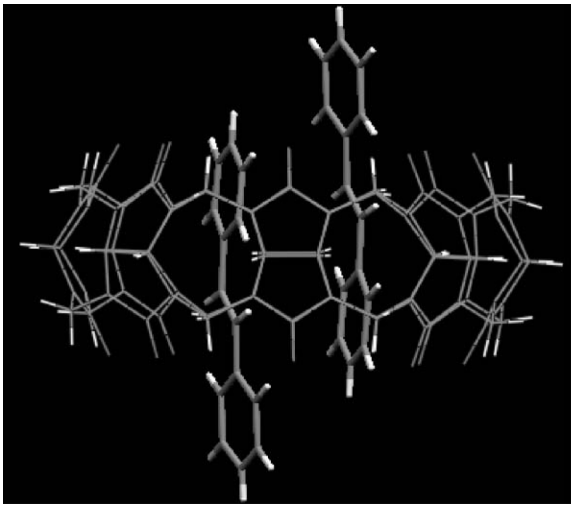
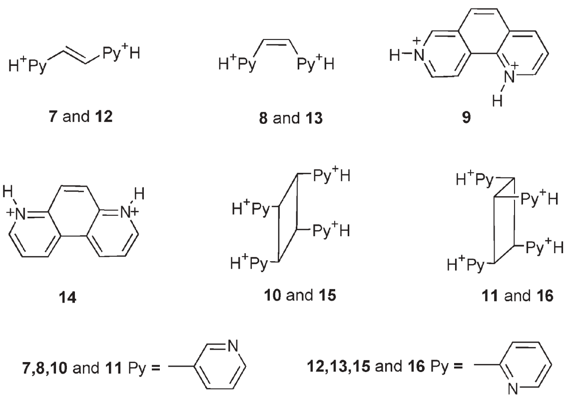


Fig. 2 X-Ray crystal structure[12] showing two **4-BPE·2HCl (1)** molecules aligned in a slipped parallel fashion within CB[8].

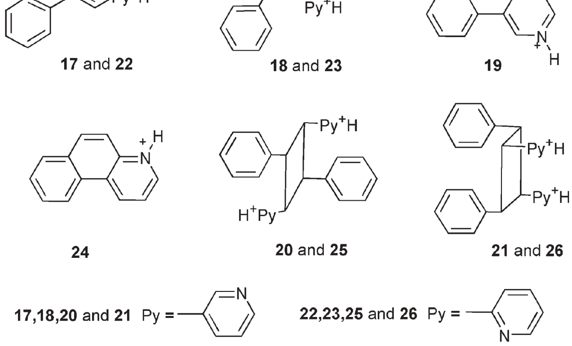


Scheme 2

Surprisingly, no dimerization occurred upon irradiation of the crystals of 1 : 2 host–guest complexes even after 48 h of irradiation. Clearly, the included olefins frozen at a distance >4.2 Å in a slipped parallel arrangement were unable to interact and photodimerize in the excited state.

To examine the general applicability of CB[8] as a template, photodimerizations of other olefins *i.e. trans*-1,2-bis(3-pyridyl)-ethylene dihydrochloride **7** (**3-BPE·2HCl**), *trans*-1,2-bis(2-pyridyl)-ethylene dihydrochloride **12** (**2-BPE·2HCl**), *trans*-4-stilbazole hydrochloride (**4-SA·HCl**) **17** and *trans*-2-stilbazole hydrochloride (**2-SA·HCl**) **22** were attempted. As per MALDI-TOF MS and ^{1}H-NMR all four olefins formed 1 : 2 CB[8]–olefin complexes.† Irradiation of an aqueous solution of **7** and **12** within CB[8] resulted in 87% and 88% of *syn* dimers **10** and **15** respectively as the major products while in the absence of CB[8] only the corresponding *cis* isomers (**8** and **13**) and the cyclization products (**9** and **14**) were produced (Scheme 2, Table 1).

Similar irradiation of *trans*-*n*-stilbazole hydrochloride **17** and **22** included in CB[8] gave **20** (92%) and **25** (91%) respectively (Scheme 3, Table 2). Irradiation in the absence of CB[8] under the same conditions (5×10^{-4} M) resulted mainly in geometric isomerization; less than 4% of the dimer (a mixture of *syn* and *anti* dimers) was formed. Based on these results, we believe that CB[8] directs all five olefins, **4-**, **3-** and **2-BPE·2HCl**, **4-SA·HCl** and **2-SA·HCl** to the corresponding *syn* dimers.



Scheme 3

Table 2 Product distribution[a] (%) upon irradiation of *trans-n*-stilbazoles in the absence and presence of CB[8] in water[b,c]

Medium				
4-SA·HCl (17)	**18**	**19**	**20**	**21**
Water	93	2	3	2
CB[8]	4	1	90	5
2SA·HCl (22)	**23**	**24**	**25**	**26**
Water	95	1	2	2
CB[8]	17	2	81	—

[a] The % were calculated based on integration of ^{1}H NMR signals. [b] See Scheme 3 for structures of **18–26**. [c] Concentration of guest: 5.5×10^{-4} M.

Cucurbit[7]uril (CB[7]), an oligomer with a slightly smaller cavity (inner cavity diameter 7.3 Å, height 9.1 Å) was able to include only one molecule of **1** and on irradiation, *cis* isomer **2** (67%), phenanthroline **3** (12%) and the hydration product **4** (21%) alone were formed. Similarly, irradiation of **7** and **12** included within CB[7] in aqueous solution resulted only in the corresponding *cis* isomers (**8** and **13**) and the cyclization products (**9** and **14**) (Table 1). Thus a larger cavity is essential for inclusion and alignment of two *trans*-1,2-bis(*n*-pyridyl)ethylenes for photodimerization in aqueous solution.

Templating photodimerization in the solid state is a well established technique.[13] In solution the templating strategy, though it has been explored, is yet to gain wide recognition.[5,14] We have shown previously that cucurbutrils can facilitate photodimerization of cinnamic acids in water.[11] In this presentation we have chosen dipyridyl ethylenes and stilbazoles as examples for three reasons: (a) These molecules in solution undergo a variety of reactions and dimerization is the least preferred pathway.[9,10] (b) A number of different templates have been designed for the solid state photodimerization of dipyridyl ethylenes.[15] However, no template has been reported to effect photodimerization of such systems in aqueous solution. (c) Solid state photodimerizations of *trans*-1,2-bis(*n*-pyridyl)ethylene and 2- and 4-stilbazoles often require different templates for each olefin. Given the fact that cucurbit[8]uril worked with a number of cinnamic acids we wished to explore whether the same template would work with different dipyridyl ethylenes and stilbazoles. As presented in this report cucurbit[8]uril is a versatile template and it has the ability to bring two olefins closer and place them in an appropriate geometry to yield a single photodimer.

We have established in this report that water insoluble CB[8] becomes water soluble in the presence of cationic olefins. The host prealigns the olefins in a specific geometry within its cavity and favors the formation of a single dimer. Thus photodimerization that is not preferred in solution becomes the main reaction in the presence of cucurbiturils. The remarkable observation that a single host is able to template a variety of olefins in water has prompted us to examine the utility of cucurbiturils in controlling other unimolecular and bimolecular photoreactions.

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12 Crystal data. $C_{72}H_{72}Cl_4N_{36}O_{16}\cdot 13.5H_2O$, $M = 2055.46$, triclinic, space group $P\bar{1}$, $a = 12.938(2)$, $b = 14.613(2)$, $c = 25.703(4)$ Å, $U = 4717(1)$ Å^3, $\rho = 1.447$ g cm^{-3}, $\mu = 0.228$ mm^{-1}, $T = 100$ K, $Z = 2$, Mo-Kα radiation ($\lambda = 0.71073$ Å), 32956 reflections measured, 16070 unique ($R_{\text{int}} = 0.0581$), final $R = 0.1289$ for reflections with $I > 2\sigma(I)$ and 0.1932 for all reflections. The H-atoms of the solvent water molecules could not be located and so are not included in the refinement or structure factor calculations. CCDC 276220. See http://dx.doi.org/10.1039/b508458j for crystallographic data in CIF or other electronic format.

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