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COMMUNICATION

Supramolecular photocatalysis: insights into cucurbit[8]uril catalyzed photodimerization of 6-methylcoumarin†‡

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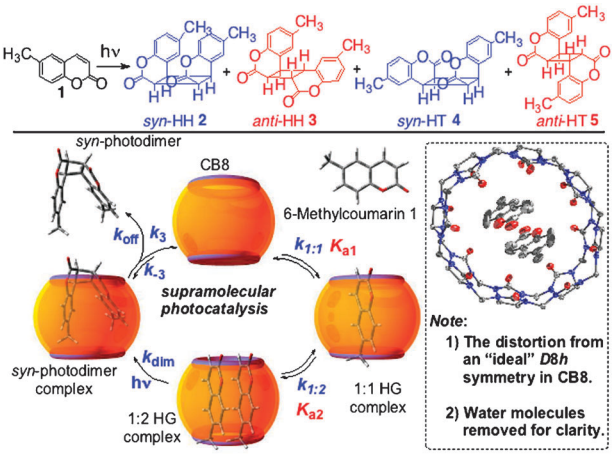
Guest induced shape change of the cucurbit[8]uril cavity is likely rate limiting in the supramolecular photocatalytic cycle for CB8 mediated photodimerization of 6-methylcoumarin.

Catalytic chemical transformations in nature carried out by enzymes stand out for their elegance and simplicity. One of the common features in such transformations is confinement of substrates within the enzyme pocket. Supramolecular cavities provide a potential avenue to carry out chemical transformations within their confined environment where the reactants are immobilized by host–guest (HG) interactions.[1] Synthetic supramolecular hosts like cyclodextrin, calixarenes, zeolites, and micelles have been utilized extensively for molecular recognition of various substrates.[2] An underexplored supramolecular container in this regard are cucurbiturils[3] (Scheme 1) that feature a cavity similar to that of cyclodextrins. Various research groups have established the superior molecular recognition properties of cucurbiturils (CBs).[3] We have been exploring the use of cucurbit[8]urils (CB8) to control the photoreactivity of coumarin derivatives. Additionally, we are interested in employing CB8 in catalytic amounts to carry out synthetic photochemical transformations to overcome a fundamental bottleneck *viz*., solubility of CB8 in higher amounts in water. In this communication, we present our findings on the physical aspects of supramolecular catalysis involving CB8 orchestrating the photodimerization of 6-methylcoumarin **1**.

Recently we reported[4–6] that CB8 as low as 10 mol% acts as a supramolecular catalytic nano reaction vessel and facilitates the photodimerization of coumarins[7,8] in water leading to *syn*-dimers exclusively (Scheme 1). Saturation kinetics showed a sigmoidal dependence with a turnover number of 3.4 min^{-1}



Scheme 1 Left: supramolecular photocatalysis of **1** mediated by CB8. Right: single crystal XRD of 1 : 2 CB8-**1** HG complex.

with a Hill constant of 1.8 indicating a co-operative mechanism in the catalytic process.[4] We also established that CB8-**1** HG complexation is a dynamic process using fluorescence lifetime measurements.[6] To understand the mechanism of supramolecular catalysis with CB8, it is critical to decipher not only the nature of the excited state but also the kinetic and thermodynamic aspects involved in the catalytic process.[4] ;In this report we present room temperature triplet–triplet absorption studies of the CB8-**1** HG complex, electrospray ionization mass spectrometry (ESI-MS)[9] of CB8-**1** and CB8-*syn*-photodimer HG complexes in aqueous solution, single crystal XRD of CB8-**1** 1 : 2 HG complex and stopped-flow measurements that provide insights into the efficiency of the catalytic cycle.

The 1 : 2 CB8-**1** host–guest (HG) complex was characterized by single crystal X-ray diffraction§ (Scheme 1) that revealed a Head-to-Tail (HT) orientation. Based on the crystal structure one would predict HT dimers as major products if the same orientation is preferred in solution. But we previously established that *syn*-dimers are favored exclusively within CB8 with a HH : HT ratio of 69 : 31. While formation of the *syn*-HT dimer **4** (minor product) can be rationalized from the orientation of guests within the CB8 in the crystalline state, the orientation of the guest molecules has to be different in solution for the formation of the *syn*-HH dimer **2** (major product). An important feature that was clearly visible from the X-ray

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‡ Electronic supplementary information (ESI) available: Experimental procedure, analysis conditions. CCDC 814052. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc11164g

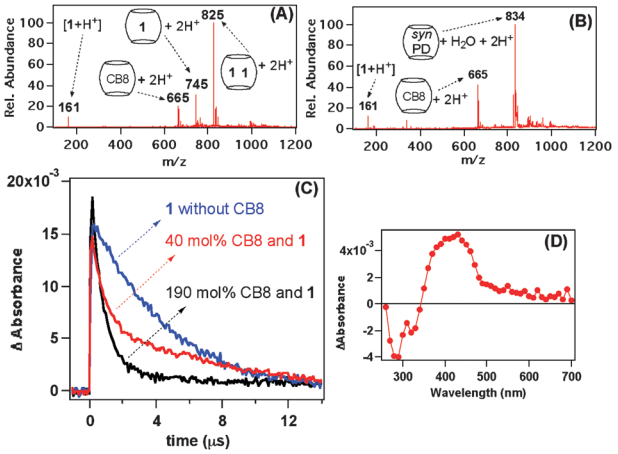

Fig. 1 Top: ESI-MS spectra of non-irradiated (A) and irradiated (>90% convn. to photoproduct) aq. solutions of CB8-**1** (B) with 0.01% HBr. Bottom: (C) transient absorption decay traces recorded at 420 nm of ^{3}(**1**)* in the absence and presence of different amounts of CB8. (D) Transient absorption spectrum of CB8-**1** HG complex (25 μM CB8 and 50 μM **1**).

structure (Scheme 1) was the distortion of the CB8 cavity by coumarin guest molecules. Guest induced shape change of CBs leading to allosterism is well established,[10] and we believe that a similar phenomenon is operating in our case.

To have a better understanding of the behavior of CB8-**1** HG complex in solution, we performed ESI-MS and MS/MS studies and observed both 1 : 1 and 1 : 2 CB8-**1** HG complexes as double charged ions (Fig. 1A). Additionally, we were able to observe the free guest and free host as mono- and di-protonated ions, respectively. MS/MS studies of the complexes confirmed these assignments.‡ LC-MS analysis of the irradiated solutions of the HG complexes showed the expected formation of the photodimer of **1**.‡ The analysis of the irradiated samples of **1**@CB8 (>90% conversion, photodimers do not absorb beyond 320 nm) by direct infusion into the mass spectrometer showed a base peak at *m*/*z* 834 (Fig. 1B). Fragmentation studies revealed that this signal corresponded to the CB8-photodimer complex.‡

Photodimerization of **1** was established to originate from the triplet state.[8] To understand the dynamics and triplet state reactivity of CB8-**1** HG complex, laser flash photolysis studies were performed. Laser excitation (308 nm, pulse width: 15 ns) of deoxygenated aqueous solutions of CB8-**1** HG complex (CB8 25 μM and 50 μM **1**) generated a transient absorption spectrum (Fig. 1D). The transient absorption centered around 420 nm was assigned to the triplet–triplet absorption of **1** based on similarities with previously published spectra.[8] Triplet absorption decay traces were recorded at different concentrations of CB8 (Fig. 1C). In the absence of CB8, ^{3}(**1**)* decayed mono-exponentially with a lifetime (τ_1) of 4.6 μs (Table 1). In the presence of ≥100 mol% of CB8 a mono-exponential triplet decay with a lifetime (τ_2) of 0.75 μs was observed. However, above 5 mol% and below 100 mol% of CB8 the triplet decay fitted best to a bi-exponential kinetic decay with a short component (τ_2 ~0.75 μs) and a long component with varying lifetimes (τ_1 = 4.6 to 13 μs; Table 1, entries 2–8). The contribution of the short component (τ_2) increases with increasing concentration of CB8 as shown

Table 1 Triplet lifetimes (τ) and pre-exponential factors (A) of transient absorption decays of ^{3}(**1**)* at 420 nm with various mol% of CB8[a]

Entry	mol% CB	τ_1 (μs)	A_1	τ_2 (μs)	A_2
1	0	4.6	25	—	—
2	5	4.6	17	0.75	0.7
3	10	5.4	14	0.75	2.6
4	20	6.4	13	0.79	5.3
5	30	7.9	11	0.80	9.5
6	40	10	7.5	0.74	11
7	50	13	6.6	0.79	14
8	70	12	2.5	0.75	20
9	100	—	—	0.74	36
10	130	—	—	0.74	34
11	160	—	—	0.75	36
12	190	—	—	0.75	37

[a] Laser pulse (308 nm, pulse width 15 ns). Refer to ESI‡ for details. The decays were fitted to: ΔAbsorbance $(t) = A_1 \exp(-t/\tau_1) + A_2 \exp(-t/\tau_2)$.

by the increase of the pre-exponential factor (Table 1). This lifetime component (τ_2) was assigned to CB8-^{3}(**1**)* HG complex (triplet excited 1 : 1 CB8-**1** HG complex). The long-lived component (τ_1) was assigned to uncomplexed ^{3}(**1**)* in aqueous solution (triplet excited **1** outside the CB8 cavity). The varying lifetime of ^{3}(**1**)* in solution is expected due to efficient self-quenching with a rate constant of 4.1×10^9 M^{-1} s^{-1}.‡ With increasing concentrations of CB8, the fraction of uncomplexed **1** in aqueous solution decreases. Consequently, the self-quenching decreases causing an increase in τ_1. The decrease in the fraction of uncomplexed **1** in aqueous solution with increasing CB8 concentrations is also reflected in the decrease in A_1 (Table 1). We believe that the 1 : 2 CB8-^{3}(**1–1***) HG complex has a very short lifetime and is not detected under our experimental conditions due to fast photochemical or thermal/photophysical deactivation (proximity effect). Further, the shorter lifetime of 0.74 μs that corresponds to 1 : 1 CB8-^{3}(**1**)* HG complex is not quenched by molecular oxygen.‡ On the other hand, uncomplexed ^{3}(**1**)* in aqueous solution is quenched with a high rate constant of 2×10^9 M^{-1} s^{-1}.‡ Quenching data‡ reveal that coumarin triplets upon encapsulation with the CB8 cavity are protected from quenching by oxygen. This is in line with our previous observation that photodimer conversion is similar in N_2, O_2 and air saturated atmospheres.[4]

Fluorescence studies on **1** (in the absence of CB8) showed a structureless emission centered around 411 nm with a lifetime shorter than 0.1 ns.[6] Complexation of **1** within CB8 resulted in an increase in the emission intensity with a noticeable red shift in the emission maximum centered around 443 nm (Fig. 2A).

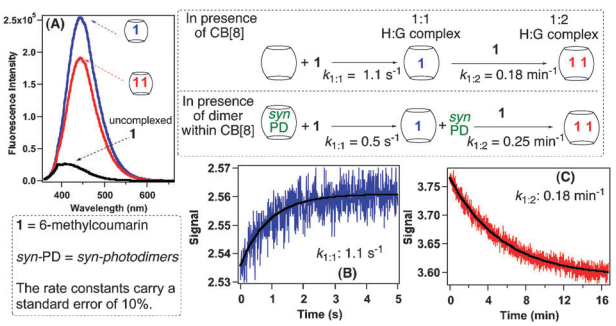

Fig. 2 Stopped-flow measurements to ascertain the complexation kinetics.

Fluorescence lifetime measurements showed an increase in the lifetime (<0.1 ns for uncomplexed **1**; 0.7 ns for 1 : 2 CB8-**1** HG complex and 3.7 ns for 1 : 1 CB8-**1** HG complex).[6] Additionally, 1 : 1 CB8-**1** HG complex had a higher fluorescence intensity than 1 : 2 CB8-**1** HG complex.[6] Thus our photophysical studies show that both the singlet and triplet excited states of **1** are involved in the photoprocesses that occur within CB8.

To understand the catalytic process involved in the photodimerization involving CB8, kinetic aspects of HG complexation were determined by stopped-flow spectrometry. Kinetic measurements were performed at both shorter (Fig. 2B) and longer (Fig. 2C) time regimes using the fluorescence signal (λ_{ex}: 325 nm; λ_{ex}: >395 nm) to ascertain the HG complexation rate constants. Mixing of **1** (0.5 mM) to an aqueous solution of CB8 (1 μM) showed an increase in the fluorescence intensity signal with a rate constant of 1.1 s^{-1} that corresponded to the formation of 1 : 1 CB-**1** HG complex (Fig. 2B). This initial rise in fluorescence intensity was followed by a slower decrease in fluorescence intensity with a rate constant of 0.18 min^{-1} that corresponded to the formation of 1 : 2 CB-**1** HG complex (Fig. 2C). To study the influence of the *syn*-photodimer (photoproduct) on the catalytic cycle, we performed the stopped-flow experiment in the presence of the *syn*-photodimer. This was to ascertain the HG complexation rate constants of **1** with CB8-*syn*-photodimer HG complex (Fig. S2, ESI‡). Addition of **1** to an aqueous solution of CB8-*syn*-photodimer (synthesized by photoreaction) showed an increase in the fluorescence intensity signal with a rate constant of 0.5 s^{-1} that corresponded to the formation of 1 : 1 CB-**1** HG complex (Fig. S2, ESI‡). This initial rise in fluorescence intensity was followed by a slower decrease in fluorescence intensity with a rate constant of 0.25 min^{-1} that corresponded to the formation of 1 : 2 CB-**1** HG complex (Fig. S2, ESI‡). Analysis of the stopped-flow data indicates that the formation of the 1 : 2 HG complex is the slow step in the catalytic cycle ($k \approx 0.2$ min^{-1}). This rate is comparable to the catalytic turnover rate of 3.4 min^{-1} that was established in our previous report.[4] Due to experimental limitations, different concentrations of CB8 and **1** were employed during stopped-flow (*e.g.* 1 μM CB8; 0.5 mM **1**) and steady-state turnover (*e.g.* 1 μM CB8; 0.1 to 0.8 mM **1**) measurements. This is reflected in the marginal difference in the catalytic turnover (3.4 min^{-1}) and the transient rate constant for the formation of the 1 : 2 complex ($k \approx 0.2$ min^{-1}). The presence of a photodimer affected the 1 : 1 complex formation as the rate constant slowed from 1.09 s^{-1} to 0.51 s^{-1}, but does not affect the slow step (formation of the 1 : 2 HG complex) in the supramolecular catalytic cycle under saturating concentration of the guest.

We believe that the slow step in the catalytic cycle *viz.*, the formation of the 1 : 2 HG complex, has its origin in the guest induced shape change of the CB8 cavity (Scheme 1). We previously reported[6] a binding constant of $K_{a1} = 1.3 \times 10^4$ M^{-1} and $K_{a2} = 2 \times 10^6$ M^{-1} for 1 : 1 and 1 : 2 CB8-**1** HG complexes respectively. Our stopped-flow data indicate that the formation of the 1 : 1 HG complex is kinetically fast and formation of the 1 : 2 HG complex is slow and it is likely to serve as the rate limiting step during the CB8 supramolecular photocatalytic process. We conjecture that the likely reason for the slow second step (formation of the 1 : 2 HG complex) in spite of being thermodynamically favorable ($K_{a2} = 2 \times 10^6$ M^{-1}) is due to the longer time required for the first coumarin guest molecule to alter the shape of the CB8 cavity to accommodate the second coumarin guest molecule. Catalytic efficiencies decided by guest induced shape changes are well established in enzyme catalysis[11] and we believe a similar phenomenon occurs in our system.

Our current study has uncovered some fundamental aspects that are responsible for the catalytic turnover involving CB8 supramolecular photocatalysis.

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Notes and references

§ Structure of the CB8-**1** HG complex: $C_{48}H_{48}O_{16}N_{32}{\cdot}2C_{10}H_8O_2{\cdot}13.5H_2O$, M = 1892.78, orthorhombic, *Pbca* (no. 61), a = 16.4918(3) Å, 22.0793(4) Å, 22.2875(4) Å, V = 8115.5(3) Å^3, Z = 4, 44 959 reflections measured, 6974 unique reflections (6587 with $I \geq 2\sigma$) which were used in all calculations R_1/wR_2 = 7.05/19.66%, R_1/wR_2 (all) = 7.70/20.84%.

1 (*a*) N. J. Turro, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 10766; (*b*) J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, New York, 1995.
2 (*a*) E. Anslyn and R. Breslow, *J. Am. Chem. Soc.*, 1989, **111**, 5972; (*b*) R. Breslow and B. L. Zhang, *J. Am. Chem. Soc.*, 1992, **114**, 5882; (*c*) A. V. Davis, R. M. Yeh and K. N. Raymond, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 4793; (*d*) J. Rebek, *Acc. Chem. Res.*, 1990, **23**, 399; (*e*) J. W. Steed and J. L. Atwood, *Supramolecular Chemistry*, John Wiley & Sons, New York, 2000; (*f*) I. Tabushi, *Acc. Chem. Res.*, 1982, **15**, 66.
3 (*a*) R. Behrend, E. Meyer and F. Rusche, *Justus Liebigs Ann. Chem.*, 1905, **339**, 1; (*b*) W. L. Mock, *Top. Curr. Chem.*, 1995, **175**, 1; (*c*) S. Y. Jon, Y. H. Ko, S. H. Park, H.-J. Kim and K. Kim, *Chem. Commun.*, 2001, 1938; (*d*) A. Day, A. P. Arnold, R. J. Blanch and B. Snushall, *J. Org. Chem.*, 2001, **66**, 8094; (*e*) J. Lagona, P. Mukhopadhyay, S. Chakrabarti and L. Isaacs, *Angew. Chem., Int. Ed.*, 2005, **44**, 4844; (*f*) R. Wang, L. Yuan and D. H. Macartney, *J. Org. Chem.*, 2006, **71**, 1237; (*g*) C. Yang, T. Mori, Y. Origane, Y. H. Ko, N. Selvapalam, K. Kim and Y. Inoue, *J. Am. Chem. Soc.*, 2008, **130**, 8574; (*h*) C. Klock, R. N. Dsouza and W. M. Nau, *Org. Lett.*, 2009, **11**, 2595.
4 B. C. Pemberton, N. Barooah, D. K. Srivatsava and J. Sivaguru, *Chem. Commun.*, 2010, **46**, 225.
5 (*a*) N. Barooah, B. C. Pemberton, A. C. Johnson and J. Sivaguru, *Photochem. Photobiol. Sci.*, 2008, **7**, 1473; (*b*) N. Barooah, B. C. Pemberton and J. Sivaguru, *Org. Lett.*, 2008, **10**, 3339.
6 B. C. Pemberton, E. Kumarasamy, S. Jockusch, D. K. Srivatsava and J. Sivaguru, *Can. J. Chem.*, 2011, **89**, 310.
7 (*a*) J. N. Moorthy, K. Venkatesan and R. G. Weiss, *J. Org. Chem.*, 1992, **57**, 3292; (*b*) K. Muthuramu and V. Ramamurthy, *J. Org. Chem.*, 1982, **47**, 3976; (*c*) X. Yu, D. Scheller, O. Rademacher and T. Wolff, *J. Org. Chem.*, 2003, **68**, 7386.
8 T. Wolff and H. Goerner, *Phys. Chem. Chem. Phys.*, 2004, **6**, 368.
9 (*a*) I. Osaka, M. Kondou, N. Selvapalam, S. Samal, K. Kim, M. V. Rekharsky, Y. Inoue and R. Arakawa, *J. Mass Spectrom.*, 2006, **41**, 202; (*b*) N. Jayaraj, M. Porel, M. F. Ottaviani, M. V. S. N. Maddipatla, A. Modelli, J. P. Da Silva, B. R. Bhogala, B. Captain, S. Jockusch, N. J. Turro and V. Ramamurthy, *Langmuir*, 2009, **25**, 13820.
10 W.-H. Huang, S. Liu, P. Y. Zavalij and L. Isaacs, *J. Am. Chem. Soc.*, 2006, **128**, 14744.
11 (*a*) K. M. Peterson and D. K. Srivastava, *Biochemistry*, 2000, **39**, 12678; (*b*) G. G. Hammes, *Biochemistry*, 2002, **41**, 8221.