Effect of Excitation on the Host–Guest Equilibrium Constants of Cyclodextrin Complexes

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The equilibrium constants for excited triplet xanthone with cyclodextrins are measured directly by spectroscopically following the decay of triplet xanthone and are shown to be much smaller than those observed for the ground state.

The paradigm of supramolecular chemistry is that organized systems alter chemical reactivity. Photophysical probe molecules have been extensively employed to characterize organized environments, such as micelles, vesicles and cyclodextrin (CD) complexes.[1,2] The difference in the quenching efficiency of excited states in homogeneous solution and in supramolecular structures has been employed to determine equilibrium constants and association and dissociation rate constants.[3–7] Most studies either assumed that the equilibrium constants for the excited and the ground state were *similar*[5,6] or no clear distinction between the two states was made.[3,4] Although it was sometimes recognized that the association process being investigated was strictly for the excited state,[7] no measurements were presented for the difference between the excited- and ground-state equilibrium constants. A recent study[8] suggested that the relocation of triplet xanthone from the CD cavity to the aqueous phase was driven by the lower association constant of the excited state. However, no estimate for the value of this constant was presented. In this communication we describe the first direct independent determination of the equilibrium constants of an excited and ground state guest molecule (xanthone) with a host (CDs). The equilibrium constant for the triplet state is much smaller than that for the ground state showing that the assumption of equal equilibrium constants for both states is not valid. These results have important implications for the use of photophysical probes in the study of supramolecular systems and caution is advised when extrapolating excited state behaviour to probes in their ground state.

Triplet xanthone has a π,π^* configuration in slightly polar and polar solvents, a triplet absorption maximum that is dependent on solvent polarity, and a larger dipole moment than the ground state.[8,9] These characteristics make triplet xanthone an excellent probe to study relocation between environments with different polarities.[8,10] In this work we determined the equilibrium constant of the excited state by studying the triplet decay at different CD concentrations. When CD complexed xanthone is excited, a non-equilibrium situation arises due to the lower equilibrium constant for the triplet, and the system relaxes to a new equilibrium. The kinetic treatment is analogous to the relaxation kinetics of temperature or pressure-jump experiments.[11] Since the triplet lifetime is much longer than the relocation phenomenon, the new equilibrium state is achieved before appreciable amount of triplet decayed to the ground state. The free CD concentration is constant and equal to its total concentration due to the large excess over the xanthone concentration. The observed rate constant for the relaxation process is given by eqn. (1).

$$k_{\mathrm{obs}} = k_- + k_+ [\mathrm{CD}] \qquad (1)$$

Here k_- and k_+ are the dissociation and association rate constants between triplet xanthone and CD and the equilibrium constant is given by eqn. (2).

$$K_{\mathrm{T}} = k_+/k_- \qquad (2)$$

We measured the relocation of triplet xanthone from CDs as a decay at 620 nm or growth at 570 nm. All samples were deaerated by bubbling nitrogen for 15 min. Samples were excited with a YAG laser† at 355 nm (Spectra Physics GCR 12, < 50 mJ) and the decay traces (500 points) were collected on a SCD1000 digitizer. Samples were irradiated with less than 50 laser shots to avoid destruction of xanthone. Most rate constants were determined by analysing decays at 620 nm (inset Fig. 1). Fitting of the growth observed at 570 nm led to the same rate constants as those obtained at 620 nm. The decay traces were fitted to the sum of two exponentials,‡ the larger rate constant corresponding to k_{obs} and the smaller rate constant to the decay of the triplet in water. The latter rate constant was fixed to the value obtained from the decay at longer times. The value for k_{obs} increased linearly with higher CD concentrations (Fig. 1). Association and dissociation rate constants were obtained by fitting the data to eqn. (1), whereas K_{T} values were obtained from eqn. (2) (Table 1). In the case of γ-cyclodextrin (γ-CD) only an upper limit for K_{T} could be obtained as the dependence of k_{obs} with γ-CD concentration was very small.

The equilibrium constants for ground-state xanthone (Table 1) were determined as previously described from the decrease of the fluorescence intensity§ when xanthone was complexed to CD.[8] The values obtained for β- and γ-CD were the same as determined earlier.[8] No relocation of singlet xanthone can occur as the lifetime of this excited state (< 2 ns) is short. Preliminary data for the complexation dynamics of ground state xanthone with β-CD were measured in an iodine laser *T*-jump experiment with fluorescence detection.[12] The observed relaxation rate constants [$(2.2 \pm 0.6) \times 10^5$ s^{-1} and $(1.6 \pm 0.4) \times 10^5$ s^{-1} at 3.2 and 11.8 °C, respectively]¶ were independent of the β-CD concentration, suggesting that the dissociation rate constant for the ground state was measured. When combining these data with the equilibrium constants (2.07×10^3 dm^3 mol^{-1} and 1.65×10^3 dm^3 mol^{-1} at 3.2 and 11.8 °C, respectively) we obtained association rate constants of $(3.3 \pm 0.9) \times 10^8$ dm^3 mol^{-1} s^{-1} and $(3.6 \pm 1.1) \times 10^8$ dm^3 mol^{-1} s^{-1} at 3.2 and 11.8 °C, respectively. Thus, the association rate constants are not very dependent on the temperature and we estimated a value of $(3.5 \pm 1.0) \times 10^8$ dm^3 mol^{-1} s^{-1} for this rate constant at 20 °C. This

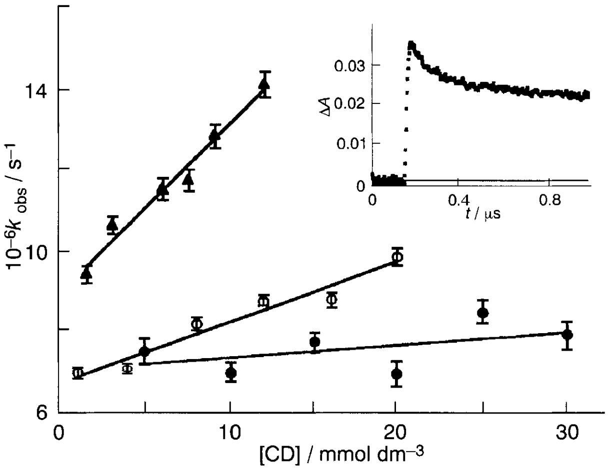

Fig. 1 Dependence of the initial rate constant (k_{obs}) for the relaxation kinetics of triplet xanthone complexed to β-CD (▲ , upper line), Hp-β-CD (○, middle line) and γ-CD (●, lower line) on the CD concentration. Error bars correspond to those from the fitting of experimental data to the sum of two exponentials. The inset shows the decay of triplet xanthone at 620 nm when complexed to 15 mmol dm^{-3} Hp-β-CD.

Table 1 Ground- (K_G)[a] and excited-state (K_T)[b] equilibrium constants and triplet association (k_+)[c] and dissociation (k_-)[c] rate constants of xanthone with cyclodextrins[d]

CD[d]	$10^{-3}\ K_G$/ dm^3 mol^{-1}	$10^{-3}\ K_T$/ dm^3 mol^{-1}	$10^{-8}\ k_+$/ dm^3 mol^{-1} s^{-1}	$10^{-6}\ k_-$/ s^{-1}	
β-CD	1.1 ± 0.2	0.048 ± 0.013	4 ± 1	8.4 ± 0.7	(12 ± 1)[e]
Hp-β-CD	1.8 ± 0.1	0.020 ± 0.004	1.4 ± 0.3	7.1 ± 0.4	
γ-CD	0.22 ± 0.03	<0.004	<0.3 ± 0.3	7.3 ± 0.5	(6 ± 2)[e]

[a] T = 20.0 ± 0.1 °C. [b] Calculated using eqn. (2). [c] T = 20 ± 2 °C, the errors are standard deviations from pooled data (three determinations for β- and Hp-β-CD and two determinations for γ-CD). [d] Xanthone (Aldrich) was recrystallized twice from ethanol and β-, γ- and hydroxypropyl-β-CD (Hp-β-CD, lot P96096-1-M, degree of substitution 5, M = 1425) was a generous gift from American Maize. Xanthone CD complexes were prepared by dissolving the solid in a water-saturated xanthone (≈50 μmol dm^{-3}) solution. [e] Ref. 8.

led to a dissociation rate constant of the ground state of $(3.2 \pm 1.1) \times 10^5\ \mathrm{s}^{-1}$.

The different equilibrium constants for the β-CDs and γ-CD can be explained by the different sizes of the cavities. The smaller β-CD cavities are clearly more suited to include xanthone. The ground-state equilibrium constant of xanthone was higher with Hp-β-CD than with β-CD, whereas the reverse was observed for triplet xanthone. These results probably reflect the more hydrophobic environment of Hp-β-CD. Thus, inclusion of a relatively hydrophobic ground-state xanthone is favoured in the more hydrophobic cavity, whereas the increase of the dipole moment for the triplet reverses the relative affinity to these CD cavities. The kinetic experiments showed that the association rate constant with β-CD is the same in the ground and excited state, suggesting that the dipole moment of xanthone does not influence the association process. Conversely, it is the increase in the dissociation rate constant of the triplet that leads to the much smaller equilibrium constant for the excited state. It is interesting to note that for the dynamics of triplet xanthone with β- and Hp-β-CD the biggest difference is in the values for the association rate constants. Temperature dependence studies are currently being performed to obtain a better insight into the complexation mechanism.

In summary, we have determined that the values for the equilibrium constants of triplet xanthone with CDs are *ca.* 20, 100 and >50 times smaller than the equilibrium constants for ground-state xanthone with β-, Hp-β- and γ-CD, respectively. The magnitude of these differences might be smaller for other probe molecules, such as the hydrocarbons previously employed. However, our results show that extrapolation from studies with excited states to behaviour of ground-state probes should be done cautiously when the dynamics of complexation occurs in a time domain shorter than the excited-state lifetime.

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Footnotes

† The laser system is based on the concepts outlined in ref. 9. A preliminary description was published in the May 1993 IAPS Newsletter and a detailed description will be published in the near future.

‡ The decay traces were fitted by using the general fit procedure of the Kaleidagraph software (Synergy Software v 2.0).

§ Fluorescence spectra were acquired with a Perkin-Elmer MPF 66.

¶ The errors are relatively large as the observed rate constants are close to the time resolution of the equipment. This is also the reason that precluded experiments at 20 °C. It was not possible to determine the relaxation kinetics by monitoring absorption as no appreciable changes in the xanthone absorption were observed.

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