The Journal of Physical Chemistry A

 VOLUME 102, NUMBER 10, MARCH 5, 1998

LETTERS

Femtochemistry in Nanocavities: Reactions in Cyclodextrins

A. Douhal,*,†,‡ T. Fiebig,†,§ M. Chachisvilis,†,|| and A. H. Zewail*,†

Laboratory for Molecular Sciences, Arthur Amos Noyes Laboratory of Chemical Physics, California Institute of Technology, Pasadena, California 91125, and Departamento de Química Física, Facultad de Químicas, Sección de Toledo, Universidad de Castilla-La Mancha, San Lucas, 3, 45002 Toledo, Spain

Received: December 15, 1997; In Final Form: January 6, 1998

We present our first studies of the femtosecond dynamics of reactions in confined nanocavities in water solutions. Intramolecular proton transfer and isomerization dynamics of a hydrogen-bonded molecule (HPMO) in liquid solutions and encapsulated in the cavity formed by β-cyclodextrin (diameter $\sim$8 Å) is studied using the technique of fluorescence up-conversion. Our results suggest that the proton transfer in aprotic solvents occurs in much less than 300 fs while upon encapsulation this initial step is slowed to the subpicosecond time scale. Furthermore, in these aprotic solvents, HPMO undergoes a picosecond twisting motion around the interaromatic single bond, which is noticeably inhibited when the molecule is inside the nanocavity. Such studies of condensed-phase femtochemistry in nanocavities offer several promising extensions.

I. Introduction

In this Letter we report on the extension of femtochemistry to the studies of reactions in nanocavities. Such structures are unique and can be formed through covalent and weak, noncovalent bonding as in the case of supramolecular and catalytic chemistry.[1] Cyclodextrin in water solutions provides an opportunity to examine intramolecular reactions and the effect of confined geometries on their dynamics. Our first effort in this direction focuses on the dynamics of intramolecular proton transfer and isomerization with femtosecond (fs) time resolution in β-cyclodextrin (β-CD) whose cavity diameter is $\sim$8 Å. In Figure 1, the guest molecule of interest is shown inside the β-CD cavity with the structure of β-CD determined by X-ray techniques.[2]

Guest HPMO, 2-(2′-hydroxyphenyl)-4-methyloxazole is a heterocyclic molecule with two moieties, capable of establishing an intramolecular hydrogen (H)-bond, and a twisting motion about the interaromatic C−C bond. Upon electronic excitation, the molecule undergoes intramolecular proton-transfer reaction in the gas phase,[3] in solution, and in polymeric media.[4] Recent ab initio calculations on an analogue structure (H atom instead of the 4-methyl group), suggest the presence of a zero- or near zero-energy barrier for the proton transfer in the S_1 state and the possible involvement of a rotational process.[4] Evidence for proton transfer in the excited state comes from the observation of a large Stokes shift in the emission spectra of the keto form of HPMO. Our emission spectra at room temperature are broad and located at $\sim$470 ($\pm$10) nm in liquid solution of 3-methylpentane. Absorption is at $\sim$320 nm, giving the Stokes shift of $\sim$10 000 cm^{-1}.

In water solutions of β-CD, a caged species of HPMO is formed with a 1:1 stochiometry. The steady-state absorption and emission spectra have been shown to depend on the diameter of the cavity of the encapsulating molecular pocket.[5] Other similar molecules exhibiting intramolecular proton transfer and incorporated into the cavity of α-, β-, or γ-CD have also been studied.[6−8] As discussed below, the spectra of HPMO change

† California Institute of Technology.
‡ Universidad de Castilla-La Mancha.
§ Postdoctoral Fellow of the Deutsche Forschungsgemeinschaft.
|| Postdoctoral Fellow of the Swedish Foundation for International Cooperation in Research and Higher Education.

S1089-5647(98)00518-5 CCC: $15.00
Published on Web 02/14/1998

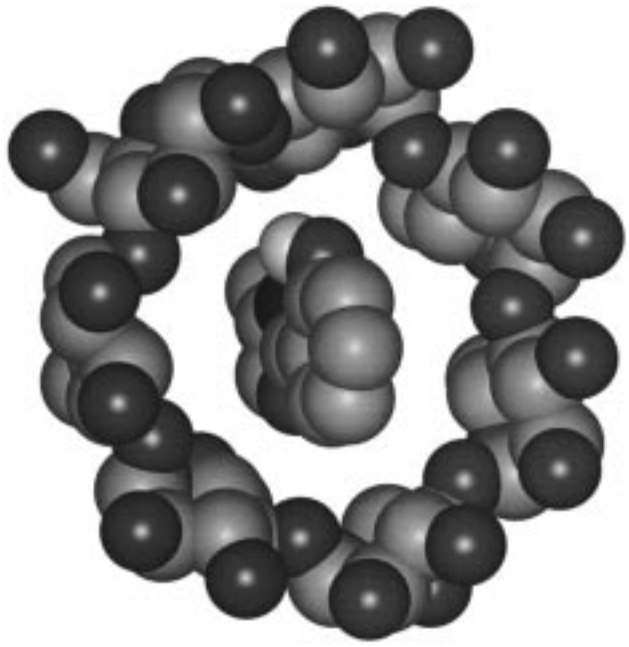

Figure 1. Molecular structure of β-cyclodextrin (β-CD) encapsulating the molecule (HPMO) which undergoes intramolecular proton-transfer and isomerization reactions. The β-CD structure was obtained by X-ray analysis (ref 2), and the larger inner diameter is ~8 Å.

noticeably on going from solvation to cavitation. In 3-methylpentane, the emission is at ~470 nm and in water at ~415 nm, while it is at ~465 nm in β-CD.

In this contribution, and subsequent reports, we examine the femtosecond dynamics of these and other reactions in nanocavities. Cyclodextrins (α-, β-, or γ-CD), which are oligosaccharides with hydrophobic interior and hydrophilic exterior, are used as cavities because of their unique structures and the fact that six (α), seven (β), or eight (γ) glucose units determine the size (see Figure 1). We investigate proton-transfer and isomerization dynamics of HPMO, first in aprotic solvents (3-methylpentane; free dynamics) and then in the caging molecular pocket (β-CD; caged dynamics). Because these cavities are expected to control the H-bonded structure and the dynamics in a size-controlled environment, we are able to observe the influence of cavitation on the intramolecular elementary dynamics, thus opening the door to other similar studies of the effect of nanostructures on reaction dynamics in the condensed phase. Together with studies[9] of solvation and intermolecular effects, we should be able to separate intra- and intermolecular relaxation pathways. Perhaps, some relevance to isomerization and proton- and electron-transfer processes of biological systems, such as those involved in bacteriorhodopsin[10] and protein folding,[11] may also emerge from future studies.

II. Experimental Section

Two femtosecond pulses were generated and used in these experiments; one for the excitation and the second for gating the fluorescence of the different species at various wavelengths. We use the technique of fluorescence up-conversion; the setup is shown schematically in Figure 2. The system consists of a femtosecond Ti:Sapphire oscillator coupled to a regenerative amplifier that generates 90 fs, 0.6 mJ light pulses. The pulses are centered around 798 nm at 1-kHz repetition rate. A beam splitter was used to divide the light beam into the excitation and gating branches with 4-to-1 ratio. The excitation pulses were trippled to yield 266-nm pulses, using two 0.2-mm BBO

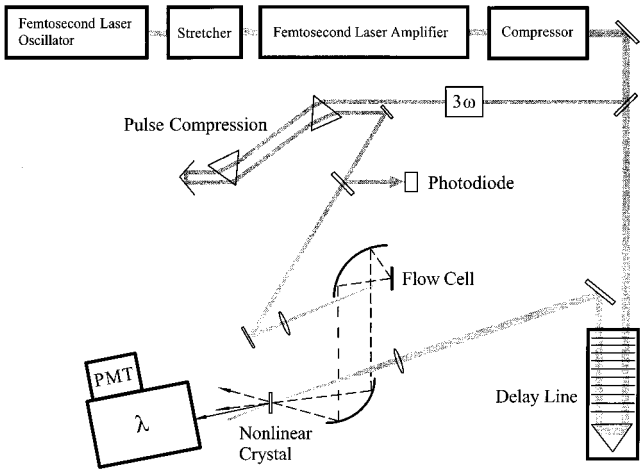

Figure 2. Femtosecond experimental apparatus. The schematic shows the key components involved in the generation, amplification, and compression of femtosecond pulses and the arrangement for fluorescence upconversion.

crystals. These pulses were subsequently compressed, using two silica prisms to compensate for group velocity dispersion, and focused into the sample that flows in a quartz cell.

Typically, the energy of the excitation pulse at the sample was ~30 nJ. To examine the population dynamics, the polarization of the excitation light was set at the magic angle (54.7°) with respect to that of the gating pulse. The sample fluorescence was collected and focused into a nonlinear crystal (0.2 mm, BBO, type I) using reflective optics. The gating pulse was delayed in time and also focused into a nonlinear crystal to overlap with the sample fluorescence.

The resulting sum-frequency signal in the UV region was filtered using a double monochromator and detected with a photomultiplier tube. When necessary, the signal was also normalized to the energy of the excitation pulse. The temporal response function of the pulses and detection is ~300 fs. Since the pulse width is ~90 fs, the resolution is only limited by the detection arrangement. The signal was processed with the help of a computer, and the fit to theoretical curves was made using least-squares analysis.

The sample of 2-(2′-hydroxyphenyl)-4-methyloxazole (HPMO) was obtained as previously described.[4] It was then purified by column chromatography, repeated crystallization from water−ethanol solutions, and vacuum sublimation. The final sample consisted of white crystals. To check for impurities, we obtained the steady-state absorption and fluorescence and the mass spectra. The purity of HPMO was further checked using high-performance liquid chromatography (HPLC); no evidence for impurities was found.

To protect the sample from atmospheric oxygen, all experiments were carried out in an atmosphere of dry argon. The steady-state absorption and fluorescence measurements were performed using a Spex FluoroMax-2 spectrometer.

III. Results and Discussion

As mentioned above, with steady-state UV excitation HPMO exhibits a broad emission band having the maximum at 470 nm in 3-methylpentane and at 465 nm when encapsulated by one molecule of β-CD in neutral water. Both bands result from the emission of the tautomers formed as result of the intramolecular proton transfer. In β-CD−water solutions, HPMO also exhibits relatively weak emission bands at 350 and 415 nm, assigned to the water-solvated enol and phenolate-type species,

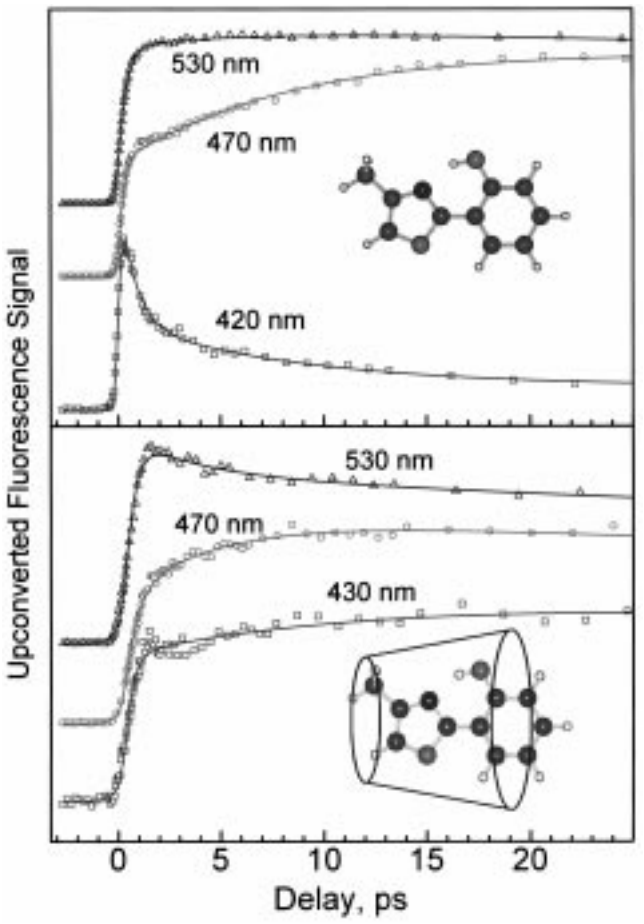

Figure 3. Femtosecond fluorescence transients observed at different wavelengths for HPMO in 3-methylpentane (upper) and in β-cyclodextrin in water solution (lower). The detection wavelengths are indicated.

respectively.[5] The emission of tautomers is largely separated from these weak bands, and thus, the specific dynamics can be studied without interference from these species.

Figure 3 shows the femtosecond-resolved fluorescence transients of the emission of HPMO in 3-methylpentane and in β-CD, when excited at 266 nm and gated at different wavelengths. In 3-methyl pentane, the fluorescence transient depends markedly on the observation wavelength. At the blue side of the emission band (420 nm), the transient shows a fast decay ($\tau_1 \sim 0.7$ ps, 60%; $\tau_2 \sim 9$ ps, 30%), followed by a subnanosecond ($\sim$0.4 ns, 11%) component. However, when the emission is gated at $\sim$470 nm, the transients display a rise with two apparent time constants ($\sim$0.2 ps, 20% and $\sim$9 ps, 30%). The nanosecond component is reached later, as found by probing in the blue region. These observations elucidate the dynamics of free HPMO in the aprotic solvent medium (3-methylpentane).

The decay at 420 nm and the rise at 470 and 530 nm are indicative of the process of proton transfer (Stokes shift), which in this case is accompanied by a twisting dynamics around the single C−C bond linking the oxazole and phenyl moieties. In earlier studies[12] of proton transfer in 7-azaindole in liquid solutions, we observed a similar behavior with two apparent time scales for the rise, reflecting two pathways for the transfer; one is a direct proton motion, and another, slower in time, is an indirect, equilibrated process. The fact that the 420-nm emission shows no detectable rise time, within our resolution, and decays with a time constant of $\sim$0.7 ps (and larger) indicates that the proton transfer is very rapid ($<$300 fs) and that the

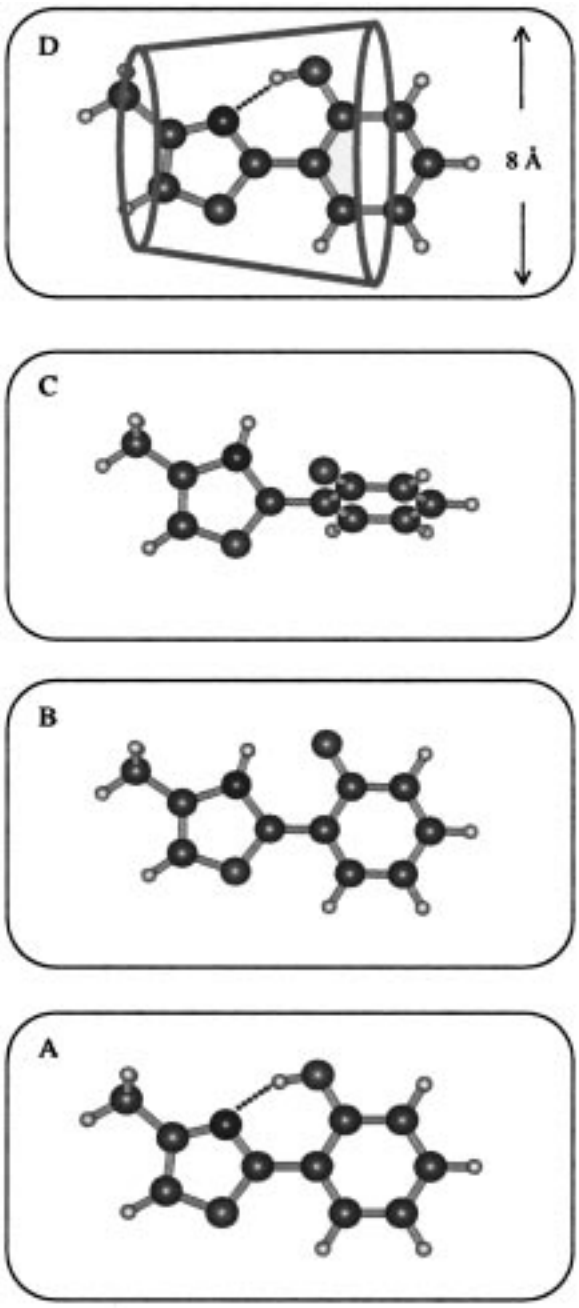

Figure 4. Molecular structures of the HPMO molecule in the enol form (A), keto tautomer (B), rotamer (C), and encapsulated into β-cyclodextrin (D).

470-nm (steady-state) emission is not that of the nascent, initial tautomer following the transfer.

The nascent tautomer is born with different vibrational distributions,[4,12−18] and its decay is due to a twisting around the C−C bond to reach different stable rotamer configuration-(s). The rotational motion involves a barrier crossing, while the proton transfer requires a small or no barrier, as suggested by ab initio calculations.[4] The very rapid proton transfer is also consistent with results from Ernsting's group[15] obtained for a similar system in solution, and with the results for methyl salicylate[18] and hydroxy phenyl oxazole derivative,[16,17] obtained in isolated, gas-phase studies.

The rise of the emission at 470 nm and at 530 nm for HPMO in 3-methylpentane is not instantaneous. In fact, at 470 nm the rise is about $\sim$0.2 ps and at 530 nm is $\sim$0.4 ps, and for both wavelengths the long-time rise component is $\sim$8 ps. These

results are consistent with the rise of a rotamer structure following the proton transfer. Of course, upon proton transfer and redistribution of charges, solvent polarization and dielectric friction will lead to different solvent configurations of some stability. Thus, the emission at longer wavelengths, for example, 530 nm, may reflect these local rotamer structures, and further studies should illuminate their extend and dynamics.

As noted in Figure 3, the transient behavior of HPMO in β-CD at 430 nm is different from that observed in 3-methylpentane. The steady-state emission in β-CD in water solutions is similar to that in 3-methylpentane except for a blue shift of $\sim$5 nm. (In water solution, there is an additional peak at 415 nm, which decreases considerably upon encapsulation.[5]) The transient at 430 nm in β-CD is not instantaneous and shows a rise of $\sim$0.3 ps. At the other wavelengths, 470 and 530 nm, the rise is similar ($\sim$0.4$-$0.5 ps). This observed rise, and the absence of the femtosecond decay, suggests that the encapsulated HPMO initial geometry requires some structural rearrangements for the proton to move. Furthermore, the twisting process is considerably reduced owing to the confined geometry of the host environment.

Because of the size of the guest (HPMO, length $\sim$9 Å and diameter $\sim$5 Å) and that of the host cavity (β-CD, largest inner diameter $\sim$8 Å),[2] we expect a reduction of the degrees of freedom involved in proton transfer and twisting when the molecule is encapsulated. From a structural point of view (Figure 4), the dynamics in the cavity can be understood. First, the existence of several configurations of encapsulated HPMO with different angles between the oxazole ring (H-bond acceptor) and phenol moiety (H-bond donor) leads to large motions of these parts in order to reach an adequate geometry for the intramolecular proton transfer. These motions need time to modulate the proton jump as well as the subsequent relaxation to the different rotamers. Second, because of confinement in β-CD, the amplitude of the motion for barrier crossing is reduced with the consequence of limiting structural changes.

The above results suggest further experiments, including the study of the cavity size effect (α, β, γ-CD), the solvent polarity, and the guest composition.

IV. Conclusion

In this Letter, femtochemistry of intramolecular reactions in nanocavities is reported. Using β-cyclodextrins as a host in water solutions, we examined the reactions of proton transfer and isomerization for the guest HPMO (2-(2′-hydroxyphenyl)-4-methyloxazole). The dynamics in cyclodextrin and in aprotic solvents are compared. In case of the free molecule in aprotic solvent, the femtosecond fluorescence transients indicate ultrafast proton transfer ($<$300 fs) as well as a slower picosecond twisting motion around the interaromatic C$-$C bond of HPMO. In contrast, the caged molecule in β-cyclodextrin exhibits dynamics that are influenced by the host environment leading to a slower proton-transfer rate and a reduction in barrier crossing. These results provide the basis for many new experiments on chemical reaction dynamics in nanocavities. Work along these lines is in progress in this laboratory.

Acknowledgment. This work was supported by the National Science Foundation. M.C. thanks the Swedish Foundation for International Cooperation in Research and Higher Education (STINT) for its generous fellowship. T.F. is grateful for financial support from the Deutsche Forschungsgemeinschaft. A.D. thanks Prof. A. H. Zewail and his group for their hospitality during his stay in Femtoland V. We thank Dr. W. Kühnle for his help with the HPLC.

References and Notes

(1) Lehn, J. M. *Supramolecular Chemistry*: *Concepts and Perspectives*; VCH Publishers: New York, 1995. Thomas, J. M.; Thomas, W. J. *Principles and Practice of Heterogeneous Catalysis*; VCH Publishers: New York, 1997. (b) Balzani, V.; Scandolla, F. *Supramolecular Chemistry*; Ellis Horwood: London, 1991.

(2) See, for example: (a) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer-Verlag: New York 1978. (b) Sjetli, J. *Cyclodextrin Technology*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1988. (c) Wenz, G. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 803. (d) Bortolus, P.; Monti, S. In *Advances in Photochemistry*; Neckers, D. C., Volman, D. H., von Bünau, G., Eds.; John Wiley & Sons, Inc.: New York, 1996 and references therein.

(3) Douhal, A.; Lahmani, F.; Zehnacker-Rentien, A.; Amat-Guerri, F. *Fast Elementary Processes in Chemical and Biological Systems*; AIP Conference Proceedings; Tramer A., Ed.; American Institute of Physics: Woodbury, NY, 1996; Vol. 346, p 383.

(4) Guallar, V.; Moreno, M.; Lluch, J. M.; Amat-Guerri, F.; Douhal, A. *J. Phys. Chem*. **1996**, *100*, 19789.

(5) Douhal et al. To be published.

(6) Cox G. S.; Turro, N. *J. Photochem. Photobiol*. **1984**, *40*, 185.

(7) Roberts, A. L.; Dey, J.; Warner, I. M. *J. Phys. Chem*. **1996**, *100*, 19681.

(8) Douhal, A.; Amat-Guerri, F.; Acuña, A. U. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 1514.

(9) (a) Duveneck, G. L.; Sitzmann, E. V.; Eisenthal, K. B.; Turro, N. J. *J. Phys. Chem*. **1989**, *93*, 7166. (b) Vajda, S.; Jimenz, R.; Rosenthal, S. J.; Fidler V.; Fleming, G. R.; Castner, E. W. *J. Chem. Soc., Faraday Trans.*, **1995**, *91*, 867. (c) Hansen, J. E.; Pines, E.; Fleming, G. R. *J. Phys. Chem*. **1992**, *96*, 6904.

(10) Tajkhorshid, E.; Paizs, B.; Suhai, S.; *J. Phys. Chem. B* **1997**, *101*, 8021 and references therein.

(11) See, for example: *Chem. Rev*. **1997**, *97* (5) and references therein.

(12) Chachisvilis, M.; Fiebig, T.; Douhal, A.; Zewail, A. H. *J. Phys. Chem. A* **1998**, *102*, 669.

(13) Douhal, A.; Amat-Guerri, F.; Acuña, A. U.; Yoshihara, K. *Chem. Phys. Lett*. **1994**, *217*, 619.

(14) Chudoba, C.; Riedle, E.; Pfeiffer, M.; Elsaesser, T. *Chem. Phys. Lett*. **1996**, *263*, 622.

(15) Arthen-Engeland, Th.; Bultman, T.; Ernsting, N. P.; Rodriguez, M. A.; Thiel, W. *Chem. Phys*. **1992**, *163*, 43.

(16) Douhal, A.; Lahmani, F.; Zehnacker-Rentien, A.; Amat-Guerri, F. *J. Phys. Chem*. **1994**, *98*, 12198.

(17) Douhal, A.; Lahmani, F.; Zewail, A. H. *Chem. Phys*. (Special issue) **1996**, *207*, 477 and references therein.

(18) Herek, J. L.; Pedersen, S.; Bañares, L.; Zewail, A. H. *J. Chem. Phys*. **1992**, *97*, 9046.