Water: An underappreciated reaction medium for photodimerizations

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Abstract

Organic solvents have been the sought-after medium to achieve light initiated transformations in laboratories and industries. Given the current emphasis on green chemistry and rising awareness of environmental pollution it may be necessary for us to utilize abundantly freely available, non-toxic and environmentally friendly water as the medium to perform photoreactions. Although water has attracted the attention of organic synthetic chemists, it is yet to receive the indispensable attention of photochemists. In this article we present examples of photocycloaddition reactions of four molecules namely coumarin, indene, cinnamic acid and acenaphthylene that are sparingly soluble in water. Photodimerization of these molecules in water is much faster and occurs at much lower concentrations than in organic solvents. Aggregation probably forced by hydrophobic association is suggested to be the cause for the increased reactivity even at lower concentrations. The dimer distribution in water is different from that in organic solvents. Further work is required to fully understand the mechanism of photodimerization in water. Although the poor solubility of organic molecules in water requires one to irradiate large volumes to collect enough useful amounts, availability of flow reactors and LEDs as light sources should help one overcome the challenges.

Key words

Water, hydrophobic effect, aggregates, photodimerization, [2+2] addition

Introduction

Water has been the preferred medium for biological reactions while non-aqueous medium is preferred by organic chemists including photochemists to perform transformations. Water has advantages, it is green, non-toxic, cheap and non-hazardous. Yet, it is not preferred because most molecules organic chemists are interested-in are insoluble in water. However, during the last two decades there has been a steady interest in carrying out reactions in water by synthetic chemists. Considerable literature including reviews and monographs authored by organic synthetic chemists are available.[1-6] In addition, due to the insistent efforts of physical chemists much of the properties of water is known.[7-9] Given that synthetic chemists have begun to embrace several aspects of photochemistry (e.g., electron and energy transfer mediated photoreactions) it is time for photochemists to learn from the experience of synthetic chemists and begin exploring the use of water as a reaction medium. Previously, organized assemblies such as micelles, cavitands and organic and inorganic hosts were employed to solubilize organic molecules in water.[10, 11] While reactions in these media have provided insight into the factors that control the behavior of confined molecules and also yielded highly selective products, the reaction does not occur in water, it does within the confined spaces of hosts. Further, often the use of host systems require either synthesis and/or disposal of host after use. Given that photocycloaddition has been a very valuable synthetic tool in constructing natural and unnatural organic molecules,[12] establishing the value of water as the reaction medium for such reactions seemed a worthwhile goal.

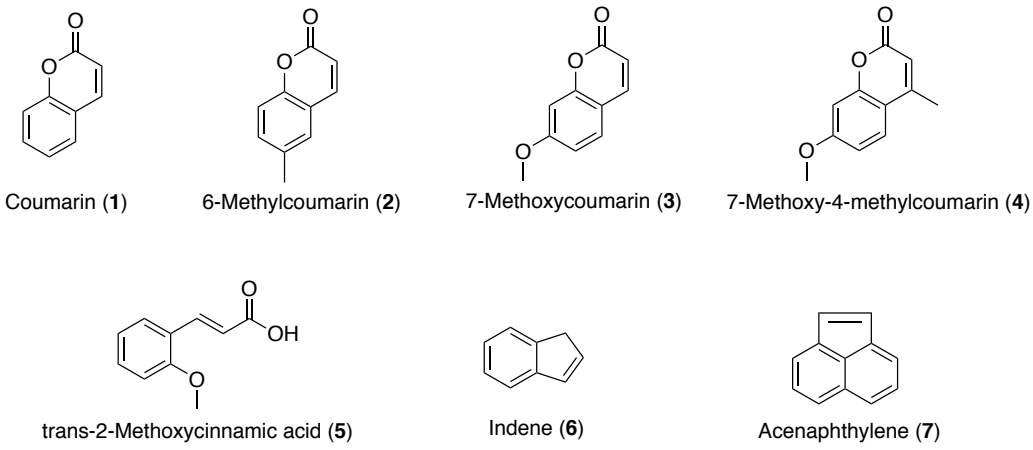
Water as the medium for organic reactions is known for over a century and in fact it was the medium of choice by Diels and Alder to perform their well-known [4+2] addition of maleic anhydride with furan.[13] The same has been utilized by Woodward and Baer in their synthesis of a natural product cantharidin.[14, 15] In spite of these, interest in this topic by the organic community had to wait for the publications of Breslow and his co-workers in 1980s.[16-19] They showed that rates of Diels-Alder reactions of a few systems are enhanced in water as well as there is a preference for endo product in some cases. Synthetic value of this strategy was established by Grieco's group.[20-25] In these examples, enhancement of rate and selectivity were attributed to hydrophobic effect.[26-29] These additions are dubbed 'in water' reactions meaning that reactant molecules are not on surface, but in bulk water either as aggregates or as dissolved molecules in low concentrations. Interest in this topic was further recently kindled by

a report by Sharpless and co-workers whose reactions were classified as 'on water'.[30] These additions occur between two molecules that are not dissolved but suspended in water. Thus, the two types 'in water' and 'on water' reactions extend to all types of molecules, the ones that are insoluble and remain as aggregates in bulk water and to those that are insoluble but remain suspended at the interface involving water as a component. It is clear from the above as well as a number of reported examples that water can be a good medium to perform various types of synthetically useful reactions.[31-33] The above studies argue favorably to undertake experiments to establish the value of water as a solvent to perform photoreactions. The fact that pure water is transparent above 220 nm is a virtue and it allows selective excitation of a large number of molecules carrying almost any type of chromophore.

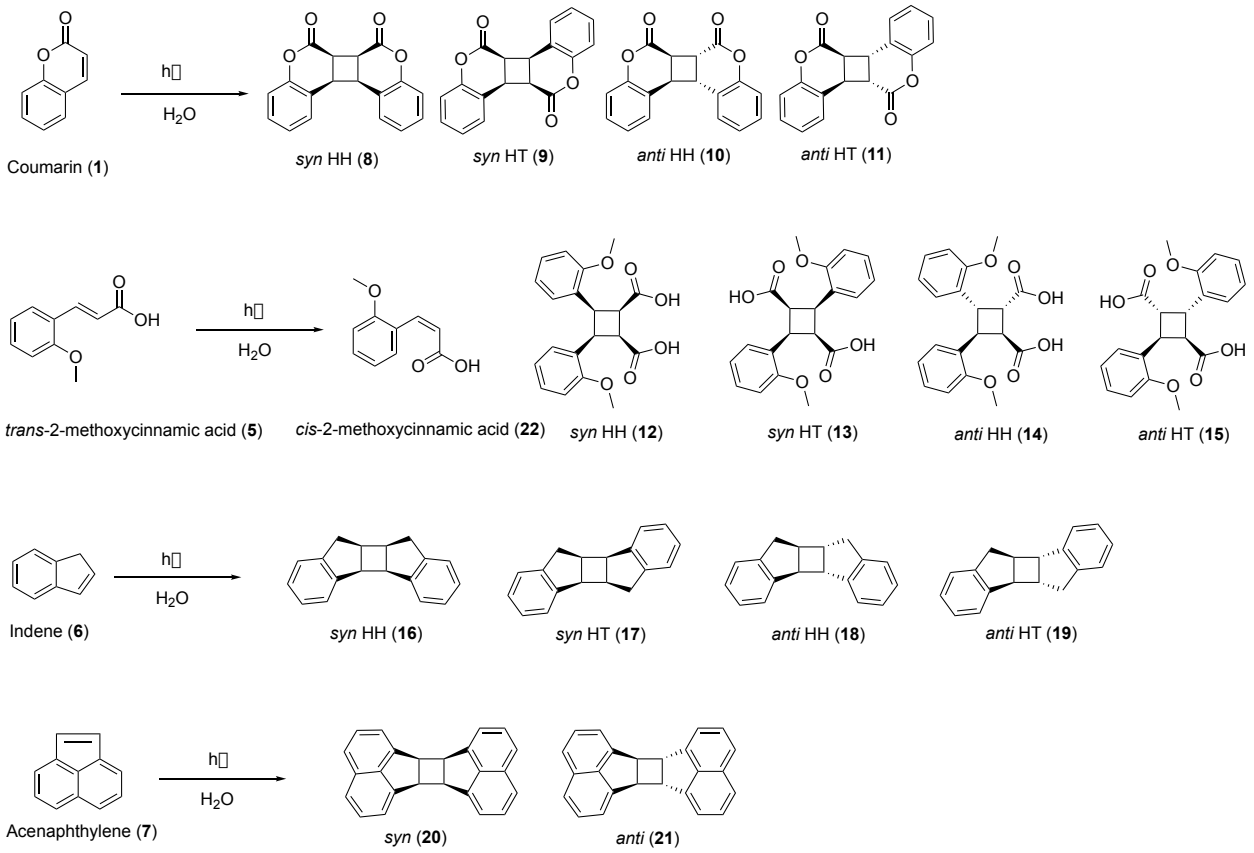
It is well-known that selective photodimerizations could be carried out in solid state even without solvents.[34-36] However, not all olefins can be photodimerized in crystalline state either due to the fact that not all olefins are crystalline or the packing is not conducive for the reaction. Thus, the value of water as the medium can't be overlooked in favor of solvent free (solid state) reactions. While the original proposal of Breslow that the unusual influence of water on organic reactions 'in water' is due to hydrophobic effect still stands, theoretical calculations have brought out the importance of additional effects such as enforced hydrophobic effect, hydrogen bonding and enhanced hydrogen bonding at the polarized transition state.[37-43] Computations also bring out the importance of hydrogen bonding between water molecules on the interface with the reactants as well as with the transition state during 'on water' reactions.[44, 45] Thus, in general three effects play a role, hydrophobic effect, enforced hydrophobic effect and hydrogen bonding. Given that the mechanisms of thermal and photochemical reactions are different it is not obvious whether these effects would play a role and enhance the rate and enforce selectivity during photochemical reactions. We provide below four examples from our laboratory of photodimerization of organic molecules in water. In all examples, the rate of dimerization is enhanced while the extent of selectivity is not obvious.

Although interest in thermal reactions in water exploded following the reports of Breslow and Sharpless, no such event took place with photoreactions. There have been scattered reports of [2+2] photocycloadditions in water. Even some of them brought out the uniqueness of water as the medium. To our knowledge the early reports on this topic dealt with photodimerization of thymine and uracil and their derivatives.[46-49] Dimerization was speculated to involve

aggregates. Following the initial report by Rideout and Breslow we reported that coumarin readily dimerizes in water and the quantum yield was higher by two orders of magnitude compared to that in methanol.[50] We followed this with the photodimerization of stilbene and alkyl cinnamates.[51-53] In addition to ours there were a few reports, but they failed to arouse the interest of photochemical community.[54-57] Considering the remarkable attention thermal reactions in water has received, we believe this is an appropriate time to re-examine the value of water as the solvent in photoreactions. With this rationale we have examined the photocycloadditions of four cyclic olefins, coumarins, indene, acenaphthylene and *trans*-2-methoxycinnamic acid (**1**-**7** ; Scheme 1) whose excited state chemistry have been extensively investigated in solution.[58-66] The products formed in organic solvents are shown in Scheme 2. Results of our investigation in water are discussed in this presentation.



Scheme 1: Structure of molecules investigated



Scheme 2. Photodimerization of reactants.

Experimental Section

General information: Commercially available materials were used as supplied without purification. ^{1}H NMR characterization and NMR titration studies were performed on Bruker Avance 400 spectrometer. Chemical shifts are reported in parts-per-million (ppm). Deuterated solvent was used as a lock and residual protonated solvent peak was used as reference. Absorption spectra were recorded on a Shimadzu UV - 3150 spectrophotometer. Dynamic Light Scattering (DLS) measurements were recorded on a Malvern zetasizer nano.

Materials: All chemicals used were purchased from commercially available sources. Coumarin and its derivatives from Aldrich and were used as received. *trans*-2-methoxycinnamic acid (≥97%) and Indene (≥ 99%) were purchased from Sigma-Aldrich. *trans*-2-methoxycinnamic acid used as received, whereas Indene was distilled prior to use. Acenaphthylene (85%) from Aldrich was subjected to vacuum sublimation thrice prior to use. Eosin-Y (93%) from Eastman

Chemical Co. was used as received. Benzophenone (99%) from Beantown Chemical was used as received. Deuterated water, chloroform and DMSO from Sigma-Aldrich were used as received. De-ionized water was used for all Pyrex tube irradiations. Triple-distilled water was used to record absorption spectra and DLS.

*General procedure for excitation of olefins in water***:** Samples in water for irradiation were prepared by weighing reactants such that they would make 0.02 M solution if completely dissolved. Due to the limited solubility in water, the reactants remain suspended in water. The reactants were taken in a test tube and charged with a magnetic stir bar. Appropriate amounts of de-ionized water were added. The samples were purged with N_2 for 30 mins and irradiated using a 450 W medium pressure Hg lamp in a water-cooled Pyrex immersion well under vigorous stirring. The photoproducts in the irradiated sample were extracted using chloroform (ethyl acetate in the case of *trans*-2-methoxycinnamic acid (**5**)) and analyzed by ^{1}H NMR.

General procedure for excitation of olefins as liquid (l) and as solids (s): A thin layer of the reactants was sandwiched in between two Pyrex glass slides and irradiated with a 450 W medium pressure Hg lamp in a water-cooled Pyrex immersion well. The glass slides were rotated occassionally to ensure even irradiation of the entire sample. The irradiated sample was analyzed by ^{1}H NMR.

General procedure for excitation of olefins in organic solvents: 600 μL of 0.02 M reactant samples in $CDCL_3$ (DMSO-d_6 in the case of *trans*-2-methoxycinnamic acid (**5**)) were taken in an NMR tube. They were purged with N_2 for 30 mins and irradiated with a 450 W medium pressure Hg lamp in a water-cooled Pyrex immersion well. The irradiated sample was analyzed by ^{1}H NMR.

UV-Visible Absorption Spectra: A suspension of coumarin (**1**) in water was sonicated for 15 mins and passed through a 0.45 μm PTFE filter to yield a stock solution of coumarin in water. UV spectra of coumarin at various concentrations were taken by further diluting the stock solution of coumarin in water obtained after passing through the filter. A 0.001 M stock solution of acenaphthylene (**7**) was prepared in DMSO-d_6. UV spectra of acenaphthylene at various concentrations were obtained by adding 1.5 μL of the stock solution into 3 mL of de-ionized water taken in a cuvette. With each addition, the concentration of acenaphthylene in water was raised by increments of 5 μM.

^{1}H NMR Spectra: A 0.24 M stock solution of coumarin (**1**) was prepared in DMSO-d_6. ^{1}H NMR spectra of coumarin at various concentrations were obtained by adding 2.6 μL of the stock solution into 600 μL of D_2O taken in an NMR tube. With each addition, the concentration of coumarin in D2O was raised by increments of 0.001 M.

Dynamic Light Scattering (DLS) Experiments: Suspensions of the reactants in water were sonicated for 15 mins and passed through a 0.45 μm PTFE filter to yield a stock solution of reactants in water. DLS measurements were run on the prepared stock solutions of the reactants in water. A 0.06 M stock solution of indene (**6**) was prepared in DMSO-d_6. Appropriate amount of this stock solution was added to de-ionized water and the DLS measurements were run at various concentrations.

Results

Four systems namely coumarins, cinnamic acid, indene and acenaphthylene structures of which shown in Scheme 1 were chosen for examination of photodimerization in water. All four systems have been investigated extensively in solution[58-61, 63, 64, 66-68] as well as in various organized assemblies.[69-83] These studies provide spectral data for product dimers as well as mechanism of dimerization in organic solvents. In this study the ^{1}H NMR data of the dimers obtained were compared with literature reports. As expected, the seven molecules (Scheme 1) examined here have very poor solubility in water and it varied between $5x10^{-5}$ M (**7**) and $9x10^{-3}$ M (**1**). For the sake of uniformity known amounts of the substrate that would make 0.02 M were taken in water. Under this condition some amounts of the substrate remained insoluble in water. Since not all the amount of the substrate taken completely dissolved in a given amount of water, we call it as 'equivalent concentration' instead of concentration, *i.e.,* had all the taken amount of olefins dissolved in water this would be the concentration (but it did not). Indene being a liquid, it was not clear whether it remained fully or partially solubilized in water. Coumarin **2**-**4** being less soluble, only solutions of $8x10^{-3}$ M were irradiated. Even if the solutions were initially turbid because of the presence of undissolved reactant molecules, both dissolved and suspended reactants were fully converted to dimers upon irradiation. This could be due to dissolution of the undissolved particles as and when the dissolved olefin molecules reacted.

The experimental procedure consisted of Pyrex test tube as reaction vessel and 450 W medium pressure mercury lamp as the light source. All irradiations were conducted under nitrogen saturated conditions and the solution was vigorously stirred while being irradiated. Upon completion of irradiation (~ 24 hrs) the products were extracted with chloroform or ethyl acetate and concentrated. ^{1}H NMR spectra of concentrated samples in $CDCl_3$ were recorded and the yields of the products were estimated by integrating relevant signals. In the case of indene, the yields were estimated by employing GC-MS. Product yields along with irradiation conditions are presented in Table 1. In addition to bulk irradiation in Pyrex test tubes, smaller amounts of the sample in D_2O (600 μL) were irradiated in NMR tubes and the reaction was followed by NMR. The latter was carried out to make sure small and large scale irradiations show similar behavior. Under NMR tube irradiation conditions, the equivalent concentration was maintained at 0.02 M by proportionally reducing the amount of the olefin and water. Since the sample after irradiation was cloudy, products were extracted with $CHCl_3$ or ethyl acetate, solvent evaporated and NMR recorded in $CDCl_3$ or DMSO-d_6. Product distribution was the same during both Pyrex test tube and NMR tube irradiations (Table S1; Supplementary Information).

In Figures 1-4, the ^{1}H NMR spectra of starting olefins **1**, **5**-**7** and products obtained following irradiation are presented. In every case the reaction was clean and the only products obtained were dimers except in the case of **5** where the *cis* isomer (**22**) accompanied the dimer. From ^{1}H NMR spectrum in the case of coumarin **1** we could identify the presence of three dimers.[58] Of the three dimers, *syn* head-head was the major. As seen in Figure 2, *trans*-2-methoxycinnamic acid (**5**) yielded single dimer along with *cis* isomer **22** in water.[84] ^{1}H NMR spectrum of the products formed upon irradiation of indene is complex (Figure 3).[65, 81] However, signals for all dimers have been assigned in the literature.[66] Comparing with literature data we were able to recognize the formation of four dimers (Table 1) with *anti*-head-head (anti HH) as the predominant one. In the case of acenaphthylene the signals for the two dimers are easily identified (Figure 4).[62] Thus, from the NMR spectra it is clear that there is dimerization in all cases in water even though the concentration is low (< 0.02 M). The dimerization in all cases in water proceeded with no complications even if the reactant molecules were not fully dissolved.

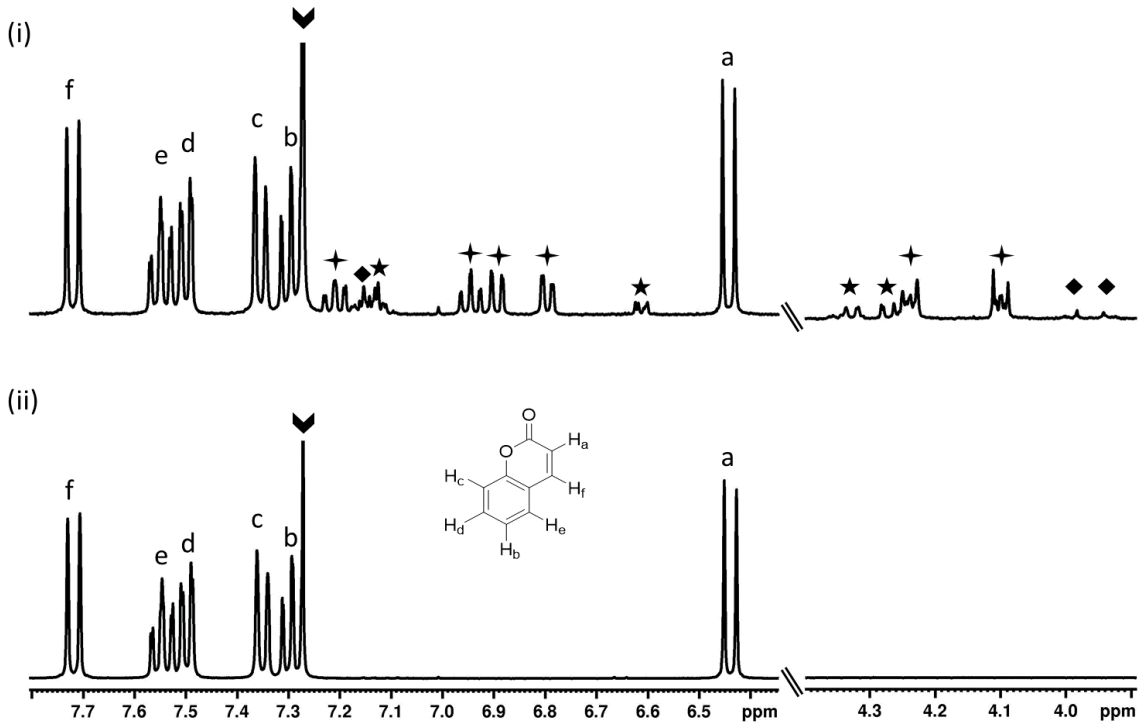


Figure 1. ^{1}H-NMR (400 MHz, $CDCl_3$) spectra of coumarin (**1**) upon direct irradiation in water. (i) coumarin sample after irradiation in water (★ represents *syn* HT dimer (**9**), ✦ represents *syn* HH dimer (**8**) and ◆ represents *anti* HH dimer (**10**)); (ii) coumarin sample before irradiation; (⮟ represents residual $CHCl_3$)

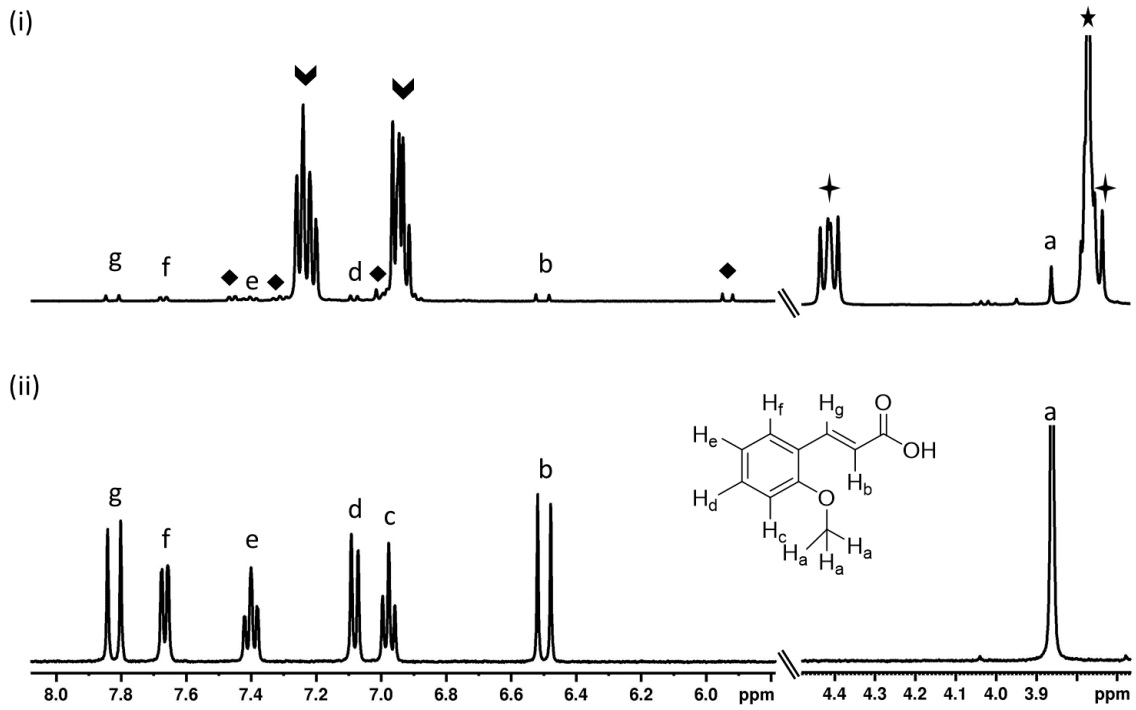


Figure 2. ^{1}H-NMR (400 MHz, DMSO-d_6) spectra of *trans*-2-methoxycinnamic acid (**5**) upon direct irradiation in water. (i) *trans*-2-methoxycinnamic acid sample after irradiation in water (✦ represents protons on the cyclobutane ring of *anti* HT dimer (**15**), ★ represents methoxy protons of **15**, ⌄ represents aromatic ring protons of **15** and ◆ represents protons of *cis*-2-methoxycinnamic acid (**22**)); (ii) *trans*-2-methoxycinnamic acid sample before irradiation.

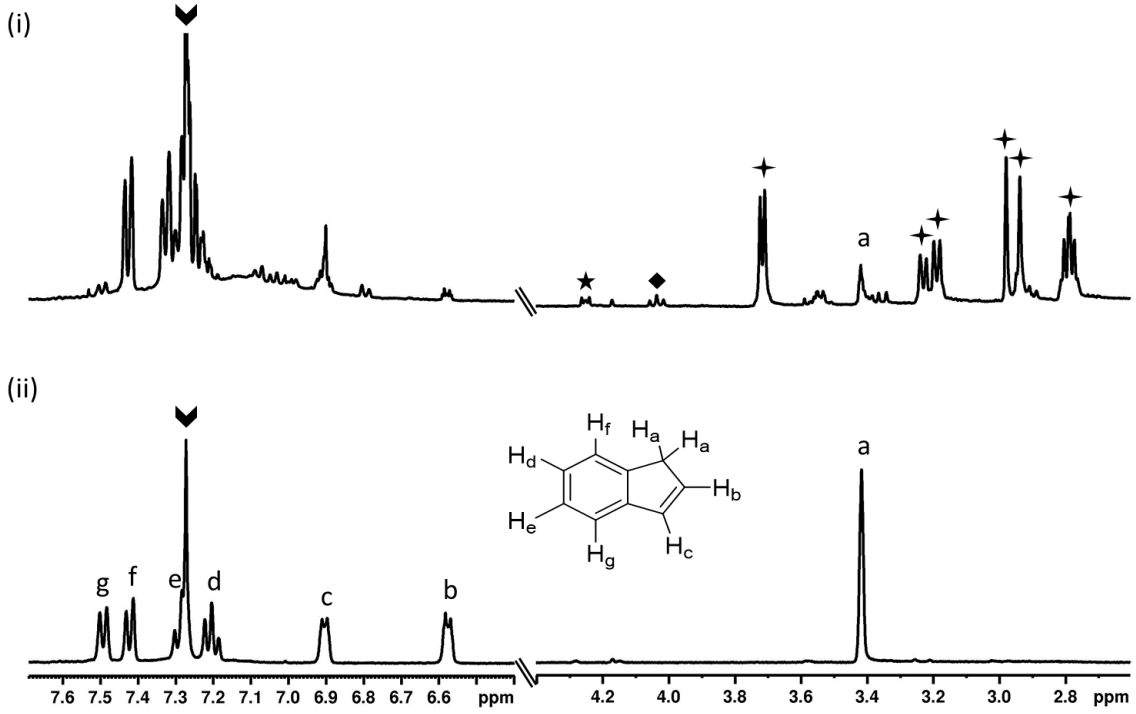


Figure 3. ^{1}H-NMR (400 MHz, $CDCl_3$) spectra of indene (**6**) upon direct irradiation in water. (i) indene sample after irradiation in water (✦ represents anti HH dimer (**18**) and ★ represents *syn* HH dimer (**16**) and ◆ represents *syn* HT dimer (**17)**; (ii) indene sample before irradiation. (⮟ represents residual $CHCl_3$)

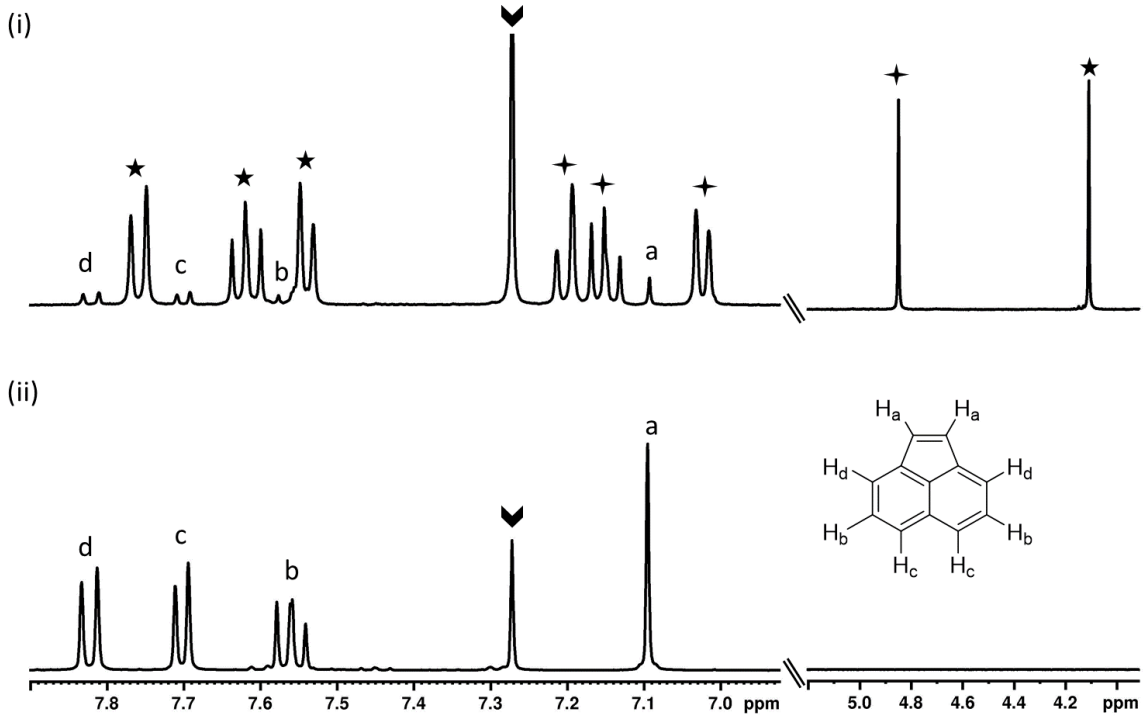


Figure 4. ^{1}H-NMR (400 MHz, $CDCl_3$) spectra of acenaphthylene (**7**) upon direct irradiation in water. (i) acenaphthylene sample after irradiation in water (✦ reresents *syn* dimer (**20**) and ★ represents anti dimer (**21**)); (ii) acenaphthylene sample before irradiation. (⮟ represents residual $CHCl_3$)

Table 1. Product distribution upon irradiation of olefins **1**-**7** in water.

(a) Direct Excitation[a,b]						
Reactants	Equivalent concentration[d]	Percent conversion, %	Product composition[c], %			
			syn HH	*syn* HT	*anti* HH	*anti* HT
Coumarin	0.02 M	47	64	28	8	-
6-methylcoumarin	0.008 M	95	35	8	57	-
7-methoxycoumarin	0.008 M	96	6	79	15	-
7-methoxy-4-methylcoumarin	0.008 M	95	75	25	-	
trans-2-methoxycinnamic acid	0.02 M	87	-	-	-	60[e]
Indene	0.02 M	97	7	7	77	9
Acenaphthylene	0.02 M	95	47 (*syn*)		53(*anti*)	
(b) **Sensitized Excitation**[a]						
Reactants	Irradiation time, hours	Sensitizer	Product composition[c], %			
			syn HH	*syn* HT	*anti* HH	*anti* HT
Coumarin (14.6 mg in 5 mL water/equivalent concentration 0.02 M)	5	Benzophenone (1.8 mg)	36	20	44	-
		Benzophenone (3.6 mg)	28	21	51	
Acenaphthylene (30 mg in 10 ml water/ equivalent concentration 0.02 M)	24	Eosin-Y[f]	48 (*syn*)		52 (*anti*)	

[a] All samples were irradiated for 24 hours using a 450-watt medium pressure Hg lamp in a water-cooled Pyrex immersion well.

[b] Sample volume in all cases were 50 mL of water.

[c] Product composition in the irradiated sample was determined by ^{1}H NMR spectroscopy. Indene (**6**) product composition was determined by GC-MS spectoscopy. Product composition is calculated based on the reacted starting material.

[d] The organic molecules studied have limited solubility in water. All samples were prepared such that if completely dissolved in water, the organic molecules would have an equivalent concentration as given in this column.

[e] *trans*-2-methoxycinnamic acid (**5**) acid also undergoes isomerization to give *cis*-2-methoxycinnamic acid.

[f] Radiations from the mercury lamp was passed through a Corning cut-off filter (3-68) that is transparent to radiations above 520 nm only.

To examine the feasibility of triplet sensitization in water, dimerization of coumarin and acenaphthylene were conducted with benzophenone and eosin-Y respectively as triplet sensitizers.[60, 62] The aim of triplet sensitized dimerization was to explore the feasibility of obtaining different dimers from two different reactive states in water. To achieve dimerization from triplet state we needed to examine the feasibility of triplet sensitization in water. For this purpose we employed eosin-Y and benzophenone as sensitizers for acenaphthylene and coumarin systems respectively. The triplet energies of eosin-Y, benzophenone, acenaphthylene and coumarin are known to be 47, 69, 43 and 62 kcal/mole respectively.[68, 85, 86] Product yields are summarized in Table 1. Under our conditions, while in the case of coumarin there was a difference in the dimer ratio between direct and sensitized irradiations, there was no such difference in the case of acenaphthylene. To be sure that triplet sensitization occurs in the case of acenaphthylene, sample without sensitizer was irradiated >520 nm. There was no dimerization. The fact that dimerization occurred in presence of eosin-Y under the same condition suggested that triplet sensitization occurred in the case of acenaphthylene in aqueous solution. However, there was not much difference in isomer ratio of the dimers. Benzophenone has been established to triplet sensitize coumarin to yield *anti* HH dimer.[60, 67] The dimer obtained during direct excitation is *syn* HH (Table 1). Since there is overlap between benzophenone and coumarin absorptions selective excitation of benzophenone, especially in water was not feasible. Therefore, irradiations were conducted where the relative concentrations of benzophenone and coumarin were different. Once again evidence in favor of triplet sensitization came from the enhanced yield of *anti* HH dimer with increased concentration of benzophenone (Table 1). The above experiments suggested that triplet sensitization in water as in organic solvents can be conducted. Indeed, this opens up opportunity to carry out both direct excited and triplet sensitized reactions in water.

The above results raise important questions: How is the rate and distribution of products differ with respect to that in isotropic organic solvents and if there is a difference what is the cause. To address these questions, we irradiated four samples **1**, **5**-**7** in organic solvents ($CDCl_3$

or DMSO) at 0.02 M concentration (the same effective concentration used in water). Results presented in Table S2 show that at such concentrations and under the same conditions of irradiation as in water the dimer yield was low (<10%) in organic solvents. In the case of *trans*-2-methoxycinnamic acid (**5**) only isomerization to the *cis* isomer (**22**) occurred. Clearly, photodimerization in water is more efficient than in organic solvents. The fact that the dimerization is more efficient in water, even at low concentrations, suggests that diffusion is not playing a role in the dimer formation.

Of the olefins investigated here, extensive mechanistic studies on photodimerization of coumarin and acenaphthylene have been conducted.[62] Morrison and co-workers have shown that the dimer ratio depends on the concentration of the substrate and solvent polarity.[87] Interestingly even at 0.31 M in various solvents the conversion is only 7% after 68 h of irradiation. The conversion appears to be lower than what we were able to achieve with 0.02 M in water. Dimerization of acenaphthylene in organic solvents was conducted at much higher concentrations (0.66 M) than what we have used in water.[62] Conversion is reported to be lower. From the reported examples we believe that water is able to enforce dimerization even at lower concentrations.

To probe the presence of aggregates we recorded dynamic light scattering spectra (DLS) of aqueous solution of **1**, **5**-**7**. Results presented in Table 2 clearly show that all four samples are aggregated in aqueous solution. Size of the aggregate from each molecule is also included in the Table. From the DLS data we conclude that each aggregate contains between 165 (in **1**) and 1450 molecules (in **5**). In the case of indene, the aggregate size increases with concentration (Figure S2). From DLS data we conclude that the molecules investigated here aggregate in water. No further additional conclusions were drawn from these data. Having inferred the presence of aggregates in water we were curious to know whether there is any electronic or magnetic interaction between molecules in the aggregates. To probe this, we recorded the absorption spectra of **1**, **5**-**7** at various concentrations (Figures S3-S6). Although as expected intensity of the absorption increased with concentration, there was no change in the spectra. Also as seen in Figure S3-S6 in SI the absorption intensity showed a linear relationship with the concentration ruling out electronic interactions between molecules in the aggregate. Had there been an aggregate with different absorption properties non-linear Beer-Lambert plot would have resulted. Based on this we conclude that in these aggregates there are no intermolecular orbital

interactions like in H and J aggregates. Based on absorption spectra we believe the aggregates are not a highly organized assemblies. However, as per ^{1}H NMR signals of coumarin there seems to be weak magnetic interaction between molecules. The ^{1}H NMR spectra of coumarin at various concentration in D_2O are presented in Figure 5. A slight shift in the aromatic and olefinic proton signals with respect to concentration is noticeable. We believe this may be an indication of coumarin molecules being close to each other in aqueous solution. Probably, this is an indication of the presence of aggregates in water.

Table 2: Aggregate size based on dynamic light scattering data in aqueous solution[a]

Reactants	Molecule Size, nm		Diameter (nm)	Intensity, %
Coumarin	(0.73 nm)	Peak 1	119.8 ± 67.08	88.9
		Peak 2	4315 ± 1040	11.1
trans-2-mmethoxycinnamic acid	(0.92 nm)	Peak 1	1327 ± 956.5	93.4
Indene	(0.65 nm)	Peak 1	139.9 ± 85.22	81.4
		Peak 2	2711 ± 1403	15.5
Acenaphthylene	(0.69 nm)	Peak 1	199 ± 126.6	89.5
		Peak 2	3410 ± 1305	7.9

a. Samples were prepared by filtering a suspension of molecules in water through 0.45 μm PTFE filter.

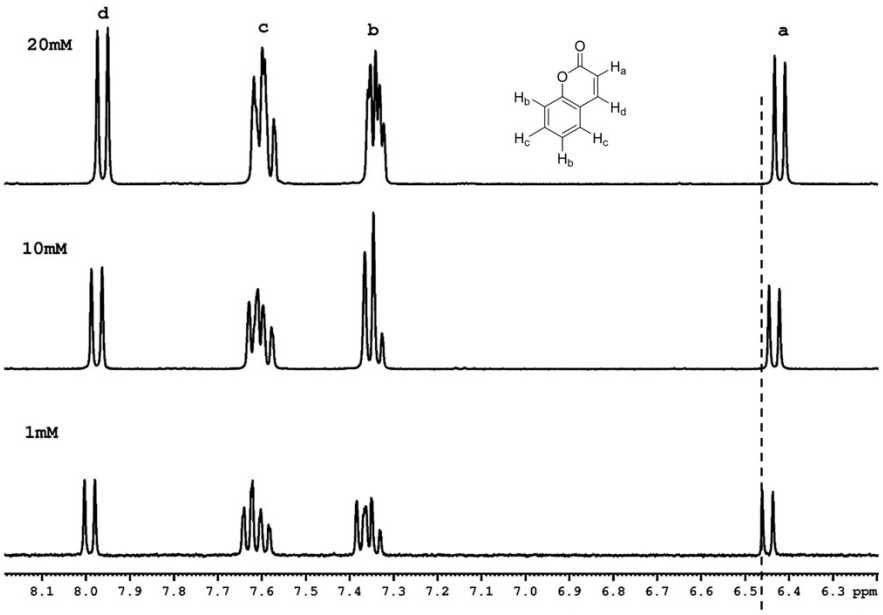


Figure 5. ^{1}H-NMR spectra of coumarin in D_2O at various concentrations.

To be sure that observed dimerization is not the result of microcrystals or microdroplets we carried out photodimerizations under solvent-free conditions. This was achieved by irradiating the samples in between Pyrex glass plates with no solvents. Of the four, indene is liquid while the rest are solids. Interestingly, under our conditions except for coumarin the other three olefins dimerized as neat samples (Table S4). Of the three solid samples both acenaphthylene and *trans*-2-methoxycinnamic acid are known to dimerize as crystals [35, 36, 88]; coumarin due to unfavorable crystal packing is known to be photostable.[80, 89] The most valuable information was provided by coumarin. The fact that coumarin that did not dimerize in solid state gave dimers in water (Table 1) suggested that photodimerizations occurring in water are not due to suspension of microcrystals. Although indene and acenaphthylene dimerized in their native state (liquid and solid respectively) the distribution of the dimers are not the same as in water. These observations lead us to conclude that dimerization in water is not due micro-crystals or micro-liquid droplets, most likely is due to aggregates of reactant molecules. It is quite likely the aggregates grow to microcrystals under favorable conditions.

During Diels-Alder reaction in water the ratio of the *endo* and *exo* isomers are reported to differ from that in organic solvents. To identify the effect of water on the ratio of isomers of photodimer, we compared the results in water with the dimerization in a polar solvent medium.

Unfortunately, the results are not easily comparable since the ratios in several examples depend on the concentration of the reactant olefin. For example, in methanol coumarin is reported to give exclusively *syn*-HH at 0.31 M and >90% *anti*-HH at 0. 01 M. Under our conditions in water the ratio of the dimers is different (*syn*-HH: 64; *syn*-HT 28 and *anti*-HH 8%). In the case of indene, the dimer ratio in acetonitrile is reported to be *syn*-HH: 74; *syn*-HT 5 and *anti*-HH 12% while in water we find it to be different: *syn* HH: 7; *syn*-HT 7; *anti*-HH 77 and *anti*-HT 9%. Finally, in the case of acenaphthylene the ratio of *syn* and *anti*-dimers in cyclohexane vary with the concentration. The *syn*-dimer composition varies between 78% and 86% in the concentration range (0.22 M to 1.32 M). The rest is the *anti*-dimer. In water the dimer composition is 47 % (*syn*) and 53 % (*anti*) at 0.02 M. From the above examples it is clear that the dimer ratio differs in water compared to that in organic solvents. Similar observations were made during triplet sensitized dimerization of coumarin and acenaphthylene. From the examples presented above it is clear that water as the reaction medium has an effect on the dimer ratio.

Overall, results presented above suggest that (a) photodimerization of several olefins occur in water at low concentrations, (b) these olefins, most likely, exist as aggregates in water, (c) there is no electronic interaction between molecules in the aggregates although there may be a very weak magnetic interactions and (d) the dimer product distributions in water and organic solvents are not the same. In the next section we analyze the results and evaluate the opportunities of using water as the reaction medium.

Discussion

It is well established that solvents have an effect on photoreactions.[11] Solvent properties can influence the rate and product distribution of a photoreaction. Also, they can indirectly influence a photochemical reaction by having an effect on various photophysical events such as rates of intersystem crossing, radiative and radiationless processes as well as by altering the nature of the excited states. These are generally attributed to inherent properties of solvents such as polarity, viscosity, dielectric constant etc. In this context, water is unique and it can enforce an effect that is unknown with other solvents, namely hydrophobic effect. In this study we have demonstrated that water as a solvent enhances the efficiency of dimerization of a few olefins as well as favors dimerization even at very low concentrations.

Photodimerization occurs by interaction of an excited and a ground state molecule. This requires the excited and the ground state molecules to come together and form a bond within the lifetime of the excited reactant molecule ($<10^{-9}$ sec). The maximum rate at which the encounter can occur would be the rate of diffusion (k_d x [olefin]^2). Diffusion constant of water being 6.5 x 10^9 L/mol/sec one would require at least 0.1 M of olefin for the dimerization to be efficient within the lifetime of the excited olefin.[86] As noted earlier the solubility of the olefins studied here varied between $5x10^{-5}$ M and 8 $x10^{-3}$ M (coumarin 8 mM; *trans*-2-methoxycinnamic acid 0.23 mM; indene 1.2 mM and acenaphthylene 0.05 mM at room temperature). With this low solubility the photodimerization that is controlled by diffusion would not be expected to be efficient in water, especially when the reaction occurs from excited singlet state whose lifetime is expected to be less than a ns. However, the fact that the reaction that is not efficient in organic solvents (compare Table 1 with Table S2) occurs in water suggests that diffusion is not the determining step. The dynamic light scattering experiments suggested that the molecules investigated here remain as aggregates in water. In such aggregates since several molecules (between 165 and 1450, Table 2) would be close to each other dimerization can occur without the need for diffusion. We visualize the photodimerization in water to occur in such aggregates of reactants and not between individually solubilized molecules. Thus, the primary reason for the enhanced reactivity of the olefins investigated here in water is the ability of water to force aggregation of molecules without precipitating them.

The origin of aggregation we believe could be traced to the hydrophobic effect.[7] Such an effect has been suggested earlier by Breslow during the now well-known Diels-Alder reaction in water.[26] Similar to the substrates used by Breslow's group the olefins investigated here have poor solubilities in water. They all possess aromatic framework that might favor π–π interaction between two or more molecules. It is quite likely that a combination of intermolecular weak interaction and hydrophobic effect might favor the formation of aggregates. In terms of classification, the dimerization we report here should be considered 'in water' reaction similar to the Diels-Alder reactions of Breslow for the following reason:[4] The dimerization occurs even at $<10^{-5}$ M when the solution is transparent and there are no floating particles. Thus, the enhanced rate of dimerization in water can be attributed to high local concentration of olefins in aggregates. We are aware there is another class of reactions known as 'on water'.[90] In these cases the water interface plays a primary role and reactions can be

effected even if the reactants are not solubilized in water. We don't believe that is the case in our systems.

In the case of Breslow Diels-Alder reaction in water, [37-39, 91] Engberts has suggested that 'forced hydrophobic effect' plays a significant role in addition to normal hydrophobic effect. According to him this effect reduces the activation energy by stabilizing the transition state more than the reactant molecules. Hydrogen bonds between water molecules and the reacting molecules, both at the beginning stage and at the transition state, are also suggested to play a role in reducing the activation energy.[42, 43, 92, 93] This operates similar to 'forced hydrophobic effect' mentioned above. Since the mechanisms of thermal Diels-Alder reaction and photochemical [2+2] additions are different, it is not obvious whether 'forced hydrophobic effect' and hydrogen bonding would play a role in enhancing the rate of addition. Photochemical reactions being an exothermic process the activation barrier, if any, is expected to be small. However, due to electronic factors a small barrier may be present between the excited bimolecular complex and the minimum (funnel) through which it enters the ground surface. It is quite likely the hydrophobic, forced hydrophobic effects and hydrogen bonding may favor a compact structure in the excited state. With the data on hand, we can't conclude whether or not such effects play a role in increasing the rate of photodimerization reactions. However, based on DLS data we are confident that aggregation enforced by hydrophobic effect is at least partially responsible for the enhanced reactivity of olefins in water. Further work is needed to fully understand all the factors that control the photoreactivity of olefins in water.

One of the most remarkable observations reported by Breslow's and Sharpless' groups is that there is selectivity in the adducts formed in water. Generally, preference for *endo* cycloadduct is noted during Diels-Alder addition in water. This is attributed to the hydrophobic effect, forced hydrophobic effect and hydrogen bonding favoring the more compact *endo* transition state.[17, 18, 26, 40] In our examples it is not obvious whether the changes observed in product distribution could be readily interpreted based on such factors. Photochemical reactions are further complicated by two different excited states from which the reaction occurs, the excited singlet and triplet states. The factors that control the amounts of isomers from these two states are unlikely to be the same. However, if the compactness of the transition state or of the structure of the complex that enters the conical intersection is the determining factor we can speculate on the role of water along the lines proposed for thermal addition reactions.[26, 31, 39,

40] At this stage we do not have sufficient data to speculate on the role of water on dimer distribution.

Detailed studies on solvent effects on photodimerization of coumarin and acenaphthylene are available.[62, 87] Interestingly there is a significant difference in the dimer formed from coumarin in polar, non-polar and hydroxylic solvents.[87] In hydroxylic solvent methanol the preferred dimer is *syn* HH. However, in our case significant amount of *syn* HT is also formed. Acenaphthylene dimerization is slightly more complicated as the dimerization occurs from both excited singlet and triplet states and is also sensitive to oxygen content and concentration of acenaphthylene. Presence of oxygen and low concentration favor reaction from triplet state that gives a mixture of dimers. If this is the case under the concentration we have used (0.02 M) one would expect a mixture of dimers. As already discussed earlier the concentration indicated above is not 'real' as the molecules exist as aggregates in water. Under this condition several acenaphthylene molecules would be close by and the effective local concentration would be significantly higher than 0.02 M. Under such conditions, the *cis* isomer from excited singlet would be expected. The fact that we isolate both isomers suggest that water influences the dimer distribution. At this stage we are not sure what factors are involved in the isomer distribution of dimers from coumarins and acenaphthylene. Further work is required to fully understand the role of water in dimer distribution in the systems investigated here.

Conclusions

We conclude our presentation by pointing out that unlike thermal reactions that have been extensively explored and synthetically utilized very little attention has been paid by photochemists in using water as a solvent. Literature contains a few publications that have demonstrated the effectiveness of water in increasing the rate of dimerization with respect to organic solvents. Dimerization at as low as 10^{-5} M has been reported.[55] Generality of photodimerization in water at low concentrations have been established with several examples.[46-52, 54] In spite of these publications the potential of water as a solvent is yet to be recognized by photochemists. In this study, with seven different examples we have shown that dimerization can be brought about even at very low concentrations. Increased reactivity most likely is due to hydrophobic effect that favors the formation of aggregates. In aggregates molecules are preassembled and dimerization can happen at any concentration as long as they

don't precipitate. In addition to conventional hydrophobic effect other effects invoked in thermal reactions such as forced hydrophobic effect and hydrogen bonding could play a role. Also it is not clear what factors are involved in the distribution of dimers in water. Further work is required. We being surrounded by water there is a possibility that a large number of organic molecules are present in ocean, rivers and pools in very low concentrations. With Sun ever present above us reactions of these molecules present in water is likely to have an influence on our life. Better understanding of the interaction between photon and molecules in water would certainly improve the quality of our life.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at -----

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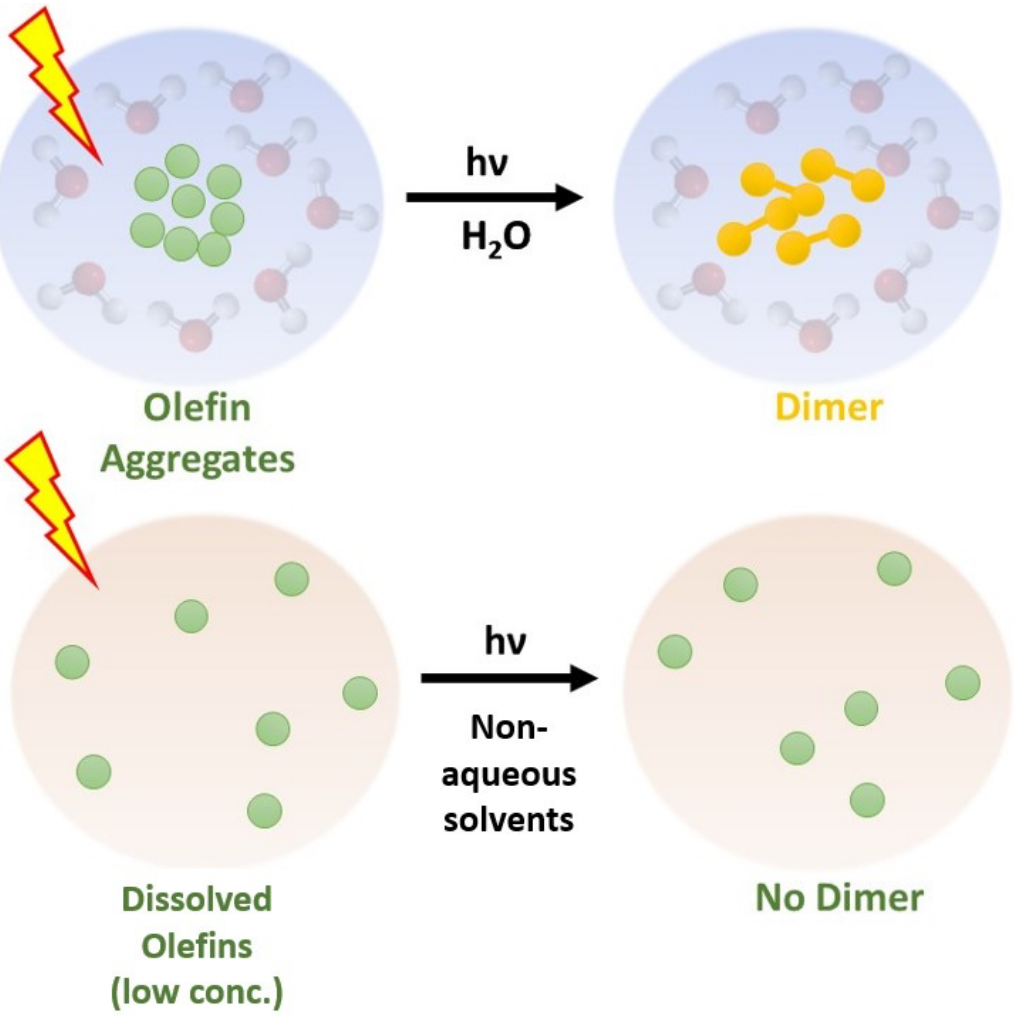
TOC Graphic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