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Ultrafast Time-Resolved Transient Absorption and Resonance Raman Spectroscopy Study of the Photodeprotection and Rearrangement Reactions of *p*-Hydroxyphenacyl Caged Phosphates

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Abstract: The kinetics and mechanism of the photodeprotection and rearrangement reactions for the *p*HP phototrigger compounds *p*-hydroxyphenacyl diethyl phosphate (HPDP) and diphenyl phosphate (HPPP) were studied using transient absorption (TA) and picosecond time-resolved resonance Raman (ps-TR^3) spectroscopy. TA spectroscopy was employed to detect the dynamics of the triplet precursor decay as well as to investigate the influence of the solvent and leaving group on the triplet quenching process. Ps-TR^3 spectroscopy was used to directly monitor the formation dynamics for the photosolvolytic rearrangement product and its solvent and leaving group dependence. The TA and TR^3 spectroscopy experiments were also used to characterize the structural and electronic properties of the triplet precursor to the HPDP and HPPP deprotection reactions. The solvent effect observed in conjunction with the leaving group dependence of the triplet decay dynamics are consistent with a concerted solvent assisted triplet cleavage through a heterolytic mechanism for the HPDP and HPPP photodeprotection process. Correlation of the dynamics between the deprotection and rearrangement processes reveals there is a consecutive mechanism and the involvement of an intermediate between the two reaction steps. The reaction rate of the deprotection and rearrangement steps and the influence of the solvent and leaving group were determined and evaluated based on kinetic modeling of the dynamical data obtained experimentally for HPDP and HPPP in H_2O/MeCN mixed solvents with varying water concentration in the solvent system. A solvation complex with a contact ion pair character was proposed to be the intermediate involved in the deprotection and rearrangement pathway. The results here combined with our previous study on the photophysical events occurring on the early picosecond time scale (Ma; et al. *J. Am. Chem. Soc.* **2005**, *127*, 1463−1472) provide a real time overall mechanistic description for the photodeprotection and rearrangement reactions of *p*HP caged phosphate phototrigger compounds.

Introduction

There is increasing interest in developing efficient phototriggers for real-time monitoring of physiological responses in biological systems.[1−7] The *p*-hydroxyphenacyl (*p*HP) protecting group has received much attention in this regard due to its practical potential as a rapid and efficient “cage” for the liberation of various biological stimulants.[8,9] Previous studies found that the photodeprotection reaction of *p*HP caged compounds is highly solvent-dependent and occurs only in aqueous or aqueous containing media while the photodeprotection reaction does not occur in neat organic solvents such as acetonitrile (MeCN) where the photoexcitation leads solely to photophysical processes resulting in the recovery of the ground-

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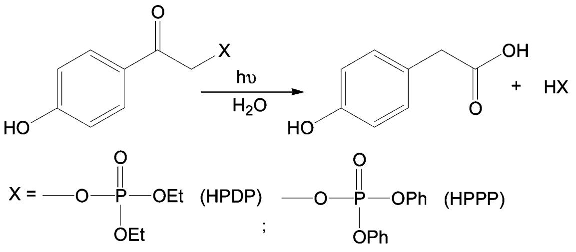
state substrate molecules.[8,10,11] In aqueous or aqueous containing solvents, along with the liberation of the leaving group, the photolysis also causes photosolvolytic rearrangement of the *p*HP cage into a *p*-hydroxyphenylacetic acid (HPAA) final product (eq 1):



(1)

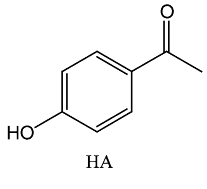
Although the products and conditions for the *p*HP deprotection have been well established in previous work,[10−12] the reaction mechanism is not well understood and there remains some uncertainty about the events and reactive intermediates involved in the photochemical pathway. By using transient absorption spectroscopy, previous mechanistic work done by Givens, Wirz and co-workers,[10] and Wan and co-workers[11] report the observation of several short-lived species after UV light (∼300 nm) excitation of *p*HP caged acetate (HPA) and diethyl phosphate (HPDP) in aqueous containing solvent systems. However, these studies present some conflicting interpretations in terms of identities of the relevant intermediates as well as the processes leading to their formation. Consequently, two distinct reaction pathways have been proposed for the *p*HP deprotection and rearrangement reaction. To clarify this ambiguity in the reaction mechanism, additional work is required. In particular, the following three issues need to be resolved: (i) multiplicity for the initial reactive precursor in order to differentiate between the triplet vs singlet mechanism suggested by Givens[8,10] and Wan,[11] respectively; (ii) dynamics and mechanism of the deprotection (in terms of homolytic vs heterolytic cleavage[8,10]) and rearrangement reactions; (iii) role played by the solvent water molecules in the deprotection reaction so as to address whether the water molecules work as a necessary mediator to assist the intramolecular proton transfer (ESIPT) that consequently facilitates the deprotection and rearrangement[11] or the water molecules simply provide a favorable solvent environment to encourage a direct cleavage of the C−O bond connecting the *p*HP cage and the leaving group.[8,10]

Our recent study employing a combination of femtosecond Kerr gated time-resolved fluorescence (KTRF) and ps-TR^3 spectroscopy[13] on HPA and HPDP provided compelling evidence that the triplet is the reactive precursor for the *p*HP photorelease reaction. This furnishes an answer to the first issue, but the next two subjects have not been addressed explicitly to the best of our knowledge. In this regard, we report here a subpicosecond TA and ps-TR^3 investigation on HPDP and a newly synthesized *p*HP caged diphenyl phosphate (HPPP). As scaled by the pK_a of a leaving group anion, the diphenyl phosphate is a much better leaving group than diethyl phosphate.[14] Since the dynamics of a cleavage process occurring by a heterolytic mechanism has a distinctly different dependence on the leaving group from that of a homolytic cleavage,[15] it is expected that comparison of the real time reaction dynamics displayed by the HPDP and HPPP phototrigger compounds can provide important evidence to help elucidate the nature of the photorelease and rearrangement mechanism of the *p*HP caged phototriggers.

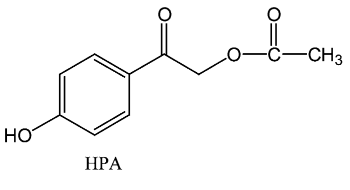
TA spectroscopy was used to examine the solvent influence and leaving group dependence of the triplet reactivity in terms of the photodeprotection reaction. Ps-TR^3 experiments were performed to directly probe and determine the formation dynamics of the HPAA rearrangement product from photoexcited HPDP and HPPP in H_2O/MeCN mixed solvents. To our knowledge, this is the first characterization of the formation time of the final rearrangement product for *p*HP phototrigger compounds. The solvent effect on the deprotection and rearrangement reactions was investigated by performing the TA and ps-TR^3 measurements for the two compounds in the mixed solvents with varying water concentration as well as in other typical solvents such as dimethyl sulfoxide (DMSO) and 2,2,2-trifluoroethanol (CF_3CH_2OH). The TA and TR^3 measurements were also done to characterize the properties of the triplet state for the new HPPP compound, and these results were compared to those for HPDP. Correlation of the triplet decay dynamics with the temporal evolution of the rearrangement product leads to a quantitative description of the dynamics of the deprotection and rearrangement reactions that was based on their respective reaction rates. The solvent and leaving group dependence was also derived and evaluated for the deprotection and rearrangement reactions. The results presented here shed more light on the overall mechanistic details of the *p*HP photochemistry and enables us to clarify the pertinent controversy of the relevant reactive intermediate(s) involved in the deprotection and rearrangement pathways of *p*HP caged phototrigger compounds given in previous studies.[8,10,11]

Experimental Methods

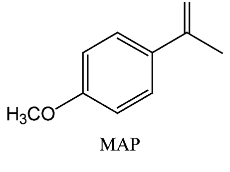
HPDP was synthesized following the method given in ref 13. The synthesis of HPPP is similar to that of HPDP, and the details are given in the Supporting Information. The identity and purity of these compounds were confirmed by analysis of MS, NMR, and UV absorption spectroscopy. HPAA is commercially available and was used after recrystallization. Model compounds *p*-hydroxyacetophenone (HA) and *p*-methoxyacetophenone (MAP) were purchased and used after recrystallization 3 times in MeCN.



HA



HPA



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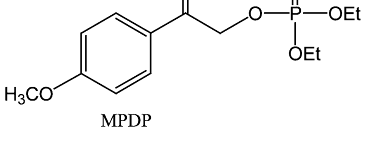

MPDP

Except for the HPDP and HPPP molecules, the molecular structures

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for the compounds used in this work (HA and MAP) and those (HPA and MPDP) important for discussion of our present results are shown below. Spectroscopic grade MeCN, CF_3CH_2OH, and DMSO as well as deionized water were used as solvents for the experiments presented in this work.

A. Photochemistry Experiments. The photochemistry of the photoinduced deprotection and solvolytic rearrangement reactions for the *p*HP caged compounds was monitored by measuring the UV−vis absorption spectrum of the sample solution (∼0.1 mM concentration) before and after exposure to an unfocused 267 nm laser line (∼5 mJ) from the fourth harmonic of a nanosecond Nd:YAG Q-switch laser. The sample solution was put in a 1 cm UV grade cell and excited by the 267 nm laser beam. As the reaction progressed, the UV−vis absorption spectrum of the photolyzed sample was measured by using a Perkin-Elmer Lambda 19 UV/vis spectrometer. The absolute quantum yield for the product formation (eq 1) was estimated based on the decrease of the optical density for the characteristic sample absorption band (see below), the period of irradiation time, and the laser energy used for the photolysis measurement.[16]

B. Femtosecond Transient Absorption (TA) Experiments. Both the TA and ps-TR^3 experiments were performed based on a commercial Ti:Sapphire regenerative amplifier laser system equipped with a homemade OPA system that provides a tunable femtosecond/picosecond light source.[16−18] The TA experiments were done utilizing a newly developed femtosecond TA setup with a 267 nm pump (the third harmonic of the 800 nm regenerative amplifier fundamental) and probed by a white light continuum pulse produced from a rotating CaF_2 plate pumped by the 800 nm fundamental laser pulses.[19] After generation, the white light continuum was collected and focused by an elliptical mirror and separated into two beams by a beam splitter. One of the beams (the sample beam) was used as the probe pulse to overlap the pump pulse (267 nm) in the sample. The other beam (the reference beam) passes through an unpumped spot in the sample and was used as a reference to monitor the intensity and spectral variation of the white light continuum pulse. After these beams passed through the sample, the two beams were focused into a monochromator and detected separately in different strips by a liquid nitrogen cooled CCD camera. The signals from the CCD were then downloaded to a PC for spectral analyzed. The transient absorbance difference spectrum (the TA spectrum) was obtained by comparison of the sample-beam spectrum recorded with the pump beam blocked and unblocked, respectively. The reference-beam spectrum permits correction of the intensity and spectral fluctuations of the white light continuum during the TA experiments. The temporal difference between the pump (267 nm) and probe (the white light continuum) pulses was controlled using an optical delay line. The time resolution of the TA measurement was about 200 fs. Sample solutions of ∼1 mM concentration were recycled and contained in a quartz cell with a 1 mm thickness. The spot sizes of the pump and probe beams at the sample were about 200 and 100 μm, respectively. TA experiments were done for HPDP and HPPP and for the model compounds HP and MAP in neat MeCN and H_2O/MeCN (1:1 by volume) mixed solvents. To examine specific solvent effects, typical solvents DMSO and CF_3CH_2OH and the mixture of these two were also used in the TA experiments for HPDP and HPPP.

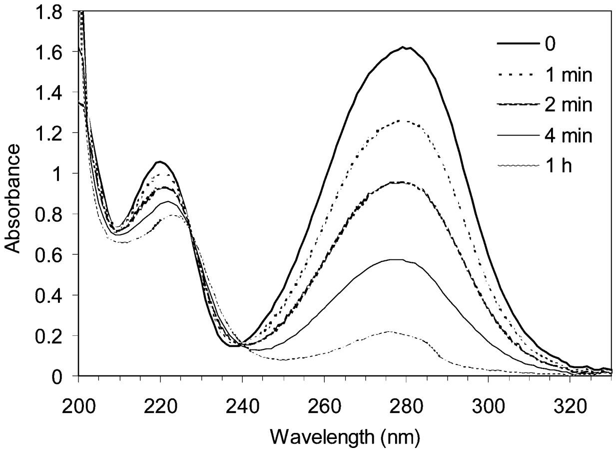

Figure 1. UV/vis absorption spectra for the conversion from HPDP to HPAA upon photolysis of HPDP in a H_2O/MeCN (1:1) mixed solvent. The time periods the sample solution is exposed to the excitation laser pulse are labeled for each of the spectral traces.

C. Picosecond Time-Resolved Resonance Raman (ps-TR^3) Experiments. For the ps-TR^3 measurements, the samples were pumped with the 267 nm laser pulse and probed by a 200 nm laser pulse made by mixing the 800 nm fundamental and the 267 nm output. The pump and probe pulse durations were ∼1.5 ps. The pulse energies at the sample were 2−3 μJ. A recirculated solution with a sample concentration of ∼1−1.5 mM was used with the pump and probe beams loosely focused onto the thin stream of the sample solution. The Raman light was collected in a backscattering configuration and detected by a nitrogen cooled CCD detector. Each ps-TR^3 spectrum shown here was obtained by accumulating over 2 min with an appropriately scaled pump only and probe only spectra being subtracted from a pump−probe spectrum. Acetonitrile Raman bands were used to calibrate the TR^3 spectrum with an estimated accuracy of ±5 cm^{-1} in absolute frequency.

Ns-TR^3 measurements with 267 nm pump and 416 nm probe laser pulses were also performed for HPPP in MeCN solvent. Ps-TR^3 experiments with 267 nm excitation and 400 probe wavelengths were done for HPDP and HPPP in neat MeCN and H_2O/MeCN (1:1) solvent to examine the influence of carbonyl H-bonding on the structure of the triplet precursor[20] to the *p*HP photochemistry. Details of the experimental apparatus and methods employed for these ns- and ps-TR^3 experiments are the same as those described in refs 17, 18, 20, and 21.

Results

A. Photochemistry of the *p*HP Caged Phosphates in H_2O/MeCN (1:1) Solvent. Photochemistry experiments were performed for HPDP and HPPP in H_2O/MeCN (1:1) solvent to estimate the quantum yields of the photodeprotection and rearrangement reactions. Figure 1 shows the UV/vis absorption spectra obtained after 267 nm photolysis of HPDP in the mixed solvent. It can be seen that, with an increase of the photolysis time, the two characteristic absorption bands (maxima at ∼280 and ∼220 nm) of the substrate HPDP decrease in optical density and shift slightly in position. The absorption spectrum finally converts into an absorption profile (the absorption trace of the 1 h spectra in Figure 1) that is identical to the absorption

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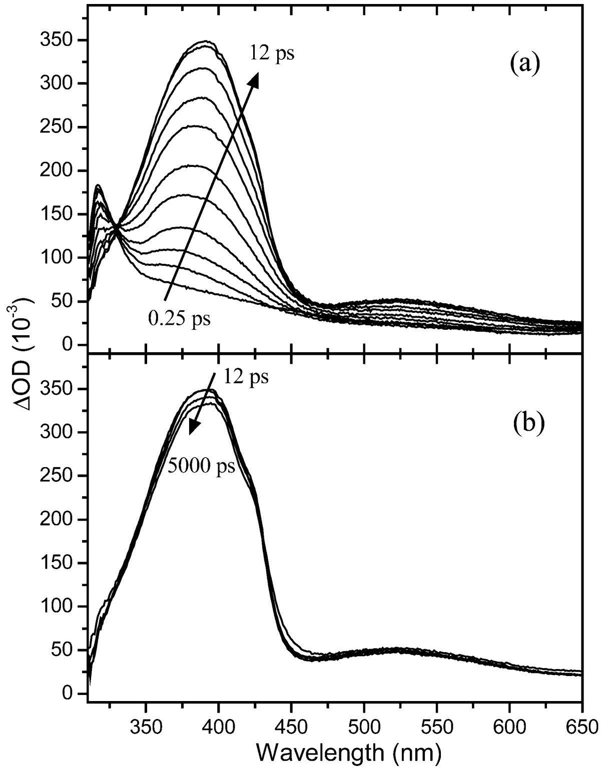

Figure 2. Transient absorption spectra of HPDP at early (a) (from 0.25 to 12 ps) and late (b) (from 12 to 5000 ps) picosecond times recorded with 267 nm excitation in MeCN solvent.

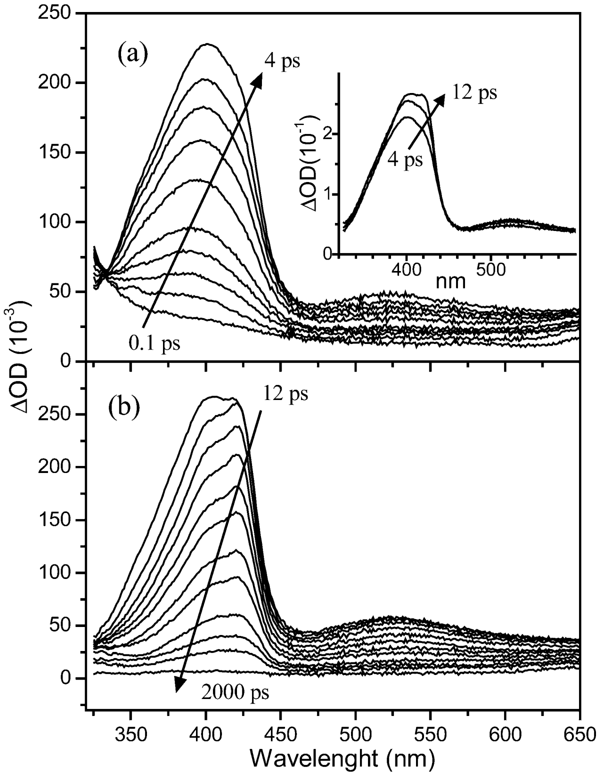

Figure 3. Transient absorption spectra of HPDP at early (a) (from 0.1 to 12 ps) and late (b) (from 12 to 2000 ps) picosecond times recorded with 267 nm excitation in H_2O/MeCN (1:1) mixed solvent. The right-hand part in (a) shows profile change of the transient absorption spectra recorded over 4−12 ps.

spectrum of an authentic sample of the HPAA product. A similar spectral transformation was also observed for HPPP in the same solvent. This spectral change reflects the photoinduced generation of the HPAA rearrangement product and is consistent with the *p*HP photoinduced reaction displayed in eq 1. Since essentially only the photodeprotection and rearrangement reactions occur upon photolysis of *p*HP caged phototriggers in the water/MeCN mixed solvent, the quantum yield for the HPAA formation should be identical to the disappearance quantum yield of the HPDP reactant. The quantum yield for HPAA formation can be estimated based on the large decrease of the lowest HPDP absorption band (~280 nm) displayed in Figure 1 along with the irradiation time and laser energy used for the photolysis experiments.[16] This was done by selectively monitoring the variation of the HPDP absorbance in the 290−310 nm region where the HPAA product shows little absorption. The quantum yields obtained are 0.40 ± 0.09 and 0.41 ± 0.01 for HPDP and HPPP, respectively. The quantum yield obtained here based on the disappearance of the starting material is very close to the corresponding value reported previously based on the appearance of the HPAA product for *p*HP phototriggers bearing phosphate esters as the leaving group.[8] This implies there is a high efficiency for the photochemical steps leading to the rearrangement reaction of the *p*HP caged phototriggers.

B. Dynamics of the HPDP Triplet Studied by TA Spectroscopy. Figure 2 shows the TA spectra for HPDP obtained in neat MeCN (267 nm excitation) with time delays from 0 to 5000 ps after excitation. To clearly indicate the spectral changes at different time scales, the spectra of the early (before 12 ps) and late (12−5000 ps) times are given separately in the figure. Corresponding TA spectra in the H_2O/MeCN (1:1) mixed solvent are displayed in Figure 3. The kinetics of the spectral changes in the early and late time regimes in the two solvents are given in Figure 4.

From Figures 2a and 3a, it can be seen that the temporal evolution of the early time spectra are very similar in both solvent systems: two absorption bands (a strong one around 400 nm and a broad and weak one at 470−620 nm) grow in rapidly at the expense of the middle strong band at ~320 nm. An isobestic point at ~330 nm indicates a dynamical conversion between two distinct states. From Figure 4a, the kinetics of the ~330 nm decay and the 400 nm and 470−620 nm growth can be fitted simultaneously by an one exponential function with a 2.5 ps time constant. This value matches well with the value of the intersystem crossing (ISC) time-constant obtained from our recent KTRF study[13] and indicates that the spectral transformation observed here is due to the ISC conversion from the lowest singlet (S_1) to triplet (T_1). This suggests the very early time spectra (such as the 0.25 and 0.1 ps spectra in Figure 2a and 3a, respectively) should be assigned to the $S_1 \rightarrow S_n$ absorption from the S_1 ($n\pi^*$) singlet state and the fully developed spectra (12 ps spectra in Figures 2a and 3a) should be assigned to the $T_1 \rightarrow T_n$ absorption from the T_1 triplet ($\pi\pi^*$) state. The triplet assignment is also corroborated by the late time decay behavior in the two solvents and the spectral resemblance to the nanosecond LFP absorption spectra recorded for the *p*HP caged compounds in MeCN.[10,11] The 267 nm excitation leads to instantaneous population of the S_3 ($\pi\pi^*$) state. The time constant for internal conversion (IC) from S_3 to S_1 has been found to be ~80 fs in both solvent systems according to our previous KTRF work.[13]

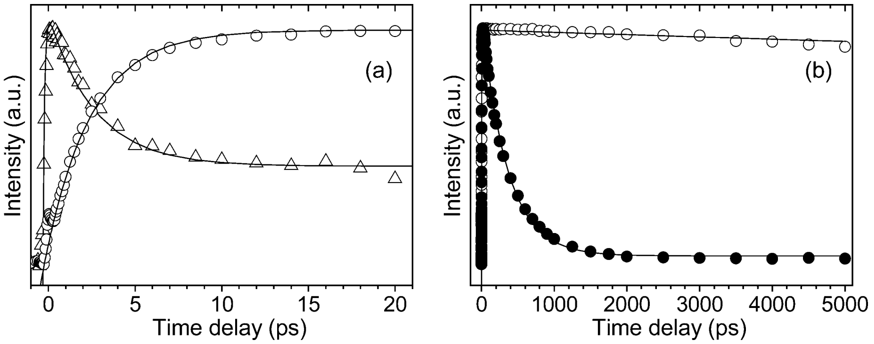

Figure 4. Temporal dependence of transient absorption spectra for HPDP recorded at early picosecond times in MeCN (a) at ~330 nm (△) and ~400 nm (○); at late picosecond times (b) in MeCN (hollow circles) and H_2O/MeCN (1:1) (●) at ~400 nm. The solid lines indicate the kinetics fittings using a one exponential function to the experimental data points.

The TA spectrum in MeCN solvent shows very little change at late picosecond times up to 5000 ps (Figure 2b). This is consistent with the HPDP triplet lifetime that has been observed to be ~150 ns in ns-TR^3 spectroscopy experiments.[17] However, the TA spectrum in the water mixed solvent shows almost complete decay at 2000 ps. As displayed in Figure 4b, the triplet decay kinetics in the water mixed solvent can be fitted by a single exponential with a time constant of 350 ± 20 ps. This value parallels the triplet decay rate reported by Wirz and coworkers employing the TA method (~400 ps)[10] and the value reported by us using ps-KTR^3 spectroscopy (~420 ± 20 ps).[13] This solvent-dependent TA decay dynamics confirms the triplet assignment on one hand and validates the triplet as a reactive precursor state to the photochemistry events observed previously in water containing solvent on the other hand.

A careful examination of the TA spectral evolution in the water mixed solvent (Figure 3) indicates that, besides the overall decrease in the optical density at late picosecond times, the TA spectrum displays a small but obvious change in its profile over the ~4 to 35 ps time period. The ~400 nm absorption band is broad and structureless before 4 ps but appears to gain some structure afterward. This temporal variation in the profile is not observed in neat MeCN (Figure 2). According to our previous ps-TR^3 work on *p*HP related compounds[17,18a] and other relevant studies,[13,20,22] this phenomenon could have two possible sources: (i) relaxation of excess energy of the initially formed energetic triplet state produced from the rapid ISC conversion;[13,17,18a] (ii) specific solute−solvent interaction, most possibly the intermolecular H-bond or solvation of the HPDP triplet by the solvent water molecule(s).[20,21] Although source (i) is certainly operative on the triplet manifold as substantiated by the HPDP ps-TR^3 study,[13,17] it is unlikely to be the particular reason for the profile change since this process is not that sensitive to the kind of solvent used in the system and is expected to result in similar spectral variations, such as a narrowing or slight spectral shift of the TA band, in both of the solvent systems. In this regard, the specific solvent effect would probably be the predominant factor to account for the profile change observed in Figure 3. TA measurements on the HA and MAP model compounds that bear no leaving group found that there is hardly any change in the spectral shape in both the water/MeCN mixed solvents and neat MeCN solvent. The TA spectra of HA and MAP in these two solvents are presented as Figure 1S and 2S in the Supporting Information. Comparing these results with the HPDP TA result implies that the profile changes in HPDP might be mainly associated with solvation of the phosphate leaving group (possibly through H-bonding interaction with the solvent water molecules).

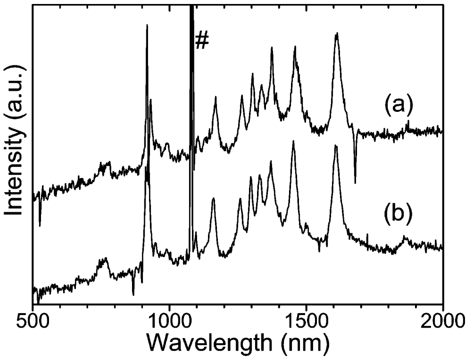

Figure 5. Nanosecond time-resolved Resonance Raman (ns-TR^3) spectrum of HPPP (a) and HPDP (b) obtained with 267 nm excitation and a 416 nm probe wavelength in MeCN solvent at 20 ns delay time. The sharp feature labeled by "#" is due to a stray laser line.

C. Triplet Properties and Decay Dynamics of HPPP Characterized by TA and TR^3 Spectroscopy. The TA experiments analogous to those done for HPDP were also performed for the newly synthesized HPPP compound in neat MeCN and mixed MeCN/H_2O solvents. The TA results for HPPP are generally similar to those for HPDP and the recorded spectra are presented in Figures 3S and 4S in the Supporting Information. It is obvious that the TA spectra and temporal evolution at early picosecond times (before 50 ps) closely resemble those observed for HPDP in the respective solvents. This suggests that similar photophysical processes like those observed for HPDP, i.e., rapid ISC conversion (with ~2 ps time constant) from the S_1 ($n\pi^*$) to T_1 ($\pi\pi^*$) state, are also being detected for HPPP in the two solvent systems. The resemblance in the spectral character for the $T_1 \rightarrow T_n$ absorption observed for both HPPP and HPDP implies further that these two compounds have triplet states with similar properties. This is firmly confirmed by comparison of the ns-TR^3 spectra (see Figure 5) from the two compounds obtained by directly probing the triplet absorption using a 416 nm probe wavelength and employing a 267 nm pump wavelength in neat MeCN solvent. The ns-TR^3 spectrum of HPDP displayed in Figure 5 is from the HPDP triplet as indicated by our previous TR^3 spectra combined with a density functional theoretical (DFT) study.[17]

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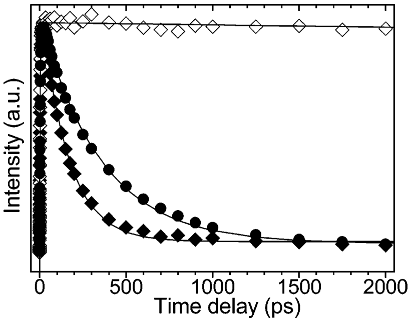

Figure 6. Temporal dependence of the transient absorption intensity for HPPP in MeCN (◇) and H_2O/MeCN (1:1) (◆) at ~400 nm. Data labeled by the filled circles are from the intensity of the HPDP TA spectra at ~400 nm obtained in the H_2O/MeCN (1:1) solvent. Solid lines indicate kinetics fitting using a one exponential function to fit the experimental data points.

Table 1. Time Constants of the Triplet Decay Dynamics and the Rearrangement Reaction of HPDP and HPPP in H_2O/MeCN Mixed Solvent

H_2O%	time constant of the triplet decay (τ_1)[a] (ps)								
(vol.)	75%	50%	40%	30%	25%	15%	10%	τ_2[c] (ps)	pK_a[d]
HPPP		150					830	600	0.4
HPDP	290	350	530	800	1280	2400	9000	470	1.39
HPA[b]		2130							4.76

[a] Uncertainty of the τ_1 time is ±20 ps. [b] Data for HPA (from ref 13) are listed for comparison. [c] Corresponds to time constants of the solvolytic rearrangement with an uncertainty of ±40 ps. [d] Values of pK_a are from ref 14.

The nearly identical features of the HPPP spectrum to that of the HPDP spectrum indicates unambiguously they have almost the same triplet structure for the two compounds in terms of the chromophore (the *p*HP cage) responsible for the $T_1 \rightarrow T_n$ absorption probed by the ns-TR^3 spectra. This reinforces our earlier suggestion that photoinduced generation of the triplet state for *p*HP caged compounds leads to a localized excitation on the *p*HP moiety and is not strongly influenced by the leaving group.[13,17,18a] In this sense, examination of the leaving group and solvent dependence of the triplet decay dynamics can provide important information for the elucidation of the photodeprotection reaction.

The triplet decay dynamics of HPPP in the two solvents is displayed in Figure 6. The decay dynamics for HPDP in the H_2O/MeCN (1:1) mixed solvent is also shown for comparison purposes. Like HPDP, the triplet of HPPP in MeCN shows little decay within 5000 ps that is consistent with the ~27 ns triplet lifetime estimated from a ns-TR^3 measurement performed for HPPP under open air conditions. These spectra and the derived triplet lifetime decay curve are presented in Figure 5S in the Supporting Information. In H_2O/MeCN (1:1) mixed solvent, the HPPP triplet decays quickly with an ~150 ps time constant. This is faster than the ~350 ps decay time of the HPDP triplet in the same solvent. These time constants together with ~2200 ps triplet decay time found for HPA in this solvent combination reveals a trend for the correlation of the triplet decay dynamics with the pK_a value of the leaving group anion (Table 1). The pK_a's of the diphenyl phosphate anion, the diethyl phosphate anion, and the acetate anion are 0.40, 1.39, and 4.76, respectively.[14] Since comparison of the pK_a values manifests the relative stability of the respective anion in aqueous containing environments as well as reflecting the leaving group ability in terms of a heterolytic dissociation of the bond bearing the corresponding group as a nucleofuge (leaving group that carries away the bond pair),[15] this correlation provides strong evidence in favor of a direct triplet heterolytic cleavage mechanism for the *p*HP deprotection process.

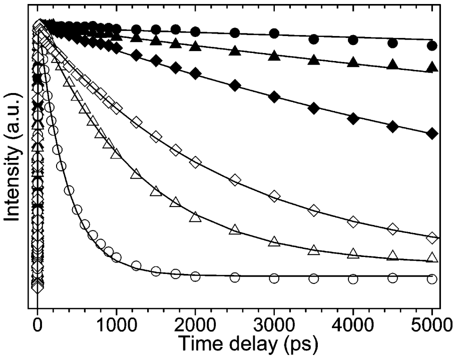

Figure 7. Triplet decay kinetics observed for HPDP by transient absorption measurements in water/MeCN mixed solvent with water concentration of 0% (●), 10% (◆), 15% (◇), 25% (△), and 50% (○). Data labeled by the filled triangles are obtained in a DMSO/CF_3CH_2OH (1:1 by volume) mixed solvent. Solid lines indicate dynamic fittings using a one exponential decay function to the experimental data points.

D. Solvent Effect on the Triplet Decay Dynamics. Influence of Water Concentration on the Triplet Decay Dynamics: To gain further mechanistic insight into the *p*HP deprotection reaction, the solvent effect on the triplet decay dynamics was examined for HPDP and HPPP by using TA spectroscopy. The TA measurements were performed for the compounds in H_2O/MeCN mixed solvents with various water concentrations. These experiments resulted in similar TA spectra and analogous triplet decay kinetics as those observed in the H_2O/MeCN (1:1) solvent (shown in Figure 3). Single exponential dynamics were observed for the triplet decay in all solvent combinations with the triplet decay time becoming substantially longer as the concentration of the water component decreased. Figure 7 displays representative results for the water concentration dependence of the HPDP triplet decay dynamics. A similar water concentration dependence was also observed from TA experiments on HPPP. The time constants for the triplet decay dynamics are summarized in Table 1 for HPDP and HPPP in the mixed solvents with varying water content. It is interesting to note that, for solvents with a water content larger than 50% (by volume ratio), the increase of the triplet decay rate becomes much more modest upon further addition of water to the solvent (Table 1). The dependence of the triplet decay dynamics on water concentration reflects the effect of the local solvent environment on the triplet quenching process. This may be associated with the preferential solvation of this solute molecule in the water/MeCN mixed solvent.[27−30] The absence of significant improvement of the triplet quenching rate at high water

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concentration (>50% H_2O) implies the predominance of the solvent water molecules in the HPDP solvation shell at these large water concentrations.

Stern−Volmer analysis based on the above triplet decay measurements leads to a curved and roughly quadratic dependence on water concentration (see Figure 6S in the Supporting Information). Providing that the addition of water generally affects a heterolytic dissociation in a nonlinear way, the curved water concentration dependence observed here corroborates further the triplet heterolytic cleavage pathway for release of the phosphate leaving groups in photoexcited HPDP and HPPP. This water concentration effect implies that the solvent water molecules not only participate in the *p*HP photochemistry at the solvolytic rearrangement step (eq 1) but also play an important role at a very early stage, and this is crucial to the deprotection process.

Concerted Solvation of the Triplet State: To be consistent with the fact that the triplet quenching does not happen in MeCN solvent, the observed significant triplet quenching especially by water could be associated with the special properties of solvent water as well as the substantial change of acid−base properties (closely related to the electronic structure) for the HPDP triplet[17,20,21] in relation to the ground state. It is well-known that water may act simultaneously as an HBD (hydrogen bond donor) and HBA (hydrogen bond acceptor) solvent. This together with the high relative permittivity ($\epsilon = 78.36$) makes water an extraordinary solvent with both a good ionizing and dissociating capability that is greatly important for many reactions involving the breaking of a polarized covalent bond.[15] To further elucidate the solvent effect on the triplet quenching effect in terms of the photodeprotection reaction, we have performed TA measurements for 267 nm photolysis of HPDP in solvents of DMSO and CF_3CH_2OH and a mixed solvent of DMSO/CF_3CH_2OH (1:1 by volume). DMSO is a typical HBA solvent with nearly zero ability to be an HBD solvent while CF_3CH_2OH is a good HBD solvent that is not able to act as a good HBA solvent.[15] This particular solvent property enables selective H-bonding with the HPDP triplet at the acidic site (phenolic proton) in the DMSO solvent and at the basic site(s) (the carbonyl oxygen and phosphate anion as leaving group) in the CF_3CH_2OH solvent. Solvation by H-bonding at both the acidic and basic sites by the respective components is possible in the DMSO/CF_3CH_2OH (1:1) mixed solvent. The TA experiment in DMSO reveals no triplet quenching, and the recorded triplet decay kinetics is the same as that found in MeCN. A small extent of triplet quenching was observed in CF_3CH_2OH solvent, but a much more obvious quenching effect was found in the DMSO/CF_3CH_2OH (1:1) mixed solvent. The triplet decay dynamics obtained in this solvent mixture is given in Figure 7 and is displayed together with the quenching dynamics caused by water in the MeCN mixed solvent. These results show that the triplet can be quenched rather efficiently in the DMSO/CF_3CH_2OH mixed solvent, but not so much in the respective neat solvent may mean that the presence of solvent with both the hydrogen bond donating and accepting capacities is essential for the triplet quenching step. This implies further that concerted solvation at both the acidic and basic sites is needed for the deprotection reaction. UV/vis photochemistry measurements found that the disappearance quantum yield of HDPD is ∼0.17 in the DMSO/CF_3CH_2OH solvent. Compared with the ∼0.4 yield in the H_2O/MeCN (1:1) solvent (∼350 ps triplet decay time), the lower yield in the DMSO/CF_3CH_2OH solvent mixture is consistent with the much slower triplet decay rate (∼25 ns triplet decay time). The lower yield and slower triplet quenching in the DMSO/CF_3CH_2OH solvent mixture compared to the H_2O/MeCN (1:1) solvent can be associated with the stronger HBA and HBD ability and high polarity of water compared to DMSO and CF_3CH_2OH.[34]

It is reasonable to suggest that the double-bonded oxygen of the phosphate leaving group and the hydrogen atom of the hydroxy moiety are the relevant basic and acidic sites, respectively, involved in the concerted triplet solvation and associated deprotection reaction. On one hand, the importance of the leaving group solvation is consistent and corroborated with results that show the triplet decay dynamics for the *p*HP compounds investigated (HPPP, HPDP,[13] and HPA[13]) is highly leaving group dependent, with the decay rate correlating with the stability of leaving group anion (Table 1). The observation that the ability of a good leaving group to stabilize the corresponding solvent solvated anion leads to an encouragement of the photoinduced dissociation has long been established to be characteristic of an excited-state heterolytic cleavage reaction.[14,15,27−31] Furthermore, the phosphate anions in HPDP and HPPP are good nucleofuges,[1,2a,32] and a photoheterolytic cleavage has been proposed for several systems bearing the phosphates as leaving groups.[14] The observed solvent and leaving group dependent nature of the triplet decay dynamics can thus be taken as convincing evidence for a triplet quenching process leading to direct heterolytic cleavage assisted by water solvation of the leaving group anion. The necessity of the leaving group solvation for the occurrence of the *p*HP photodeprotection also helps to explain the complete lack of reactivity for HPDP in MeCN[10,11] and DMSO solvents. The two solvents are highly dipolar, but they cannot act as H-bond donors so they are poor at solvating the departing group.[15]

On the other hand, solvation of the phenolic proton by a solvent with HBA capability is associated with the much-increased acidity of the hydroxy group in the triplet state compared to the ground state (pK_a values of the HA model compound are 7.9 and 3.6, respectively, in the ground state and triplet state[10]).[33−38] Water solvation of the phenolic proton is also required to interpret the previous observation that photolysis of MPDP (the *p*-methoxy counterpart of HPDP) in a H_2O/MeCN (1:1) solvent results in hardly any deprotection products.[8,11] Since the hydroxy and methoxy group have similar electronic effects on the intrinsic property of the triplet states,[17,20,21] the absence of reactivity for MPDP argues against a primary step involving simply the C−O bond heterolysis in the HPDP triplet and suggests that the proton donating function of the hydroxy moiety in the *p*HP triplet[10,11,21,35,36] could be crucial to under-

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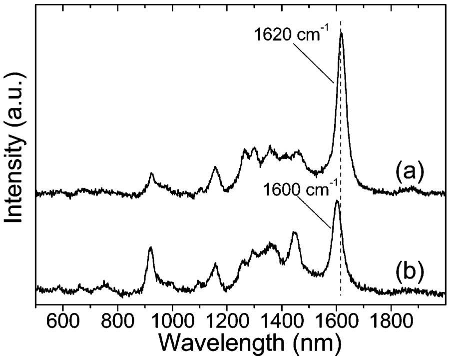

Figure 8. Ps-TR^3 spectrum of HPDP in H_2O/MeCN (1:1) (a) and neat MeCN (b) obtained with 267 nm excitation and a 400 nm probe wavelength at a 50 ps delay time.

stand the different photochemical reactivities of MPDP from HPDP in the same water/MeCN mixed solvent. Additionally, the concerted solvation perspective has important implications for the identification of the key intermediate involved in the deprotection and rearrangement reactions (see below).

Carbonyl H-Bonding Effect on the Properties of the Triplet: The carbonyl oxygen of the *p*HP cage becomes more basic in the triplet state compared to ground state.[11,34,37−39] This leads to strengthened intersolute−solvent carbonyl H-bonding interaction in the triplet state relative to the ground state. Our previous combined TR^3 and DFT study on the MAP[20] and HA[21] model compounds reveals that the carbonyl H-bonding can cause a profound modification of the triplet property and is responsible for the prolonged triplet lifetime of MAP observed in water containing MeCN solvents compared to neat MeCN solvent.[20] The free triplet state observed in neat MeCN has a delocalized $\pi\pi^*$ character (π^* electron delocalizes over the ring and carbonyl subgroups)[17,20,21] while the H-bonded triplet recorded in a H_2O/MeCN solvent has a phenyl ring localized biradical $\pi\pi^*$ character with an enhanced quinoidal ring configuration.[20,21] The small influence of the leaving group on the properties of the triplet[13,17] implies that the H-bonding effect and associated property variation may apply generally to the *p*HP caged compounds. This is confirmed by comparison of the ps-TR^3 spectra for HPDP and HPPP triplet states obtained in neat MeCN and H_2O/MeCN (1:1) solvents. The corresponding spectra for HPDP are displayed in Figure 8 (similar results were also obtained for HPPP). It can be seen that there are distinct differences, though modest, between the two spectra. Especially, the frequency upshift of the ring center C−C stretching vibration observed in the mixed solvent (~1620 cm^{-1}) from the neat MeCN (~1600 cm^{-1}) is a characteristic indication for the increased quinoidal feature in the former than latter solvent environment.[20,21] The broad character of the recorded Raman bands limits a detailed discussion on the differences of the two spectra. Nevertheless DFT calculations that consider the carbonyl H-bonding interaction on the HPDP triplet confirms it has a nearly planar biradical $\pi\pi^*$ character and indicates that the change of the HPDP triplet property upon carbonyl H-bonding closely resembles those observed for the HP and MAP model compounds. The DFT optimized structure of the carbonyl H-bonded triplet and comparison of the corresponding calculated spectrum with the experimental spectrum (Figure 8a) are given in Figure 7S in the Supporting Information. The structural parameters for the optimized structures are also listed in Table 1S in the Supporting Information.

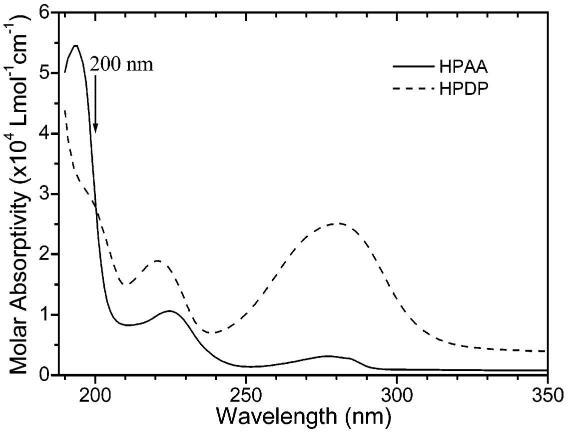

Figure 9. UV−vis absorption spectra of the HPAA product (solid line) and the HPDP substrate (dash line) in a H_2O/MeCN (1:1) mixed solvent.

We note that the triplet decay leading to the deprotection reaction occurs on the hundreds of picoseconds or even longer time scale (depending on the water concentration). However, the solvent reorganization required for changing the carbonyl H-bonding configuration on the triplet manifold takes place in the early picosecond time regime (within ~10 ps).[20,40] These preceding results suggest that it is the carbonyl H-bonded triplet that actually acts as the reactive precursor to the HPDP and HPPP deprotection reactions. The intrinsic ring localized $\pi\pi^*$ nature of such a precursor triplet state determines that the deprotection chemistry of *p*HP caged compounds is fundamentally different from the radical cleavage mechanism proposed for the deprotection of certain phenacyl caged phototriggers that occurs from an nπ^* triplet and initiated by a hydrogen abstraction reaction.[41]

E. Dynamics of the Rearrangement Reaction Studied by ps-TR^3 Spectroscopy. Ps-TR^3 measurements were performed to determine the formation dynamics of the rearrangement product HPAA for photoexcited HPDP and HPPP in a H_2O/MeCN (1:1) mixed solvent. The UV absorption spectrum of HPAA (displayed in Figure 9) shows that its lowest two absorption bands are weak but it absorbs strongly around 190−200 nm. A 200 nm probe wavelength was therefore chosen for the ps-TR^3 measurements. Figure 10 displays representative ps-TR^3 spectra of HPDP at various delay times obtained with a 267 nm pump and 200 nm probe wavelengths in a H_2O/MeCN (1:1) solvent. An overview of all the TR^3 spectra recorded under these conditions is given as Figure 8S in the Supporting Information. The resonance Raman spectrum from an authentic sample of HPAA obtained under the same conditions and using a 200 nm excitation wavelength is also shown in Figure 10 to compare with and to help identify the transient observed in the TR^3 spectra. The most important observation in the TR^3 spectra is the simultaneous growth of a series of a new feature at later picosecond times (~200 ps and afterward) that reflects the generation of a new species in this time regime. It is obvious that the newly developed transient spectra are essentially identical to the 200 nm resonance Raman spectrum of an authentic sample of HPAA. This indicates explicitly that the

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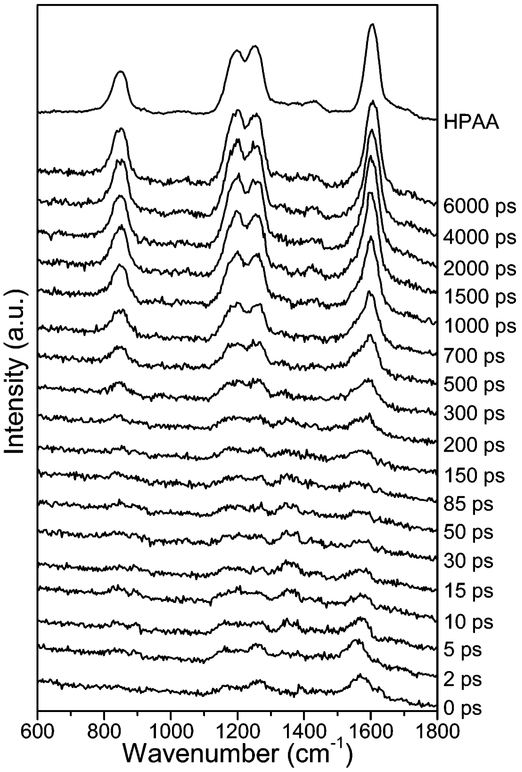

Figure 10. Picosecond time-resolved resonance Raman (ps-TR^3) spectra of HPDP obtained with a 267 nm pump and 200 nm probe wavelengths in a H_2O/MeCN (1:1) mixed solvent. Resonance Raman spectrum of an authentic sample of HPAA recorded with 200 nm excitation is displayed at the top.

new species can be attributed unambiguously to the HPAA rearrangement product. The spectral evolution displayed in Figure 10 thus represents a real time monitoring of the dynamic transformation from the photoexcited HPDP to the HPAA final product. To the best of our knowledge, the TR^3 results presented here provide the first direct time-resolved detection of the solvolytic rearrangement reaction for *p*HP phototrigger compounds.

Considering the ~2.5 ps ISC time,[13,17] the weak Raman feature (mainly the band at ~1550 cm^{-1}) at very early times (before 5 ps, Figure 10) can be attributed to the S_1 singlet state. The weakness of the S_1 feature implies the absorption of $S_1 \rightarrow S_n$ is weak at the 200 nm probe wavelength. Since the HPDP triplet has an ~350 ps lifetime in H_2O/MeCN (1:1) solvent, the observation that TR^3 spectra in Figure 10 display no recognizable features over the 10−200 ps time period implies that the triplet $T_1 \rightarrow T_n$ absorption is either absent or very weak around the 200 nm probe wavelength. To further confirm the dynamic observation for the rearrangement reaction in the water mixed solvent, parallel ps-TR^3 measurements (267 nm pump and a 200 nm probe) were also done for HPDP in neat MeCN solvent. The TR^3 spectra obtained in MeCN (presented as Figure 9S in the Supporting Information) is essentially featureless at the corresponding late delay times. This is in agreement with the absence of the HPDP deprotection and rearrangement reaction in MeCN solvent.[8,10,11]

The temporal change of the transient HPAA band area obtained in the TR^3 spectra (Figure 10) reflects the kinetics of the rearrangement reaction. The time-dependence of the Lorentzian fitted ~850 cm^{-1} band area of the transient HPAA TR^3 spectra (Figure 10) is displayed in Figure 11 (the data series indicated by circles). A rough fit of these data by a one exponential growth function results in a time constant of ~1100 ps. Comparison of this time constant with the ~350 ps time constant triplet delay time observed for HPDP in the same solvent indicates clearly that the occurrence of the rearrangement reaction is actually delayed relative to the triplet quenching process. The delayed formation of the rearrangement product was observed similarly for HPPP in a H_2O/MeCN (1:1) mixed solvent (Figure 11, data points in squares). Since the triplet decay time can be considered as the time constant for the release of the phosphate leaving groups, the delayed rearrangement dynamics implies a consecutive mechanism and the existence of an additional intermediate. This additional intermediate is the direct product of the triplet deprotection and acts simultaneously as the immediate precursor to the rearrangement process. This new intermediate is denoted temporally as “M” in the following kinetic analysis. The above correlation of the dynamics leads to the following equation (eq 2) to describe the deprotection and rearrangement reactions of HPDP and HPPP in a H_2O/MeCN mixed solvent. The “T” in the equation represents the triplet precursor of the deprotection reaction.

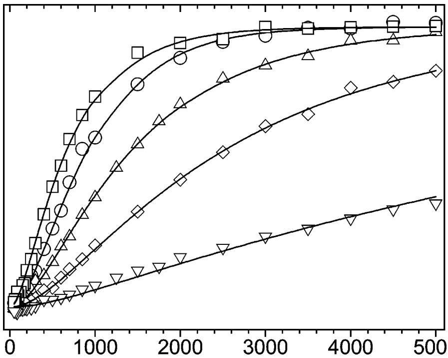

Figure 11. Time dependence of the HPAA 850 cm^{-1} band areas observed in the ps-TR^3 spectra obtained with 267 nm excitation and 200 nm probe wavelengths for HPDP in H_2O/MeCN mixed solvent with H_2O concentration of 50% (○), 25% (△), 15% (◇), and 10% (▽) and for HPPP in a H_2O/MeCN (1:1) solvent (□). The solid lines represent fitting results of the data points according to eq 3 (see text for details).

$$\mathrm{T} \xrightarrow[\text{deprotection}]{k_1} \mathrm{M} \xrightarrow[\text{rearrangement}]{k_2} \text{HPAA} + \text{phosphate anion (solvated)} \quad (2)$$

In this reaction scheme, the temporal variation of the HPAA concentration ([HPAA]) is expressed by eq 3[42]

$$[\mathrm{HPAA}] = \frac{[\mathrm{T}]_0}{k_2 - k_1}[k_2(1 - e^{-k_1 t}) - k_1(1 - e^{-k_2 t})] \quad (3)$$

where $[\mathrm{T}]_0$ stands for the initial concentration of the triplet precursor; k_1 and k_2 represent the rate constants of the deprotection and rearrangement reactions, respectively.

Providing that the decay of the HPDP triplet due to the occurrence of the deprotection is much faster (~500−20 times faster depending on the water concentration in the range of 75% −10 vol % water) than the natural triplet decay time (~150 ns), it is reasonable to assume that the contribution of the triplet

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[42] Laidler, K. J. *Chemical Kinetics*; Happer & Row, Publishers: 1987.

decay by natural photophysical processes can be ignored and the k_1 in eq 3 can be taken as the triplet decay rate determined in the preceding TA measurements ($k_1 = 1/\tau_1$, Table 1 for τ_1). We note that similar results are also observed for HPPP. To estimate the rearrangement rate of k_2 and its influence by the solvent, the ps-TR^3 measurements with a 267 nm pump and a 200 nm probe wavelengths were done for HPDP in water mixed solvent with the water content varying from 10% to 75% (by volume). The HPAA formation dynamics obtained represented by the integrated HPAA $\sim$850 cm^{-1} band area are also displayed in Figure 11. Dynamic fitting of the data series was done using eq 3, and it was found that the k_2 is not that sensitive to the water concentration. The data obtained in all of the examined H_2O/MeCN combinations can actually be fitted fairly well by a k_2 of $\sim 2.13 \times 10^{-9}$ s^{-1} rearrangement rate (with $k_2 = 1/\tau_2$, this corresponds to a τ_2 of $\sim$470 ps for the time constant). The lines in Figure 11 display these fitting results. The insensitivity of k_2 on the water concentration may imply that, for solvents with a water content ranging from 10% to 75% (by volume), the local solvent environments around the HPDP and HPPP excited precursor are quite similar in the hundreds to thousand picosecond time regime (when the rearrangement occurs). Thus, the difference in the water concentration shows no significant water concentration dependence on the solvolytic rearrangement reaction.

An analogous fitting procedure was also adopted to obtain the k_2 for the HPPP rearrangement reaction, and this results in a k_2 of $\sim 1.67 \times 10^{-9}$ s^{-1} rate (corresponding to a τ_2 time constant of 600 ps). The fitting result is shown in Figure 11) in a H_2O/MeCN (1:1) solvent. The time constants of the deprotection (τ_1) and the rearrangement (τ_2) for HPDP and HPPP are summarized in Table 1. The slower rearrangement time in HPPP ($\sim$600 ps) than in HPDP ($\sim$470 ps) appears to be unexpected since our TA result shows that, in a H_2O/MeCN (1:1) solvent, the deprotection time is faster for HPPP ($\sim$150 ps) than for HPDP ($\sim$350 ps). However, this leaving group dependence of the rearrangement rate has important implications for understanding the rearrangement process and may help in the identification of the "M" intermediate. Considering the more bulky nature of the diphenyl phosphate moiety than the diethyl phosphate leaving group, the slower k_2 in HPPP may simply reflect the steric influence of the leaving group on the rearrangement reaction. It could also imply there is a close involvement of the leaving group in the "M" precursor to the solvolytic rearrangement step.

Discussion

A. Spectral Character and Probable Identification of the Intermediate "M". Because of its important role, it is necessary to discuss the spectral features and probable attribution of the "M" intermediate. Although our present data contain no direct indication for the identity of this intermediate, it is quite certain that the species (i) is transparent in the region from 300 to 700 nm and (ii) shows very weak or no appreciable absorption around 200 nm and (iii) the temporal occurrence of this species is highly water concentration dependent. Point (i) is based on the spectral and dynamics of the relevant TA spectra. In the H_2O/MeCN (1:1) solvent (Figure 3b and 4b), the entire TA spectrum ($T_1 \rightarrow T_n$ absorption) follows a one exponential decay function and decays back to the prepulse baseline at later times. This indicates that there is no subsequent species exhibiting an appreciable absorption over the 300−700 nm detection range. Point (ii) comes from the ps-TR^3 data (Figure 10) displaying only vibrational features from the HPAA product (late times) and the S_1 state (very early times) and no interference from other unidentified species. Point (iii) is based on the consecutive reaction scheme of the deprotection and rearrangement reaction (eq 2). According to the reaction scheme (eq 2), the temporal dependence of the "M" concentration ([M]) follows[42]

$$[M] = [T]_0 \frac{k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}) \quad (4)$$

It is obvious from this equation that a significant accumulation of [M] can only be observed when $k_1 \gg k_2$. In the case where $k_1 \ll k_2$ a steady-state treatment becomes appropriate and M cannot be easily observed experimentally due to a rapid conversion of the nascent M into the HPAA product. This provides a quantitative correlation to the dynamics data we obtained for the triplet decay (Figure 7) and HPAA growth (Figure 11) from HPDP in a solvent with varying water concentrations. That is, the development time of HPAA shows a noticeable delay relative to the triplet decay dynamics in high water content solvents (such as 50% and 75% water content), while the two times become close in low water content solvent (such as those with a 15% and 10% water content). Based on this, detection of the M intermediate is only possible in largely water containing solvent (>50 vol %) where $k_1 > k_2$.

As to attribution of the M species, it is instructive to consider the importance of a concerted leaving group and hydroxy solvation to the deprotection reaction. The solvation of phosphate leaving groups in HPDP and HPPP can operate by H-bonding interaction between the double-bonded oxygen (as a H-bonding acceptor) and the solvent water molecule (as a H-bonding donor) so as to exert an electrophilic pull on the departing leaving group anion. This consequently facilitates dissociation of the corresponding C−O bond. Simultaneously, solvation of the phenolic proton (as a H-bonding donor) by the solvent water (as a HBA) results in a certain loss of the proton from the hydroxy group to the associated water molecule. This induces an increased electron density on the phenyl ring due to an improved electronic conjugation from the hydroxy oxygen to the ring system.[21] The electron-enriched ring may in turn become capable of performing a good nucleophilic attack to the carbon atom connecting the leaving group so as to exert an electronic push and facilitate departure of the water solvated leaving group. This cooperative push−pull scenario is in excellent agreement with the well-established neighboring group participation mechanism proposed for the intermolecular rearrangement and solvolytic reaction of β-anisylethyl, tosylates, brosylates, bromides, etc.[43−45] The push−pull interaction leads directly to generation of a transient species analogous to the spiroketone intermediate (shown below) which has been proposed to be essential for the occurrence of the solvolytic rearrangement reaction.[8,11,46] This in conjunction with the steric effect of the leaving group on the solvolytic rearrangement step as well as the effect of the carbonyl H-bonding leads us to

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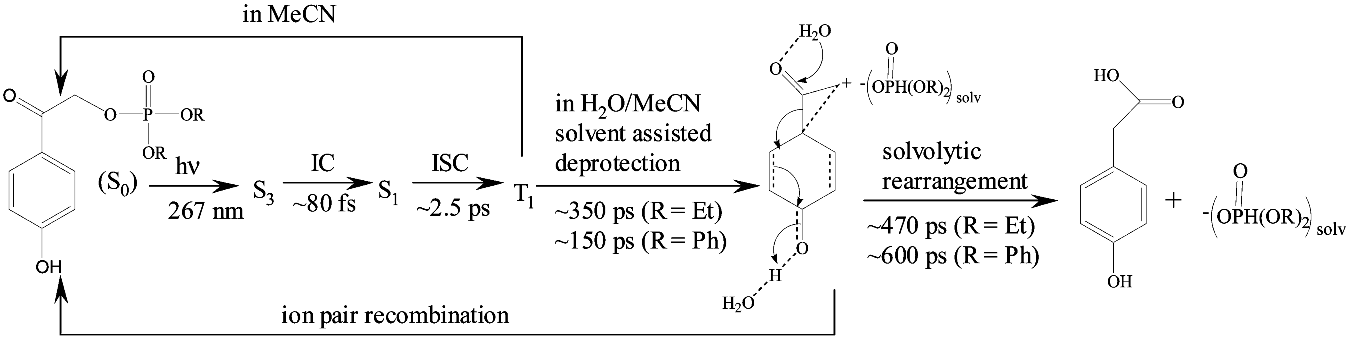
(43) (a) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3863−3870. (b) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2129−2137. (c) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3875−3883.

(44) Swain, C. G.; Eddy, R. W. *J. Am. Chem. Soc.* **1948**, *70*, 2989−2994.

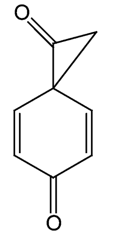
(45) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151−4162.

(46) Park, C-H.; Givens, R. S. *J. Am. Chem. Soc.* **1997**, *119*, 2453−2463.

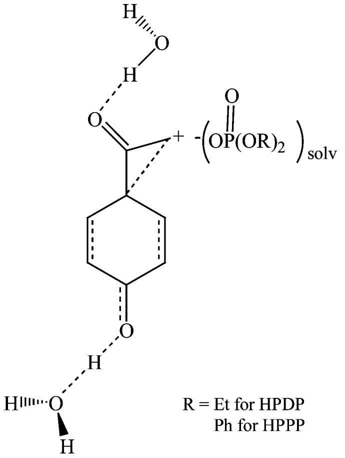
Scheme 1



propose a likely candidate for this intermediate species. This species is suggested to be a solvation complex with contact ion pair character (shown below).



spiroketone



Recombination of the contact ion pair may lead to the recovery of the HPDP and HPPP substrate; separation of the ion pair accompanied by water solvolysis at the carbonyl carbon leads to the HPAA product. The solvent water with its high dissociating ability and nucleophilic capability is ideal for the successful and efficient ion pair separation and solvolytic rearrangement reaction to occur.[43−46]

Considering the nearly planar structure of the precursor triplet (Table 7S and Table 1S in the Supporting Information), it is reasonable to suggest that the major chromophore (the phenyl ring and the joined cyclopropane and solvated hydroxy group) of the M intermediate may also be mainly planar. It is interesting that this chromophore may resemble the spiroketone species[8,10,11] and they may have parallel electronic properties. DFT computations at the random-phase approximation (RPA) employing the Gaussian 98 program suite[47] suggest that the spiroketone species has an electronic transition carrying a reasonably large oscillator strength at ∼274 nm (the RPA calculated results are given as Table 2S in the Supporting Information). The ∼274 nm electronic transition appears to be consistent with the spectral character found for the M intermediate (points (i) and (ii) above). We have thus performed a Kerr-gated ps-TR^3 experiment with a 273 nm pump and 273 nm probe wavelength aiming to detect the M intermediate for both HPDP and HPPP in largely water containing solvent. However, these spectra reveal no clear features that can be readily assigned to the M intermediate. This may be due to the following: (i) The concentration of M is too low to allow easy detection by TR^3. This is possible since the requirement of $k_1 \gg k_2$ is not fulfilled even under the most favorable conditions of the present experiment (Table 1). (ii) The species does not have a strong enough absorption at the 273 nm probe wavelength.

B. Mechanism for the Photodeprotection and Rearrangement Reaction of *p*HP Caged Phosphate Compounds. The data presented here provide strong evidence suggesting a direct triplet heterolytic cleavage mechanism for the deprotection reaction. It also provides evidence that concerted solvation of the leaving group and phenolic hydrogen are important and may work as a driving force to promote the cleavage reaction. Correlation of the dynamics of the deprotection and rearrangement reactions indicates a consecutive reaction scheme and involvement of an intermediate that has been tentatively attributed to a solvation complex with contact ion pair character. Reaction rates of the deprotection and rearrangement reaction have been derived based on a kinetic analysis of the dynamics data recorded experimentally. It was found that the deprotection rate depends strongly on both the leaving group and water concentration while the rearrangement rate is only leaving group dependent but insensitive to the water content. The present work represents one of the first in terms of real time monitoring and determination of the reaction pathway and reaction rates for the *p*HP photodeprotection and rearrangement reactions and addressing the important effect of water solvation on the overall reaction mechanism. This in conjunction with our earlier femtosecond KTRF[13] and relevant TR^3 studies[17,18a,20,21] on the photophysics of the *p*HP compounds leads to the following mechanistic scheme (Scheme 1). The proposed mechanism provides an overall account in terms of the early time photophysics and deprotection and rearrangement photochemistry for 267 nm photolysis of *p*HP caged phosphates in H_2O/MeCN mixed solvents (1:1 by volume for example).

In the proposed mechanism, the solvent assisted triplet heterolytic cleavage is the key initiating step to the photochemistry of *p*HP caged phosphates. Special structural and dynamical effects of the solvent water to solvate the HPDP triplet state thus play a crucial role in such a process. In this aspect, the *p*HP triplet deprotection appears to be analogous to the cleavage reaction of anion radicals in a series of α-substituted acetophenone compounds studied by Savéant and co-workers[48] and Wagner and co-workers.[49] In both cases, the mode of the

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(47) Frisch, M. J.; et al. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(48) Andersen, M. L.; Long, W.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1997**, *119*, 6590−6595.

(49) Andrieux, C. P.; Savéant, J.-M.; Tallec, A.; Tardivel, R.; Tardy, C. *J. Am. Chem. Soc.* **1996**, *118*, 9788−9789.

cleavage can be viewed as an intramolecular dissociative charge transfer, where the electron is transferred from a π^* orbital on the *p*-hydroxyphenacyl moiety (for the triplet of the *p*HP caged phosphates) or the acetophenone moiety (for the radical anion cleavage) to a σ^* orbital of the breaking bond between the phenacyl CH_2 and the leaving group. A significant degree of solvent reorganization is required to accommodate the flow of charge from the π^* to the dissociating σ^* orbital, and solvent reorganization has been found to be the main factor in dictating the height of the intrinsic reaction barrier.[48,49] This is consistent with the solvent effect and relevant interpretation we have presented here for the HPDP and HPPP triplet quenching process. For example, the concerted solvation perspective suggested in this work requires the dynamic rebuilding of the triplet solvation shell through rearrangement of the surrounding water molecules that may promote a favorable electronic shift and structural modification so as to deactivate the triplet efficiently and consequently account for the deprotection reaction. It is thus reasonable to suggest that the barrier height of the triplet photodeprotection for the *p*HP phosphates might also be controlled largely by the dynamical reorganization of the nearby solvent molecules. We note in this regard that a recent combined experimental and theoretical work by Phillips and co-workers demonstrates nicely that water-catalyzed solvation of a neutral leaving group into ions can act as a driving force to account for photodecomposition of isopolyhalomethanes in water solvated environments.[16] Further theoretical work could be helpful to provide a detailed molecule-level description of the reaction pathway for the solvent assisted *p*HP triplet deprotection and its subsequent rearrangement reaction.

C. Relevance of Previously Suggested Intermediates to the Deprotection Reaction. The spectral and dynamical properties of the intermediate M obtained in the present work enable us to comment on one of the relevant issues raised from previous work[8,10,11] about the *p*HP deprotection mechanism, that is, the possible involvement of the *p*HP deprotonation related intermediates in the photodeprotection reaction. A TA study on the photochemistry of the model compound HA in water or water mixed MeCN solvent found that the HA triplet deprotonation reaction leads to formation of the ionized HA triplet anion ($^3HA^-$) and subsequently the ground-state anion (HA^-) by ISC conversion.[10,21] The $^3HA^-$ and HA^- transient species was observed to have an absorption band with λ_{max} at ~400 and 350 nm, respectively.[10] Our conclusion here that the reactive intermediate is transparent at the 300−700 nm spectral range precludes involvement of any of the two species in the deprotection and rearrangement pathway for the *p*HP caged phosphates. This is further corroborated by comparison of the reaction rate between the phenolic deprotonation and release of the phosphate leaving groups. Our recent ps- and ns-TR^3 work found that time constants for the generation of the $^3HA^-$ and HA^- are ~10 ns and ~90 ns, respectively, in a H_2O/MeCN (1:1) solvent.[21] In so far as the leaving group has little influence on the deprotonation kinetics, the deprotonation is too slow to compete with the release of phosphate leaving groups that have been found to occur with time constants of ~350 and 150 ps, respectively, for HPDP and HPPP in the same H_2O/MeCN solvent.

In this aspect, we note also that, in the nano- to micro-second LFP study of the photorelease mechanism for HPA, a transient absorption band at 300−360 nm has been reported in a H_2O/MeCN (1:1) mixed solvent (this band was not seen in neat MeCN).[11] Based on the two exponential decay kinetics of this absorption band and the observation that the relative contributions of the two exponential components were sensitive to the solvent pH value, the band has been associated with two intermediates, the *p*-quinone methide (*p*QM) and its conjugated base. The *p*QM intermediate was suggested to be formed by a water mediated formal proton transfer of the phenolic proton to the ketone carbonyl and proposed to be the key reactive precursor for the deprotection reaction (ESIPT model).[11] It is obvious that this band does not appear for photoexcited HPDP and HPPP in a H_2O/MeCN (1:1) solvent (Figure 3, 4, 3S, and 4S) especially in the time period (0−10 ns) when the photorelease and rearrangement reaction occurs. This means that the so-called *p*QM intermediate must not be relevant to deprotection of these *p*HP caged phosphates. This suggests that the *p*QM may not necessarily be the reactive intermediate to the *p*HP photodeprotection reaction, even for the case of HPA. This reasoning is consistent with the calculation results reported by Wirz and co-workers that show that the energy of the *p*QM triplet is too low to be capable of expelling a leaving group.[10]

The mechanism shown in the Scheme 1 represents a general description of the dynamics and reaction pathway followed by the photophysical and deprotection related photochemical processes for the *p*HP caged phosphates. It is believed that this deprotection and rearrangement mechanism is applicable generally to various *p*HP caged phototriggers. It is however worthwhile to point out that although the early picosecond photophysical events (the IC and ISC) are relatively leaving group independent and thus the corresponding pathway is expected to apply generally to all *p*HP caged compounds, there might be additional channel(s) to deactivate the triplet state and the relative importance of these channel(s) to the deprotection pathway may depend highly on the ability of the leaving group. This is based on the triplet heterolytic cleavage mechanism and the consideration that, in the case of a slow triplet deprotection, the *p*-hydroxyphenacyl prototropic related process(es) (such as the deprotonation and tautomerization of the *p*HP cage occur on the nanosecond time regime[10,11,21]) could become an effective competing channel to depopulate the triplet. This prospect enables one to interpret the observation of additional transient species (assigned to be responsible for the 300−360 nm TA band observed in the nanosecond to microsecond time regime) observed for photolysis of HPA[11] compared to the absence of this band for photolysis of HPDP and HPPP in the H_2O/MeCN (1:1) solvent. In contrast to the high sensitivity of the deprotection dynamics on the stability of the leaving group anion, the prototropic related processes localize on the *p*HP moiety and its dynamics are expected to be relatively insensitive to that kind of leaving group.[13,21] On one hand, for a good leaving group such as the diphenyl and diethyl phosphates, respectively, in HPDP and HPPP, the cleavage process (~150 and 350 ps for HPPP and HPDP, respectively) is rapid so that it becomes the predominant pathway to deactivate the triplet state. Consequently no transient species related to the prototropic process could be observed after photolysis of HPDP and HPPP in water containing solvent. On the other hand, for the acetate leaving group in HPA, due to the slower deprotection rate (2200 ps triplet decay time), the prototropic related reaction could turn into an efficient competing process and they both make contributions to the triplet depopulation dynamics. This may provide an explanation for the observation of the prototropic related transient species for the photolysis of HPA in the water mixed solvent.[11] Further work is in progress to better understand the interesting variation of the triplet deactivation pathway with the nature of the solvent medium (such as the pH condition) and on the nature of the leaving group.

Conclusion

We report here a TA and ps-TR^3 spectroscopy study of the photodeprotection and rearrangement reactions for HPDP and HPPP in H_2O/MeCN mixed solvents. TA spectroscopy was used to detect the solvent dependent decay dynamics of the triplet precursor, and TR^3 was used to monitor the formation dynamics of the HPAA rearrangement product in the mixed solvent systems. The solvent effect observed in the TA experiments is consistent with a solvent assisted triplet heterolytic cleavage pathway for the release of the phosphate leaving groups. These results provide an indication for the strong coupling of water that may manifest itself as site-specific concerted solvation of the hydroxy proton and phosphate leaving group anion through their respective intermolecular H-bondings with solvent water molecules to promote the photodeprotection reaction. Correlation of the dynamics of the deprotection and rearrangement reactions reveals there is a consecutive mechanism with the rearrangement occurring subsequently to the deprotection and there is an involvement of an intermediate between the two reactions. The reaction rates for the two processes are derived based on a kinetic modeling of the dynamics data obtained for HPDP and HPPP in H_2O/MeCN mixed solvents with varying water concentrations. The deprotection rate was found to be sensitive to the solvent water concentration and is faster for HPPP than HPDP in the same solvent environment. The rearrangement rate is generally insensitive to the water content (for water concentration ranges from 10% to 75 vol %) but was estimated to be slower for HPPP (∼600 ps) than for HPDP (∼470 ps). The observed dynamics dependence on the solvent and the leaving group leads to the suggestion of a solvation complex with contact ion pair character as an intermediate involved in the pathway of the deprotection and rearrangement reactions. The results here provide important kinetics and structural data that allows an overall mechanistic characterization for the photophysical and photochemical events occurring after photolysis of *p*HP caged phosphates in various solvent environments.

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Supporting Information Available: Details for the synthesis and characterization of HPPP. Figure 1S. Transient absorption spectra of the HA model compounds obtained in MeCN (a) and H_2O/MeCN (1:1) solvent (b) with 267 nm photoexcitation; Figure 2S. Transient absorption spectra of the MAP model compounds obtained in MeCN (a) and H_2O/MeCN (1:1) solvent (b) with 267 nm photoexcitation; Figure 3S. Transient absorption spectra of HPPP in MeCN at early (a) and late (b) picosecond times. Figure 4S. Transient absorption spectra of HPPP in H_2O/MeCN (1:1) at early (a) and late (b) picosecond times. Figure 5S. (a) Nanosecond time-resolved resonance Raman (ns-TR^3) spectra of HPPP obtained in MeCN with 267 nm excitation and 416 nm probe wavelength at various delay times. (b) Lifetime decay of HPPP triplet fitted by one exponential function of the $\sim$1600 cm^{-1} Raman band. Figure 6S. Stern−Volmer plot for triplet quenching dynamics of HPDP by water (in MeCN). Figure 7S. DFT (UB3LYP/6-311G**) optimized structure for carbonyl H-bonded triplet of HPDP (a) and comparison of the calculated spectrum with experimental result (b). Figure 8S. Picosecond time-resolved resonance Raman spectra of various delay times for HPDP obtained with 267 nm pump and 200 nm probe wavelength in H_2O/MeCN (1:1) solvent; Figure 9S. Picosecond time-resolved resonance Raman spectra of various delay times for HPDP obtained with 267 nm pump and 200 nm probe wavelength in MeCN solvent; Table 1S. DFT (UB3LYP/6-311G**) optimized structural parameters for carbonyl H-bonded triplet state of HPDP. Table 2S. Time dependent DFT (B3LYP/6-311G**) RPA calculated result obtained for excited-state energies and oscillator strengths from the ground state of the spiroketone species; Complete ref 47. This material is available free of charge via the Internet at http://pubs.acs.org.

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