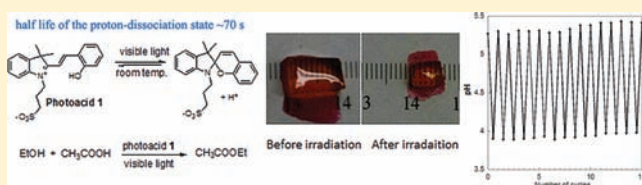


# Long-Lived Photoacid Based upon a Photochromic Reaction

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**ABSTRACT:** A visible-light activatable photoacid has been studied, which upon irradiation, changes from a weak acid, with a  $pK_a$  of 7.8, to a strong acid, which achieves nearly complete proton dissociation. This process is reversible and the half-life of the proton-dissociation state is  $\sim 70$ s. The long lifetime of the proton-dissociation state is due to a sequential intramolecular photochromic reaction. Using this photoacid, a pH change of 2.2 units has been achieved. In addition, we demonstrated that the photoinduced proton concentration can catalyze an esterification reaction, and greatly alter the volume of a pH-sensitive polymer. This work shows that acid-catalyzed and pH-sensitive processes can be photochemically controlled by using this type of photoacid.



## 1. INTRODUCTION

Proton transfer is one of the most fundamental processes in nature. It is involved in numerous chemical reactions, biological functions, and material properties.<sup>1</sup> Photoacids that undergo proton dissociation upon irradiation promise spatial and temporal control of these processes in a noncontact way, and could provide a way to convert photoenergy into other types of energy. Herein the term “photoacids” refers to the molecules that reversibly undergo proton photodissociation and thermal reassociation. Photoacid generators (PAGs) and other compounds that are consumed in the photoprocesses are not considered. In fact, photoacids have been studied since the 1970s, and reviews have been published every decade since then.<sup>2–6</sup> Photoacids have been used to study molecular proton transfer, and have been exploited to control molecular and supramolecular events.<sup>7,8</sup> However, the photoinduced proton concentration of previously reported photoacids has not been large enough to drive or control many acid-catalyzed or pH-sensitive processes, and the great potential of photoacid has yet to be explored. For example, catalyzing reactions using photoacids was proposed in the 1970s and is still described as a potential application in recent papers.<sup>9</sup> The major challenge is that the lifetime of the proton-dissociation state is limited by the lifetime of the conjugated base of the photoacid in the ground state. The short lifetime of the proton dissociation state is useful for studying some fast processes; however, the liberated proton does not have enough time to diffuse away from its counterion and thus cannot catalyze a chemical process or significantly alter a macroscopic property even though the theoretical excited-state  $pK_a^*$  can be very low. A recent work reported a photoacid with a relaxation time of the proton-dissociation state close to 1 s, which was estimated by pump–probe absorption spectroscopy.<sup>9</sup>

Using an intramolecular photoreaction to stabilize the proton dissociation state can be an effective way to increase the lifetime of the proton dissociation state. The most extensively studied intramolecular photoreactions are photochromic reactions.<sup>10</sup> As a matter of fact, photochromic compounds have been used to

induce proton transfer and consequent molecular events before, but the lifetime of their proton-dissociation state was not reported.<sup>8</sup> These photochromic compounds include protonated merocyanines and 2-hydroxyazobenzenes. Herein we report a long-lived photoacid based on a photochromic reaction, and demonstrate its applications by catalyzing an esterification reaction, as well as altering the volume of a pH-sensitive polymer.

## 2. EXPERIMENTAL PROCEDURE

**General.** The photoreactions were performed using a RPR-100 Rayonet photochemical reactor equipped with 16 lamps with emission wavelength of 419 or 570 nm. Products of the esterification reaction were analyzed by a PerkinElmer series 200 HPLC. Fisher Scientific Accumant AR15 benchtop meter and pH combination electrodes were used to measure the pH change. The UV absorption spectral studies were performed using a Varian Cary 50 Scan UV–vis spectrophotometer.

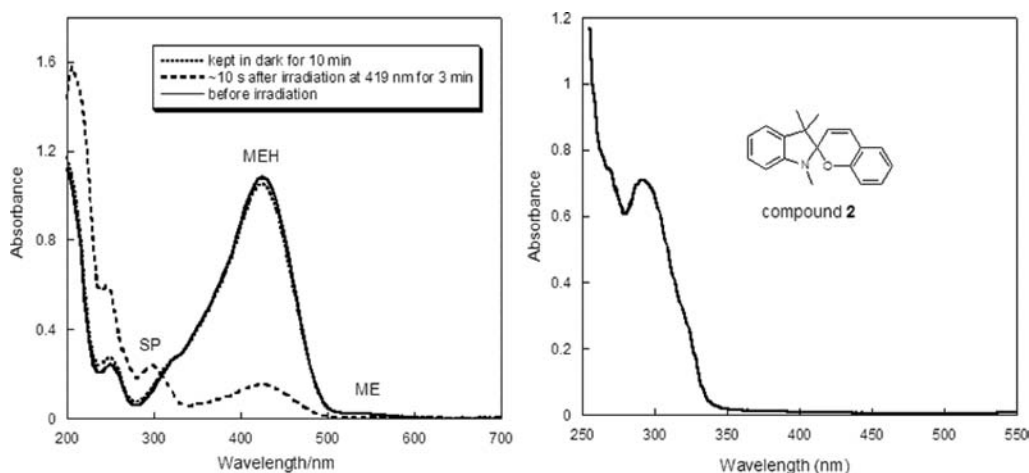
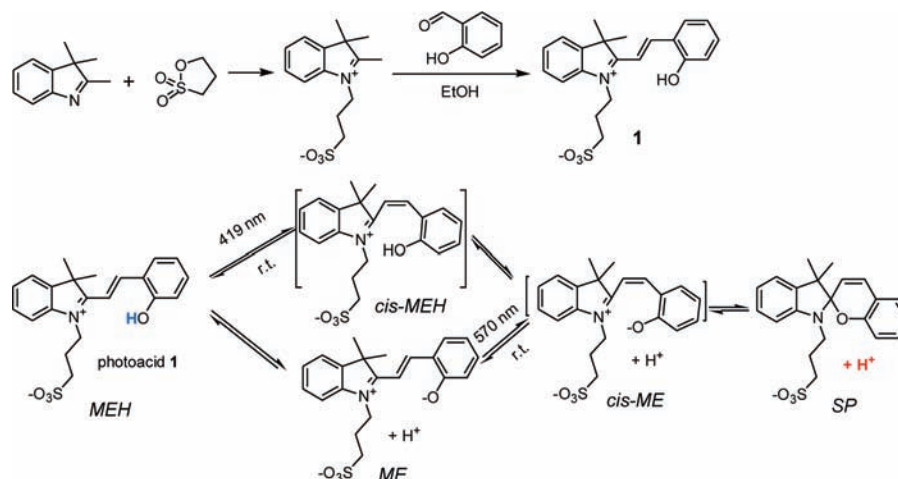
**Photoreaction Conditions.** In the photocatalyzed esterification reaction, a solution of the reactants and the photoacids was divided into two solutions and placed in Pyrex test tubes. One of the test tubes was wrapped with aluminum foil and used as the control. The two test tubes were placed together in a RPR-100 Rayonet photochemical reactor and were irradiated with a 419 and/or a 570 nm light. The photoreactor was equipped with a ventilation fan, which kept the temperature close to room temperature. The concentration of the solution, the irradiation time, and the yields were given in the text. In the experiment that demonstrated the photoinduced volume change, the hydrogel cuboid was placed in an open beaker filled with an aqueous solution of the photoacid. The mixture was irradiated in the photochemical reactor, and the size of the cuboid was measured by placing the wet cuboid on a ruler.

**Synthesis of Photoacid 1.** Scheme 1 shows the details. Starting material 2,3,3-trimethyl-1-(3-sulfonatepropyl)-3H-indolium was synthesized following a literature method.<sup>11</sup> Thus, 2,3,3-trimethylindolenine (1.65 g, 0.01 mmol, Aldrich) was added into propane sultone (1.26 g, 0.01 mmol, TCI). The mixture was stirred at 90 °C for 4 h under  $N_2$ .

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Scheme 1. Synthesis (Top) and Photochemical Reaction (Bottom) of Photoacid 1



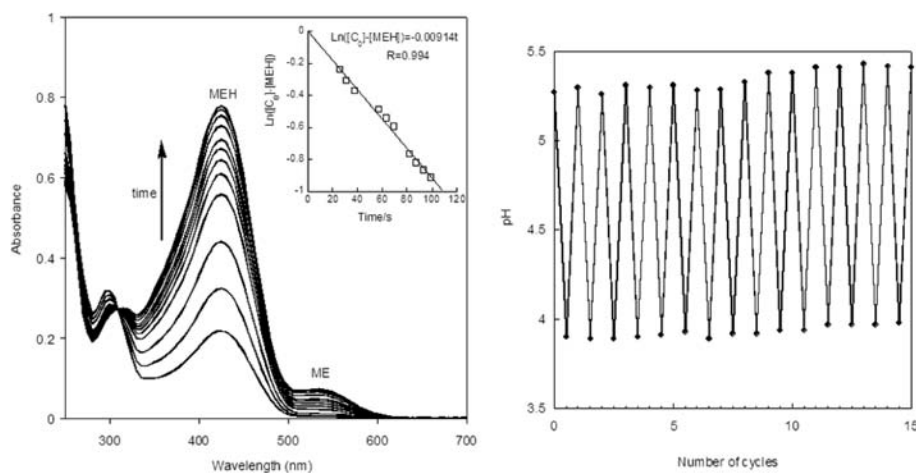
**Figure 1.** UV–vis absorption of a solution of photoacid **1** before irradiation,  $\sim 10$  s (time between the end of the irradiation and the end of UV–vis measurement) after irradiation at 419 nm for 3 min, and kept in the dark for 10 min after irradiation (left), and UV–vis absorption of **2**, an analogue of the SP form of **1** (right).

The purple solid was collected by filtration, washed with cold diethyl ether, and dried in vacuo (2.61 g, 89% yield).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.04 (d, 1H,  $J$  = 7.0), 7.81 (d, 1H,  $J$  = 6.5), 7.61 (m, 2H), 4.65 (t, 2H,  $J$  = 8), 2.82 (s, 3H), 2.62 (t, 2H,  $J$  = 6.5), 2.14 (m, 2H), 1.52 (s, 6H).

For the synthesis of **1**, 2,3,3-trimethyl-1-(3-sulfonatepropyl)-3H-indolium (100 mg, 0.36 mmol) and 2-hydroxybenzaldehyde (48 mg, 0.39 mmol) were added into anhydrous ethanol (2 mL). The mixture was allowed to reflux overnight. The orange solid was obtained by filtration (110 mg, 80% yield).  $^1\text{H}$  NMR (500 MHz,  $d_6$ -DMSO):  $\delta$  = 11.05 (s, 1H), 8.60 (d, 1H,  $J$  = 16.5), 8.28 (d, 1H,  $J$  = 7.0), 8.02 (d, 1H,  $J$  = 7.0), 7.87 (m, 2H), 7.62 (m, 2H), 7.45 (t, 1H,  $J$  = 8.4), 7.04 (d, 1H,  $J$  = 8.5), 6.96 (t, 1H,  $J$  = 7.0), 4.80 (t, 2H,  $J$  = 7.5), 2.65 (t, 2H,  $J$  = 6.0), 2.15 (m, 2H), 1.77 (s, 6H).  $^{13}\text{C}$  NMR (500 MHz,  $d_6$ -DMSO):  $\delta$  = 25.1, 26.9, 45.9, 47.8, 52.3, 111.9, 115.5, 117.1, 120.5, 121.8, 123.4, 129.5, 129.6, 130.2, 136.2, 141.4, 143.9, 149.1, 159.5, 182.2. HRMS (ESI):  $[\text{M} - \text{H}]^-$  = 384.1275,  $[\text{M} - 2\text{H} + \text{Na}]^-$  = 406.1094. UV–vis absorption in water:  $\lambda_{\text{max}}$  = 424 nm. The solubility of MEH in water at room temperature is  $\sim 2 \times 10^{-4}$  M. Assisted by gentle heating,  $\sim 6 \times 10^{-4}$  M solution can be obtained. However, the solution became slightly cloudy after being kept overnight.

### 3. RESULTS AND DISCUSSION

Photoacid **1** is a protonated merocyanine with a propyl sulfonate group on the nitrogen of the indoline moiety. It was synthesized following the procedure in Scheme 1. In an aqueous solution, the protonated merocyanine (MEH) form of **1** is predominant at room temperature in the dark, which is proven by UV–vis (Figure 1) and NMR spectroscopy. In the UV–vis spectrum, the absorption of the deprotonated merocyanine (ME) can also be observed, which indicates that **1** is weakly acidic. A  $5.88 \times 10^{-4}$  M aqueous solution of photoacid **1** has a pH value of 5.5, from which the  $\text{pK}_a$  of **1** was calculated to be 7.8. When the solution was irradiated with 419 nm light, which is close to the  $\lambda_{\text{max}}$  of MEH (424 nm), pH drops more than 2 units to 3.3. This value is close to the theoretical value for complete proton dissociation (3.2) indicating that **1** is a strong acid under irradiation. When the light was turned off, pH value increased quickly to  $\sim 4.5$  in  $\sim 1$  min, gradually returning to its original level in  $\sim 5$  min. This cycle can be repeated many times (Figure 2). Therefore, proton concentration can be simply controlled by switching a light on and off. This process does not require control

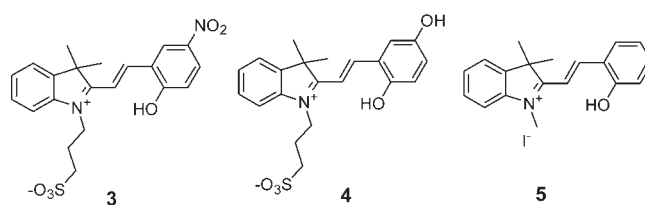


**Figure 2.** UV–vis absorption of a solution of photoacid **1** 25–340 s after irradiation (left) (the inset plot shows the data in the first 100 s fitted to a first order reaction equation), and cycles of pH change under irradiation and in the dark (right). For each cycle, a solution of **1** ( $1.5 \times 10^{-4}$  M) was irradiated with 419 nm light for 3 min and kept in the dark for 10 min.

of two light sources with different wavelengths, nor does it involve irradiation with UV light.

The photochemical reaction was studied by UV–vis absorption spectroscopy (Figures 1 and 2). Upon irradiation, the absorption of MEH decreased, and an absorption peak at 300 nm appeared. This absorption peak is assigned to the SP form of **1** based on the UV–vis spectrum of an analogue, **2**, in Figure 1. The absorption of ME disappeared quickly upon irradiation, leaving only the MEH and SP absorption to be observed. This indicates that ME is not likely as an intermediate in the MEH-to-SP process. The disappearance of ME should be due to the equilibrium between the MEH and ME, and the increased acidity caused by the MEH-to-SP transformation, which changes ME to MEH. In the dark, the absorption intensity of MEH recovered to the level before irradiation in  $\sim 5$  min. The absorption of ME increased with that of MEH with no isosbestic point (Figure 2), which indicates that MEH is not generated from ME in the SP-to-MEH transformation. On the basis of these analyses and previous studies of photochromism,<sup>12</sup> the mechanism of the photoreaction is proposed as in Scheme 1. Photoirradiation with 419 nm light induces a trans–cis isomerization of MEH. Proton dissociation of the cis-MEH produces cis-ME, which undergoes a nucleophilic ring closing reaction to yield SP. The process is reversible, and SP reverts back to MEH in the dark. In addition, irradiation at 570 nm, which is only absorbed by ME, also induced MEH-to-SP transformation. This supports the idea that photoirradiation induces trans–cis isomerization rather than proton dissociation. Absorption peaks of cis-ME and cis-MEH were not observed, which may be due to their low stability in addition to absorption overlaps with those of MEH, ME, and SP.

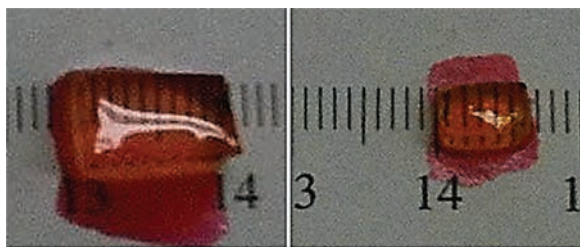
The lifetime of the proton-dissociation state was calculated from the rate of MEH formation after irradiation, which was monitored by UV–vis spectroscopy. UV–vis spectra were collected every 10 s after irradiation (Figure 2). The proton concentration equals the overall concentration subtracted by the MEH concentration. The experimental data in the first 100 s were fit to a first order kinetic equation, and a rate constant  $k = 0.00914 \text{ s}^{-1}$  was obtained (Figure 2). The half-life of the proton dissociation state ( $t_{1/2} = 0.693/k$ ) was calculated to be 76 s. This lifetime is only an estimation, since the process is a reversible



**Figure 3.** Derivatives of **1** synthesized and studied in this work.

multistep process, and thus may not strictly follow first-order kinetics. Nonetheless, the calculated half-life is consistent with the pH measurements, which shows that first order decay is a reasonable approximation for the early stage of the proton concentration decay.

To further improve the photoacidity and understand the factors that affect it, analogues of **1** (**3–5** in Figure 3) were synthesized. Compound **3** has an electron-withdrawing  $\text{NO}_2$  group on the phenol moiety, and **4** has an electron-donating OH group. Both **3** and **4** are less effective than **1** in lowering the pH on photolysis. The electron-withdrawing group of **3** increased its acidity in the dark. The  $\text{pK}_a$  of **3** in the dark is 6.36, which is 1.5 units lower than that of **1**. The pH of a  $3.7 \times 10^{-4}$  M solution of **3** changed from 4.9 to 3.9 upon irradiation, while a solution of **1** of the same concentration can change its pH from 5.5 to 3.5. The acidity of **3** after irradiation is lower than that of **1**, which should be due to a less efficient nucleophilic cis-ME-to-SP reaction. For compound **4**, photoirradiation does not effectively induce MEH-to-SP transformation, and thus produces little pH change. This may be because the cis-MEH cannot undergo proton dissociation efficiently to generate cis-ME. Detailed mechanistic study is required to quantitatively define the suitable photoreactivities and energy levels of MEH, SP, and ME, which is beyond the scope of this article. Solubility of the photoacid is important for inducing a large pH change in solution. The saturation concentration of **1** in water is  $\sim 6 \times 10^{-4}$  M, which limits the photoinduced pH change to  $\sim 2$  units. The solubility of **5** is too low in both organic solvents and water for a significant change of proton concentration to be realized. Comparing **1** with **5**, we can see that the propyl sulfonate group increases the solubility of **1**. In addition, it has been reported that alkyl sulfonate groups on the



**Figure 4.** pH sensitive hydrogel before (left) and after (right) being irradiated in a solution of **1**. (The cuboid was taken out of the solution and measured on a ruler.)

nitrogen of the indoline moiety can stabilize the open ring forms (MEH and ME).<sup>13</sup> The positive charge of N<sup>+</sup> on the indoline moiety is shielded by SO<sub>3</sub><sup>-</sup>, which disfavors the nucleophilic ring-closing reaction of the phenoxy anion, and thus stabilizes open ring structures.

Two experiments were conducted to demonstrate the applications of this type of photoacid. In the first experiment, **1** was used to catalyze a Fisher esterification reaction, which often requires a strong acid catalyst, such as sulfuric acid. Thus, a mixture of acetic acid (12.5 mM) and **1** (3.1 mM) in ethanol was irradiated at 419 and 570 nm. Ethyl acetate was produced and analyzed by HPLC. The yields were 33%, 50%, and 66% for 1, 2, and 3 h reaction, respectively. No reaction was detected when the mixture was kept in the dark. In a control experiment, **1** was substituted by **2**. No esterification reaction was detected after the mixture was irradiated for 3 h. This experiment shows that acid-catalyzed reactions could be photocatalyzed. In the second experiment, a solution of **1** was used to alter the volume of a pH sensitive polymer. The idea was proposed before, but no experimental demonstration has been made to date.<sup>14</sup> Thus, a hydrogel of cross-linked polyacrylamide was prepared following a literature procedure.<sup>15</sup> It was partially hydrolyzed to a copolymer of poly(acrylic acid) and polyacrylamide by 1 M NaOH solution. The hydrogel was cut into cuboids, which were then soaked in a mixture of **1** in water (1 mg/mL). After irradiation, the volume of the hydrogel changed to  $\sim 1/8$  of its initial volume (Figure 4). The hydrogel did not change back to its original volume when left in the dark although the pH of the solution did revert back to its original value. This is due to the property of the hydrogel, not the photoacid, since the hydrogel showed the same behavior when placed in different buffer solutions with different pH values. Given that these experiments are for demonstration only, no effort was put forth to optimize the conditions. For real applications, the photoacid should be covalently linked to polymers, which could lead to recyclable heterogeneous catalysts that eliminate the requirements of strong acids, as well as photo-responsive actuators and artificial muscles that can be controlled using fiber optics or noncontact irradiation.

#### 4. CONCLUSION

In conclusion, we have discovered a visible-light activatable photoacid that has a proton-dissociation state lifetime of  $\sim 70$  s and can alter the pH value of its solution unprecedentedly. The long lifetime of its proton-dissociation state is due to a sequential intramolecular reaction. The magnitude of photoinduced proton concentration reported in this work is so large that it can catalyze an esterification reaction and alter the volume of a pH sensitive polymer. None of these have been achieved with other photoacids.

These are only two examples of the potential of photoacids. Given that proton transfer is one of the most fundamental processes in nature, this type of photoacid may provide a way to utilize photoenergy to control or drive numerous processes that involve proton concentration.

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