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Journal:	<i>ChemComm</i>
Manuscript ID	CC-COM-12-2024-006465.R1
Article Type:	Communication

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A novel metastable-state photoacid for reversible protonation of strong bases

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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Metastable-state photoacid (mPAH) has become a common tool for controlling and driving chemical processes with light. However, previously developed mPAHs could not be used for reversible protonation of strong bases, including many common amines and heterocycles. In this work, we developed a novel mPAH using benzimidazole as the structural moiety with the active proton. The very low dark acidity of the photoacid avoids the protonation of strong bases in the absence of irradiation. Absorption spectroscopy and NMR studies showed that the photoacid could be paired with NEt_3 and DMAP and underwent reversible photoreaction and proton transfer. This new type of photoacid allows the photocontrol of functional materials with strong proton acceptors.

Metastable-state photoacids (mPAHs), which can reversibly generate a high proton concentration under moderate irradiation, have become a common tool for driving and controlling chemical processes with light in the past decade.¹ Not only have many applications in chemical, material, biological, medical, and energy areas been demonstrated in research labs, but companies are also developing the technology utilizing mPAHs.² For example, Kim and coworkers invented a new route to harvest solar energy utilizing a proton gradient generated by asymmetrically irradiating a solution of an mPAH. The device, which was called PA-driven liquid-state photoenergy harvester, generated electricity from natural sunlight with an electrochemical energy conversion efficiency of 59%.³ Sleiman group utilized an mPAH to create a proton dissipation, which was utilized to generate otherwise inaccessible morphologies of fibers made of DNA and cyanuric acid.⁴ Pezzato group achieved a persistent pH gradient of 4 pH units using an mPAH solution and obtained an open circuit

potential as high as 240 mV, comparable to the biological transmembrane proton pumps.⁵ Several groups demonstrated that mPAHs can be applied to regenerate carbon dioxide sorbent with visible light at room temperature.⁶⁻¹⁰ The photo-induced acidity was utilized to release the CO_2 captured by the sorbent. The sorbent can then be reused, and the concentrated CO_2 obtained in the process can be used as an industrial material.

The main advantage of using mPAHs to develop a photoresponsive system is that the functional component does not need to be photosensitive. It only needs to possess a certain basicity to accept the proton from an mPAH. Basicity is a common property of chemicals. Even hydrocarbon aromatic rings have been used as proton acceptors of mPAHs.¹¹ Therefore this is a highly versatile approach. The pK_a of the proton acceptor or the pH of the proton accepting system must fall into the range between the pK_a of the acidic metastable state (pK_a_{MS}) generated by irradiation and the ground-state pK_a (pK_a_{GS}) of the mPAH, i.e. $\text{pK}_a_{\text{GS}} > \text{pK}_a_{\text{acceptor}} > \text{pK}_a_{\text{MS}}$. If the pK_a of the proton acceptor is lower than pK_a_{MS} , the mPAH cannot transfer the proton to the acceptor under irradiation. If the pK_a of the proton acceptor is higher than pK_a_{GS} , meaning the acceptor is very basic, the mPAH releases the proton to the acceptor without irradiation. Therefore, the range between pK_a_{GS} and pK_a_{MS} is critical for the applications of an mPAH.

There are three types of mPAHs reported before, which are merocyanine, TCF, and indazole mPAHs.¹ Many derivatives have been developed since they were reported about a decade ago. The lowest pK_a_{MS} is near 1 possessed by merocyanine mPAHs¹², and the highest pK_a_{GS} is around 9 for indazole mPAHs^{6,13}, allowing a wide range of molecular systems to be controlled by light. However, photocontrol of strongly basic systems is still a changing problem. For example, amines, which are the most used organic bases, often have

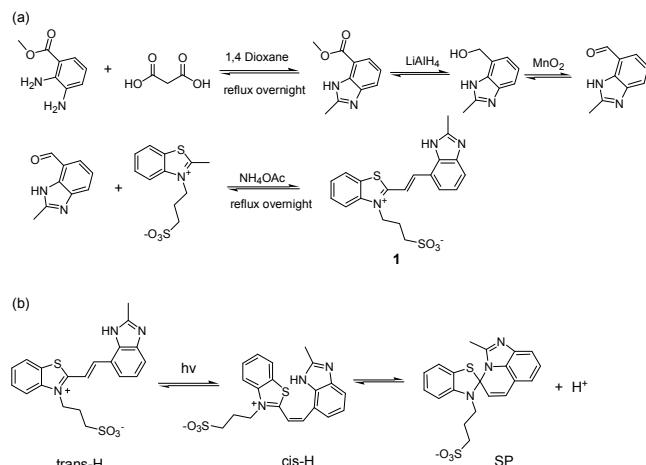
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Supplementary Information available: [details of any supplementary information av included here]. See DOI: 10.1039/x0xx00000x

$pK_a \sim 10$. Previously developed mPAHs transfer protons to these bases at the ground state without irradiation. Herein, we report a new type of mPAH with high pK_a _GS, allowing reversible proton transfer to strong organic bases including triethyl amine (NEt_3) and 4-dimethylaminopyridine (DMAP).

The new photoacid **1** was synthesized following the route shown in Scheme 1. The 2-methyl benzimidazole carboxylate was synthesized from 2,3-diaminobenzoate based on a literature procedure.¹⁴ The ester was converted to the corresponding aldehyde by a common method using LiAlH_4 reduction followed by MnO_2 oxidation. The resultant aldehyde was reacted with a methyl benzothiazolium, which was synthesized according to a literature method¹³, to yield the mPAH **1**. The detailed procedure is described in the Supporting Information (SI). Comparing **1** with the previous types of mPAHs, the major difference is that benzimidazole was used as the structural moiety with active proton, instead of phenol or indazole as in the other mPAHs. MPAH **1** is poorly soluble in water but well dissolved in organic solvents including methanol and DMSO. The absorption spectrum of **1** in a methanol solution is shown in Fig. 1. The strong absorption band in the visible range has a λ_{max} at 419 nm with molar absorptivity $\epsilon = 2.85 \times 10^4 \text{ M}^{-1}\text{cm}^{-1}$. The photoreaction of an mPAH generally involves photoinduced trans-cis isomerization followed by nucleophilic ring-closing reaction, which forms an acidic spiro (SP) structure and releases proton. (Scheme 1b) Irradiation of **1** with 470 nm LED light significantly reduced the absorption peak at 419 nm and increased the absorption near 300 nm. (Fig. 1a) Prolonged irradiation did not further reduce the absorption in the visible range. Due to the broken conjugated structure, the SP does not absorb light in the visible range. The remaining absorption in the visible range showed that the conversion to SP was not effective. A complete conversion to SP was achieved by irradiating a solution of **1** in the presence of 1 mM of NEt_3 . (Fig. 1b) The base (NEt_3) reacted with the proton released from SP and shifted the equilibrium to SP. Comparing Fig 1a with 1b clearly shows that the major product of irradiation without base is not SP, which has a strong absorption peak at 285 nm. Based on the mechanism and previous work^{1,15}, the major



Scheme 1. (a) synthesis of mPAH **1** and (b) mechanism of photoreaction.

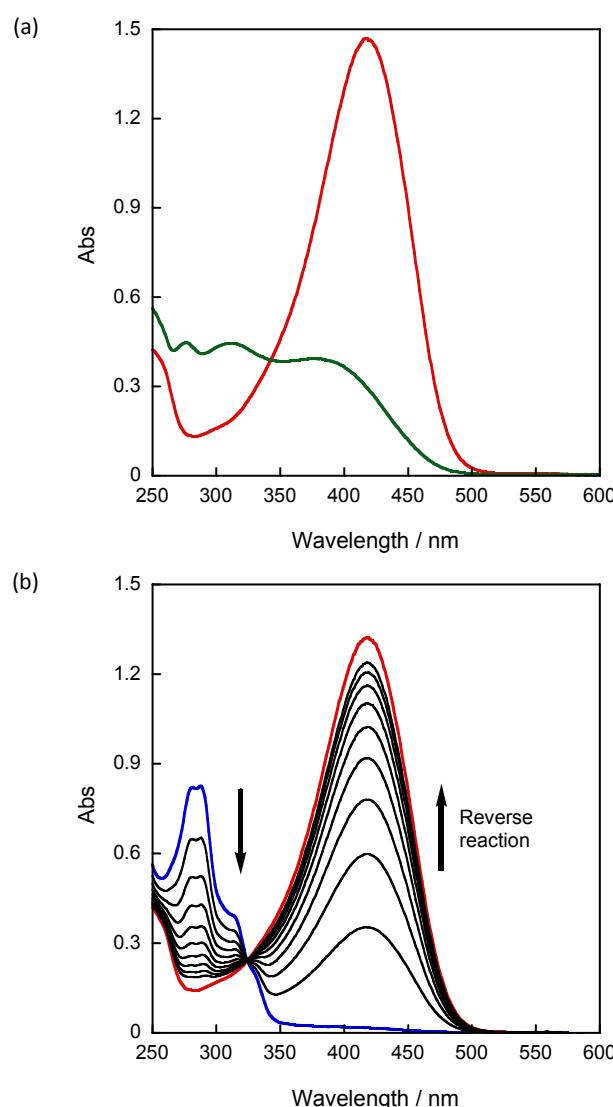


Fig. 1 (a) Absorption spectra of a solution of **1** in methanol before irradiation (red) and immediately after irradiation (green) and (b) Absorption spectra of **1** in 1 mM of NEt_3 solution before irradiation (red), immediately after irradiation (blue), and during the reverse process (black, the arrows indicate the direction of product is assigned to the cis-H conformer (Scheme 1b).

The absorption peak at 419 nm was only slightly reduced in the presence of 1 mM NEt_3 , indicating a very low ground state acidity (dark acidity). (Fig. 2a) For comparison, other types of mPAHs were deprotonated under similar conditions and formed SP and trans- without irradiation. The photoreaction was reversible. (Fig. 1b) After the light was switched off, the absorption spectrum returned to the original pattern in about 2 hours. Since the concentration of the base is much higher than that of **1**, the $[\text{H}^+]$ is approximately constant, and thus, the reverse reaction was treated as a first-order reaction. Fitting the data to the first-order kinetic equation resulted in a rate constant of $3.8 \times 10^{-4} \text{ s}^{-1}$.

Although the ground-state acidity (pK_a _GS) could be analyzed based on the equilibrium among trans-H, trans-, and SP,¹⁶ a convenient method is finding a pH buffer, at which half of trans-

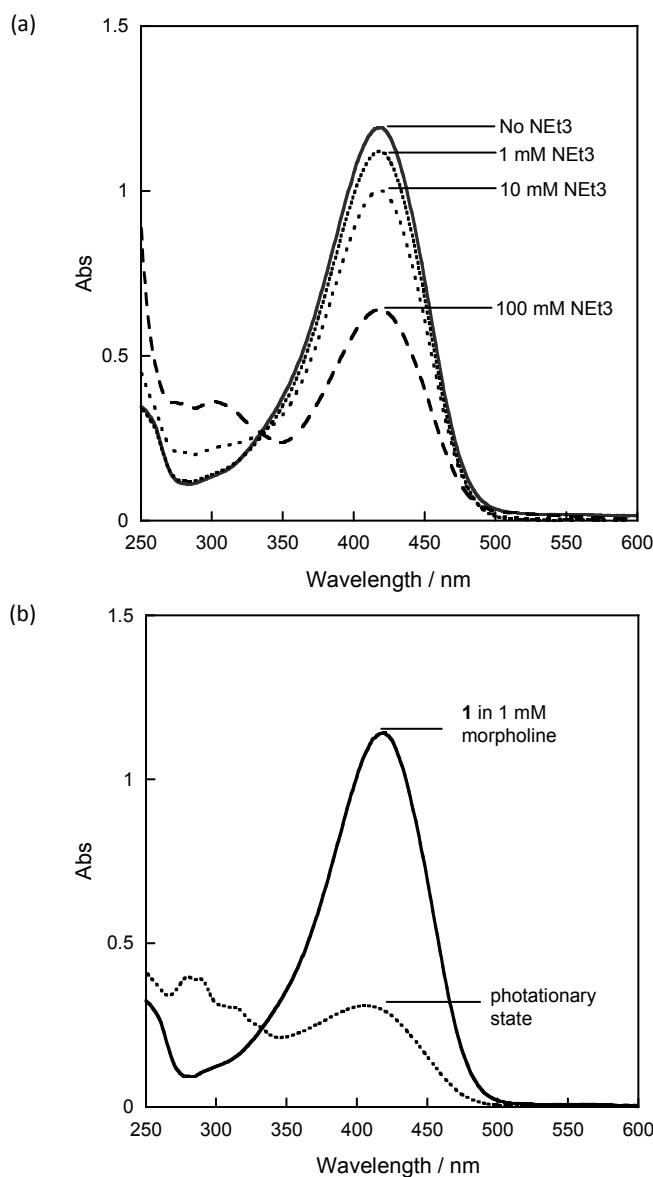


Fig. 2 (a) Decrease of the trans-H absorption in 1 mM, 10 mM, and 100 mM NEt_3 solutions and (b) absorption spectra of **1** in 1 mM Morpholine solution without irradiation and at a photostationary state.

1 is converted to either SP or trans⁺. ¹³ The $\text{pK}_{\text{a}}\text{-GS}$ is approximately the pH of the buffer. Fig. 2a shows the spectra of **1** in 1 mM, 10 mM, and 100 mM NEt_3 solutions. Since the concentration of **1** ($\sim 10^{-5}$ M) is much smaller than that of NEt_3 , the solutions can be considered as buffers. In 100 mM NEt_3 solution, the absorption peak of trans-H at 419 nm was reduced to nearly half of the absorption without base. Using the pK_{a} of NEt_3 in methanol (10.78), the pH of the solution was calculated to be 11.9. Therefore, the $\text{pK}_{\text{a}}\text{-GS}$ is estimated to be as high as ~ 11.9 .

The photoacidity ($\text{pK}_{\text{a}}\text{-MS}$) of an mPAH is often calculated from the pH of a solution under irradiation. The pH is determined by either a pH meter or a pH indicator. However, the solubility of **1** in water is low, and a common pH meter is not capable of measuring pH in

organic solvents, including methanol. It is also difficult to find a suitable pH indicator for a basic methanol solution. For example, common pH indicators used for aqueous solutions are based on deprotonation of phenols, which greatly change their pK_{a} s in methanol. It is well-accepted that photoacidity of an mPAH is defined by the equilibrium between the cis-H and SP ¹⁶, and $\text{K}_\text{a} = [\text{SP}][\text{H}^+]/[\text{cis-H}]$. Therefore, if a photostationary state possessing a significant amount of both cis-H and SP can be achieved, K_a can be calculated. Since both cis-H and SP form equilibria with trans-H, the photostationary state also possesses trans-H. We found that such photostationary state can be obtained by irradiating **1** in a morpholine (adjusted $\text{pK}_{\text{a}} \sim 8.5$ in methanol ¹⁷) solution (1-10 mM) in methanol. (Fig. 2b) The concentration of SP, cis-H, and trans-H can be obtained by analyzing the absorption spectra of the photostationary state, and the $\text{pK}_{\text{a}}\text{-MS}$ in methanol was calculated to be 9.8. The detailed spectroscopy analysis and calculation are described in SI.

MPAH **1** is not a conventional photoacid, which normally has a pK_{a} lower than 7 for the photo-generated acidic state. It has both low dark acidity and low photoacidity and is suitable for photo-controlled proton transfer to strong bases, which could not be achieved with previous mPAHs. The proton transfer between **1** and a strong base was further studied using ^1H NMR. DMAP was used as the proton acceptor. DMAP is a commonly used organic base with a pK_{a} of 9.7 in water and the adjusted pK_{a} in methanol is ~ 10 . ¹⁷ It was chosen mainly because the shifts of the aromatic protons of DMAP are relatively easy to analyze. An approximate 1:1 solution of **1** and DMAP was studied by ^1H NMR. (Fig. 3) Before irradiation, no SP conformer of **1** (represented by a' and b') was observed, consistent with its low dark acidity. The two pairs of the aromatic protons of DMAP (1 and 2) showed two doublets centered at 8.12 and 6.67 ppm, respectively. The solution was irradiated for 5 min and scanned by NMR again. Peaks of SP appeared accompanied by the reduction of the trans-H peaks. The SP peaks were smaller than that of trans-H due to the reverse reaction, which occurred during the NMR experiment, and the relatively high concentration, which made it difficult to complete the conversion with irradiation. Most importantly, the peaks of DMAP not only shifted to the low field at ~ 8.16 and 6.79 ppm, but also the peaks are significantly broadened, clearly indicating the proton transfer to DMAP. The protonation of

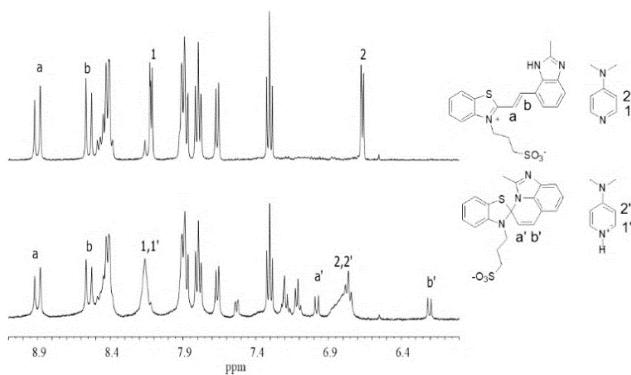


Figure 3. ^1H NMR of a 1:1 solution of **1** and DMAP in DMSO before and after irradiation. For clarity's sake, only the aromatic and double bond proton signals are shown and the double bond protons and DMAP protons are labelled.

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DMAP on the nitrogen (Fig. 3) deshielded the protons (1' and 2') on the aromatic ring resulting in the peak shift to the lower field. Due to the quick proton exchange, the protons on the free DMAP (1 and 2) and protons on the protonated DMAP (1' and 2') did not show two pairs of peaks but showed two broadened peaks.

In conclusion, although many mPAHs have been developed and used for various applications in the past decade, they cannot be applied to control the protonation of strong bases, including many commonly used amines. In this work, we developed a novel mPAH with very low dark acidity, avoiding proton transfer to strong bases without irradiation. The $\text{pK}_{\text{a}}\text{-GS}$ and $\text{PK}_{\text{a}}\text{-MS}$ were estimated to be 11.9 and 9.8 in methanol. Most importantly, absorption spectroscopy and NMR studies showed that **1** could be paired with NEt_3 and DMAP and underwent reversible photoreaction and proton transfer. This new type of photoacid will allow reversible photo-control of proton transfer in basic conditions and the development of functional materials with strong proton acceptors.

Conflicts of interest

There are no conflicts to declare.

Data availability

A data availability statement (DAS) is required to be submitted alongside all articles. Please read our full guidance on data availability statements for more details and examples of suitable statements you can use.

Acknowledgements

This research was supported by the US Department of Energy, Office of Science, Office of Basic Energy Sciences, Chemical Sciences, Geosciences, and Biosciences Division, Separation Sciences, under Contract No. AC05-00OR22725.

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Data Availability Statement

The data supporting the article A novel metastable-state photoacid for reversible protonation of strong bases have been included in the Supplementary Information.