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Reversible Photo Control of Proton Chemistry

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Abstract:

Spatial, temporal, and remote control of proton chemistry can be achieved by using photoacids, which are molecules that transform from weak to strong acids under light. Most of proton chemistry is driven by a high concentration of proton ($[H^+]$), which is difficult to obtain using excited-state photoacids. Metastable-stable state photoacid (mPAH) can reversibly generate a high $[H^+]$ under visible light with moderate intensity. It has been widely applied to different fields, e.g. fueling dissipative assemblies, driving molecular machines, controlling organic reactions, powering nanoreactors, curing diseases, manipulating DNA and protein, developing smart materials and capturing carbon dioxide in air etc. This article compares mPAH with excited-state photoacid as well as common acids e.g. HCl to explain its advantages. Recent studies on the thermal dynamics, kinetics, and photoreaction of mPAHs are described. Advantages and disadvantages of the three types of mPAHs, i.e. merocyanine, indazole, and TCF mPAH are compared with regard to photo-induced $[H^+]$, switching rate, and other properties. The mechanisms of controlling or driving functional systems, which involve acid-base reaction, acid catalyzed reaction, ionic bonding, coordination bonding, hydrogen bonding, ion exchange, cation-π interaction, solubility, swellability, permeability, and pH change in biosystems are described. Applications of mPAHs in chemical, material, energy, biotechnology and biomedical areas published in the past 5 years are reviewed. Prospects in the development and application of mPAH are discussed.

1. Introduction

Proton transfer is one of the most fundamental processes in nature and numerous chemical, material, and biological processes are driven by protonation. For example, many organic reactions are catalyzed by protic acids; the function of enzymes are sensitive to the proton concentration (pH); mitochondria use proton gradient as an energy form to synthesize ATP; and many materials alter their properties upon protonation. Proton transfer can be photochemically controlled with photoacids, which are molecules that transform to a strong acid and release protons upon irradiation. This type of molecule allows remote, spatial, and temporal control of proton chemistry and provides a way to convert photo-energy into other types of energy.

A photoacid can be either reversible or irreversible. A reversible photoacid can take back the proton and return to its original state after it is converted to the acidic state by light. Irreversible photoacids are normally called photoacid generators (PAGs), which permanently decompose to acids and other side products under irradiation.[1] PAGs have been extensively studied as photo initiators for cationic polymerization and have been applied to photolithography. Reversibility of a photoacid is desirable. Using a reversible photoacid, we can not only initiate a process with light, but the process also can be stopped or reversed by turning off the light, thus achieving complete control of the process. This article focuses on photo-control of proton chemistry by reversible photoacids.

There are two common types of reversible photoacids, i.e. excited-state photoacid and metastable-state photoacid (mPAH). Excited-state photoacid, e.g. naphthol derivatives, possesses high acidity at the photo excited state. [2] MPAH undergoes a reversible photoreaction to form a metastable photo product, which has high acidity. In both cases, the acidic states can relax back to the ground state. However, the lifetime of the acidic states of the two types is enormously different. For an excited-state photoacid, the lifetime of the acidic state is similar to that of the excited state, which is normally nanoseconds or less. The acidic state of mPAH has a lifetime from seconds to hours. Due to the short lifetime of the acidic state, it is difficult for excited-state photoacids to achieve a high proton concentration ($[H^+]$). This can be explained by a simple model. A sample containing a photoacid is irradiated. The photon flux is q; the depth of the sample (or the path length of light) is L; the fraction of the photon absorbed is f; and the quantum yield is ϕ. Under irradiation, the photoacid changes from its ground state to the acidic state A. At the stationary state, the photoreaction rate is the same as the reverse reaction rate. Assuming the reverse reaction is a first order reaction with a rate constant of k, we can obtain equation 1:

$$qf\phi/L = k[A] \quad [1]$$

Since the half-life of the acidic state $\tau = \ln 2/k$, equation 1 can be transformed to equation 2. In equation 2, we assume that [A] is approximately the same as $[H^+]$ since the acidity is high.

$$[H^+] = qf\phi\tau/(\ln 2 \cdot L) \quad [2]$$

One may input some reasonable numbers to Equation [2] and find out that it is practically impossible to generate a significant $[H^+]$ with an excited state photoacid. For example, when the power is as high as 1 W/cm^2 (q = 34mmol.m^{-2}.s^{-1} for 400 nm light), the absorption and quantum yield are both 100%, and the

light path is 1 cm, a half-life of 1 ns yields a $[H^+]$ of only 4.9×10^{-12} M. For comparison, mPAHs can generate mM or higher $[H^+]$ under moderate intensity (mW/cm^2) of light from LED or sunlight. The magnitude of $[H^+]$ under irradiation can often be estimated by ignoring the reverse reaction and treating the mPAH as a normal acid with a pK_a same as that of the metastable state. Since most of proton transfer processes are driven by a high $[H^+]$, mPAHs, which convert photoenergy to a high $[H^+]$, can be used to control and drive various proton chemistry. This analysis by no means undervalues the significance of excited-state photoacid. Study of excited-state photoacid has advanced our knowledge of some important proton-transfer events in nature. For example, the excited-state proton transfer in green fluorescent protein has been extensive studied. [2] The first mPAH was reported by our group in 2011. Since then it was quickly adapted by other researchers for different applications. The study of mPAHs and their applications before 2017 has been reviewed before.[3] This article focuses on the progress in this area after that.

2. Structure and mechanism of mPAH

MPAHs are generally designed by connecting an electron accepting moiety and a weakly acidic nucleophilic moiety with a double bond.[3] Photoinduced *trans-cis* isomerization of the double bond followed by a nucleophilic reaction between the two moieties generates an acidic metastable state. This process is reversible. The metastable photoproduct spontaneously undergoes a ring-opening reaction and relaxes back to the ground state. Figure 1 shows the three types of mPAHs that have been reported, i.e. merocyanine mPAH,[4] indazole mPAH,[5] and TCF mPAH.[6,7] The merocyanine photoacid **1** is the first reported and the most used mPAH to date. Its photoreaction is also shown in Figure 1.

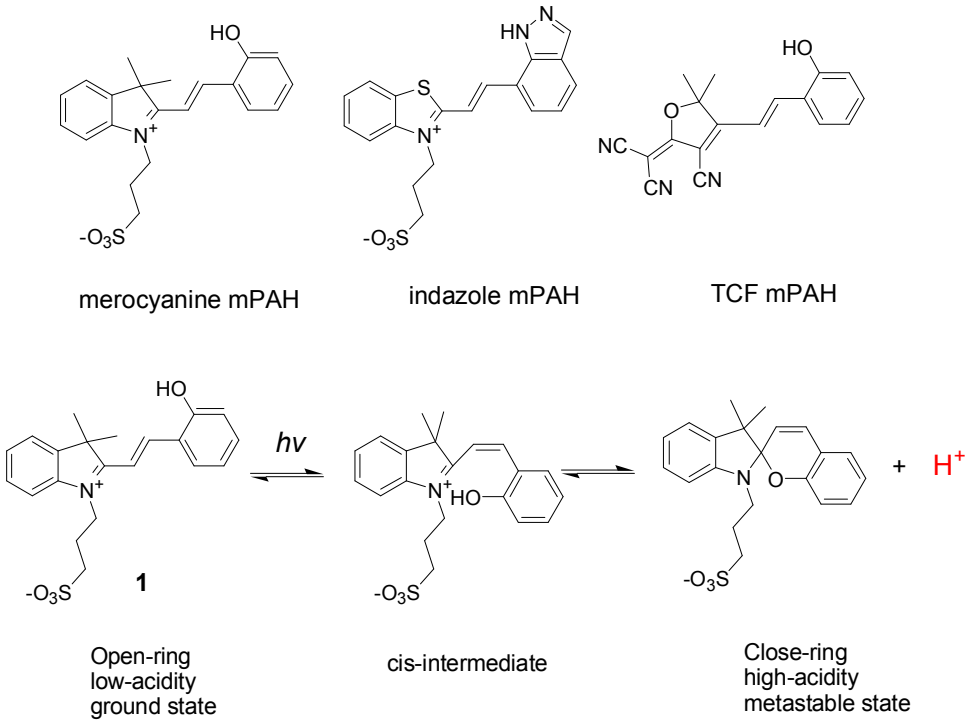

Figure 1. Structure of the three types of mPAHs (top) and the photoreaction of the most studied mPAH 1

Among the three types, merocyanine mPAH is the most studied and used. Crystal structures of some merocyanine mPAHs have been reported. [8,9] It is worth mentioning that the hydroxy group is at the trans position of the iminium group in all the crystal structures reported. A thorough study of thermal dynamics and kinetics was published recently by Pezzato and coworkers,[8] although some physicochemical studies were previously conducted by Coudret,[10] Zhang,[11] and our group [12]. Pezzato group quantitatively examined the equilibrium between the protonated, deprotonated and close-ring states of **1**. The dynamics and kinetics of the forward and reverse reaction were studied experimentally and theoretically. The effective pK_as of **1** in the dark and under irradiation were determined to be 6.2 and 2.5 respectively. It is worth mentioning that the dark acidity of mPAH is not only determined by the proton dissociation of the open-ring form. The thermal equilibrium between the open-ring form and the acidic close-ring form also affects it. Although the effective dark pK_a can be precisely determined by Pezzato's method, a simple way is examining the UV-Vis absorption in a serious of pH buffers. The effective dark pK_a is approximately the pH of the buffer, in which the absorption of the protonated open-ring state is reduced to half. [5] Pezzato's work also showed that the reverse reaction was a complex process, and reprotonation was not involved in the rate determining step. The mechanism of the photoreactions of merocyanine and indazole mPAHs was recently studied by Sension group using transient absorption spectroscopy. [13] This work revealed the importance of the cis-conformer in the photoreaction and photoacidity, which is consistent with the Pezzato's study. Session and coworkers also conducted quantum mechanical calculations to study the path of the reaction. The mechanism of **1** based on the works mentioned above is summarized in Fig. 2. Both experimental and calculation results indicated the absence of protonated metastable state (MSH) of **1**. The photoacidity was defined by the equilibrium between the deprotonated metastable state and the protonated *cis*-intermediate.[8] The mechanism shown in Fig 2. is based on study of **1** in water. Different photoacids and/or different solvents may lead to different mechanism. Transient absorption spectroscopy was also used by Wachtveitl group to study the photoreaction of a pyridinyl merocyanine photoacid. [14] Physicochemical properties e.g. acidity, reverse reaction rate etc. of some TCF mPAHs have been reported by Levlev group[15,16] and our group [6,7].

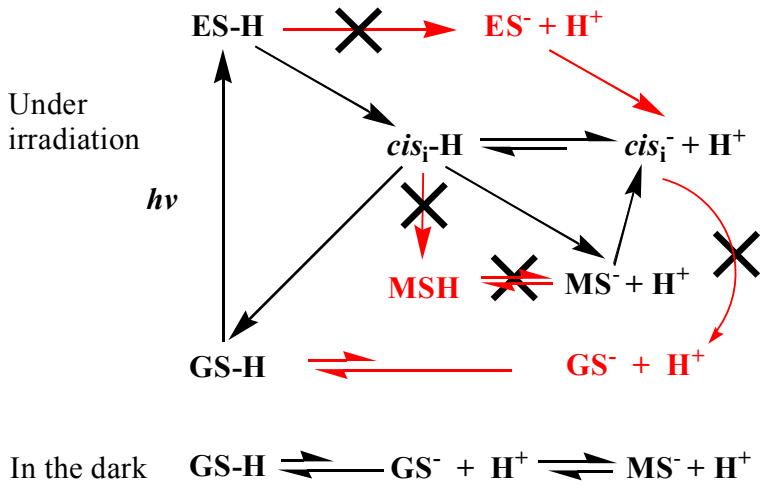

Figure 2. Mechanism of mPAH **1** (GS: ground state, ES: excited state, MS: metastable state, cis_i: cis intermediates, red coloured states: the states that do not involve in the mechanism of **1**, but may involve in other mPAH's mechanisms.)

3. Coupling mPAHs with functional systems

MPAH can be conveniently used in aqueous, organic solutions and polymer materials. Under visible light, mPAHs are converted to acids and release protons. This process generates a unequilibrated proton concentration, which protonates chemical systems, changes their covalent and/or noncovalent structures, and alter their properties and functions. (Fig. 3) One of the major advantages is that *the controlled systems do not have to be photosensitive themselves*. They only need to have certain basicity to accept the protons from mPAHs. Basicity is a common property of chemicals. Even a hydrocarbon may have certain basicity and interact with protons via e.g. cation-π interaction. Therefore, this is a highly versatile method. *A common question is why not simply use a common acid such as HCl instead of an mPAH to control chemical systems by protonation.* Control of a chemical system implies turning on/off certain functions or properties on demand, which requires that the protonated and deprotonated states can be reversibly and repeatedly created. Protonation/deprotonation by adding acids and bases alternatingly or transferring the system repeatedly between an acidic and a basic solution is apparently not practical for applications. An mPAH functions as an acid under light and protonates the system. When the light is removed, it takes back the proton like a base and deprotonates the system. The process does not require adding or removing chemicals repeatedly. Nor does it create or accumulate any chemical waste. Another advantage of using mPAH is that it allows the system to be spatially, temporally, and remotely controlled.

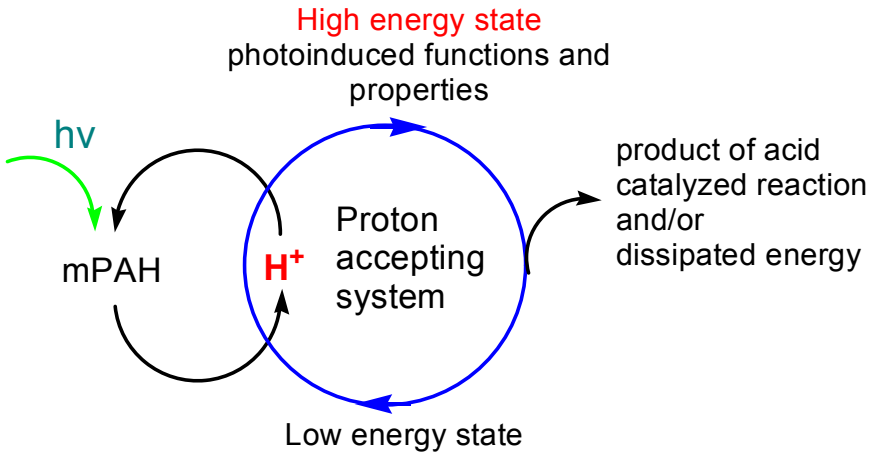

Figure 3. General scheme of coupling mPAH with functional systems.

This section first describes the mechanisms of photocontrol or photoenergy input using mPAHs. Some of the mechanisms, e.g. coordination bond dissociation, cation-π interaction, stoichiometric acid base reaction etc. were utilized only in recent years. The mechanisms are summarized in Table 1, which also lists the applications based on the corresponding mechanism. The requirements of the mPAHs for different chemical systems are discussed next. The physicochemical properties of the three types of mPAHs were compared based on the results from recent works. This section is to answer two questions: *what kind of chemical system can couple with mPAH* and *how to choose a suitable mPAH for certain chemical system.*

Table 1. Different mechanisms of photocontrol by mPAHs and the corresponding applications. (* m, t, i are merocyanine, TCF and indazole mPAHs respectively.)

Mechanism	**Examples of applications**	**type of mPAH***
stoichiometric reaction with a base	CO_2 capture/release[17]	m
Acid catalyzed reaction	Thiol-ene reaction,[18] ring-opening polymerization,[19,20] Fenton reaction,[38] supramolecular patterning (hydrazone formation),[21] odorant and drug release [22,23] (hydrolysis reaction),	m
Change of ionic interaction due to protonation	Dissipative assemblies of metallic and organic nanoparticles[24-27], chitosan,[28] volume change hydrogel [3]	m
Ion exchange due to proton release	Cation sensor [29]	m, t
protonation induced cation-π interaction	Molecular machine,[30] organic inclusion complex [31]	m
Hydrogen bond formation or breaking due to protonation	Assembly of DNA[32,33] and synthetic polymer[27]; molecular switch[34]	m
Coordination bond breaking due to protonation of the ligand	Metallasupromolecular assemblies [35-37]	m
Protonation induced hydrophilicity, water solubility, swellability, permeability change	Drug activation,[38] microbial fuel cell,[39] enzymatic nanoreactor [40]	m, i
Protonation induced change of electronic and optical properties	Photoswitchable conducting polymer,[41] single molecular junction, [42] photochromic material [43-45]	m, i
Modulating pH in biological systems	anticancer,[38] antibacterial,[46] wound healing,[47] ion channel switch,[48] ATP production of chloroplast,[49] peptide assembly [50]	m, i

3.1. Mechanism of photocontrol with mPAHs

As a reversible photoacid, mPAH has been used to react with a base directly.[17] The base was neutralized by the mPAH under irradiation, and recovered its basicity after the light was turned off. In other words, mPAH can convert a regular base to a negative photobase, which lowers its basicity under irradiation. MPAHs have also been used as acid catalyst for organic reactions[18-23], and Fenton reaction[38] These reactions can be turned on/off or spatially controlled with light.

Proton transfer from mPAH to a proton acceptor adds a positive charge to the proton acceptor. If the proton acceptors are neutral, the added positive charge will induce repulson among them. On the contrary, if the proton acceptors are negatively charged, protonation will neutralize the charge and diminish the repulsion among them. [24-27] The positive charge may also allow the proton acceptor to attract other anionic species including the deprotonated mPAH.[28] The mPAH becomes an anionic molecule after it releases its proton, and can attract other cations, e.g. Ca^{2+}. This ion exchange mechanism has been utilized to develop cationic sensors. [29] Beside ionic interaction, the positively charged proton acceptor can bind to electron-rich aromatic molecules via cation-π interaction.[30,31]

MPAHs have been utilized to reversibly introduce hydrogen bonding between two bases. [32,33] They can also be used to break existing hydrogen bonds by protonating the hydrogen bond acceptor.[27,34] Similar approach has been applied to coordination complexes in recent years.[35-37] Ligands in coordination compounds are Lewis bases and can be photo protonated by mPAHs. The protonated ligands can no longer coordinate with the metal and consequently the coordination bond is cleaved under light.

Protonation by mPAHs has also been used for reversibly altering the properties of molecules or materials including hydrophilicity, optical, and electronic properties. As mentioned above, when the proton acceptor is neutral, protonation will convert it to a cation, which increases its hydrophilicity. The increase of hydrophilicity consequently enhances water solubility,[38] permeability of ion [39] and hydrophilic molecules [40], and swelling capacity [40]. When the proton acceptor is anionic, protonation neutralizes its charge, which often reduces its hydrophilicity and the related properties. [4]

Protonation of materials alter their electronic structures and consequently electronic properties. Conductance switching at both material [41] and single molecular level [42] has been demonstrated using mPAHs. However, the magnitude of the conductivity change of material is small and needs to be much improved. Similar to the mechanism of pH indicators, protonation of chromatic molecules changes their optical properties. Photochromic materials based on photo-induced proton transfer from mPAHs to acidochromic dyes have been developed. [43-45]

Upon irradiation, mPAHs convert the photoenergy to chemical energy through generating a unequilibrated proton concentration. This energy conversion mechanism has been utilized to fuel dissipative assemblies with photoenergy.[25-28,32,33,35-37] No chemical waste is generated during the dissipative process and spatial, temporal and intensity control can be easily achieved. Such system may also be used to mimic the dissipative assemblies sustained by chemical energy as those in living systems because the energy form that directly interacts with the assembly is chemical energy of a high proton concentration.

It is well-known that the properties of biological systems change with pH. Since mPAHs are capable of change pH significantly under light, they have found applications in biotechnology and biomedical areas,[32, 33,38,46-50] which are described in Section 3. It is worth mentioning that the pH of biological systems is often maintained by pH buffers. However, temporary and reversible pH change can be locally produced by localized mPAHs, which can be achieved by polymerizing mPAHs [44,51,52] or encapsulating mPAHs in nanomaterials [23,38]. For example, our group showed that pH pulses of ~1.7 unit can be repeatedly generated in a micrometer film of an mPAH hydrogel in PBS.[52]

3.2. Requirements of mPAH for certain system

As described in Introduction, different types of mPAHs have been developed. While the merocyanine mPAHs are the most widely used, they are not always the best choice. A suitable mPAH for a certain system must meet requirements of acidity, reverse reaction rate, compatibility, activating wavelength, stability etc.

The first thing that needs to be considered is the acidity of mPAH in the dark and under light, which are defined by the effective dark pK_a and photo pK_a respectively. The mPAH must be able to hold most of its protons in the dark and efficiently release protons under irradiation. For a solution system, the desired pH change is often known. The dark pK_a of the mPAH must be higher than the desired pH before irradiation. The photo pK_a is better to be lower than the desired pH under irradiation although it is possible to achieve a pH lower than the photo pK_a by using a large concentration. For material applications, mPAHs are often paired with functional proton acceptors. The dark pK_a of mPAH must be higher than the pK_a of the proton acceptor, and the photo pK_a must be lower than that. The merocyanine mPAHs have effective dark pK_as between 6 and 7,[8] and the indazole mPAHs have much lower dark acidity and higher dark pK_as (~10).[5] (The pK_as are pK_as in water unless otherwise specified.) It has been reported that more than 80% of the merocyanine mPAH **1** released their protons without irradiation at a physiological pH of 7.4, while an indazole mPAH showed little proton dissociation at this pH. [5] The photo pK_a of merocyanine mPAH is 2-3 in water,[7,8] which is lower than that of indazole mPAH (4-6).[5,53] So the merocyanine mPAH is suitable for creating a large $[H^+]$ but cannot be used in basic conditions. In fact, pH change of 2-3 units has been routinely produced by merocyanine mPAHs. The indazole mPAH can be used in basic conditions but has less photoacidity. The reported dark pK_a and photo pK_a of a water soluble TCF mPAH are 6.6 and 3.9 respectively.[15] It needs to be noted that the pK_as in nonaqueous media are different from those in aqueous solutions.

The reverse reaction rate of mPAH determines how fast the controlled system can be switched between the protonated state and deprotonated state. As described above, the relaxation of mPAH from the acidic metastable state to the ground state is slow, which means the photo-induced acidity is not instantly turned off after light is removed. Although the reverse reaction is a complex process, it is often treated as a pseudo first order reaction especially at the early stage of the reverse process. The rate constant of merocyanine mPAH **1** in water is 9.2×10^{-3} s^{-1}, which corresponds to a τ of 75 s.[4] The reverse reaction depends on the media and becomes slower in organic solvents due to the change of hydrogen bond donor acidity [12] and hydrogen bond acceptor

basicity [20]. The latter can be used to predict the trend of the reverse reaction rate in aprotic organic solvents.[20] The reverse reactions of merocyanine photoacids in methanol have been systematically studied, and the rate constants are in the range of ~10^{-5} – 10^{-2} s^{-1}.[11] It is worth mentioning that the mPAH with a electron-donating methoxy group at the meta-position of the phenol hydroxy group possesses a reverse reaction rate more than 50 times faster than the one without substituent.[22] The reverse reaction of indazole mPAHs are much slower. Although no systematic study has been conducted, the half life of the reported mPAHs were several hours.[5,52] In contrast, the reverse reaction of TCF mPAH is faster than the other two types.[7] For example, the first order reverse reaction rate of a TCF mPAH was reported to be 6.0 × 10^{-2} s^{-1} in water [15] even though the electron-withdrawing sulfonate group on the phenol side is expected to slow the reaction.

Many applications require both high [H^+] and fast switching (reverse) rate. According to Equation 2, a fast reverse reaction will inevitably lower the achievable [H^+]. There are several approaches to solve this problem. If it is practical acceptable, a high-power light source can be used to push a photoacid with a fast reverse reaction to its acidic state and achieve a high [H^+]. For mPAHs with slow reverse reaction at room temperature, heating can be used to faster the reverse reaction. This method has been applied to polymer thin films containing mPAHs.[44,45] Recently, our group reported a indazole mPAH, which has very slow thermal reverse reaction.[53] However, the reverse reaction can be quickly induced by a different wavelength (365 nm) from that of the forward reaction (470 nm). Such photoacid allows both high [H^+] and fast switching. Although the quantum yield of the photo reverse reaction is as high as 0.83, the photo stationary state at 365 nm favors the acidic state and only allows 22% of the photoacid to return to the ground state.

Besides acidity and reverse reaction rate, other properties, e.g. quantum yield, activating wavelength, compatibility, photo and chemical stability etc. may also need to be considered. The quantum yield of the photoreaction is fairly high (>0.1) for all the mPAHs that have been measured except one. This unique mPAH can be activated by red light (700 nm) in comparison to blue or green light for other mPAHs. [54] However, the quantum yield (0.007) is much lower than other MPAHs. Given the long lifetime of the acidic state, the achievable [H^+] of most mPAHs is mainly limited by the concentration in solution or loading in polymer. Some mPAHs have been developed to enhance the solubility in water and organic solvents as well as compatibility with polymers.[8,20,48] MPAHs have high photostability partially due to low-energy visible light activation. Previous work showed that an mPAH underwent 100 irradiation/recovery cycles in air without significant degradation.[55] However, they are slowly hydrolyzed in aqueous solutions.[56] One strategy to enhance hydrolytic stability involved adding electron-donating substituents conjugated to the bridging double bond, which presumably decreases the positive charge on the hydrolytic center.[56] It was reported that increasing the length of the alkly-1-sulfonate side chain improved stability, but the role of the sulfonate group has not been well understood. [8]

4. Recent applications

This section reviews the works related to the applications of mPAHs in chemical, material, energy, and biomedical areas in the past 5 years. The applications reported before late 2016, e.g. volume-changing hydrogels, photochromatic materials, photo-conducting material, photopatterning, odorant release, ring-opening polymerization, nanoparticle formation and assembly, supramolecular assembly, molecular switch, microbial fuel cells, cationic sensors, and bacteria killing etc. have been reviewed in a previous article (Reference 3). Interested readers may check this article and the cited works.

In recent years, mPAHs have been applied to biomedical and biotechnology areas. Bu, Zhang and coworkers encapsulated an mPAH and a photodynamic therapy (PDT) drug in a porous upconversion nanoparticle (UCNP).[38] Under near-infrared (NIR) light (980 nm), the emission light of the UCNP activated the mPAH, which cannot be activated directly by NIR light. The protons released from the mPAHs changed the pH of tumor microenvironment and made the PDT drug more effective. This work was the first example of *in vivo* study of mPAH. It is worth mentioning that a indazole mPAH instead of commonly use merocyanine mPAH was used in this work, which allowed local pH change in physiological condition. In a latter work, the group discovered that the [H^+] generated by the mPAH deactivated cofilin, which prevented tumor cell migration.[38] Hou and coworkers also utilized UNCP to activate mPAHs with NIR light for drug delivery.[23] They encapsulated an mPAH and a drug in a porous UNCP coated with an acid-labile cap. The photoactivated mPAH cleaved the cap and the drug was released. An mPAH has been combined with a CuS nanoparticle, which mimicked peroxidase, for treatment of bacteria-infected wound.[47] The photo-induced pH drop by the mPAH enhanced the antibacterial activity of the nanozyme.

Gray, Dougherty and coworkers showed that ion channels associated with vision and pain can be reversibly activated with light using an mPAH, which generated a pH drop from 6 to 3.2 under irradiation.[48] Li group reported that chloroplast entrapped with an mPAH conducted photosynthesis much more efficiently, and produced 2.9 times more ATP than natural chloroplast.[49] Appelhans, Lederer, and co-workers developed a photoswitchable enzymatic nanoreactor, which contained glucose oxidase encapsulated in a pH sensitive polymersome.[40] Under the low pH condition created by an mPAH, the polymersome swelled and its permeability increased. Glucose could then penetrate into the nanoreactor and be oxidized by the enzyme.

MPAH has become a convenient tool for fueling dissipative assemblies with photoenergy. In fact, most of natural and synthetic assemblies do not possess photosensitive functional groups. Incorporating photosensitive groups, especially those respond to long wavelength light, is a formidable work. Using mPAH, assemblies without photosensitive groups can be controlled by light. Li group showed that an assembly of a simple dipeptide (diphenylalanine) became photosensitive in the presence of an mPAH.[50] Yang, Chen, Li and coworkers developed a functional nanoassembly of chitosan and an mPAH. [28] The mPAH was noncovalently incorporated into the assembly instead of only in the medium. The group further incorporated fluorophores into the assembly. The photo-controlled assembly and disassembly induced fluorescence change in cancer cells. Kuzyk group utilized the photo-induced pH drop by an mPAH to induce the formation of DNA triplex, which led to reversible reconfiguration of the corresponding chiral plasmonic molecules.

It is interesting that the reconfiguration can be tuned by the intensity of light.[32] Sleiman group utilized an mPAH to create a proton dissipation and showed that the proton dissipation led to otherwise inaccessible morphologies of fibres built from DNA and cyanuric acid.[33]

In recent year, reversible destruction of coordination bonds by protonation of ligand has become an approach for controlling coordination assembles with light. Severin group constructed metallasupramolecular assemblies with palladium coordination structures. [35,36] They were switched between disassembled and assembled states with light due to reversible protonation by an mPAH. Liu group reported a nanorod constructed by coordination of zinc ions with a inclusion complex of dipyridine in β-cyclodextrin, which became photosensitive in the presence of an mPAH.[37] Organic inclusion complex of helic[6]arene and an pyridium salt controlled by mPAH was reported by Shi and Chen. [31] Photo-induced protonation led to the formation of the complex due to cation- π interaction.

Dissipative assemblies with novel behaviors have been reported in recent years. Ikkala group demonstrated a programable hydrogel containing gold nanoparticles and an mPAH. [24] The sol-gel state of hydrogel is thermal sensitive and the assembly state of the nanoparticle is photosensitive due to neutralization of the surface charges by the protons from the mPAH. However, the assembly of the nanoparticle also depends on the state of the hydrogel. This led to the complex behavior of the system, which can be programed by the sequence of the thermal and photo stimuli. Kuehne and coworkers developed a dissipative assembly of microgels controlled by an mPAH. [25] A pronounced feature of this system is that the microgels formed well-ordered crystalline structure under irradiation.

MPAHs have also found applications in photoresponsive material. The mechanism of photochromism based on proton transfer from mPAHs to acidochromic dyes has been described in the last section. Based on this mechanism, Zhang group developed rewritable paper with high color contrast and resolution, appropriate legible time of prints, excellent reversibility, and easiness to achieve multicolor prints. [45] The erasing process of this type of thin film photochromic material is often accelerated by heating since the reverse process of mPAHs are generally slow in polymers. [44,45] Our group demonstrated a polymer photochromic material, which can be patterned and erased with different wavelengths of light.[53] The mPAH used in this material was the photoswitchable indazole mPAH described in the last section. Photoresponsive molecular systems are essential for molecular optoelectronic devices. Cai et al. built a single molecular junction with a proton sensitive azulene molecule. In the presence of an mPAH, the charge transport through this junction can be switched on and off by light. [42] Landfester group reported a novel polymer of mPAH, which was controlled by both photo and thermal stimuli.[51] The mPAHs in the polymer can be reversibly deactivated and activated by tuning temperature above and below a critical value respectively.

Carbon dioxide (CO_2) capture from air is one of the most important research topics today. One of the challenges is controlled release of CO_2 from the basic media after it is captured, so that the basic media can be repeatedly used and the CO_2 can be utilized as a starting material for chemical

synthesis. Bennett and coworkers demonstrated an approach based on photo-induced pH change by an mPAH.[17] The pH drop reduced the solubility of CO_2 and led to CO_2 release. Although the pH change was small in this preliminary work, this approach is promising since no chemical waste is generated and solar energy could be used in the process. Photocontrol of ring-opening polymerization, hydrazone formation, hydrolysis and esterification using mPAHs as photo-catalysts have been reported before. (Table 1) Recently Kloxin group have used an mPAH to control a novel acid-catalyzed thiol-ene reaction.[18] Hua and coworkers applied mPAH to mass spectrometry and conducted a real-time study of pH-dependent water clusters. [57] This is an example of using non-optical instrument to study proton chemistry with mPAH. MPAHs have also been utilized to drive molecular shuttles with light,[30,58] control foam formation at air-water interface,[59] and direct the movement of water drop in oil [60] etc. in recent years.

5. Future Prospects

As described earlier, different types of mPAHs have their advantages and disadvantages. For example, merocyanine mPAH has high photoacidity and a moderate reverse rate suitable for many applications. However, its dark acidity is high, and the stability in aqueous solution is low. Indazole mPAH has low dark acidity and large working pH range, but also relatively low photoacidity and solubility in water. Especially, the reverse reaction of indazole mPAH is slow comparing to the other two types, which is not well-understood. Improving the properties of mPAHs by modifying their structures is a necessary work in near future. This work shall be assisted by theoretical calculations and mechanistic studies, especially for indazole and TCF mPAH. Quantum mechanical calculation of mPAH photoreaction, which involves intramolecular and intermolecular proton transfer, is a challenging work. Progress in this direction will greatly assist the design of mPAH.

Although mPAHs have been used in light-sustained dissipative systems, the energetic aspects of photo-induced proton transfer have seldomly been studied. Under irradiation, an mPAH is converted to its metastable state and protonates a proton acceptor. The photo energy is partially converted to the chemical energy of the metastable state and the protonated acceptor. The latter is related to not only the basicity of the acceptor but also the concentration. A model for calculating the energy conversion is desirable. The chemical energy converted from the photoenergy by mPAH may be used for practical purposes. MPAHs have been applied for temporal and spatial control of acid-catalyzed reactions. It may be possible to utilize the energy of the metastable state to drive uphill reactions.

New type of mPAH with novel properties may be developed. For example, reversible photoacid that can be switched by two different wavelengths of light has great potential in photoresponsive material. As described earlier, the one reported before only allowed about 20% of the acidic state to be switched to the ground state with light. There is much room for improvement, which may require not only modification of peripheral structure but also design of new core structure. Another example would be designing mPAHs with multi-proton release trigged by a single photon

event, which could not only enhance the efficiency of the photoreaction but also significantly lower the mass loading for generating certain [H^+].

While there is no doubt that more applications will emerge in near future, it is important to explore further in some important areas, in which the usage of mPAH has been demonstrated. For example, mPAH has become a popular tool for development of dissipative assemblies. With the convenience provided by mPAH, it shall be possible to develop complex dissipative assemblies mimicking living systems or possessing novel functions. In fact, some recent works have shown this trend.[24,28,33] Another example would be the CO_2 capture, which is a highly important task. Although using mPAH for releasing captured CO_2 with solar light is a promising approach, little has been done in this direction. Remote, temporal, and spatial control of pH has much potential in biotechnology. Although photocontrol of various biomolecules, e.g. protein, DNA, polysaccharide, etc. using mPAH has been demonstrated, practical applications remain to be developed. Coupling mPAH with instruments other than UV-Vis absorption spectrometer to study proton chemistry is another direction worth to explore since proton acceptors do not often have an absorption band that can be conveniently monitored. The mass spectroscopy work by Hua group [58] demonstrated the potential in this area. It should be pointed out that understanding the properties of mPAHs is necessary for their applications. For example, although mPAH **1** has been widely used, it is not an ideal one even for some that have been demonstrated. Communication and collaboration among the researchers in development, mechanistic study, and applications of mPAH will make this area more fruitful.

Conflicts of interest

There are no conflicts to declare.

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