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A diaryl Schiff base was explored as a new type of photo- and pH-responsive bifunctional molecule. Its regulation mechanism is probably related to an irreversible photo-cyclization and a reversible pH-promoted bond cleavage.

Stimuli-responsive molecules with properties that can be regulated by light and/or pH have attracted increasing attention in many scientific areas.¹ Due to the pH gradients existing in both normal and physiological states, pH-responsive molecules (*e.g.* hydrazones,² imines,³ and esters,⁴ *etc.*) can be explored for their potential use in polymers and nanoparticles for drug delivery.⁵ Besides, the spectroscopic properties of some photo-sensitive molecules, such as diarylethenes,⁶ stilbenes,⁷ viologens,⁸ spirooxazines,⁹ azobenzenes¹⁰ and quinones,¹¹ *etc.*, have been fully explored and their regulation mechanisms are well understood, which involve bond cleavage and reformation, *trans-cis* isomerization, reversible photo-cyclization, *etc.*¹² Among stimuli-responsive molecules, diaryl Schiff bases (*e.g.* *N*-salicylideneanilines) are usually studied as photochromic switches because of their excellent reversible photo-isomerization characteristic.¹³ However, reports about the photo-cyclization of these Schiff bases are rare, especially the free radical transfer-promoted photo-cyclization, and further investigation is needed in to the pH-responsive properties of this kind of stimuli-responsive molecule.

In this communication, we report a diaryl Schiff base **1a**, which can serve as a new type of photo- and pH-responsive bifunctional molecule (Fig. 1). The structural function system of compound **1a** consists of two main parts: (i) the nitro group and the C=N conjugated double bond to absorb certain wavelengths of light and respond to the light stimulus, (ii) the anilino-group and phenol hydroxyl group to recognize the acid-base pH changes and adjust the molecular structure. The two

parts are linked together using a C=N double bond as a bridge to achieve the objective of dual-directional regulation between light and pH.

The UV modulation for compound **1a** upon exposure to UV light is illustrated in Fig. 2. An ethanol solution containing compound **1a** was irradiated with UV light (at 302 nm). After twenty, forty and sixty minutes, it was immediately moved into the ultraviolet spectrometer and fluorescence spectrophotometer to record the ultraviolet absorption spectrum and fluorescent emission spectrum, respectively. The characteristic ultraviolet absorption of compound **1a** (at 375 nm) was significantly reduced over time (Fig. 2a), but on the contrary the photoluminescence (PL) intensity at 365 nm increased rapidly (Fig. 2b). In addition, the intensity of the ultraviolet absorption peak at 307 nm remained almost unchanged. Accompanying the UV modulation process, the ethanol solution of compound **1a** changed its colour from translucent to bluish-violet when visualized under UV-light irradiation (at 302 nm) (Fig. 1b). Interestingly, the bluish-violet colour faded away when the solution was exposed to visible light. It appears that a structural change of compound **1a** is caused by the UV light stimulus, and

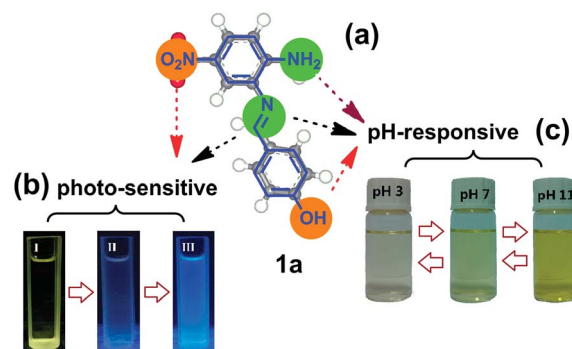


Fig. 1 (a) Structure for the photo- and pH-responsive diaryl Schiff base **1a**. (b) Photograph I was taken in visible light, and photographs II (irradiated for 10 minutes) and III (irradiated for 60 minutes) were taken under UV light (at 302 nm). (c) Colour changes of compound **1a** in ethanol solution at different pH values.

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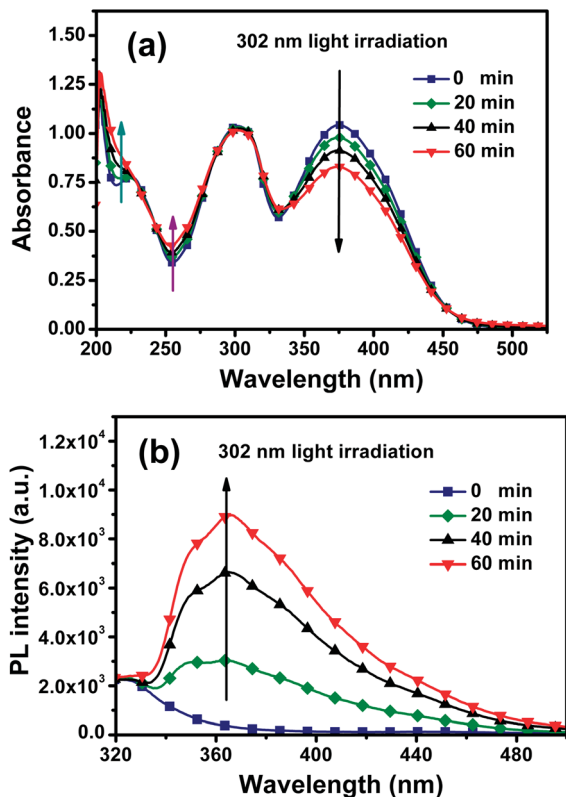


Fig. 2 Spectral changes of compound **1a** (50 μ M in ethanol) upon UV light irradiation (at 302 nm) over 0–60 minutes. (a) UV-vis absorption (slit width 2.0 nm) and (b) fluorescent emission (λ_{ex} = 270 nm, slit width 5.0 nm).

this is a typical characteristic of photosensitive molecular switches.¹⁴

To determine what kind of structural change might be happening, NMR spectra were used to analyze the configurations of compound **1a** with UV light irradiation and no UV light irradiation. The ^1H NMR spectral changes are shown in Fig. 3. The proton chemical shifts for $-\text{CH}=\text{N}-$ (marked with b in Fig. 3b) and $-\text{NH}_2$ (marked with h in Fig. 3b) have clearly disappeared from the ^1H NMR spectrum of the irradiated compound **1a** (Fig. 3c), and the other proton chemical shifts were found to vary after being irradiated by UV light for 2 hours. Therefore, we speculate that compound **1a** is transformed into compound **1a'**, which contains a five-membered imidazole ring (the proton chemical shift of $-\text{NH}-$ in the imidazole ring is not observed in Fig. 3c, probably because of chemical exchange with d_6 -DMSO solvent after UV light irradiation). In other words, photo-cyclization causes the structural change of compound **1a**, not *trans-cis* isomerization or tautomerism (Fig. 3a). However, note that the photo-cyclization of compound **1a** looks very strange for a photo-cyclization that simply changes the buckling mode of a structure when compared with the general pattern of photo-cyclization of molecular switches.¹⁵ More work needs to be done to explain such a phenomenon.

In order to explore the detailed cyclization mechanism of compound **1a**, a derivative of compound **1a** without the nitro group (compound **2a**) was synthesized according to the preparation method used for compound **1a** (see ESI† for the synthesis

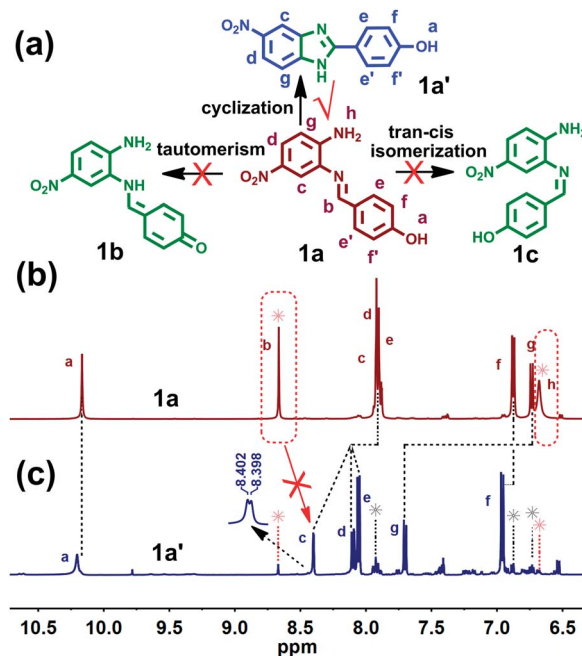


Fig. 3 Conceivable structural changes (a) and ^1H NMR spectral changes of compound **1a** in d_6 -DMSO: (b) no UV light irradiation and (c) UV light irradiation (at 302 nm) for 2 hours.

and structural characterization of compounds **1a** and **2a**). However, the typical characteristic of the photosensitive molecule **1a** was not observed after irradiating compound **2a** with UV light (at 254 nm, 302 nm and 365 nm). Thus, it is speculated that the nitro group of compound **1a** may play a key role in responding to UV light and may be responsible for the structural change. Theoretical calculations based on DFT were also used to study the photo-sensitivity of compounds **1a** and **2a**, and the nature of the frontier orbitals has been investigated using Gaussian 09 (Gaussian, Inc.)¹⁶ at the DFT(B3LYP)/6-31G(d) level.

The frontier orbital energies of compounds **1a** and **2a** are given in Table 1. The HOMO/LUMO energy levels of compound **1a** were calculated as -5.69 eV and -1.84 eV, respectively, which were significantly decreased by 0.65 eV and 0.48 eV compared with compound **2a**. Obviously, the π -conjugation effect is enhanced by the introduction of the nitro group on the aromatic skeleton, and the π -conjugation destabilizes both the HOMO and LUMO of compound **1a**. However, it is noteworthy that the HOMO–LUMO energy gaps (E_{gap}) of compounds **1a** and **2a** are almost the same, resulting in similar UV-absorbing wavelengths but different absorbance intensities (see Fig. S1 in ESI†).

Table 1 Frontier orbital energies of compounds **1a** and **2a**. The energy values are reported in eV

Compound	E_{HOMO}	E_{LUMO}	E_{gap}
1a	-5.69	-1.84	3.85
2a	-5.04	-1.36	3.68

Upon closer inspection of the HOMO/LUMO of compound **1a**, the HOMO is localized on the 4-nitro-*o*-phenylenediamine, and extends over the 4-hydroxy benzylidene linker (C=N) (Fig. 4a). However, the LUMO is principally localized on the 4-nitro-*o*-phenylenediamine moiety (Fig. 4b) and not on the *p*-hydroxybenzaldehyde moiety, which is markedly different from that of compound **2a** (Fig. 5b). Thus the 4-nitro-*o*-phenylene-diamine subunit acts as both the photo-induced electron acceptor and donor, specifically the nitro group mainly serves as a strong electron acceptor and the amino group a strong electron donor. Since intramolecular electron transfer is likely to occur, a rotation of 4-nitro-*o*-phenylenediamine results when the electron is transferred from HOMO to LUMO in the form of a hydrogen free radical under irradiation by UV light. This results in an instantaneous isomerization of compound **1a** and an unstable nitrogen free radical. It seems very likely that the five-membered ring is formed due to the photo-induced free radical transfer under irradiation by UV light. The proposed cyclization mechanism is shown in Fig. 4c.

The formation and hydrolysis of Schiff bases are generally considered to be reversibly pH-dependent.¹⁷ To explore the pH-responsive properties, the UV absorption of compounds **1a** and **1a'** were investigated in ethanol solutions with different pH gradients using HCl (37% liquor) and KOH to regulate the pH. The UV absorption peaks of compound **1a** varied greatly in intensity and shape when the pH was changed from 3 to 11 and then back to 3 (Fig. 6a), and the colour of the solution reversibly changed from colourless transparent to slight yellow to bright orange (Fig. 1c). The C=N double bond of compound **1a** may be hydrolyzed when the pH value is 5, and the hydrolysis is complete when the pH value reaches 3. In addition, when the pH > 10, the UV absorption peak at 307 nm vanishes and the absorption intensity at 375 nm is twice that of when the pH = 8.

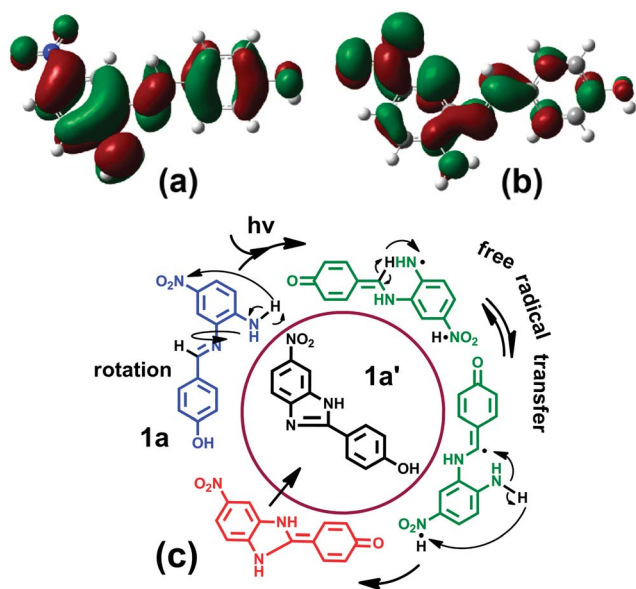


Fig. 4 B3LYP/6-31G(d) calculated molecular orbitals and the proposed photocyclization mechanism of compound **1a**: (a) HOMO, (b) LUMO, and (c) proposed cyclization mechanism.

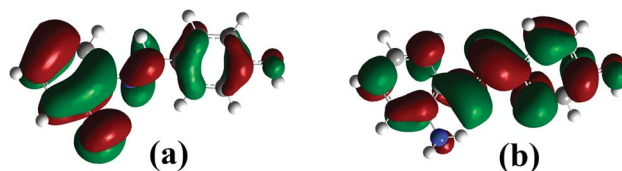


Fig. 5 B3LYP/6-31G(d) calculated molecular orbitals of compound **2a**: (a) HOMO and (b) LUMO.

Compared with compound **1a**, the hydrolysis of the C=N double bond of compound **1a'** is more difficult and slower, and is observed only slightly under stronger acidic pH conditions (Fig. 6b). However, the two UV absorption peaks of compound **1a'** share the same absorption intensity instead of vanishing or increasing like compound **1a** under alkaline pH conditions. As a result, both compounds **1a** and **1a'** are pH-responsive molecules and the five-membered imidazole ring of compound **1a'** could be hydrolyzed to an amide by a ring-opening reaction of pH-promoted bond cleavage under strong acidic conditions. Besides, compound **1a** undergoes a reversible pH-promoted C=N bond cleavage, which may find widespread use in the field of pH-regulated release in drug delivery systems (DDSs) (as part of the drug carrier to effectively recognize the pH gradients and selectively release bioactive drugs at pathological locations). Meanwhile, the pH-dependent reversible hydrolysis of

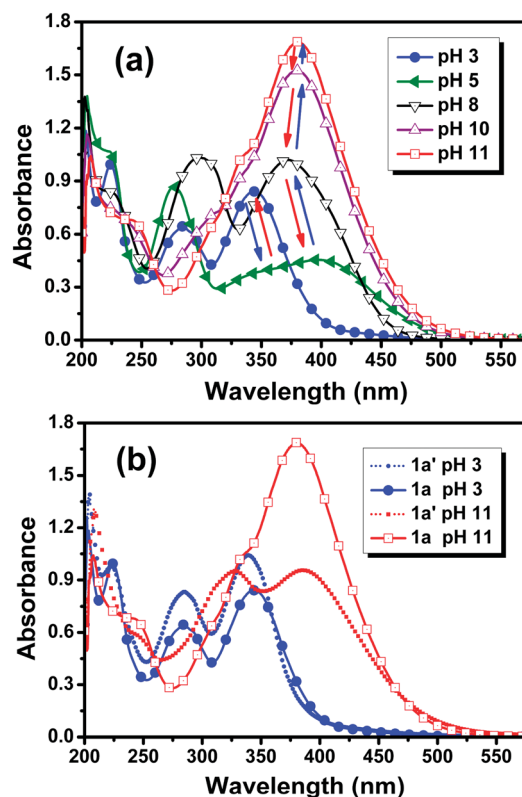


Fig. 6 UV absorption of compounds **1a** and **1a'** in ethanol solutions with different pH gradients: (a) compound **1a** and (b) compounds **1a** and **1a'**, blue: pH 3, red: pH 11.

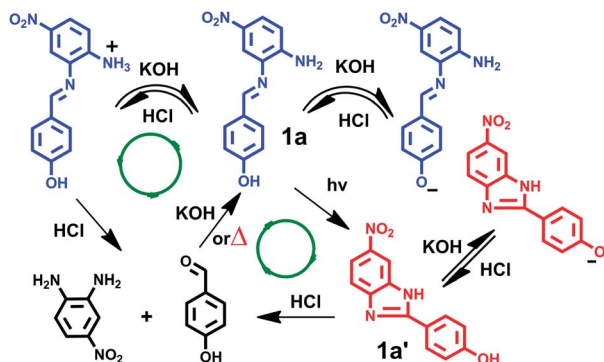


Fig. 7 The proposed co-regulation mechanism of compounds **1a** and **1a'**.

compound **1a** acts as a hub of dual functions and plays a significant role in the co-regulation of light and pH. The proposed co-regulation mechanism is given in Fig. 7.

To sum up, we synthesized a photo- and pH-responsive bifunctional molecule that can be developed into a potential co-regulated molecular switch. The regulation mechanism was preliminarily explored, and the bifunctional molecule can be co-controlled by UV light and pH. The photo-induced free radical transfer could be the reason for the irreversible photocyclization of the diaryl Schiff base, and the reversible pH-promoted bond cleavage is attributed largely to the hydrolysis of the Schiff base C=N double bond, resulting in the ring opening of the five-membered imidazole ring under strong acidic conditions. This study will be meaningful and helpful to the design of new diaryl Schiff bases as photo- and pH-responsive molecular devices, which may find a wide range of applications in drug delivery, coordination chemistry and materials science.

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