

Basic-to-acidic reversible pH switching with a merocyanine photoacid

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The application of merocyanine photoacids has been previously largely limited to neutral and acidic pH values. Here we introduce a new merocyanine photoacid with superior pH switching qualities. By increasing the pK_a in the dark (pK_a^{dark}) and the solubility we increased the reversible visible light induced pH jump to 3.5 units. Moreover, it is the first demonstration of a merocyanine photoacid able to generate a significant pH drop from a basic (pH 8.3) to an acidic (pH 5.2) environment.

Every process occurring in an aqueous environment will be sensitive to pH, whether it is enzyme functionality, controlling chemical reactivity, or the ocean's capacity to store carbon dioxide. By using light to induce proton dissociation, pH can be modified externally and non-invasively with high precision in space and time. Spiropyran/merocyanine photoswitches are reversible metastable photoacids that can significantly decrease the pH of an aqueous solution when irradiated with visible light, with subsequent recovery to the initial pH occurring thermally. The first reported merocyanine photoacid able to generate a substantial reversible pH jump of 1.5 units ($R_1 = \text{H}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$, Fig. 1)¹ sparked interest in a wide-spread range of applications in supramolecular² and materials chemistry.³ Recently developed merocyanines demonstrated increased pH jumps ranging from 2.5 ($R_1 = \text{H}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_4\text{SO}_3^-$ ⁴ and $R_1 = \text{H}$, $R_2 = \text{polymer}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$ ⁵) and 3.0 pH units ($R_1 = \text{MeO}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$)⁶ to the highest reported value of 3.2 pH units ($R_1 = \text{MeO}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{NMe}_3^+$).⁷ The pH ranges these examples^{4, 6-7} can be used for is limited to near neutral or acidic environments.⁸ Herein we report a new merocyanine derivative **1** with a butyl sulfonate group (R_3) and substituents $R_1 = \text{MeO}$ and $R_2 = \text{H}$ capable of generating an unsurpassed pH jump of 3.5 units. Moreover, it is the first demonstration of a pH jump covering a significant part of the basic region.

Merocyanine photoacid **1** was synthesized over three-steps (for full characterisation and data, see Supporting Information S2). The proton dissociation behaviour of **1** was studied in the dark and under visible light irradiation ($\lambda = 455 \text{ nm}$) by established methods.^{4, 7} In the dark the protonated

merocyanine form (MCH) is in equilibrium with the deprotonated merocyanine form (MC) and the ring-closed spiropyran form (SP) (Figure 2ai).⁹ The pK_a^{dark} value was determined by measuring the UV-vis absorption spectra of equilibrated samples at pH 5.1–9.6 (Figure 2ai,iii see S4.3 in Supporting Information). This parameter accounts for the coupled equilibria between MCH, MC and SP. The corresponding pK_a value under irradiation, pK_a^{hv} , is determined by the equilibrium between the metastable *cis*-MCH and SP form (Fig 2bi)^{4, 7} and was calculated from the absorption spectra of equilibrated samples under visible light irradiation ($\lambda = 455 \text{ nm}$) over a pH range from 2.2 to 6.6 (Fig. 2bii, iii).

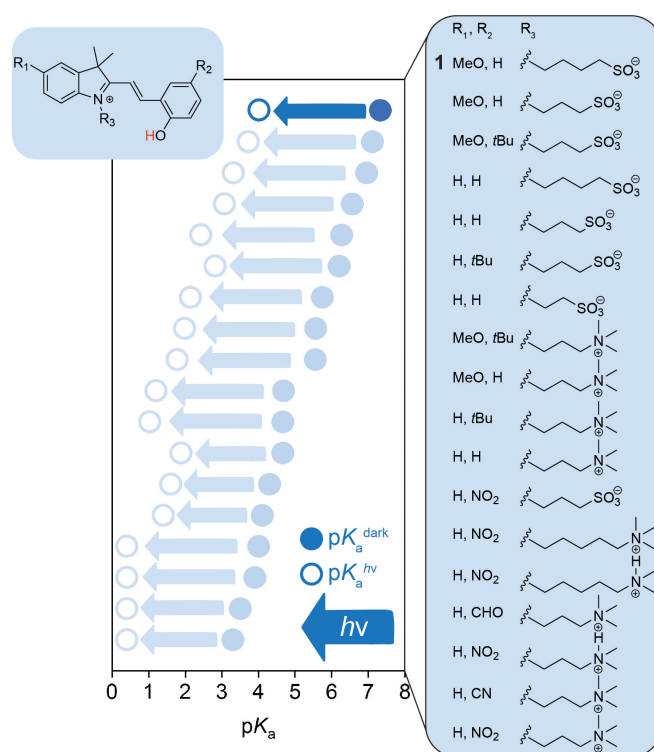


Fig. 1 Overview over pK_a^{dark} and pK_a^{hv} values of reported^{4, 6-7, 10} merocyanine photoacids and derivative **1** with respective substitution patterns (right).

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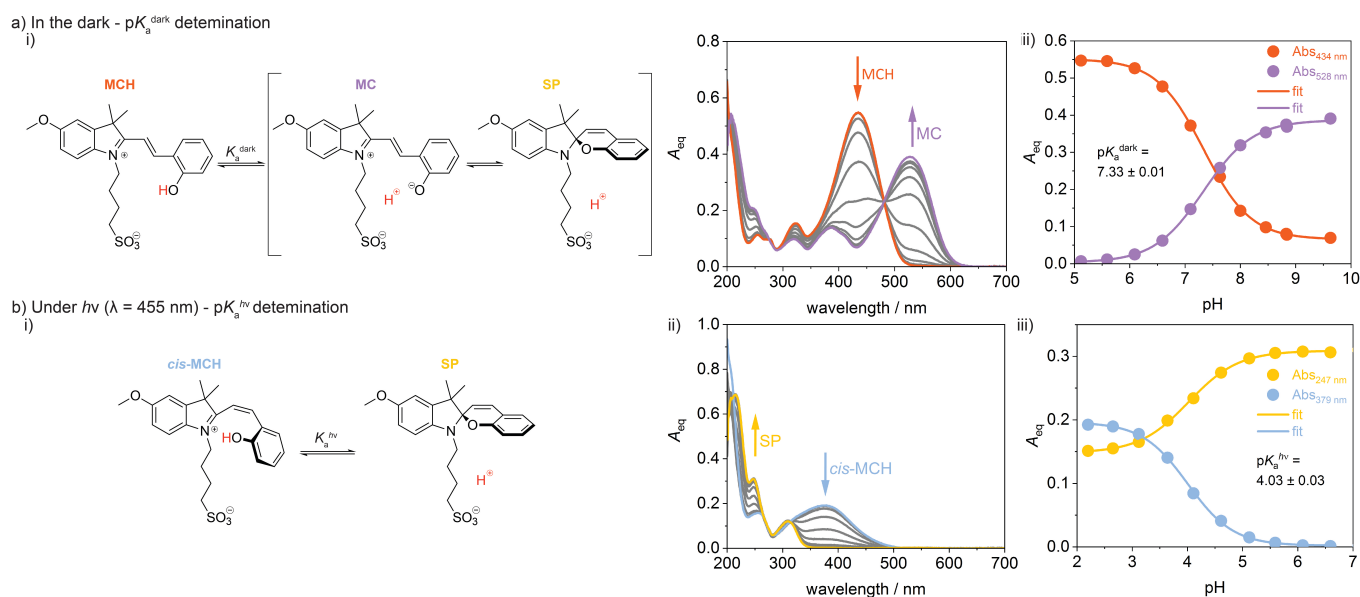


Fig. 2 Determination of pK_a^{dark} and $pK_a^{h\nu}$ by UV-vis absorption measurements of merocyanine photoacid **1**. ai) Equilibrium in the dark between the protonated merocyanine form (MCH) and the deprotonated form (MC) or respective ring closing product of MC – the spiropyran form (SP). aii) Absorption spectra of equilibrated samples in the dark at increasing pH values (orange: pH = 5.1, purple: pH = 9.6). aiii) Absorbance traces over the pH range of maxima characteristic for the MCH (orange, $\lambda = 434$ nm) and MC forms (purple, $\lambda = 528$ nm) with respective sigmoidal fit. Experimental conditions: [**1**] = 20.0 μM , [phosphate buffer] = 20 mM, pH 5.1-9.6, $T = 22$ $^{\circ}\text{C}$. bi) Equilibrium under 455 nm light irradiation between the protonated metastable *cis*-merocyanine form (*cis*-MCH) and the deprotonated ring closing product – the spiropyran form (SP). bii) Absorption spectra of equilibrated samples under 455 nm light irradiation at increasing pH values (blue: pH = 2.2, yellow: pH = 8.8). biii) Absorbance traces over the pH range of maxima characteristic for the *cis*-MCH (blue, $\lambda = 379$ nm) and SP forms (yellow, $\lambda = 247$ nm). Experimental conditions: [**1**] = 20.0 μM , [phosphate buffer] = 20 mM, pH 2.2-6.6, $T = 22$ $^{\circ}\text{C}$.

Both pK_a^{dark} and $pK_a^{h\nu}$ are “pseudo” pK_a values as they involve equilibria between other species than just the acid and the base,¹¹ but are useful to describe the effective proton dissociation behaviour of merocyanine photoacids. The pK_a^{dark} of **1** was determined as 7.33 ± 0.01 which is higher than reported values for related compounds (7.11 ± 0.03 :⁷ $R_1 = \text{MeO}$, $R_2 = t\text{Bu}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$; 6.95 ± 0.03 :⁶ $R_1 = \text{MeO}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$). The proton dissociation behaviour of **1** under light irradiation was also shifted to higher pH ($pK_a^{h\nu} = 4.03 \pm 0.03$) compared to reported values of related compounds (3.72 ± 0.01 :⁷ $R_1 = \text{MeO}$, $R_2 = t\text{Bu}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$; 3.43 ± 0.04 :^{6,12} $R_1 = \text{MeO}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{SO}_3^-$). This also confirms the trend⁷ that the difference between pK_a^{dark} and $pK_a^{h\nu}$, defined as the photoacidity parameter⁴ ($\Pi = pK_a^{\text{dark}} - pK_a^{h\nu}$) is relatively constant across different merocyanine compounds. The photoacidity parameter of photoacid **1** is 3.29 ± 0.03 which is in the range of previous examples (derivatives in Fig.1 with R_2 : H or $t\text{Bu}$) of 3.38 ± 0.03 to 3.85 ± 0.08 .^{4, 6-7}

Increasing the length of the side chain (R_3) by just one methylene group led to increased solubility in line with previously reported compound ($R_1 = \text{H}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_4\text{SO}_3^-$).⁴ We were able to prepare 3 mM solutions of merocyanine **1** which is around one order of magnitude higher than the solubility of propyl sulfonate analogue⁶ ($c = 0.4$ mM). As expected, the increased solubility of **1** resulted in improved pH switching properties. A 3 mM solution of **1** in 20 mM KCl was adjusted to pH 7.3 by adding minimal amounts of aqueous potassium hydroxide solution (1.0 M). Exposure to visible light at $\lambda = 450$ nm resulted in a drop to pH 3.8, equivalent to a 3.5

unit reversible pH jump (Fig. 3a). This switching process was repeated over 10 cycles with only minimal loss in the pH jump (98% recovery/cycle, Fig. 3b). Adjusting the initial pH to 8.3 yielded a light-induced pH jump of 3.2 units to pH 5.2 (Fig. 3 c). By comparison, the corresponding switching of a previously reported merocyanine ($R_1 = \text{MeO}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_3\text{NMe}_3^+$) at an initial pH of 7.5 resulted in a pH drop of only 1.6 units whereas an initial pH of 8.8 gave a drop of just 0.1 units.⁷ Repeated cycling of the pH jump for compound **1** from basic (pH 8.3) to acidic (pH 5.2) over 10 cycles also showed good stability (99% recovery/cycle, Fig 3 d). Slightly improved stability at higher pH values confirms the behaviour observed for hydrolytic degradation in previous studies.^{4, 6} The pH switching capacity for initial pH values in the range of pH 7.2 to pH 8.3 was similarly good with pH jumps of 2.6–3.5 units, demonstrating that the initial pH can be adjusted as needed for relevant applications (details see Supporting Information S5.1). The light induced pH jump decreases significantly beyond pH 8.3 due to incomplete bleaching of the MC(H) form (isomerization to the SP form), as shown by *in situ* NMR irradiation experiments in neutral to basic environments (see Supporting Information S3.3). The pH jump was only minimally influenced by temperature changes of 25 ± 3 $^{\circ}\text{C}$ with an observed variation of < 0.1 pH units (see Supporting Information S5.2).

For application purposes it is also important to know the timeframe of the pH response. A quick pH response is useful when an abrupt change in environment is required, whereas a slow response can be advantageous for processes requiring slower pH changes (i.e. to control kinetic processes like gel

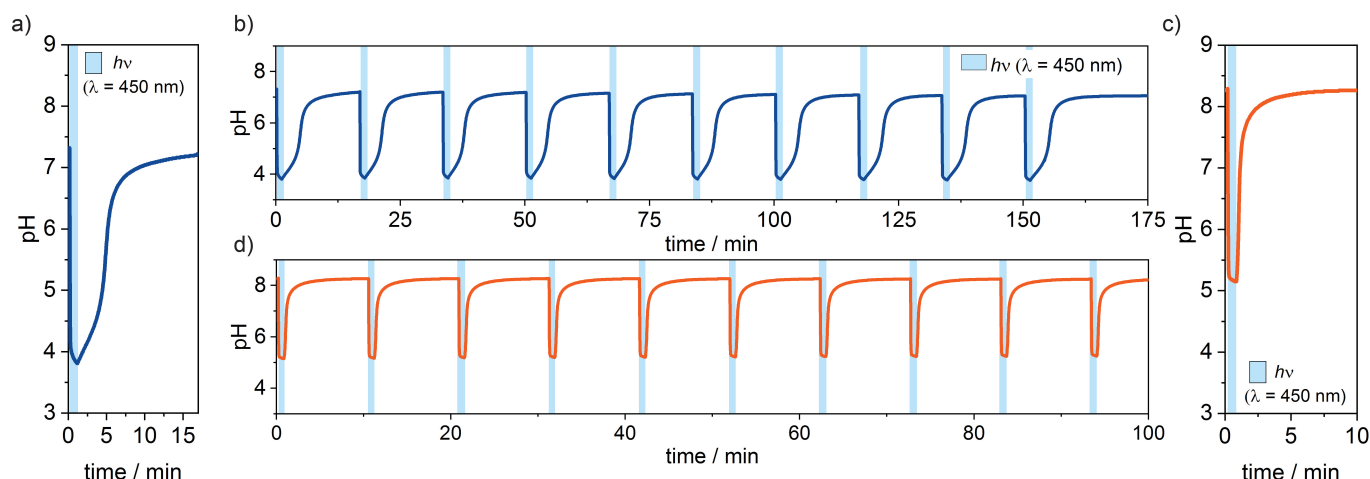


Fig. 3 Reversible visible light induced pH switching of a 3 mM aqueous solution of merocyanine photoacid. **a)** pH jump from 7.3 to 3.8 units, **b)** pH switching from neutral to acidic repeated for 10 cycles, **c)** pH jump from 8.3 to 5.1 units, **d)** pH switching from basic to acidic repeated for 10 cycles.

formation). We show that merocyanine **1** could achieve pH drops within seconds (< 5 s) under light irradiation whereas the thermal recovery occurred over minutes (< 20 min). As expected, the thermal recovery is more sensitive to temperature than the photoisomerization. At 28°C the thermal recovery took approximately a third of the time than at 22°C (7 min vs 18 min).

In conclusion, we report a new merocyanine photoacid with improved solubility and the highest $\text{pK}_a^{\text{dark}}$ value with respect to reported examples.^{4, 6-7, 10} These improved properties enabled the highest visible-light-induced pH jump of 3.5 units (pH 7.3 to 3.8) with good stability over 10 cycles. Visible-light-induced pH switching was extended well into the basic pH range for the first time with significant reversible pH drops from pH 8.3 to 5.2 that could be repeated over 10 cycles with minimal loss in function. These switching cycles of considerable magnitude and access to pH switching from basic to acidic environments make merocyanine **1** a useful tool to control chemical and biological activity with visible light. Application of merocyanine **1** will significantly broaden the scope of pH sensitive systems that can now be externally (and non-invasively) controlled with visible light.

Notes and references

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- See Ref. 7: Reported merocyanine ($\text{R}_1 = \text{MeO}$, $\text{R}_2 = \text{H}$, $\text{R}_3 = (\text{CH}_2)_3\text{NMe}_3^+$) achieved a pH drop of 1.6 units at an initial pH of 7.5 whereas an initial pH of 8.8 gave a drop of just 0.1 units.
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- Described in more detail in Ref. 4, 6-7.
- with 425 nm excitation. When excited with 500 nm light the $\text{pK}_a^{h\nu}$ was 3.31 ± 0.04

TOC:

