

Photoswitchable triple hydrogen-bonding motif†‡

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Photochromic bis(thiazol-4-yl)maleimides, displaying enhanced binding affinity to complementary melamine receptors in their ring-closed switching state, have been developed and could pave the way to light-responsive supramolecular assemblies.

The “bottom-up” organization of molecules to defined superstructures and resulting materials requires the use of weak and reversible non-covalent interactions between the molecular building blocks as they enable the generation of defect free structures. As structure formation relies on the primary event of molecular recognition, hydrogen-bonds have been extensively exploited as they offer directionality as well as complementarity and can be adjusted in their strength.^{1,2} Another advantage of using the supramolecular assembly approach relies on its ability to respond to external stimuli giving rise to “smart” materials.³ For this purpose, hydrogen-bonding interactions can be controlled by changes in temperature, solvent, and pH.^{1,2} The formation of multiple hydrogen bonding interactions can also be tuned by oxidation/reduction, altering the intrinsic ability of one partner to act as a hydrogen-bond acceptor and/or donor.⁴ In contrast to the above mentioned stimuli, light represents a truly non-invasive stimulus combined with unprecedented spatio-temporal resolution that, in principle, constitutes an exquisite tool to remotely control hydrogen-bonding interactions.^{2a,c} Thus far such photochemical control has been achieved primarily by manipulating the geometry and flexibility of the key building blocks involved in the formation of hydrogen-bonding networks⁵ and their higher aggregates.⁶ Another example relies on the photomodulation of secondary interactions and their impact on the formation of a discrete hydrogen-bonding complex.⁷ Here, we present an alternative approach to photochemically modulate the inherent binding strength of a triple hydrogen-bonding motif by means of changing its electronic nature during the course of a photochromic reaction.⁸

Inspired by the possibility of influencing the strength of multiple hydrogen-bonding motifs by variation of π -conjugated electron-donating/accepting groups⁹ and intrigued by Irie's diarylethene photochromes,¹⁰ which allow for significant changes in π -conjugation when switching from the open to the closed form, we chose to merge both aspects in our design (Fig. 1).¹¹ The central maleimide core is acting as a triple hydrogen-bonding acceptor–donor–acceptor (ADA) site, which

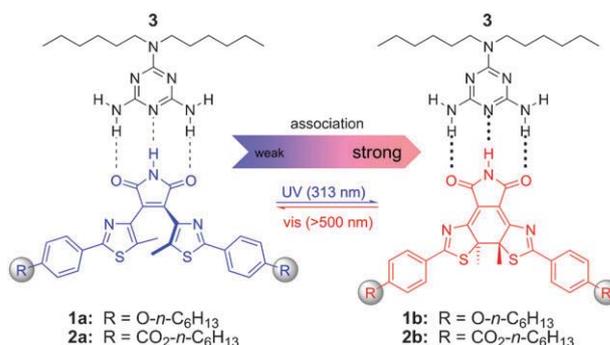


Fig. 1 Photoswitchable triple hydrogen-bonding motif: reversible photochemical ring-closure (opening) leads to an enhanced (diminished) binding of the central ADA imide moiety in **1b/2b** (**1a/2a**) to a complementary DAD melamine receptor **3**.

in the open form is largely decoupled from the termini, whereas in the closed form the terminal donor/acceptor groups are in π -conjugation and hence should influence the association with a complementary *N,N*-dialkylmelamine DAD moiety.

In order to readily vary the substitution pattern, a modular synthesis of compounds **1a** and **2a** was devised, involving Suzuki cross-coupling between the dibromomaleimide core and suitable 5-methyl-2-phenylthiazol-4-ylboronic esters, carrying either electron-donating ether or electron-accepting ester groups in the *para*-position of the 2-phenyl moiety. Thiazole termini were chosen as they are readily available and offer great performance, in particular with regard to their thermal and photochemical stability.¹² To facilitate solubility, *n*-hexyl chains were attached to both termini in each case (**1a**, **2a**) and furthermore incorporated into the complementary melamine moiety **3**. The respective ring-closed isomers **1b** and **2b** were isolated after preparative irradiations of their ring-open derivatives and subsequent column chromatography.

Compounds **1a/b** and **2a/b** display excellent photochromic behaviour (Fig. 2). Irradiation with UV-light ($\lambda_{\text{irr}} = 313 \text{ nm}$) of a solution of **1a** or **2a** in methylene chloride leads to rapid change in colour from yellow to deep-red, reflected in new bands arising at 540 nm and 545 nm, respectively. Isosbestic points at 329 nm in the case of **1a/b** and at 256, 336, 352, 379, and 408 nm in the case of **2a/b** indicate clean two-component processes. The thus reached photostationary states (PSSs) contain 87% of **1b** and 82% of **2b**, respectively (Table 1). Subsequent irradiation with visible light ($\lambda_{\text{irr}} > 500 \text{ nm}$) effects decolorization and the original UV-spectra are completely restored, *i.e.* the ring-closed isomers are quantitatively converted into their ring-opened forms. Repetitive switching cycles revealed slight decomposition of **1a/b**¹³ while **2a/b** showed excellent fatigue resistance (Fig. 2, insets). Furthermore, both ring-closed isomers were found to be thermally stable

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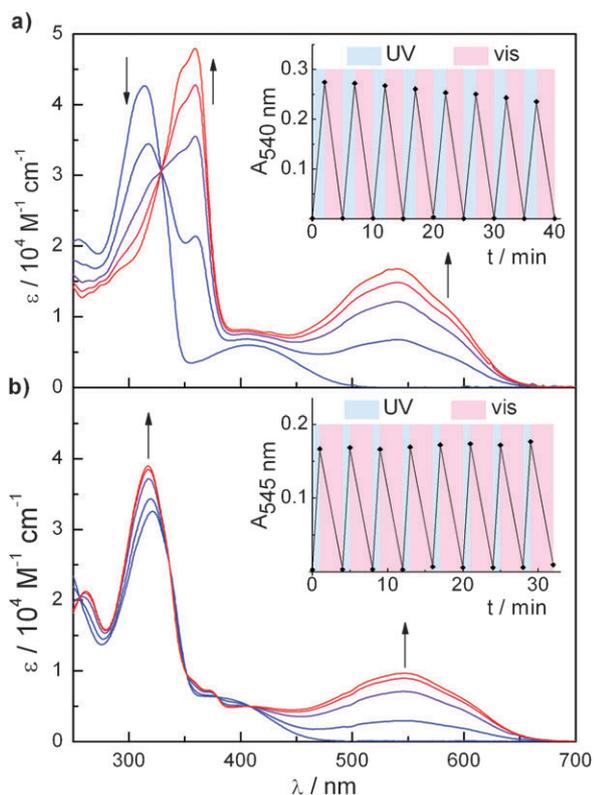


Fig. 2 Photochromic behaviour: UV/vis absorption spectra during the course of irradiation ($\lambda_{\text{irr}} = 313$ nm) until reaching the PSS of (a) **1a** (time intervals: $t = 0, 60, 120, 180,$ and 500 s) and (b) **2a** (time intervals: $t = 0, 10, 30, 60,$ and 120 s) in CH_2Cl_2 ($c = 2 \times 10^{-5}$ M, 25°C). Insets show repetitive switching cycles ($\lambda_{\text{irr}} = 313$ nm for ring-closure, $\lambda_{\text{irr}} > 500$ nm for ring-opening) between (a) **1a** and **1b** as well as (b) **2a** and **2b**.

Table 1 Photochromic and association properties of both switch pairs

	Photochromism ^a			Association ^c	
	$\lambda_{\text{max}}/\text{nm}$	$\Phi_{\text{a} \rightarrow \text{b}}^{313 \text{ nm}}$	$\Phi_{\text{b} \rightarrow \text{a}}^{546 \text{ nm}}$	Conv. ^b (%)	$K_{\text{a}}/\text{M}^{-1}$
1a	313, 408	0.08	0.02	87	7.57 ± 0.02 132 ± 11
1b	359, 540				7.72 ± 0.06 231 ± 23
2a	321, 380	0.18	0.02	82	7.75 ± 0.05 142 ± 13
2b	317, 545				7.99 ± 0.03 318 ± 30

^a In CH_2Cl_2 at 25°C . ^b Composition of the PSS upon irradiation of the open form (**1a** or **2a**) with UV-light ($\lambda_{\text{irr}} = 313$ nm) determined by UPLC. ^c Derived from NMR-titration data in CDCl_3 , 25°C . †

over extended periods of time (days and weeks). Interestingly, the photochromic performance of **1a/b** is strongly dependent on solvent polarity since in acetonitrile prolonged irradiation times are necessary to reach the PSS, which is composed of only 44% of **1b**. This finding is further supported by comparing the quantum yields for ring closure, which show a marked decrease when going from methylene chloride to acetonitrile. ‡ This effect can be attributed to the generation of a twisted intramolecular charge transfer (TICT) state upon excitation of **1a** as suggested previously to explain solvent-dependent photochromism of related donor–acceptor dithienylethenes.¹⁴

To investigate the association behaviour of each photochromic ADA maleimide pair (**1a/b** and **2a/b**), NMR titrations with the complementary DAD receptor (**3**) were carried out in CDCl_3 . Changing chemical shifts of the central imide NH-proton were monitored with increasing amount of receptor and show characteristic binding isotherms (Fig. 3). In both cases, the binding curve of ring-closed isomer (**1b** or **2b**) displays a steeper slope that is indicative of a stronger association. Evaluation of the data following established procedures¹⁵ allowed us to determine the respective association constants K_{a} (Table 1), which are in the expected range of related imide–melamine complexes.^{9d,15c} Indeed, the association of each of the ring-closed isomers to the melamine receptor is stronger as compared to the respective ring-opened isomers. The K_{a} values approximately double upon switching to the ring-closed forms and a slightly stronger enhancement of binding was observed in the case of the ester derivatives **2a/b**. The 1 : 1 binding stoichiometry was verified by Job plots showing maxima at molar fractions $x_{\text{receptor } 3} = 0.5$. ‡ Most importantly, photochemical switching behaviour remains unaffected by the presence of melamine **3**, as essentially the same quantum yields are observed even if the majority of the switch is complexed. ‡

The observed general enhancement in the association of the ring-closed isomers with the receptor can primarily be related to the reduced electron-density of the maleimide core.¹⁶ This is nicely reflected in the significantly reduced reduction potential

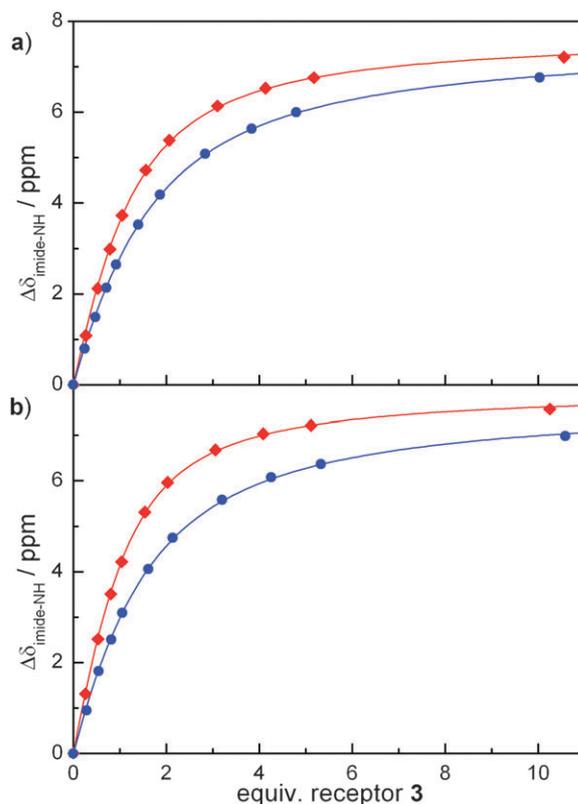


Fig. 3 Association behaviour: NMR-titration of ring-open isomers (blue circles) and ring-closed isomers (red diamonds) with receptor **3** in CDCl_3 at 25°C for (a) **1a** and **1b** as well as (b) **2a** and **2b** (lines show fitted curves for the 1 : 1 binding isotherms).

of **2b** ($E_p^{\text{red}} = -1.253$ V) as compared to its ring-opened analogue **2a** ($E_p^{\text{red}} = -1.497$ V). In the case of the **1a/b**, the reduction potential is also reduced in the ring-closed form yet to a smaller extent ($\Delta E_p^{\text{red}} = -74$ mV for **1a/b** instead of $\Delta E_p^{\text{red}} = -244$ mV for **2a/b**, all values relative to an Fc/Fc^+ standard).[‡] Clearly when comparing both ring-closed isomers, the larger K_a value for **2b** is due to the presence of the coupled electron-accepting ester groups, which further diminish electron density in the maleimide core. The overall reduction of electron density upon ring-closure is associated with an increased acidity of the central imide N–H group, whose interaction with the melamine's endocyclic N-atom seems to dominate the association event. This finding is in line with the geometry of the five-membered maleimide ring that leads to elongated and hence weaker interactions of both terminal imide carbonyl O-atoms with the two exocyclic N–H groups of the melamine receptor. From our experiments it seems that ring-closure in combination with π -conjugated electron-accepting groups is best suited for achieving enhanced binding constants for the presented photoswitchable imides.

The first encouraging example of a photoswitchable triple hydrogen-bonding motif, based on an electronic modulation of the participating basicity/acidity and therefore binding strength, has been developed. Ongoing efforts in our laboratories are concerned with the design of improved systems, which provide larger differences in association strength (ON/OFF ratios) as well as inherently stronger association. The latter could be accomplished by introducing more hydrogen-bonding sites, for example Meijer's quadruple hydrogen-bonding ureidopyrimidines,^{2b} or simply by working in less polar media.^{15c} In principle, such photoswitchable supramolecular "glue" should allow for the construction of light-responsive soft materials, for example by utilizing multivalent constructs as photochromic monomers or crosslinkers. Furthermore, our approach of exploiting the bridge of diarylethenes as a tunable functionality,^{16,17} which is electronically modulated by coupling terminal donors/acceptors appears to be a general strategy to photomodulate various functions and work along these lines will be reported in due course.

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