

# Photoswitchable triple hydrogen-bonding motif†‡

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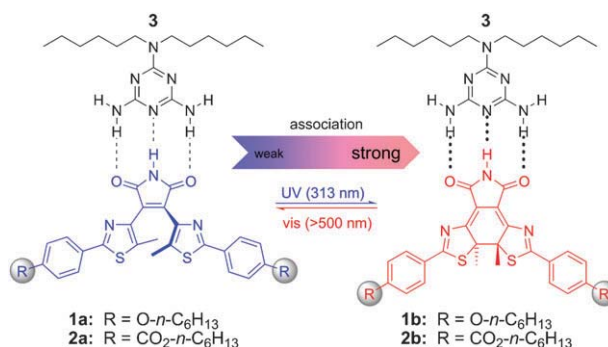
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**Photochromic bis(thiazol-4-yl)maleimides, displaying enhanced binding affinity to complementary melamine receptors in their ring-closed switching state, have been developed and could pave the way to light-responsive supramolecular assemblies.**

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.<sup>1,2</sup> Another advantage of using the supramolecular assembly approach relies on its ability to respond to external stimuli giving rise to “smart” materials.<sup>3</sup> For this purpose, hydrogen-bonding interactions can be controlled by changes in temperature, solvent, and pH.<sup>1,2</sup> 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.<sup>4</sup> 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.<sup>2a,c</sup> 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 networks<sup>5</sup> and their higher aggregates.<sup>6</sup> Another example relies on the photomodulation of secondary interactions and their impact on the formation of a discrete hydrogen-bonding complex.<sup>7</sup> 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.<sup>8</sup>

Inspired by the possibility of influencing the strength of multiple hydrogen-bonding motifs by variation of  $\pi$ -conjugated electron-donating/accepting groups<sup>9</sup> and intrigued by Irie's diarylethene photochromes,<sup>10</sup> which allow for significant changes in  $\pi$ -conjugation when switching from the open to the closed form, we chose to merge both aspects in our design (Fig. 1).<sup>11</sup> 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  $\pi$ -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.<sup>12</sup> 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.

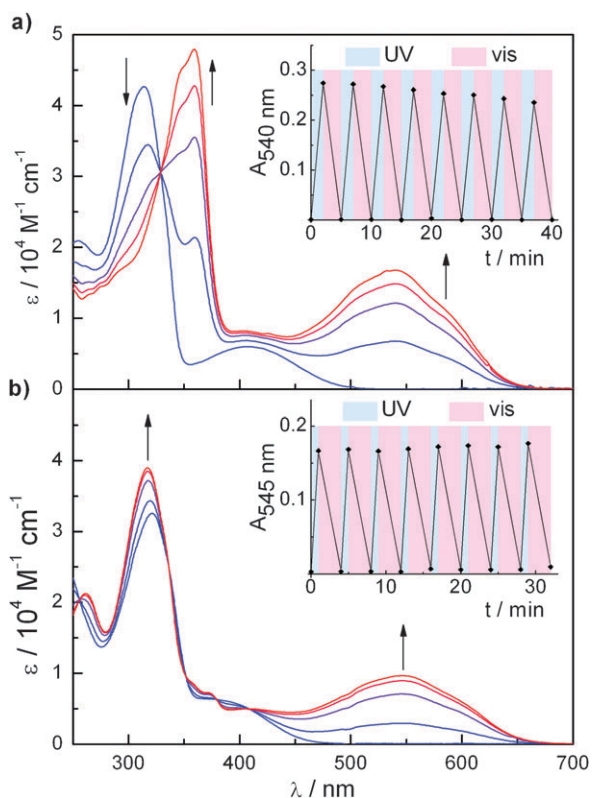
Compounds **1a/b** and **2a/b** display excellent photochromic behaviour (Fig. 2). Irradiation with UV-light ( $\lambda_{\text{irr}} = 313 \text{ nm}$ ) of a solution of **1a** or **2a** in methylene chloride leads to rapid change in colour from yellow to deep-red, reflected in new bands arising at 540 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**<sup>13</sup> 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  $\text{CH}_2\text{Cl}_2$  ( $c = 2 \times 10^{-5}$  M,  $25^\circ\text{C}$ ). 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

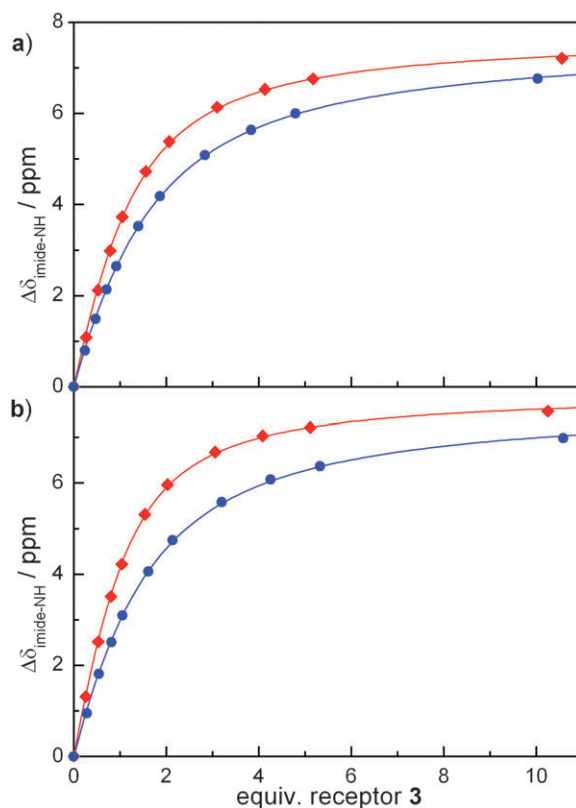
	Photochromism <sup>a</sup>			Association <sup>c</sup>	
	$\lambda_{\text{max}}/\text{nm}$	$\Phi_{\text{a} \rightarrow \text{b}}^{313 \text{ nm}}$	$\Phi_{\text{b} \rightarrow \text{a}}^{546 \text{ nm}}$	Conv. <sup>b</sup> (%)	$K_{\text{a}}/\text{M}^{-1}$
<b>1a</b>	313, 408	0.08	0.02	87	$7.57 \pm 0.02$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

<sup>a</sup> In  $\text{CH}_2\text{Cl}_2$  at  $25^\circ\text{C}$ . <sup>b</sup> Composition of the PSS upon irradiation of the open form (**1a** or **2a**) with UV-light ( $\lambda_{\text{irr}} = 313$  nm) determined by UPLC. <sup>c</sup> Derived from NMR-titration data in  $\text{CDCl}_3$ ,  $25^\circ\text{C}$ . †

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.<sup>14</sup>

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  $\text{CDCl}_3$ . 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 procedures<sup>15</sup> allowed us to determine the respective association constants  $K_{\text{a}}$  (Table 1), which are in the expected range of related imide–melamine complexes.<sup>9d,15c</sup> 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  $K_{\text{a}}$  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.<sup>16</sup> 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  $\text{CDCl}_3$  at  $25^\circ\text{C}$  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  $\text{Fc}/\text{Fc}^+$  standard).<sup>‡</sup> 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  $\pi$ -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,<sup>2b</sup> or simply by working in less polar media.<sup>15c</sup> 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,<sup>16,17</sup> 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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## Notes and references

- G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, New York, 1997.
- For multiple hydrogen-bonding motifs: (a) A. J. Wilson, *Soft Matter*, 2007, **3**, 409–425; (b) R. P. Sijbesma and E. W. Meijer, *Chem. Commun.*, 2003, 5–16; (c) G. Cooke and V. M. Rotello, *Chem. Soc. Rev.*, 2002, **31**, 275–286; (d) C. Schmuck and W. Wienand, *Angew. Chem.*, 2001, **113**, 4493–4499 (*Angew. Chem., Int. Ed.*, 2001, **40**, 4363–4369); (e) S. C. Zimmerman and P. S. Corbin, *Struct. Bonding*, 2000, **96**, 63–94.
- For recent overviews, in particular dealing with photoresponsive materials, see: (a) F. Ercole, T. P. Davis and R. A. Evans, *Polym. Chem.*, 2010, **1**, 37–54; (b) M.-M. Russew and S. Hecht, *Adv. Mater.*, 2010, **22**, 3348–3360.
- (a) E. Breinlinger, A. Niemz and V. M. Rotello, *J. Am. Chem. Soc.*, 1995, **117**, 5379–5380; (b) Y. Ge, R. Lilienthal and D. K. Smith, *J. Am. Chem. Soc.*, 1996, **118**, 3976–3977; (c) Y. Ge, L. Miller, T. Ouimet and D. K. Smith, *J. Org. Chem.*, 2000, **65**, 8831–8838; (d) J. Bu, N. D. Lilienthal, J. E. Woods, C. E. Nohrden, K. T. Hoang, D. Truong and D. K. Smith, *J. Am. Chem. Soc.*, 2005, **127**, 6423–6429.
- (a) S. Yagai, T. Karatsu and A. Kitamura, *Chem.–Eur. J.*, 2005, **11**, 4054–4063; (b) S. Yagai, T. Nakajima, T. Karatsu, K. Saitow and A. Kitamura, *J. Am. Chem. Soc.*, 2004, **126**, 11500–11508; (c) F. Rakotonradany, M. A. Whitehead, A.-M. Lebus and H. F. Sleiman, *Chem.–Eur. J.*, 2003, **9**, 4771–4780.
- (a) M. S. Vollmer, T. D. Clark, C. Steinem and M. R. Ghadiri, *Angew. Chem.*, 1999, **111**, 1703–1706 (*Angew. Chem., Int. Ed.*, 1999, **38**, 1598–1601); (b) L. N. Lucas, J. van Esch, R. M. Kellog and B. L. Feringa, *Chem. Commun.*, 2001, 759–760; (c) J. J. D. de Jong, L. N. Lucas, R. M. Kellog, J. van Esch and B. L. Feringa, *Science*, 2004, **304**, 278–281; (d) M. Takeshita, M. Hayashi, S. Kadota, K. H. Mohammed and T. Yamato, *Chem. Commun.*, 2005, 761–763; (e) M. Takeshita, M. Hayashi and T. Miyazaki, *Chem. Lett.*, 2010, **39**, 82–83.
- A. Goodman, E. Breinlinger, M. Ober and V. M. Rotello, *J. Am. Chem. Soc.*, 2001, **123**, 6213–6214.
- An impressive, conceptually related example of a photoswitchable fulgimide has been described in T. Okuyama, Y. Yokoyama and Y. Yokoyama, *Bull. Chem. Soc. Jpn.*, 2001, **74**, 2181–2187.
- (a) Y. Kyogoku, R. C. Lord and A. Rich, *Proc. Natl. Acad. Sci. U. S. A.*, 1967, **57**, 250–256; (b) C. S. Wilcox, E. Kim, D. Romano, L. H. Kuo, A. L. Burt and D. P. Curran, *Tetrahedron*, 1995, **51**, 621–634; (c) R. Deans, G. Cooke and V. M. Rotello, *J. Org. Chem.*, 1997, **62**, 836–839; (d) F. Würthner and S. Yao, *J. Org. Chem.*, 2003, **68**, 8943–8949.
- M. Irie, *Chem. Rev.*, 2000, **100**, 1685–1716.
- Please note that dithienylethenes have been utilized to photomodulate aggregation via H-bonding, see ref. 6b–e, and via  $\pi$ , $\pi$ -stacking in combination with hydrophobic forces: (a) T. Hirose, K. Matsuda and M. Irie, *J. Org. Chem.*, 2006, **71**, 7499–7508; (b) T. Hirose, M. Irie and K. Matsuda, *Adv. Mater.*, 2008, **20**, 2137–2141. Photochromic purine analogues and their base pairing with thymidine have recently been reported in: (c) M. Singer and A. Jäschke, *J. Am. Chem. Soc.*, 2010, **132**, 8372–8377.
- (a) K. Uchida, T. Ishikawa, M. Takeshita and M. Irie, *Tetrahedron*, 1998, **54**, 6627–6638; (b) S. Takami, S. Kobatake, T. Kawai and M. Irie, *Chem. Lett.*, 2003, **32**, 892–893.
- Upon prolonged UV-irradiation ( $\lambda_{\text{irr}} = 260$ –380 nm) irreversible bleaching of the absorption band is observed, yet no by-product could be detected.
- (a) M. Irie and K. Sayo, *J. Phys. Chem.*, 1992, **96**, 7671–7674; (b) M. Ohsumi, M. Hazama, T. Fukaminato and M. Irie, *Chem. Commun.*, 2008, 3281–3283.
- (a) K. A. Connors, *Binding Constants*, Wiley & Sons, New York, 1987; (b) C. S. Wilcox, in *Frontiers of Supramolecular Chemistry and Photochemistry*, ed. H. J. Schneider and H. Dürr, VCH, Weinheim, 1991, pp. 123–143; (c) F. Würthner, C. Thalacker, A. Sautter, W. Schärtl, W. Ibach and O. Hollricher, *Chem.–Eur. J.*, 2000, **6**, 3871–3886.
- This effect is somewhat related to photoswitchable changes in Lewis-acidity observed by Branda and coworkers in dioxaborolane bridged dithienylethenes, which interconvert between a (hetero)-aromatic open and a cross-conjugated closed isomer: V. Lemieux, M. D. Spantulescu, K. K. Baldrige and N. R. Branda, *Angew. Chem., Int. Ed.*, 2008, **47**, 5034–5037.
- For elegant examples exploiting chemical reactivity differences of the bridge functionality, see: (a) D. Sud, T. J. Wigglesworth and N. R. Branda, *Angew. Chem., Int. Ed.*, 2007, **46**, 8017–8019; (b) V. Lemieux, S. Gauthier and N. R. Branda, *Angew. Chem., Int. Ed.*, 2006, **45**, 6820–6824; (c) V. Lemieux and N. R. Branda, *Org. Lett.*, 2005, **7**, 2969–2972.