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 hydrogenbonding 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 ($\lambda_{irr} = 313$ 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 ($\lambda_{irr} > 500 \text{ nm}$) 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/bshowed 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 ($\lambda_{irr} = 313$ 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 CH₂Cl₂ ($c = 2 \times 10^{-5}$ M, 25 °C). Insets show repetitive switching cycles ($\lambda_{irr} = 313$ nm for ring-closure, $\lambda_{irr} > 500$ 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	
	λ_{max}/nm	$\Phi^{313 \text{ nm}}_{\mathbf{a} \rightarrow \mathbf{b}}$	$\Phi^{546 nm}_{\mathbf{b} ightarrow \mathbf{a}}$	Conv. ^b (%)	$\Delta \delta_{ m max}/ m ppm$	$K_{\rm a}/{ m M}^{-1}$
1a 1b	313, 408 359, 540	0.08	0.02	87	7.57 ± 0.02 7.72 ± 0.06	$132 \pm 11 \\ 231 \pm 23$
2a 2b	321, 380 317, 545	0.18	0.02	82	$\begin{array}{c} 7.75 \pm 0.05 \\ 7.99 \pm 0.03 \end{array}$	$\begin{array}{c} 142\pm13\\ 318\pm30\end{array}$

^{*a*} In CH₂Cl₂ at 25 °C. ^{*b*} Composition of the PSS upon irradiation of the open form (**1a** or **2a**) with UV-light ($\lambda_{irr} = 313$ nm) determined by UPLC. ^{*c*} Derived from NMR-titration data in CDCl₃, 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 CDCl₃. 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 $K_{\rm a}$ (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 $x_{\text{receptor }3} = 0.5.\ddagger$ 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 CDCl₃ at 25 $^{\circ}$ 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 ($E_{\rm p}^{\rm red} = -1.497$ V). In the case of the 1a/b, the reduction potential is also reduced in the ring-closed form yet to a smaller extent ($\Delta E_{p}^{red} = -74$ mV for **1a/b** instead of $\Delta E_{\rm p}^{\rm red} = -244$ 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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Notes and references

- 1 G. A. Jeffrey, An Introduction to Hydrogen Bonding, Oxford University Press, New York, 1997.
- 2 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.
- 3 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.

- 4 (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.
- 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. Rakotondradany, M. A. Whitehead, A.-M. Lebuis and H. F. Sleiman, *Chem.-Eur. J.*, 2003, 9, 4771–4780.
- 6 (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.
- 7 A. Goodman, E. Breinlinger, M. Ober and V. M. Rotello, J. Am. Chem. Soc., 2001, **123**, 6213–6214.
- 8 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.
- 9 (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.
- 10 M. Irie, Chem. Rev., 2000, 100, 1685-1716.
- 11 Please note that dithienylethenes have been utilized to photomodulate aggregation via H-bonding, see ref. 6b-e, and via π,π-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.
- 12 (a) K. Uchida, T. Ishikawa, M. Takeshita and M. Irie, *Tetra-hedron*, 1998, **54**, 6627–6638; (b) S. Takami, S. Kobatake, T. Kawai and M. Irie, *Chem. Lett.*, 2003, **32**, 892–893.
- 13 Upon prolonged UV-irradiation ($\lambda_{irr} = 260-380$ 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.
- 15 (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.
- 16 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. Baldridge and N. R. Branda, *Angew. Chem., Int. Ed.*, 2008, **47**, 5034–5037.
- 17 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.