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# Anion-tunable control of thermal $Z \rightarrow E$ isomerisation in basic azobenzene receptors

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Herein, we report that thermal  $Z \rightarrow E$  isomerisation of simple azobenzene urea derivatives is selectively and predictably controlled by anion binding. The rate of this process depends strictly on the anion concentration and its binding affinity to the Z-isomer of the azobenzene host, i.e. increased rate constants are observed for higher anion concentration as well as for more strongly bound guests. The origin of this phenomenon is attributed to electron density transfer from the anion to the host  $\pi$ -system, resulting in increased repulsion between the lone electron pairs in the N=N bond.

Light induced control of the geometry of molecules and the spatial arrangement of their assemblies is of fundamental importance in material and medicinal sciences. This arises from the fact that, contrary to other external stimuli, light possesses an electrically neutral character and ensures that the resulting transformation is rapid, strictly localized in space, and generally reversible.<sup>1</sup> The photoactive moieties that are often applied in such transformations include diaryl- and dithienylethene, spiropyrane, and azobenzene (AB) derivatives.<sup>1-3</sup> Among these, the latter appear to be the most useful owing to their synthetic availability and robustness.<sup>4-6</sup> In general, upon irradiation of ABs with UV or visible light, photostationary equilibrium is established between the near planar E-isomer and the more compact Vshaped Z-isomer. However, when the light is off, the Z-isomer spontaneously reequilibrates to the thermodynamically more stable E-isomer. For some practical applications control of this back process is desirable since this precludes the use of a second light stimulus for regenerating the initial state of the sample.7-9 One unusual option for this control comes from the covalent introduction of a strong electron withdrawing fluorine substituents to the AB ring, which, by decreasing the electron density of the N=N bond, result in considerably long-lived AB derivatives.<sup>10</sup> Analogically, the reverse situation should facilitate the rate of thermal back-isomerization by increasing the repulsion between lone electron pairs in the azo bond. Based on our activity in anion coordination chemistry,<sup>11-13</sup> we assumed that anionic species could be utilized here since an increase of the electron density in the  $\pi$ -conjugated host system is observed upon anion binding.<sup>12,14</sup> Furthermore, although recognition and transport of anions is one of the most important areas of supramolecular chemistry,15 so far a limited amount of work has been done.<sup>16</sup> Therefore, we decided to synthesize and examine the thermodynamic and kinetic properties of para- substituted mono- (1a) and diphenylurea (1b) AB derivatives as model hosts for basic studies of their anion controlled  $Z \rightarrow E$  isomerization. We utilize the urea group as primary binding site, due to its excellent affinity to oxo-anions,13,17,18 Preliminary quantum calculations confirm our assumption that a slight elongation of the N=N bond and a more negative electrostatic potential surface (EPS), which describes increased electron density, is observed for the anion complex than for free receptor Z-1 (a representative complex of Z-1b with benzoate is shown in Fig. 1).



**Fig.** 1 Energy minimized structures (DFT/ $\omega$ b97x-d/6-31G+/DMSO) of the Z-**1b** (a) and Z-**1b** $\supset$ PhCO<sub>2</sub><sup>-</sup> (b) along with electrostatic potential surfaces (EPS) mapped onto electron density (0.001 au); values in the legend are given in kJ·mol<sup>-1</sup>.

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The *E*-1 hosts were readily synthesized from commercially available azo-precursors 2 and 3 whereas *Z*-1 hosts could be obtained by irradiating the samples of *E*-1 with UV light (Scheme 1).



The E- and Z-isomers of 1 exhibit distinct spectral properties and the two isosbestic points in the UV-VIS spectra indicate that only one process is present during both photo, as well as thermal  $Z\rightarrow E$  isomerisation (Fig. 2a).<sup>19</sup> In addition, after several cycles of alternate irradiation with UV and visible light, receptors 1 still showed very good recoverability with no photodegradation products (Fig. 2b).



Fig. 2 (a) Thermal isomerization of Z-1b to E-1b; (b) photoswitching between E-1b and Z-1b isomers using UV (368 nm) and blue light (410 nm).

Subsequently, we determined the first-order rates of thermal isomerization for the *Z*-**1** hosts by monitoring the absorption change in the corresponding *Z*- and *E*-isomers in darkness and non-linear fitting of the experimental data using the Marquard technique.<sup>20</sup> In all cases, practically linear Arrhenius and Eyring plots indicate that only one mechanism occurs, namely via inversion of one of the *sp*-hybrydised nitrogen atoms of the azo bond.<sup>21</sup> Note that our measurements were conducted in a highly polar solvent mixture, i.e. DMSO + 0.5% H<sub>2</sub>O, which is known to significantly accelerate thermal isomerization of ABs.<sup>4,22,23</sup> Fortunately, the half-life of pure *Z*-**1** isomers was sufficiently large<sup>24</sup> for subsequent studies with anions. Table 1 shows the relevant spectral, kinetic, and thermodynamic data for these photoswitchable hosts.

<b>Tab. 1</b> Spectra, kinetic, and thermodynamic data for thermal $Z \rightarrow E$ isomerization of azobenzene (AB) and hosts <b>1</b> at 298±0.1K <sup>[a]</sup>											
Host	$\lambda_{E}$ (nm)	$\lambda_Z$ (nm)	$\tau_{1/2}$ (h)	$E_{\rm a}$	$\Delta H^{*}$	$T\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$				
AB	321	~290	213.6	103	100	-7.8	107				
1a	372	337	13.1	92	89	-11	101				
1b	392	336	1.8	88	86	-10	96				

[a]  $\lambda_E$  and  $\lambda_Z$  denotes maximum absorption transition ( $\pi \rightarrow \pi^*$ ) for the *E*- and *Z*isomer, respectively; values for  $E_a$ ,  $\Delta H^{\dagger}$ ,  $T\Delta S^{\dagger}$ , and  $\Delta G^{\dagger}$  are given in kJ·mol<sup>-1</sup>.

The data presented in Table 1 reveal that introducing the urea group to the AB scaffold significantly decreases the stability of *Z*-1 and shift the  $\pi$ - $\pi$ \* (S<sub>2</sub>) bands of both *E*-1 and *Z*-1 toward higher

wavelengths in comparision to the parent AB. These results are in line with the reported data for *para*-substituted ABs,<sup>22,23,25</sup> but explaining why any substituent in this position facilitates the thermal isomerisation is not always clear.<sup>22</sup> In our model system, this phenomenon can be rationalized in a simple way, in terms of extended  $\pi$ -electron conjugation caused by the strong positive mesomeric effect of urea groups, as pointed out by Woolley.<sup>26</sup> This is supported by molecular orbital calculations which predict that for *Z*-1 energy of the n orbitals is much higher than for the  $\pi$ orbitals due to mixing with  $\pi$  orbitals of the phenylurea moiety.

In the next step, we studied the thermal kinetics of Z-1 in the presence of a constant quantity of representative anionic guests, i.e.: spherical halogens (F, Br), Y-shaped carboxylates (MeCO<sub>2</sub>,  $PhCO_{2}$ ), and tetrahedral bisulfate  $(HSO_4)$ and dihydrogenphospate (H<sub>2</sub>PO<sub>4</sub><sup>-</sup>), added as tetra-n-butylammonium (TBA) salts. The results of these measurements are given in Table 2 and they clearly demonstrate that even a small quantity of an anion has a tremendous impact on accelerating the rate of thermal  $Z \rightarrow E$  isomerisation. Moreover, effect of the anion added is simply hindered by the addition of TFA, and restored again by the addition of Et<sub>3</sub>N.<sup>27</sup>

<b>Tab. 2</b> Spectral and kinetic data for thermal $Z \rightarrow E$ isomerization of complexes of Z-1 with 10 equiv of anions at 298±0.1K <sup>[a]</sup>										
Host	Value	F-	MeCO <sub>2</sub> -	PhCO2-	HSO4 <sup>-[b]</sup>	$\mathrm{H}_{2}\mathrm{PO}_{4}^{-}$				
1a	$\Delta\lambda_{\pi\text{-}\pi^*}(nm)$	15	18	10	8	17				
	$k_{\Delta} \cdot 10^{-4}$ (s)	19	31	3.9	3.2	4.9				
	$\tau_{1/2}(min)$	6	4	30	37	24				
1b	$\Delta\lambda_{\pi\text{-}\pi^*}(nm)$	4	14	8 (19) <sup>[c]</sup>	1	6				
	$k_{\Delta} \cdot 10^{-4} (s)$	7.6	14	4.6 (14) <sup>[c]</sup>	1.4	4.1				
	$\tau_{1/2}(min)$	15	8	25 (8) <sup>[c]</sup>	8	28				

[a] Anions added as TBA salts,  $\Delta \lambda_{\pi-\pi^*}$  denotes the shift in maximum absorption between free Z-1 and its anion complexes; [b] 200 and [c] 555 equiv of anion, respectively, were added.

The effect of the added anions is much more pronounced for mono-substituted Z-1a than for Z-1b; this is attributed to the extended delocalisation of the negative charge from anion over the second phenylurea moiety in the latter case. In addition, those anions which most accelerate reaction rates also induced the highest red-shift of the Z-1 host  $\pi$ - $\pi^*$  bands which is supported by quantum chemical DFT calculations. These effects depend on the type of anion added and its concentration, and may be rationalized by the binding affinity of the Z-1 hosts to anions. This affinity primarily depends on two factors: anion basicity (F > MeCO<sub>2</sub> > PhCO<sub>2</sub> ~  $H_2PO_4$  > HSO<sub>4</sub> >> Br) and the geometric match between the anion and binding groups of Z-1. Therefore, the highest rate constant enhancement and largest red shifts of the  $\pi$ - $\pi^*$  band are observed for the acetate anion, which is highly basic and has geometry complementary to the urea group<sup>18,28</sup> (209 and 13 for Z-1a and Z-1b, respectively), whereas the bulky and weakly basic Br<sup>-</sup> anion only influences  $k_{\Lambda}$ marginally. In continuation, we decided to investigate the exact influence of the anion concentration on the thermal  $Z \rightarrow E$ isomerisation of Z-1 in detail. Assuming that the anion modifies the thermal rate constant according to the binding affinity of the AB derivatives used, and that the equilibria shown in Scheme 2

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are valid, we can conclude that the observed kinetic rate constant describing  $Z \rightarrow E$  isomerisation depends on three parameters: namely the association constant of the *Z*-isomer with the anion ( $K_{a,Z}$ ), and two first-order rate constants for free *Z*-**1** ( $k_1$ ) and its saturated complex with the corresponding anion ( $k_2$ ).

Z-H + G 
$$\xrightarrow{k_1} E$$
-H + G  
 $K_{a,Z}$   $K_{a1,E}$   $K_{a2,E}$   
Z-HG  $\xrightarrow{k_2} E$ -HG  $\xleftarrow{k_{a2,E}} E$ -HG<sub>2</sub>

**Scheme 2** Equilibria describing anion complexation and  $Z \rightarrow E$  thermal isomerization in solution, H – host, G – guest.

After solving the equations describing the above equilibria we arrive at eqn (1), which affords the concentration of the complex of Z-H with an anion at any given time, and eqn (2), which describes the dependence of the observed first-rate constant on the initial concentration of the guest (assuming that  $[G]_0 \cong [G]$ ).

$$[Z - HG]_{J} = [Z - HG]_{0} e^{-\kappa t}$$
(1)  
$$\kappa_{obs} \equiv f_{H}k_{1} + f_{HG}k_{2} = \frac{k_{1} + k_{2}K_{a,Z}[G]_{0}}{1 + K_{a,Z}[G]_{0}}$$
(2)

And so, the parameters of interest from eqn (2) ( $K_{a,Z}$  and  $k_2$ ) could be determined using a nonlinear regression technique with experimentally determined rate constants for various quantities of added guest.<sup>29</sup> The representative results of this approach for complexes of *Z*-1 with a benzoate anion are shown in Figure 3.



Fig. 3 Change in the observed first-order rate constant of thermal  $Z \rightarrow E$  isomerization of receptors Z-1a (red diamonds) and Z-1b (blue diamonds) upon addition of TBA benzoate determined under isothermal conditions (298.0±0.1 K) by UV-Vis spectroscopy, errors estimated to be less than 5%.

Evaluation of the data indicates that the dependence between guest added and observed rate constant is accurately described by non-linear fitting using Eq. 2 and provides precise values for both association constants  $K_a$  for *Z*-**1** and rates of back-isomerization for the saturated anionic complex. Unlike routinely used titration under <sup>1</sup>H NMR control, this method is independent

of the host concentration, and prior determination of the association constant for the E-isomer is not necessary. Interestingly, Z-1a binds benzoate 4.5 times stronger than Z-1b. The explanation of such phenomena appears to be nontrivial,<sup>30</sup> and we plan to investigate this issue in detail in the future. On the other hand, as expected, higher rate constant enhancement  $(k_{2}/k_{1})$  is observed for Z-1a than for Z-1b, which corresponds with the former's lower ability to diffuse electronic density (vide supra). Notably, these findings are fully consistent with the early work of Shinkai who has shown that thermal isomerization of azacrown ethers is hampered by certain cations.<sup>31</sup> Although corresponding binding constants with Z-isomer were not reported, we can conclude that the most strongly bound cations with a large ionic radius (Rb<sup>+</sup> and Cs<sup>+</sup>) caused the highest inhibition of this process. Furthermore, to our knowledge, there are no contraindications to using our procedure in this case. Finally, for the purpose of validating this method we determined the affinities of hosts 1 to benzoate anions using the <sup>1</sup>H NMR titration technique in DMSO + 0.5% H<sub>2</sub>O, which provides very consistent results ( $K_a$  = 1130 and 230 M<sup>-1</sup> for Z-1a and Z-1b, respectively). In addition, <sup>1</sup>H NMR titrations reveal a lack of selectivity between Z-1a and E-1a ( $K_a = 1290 \text{ M}^{-1}$ ), which is in full accordance with DFT calculations. Interestingly, for E-1b the first binding constant ( $K_{a,1} = 990 \text{ M}^{-1}$ ) is 3 times higher than for Z-1b, which could partially be attributed to repulsion between the phenyl rings of Z-1b and the benzoate.

In conclusion, we obtained two photoswitchable AB derivatives 1 which readily undergo photo and thermal isomerization. E and Z isomers possess different spatial arrangements of binding pockets, which affect their binding properties. In our studies, the more compact Z-1b bound anions more weakly and in a 1:1 fashion, whereas the corresponding E-1b bound them more strongly and in a 1:2 mode. It seems evident that varying the anions and their concentration can be used for precise control of the thermal  $Z \rightarrow E$  isomerization rates and these changes could be easily hindered by the simple addition of an acid, and restored again by the addition of the base. This approach would seem to be important for biological applications, as has been shown in several reports devoted to AB photoswitches.32-34 Finally, we show that kinetic data could be used as a simple and accurate method for determining both the association constant for the Zisomer with an ionic guest and the maximum rate constant change for the thermal  $Z \rightarrow E$  isomerisation. The influence of variously substituted azobenzene core receptors, based on 1, on anion recognition and E-Z isomerization is currently under study in our laboratory.

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#### Notes and references

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<sup>†</sup> Electronic Supplementary Information (ESI) available: Synthesis and characterization of hosts **1**, details of quantum calculations, photoisomerisation, and binding studies; Cartesian coordinates and visualization of MOs of the compounds studied, see DOI: 10.1039/c000000x/

- H. Dürr and H. Bouas-Laurent, *Photochromism: Molecules and Systems: Molecules and Systems*, Elsevier Science, 2003.
- W. Szymański, J. M. Beierle, H. A. V. Kistemaker, W. A. Velema and B. L. Feringa, *Chem. Rev.*, 2013, **113**, 6114-6178.
- C. Brieke, F. Rohrbach, A. Gottschalk, G. Mayer and A. Heckel, Angew. Chem., Int. Ed., 2012, 51, 8446-8476.
- H. M. D. Bandara and S. C. Burdette, *Chem. Soc. Rev.*, 2012, 41, 1809-1825.
- A. A. Beharry and G. A. Woolley, *Chem. Soc. Rev.*, 2011, 40, 4422-4437.
- 6. E. Merino, Chem. Soc. Rev., 2011, 40, 3835-3853.
- J. Garcia-Amorós, M. Díaz-Lobo, S. Nonell and D. Velasco, *Angew. Chem.*, *Int. Ed.*, 2012, 51, 12820-12823.
- J. A. Ihalainen, J. Bredenbeck, R. Pfister, J. Helbing, L. Chi, I. H. M. van Stokkum, G. A. Woolley and P. Hamm, *Proc. Natl. Acad. Sci.* USA, 2007, 104, 5383-5388.
- 9. J.-H. Ha and S. N. Loh, Chem. Eur. J., 2012, 18, 7984-7999.
- D. Bléger, J. Schwarz, A. M. Brouwer and S. Hecht, J. Am. Chem. Soc., 2012, 134, 20597-20600.
- 11. J. M. Granda and J. Jurczak, Chem. Eur. J., 2014, 20, 12368-12372.
- K. Dąbrowa, M. Pawlak, P. Duszewski and J. Jurczak, Org. Lett., 2012, 14, 6298-6301.
- P. Dydio, D. Lichosyt and J. Jurczak, Chem. Soc. Rev., 2011, 40, 2971-2985.
- D. E. Gomez, L. Fabbrizzi, M. Licchelli and E. Monzani, *Org. Biomol. Chem.*, 2005, 3, 1495-1500.
- P. A. Gale, N. Busschaert, C. J. E. Haynes, L. E. Karagiannidis and I. L. Kirby, *Chem. Soc. Rev.*, 2014, 43, 205-241.
- For recent example, see: K.-S. Jeong,Y. R. Choi,G. C. Kim,H.-G. Jeon,J. Park and W. Namkung, Chem. Commun., 2014, doi:10.1039/C4CC07560A, for the recent review, see: S. Lee and A. H. Flood, J. Phys. Org. Chem., 2013, 26, 79-86.
- V. Amendola,L. Fabbrizzi and L. Mosca, Chem. Soc. Rev., 2010, 39, 3889-3915.
- A.-F. Li, J.-H. Wang, F. Wang and Y.-B. Jiang, Chem. Soc. Rev., 2010, 39, 3729-3745.
- In all UV-Vis experiments we used 5•10-5 M concentration of the host 1 and DMSO+0.5% water as a solvent mixture.
- 20. L. M. Schwartz and R. I. Gelb, Anal. Chem., 1978, 50, 1592-1594.
- 21. T. Asano and T. Okada, J. Org. Chem., 1986, 51, 4454-4458.
- 22. J. Dokic, M. Gothe, J. Wirth, M. V. Peters, J. Schwarz, S. Hecht and P. Saalfrank, *J. Phys. Chem. A*, 2009, **113**, 6763-6773.
- N. Nishimura, T. Sueyoshi, H. Yamanaka, E. Imai, S. Yamamoto and S. Hasegawa, *Bull. Chem. Soc. Jpn.*, 1976, 49, 1381-1387.
- 24. In comparison, structurally similar urea-based host reported in ref 26 back-isomerize in the matter of seconds in the polar environment.
- A. A. Blevins and G. J. Blanchard, J. Phys. Chem. B., 2004, 108, 4962-4968.
- O. Sadovski, A. A. Beharry, F. Zhang and G. A. Woolley, *Angew. Chem.*, *Int. Ed.*, 2009, 48, 1484-1486.

- Control experiments with H3PO4 and Et3N reveal that pH has virtually no effect on the thermal Z-E isomerisation of Z-1, which is common for push-pull ABs (see A. M. Sanchez and R. H. Rossi, J. Org. Chem., 1995, 60, 2974-2976).
- B. P. Hay, T. K. Firman and B. A. Moyer, J. Am. Chem. Soc., 2005, 127, 1810-1819.
- 29. C. Bohne, Chem. Soc. Rev., 2014, 43, 4037-4050.
- 30. The reports available in the literature on photoswitchable anion receptors are inconclusive in this regard, see ref 16.
- S. Shinkai, T. Nakaji, T. Ogawa, K. Shigematsu and O. Manabe, J. Am. Chem. Soc., 1981, 103, 111-115.
- M. R. Banghart, M. Volgraf and D. Trauner, *Biochemistry*, 2006, 45, 15129-15141.
- P. Gorostiza, M. Volgraf, R. Numano, S. Szobota, D. Trauner and E. Y. Isacoff, *Proc. Natl. Acad. Sci. USA*, 2007, **104**, 10865-10870.
- A. A. Beharry, L. Wong, V. Tropepe and G. A. Woolley, *Angew. Chem.*, *Int. Ed.*, 2011, 50, 1325-1327.

4 | J. Name., 2012, 00, 1-3