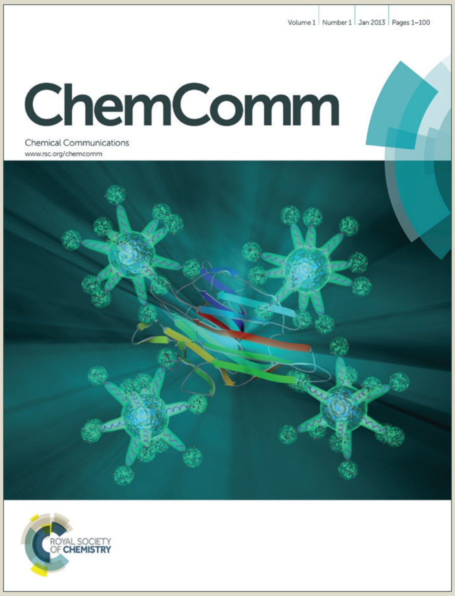
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name RSCPublishing

COMMUNICATION

A supramolecular keypad lock

Cite this: DOI: 10.1039/x0xx00000x

Cátia Parente Carvalho,[a] Zoe Domínguez,[a] José Paulo Da Silva[b] and Uwe Pischel[a]*

Received 00th January 2012,
Accepted 00th January 2012

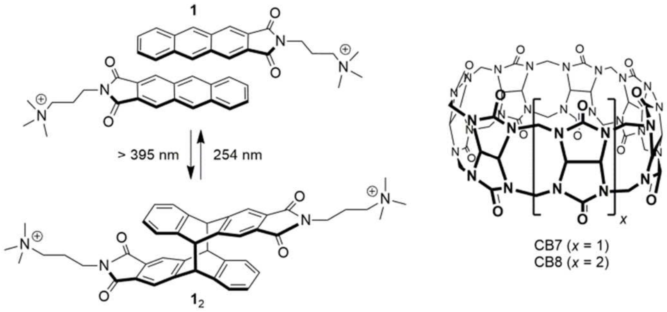
DOI: 10.1039/x0xx00000x

www.rsc.org/

The reversible photoswitching between an anthracene derivative and its [4+4] dimer, using the template effect of the CB8 macrocycle, was demonstrated. This example of supramolecular chemistry in water was harnessed to demonstrate the operation of a keypad lock device that is driven by means of light and chemicals as inputs.

The use of molecular species for achieving information processing of chemical, photonic or electrochemical signals according to the principles of binary coding (0 and 1) and Boolean language continues to receive wide attention.[1-3] The challenge of the design of molecules that are capable of a pre-determined logic operation has received important backup from smart applications of molecular logic gates in sensing, drug delivery, theranostics, and materials chemistry.[4-10] Among the different logic operations, those that imply a memory function belong to the most demanding ones in terms of their chemical design.[11] This type of logic, known as sequential logic, results in differentiated outputs depending on the input history of the device. Current research activities along these lines have their focus on the implementation of flip-flops and molecular keypad locks. Photochromic switches have been often exploited for these purposes.[12-15] However, also chemically-addressable systems served for the demonstration of molecular keypad locks[16-19] and redox-switchable devices were used as flip-flops.[20, 21]

Surprisingly, the exploitation of supramolecular host-guest phenomena for the demonstration of keypad lock functions has no precedence in the literature. In recent works host-guest complexes with cucurbit[7]uril (CB7) and cucurbit[8]uril (CB8) were used to demonstrate the reconfigurable and resettable operation of logic gates in aqueous solution.[22, 23] Cucurbiturils have drawn much attention for their very high binding constants of cationic guests (up to 10^{17} M^{-1})[24] and their supramolecular application potential with a strong focus on biological and pharmacological contexts, and analytical problems is beginning to reveal.[25-35]



Scheme 1 Reversible photoswitching between the anthracene derivative **1** and its photodimer **1**$_2$; structures of CB7 and CB8.

In the present work we take advantage of the specific complexation properties of the CB8 macrocycle. Unlike the smaller homologues CB6 and CB7, that commonly offer space for only one guest molecule, the larger CB8 accommodates often two guests and the resulting complexes may feature new emission properties (e.g., excimer fluorescence) or lead to fluorescence self-quenching.[35-38] Additionally, the resulting pre-organization of the two guests may facilitate intracomplex photoreactions that would not happen at the dilute concentrations of the free dye molecules.[38-40] In a wider context, host-templated photodimerizations have been used for the design of photoswitchable supramolecular polymers.[40-42]

Herein we designed the anthracene derivative **1** (see ESI for details on the synthesis and Scheme 1 for the structure) which contains a positively charged tetraalkylammonium side chain, known to interact efficiently with the carbonyl-lined portals of CB8. The aromatic parts of the guests should be immersed in the hydrophobic inner cavity of the host macrocycle leading to a 2:1 (guest:host) complex. This situation can give rise to a template effect in a [4+4] photodimerization,[40] a well-known photoreaction of anthracenes.[43] The ammonium arms are expected to be oriented in opposite directions occupying the two portals of the macrocycle and thereby avoiding destabilization of the complex by electrostatic repulsion of the positive charges. This binding mode and the long-axis symmetry of **1** would lead to a single dimerization product ($\mathbf{1}_2$; see Scheme 1). A drawback for photoswitching are undesired secondary photoreactions that can hamper the efforts to achieve complete reversibility by cycloreversion of the photodimer.[40] Photooxidation reactions of anthracenes may interfere, especially when working with highly energetic UV light in aerated solutions. This obstacle can be potentially avoided by using electron-poor aromatic systems such as dye **1**.

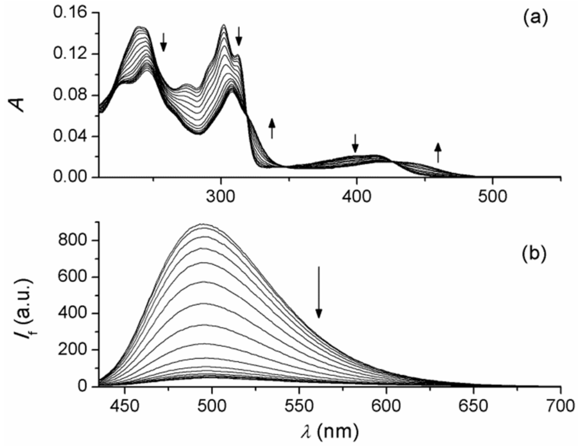


Fig 1 Spectral changes of the UV/vis absorption (a) and the fluorescence (b) upon titration of **1** (3.6 μM) with CB8 (0-6.2 μM) in pH-neutral aqueous solution.

With these design outsets we started the characterization of the supramolecular interactions between dye **1** and CB8. In the titration of a 10 μM aqueous solution of **1** with CB8 at neutral pH significant changes in the UV/vis absorption spectrum were observed (see Fig. 1a). The characteristic long-wavelength absorption of free **1** at λ_{max} = 412 nm is bathochromically shifted. The uniformity of the interaction was confirmed by the occurrence of various isosbestic points at 319, 350, and 427 nm. The absorption titration curve levelled-off sharply at ca. 0.5 equivalents of CB8, pointing to the predicted formation of the **1•1•**CB8 complex (see ESI). This stoichiometry was independently verified by Job's method (see ESI). In electrospray-ionization mass spectrometry the existence of the 2:1 complex was also corroborated for the gas phase (see ESI). Furthermore, ^{1}H NMR studies evidenced pronounced upfield shifts of the aromatic proton signals of the guest dye, coinciding with its deep immersion into the CB8 macrocycle (see ESI). The fluorescence of **1** (λ_{max} = 494 nm, Φ_f = 0.44, τ_f = 6.72 ns) underwent significant variations in the course of the titration with the CB8 host, leading to the observation of a strong emission quenching; see Fig. 1b. This is explained with an enhanced non-radiative deactivation caused by π-π interactions between the face-to-face organized aromatic guest molecules. The fitting of the titration data gave a binding constant of $K = 4.5 \times 10^{12}$ M^{-2}, which is indicative of a strong supramolecular interaction and the avoidance of electrostatic repulsion of the positively charged arms of **1** (see above).

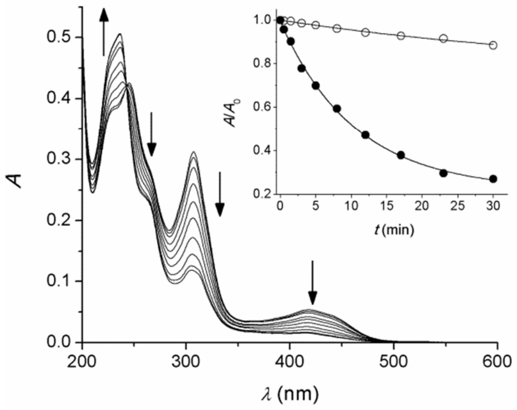


Fig 2 UV/vis absorption spectral changes upon irradiation of **1** (10 μM) in the presence of CB8 (5 μM) at λ > 395 nm in pH-neutral aqueous solution. The inset shows the kinetic curves and the mono-exponential fittings for the irradiation of **1** in absence (empty circles) and presence of CB8 (filled circles); observation at 412 nm (free dye) or 424 nm (presence of CB8).

Having established the strong binding of **1** to CB8, the intracomplex photodimerization of the dye was attempted. Irradiation (150 W Xe-lamp, λ_{exc} > 395 nm) of a diluted solution of **1** (10 μM in neutral water) in the presence of CB8 (5 μM) resulted in a uniform photoreaction that was followed by UV/vis absorption spectroscopy, liquid chromatography, and NMR spectroscopy (see ESI). Under the applied conditions ca. 75% of the long-wavelength absorption band (between ca. 350 and 500 nm) of the complex depleted within 30 min of irradiation; Fig. 2. In comparison, the free dye (i.e., in absence of CB8) showed only ca. 10% decrease of the long-wavelength absorption band under identical irradiation conditions (inset of Fig. 2). Hence, a much faster photoreaction (by a factor of ca. 10) resulted in the presence of CB8. By means of liquid chromatography with mass spectrometric detection the CB8-templated formation of the dimerization product was unequivocally confirmed by the observation of a molecular ion peak at m/z = 347 with an isotope pattern spacing of Δm = 0.5 amu (see ESI). ^{1}H NMR studies provided structural proof for the formation of photodimer $\mathbf{1}_2$. Namely, pronounced changes in the aromatic region and a new signal at ca. 4.4 ppm, indicative of the bridgehead protons of the dimer, were detected (see ESI). On the other hand, no photodimer was noted for the irradiation of the noncomplexed dye at λ > 395 nm (see ESI).[†] The cycloreversion of the photodimer $\mathbf{1}_2$ (see Scheme 1) back to the monomeric dye **1** was achieved by irradiation at 254 nm for a short period of time (30 s). The efficient back reaction was signalled by the recovery of more than 90% of **1** as rated by UV/vis absorption spectroscopy. Also in the ^{1}H NMR spectra the recovery of the aromatic signals that correspond to the complexed monomeric dye and the concomitant disappearance of the respective photodimer signals was evident (see ESI). The recycling of the dimerization/cycloreversion sequence was shown for at least 5 cycles, submitting the CB8 complexes to successive irradiations at > 395 nm and 254 nm (see ESI).

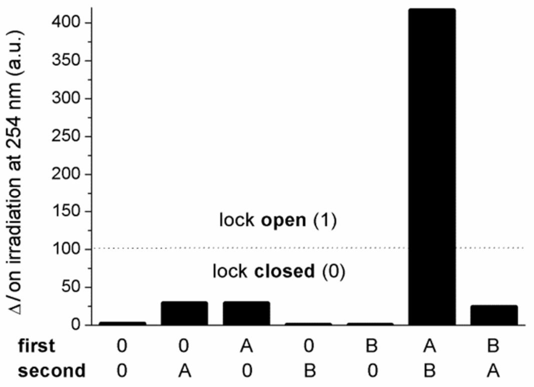
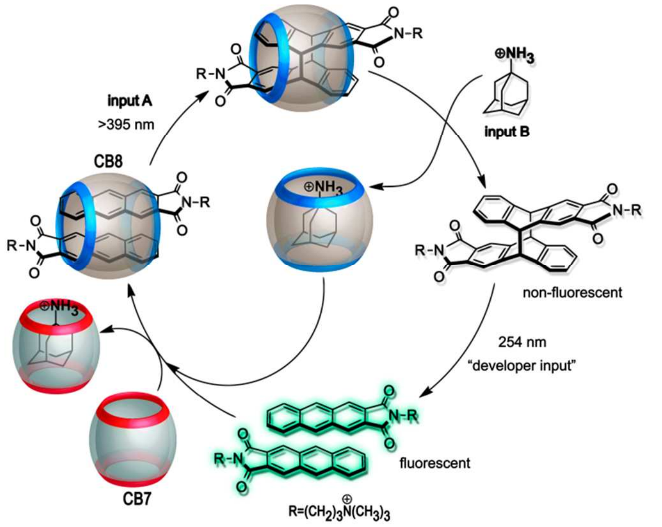


Fig 3 Operation of the supramolecular keypad lock (10 μM **1**, 5 μM CB8) upon application of the corresponding inputs (A: irradiation at λ > 395 nm for 45 min; B: addition of 1-aminoadamantane; 20 μM). The output is read as change of the fluorescence upon irradiation at 254 nm for 30 s. The dotted line shows the threshold. With respect to Input A, stronger light sources would enable the shortening of the irradiation time. Note that the input combinations contemplate that also one or both inputs may not be activated (binary 0).

The described CB8-template effect on the photodimerization of **1** as well as the reversible photoswitching form the chemical basis for the realization of the announced supramolecular keypad lock (see Scheme 2). For this purpose the inputs were chosen as the irradiation at λ > 395 nm (input A) and the addition of the strongly binding competitor 1-aminoadamantane (input B).[35, 44] Noteworthy, the latter is able to displace the monomeric dye **1** as well as the dimer $\mathbf{1}_2$ from the CB8 macrocycle. The output of the system was defined as the observation of noncomplexed photodimer. The detection of this situation would in principle demand a cumbersome analysis, for example, by NMR spectroscopy. In order to visualize the output situation more conveniently, the irradiation at 254 nm ("developer input" in Scheme 2) together with monitoring the resulting change of the fluorescence intensity ($\Delta I = I_{254} - I_0$; the subscripts 254 and 0 refer to after and before irradiation at 254 nm, respectively) was employed. The photodimer $\mathbf{1}_2$ is non-fluorescent both in absence and presence of CB8. However, the cycloreversion of the noncomplexed dimer back to **1** is accompanied by a recovery of the fluorescence, while the same process inside CB8 leads to no significant fluorescence increase due to efficient quenching (see ESI). In accordance, the only high output in form of ΔI (being defined as binary 1 and corresponding to the situation of the *open lock*) was observed for the sequential input order of first A and then B. This coincides with the formation of noncomplexed photodimer (see Scheme 2). All other combinations led to no photodimer (input combinations 00, B0, 0B, BA) or the formation of photodimer residing inside the CB8 cavity (A0 and 0A), see Fig. 3.

The resetting of the system to its initial state would be a valuable asset. The reversible nature of the photoreaction and of the involved supramolecular interactions enable such feature. Taking for example the situation of the open keypad lock (illustrated in Scheme 2), the competitor 1-aminoadamantane is encapsulated by CB8 ($K = 3.3 \times 10^{7}\ \mathrm{M}^{-1}$)[35] and the dye **1** is a noncomplexed species after application of the "developer input" (see Scheme 2). Given the fact that the binding constant of 1-aminoadamantane to CB7 is three orders of magnitude larger ($K = 1.2 \times 10^{10}\ \mathrm{M}^{-1}$)[35] than for CB8 and that dye **1** has a much smaller binding constant with CB7 ($K = 3.0 \times 10^{5}\ \mathrm{M}^{-1}$; this work), thermodynamic self-sorting can be used to achieve resetting.[44] Indeed, the addition of CB7 to the mixture that was obtained after irradiation at 254 nm led to the complexation of 1-aminoadamantane by CB7 and of **1** by CB8, thereby closing the cycle shown in Scheme 2. The spectral signature of the **1•1•**CB8 complex was re-constituted by addition of CB7 (see ESI). At this point the logic operations can be repeated. This was shown for 5 cycles, after which a fatigue effect of ca. 30% was noted (see ESI). A concentration optimization of the 4 components that are involved in the resulting intricate multi-equilibrium situation[45] should improve the performance further.



Scheme 2 Supramolecular keypad lock by applying the correct input order, reading the output with the help of the "developer input", and resetting by CB7.

Conclusions

The anthracene dye **1** forms a reversibly photoswitchable complex with CB8, harnessing the template effect exerted by the organic macrocycle.[40] This was used to demonstrate a supramolecular keypad lock where the formation of noncomplexed photodimer, indirectly signalled by the fluorescence enhancement upon photoinduced cycloreversion, was the output. Only by application of the right input order (first irradiation at λ > 395 nm and then addition of 1-aminoadamantane) the lock was opened. By exploitation of self-sorting on addition of CB7 the system was reset to the initial **1•1•**CB8 complex. These results demonstrate the utility of cucurbituril chemistry for the realization of resettable complex logic operations with all-organic systems in aqueous solution. Applications as functional switches in bio-relevant contexts are foreseen.

The financial support by the Spanish MINECO (CTQ2011-28390 for U.P), the COST Action “Supramolecular Chemistry in Water” (CM1005), and the Portuguese FCT

(REEQ/717/QUI/2005 for J.P.S and PhD grant SFRH/BD/81628/2011 for C.P.C) is gratefully acknowledged.

Notes and references

[a] CIQSO - Center for Research in Sustainable Chemistry and Department of Chemical Engineering, Physical Chemistry and Organic Chemistry, University of Huelva, Campus El Carmen s/n, E-21071 Huelva, Spain. Fax: +34 959 21 99 83; Tel: +34 959 21 99 82; E-mail: uwe.pischel@diq.uhu.es.

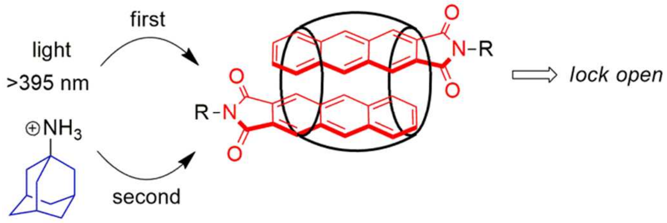
[b] Faculdade de Ciências e Tecnologia, Universidade do Algarve, Campus de Gambelas, 8005-139 Faro, Portugal.

† Applying the Stern-Volmer formalism and the fluorescence lifetime of **1** (see text) leads to the conclusion that even a diffusion-controlled [4+4] photodimerization (k_{diff} ca. 10^{10} $M^{-1}s^{-1}$) of noncomplexed **1** would be very inefficient (< 1%) in diluted solution (10 μM).

Electronic Supplementary Information (ESI) available: Details on experimental conditions, synthesis of **1**, supramolecular and photochemical characterization, resetting, mass spectrometry, NMR spectroscopy, and liquid chromatography. See DOI: 10.1039/c000000x/

1. K. Szaciłowski, *Chem. Rev.*, 2008, **108**, 3481-3548.
2. J. Andréasson and U. Pischel, *Chem. Soc. Rev.*, 2010, **39**, 174-188.
3. A. P. de Silva, *Molecular Logic-based Computation*, The Royal Society of Chemistry, Cambridge, 2013.
4. A. P. de Silva, M. R. James, B. O. F. McKinney, D. A. Pears and S. M. Weir, *Nat. Mater.*, 2006, **5**, 787-790.
5. M. Hammarson, J. Andersson, S. M. Li, P. Lincoln and J. Andréasson, *Chem. Commun.*, 2010, **46**, 7130-7132.
6. Z. Xie, L. Wroblewska, L. Prochazka, R. Weiss and Y. Benenson, *Science*, 2011, **333**, 1307-1311.
7. M. Elstner, K. Weisshart, K. Müllen and A. Schiller, *J. Am. Chem. Soc.*, 2012, **134**, 8098-8100.
8. S. J. Chen, Y. H. Yang, Y. Wu, H. Tian and W. H. Zhu, *J. Mater. Chem.*, 2012, **22**, 5486-5494.
9. S. Erbas-Cakmak and E. U. Akkaya, *Angew. Chem. Int. Ed.*, 2013, **52**, 11364-11368.
10. U. Pischel, J. Andréasson, D. Gust and V. F. Pais, *ChemPhysChem*, 2013, **14**, 28-46.
11. U. Pischel, *Angew. Chem. Int. Ed.*, 2010, **49**, 1356-1358.
12. J. Andréasson, S. D. Straight, T. A. Moore, A. L. Moore and D. Gust, *Chem. Eur. J.*, 2009, **15**, 3936-3939.
13. J. Andréasson, U. Pischel, S. D. Straight, T. A. Moore, A. L. Moore and D. Gust, *J. Am. Chem. Soc.*, 2011, **133**, 11641-11648.
14. P. Remón, M. Bälter, S. M. Li, J. Andréasson and U. Pischel, *J. Am. Chem. Soc.*, 2011, **133**, 20742-20745.
15. Q. Zou, X. Li, J. J. Zhang, J. Zhou, B. B. Sun and H. Tian, *Chem. Commun.*, 2012, **48**, 2095-2097.
16. Z. Q. Guo, W. H. Zhu, L. J. Shen and H. Tian, *Angew. Chem. Int. Ed.*, 2007, **46**, 5549-5553.
17. D. Margulies, C. E. Felder, G. Melman and A. Shanzer, *J. Am. Chem. Soc.*, 2007, **129**, 347-354.
18. M. Kumar, R. Kumar and V. Bhalla, *Chem. Commun.*, 2009, 7384-7386.
19. B. Rout, P. Milko, M. A. Iron, L. Motiei and D. Margulies, *J. Am. Chem. Soc.*, 2013, **135**, 15330-15333.
20. G. de Ruiter, L. Motiei, J. Choudhury, N. Oded and M. E. van der Boom, *Angew. Chem. Int. Ed.*, 2010, **49**, 4780-4783.
21. G. de Ruiter, E. Tartakovsky, N. Oded and M. E. van der Boom, *Angew. Chem. Int. Ed.*, 2010, **49**, 169-172.
22. U. Pischel, V. D. Uzunova, P. Remón and W. M. Nau, *Chem. Commun.*, 2010, **46**, 2635-2637.
23. C. Gao, S. Silvi, X. Ma, H. Tian, M. Venturi and A. Credi, *Chem. Commun.*, 2012, **48**, 7577-7579.
24. L. P. Cao, M. Šekutor, P. Y. Zavalij, K. Mlinarić-Majerski, R. Glaser and L. Isaacs, *Angew. Chem. Int. Ed.*, 2014, **53**, 988-993.
25. A. Hennig, H. Bakirci and W. M. Nau, *Nat. Methods*, 2007, **4**, 629-632.
26. J. M. Chinai, A. B. Taylor, L. M. Ryno, N. D. Hargreaves, C. A. Morris, P. J. Hart and A. R. Urbach, *J. Am. Chem. Soc.*, 2011, **133**, 8810-8813.
27. C. Parente Carvalho, V. D. Uzunova, J. P. Da Silva, W. M. Nau and U. Pischel, *Chem. Commun.*, 2011, **47**, 8793-8795.
28. R. N. Dsouza, U. Pischel and W. M. Nau, *Chem. Rev.*, 2011, **111**, 7941-7980.
29. D.-W. Lee, K. M. Park, M. Banerjee, S. H. Ha, T. Lee, K. Suh, S. Paul, H. Jung, J. Kim, N. Selvapalam, S. H. Ryu and K. Kim, *Nat. Chem.*, 2011, **3**, 154-159.
30. F. Biedermann, E. Elmalem, I. Ghosh, W. M. Nau and O. A. Scherman, *Angew. Chem. Int. Ed.*, 2012, **51**, 7739-7743.
31. D. Ma, G. Hettiarachchi, D. Nguyen, B. Zhang, J. B. Wittenberg, P. Y. Zavalij, V. Briken and L. Isaacs, *Nat. Chem.*, 2012, **4**, 503-510.
32. F. Biedermann and W. M. Nau, *Angew. Chem. Int. Ed.*, 2014, **53**, 5694-5699.
33. H. H. Lee, T. S. Choi, S. J. C. Lee, J. W. Lee, J. Park, Y. H. Ko, W. J. Kim, K. Kim and H. I. Kim, *Angew. Chem. Int. Ed.*, 2014, **53**, 7461-7465.
34. J. P. Da Silva, R. Choudhury, M. Porel, U. Pischel, S. Jockusch, P. C. Hubbard, V. Ramamurthy and A. V. M. Canário, *ACS Chem. Biol.*, 2014, **9**, 1432-1436.
35. J. Vázquez, P. Remón, R. N. Dsouza, A. I. Lazar, J. F. Arteaga, W. M. Nau and U. Pischel, *Chem. Eur. J.*, 2014, **20**, 9897-9901.
36. R. B. Wang, L. Yuan, H. Ihmels and D. H. Macartney, *Chem. Eur. J.*, 2007, **13**, 6468-6473.
37. J. Mohanty, S. Dutta Choudhury, H. P. Upadhyaya, A. C. Bhasikuttan and H. Pal, *Chem. Eur. J.*, 2009, **15**, 5215-5219.
38. B. C. Pemberton, R. K. Singh, A. C. Johnson, S. Jockusch, J. P. Da Silva, A. Ugrinov, N. J. Turro, D. K. Srivastava and J. Sivaguru, *Chem. Commun.*, 2011, **47**, 6323-6325.
39. C. Yang, T. Mori, Y. Origane, Y. H. Ko, N. Selvapalam, K. Kim and Y. Inoue, *J. Am. Chem. Soc.*, 2008, **130**, 8574-8575.
40. F. Biedermann, I. Ross and O. A. Scherman, *Polym. Chem.*, 2014, **5**, 5375-5382.
41. Q. W. Zhang, D.-H. Qu, X. Ma and H. Tian, *Chem. Commun.*, 2013, **49**, 9800-9802.
42. Q. W. Zhang, D.-H. Qu, J. C. Wu, X. Ma, Q. C. Wang and H. Tian, *Langmuir*, 2013, **29**, 5345-5350.
43. H. Bouas-Laurent and J.-P. Desvergne, in *Photochromism: Molecules and Systems*, eds. H. Dürr and H. Bouas-Laurent, Elsevier, Amsterdam, 2003, pp. 561-630.
44. S. M. Liu, C. Ruspic, P. Mukhopadhyay, S. Chakrabarti, P. Y. Zavalij and L. Isaacs, *J. Am. Chem. Soc.*, 2005, **127**, 15959-15967.
45. Q. W. Zhang and H. Tian, *Angew. Chem. Int. Ed.*, 2014, **53**, 10582-10584.

Table of Contents



The first supramolecular keypad lock based on cucurbituril chemistry in water is presented.