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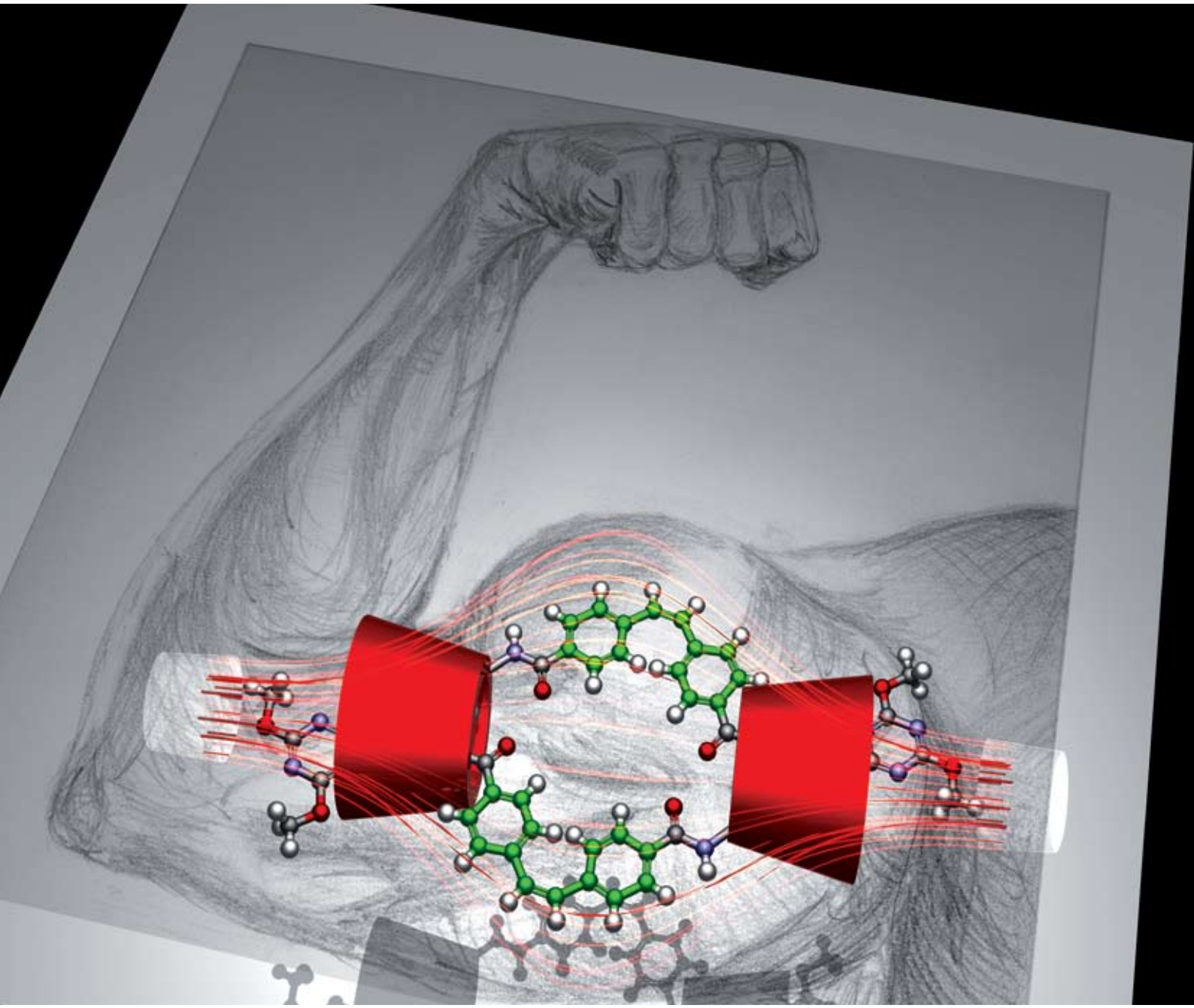

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The foundation of a light driven molecular muscle based on stilbene and α-cyclodextrin†

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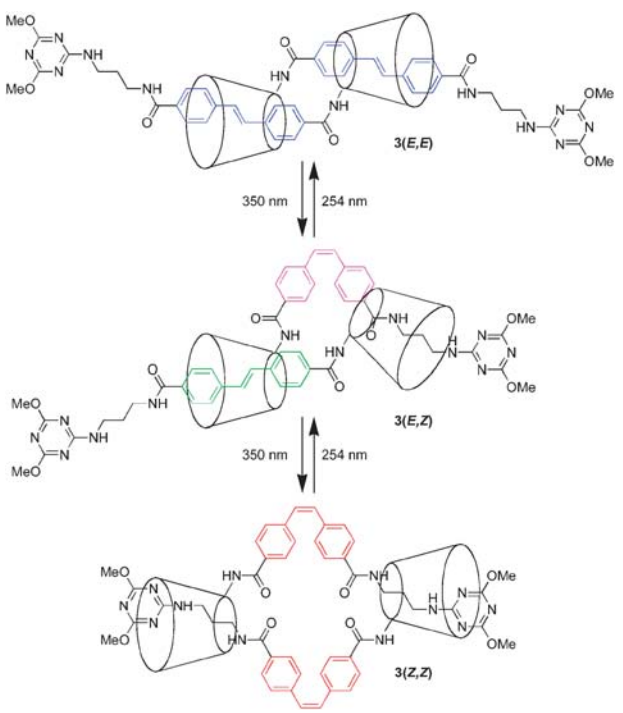
The rotaxane 3(*E*,*E*) serves as the basis of a light driven molecular muscle, where reversible photoisomerisation of the stilbene units causes the cyclodextrins to move off and on the stilbene units, contracting and extending the distance between the blocking groups.

In nature, biological machines perform tasks that enable life to proceed.[1–4] For example, the contraction and expansion of muscle fibres, caused by the simultaneous sliding of the stacked filaments of the myosin and actin upon chemical stimulation by ATP hydrolysis, enables our controlled movement.[3,4] In the pursuit of nanoscale machines, chemists are inspired to mimic nature, to produce synthetic structures that perform tasks at our discretion.[5–9] Recently, examples of molecular mimics of muscle fibres have appeared in the literature.[10–18] Methods for synthesising these have centred on the formation of [2]-rotaxanes, which are well-suited for the construction of molecular machines as the relative motions of their mechanically interlocked components can be controlled.[19,20] Previous examples of molecular muscle fibre mimics have primarily depended on transition metal complexation[10–15] and redox chemistry[16,17] to operate. In this communication we describe the use of α-cyclodextrin (αCD) and a stilbene in the construction of a reversible molecular mimic of a muscle fibre, that instead relies on hydrophobic forces and size constraints, and photochemical isomerisation of the stilbene units, to function.

In aqueous solutions, αCD forms host–guest complexes with hydrophobic guests having the appropriate size to fit inside the CD annulus.[21–25] Hermaphroditic CDs, where the guest is bonded to the CD, form complexes with a doubly threaded topology, termed Janus complexes. Capping these with bulky blocking groups, to prevent dissociation of the components, affords [2]-rotaxanes called c_2-daisy chains.[10,26–29] *trans*-Stilbenes are readily complexed by αCD, much more so than the *cis*-isomers, and the complexes have been capped to give rotaxanes.[30–33] Accordingly, we report the construction of the molecular muscle fibre mimic **3** having a ditopic axle comprising both a stilbene and an aliphatic group for CD binding. Interconversion between the *trans*- and *cis*-stilbene isomers causes the CDs to move between the binding sites, expanding and contracting the distance between the capping groups, as illustrated in Scheme 1. Kaneda and co-workers[18] have reported the synthesis of oligomers of an azobenzene based rotaxane, where the movement resulting from photoisomerisation was not demonstrated but only predicted using molecular simulations. In our case, each of the extended, intermediate and contracted states of the rotaxane **3(*E*,*E*)**, **3(*E*,*Z*)** and **3(*Z*,*Z*)** has been isolated and fully characterised using 2D NMR spectroscopy, thus directly establishing the changes in geometry and function akin to that of a muscle fibre.

The *trans*,*trans*-isomer of the muscle **3(*E*,*E*)** was synthesised as shown in Scheme 2 (see ESI for details†). In the final step, the hermaphroditic cyclodextrin **1** reacted with the dimethoxychlorotriazine **2** to give the rotaxane **3(*E*,*E*)** in 30% yield, after purification using HPLC. The symmetrical dimeric nature of this material was determined from the ESI mass spectrum and the simplicity of the 1D ^{1}H and ^{13}C NMR spectra, while the *trans*-geometry was confirmed by the coupling constant of 16.5 Hz between the olefinic protons in the ^{1}H NMR spectrum. Irradiation at 350 nm of an aqueous solution of the rotaxane **3(*E*,*E*)** gave the *cis*,*trans*- and *cis*,*cis*-isomers **3(*E*,*Z*)** and **3(*Z*,*Z*)**, and recovered starting material, in yields of 21, 11 and 36%, respectively, again after purification through HPLC (Scheme 1). The 1D ^{1}H and ^{13}C NMR spectra of the *cis*,*trans*-isomer **3(*E*,*Z*)**



Scheme 1 Contraction and expansion of the molecular muscle **3**.

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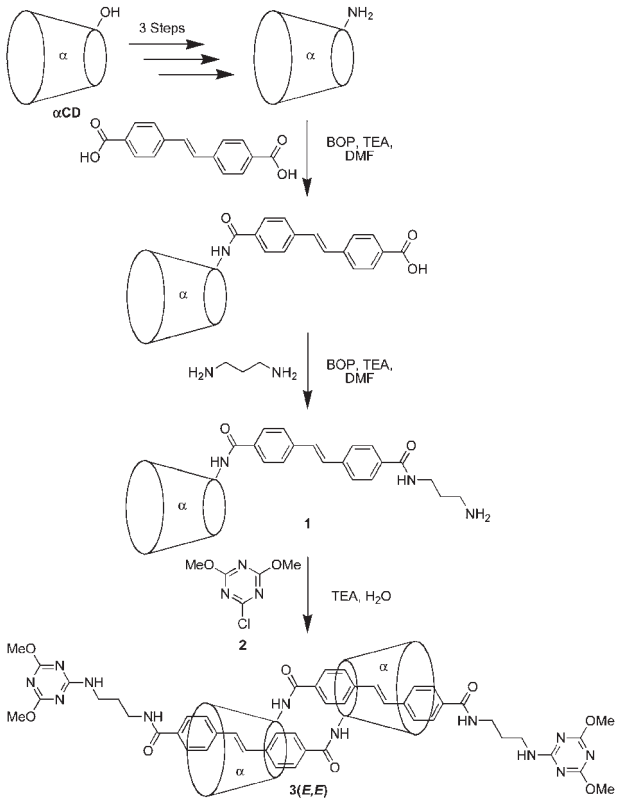

Scheme 2 Synthesis of the hermaphroditic [2]-rotaxane **3(*E*,*E*)**.

show two sets of stilbene resonances, including two pairs of olefinic proton resonances with coupling constants of 12 and 16.5 Hz, while the corresponding spectra of the *cis*,*cis*-rotaxane **3(*Z*,*Z*)** are again characteristic of a symmetric dimer but in this case the ^{1}H NMR coupling constant between the olefinic protons is 12.5 Hz. In aqueous solution, the ultraviolet–visible spectra of the rotaxanes **3(*E*,*E*)** and **3(*Z*,*Z*)** show λ_{max} 334 nm (ε_{max} 105 100) and λ_{max} 305 nm (ε_{max} 10 300), typical of the *trans*- and *cis*-stilbene moieties, respectively. For the *cis*,*trans*-isomer **3(*E*,*Z*)**, λ_{max} 330 nm (ε_{max} 40 000) with a shoulder at lower wavelength is also characteristic.

When the irradiation of the *trans*,*trans*-rotaxane **3(*E*,*E*)** at 350 nm was monitored using ultraviolet–visible spectroscopy and HPLC, some decomposition was observed but a photostationary mixture of the isomers **3(*E*,*E*)**, **3(*E*,*Z*)** and **3(*Z*,*Z*)** formed, in the ratio *ca.* 2 : 2 : 1. This wavelength was chosen based on the ultraviolet–visible spectra, to selectively excite the *trans*-stilbene moieties. Subsequent irradiation with 254 nm light, to target *cis*-stilbene residues, afforded a photostationary mixture of the isomers **3(*E*,*E*)** and **3(*E*,*Z*)** in the ratio *ca.* 6 : 1. These ratios are typical of stilbene photoisomerisations[34] and do not appear to be substantially affected by the presence of a cyclodextrin. The reversibility of the photoinduced interconversion between the rotaxanes **3(*E*,*E*)**, **3(*E*,*Z*)** and **3(*Z*,*Z*)** was studied by preparing a 6.4×10^{-6} M solution of the *trans*,*trans*-isomer **3(*E*,*E*)** in H_2O, and sequentially and repeatedly irradiating it with light of wavelength 350 nm for 3 min, followed by light of wavelength 254 nm for 3 min. Under these conditions, approximately 2–3% decomposition accompanied each cycle (see Fig. S1 in the ESI†).

The structural changes associated with interconversion between the isomers **3(*E*,*E*)**, **3(*E*,*Z*)** and **3(*Z*,*Z*)** were examined by analysing each compound using 2D NMR spectroscopy. A section of the ROESY contour plot of the *trans*,*trans*-rotaxane **3(*E*,*E*)** is shown in Fig. 1. The resonances of the stilbene protons designated B, C and D show NOE interactions with the signals of the CD-H5 protons, while those of the stilbene protons E and F show interactions with the resonances of the CD-H3 protons. The signal of the stilbene protons A shows relatively weak interactions with what could be the resonances of the CD-H6 protons of either the same or the other monomeric unit of the dimer. In any event, the other interactions show that the stilbenes are included within the CD cavities and the structure of the rotaxane **3(*E*,*E*)** is as illustrated in Fig. 1.

For the *cis*,*trans*-rotaxane **3(*E*,*Z*)**, the corresponding section of the ROESY spectrum is shown in Fig. 2. All of the resonances of the *trans*-stilbene moiety show NOE interactions with CD proton signals, whereas the resonances of protons B, C and D of the *cis*-stilbene group do not. *cis*-Stilbene protons A, E and F interact with CD protons and, in the absence of interactions involving protons B, C and D, this indicates that *cis*-stilbene protons A interact with protons of the CD of the same monomeric unit, while E and F interact with protons of the other CD. The structure of the rotaxane **3(*E*,*Z*)** is therefore as illustrated in Fig. 2, where the *trans*-stilbene is included within a CD and the other CD is located over the far end of the *cis*-stilbene and the propyl group. NOE interactions between CD and propyl group protons are indistinguishable from those between different CD protons.

With the *cis*,*cis*-rotaxane **3(*Z*,*Z*)**, for which the most relevant section of the ROESY spectrum is shown in Fig. S2 of the ESI,†

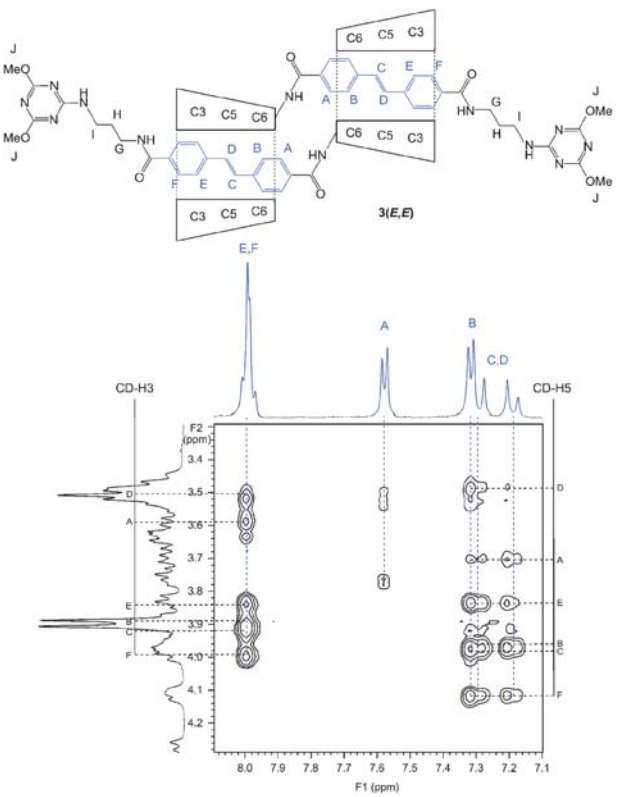

Fig. 1 A section of the 500 MHz ROESY NMR spectrum of the hermaphroditic [2]-rotaxane **3(*E*,*E*)** in D_2O at 25 °C, of the region where crosspeaks are observed between aromatic and cyclodextrin proton signals.

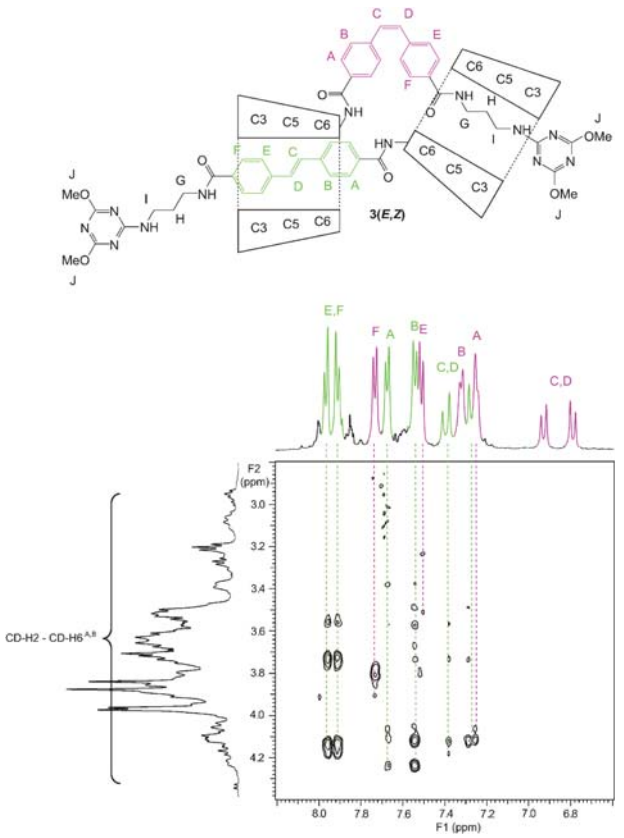

Fig. 2 A section of the 500 MHz ROESY NMR spectrum of the hermaphroditic [2]-rotaxane **3(*E*,*Z*)** in D_2O at 25 °C, of the region where crosspeaks are observed between aromatic and cyclodextrin proton signals.

stilbene protons B–E show no NOE interactions with CD protons. Protons A and F do, logically with protons of the CD of the same monomer and the other CD, respectively. The structure of the rotaxane **3(*Z*,*Z*)** is therefore as illustrated in Fig. 3, with each CD located over the propyl group and far end of the *cis*-stilbene of the other component of the cyclic dimer.

In summary, it follows that *trans*-stilbene moieties are readily accommodated within αCD, while *cis*-stilbene groups are not. Consequently, when irradiation at 350 nm causes photoisomerisation of the *trans*,*trans*-rotaxane **3(*E*,*E*)** to the *cis*,*trans*- and *cis*,*cis*-isomers **3(*E*,*Z*)** and **3(*Z*,*Z*)**, the CDs are moved off the *cis*-stilbene moieties towards the propyl and blocking groups. Irradiation at 254 nm reverses the isomerisation and the movement of the CDs. The movement of the CDs

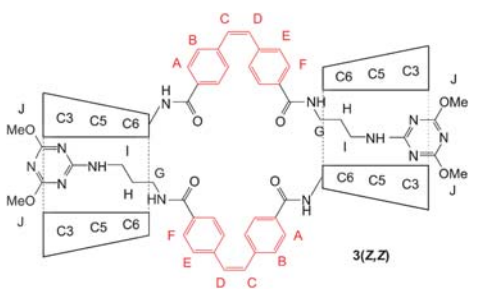

Fig. 3 Structure of the rotaxane **3(*Z*,*Z*)** and proton designations.

off the stilbene shortens the length of the rotaxane **3** and the distance between the blocking groups, so the isomers **3(*E*,*E*)**, **3(*E*,*Z*)** and **3(*Z*,*Z*)** represent the extended, intermediate and contracted states of a reversible, light driven molecular mimic of a muscle fibre (Scheme 1).

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Notes and references

1 J. Howard, *Nature*, 1997, **389**, 561.
2 T. Elston, H. Wang and G. Oster, *Nature*, 1998, **391**, 510.
3 K. Kitamura, M. Tokunaga, A. H. Iwane and T. Yanagida, *Nature*, 1999, **397**, 129.
4 M. A. Geeves, *Nature*, 2002, **415**, 129.
5 D. Philp and J. F. Stoddart, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1154.
6 V. Balzani, A. Credi, S. Silvi and M. Venturi, *Chem. Soc. Rev.*, 2006, **35**, 1135.
7 H. Murakami, A. Kawabuchi, R. Matsumoto, T. Ido and N. Nakashima, *J. Am. Chem. Soc.*, 2005, **127**, 15891.
8 X. Ma, D. Qu, F. Ji, Q. Wang, L. Zhu, Y. Xu and H. Tian, *Chem. Commun.*, 2007, 1409.
9 R. J. Coulston, H. Onagi, S. F. Lincoln and C. J. Easton, *J. Am. Chem. Soc.*, 2006, **128**, 14750.
10 M. C. Jiménez, C. Dietrich-Buchecker and J.-P. Sauvage, *Angew. Chem., Int. Ed.*, 2000, **39**, 3284.
11 J.-P. Collin, C. Dietrich-Buchecker, P. Gaviña, M.-C. Jimenez-Molero and J.-P. Sauvage, *Acc. Chem. Res.*, 2001, **34**, 477.
12 B. X. Colasson, C. Dietrich-Buchecker, M. C. Jimenez-Molero and J.-P. Sauvage, *J. Phys. Org. Chem.*, 2002, **15**, 476.
13 M. C. Jimenez-Molero, C. Dietrich-Buchecker and J.-P. Sauvage, *Chem. Commun.*, 2003, 1613.
14 C. Dietrich-Buchecker, M. C. Jimenez-Molero, V. Sartor and J.-P. Sauvage, *Pure Appl. Chem.*, 2003, **75**, 1383.
15 J.-P. Sauvage, *Chem. Commun.*, 2005, 1507.
16 T. J. Huang, B. Brough, C.-M. Ho, Y. Lui, A. H. Flood, P. A. Bonvallet, H.-R. Tseng, J. F. Stoddart, M. Baller and S. Magonov, *Appl. Phys. Lett.*, 2004, **85**, 5391.
17 Y. Liu, A. H. Flood, P. A. Bonvallet, S. A. Vignon, B. H. Northrop, H.-R. Tseng, J. O. Jeppesen, T. J. Huang, B. Brough, M. Baller, S. Magonov, S. D. Solares, W. A. Goddard, C.-M. Ho and J. F. Stoddart, *J. Am. Chem. Soc.*, 2005, **127**, 9745.
18 S. Tsuda, Y. Aso and T. Kaneda, *Chem. Commun.*, 2006, 3072.
19 S. Saha and J. F. Stoddart, *Chem. Soc. Rev.*, 2007, **36**, 77.
20 E. R. Kay, D. A. Leigh and F. Zerbetto, *Angew. Chem., Int. Ed.*, 2007, **46**, 72.
21 G. Wenz, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 803.
22 S. A. Nepogodiev and J. F. Stoddart, *Chem. Rev.*, 1998, **98**, 1959.
23 C. J. Easton and S. F. Lincoln, *Modified Cyclodextrins: Scaffolds and Templates for Supramolecular Chemistry*, Imperial College Press, London, 1999.
24 A. Harada, *Acc. Chem. Res.*, 2001, **34**, 456.
25 G. Wenz, B.-H. Han and A. Muller, *Chem. Rev.*, 2006, **106**, 782.
26 S. J. Rowan, S. J. Cantrill, J. F. Stoddart, A. J. P. White and D. J. Williams, *Org. Lett.*, 2000, **2**, 759.
27 T. Fujimoto, Y. Sakata and T. Kaneda, *Chem. Commun.*, 2000, 2143.
28 H. Onagi, C. J. Easton and S. F. Lincoln, *Org. Lett.*, 2001, **3**, 1041.
29 S. Tsukagoshi, A. Miyawaki, Y. Takashima, H. Yamaguchi and A. Harada, *Org. Lett.*, 2007, **9**, 1053.
30 C. J. Easton, S. F. Lincoln, A. G. Meyer and H. Onagi, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2501.
31 H. Onagi, B. Carrozzini, G. L. Cascarano, C. J. Easton, A. J. Edwards, S. F. Lincoln and A. D. Rae, *Chem.–Eur. J.*, 2003, **9**, 5971.
32 H. Onagi, C. J. Blake, C. J. Easton and S. F. Lincoln, *Chem.–Eur. J.*, 2003, **9**, 5978.
33 W. Herrmann, S. Wehrle and G. Wenz, *Chem. Commun.*, 1997, 1709.
34 H. Görner and H. J. Kuhn, in *Advances in Photochemistry*, ed. D. C. Neckers, D. H. Volman and G. von Bünau, John Wiley & Sons Inc., New York, 1995, vol. 19, pp. 1–117.

