



Project no.
NMP4-CT-2004-013525

Project acronym
Hy3M

Project title
Hydrogen-bond geared Mechanically interlocked Molecular Motors

Instrument
Specific Targeted Research Project

Thematic Priority
Nanotechnologies and nano-sciences, knowledge-based multifunctional materials and new production processes and devices

Publishable final activity report

Period covered: from 1.4.2005 to 31.3.2008

Date of preparation: 15.6.2008

Start date of project: 1.4.2005

Duration: 36 months

Project coordinator name: Wybren Jan Buma
Project coordinator organisation name: UvA/HIMS

Project execution

Hy3M seeks to create new types of synthetic molecular motors - fuelled by energy in the form of light, heat, electrons, *etc.* - that transmit the effects of mechanical motion from the *molecular* level through to the *macroscopic* world. To this purpose *Hy3M* has set out to (i) develop new methods and mechanisms for controlling sub-molecular translational and rotary motion through manipulation of hydrogen bonding interactions and (ii) find out how to link such movements to the outside world in order to do useful work. Primary objectives of the Project are to “*Design, Synthesize, Assemble, Characterize and Evaluate Functional Materials that act through Mechanical Motion at the Molecular Level*”. With this objective we aim to demonstrate the feasibility of exploiting molecular motion at the macroscopic level in general, using key strategic targets as particular examples.

Six workpackages are aimed at obtaining an assessment of both the static and dynamic influences of mechanical interlocking at the molecular level, the ability to assemble the structures into films or polymers which must be engineered into a useful material, and an understanding of how key proximity effects could be “designed in” to tailor specific properties. The knowledge generated from these workpackages is employed to produce materials that exhibit various types of macroscopic responses from mechanical motion at the molecular level (surface-property change, shape-change, movement of object) as well as a synthetic molecular motor coupled to the outside world to do work.

The contractors involved in *Hy3M* are given in the following Table:

Partic. Role*	Partic. no.	Participant name	Participant short name	Country	Date enter project	Date exit project
CO	1	Universiteit van Amsterdam	UvA-HIMS	NL	Month 1	Month 36
CR	2	University of Edinburgh	UniEd	UK	Month 1	Month 36
CR	3	Università di Bologna	UniBo	I	Month 1	Month 36
CR	4	University of Groningen	RUG	NL	Month 1	Month 36
CR	5	University of Angers	UniAn	F	Month 1	Month 36
CR	6	Consiglio Nazionale delle Ricerche	CNR	I	Month 1	Month 36
CR	7	Intertek ASG	ASG	UK	Month 1	Month 36

*CO = Coordinator; CR = Contractor

The overall project management is in the hands of HIMS (Van 't Hoff Institute of Molecular Sciences) of the Faculty of Science of the Universiteit van Amsterdam. Prof. dr Wybren Jan Buma (1961) is the co-ordinator. Contact details of the co-ordinator are:

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The *Hy3M* project has gone extremely well with several important breakthroughs. During the first year, new synthetic routes towards mechanically interlocked architectures that only require a catalytic quantity of template have been developed.¹ We have synthesized several new rotaxane architectures that can be addressed by a variety of external chemical and physical stimuli.²⁻⁴ In order to follow the elementary mechanical motions of molecular devices in real time, experimental techniques have been developed that enable us to determine the absolute conformation of mechanically-interlocked molecules on a 100 fs timescale.⁵ This offers us a unique view into the functioning of molecular devices that is difficult to obtain with other experimental methods. In addition to using many new techniques to characterize the signatures of these compounds, we have developed methods to electrochemically, photochemically, thermally, and mechanically switch rotaxane molecules. Two new types of simple molecular machines have been developed that perform the task of transporting a Brownian substrate between two distinguishable binding sites.⁶

Highlights of the first year include our report of the first prototypical system where a fluorescent pattern can be written into a polymer film using submolecular motion (Figure 1).⁷ The rotaxane contains a fluorescent anthracene group on the thread and a quenching group on the macrocycle. When the macrocycle is held close to the anthracene unit, the fluorophore is quenched and no fluorescence is observed. However, translocating the macrocycle along the thread with an external stimulus (polarity of environment, electrons or light) moves the quenching unit away from the anthracene and it fluoresces freely. This two-state molecular mechanical “switch” can be incorporated into polymethylmethacrylate and a visible image stored arising solely from controlled submolecular motion!

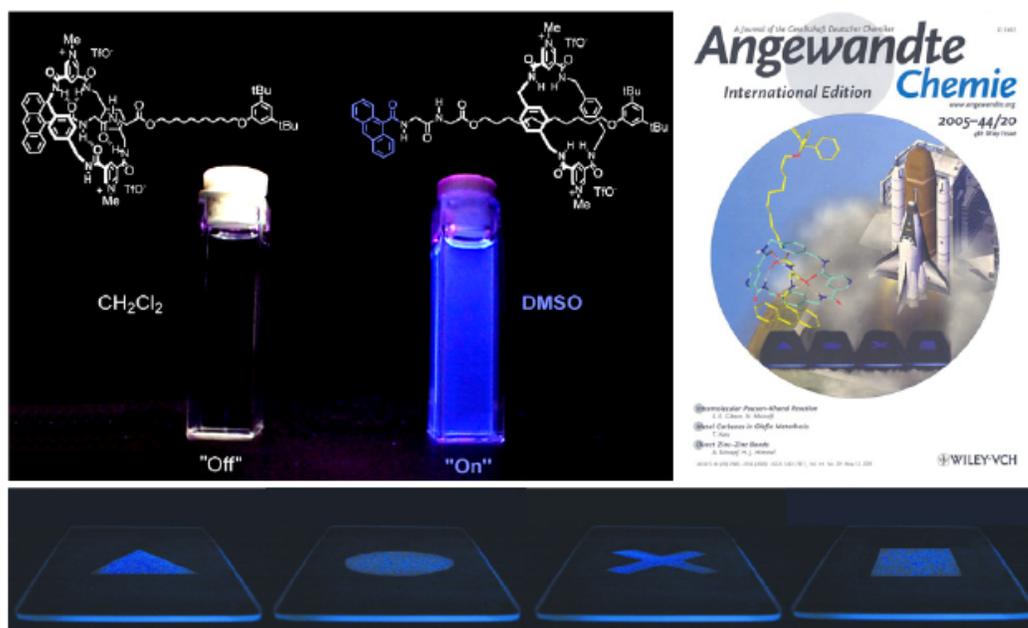


Figure 1. Optical readout and patterning in a polymer film, caused by the controlled translocation of the components of a molecular shuttle.

Additionally, we developed in the first several ways to assemble rotaxanes on a variety of surfaces, that have been characterized extensively using experimental and theoretical methods.⁸ Thin films of rotaxanes, once triggered by thermal or mechanical perturbations, have been shown to self-organise across multiple length scales (from nm to μm) into functional structures with controllable size and position (Figure 2), paving the way for nano-patterning applications.⁹ A theoretical study has demonstrated that interconversion of crystallographic planes through the motion of the macrocycle

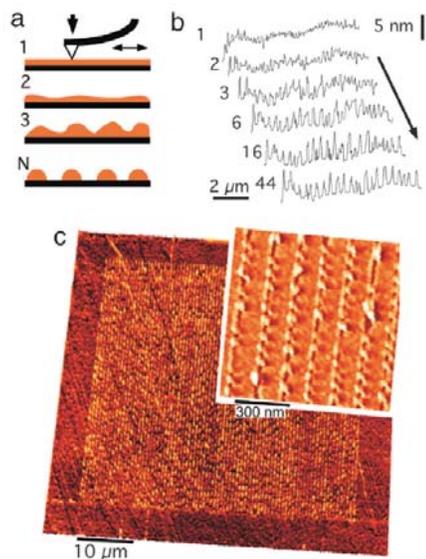


Figure 2 Patterning of rotaxane films by AFM triggered self-organization. (a) Scheme of the process. (b) Sequence of topography line scans recorded at the threshold force. (c) Array of dots fabricated by individual line scans of the AFM tip. Large area pattern of dots is shown. (Inset) An example of a high-resolution pattern.

is at the basis of these phenomena.¹⁰ This is the first example of molecules that, once triggered, self-organise across multiple length scales into functional structures with controllable size and position. This is a genuine, almost school book, example of bottom-up fabrication using molecules with built-in “smartness” through their intermolecular interactions on one hand, their mobility in the solid state, and a happy marriage with collective reorganisation phenomena on large length scales. This result has been patented and is presently finding practical applications in data and information storage.

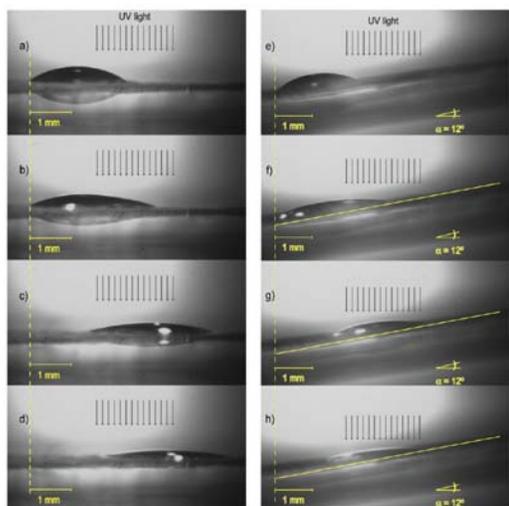
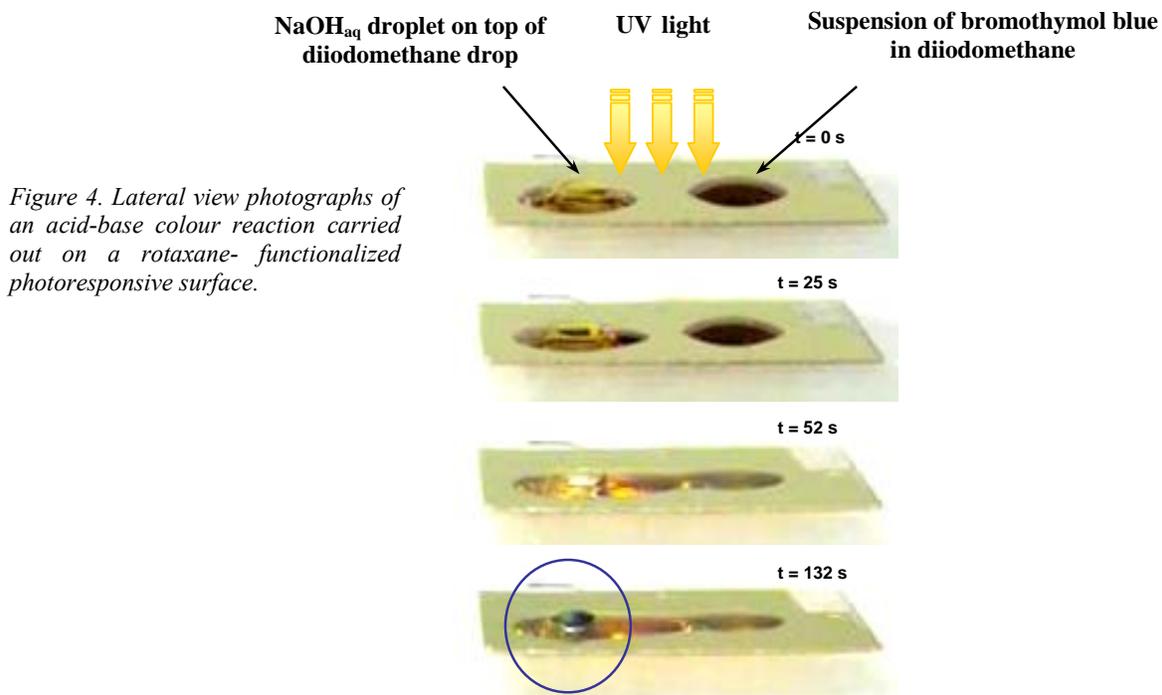


Figure 3. Lateral photographs of light-driven directional transport of a 1.25 μl diiodomethane drop across the surface of a monolayer of a fluorinated rotaxane substrate on mica, both horizontally (a)-(d) and up a twelve degree

An important step forward has been achieved by the demonstration of macroscopic property effects that occur through mechanical motion at the molecular level through fluorinated molecular shuttles that could be driven with light to change the contact angle of liquid droplets (Figure 3).¹¹ Remarkably, this effect is powerful enough to actually transport the droplets across the surface, the first example of the transport of a macroscopic object by synthetic molecular machines. The nanomotors can even be used to drive the liquid droplets up a slope, the synthetic molecular motors—fuelled by light—doing work against gravity. This new breakthrough on the use of rotaxanes as molecular machines to displace macroscopic objects is the first-ever example of exploitation of such molecules, and has been successfully employed to provide a first proof of feasibility for delivering analytes in a lab-on-chip environment, and for performing chemical reactions on a tiny scale without reaction vessels (Figure 4).



During the second year of the Project we showed that information about the location of a macrocycle in a rotaxane can be used, on the input of light energy, to alter the kinetics of the shuttling of the macrocycle between two compartments on the axle. The selective transport of particles between two compartments by Brownian motion in this way bears similarities to the hypothetical task performed without an energy input by a ‘demon’ in Maxwell’s famous thought experiment. Our observations demonstrate that synthetic molecular machines can operate by an information ratchet mechanism, in which knowledge of a particle’s position is used to control its transport away from equilibrium (Figure 5).¹² We have developed new synthetic routes and prepared a host of new molecules.^{13,14} In addition to using many new techniques to characterize the signatures of these compounds¹⁵⁻¹⁷, we have developed methods to electrochemically, photochemically, thermally, and mechanically switch rotaxane molecules. The material acquired from the synthetic and spectroscopic studies have formed a major input for an extensive review.¹⁸

Extensive progress has been made in assembling arrays of catenanes and rotaxanes. Contrary to other reports, we have demonstrated that ordered acid-terminated self-assembled monolayers are obtained with the same preparation conditions as those of the methyl-terminated ones, without any additional treatment.¹⁹ We have further exploited the fact that when a local mechanical perturbation

is applied to the surface of a thin film of a rotaxane, the molecules self-organize into periodic arrays of discrete dots or lines. The phenomenon is now applied as a bottom-up nanofabrication method.

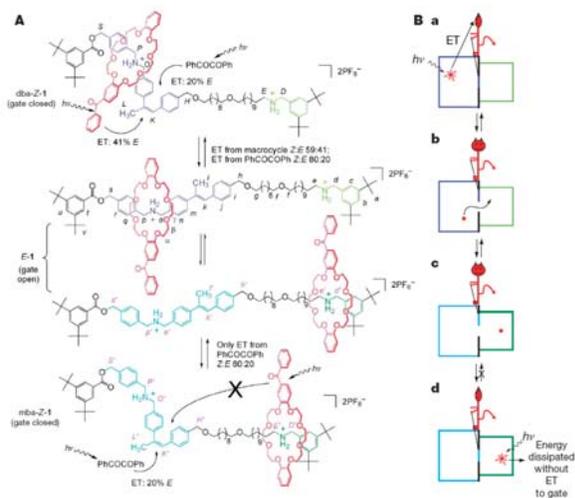


Figure 5. A photo-operated molecular information ratchet. A, Irradiation of rotaxane **1** (1mM) at 350nm in CD₃OD at 298K interconverts the three diastereomers of **1** and, in the presence of benzil (PhCOCOPh), drives the ring distribution away from the thermodynamic minimum, increasing the free energy of the molecular system without ever changing the binding strengths of the macrocycle or ammonium binding sites. For clarity, the photoinduced energy transfer (ET) pathways are only illustrated on the Z- (gate closed) forms of **1** although the same processes occur for the equivalent E- (gate open) translational isomers. When the macrocycle is on the mba binding site (green), intramolecular ET from the macrocycle is inefficient and intermolecular ET from benzil dominates (the cross on the intramolecular ET arrow is used to indicate that it is a rare event compared to other relaxation pathways). When the macrocycle is on the dba binding site (blue), both ET mechanisms can operate efficiently. The amount of benzil present determines the relative contributions of the two ET pathways and thus the nanomachine's effectiveness in pumping the macrocycle distribution away from equilibrium. The mechanism requires the shuttling of the ring between the two ammonium groups in E-1 to be slow with respect to the lifetime of the macrocycle-sensitizer triplet excited state. B, Cartoon illustration of the operation of **1** in terms of a non-adiabatic Maxwellian pressure demon.

In the third year of the Project we have shown that the rotaxane architecture can be used to construct molecular machines that actively control the shape of floppy molecules (Figure 6)²⁰. By suitable design of the molecular mould, these machines make it possible to study the properties of

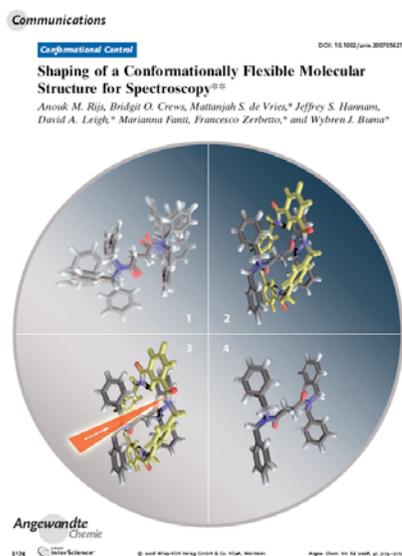


Figure 6. Architecture of a molecular-shaping device. Incorporation of a flexible molecular structure into a rotaxane architecture severely restricts the conformations it can adopt. Light-induced cleavage of the macrocycle releases the molecule in a conformationally shaped form that can be controlled through the appropriate choice of the macrocycle.

specific, user-selected conformations, including highly-strained ones. We have developed new synthetic routes for rotaxanes using an ‘*active-metal*’ template strategy^{21,22} and shown that one can control the shuttling rate of the macrocycles by a judicious choice of the metal ion.²³ New systems with weak interactions between the mechanically interlocked components have been devised allowing for easier access to their large-amplitude motions.²⁴ In a second generation of redox-active imide molecular shuttles, the positional discrimination and rapid shuttling kinetics of the original system have been improved upon in a shuttle that now exhibits three distinct macrocycle distributions, all accessible using only electrochemistry.²⁵ Spectacular advances have been made in preparing functionalized surfaces, using a wide variety of materials and under conditions that are relevant for technological applications.

During the lifetime of the Project the consortium has been able to achieve its final Primary Scientific/Technological Objectives, *Demonstration of macroscopic surface-property change through mechanical motion at the molecular level, Demonstration of macroscopic shape-change through mechanical motion at the molecular level, Demonstration of macroscopic movement of an object across a surface through mechanical motion at the molecular level*, and the accompanying Deliverables. Although all components are in place to accomplish *Demonstration of a fully operational synthetic molecular motor*, an actual demonstration in the spirit of what we had in mind has so far not been possible.

During the last three years the *Hy3M* consortium has taken the chance discovery of a catenane synthesis in a chemistry lab forward to produce some of the first working examples of synthetic molecular motors and nanomachines. Preparing experimental molecular-level systems that employ motion in a useful manner can teach us much about the fundamental mechanical behaviour of matter at small length scales. This in turn may help scientists to unravel how the sophisticated and complicated biomachines of the cell work – crucially important because of the central role they play in many disease states. But the ultimate goal for synthetic molecular machines is to harness their abilities for our own technological use; the creation of artificial nanotechnology. Transmission of the effects of mechanical motion from the molecular level through to the macroscopic world could lead to breakthroughs in areas of technology that today sound like science fiction. Some of these are still far in the future, but we believe others have been brought significantly closer to fruition - and the whole field significantly advanced - by the *Hy3M* Project.

The results illustrate that the major developments world-wide over the past three years on hydrogen bond-assembled molecular machines have occurred as part of the *Hy3M* Project. It is therefore not surprising that the *Hy3M* Project has attracted considerable attention in the form of highlights and commentaries in Journals like *Nature*, *Science*, and *PNAS*, as well as radio and television interviews, and innumerable newspaper articles, and that its participants are frequently invited to give their expert opinion on new results in this exciting field.²⁶ The appreciation for the achievements of *Hy3M* is perhaps best illustrated with the observation that its participants received March 12, 2008 the 2007 Descartes Prize for Transnational Collaborative Research.

[1] V. Aucagne, K.D. Haenni, D.A. Leigh, P.J. Lusby, D.B. Walker, *J. Am. Chem. Soc.* **2006**, *128*, 2186-2187; [2] D.S. Marlin, D. González Cabrera, D.A. Leigh and A.M.Z. Slawin, *Angew. Chem. Int. Ed.* **2006**, *45*, 77-83; [3] D.S. Marlin, D. González Cabrera, D.A. Leigh and A.M.Z. Slawin, *Angew. Chem. Int. Ed.* **2006**, *45*, 1385-1390; [4] V. Aucagne, D.A. Leigh, J.S. Lock and A.R. Thomson, *J. Am. Chem. Soc.* **2006**, *128*, 1784-1785; [5] O.F.A. Larsen, P. Bodis, W.J. Buma, J.S. Hannam, D.A. Leigh, S. Woutersen, *Proc. Natl. Acad. Sci.* **2005**, *102*(38), 13378-13382; [6] M.N. Chatterjee, E.R. Kay and D.A. Leigh, *J. Am. Chem. Soc.* **2006**, *128*, 4058-4073; [7] D.A. Leigh, M.Á.F. Morales, E.M. Pérez, J.K.Y. Wong, C.G. Saiz, A.M.Z. Slawin, A.J. Carmichael, D.M. Haddleton, A.M. Brouwer, W.J. Buma, G.W.H. Wurpel, S. León and F. Zerbetto, *Angew. Chem. Int. Ed.* **2005**, *44*, 3062-3067; [8] S. Mendoza, C.M. Whelan, J.-P. Jalkanen, M. Lubomska, F. Gatti, E.R. Kay, D.A. Leigh, F. Zerbetto, and P. Rudolf, *J. Chem. Phys.* **2005**, *123*, 244708/1-244708/7; [9] F. Biscarini, M. Cavallini, R. Kshirsagar, G. Bottari, D.A. Leigh, S. León, F. Zerbetto, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 17650-17654; [10] J.-F. Moulin, J.C. Kengne, R. Kshirsagar, M. Cavallini, F. Biscarini, S. Leon, F. Zerbetto, G. Bottari, D.A. Leigh, *J. Am. Chem. Soc.* **2006**, *128*, 526-532; [11] J. Berná, D.A. Leigh, M. Lubomska, S.M. Mendoza, E.M. Pérez, P. Rudolf, G. Teobaldi and F. Zerbetto, *Nature Materials* **2005**, *4*, 704-710; [12] V. Serreli, C.-F. Lee, E.R. Kay and D.A. Leigh, *Nature* **2007**, *445*, 523-527; [13] S. Djurdjevic, D.A. Leigh, H. McNab, S. Parsons, G. Teobaldi, F. Zerbetto, *J. Am. Chem. Soc.* **2007**, *129*(3), 476-477; [14] J. Berná, A.M. Brouwer, S.M. Fazio, N. Haraszkiwicz, D.A. Leigh and C.M. Lennon (né Keaveney) *Chem. Commun.* **2007**, 1910-1912; [15] [P. Bodis, R. Timmer, S. Yeremenko, W.J. Buma, J.S. Hannam, D.A. Leigh, and S. Woutersen, *J. Phys. Chem. C* **2007**, *111*(18), 6798-6804 (2007); [16] C.M. Whelan, F.G. Gatti, D.A. Leigh, P. Rudolf, S. Rapino and F. Zerbetto, *J. Phys. Chem. B* **2006**, *110*(34), 17076-17081; [17] J. Niziol, K. Nowicka and F. Kajzar, in "Nonlinear optical properties of matter: From molecules to condensed phases", M.G. Papadopoulos, J. Leszczynski and A.J. Sadlej, Eds, Berlin: Springer, 2006 - s. 609-643 - ISBN: 978-1-4020-4849-4; [18] E.R. Kay, D.A. Leigh and F. Zerbetto, *Angew. Chem. Int. Ed.* **2007**, *46*, 72-191; [19] S.M. Mendoza, I. Arfaoui, S. Zanarini, F. Paolucci, and P. Rudolf, *Langmuir* **2007**, *23*, 582-588; [20] A.M. Rijs, B.O. Crews, M.S. de Vries, J.S. Hannam, D.A. Leigh, M. Fanti, F. Zerbetto, and W.J. Buma, *Angew. Chem. Int. Ed.* **2008**, *47*, 3174-3179; [21] J. Berná, J.D. Crowley, S.M. Goldup, K.D. Hänni, A.-L. Lee, and D.A. Leigh, *Angew. Chem. Int. Ed.* **2007**, *46*, 5709-5913; [22] J.D. Crowley, K.D. Hänni, A.-L. Lee, and D.A. Leigh, *J. Am. Chem. Soc.* **2007**, *129*, 12092-12093; [23] V. Aucagne, J. Berná, J.D. Crowley, S.M. Goldup, K.D. Hänni, D.A. Leigh, P.J. Lusby, V.E. Ronaldson, A.M.Z. Slawin, A. Viterisi, and D.B. Walker, *J. Am. Chem. Soc.* **2007**, *129*, 11950-11963; [24] J. Berná, S.M. Goldup, A.-L. Lee, D.A. Leigh, M.D. Symes, G. Teobaldi, and F. Zerbetto, *Angew. Chem. Int. Ed.* **2008**, *47*, 4392-4396; [25] G. Fioravanti, N. Haraszkiwicz, E.R. Kay, S.M. Mendoza, C. Bruno, M. Marcaccio, P.G. Wiering, F. Paolucci, P. Rudolf, A.M. Brouwer, D.A. Leigh, *J. Am. Chem. Soc.* **2008**, *130*, 2593-2601; [26] E.R. Kay and D.A. Leigh, *Nature* **2006**, *440*, 286-287.