Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 301–304

An investigation of the complexation properties of cyclobis(paraquat-*p*-phenylene) in water

Marc Bria,[a] Graeme Cooke,[b,*] Alan Cooper,[b] James F. Garety,[b] Shanika Gunatilaka Hewage,[b] Margaret Nutley,[b] Gouher Rabani[b] and Patrice Woisel[c]

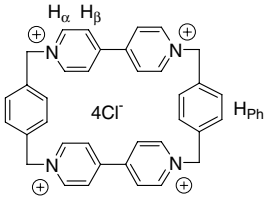
[a]*CCM-RMN Lille 1, Université des Sciences et Technologies de Lille, Villeneuve d'Ascq 59655, France*
[b]*WestCHEM, Department of Chemistry, Joseph Black Building, University of Glasgow, Glasgow G12 8QQ, UK*
[c]*Laboratoire de Chimie Organique et Macromoléculaire, Université des Sciences et Technologies de Lille, Villeneuve d'Ascq 59655, France*

Received 15 September 2006; revised 13 October 2006; accepted 2 November 2006
Available online 27 November 2006

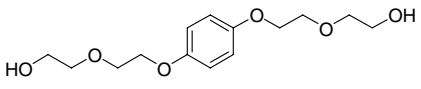
Abstract—This article reports the characterization of pseudorotaxanes fabricated from cyclobis(paraquat-*p*-phenylene) **1**, and 1,4-dialkyloxyphenyl derivative **2** or 1,5-dialkyloxynaphthalene derivative **3** in water. Addition of competing guest **3** to **1.2** or the electrochemical reduction of the cyclophane of **1.3** results in a dethreading of the original pseudorotaxane architecture.
© 2006 Elsevier Ltd. All rights reserved.

The tetracationic cyclophane cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) has arguably become one of the most important building blocks to furnish functional systems in contemporary supramolecular chemistry.[1] This has arisen primarily due to the ability to synthesize this unit on reasonable scales,[2] its ability to have its recognition properties tuned by redox events[3] and its ability to form complexes in both organic and aqueous media.[4] Here, we report an investigation of the complexation properties of **1** with **2** or **3** in aqueous environments.[5] We have shown that **2** and **3** both form pseudorotaxanes with **1** with large association constants in water. Furthermore, pseudorotaxane **1.2** can be disrupted upon the addition of **3**, whilst **1.3** can be disassembled upon the electrochemical reduction of the cyclophane moiety.

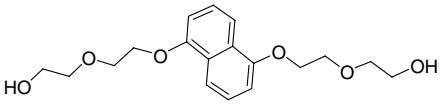
Compounds **1**, **2** and **3** were prepared according to the literature methods.[2,3] ^{1}H NMR and 2D NMR (COSY, NOESY) spectroscopies were used to determine the nature of the complexes formed between **1** and **2** or **3** in D_2O. Addition of aliquots of either **2** or **3** to a solution of **1** showed significant changes in the chemical shifts relative to those of non-complexed species (see Fig. 1 and Supplementary data). It is particularly noteworthy that dramatic chemical shift changes for the $H_{2/6}$, $H_{3/7}$ and $H_{4/8}$ protons of the naphthalene unit occur ($\Delta\delta \approx -1.5$, -1.4 and -4.5 ppm, respectively) during the formation of pseudorotaxane **1.3**. An interesting feature of the spectrum for **1.3** is the existence of two sets of signals for H_α, H_β and H_{Ph}, suggesting that the local C_{2h} symmetry of **3** imposes two different environments on the bipyridium protons of **1**[2,6] and/or that a slow



1



2



3

Keywords: Supramolecular chemistry; Pseudorotaxanes; Tuneable.
* Corresponding author. Tel.: +44 141 330 5500; fax: +44 141 330 4888; e-mail: graemec@chem.gla.ac.uk

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.11.003

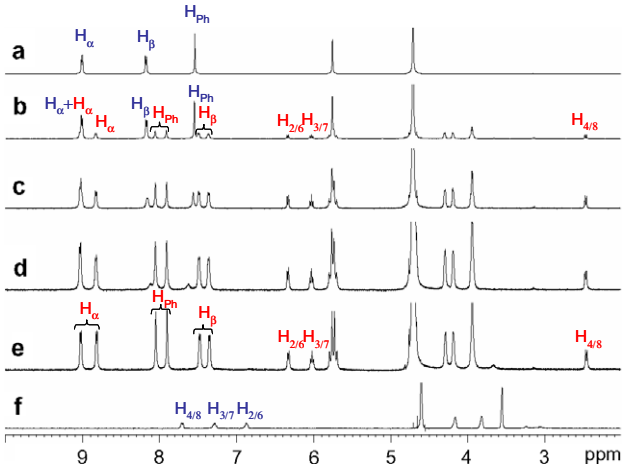


Figure 1. Partial ^{1}H NMR spectra of (a) **1** ($\sim 2 \times 10^{-3}$ M) and upon the addition of (b) 0.25, (c) 0.5, (d) 0.75, (e) 1.0 equivalents of **3**, (f) = **3** alone. Recorded in D_2O at 298 K.

exchange occurs (at least on NMR timescale) between the complexed and the uncomplexed forms.

Further proof regarding the formation of pseudorotaxane **1.3** was also obtained from its 2D NOESY spectrum (Fig. 2). The spectrum recorded in D_2O at 298 K clearly displays strong dipolar correlations between the $H_{4/8}$, $H_{3/7}$ protons of **3** and the H_{Ph} and H_β protons of cyclophane **1**, respectively.

The addition of **2** to a solution of **1** in water resulted in the formation of a red solution, corresponding to the appearance of an absorption at 442 nm in its UV–vis spectrum, whereas the addition of **3** to a separate solution of **1** resulted in the formation of a purple solution corresponding to an absorption centred around 519 nm. A graph of the ratio between the concentration (C) and absorbance (A) versus $1/\sqrt{A}$ for equimolar solutions of **1** and **3** (10^{-2} to 10^{-4} M), provided a straight line indicating that the stoichiometry of the complex does not vary significantly over this concentration range (see Supplementary data).[2]

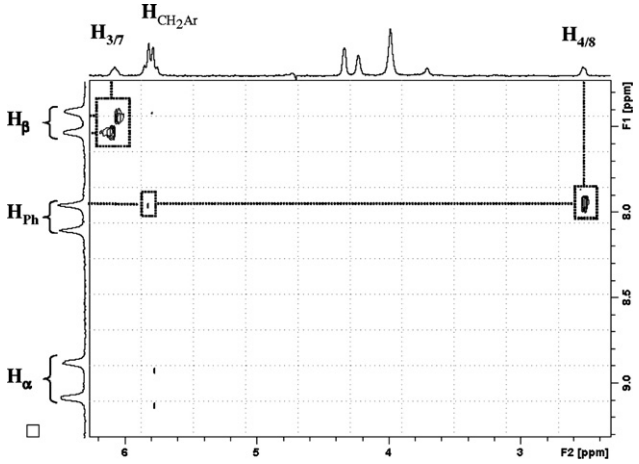


Figure 2. Partial NOESY NMR spectrum of the binary complex **1.3** in D_2O at 298 K.

Isothermal titration microcalorimetry (ITC) experiments (see Fig. 3 and Supplementary data) show that addition of **2** or **3** to dilute solutions of **1** in water at 25 °C gives rise to an exothermic response consistent with reversible non-covalent 1:1 host–guest complexation. Analysis of the thermal titration data gives $K_a = 7300$ (± 150) M^{-1}, $\Delta H = -8.3$ (± 0.2) kcal mol^{-1} for **1.2**, whereas formation of **1.3** is about 200-fold stronger under these conditions, with $K_a = 1.48$ (± 0.02) $\times 10^6$ M^{-1}, $\Delta H = -15.7$ (± 0.1) kcal mol^{-1}. The stoichiometry of the complex **1.2** (see Supplementary data) was confirmed to be 1:1 by producing a continuous variation plot of the chemical shift of the phenyl protons of **1** versus its molar fraction, which gave a maximum value of chemical shift when the molar fraction was equal to 0.5. The stoichiometry of the complex **1.3** was also assumed to be 1:1 as a total disappearance of all protons belonging to the free host **1** is observed at a 1:1 ratio of host and guest (see Fig. 1e and Supplementary data).

We next turned our attention to whether pseudorotaxane formation could be controlled using an external stimulus. Firstly, we have exploited the well-documented ability of $CBPQT^{4+}$-based pseudorotaxanes to have their supramolecular architecture disassembled by electrochemical reduction of the cyclophane to its diradical dicationic state.[3] To investigate whether this methodology can be extended to aqueous environments, we have recorded the cyclic and square wave voltammograms of compound **1** (dissolved in water containing 0.1 M NaCl) and upon the addition of excess **3** (see Supplementary data).[7] In accordance with previous reports, cyclic voltammetry indicated that the electrochemistry of this macrocycle was considerably more complicated than that of $CBPQT^{4+}$ ($4PF_6^-$) recorded in acetonitrile.[3] The first reduction process corresponding to the formation of the diradical dication state of **1** gave rise

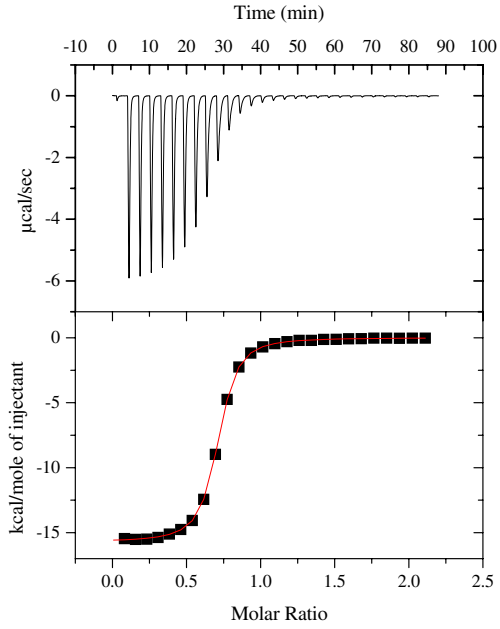


Figure 3. Isothermal titration calorimetry data for the addition of aliquots of **3** to **1**. Recorded in H_2O at 298 K.

to a pseudoreversible reduction wave, whereas the wave for the subsequent two electron reduction was irreversible, presumably due to precipitation of the highly insoluble (in aqueous environments) fully reduced species (see Supplementary data).[4b] Upon the addition of **3** to a solution of **1**, the square wave voltammetry (SWV) data showed that the first redox wave is shifted by ~−60 mV. This shift is presumably due to donor–acceptor interactions (resulting from pseudorotaxane formation between the naphthalene and cyclophane moieties) destabilizing the diradical dication state of the macrocycle (see Supplementary data).[3]

Spectroelectrochemistry measurements were undertaken on **1.3** to indicate whether reduction causes disassembly of the pseudorotaxane, as the electrochemically mediated disassembly should result in the cessation of the CT band in their UV–vis spectra. Increasing the negative potential applied to a solution of the pseudorotaxane in water in an OTTLE cell, indeed resulted in the disappearance of the CT band at 519 nm (Fig. 4). Thus, the data indicate pseudorotaxane formation is disrupted upon reduction of the cyclophane.

As a strategy for disassembling pseudorotaxane **1.2**, we have explored the addition of **3** to a solution of the aforementioned pseudorotaxane,[8] as we have established that **3** is a considerably more effective guest for $CBPQT^{4+}$ than **2** in water. The addition of aliquots of **3** to a cuvette containing **1** and **2** resulted in the formation of a purple solution characteristic of the **1.3** complex in water (Fig. 5). Thus, the UV–vis data are consistent with **3** disrupting pseudorotaxane formation between **1** and **2**.

To prove further that **3** can effectively compete with **2** to form a pseudorotaxane with **1**, we have investigated the change in the ^{1}H NMR spectra of a 1:1 solution of **1** and **2** upon the addition of **3** (Fig. 6). The addition of **2** to a solution of **1** in D_2O resulted in a significant change in the chemical shift of the aromatic protons of the former (~−3 ppm) (compared to a solution of **2** alone). Small shifts were also observed for the cyclophane protons. Upon the addition of one equivalent of **3**, a large upfield shift in the $H_{4/8}$ protons occurred (very similar to those obtained in Fig. 1e), which is diagnostic of the pseudorotaxane formation between **1** and **3**. Furthermore, the aromatic protons of **2** returned to their normal position,

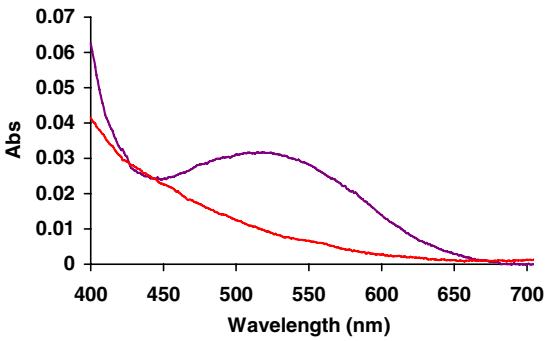


Figure 4. Spectroelectrochemistry of **1.3** (~7×10^{-4} M) in acetonitrile. (—) = 0 V, (—) = −0.6 V.

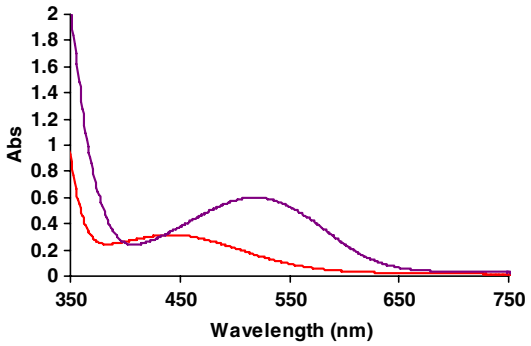


Figure 5. UV–vis spectra of the pseudorotaxane formed between **1** and **2** (~1.5×10^{-3} M) (—) and upon the addition of 2 equiv of **3** (relative to **2**). Recorded in water at 298 K.

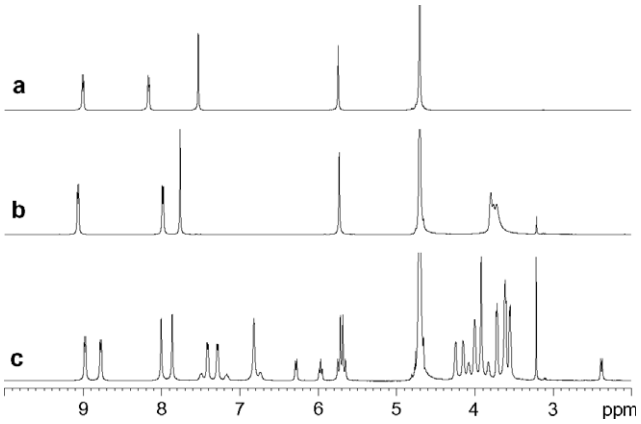


Figure 6. Partial ^{1}H NMR spectra showing (a) **1** (~2×10^{-3} M); (b) 1:1 admixture of **1** and **2**; (c) upon the addition of 1 equiv of **3**. Recorded in D_2O at 298 K.

indicating that **2** is no longer bound to cyclophane **1** to any significant extent.

In conclusion, we have shown that pseudorotaxanes with large association constants can be formed between **1** and **2** or **3** in water. Furthermore, we have shown that complexation can be disrupted by, in the case of **1.2**, the addition of **3**, or in the case of **1.3**, by the electrochemical reduction of the cyclophane. Further work in our laboratory will focus upon the application of these and related systems as a means of reversibly functionalizing biological macromolecules and surfaces. Our work in this area will be reported in due course.

Acknowledgements

We thank the EPSRC for funding this work, and the EPSRC/BBSRC Biological Microcalorimetry facility at Glasgow for performing the ITC measurements.

Supplementary data

Further characterization of pseudorotaxanes formed between **1** and **2** or **3**. Supplementary data associated with

this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.11.003.

References and notes

1. For an early report describing this cyclophane see: Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1547–1550.
2. Asakawa, M.; Dehaen, W.; L'Abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Org. Chem.* **1996**, *61*, 9591–9595.
3. For a discussion of the electrochemically tuneable binding characteristics of $CBPQT^{4+}$ see: Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, M. V.; Spencer, A. M. Z.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 193–218.
4. For examples see: (a) Goodnow, T. T.; Reddington, M. V.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1991**, *113*, 4335–4337; (b) Bernardo, A. R.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1992**, *114*, 10624–10631; (c) Staley, S. A.; Smith, B. D. *Tetrahedron Lett.* **1996**, *37*, 283–286.
5. For examples of previous reports of pseudorotaxane formation between **1** and **3** in aqueous conditions see: (a) Ballardini, R.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; Venturi, M.; Philp, D.; Ricketts, H. G.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1301–1303; (b) Ashton, P. R.; Ballardini, R.; Balzani, V.; Boyd, S. E.; Credi, A.; Gandolfi, M. T.; Gómez-López, M.; Iqbal, S.; Philp, D.; Preece, J. A.; Prodi, L.; Ricketts, H. G.; Stoddard, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1997**, *3*, 152–170; (c) Chia, S.; Cao, J.; Stoddart, J. F.; Zink, J. I. *Angew. Chem., Int. Ed.* **2001**, *40*, 2447–2451; (d) Hernandez, R.; Tseng, H.-R.; Wong, J. W.; Stoddart, J. F.; Zink, J. I. *J. Am. Chem. Soc.* **2004**, *126*, 3370–3371; (e) Venturi, M.; Dumas, S.; Balzani, V.; Cao, J.; Stoddart, J. F. *New J. Chem.* **2004**, *28*, 1032–1037.
6. For similar NMR data reported for related rotaxanes in non-aqueous solvents see: Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Eur. J. Org. Chem.* **1998**, 2565–2571.
7. All electrochemical experiments were performed using a CH Instruments 620A electrochemical workstation. The electrolyte solution (0.1 M) was prepared from recrystallized NaCl and distilled water. A three electrode configuration was used with a Pt disc working electrode, a Ag/AgCl reference electrode and a platinum wire as the counter electrode. The solution was vigorously purged with nitrogen prior to recording the electrochemical data. All voltammetry measurements were recorded under a nitrogen atmosphere.
8. (a) Ashton, P. R.; Gomez-Lopez, M.; Iqbal, S.; Preece, J. A.; Stoddart, J. F. *Tetrahedron Lett.* **1997**, *38*, 3635–3638; (b) Credi, A.; Montalti, M.; Balzani, V.; Langford, S. J.; Raymo, F. M.; Stoddart, J. F. *New J. Chem.* **1998**, 1061–1065.