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Electrochemically tuneable hydrogen bonding interactions between a phenyl-urea terminated dendrimer and phenanthrenequinone†

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Electrochemically tuneable hydrogen bonding interactions are described between a phenyl-urea terminated dendrimer and phenanthrenequinone.

The construction of hyperbranched macromolecular architectures featuring engineered non-covalent interactions is a burgeoning area within contemporary dendrimer chemistry.[1] In particular, the strength, directionality and selectivity of hydrogen bonding processes have proved to be particularly successful supramolecular interactions for modifying the periphery of dendrimer architectures.[2] Indeed, the reversibility of assemblies of this type has allowed the creation of responsive supramolecular dendrimers with architectures that can be assembled/disassembled under the control of an external stimulus.[3] It is likely that responsive dendrimers constructed using supramolecular interactions will continue to be an attractive alternative to their covalently functionalised brethren, as the self-assembly method significantly reduces the lengthy synthetic routes required to fabricate elaborate functional macromolecules of this type.

The application of electrochemistry to modulate the efficiency of hydrogen bonded interactions is a rapidly developing field within supramolecular chemistry.[4] For example, it has been shown that the electrochemical reduction of the phenathrenequinone component of complex **1.2**, results in a significant increase in hydrogen bonding efficiency between these units.[5] Moreover, it was also shown that the efficiency could be modulated in polar (DMF) and non-polar (CH_2Cl_2) environments, thereby nominating this system as an attractive building block for the construction of dendrimers with electrochemically controllable complexation properties.[6] Here, we report the electrochemically tuneable hydrogen bonding interactions between phenyl-urea terminated dendrimer **4** and **1** (Fig. 1).[7]

Dendrimer **4**‡ was readily synthesised from commercially available polypropylenimine hexadecaamine dendrimer (DAB–Am-16) and excess phenyl isocyanate using a similar method to that previously reported.[8] ^{1}H NMR spectroscopy was used to confirm the formation of hydrogen bonds between electroactive guest **1** and hosts **3** and **4**. The addition of aliquots of **1** to a solution of **3** or **4** in DMF-d_7 led to a broadening and small downfield shifts (~0.1 ppm) of the resonances for both urea protons, thereby indicating the formation of a low-affinity hydrogen bonded complex (see ESI†).

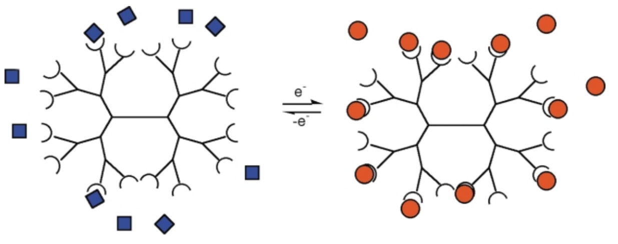
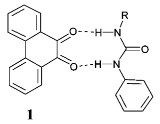
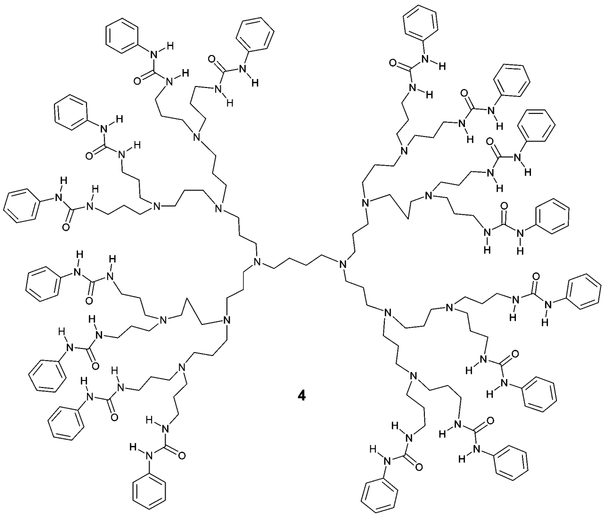


Fig. 1 Schematic representation of the electrochemically controlled complexation of dendrimer **4** with phenanthrenequinone **1**.



1

2 R = Ph
3 R = Bu



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With hydrogen bond formation confirmed between the urea hosts and **1** in DMF, we next investigated their electrochemically controlled complexation using cyclic voltammetry (CV).[9] The addition of an excess of dendrimer **4** to a solution of **1** (in DMF containing 0.1 M Bu_4NPF_6) immediately resulted in a +90 mV shift in the half-wave potential of the reduction wave of **1** (Fig. 2). This positive shift indicates a substantial stabilization (8.7 kJ mol^{-1}) of the radical anionic state of **1**, corresponding to over a 30-fold increase in binding affinity between this unit and the dendrimer periphery.[10] A notable

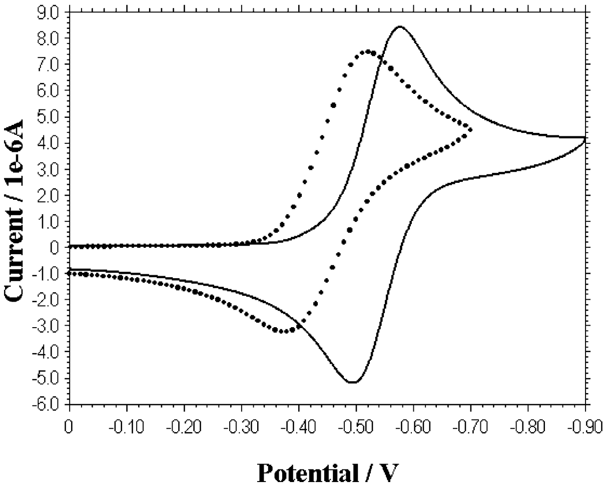

Fig. 2 CV data for **1** (~9×10^{-4} M in DMF) recorded in the absence (——) of and in the presence (······) of an excess (~6×10^{-3} M) of urea dendrimer **4**.

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† Electronic supplementary information (ESI) available: ^{1}H NMR titration and cyclic voltammetry data. See http://www.rsc.org/suppdata/cc/b2/b211370h/

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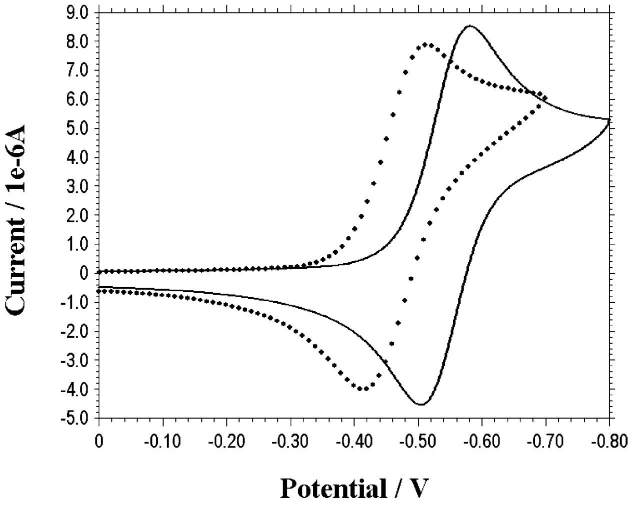

Fig. 3 CV data for **1** (~ 9×10^{-4} M in DMF) recorded in the absence (——) of and in the presence (······) of an excess (~ 9×10^{-2} M) of urea **3**.

feature of the CV of **1** following the addition of an excess of dendrimer **4**, is the ~ 20–30% decrease in peak currents for this reduction wave, which is particularly evident during the re-oxidation of the $\mathbf{1}^{\cdot -}$ to the **1** state. This observation further supports complex formation between dendrimer **4** and **1**, by indicating that hydrogen bonding interactions with the relatively large dendrimer species slows down diffusion of **1** to the working electrode surface.[11] Evidence supporting the reduced reversibility of the redox wave of **1** being a consequence of the slower diffusion rate of the dendrimer/phenanthrenequinone complex, was obtained by measuring the effect scan rate has on the reversibility of the redox wave of **1**. At low scan rates (*e.g.* 25 mV s^{-1}), a reversible waveform was obtained for the reduction of **1** to $\mathbf{1}^{\cdot -}$ in the presence of excess **4**, however, at faster scan rates (*e.g.* 5 V s^{-1}) the waveform became considerably more irreversible (see ESI†).

To further corroborate electrochemically controlled host–guest complexation between **1** and **4**, we explored the changes in solution electrochemistry of **1** following the addition of an excess of model compound **3**.[12] A slightly smaller shift of + 83 mV was observed for the redox wave of **1** following the addition of **3**. However, in contrast to the CV data obtained for dendrimer **4**, a relatively small decrease (~ 5–10%) in peak currents was typically observed (Fig. 3). This result is to be expected as host–guest complexation between **1** and **3** should not significantly perturb the diffusion rate of **1** to the working electrode.

In summary, we have established that the efficiency of hydrogen bonds formed between dendrimer **4** and **1** can be significantly enhanced upon electrochemical reduction of the latter to its radical anion state. In particular, by relating the perturbation of the redox potential of **1** to the thermodynamic data obtained for an analogous hydrogen bonded complex, the very weak hydrogen bonds formed between the neutral species (‘off’ state) can be increased 33-fold by reduction of **1** (‘on’ state). Therefore, this study paves-the-way for the development of new electrochemically controlled dendrimer architectures with biomimetic and device applications; the results of our investigations towards these goals will be reported in due course.

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Notes and references

‡ *Selected data for* **4**: Yield 60%. IR (KBr) ν (cm^{-1}) 3339, 2945, 2805, 1650, 1598, 1554, 1499, 1441, 1312, 1240, 753, 693; ^{1}H NMR (200 MHz, DMSO-d_6): δ 8.40 (br. 16H, PhN*H*CONH), 7.36 (d, 32H, J = 7.9 Hz, Ph), 7.15 (t, 32H, J = 7.7 Hz, Ph), 6.85 (t, 16H, J = 7.2 Hz, Ph), 6.23 (br. t, 16H, PhNHCON*H*), 3.10 (br. 32H, NHCH_2), 2.33 (br. 84H, CH_2NCH_2), 1.51 (br. 56H, CH$_2$CH_2CH$_2$) 1.38 (br, 4H, NCH$_2$CH_2CH_2CH$_2$N); ^{13}C NMR (50 MHz, DMSO-d_6): δ 155.85, 140.87, 129.03, 121.50, 118.31, 52.15, 51.51, 38.64, 27.84; MS (MALDI-TOF): m/z = 3592.7 (M^+).

1 For examples of recent reviews which focus upon supramolecular dendrimers see: (*a*) F. Zeng and S. C. Zimmerman, *Chem. Rev.*, 1997, **97**, 1681; (*b*) D. A. Tomalia and I. Majoros, *Supramolecular Polymers*, ed. A. Ciferri, Dekker, New York, 2000, 359; (*c*) D. K. Smith and F. Diederich, *Top. Curr. Chem.*, 2000, **210**, 183; (*d*) S. C. Zimmerman and L. J. Lawless, *Top. Curr. Chem.*, 2001, **217**, 95; (*e*) J. M. J. Fréchet, *Proc. Nat. Acad. Sci. USA*, 2002, **99**, 4782.

2 For recent examples of hydrogen bonding interactions between peripherally functionalised dendrimer hosts and complementary guests see: (*a*) U. Boas, S. H. M. Söntjens, K. Jensen, J. B. Christensen and E. W . Meijer, *Chem. Biochem.*, 2002, **3**, 433; (*b*) J. W. Lee, Y. H. Ko, S.-H. Park, K. Yamaguchi and K. Kim, *Angew. Chem., Int. Ed.*, 2001, **40**, 746; (*c*) H. W. Gibson, N. Yamaguchi, L. Hamilton and J. W. Jones, *J. Am. Chem. Soc.*, 2002, **124**, 4653.

3 G. M. Dykes, D. K. Smith and G. J. Seeley, *Angew. Chem., Int. Ed.*, 2002, **41**, 3254.

4 (*a*) A. E. Kaifer and M. Gómez-Kaifer, *Supramolecular Electrochemistry*, Wiley-VCH, Weinheim, 1999; (*b*) P. L. Boulas, M. Gomez-Kaifer and L. Echegoyen, *Angew. Chem., Int. Ed.*, 1998, **37**, 216; (*c*) V. M. Rotello and A. Niemz, *Acc. Chem. Res.*, 1999, **32**, 44; (*d*) A. E. Kaifer, *Acc. Chem. Res.*, 1999, **32**, 62; (*e*) J. H. R. Tucker and S. R. Collinson, *Chem. Soc. Rev.*, 2002, **31**, 147; (*f*) G. Cooke and V. M. Rotello, *Chem. Soc. Rev.*, 2002, **31**, 275.

5 (*a*) Y. Ge, R. R. Lilienthal and D. K. Smith, *J. Am. Chem. Soc.*, 1996, **118**, 3976; (*b*) Y. Ge, L. Miller, T. Ouimet and D. K. Smith, *J. Org. Chem.*, 2000, **65**, 8831.

6 For examples of metallocene terminated dendrimers that can undergo electrochemically controlled binding to β-cyclodextrin see: (*a*) R. Castro, I. Cuadrado, B. Alonso, C. M. Casado, M. Morán and A. E. Kaifer, *J. Am. Chem. Soc.*, 1997, **119**, 5760; (*b*) B. González, C. M. Casado, B. Alonso, M. Morán, Y. Wang and A. E. Kaifer, *Chem. Commun.*, 1998, 2569.

7 For examples of metallocene terminated dendrimers which electrochemically respond to inorganic anions see: (*a*) C. Valério, J.-L. Fillaut, J. Ruiz, J. Guittard, J.-C. Blais and D. Astruc, *J. Am. Chem. Soc.*, 1997, **119**, 2588; (*b*) C. Valério, E. Alonso, J. Ruiz, J.-C. Blais and D. Astruc, *Angew. Chem., Int. Ed.*, 1999, **38**, 1747; (*c*) C. M. Casado, I. Cuadrado, B. Alonso, M. Morán and J. Losado, *J. Electroanal. Chem.*, 1999, **463**, 87; (*d*) B. Alonso, C. M. Casado, I. Cuadrado, M. Morán and A. E. Kaifer, *Chem. Commun.*, 2002, 1778.

8 U. Boas, A. J. Karlsson, B. F. M. de Waal and E. W. Meijer, *J. Org. Chem.*, 2001, **66**, 2136.

9 All electrochemical experiments were performed using a CH120A electrochemical workstation. The electrolyte solution was prepared from recrystallised Bu_4NPF_6 using spectroscopic grade dimethylformamide (0.1 M). A three electrode configuration was used with a Pt working electrode, a Ag/AgCl reference electrode and a platinum wire as the counter electrode. Scan rate = 100 mVs^{-1} (unless otherwise stated). T = 25 °C. The solution was purged for several minutes with N_2 prior to recording the electrochemical data; the voltammograms were recorded under an atmosphere of N_2.

10 We expect that the addition of an excess of dendrimer **4** to a solution of **1** would principally result in the formation of complex of stoichiometry **1.4**. Thus, we can estimate the change in K_a following the electrochemical formation of $\mathbf{1}^{\cdot -}.\mathbf{4}$ using a thermodynamic cycle which can be expressed mathematically using: $K_a(\text{red})/K_a(\text{ox}) = e^{(nF/RT)(E_{1/2}(\text{bound}) - E_{1/2}(\text{unbound}))}$. K_a(red) and K_a(ox) are the association constants in the reduced and oxidised forms, and $E_{1/2}$ (bound) and $E_{1/2}$ (unbound) are the half-wave redox potentials in the receptor bound and unbound states. A K_a(ox) of 1 M^{-1} has previously been determined for the hydrogen bonded complex formed between 1-phenyl-3-propyl urea and **1** using simulated electrochemical data. As it was not possible to fully reach saturation in our electrochemical experiments, a lower limit for K_a(red) for $\mathbf{1}^{\cdot -}.\mathbf{4}$ complex can be estimated to be 33 M^{-1}.

11 A similar decrease in peak currents is often observed in the cyclic voltammograms of encapsulated redox-active units. For a review see: C. M. Cardona, S. Mendoza and A. E. Kaifer, *Chem. Soc. Rev.*, 2000, **29**, 37.

12 In order to ensure comparability between electrochemical measurements (*i.e.* maintaining the same number of urea recognition units per molecule of **1**), 16 molar equivalents (compared to the amount of dendrimer **4** added in the previous experiment) of model compound **3** was added to the CV cell.