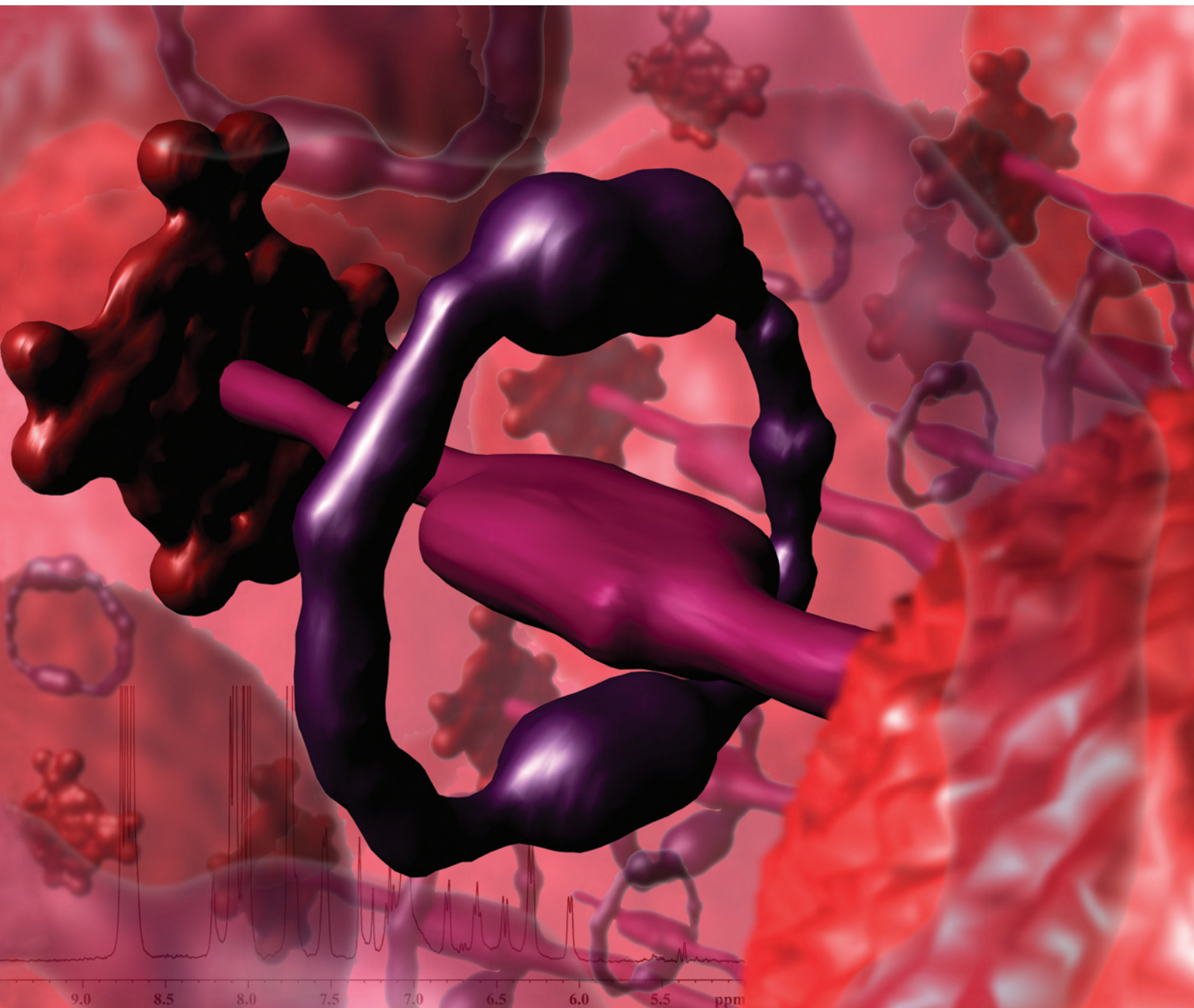


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FULL PAPER

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Monitoring the thermodynamically-controlled formation of diimide-based resin-attached rotaxanes by gel-phase HR MAS ^1H NMR spectroscopy†

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The thermodynamically controlled self-assembly of rotaxane and pseudorotaxane systems consisting of (i) a naphthodiimide thread unit terminated at one end with a pyridine ligand, and covalently linked at the other to a gel-phase polystyrene resin support, (ii) a dinaphtho-crown ether shuttle unit, and (iii) a ruthenium carbonyl metalloporphyrin stopper unit, is investigated by high resolution magic angle spinning proton (HR MAS ^1H) NMR spectroscopy. The effects of variable concentration of the solution-phase components, the temperature, and added Li^+ and Na^+ ions are described, and the limitations of the technique are addressed. The dynamic behaviour is compared directly to the solution-phase analogues, where a bulky stopper group is substituted for the polystyrene resin bead.

Introduction

One of the most appealing aspects of supramolecular chemistry is its promise to deliver real nanoscale working devices with a minimum of synthetic investment.^{1,2} Accordingly, the concepts of molecular recognition leading to self organization and self-assembly have assumed particular prominence^{3,4} and from this has evolved a modular approach where individual appropriately designed molecular components are brought together in such a way as to ensure structural integrity and coherence of the final assemblage.⁵ Inevitably, this has required a full understanding of the recognition principles involved, but the process is even then often constrained by the efficiency of kinetically controlled bond-forming reactions between the components.⁶ A thermodynamically-based process, where the components are assembled under equilibrating conditions, can lead to efficient selectivity with inbuilt error correction.^{7,8} Furthermore, the principles of dynamic combinatorial chemistry can then be utilised to advantage, so that selection from a library of components can lead to the most thermodynamically favoured outcome.^{9,10}

While thermodynamic control has the advantage of simplicity of construction, the stability of the final assembly is at the mercy of the principles of dynamic equilibrium, at least in solution. For robust working devices, this represents a serious impediment. A logical next step is to use an irreversible kinetic fixing process after equilibration, and this has been used to advantage in isolation of the major component from a dynamic combinatorial library,^{8,10,11} or for supramolecular synthesis.^{4,12}

We have previously reported on the assembly of rotaxanes and catenanes under conditions of thermodynamic control in the solution-phase.^{13–15} These systems utilise the pseudorotaxane-like stabilisation offered by a naphthodiimide and a dibenzo-crown ether, and the threaded unit, which is itself appended at each end by a pyridine-derived Lewis base moiety, is then stoppered essentially reversibly by a coordinate covalent bond to a suitable metalloporphyrin.

In working electronic or mechanical devices, the molecular scale systems need to be attached in an ordered array at some interface or solid surface. Usually, one of the constituent units is attached, and the other component(s) is (are) then assembled from the surrounding solution. Although a number of solid-supported supramolecular systems has been reported^{2,16,17} the majority involve either the incorporation of supramolecular systems into polymer matrixes,¹⁸ the use of Langmuir–Blodgett (LB) films,¹⁹ or more commonly, the formation of self-assembled monolayers on gold or other surfaces.²⁰

Because of the limited number of techniques that can be applied to solid-appended systems, and especially those under dynamic equilibrium, the structural integrity and dynamics of the array need to be inferred by analogy to the solution-phase behaviour. In some instances, it has been possible to detach the supramolecule from the solid support to enable solution-phase characterisation, but this is only feasible for intact non-equilibrating systems.

To this end, we have described a series of neutral rotaxane and catenane systems and have compared their synthesis, behaviour and properties in solution with those of analogous systems tethered to solid-phase polystyrene supports.^{14,21,22} While these particular polymeric supports offer little in terms of electrical conductivity that might be utilised in nanoscale electronic devices, they have a particular advantage in the fact that they can be readily studied by high resolution gel-phase magic angle spinning (HR MAS) ^1H NMR spectroscopy. This allows high quality well-resolved proton spectra to be obtained with linewidths comparable to conventional solution-phase spectra, not only for the solid-attached molecular components, but also the solution-phase

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entities in the surrounding solution.^{21–23} Hence, a direct view of the equilibrium processes between solid-attached and solution-phase components can be obtained in real time. For self-assembling supramolecular systems, this represents a convenient way to compare the solution state behaviour with that of the solid-attached analogues, which in turn provides confidence in an assumed correspondence of structural integrity and properties of similar types of systems that are ultimately attached to conducting surfaces or assembled at interfaces or in membranes.

The fundamental components of these systems in both solution and solid-phase studies are the neutral naphthodiimide thread **1**, the dinaphtho 38-crown-10 macrocycle **2**, and the ruthenium carbonyl porphyrin **3**. In a typical solution-phase rotaxane system illustrated in Scheme 1, the thread unit is encircled by the crown ether through a combination of dipolar, π - π and charge transfer intermolecular forces, and the rotaxane **4** is completed by stoppering as a result of coordination of the terminal pyridine units of the thread with the ruthenium carbonyl porphyrin. The assembly of this system is completely reversible and the thermodynamically most stable product, the rotaxane, self-assembles in solution by simple mixing of the components in a suitable solvent.^{13,15}

Based on the same principles, the self-assembly of analogous rotaxanes on solid supports was also studied (Scheme 2). A naphthodiimide thread terminated with a single pyridine group was tethered at the opposite end to polystyrene beads. The functionalised beads **5** were then allowed to swell in solutions containing the crown **2** and porphyrin **3** stopper components, and the system was analysed by HR MAS ¹H NMR spectroscopy. This allowed the dynamic equilibrium between the solid- and solution-phases to be easily monitored as the polymer-bound rotaxane **6** assembled from its component parts.^{14,21} We have also reported the

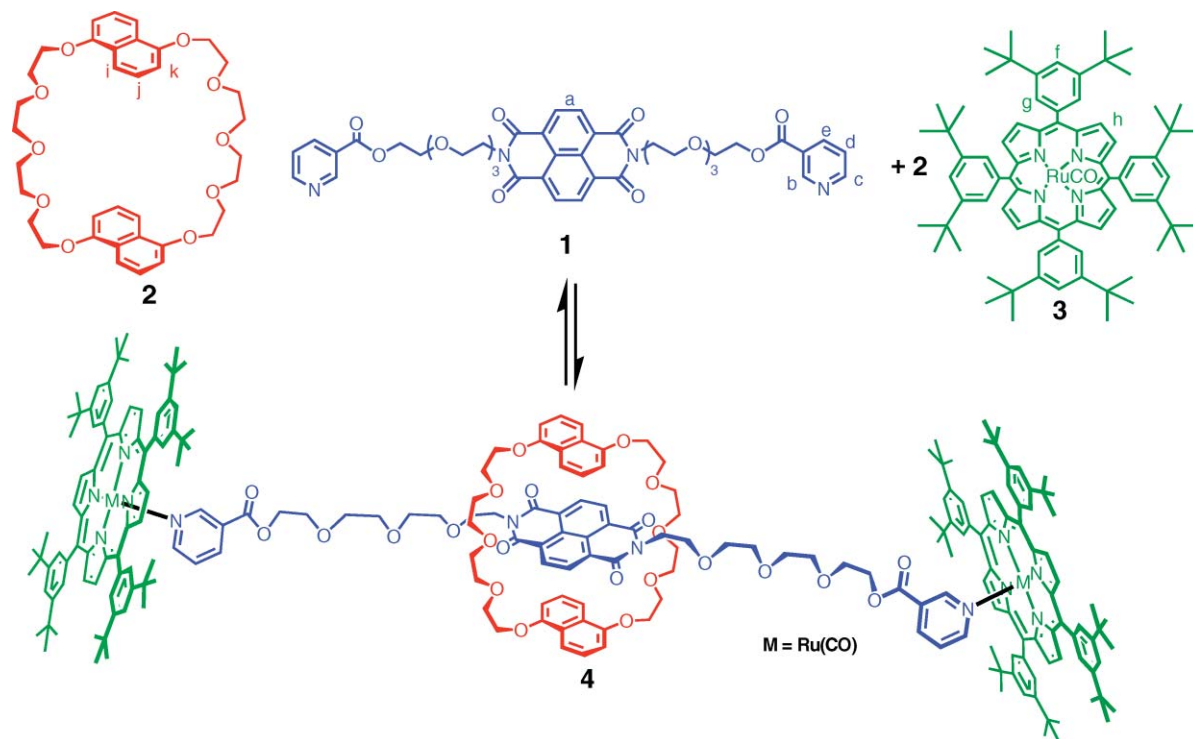
non-equilibrium counterparts to these systems, where rotaxane and catenanes were covalently attached to these beads under kinetically controlled conditions.²²

We now present a more detailed description of this system, and extend the study to examine the full correspondence between solution and solid-phase-attached behaviour, as revealed by HR MAS spectroscopy. Further, we report on the effect of temperature, added metal ions, and relative concentrations on the assembly processes both in solution-phase and solid-attached gel-phase systems.

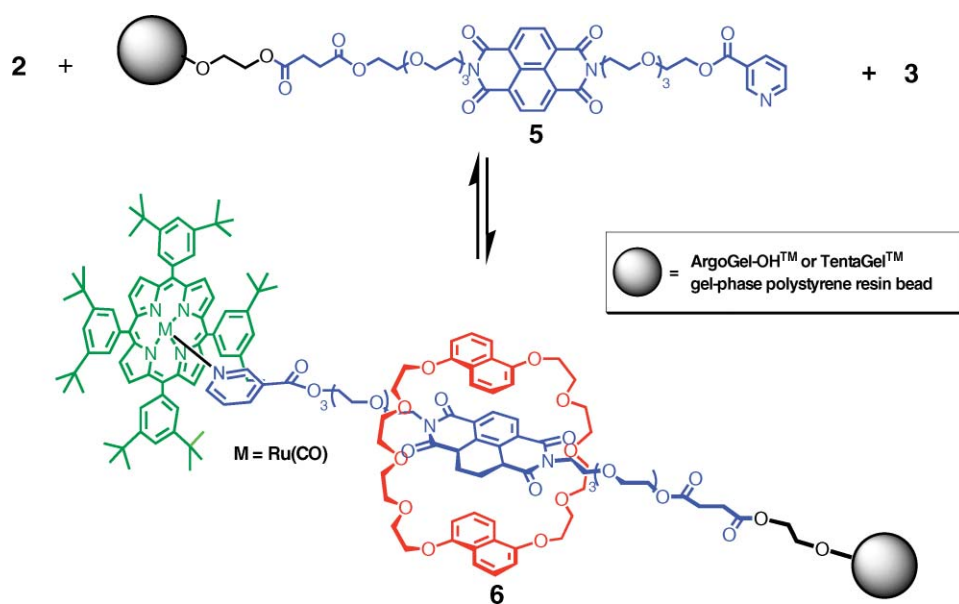
Results and discussion

Solution-phase analogues of a mono-stoppered naphthodiimide-threaded rotaxane

Previous solution studies of the three component system referred to above have involved the use of the *bis*-pyridine functionalised thread **1**, in which two stoppering porphyrin units are required for the rotaxane.^{13,14} However, for a solid-tethered thread unit **5**, one end is effectively stoppered by the solid support and thus only one porphyrin equivalent is needed for rotaxane formation. Thus, a more appropriate solution analogue was reasoned to be one in which one end of the thread is stoppered by a bulky, non-porphyrinic entity designed to prevent slippage of the macrocycle from one end. This would provide a solution-phase counterpart for direct comparisons of thermodynamic, kinetic and structural factors. The stopper group of choice was based on **7**, and is similar to those used extensively by Stoddart and others as effective stoppers in related bipyridinium-based, dialkylammonium, and other rotaxanes.^{24,25}



Scheme 1



Thus, the mono-stoppered naphthodiimide thread **9** was synthesised *via* reaction between **7** and the acid chloride derivative of **8** (Scheme 3).

An ^1H NMR spectrum (2% MeOD- CDCl_3) of an equimolar solution of **2** and **9** was consistent with the formation of the pseudorotaxane **10**. It showed upfield shifted and broadened resonances for the diimide protons (8.72 to 8.59 ppm) and crown aromatic protons (7.54, $\Delta\delta = -0.16$; 7.05, $\Delta\delta = -0.13$; and 6.42 ppm, $\Delta\delta = -0.08$ ppm), indicating that the system was in fast exchange on the NMR chemical shift time scale, similar to that previously observed for the analogous system with the *bis*-pyridyl-substituted naphthodiimide thread **1** (Fig. 1).¹³

At lower temperatures, two sets of peaks became evident for both the diimide and crown resonances, indicating a change in dynamics from a fast to a slow exchanging system on the NMR chemical shift timescale (Fig. 1): the diimide proton resonance (a) at 8.59 ppm splits into unbound (a_{out} , 8.61 ppm) and bound (a_{in} , 8.08 ppm) resonances, with the bound resonance increasing in proportion relative to its unbound counterpart as the temperature decreased.

Likewise, two sets of crown peaks (i, j, k) were observed with those belonging to the unbound crown appearing at 7.62, 7.18 and 6.54 ppm, and those belonging to its bound partner appearing at 6.67, 6.59, 6.03 ppm. This temperature dependence was comparable to that of the binding of the *bis*-pyridine thread **1**, indicating that any effect on the binding or stability of having one end of the thread stoppered is negligible in this time frame and concentration range. At -70°C , a fine structure around the bound diimide peak (a_{in}) was evident. This has been seen in similar systems involving crowns complexed with diimides and has been shown to be due to the rocking back and forth and “yawing” from side to side of the diimide inside the crown.^{15,26}

Addition of one equivalent of ruthenium carbonyl porphyrin **3** to the 1 : 1 mixture of **9** and **2** completed the rotaxane formation, **11**, through stoppering of the single pyridine terminus of the thread *via* a coordinate covalent bond to the ruthenium. Similar to the

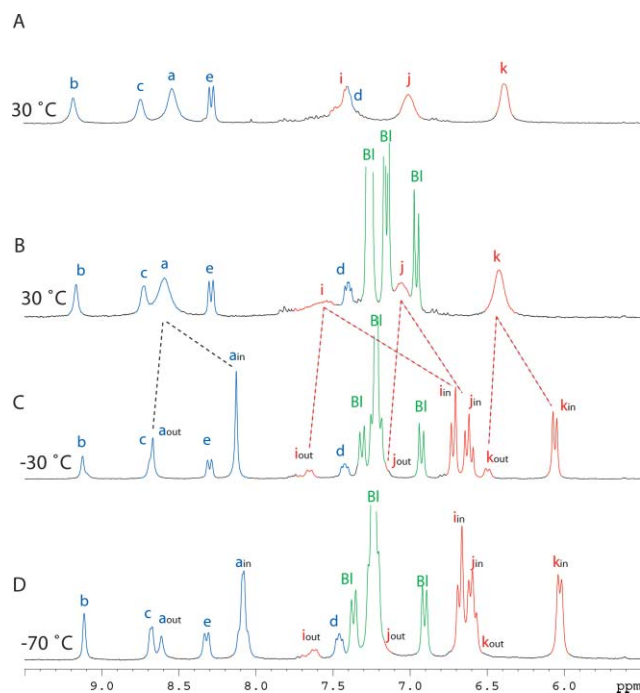
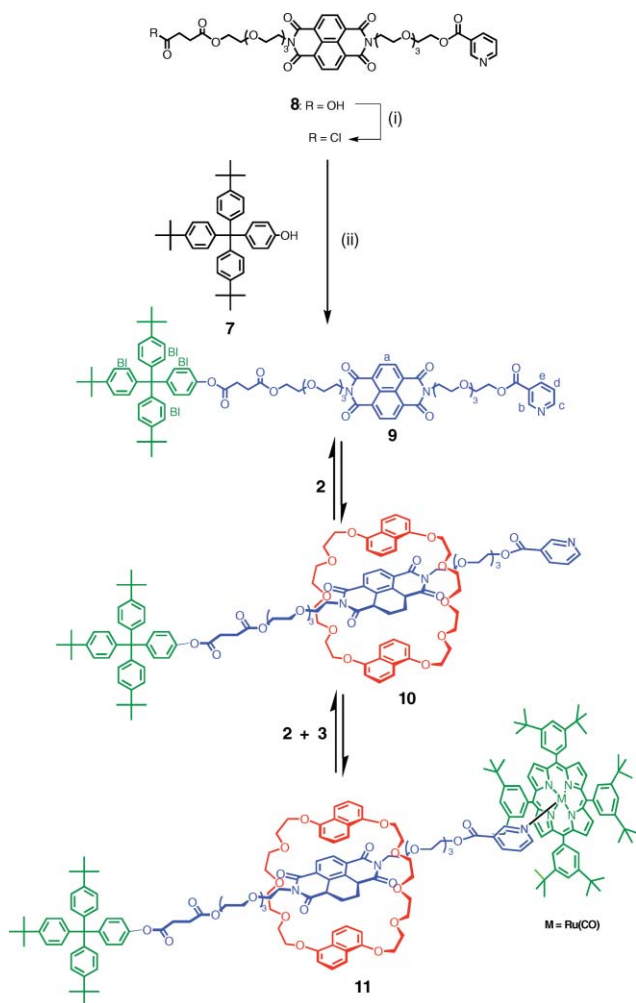


Fig. 1 ^1H NMR temperature comparison of equimolar mixtures of **1** and **2** (A); and **9** and **2** (B, C and D). Numbering and colouring refer to those indicated in Schemes 1 and 3.

behaviour previously observed for the analogous system with **1**, the ^1H NMR spectrum showed dramatic upfield shifts of the pyridine proton resonances from their unbound positions of 9.17, 8.73, 8.29 and 7.40 ppm to typical coordinated positions of 6.74, 5.39, 2.20 and 1.78 ppm. Notably, even at room temperature, two sets of resonances for the crown and diimide protons were observed indicating the system was now in slow exchange on the NMR chemical shift timescale. Variable temperature NMR experiments were performed and again similar ratios of bound *versus* unbound



Scheme 3 Reagents and conditions (i) oxalyl chloride, toluene, quantitative yield; (ii) dry DCM, room temperature, 12 h, 81%. Also indicated in this and Schemes 1 and 2 is the non-systematic aromatic group labelling and colouring system used for the NMR analysis of **9** and its related supramolecular systems **10** and **11**.

crown were obtained compared to the symmetrical diimide thread **1**.¹³

Thus, it is established that the covalent stoppering of one end of the diimide thread has no significant effect on the dynamic self-assembly of this system.²⁷ This is expected to translate directly to the polymer-attached thread, where the polymer matrix acts as an inbuilt stopper.

Enhancing the crown–diimide interaction using alkali metal ions

It has been demonstrated that alkali metal ions can enhance binding and can be used to control molecular motion in assembled catenanes and rotaxanes incorporating the diimide-dinaphtho-crown motif.^{28,29} This effect has been especially significant using LiI in pyromellitic diimide systems, while more complex behaviour has been reported for the naphthodiimide counterparts in the presence of sodium salts, and particularly NaI.³⁰ Thus, NMR studies in 2% MeOD–CD₂Cl₂ (a solvent system which had been shown to maximise the effects of the added cations) pseudorotaxane formation involving the mono-stoppered thread unit **9** and the

dinaphtho-crown **2** was only minimally enhanced by the addition of LiI, while a greater effect was seen in the case of NaI. This was evidenced by an upfield shift in both crown and diimide aromatic resonances at 30 °C in the presence of an excess of NaI in an equimolar mixture of diimide and crown (Fig. 2). At lower temperatures, these broadened and shifted (fast exchange) resonances split into bound and unbound crown peaks as the system moved into the slow exchange regime (bound at 6.62 ppm i and j, and 6.09 ppm k; and unbound at 7.55 i, 6.89 j and 6.76 k ppm at –30 °C) (Fig. 2). Furthermore, three distinct peaks were evident for the diimide protons (8.64, 7.97 and 8.57 ppm), as a result of the asymmetry induced in the diimide–crown interaction geometry by the Na⁺ ion, as previously reported.^{29,30} At lower temperatures, the spectra showed additional fine structure, which is again indicative of rocking and yawing of the diimide inside the crown as described above.

When the ruthenium porphyrin stopper **3** was subsequently added to the equimolar mixture of diimide **9** and crown **2** in the presence of NaI, clear bound (6.64 ppm for protons i and j overlapping, and 6.14 ppm) and unbound (7.58, 6.86, 6.79 ppm) resonances for the crown, and similarly bound (8.05 ppm) and unbound (8.69 ppm) diimide peaks were observed. An increase in the proportion of bound *versus* unbound crown was clear evidence of enhanced stabilisation of the crown–diimide complex by the Na⁺ cation. Again at low temperatures the appearance of the third peak due to the asymmetry resulting from binding of the sodium cations was observed at 8.50 ppm, as was the fine structure around both bound diimide peaks due to the “yawing” and “rocking” phenomena.

Thus it was established that the addition of NaI enhances the crown–diimide interaction and it can be anticipated that subsequent experiments on solid supports will be able to incorporate this to advantage.

Polymer-tethered pseudorotaxanes and rotaxanes

The principles thus established for the incorporation of singly-stoppered thread units in these thermodynamically driven systems could now be transferred to the polymer-tethered analogues.

Previously we reported²¹ that an equilibrated mixture of the polymer-bound thread **5** and the crown **2** in CDCl₃ containing excess crown showed an upfield shifted diimide resonance, as well as large crown peaks not significantly shifted from their free positions. This is consistent with the formation of the pseudorotaxane system, which is in fast exchange on the NMR timescale; the crown resonance positions are dominated by the large contribution from the excess crown, which on the other hand has caused a substantial upfield shift of the diimide, which is predominantly bound under these conditions. We have previously alluded to the logistical difficulties inherent in the measurement technique, of precise quantification of added reagents with respect to the loading of the bead component.³¹ Nevertheless, when the experiment is performed (in this case in 2% CD₃OD–CDCl₃) with a lower concentration of added crown, then instead of large and dominant excess crown resonances, now *two* distinct sets of peaks can be identified for the crown, each somewhat broadened and moved from its free position (Fig. 3). Apparently in contradiction, there is only *one* upfield shifted and broadened diimide resonance. Since it was expected that the system should still be in fast

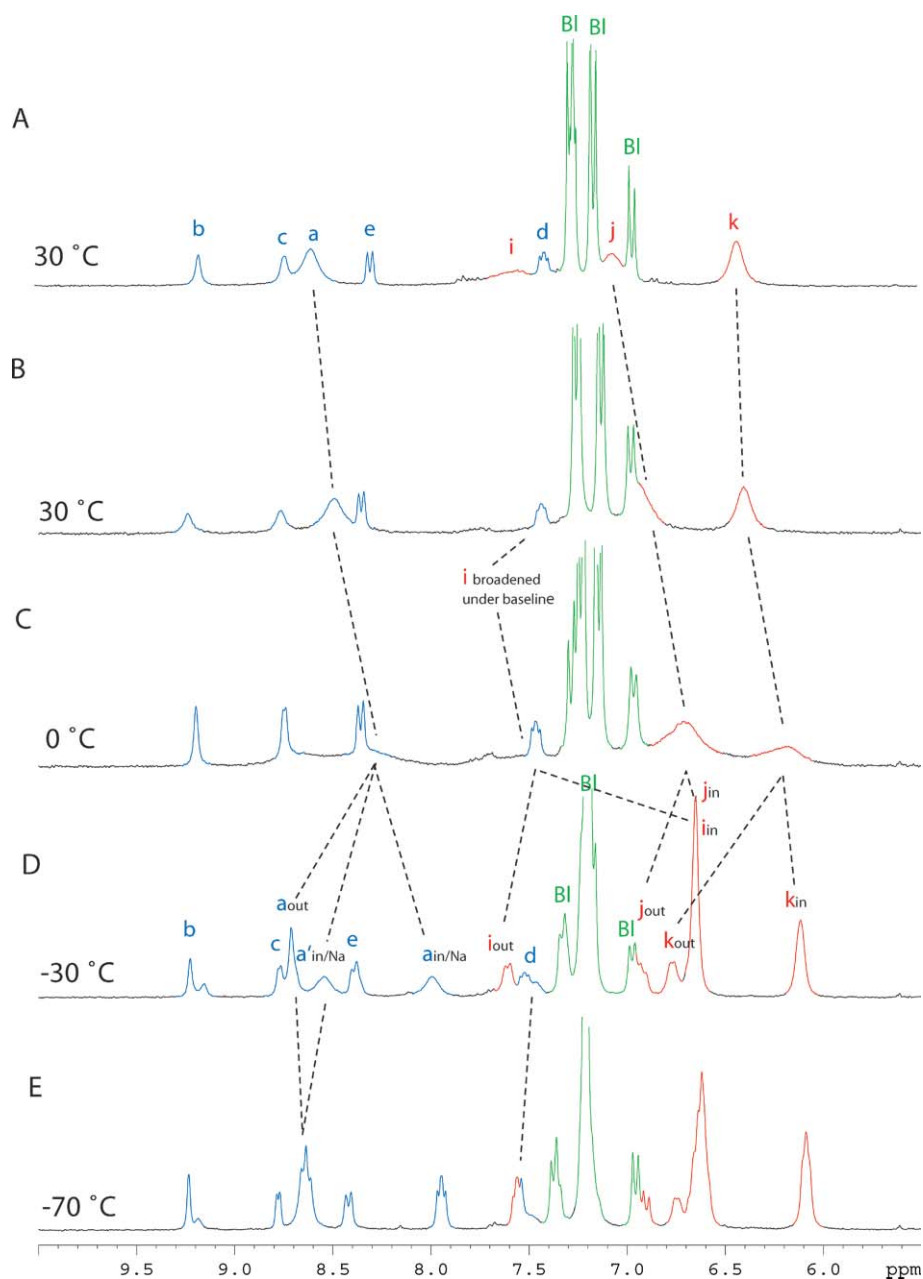


Fig. 2 ^1H NMR comparison of diimide thread **9** binding equimolar proportions of crown ether **2** at 30 °C (A); and in the presence of NaI at various temperatures (B, C, D, and E). All spectra were run in 2% MeOD- CD_2Cl_2 . Bound crown and diimide peaks are depicted as i_{in} , j_{in} etc, while unbound peaks are depicted as i_{out} , j_{out} etc.

exchange (as in the solution studies above, and from our previous results), the presence of a second set of crown peaks was puzzling. Measuring the HR MAS spectrum of the same sample at low temperature ($-15\text{ }^\circ\text{C}$) resolved the issue: the diimide resonance and *one* set of the crown peaks (labelled i_{in} , j_{in} and k_{in} in Fig. 3) sharpened and shifted upfield. This is indicative of their being involved in an equilibrium between free components and bead-bound pseudorotaxane, where the lower temperature has increased the proportion of the latter, with concomitant upfield shifts. On the other hand, the *second* set of crown peaks remained unmoved, and unchanged in intensity and broadness, clearly indicating that it is not involved in the equilibrium. Being downfield of the

diimide-bound set, we attribute this set of peaks to ‘entrapped’ or ‘intertwined’ in the bead core and thus unable to access the diimide.³² These peaks are labelled i_{bead} , j_{bead} and k_{bead} in Fig. 3. This phenomenon is not seen when a large excess of crown is added (as reported in our previous studies), where the peaks appear in the typical unbound region of the spectrum, overlapping and obscuring the region where the entrapped crown peaks appear.

Thus it is important to ensure that analysis of these systems is carried out with both concentrated and more dilute solutions so that the different behaviour can be monitored. It is also clear that the use of variable temperature HR MAS can be of considerable

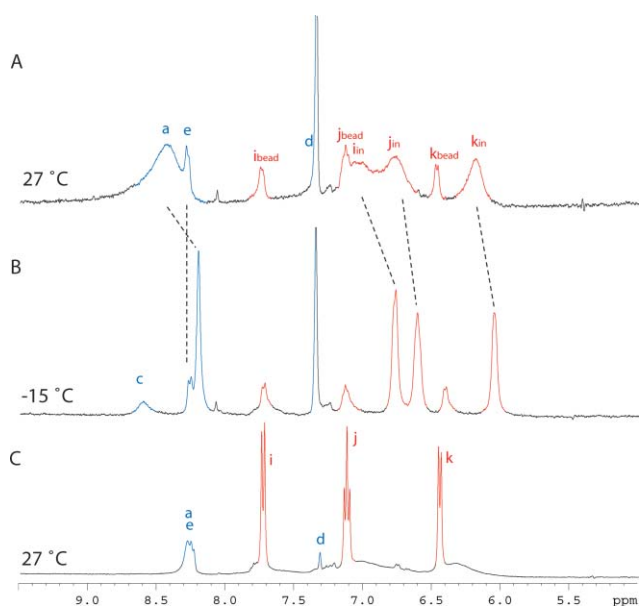


Fig. 3 HR MAS proton NMR spectral comparisons of a mixture of diimide tethered bead **5** with crown **2** in 2% MeOD-CDCl₃ at the temperatures indicated. A and B are spectra of the same sample at different temperatures. C is a spectrum of a sample with an excess of crown **2**. The differences in spectrum C compared to a previous report²¹ is due to both a different solvent system and concentration of crown (the previous spectrum was obtained in CDCl₃ with a significantly higher concentration of added crown, resulting in stronger diimide complexation, as evidenced by a higher field diimide proton a chemical shift. It should also be noted that some pyridine proton resonances that are apparent in our previous reported spectrum of this system, are not visible here due to their being filtered out as a result of a 2 K CPMG loop pulse sequence used to suppress core bead proton resonances (see Experimental and the electronic supplementary information†). Nevertheless, all samples were routinely run with 0, 32, and 2 K CPMG loop pulse sequences to ensure visualisation of all components. Clear NMR signals for the pyridine protons b–e were visualised in the basic proton pulse acquisition where no CPMG sequences were used. Labelling and colouration is as discussed in the text, and correspond to those indicated in Scheme 1.

utility in understanding the dynamic behaviour of these systems on solid supports.

A similar concentration dependence was observed for the ruthenium porphyrin fully stoppered rotaxane **6**. Previously, we have reported that an equilibrated mixture of the polymer-bound thread **5**, the crown **2** and the ruthenium porphyrin **3** showed the presence of three distinct sets of crown-derived peaks in the HR MAS spectrum. These were attributed to unbound crown **2**, crown belonging to the polymer-linked and porphyrin-stoppered rotaxane **6**, and the third set to crown encircling the inner polyethylene glycol linkers on the ArgoGel beads. We now show that the appearance of this third set of crown resonances is also concentration dependent, and if a lower concentration of crown is used in the solution surrounding the functionalised beads, then these resonances can be effectively eliminated. Under (estimated) similar relative concentration conditions as used above, addition of an equimolar solution of **2** and **3** to the diimide tethered beads **5** resulted in a large upfield shift of the pyridyl protons (to 6.68, 5.35, 2.18 and 1.76 ppm) as the pyridine group coordinated to the ruthenium porphyrin. Stoppering by this porphyrin slows

the dynamics of this system from fast to slow exchange on the NMR chemical shift timescale, resulting in observable bound (6.75, 6.57, 6.02 ppm) and unbound (7.70, 7.14, 6.48 ppm³³) crown, and likewise bound (8.18 ppm) and unbound (8.71 ppm) diimide peaks (Fig. 4). Unlike our previous report however, no third set of crown peaks due to polyethylene glycol bound crown around the polyethylene glycol tentacles of the ArgoGel beads were observed under these more dilute conditions. Variable temperature experiments showed that as the temperature decreased, the proportion of bound *versus* unbound crown increased, indicating that rotaxane formation is thermodynamically favoured at lower temperatures, which is comparable behaviour to that observed on the analogous solution-state rotaxane systems discussed above.

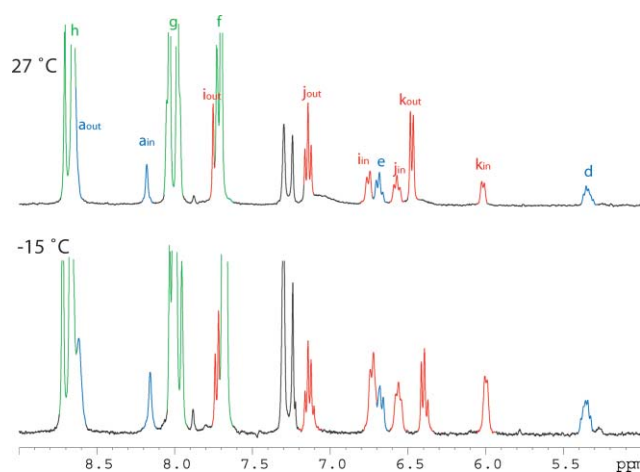


Fig. 4 HR MAS ¹H NMR comparison, at the temperatures indicated, of diimide tethered bead **5** with an added excess of an equimolar mixture of crown **2** and porphyrin stopper **3**.

Nevertheless, the reproducibility of this technique was demonstrated by the use of more concentrated solutions of crown and porphyrin. The HR MAS spectra obtained were now identical to those previously reported, with the pseudorotaxane showing only one set of peaks, and the sample containing both crown and porphyrin revealing the third set of crown peaks, identical to those previously reported.²¹ This confirms that the technique is indeed reproducible and the differences between samples and sets of measurements are a function of the ratio of diimide to crown and porphyrin, and not to any anomaly in either the synthesis/loading of the beads or an experimental artefact of the HR MAS technique (see also the electronic supplementary information†).

Since we had previously observed Na⁺-enhanced rotaxane formation in solution-phase studies of the analogous system containing the stoppered diimide **9**, it was of interest to determine whether this effect could be seen in the analogous systems tethered to solid polystyrene beads. However, as quantitation is difficult in this technique, care must be taken to ensure that any observed relative enhancement of binding is due to the addition of sodium cations, and not as a result of variation in crown concentration in the solution surrounding the beads in the different samples during their preparation for HR MAS analysis.

In a typical experiment, a solution of crown **2** and NaI in 2% MeOD-CDCl₃ was sonicated for several minutes to ensure solubilisation of the sodium iodide and then this solution was

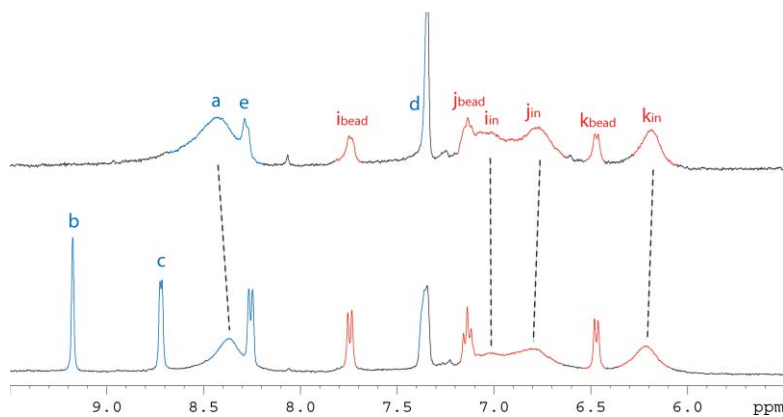


Fig. 5 HR MAS ^1H NMR comparison of polymer-tethered pseudorotaxane with and without added NaI at 300 K in 2% MeOD- CDCl_3 . Top spectrum is tethered diimide **5** + crown **2**. Bottom spectrum is tethered diimide **5** + crown **2** + excess NaI.

added to the diimide tethered beads **5** and HR MAS ^1H NMR spectrum recorded (Fig. 5).

HR MAS NMR spectra recorded in the presence of NaI invariably show much sharper peaks. Indeed, in these cases, the pyridine protons are clearly distinguished; they are not filtered by the application of the CPMG pulse sequence, an experimental artefact that is commonly encountered in preparations without added salt (see for example the caption under Fig. 3), presumably due to different relaxation effects caused by the presence of the NaI. In the comparable samples shown in Fig. 5, the addition of NaI has caused an upfield shift in the diimide proton from 8.43 to 8.37 ppm. In this case however, the crown peaks are seen to be deshielded slightly, moving from 6.92, 6.77 and 6.19 ppm to 7.01, 6.79 and 6.22 ppm. This suggests an excess of crown added to the beads in this sample, and thus the upfield shift of the diimide peak may be a result of additional crown causing a shift in the equilibrium to a larger proportion of bound species. Nevertheless, the sharpening of the spectra suggests that the exchange process is slower and that the formation of pseudorotaxane is indeed stabilised, although the relative magnitudes of the shifts of the peaks in this case is not entirely definitive.

Addition to the diimide-attached beads **5** of a solution containing the same crown **2**, but now with added porphyrin stopper **3** and NaI, showed more definitive evidence of the effect of the sodium ion (Fig. 6). In this case, addition of NaI clearly increases both the proportion of bound diimide and bound crown relative to their unbound counterparts. It could be established that this is not due to excess crown, as otherwise the spectrum would show an increase in bound diimide but a decrease in bound crown. Conversely, it cannot be due to a lower amount of added crown, which would result in increased bound crown peaks but a reduction of bound diimide. Thus, it can be concluded that the sodium cation enhances the rotaxane formation on solid supports just as it does in the solution-phase analogues **10** and **11**.

Conclusions

The results presented here show that there is no significant difference in the behaviour of the solid-tethered diimide thread system compared to that observed in their solution-phase analogues. The enhancement of rotaxane formation by the addition of Na^+ ions

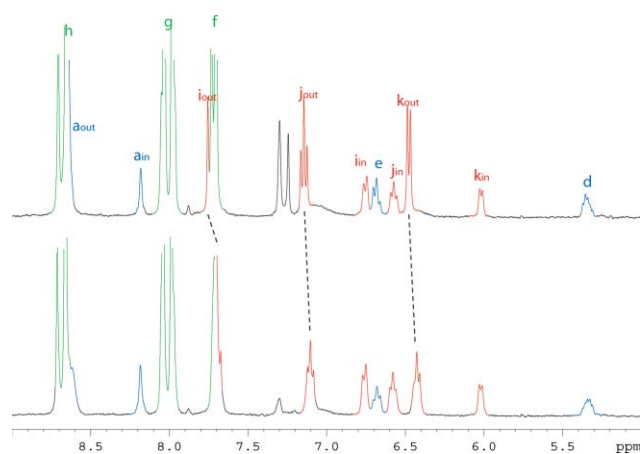


Fig. 6 HR MAS ^1H NMR comparison of pseudorotaxane formation with and without NaI at 300 K. Top spectrum is of tethered diimide **5** + crown **2** + porphyrin stopper **3**. Bottom spectrum is of the same mixture + NaI.

observed in solution is also paralleled in the gel-phase system. We have also confirmed that within certain limitations imposed by experimental difficulties associated with precise stoichiometric quantitation, the spectra are reproducible, which shows that this technique is reliable and robust. The ability to use variable temperature makes this a very versatile technique and extends its potential considerably.

Experimental

Synthesis

2-(2-(2-(2-(2-Nicotinoyloxyethoxy)ethoxy)ethoxy)ethyl)-7-(2-(2-(2-(2-(3-carboxypropionyloxy)ethoxy)ethoxy)ethyl)-benzo[*lmn*]-3,8)phenanthroline-1,3,6,8-tetraone (**8**)

2-(2-(2-(2-(2-Nicotinoyloxyethoxy)ethoxy)ethoxy)ethyl)-7-(2-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)benzo[*lmn*]-3,8)-phenanthroline-1,3,6,8-tetraone¹⁵ (325 mg, 450 μmol), succinic anhydride (90 mg, 900 μmol), 4-(*N,N*-dimethylamino)pyridine (DMAP, 11.0 mg, 90 μmol) and triethylamine (125 μL , 900 μmol) were dissolved in dichloromethane (DCM, 40 mL) and stirred at room temperature for 5 days then heated to 48 $^\circ\text{C}$ for 1 day. The

solvent was evaporated and the residue taken up in chloroform-water. The organic layer was separated, dried (Na₂SO₄) and the solvent evaporated. The crude product was subjected to column chromatography (SiO₂: DCM to 10% MeOH-DCM) to yield the pure product as a yellow oil (300 mg, 81%); *m/z* (ES-MS) [M + H]⁺ 824.2880 C₄₀H₄₆N₃O₁₆ (calc. 824.2878); ¹H NMR (300 MHz, CDCl₃) δ 9.18 (1H, d, Ar-H), δ 8.72 (4H, s, Ar-H), δ 8.76 (1H, dd, Ar-H), δ 8.31 (1H, dd, Ar-H), δ 7.42 (1H, dd, Ar-H), δ 4.46 (6H, m, OCH₂), δ 4.19 (2H, t, OCH₂), δ 3.82 (6H, m, OCH₂), δ 3.57–3.71 (18H, m, OCH₂), δ 2.60 (4H, s, CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 176.3, 176.0, 175.3, 172.4, 172.2, 171.5, 165.0, 162.9, 152.8, 150.4, 137.7, 131.0, 126.7, 126.6, 126.3, 123.5, 70.6, 70.4, 70.1, 69.0, 67.8, 64.6, 63.7, 60.7, 45.5, 42.2, 42.0, 40.7, 39.6, 30.4, 30.1, 29.7, 29.3, 29.2, 29.1, 28.0, 14.1, 14.0, 12.9, 8.5.

Mono-(2-(2-(2-(1,3,6,8-tetraoxo-7-(2-(2-(2-(2-(pyridine-3-carboxyloxy)ethoxy)ethoxy)ethyl)-3,6,7,8-tetrahydro-1H-benzo[lmn](3,8)phenanthroline-2-yl)ethoxy)ethoxy)ethoxy)-mono-4-(tris-(4-tert-butylphenyl)-methyl)-phenyl) succinate (9)

Succinic acid mono-ester **8**^{15,22} (50 mg, 0.06 mmol) was dissolved in toluene (5 mL) and excess oxalyl chloride (2 mL) was added. The mixture was stirred at room temperature under N₂ for 4 h. The reaction mixture was then pumped dry, solubilized in CHCl₃ (1 mL) and pumped dry. This procedure was repeated 4 times to remove all excess oxalyl chloride. The produced acid chloride diimide thread (quantitative yield) in dry CHCl₃ (10 mL) was then added to a solution of phenol stopper **7**²⁴ (34 mg, 0.06 mmol) in dry CHCl₃ (30 mL). The reaction mixture was then stirred at room temperature under N₂ for 12 h. After this time, the mixture was diluted with CHCl₃ (30 mL) and washed with sat. NaHCO₃ (20 mL) and H₂O (20 mL). The crude product was purified by chromatatratron (2 mm silica plate) using 5% MeOH-DCM as the eluent to give the pure product **9** as a yellow solid (66 mg, 81%); *m.p.* 168–170 °C; *m/z* (ESI-MS) [M+H]⁺ 1310.6165 C₇₇H₈₈N₃O₁₆ (calc. 1310.6086); ¹H NMR (300 MHz, CDCl₃) δ 9.24 (1H, s, py-H), 8.76 (5H, s, py-H, NDI), 8.35 (1H, d, *J* 8, py-H), 7.45 (1H, t, *J* 6, py-H), 7.18–7.28 (8H, m, Ar-H), 7.08–7.11 (6H, m, Ar-H) 6.97 (2H, d, *J* 6, OAr-H), 4.45–4.52 (8H, m, OCH₂), 4.24–4.27 (2H, m, OCH₂), 3.84–3.87 (8H, m, OCH₂), 3.60–3.72 (14H, m, OCH₂), 2.86 (2H, m, CH₂), 2.77 (2H, m, CH₂), 1.31 (27H, s, t-Bu); ¹³C NMR (75 MHz, CDCl₃) δ 172.0, 170.8, 165.1, 162.8, 153.1, 150.7, 148.5, 145.0, 143.7, 137.3, 132.2, 131.0, 130.7, 126.8, 126.6, 124.1, 119.9, 70.7, 70.6, 70.1, 69.0, 67.8, 64.5, 63.9, 63.4, 39.6, 34.3, 31.4, 29.3, 29.1.

ArgoGel(tm)-OH bound 2-(2-(2-(2-(2-nicotinoyloxy-ethoxy)-ethoxy)-ethoxy)-ethyl)-7-(2-(2-(2-(2-(3-carboxy-propionyloxy)-ethoxy)-ethoxy)-ethoxy)-ethyl)benzo[lmn]-(3,8)phenanthroline-1,3,6,8-tetraone (5)

ArgoGel-OHTM or TentaGelTM beads (50 mg) and mono-succinate ester **8** (337 mg, 409 μmol) were stirred at room temperature under nitrogen with CHCl₃ (5 mL). Triethylamine (62 μL, 450 μmol) was added to the mixture *via* a syringe, followed by 1-hydroxybenzotriazole, HOBT (81 mg, 600 μmol) and EDC (115 mg, 600 μmol). The mixture was heated to 50 °C and stirred for 7 days under N₂. Then the beads were filtered and washed successively with CHCl₃ (5 mL), acetone (5 mL), water (5 mL), HCl (aq, 2 M, 5 mL), sodium bicarbonate (sat aq, 5 mL), water (5 mL) acetone (5 mL), petroleum spirit (5 mL) and CHCl₃ (5 mL). The beads were then dried under high vacuum. The resulting component-attached beads **5** were coloured yellow. ¹H NMR

(400 MHz, 2% MeOD-CDCl₃) δ 9.16 (1H, d, Ar-H), 8.72 (5H, s, Ar-H), 8.28 (1H, dd, Ar-H), 7.39 (1H, dd, Ar-H), 4.43 (4H, m, OCH₂), 4.19 (8H, m, OCH₂), 3.44–3.79 (20H, m, OCH₂), 2.60 (4H, s, CH₂). This compound was also attached to TentaGel resin beads giving an identical HR MAS NMR spectrum.

Methods and procedures for gel-phase HR MAS spectroscopy

Solution NMR spectra were acquired on a 300 MHz Bruker AC-300P FT spectrometer at 303 K. HR MAS NMR spectra were acquired on a Bruker DRX400 spectrometer at room temperature or below using a Bruker HR MAS microprobe. Rotors containing a suspension of the beads in CDCl₃ were spun at 4 kHz. One-dimensional HR MAS spectra were obtained with 64 scans. CPMG pulse sequence contained 32 or 2000 π-pulses with a repetition time of 30 ms. Chemical shifts (δ) are reported in parts per million relative to residual solvent.

Limitations of the technique and difficulties associated with accurate quantitation and spectral reproducibility between samples are discussed in the electronic supplementary information.†

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- 27 This is to be expected as stoppering of one end of the thread, instead of both ends, alters both the on and off rates equally (by a factor of 1/2), having no net effect on the overall K_a . However, this would not be the case in situations in which the stopper directly interacts with the binding either positively or negatively, so this possibility needed to be discounted.
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- 31 The loading of the diimide thread on the polystyrene beads was determined by spectroscopic techniques and elemental analysis. Details of the procedures and the results are described in the electronic supplementary information. The loading of the naphthodiimide tethered beads 5 was determined to be approximately 0.19 mmol g⁻¹. This is a higher figure than we reported previously,²¹ which was in error. Limitations inherent in the technique with regard to precise quantitation and reproducibility are also discussed in the electronic supplementary information†.
- 32 The crown may be threaded on the polyether chains, or more simply entangled in them; the spectra are unable to distinguish between these possibilities. In either case, the environment provided by the polyethylene glycol chains would be sufficiently different to that of the solvated uncomplexed crown to account for the slight upfield shifts.
- 33 It should be noted that this unbound crown set will include both crown “entrapped” in the bead core, which is not involved in the equilibrium with the diimide, and unbound crown which is.