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An imidazolium-functionalized self-assembling calix[4]pyrrole†

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A calixpyrrole bearing a tethered imidazolium functional group was prepared in the form of its bromide salt. This compound was found to undergo self-assembly to produce supramolecular polymers, wherein both the bromide anion and the imidazolium cation are bound to the calixpyrrole core.

Since Lehn's seminal report,[1] supramolecular polymers have been widely investigated. They represent an interesting class of macromolecules in which non-covalent forces and reversible bonding interactions serve to assemble monomeric subunits. Supramolecular polymers combine the useful features of conventional polymers with the dynamic nature of non-covalent interactions.[2] To date, a variety of non-covalent intermolecular forces, including hydrogen bonding, host–guest interactions, metal–ligand coordination, π–π donor–acceptor and hydrophobic effects, have been exploited to produce non-covalent polymers. Control of these systems has been achieved using a number of stimuli and triggers, such as pH, temperature, changes in metal coordination, and light.[2l] During last decade, remarkable advances in the supramolecular polymer field have been made using well-known receptors, such as cyclodextrins,[2b] crown ethers,[3] calixarenes,[4] cucurbiturils,[5] cyclophanes,[6] cryptands[2n] and pillar[5]arenes.[2l] This has allowed production of *inter alia* self-healing materials[2l] and integrated motion systems that mimic muscle action.[2k] Nevertheless, to exploit fully the inherent promise of the supramolecular material paradigm, new synthetic platforms that permit the construction of self-assembled polymers would be useful. Here, we report a new class of supramolecular constructs based on calix[4]pyrroles.

Calix[4]pyrroles are non-aromatic, oligopyrrole macrocycles that display anion and ion pair recognition capabilities. They have been used for various applications, including as phase-transfer catalysis,[7] ion-selective sensors,[8] trans-membrane ion transporters,[9] extractants for anions and cations,[10] and as solid supports for the sensing and separation of anions.[10d] Recently, we reported supramolecular polymeric materials stabilized by a combination of donor–acceptor and hydrogen bonding interactions using tetrathiafulvalene-functionalized and bis(dinitrophenyl)-*meso*-substituted calix[4]pyrroles.[2i] While good fidelity and easy-to-observe optical changes were seen during assembly and disassembly, the use of two components complicated the analyses and required a relatively larger synthetic investment. In principle these deficiencies could be overcome by combining a calixpyrrole core with a moiety that would promote interactions with another calixpyrrole. We had found in separate work that pyridinium and imidazolium bis-cations were able to link calix[4]pyrrole anion complexes, both in solution and in the solid state. This linking, which was ascribed to the electron deficient bis-cations binding within the electron-rich bowl-shaped cavities of two separate anion-bound calixpyrroles, resulted in the stabilization of discrete, non-covalently linked sandwich-type dimers.[2j]

These findings prompted us to consider that heteroditopic calix[4]pyrroles bearing an imidazolium subunit connected to a tetrapyrrolic core through an alkyl chain ($\mathbf{4}^{+}$) would act as an autonomous building block that could be used to create synthetic, self-assembled supramolecular polymeric materials without requiring the concordant use of other functional monomers (Fig. 1). As detailed below, these design expectations were met as inferred from ^{1}H- and DOSY NMR spectroscopic analyses, as well as viscosity measurements.

Scheme 1 provides a summary of the synthesis of the bromide salt of the imidazolium-functionalized calixpyrrole of this study (*i.e.*, **4**), as well as the corresponding control imidazolium salt. Briefly, the carboxylic acid substituted calix[4]pyrrole **2**[10e] was reacted with 11-bromo-1-undecanol in dichloromethane in the presence of dicyclohecylcarbodiimide–4-dimethylaminopyridine (DCC–DMAP). This provided compound **3** in 64% yield. Compound **3** was then reacted with 1,2-dimethylimidazole in acetonitrile at 70 °C to afford the bromide salt of the imidazolium-functionalized

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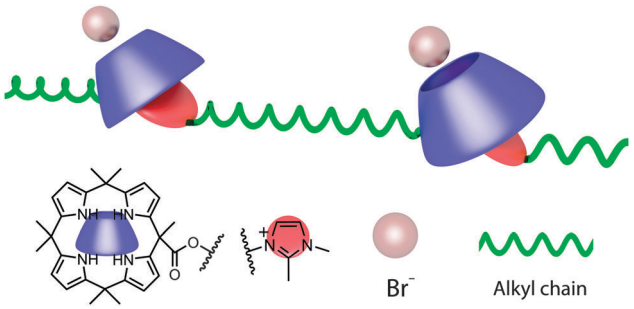
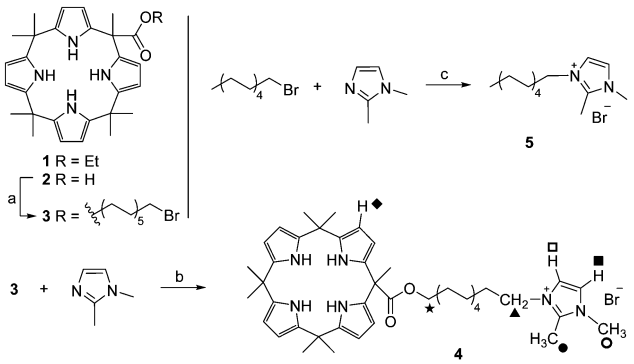


Fig. 1 Representation of the supramolecular polymer formed *via* the self-assembly of **4**.



Scheme 1 Synthesis of imidazolium-functionalized calix[4]pyrrole and control compounds. Reagents and conditions: (a) 11-bromo-1-undecanol, DCC–DMAP, CH_2Cl_2, r.t.; (b) CH_3CN, 70 °C, 24 h; (c) *n*-propanol, reflux, 24 h.

calixpyrrole target (**4**) in 93% yield. A control imidazolium salt (**5**) was prepared in 96% yield by reacting 1-bromodecane with 1,2-dimethylimidazole in 1-propanol at reflux.

To assess the self-assembly properties of the imidazolium-functionalized calix[4]pyrrole **4**, it and the imidazolium-free calix[4]pyrrole **3** were analyzed by ^{1}H-NMR spectroscopy in $CDCl_3$. The spectra of these two calixpyrroles differ dramatically (Fig. 2). For instance, as compared to **3**, the NH peaks of **4** are shifted to lower field, while the pyrrolic –CH peaks are shifted upfield. The nature and direction of these two sets of peak shifts are typical of what is observed when a calix[4]pyrrole adopts a cone conformation and acts an ion pair receptor, binding the anion and cation *via* pyrrole NH hydrogen bonds and "cup-like" cation–π interactions, respectively.[11]

Also shown in Fig. 2 are the spectra for control compounds. Based on comparisons, upfield shifts in the imidazolium peaks are seen in the case of **4** relative to **5**. These shifts are consistent with an interaction between the imidazolium cation and the calixpyrrole in the case of **4**. These interactions are, of course, precluded in the case of **5**. Noteworthy is that the imidazolium –CH protons in **4** resonate at 6.76 and 6.63 ppm, whereas the corresponding peaks are observed at 7.40 and 7.70 ppm in the case of **5**. Similarly, the imidazolium $-CH_3$ protons of **4** are observed as broad peaks at 2.69 and 2.13 ppm, whereas the corresponding signals appear as sharp peaks at 4.02 and 2.81 in the case of **5**. Finally, the $-CH_2$ protons adjacent to the imidazolium unit in **4**

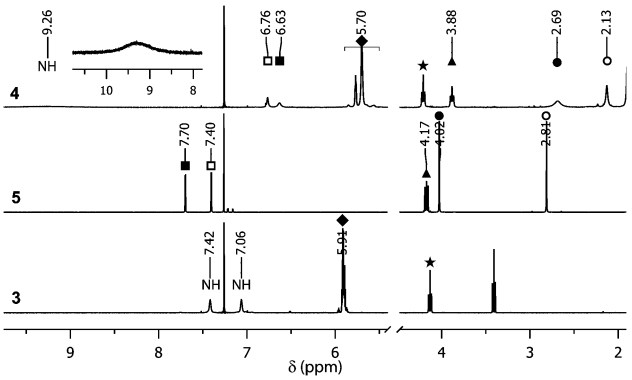


Fig. 2 Partial ^{1}H-NMR spectra of compounds **3**, **4**, and **5** recorded at 7 mM in $CDCl_3$. Peak labels: imidazolium $-CH_3$ (○ and ●) and –CH peaks (□ and ■); alkyl $-CH_2$ (▲); pyrrole –CH (◆); ester $-CH_2$ (★).

are shifted upfield by 0.29 ppm as compared to **5**. These shifts mimic what is seen when imidazolium cations interact with the anion-bound cone form of calix[4]pyrrole.[2j,m] They are consistent with an interaction between the calixpyrrole core and the imidazolium subunit of **4**.

Further support for the proposed interaction between the bromide and the tethered imidazolium ion attached to the calixpyrrole core came from a ^{1}H-NMR spectral titration of control compound **5** with **1**. This titration revealed that both the imidazolium –CH resonances (from 7.6 to 6.8 ppm) and the imidazolium $-CH_3$ signals (from 4 ppm to 2.9 ppm and 2.8 ppm to 2.3 ppm) of **5** undergo an upfield shift as the concentration of **1** increases (*cf.* Fig. 3 and Fig. S7, ESI†). The signals ascribed to the $-CH_2$ protons (▲) also shift to higher field (from 4.15 ppm to 3.9 ppm). By monitoring the imidazolium $-CH_3$ (●) proton shifts over the course of the above titrations, the binding constant between the calixpyrrole core of **1** and the imidazolium cation **5** could be calculated, giving a value of $(1.44 \pm 0.2) \times 10^4$ M^{-1} for the equilibrium in question (*cf.* Fig. S19 and S20, ESI†).

The concurrent binding of the bromide anion of **4** (*via* hydrogen bonds) to the calixpyrrole NH protons and the imidazolium cation within the "cup" produced in the anion-bound cone conformation allows for oligomer-forming self-assembly (as illustrated in Fig. 3a). The chemical shifts observed above are consistent with such a

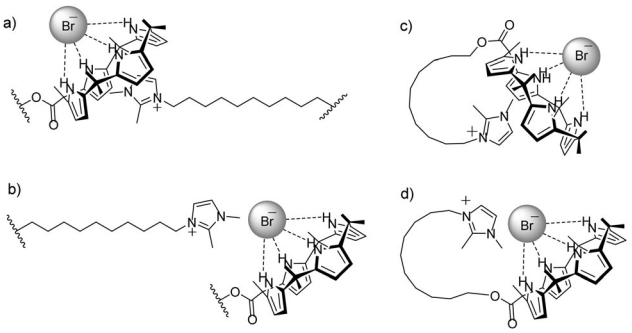


Fig. 3 (a) Schematic representation of the supramolecular polymer formed *via* the self-association of **4**. Also shown (b–d) are other possible binding modes for the imidazolium cation present in **4**.

Table 1 List of peak shifts seen upon dilution of **4** in $CDCl_3$/DMSO-d_6 (97.5/2.5)

	Pyrrole (ppm)		Imidazolium (ppm)				
[**4**] (mM)	–NH	–CH (◆)	–CH (◘)	–CH (■)	$–CH_2$ (▲)	$–CH_3$ (●)	$–CH_3$ (○)
14.5	9.60	5.69	6.85	6.68	3.88	2.72	2.08
0.94	8.65	5.80	7.13	7.13	4.05	3.40	2.59

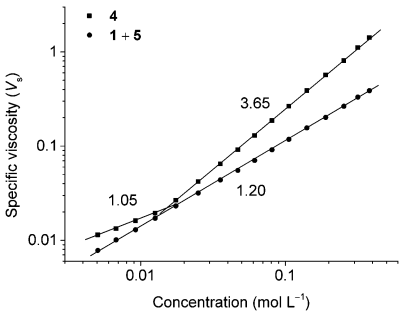


Fig. 4 Specific viscosity (303 K) of **4** and a mixture of **1** and **5** plotted against the monomer concentration.

binding mode. They also serve to rule out a number of alternative scenarios, including intra- and intermolecular interactions wherein the imidazolium cation is bound directly to the bromide anion (*cf.* Fig. 3b and d). However, the spectral analyses associated with Fig. 2 do not in themselves allow a distinction between the formation of a supramolecular polymer (the binding mode shown in Fig. 3a) and self-associating structures wherein the binding interactions are intramolecular in nature (*cf.* Fig. 3c).

To distinguish between inter- and intramolecular binding modes, (Fig. 3a and c, respectively), receptor **4** was studied as a function of concentration. This was done by subjecting a stock solution of **4** in DMSO-d_6/$CDCl_3$ (2.5 : 97.5 v/v) to dilution, while recording the changes in the ^{1}H-NMR spectrum (Table 1 and Fig. S8, ESI†). From an inspection of Table 1, the pyrrole –NH protons were found to shift to higher field, while the calixpyrrole –CH protons shifted to lower field as the concentration was reduced from 14.5 mM to 0.94 mM. Similarly, the imidazolium $–CH_3$ (●) resonance of **4** was found to shift from 2.72 to 3.40 ppm over the concentration range in question. For reference, the same signal in **5** resonates at 4.02 ppm, with the chemical shift being insensitive to concentration. These peak shifts are thus consistent with an intermolecular association (Fig. 3a) and the corollary expectation that both the anion and imidazolium cation become bound less effectively to the calixpyrrole as the concentration is lowered.

Using the effective affinity constant derived in the case of the model system (**5**⊃**1**, for which $K_a = 1.44 \pm 0.2 \times 10^4$ M^{-1}) in conjunction with an isodesmic model, the degree of polymerization (DP $\approx (K_aC)^{1/2}$), could be calculated.[12] The resulting value, which corresponds to the average number of subunits in the oligomer, was found to be 14.4 for **4** at a concentration of 14.5 mM in $CDCl_3$ at room temperature.

To analyze further the supramolecular aggregates obtained from **4**, viscosity measurements were carried out in $CHCl_3$/DMSO (95/5 v/v) using an Ubbelohde semi-micro dilution viscometer. As presented in Fig. 4, the aggregates assembled from **4** exhibited viscosity transitions, which were reflected in a change in slope in the logarithmic plots of the specific viscosity *versus* concentration.

At low concentration, the curve had a slope of nearly 1, indicating a linear relationship between specific viscosity and concentration.[13] When the concentration exceeds the critical polymerization concentration (CPC; approximately 12.5 mM for **4**), a sharp increase in the viscosity was observed (slope = 3.65). In contrast, a relatively lower viscosity was found for a mixture of **1** and **5** (slope = 1.20), reflecting non-covalent interactions that cannot lead to formation of a supramolecular polymer. The CPC value of **4** was found to be relatively low compared to what is seen for analogous systems based on calixarenes, pillar[5]arenes, crown ethers, and cryptands. This result seems reasonable since most of these latter systems have been studied in more polar media (*e.g.*, acetonitrile).[2]

2D diffusion-ordered NMR spectroscopy (DOSY) analyses of **4** provided further support for the conclusion that **4** self-assembles to produce supramolecular oligomers (Fig. S16, ESI†). Specifically, solutions of **4** at 14.1 mM, 6 mM, and 1.1 mM, respectively, in $CDCl_3$ were subjected to DOSY analyses. In accord with the design expectations, the concentrated solution was found to show a diffusion order of $(6 \pm 0.1) \times 10^{-10}$ m^2 s^{-1}, while the dilute solutions were characterized by higher diffusion orders (*i.e.*, $(10 \pm 0.1) \times 10^{-10}$ m^2 s^{-1} and $(20 \pm 0.1) \times 10^{-10}$ m^2 s^{-1}, respectively). Additionally, correlated 2D-NOESY signals were observed between the pyrrole –CH, ester $–CH_2$ and imidazolium –CH and $–CH_3$ protons. These findings provide further support for the proposed inclusion of the imidazolium subunit within the electron-rich cup of the calixpyrrole (Fig. S18, ESI†).

Further support for the proposed supramolecular polymerization of **4** came from a titration of **4** with **5**. The rationale for this titration is that if a competing imidazolium bromide were added to a $CDCl_3$ solution of **4**, the proposed self-assembly of **4** would be disrupted. This, in turn, should lead to disassembly of the supramolecular polymer. Fig. S9, ESI,† shows the results of the titration of **4** with **5** as monitored by ^{1}H-NMR spectroscopy. As the number of **5** equivalents is increased, the signals corresponding to the imidazolium $–CH_3$ protons (○ and ●; Fig. S9, ESI†) of **4** were found to shift to lower field. For instance, the signals that appear at 2.21 and 2.79 ppm in the absence of **5**, were observed at 2.53 and 3.46 ppm in the presence of 3.2 equivalents of **5**. Concurrently, the imidazolium –CH proton resonances of **4** (◘ and ■) were found to undergo a downfield shift as the relative concentration of **6** increased. These signals are observed at 6.70 and 6.80 ppm in the absence of **5** but appear at 7.19 and 7.25 ppm in the presence of 3.2 equiv. of **4**. On treatment with **5**, the protons of the bridging alkyl tether of **4** (▲) shift to lower field and are observed as a triplet centered

at 3.91 ppm that overlaps with the corresponding signals for **5** (centered at 4.1 ppm).

DOSY NMR spectral analyses (Fig. S17, ESI†) revealed that while **4** (6.3 mM) gives rise to a diffusion constant of $(8 \pm 0.1) \times 10^{-10}$ m^2 s^{-1}, the corresponding value increases to $(15 \pm 0.1) \times 10^{-10}$ m^2 s^{-1} when the same solution is treated with 3.2 equivalents of **5**. Taken in concert with the results of the 1D NMR spectral analysis, these results are consistent with the expectation that the supramolecular oligomer formed from **4** deaggregates when treated with a suitable competitive binding agent, such as **5**.

In summary, we have prepared a novel supramolecular polymer, **4**, that self-assembles as the result of the dual recognition of both a bromide anion and an imidazolium cation tethered to a calix[4]pyrrole unit. The present results thus highlight a new approach to creating self-assembled materials.

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