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Countercation-Dependent Proton-Driven Self-Assembly of Linear Supramolecular Oligomers Based on Amino-Calix[5]arene Building Blocks


Dedicated to Professor Sir J. Fraser Stoddart on the occasion of his 65th birthday

Abstract: Self-assembly of a calix[5]arene bearing a 12-aminododecyl pendant group on the lower rim into supramolecular oligomers through intermolecular iterative inclusion events is readily triggered by contact with acid solutions and is reversed to the amino monomer precursor by treatment with a base. 1H NMR data are consistent with the formation of head-to-tail assemblies derived from endo-cavity inclusion of the alkylammonium moiety. Diffusion NMR and light-scattering studies provide evidence for the presence of oligomers in solution and show that different counterions and concentrations result in different oligomer sizes, whereas ESI-MS and SEM investigations, respectively, indicate that self-assembly also takes place in the gas phase and in the solid state. The growth of these supramolecular oligomers is concentration-dependent; however, as a consequence of the saline nature of the monomer, it also shows a distinct counterion-dependence owing to ion-pairing/solvation effects.

Keywords: calixarenes · ion pairs · light scattering · NMR spectroscopy · supramolecular polymers

Introduction

Supramolecular polymers[1] are one of the latest developments in modern materials research. Over the past few years, a great deal of energy has been devoted to the construction of polymeric architectures, starting from simple molecules that can recognize each other and then self-assemble through weak intermolecular interactions. Several authors have focused on the use of complementary hydrogen-bonding building blocks, such as uracil derivatives and dianimopyridines,[2] cyanuric acid and melamine,[3] cyanuric acid and bis-diaminopyridines,[4] ureidopyrimidinone,[5] or even calix[4]arene tetraurea dimers,[6] to name a few representative examples. Others have investigated the possibility of using arene–arene interactions for the self-assembly of supramolecular polymers from discotic molecules, which has led to the production of a number of superstructures displaying liquid crystalline properties.[7] On the other hand, examples of supramolecular polymers obtained by exploiting iterative host–guest inclusion events are less common.[8] Relevant examples are the linear arrays of (pseudo)rotaxanes based on cyclodextrins with an apolar pendant group attached to the primary face, described by Harada et al.,[9] or the heteroditopic monomer composed of a bipyridinium moiety linked to a dibenzo[32]crown-10, reported by Gibson and co-workers.[10] In-depth studies on the formation of cyclic versus linear oligomers derived from secondary ammonium ion-substituted dibenzo[24]crown-8 have been described by the group of Stoddart.[11] Alternatively, formation
of supramolecular polymers that rely on host–guest interactions has involved the use of complementary homoditopic monomers, such as bis-crown ethers and secondary diammonium ions,[12] or bis-cyclodextrin and bis-adamantyl guest molecules.[13] Within the framework of a general project aimed at the synthesis of supramolecular entities based on the calix[5]arene–primary alkylammonium ions recognition motif, we have recently described the formation of inclusion networks derived from the self-assembly of a bis-calix[5]arene receptor and long-chain α,ω-alkylldiammonium ions.[14] In this context, besides the studies on the self-assembly of the aforementioned AA/BB-type complementary homoditopic monomers, we have also been interested in the development of polymeric supramolecular structures by harnessing AB-type[15] heteroditopic monomers. Prompted by a very recent paper on the self-assembly of a pyridinium-containing calix[4]arene,[16] we now wish to report full details on the synthesis of a cone calix[5]arene derivative, bearing a long-chain alkylamino pendant group on the lower rim, and its self-assembly behavior in the presence of different acids. The self-assembly process was followed by NMR spectroscopy, diffusion NMR, static and dynamic light scattering, mass spectrometry and scanning electron microscopy. The combination of all these techniques provides conclusive evidence for the existence of self-assembled aggregates in solution, in the solid state and in the gas phase.

**Results and Discussion**

**Synthesis of the monomer precursor 1**: The target amino-calix[5]arene 1 (Scheme 1) was synthesized in three steps starting from p-tert-butylicalix[5]arene[17] (2). An excess of 2 was treated with N-(12-bromododecyl)phthalimide[18] to yield the phthalimidododecyloxy derivative 3 (73%), which was then exhaustively alkylated with 4-methyl-1-bromopentane to produce calix[5]arene 4 (81%). Conversion of the phthalimido moiety into an amino group by treatment with hydrazine, under standard Gabriel conditions, yielded the monomer precursor 1 (56%). Amino-calix[5]arene 1 was characterized by 1H and 13C NMR spectroscopy, as well as by MALDI-TOF mass spectrometry. NMR data for 1 are consistent with a C₅-symmetric structure blocked in a cone conformation.[19]

**1H NMR studies**: Based on the known tendency of p-tert-butylcalix[5]arene derivatives to recognize and tightly bind unbranched primary alkylammonium ions,[20] we anticipated that simple conversion of 1 into a corresponding ammonium derivative would readily generate self-assembling monomeric species. To verify this hypothesis, a solution of amino-calixarene 1 in CD₂Cl₂ was exposed to aqueous 1 m HCl, dried (MgSO₄) and directly investigated by 1H NMR spectroscopy. As expected, protonation of the amino group activates the self-assembly of monomer 1·HCl, as the result of an iterative intermolecular inclusion process between the dodecylammonium moiety of one calixarene monomer and the cavity of another. This process of intermolecular complex formation/dissociation is slow on the 1H NMR timescale and, accordingly, two distinct sets of resonances were observed for the end-group (unthreaded moieties)[21] and core (threaded moieties) hydrogen atoms of the resulting noncovalent oligomers (1·HCl)n (Figure 1). With respect to the amino precursor 1, in CD₂Cl₂, the resonances of the oligo-

![Scheme 1. Synthesis of the calix[5]arene monomer precursor 1.](image)

![Figure 1. 1H NMR spectra (300 MHz, CD₂Cl₂, 10 mm, 295 K) of: a) 1; b) 1·HCl. The asterisk indicates the residual solvent peak.](image)
mer end-groups (calixarene cavity at one end and dodecylammonium moiety at the other, see Figure 1b) change very little. The most significant variations are associated with a peak (δ = 8.54 ppm) for the newly formed NH₃⁺ group and a downfield shift (Δδ = 0.30 ppm) for the adjacent methylene (CH₂NH₃⁺). On the other hand, the resonances assigned to the oligomer core undergo substantial complexation-induced shifts. Intermolecular inclusion of the dodecylammonium moiety of 1·HCl within the cavity of another calixarene is unambiguously demonstrated by the appearance, in the high-field region (δ = –2.0 to 1.0 ppm), of five peaks consistent with the methylene groups closest to the ammonium moiety (α- to ε-CH₂) and by the upfield shift of the NH₃⁺ resonance (δ = 5.63 ppm). NMR data (chemical shift as well as diffusion measurements, see below) and inspection of CPK models rule out the alternative process of endo-cavity intramolecular inclusion (self-threading) of the dodecylammonium moiety, either via the upper or the lower rim.

According to Equation (1), in the present case, the number-average degree of polymerization (X̄ₙ) depends on the stability constant (K) of the interaction between the host and guest subunits of the monomers.

\[ X_n \approx (K \cdot \text{monomer})^{1/2} \]  

(1)

As mentioned above, in the case under study, formation and dissociation of the oligomers were found to be slow on the NMR time-scale, so that direct integration of key resonances (NH₃⁺, ArH and -CH₂) of both the threaded and unthreaded species (core vs end-groups) of (1·HCl), were used to determine the value of \( X_n \) and derive the stability constant from it by means of Equation (1) (Table 1).

One of the attractive features of noncovalent polymers over covalently bound ones is their ability to reversibly vary the degree of polymerization in response to changes in the environmental conditions. In this respect, amino-calixarene 1 is, in principle, an extremely useful precursor for polymer formation because it promptly responds to simple chemical stimuli (i.e. acid/base treatment) by activating or deactivating the self-assembly process. Calixarene 1 acts as a proton scavenger, and even trace amounts of acid present in commercial CDCl₃ or CD₂Cl₂ are sufficient to induce protonation and set off the self-assembly process. Similarly, the (1·HCl), oligomers, in agreement with their non-covalent nature, were easily deprotonated to the free amino precursor 1 by treatment with a mild base (e.g. 1 M aqueous KOH).

Furthermore, 1 could be successfully reconverted to (1·HCl), upon subsequent exposure to an aqueous 1 M HCl solution, demonstrating that the oligomerization process can be controlled and turned on and off. Conversion of amino-calixarene 1 into an ammonium salt species (e.g. 1·HCl) is a mandatory step for oligomerization/polymerization to occur. The stability constants between neutral hosts and ionic guests in low polarity media, on the other hand, are known to be influenced by ion-pairing interactions. It was therefore envisaged that use of different acids would produce a variety of ammonium-calixarene salts which, as a result of the dependence of the monomer–monomer stability constant on the extent of ion-pairing, would ultimately yield oligomers of different sizes at a given monomer concentration. This hypothesis was fully confirmed by the conversion of monomer precursor 1 into (1·HBr) and (1·HPic), upon treatment with 1 M hydrobromic acid and 1% aqueous solution of picric acid, respectively. The end-group titration data, summarized in Table 1, indicate that in the case of 1·HCl, a 20-fold increase in the monomer concentration hardly affects the size of the oligomers formed (\( X_n = 1.8–1.9 \)), whereas variations of the bromide or picrate salt monomer concentrations produce a moderate-to-marked increase of the \( X_n \) values (3–5 and 9–20 for 1·HBr and 1·HPic, respectively) as a consequence of a progressive loosening of the ion-pairing.

**Diffusion NMR studies**: Extensive diffusion NMR experiments on CD₃Cl solutions of 1·DCI and 1·HPic unambiguously confirm intermolecular self-assembly and strongly support the formation of linear vs cyclic oligomers. In the event of intramolecular self-inclusion of the dodecylammonium moiety, the diffusion coefficient (D) of the protonated or deuterated monomers (1·HPic and 1·DCI) would have remained similar to that of the amino-precursor 1. On the contrary, diffusion data (Table 2) show that a dramatic decrease in the diffusion coefficient values follows upon protonation/deuteration of 1. This observation is only consistent with the formation of oligomeric species (see below). Figure 2 shows stack plots of the signal decay of representative peaks of 1, biscalix[5]arene 2 (chosen as a model compound for a species with a molecular weight roughly similar to that of the dimer of 1), 1·DCI and 1·HPic as a function of the gradient strength (G) for 10 mM CD₂Cl₂ solutions at 298 K.

Stack plots (c) and (d) (see Figure 2), assigned to a pair of oligomer core peaks (i.e. cavity included α- and β-CH₂) of

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Table 1. Percentages of threading for 1·HCl, 1·HBr and 1·HPic and corresponding calculated number-average degree of polymerization (\( X_n \)) and “apparent” stability constants (K).

<table>
<thead>
<tr>
<th>[%]</th>
<th>2</th>
<th>10</th>
<th>25</th>
<th>40</th>
<th>2</th>
<th>10</th>
<th>25</th>
<th>40</th>
<th>2</th>
<th>10</th>
<th>25</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xₙ</td>
<td>1.8</td>
<td>1.8</td>
<td>1.9</td>
<td>1.9</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>9</td>
<td>13</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>K</td>
<td>1620</td>
<td>324</td>
<td>144</td>
<td>90</td>
<td>5120</td>
<td>1369</td>
<td>740</td>
<td>576</td>
<td>34445</td>
<td>15625</td>
<td>11156</td>
<td>10000</td>
</tr>
</tbody>
</table>

[a] For calculation of \( X_n \) values see text. [b] Determined by ¹H NMR (300 MHz) at 295 K in CD₂Cl₂. Values derived from the average of three independent measurements. [c] Standard error ± 10%.

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The data in Table 2 show that, at any given concentration, both 1-DCI and 1-HPic always have much lower diffusion coefficients than 1 or even the model biscalixarene 5. These observations are consistent with the formation of non-covalent oligomers (i.e., (1-DCI), and (1-HPic)), in the case of 1-DCI and 1-HPic. It is also clear from the smaller $D$ values measured for 1-HPic over 1-DCI that the former generates larger aggregates. Diffusion NMR provides a means to simultaneously obtain the diffusion coefficients of all the different supramolecular species co-existing in solution, as long as they display distinct and not superimposed peaks. As mentioned above, two distinct sets of $^1$H NMR peaks were found for the end-groups and core of oligomers (1-DCI), and (1-HPic). Figure 4 shows the stack plots of the signal decay as a function of the gradient strength ($G$) for the ArCH$_2$Ar peaks assigned to the end-groups (traces 4a,c) and core (traces 4b,d) of the oligomers derived from 1-DCI and 1-HPic (traces 4a,b and 4c,d, respectively). Figure 5 shows the plot of the natural logarithm of the normalized signal decay as a function of the $b$ values for the peaks shown in Figure 4. Interestingly, we found different diffusion

**Table 2. Diffusion coefficients ($D$) for 1, 5, 1-DCI, and 1-HPic at different concentrations in CD$_2$Cl$_2$ at 298 K.$^{[a]}$**

<table>
<thead>
<tr>
<th>System</th>
<th>Peak [ppm]</th>
<th>40 nm</th>
<th>25 nm</th>
<th>$D$ [$\times 10^{-5}$ cm$^2$ s$^{-1}$]</th>
<th>10 nm</th>
<th>2 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.58</td>
<td>–</td>
<td>–</td>
<td>0.65 ± 0.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>4.56</td>
<td>–</td>
<td>–</td>
<td>0.44 ± 0.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>1-DCI</td>
<td>-1.82$^{[h]}$</td>
<td>0.21 ± 0.01 (0.25 ± 0.01)</td>
<td>0.22 ± 0.01 (0.27 ± 0.01)</td>
<td>0.30 ± 0.01 (0.30 ± 0.01)</td>
<td>0.33 ± 0.01 (0.35 ± 0.01)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.47$^{[h]}$</td>
<td>0.22 ± 0.01 (0.25 ± 0.01)</td>
<td>0.24 ± 0.01 (0.28 ± 0.01)</td>
<td>0.30 ± 0.01 (0.31 ± 0.01)</td>
<td>0.35 ± 0.01 (0.36 ± 0.01)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.57$^{[h]}$</td>
<td>0.23 ± 0.01 (0.26 ± 0.01)</td>
<td>0.25 ± 0.01 (0.29 ± 0.01)</td>
<td>0.31 ± 0.01 (0.32 ± 0.01)</td>
<td>0.36 ± 0.01 (0.36 ± 0.01)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.02$^{[h]}$</td>
<td>0.23 ± 0.01 (0.27 ± 0.01)</td>
<td>0.25 ± 0.01 (0.29 ± 0.01)</td>
<td>0.31 ± 0.01 (0.32 ± 0.01)</td>
<td>0.36 ± 0.01 (0.37 ± 0.01)</td>
<td></td>
</tr>
<tr>
<td>1-HPic</td>
<td>-1.82$^{[h]}$</td>
<td>0.07 ± 0.01</td>
<td>0.10 ± 0.01</td>
<td>0.15 ± 0.01</td>
<td>0.27 ± 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.47$^{[h]}$</td>
<td>0.07 ± 0.01</td>
<td>0.10 ± 0.01</td>
<td>0.15 ± 0.01</td>
<td>0.27 ± 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.61$^{[h]}$</td>
<td>0.11 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>0.18 ± 0.01</td>
<td>0.31 ± 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.02$^{[h]}$</td>
<td>0.10 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>0.19 ± 0.01</td>
<td>0.30 ± 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.30$^{[h]}$</td>
<td>0.07 ± 0.01</td>
<td>0.09 ± 0.01</td>
<td>0.15 ± 0.01</td>
<td>0.26 ± 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.93$^{[h]}$</td>
<td>0.64 ± 0.01</td>
<td>0.62 ± 0.01</td>
<td>0.57 ± 0.01</td>
<td>0.64 ± 0.01</td>
<td></td>
</tr>
</tbody>
</table>

[a] Diffusion experiments were performed in triplicate and the reported values are the mean ± standard deviation of the mean. Values for 1-DCI refer to CD$_2$Cl$_2$ solutions containing 1.33% of DCI/D$_2$O (see ref. [31]), corresponding values for D$_2$O-free CD$_2$Cl$_2$ solutions (see ref. [35]) are reported in parentheses. [b] Peak assigned to the core of the oligomers. [c] Peak assigned to the end-groups of the oligomers. [d] Peak assigned to the picrate anion.
coefficients for the two sets of peaks that were assigned to the end-groups and core of these oligomers, the D values of the former being always higher than those of the core (Table 2). The most plausible explanation for these findings is that core and end-group units are in slow exchange with each other, while the latter are, in turn, rapidly exchanging with the fraction of free monomer present in solution. Because it is reasonable to assume that the diffusion coefficients of monomers 1·DCl and 1·HPic are as high as that of the monomer precursor 1, it was therefore concluded that the D values referring to the oligomer end-groups express a weighted average of the diffusion coefficients of the free monomer and the oligomers present in solution at a given concentration. By the same token, the different diffusion coefficients measured for the two sets of peaks (core versus end-groups) of both (1·DCl)n and (1·HPic)n, corroborate, at the same time, the formation of linear rather than cyclic oligomers.

Assuming cyclic oligomers[32] were formed in a preponderant amount, for a cyclic aggregate one should expect to find only one set of peaks characterized by a single averaged value of the diffusion coefficient. This is clearly not the case here (Table 2): the D values found for the unthreaded set of calixarene peaks (e.g. ArCH2Ar at δ = 4.57 and 4.61 ppm for 1·DCl and 1·HPic, respectively) are far too low to be compatible with that of the monomer (or its unprotonated precursor 1, δ = 4.61 ppm). The diffusion coefficients, extracted from the plots of $\ln(I/I_0)$ versus b values (Figure 6), unambiguously indicate that the size of the non-covalent oligomers formed from 1·DCl and 1·HPic is both concentration- and anion-dependent. Data from Table 2 were also conveniently used to calculate the average number of monomer units present in the oligomers by means of a recent hydrodynamic model[33] that takes into account the effect of the number of repeating units on the diffusion coefficient of a cylindrical molecular assembly. According to this model, the number-average degree of polymerization was found to be 5, 6, and 10 for 1·DCl and 8, 20, and 36 for 1·HPic when the concentrations were 2, 10, and 25 mM, respectively.

The $\bar{X}_n$ values determined in this way, together with those obtained by end-group titration (although in some cases quite different, see Table 1) provide qualitative clear-cut evidence of the crucial role played by the calixarene counterion. From these data, it is evident that non-covalent oligomers derived from 1·HCl and 1·DCl are, at any given concentration, smaller than those obtained from 1·HPic. The two sets of $\bar{X}_n$ values obtained for the latter compare better at lower concentrations (e.g. 2 mM) because the $^1$H NMR in-
tential accuracy is more reliable, being closer to the useful 20–80% range.\[34\]

Besides, it should also be mentioned that—in the case of the diffusion data—viscosity effects cannot be ruled out for CD2Cl2 solutions at 25 m\(m\) or higher concentrations, and as a consequence an overestimation of the \(X_\bar{m}\) values is also likely. The discrepancy observed between \(1\text{-HCl}\) and \(1\text{-DCl}\) data, on the other hand, deserves comment. These differences in the degree of polymerization obtained by \(^1\)H NMR integration and diffusion NMR data can be attributed, to some extent, to the different preparation procedures of the samples or to some self-aggregation of the charged oligomeric chains formed in the CD2Cl2 solution. Self-aggregation between chains, which would result in a decrease in the observed diffusion coefficients and in an overestimation of the average aggregation number \((X_m)\), would be concentration-dependent and much more significant at high concentrations. It should be remembered that \(1\text{-DCl}\) samples, obtained in situ by DCI/D2O addition to a CD2Cl2 solution of \(1\), inevitably undergo ion solvation and the extent of ion-pairing varies as a result (see below).\[31\] In addition, one should also bear in mind that the end-group integration includes a contribution from the monomer present in the solution.

It is worth noticing that, in agreement with the Hofmeister trend,\[36\] the increasing efficiency of the self-assembly processes can be correlated to the decreasing intensity of ion-pairing interactions between the ammonium monomer \(1\text{-H}^+\) and its counterion \((\text{Pic}^-<\text{Br}^-<\text{Cl}^-)\).\[37\] This trend is reflected in a qualitative fashion by the chemical shifts of the uncomplexed ammonium end-group (\(\delta=8.54, 8.13,\) and 7.87 ppm for \(1\text{-HCl}, 1\text{-HBr}\) and \(1\text{-HPic}\), respectively), which show that the tighter the ion pair, the higher the deshielding observed on this resonance, and by the much lower diffusion coefficient of \(1\text{-HPic}\) compared to that of \(1\text{-DCl}\) at a given concentration. Indeed, the diffusion coefficients listed in Table 2 clearly demonstrate that the picrate anion is not ion-paired to the oligomer.\[37\] The diffusion coefficient for this counterion (\(\delta=8.93\) ppm) is concentration-independent and its value is close to that of simple alkylammonium salts (e.g., hexylammonium picrate) and in comparison much higher than the one measured for the oligomers present in the same CD2Cl2 solution. On the one hand, our findings suggest that the degree of polymerization can, to some extent, be modulated by changing the calixarene counterion in the initial protonation step leading to the formation of the monomer salt. On the other hand, a closer look at the data reported in Tables 1 and 2 reveals that unavoidable ion-pairing effects, intrinsic to saline monomers in apolar solvents, are responsible for reducing the self-assembly efficiency of these systems at high concentration. For a given monomer, on going from a lower to a higher concentration, the number-average degree of polymerization does not increase as fast as would be expected on the basis of Equation (1) as a result of a parallel decrease in the \(K\) value. This dependence of the “apparent” \(K\) values on the concentration is consistent with the monomers being ion-paired while their corresponding oligomers are not. If both monomers and oligomers were ion-paired no such trend would be observed, although each salt would behave differently. In our cases the “active” monomeric species undergoing oligomerization is the cation rather than the ion-paired salt, and consequently the latter has to dissociate prior to self-assembly. As a result of this, comparatively more efficient self-assembly processes (higher “apparent” \(K\) values)\[24\] take place at lower monomer concentrations (i.e., 2 m\(m\)), where the extent of salt dissociation is higher.

Light-scattering studies: To gain further evidence of oligomer formation in solution and obtain at the same time an independent evaluation of their (average) size and mass, both static and dynamic light scattering (SLS and DLS) measurements\[38\] were carried out. The SLS technique is able to measure the absolute molecular weight of a macromolecule by making use of the time-averaged intensity of the scattered light as a function of the sample concentration. Accordingly, from the scattered intensity at 90° of a 10 m\(m\) CH2Cl2 solution of \(1\text{-HPic}\), an intensity-weighted average aggregation number of approximately 17 was calculated, using the Rayleigh expression (see the Experimental Section). Interestingly, this value is in good agreement with that determined at the same concentration by diffusion NMR \((X_\bar{m}=20)\). An insight into the oligomer-size distribution in solution came from DLS\[39\] data, which indicate the presence of two families of aggregates having hydrodynamic radii \((R_H)\) of about 2 and 35 nm, respectively (Figure 7). From the spectral contribution of both aggregates to the correlation function, after an appropriate correction for the scattering efficiency, it emerges that the smaller aggregates are predominant, but about 0.04% of the total mass of \((1\text{-HPic})_n\) is assembled in larger aggregates. Assuming that the mass of the aggregates is homogeneously distributed,\[40\] the aggregation numbers were estimated to be 6 and 30000 for \(R_H=2\) and \(R_H=35\) nm, respectively. In the case of a 10 m\(m\) CH2Cl2 so-
lution of 1·HBr, a similar DLS investigation revealed the presence of only one type of aggregate with \( R_0 \approx 1.5 \) nm and an aggregation number of \( \approx 5 \).

**ESI-MS and SEM studies:** Electron-spray ionization mass spectroscopy (ESI-MS)\(^{[41]}\) investigations (Figure 8) on a 0.5 mm sample solution of 1·HPic in CH\(_2\)Cl\(_2\)/CH\(_3\)OH (5:4, v/v) show the presence of a prominent peak at \( m/z \) 1332.1 corresponding to [1·H\(^+\)] (base peak), along with a diagnostically important series of multi-charged ion peaks of much lower intensity (\( \leq 5\% \)) at \( m/z \) 2113.0, 1853.4, and 1723.4 corresponding to the general formulation \([1·H]+Pic\)\(^{n-1}\)+ (\( n = 3, 4, 5 \)). The latter demonstrate the existence of oligomeric fragments—containing up to five monomer units—also in the gas phase.

In addition to the solution studies discussed above, a scanning electron microscopy (SEM) analysis of gold-coated fibers, obtained by slow evaporation of a 10 mm chloroform solution of 1·HPic, provided direct evidence of the formation of supramolecular assemblies of nanoscopic dimensions in the solid state. The secondary electron SEM images (Figure 9) show a quite uniform material, having a typical interwoven fibrous morphology with individual fibers up to 100 \( \mu \)m long and about 800 nm wide.

**Conclusion**

In conclusion, we have shown that a calix[5]arene bearing an alkylamino pendant group of an appropriate length is able to form, upon protonation, supramolecular oligomers as a result of iterative intermolecular inclusion processes. With this type of molecule, oligomer formation or reversal to the original monomer precursor can be controlled (on and off switching) by means of simple acid/base treatment and, since oligomerization is influenced by ion-pairing effects between the cationic monomer and its counterion, the oligomer size can be tuned, to some extent, via the formation of a variety of monomeric salt species (exposure to different acids). The self-assembly of calixarene monomers 1·HX in solution has been investigated by a number of techniques (\(^1\)H and diffusion NMR, SLS, DLS), which in combination have provided conclusive evidence on the formation of linear head-to-tail oligomers, whose size is both concentration- and counterion-dependent. Oligomeric assemblies have also been detected in the gas phase (ESI-MS) and additionally confirmed in the solid state by SEM (fibrous structures were observed upon solvent evaporation).

We believe that these studies provide the basis for the future design of linear supramolecular polymers based on heteroditopic salt monomers. The drawback represented by ion-pairing effects on the growth of such polymers calls for the synthesis of new heteroditopic compounds that will also incorporate an auxiliary counterion binding site in their structure. It is likely that such an additional structural feature would facilitate salt dissociation (by overriding ion-pair interactions) and ultimately make polymer formation more efficient. The strategy of harnessing non-covalent host–guest interactions between building blocks derived from pH-sensitive calixarene monomer precursors—equipped with an additional anion recognition site—for the construction of new supramolecular polymers as novel “daptive materials”\(^{[14]}\) is currently under investigation.

**Experimental Section**

**General:** Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Unless otherwise stated, \(^1\)H and \(^13\)C NMR spectra were recorded at 295 K in CDCl\(_3\), at 300 and 75 MHz respectively, using TMS as an internal standard. CH\(_3\)CN was dried by standard methods; HCl-free CHCl\(_3\) and CDCl\(_3\), employed for the synthesis and the NMR analysis of I, were passed through neutral alumina prior to use; all other chemicals were reagent grade and were used without further purification. Column chromatography was performed on silica gel (Merck; 230–400 mesh). All reactions were carried out under an argon atmosphere. \( p \)-tert-Butylcalix[5]arene 2\(^{[17]}\) and bis-calix[5]arene 5\(^{[24]}\) were synthesized according to a literature procedure.

**Diffusion NMR spectroscopy:** Diffusion NMR experiments were carried out on a 400 MHz NMR spectrometer equipped with a z-gradient system.
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Mass spectrometry: Matrix-assisted laser desorption-time (MALDI-TOF) mass spectra were recorded in the reflector mode on a Voyager STR instrument (Applied Biosystems, Framingham, MA, USA) equipped with a nitrogen laser (λ = 337 nm) and provided with delayed extraction technology. Ions formed by the pulsed laser beam were accelerated through 24 kV. Each spectrum is the result of approximately 200 laser shots. External calibration was applied, calibration was about 12000 (FWHM). 2.5-Dihydroxybenzoic acid (DHB) was used as the matrix. Electron-spray ionization (ESI) mass spectra were recorded on a Finnigan LCQDECA ThermoQuest mass spectrometer with the following main settings: source voltage, 5 V; capillary voltage, 40 V; capillary temperature, 225°C; standard calibration. Sample solutions were introduced into the mass spectrometer source with a syringe pump at a flow rate of 5 μL min⁻¹. The final spectrum is the sum of several scans.

Scanning electron microscopy: Investigations were carried out on a Leo S420 instrument operating at an energy of 10 keV, an I probe of 9 pA and a working distance of 9 mm. All observations were performed from low to higher magnifications up to ×45000.

N-(12-Bromododecyl)phthalimide: Potassium phthalimide (0.93 g, 5.0 mmol) and 1,12-dibromododecane (4.9 g, 15.0 mmol) were stirred at 100°C for 16 h. The reaction mixture was cooled, filtered, and the filtrate was evaporated to dryness. Unreacted potassium phthalimide was filtered off after sonication with petroleum ether. The crude product obtained after solvent evaporation was purified by column chromatography (SiO2, petroleum ether/ACeOEt 95:5) followed by recrystallization from petroleum ether to yield pure N-(12-bromododecyl)phthalimide (1.0 g, 51%). M. P. 59-62°C (petroleum ether, i.r.,[9] 26–63°C). 1H NMR spectral data were in agreement with those reported in the literature.[18]

[31][12-N’-(Phthalimidododecyl)oxy]-32,33,34,35-tetrahydroxy-5.11.17.23.29-penta-tert-butylcalix[5]arene (3): A stirred mixture of 2 (1.16 g, 1.43 mmol), N-(12-bromododecyl)phthalimide (0.2 g, 0.5 mmol) and KHCO3 (0.29 g, 2.9 mmol) in anhydrous CH2CN (40 mL) was refluxed for 42 h. The solvent was evaporated under reduced pressure, and the residue was partitioned between chloroform and aqueous HCl (0.1M). The organic layer was dried (Na2SO4) and concentrated. The crude product was purified by column chromatography (SiO2, petroleum ether/CH2Cl2 95:5 to remove the excess of 2, then CHCl3) to give 3 (410 mg, 73%). M. P. 107–109°C; 1H NMR: δ = 1.09, 1.23, 1.32 (s, 12, 2H; CH2, C); 4.06, 4.15 (d, J = 20.6, 20.6, 28.6, 29.2, 29.4, 29.5, 29.7, 29.9, 29.9, 32.0, 30.6, 31.6, 31.3, 31.4, 31.5, 31.7, 33.8, 34.1, 38.1, 75.9, 123.1, 125.4, 125.5, 125.6, 125.8, 126.8, 126.9, 132.1, 132.9, 133.8, 142.6, 142.7, 142.8, 147.6, 149.2, 150.3, 168.5 ppm; MALDI-TOF MS: m/z: 1146.7 [M+Na]+; 1162.7 [M+K]+; elemental analysis calcd (%) for C32H59NO3S: C 80.10, H 6.89, N 1.25; found: C 80.34, H 8.81, N 1.22.

[31][12-N’-(Phthalimidododecyl)oxy]-32,33,34,35-tetra-(4-methyl-pentyl)-oxy)-5.11.17.23.29-penta-tert-butylcalix[5]arene (4): Calix[C5]arene 3 (380 mg, 0.34 mmol), 1-bromo-4-methylpentane (677 mg, 4.1 mmol) and K2CO3 (560 mg, 4.1 mmol) were suspended in anhydrous CH2CN (50 mL) and refluxed for 16 h, under a vigorous stirring. Inorganic salts were filtered off and washed with CHCl3. The combined filtrates were evaporated to dryness under reduced pressure, and the residue was triturated with MeOH to give 4 (400 mg, 81%). M. P. 124–126°C; 1H NMR: δ = 0.95 (d, J = 6.6 Hz, 6H, CH(CH3)2), 1.01, 1.06, 1.09 (s, 2.21, 4H, C- (CH3)2), 1.26–1.50 (m, 22H, 1.58–1.75 (m, 8H, 1.84–1.95 (m, 10H, 3.25 and 4.55 (AX system, J = 13.8 Hz, 10H, CH2-CH2), 3.56 (t, J = 7.0 Hz, 2H, OCH2-CH2), 3.65 (t, J = 7.3 Hz, 8H, OCH2-CH2), 3.69 (t, J = 7.2 Hz, 2H, NCH2), 6.69, 6.94, 6.97 (s, 2.21, 10H, Ar), 7.66–7.74 and 7.81–7.88 ppm (AA’BB’ system, 4H, Ph’); 13C NMR: δ = 22.8, 26.3, 26.9, 28.3, 28.4, 28.6, 29.26, 29.33, 29.4, 29.6, 29.7, 29.8, 30.1, 30.2, 30.6, 31.4, 31.41, 31.44, 33.22, 33.94, 33.95, 35.1, 35.2, 38.1, 73.9, 74.3 (2×).
1.02. 8172 spectra, and Prof. G. Malandrino (Università di Catania) for useful discussions; 13C NMR: 144.4, 152.7, 152.8, 168.5 ppm; MALDI-TOF MS: m/z: 1483.1 [M+Na]+; elemental analysis calcd (%) for C91H143NO5: C 82.11, H 10.83, N 1.05; found: C 82.67, H 11.07, N 1.02.

The residue was dissolved in CHCl3, CH2Cl2 (or CH2Cl2) was dispensed out of a literature procedure. See: M. J. Pfammatter, V. Siljegovic, T. Darbre, R. Keese, Helv. Chim. Acta 2001, 84, 678–689.

This presence of free monomeric species cannot be ruled out by 1H NMR. In fact the diffusion NMR data did show that some unthreaded monomeric species are indeed present in the solution.

Assignments reported in Figure 1b follow from a 1H–1H COSY experiment (see the Supporting Information).

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The iterative inclusion of the alkyl chain is far too short to bend alongside the aromatic unit, fold over the tert-butyl group and reach the interior of the cavity to relieve steric hindrance. In this event, however, the loss of symmetry of the cavity would have been detected by $^1$H NMR spectroscopy. See: G. De Salvo, G.Gattuso, A. Notti, M. F. Parisi, J. Am. Chem. Soc. 2006, 67, 684–692.


The dodecylammonium alkyl chain is far too short to bend alongside the aromatic unit, fold over the tert-butyl group and reach the interior of the cavity to relieve steric hindrance. In this event, however, the loss of symmetry of the cavity would have been detected by $^1$H NMR spectroscopy. See: G. De Salvo, G. Gattuso, A. Notti, M. F. Parisi, J. Org. Chem. 2002, 67, 684–692.

[24] The dodecylammonium alkyl chain is far too short to bend alongside the aromatic unit, fold over the tert-butyl group and reach the interior of the cavity to relieve steric hindrance. In this event, however, the loss of symmetry of the cavity would have been detected by $^1$H NMR spectroscopy. See: G. De Salvo, G. Gattuso, A. Notti, M. F. Parisi, J. Org. Chem. 2002, 67, 684–692.


[27] The iterative inclusion of 1-HX was assumed to be isodesmic (R. B. Martin, Chem. Rev. 1996, 96, 3043–3064). The number-average degree of polymerization was calculated by the Carothers equation (C. H. Carothers, Trans. Faraday Soc. 1936, 32, 39–49). $X_{\text{ave}} = 1/(1–p)$, where $p$ is the fraction of complexed species. This expression assumes that cyclic species are not present in significant amounts.

[31] Oligomerization was directly carried out in the NMR tube by adding 4% of 20% DCl to 300 µL of the CD3Cl solution of 1.


[35] When solutions of DCl (prepared as described in the “Experimental Section” under the subheading “General procedure for the formation of the ammonium salt monomers”) in D2O-free CD3Cl (dispensed out of a freshly-opened bottle) were used, the diffusion coefficients (Table 2) were consistently found to be slightly higher than those observed for 1-DCl obtained by in situ addition of DCl/CD3O (see ref. [31]). Furthermore, under these conditions, $^1$H NMR integration (data not shown) displayed an average decrease ($\approx 6\%$) in the percentages of threading. These observations indicate that in the absence of D2O, both the lack of ion solvation and greater extent of ion-pairing result in a modest but detectable decrease in the self-assembly.


