Supramolecular Polymers

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Anion-Assisted Supramolecular Polymerization: From Achiral AB-Type Monomers to Chiral Assemblies**

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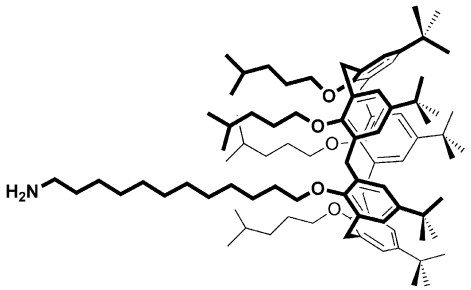
Control over the self-assembly process of monomeric species by functional group modulation is highly desirable in the context of supramolecular polymer design. These materials, unlike covalently linked polymers, consist of monomeric arrays held together by reversible and highly directional noncovalent bonds.[1] Owing to the dynamic and reversible nature of noncovalent interactions, supramolecular polymers display unique topologies and unconventional properties (such as stimuli responsiveness[2] and self-healing[3]) and are thus becoming cutting-edge species in modern materials science. Multiple hydrogen bonds, metal–ligand coordination, and π–π stacking are, by far, the most common weak forces used for engineering supramolecular polymers.[4] Recently, however, oligomeric and polymeric architectures based on host–guest inclusion complexes have started to become more and more popular.[5]

Within this research frame, we have recently described a pH-responsive aminododecyloxy-calix[5]arene derivative (**C5-NH$_2$**) that, upon exposure to a variety of acids, self-assembles into linear oligomers.[6] Protonation activates the two latent self-complementary binding sites of this heteroditopic monomer precursor (i.e. a preorganized cone-shaped π-rich calix[5]arene cavity and a linear alkylamine pendant chain) and, according to a well-established host–guest recognition pattern,[7] which involves a concerted set of weak interactions (NH···O, CH–π, cation–π),[8] supramolecular oligomer formation readily occurs. However, because of the intrinsically saline nature of the monomers used, the growth of these supramolecular assemblies was found to be anion-dependent. More specifically, the looser the ion-pairing interactions between the ammonium monomer and its counterion, the higher the degree of polymerization observed.[9]



C5-NH$_2$

Although ion-pairing effects have been analyzed extensively in relation to simple one-to-one host–guest systems,[10] to the best of our knowledge they have not yet been examined in the context of supramolecular polymers derived from charged monomers. Elegant examples of polymeric species derived from crown ethers,[11] cryptands,[12] cyclodextrins,[13] cucurbiturils,[14] calixarenes,[15,16] and resorcinarenes[17] have been described, but in none of these instances—neither AB-type (self-complementary heteroditopic)[11a,b,d,e,12a,b,13a,17a] nor AA/BB-type (complementary homoditopic)[11c,12c,14,15,17b] systems—has the role of the counterion in the growth of the polymer or the tuning of the supramolecular properties been addressed.

Drawing on our earlier investigations on the simultaneous complexation of cations and anions[8,18] and on the design of heteroditopic[19] and heterotetratopic receptors[20] in an attempt to override the drawback of ion-pairing effects in AB-type salt monomers, we have now incorporated an ancillary anion-binding site (namely a ureido moiety)[21] into calix[5]arene **C5-NH$_2$** with the aim of facilitating salt dissociation and ultimately making polymer formation more efficient. In this communication we demonstrate that the addition of this anion-binding site to the monomer scaffold is beneficial to the supramolecular polymerization process and, most importantly, we show that modulation of the properties

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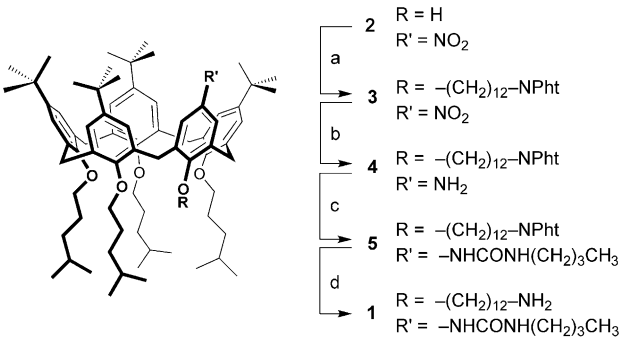

Scheme 1. Synthesis of the calix[5]arene monomer precursor **1**: a) PhtN-$(CH_2)_{12}$Br, K_2CO_3, CH_3CN, reflux, 8 days, 68%; b) H_2, Raney-Ni, THF, RT, 4 h, 70%; c) $CH_3(CH_2)_3NCO$, CH_2Cl_2, RT, 48 h, 91%; d) $H_2NNH_2{\cdot}H_2O$, EtOH, reflux, 3 h, 68%. NPht = *N*-phthalimido.

of the resulting polymer (e.g. chirality) is feasible as a result of anion binding to the ureido moieties of the polymer backbone.

The target calix[5]arene monomer precursor **1** was synthesized from the known nitro-calix[5]arene[20] **2** in four steps (Scheme 1).[22] ^{1}H and ^{13}C NMR spectroscopic data for **1** were found to be consistent with a C_s symmetric structure locked in a cone conformation.[23] As expected, exposure[22] of the amino-calixarene precursor **1** to an aqueous 1 M HCl solution triggered the self-assembly of monomer **1**·HCl and, as a result of an iterative intermolecular inclusion process of the dodecylammonium moiety of one calixarene monomer into the cavity of another, formation of polymer $(\mathbf{1}{\cdot}HCl)_n$ readily occurred (Figure 1). Conversion of the amino precursor **1** into polymer $(\mathbf{1}{\cdot}HCl)_n$ caused a substantial broadening of the ^{1}H NMR spectrum, along with the appearance, in the high-field region ($\delta = -2.0$ to 1.0 ppm), of a series of diagnostic signals[24] consistent with the intermolecular *endo*-cavity inclusion[25] of the five methylene groups closest to the ammonium moiety (α- to ε-CH_2) of the lower-rim pendant chain inside a calix[5]arene cavity.[26] Polymerization of the salt monomer was also indicated by the presence of a broad singlet at $\delta = 5.33$ ppm for the newly formed and cavity-included NH_3^+ group and by a substantial low-field shift of the resonances of the two ureido-NH protons ($\Delta\delta = 2.15$ and 3.96 ppm, for NH_a and NH_b, respectively), the latter indicating that the chloride counterion is bound to the designated anion-binding site.

Concentration-dependent diffusion NMR[27] studies were used to estimate the number-average degree of polymerization ($\bar{X}_n$) of monomer **1**·HCl in CD_2Cl_2 solutions, as its assessment by direct ^{1}H NMR integration (end-group titration) was prevented by the lack of detectable resonances that belong to the monomer/polymer end groups. Upon increase of the **1**·HCl monomer concentration from 2 to 25 mM, the average diffusion coefficients (D), extracted from the signal decay of two representative signals (i.e. β-CH_2 and ArCH_2Ar), decreased from $(3.4 \pm 0.1) \times 10^{-6}\,cm^2\,s^{-1}$ to $(1.1 \pm 0.1) \times 10^{-6}\,cm^2\,s^{-1}$, hence indicating the formation of larger aggregates (Figure 2).[28] Calculations, according to the hydrodynamic model proposed by Wu and co-workers,[29] revealed that the $\bar{X}_n$ of the species present in solution grew from 5 to 14 and then to 28–29 (Table 1). That is, a threefold increase of $\bar{X}_n$ for $[\mathbf{1}{\cdot}HCl] = 25$ mM with respect to the analogous calix[5]arene monomer (**C5-NH$_2$**·HCl) devoid of the butylureido moiety at the upper rim.[6]

Additional evidence on the oligo-/polymeric nature of the species formed upon self-assembly of **1**·HCl in solution was obtained by dynamic light scattering experiments (DLS). Our data indicate that the self-assembly process of the monomer (10 mM, CH_2Cl_2) gives rise to $(\mathbf{1}{\cdot}HCl)_n$ aggregates with an average diffusion coefficient $D = 1.5 \times 10^{-6}\,cm^2\,s^{-1}$, in good agreement with the diffusion NMR spectroscopic results.

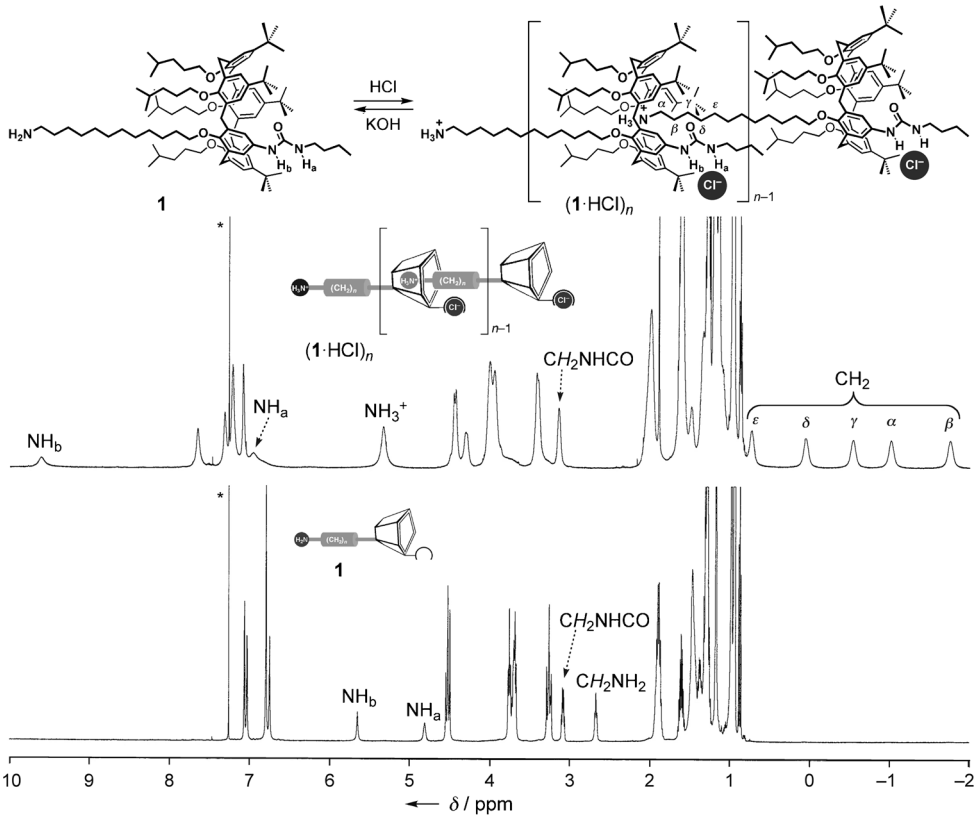

Figure 1. ^{1}H NMR spectra (500 MHz, $CDCl_3$, 5 mM, 298 K) of: a) **1** and b) $(\mathbf{1}{\cdot}HCl)_n$. The asterisk indicates residual solvent signals.

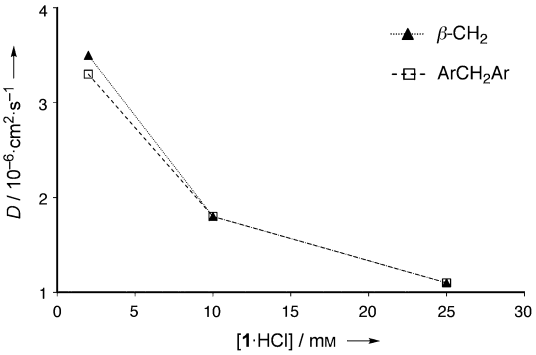

Figure 2. Diffusion coefficients (D) of two representative signals of $(\mathbf{1}\cdot HCl)_n$ at different concentrations in CD_2Cl_2 at 298 K.

Table 1: Diffusion coefficients[a] (D) for **1** and $(\mathbf{1}\cdot HCl)_n$ at different concentrations in CD_2Cl_2 at 298 K and corresponding calculated number-average degree of polymerization[b] ($\bar{X}_n$).

		D [$\times 10^{-6}$ cm^2 s^{-1}] ($\bar{X}_n$)		
Compound	Signal [ppm]	2 mM	10 mM	25 mM
1	2.66	–	6.6 ± 0.1	–
$(\mathbf{1}\cdot HCl)_n$	−1.73	3.5 ± 0.14 (5)	1.8 ± 0.1 (14)	1.1 ± 0.1 (28–29)
	4.36–4.49	3.3 ± 0.14 (5)	1.8 ± 0.1 (14)	1.1 ± 0.1 (28–29)

[a] See the Supporting Information for experimental details. [b] See Ref. [29].

From the size distribution, a mass-average hydrodynamic radius[30] (R_H) of about 3 nm is obtained (Figure S7, see the Supporting Information).

In solution $(\mathbf{1}\cdot HCl)_n$ was found to be thermally stable over a wide temperature range (−60 to 100 °C). Variable-temperature ^{1}H NMR experiments, carried out on 5 mM solutions ($C_2D_2Cl_4$ and CD_2Cl_2) of $(\mathbf{1}\cdot HCl)_n$, showed that complete disassembly occurs above 100 °C, whereas at temperatures below room temperature substantial broadening of all signals suggests a higher degree of aggregation of the polymeric material (Figure S4). Polymer $(\mathbf{1}\cdot HCl)_n$ also survives in the presence of considerable amounts of protic and ureido-coordinating[31] solvents (e.g. $CDCl_3/CD_3OD$ 2:1 and $CDCl_3$/[D$_6$]DMSO 4:1). Even in the gas phase, $(\mathbf{1}\cdot HCl)_n$ proved to be extremely robust. The ESI-MS spectrum of a 0.5 mM solution of **1**·HCl in $CHCl_3/CH_3OH$ (2:1 v/v) shows several signals corresponding to the general formulation $[(\mathbf{1}\cdot H)_n + m\,Cl]^{(n-m)+}$, which can be assigned to multicharged ions composed of up to eleven monomer units (namely, m/z 3885.1, $[(\mathbf{1}\cdot H)_{11} + 7Cl]^{4+}$; see Table S1).

In line with its pH-responsive nature, on the other hand, $(\mathbf{1}\cdot HCl)_n$ readily disassembles by simple treatment with an aqueous solution of base (1M KOH, room temperature) to give the parent monomer precursor **1**. Moreover, protonation of **1** with acids other than HCl sets off the self-assembly of the resulting monomers **1**·HX ($X^- = I^-$, Br^-, and AcO^-) to give the corresponding supramolecular assemblies $(\mathbf{1}\cdot HX)_n$ (Figure S8).[22] The ^{1}H NMR spectra of the different assemblies under study show consistent and virtually invariant chemical

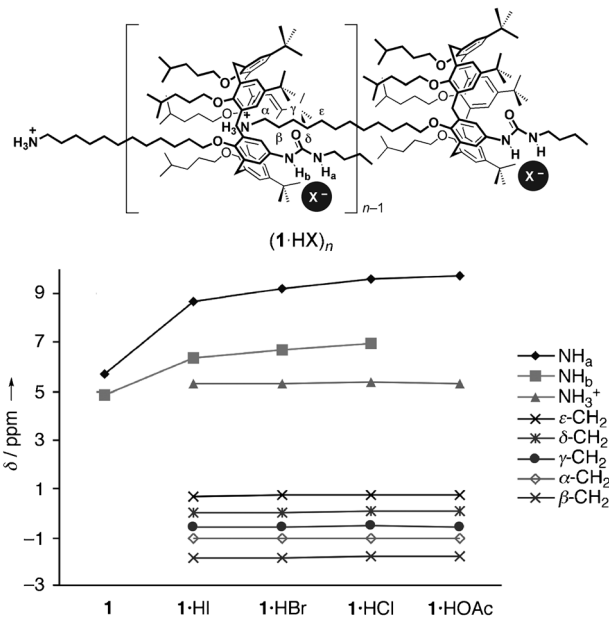

Figure 3. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) chemical shifts (δ) of the diagnostic resonances (NH_a, NH_b, NH_3^+, α-ε-CH_2) of 5 mM solutions of $(\mathbf{1}\cdot HX)_n$.

shift values for the resonances of the NH_3^+ and α-ε-CH_2 groups whereas, in sharp contrast, the ureido NH signals display a considerable anion-complexation-induced shift dependence (Figure 3).

These data suggest that: 1) all the anions dock onto the ancillary ureido binding site and 2) the alkylammonium chain of one monomeric unit—irrespective of its counterion—always rests at the same depth inside the cavity of the adjacent monomer. Both intermolecular inclusion of the alkylammonium chain and ureido-counterion binding are slow on the NMR time-scale, as suggested by the fact that the chemical shifts of the diagnostic ^{1}H NMR signals (NH_3^+, α-ε-CH_2 and NHs) are concentration independent.

Given the proclivity with which carboxylate anions bind to ureido moieties,[21,32] addition of a chiral carboxylic acid to the monomer precursor **1** was envisaged as an easy and convenient way to generate chiral supramolecular polymers. Thus it was anticipated that protonation of the amino moiety would start self-assembly, while the concurrent binding of the released carboxylate ion to the ureido group would induce chirality in the final supramolecular assembly.[33] To verify this hypothesis, 1 equiv of either (*R*)- or (*S*)-mandelic acid ((*R*)- and (*S*)-**Ma**H, respectively) was added to a solution of **1** (CD_2Cl_2 or CH_2Cl_2) and the samples were examined by ^{1}H NMR (Figure S9) and by circular dichroism (CD) spectroscopy. In addition, blank experiments in the presence of phthalimido derivative **5** (in which self-assembly is prevented by the presence of the *N*-phthaloyl protecting group) and *n*-dodecylammonium (*R*)- or (*S*)-mandelate ((*R*)- and (*S*)-$\mathbf{Ma}^-\mathbf{C_{12}}$-$NH_3^+$, respectively) were also carried out.

Formation of two pairs of enantiomeric assemblies (((*S*)-**Ma**H·**1**)$_n$/((*R*)-**Ma**H·**1**)$_n$ and (*S*)-$\mathbf{Ma}^-\subset\mathbf{5}\supset\mathbf{C_{12}}$-$NH_3^+$/(*R*)-$\mathbf{Ma}^-\subset\mathbf{5}\supset\mathbf{C_{12}}$-$NH_3^+$, respectively (Figure 4b and d)) upon addition of (*S*)- or (*R*)-**Ma**H to **1** and (*S*)- or (*R*)-$\mathbf{Ma}^-\mathbf{C_{12}}$-

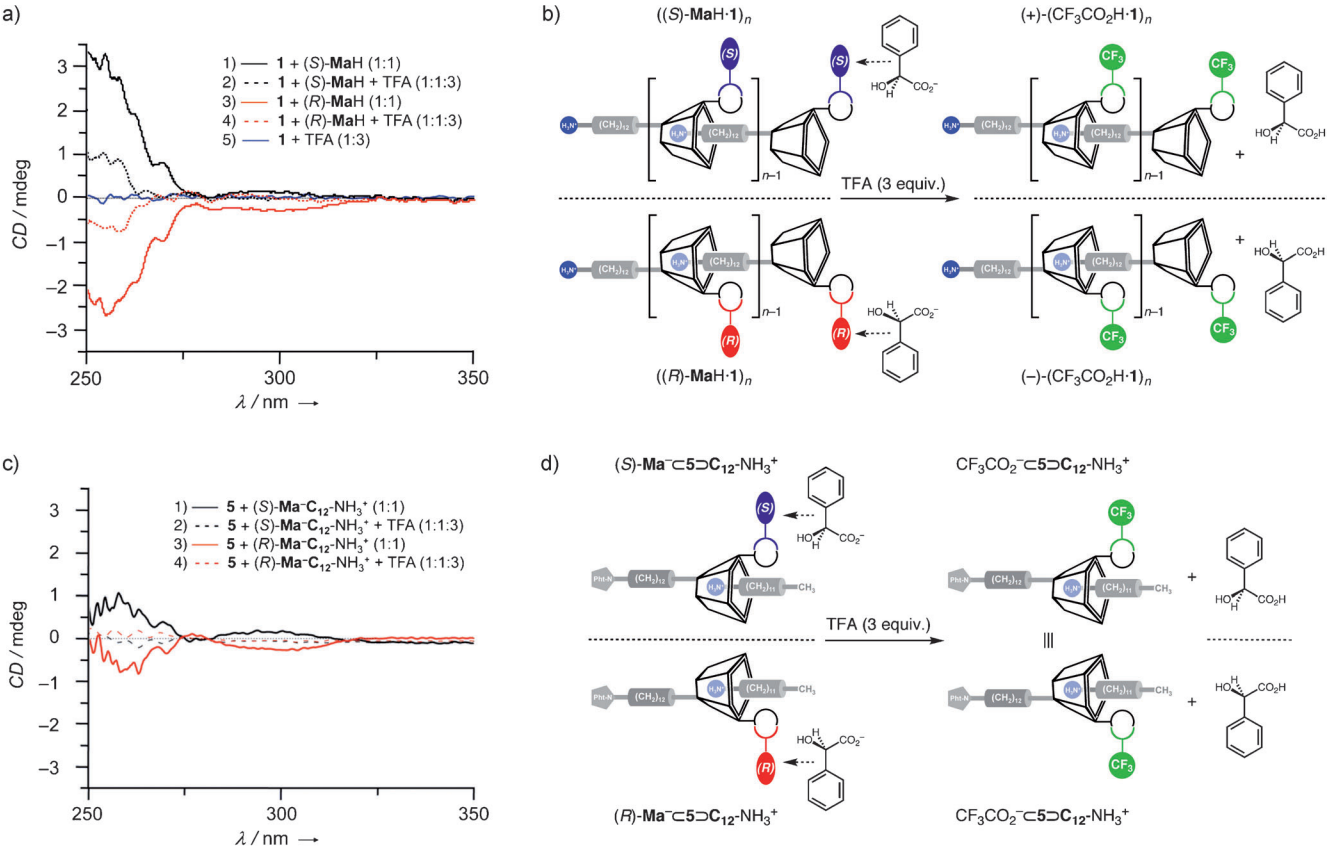

Figure 4. a) CD spectra of CH_2Cl_2 solutions of: [**1**] = [(*S*)-**Ma**H] = 1 mM (trace 1); [**1**] = [(*S*)-**Ma**H] = 1 mM and [TFA] = 3 mM (trace 2); [**1**] = [(*R*)-**Ma**H] = 1 mM (trace 3); [**1**] = [(*R*)-**Ma**H] = 1 mM and [TFA] = 3 mM (trace 4); [**1**] = 1 mM and [TFA] = 3 mM (trace 5). b) Schematic representation of the two pairs of enantiomeric assemblies ((*S*)-**Ma**H·**1**)$_n$/((*R*)-**Ma**H·**1**)$_n$ and (+)-(CF_3CO_2H·**1**)$_n$/(−)-(CF_3CO_2H·**1**)$_n$ formed upon mixing **1** with (*S*)-**Ma**H or (*R*)-**Ma**H prior and after addition of TFA (3 equiv). c) CD spectra of CH_2Cl_2 solutions of: [**5**] = [(*S*)-**Ma**$^-$**C**$_{12}$-NH_3^+] = 1 mM (trace 1); [**5**] = [(*S*)-**Ma**$^-$**C**$_{12}$-NH_3^+] = 1 mM and [TFA] = 3 mM (trace 2); [**5**] = [(*R*)-**Ma**$^-$**C**$_{12}$-NH_3^+] = 1 mM (trace 3); [**5**] = [(*R*)-**Ma**$^-$**C**$_{12}$-NH_3^+] = 1 mM and [TFA] = 3 mM (trace 4). d) Schematic representation of the two enantiomeric complexes (*S*)-**Ma**$^-$⊂**5**⊃**C**$_{12}$-NH_3^+/(*R*)-**Ma**$^-$⊂**5**⊃**C**$_{12}$-NH_3^+ formed upon mixing **5** with (*S*)-**Ma**$^-$**C**$_{12}$-NH_3^+ or (*R*)-**Ma**$^-$**C**$_{12}$-NH_3^+ and of the resulting optically silent complex $CF_3CO_2^-$⊂**5**⊃**C**$_{12}$-NH_3^+ obtained after addition of TFA (3 equiv).

NH_3^+ to **5** is consistent with the presence of bands with opposite sign in their CD spectra (Figure 4a and c, traces 1 and 3). A comparative analysis of the intensity of these two sets of induced CD signals, however, demonstrates that chiral induction is higher in the case of the monomer precursor **1**, where oligo-/polymerization takes place.[34] TFA addition (3 equiv) to the original solutions of ((*S*)-**Ma**H·**1**)$_n$ or ((*R*)-**Ma**H·**1**)$_n$ and (*S*)- or (*R*)-**Ma**$^-$⊂**5**⊃**C**$_{12}$-NH_3^+ readily promotes anion exchange at the ureido-binding sites of these species with a concomitant release of one molecule of (*S*)- or (*R*)-mandelic acid (Figure 4b and 4d). As expected, in the case of (*S*)-**Ma**$^-$⊂**5**⊃**C**$_{12}$-NH_3^+ and (*R*)-**Ma**$^-$⊂**5**⊃**C**$_{12}$-NH_3^+, replacement of the enantiomeric (*S*)- and (*R*)-mandelate counterions with trifluoroacetate ions makes the two complexes lose their CD-footprint[35] (Figure 4c, traces 2 and 4; see also Figure S11 for ^{1}H NMR evidence) as a consequence of the formation of the same optically silent species (i.e. $CF_3CO_2^-$⊂**5**⊃**C**$_{12}$-NH_3^+). Conversely, TFA-induced counterion exchange on ((*S*)-**Ma**H·**1**)$_n$ and ((*R*)-**Ma**H·**1**)$_n$ produces two new enantiomeric supramolecular species (+)-(CF_3CO_2H·**1**)$_n$ and (−)-(CF_3CO_2H·**1**)$_n$, respectively). Despite the fact that the chiral auxiliary is no longer bound to the backbone of the two newly formed species (Figure 4b), these still exhibit chiral features. (+)- and (−)-(CF_3CO_2H·**1**)$_n$ show CD signals of opposite sign and, most remarkably, each of them retains the same handedness of its enantiomeric precursor (Figure 4a, traces 2 and 4). The persistence of these induced CD signals is consistent with the so-called "chiral memory"[36] effect, whereby, in our case, replacement of the enantiomeric counterions with optically inactive ones only partially erases the chirality memorized within the supramolecular structure in the initial self-assembly process.

In summary, we have demonstrated a simple method for enhancing the degree of polymerization of ionizable AB-type supramolecular monomers. The strategy presented herein relies on the simultaneous trapping—in an ancillary binding site—of the counterion released in the initial acid-promoted polymerization step of an amino-calix[5]arene monomer precursor. Our data, however, most significantly show that a given anion can modulate the properties of an entire supramolecular assembly by simply docking into the additional binding sites present on its backbone. These results

suggest that, in principle, any molecular property (e.g. optical, redox, etc.) can easily be transferred to a supramolecular polymer just by choosing an appropriate off-the-shelf acid.

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[1] a) L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071 – 4098; b) J.-M. Lehn, *Polym. Int.* **2002**, *51*, 825 – 839; c) *Supramolecular Polymers*, 2nd ed. (Ed.: A. Ciferri), CRC, Boca Raton, FL, **2005**.

[2] M. A. Cohen Stuart, W. T. S. Huck, J. Genzer, M. Müller, C. Ober, M. Stamm, G. B. Sukhorukov, I. Szleifer, V. V. Tsukruk, M. Urban, F. Winnik, S. Zauscher, I. Luzinov, S. Minko, *Nat. Mater.* **2010**, *9*, 101 – 113.

[3] a) P. Cordier, F. Tournilhac, C. Soulie-Ziakovic, L. Lieber, *Nature* **2008**, *451*, 977 – 980; b) M. D. Hager, P. Greil, C. Leyens, S. van der Zwaag, U. S. Schubert, *Adv. Mater.* **2010**, *22*, 5424 – 5430.

[4] a) T. F. A. De Greef, M. M. J. Smulders, M. Wolffs, A. P. H. J. Schenning, R. P. Sijbesma, E. W. Meijer, *Chem. Rev.* **2009**, *109*, 5687 – 5754; b) D. González-Rodríguez, A. P. H. J. Schenning, *Chem. Mater.* **2011**, *23*, 310 – 325.

[5] a) T. Haino, Y. Matsumoto, Y. Fukazawa, *J. Am. Chem. Soc.* **2005**, *127*, 8936 – 8937; b) F. Huang, J. W. Jones, *Prog. Polym. Sci.* **2005**, *30*, 982 – 1018; c) G. Gattuso, A. Notti, A. Pappalardo, M. F. Parisi, I. Pisagatti, S. Pappalardo, D. Garozzo, A. Messina, Y. Cohen, S. Slovak, *J. Org. Chem.* **2008**, *73*, 7280 – 7289; d) A. Harada, Y. Takashima, H. Yamaguchi, *Chem. Soc. Rev.* **2009**, *38*, 875 – 882; e) A. Harada, A. Hashidzume, H. Yamaguchi, Y. Takashima, *Chem. Rev.* **2009**, *109*, 5974 – 6023; f) T. Haino, E. Hirai, Y. Fujiwara, K. Kashihara, *Angew. Chem.* **2010**, *122*, 8071 – 8075; *Angew. Chem. Int. Ed.* **2010**, *49*, 7899 – 7903; g) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma, F. Huang, *Angew. Chem.* **2011**, *123*, 1433 – 1437; *Angew. Chem. Int. Ed.* **2011**, *50*, 1397 – 1401.

[6] S. Pappalardo, V. Villari, S. Slovak, Y. Cohen, G. Gattuso, A. Notti, A. Pappalardo, I. Pisagatti, M. F. Parisi, *Chem. Eur. J.* **2007**, *13*, 8164 – 8173.

[7] a) F. Arnaud-Neu, S. Fuangswasdi, A. Notti, S. Pappalardo, M. F. Parisi, *Angew. Chem.* **1998**, *110*, 120 – 122; *Angew. Chem. Int. Ed.* **1998**, *37*, 112 – 114; b) D. Garozzo, G. Gattuso, F. H. Kohnke, P. Malvagna, A. Notti, S. Occhipinti, S. Pappalardo, M. F. Parisi, I. Pisagatti, *Tetrahedron Lett.* **2002**, *43*, 7663 – 7667.

[8] G. Gattuso, A. Notti, S. Pappalardo, M. F. Parisi, T. Pilati, G. Resnati, G. Terraneo, T. Pilati, *CrystEngComm* **2009**, *11*, 1204 – 1206.

[9] At a 40 mM monomer concentration the number-average degree of polymerization ($\bar{X}_n$) was found to be approximately 40 and 2 in the case of the picrate and chloride derivatives, respectively; see Ref. [6].

[10] a) J. W. Jones, H. W. Gibson, *J. Am. Chem. Soc.* **2003**, *125*, 7001 – 7004; b) F. Huang, J. W. Jones, C. Slebodnik, H. W. Gibson, *J. Am. Chem. Soc.* **2003**, *125*, 14458 – 14464; c) T. B. Gasa, J. M. Spruell, W. R. Dichtel, T. J. Sørensen, D. Philp, J. F. Stoddart, P. Kuzmic, *Chem. Eur. J.* **2009**, *15*, 106 – 116; d) S. Roelens, A. Vacca, O. Francesconi, C. Venturi, *Chem. Eur. J.* **2009**, *15*, 8296 – 8302; e) S. K. Kim, J. L. Sessler, *Chem. Soc. Rev.* **2010**, *39*, 3784 – 3809; f) T. B. Gasa, C. Valente, J. F. Stoddart, *Chem. Soc. Rev.* **2011**, *40*, 57 – 78.

[11] For representative examples, see: a) P. R. Ashton, I. W. Parsons, F. M. Raymo, J. F. Stoddart, A. J. P. White, D. J. Williams, R. Wolf, *Angew. Chem.* **1998**, *110*, 2016 – 2019; *Angew. Chem. Int. Ed.* **1998**, *37*, 1913 – 1916; b) N. Yamaguchi, D. S. Nagvekar, H. W. Gibson, *Angew. Chem.* **1998**, *110*, 2518 – 2520; *Angew. Chem. Int. Ed.* **1998**, *37*, 2361 – 2364; c) N. Yamaguchi, H. W. Gibson, *Angew. Chem.* **1999**, *111*, 195 – 199; *Angew. Chem. Int. Ed.* **1999**, *38*, 143 – 147; d) F. Wang, C. Han, C. He, Q. Zhou, J. Zhang, C. Wang, N. Li, F. Huang, *J. Am. Chem. Soc.* **2008**, *130*, 11254 – 11255; e) X. Yan, M. Zhou, J. Chen, X. Chi, S. Dong, M. Zhang, X. Ding, Y. Yu, S. Shaod, F. Huang, *Chem. Commun.* **2011**, *47*, 7086 – 7088.

[12] For representative examples, see: a) F. Wang, J. Zhang, X. Ding, S. Dong, M. Liu, B. Zheng, S. Li, L. Wu, Y. Yu, H. W. Gibson, F. Huang, *Angew. Chem.* **2010**, *122*, 1108 – 1112; *Angew. Chem. Int. Ed.* **2010**, *49*, 1090 – 1094; b) Y.-S. Su, J.-W. Liu, Y. Jiang, C.-F. Chen, *Chem. Eur. J.* **2011**, *17*, 2435 – 2441; c) Z. Niu, F. Huang, H. W. Gibson, *J. Am. Chem. Soc.* **2011**, *133*, 2836 – 2839.

[13] For representative examples, see: a) K. Ohga, Y. Takashima, H. Takahashi, Y. Kawaguchi, H. Yamaguchi, A. Harada, *Macromolecules* **2005**, *38*, 5897 – 5904; b) V. H. Soto Tellini, A. Jover, J. Carrazana García, L. Galantini, F. Meijide, J. Vázquez Tato, *J. Am. Chem. Soc.* **2006**, *128*, 5728 – 5734; c) P. Kuad, A. Miyawaki, Y. Takashima, H. Yamaguchi, A. Harada, *J. Am. Chem. Soc.* **2007**, *129*, 12630 – 12631.

[14] For representative examples, see: a) U. Rauwald, O. A. Scherman, *Angew. Chem.* **2008**, *120*, 4014 – 4017; *Angew. Chem. Int. Ed.* **2008**, *47*, 3950 – 3953; b) Y. Liu, Y. Yu, J. Gao, Z. Wang, X. Zhang, *Angew. Chem.* **2010**, *122*, 6726 – 6729; *Angew. Chem. Int. Ed.* **2010**, *49*, 6576 – 6579.

[15] D.-S. Guo, S. Chen, H. Qian, H.-Q. Zhang, Y. Liu, *Chem. Commun.* **2010**, *46*, 2620 – 2622.

[16] For examples of calixarene-based supramolecular polymers relying on multiple-hydrogen bonds as well as guest encapsulation, see: a) R. K. Castellano, C. Nuckolls, S. H. Eichhorn, M. R. Wood, A. J. Lovinger, J. Rebek, Jr., *Angew. Chem.* **1999**, *111*, 2764 – 2768; *Angew. Chem. Int. Ed.* **1999**, *38*, 2603 – 2606; b) H. Xu, D. M. Rudkevich, *Chem. Eur. J.* **2004**, *10*, 5432 – 5442.

[17] a) R. M. Yebeutchou, F. Tancini, N. Demitri, S. Geremia, R. Mendichi, E. Dalcanale, *Angew. Chem.* **2008**, *120*, 4580 – 4584; *Angew. Chem. Int. Ed.* **2008**, *47*, 4504 – 4508; b) F. Tancini, R. M. Yebeutchou, L. Pirondini, R. De Zorzi, S. Geremia, O. A. Scherman, E. Dalcanale, *Chem. Eur. J.* **2010**, *16*, 14313 – 14321.

[18] G. Cafeo, G. Gattuso, F. H. Kohnke, A. Notti, S. Occhipinti, S. Pappalardo, M. F. Parisi, *Angew. Chem.* **2002**, *114*, 2226 – 2230; *Angew. Chem. Int. Ed.* **2002**, *41*, 2122 – 2126.

[19] a) G. Gattuso, C. Gargiulli, C. Liotta, A. Notti, M. F. Parisi, I. Pisagatti, S. Pappalardo, *J. Org. Chem.* **2009**, *74*, 4350 – 4353; b) C. Capici, R. De Zorzi, C. Gargiulli, G. Gattuso, S. Geremia, A. Notti, S. Pappalardo, M. F. Parisi, F. Puntoriero, *Tetrahedron* **2010**, *66*, 4987 – 4993.

[20] D. Garozzo, G. Gattuso, A. Notti, A. Pappalardo, S. Pappalardo, M. F. Parisi, M. Perez, I. Pisagatti, *Angew. Chem.* **2005**, *117*, 4970 – 4974; *Angew. Chem. Int. Ed.* **2005**, *44*, 4892 – 4896.

[21] a) B. P. Hay, T. K. Firman, B. A. Moyer, *J. Am. Chem. Soc.* **2005**, *127*, 1810 – 1819; b) V. Amendola, L. Fabbrizzi, L. Mosca, *Chem. Soc. Rev.* **2010**, *39*, 3889 – 3915.

[22] See the Supporting Information for experimental details.

[23] a) D. R. Stewart, M. Krawiec, R. P. Kashyap, W. H. Watson, C. D. Gutsche, *J. Am. Chem. Soc.* **1995**, *117*, 586 – 601; b) G. De Salvo, G. Gattuso, A. Notti, M. F. Parisi, S. Pappalardo, *J. Org. Chem.* **2002**, *67*, 684 – 692.

[24] For previous examples of *endo*-cavity inclusion of alkylammonium and alkanediyldiammonium ions inside calix[5]arene derivatives, see: Refs. [6–8] and [18–20].

[25] The alternative process of *endo*-cavity intramolecular inclusion of the pendant chain had been previously ruled out by ^{1}H NMR diffusion experiments on the protonated form of **C5-NH$_2$** (see Ref. [6]). For an example of self-threading, see: Y. Inoue, M.

Miyauchi, H. Nakajima, Y. Takashima, H. Yamaguchi, A. Harada, *J. Am. Chem. Soc.* **2006**, *128*, 8994 – 8995.

[26] Signal assignments, reported in Figure 1, follow from DQF-COSY and 1D TOCSY experiments (see the Supporting Information).

[27] For a review on the application of diffusion NMR spectroscopy in supramolecular chemistry, see: Y. Cohen, L. Avram, L. Frish, *Angew. Chem.* **2005**, *117*, 524 – 560; *Angew. Chem. Int. Ed.* **2005**, *44*, 520 – 554. For a selection of recent articles on the same topic see: a) L. Avram, Y. Cohen, *J. Am. Chem. Soc.* **2004**, *126*, 11556 – 11563; b) T. Evan-Salem, I. Baruch, L. Avram, L. C. Palmer, J. Rebek, Jr., *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 12296 – 12300; c) T. Evan-Salem, L. Frish, F. W. B. van Leeuwen, D. N. Reinhoudt, W. Verboom, M. S. Kaucher, J. T. Davis, Y. Cohen, *Chem. Eur. J.* **2007**, *13*, 1969 – 1977; d) L. Avram, Y. Cohen, *Org. Lett.* **2008**, *10*, 1505 – 1508; e) S. Slovak, L. Avram, Y. Cohen, *Angew. Chem.* **2010**, *122*, 438 – 441; *Angew. Chem. Int. Ed.* **2010**, *49*, 428 – 431; f) A. Lledó, J. Rebek, Jr., *Chem. Commun.* **2010**, *46*, 8630 – 8632.

[28] The stack plots of the β-CH_2 peak of **1** and (**1**·HCl)$_n$ at different concentrations and the respective natural logarithm of the normalized signal decay of these peaks are shown in the Supporting Information (Figure S5 and S6, respectively).

[29] A. Wong, R. Ida, L. Spinder, G. Wu, *J. Am. Chem. Soc.* **2005**, *127*, 6990 – 6998. The model takes into account the effect of the number of repeating units on the diffusion coefficient of cylindrical molecular assemblies that do not interact with each other and is based on M. M. Tirado, C. Lopez Martinez, J. García de La Torre, *J. Chem. Phys.* **1984**, *81*, 2047 – 2052.

[30] The hydrodynamic radius is defined as the radius of an equivalent sphere experiencing the same viscous friction as the (**1**·HCl)$_n$ species.

[31] Heteroditopic calix[4]arenes endowed with a ureido functionality have been reported to strongly coordinate through hydrogen bonding to DMSO molecules; see: A. Arduini, E. Brindani, G. Giorgi, A. Pochini, A. Secchi, *Tetrahedron* **2003**, *59*, 7587 – 7594.

[32] F. P. Ballistreri, A. Notti, S. Pappalardo, M. F. Parisi, I. Pisagatti, *Org. Lett.* **2003**, *5*, 1071 – 1074.

[33] J. Lacour, D. Morelda, *Chem. Commun.* **2009**, 7073 – 7079.

[34] Induced CD signals likely arise as the result of an asymmetric arrangement of the calixarene framework (i.e. clockwise and counter-clockwise orientation of the NH groups of the ureido moiety, with respect to the macrocyclic cavity) induced by the binding of the enantiomeric mandelate counterions. An additional helical arrangement (instilled by steric hindrance during the monomer-to-monomer self-assembly process) may also be invoked in the case of the ((*S*)-**Ma**H·**1**)$_n$ and ((*R*)-**Ma**H·**1**)$_n$ assemblies to justify the enhanced intensity of their CD bands.

[35] The low-intensity CD signals, observed in Figure 4c (traces 2 and 4), account for the CD spectra of (*S*)- and (*R*)-mandelic acid, respectively, released in solution upon the addition of trifluoroacetic acid (TFA; see the Supporting Information, Figure S11).

[36] For representative examples, see: a) Y. Furusho, T. Kimura, Y. Mizuno, T. Aida, *J. Am. Chem. Soc.* **1997**, *119*, 5267 – 5268; b) L. J. Prins, F. De Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **2000**, *408*, 181 – 184; c) Y. Mizuno, T. Aida, K. Yamaguchi, *J. Am. Chem. Soc.* **2000**, *122*, 5278 – 5285; d) J. M. Rivera, S. L. Craig, T. Martin, J. Rebek, Jr., *Angew. Chem.* **2000**, *112*, 2214 – 2216; *Angew. Chem. Int. Ed.* **2000**, *39*, 2130 – 2132; e) H. Onouchi, T. Miyagawa, K. Morino, E. Yashima, *Angew. Chem.* **2006**, *118*, 2441 – 2444; *Angew. Chem. Int. Ed.* **2006**, *45*, 2381 – 2384; f) A. Mammana, A. D'Urso, R. Lauceri, R. Purrello, *J. Am. Chem. Soc.* **2007**, *129*, 8062 – 8063; g) R. Randazzo, A. Mammana, A. D'Urso, R. Lauceri, R. Purrello, *Angew. Chem.* **2008**, *120*, 10027 – 10030; *Angew. Chem. Int. Ed.* **2008**, *47*, 9879 – 9882; h) F. Helmich, C. C. Lee, A. P. H. J. Schenning, E. W. Meijer, *J. Am. Chem. Soc.* **2010**, *132*, 16753 – 16755.

