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Anion-controlled foldamers†‡

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This *tutorial review* provides a summary of anion-mediated folding of linear and cyclic oligomers as well as anion-responsive behaviours of related polymeric architectures. Anions have emerged as a significant focus of the supramolecular community and here we review their impact on directing the secondary structures of synthetic oligomers and polymers while modulating physical properties *e.g.* molecular recognition. Oligomers and polymers responsive to anionic guests are typically constructed with hydrogen bond donors complementary to the target anions. Anion binding within the cavities leads to folding and helical wrapping of linear and cyclic oligomers as well as control over macromolecular properties of polymers. This review covers the impact of anion binding on guiding the secondary structures of single-stranded folded oligomers (foldamers) and cyclic oligomers (macrocycles), and on modulating the physical properties of select polymer architectures.

1. Introduction

Anion recognition chemistry has emerged as an exciting research field in supramolecular chemistry in recent years owing to the biological and environmental relevance of anions.[1] Most anions are good hydrogen bond acceptors, and their receptors commonly possess appropriate donor groups for binding. Directionality of the hydrogen bond allows for designing receptors of specific shapes that are capable of differentiating between anions of different size, geometry and hydrogen-bonding modes. The lock and key principle has inspired organic and supramolecular chemists to implement the concepts of preorganization and complementarity in the design of synthetic anion receptors with high affinity and selectivity.[2]

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† Dedicated to the memory of Professor Chi Sun Hahn.

‡ Part of a themed issue on the supramolecular chemistry of anionic species.

Conventional synthetic receptors like macrocycles and molecular clefts possess binding sites that are constructed by covalent bonds. In contrast, natural receptors such as proteins and enzymes are essentially linear polymers that fold to create binding cavities. The encapsulation and isolation of anionic guests enables complex functions such as transport, signaling, catalysis, *etc* and are the direct result of folding which is fundamentally governed by noncovalent interactions. Many groups have prepared unnatural oligomers or polymers that exhibit strong tendencies to form well ordered secondary structures by a combination of noncovalent interactions, resembling those found in Nature.[3–5] These synthetic molecules have been known as *foldamers*, and provide an opportunity to understand fundamental principles of protein folding, to probe the relationship between structure and function in biomacromolecules, and to develop novel, functional materials inspired by biological self-assembly.

Foldamers have unique features or merits as synthetic receptors. In the context of molecular recognition, programmed folding can replace a synthetically challenging cyclisation with

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a facile conformational change. Foldamers can bind guests by encapsulating them in their internal cavities, and the degree of encapsulation depends on the length of foldamers, which in general determines the dimensions of the binding cavity. The dimension, size and shape of the binding cavity in the foldamer can be conveniently manipulated by controlling the number of repeating monomer units and changing the kind of molecular components connecting the monomers. Furthermore, the weak noncovalent character of the stabilizing interactions provides foldamers with some degree of flexibility, an advantage over rigid synthetic receptors because small conformational changes in receptors lead to optimal distance and geometry to exert maximum interaction with target guests.[6,7]

In the context of this review, examples of foldamers and related folding structures controlled by anion binding have been overviewed. First, foldamers of acyclic oligomers that contain helical cavities for binding complementary anions are described. Next, cyclic oligomers such as cyclic oligopyrroles and oligoureas are included which fold to generate two binding cavities for anions, resembling a figure of eight. The last section contains supramolecular polymers whose formation or dissipation is mediated by anions as well as helical polymers whose structures or chiral bias can be modulated by anion binding. Anion-binding foldamers based on amino acids have not been included here as an extensive review by Kubik has recently been published.[8]

2. Acyclic oligomers

Sequential linking of monomers in a programmed manner affords foldamers that fold into well-defined secondary structures, *e.g.* helical structures. The information necessary for folding should be prescribed in the design of the monomers. To prepare foldamer-based anion receptors, the monomers need to have hydrogen bond donors to interact with anions. Examples include the NH protons of amides, ureas, pyrroles and indoles, and the polarized CH protons of neutral or positively charged aromatic heterocycles such as 1,2,3-triazoles. In particular, pyrroles, indoles and related molecules contain only hydrogen bond donors, not acceptors. This is an important feature to prevent their oligomeric strands from forming intra- and interstrand hydrogen bonds that could possibly lead to the collapse of the binding cavity or severe aggregation of the foldamers. Herein, we first describe acyclic oligopyrroles, comprising four or six pyrrole rings, in which anion binding gives rise to well-defined S- or C-shaped conformations. Then, oligoindoles, oligotriazoles, and other oligomers have been described, which fold into helical conformations in the presence of anionic species in solution.

2.1 Oligopyrroles

Pyrrole contains a built-in NH proton which forms a strong hydrogen bond with anions as demonstrated for the first time by Sessler *et al.*[9] Hexapyrrole **1** is fully conjugated and the X-ray crystal structure of the dihydrochloride salt shows the molecule to exist in a planar, extended S-shaped conformation comprising two clefts, each occupied by a chloride ion held by three NH$\cdots$Cl$^-$ hydrogen bonds (Fig. 1).[10] ^{1}H NMR experiments also support the solid-state structure as NOEs between the

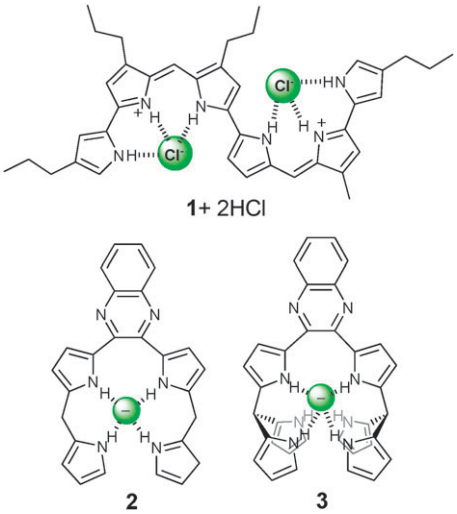

Fig. 1 Oligopyrroles **1–3** depicted in their proposed anion binding modes.

pyrrole NH and the CH within the cavity confirmed the prevalence of the S-shaped conformation in solution.

Also developed by Sessler and co-workers were oligopyrroles **2** and **3** which consisted of either di- or tripyrrolic moieties directly connected to a chromophore, quinoxaline (Fig. 1).[11,12] In the absence of anions, the pyrrole arms rotate freely in solution at room temperature, but in the presence of anions the spatial arrangements of the arms are adjusted to create a concave pocket that comprises four or six NH donor groups in a convergent manner suitable for binding an anion. Binding constants (K_a) of chloride were determined to be 550 M^{-1} and 5800 M^{-1} in CH_2Cl_2 for **2** and **3**, respectively, while those of dihydrogenphosphate were 4300 M^{-1} and 3×10^5 M^{-1}.

Maeda and co-workers reported the diketo-substituted boron complex of oligopyrrole **4** in which anion binding implemented a distinct conformational change of the oligomer (Fig. 2).[13] In the presence of anions the pyrrole arms inverted from their free conformations to form a well-defined C-shaped cavity comprising four convergent NH hydrogen bond donors that can complex anions. The diketo-boron bridge offers a modular way of controlling the electronic and subsequent binding properties of the oligomer. Oligomer **4** binds chloride, acetate and dihydrogenphosphate with association constants (K_a) of approximately 10^6 M^{-1} in $CHCl_3$ as determined by UV-Vis spectroscopy. X-Ray diffraction analysis of **4** and TBA$^+$Cl$^-$ describes a pentacoordinated [1 + 1] complex where the anion is held by four NH$\cdots$Cl$^-$ hydrogen bonds and one

Fig. 2 Diketo-boron derivatized oligopyrrole **4** hydrogen bonds to an anion yielding a curved conformation.

$CH\cdots Cl^-$ from the enol bridge. They expanded upon the boron-derivatized motif by synthesizing longer oligomers, but anion binding and folding studies have not been reported.[14,15]

2.2 Oligoindoles

In 2005, Jeong and co-workers first reported single strand oligoindoles, containing four, six, and eight indoles, which helically folded around anions.[16] A series of oligoindoles were synthesized in which monomeric indole units were connected sequentially by ethynyl linkers (Fig. 3). First, oligomers **5** adopted an expanded conformation in the absence of an anion, but folded into helical conformations in the presence of a chloride, thus encapsulating the anion within a helical cavity. This was proven by ^{1}H NMR spectroscopy where addition of chloride gave rise to large downfield shifts of the ^{1}H NMR signals of the indole NHs due to $NH\cdots Cl^-$ hydrogen bonds. In addition, characteristic upfield shifts of the aromatic CH signals of the longer oligoindoles **5** (n = 1, 2) were observed as a result of π-stacking between adjacent helical turns, where one turn was composed of about four indole rings. The anion-induced, helical folding was further proved by 2D ^{1}H–^{1}H ROESY experiments where NOE cross-peaks between stacked aromatic protons were observed only in the presence of TBA^+Cl^-. The association constants (K_a) between **5** and chloride were determined to be in the range of 10^5–10^7 M^{-1} in acetonitrile, depending on the chain length of the oligomers. In a more competitive medium for hydrogen bonding (10% v/v H_2O–CH_3CN), the association constants were greatly reduced to 210–23 000 M^{-1}, proving that the complex formation is driven mainly by hydrogen bonds.

A strongly fluorescent oligoindole **6** was prepared by modification of the oligomer termini, to compare relative binding affinities between anions.[17] Upon binding an anion, oligomer **6** displayed bathochromic and hypochromic shifts ($\Delta\lambda$ up to 65 nm) of the emission spectra due to intramolecular excimer formation by π–π stacking in the helical array, resulting in a color change from bright blue to bluish green. Oligomer **6** was shown to bind a variety of anions ($F^- > Cl^- > N_3^- \approx CN^- > AcO^- > Br^- > I^- \approx NO_3^-$) with association constants (K_a) ranging from 10^3 to 10^6 M^{-1} in 20% MeOH–CH_2Cl_2 determined by fluorescence spectroscopy.

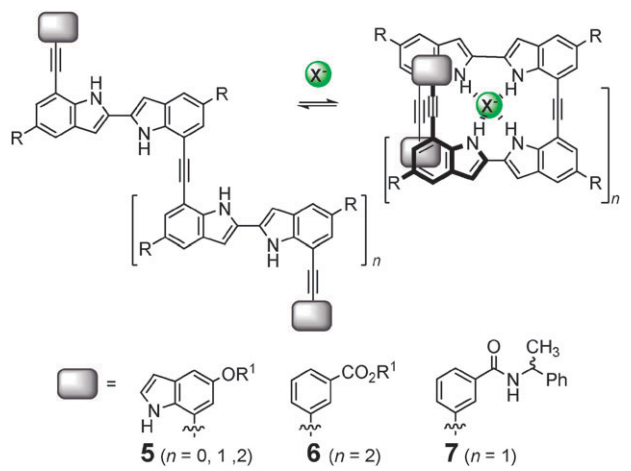

Fig. 3 Oligoindole based foldamers **5–7** fold into helical structures in the presence of anions.

Next, chiral segments were introduced to the foldamer termini to investigate whether the preferential formation of a left- or right-handed helix could be controlled in the presence of an anionic stimulus.[18] Chiral oligomer **7** showed no circular dichroism (CD) signal by itself, but a strong Cotton effect was observed upon the addition of TBA^+Cl^- in CH_2Cl_2. The signal intensity gradually increased and saturated upon addition of approximately one equivalent of the chloride ion, and the enantiomer of **7** showed identical behaviour but the opposite Cotton effect. The association constant between **7** and TBA^+Cl^- was determined to be 2.9×10^5 M^{-1} in 1% (v/v) MeOH–CH_2Cl_2. These results demonstrate that the chirality of terminal groups induces the formation of a particular helix over the other at least preferentially in the presence of an anion.

The same group synthesized indolocarbazole oligomers that possessed extended π-surfaces relative to the corresponding biindole-based ones, thus possibly providing increased π–π stacking and hydrophobic interactions.[19] A water-soluble foldamer **8** folded into a helical conformation with an internal cavity encircled by multiple neutral hydrogen bond donors (Fig. 4). In water, **8** bound halides such as fluoride (K_a = 46 M^{-1}), chloride (65 M^{-1}), and bromide (19 M^{-1}) as determined by ^{1}H NMR titrations. Interestingly, the chloride ion was bound more strongly in water than the fluoride ion, possibly attributed to the higher degree of solvation of fluoride. This study is a rare example of synthetic receptors that achieve binding of hydrophilic anions by neutral hydrogen bonds in water.

The indolocarbazole building block was further utilised to synthesize oligomer **9** which contained six indole NHs and two aliphatic OHs (Fig. 4).[20] The sulfate complex of **9** yielded single crystals suitable for X-ray diffraction analysis. The tetrahedral sulfate ion was encapsulated in a helical cavity

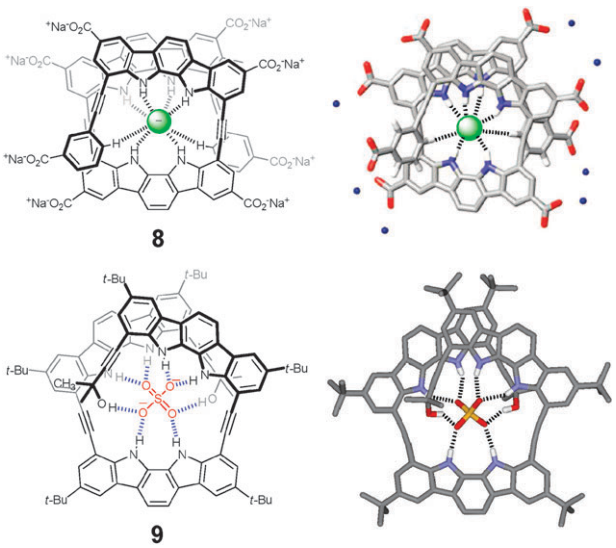

Fig. 4 Oligomers **8** and **9** in the hydrogen bonding modes with anions. An energy-minimized structure of **8**·Cl^-(top right) and a crystal structure of **9**·SO_4^{2-} (bottom right) depict a helical cavity encapsulating anions by hydrogen bonds.

by a total of eight hydrogen bonds, each oxygen forming two hydrogen bonds. Interestingly, the crystal was found to be a racemic compound in which *M*- and *P*-helices were alternately stacked to give higher order aggregates. Folding observed in the solid state was also evident *via* ^{1}H–^{1}H NOESY studies where π–π stacking of the terminal arms of the oligoindolocarbazole resulted in cross peaks between non-adjacent aromatic protons. Oligomer **9** displayed a high binding strength and selectivity towards sulfate (K_a = 6.4 × 10^5 M^{-1} in 10% v/v CH_3OH–CH_3CN). It should be mentioned that other anions (Cl^-, Br^-, I^-, AcO^-, CN^-, N_3^-, $H_2PO_4^-$) yielded binding strengths at least two orders of magnitude lower than sulfate.

2.3 Oligotriazoles

1,2,3-Triazoles have recently come to prominence due to their extremely efficient synthesis *via* "click chemistry" and their subsequent use as universal ligation tools with negligible independent function.[21] However, recent reports have suggested that the size and dipole moment (~5 D) of the heterocycle, make them suitable candidates as amide bond surrogates and 1,2,3-triazoles have been implemented in the synthesis and study of peptidotriazoles and foldamers. Of particular interest to the anion recognition community is the distinct dipole of the ring which results in an electropositive CH, thus capable of forming the hydrogen bond with anions.

In a series of almost simultaneous reports, the groups of Flood, Craig and Hecht independently reported the use of aryl-1,2,3-triazoles to develop synthetic anion receptors. Li and Flood reported a rigid, planar tetrameric macrocycle that formed a complex with chloride only by means of CH···Cl^- hydrogen bonds.[22] The internal cavity is lined with hydrogen atoms from the aryl moieties and the more electropositive CHs of the triazoles, resulting in a complementary environment for chloride.

Craig and co-workers reported acyclic oligomers based on the aryl 1,2,3-triazole motif (Fig. 5).[23,24] It was shown that linear oligomer **10** comprising four 1,2,3-triazole rings coupled with phenyl spacers complexed anions by folding around the anion in a helical fashion. Devoid of conventional NH hydrogen bond donors, binding of chloride by **10** was exclusively carried out by CH···Cl^- bonds and ^{1}H NMR titrations with chloride and bromide yielded association constants (K_a) of 10^4 M^{-1} in d_6-acetone. The helical cavity formed upon folding of **10** in the presence of the anion is characterized in solution by ^{1}H–^{1}H NOESY experiments, showing that in the absence of an anion, the oligomer exists in a random, extended conformation that switches to a wrapped helix upon anion complexation. The size of the binding cavity was shown to be complementary to chloride as studies with larger anions gave lower association constants due to an improper fit within the cavity (*e.g.* for I^-, K_a = 1300 M^{-1} in d_6-acetone). In a following publication, it was shown that the association constants with anions in the case of oligomer **10** were largely dependant on effective ionic radius with small but measurable deviations in the case of non-spherical anions. The short and flexible oligomer **10** was also used as a model to understand the relationship between

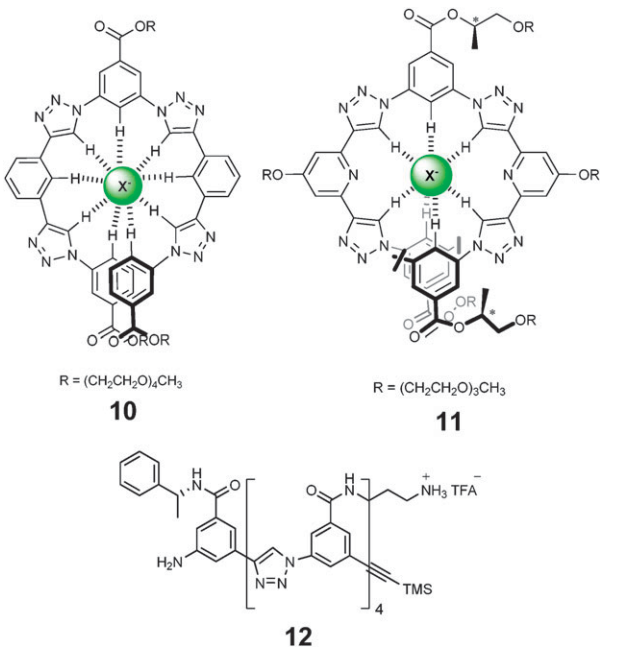

Fig. 5 Oligotriazoles **10** and **11** in their folded anion binding modes, and a cationic oligotriazole **12**.

anion size/geometry and solvent effects, particularly in the case of CH···X^- interactions which are still considered unconventional hydrogen bonding interactions and compared to NH···X^- interactions, largely unexplored.

Meudtner and Hecht independently reported structurally related oligomer **11** by alternating aryl, pyridyl and 1,2,3-triazole moieties (Fig. 5).[25] As previously mentioned, dipole effects in 1,2,3-triazoles are significant and dipole–dipole repulsion between the heterocycles caused **11** to adopt a helical conformation in water–acetonitrile that was further stabilized by π-stacking of the overlapped strand and solvophobic effects. Addition of HCl did not disrupt the helicity as was observed by CD studies, but the role of the counter anion was investigated further at neutral pH. Fluoride was shown to increase the intensity of the CD signal while chloride and bromide caused inversion of helicity with bromide having the most significant effect. Of importance is that the foldamer interaction with achiral, spherical halides leads to an opposite helical preference. It was hypothesized that halide interaction with the chiral ethylene glycol side chains of **11** transferred helicity to the aromatic backbone, resulting in an inversion between left- and right-handed helices.

Jiang and co-workers reported the folding and higher-order aggregation behaviors of cationic oligotriazole **12** (Fig. 5).[26] Using similar design principles of alternating *meta*-phenyl groups with 1,2,3-triazoles, a series of water-soluble oligomers were synthesized by attaching ammonium side chains. The authors hypothesized that solvophobic and van der Waals interactions would force the cationic oligomer **12** to adopt compact, helical conformations in polar solvents such as water and methanol, thus providing helical binding cavities for anions. While the focus of their report involved the aggregation and assembling behaviors of the oligomers in solution, in the context of this review it is important to note that similar

$CH\cdots X^-$ interactions guided the recognition of chloride and fluoride in mixtures of water and methanol. Furthermore, the anion binding of these oligomers prevented the higher order aggregation of the oligotriazoles by destabilizing the inter-strand attractions.

From these reports it is clear that even though not traditionally included in the list of hydrogen bond donors, sufficiently polar CH bonds interact with anions in a manner that makes them useful building blocks for anion receptors. In the context of anion-controlled foldamers, 1,2,3-triazoles are useful building blocks due to their ease of synthesis, and also due to their inherent electronic (strong dipole, electropositive CH), and structural (planar, π-rich) properties.

2.4 Others

de Mendoza and co-workers reported the first example of using anions as a template for generating helical oligomers in 1996.[27] Chiral oligomer **13** comprised four bicyclic guanidinium salts connected by a CH_2SCH_2 spacer unit (Fig. 6). **13** was designed for the complexation and transport of oligonucleotides across cell membranes as the thioether spacer spans the distance between two anionic subunits of the phosphodiester backbone. In the presence of sulfate, the spacer was not long enough to wrap the two guanidinium subunits around a single anion and instead two strands of **13** folded into a double-helical structure around sulfate. The helical complex was of specific handedness due to the chirality imposed by the individual oligomers, which was proven by circular dichroism (CD) spectroscopy. Almost a decade later the same group reported the utility of **13** as a novel cell-penetrating vector that gets efficiently internalized in human tumor cells, specifically in mitochondria.[28,29]

Kruger and Martin reported bispyridyl ligand **14** that formed a helical dimer in the presence of hydrogen chloride (Fig. 7).[30] The crystal structure of the complex consists of two ligand strands complexed with two chloride anions in a double

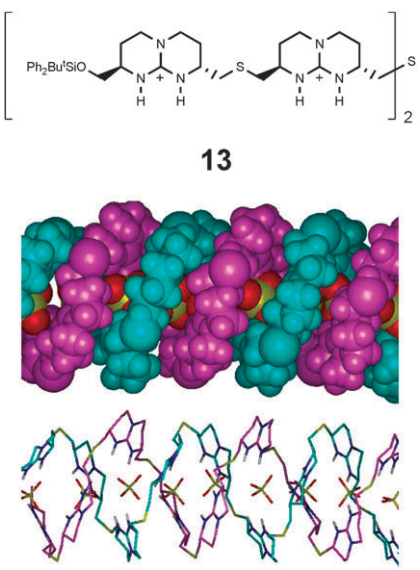

Fig. 6 Tetrakis guanidinium oligomer **13** and optimized models of a sulfate helicate from (*S*,*S*)-guanidines. Reproduced with permission from ref. 29. Copyright 2007 RSC Publishing.

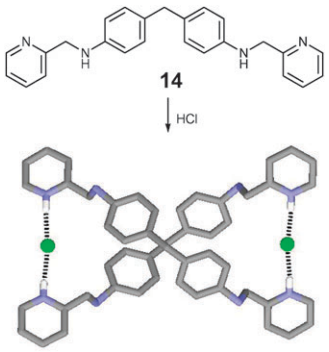

Fig. 7 Bispyridyl ligand **14** forms a helical dimer in the presence of hydrogen chloride in the solid state.

helical arrangement. The chloride ions are coordinated in a pincer fashion by the two pyridinium moieties by ionic hydrogen bonds and also by weaker interactions with methylene and aromatic hydrogens within the binding pocket.

Gale and co-workers reported the fluoride-directed assembly of isophthalamide cleft **15** into a double helix.[31] Single-crystal X-ray diffraction analysis of the fluoride complex of **15** revealed a double helix wrapped around two fluoride anions that were each held by two $NH\cdots F^-$ hydrogen bonds (Fig. 8). The helical complex was further stabilized by π–π interactions between the terminal nitroaromatic arms of the clefts.

Mellet and Fernandez designed **16**, a carbohydrate-thiourea hybrid, to investigate the role of long-range hydrogen bonds between the carbohydrate and thiourea NHs in stabilizing helical structures (Fig. 9).[32] The foldamer **16** was shown to possess a 15-membered hydrogen bond involving the sugar oxygen and the thiourea NH leading to either *P*- or *M*-helices. The difference here is the role that anion complexation plays in helix destabilization and uncoiling, in contrast to reports discussed earlier in this review where anion binding induces helicity. Upon binding to benzoate (K_a = 1930 M^{-1} in $CDCl_3$), the long-range hydrogen bonds are disrupted and the helical folding pattern is destabilized leading to uncoiling of the oligomer.

Li and co-workers reported the folding of a linear arylamide oligomer **17** in DMSO in the presence of benzene-1,3,5-tricarboxylate anion (Fig. 10).[33] The oligomer consisted of

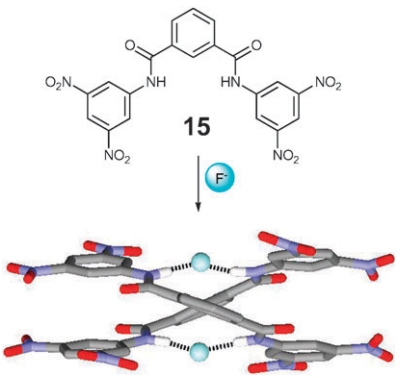

Fig. 8 Isophthalamide oligomer **15** hydrogen bonds to fluoride forming a double helix in the solid state.

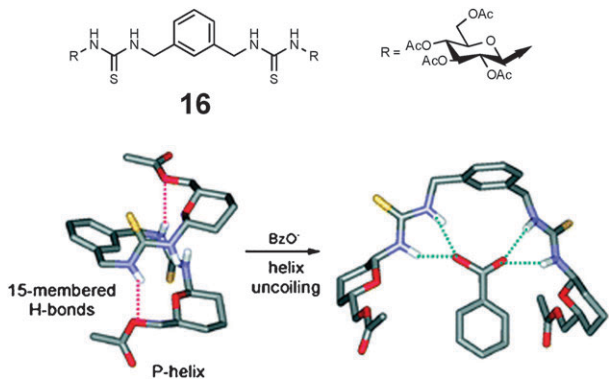

Fig. 9 Carbohydrate-thiourea hybrid oligomer **16** forms 15-membered hydrogen bonds which are disrupted by hydrogen bonding to benzoate resulting in helix uncoiling. Reproduced with permission from ref. 32. Copyright 2007 RSC Publishing.

naphthalene-2,7-diamine and 1,3,5-benzenetricarboxylic acid segments. According to ^{1}H–^{1}H NOESY, ^{1}H NMR, fluorescence and UV-Vis studies, **17** did not adopt compact conformations in the absence of the anionic template, but folded into a helical structure upon hydrogen bonding to benzenetricarboxylate. Upon folding, a helical cavity was formed with NH and CH donor groups arranged in a complementary fashion to stabilize the complex ($K_a = 8.6 \times 10^5$ M^{-1} in DMSO). The hydrogen bonding complementarity towards tricarboxylate is imperative in generating the helical folded structure, as anions such as chloride, bromide, nitrate, acetate and isophthalate did not induce a helical complex.

3. Cyclic oligomers

Cyclic oligomers that display interesting dynamic conformational behavior can be considered as a type of foldamer comprising monomeric repeating units. Cyclic oligomers of short length are relatively rigid macrocycles with limited conformational freedom, thus possessing a single binding cavity. As the ring size increases, however, cyclic oligomers are flexible enough to display unique twisting and folding behaviors similar to their acyclic counterparts. The resulting secondary structures adopted by these oligomers resemble a "figure-of-eight" containing two binding pockets which are geometrically separated from each other as demonstrated in cyclic oligoureas and cyclic oligopyrroles discussed below.

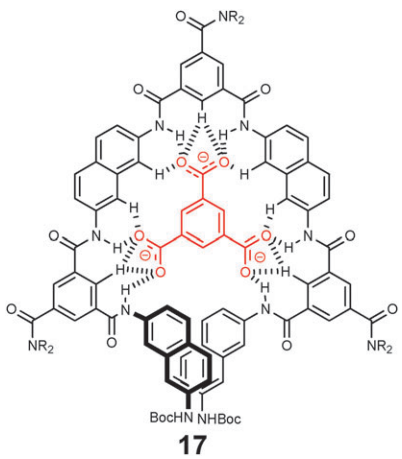

Fig. 10 Arylamide oligomer **17** in hydrogen bonding mode with complementary benzene-1,3,5-tricarboxylate.

3.1 Cyclic oligoureas

The utility of urea in synthetic anion receptors stems directly from its ability to simultaneously form two hydrogen bonds, and offers a hydrogen-bonding motif complementary to oxoanions. The NH protons of urea are strong hydrogen bond donors and when linked to aryl units in the form of a macrocycle offer a good balance of both structural rigidity and flexibility.[34]

Böhmer and co-workers described a cyclic hexaurea **18** which consisted of four rigid xanthene units and two flexible diphenyl ether units connected *via* the urea functional group (Fig. 11).[35] The aryl ureas are responsible for the prearrangement of the donor NHs while the flexible ether linkages offer the ability to adapt to the target guest by twisting. The resulting macrocyclic cavity contained twelve NH hydrogen bond donors; two from each urea. The X-ray crystal structure showed that in the presence of chloride **18** folded to create two binding cavities resembling a figure of eight. In each cavity, three adjacent ureas bind to one chloride resulting in 1 : 2 **18**/Cl^- stoichiometry. The UV-visible titration by the addition of tetrabutylammonium chloride to a solution of **18** in CH_3CN–THF (3 : 1 v/v) allowed the elucidation of the stability constants, log K_{11} = 6.16 and log K_{12} = 5.25. Microcalorimetric titrations afforded thermodynamic parameters; $\Delta H = -23$ kJ mol^{-1} and $T\Delta S = 12$ kJ mol^{-1} for the first step (**18** + Cl^- → **18**·Cl^-), and $\Delta H = -44$ kJ mol^{-1}

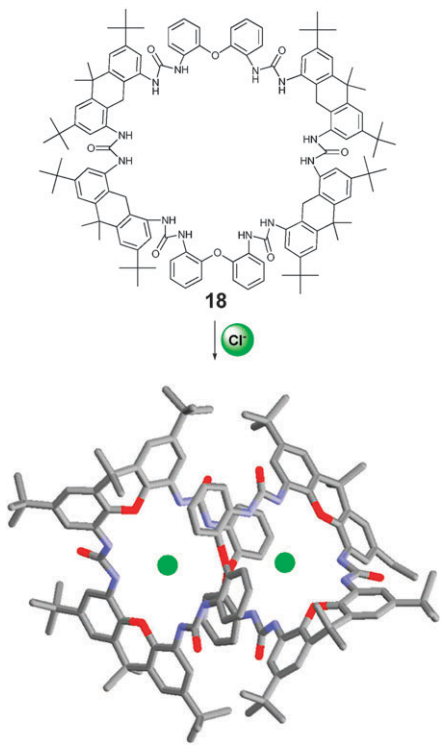

Fig. 11 Cyclic hexaurea **18** twists and wraps around two chloride ions yielding a figure-of-eight structure in the solid state.

and $T\Delta S = -14$ kJ mol^{-1} for the second step (**18**·Cl$^-$ + Cl$^-$ → **18**·(Cl$^-$)$_2$), respectively. Interestingly, the first step is entropically favorable possibly owing to desolvation, and the stronger interactions (more negative ΔH) are formed upon the second guest binding. This result suggests that anion binding occurs *via* an "induced fit" model due to the combination of both rigid and flexible units in the cyclic oligomer, allowing for the accommodation of two anionic guests. The same group also described related cyclic oligoureas which have different combination of monomers, xanthene and diphenyl ether, and display more complicated folding structures.[36,37]

3.2 Cyclic oligopyrroles

Sessler and co-workers have reported a number of oligopyrrole-based macrocycles known as "expanded porphyrins" that display unique anion binding properties.[38] A cyclic decapyrrole **19** called turcasarin can twist to adopt left- and right-handed enantiomeric figure-of-eight loops (Fig. 12).[39] The crystal structure of the tetraprotonated chloride complex of **19** demonstrated a nearly C_2-symmetric "twisted ribbon" conformation and not a circular "loop" conformation. The twist observed in the crystal structure affords two binding compartments, each of which accommodates two chloride ions hydrogen bonded to the NHs of pyrroles. These hydrogen binding interactions resulted in the slow conformational interconversion of **19**, observed on the NMR timescale in $CDCl_3$ solution at room temperature. It is worthwhile noting that at the point of crossing of the macrocyclic loops, the two pyrrole containing π-systems are separated by a van der Waals distance of 3.268 Å, indicative of the folded conformation additionally stabilised by π-stacking. Of interest is that conjugated macrocycles need not necessarily be considered rigid and flat structures but can also display interesting dynamic behaviours like twisting and folding that make them potentially chiral.

The same group also reported a cyclic oligopyrrole **20** in which bipyrroles were connected to 2,6-diamidopyridine units *via* imine linkages (Fig. 12).[40] The imine macrocyclization of the precursors, a bipyrrole dialdehyde and a diamidopyridine diamine, was carried out in the presence of various acids (HCl, HBr, CH_3CO_2H, CF_3COOH, H_3PO_4, H_2SO_4, HNO_3). The presence of only H_2SO_4 led to the desired macrocycle, nearly free of side products, but all other acids resulted in higher oligomers or uncharacterized side products. Single-crystal

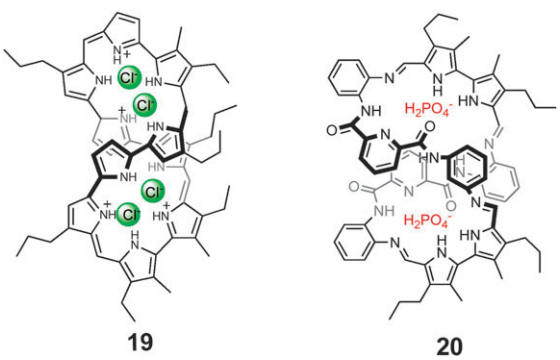

Fig. 12 Cyclic oligopyrroles **19** and **20** twist into figure-of-eight loops and encapsulate anions by hydrogen bonds in two distinct cavities.

X-ray diffraction analysis of **20** revealed that the macrocycle adopted a figure-of-eight conformation whose structure was stabilized by intra- and intermolecular hydrogen bonds between the pyrrole NHs, the amide carbonyl oxygens and two water molecules. Anion binding studies of **20** showed selective binding toward tetrahedral anions such as dihydrogen phosphate and hydrogen sulfate; **20** bound two equivalents of dihydrogen phosphate with association constants of $K_{11} = 1.9 \times 10^5$ M^{-1} and $K_{12} = 6.0 \times 10^4$ M^{-1} in CH_3CN, but bound one equivalent of hydrogen sulfate with $K_a = 6.3 \times 10^4$ M^{-1}. No binding was observed with chloride, bromide and nitrate, possibly due to the shape mismatch of these anions to the binding pocket generated by a tetrahedral template as explained by the authors.

In the presence of dihydrogen phosphate and hydrogen sulfate, **20** slowly underwent a rearrangement and subsequent ring expansion resulting in a complex, double-twisted, diprotonated macrocyclic dication that could encapsulate a sulfate dianion, coordinated through an intricate network of hydrogen bonds.[41] Authors used this expanded macrocyclic complex with dihydrogen phosphate to draw comparisons to the active site in the phosphate-binding protein and similar structural analogies to the sulfate-binding protein with the corresponding hydrogen sulfate complex.

4. Anion responsive polymers

Described in this section are anion binding effects on directing polymeric self-assembly and morphology. Here, anion binding to the polymeric cavities or side-chains has pronounced effects on the structures and functions of the polymers. We briefly overview selected examples of anion-directed assembly and disassembly of supramolecular polymers, and the anion binding effect on the morphology of helical polymers. Supramolecular polymeric architectures and gels induced by anion binding have been recently reviewed in detail and will not be included here.[42–44]

4.1 Assembly and disassembly

Gale and co-workers reported an anionic supramolecular polymer consisting of 3,4-dichloro-2,5-diamido-substituted pyrrole units.[45] Compound **21** dimerized in an orthogonal manner *via* NH···N$^-$ hydrogen bonds when the added fluoride ion gave rise to the deprotonation of the pyrrole NH. Crystals of the amidopyrrole **21** obtained in the presence of excess TBA$^+$F$^-$ depicted the doubly deprotonated pyrrole anions (**21**-2H$^+$) forming interlocked chains of anions that were stabilized by NH···N$^-$ hydrogen bonds (Fig. 13). These interactions extended to yield a polymeric chain consisting of twisted molecules at every other position resulting in a unique zig-zag architecture. The same group has described several other examples of solid-state supramolecular polymeric architectures formed by hydrogen bonds between anionic species and small molecular building blocks with bis- and tetraureido groups.[46]

Maeda and Kusunose reported the formation of a chloride bridged supramolecular polymeric network with BF_2 complexes of acyclic dipyrrolyldiketone **22** by means of CH···Cl$^-$ and NH···Cl$^-$ hydrogen bonds (Fig. 14).[47] In the solid state, the

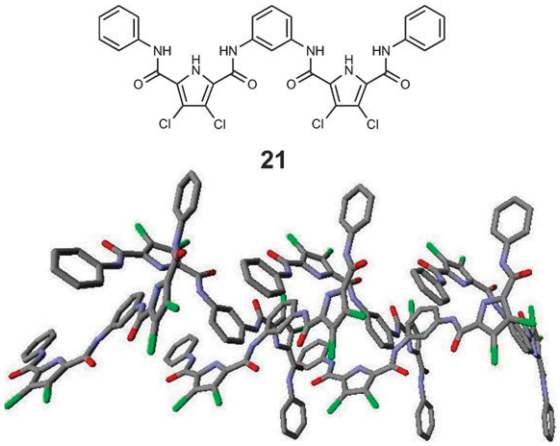

Fig. 13 Amido-pyrrole oligomer **21** forms an extended supramolecular polymeric chain in the solid state upon deprotonation of the pyrrolic NH by fluoride.

CH proton and one of the two pyrrole NH protons hydrogen bond with chloride. The second pyrrolyl NH of **22** turns away and binds to another chloride forming an anion-bridged 1D chain polymeric network. This binding mode is responsible for the supramolecular extension of the polymeric chain. The chlorides are alternately arranged in an almost linear array with a distance of 9 Å.

Haley and Johnson described an aniline derivatized ethynyl–pyridine **23** in which hydrogen bonds and π-stacking guides supramolecular polymeric chain formation in the solid state (Fig. 15).[48] Upon protonation of the pyridyl nitrogen, **23** undergoes a drastic conformational rearrangement that facilitates hydrogen bonding with Cl^-, subsequently forming a helical assembly in solution and the solid state. The crystal structure of the **23**-$H^+ \cdot Cl^-$ complex reveals a helical assembly stabilized by three NH$\cdots$$Cl^-$ and two CH$\cdots$$Cl^-$ hydrogen bonds.

Steed and co-workers reported the effect of hydrogen bonding to anions on the shape and symmetry of helical coordination polymers.[49] A bifunctional bis(pyridylurea) ligand **24** was designed to form a linear strand coordination polymer by metal coordination to the pyridines while the ureas hydrogen bond to the counter anions (Fig. 16). The ligand **24** alternately bridges Ag(I) to form a helical chain, and the helical chains can

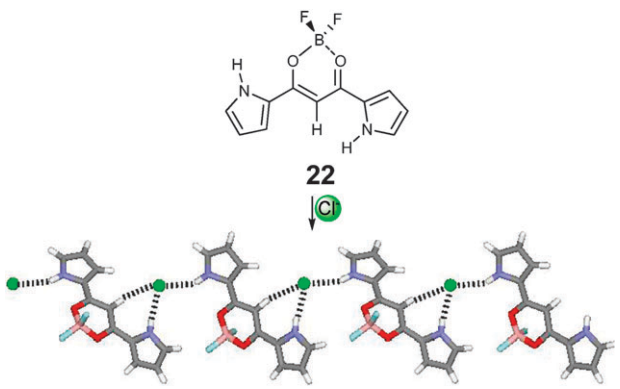

Fig. 14 Diketo-boron bridged oligopyrrole **22** forms an extended hydrogen bonded supramolecular chain with chloride in the solid state.

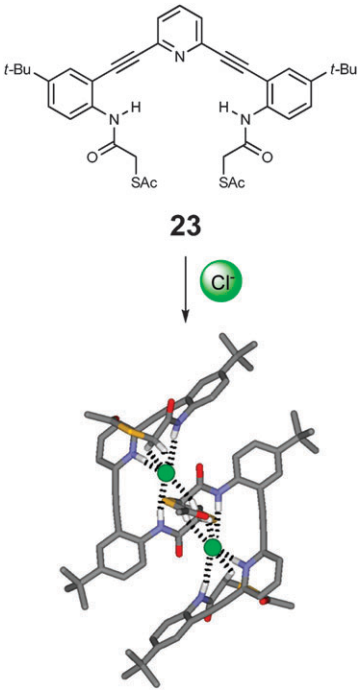

Fig. 15 Hydrogen bonding of protonated oligomer **23** with chloride ions yields a supramolecular helical assembly in the solid state.

intertwine to generate a higher order helical structure. The counter anion had a profound impact on the network topology presumably due to the variable coordinations and bridging modes. Nitrate promoted the formation of a planar helical coordination polymer while tetrafluoroborate yielded a twisted, quintuple helical coordination polymer.

Thodarson and co-workers reported the anion-mediated disassembly of a pyromellitamide polymeric gel.[50] The pyromellitamide **25** was found to be capable of both intermolecular self-assembly and anion binding (Fig. 17). In the absence of anions, **25** self-assembles in non-polar solvents to yield a gel comprising of one-dimensional columnar stacks that are stabilized by hydrogen-bonding, as proven by X-ray

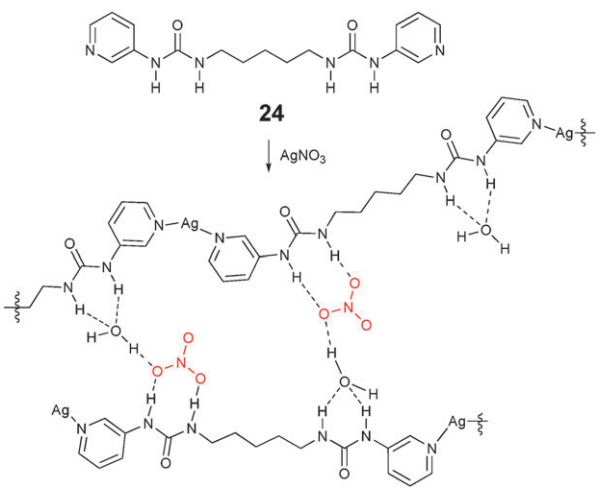

Fig. 16 Nitrate binding to pyridyl urea oligomer **24** effects the formation of helical polymeric strands upon Ag(I) coordination.

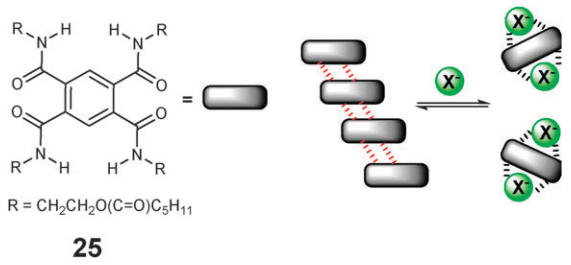

Fig. 17 Supramolecular polymeric gel obtained from intermolecular stacking of **25** where anion binding induces collapse of the gel.

crystallography. **25** was also shown to bind to anions in 1 : 2 host/guest stoichiometry which was in direct competition to the intermolecular aggregation, hereby offering a stimulus for gel collapse. Under the same conditions that promote gel formation, addition of as little as 0.25 equivalents of either TBA^+Cl^- or TBA^+Br^- prevented self-assembly by intermolecular hydrogen bonding and subsequent gelation. Similarly, addition of anions to preformed gels of **25** causes the gels to collapse. It is interesting that the time taken for the anions to induce gel collapse correlates directly to the anion binding strength in the order of $Cl^- > AcO^- > Br^- > NO_3^- > I^-$; chloride ($K_a > 10^5$ M^{-1} in d_6-acetone) causes the quickest collapse (10 s) while iodide ($K_a = 420$ M^{-1}) induces the slowest collapse (1 h).

Sessler and co-workers recently reported a tetracationic imidazolium macrocycle **26** that was capable of binding the mono-terephthalate anion, forming pseudorotaxanes (Fig. 18).[51] Under dilute conditions, **26** binds to mono-terephthalate anion with an association constant $K_a = 2.1 \times 10^3$ M^{-1} in d_6-DMSO with 1 : 1 binding stoichiometry. At high concentrations, the complexes self-assemble into short supramolecular oligo-pseudorotaxanes in solution and more extended supramolecular poly-pseudorotaxanes in the solid state. The supramolecular complex of **26** with mono-terephthalate was shown to be sensitive to environmental perturbations as disassembly was observed at lowered concentrations, higher temperatures and when the protonation state of the mono-terephthalate anion was altered.

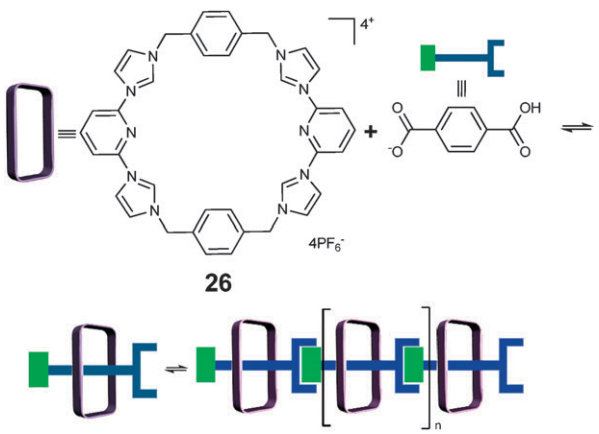

Fig. 18 Threading of mono-terephthalate anion into cyclic oligomer **26** yields supramolecular oligo/poly-pseudorotaxanes.

Wang and Yan reported the phosphate-directed self-assemblies of indole-based receptors in the solid state.[52] A representative example is anion receptor **27** which consisted of two indolocarbazole binding sites bridged by pyrazino-quinoxaline. Solid-state studies proved that **27** hydrogen bonded to dihydrogen phosphate to yield a self-associated polymeric chain (Fig. 19). Each binding site contains two dihydrogen phosphate anions bound by $NH\cdots O^-$ hydrogen bonds. Furthermore, the dihydrogen phosphates form hydrogen bonded infinite chains between the indolocarbazole units which resulted in the formation of a two-dimensional coordination polymer.

4.2 Modulation of helical structures

Kakuchi and co-workers developed helical polymers **28** capable of size-specific and colorimetric anion detection by attaching amino acids to a helical poly(phenylacetylene) backbone by urea linkers (Fig. 20).[53] Helical polymer **28** consists of poly(phenylacetylene) conjugated to L-leucine through urea groups which serve as hydrogen bond donors.

The system demonstrated a chiral translation from the pendant amino acid unit to the helical backbone that caused the three-dimensional organization of the urea linkers, making anion binding more efficient. The biased helical conformation of **28** was proven through observed Cotton effects in the circular dichroism (CD) spectra. The addition of acetate, chloride and bromide as their tetrabutylammonium salts into a solution of **28** intensified the Cotton effects indicating the chiral adjustment of the urea groups upon anion binding. Also of interest was the dramatic color change in the absorption spectra from pale yellow to red observed upon the addition of anions. This behavior was highly dependant on anion size and only observed with anions whose radius is between 160–190 pm (AcO^-, Cl^-, Br^-). Anions of other sizes had no effect on either the CD or UV/Vis profiles of polymer **28**. Similar behavior was reported in amide functionalized poly(phenylacetylene)-L-leucine which displayed a selectivity for acetate and fluoride.[54]

Lee and co-workers reported the cation-directed self-assembly of a coordination polymer whose secondary structures could be tuned by the counteranions (Fig. 21).[55] A bent shaped ethynylene-modified pyridine ligand **29** comprising a dendritic ethylene glycol side chain complexed with silver ion and its self-assembly into supramolecular structures was shown to be highly dependant upon counteranion size. As the anion size increased, the secondary structure of the coordination chain changed from a folded helix to a dimeric cycle, and then to an unfolded zigzag chain in the solid state. In the presence of small anions (NO_3^-, BF_4^-), the coordination

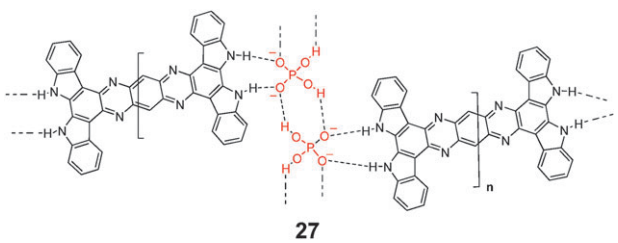

Fig. 19 Indole-based receptor **27** hydrogen bonds to dihydrogen phosphate to yield a polymeric chain in the solid-state.

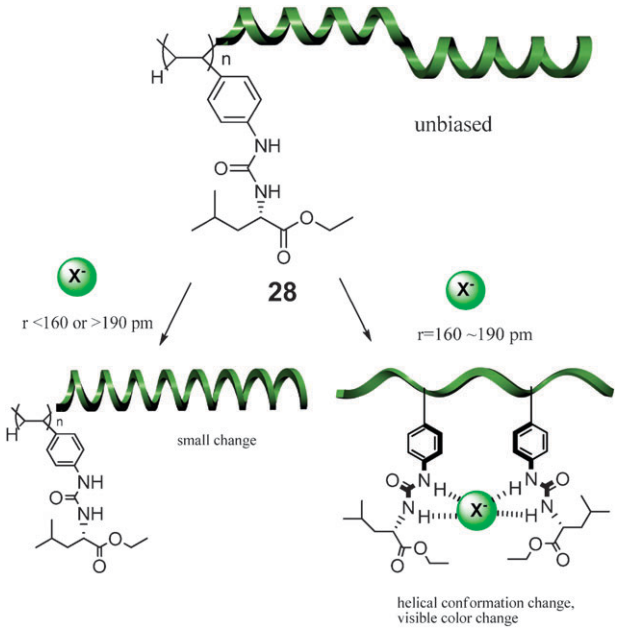

Fig. 20 Hydrogen bonding of anions of specific radii to side chains in helical polymer **28** induces a helical conformational and visible color change.

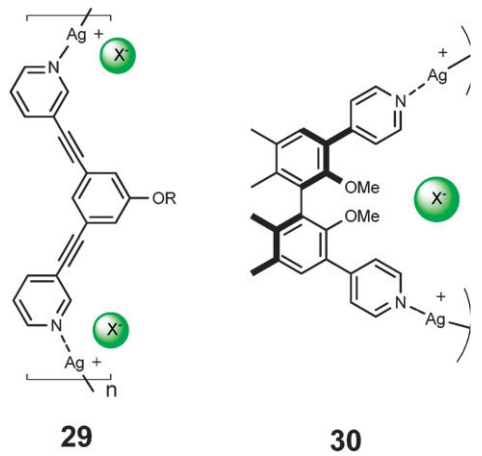

Fig. 21 Helical coordination polymers **29** and **30** whose morphologies are sensitive to the size of the counteranions.

chains self-assembled into helical chains that organized into a 2D hexagonal lattice. The triflate (TfO^-) complex of **29** formed dimeric cycles that stacked into columns that laterally assembled in a hexagonal fashion. A larger anion such as heptafluorobutyrate induced the organization of the coordination chains of **29** into a lamellar structure.

Cui and co-workers also reported the anion-mediated behavior of homochiral helical coordination polymers.[56] Bipyridine modified biphenyl ligand **30** was shown to assemble in a helically ordered array upon coordination to Ag(I) ions (Fig. 21). The conformation of this cationic helical chain was highly dependant on the counteranions; NO_3^-, PF_6^- and ClO_4^- directed the polymeric strand to fold into 2_1, 3_1 and 4_1 helices, respectively.

5. Conclusions

In this review, the anion-controlled behaviors of linear foldamers, cyclic oligomers and related polymers have been described. Anion recognition is an emergent field in the supramolecular community and in the context of foldamers, provides the impetus for generating novel structures and functions for linear and cyclic oligomers. Hydrogen bonding of anions within oligomeric cavities modulates the secondary structures, resulting in well-defined helically folded and wrapped species. The control over polymeric architecture is important to the materials community and anion binding within or to polymers has been shown to have a profound impact on overall polymer morphology. A variety of structures including curved and helical single stranded oligomers, twisted macrocycles, and helical polymers can all be tuned by their interactions with anions. To meet the growing need for novel functional molecules and materials, new methods of directing structures have to be devised. In this regard, both foldamers and anion recognition have grown in importance, and the confluence of these fields is sure to produce exciting and impactful chemistry.

Acknowledgements

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