Self-Assembly

Very Important Paper



Hydrogen bond-Driven Self-Assembly between Amidinium Cations and Carboxylate Anions: A Combined Molecular Dynamics, NMR Spectroscopy, and Single Crystal X-ray Diffraction Study

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Abstract: A combination of molecular dynamics (MD), NMR spectroscopy, and single crystal X-ray diffraction (SCXRD) techniques was used to probe the self-assembly of paraand meta-bis(amidinium) compounds with para-, meta-, and ortho-dicarboxylates. Good concordance was observed between the MD and experimental results. In DMSO solution, the systems form several rapidly exchanging assemblies, in part because a range of hydrogen bonding interactions is possible between the amidinium and carboxylate moieties. Upon crystallization, the majority of the systems form 1D supramolecular polymers, which are held together by short N-H-O hydrogen bonds.

Introduction

Hydrogen bonds are one of the key driving forces of self-assembly in both synthetic and biological systems. As hydrogen bonds can be significantly weakened by competing interactions with protic solvents, supramolecular chemists have explored the use of charge-assisted hydrogen bonds where ionic attractions increase the strength of noncovalent interactions. In particular, favorable interactions between amidinium cations and sulfonate or carboxylate anions, and between quanidinium cations and sulfonate anions have allowed the synthesis of a range of elegant self-assembled systems.^[1-6]

Pioneering work in the 1990s by the Hosseini group demonstrated that cyclic alkylbis(amidiniums) could assemble with terephthalate or isophthalate anions into 1D supramolecular polymers (Figure 1 a).^[1] Subsequent studies using amidinium cations reported the preparation of capsules,^[2] helices,^[3] [2+2]

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Figure 1. Examples of self-assembled structures prepared using charge-assisted hydrogen bonds: a) Wais Hosseini's synthesis of 1D supramolecular polymers,^[1] b) general representation of Ward's synthesis of a family of guanidinium-sulfonate frameworks,^[6] and c) White's synthesis of amidinium-carboxvlate frameworks.^[7]

macrocycles,^[4] and [2]catenanes,^[5] typically from relatively large and complex amidinium and carboxylate/sulfonate components.

Ward's group has pioneered the assembly of simple guanidinium cations with polysulfonate molecules to give ready access to a large family of guanidinium-sulfonate frameworks (Figure 1 b), many of which encapsulate organic guest molecules.^[6] Inspired by these studies, we recently reported the synthesis of supramolecular organic frameworks in water based on the favorable interactions between a tetraamidinium cation and terephthalate anions (Figure 1 c).^[7]

Very recently, two papers reported investigations into the solid state assembly of amidinium and carboxylate compounds: McArdle and Erxleben demonstrated that a range of hydrogen bonding interactions was present in the carboxylate salts of druglike amidinium compounds.^[8] These authors showed that the idealized "paired" hydrogen bond (Figure 2) is far from the only possible interaction between amidiniums and carboxylates in the solid state. While the work described herein was being prepared for publication, Grosu and Legrand reported that two *para*-benzenebis(amidiniums) assembled into solid state macrocyclic assemblies with either dicarboxylate or disulfonate compounds through charge-assisted hydrogen bonding.^[9]



Figure 2. Structures of bis(amidinium) cations and dicarboxylates used in this study and descriptors used to describe observed hydrogen bonding geometries. Other hydrogen bonding geometries between amidiniums and carboxylates have been observed by other authors.^[8]

In this study, we sought to explore amidinium--carboxylate self-assembly further, in particular to see if the varied hydrogen bonding interactions observed by McArdle and Erxleben persist in solution. We were interested to see whether molecular dynamics (MD) simulations could provide insight into the self-assembly of (potentially) discrete supramolecular systems. Although MD has been used to explore the self-assembly and interactions of a range of extended structures, including miccelles,^[10] bilayers,^[11] and membrane proteins,^[12] we are unaware of its use in this type of supramolecular system. NMR spectros-copy is often relatively uninformative for this type of assembly, and so we hoped that MD would be able to provide more detailed information.

Our initial goal was to take simple, readily prepared bis(amidiniums) and dicarboxylates to see if these could be used to assemble hexagonal macrocycles (Scheme 1) by analogy with the elegant synthesis of similar structures reported using transition metal coordination^[13] or the hydrogen bonded self-assembly of carboxylic acids^[14] or DNA bases.^[15]



Scheme 1. Targeted self–assembly of hexagonal macrocycles through charge-assisted hydrogen bonding.

In this report, we describe the results of our studies on bis(amidinium)---dicarboxylate self-assembly (Figure 2) in a range of solvents and in the solid state. A combination of NMR spectroscopy experiments and MD simulations was used to give detailed understanding of the solution phase self-assembly. Although we were not able to isolate the targeted hexagonal macrocycles, a family of crystalline self-assembled 1D polymers was prepared in water.

Results and Discussion

Synthesis of building blocks

The *para-* and *meta-*benzenebis(amidiniums) were prepared as the chloride salts (i.e., **1**·2 Cl and **2**·2 Cl, respectively) from the corresponding bis(nitriles) using lithium hexamethyldisilazide (LiHMDS) followed by workup with ethanolic HCl, according to the general procedure described by Zhu^[16] (Scheme 2). In both cases, analysis of the crude reaction mixture by ¹H NMR spectroscopy indicated clean and complete conversion of the bis(-nitrile) into the bis(amidinium), as well as the formation of a significant amount of an ammonium salt (presumably ammonium chloride).

In the case of the *para* isomer, workup was facile, and **1**·2Cl was obtained in 72% yield following thorough sonication and washing. With the *meta* isomer, separation of **2**·2Cl from the ammonium chloride formed during the reaction was difficult owing to the similar solubilities of these compounds, and this resulted in a relatively low yield of the isolated product (23%).



Scheme 2. Synthesis of bis(amidinium) compounds 1²⁺ and 2²⁺.

An alternative synthetic route to these compounds has been reported using gaseous HCl followed by gaseous NH_3 , but we were unable to obtain either 1-2Cl or 2-2Cl cleanly using this approach.^[14,17]

The potentially coordinating chloride anions were exchanged for noncoordinating tetraphenylborate (BPh₄⁻) anions to give 1.2 BPh₄ and 2.2 BPh₄ in good yields by precipitation from water. Low-quality crystal structures of these compounds were obtained and are presented in the Supporting Information.

Investigation of solution state self-assembly

NMR spectroscopy investigation of solvent effects on the selfassembly of 1^{2+} and IP^{2-}

In the first instance, we focused on the assembly of linear 1^{2+} cations and isophthalate (IP^{2-}) anions, which contain a 120° angle between the carboxylate groups, and used NMR spectroscopy to investigate the effect of solvent on this assembly. We started using 1.2 BPh_4 and tetrabutylammonium isophthalate ($TBA_2 IP$), as these salts (containing lipophilic counterions) have good solubility in a range of organic solvents. Mixing solutions of these two compounds in acetone, acetonitrile, methanol, and DMF resulted in immediate precipitation of $1 \cdot IP$ (as determined by ¹H NMR spectroscopy). This immediate precipitation suggested the rapid formation of a polymeric assembly, and so, more competitive solvents were used, which resulted in no precipitation (DMSO or water; when using water as the solvent it was necessary to use 1.2 CI instead of 1.2 BPh_4 for solubility reasons).

The assembly in these solvents was further investigated by ¹H NMR spectroscopy, which showed evidence of interactions between the two components in 10 mM solution (Figure 3). Upon addition of one molar equivalent of TBA₂·IP to 1·2BPh₄ in [D₆]DMSO solution, a small downfield shift in the CH resonance of 1²⁺ was observed (δ =0.054 ppm), as was a much larger downfield shift in the amidinium NH resonance (δ = 1.14 ppm), which also broadened significantly upon anion addition. These downfield shifts are consistent with hydrogen bonding interactions in solution withdrawing electron density from the bis(amidinium) compound.



Figure 3. Partial ¹H NMR spectrum of 1.2 BPh_4 upon addition of TBA₂·IP; signals labeled IP are from the IP²⁻ anion. Inset: expansion of the downfield region of the spectrum showing the NH signal after the addition of 1.0 equivalent of TBA₂·IP (10 mM,^[18] 298 K, [D₆]DMSO).

Conversely, when TBA₂·IP was added to 1·2 Cl in D₂O, the CH resonance of 1²⁺ showed a small upfield shift upon anion addition ($\delta = 0.056$ ppm; Figure S19, Supporting Information). This upfield shift suggested the presence of hydrophobic/donor-acceptor stacking interactions^[19] in this solvent (see below). The amidinium NH resonance largely disappears in D₂O owing to H/D exchange.

As ¹H NMR spectroscopy suggested the presence of significant interactions between 1^{2+} and IP^{2-} in $[D_6]DMSO$ solution, we used DOSY NMR spectroscopy to probe the size of any aggregates in this solvent. While this indicated the presence of species larger than the individual building blocks, it did not give conclusive evidence for a species large enough to be the hexagonal macrocycle. To probe this further, MD simulations of the interaction between 1^{2+} and IP^{2-} were conducted in a range of solvents.

MD investigation of solvent effects on the self-assembly of 1^{2+} and $1P^{2-}$

MD simulations were performed on mixtures of 1^{2+} and IP^{2-} solvated in benzene, acetonitrile, phenol, methanol, DMSO, and water. Visual inspection of trajectories showed significant interaction between the components in all solvents except for phenol. In benzene, acetonitrile, and methanol, globular morphologies (i.e., "clumps" of large numbers of 1^{2+} and IP^{2-} mol-

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ecules) were formed. This is consistent with the solution state behavior of these systems, for which precipitation was observed upon mixing 1·2 BPh₄ and TBA₂·IP in acetonitrile or methanol. In water, 1^{2+} and IP²⁻ molecules form face-to-face stacks, which then aggregate, again consistent with the ¹H NMR spectroscopy data, which suggest hydrophobic stacking.

In DMSO, distinctly different behavior was observed: 1D tape structures, larger cyclic assemblies, and [2+2] cyclic architectures were all observed (Figure 4) with rapid exchange between the various assemblies (exchanging on the tens of nanoseconds timescale on the basis of visual inspection of the trajectories). Again, this is consistent with the 1D and DOSY NMR spectroscopy data, which indicate significant interactions between 1^{2+} and IP^{2-} , but without formation of the targeted large architectures.



Figure 4. Representative snapshots of frequently observed motifs in MD simulations of 1-IP: a) 1D tapes, b) [2+2] small cyclic structure, and c) larger cyclic assembly.

By considering the distances between the centroid of the phenyl rings of 1^{2+} and IP^{2-} , we can graphically represent the different interactions observed in the different solvents (Figure 5). This allows us to compare the dominant interactions in each solvent.

There are clear clusters of interaction distances: a distance of approximately 4 Å corresponding to a donor-acceptor stacked arrangement, a distance of approximately 6 Å corresponding to a side-by-side hydrogen bonding arrangement, and a distance of approximately 10 Å corresponding to the targeted d_2a_2 hydrogen bonding interaction (Figure 5 a–c). The most noticeable difference between the interactions in DMSO and those in all of the other solvents is the distinct lack of a peak at 4 Å, showing almost no stacking in this solvent. The attenuation of this interaction seems to prevent the formation of globular morphologies, and instead, hydrogen bonding dominates, which leads to the observed tape and cyclic structures (Figure 4). The histogram peaks are broadened owing to the fact that a range of hydrogen bonding interactions is observed (e.g., d_1a_1 , d_2a_1 , d_2a_2) and because of thermal motion within these geometries. Single-stranded ribbons are dominat-





Figure 5. Histogram^[20] of center-of-mass distances between 1^{2+} and IP^{2-} observed in MD simulations in a range of solvents, and representation of three major types of possible interactions: a) stacked, b) side by side, and c) end-to-end d_2a_2 .

ed by end-to-end interactions, whereas larger sheets are made up of ribbons joined by side-to-side interactions (i.e., additional d_1a_1 interactions).

Given the large number of possible interactions and close contacts between 1^{2+} and IP^{2-} in most organic solvents, it is perhaps unsurprising that the systems precipitate from, for example, acetonitrile and methanol. Conversely, the range of possible interactions is limited in DMSO, and this leads to regular and morphologically interesting solution structures.

MD investigation of self-assembly of other bis(amidinium) and dicarboxylate isomers

Given the interesting solution assembly observed by both NMR spectroscopy and MD for 1^{2+} and IP^{2-} , we next used MD simulations to explore the self-assembly of 1^{2+} and 2^{2+} with

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Figure 6. Histogram^[20] of center-of-mass distances between bis(amidinium) compounds and dicarboxylate anions in DMSO.

terephthalate (TP²⁻), IP²⁻, and phthalate (P²⁻) [i.e., assemblies of **1**-TP, **1**-IP, **2**-TP, **2**-IP, and **2**-P; no simulation was performed for **1**-P, as no single crystal X-ray diffraction (SCXRD) data was available for this system for comparison purposes, see below]. The combined data are presented in histogram form in Figure 6 and are then subsequently discussed briefly for each system. In all five systems, end-to-end interactions are common—as evidenced by the large peaks in the histogram at approximately 10 Å. In all of the systems containing **2**²⁺, an additional peak is observed with a ring…ring distance of approximately 7.5 Å. This corresponds to an arrangement in which the two amidinium groups form a hydrogen bonding chelate to both oxygen atoms of a carboxylate (e.g., see Figure 7).



Figure 7. Representative snapshot of long-lived cyclic structures of 2·TP observed in MD simulations in DMSO.

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1·TP

The system comprises linear components that form 1D tape motifs, which sometimes assemble into sheets, and stacked sheets (Figure S20), as observed in the SCXRD structure of this compound (see below). This efficient packing allows the ring centers of the two compounds to get close together, which results in the large peak at approximately 4.5 Å in Figure 6.

2∙TP

Despite the fact that the 1-IP and 2-TP assemblies contain components with relatively similar geometries, that is, one linear tecton and one containing a 120° angle between hydrogen bonding groups, MD simulations indicate quite different behaviors. Similar to 1-IP, 2-TP frequently forms 1D tape motifs, but additionally, 2-TP occasionally forms long-lived [3+3] cyclic structures, which, once formed, remain stable until the end of the MD simulation (Figure 7). These structures are assembled through a mixture of d_2a_2 hydrogen bonds as well as other hydrogen bonding arrangements. Presumably, the fact that the *meta*-bis(amidinium) compound can form a chelating interaction explains the presence of the additional cyclic structures that are not observed for 1-IP.

2·IP

The structure of **2**·IP is the most globular of all the structures studied in DMSO. This is consistent with the solution data, as this compound shows the lowest solubility in DMSO of any of the structures apart from **1**·TP (which presumably has very low solubility as it rapidly forms a 2D sheet). This globular structure results from a wide range of possible interactions; indeed, this system has the largest spread of interaction distances (Figure 6). Few persistent structures are seen, although [2+2] macrocycles are sometimes observed (Figure S21).

2∙P

Whereas some assemblies of **2**·P have a globular structure, well-defined [2+2] macrocyclic systems are also observed (Figure 8). The formation of these persistent macrocycles contrasts with all the other simulated systems, which form a range of architectures. These structures are very similar to those observed by SCXRD (see below).

Solid state structures

The combined MD/NMR spectroscopy solution self-assembly studies reveal that a range of amidinium/carboxylate assemblies exists in solution. We next decided to see if this dynamic range of structures could be reduced to one product by crystallization. To this end, we attempted to crystallize 1^{2+} and 2^{2+} with the three dicarboxylate anions. It was found that mixing solutions of 1.2BPh₄ and 2.2BPh₄ with dicarboxylate anions in most organic solvents was not a viable method of preparing crystals owing to immediate precipitation (see above). Most of





Figure 8. Representative snapshot of long-lived [2+2] cyclic structures of 2-P observed in MD simulations in DMSO.

the assemblies have limited solubility, even in DMSO (e.g., 10 mM solutions of 1^{2+} and TP^{2-} , 1^{2+} and IP^{2-} , and 2^{2+} and IP^{2-} form precipitates upon standing for extended periods; these precipitates are not single crystals).

The most generalizable way to prepare co-crystals was using water as the solvent starting from the chloride salts of the bis(amidinium) compounds (1.2 BPh₄ and 2.2 BPh₄ are insoluble in water). In the case of $[1 \cdot TP]_n$, which contains both a linear bis(amidinium) and a linear dicarboxylate, crystals were obtained by simply layering aqueous solutions of tetrabutylammonium terephthalate (TBA2·TP) and 1·2Cl, and crystals were formed within minutes. Crystalline solids of the other five possible cocrystals were obtained by diffusing acetone vapor into aqueous solutions containing the dicarboxylate anion and either 1.2Cl or 2.2Cl. These materials could be obtained "in bulk" in good yields and were characterized by NMR spectroscopy, IR spectroscopy, and powder X-ray diffraction (PXRD) experiments. In all cases except for $[1 \cdot P]_n$, crystals suitable for SCXRD studies were also obtained, and the structures of these materials are discussed in the following section.^[21]



Figure 9. Views of the X-ray crystal structure of [1-TP]_n: a) 1D tape motif and b) 2D sheet generated through orthogonal hydrogen bonding.

Structure of [1.TP]_n

Unsurprisingly, if the two linear 1^{2+} and TP^{2-} components are combined, the crystalline product, $[1\cdotTP]_n$, contains 1D chains of bis(amidinium) cations and dicarboxylate anions (Figure 9a). No solvent is present in the crystal structure, and the chains are assembled through short, linear paired d_2a_2 N–H···O hydrogen bonds. Additional N–H···O hydrogen bonds perpendicular to these 1D chains assemble the structure into 2D sheets (Figure 9b). The observed tape/sheet structure is very similar to the arrangements observed in the MD simulations (Figure S20).

Structure of [1·IP]_n

It is possible to crystallize $[1\cdotIP]_n$ by diffusing methanol into a DMSO solution^[22] of $1\cdot2BPh_4$ and $TBA_2\cdotIP$ or by diffusing acetone into an aqueous solution of $1\cdot2CI$ and $TBA_2\cdotIP$. If $[1\cdotIP]_n$ is crystallized from organic solvents, a zig-zag 1D polymer forms (Figure 10a), and no solvent is incorporated into the crystal lattice. The hydrogen bonded polymer is held together by paired d_2a_2 hydrogen bonds. Despite the use of a bent tecton, a cyclic product is not produced. If $[1\cdotIP]_n$ is crystallized from acetone/water, a 1D polymer is again formed (Figure 10b), but in this case, there are three water molecules of crystallization



Figure 10. X-ray crystal structures of [1-IP]_n zigzag polymers: a) solventless [1-IP]_n, crystallized from DMSO and b) [1-IP]_n crystallized from acetone/water (three water molecules per 1-IP pair are omitted for clarity).

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Figure 11. X-ray crystal structures of zigzag polymers: a) [2-TP]_n and b) [2-IP]_n (one water molecule per 2-TP or 2-IP pair is omitted for clarity).

for each bis(amidinium)/dicarboxylate pair. One amidinium group undergoes a d_2a_2 hydrogen- bonding interaction with both oxygen atoms from a carboxylate group, whereas the other crystallographically independent amidinium group hydrogen bonds to one carboxylate oxygen atom in a d_2a_1 fashion. The other carboxylate oxygen atom accepts a hydrogen bond from an adjacent amidinium NH group linking the 1D chains orthogonally.

 $[1-TP]_n$, the polymers are held together by short d_2a_2 N–H···O hydrogen bonds. In both cases, crystals are obtained from water/acetone, and one water molecule is present per bis(amidinium)/dicarboxylate pair.

Structure of [2·P]_n

Structures of [2·TP]_n and [2·IP]_n

If 2^{2+} is crystallized with TP²⁻ or IP²⁻, the product is again a zig-zag 1D polymer (Figure 11) and not the desired hexagonal macrocycle. As with the linear structure observed for If 120°-containing tecton 2^{2+} is crystallized with 60° tecton P^{2–} from methanol/diethyl ether, a simple 1D chain does not form. Instead a [2+2] cyclic structure, reminiscent of those observed by Grosu and Legrand,^[9] is observed (Figure 12a). Again, this structure is very similar to the persistent [2+2] macrocycles observed in the MD simulations.



Figure 12. X-ray crystal structures of [2-P]_n: a) crystallized from methanol/diethyl ether (PLATON-SQUEEZE^[23] used) and b) crystallized from water/acetone (one water molecule per 2-P pair omitted for clarity).

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globular aggregates

1D tapes, 2D sheets

One of the two carboxylate groups on each phthalate anion twists approximately perpendicular to the benzene ring, and one of the oxygen atoms from this carboxylate group hydrogen bonds to an amidinium group of a neighboring [2+2]cyclic structure, which links the supramolecular macrocycles into chains. A region of disordered solvent appears to be present, but this could not be refined satisfactorily, and so, PLATON-SQUEEZE^[23] was used to include this electron density in the refinement. Upon crystallizing 2^{2+} and P^{2-} from water/ acetone, a 1D chain structure is obtained (Figure 12b). As observed in the structure of $[1\cdot IP]_n$ crystallized from water/acetone, one of the crystallographically independent amidinium groups hydrogen bonds to a carboxylate group in a d_2a_2 fashion, whereas one does not. The other amidinium group has a d_2a_1 hydrogen bonding arrangement with a carboxylate oxygen atom, and the other oxygen atom of this carboxylate receives a hydrogen bond from a water solvent molecule (there is one water molecule per 1·IP pair).

Hydrogen bonding interactions

In four of the seven structures, all amidinium and carboxylate groups are involved in a d_2a_2 hydrogen bonding interaction. In the other structures, one crystallographically independent amidinium/carboxylate couple has a d_2a_2 arrangement, whereas the other is involved in either a d_2a_1 or d_1a_1 interaction. Parameters for these hydrogen bonding interactions are given in Table S1 and Figure S26.

Briefly, hydrogen bonds are generally short, with N···O distances of approximately 2.8 Å. The shortest H--O distance is 1.84 Å, which corresponds to 68% of the sum of the van der Waals radii of hydrogen and oxygen,^[24] and most H--O distances are between 1.9 and 2.0 Å (70-75% of the sum of the van der Waals radii). There is some variability in the N-H-O angles, presumably as a result of the hydrogen bonds twisting slightly to give favorable crystal packing. Notably, the N-H bond lengths (or indeed any R-H bond length) are systematically underestimated by crystallographic techniques, typically by approximately 0.1 A.^[25] As a result, the H--O values will be systematically overestimated by a similar amount (i.e., the real H---O distances are shorter than those reported).

Figures S24 and S25 show the radial distribution functions (RDFs) for the H--O distances for the five systems studied, and in all cases, the first peak (i.e. shortest interaction) is centered at approximately 1.8 Å. Accounting for the underestimation of H...O by X-ray crystallographic techniques, good concordance is observed between MD and SCXRD measurements. Upon considering one system $(1^{2+} \text{ and } IP^{2-})$ in a range of solvents (Figure S24), no difference is observed in the hydrogen bonding lengths upon changing the solvent. What does change is the frequency of the interaction occurring, with very few hydrogen bonding interactions in phenol and slightly more in methanol and water.

Integrating the RDFs allows us to calculate the average number of hydrogen bonds per potential hydrogen bond donor/acceptor and to compare this with the system morphology (Table 1, hydrogen bonds to solvent molecules are exclud-

bond acceptor or donor determined by MD simulations.				
System	Solvent	No. of hydrogen bonds per donor/acceptor ^[a]	System morphology	
1. IP	phenol	0.22	few interactions	
1.IP	water	0.83	globular aggregates	
1.IP	methanol	0.85	globular aggregates	
1.IP	DMSO	1.30	1D tapes, cycles	
1.IP	acetonitrile	1.54	globular aggregates	

Table 1 Average number of hydrogen bonds per potential hydrogen

DMSO 1D tapes, cycles 2.TP DMSO 1.07 1D tapes, cycles 2.IP DMSO 1.40 cycles, globular aggregates 2.P DMSO 1.24 cycles [a] A H---O distance of 2.3 Å was used as the cut-off for what constitutes a hydrogen bond, as this appears to be the natural end of the initial peak in the RDF. Solvent molecules were not considered in this hydrogen bonding analysis.

1.59

1.11

1.30

benzene

DMSO

ed from this analysis). In the aprotic solvents benzene and acetonitrile, a very high number of hydrogen bonding interactions are apparent, which results from the amidinium and carboxylate molecules forming very tightly packed globular assemblies. In DMSO, an intermediate number of hydrogen bonding interactions is observed, as the compounds interact regularly, but not so frequently that tightly packed aggregates form. In phenol, methanol, and water, far fewer hydrogen bonds are present, and this is consistent with the cations and anions either not interacting significantly (phenol) or interacting mainly through stacking interactions.

Discussion of self-assembly

1·IP

1.TP

1.IP

The MD data indicate that in less-polar solvents (e.g., acetonitrile), bis(amidinium) cations and dicarboxylate anions associate strongly and that these interactions have a variety of geometries, presumably because a range of favorable interactions is present in these solvents. Consistent with this modeling, mixing the amidinium and carboxylate species in acetonitrile results in immediate precipitation of an insoluble solid. Moving to DMSO reduces the range of interactions possible, and so a range of oligomeric structures is observed in MD, with no clear preference for any one species. Again, this is consistent with the 1D and 2D NMR spectroscopy data, which show that although there are interactions present between the amidinium and carboxylate compounds, and that the average size of the species in solution is greater than the substituent components, there is no clear evidence for the targeted hexagonal macrocycles. MD simulations in water suggest the presence of aromatic stacking interactions, presumably arising from a combination of ionic and hydrophobic factors. The ¹H NMR spectroscopy data are again consistent with this modeling.

A key point from this work is that a range of amidinium...carboxylate interactions is common in solution, in line with previous results from the solid state.^[8,9] It is notable that in many previous reports in which the amidinium--carboxylate

motif was used to prepare self-assembled structures, additional factors were present that favored the "forward" (i.e., d_2a_2) interaction. For example, many of Yashima's systems involved *N*-al-kylated amidinium motifs,^[3] which preclude many "unwanted" hydrogen bonding interactions. Similarly, the 3D polymeric structure of our previously reported frameworks presumably drives the system towards a d_2a_2 arrangement.^[7]

Whereas the solution structures of the systems reported herein are dominated by small discrete structures, in the solid state the products are polymeric systems. This can presumably be attributed to the reduced solubility of these polymers, which first results in their crystallization. To a first approximation, the smallest nonstrained supramolecular species would be expected to form, as this would maximize the number of favorable hydrogen bonding interactions and minimize the entropic cost.^[26] However, this analysis is valid for an equilibrium mixture and ignores the effects of an insoluble solid precipitating. It would seem that in this system, solubility effects dominate, which results in the observed polymeric products.

Conclusions

The interaction between relatively simple bis(amidinium) and dicarboxylate compounds was thoroughly investigated by a combination of NMR spectroscopy, molecular dynamics, and single crystal X-ray diffraction techniques. In less competitive solvents such as acetonitrile, a range of strong interactions was found to be present between the 2^+ and 2^- components, which resulted in aggregation and precipitation of insoluble solids. Using a more competitive solvent such as DMSO or water attenuated many of these interactions, which resulted in the formation of more ordered structures. In the majority of the cases studied, a number of different assemblies were present, and no one architecture dominated. It is, thus, perhaps unsurprising that if the systems were crystallized, 1D hydrogen bonded polymers were observed, as the self-assembly equilibria collapsed to give the least-soluble product. It would be interesting to prepare solubilized versions of these components to broaden the range of useable solvents and to allow more control over the crystallization processes.

Importantly, good concordance was observed between the experimental and computational data, which suggests that MD simulations have wider applicability if studying supramolecular self-assembly processes. Further studies using MD techniques to gain insight into these processes are continuing in our laboratories.

Experimental Section

General methods

Solvents and reagents were bought from commercial suppliers and were used as received, except for THF, which was distilled from sodium prior to use. TBA₂·TP and TBA₂·IP were prepared from the corresponding carboxylic acids and tetrabutylammonium hydroxide in a manner similar to that described by Pfeffer for TBA₂·TP.^[27] The procedure used to prepare 1·2Cl and 2·2Cl was a modification of Zhu's procedure.^[16] Details of instrumentation are given in the Supporting Information.

Synthesis

1.2 Cl: 1,4-Dicyanobenzene (0.500 g, 3.90 mmol) was dissolved in dry THF (20 mL) and cooled to $-78\,^\circ\text{C}$ under a nitrogen atmosphere. A solution of LiHMDS in THF (1.0 m, 12 mL, 12 mmol) was added, and the solution was warmed to room temperature and stirred under a nitrogen atmosphere overnight. Ethanolic HCl was prepared by cautiously adding acetyl chloride (3 mL) to ethanol (10 mL), and this was added to the reaction mixture, which resulted in the precipitation of a white solid. The solid was isolated by filtration, suspended in ethanol (10 mL), and sonicated for 1 h. The resulting solid was isolated by filtration, again suspended in ethanol, and again sonicated for 1 h. The resulting white solid was isolated by filtration, washed with ethanol, and dried in vacuo to give **1.**2 Cl. Yield: 0.660 g (2.81 mmol, 72%). ¹H NMR ([D₆]DMSO): $\delta =$ 9.60 (br.s, 4H), 9.34 (br.s, 4H), 8.02 ppm (s, 4H). ¹³C NMR ([D₆]DMSO): $\delta = 164.5$, 132.6, 128.6 ppm. MS (ESI+): m/z: 163.1 $[C_8H_{11}N_4]^+$. IR: $\tilde{v} = 1693$ (s, C=N stretch), 1660 cm⁻¹ (s, C=N stretch).

1-2 BPh₄: A solution of 1-2 Cl (0.024 g, 0.10 mmol) in water (5 mL) was added to a solution of sodium tetraphenylborate (0.075 g, 0.22 mmol) in water (25 mL), which resulted in the immediate formation of a precipitate. The solid was isolated by filtration, washed with water (3×10 mL), and dried in vacuo to give 1-2 BPh₄ as a cream-colored powder. Yield: 0.068 g (0.085 mmol, 85%). ¹H NMR ([D₆]DMSO): δ =9.23 (br.s, 8H), 7.98 (s, 4H), 7.17 (br.s, 16H), 6.92 (app t, *J*=7.3 Hz, 16H), 6.79 ppm (t, *J*=7.1 Hz, 8H). ¹³C NMR ([D₆]DMSO): δ =164.4, 162.6–164.1 (m), 135.5, 132.7, 128.6, 125.3, 121.5 ppm. MS (ESI+): *m/z*: 163.1 [C₈H₁₁N₄]⁺. MS (ESI-): *m/z*: 319.1 [C₂₄H₂₀¹¹B]⁻. IR: $\tilde{\nu}$ =1669 cm⁻¹ (s, C=N stretch).

2.2 Cl: 1,3-Dicyanobenzene (0.500 g, 3.90 mmol) was dissolved in dry THF (20 mL) and cooled to $-78\,^\circ\text{C}$ under a nitrogen atmosphere. A solution of LiHMDS in THF (1.0 m, 12 mL, 12 mmol) was added, and the solution warmed to room temperature and stirred under a nitrogen atmosphere overnight. Ethanolic HCl was prepared by cautiously adding acetyl chloride (3 mL) to ethanol (10 mL), and this was added to the reaction mixture, which resulted in the precipitation of a white solid. This solid was isolated by filtration, suspended in ethanol (10 mL), and sonicated for 1 h. The resulting solid was dissolved in water (10 mL), and acetone (50 mL) was added, which resulted in the precipitation of a fluffy white solid. This solid was isolated by filtration, washed with acetone, and dried in vacuo to give 2.2Cl. Yield: 0.210 g (0.893 mmol, 23%). ¹H NMR ([D₆]DMSO): δ = 9.74 (br. s, 4H), 9.46 (br. s, 4H), 8.53 (s, 1H), 8.16 (d, J=7.7 Hz, 2 H), 7.84 ppm (t, J=7.7 Hz, 1 H). ¹³C NMR ([D₆]DMSO): $\delta = 164.7$, 133.1, 129.5, 129.0, 128.2 ppm. MS (ESI+): m/z: 163.1 [C₈H₁₁N₄]⁺. IR: $\tilde{\nu}$ = 1686 (s, C = N stretch), 1658 cm⁻¹ (s, C = N stretch).

2·2 BPh₄: A solution of **2**·2 Cl (0.024 g, 0.10 mmol) in water (5 mL) was added to a solution of sodium tetraphenylborate (0.075 g, 0.22 mmol) in water (25 mL), which resulted in the immediate formation of a precipitate. This solid was isolated by filtration, washed with water (3×10 mL), and dried in vacuo to give **2**·2 BPh₄ as a white powder. Yield: 0.065 g (0.081 mmol, 81%). ¹H NMR ([D₆]DMSO): δ = 9.26 (br.s, 8H), 8.20 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 2H), 7.89 (t, *J* = 7.9 Hz, 1H), 7.18 (br.s, 16H), 6.93 (app. t, *J* = 7.3 Hz, 16H), 6.79 ppm (t, *J* = 7.1 Hz, 8H). ¹³C NMR ([D₆]DMSO): δ = 164.4, 162.6–164.1 (m), 135.5, 133.1, 129.7, 128.7, 128.1, 125.3, 121.5 ppm. MS (ESI +): *m/z*: 163.1[C₈H₁₁N₄]⁺. MS (ESI –): *m/z*: 319.1 [C₂₄H₂₀¹¹B]⁻. IR: $\tilde{\nu}$ = 1671 cm⁻¹ (s, C = N stretch).

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TBA2•TP: Terephthalic acid (0.332 g, 2.00 mmol) was suspended in water (10 mL) and a 1.0 M solution of tetrabutylammonium hydroxide in methanol (4.00 mL, 4.00 mmol) was added, which caused most of the acid to dissolve. The solution was stirred at room temperature for 2 min, filtered to remove a small amount of insoluble solid, and taken to dryness under reduced pressure. Analysis at this point by ¹H NMR spectroscopy indicated a product of approximately 95% purity. This was taken up in methanol (30 mL) and filtered to remove a small amount of insoluble solid, which was washed with more methanol (2×5 mL). The combined filtrate was taken to dryness under reduced pressure. The resulting white solid was dried in vacuo to give TBA2·TP as white powder. Yield: 0.931 g (1.43 mmol, 72%). ¹H NMR ([D₆]DMSO): δ = 7.62 (s, 4H), 3.16 (t, J = 7.5 Hz, 16H), 1.52-1.60 (m, 16H), 1.26-1.35 (m. 16H), 0.93 ppm (t, J = 7.5 Hz, 24H). ¹³C NMR ([D₆]DMSO): $\delta = 168.4$, 141.6, 127.4, 57.5, 23.1, 19.2, 13.5 ppm. MS (ESI+): *m/z*: 242.4 [C₁₆H₃₆N]⁺. MS (ESI-): m/z: 165.1 $[C_8H_4O_4 \cdot H]^-$. IR: $\tilde{\nu} = 1577$ (s, C = O stretch), 1348 cm⁻¹ (s, C-O stretch).

TBA2·IP: Isophthalic acid (0.332 g, 2.00 mmol) was suspended in water (10 mL) and a 1.0 M solution of tetrabutylammonium hydroxide in methanol (4.00 mL, 4.00 mmol) was added, which caused most of the acid to dissolve. The solution was stirred at room temperature for 2 min, filtered to remove a small amount of insoluble solid, and then taken to dryness under reduced pressure. Analysis at this point by ¹H NMR spectroscopy indicated a product of approximately 95% purity. This was sonicated in acetone/methanol (2:1 v/v, 15 mL) and filtered to remove a white solid. The filtrate was dried in vacuo to give $\mathsf{TBA}_2\text{-}\mathsf{IP}$ as a hygroscopic white solid. Yield: 1.02 g (1.57 mmol, 79%). ¹H NMR ([D₆]DMSO): $\delta = 8.28$ (s, 1 H), 7.66 (d, J=7.4 Hz, 2 H), 7.01 (t, J=7.4 Hz, 1 H), 3.14-3.20 (m, 16H), 1.52–1.60 (m, 16H), 1.25–1.34 (m. 16H), 0.92 ppm (t, J= 7.3 Hz, 24 H). ^{13}C NMR ([D_6]DMSO): $\delta\!=\!169.1,$ 140.8, 130.0, 128.6, 124.9, 57.5, 23.1, 19.2, 13.5 ppm. MS (ESI+): *m/z*: 242.4 [C₁₆H₃₆N]⁺. MS (ESI–): 165.1 $[C_8H_4O_4\cdot H]^-$, 406.3 $[C_{16}H_{36}N\cdot C_8H_4O_4]^-$. IR: $\tilde{\nu} = 1604$ (s, C=O stretch), 1343 cm⁻¹ (s, C–O stretch).

[1·TP]_n: A solution of 1·2Cl (24 mg, 0.10 mmol) in water (5 mL) was layered with water (2.5 mL) and then TBA₂·TP (65 mg, 0.10 mmol) in water (2.5 mL). Within a few minutes, a white microcrystalline solid was visible. After a few days, the solid was isolated by filtration, washed with water (3×5 mL), and dried in vacuo. Yield: 20 mg (0.061 mmol, 61%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): δ = 9.77* (br.s), 9.51* (br.s), 8.05 (s, 4H), 8.02 ppm (s, 4H). *These signals integrate to a value lower than the expected value of 4H, presumably as a result of H/D exchange. IR: $\tilde{\nu}$ = 1706, 1476 (s), 1373 cm⁻¹ (s). Crystals suitable for SCXRD were obtained by repeating the synthetic procedure described above at a lower concentration (1–2 mg of 1·2Cl in ≈ 1 mL water).

General procedure for synthesis of $[1\cdot IP]_n$, $[1\cdot P]_n$, $[2\cdot TP]_n$, $[2\cdot IP]_n$, and $[2\cdot P]_n$: A solution of TBA₂·TP or TBA₂·IP (65 mg, 0.10 mmol) or Na₂·P (21 mg, 0.10 mmol) in water (2.5 mL) was added to a solution of 1·2 Cl or 2·2 Cl (24 mg, 0.10 mmol) in water (2.5 mL). The resulting clear, colorless solution was subjected to acetone vapor diffusion, which resulted in the formation of colorless crystals or white microcrystals that were isolated by filtration, washed with acetone (5×2 mL), and dried in vacuo.

[1·IP]_n: White crystals. Yield: 25 mg (0.076 mmol, 76%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): δ =9.76* (br.s), 9.46* (br.s), 8.43 (s, 1 H), 8.13 (d, *J*=7.7 Hz, 2 H), 8.03 (s, 4 H), 7.62 (t, *J*=7.7 Hz, 1 H). *These signals integrate to a value lower than the expected value of 4 H, presumably as a result of H/D exchange. IR: $\tilde{\nu}$ =1673, 1604, 1550 (s), 1372 cm⁻¹ (s).

[1·P]_n: White crystals. Yield: 24 mg (0.073 mmol, 73%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): δ =9.76* (br.s), 9.46* (br.s), 8.03 (s, 4H), 7.61–7.65 (m, 2H), 7.54–7.58 ppm (m, 2H). *These signals integrate to a value lower than the expected value of 4H, presumably as a result of H/D exchange. IR: $\tilde{\nu}$ =1693, 1542 (s), 1388 cm⁻¹ (s).

[2·TP]_n: White crystals. Yield: 13 mg (0.040 mmol, 40%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): δ =9.77* (br.s), 9.48* (br.s), 8.47 (s, 1 H), 8.15 (d, *J*=7.9 Hz, 2 H), 8.01 (s, 4 H), 7.80 ppm (t, *J*=7.9 Hz, 1 H). IR: $\tilde{\nu}$ =1501 (s), 1372 cm⁻¹ (s).

[**2**·IP]_{*n*}: White crystals. Yield: 24 mg (0.073 mmol, 73%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): δ = 9.76* (br.s), 9.46* (br.s), 8.45 (s, 1 H), 8.43 (s, 1 H), 8.11–8.16 (m, 4 H), 7.98 (t, *J*=7.9 Hz, 1 H), 7.62 (t, *J*=7.7 Hz, 1 H). *These signals integrate to a value lower than the expected value of 4H, presumably as a result of H/D exchange. IR: $\tilde{\nu}$ = 1604, 1518 (s), 1375 cm⁻¹ (s).

 $[2 \cdot P]_n$: White crystals. Yield: 20 mg (0.061 mmol, 61%). ¹H NMR ([D₆]DMSO containing 2 drops conc. DCl_(aq)): $\delta = 9.77^*$ (br.s), 9.47* (br.s), 8.48 (s, 1H), 8.15 (d, J = 7.9 Hz, 2H), 7.81 (t, J = 7.9 Hz, 1H). 7.61–7.66 (m, 2H), 7.55–7.59 ppm (m, 2H). *These signals integrate to a value lower than the expected value of 4H, presumably as a result of H/D exchange. IR: $\tilde{\nu} = 1669$, 1513 (s), 1373 cm⁻¹ (s).

MD simulations

The GROMACS version 5.1.2 molecular dynamics package,^[28] in conjunction with the GROMOS 54A7 force field,^[29] was used in all MD simulations. This force field was chosen primarily for its ability to generate parameters automatically and accurately for carboxylate and amidinium species using the Automated Topology Builder (ATB).^[30] Parameters generated by the ATB are able to reproduce the free energy of solvation for small organic molecules with a mean unsigned error of 6.7 kJ mol⁻¹ based on a test set of 214 molecules including many relevant to the systems studied in this work.^[31]

Water was represented explicitly using the simple point charge (SPC) model. $^{\scriptscriptstyle [32]}$ Parameters for all other molecules were taken from the Automated Topology Builder.^[30] Each system contained 10 bis(amidinium) cations, 10 dicarboxylate anions, and 5700 solvent molecules and was simulated under periodic boundary conditions in a rectangular simulation box with a timestep of 2 fs. The temperature of the system was maintained by coupling each component of the system to an external temperature bath at 298 K with a coupling constant of $\tau_T = 0.1$ ps using a velocity rescaling thermostat. The pressure was maintained at 1 bar (1 bar = 0.1 MPa) by weakly coupling the system to a semi-isotropic pressure bath using an isothermal compressibility of 4.5×10^{-5} bar⁻¹ and a coupling constant of $\tau_{\rm P}$ = 0.5 ps. During the simulations, the length of all bonds within the tectons and non-water solvents were constrained using the LINCS algorithm.^[33] The SETTLE algorithm^[34] was used to constrain the geometry of the water molecules. Electrostatic interactions were calculated using particle mesh Ewald summation, and nonbonded interactions were calculated with a cut-off of 1.0 nm. Both were updated each timestep. Each simulation system was simulated in triplicate for 100 ns. All images were prepared in VMD.[35]

X-ray crystallography

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Single crystal data were collected using mirror-monochromated CuK_{α} radiation at 150 K with an Agilent Supernova diffractometer. Raw frame data (including data reduction, interframe scaling, unitcell refinement, and absorption corrections) were processed using CrysAlis PRO.^[36] Structures were solved with SUPERFLIP^[37] and were

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refined using full-matrix least-squares on F^2 within the CRYSTALS suite.^[38] All non-hydrogen atoms were refined with anisotropic displacement parameters. C—H hydrogen atoms were generally visible in the Fourier difference map and were initially refined with restraints on bond lengths and angles, after which the positions were used as the basis for a riding model.^[39] O—H and N—H hydrogen atoms were generally visible in the Fourier difference map, and their positions were refined with restraints on bond lengths and angles. Selected crystallographic data are summarized in Tables S2 and S3, and full crystallographic data are provided in CIF format in the Supporting Information.

 $\begin{array}{ccccccc} 1537445 \mbox{ (1-TP),} & 1537446 \mbox{ (1-IP),} & 1537447 \mbox{ (1-IP),} \\ 1537448 \mbox{ (2-TP),} & 1537449 \mbox{ (2-IP),} & 1537450 \mbox{ (2-P),} & 1537451 \mbox{ (2-P),} \\ 1537452 \mbox{ (1-2BPh}_4), \mbox{ and} & 1537453 \mbox{ (2-2BPh}_4) \mbox{ contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.} \end{array}$

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Conflict of interest

The authors declare no conflict of interest.

Keywords: hydrogen bonding • molecular dynamics • selfassembly • supramolecular chemistry • X-ray crystallography

- M. W. Hosseini, R. Ruppert, P. Schaeffer, A. De Cian, N. Kyritsakas, J. Fischer, J. Chem. Soc. Chem. Commun. 1994, 2135–2136.
- [2] a) F. Corbellini, R. Fiammengo, P. Timmerman, M. Crego-Calama, K. Versluis, A. J. R. Heck, I. Luyten, D. N. Reinhoudt, J. Am. Chem. Soc. 2002, 124, 6569–6575; b) F. Corbellini, L. Di Costanzo, M. Crego-Calama, S. Geremia, D. N. Reinhoudt, J. Am. Chem. Soc. 2003, 125, 9946–9947; c) H. Katagiri, Y. Tanaka, Y. Furusho, E. Yashima, Angew. Chem. Int. Ed. 2007, 46, 2435–2439; Angew. Chem. 2007, 119, 2487–2491.
- [3] a) Y. Tanaka, H. Katagiri, Y. Furusho, E. Yashima, Angew. Chem. Int. Ed. 2005, 44, 3867–3870; Angew. Chem. 2005, 117, 3935–3938; b) M. Ikeda, Y. Tanaka, T. Hasegawa, Y. Furusho, E. Yashima, J. Am. Chem. Soc. 2006, 128, 6806–6807; c) E. Yashima, K. Maeda, Y. Furusho, Acc. Chem. Res. 2008, 41, 1166–1180; d) W. Makiguchi, J. Tanabe, H. Yamada, H. Iida, D. Taura, N. Ousaka, E. Yashima, Nat. Commun. 2015, 6, 7236.
- [4] a) T. Kusukawa, K. Matsumoto, H. Nakamura, W. Iizuka, K. Toyama, S. Takeshita, Org. Biomol. Chem. 2013, 11, 3692–3698; b) T. Kusukawa, S. Tanaka, K. Inoue, Tetrahedron 2014, 70, 4049–4056.
- [5] Y. Nakatani, Y. Furusho, E. Yashima, Angew. Chem. Int. Ed. 2010, 49, 5463–5467; Angew. Chem. 2010, 122, 5595–5599.
- [6] a) M. J. Horner, K. T. Holman, M. D. Ward, J. Am. Chem. Soc. 2007, 129, 14640–14660; b) W. Xiao, C. Hu, M. D. Ward, J. Am. Chem. Soc. 2014, 136, 14200–14206; c) Y. Liu, W. Xiao, J. J. Yi, C. Hu, S.-J. Park, M. D. Ward, J. Am. Chem. Soc. 2015, 137, 3386–3392; d) T. Adachi, M. D. Ward, Acc. Chem. Res. 2016, 49, 2669–2679.
- [7] M. Morshedi, M. Thomas, A. Tarzia, C. J. Doonan, N. G. White, Chem. Sci. 2017, 8, 3019–3025.
- [8] N. Kamali, M. Aljohani, P. McArdle, A. Erxleben, Cryst. Growth Des. 2015, 15, 3905–3916.
- [9] L. Pop, N. D. Hadade, A. van der Lee, M. Barboiu, I. Grosu, Y.-M. Legrand, Cryst. Growth Des. 2016, 16, 3271 – 3278.

- [10] a) S. J. Marrink, D. P. Tieleman, A. E. Mark, J. Phys. Chem. B 2000, 104, 12165–12173; b) P. Brocos, P. Mendoza-Espinosa, R. Castillo, J. Mas-Oliva, A. Pineiro, Soft Matter 2012, 8, 9005–9014.
- [11] a) S. J. Marrink, A. E. Mark, *J. Am. Chem. Soc.* 2003, *125*, 15233–15242;
 b) S. J. Marrink, H. J. Risselada, S. Yefimov, D. P. Tieleman, A. H. de Vries, *J. Phys. Chem. B* 2007, *111*, 7812–7824.
- [12] E. Lindahl, M. S. P. Sansom, Curr. Opin. Struct. Biol. 2008, 18, 425-431.
- [13] a) P. J. Stang, N. E. Persky, J. Manna, J. Am. Chem. Soc. 1997, 119, 4777–4778; b) H. Abourahma, B. Moulton, V. Kravtsov, M. J. Zaworotko, J. Am. Chem. Soc. 2002, 124, 9990–9991; c) R. Chakrabarty, P. S. Mukherjee, P. J. Stang, Chem. Rev. 2011, 111, 6810–6918.
- [14] A similar hexagonal amidinium carboxylate construct was proposed by Hamilton, but no studies on attempts to prepare it have been reported: J. Yang, R. Melendez, S. J. Geib, A. D. Hamilton, *Struct. Chem.* **1999**, *10*, 221–228.
- [15] M. Mascal, N. M. Hext, R. Warmuth, M. H. Moore, J. P. Turkenburg, Angew. Chem. Int. Ed. Engl. 1996, 35, 2204–2206; Angew. Chem. 1996, 108, 2348–2350.
- [16] G.-L. Song, H.-J. Zhu, L. Chen, S. Liu, Z.-H. Luo, *Helv. Chim. Acta* 2010, 93, 2397–2405.
- [17] A. Petitjean, L. A. Cuccia, M. Schmutz, J.-M. Lehn, J. Org. Chem. 2008, 73, 2481–2495.
- [18] The spectrum had to be collected relatively quickly after mixing 1-2 BPh_a and TBA₂-IP: a precipitate formed within approximately 10 min.
- [19] These upfield shifts are often indicative of these kinds of hydrophobic/ donor-acceptor stacking interactions; for example, see: M. S. Cubberley, B. L. Iverson, J. Am. Chem. Soc. 2001, 123, 7560-7563.
- [20] Each value was weighted by $1/r^2$ to remove noise from this distribution; see the Supporting Information for details and unweighted histograms.
- [21] It should be noted that Grosu and Legrand reported crystal structures of 1-P and of 1-IP (which have a different morphology to ours). Crystals were reported as being obtained from water, although no further information was given as to how this was achieved. See Ref. [9]
- [22] Crystals containing the same asymmetric unit cell could also be obtained by diffusing dichloromethane or THF into a DMSO solution of 1.2 BPh_4 and TBA_2 ·IP.
- [23] a) P. van der Sluis, A. L. Spek, Acta Crystallogr. Sect. A 1990, 46, 194–201;
 b) A. Spek, J. Appl. Crystallogr. 2003, 36, 7–13.
- [24] S. Alvarez, Dalton Trans. 2013, 42, 8617-8636.
- [25] a) R. Taylor, O. Kennard, Acta Crystallogr. Sect. B 1983, 39, 133–138; b) R. Taylor, O. Kennard, Acc. Chem. Res. 1984, 17, 320–326.
- [26] R. Kramer, J. M. Lehn, A. Marquis-Rigault, Proc. Natl. Acad. Sci. USA 1993, 90, 5394-5398.
- [27] A. J. Lowe, F. M. Pfeffer, Chem. Commun. 2008, 1871-1873.
- [28] M. J. Abraham, T. Murtola, R. Schulz, S. Páll, J. C. Smith, B. Hess, E. Lindahl, *SoftwareX* 2015, 1, 19–25.
- [29] N. Schmid, A. P. Eichenberger, A. Choutko, S. Riniker, M. Winger, A. E. Mark, W. F. van Gunsteren, *Eur. Biophys. J.* 2011, 40, 843.
- [30] A. K. Malde, L. Zuo, M. Breeze, M. Stroet, D. Poger, P. C. Nair, C. Oostenbrink, A. E. Mark, J. Chem. Theory Comput. 2011, 7, 4026–4037.
- [31] K. B. Koziara, M. Stroet, A. K. Malde, A. E. Mark, J. Comput.-Aided Mol. Des. 2014, 28, 221–233.
- [32] J. Hermans, H. J. C. Berendsen, W. F. Van Gunsteren, J. P. M. Postma, *Biopolymers* 1984, 23, 1513–1518.
- [33] B. Hess, H. Bekker, H. J. C. Berendsen, J. G. E. M. Fraaije, J. Comput. Chem. 1997, 18, 1463-1472.
- [34] S. Miyamoto, P. A. Kollman, J. Comput. Chem. 1992, 13, 952–962.
- [35] W. Humphrey, A. Dalke, K. Schulten, J. Mol. Graphics 1996, 14, 33-38.
- [36] CrysAlis PRO, **2014**, Agilent Technologies.
- [37] L. Palatinus, G. Chapuis, J. Appl. Crystallogr. 2007, 40, 786-790.
- [38] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout, D. J. Watkin, J. Appl. Crystallogr. 2003, 36, 1487.
- [39] R. I. Cooper, A. L. Thompson, D. J. Watkin, J. Appl. Crystallogr. 2010, 43, 1100-1107.

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FULL PAPER



Self–Assembly

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 With Hydrogen bond-Driven Self-Assembly
 between Amidinium Cations and Carboxylate Anions: A Combined Molecular Dynamics, NMR Spectroscopy, and Single Crystal X-ray Diffraction Study



Understanding self-assembly: The interaction between bis(amidinium) cations and dicarboxylate anions was studied in a range of solvents using NMR spectroscopy and molecular dynamics techniques. The results indicate that both linear and cyclic architectures are present in solution, and they can be crystallized to give 1D hydrogen bonded polymeric systems.

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