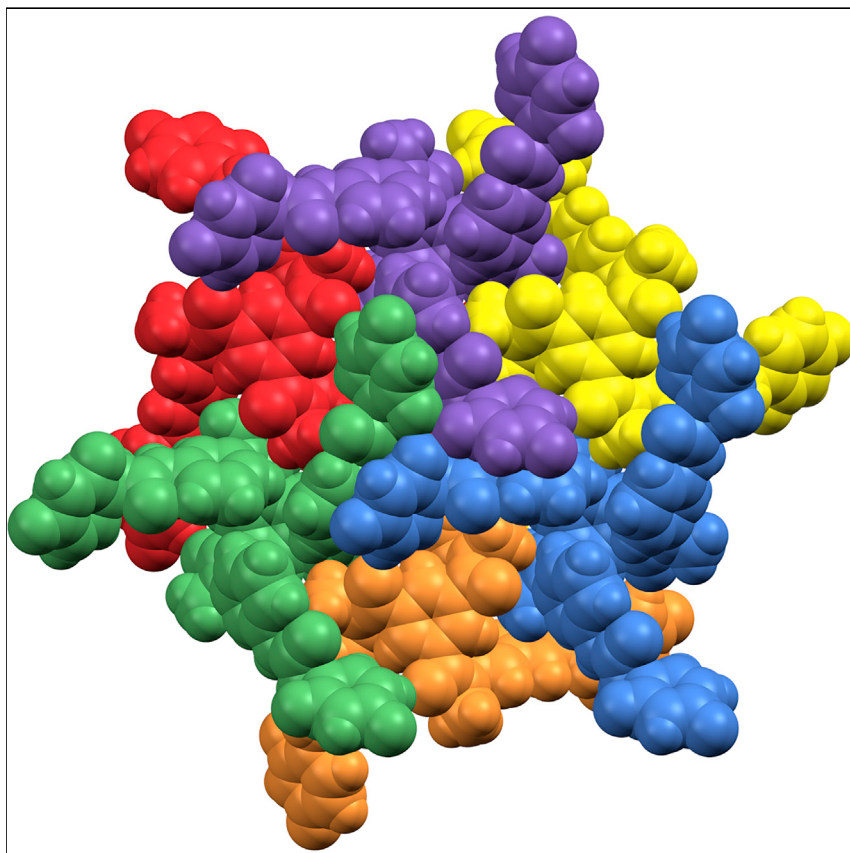


## Article

## Sulfate-Templated 2D Anion-Layered Supramolecular Self-Assemblies



Tripodal *N*-methylated(1,3,5-benzene-tricarboxamide)-tris(phenylurea) BTA ligands, possessing urea functionalities in the *meta* position, are able to form extended self-assembly 2D networks via hydrogen bonding templated by sulfate ( $\text{SO}_4^{2-}$ ). Studies in solution and in the solid state, as well as scanning electron microscopy (SEM) on the self-assembly properties of the ligands showed that the convergence also leads to the formation of hierarchical structures, including porous films and spherical nano-sized particles, with the morphological outcome being highly solvent dependent.

Anna B. Aletti, Salvador Blasco, Savyasachi J. Aramballi, Paul E. Kruger, Thorfinnur Gunnlaugsson

paul.kruger@canterbury.ac.nz (P.E.K.)  
gunnlaut@tcd.ie (T.G.)

## HIGHLIGHTS

Synthesis of urea-based tripodal ligands, with propeller-like appearance, is described

These structures form hydrogen bonding networks with  $\text{SO}_4^{2-}$

These self-assemblies give rise to highly ordered layered materials

The formation of hierarchical structures, including nano-sized particles, is observed

Article

# Sulfate-Templated 2D Anion-Layered Supramolecular Self-Assemblies

Anna B. Aletti,<sup>1</sup> Salvador Blasco,<sup>1,2</sup> Savyasachi J. Aramballi,<sup>1</sup> Paul E. Kruger,<sup>3,\*</sup> and Thorfinnur Gunnlaugsson<sup>1,4,\*</sup>

## SUMMARY

Using solution and solid-state analyses, we demonstrate that the tripodal *N*-methylated(1,3,5-benzene-tricarboxamide)-tris(phenylurea) BTA ligands, possessing urea functionalities in the meta position, are able to form extended self-assembly 2D networks via hydrogen bonding templated by sulfate ( $\text{SO}_4^{2-}$ ). The divergence of the urea binding sites confers a propeller-like conformation to the ligands and is key to formation of the self-assemblies. Studies in solution and in the solid state as well as scanning electron microscopy (SEM) on the self-assembly properties of the ligands showed that the convergence also leads to the formation of hierarchical structures, including porous films and spherical nano-sized particles; the morphological outcome is highly solvent dependent.

## INTRODUCTION

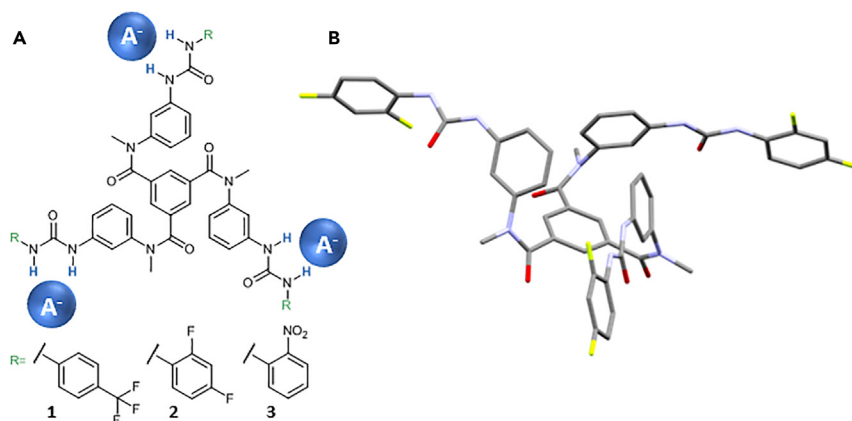
Supramolecular anion chemistry is a topical area of research with a large number of organic and coordination structures developed for the recognition, sensing, and transport of anions.<sup>1–3</sup> Anions play a critical role as counter ions in the formation of coordination networks and MOFs<sup>4</sup> and in directing self-assembly processes, such as in the formation of clusters,<sup>5</sup> metallo-macrocycles and cages,<sup>6</sup> helicates,<sup>7</sup> knots,<sup>8</sup> and mechanically interlocked structures.<sup>9</sup> Their application in supramolecular gel formation is also well studied.<sup>10,11</sup> In contrast, examples of anions directing the formation of higher order organized self-assemblies and functional hierarchical materials from charge neutral organic building blocks is limited. Noteworthy examples include that of Basarić et al.,<sup>12</sup> who used phosphate to mediate the formation of self-assembly structures from adamantane bisurea derivatives and that of Das et al.<sup>13</sup> who used carbonate to induce the formation of dimeric capsular hexagonal assemblies. Recently, Bielawski et al.<sup>14</sup> used bis-anions in the formation of anion cross-linked soft materials, while Granja et al.<sup>15</sup> formed higher order organized self-assemblies of spherical aggregates from cyclic peptides. In the last decade, several examples of anion coordination polymer (ACP) have also been developed which normally give 1D structures<sup>16,17</sup> and other anion based polymeric systems.<sup>18,19</sup> In fact, anion supramolecular self-assembly chemistry has become an import and fast growing area of research.<sup>20–22</sup> The BTA (1,3,5-benzenetricarboxamide) moiety is a tripodal building block that has been extensively used in the formation of a range of supramolecular structures and materials.<sup>23</sup> Recently, Stefankiewicz et al. used BTA ligands in the formation of a large enantiopure nanocapsule as a host for  $\text{C}_{60}$ .<sup>24</sup> We have recently shown that the BTA scaffold can form anion-templated self-assembly cages using  $\text{SO}_4^{2-}$  in 2:1 stoichiometry and self-sorting self-assembled clusters with 4:4 stoichiometry.<sup>25</sup> Here, we demonstrate that the high coordination requirement of  $\text{SO}_4^{2-}$  and its templating ability can be capitalized upon in the formation of a supramolecular layered polymeric 2D network, and that

## The Bigger Picture

Anions are widespread in our world, and many anions carry out specific roles in nature, for both living and inanimate matter. Because these processes are often accompanied by specificity, when changes occur in these interactions, the results can be of harm to life and the environment. For this reason, the study of the noncovalent bonds of anions has been of interest to scientists for many years, with a focus on hydrogen bonding, imitating the way proteins and enzymes can interact with anions in nature.

A deep understanding of these interactions is needed to comprehend how their activity can be actively used toward the formation of hierarchical assemblies to control their functions and activities in their environment.

The development of anion-templated self-assemblies is of interest for their potential in the removal of hazardous and polluting anions from the environment using new improved methodologies.



**Figure 1. Structure of Tripodal Ligands 1–3**

(A) Structures of 1–3.

(B) The X-ray crystal structure of **2**, viewed from the BTA core demonstrating the open propeller conformation with divergent urea binding sites. Hydrogen atoms and solvent molecules omitted for clarity.

these self-assemblies form nano-sized hierarchical aggregates in solution. We demonstrate by using SEM imaging that the nature of the solvent mixture dictates the way that these 2D networks aggregate to form higher-ordered hierarchical materials, the morphology of which are highly solvent dependent.

## RESULTS AND DISCUSSION

### Synthesis and Characterization

Inspired by the ability of the  $\text{SO}_4^{2-}$  anion to form anion-templated capsules, the *N*-methylated BTA structures **1–3**, Figure 1A, possessing three inner-core phenyl urea groups substituted in the *meta* position were synthesized in three steps. Starting from 1,3,5-benzenetricarbonyltrichloride and *N*-methyl-3-nitroaniline, which were coupled to give a tripodal nitro precursor, which, once catalytically reduced to the corresponding amine, was reacted with the relevant phenyl isocyanate to give the desired ligands (see Scheme S1 and Supplemental Information for full details). Our objective was to investigate whether these ligands could be used to direct self-assembly formation away from the “capsule” structure<sup>18</sup> toward the formation of higher-ordered hierarchical structures. Slow evaporation of DMSO and  $\text{CH}_3\text{CN}$  solutions of **2** and **3**, respectively, resulted in the formation of diffraction-quality single crystals. The crystal structures are shown in Figures 2A–2D. Unfortunately, attempts to grow suitable crystals of **1** failed. Ligand **2** crystallized in the triclinic P-1 space group and showed the three *N*-methyldamido groups of the BTA unit to be directed away from the plane of the central benzene core (Figures 1B, 2A, and 2B). The three amide oxygen atoms bend away from the plane defined by the central benzene ring with torsion angles of ca.  $43^\circ$  for two arms and  $62^\circ$  for the third. The coplanar conformation of two of the arms is further stabilized by low angle, ca.  $120^\circ$ , hydrogen bonds between aromatic C–H donors, and the acceptor oxygen atom of the ureas (Table S7). These interactions as well as  $\pi$ – $\pi$  interactions stabilize the conformation of 2,4-difluorophenyl moiety which, in principle, can rotate freely. These two ureas are also engaged in hydrogen bonding with two DMSO molecules, reflecting solvation of the potential binding site of the receptor. The third arm exhibits a wider angle because of bifurcated intermolecular hydrogen bonding of the urea with another arm of a neighboring molecule of **2**. The crystals of **3** were also formed in the triclinic P-1 space group, with the asymmetric unit containing one molecule of ligand and

<sup>1</sup>School of Chemistry and AMBER (Advanced Materials and BioEngineering Research) Centre, Trinity College Dublin, The University of Dublin, Dublin 2, Ireland

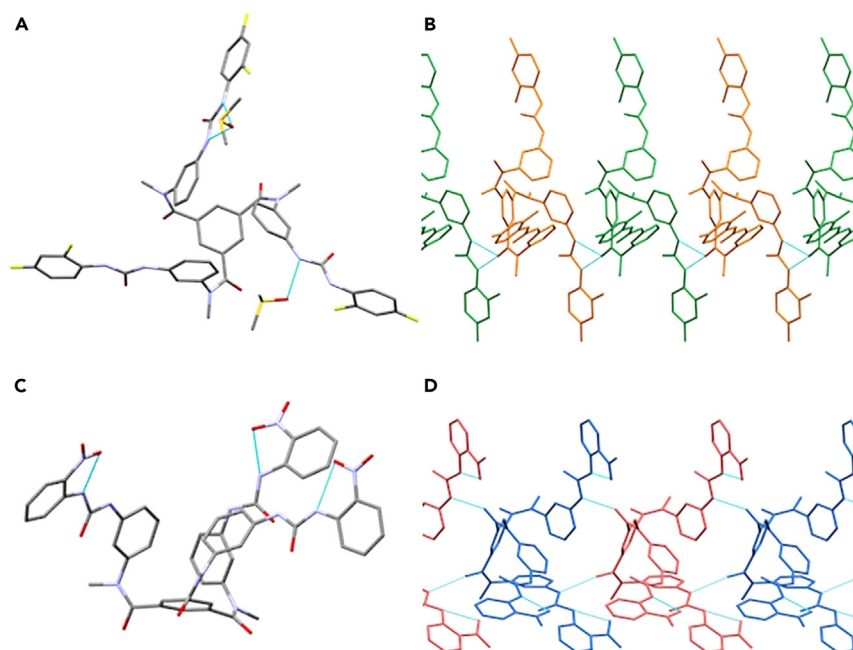
<sup>2</sup>Departamento de Química, Inorgánica, Universidad de Valencia, Instituto de Ciencia Molecular, Edificio de Institutos de Paterna, C/Catedrático José Beltrán Martínez 2, Paterna, Valencia 46980, Spain

<sup>3</sup>MacDiarmid Institute for Advanced Materials and Nanotechnology, School of Physical and Chemical Sciences, University of Canterbury, Private Bag 4800, Christchurch 8041, New Zealand

<sup>4</sup>Lead Contact

\*Correspondence:  
[paul.kruger@canterbury.ac.nz](mailto:paul.kruger@canterbury.ac.nz) (P.E.K.),  
[gunnlaut@tcd.ie](mailto:gunnlaut@tcd.ie) (T.G.)

<https://doi.org/10.1016/j.chempr.2019.06.023>



**Figure 2. Crystal Structures of 2 and 3**

Structure of **2**. Shown in (A) is a capped stick representation demonstrating the open propeller conformation, with divergent urea binding sites, that are involved in H-bond with 2 solvent molecules (DMSO), and in (B) is the packing showing hydrogen bonding from one of the urea groups NH to the BTA C=O on a neighboring molecule. Shown is the structure of **3**: in (C) is a capped stick representation showing the formation of internal hydrogen bond from one urea NH and the Ortho NO<sub>2</sub> group and in (D) is packing showing hydrogen bonding from two of the urea groups NH (the one not involved in the intramolecular H-bond) to the BTA C=O on a neighboring molecule. Hydrogen atoms omitted for clarity.

some solvent molecules. As was seen for **2**, the central BTA moiety adopts a conformation where all three amide oxygen atoms locate on the same side of the central ring, and a range of different supramolecular interactions (intermolecular hydrogen bonds,  $\pi$ - $\pi$  stacking, and CH- $\pi$  bonds) are evident in the crystal packing. Furthermore, an intramolecular hydrogen bond between the nitro-substituted distal phenyl ring and urea NHs exists for all three arms (Figure 1C). We<sup>26</sup> and others<sup>27</sup> have demonstrated such interactions in structurally similar urea-based receptors. As was observed for **2**, intermolecular hydrogen bonds between the arms of neighboring molecules also exist in **3** and give rise to a 1D network in the crystallography a axis (Figure 2D).

## Anion Binding Studies

### Anion Binding Studies in Solution

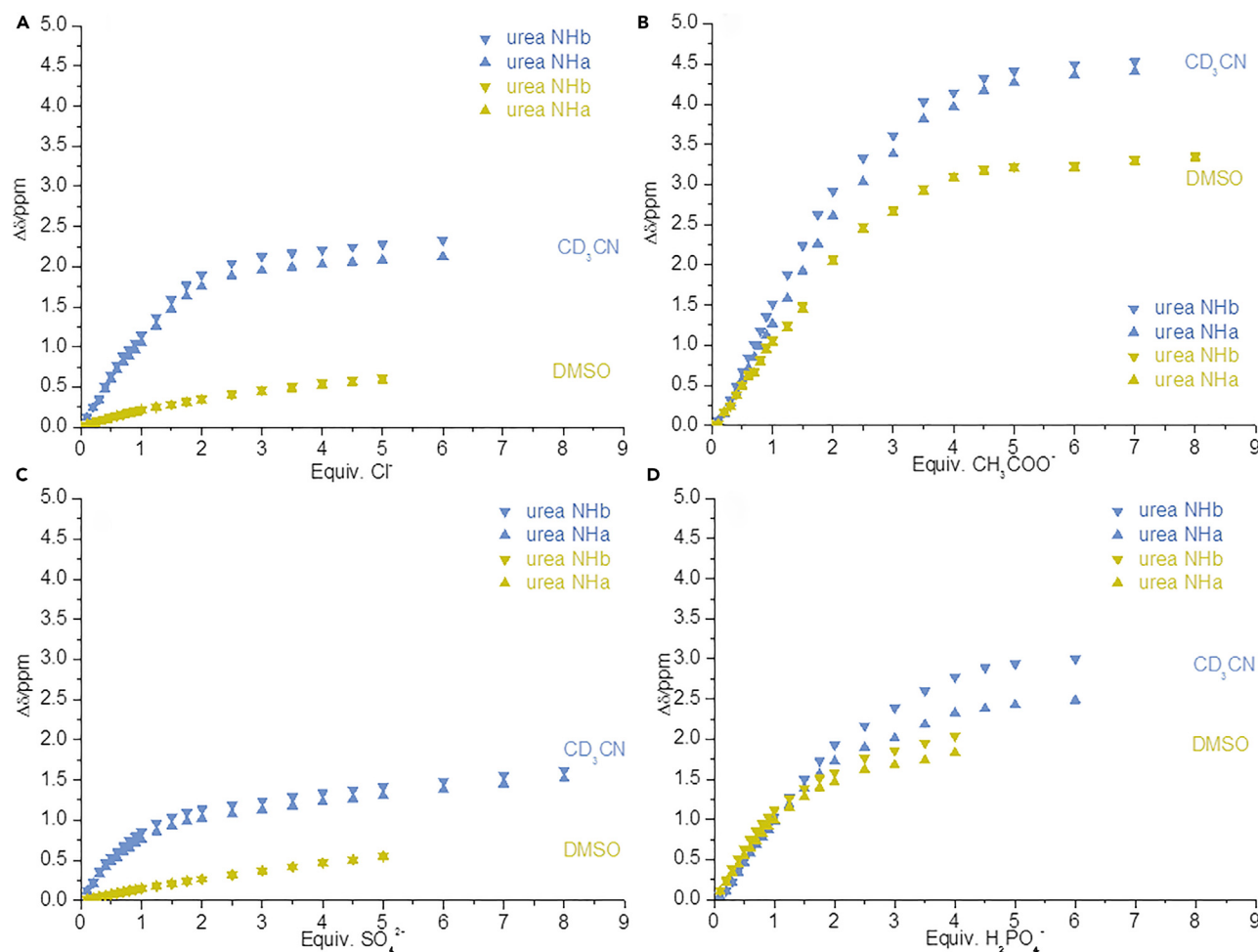
The solid-state analysis above demonstrated the presence of the anticipated open “propeller-like” conformation for both **2** and **3** and suggests that this preorganization may be appropriate to form anion-templated networks. With this in mind, we investigated the affinity of **1–3** for different anions (tetrabutyl-ammonium salts of AcO<sup>−</sup>, SO<sub>4</sub><sup>2−</sup>, H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, and Cl<sup>−</sup>)<sup>26</sup> in CH<sub>3</sub>CN solution using UV-vis absorption spectroscopy. The absorption spectra consisted of a broad band at high energy for the BTA core, and a shoulder for **1** and **2**, or a band for **3**, that was significantly red shifted, because of internal charge transfer. All the anion titrations clearly demonstrated that **1–3** participated in anion binding, with concomitant formation of

different isosbestic points (Figures S58–S69). However, the overall changes were in some cases relatively small, and the titration data could not be fit easily to give reliable anion binding constants (see Table S1 for fitting). Therefore, titrations were carried out in DMSO- $d_6$  solutions and followed using  $^1\text{H}$  NMR spectroscopy.

Full NMR characterization of 1–3 was completed using 2D NMR experiments (i.e., HMBC, C–H, and N–H HSQC) combined with selective  $^1\text{H}$  ROESY, which allowed us to identify, and confidently monitor, the shift of each proton during the binding events. Titration of these ligands with the aforementioned anions caused de-shielding to occur in the urea proton resonances, indicating hydrogen bonding interaction with the anions. From these changes, the anion binding stoichiometry and constants could be determined using the non-linear regression analysis program HypNMR.<sup>28,29</sup> The analysis showed the formation of 1:1 complexes (ligand 1:  $K_{1:1} = 32, 200$  and  $8\text{ M}^{-1}$  for  $\text{Cl}^-$ ,  $\text{H}_2\text{PO}_4^-$ , and  $\text{SO}_4^{2-}$ , respectively; for other ligands see Table S2), while with  $\text{AcO}^-$  ligands 2 and 3 formed the 1:1, and ligand 1 showed the formation of two species, 1:1 and 1:3. This behavior is in line with the Hofmeister series and the solvation of the anions. The formation of 1:1 complexes for  $\text{Cl}^-$ ,  $\text{SO}_4^{2-}$ , and  $\text{H}_2\text{PO}_4^-$  was also confirmed by MALDI-TOF analysis (Figures S37–S41), with the isotopic distribution patterns matching those of the calculated species. Unfortunately, ligand 1 was the only host that displayed sufficient solubility in  $\text{CD}_3\text{CN}$  for  $^1\text{H}$  NMR titrations to be carried out. In this media, all anions induced a greater downfield shift in the urea proton resonances than seen in DMSO- $d_6$  and less selective binding was observed ( $\text{SO}_4^{2-}$  and  $\text{Cl}^-$  showed shifts that were 2 and 4 times those seen in DMSO- $d_6$ ) (Figure 3). This reflects their stronger interactions in less competitive media (Table S3). These titrations were fit to the same binding models as employed above, showing both 1:1 and 1:3 (L:A) stoichiometry for  $\text{Cl}^-$ ,  $\text{SO}_4^{2-}$  and  $\text{H}_2\text{PO}_4^-$  (Table S3). Having determined the binding affinity of 1–3 and possible species distributions, we next set out to investigate if these ligands, in the presence of high-coordinating oxanions, could be used to form extended anion-templated self-assemblies as outlined above (in either solution or in the solid state).

#### Solid-State Studies: Formation of Anion-Templated 2D Materials

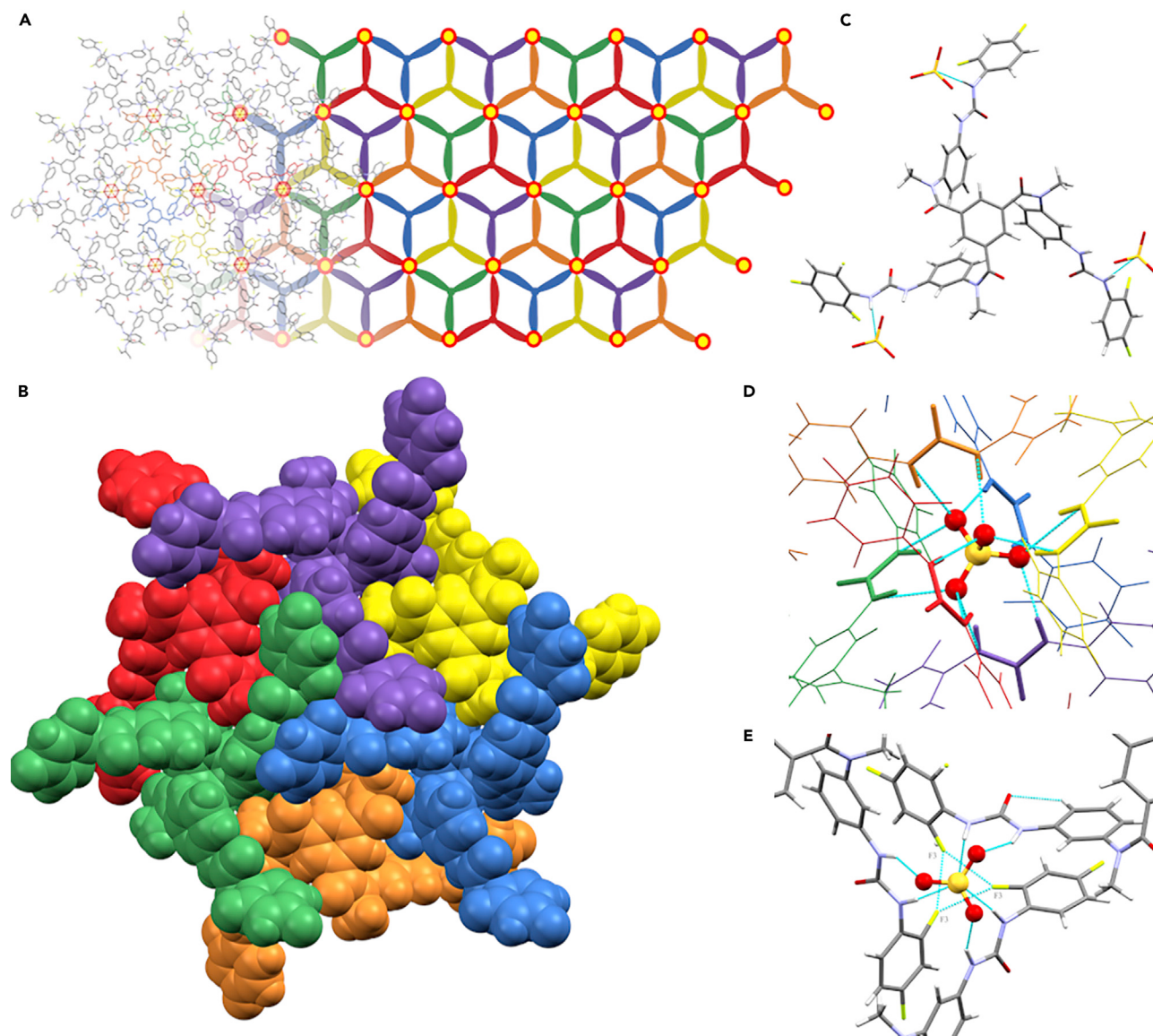
The crystallization of 1–3 in the presence tetrabutyl-ammonium salts of  $\text{SO}_4^{2-}$ ,  $\text{AcO}^-$ ,  $\text{H}_2\text{PO}_4^-$ , and  $\text{Cl}^-$  was carried out in both DMSO or  $\text{CH}_3\text{CN}$  solutions, using various methodologies. However, of these, only 2 in the presence of  $\text{SO}_4^{2-}$  yielded crystals. The slow evaporation of DMSO or  $\text{CH}_3\text{CN}$  solutions of 2 (in excess  $\text{SO}_4^{2-}$ ) resulted, on both occasions, in the formation of crystals that were suitable for single crystal X-ray diffraction analysis (Figure 2) and the structural details showed them to be isostructural (Table S4). The complex of 2 with  $\text{SO}_4^{2-}$  ( $2 \cdot \text{SO}_4^{2-}$ ) crystallized in the trigonal  $R\bar{3}$  space group, with each of the  $\text{SO}_4^{2-}$  anions positioned on a hexagonal axis, within a tight hydrogen binding pocket. The asymmetric unit contains 1/3 of a molecule of 2, 1/6 of a  $\text{SO}_4^{2-}$  anion. Solvent molecules and the counter cations were present, however, these were disordered and not interacting with their host receptor or guest anion. Each  $\text{SO}_4^{2-}$  ion is surrounded by six urea groups, from six different molecules of 2 (Figures 4A–4D) with a total of 12 hydrogen bonds (Figure 4D) with N–H $\cdots$ O(S) bond lengths ranging from 1.923–2.240 Å, with an average N–H $\cdots$ O bond length of 2.22 Å (Table S10). Within the  $2 \cdot \text{SO}_4^{2-}$  assembly, each ligand binds to three different  $\text{SO}_4^{2-}$  ions (Figures 4B and 4C). This demonstrates that the high coordination preference of the anion is fulfilled within this binding arrangement.<sup>30</sup> In contrast to the structure of 2 (cf. Figure 2A), in  $2 \cdot \text{SO}_4^{2-}$ , all three 2,4-difluorophenyl moieties are equally rotated at  $77^\circ$  with respect to the urea groups, the amide carbonyls and the *N*-methyl groups pointing away from the central  $C_3$  axis, and it is



**Figure 3.  $^1\text{H}$  NMR Binding Studies of Ligand 1**

(A–D) Binding isotherms of urea protons comparing results between  $\text{CD}_3\text{CN}$  (blue) and  $\text{DMSO-d}_6$  (green) titration of 1 with (A)  $\text{Cl}^-$ , (B)  $\text{CH}_3\text{COO}^-$ , (C)  $\text{SO}_4^{2-}$ , (D)  $\text{H}_2\text{PO}_4^-$ .

clear that the preorganization observed in 2 is to greater extent maintained in  $2 \cdot \text{SO}_4^{2-}$ , where 2 maintains its “propeller-like” conformation. The anion templation results in an overall  $\text{C}_3$  symmetry, which tessellates the ligands around the  $\text{SO}_4^{2-}$  anion, resulting in the formation of an extended 2D layer along the  $ab$  plane. These planes are stacked along the  $c$  axis, each one rotated  $\pm 120^\circ$  with respect to surrounding planes. This network is further stabilized by inter-ligand  $\pi$ – $\pi$  stacking and additional hydrogen bonding interactions. The  $\pi$ –stacking interactions differ from the ligand crystal where face-to-face interactions were seen between distal phenyl rings from the neighboring molecules. This places the ortho-fluorine atoms in one of two sites within the structure, with a similar occupancy distribution to the ligand crystal, where 32% has a potential aromatic  $\text{CH} \cdots \text{O}(\text{amide})$  hydrogen bond in place and 68% in the alternate conformation. The  $\text{SO}_4^{2-}$  anion can be found in two different orientations along the  $c$  axis, up or down, producing two crystallographically different oxygen atoms in axial or equatorial orientations. One of the ortho-fluorine atoms is situated very close to this axis, so it has two symmetry generated F at 2.54(3) Å, suggesting the possibility of a F–F interaction (Figure 4E), as we<sup>31</sup> have observed in other self-assembly structures.<sup>32</sup> The above results demonstrate that our design strategy has been successful, and that the “propeller-like”



**Figure 4. Crystal Structure of 2·SO<sub>4</sub><sup>2-</sup>**

- (A) Packing details viewed down the c axis (only one layer shown) and schematic representation of the 2D network formed by the SO<sub>4</sub><sup>2-</sup>-templated self-assembly of the propeller-like molecule.
- (B) Detail of a cluster formed by 6 molecules of **2** around 1 molecule of SO<sub>4</sub><sup>2-</sup>.
- (C) Details of the interaction of 1 molecule of **2** interacting with three SO<sub>4</sub><sup>2-</sup> molecules.
- (D) Detail of 1 molecule of SO<sub>4</sub><sup>2-</sup> interacting with 6 different molecules of **2**.
- (E) Details of the F–F interactions between three different molecules.

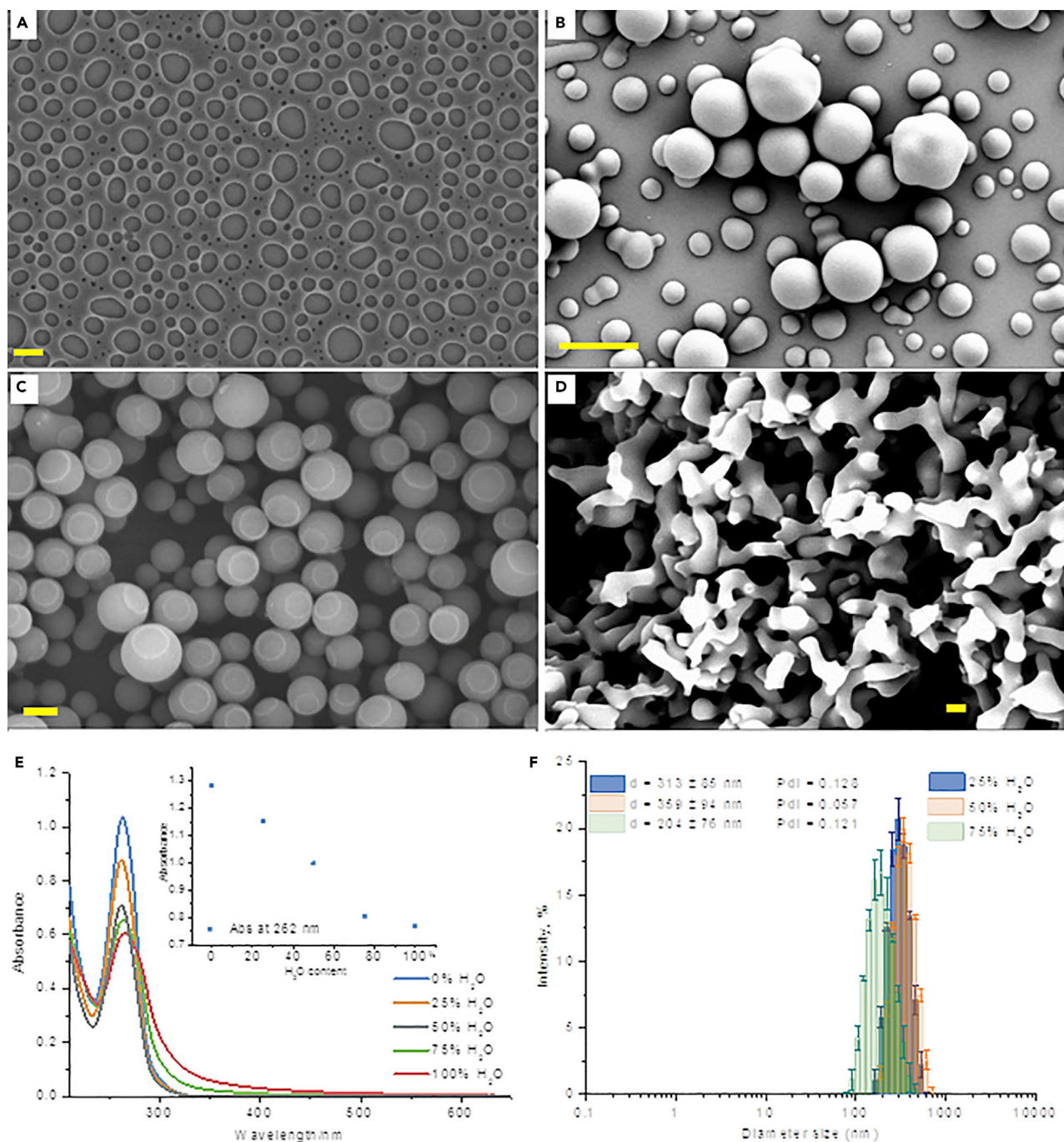
preorganization of **2** results in the formation of an extended 2D network upon binding to SO<sub>4</sub><sup>2-</sup> (Figure 4A). This is, to the best of our knowledge, the first example of the use of SO<sub>4</sub><sup>2-</sup> anion to generate such a higher order 2D self-assembly in preference to the more commonly seen capsule formation.<sup>24,25,33</sup>

### Self-Aggregation Studies

Aggregates and hierarchical materials such as extended 2D and 3D networks are formed because of inter- and intra- molecular supramolecular interactions and solvent effects.<sup>23</sup> Given that the 2·SO<sub>4</sub><sup>2-</sup> assembly gives rise to crystalline 2D networks,

and that **1–3** and **1–3**·SO<sub>4</sub><sup>2–</sup>, all have the ability to partake in such extended supramolecular network formation, we investigated the hierarchical formation for **1–3** in solution, both in the absence and presence of anions. <sup>1</sup>H NMR dilution studies (5 × 10<sup>–6</sup> → 1 × 10<sup>–2</sup> M) were first undertaken and these showed that in DMSO-*d*<sub>6</sub> only minor changes were observed for the free ligands. However, such dilution studies in the presence of SO<sub>4</sub><sup>2–</sup> clearly showed aggregation effects occurring for **1**·SO<sub>4</sub><sup>2–</sup> and **2**·SO<sub>4</sub><sup>2–</sup> (Figures S81 and S85). In the case of **1**, aggregation effects were seen in both CD<sub>3</sub>CN and CD<sub>3</sub>OD, with sharpening and shifts in key resonances observed at higher concentrations (Figures S82–S83). Next, solutions of **1** (1 mM in DMSO, CH<sub>3</sub>CN, and CH<sub>3</sub>OH), **2**, and **3** (in DMSO)<sup>34</sup> were deposited on silica plates; these were dried in vacuum and imaged using scanning electron microscopy (SEM). The formation of thin films was observed in the SEM for **1–3** in DMSO (Figure S87) and for **1** CH<sub>3</sub>CN, Figure 5A. However, for ligand **1** in CH<sub>3</sub>OH, the formation of micro-spherical aggregates of ca. 1–2 μm size was observed, Figure 5B.<sup>35</sup> It is clear from the SEM imaging that the solvent has a major effect on the supramolecular interactions of these 2D structures, which results in the formation of the hierarchical structures. While it is difficult to elucidate what self-assembly pathways these 2D structures take to form these higher order structures, it is clear that the polarity, and hydrogen bonding ability, of the solvent is an important factor. As **1** is hydrophobic in nature, we investigated the effect of H<sub>2</sub>O on the assembly process of **1** in CH<sub>3</sub>OH by adding various aliquots of H<sub>2</sub>O to the 1 mM solution of **1** in CH<sub>3</sub>OH above. This instantly generated off-white precipitates that would remain dispersed in solution for days. Samples of these suspensions were analyzed by SEM and all showed the formation of spheres, Figure 5C. However, unlike that seen from pure CH<sub>3</sub>OH solution, these were more uniform and nano-sized (ca. 150–300 nm), demonstrating the effect of water on the aggregation pathway, and that the ligand alone can form hierarchical material. The formation of the spherical structures of **1** was also observed at even lower concentrations. This prompted us to monitor their formation as a function of both concentration of **1** (between 10<sup>–6</sup> → 10<sup>–5</sup> M) and in different H<sub>2</sub>O:CH<sub>3</sub>OH compositions, using UV-vis absorption spectroscopy. The results showed that at 8 × 10<sup>–6</sup> M concentration of **1**, the aggregate formation instantaneously occurred upon addition of H<sub>2</sub>O and the absorption of **1** at 263 nm, being initially slightly blue shifted (0% → 50% H<sub>2</sub>O), was followed by a red shift (265 nm) with the formation a broad shoulder (~300 nm) (Figure 5E). DLS studies of these samples confirmed their monodispersed nature and size distribution between 150–350 nm (Figure 5F).

Next, we investigated what effect SO<sub>4</sub><sup>2–</sup> (1 equiv) would have on such hierarchical formations. The addition of SO<sub>4</sub><sup>2–</sup> to DMSO solutions of **1** and **3** resulted in the formation of aggregates from deposited solutions, these clearly being formed as discrete microspheres for **3** (Figure S88), while **1**, consisted of “film” covered particles (Figure 6A). In contrast, **2** showed the formation of microcrystals within a film structure (Figure 6C). Addition of H<sub>2</sub>O (50%) to these solutions showed the formation of smooth spherical particles for **1** (Figure 6B) and **3** (Figure S88), while **2** showed a spherical aggregate with a microcrystalline texture (Figure 6D). We also added SO<sub>4</sub><sup>2–</sup> to preformed spheres of **1** in 1:1 CH<sub>3</sub>OH:H<sub>2</sub>O solutions causing the precipitation of the microparticles. SEM imaging of these showed that further aggregation of the spheres occurred (Figure 5D), giving rise to the formation of “coral”-like aggregates. This clearly demonstrates that the 2D self-assembly material forms alternative hierarchical structures in highly competitive hydrogen bonding media, which could possibly be due to the combination of hydrophobic effects between the layered material and the solvent, as well as a degree of hydrogen bonding interactions with the urea oxygen atoms. Although we have not been able to prove this experimentally, it is clear that the polarity of the urea arms (e.g., due to the nature

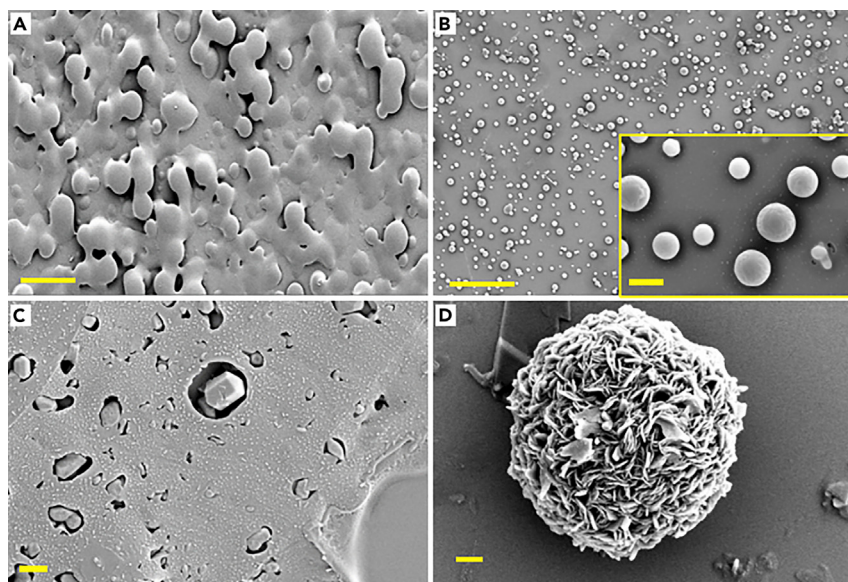


**Figure 5. Self-Assembly Studies of 1 in CH<sub>3</sub>CN and CH<sub>3</sub>OH**

(A–D) SEM images of self-assembled nanospheres of 1 in: (A) CH<sub>3</sub>CN (bar; 1  $\mu$ m), (B) CH<sub>3</sub>OH (bar; 2  $\mu$ m), (C) 1:1 CH<sub>3</sub>OH–H<sub>2</sub>O mixture (1 wt %) (bar; 200 nm), (D) 1:1 CH<sub>3</sub>OH–H<sub>2</sub>O mixture (1 wt %) and 3 equiv of SO<sub>4</sub><sup>2–</sup> (bar; 200 nm).

(E) UV-vis plot; (inset) plot of absorbance at 262 nm against H<sub>2</sub>O content in solution. Ligand concentration  $8 \times 10^{-6}$  M.

(F) Average particle size distribution determined using DLS technique from suspensions of ligand 1, prepared in CH<sub>3</sub>OH:H<sub>2</sub>O in different ratios ( $c = 8 \times 10^{-6}$  M, at 25°C).



**Figure 6. Self-Assembly Studies for 1 and 2 in DMSO**

(A and B) SEM images of deposited solutions of **1**·SO<sub>4</sub><sup>2−</sup> in: (A) DMSO (scale bar, 20 μm), (B) 1:1 DMSO-H<sub>2</sub>O (scale bar, 10 μm, inset = 1 μm).

(C and D) SEM images of deposited solutions of **2**·SO<sub>4</sub><sup>2−</sup> in: (C) DMSO (scale bar, 2 μm), (D) 1:1 DMSO-H<sub>2</sub>O (scale bar, 2 μm).

of the substituents; e.g., CF<sub>3</sub> versus F) allows us to gain some degree of tuning of the morphological outcome.

Using Cl<sup>−</sup>, AcO<sup>−</sup>, and H<sub>2</sub>PO<sub>4</sub><sup>−</sup> caused similar effect (Figure S89). In contrast, SEM images of samples where SO<sub>4</sub><sup>2−</sup> was first added to a solution of **1** in CH<sub>3</sub>OH solution, followed by the addition of H<sub>2</sub>O, gave no evidence of sphere formation, and only the formation of films, similar to that seen above, was observed (Figure S90). These studies showed that the self-assembly properties of the ligand would be highly affected by the solvent, which can influence both the self-assembly of the free ligand and of its SO<sub>4</sub><sup>2−</sup> complexes.<sup>36,37</sup>

## Conclusions

In summary, we have demonstrated that supramolecular self-assembly networks and aggregates, including uniform nano- and microspheres, can be formed from *N*-methylated BTA structures possessing *meta* phenyl urea groups, in both the presence and absence of SO<sub>4</sub><sup>2−</sup>. Using X-ray crystallography, we showed that **2**·SO<sub>4</sub><sup>2−</sup> formed a 2D hydrogen bonded network, where each anion is bound in a symmetrical way to six **2** “hosts”. To the best of our knowledge, these are the first examples of such SO<sub>4</sub><sup>2−</sup> based or connected supramolecular self-assembled structures hierarchical materials using BTA based urea ligands, demonstrating the powerful role anions can have in generating novel functional material owing to its high coordination requirement.

## EXPERIMENTAL PROCEDURES

All solvents and chemicals were purchased from commercial sources and used without further purification. Deuterated solvents used for NMR analysis (CD<sub>3</sub>CN, DMSO-*d*<sub>6</sub>) were purchased and used as received. Silica chromatography was carried out on a Teledyne Isco CombiFlash automated machine using pre-packed RediSep

cartridges. Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer fitted with a universal ATR sampling accessory. Melting points were determined using an Electrothermal IA9100 digital melting point apparatus. Where applicable, elemental analysis (CHN) was carried out by the School of Chemistry, University College Dublin.

### Mass Spectroscopy

Mass spectrometry was completed in the departmental mass spectrometry service of the School of Chemistry, Trinity College Dublin. Electrospray mass spectra were measured on a Micromass LCT spectrometer calibrated against a leucine enkephalin standard. MALDI Q-ToF mass spectra were recorded on a MALDI Q-TOF Premier (Waters Corporation, Micromass MS Technologies, Manchester, UK) and high-resolution mass spectrometry was performed using Glu-Fib as an internal reference ( $m/z = 1,570.677$ ).

### Dynamic Light Scattering

DLS measurements were made from back scatter in using Malvern Instrument Zetasizer Nano Series at 25°C in quartz cuvette with a path length of 10 mm. Statistical distribution by intensity were determined using the instrument software with standard deviations determined from triple replicate measurements. Samples were prepared using HPLC-grade CH<sub>3</sub>OH and H<sub>2</sub>O filtered six times through a 0.45 µm syringe filters (Acrodisc, PTFE).

### UV-Vis Absorption Studies

UV-visible absorption spectra were recorded using a Varian Cary 50 spectrophotometer, a spectroscopic window of 450–200 nm was used for all spectra with applied baseline correction from blank solvent. All UV-vis measurements were performed at 298 K in CH<sub>3</sub>CN or DMSO:CH<sub>3</sub>CN (spectroscopic grade) solutions. UV-vis absorption spectra were measured in 1 cm quartz cuvettes, except for the aggregation measurements for which 0.2 cm quartz cuvette was used. Baseline correction was applied for all spectra. Spectroscopic solutions were prepared from stock solutions using Pipetman Classic micropipettes (Gilson, Inc.).

### Preparation of Solutions for UV-Vis Titrations with Anions

The TBA salts of the anions used in the titrations were of spectroscopic grade and were purchased from Sigma Aldrich. All TBA salts were dried over P<sub>2</sub>O<sub>5</sub> at room temperature under vacuum. Solutions of these salts were prepared at varying concentrations of ca. 0.1 M,  $5 \times 10^{-2}$  M,  $1 \times 10^{-2}$  M, and  $1 \times 10^{-3}$  M. Host solutions of ca.  $1 \times 10^{-3}$  M were prepared and then diluted before titration (ca.  $1 \times 10^{-5}$  M).

### <sup>1</sup>H NMR Studies

The <sup>1</sup>H NMR spectra were recorded at either 400 or 600 MHz on Bruker instruments (AV3-400 or AV2-600). <sup>13</sup>C NMR spectra were recorded, on the same instruments, at either 150.9 or 100.6 MHz, while <sup>19</sup>F NMR spectra were recorded at 376.5 MHz. All <sup>13</sup>C NMR spectra were decoupled from <sup>1</sup>H, couplings to other nuclei are specified where appropriate. All spectra were recorded in commercially sourced per-deuterated solvents and referenced to residual proton signals of those solvents. Recorded free-induction decay signals were Fourier-transformed and processed using MestreNova v.6 without apodization and chemical shifts expressed in parts per million (ppm/δ) and coupling constants (*J*) in Hz. Residual solvent resonances were used as the internal reference, while 2D spectra were graphically referenced. All NMR spectra were carried out at 298 K.

### Preparation of Solutions for $^1\text{H}$ NMR Titrations with Anions

Spectroscopic solutions were prepared from stock solutions using Pipetman Classic micropipettes (Gilson, Inc.). The concentrations of these solutions were prepared in deuterated solvent such that 2  $\mu\text{L}$  would give ca. 0.1 molar equivalents of the anion. Host solutions of  $7 \times 10^{-3}$  M were prepared by dissolving a known amount of host in 0.7 mL of deuterated solvent. All measurements were performed at 25°C in  $\text{CD}_3\text{CN}$ . Receptors were titrated with a 100-fold more concentrated solution of the anion, as  $\text{TBA}^+$  salt. After each addition of the titrant solution, the  $^1\text{H}$ -NMR spectrum was recorded. TBA salts were dried in vacuum over  $\text{P}_2\text{O}_5$ . The  $^1\text{H}$  NMR spectra were recorded at 400 MHz on Bruker instruments AV3-400.

### SEM

Microscopy analysis of gel-aggregate samples by SEM was carried out using the facilities of the Advanced Microscopy Laboratory (AML) in Trinity College Dublin. Samples were prepared by a drop-casting methodology onto clean silicon wafers (cleaned by sonication in HPLC-grade acetone followed by HPLC-grade propan-2-ol) from glass Pasteur pipettes.<sup>24</sup> The manually drop cast samples were dried overnight in ambient conditions (a week in the case of DMSO solutions) and under high vacuum for 2 h immediately prior to their imaging. Samples were coated with a conductive Au layer, by sputtering, in order to improve contrast where static charging interfered with the imaging. Low kV SEM was carried out using the Zeiss ULTRA Plus using an SE2 detector.

### X-Ray Crystallography

X-ray data were collected on a Rigaku Saturn 724 CCD Diffractometer using graphite-monochromated  $\text{Mo-K}\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The data were collected using Crystalclear-SM 1.4.0 software. Data integration, reduction, and correction for absorption and polarization effects were all performed using Crystalclear-SM 1.4.0 software. Space group determination was obtained using Crystal structure version 3.8. Data for structure ( $2 \cdot \text{SO}_4^{2-}$ ).<sup>22</sup> was collected on an APEX Duo diffractometer using  $\text{Cu-K}\alpha$  radiation ( $\lambda = 1.54056 \text{ \AA}$ ). The data collection, integration, and reduction were made with Bruker Apex II software. The structures were solved by direct methods (SHELXS-97) and refined against all F2 data (SHELXL97). All H-atoms, except for N-H protons, were positioned geometrically and refined using a riding model with  $d(\text{CH}_{\text{ar}}) = 0.95 \text{ \AA}$ ,  $U_{\text{iso}} = 1.2 \text{ Ueq (C)}$  for aromatic and  $0.98 \text{ \AA}$ ,  $U_{\text{iso}} = 1.2 \text{ Ueq (C)}$  for  $\text{CH}_3$ . N-H protons were found from the difference map and fixed to the attached atoms with  $U_{\text{H}} = 1.2 \text{ UN}$ . In some cases, disordered solvent molecules were removed using SQUEEZE program from the PLATON crystallographic software.<sup>37</sup>

### DATA AND CODE AVAILABILITY

X-ray crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Center ([www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif)) under access numbers CCDC: Structure 2: 1874341; structure  $2 \cdot \text{SO}_4^{2-}$ : 1874342, and structure 3: 1874344.

### SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.chempr.2019.06.023>.

### ACKNOWLEDGMENTS

Financial support from Science Foundation Ireland (SFI PI 2013 to T.G. and the Phase II Funding [Research Centres Phase 2 12/RC/2278\_P2] to the SFI AMBER Centre),

School of Chemistry and the University of Dublin (Postgraduate Scholarship to A.A.), Marie Skłodowska-Curie actions (MSCA to S.B.) is acknowledged. We acknowledge Dr. Samuel Bradberry for continued support, fruitful discussions, and preparation of the final manuscript. We would also like to thank Drs. J.E. O'Brien, M. Reuther, and G. Hessman for helping with NMR and MS analysis and for their continuous support of our research efforts.

## AUTHOR CONTRIBUTIONS

A.B.A. carried out the synthesis, anion binding, and aggregation studies. Crystal structures were solved by S.B. Samples for SEM were prepared by A.B.A. and S.A.J., and images were collected by S.A.J. A.B.A. and T.G. co-wrote the manuscript with support from all authors. All research was performed under the guidance and supervision of T.G. and P.E.K.

## DECLARATION OF INTERESTS

The authors declare no competing interests.

Received: October 25, 2018

Revised: December 6, 2018

Accepted: June 27, 2019

Published: July 25, 2019

## REFERENCES AND NOTES

- Wu, X., Judd, L.W., Howe, E.W., Withecombe, A.M., Soto-Cerrato, V., Li, H., Busschaert, N., Valkenier, H., Pérez-Tomás, R., Sheppard, D.N., et al. (2016). Nonprotonophoric electrogenic Cl<sup>−</sup> transport mediated by valinomycin-like carriers. *Chem* 1, 127–146.
- Aletti, A.B., Gillen, D.M., and Gunnlaugsson, T. (2018). Luminescent/colorimetric probes and (chemo-) sensors for detecting anions based on transition and lanthanide ion receptor/binding complexes. *Coord. Chem. Rev.* 354, 98–120.
- Gale, P.A., Howe, E.N.W., Wu, X., and Spooner, M.J. (2018). Anion receptor chemistry: highlights from 2016. *Coord. Chem. Rev.* 375, 333–372.
- Hoque, M.N., and Das, G. (2017). Overview of the strategic approaches for the solid-state recognition of hydrated anions. *CrystEngComm* 19, 1343–1360.
- He, Q., Tu, P., and Sessler, J.L. (2018). Supramolecular chemistry of anionic dimers, trimers, tetramers, and clusters. *Chem* 4, 46–93.
- Yang, D., Zhao, J., Yang, X.J., and Wu, B. (2018). Anion-coordination-directed self-assemblies. *Org. Chem. Front.* 5, 662–690.
- Bai, X., Jia, C., Zhao, Y., Yang, D., Wang, S.C., Li, A., Chan, Y.T., Wang, Y.Y., Yang, X.J., and Wu, B. (2018). Peripheral Templatation-modulated interconversion between an A4 L6 tetrahedral anion cage and A2 L3 triple helicate with guest capture/release. *Angew. Chem. Int. Ed. Engl.* 57, 1851–1855.
- Bilbeisi, R.A., Prakasam, T., Lusi, M., El Khoury, R., Platas-Iglesias, C., Charbonnière, L.J., Olsen, J.C., Elhabiri, M., and Trabolsi, A. (2016). C-H...anion interactions mediate the templation and anion binding properties of topologically non-trivial metal-organic structures in aqueous solutions. *Chem. Sci.* 7, 2524–2531.
- Lim, J.Y.C., Marques, I., Félix, V., and Beer, P.D. (2018). A chiral halogen-bonding [3]rotaxane for the recognition and sensing of biologically relevant dicarboxylate anions. *Angew. Chem. Int. Ed. Engl.* 57, 584–588.
- Offiler, C.A., Jones, C.D., and Steed, J.W. (2017). Metal 'turn-off', anion 'turn-on' gelation cascade in pyridinylmethyl ureas. *Chem. Commun. (Camb.)* 53, 2024–2027.
- Okesola, B.O., and Smith, D.K. (2016). Applying low-molecular weight supramolecular gelators in an environmental setting - self-assembled gels as smart materials for pollutant removal. *Chem. Soc. Rev.* 45, 4226–4251.
- Blažek, V., Molčanov, K., Mlinarić-Majerski, K., Kojić-Prodić, B., and Basarić, N. (2013). Adamantane bisurea derivatives: anion binding in the solution and in the solid state. *Tetrahedron* 69, 517–526.
- Basu, A., and Das, G. (2014). A C(3v)-symmetric tripodal urea receptor for anions and ion pairs: formation of dimeric capsular assemblies of the receptor during anion and ion pair coordination. *J. Org. Chem.* 79, 2647–2656.
- Silver, E.S., Rambo, B.M., Bielawski, C.W., and Sessler, J.L. (2014). Reversible anion-induced cross-linking of well-defined calix(4)pyrrole-containing copolymers. *J. Am. Chem. Soc.* 136, 2252–2255.
- Rodríguez-Vázquez, N., Amorín, M., Alfonso, I., and Granja, J.R. (2016). Anion recognition and induced self-assembly of an alpha,gamma-cyclic peptide to form spherical clusters. *Angew. Chem. Int. Ed. Engl.* 55, 4504–4508.
- Morshedi, M., Willis, A.C., and White, N.G. (2016). Anion-templated 2D frameworks from hexahydroxytriphenylene. *CrystEngComm* 18, 4281–4284.
- White, N.G., Carta, V., and MacLachlan, M.J. (2015). Layered 2D sheetlike supramolecular polymers formed by O-H...anion hydrogen bonds. *Cryst. Growth Des.* 15, 1540–1545.
- White, N.G., and MacLachlan, M.J. (2015). Anion and cation effects on anion-templated assembly of tetrahydroxytryptylene. *Cryst. Growth Des.* 15, 5629–5636.
- Zhao, W., Qiao, B., Tropp, J., Pink, M., Azoulay, J.D., and Flood, A.H. (2019). Linear supramolecular polymers driven by anion-anion dimerization of difunctional phosphonate monomers inside cyanostar macrocycles. *J. Am. Chem. Soc.* 141, 4980–4989.
- Qiao, B., Hirsch, B.E., Lee, S., Pink, M., Chen, C.H., Laursen, B.W., and Flood, A.H. (2017). Ion-pair oligomerization of chromogenic triangulenium cations with cyanostar-modified anions that controls emission in hierarchical materials. *J. Am. Chem. Soc.* 139, 6226–6233.
- Li, S., Jia, C., Wu, B., Luo, Q., Huang, X., Yang, Z., Li, Q.S., and Yang, X.J. (2011). A triple anion helicate assembled from a bis(biurea) ligand and phosphate ions. *Angew. Chem. Int. Ed. Engl.* 50, 5721–5724.
- Barry, D.E., Hawes, C.S., Blasco, S., and Gunnlaugsson, T. (2016). Structure direction, solvent effects, and anion influences in halogen-bonded adducts of

- 2,6-bis(iodoethyl)pyridine. *Cryst. Growth Des.* **16**, 5194–5205.
23. Savyasachi, A.J., Kotova, O., Shanmugaraju, S., Bradberry, S.J., O'Maille, G.M., and Gunnlaugsson, T. (2017). Supramolecular chemistry: a toolkit for soft functional materials and organic particles. *Chem* **3**, 764–811.
24. Markiewicz, G., Jenczak, A., Kołodziejewski, M., Holstein, J.J., Sanders, J.K.M., and Stefankiewicz, A.R. (2017). Selective C70 encapsulation by a robust octameric nanospheroid held together by 48 cooperative hydrogen bonds. *Nat. Commun.* **8**, 15109.
25. Pandurangan, K., Kitchen, J.A., Blasco, S., Boyle, E.M., Fitzpatrick, B., Feeney, M., Kruger, P.E., and Gunnlaugsson, T. (2015). Unexpected self-sorting self-assembly formation of a [4:4] sulfate:ligand cage from a preorganized tripodal urea ligand. *Angew. Chem. Int. Ed. Engl.* **54**, 4566–4570.
26. Pandurangan, K., Kitchen, J.A., Blasco, S., Paradisi, F., and Gunnlaugsson, T. (2014). Supramolecular pyridyl urea gels as soft matter with antibacterial properties against MRSA and/or *E. coli*. *Chem. Commun.* **50**, 10819–10822.
27. Solomos, M.A., Watts, T.A., and Swift, J.A. (2017). Ortho-substituent effects on diphenylurea packing motifs. *Cryst. Growth Des.* **17**, 5065–5072.
28. Frassinetti, C., Alderighi, L., Gans, P., Sabatini, A., Vacca, A., and Ghelli, S. (2003). Determination of protonation constants of some fluorinated polyamines by means of <sup>13</sup>C NMR data processed by the new computer program HypNMR2000. Protonation sequence in polyamines. *Anal. Bioanal. Chem.* **376**, 1041–1052.
29. Frassinetti, C., Ghelli, S., Gans, P., Sabatini, A., Moruzzi, M.S., and Vacca, A. (1995). Nuclear magnetic resonance as a tool for determining protonation constants of natural polyprotic bases in solution. *Anal. Biochem.* **231**, 374–382.
30. Jia, C., Wu, B., Li, S., Huang, X., Zhao, Q., Li, Q.S., and Yang, X.J. (2011). Highly efficient extraction of sulfate ions with a tripodal hexaurea receptor. *Angew. Chem. Int. Ed. Engl.* **50**, 486–490.
31. Gunnlaugsson, T., Kruger, P.E., Jensen, P., Tierney, J., Ali, H.D.P., and Hussey, G.M. (2005). Colorimetric “Naked Eye” sensing of anions in aqueous solutions. *J. Org. Chem.* **70**, 10875–10878.
32. Martínez-Calvo, M., Kotova, O., Möbius, M.E., Bell, A.P., McCabe, T., Boland, J.J., and Gunnlaugsson, T. (2015). Healable luminescent self-assembly supramolecular metallogels possessing lanthanide (Eu/Tb) dependent rheological and morphological properties. *J. Am. Chem. Soc.* **137**, 1983–1992.
33. Custelcean, R., Williams, N.J., and Seipp, C.A. (2015). Aqueous sulfate separation by crystallization of sulfate–water clusters. *Angew. Chem. Int. Ed. Engl.* **54**, 10525–10529.
34. dos Santos, C.M.G., De Solis, S., Kruger, P.E., and Gunnlaugsson, T. (2011). Selective and tuneable recognition of anions using C3v-symmetrical tripodal urea-amide receptor platforms. Unfortunately, the poor solubility of **2** and **3** (a possible sign of potential aggregates formation) limited the use of DMSO. However, for **1**, UV-Vis absorbance dilution experiments (5×10<sup>−6</sup>→3×10<sup>−4</sup> M) were carried out in both CH<sub>3</sub>CN and CH<sub>3</sub>OH solutions, but saturation effects prevented reliable analysis at higher concentrations. We have seen such effect in other urea building blocks, which is also the reason we (and others) have employed TBA anion salts for such host-guest studies. *Chem. Commun.* **47**, 12176–12178.
35. No aggregates were found in CH<sub>3</sub>OH at low concentrations using either UV-vis absorption spectroscopy or by DLS analysis. This would indicate that the formation of aggregates occurs at higher concentrations and is very likely aided by evaporation of the solvent (see Supplemental Information).
36. Van Zee, N.J., Adelizzi, B., Mabesoone, M.F.J., Meng, X., Aloï, A., Zha, R.H., Lutz, M., Filot, I.A.W., Palmans, A.R.A., and Meijer, E.W. (2018). Potential enthalpic energy of water in oils exploited to control supramolecular structure. *Nature* **558**, 100–103.
37. Spek, A.L. (2005). Platon, a multipurpose crystallographic tool (Utrecht University).