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# Anions in crystal engineering†

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This *tutorial review* presents a current account of anions in crystal engineering, organized around two main questions: (i) how do anions influence and control crystal structures, and (ii) how do crystal environments recognize and select anions? The first part pertains to deliberate assembly of new crystalline materials using anionic components, by taking advantage of the strong and directional interactions of anions in the solid state. Along this line, the various structural roles of anions in crystals are examined. The second question is related to selective separation of anions by crystallization, by exploiting chemical recognition phenomena in the well-defined and highly structured environment inside crystals.

## Introduction

*Crystal engineering* may be defined as the design and synthesis of crystalline solids with targeted structures and properties from molecular or ionic building blocks.<sup>1</sup> As the main goal of this discipline is to synthesize new crystals, it was also appropriately referred to as *synthetic crystallography*.<sup>2</sup> Unlike molecular synthesis, which involves strong covalent bonds, crystal engineering generally relies on noncovalent or weakly covalent interactions, like hydrogen bonds, coordinative bonds, dipole–dipole, ion–dipole, or van der Waals forces,

for the assembly of crystalline structures. The utilization of such weaker intermolecular interactions, with shallow potential energy surfaces, is typically necessary to guarantee a fast and reversible self-assembly leading to a crystalline solid. A negative consequence, though, is that structural predictability and control is difficult to achieve due to the small energetic differences among alternative crystal structures. As a result, *bona fide* engineering of crystals, which requires *a priori* knowledge of their exact three-dimensional structures, remains rare. Nevertheless, partial structure prediction and control may often be achieved through a detailed understanding of intermolecular interactions involved, based on prior empirical observations. While absolute structure prediction and control remains the ultimate goal of crystal engineering, generation of new structural observations and structure–property relationships in crystalline solids continues to be, at this stage in time, a worthwhile endeavor.

Crystal engineering commonly involves neutral building blocks. Organic ions such as ammonium, guanidinium, amidinium, carboxylates, or sulfonates are also often utilized, as one can take advantage of their stronger, charge-assisted interactions.<sup>3,4</sup> Metal cations are common constituents of a large and popular class of crystalline solids: metal–organic frameworks (MOFs).<sup>5</sup> On the other hand, common inorganic anions, such as halides, nitrate, sulfate, *etc.*, have rarely been utilized in a deliberate way for the synthesis of crystalline solids. In a way, this comes as a surprise, as these anions are ubiquitous in Nature. Furthermore, the high charge density associated with such small anions translates into relatively strong interactions in crystals. However, the same high charge density is also responsible for the strong solvation of these anions, making it difficult to completely strip out the solvating molecules during crystallization, which complicates the crystal design process.

Along a different line of research, recognition of anions by molecular receptors has been extensively studied in solution and solid state, motivated by the need for selective anion sensing or separation.<sup>6</sup> Many of these studies involved crystal structure determinations by X-ray diffraction, providing a wealth of structural data about anion interactions in the solid state. Most of this information, however, was not analyzed

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from a crystal engineering perspective. The purpose of this tutorial review is to present a contemporary account of anions in crystal engineering, gravitating around two principal questions: (i) how do anions influence and control crystal structures, and (ii) how do crystal environments recognize and select anions? Whereas the first question pertains to predictably employing anions in the assembly of new crystalline materials, the second question is relevant to selective separation of anions through crystallization. The purpose of the review is limited to small inorganic anions, and does not include organic anions such as carboxylates or sulfonates, common components of popular classes of materials like MOFs<sup>5</sup> or guanidinium sulfonate frameworks<sup>3</sup> that were the subject of recent reviews.

## Anion interactions in crystals

Predictive design of crystal structures and properties requires, in the first place, a good understanding of the intermolecular interactions involved.<sup>1</sup> Specifically, the following interactions involving anions may be present in crystals (Fig. 1):

(i) *Coulombic and van der Waals*: These purely electrostatic interactions are ubiquitous, operating in the background of all crystals. They are, however, non-directional and therefore difficult to exploit for structure control.

(ii) *Metal coordination bonds* ( $M^+-A^-$ ): These Lewis acid–base interactions are relatively strong and specific, and often have a high degree of directionality. As a result, anion–metal coordination bonds are often found to strongly influence the structures of crystals. Their nature varies from purely electrostatic to significantly covalent.

(iii) *Hydrogen bonds* ( $D-H\cdots A^-$ ): These mainly electrostatic interactions are highly directional ( $<D-H-A$  close to linear) and therefore commonly employed in crystal design.<sup>1–4</sup> Small anions in particular often act as strong hydrogen-bond acceptors due to their relatively high charge density. While traditional O–H or N–H groups are most often utilized as hydrogen-bond donors, recent studies suggested that C–H groups may also act as effective partners in hydrogen bonds to anions.<sup>7,8</sup>

(iv) *Halogen bonds* ( $D-X\cdots A^-$ ): These interactions are formed between an electrophilic halogen ( $X = \text{Br}, \text{I}$ ) and a high electron density centre (in this case the anion), acting as

the halogen bond donor and acceptor, respectively. Halogen bonds are highly directional ( $<D-X-A$  close to linear), in many respects behaving like hydrogen bonds.<sup>9</sup>

(v) *Anion– $\pi$  interactions*: These are purely electrostatic attractions between anions and the centers of electron-deficient arenes. Although many such interactions involving charge-neutral arenes have been described theoretically in the gas phase, true examples of anion– $\pi$  interactions in crystals remain extremely rare.<sup>10</sup> The main reason for this paucity is the competition with  $C-H\cdots A^-$  hydrogen bonds, which tend to prevail.<sup>7</sup> Another competitor is the weak  $\sigma$  interaction involving a small amount of charge transfer from the anion to arene, which is geometrically characterized by the anion being situated above the periphery rather than the centre of the arene.<sup>7</sup> Some examples of anion– $\pi$  interactions involving positively-charged arenes can be found in crystals, although in such cases it is difficult to distinguish their contribution from that of the trivial coulombic interactions intrinsically present between the two counterions.

## Structural roles of anions in crystals

From a structural point of view, anions may play different roles in crystals (Fig. 2):

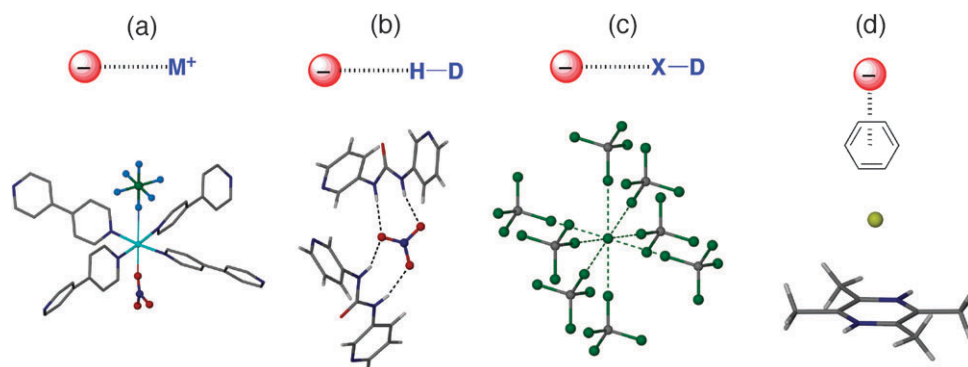
(a) *Spectator*: the anion is present merely for charge balance and does not play any structural role in the crystal; this situation is common in crystals of cationic frameworks (such as coordination polymers or MOFs) containing large pores or channels filled with weakly interacting, often disordered counterions and solvent molecules.

(b) *Structure-directing*: the anion plays a decisive role in the crystal, templating the formation of a particular structure among different alternatives, without necessarily participating directly to framework assembly.

(c) *Building unit*: the anion directly participates as a structural component to framework assembly through the formation of well-defined and directional interactions.

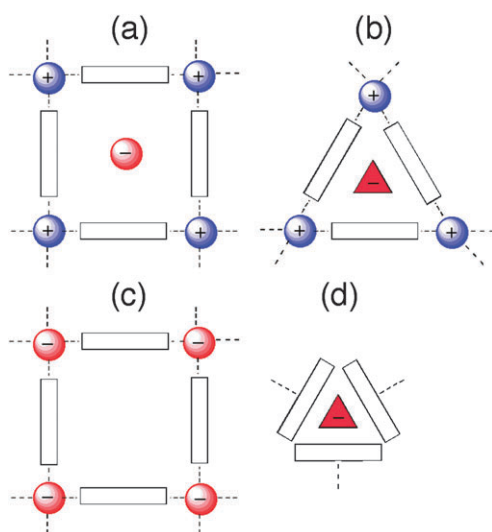
(d) *Secondary building unit (SBU)*: the anion is a central component of a larger aggregate that plays the role of building block in framework assembly.

In the next sections, selected recent examples from the literature illustrating some of the structural roles of anions



**Fig. 1** Examples of directional intermolecular interactions involving anions in crystals: (a) metal coordination by  $\text{NO}_3^-$  and  $\text{PF}_6^-$  anions;<sup>11</sup> (b) hydrogen bonding of  $\text{NO}_3^-$  by urea donors;<sup>12</sup> (c) halogen bonding of  $\text{Cl}^-$  by  $\text{CBr}_4$  donors;<sup>13</sup> (d) anion– $\pi$  interaction between  $\text{I}^-$  and tetramethylpyrazinium.<sup>14</sup>





**Fig. 2** Different structural roles of anions in crystals: (a) spectator; (b) structure-directing (templating); (c) building unit; (d) SBU component.

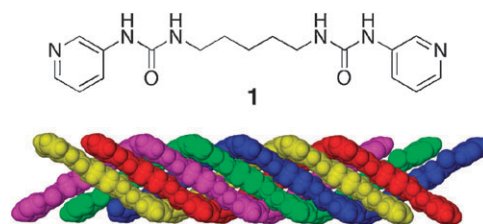
(b–d) will be highlighted. In many cases the anion's role in the crystal is clear-cut, but there are situations where the anion may play multiple roles and it may be difficult to pigeonhole it in one category or another.

### Anions as structure-directing agents

Anions may strongly influence the structure of crystals without being active structural components of the crystalline assembly. In other words, the anion does not participate as a principal building block to the assembly, but rather as a templating agent around which the framework grows. Sometimes the structure-directing role of the anion can be clearly identified from the examination of the final crystal structures, but there are cases where the anion's role is subtler, and the only hint that it has a decisive structural influence comes from the comparison of different crystal structures obtained in the presence of various anions under otherwise identical conditions.

Steed and coworkers recently demonstrated how the anion can dramatically influence the structure of a coordination polymer assembled from the flexible bis(pyridylurea) ligand **1** (Fig. 3).<sup>15</sup> **1** self-assembles with  $\text{AgX}$  ( $\text{X} = \text{NO}_3^-$ ,  $\text{BF}_4^-$ ) into a 1D coordination chain, with the urea functional group hydrogen-bonding to the counteranion. The  $\text{NO}_3^-$  anion, with its planar shape, links the coordination chains into planar hydrogen-bonded sheets. On the other hand, the tetrahedral  $\text{BF}_4^-$  interacts with urea groups orthogonally, inducing the ligands to form a two-fold helical arrangement. Because of the long pentamethylene chains between the urea groups, the helices intertwine into quintuple molecular braids (Fig. 3).

Another example of anion-directed helical assembly was provided by Cui *et al.*, using the axially chiral ligand **2**, which forms 1D coordination polymers with  $\text{Ag}^+$ .<sup>16</sup> By varying the counteranion from  $\text{NO}_3^-$  to  $\text{PF}_6^-$ , and  $\text{ClO}_4^-$ ,  $2_1$ -,  $3_1$ -, and  $4_1$ -symmetrical helices were obtained upon crystallization (Fig. 4). As other variables such as the reaction stoichiometry,

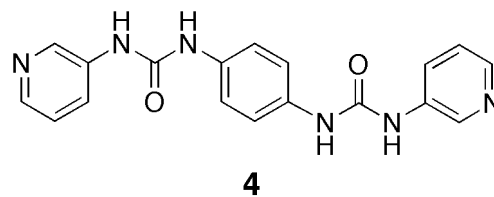


**Fig. 3** Quintuple helical molecular braid self-assembled from **1** and  $\text{AgBF}_4$  in the crystalline state.

solvent, and concentrations were kept constant, the observed structural differences may be clearly attributed to changing the anion. The smaller and more basic nitrate was found to double-bridge silver cations, thereby promoting the formation of  $\text{Ag}$ – $\text{Ag}$  bonds and folding into a  $2_1$  helix. The larger, and non-coordinating  $\text{PF}_6^-$  and  $\text{ClO}_4^-$  anions, on the other hand, templated the formation of  $3_1$  and  $4_1$  helices, respectively.

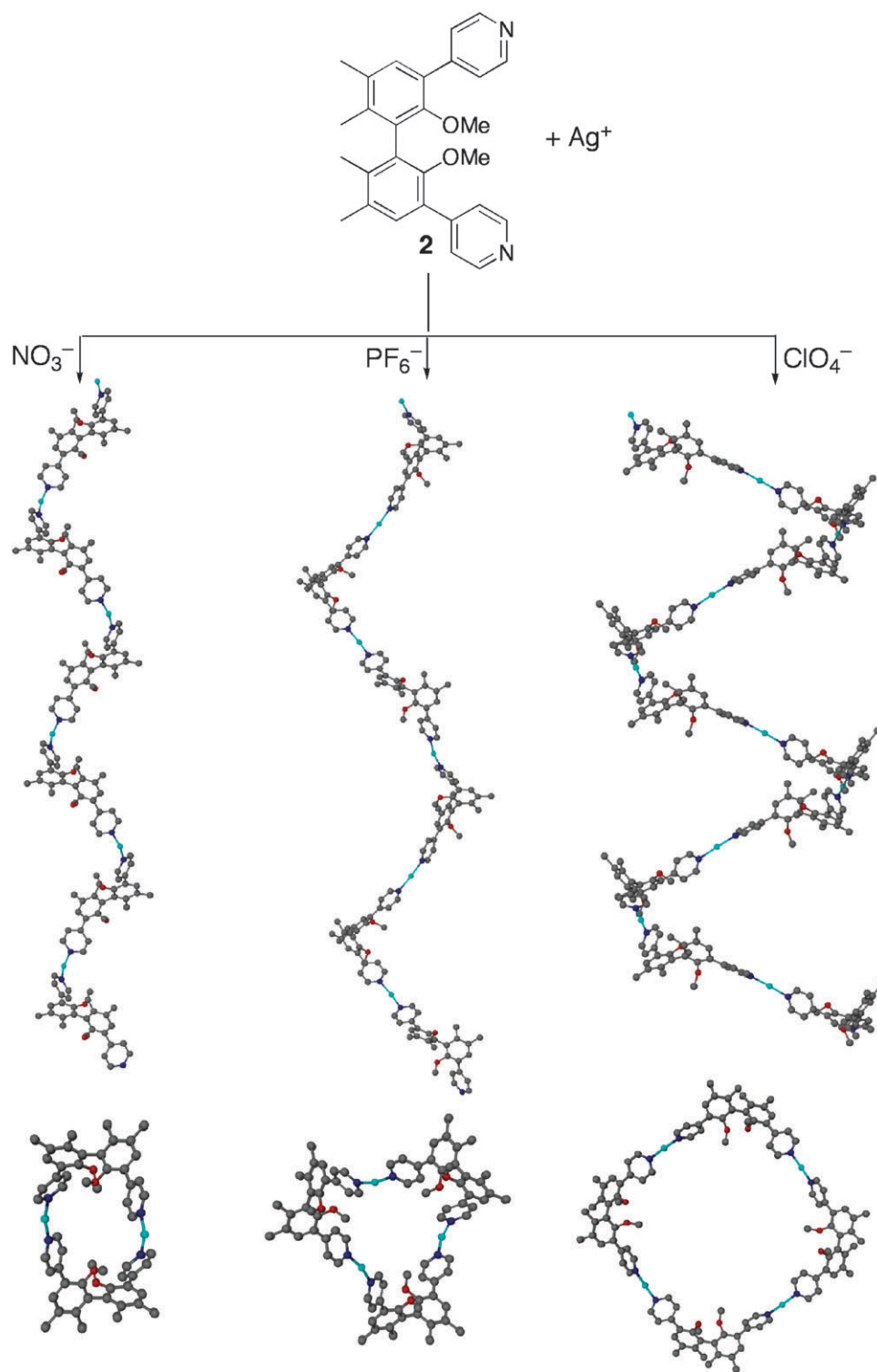
Anion templating played a decisive role in the formation of a Borromean weave coordination polymer from the bis(pyridylurea) ligand **3** and  $\text{AgNO}_3$ , as reported by Steed *et al.* (Fig. 5).<sup>17</sup> The ligand and the silver cation self-assembled into a (6,3) 2D coordination network containing hexanuclear rings connected by trigonal  $\text{Ag}^+$  nodes. The nitrate anions templated the Borromean structure, by chelating to three urea hydrogen-bond donor groups, each belonging to a separate coordination network. Each nitrate is thus coordinatively saturated by six hydrogen bonds. It may be argued that the anion plays here more than just a templating role, acting in the same time as a building unit (*vide infra*), as it enhances the dimensionality of the framework from 2D to 3D.

More recently, Adarsh and Dastidar self-assembled a structurally similar Borromean weave coordination polymer from the bis(pyridylurea) ligand **4** and  $\text{ZnSO}_4$ .<sup>18</sup> In this case, the three independent coordination networks are interlinked by urea hydrogen bonds to a sulfate anion, which plays the role of the template.



### Anions as building units

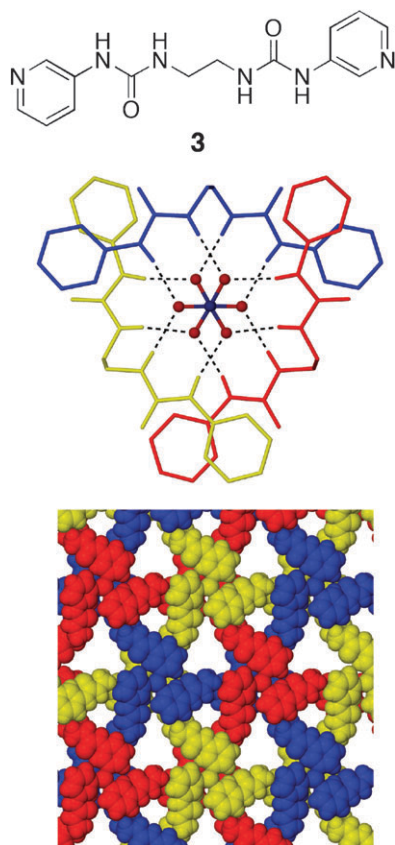
In this role, the anion behaves as a structural link interconnecting the other components in the crystal and thus becoming an integral part of the framework. Two situations may be generally encountered. In the first circumstance, the framework is mainly held together by other components, with the anion playing a secondary role and merely enhancing the connectivity of the framework. This is often the case with coordination polymers, where one can clearly identify the metal–ligand coordination as the primary 'glue' holding the crystal together. The anions then act as dimensionality enhancers, by connecting for instance coordination chains



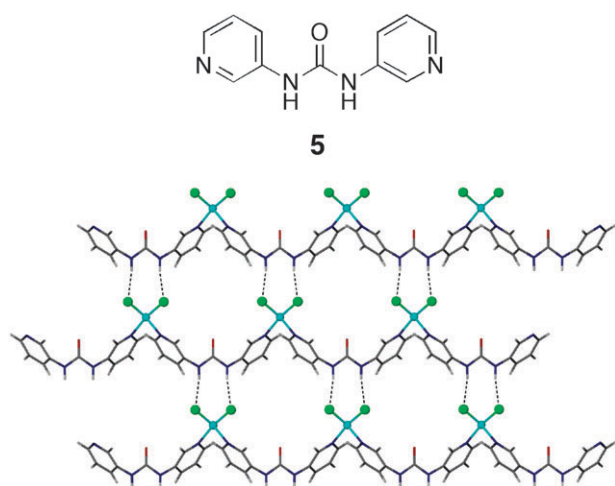
**Fig. 4** Anion-directed self-assembly of **21** (left), **31** (middle), and **41** (right) helical coordination polymers from **2** and  $\text{AgX}$  ( $\text{X} = \text{NO}_3^-$ ,  $\text{PF}_6^-$ ,  $\text{ClO}_4^-$ ).

into layers, or layers into 3D frameworks. One such example is illustrated in Fig. 6, where bis(*m*-pyridylurea) **5** forms 1D coordination chains with  $\text{Zn}^{2+}$ , further linked into 2D layers by  $\text{Cl}^-$  through Zn–Cl coordination bonds and  $\text{Cl} \cdots \text{urea}$  hydrogen bonds.<sup>19</sup>

In the second circumstance, the anion is involved as a primary component holding the crystalline assembly together through strong and directional interactions. Fig. 7 illustrates an example of anions acting as primary building units through strong charge-assisted hydrogen bonding. The dicationic organic

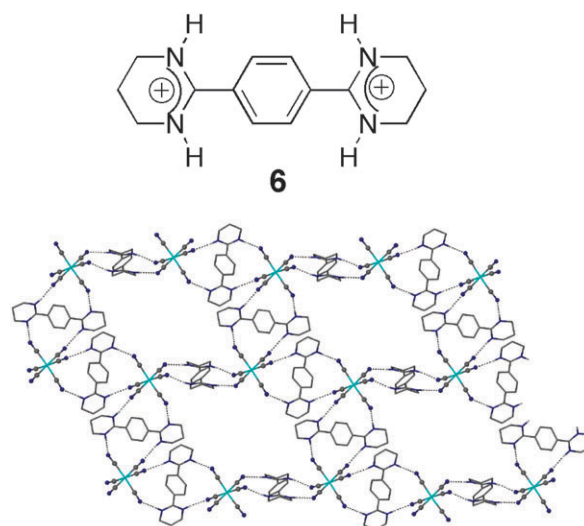


**Fig. 5** Borromean coordination network self-assembled from bis(pyridylurea) ligand **3** (top) and  $\text{AgNO}_3$ . Two nitrate anions, each hydrogen-bonding to three urea groups (middle), link three independent coordination networks into a Borromean weave (bottom).



**Fig. 6** Coordination network self-assembled from bis(*m*-pyridylurea) **5** and  $\text{ZnCl}_2$ . Chains consisting of **5** and  $\text{Zn}^{2+}$  (cyan balls) are linked into layers by  $\text{Cl}^-$  (green balls) through  $\text{Zn}-\text{Cl}$  coordination and  $\text{Cl}^- \cdots \text{urea}$  hydrogen bonds (black dotted lines).

building block **6** self-assembles with  $[\text{M}(\text{CN})_6]^{3-}$  ( $\text{M} = \text{Fe}, \text{Co}$ ) in a 3/2 ratio into a 2D network held together by  $\text{NH}^+ \cdots \text{NC}$  hydrogen bonds.<sup>4</sup> There is a good complementarity between the donor **6** and acceptor  $[\text{M}(\text{CN})_6]^{3-}$ , both acting as



**Fig. 7** Hydrogen-bonded network self-assembled from organic dicationic **6**, and anionic  $[\text{M}(\text{CN})_6]^{3-}$  ( $\text{M} = \text{Fe}, \text{Co}$ ) building blocks. Hydrogen bonds are shown as black dotted lines.

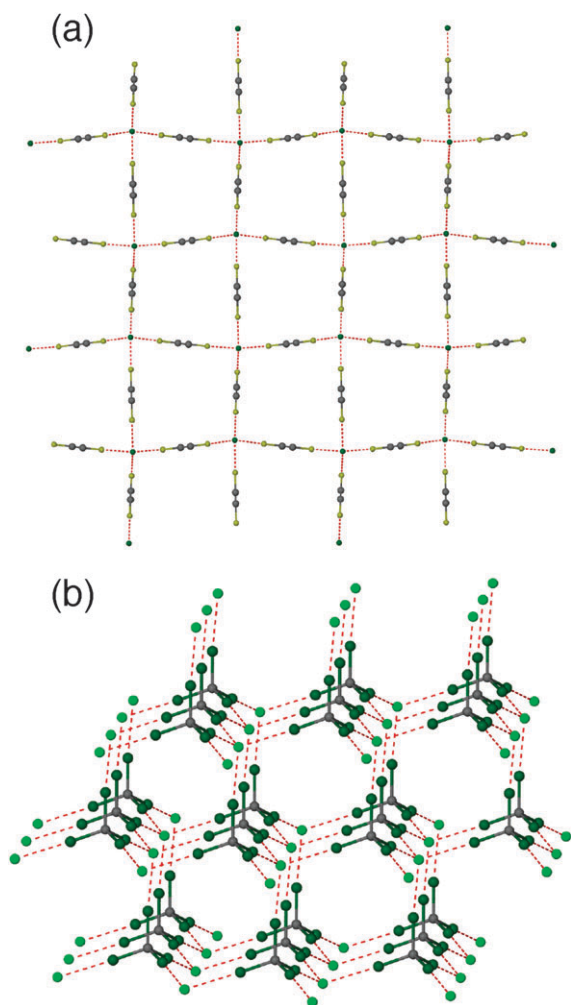
chelators, which results in the complete utilization of all hydrogen bonding groups.

Halogen bonding is another directional interaction that can be exploited for crystal assembly involving anions as building units.<sup>9</sup> Some anions have relatively high charge density, which makes them good halogen-bond acceptors. Chloride anions, for example, can self-assemble into highly symmetrical 2D or 3D structures, by halogen bonding with appropriate donors (Fig. 8). With the linear diiodoacetylene as a donor,  $\text{Cl}^-$  accepts four halogen bonds, leading to a 2D (4,4) network.<sup>20</sup> Using the tetrahedral  $\text{CBr}_4$  donor, on the other hand, a 3D diamondoid halogen-bonded framework is obtained.<sup>13</sup>

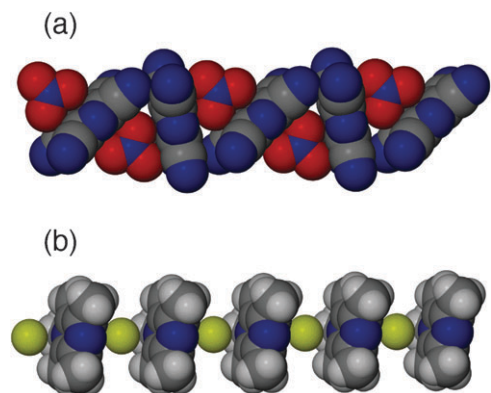
Interactions of anions with electron-deficient arenes have also been exploited for crystal assembly. Kochi *et al.* recently demonstrated that prototypical neutral  $\pi$ -acids such as trinitrobenzene, tetracyanobenzene, and tetracyanopyrazine can self-assemble with various anions like  $\text{SCN}^-$ ,  $\text{NO}_2^-$ ,  $\text{NO}_3^-$ ,  $\text{HSO}_4^-$ ,  $\text{CH}_3\text{SO}_3^-$ , and  $\text{MX}_4^{2-}$  ( $\text{M} = \text{Mn}, \text{Zn}, \text{Cd}$ ;  $\text{X} = \text{Cl}, \text{Br}, \text{I}$ ) into 1D wires.<sup>21</sup> Fig. 9a depicts the molecular wire obtained by self-assembly of tetracyanopyrazine with the nitrate anion. Alternatively, pentamethylpyrazinium cations also form similar molecular wires with anions like  $\text{I}^-$  (Fig. 9b) or  $\text{I}_3^-$ .<sup>14</sup> There is substantial charge transfer between the anions and the arenes, and the anions are situated over the edge of the aromatic rings rather than above their center. These interactions therefore fall in the category of weak  $\sigma$  rather than anion- $\pi$ .<sup>7</sup>

## Anions as secondary building unit (SBU) components

The SBU was originally defined when describing the structures of zeolites<sup>22</sup> and MOFs,<sup>23</sup> as a relatively rigid aggregate or cluster built from simpler components, acting as the basic building block of a framework. The SBU concept is useful for analyzing crystal structures, and does not necessarily imply that such clusters are preformed in solution or can be identified

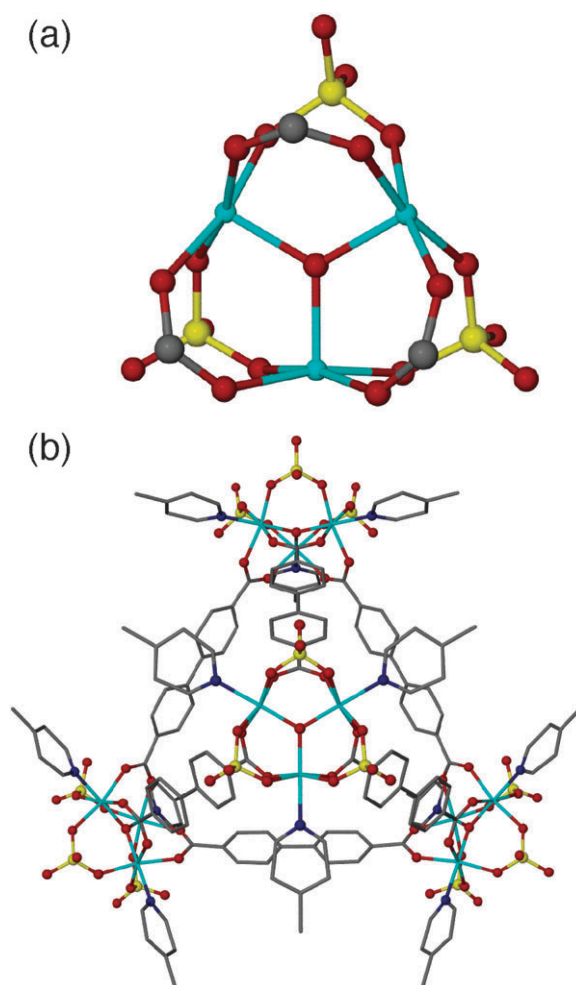


**Fig. 8** Halogen-bonded crystals involving  $\text{Cl}^-$  building units, forming a 2D network with diiodoacetylene (a), or a 3D diamondoid framework with  $\text{CBr}_4$  (b). Halogen bonds are shown as red dotted lines. The  $\text{Ph}_4\text{P}^+$  and  $\text{Et}_4\text{N}^+$ , acting as counterions in the two crystals, respectively, are not shown.



**Fig. 9** Crystal structures of anions with electron-deficient arenes. (a) Molecular wire self-assembled from tetramethylpyrazine and  $\text{NO}_3^-$ . The  $[\text{Na}(15\text{-crown-5})]^+$  counterion is not shown. (b) Molecular wire self-assembled from pentamethylpyrazinium and  $\text{I}^-$ .

as intermediates in the crystallization process.<sup>22,24</sup> From the beginning, some of the early SBUs identified within zeolitic



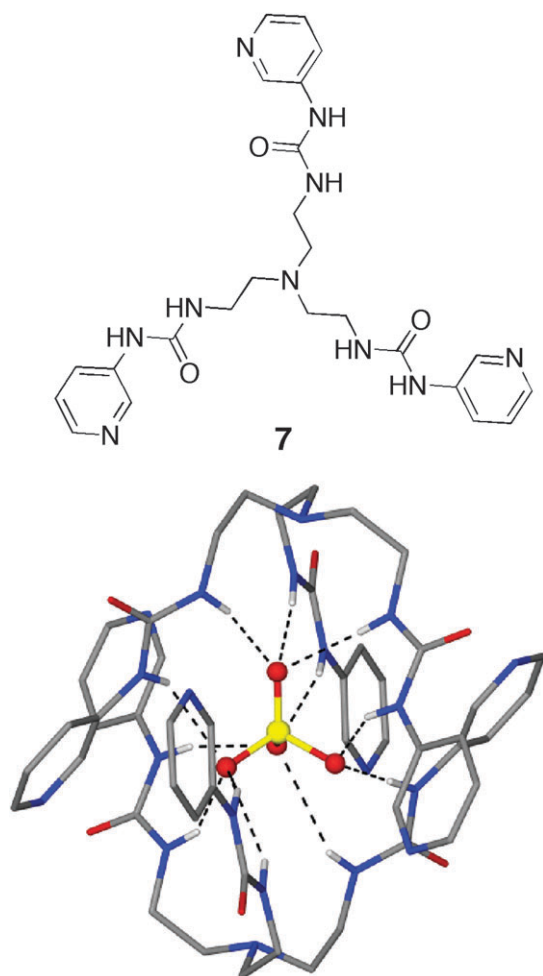
**Fig. 10** (a) Trigonal-prismatic SBU of composition  $[(\text{Fe}_3\text{O})(\text{CO}_2)_3(\text{SO}_4)_3]$ . The Fe centers (cyan balls) are capped by pyridine groups (not shown). (b) Tetrahedral cage self-assembled from 4 SBUs connected by 4,4'-biphenyl linkers. The cages can be further assembled into a MOF by bipyridine linkers.

structures contained anionic components.<sup>22</sup> More recently, anions have been identified as SBU components for the construction of MOFs, hydrogen-bonded frameworks, or molecular crystals.

A sulfate-containing SBU that forms the basis of a MOF is shown in Fig. 10.<sup>25</sup> The trigonal-prismatic SBU is composed of a  $\text{Fe}_3\text{O}$  central core coordinated by three carboxylate ligands and three capping  $\text{SO}_4^{2-}$  anions (Fig. 10a). Pyridine groups also cap the three Fe centres. Four such trigonal-prismatic SBUs can act as vertices of a tetrahedral cage, joined together by dicarboxylate linkers (Fig. 10b). The tetrahedral cages can be further linked into an extended porous MOF by replacing the monopyridine caps by bipyridine linkers. The sulfate anions do not play any connectivity role in the framework, but are nevertheless important components of the basic SBU in this hierarchical structure.

Sulfate anions are central components of SBUs based on the tris(pyridylurea) ligand **7**, developed independently by Custelcean *et al.*<sup>26</sup> and Wu *et al.*<sup>27,28</sup> Ligand **7** belongs to a series of tren-based anion receptors designed to be





**Fig. 11** Sulfate encapsulation in the crystalline state by two molecules of **7**, through the formation of 12 hydrogen bonds from the six urea donors.

complementary to  $\text{SO}_4^{2-}$  and other tetrahedral oxoanions, by providing six hydrogen bonds from its three urea groups.<sup>29,30</sup> Two such ligands can fully encapsulate sulfate, saturating its coordination sphere with 12 hydrogen bonds (Fig. 11), and resulting in an SBU with quasi- $S_6$  symmetry.

Both  $[(\text{SO}_4)(\mathbf{7})]^{2-}$  (**A**) and  $[(\text{SO}_4)(\mathbf{7})_2]^{2-}$  (**B**) can act as SBUs for the assembly of coordination and hydrogen-bonded frameworks, as illustrated in Fig. 12. These SBUs form and persist in water–methanol mixtures, as demonstrated by ESI-MS.<sup>28</sup> The nature of the resulting frameworks depends on the cation present. Thus, in the presence of  $\text{Fe}(\text{DABP})_3^{2+}$  (DABP = 4,4'-diamino-2,2'-bipyridine) the  $C_3$ -symmetrical SBU **A** is formed, leading to a 2D network with BN topology linked by hydrogen bonds between the NH donors of the cation and urea C=O acceptors from **A**.<sup>28</sup> When the cation is  $\text{M}(\text{H}_2\text{O})_6^{2+}$  (M = Mg, Zn, Mn, Co, Cd), the quasi-octahedral SBU **B** is formed, connected into a 3D framework with NaCl topology *via* water hydrogen bonding to the urea C=O and pyridine groups of **B**.<sup>26,27</sup>

In the presence of  $\text{Li}(\text{H}_2\text{O})^+$  as the cation, **B** adopts a geometry with perfect  $S_6$ -symmetry and forms a cubic framework with pyrite ( $\text{FeS}_2$ ) topology.<sup>31</sup> In this structure, each

$\text{Li}(\text{H}_2\text{O})^+$  cation acts as a  $C_3$ -symmetrical node, connecting three units of **B** by  $\text{C}=\text{O} \cdots \text{Li}$  coordination and pyridine  $\cdots \text{H}_2\text{O}$  hydrogen bonds. It could be argued that in these examples, sulfate acts not just as an SBU component, but also as a template for the formation of **A** and **B**, and of their corresponding frameworks, respectively.

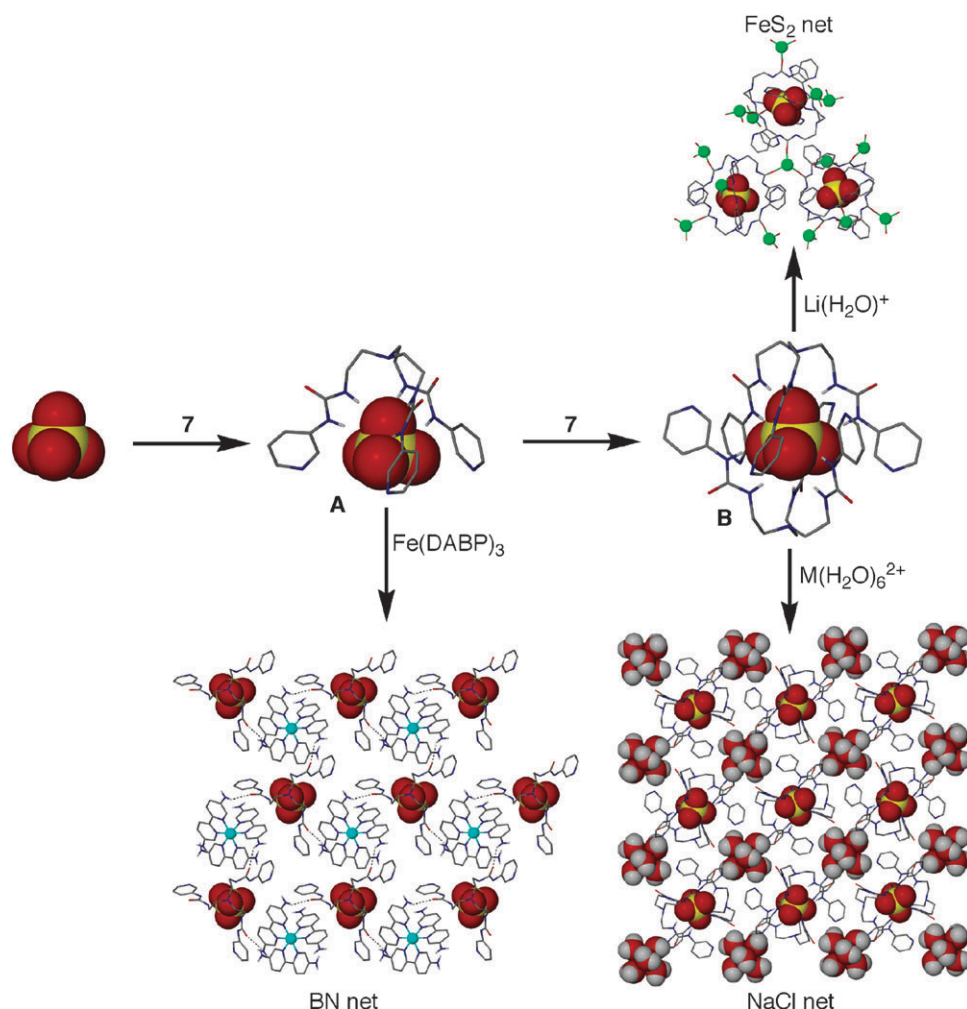
Sulfate or nitrate can also form  $C_3$ -symmetrical SBUs with the cationic ligand **8**, with the anions accepting 12  $\text{NH} \cdots \text{O}$  hydrogen bonds from three component ligands. The resulting SBU acts as a 6-connecting node, assembling into a cubic crystal *via*  $\text{CH} \cdots \text{O}$  and  $\text{CH} \cdots \pi$  interactions (Fig. 13).<sup>32</sup>

## Anion separation by selective crystallization

Inclusion of an anion in a crystal involves mutual recognition between the anion and the ensuing crystal lattice. In the previous sections we asked how anions influence or control the structures of crystals. It is equally important to consider the reverse question: how does a particular crystalline environment determine what anions are included? This is equivalent to asking: given a series of anions in solution, which anion will form the most stable (least soluble) crystal? Such a question pertains to selective separation of anions through crystallization,<sup>33,34</sup> which is relevant to many environmental applications. In trying to address this question, one needs to remember that the crystallization process involves, in addition to crystal lattice formation, desolvation of all components, including the anions. If crystallization is done from water (really the only environmentally relevant solvent), it has been observed that the larger, more charge-diffuse anions are typically preferred, due to their comparatively lower free energy of hydration. This is the so-called Hofmeister bias,<sup>33</sup> which dictates that crystallization of less hydrophilic anions, such as  $\text{NO}_3^-$  ( $\Delta G_h^\circ = -306 \text{ kJ mol}^{-1}$ ) is inherently favored over that of strongly hydrophilic ones, such as  $\text{SO}_4^{2-}$  ( $\Delta G_h^\circ = -1080 \text{ kJ mol}^{-1}$ ). This bias can be reversed by selecting a crystal environment that is highly stabilizing to anions, for example through the formation of hydrogen bonds that are stronger than those offered by the water solvent.<sup>35</sup> However, in the absence of steric constraints, with the crystal lattice being able to freely rearrange and optimize the binding of all competing anions, the resulting selectivity is still biased, with the anions that now are the strongest H-bond acceptors (strongest bases) being preferred (*e.g.*,  $\text{CO}_3^{2-}$  favored over  $\text{SO}_4^{2-}$ ). Then how can peak selectivity for a particular anion be achieved by crystallization? It turns out that two conditions need to be satisfied for realizing peak selectivity: (i) the anion-binding sites in the crystal must be complementary to the targeted anion, which requires that the binding groups be arranged in such a way as to recognize the anion's shape; and (ii) the crystal must have organizational rigidity, implying both lattice stiffness and inability to rearrange into other frameworks, so the binding sites cannot rearrange to accommodate undesired anions.<sup>33,34</sup>

For rationalizing the anion selectivity observed in competitive crystallizations, it is convenient to analyze series of isomorphous crystals (same space group and packing, and close lattice parameters), so the observed trends can be directly correlated





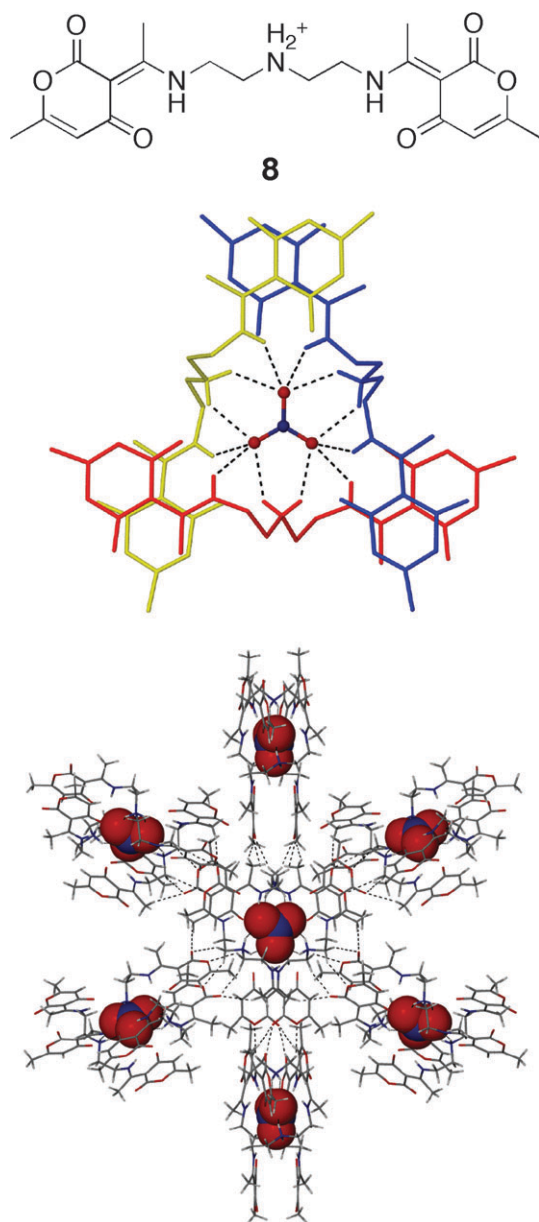
**Fig. 12** Self-assembly of SBU **A** into a BN-type net with  $\text{Fe}(\text{DABP})_3^{2+}$ , and of SBU **B** into a NaCl-type net with  $\text{M}(\text{H}_2\text{O})_6^{2+}$ , and a  $\text{FeS}_2$ -type net with  $\text{Li}(\text{H}_2\text{O})^+$ .

to the anion coordination geometries measured by X-ray diffraction. Otherwise, if completely different crystal structures are obtained with different anions, the interpretation of the observed selectivity becomes very difficult, as many factors such as dimensionality of the framework, packing efficiency, or nature of the groups exposed on crystal surfaces may determine the relative solubilities and thereby anion selectivities. Next, some recent examples of anion separation by selective crystallizations, studied in our group, will be presented to illustrate these concepts.

The bis(*m*-pyridylurea) **5** self-assembles into an isomorphous series of crystalline hydrogen-bonded helices in the presence of one equivalent of  $\text{HX}$  ( $\text{X} = \text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{NO}_3^-$ ,  $\text{ClO}_4^-$ ) (Fig. 14).<sup>36</sup> The helices were formed as a result of monoprotection of one of the pyridine groups of **5**, which then hydrogen-bonded to the free pyridine group of the adjacent ligand, symmetry-related to its neighbor by a  $2_1$  screw axis. The orthogonal urea groups therefore remained available for binding the anions, which also formed  $\text{CH}\cdots\text{X}$  hydrogen bonds and weak  $\sigma$  interactions with the pyridine groups. This binding environment is rather generic, and does not provide specific shape recognition to any particular anion.

Furthermore, crystal structure analyses revealed that these helices are quite flexible, contracting or expanding as necessary to accommodate each anion. This is therefore a good example of a crystalline system with weak anion complementarity and poor organizational rigidity. Accordingly, competitive crystallization experiments in water indicated a selectivity trend that largely followed the increase in anions' free energy of hydration (Hofmeister bias):  $\text{I}^- > \text{ClO}_4^- > \text{NO}_3^- > \text{Br}^- > \text{Cl}^-$ .

Let's examine now a crystalline system with strong charge and shape recognition, and high organizational rigidity, and the impact these factors have on anion selectivity. Crystallization of **7** with  $\text{MgSO}_4$  from water afforded crystals with the composition  $\text{MgSO}_4(\text{7})_2(\text{H}_2\text{O})_6$ , in which  $\text{SO}_4(\text{7})_2$  capsules are linked by  $\text{Mg}(\text{H}_2\text{O})_6^{2+}$  cations into a 3D hydrogen-bonded framework with NaCl topology (Fig. 12).<sup>26</sup> The capsules are highly complementary to sulfate, providing 12 hydrogen bonds from the six urea groups functionalizing the cavities (Fig. 11). As a result of the charge mismatch relative to the  $\text{Mg}(\text{H}_2\text{O})_6^{2+}$  dications, all monoanions are completely excluded. This allowed exclusive separation of sulfate from 100-fold excess of  $\text{NaNO}_3$ , despite the huge difference in the free energy of hydration between the two anions that strongly



**Fig. 13**  $C_3$ -Symmetrical  $[(NO_3)(8)_3]^{2+}$  SBU and its self-assembly into a cubic framework.

favors nitrate. Crystallization of these capsules may therefore potentially offer a solution to sulfate separation from legacy nuclear waste, which is otherwise difficult to vitrify owing to the low solubility of this anion in borosilicate glass.<sup>37</sup> Even more remarkable was the fact that sulfate was selectively separated against dianions of different shape, like trigonal-pyramidal  $SO_3^{2-}$  or trigonal-planar  $CO_3^{2-}$ , despite the fact that these anions are intrinsically stronger H-bond acceptors than  $SO_4^{2-}$ . X-Ray structural analysis indicated that while sulfite and carbonate formed crystals that were isomorphous with the sulfate analogue, they did not fit well inside the capsules, engaging in repulsive  $NH \cdots S$  and  $NH \cdots C$  interactions.<sup>26</sup> Equally important, the crystalline capsules proved to be exceptionally rigid, not distorting their shape to avoid these repulsive interactions and optimize the binding of  $SO_3^{2-}$

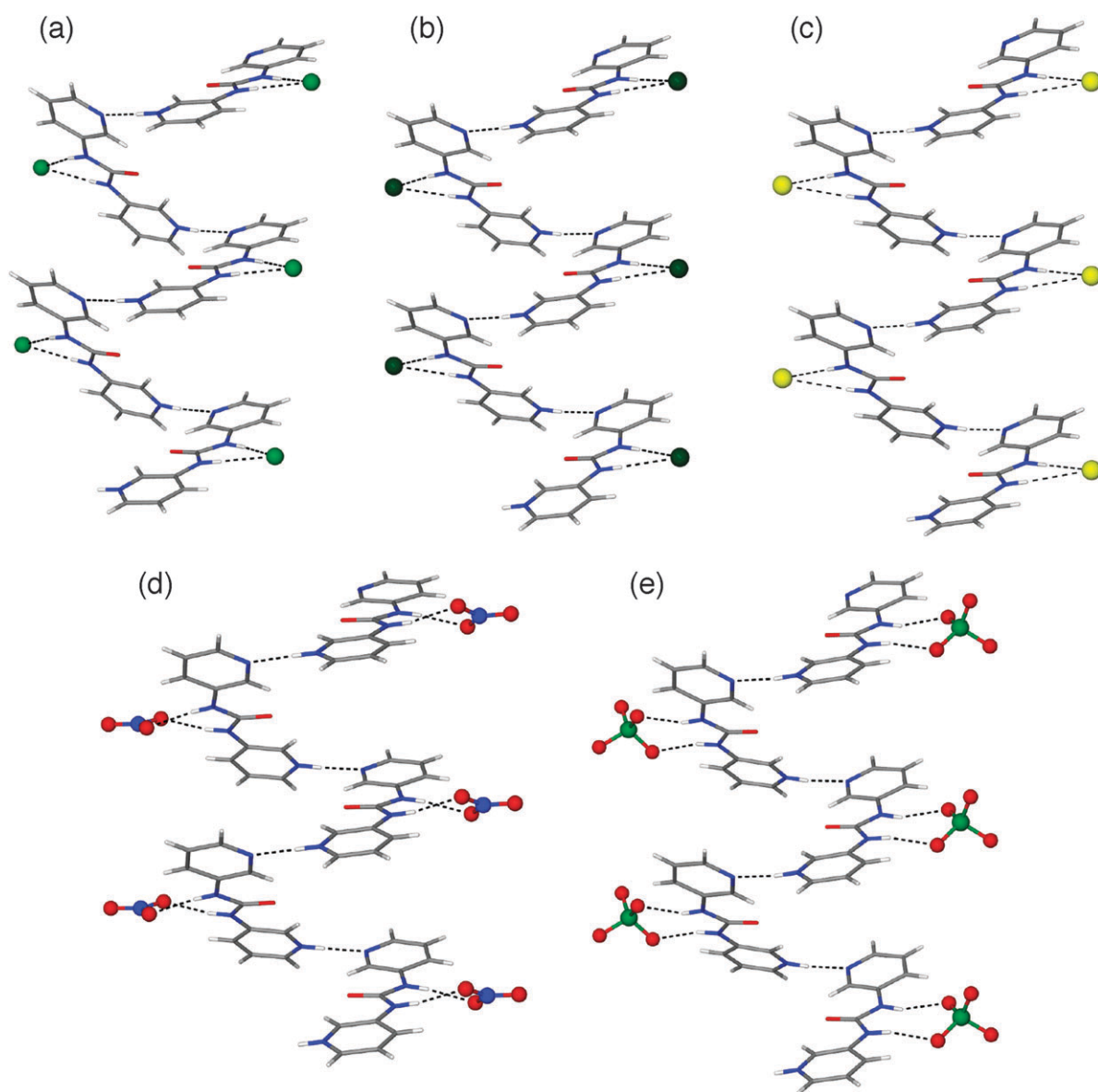
and  $CO_3^{2-}$ . On the other hand, the sulfate selectivity over selenate, which has similar tetrahedral shape but slightly larger size, was found to be modest (selectivity factor of 5) due to the tendency of the two anions to form solid solutions. Thermodynamic measurements showed that crystallization of the capsules is highly exothermic, with the most favorable enthalpy of crystallization of  $-99.1$  and  $-108.5$   $\text{kJ mol}^{-1}$  corresponding to sulfate and selenate, respectively, in agreement with the structural data. In direct contrast, sulfite has a much lower enthalpy of crystallization of  $-64.6$   $\text{kJ mol}^{-1}$ , consistent with its poor fit inside the capsule. Entropy, however, had a compensatory effect, strongly favoring sulfite and thereby offsetting some of the enthalpic advantage of the tetrahedral anions.<sup>38</sup>

When **7** was cocrystallized with  $Li_2SO_4$ , similar sulfate-encapsulating capsules were formed, linked by  $Li(H_2O)^+$  cations into a cubic framework with pyrite topology (Fig. 12). Compared with the previous system, these capsules are almost  $0.5$  Å shorter (measured between the tertiary N atoms of the two ligands). As a result, significantly higher selectivity for sulfate over the larger selenate was observed, which even surpasses the selectivity of the sulfate-binding protein.<sup>31</sup>

## Conclusions

Anions may play important roles in crystals, engaging in relatively strong and specific interactions such as metal coordination, hydrogen bonding, halogen bonding, and anion- $\pi$  (or weak  $\sigma$ ) interactions. From a structural perspective, anions often decisively influence crystal structures, by acting as templates, or/and participating directly to crystal assembly as building units or SBU components. Like in the case of crystal engineering with neutral building blocks, structure prediction of the anion-containing crystals remains a challenge. Nevertheless, as our understanding of anions' intermolecular interactions in crystals continues to improve, so will the accuracy of the crystal design involving anionic components.

A different, recently explored facet of crystal engineering with anions is concerned with selective anion separation by competitive crystallization. In this approach, the crystal may be considered as an extended 'host' that selectively includes an anion 'guest' from an anionic mixture upon self-assembly. Like in the case of traditional anion receptors in solution, crystal functionalization with strong and specific binding groups spatially oriented to complement the shape of the targeted anion, in combination with a high degree of organizational rigidity, is typically needed to overcome the anion solvation and realize high selectivities. Though some success along this direction has been achieved, obtaining predetermined selectivities through accurate design of the anion-binding sites in crystals will likely continue to be a grand challenge for years to come. Meanwhile, the empirical method, based on systematic studies of structure/selectivity relationships in crystals, remains a valuable approach that will contribute to our understanding of the anion selectivity principles in crystallizations, and potentially offers solutions to real-world problems requiring selective anion separations.



**Fig. 14** Isomorphous series of crystalline hydrogen-bonded helices of **5-HX**;  $X = \text{Cl}^-$  (a),  $\text{Br}^-$  (b),  $\text{I}^-$  (c),  $\text{NO}_3^-$  (d), and  $\text{ClO}_4^-$  (e). Reproduced with permission from ref. 36.

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