Thermodynamic and Kinetic Effects in the Crystallization of Metal-Organic Frameworks

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CONSPECTUS

The evolution of metal-organic frameworks (MOFs) has been one of the most exciting aspects of materials chemistry over the last 20 years. In the present article we discuss the development during this period in our understanding of the factors that control the crystallization of MOFs from solution. Both classical porous MOFs as well as dense MOF phases are considered. This is an opportune time at which to examine this complex area because the experimental tools now available to interrogate crystallization processes have matured significantly in the last 5 years, particularly with the use of *in situ* synchrotron X-ray diffraction. There have also been impressive developments in the use of Density Functional Theory (DFT) to treat not only the energies of very complex structures but also their entropies. This is particularly important in MOF frameworks because of their much greater flexibility compared with inorganic structures such as zeolites.

The first section of the article describes how early empirical observations on the crystallization of dense MOFs pointed to a strong degree of thermodynamic control, with both enthalpic and entropic factors playing important roles. For example, reactions at higher temperatures tend to lead to denser structures with higher degrees of frameworks connectivity and lower levels of solvation, and polymorphs tend to form according to their thermodynamic stabilities. In the case of metal tartrates, these trends have been validated by calorimetric studies. It has been clear for more than a decade, however, that certain phases crystallize under kinetic control, especially when a change in conformation of the ligand, or coordination around a metal center, might be necessary to form the thermodynamically preferred product. We describe how this can lead to time-dependent crystallization processes that evolve according to the Ostwald Rule of Stages and can be observed by *in situ* methods.

We then consider the crystallization of porous MOFs, which presents additional challenges because of solvation effects. In spite of these problems, much has been learnt about the energetics of the underlying frameworks, where the relationship between porosity and stability initially seemed to mirror the behavior of zeolites, with more porous structures being less stable. Recently, however, this simple relationship has had to be reconsidered with the emergence of some very flexible structures wherein the open structures are more stable than their denser analogues at finite temperatures due to their large vibrational entropies.

In the final section we describe how the concepts developed in the MOF work have been extended into the closely-related area of hybrid organic-inorganic perovskites. We describe recent studies on polymorphism in hybrid perovskites, which is amenable to total free energy calculations using a combination of DFT and lattice dynamics methods.

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▪ INTRODUCTION

Over the past 10-15 years, research on crystalline metal-organic frameworks (MOFs) has evolved into one of the fastest growing areas of chemistry and materials science. Most of the focus has been on porous MOFs,¹ but there has also been growing interest in *dense* MOF frameworks,² and both groups offer a limitless range of chemical and structural diversity along with vast opportunities for creating technologically relevant properties.³ Due to their relatively high surface areas and chemical tuneability, porous MOFs such as the zeolitic imidazolate frameworks (ZIFs) were initially seen primarily as promising materials for gas storage, separations and catalysis,⁴ but recently the flexibility and defect chemistry of frameworks has grown in prominence,^{5,6} with fascinating opportunities in areas such as chemical sensing. Dense MOFs, on the other hand, can exhibit fascinating multiferroic⁷ and electronic⁸ properties, opening up a wide range of alternative applications. In spite of the importance of this growing class of exciting materials, the fundamental energetics of MOF synthesis are not well understood, with the consequence that much of the synthetic work in the area is carried out empirically. The present article addresses this issue by discussing the developments over the last 10-15 years in our understanding of the factors that control the crystallization of MOFs from solution. This is an opportune time at which to examine this complex area because the experimental and computational tools now available for investigating crystallization processes have matured significantly in the last 5 years.

We shall set the scene in the next section by describing early empirical observations *ca.* 2004 on reactions at different temperatures that pointed to a strong degree of thermodynamic control during MOF synthesis. Both enthalpic and entropic factors were clearly at play in these experiments, but it soon became apparent (*ca.* 2006) that certain phases formed under kinetic control, especially when a change in

conformation of the ligand might be necessary to form the thermodynamically preferred product. Our understanding of these effects was greatly enhanced about a decade ago by further developments in Density Functional Theory (DFT), which enabled an assessment of the relative stabilities of structurally complex MOFs, at first from an enthalpic perspective but also, more recently, including entropic contributions. We shall then show that developments in *in situ* synchrotron X-ray methods now enable us to map out a quantitative reaction profile for the successive formation of a series of polymorphs.

▪ EARLY WORK ON METAL DICARBOXYLATES – EVIDENCE FOR THERMODYNAMIC CONTROL

Much of the early work on porous MOFs focused on the use of *rigid*, aromatic carboxylate ligands, such as benzene 1,4-dicarboxylate, which was used by Yaghi and co-workers to construct the iconic, Zn-based MOF-5 in 1999,⁹ and benzene 1,3,5-tricarboxylate, which the Williams group used to prepare Cu-containing HKUST-1 in the same year.¹⁰ At about the same time, and in collaboration with the late Gérard Férey in Paris, we began to explore the use of *flexible* dicarboxylates, diphosphonates and carboxyphosphonates in combination with a range of transition metals. In contrast to the case with rigid linkers, the strategy often led to *dense* rather than porous frameworks, such as a family of Ni(II) methylene-diphosphonates, $\text{Ni}_4(\text{O}_3\text{P-CH}_2\text{-PO}_3)_2 \cdot n\text{H}_2\text{O}$ ($n = 0, 2, 3$).¹¹ What was particularly interesting, however, was the fact that dimensionality of the phases increased due to the loss of water and condensation of the NiO_x polyhedra when the layered trihydrate was heated, leading to an interesting family of 3-D ferromagnetic frameworks. This was, perhaps, the first clear sign of the thermodynamic control of framework architecture, albeit carried out by post-synthesis treatment rather than during the synthesis itself.

Shortly afterwards in the early 2000s, we carried out a series of reactions between $\text{Co}(\text{OH})_2$ and succinic acid in water, wherein the only variable was the reaction temperature.¹² The formation of five distinct cobalt succinates at different temperatures enabled the relationship between reaction temperature and phase behavior to be definitively established. A clear set of trends emerged: with increasing reaction temperature from 60 °C to 250 °C, the density, dimensionality and number of coordinated Co^{2+} ions per succinate ligand in the products increased, while hydration decreased (Figure 1). The main driving force for such trends was clearly the entropic gain associated with the release of water molecules from confinement in the solid state to the relative freedom of the aqueous state. Thus, the vacated coordination sites on Co^{2+} became filled either by hydroxide ions or carboxylate ligands, resulting in increased connectivity between metal centers and simultaneous densification of the framework. This result provided clear evidence for thermodynamic control during MOF synthesis, and provided a blueprint for using temperature to control the outcome of a reaction.

Figure 1. Progression of the five phases of cobalt succinate, from low temperature (far left) to high temperature (far right) in the same reaction mixture. Adapted from with permission from ref. 12. Copyright 2004 The Royal Society of Chemistry.

Further investigation of the same system using high-throughput methods¹³ revealed the additional importance of other reaction variables, including pH, concentration and time. Increasing the fraction of the $\text{Co}(\text{OH})_2$ precursor, which acted to increase the pH, had a similar effect to increasing temperature by promoting condensation of Co-O-Co connectivity. On the other hand, concentration and time had much less effect on the phase behavior, except to allow the formation of kinetic products at very short times (in this case less than 1 day) and very low concentrations. One side-effect of decreasing concentration was to qualitatively increase the size of crystals produced, which is likely to occur as a result of having fewer nucleation sites.

▪ ZINC DICARBOXYLATES - EVIDENCE FOR KINETIC CONTROL

In the case of 2-dimensional zinc 4-cyclohexene-1,2-dicarboxylates,¹⁴ temperature was again found to be the critical factor in determining the phase behavior between a hydrated compound and two anhydrous analogues. The hydrated phase, $\text{Zn}(\text{C}_8\text{H}_8\text{O}_4) \cdot 2\text{H}_2\text{O}$, forms at temperatures $< 100^\circ\text{C}$, but at 150°C it is replaced by $\alpha\text{-Zn}(\text{C}_8\text{H}_8\text{O}_4)$, which is converted to a denser, isomorphous phase, $\beta\text{-Zn}(\text{C}_8\text{H}_8\text{O}_4)$ at higher temperatures and longer reaction times. Plane wave based DFT calculations revealed that the hydrate is more stable than the anhydrous phases by $\sim 100 \text{ kJ mol}^{-1}$, indicating that, as in the case of the Co-succinates, the driving force towards dehydration at high temperatures is entropic in origin. Between the two anhydrous analogues, the denser β phase, which contains the ligand in the *trans*-configuration, is more stable by $\sim 13.5 \text{ kJ mol}^{-1}$. However, owing to the *cis*-cyclohexene dicarboxylic acid being the starting reagent, the barrier to ligand isomerization is enough initially

to permit the kinetic crystallization of the α phase, which contains the same ligand configuration. Therefore, in contrast to evidence at the time that most hydrothermal syntheses of MOFs proceeded under thermodynamic control, kinetics also play an important role in the delicate balance at higher temperatures between the rate of ligand isomerization and the rates of formation of the MOF products.

If, on the other hand, the starting mixtures are different but have the potential to form the same product, it may reasonably be expected that thermodynamic conditions will lead to the most stable phase in all cases. This scenario was observed in the layered zinc 1,2-cyclohexane dicarboxylates (Figure 2),¹⁵ in which a racemic mixture of starting ligands did not spontaneously resolve into separate homochiral MOFs, despite the crystal structure of the chiral isomer being over 8 % denser than its racemic analogue and thus potentially more energetically favorable (we shall discuss the relationship between density and stability below in the context of ZIFs). Instead, DFT calculations, which showed excellent agreement with calorimetry, revealed that stronger intra-layer dispersion interactions in the racemic phase far outweigh weaker inter-layer ones, while the Coulomb forces are very similar in all cases. Therefore, the racemic isomer formed from racemic starting materials in preference to a chiral conglomerate, and is more stable in spite of being less dense. Similar ligand-directed stacking preferences have been observed in porous layered aluminium diphosphonates¹⁶ and dense manganese dicarboxylates.¹⁷

Figure 2. Configurations of a) *trans*-*R,R*- and b) *trans*-*S,S*-cyclohexane dicarboxylic acid, and extended crystal structures of c) the racemic Zn-dicarboxylate, **1**, and d) the homochiral Zn-dicarboxylate, **2**. Reproduced with permission from ref. 15. Copyright 2008 John Wiley and Sons.

▪ METAL TARTRATES – CONTROL OF CHIRALITY

Tartaric acid, (C₄H₆O₆), exists in two chiral (L- and D-) forms, one achiral (*meso*-) and one racemic (D,L-) form. This diversity gives rise to the potential to form MOFs with

multiple structural isomers and intrinsic homochirality in the chiral forms, which lends itself to important applications in ferroelectricity, catalysis, optics and magnetism. In 2007, we reported that hydrothermal syntheses between 100 °C and 200 °C resulted in the formation nine different magnesium tartrates.¹⁸ All three ligand systems studied – *meso*-, D- and D,L- – showed decreasing hydration and more extended connectivity with increasing temperature (Table 1). This phase behavior suggested, as with the cobalt succinates,¹² that the reactions proceeded under thermodynamic control and entropic release of water was the major driving factor.

	Racemic (D, L)	Chiral D-	Meso-
200 °C	Structure 4 Conglomerate Mg(<i>D</i> -tart)·H ₂ O / Mg(<i>L</i> -tart)·H ₂ O C222 ₁ 3-D Mg/1000Å ³ : 5.65	Structure 4 Chiral Mg(<i>D</i> -tart)·H ₂ O C222 ₁ 3-D Mg/1000Å ³ : 5.65	Structure 9 Mg(<i>m</i> -tart) C2/c 3-D Mg/1000Å ³ : 7.04
180 °C	Structure 4 Conglomerate Mg(<i>D</i> -tart)·H ₂ O / Mg(<i>L</i> -tart)·H ₂ O C222 ₁ 3-D Mg/1000Å ³ : 5.65	Structure 4 Chiral Mg(<i>D</i> -tart)·H ₂ O C222 ₁ 3-D Mg/1000Å ³ : 5.65	Structure 8 Mg(<i>m</i> -tart)(H ₂ O) ₂ P2 ₁ /c 1-D Mg/1000Å ³ : 5.2
125-150 °C	Structure 2 Racemic Mg(<i>D,L</i> -tart)(H ₂ O)·H ₂ O P2/c 2-D Mg/1000Å ³ : 5.4	Structure 4 Chiral Mg(<i>D</i> -tart)·H ₂ O C222 ₁ 3-D Mg/1000Å ³ : 5.65	Structure 7 Mg(<i>m</i> -tart)(H ₂ O) ₂ ·H ₂ O Pbca 1-D Mg/1000Å ³ : 4.7
100 °C	Structure 1 Racemic Mg(<i>D,L</i> -tart)(H ₂ O) ₂ ·3H ₂ O Pban 0-D Mg/1000Å ³ : 3.6	Structure 3 Chiral Mg(<i>D</i> -tart)(H ₂ O)·1.5H ₂ O P2 ₁ 2 ₁ 2-D Mg/1000Å ³ : 4.95	Structure 6 Mg(<i>m</i> -tart)(H ₂ O) ₂ ·H ₂ O P2 ₁ /n 1-D Mg/1000Å ³ : 4.7

Table 1. Compositions, space groups, dimensionalities and Mg atom density of magnesium tartrates formed between 100 °C and 200 °C. Reproduced with permission from ref. 18. Copyright 2007 American Chemical Society.

An extended investigation into the other alkaline earth metal (Ca, Sr and Ba) tartrates in 2009 revealed similar thermodynamic trends in hydration and connectivity, showing in particular that removing water serves to condense metal units within the structures.¹⁹ However, the observation of “disappearing polymorphs”²⁰ in the hydrated strontium tartrates indicated that kinetic effects, particularly relating to the nucleation of different phases, could be important. In addition, ligand isomerization was observed for Sr and Ba but not Ca, suggesting that nature of the metal ion affects such processes.

Furthermore, this system provided a rare opportunity to investigate the relative stabilities of three pairs of anhydrous polymorphs (*meso*- and L- for Ca and Sr, L- and D,L- for Ba) by computation and calorimetry. The *meso*- Ca and Sr phases were shown to be more stable than their chiral polymorphs by 9.1 kJ/mol and 13.4 kJ/mol, respectively, in good agreement with experiment (2.9 ± 1.6 kJ/mol and 8.2 ± 1.4

kJ/mol, respectively). In the case of Ba, the L- phase was more stable but found experimentally to form only at low temperatures: it was replaced at higher temperatures by its racemic analogue. This was perhaps the first indication that entropic factors could determine phase stability in anhydrous structures, and the beginning of our interest in the entropy of the MOFs themselves. This interest has led to, amongst others, the use of first principles calculations to quantify the entropy differences of metal formate MOFs²¹ and will be discussed further in later sections.

More recently, our studies have focused on lithium tartrates, which include eight different anhydrous polymorphs of formula $\text{Li}_2(\text{tartrate})$.²²⁻²⁴ Relative energies from DFT – including dispersion corrections and vibrational contributions – were found to correlate with density (Figure 3), indicating again that dispersion forces play a central role in phase stability.

Figure 3. Correlation between the calculated relative energies and density in anhydrous dilithium tartrates. Reproduced with permission from ref. 24. Copyright 2013 American Chemical Society.

A study of different isomers, temperatures and solvents revealed that lithium tartrate phase behavior depended on a complex interplay between several thermodynamic and kinetic factors (Fig. 4).²² The fundamental importance of solvent was clearly demonstrated in water:ethanol mixtures, which generally gave rise to more thermodynamically stable products than pure ethanol. Calculations had shown that low energy (heavy atom backbone) vibrational modes gave substantial contributions to relative energies at room temperature; this was borne out in the formation of low energy products **6** (*meso*-), **9** (L-) and **8** (D,L-) from water:ethanol. Reactions in ethanol were also subject to an alternative form of thermodynamic control: phases such as **2** (L-) and **4** (*meso*-) that contained weaker, more entropically favourable hydrogen bonds were observed in increasing amounts as the temperature was increased.

Phase behavior appeared to be complicated by a number of kinetic factors, most noticeably in the changes in binding mode and ligand conformation between reactants and products. More pronounced changes were found to require harsher conditions to come into effect, such that more stable phases replaced metastable polymorphs as

solvent polarity and temperature were increased. For example, in water:ethanol mixtures the solution-stable *gauche*-form of *meso*-tartaric acid and Li binding by chelation are reflected in the formation of metastable phase **7** at low temperatures. Temperatures above 100 °C result in a conformational change to the global thermodynamic product, **6**, which features the *trans*- ligand and monodentate tartrate binding. On the other hand, the kinetic barrier to ligand isomerization – *configurational* change – was overcome above 180 °C, such that **6** could form irrespectively of the starting materials.

Figure 4. Phase behavior of lithium tartrates; the colours of each box represent the mixture of phases produced from a particular combination of ligand isomer, solvent system and temperature. Phases are numbered as in ref. 22; **2-9** are anhydrous dilithium tartrates; phase **13** is $\text{LiH}(\text{L-C}_4\text{H}_4\text{O}_6)(\text{H}_2\text{O})$. Reproduced with permission from ref. 22. Copyright 2014 The Royal Society of Chemistry.

■ IN-SITU STUDIES OF CRYSTALLIZATION

While determination of the relative thermodynamic stabilities of MOFs is now routinely possible using computation and calorimetry, quantification of the kinetics of MOF formation remains a difficult and largely unexplored task.²⁶ In a very recent study,³⁸ we probed the evolution of lithium *meso*-tartrates using *in-situ* X-ray diffraction,³² a bulk technique for monitoring the phase behavior, composition and particle morphology of MOFs as a function of synthesis time.³³⁻³⁷ As expected from Ostwald's rule of stages,³⁹ the lowest energy phase **6** was slower to form than the metastable polymorph **7**. At low temperatures, formation of the anhydrous phases was also preceded by a hydrated phase, **11**, lending credence to the hypothesis that crystallization of products with structures most similar to the starting materials occurs fastest; in this case both the lithium source and acid were hydrated. Rate constants and activation energies for the competing formation and dissolution processes could be extracted from fitting the changes in X-ray diffraction peak intensities to semi-empirical crystallization models modified from those of Avrami and Gualtieri.⁴⁰ This enabled us to quantify fully the reaction energy profile - including intermediate phases - for the successive MOF crystallizations (Figure 5).

Figure 5. Reaction energy profile for the formation of lithium *meso*-tartrates, showing crystal structures and relative energy changes as a function of reaction progress. The energy profile of **11**, currently undetermined, is shown qualitatively for comparison. Adapted with permission from ref. 38. Copyright 2016 John Wiley and Sons.

▪ **ENERGETICS OF ZEOLITIC IMIDAZOLATE FRAMEWORKS**

In general, crystal chemistry favors dense structures, which has led to the well-known guidelines by Pauling and Goldschmidt.⁴¹ Under these circumstances it is no surprise that only a few classes of crystalline materials, such as zeolites or MOFs, are known to show a level of porosity that is sufficiently large for useful applications. To maintain a stable framework while incorporating porosity, relatively high bonding energies are necessary to obtain a thermodynamically (meta)stable framework. For instance, in zeolites, strong Si-O bonds allow for the formation of porous structures that are stable to high temperatures, e.g. several hundred degrees above room temperature.⁴² This section will focus on the important family of zeolitic imidazolate frameworks (ZIFs) – a large class of porous MOFs with topologies that are often analogous to their zeolite counterparts.⁴³

The close relation between ZIFs and zeolites stems from the tetrahedral coordination of Zn combined with a Zn-imidazole-Zn angle, which is similar to the Si-O-Si 145° angle found in zeolites (Figure 6a). In contrast to zeolites, ZIFs show an additional degree of chemical freedom due to the possibility of manipulating the chemistry by substitutions in the 2, 4 and 5 positions of the imidazolate ring, e.g. by replacing a hydrogen atom with a methyl group to make it 2-methylimidazolate. Typical syntheses of ZIFs rely on solvothermal reactions between the imidazolate ligand and a metal source at temperatures between 80 and 140°C, although some can be produced under ambient conditions. For example, mechanochemistry by liquid-assisted grinding can be used to synthesize ZIFs in a matter of minutes at room temperature.⁴⁴

Figure 6. (a) Bond angle in ZIFs and energies of ZIFs (b) at 0 K from DFT calculations with dispersion corrections. Adapted with permission from ref. 46. Copyright 2012 The Royal Society of Chemistry.

In a similar manner to zeolites, quantum chemical calculations of ZIFs reveal a decrease in energy with increasing density (Figure 6b).^{45,46} The earlier calculations⁴⁵ did not include non-bonding interactions, but the later ones^{46,46A} demonstrated clearly that the greater stability of the denser structures, in particular the non-porous ZIF-zni, was primarily due to these short-range interactions. Note that the calculations relate to ZIFs with no solvent molecules in the cavities. It should also be noted that the calculations shown in Figure 6b reflect the trend at 0 K and do not take account of entropic contributions, which can become important at higher temperatures (see below). The trend in enthalpic stabilities of the unsolvated ZIFs has been confirmed experimentally by solution calorimetry at room temperature.⁴⁷ In general, the energy landscape of the ZIFs is quite shallow, and even the amorphous form of Zn(Im)₂ is only 4.5 kJ/mol less enthalpically stable than ZIF-zni. The chemistry of the amorphous ZIFs has been described in a previous *Accounts of Chemical Research*⁴⁸ and will not be discussed further here.

Contrary to the widely held view that porous MOFs are less stable than their dense analogues, it is now known that *entropic* contributions to the free energy of MOFs can lead to porous structures being more stable than dense polymorphs at higher temperatures. This is nicely illustrated by the temperature-dependent crystal chemistry of desolvated ZIF-4, which adopts the **cag** topology with large pores at room temperature. On cooling below 140 K, desolvated ZIF-4 undergoes a first-order phase transition to a structure that is 23 % more dense.⁴⁹ The phase transition is reversible, so the dense LT structure of ZIF-4 opens up to form the porous phase on heating above 140 K. Calorimetric results indicate that the dense to open transition is accompanied by an increase in enthalpy of 8.5 kJ/mol, leading to the conclusion that the entropy must increase by ~60 J K⁻¹ mol⁻¹ in order to drive the phase transition.

The origin of the large entropy increase lies in the much greater *vibrational entropy* that is found in porous ZIF frameworks. We believe that this is a general phenomenon because similar behavior has been seen in other porous MOF systems, such as MIL-53, in which vibrational entropy is purported to overcome dispersion

forces during the transition from narrow to large pore form.⁵⁰ Similarly, in the world of zeolites it is known that the entropies of large pore systems are higher than those of their dense analogues,⁵¹ but the effect is considerably smaller ($\sim 3\text{--}4\text{ J K}^{-1}\text{ mol}^{-1}$). The difference can be ascribed to the greater flexibility of MOFs compared with zeolites, and the larger number of atoms in the formula unit.

▪ METAL-ORGANIC FRAMEWORKS WITH THE PEROVSKITE STRUCTURE

Finally, we focus on one of the most versatile structural motifs in materials science – the perovskite architecture of general composition ABX_3 . The hybrid organic-inorganic perovskites are a very large family⁵² that at first glance could be classified as an independent class of materials.⁵³ However, on looking at compounds such as the formate-containing $[(\text{CH}_3)_2\text{NH}_2]\text{Zn}(\text{HCOO})_3$ ⁵⁴ we can see that the bonding situation is very similar to that in dense MOFs, with coordination bonds forming a three dimensional metal-organic framework without accessible porosity. The formate family, itself, is quite extensive and exhibits a range of interesting ferroelectric and multiferroic properties.⁵⁵ There are other hybrid perovskites in which the framework is purely inorganic, such as the photovoltaic material $[\text{CH}_3\text{NH}_3]\text{PbI}_3$, but these are beyond the scope of our MOF theme.

Looking at their basic crystal chemistry, the hybrid perovskites of general formula AmBX_3 (Am = amine cation) show a strong relation to their solid-state analogues, *e.g.* BaTiO_3 . An ReO_3 -type lattice is formed by the BX_3 framework and the protonated amine can be found in the open void for charge balance. We have shown that the size-based concept of the Goldschmidt's Tolerance Factor (TFs) can be extended to hybrid perovskites,^{56,57} providing a useful guideline for predicting their formation. For compositions that are at the upper or lower bounds of the normal TF range between 0.8 and 1, polymorphism is often found, as we have seen with other MOF materials. For example, in the case of $[\text{NH}_3\text{NH}_2]\text{M}(\text{HCOO})_3$ (M = Zn, Mg) the TF is close to the borderline of 0.8 and formation of the perovskite-structure competes with a chiral channel-structure.²¹ Under these circumstances, entropic effects can control the outcome of the crystallization step. Figure 7a,b shows both structure-types schematically with an emphasis on the location of the protonated amines. DFT lattice calculations were performed for M = Zn^{2+} and Mg^{2+} in both structure-types, with 0 K enthalpies preferring the perovskite structure for both metals, $\Delta E = 0.07\text{ eV}$ (Zn) and $\Delta E = 0.05\text{ eV}$ (Mg). In practice, the Zn compound crystallizes in the perovskite structure whilst the Mg species prefers the chiral channel structure under ambient conditions. In a next step, the full Gibbs free energy was calculated by explicitly accounting for vibrational entropy using lattice dynamics, as shown in Figure 7c for $[\text{NH}_3\text{NH}_2]\text{Zn}(\text{HCOO})_3$. At $T_c = 330\text{ K}$, a crossover of the free energies is observed between the two structure types, driven by the higher vibrational entropy in the less dense channel structure (Figure 7d). A similar trend is observed for the Mg-based phase, where the crossover temperature is shifted down to $T_c = 300\text{ K}$ as a direct consequence of longer average HBs in comparison to $[\text{NH}_3\text{NH}_2]\text{Zn}(\text{HCOO})_3$. The

entropic effect of hydrogen bonds is a quite general phenomenon, as has been found historically in molecular crystal polymorphs,^{58,59} and which we noted in the preferential formation of lithium tartrates with weak hydrogen bonding at higher temperatures.²²

Figure 7. Crystal structures of $[\text{NH}_3\text{NH}_2]\text{Zn}(\text{HCOO})_3$ in the perovskite architecture (a) and in the metastable channel polymorph (b). Blue – nitrogen, red – oxygen, grey – carbon, white – hydrogen and red dashed lines – hydrogen bonds. The calculated Gibbs free energy (c) and entropy (d) for both polymorphs, perovskite (blue) and channel-structure (orange) as function of temperature. Adapted with permission from ref. 21. Copyright 2015 The Royal Society of Chemistry.

In cases where two alternative structures have very similar energies, it is possible to alter the outcome of the crystallization by changing the reaction temperature or modifying the underlying kinetics of nucleation. For example, it was found that the use of trimethylamine $(\text{C}_2\text{H}_5)_3\text{N}$ as an additional coordinating agent led to the formation of $[\text{NH}_3\text{NH}_2]\text{Zn}(\text{HCOO})_3$ in the chiral channel structure at room temperature.

▪ CONCLUDING REMARKS

A great deal of progress has been made over the last 15 years in our understanding of the energetics of MOFs and the kinetic and thermodynamic factors that underpin their crystallization from solution. In part this is due to the gradual accumulation of empirical knowledge, which can now be placed in a broader setting, but progress has also been made due to substantial advances in both *in situ* experimental probes and computational methods. However, a number of challenges remain in the field. In particular, the thermodynamic and kinetic effects of crystallizing *porous* MOFs under typical solvothermal conditions remains poorly understood, even though some of the key elements are now understood in the case of ZIFs, as described above. For instance, given that MOFs are known to be relatively compliant, the autogenous pressure generated in solvothermal syntheses may well affect relative phase stabilities but has not yet been systematically studied. Solvation effects are also poorly understood, yet porous MOF reaction products typically contain extra-framework solvent molecules in the cavities. It is difficult to compare the energetics of forming a large pore product containing substantial quantities of solvent molecules with a smaller pore system with fewer solvent molecules, especially in cases where the solvent itself may be a mixed system. Mixed-component and defective MOFs represent an exciting area in which nanoscopic structure may be altered to tune

properties; an understanding of the kinetics and thermodynamics of their formation would be most useful in controlling disordered structure in MOFs. Finally, computational prediction of MOFs has recently reached a level that arguably exceeds our understanding of their crystallization, particularly of metastable phases. In order to reliably create such new materials, which may be predicted to have dramatically improved physical properties, we must improve our understanding of how different synthesis parameters can be chosen to target specific phases. These problems are certainly challenging but, as the last 15 years have shown, the rapid rate of developments in experiment and theory gives us optimism that they will be met with ever increasing insight.

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