Crystallization Matrices

International Edition: DOI: 10.1002/anie.201501545
German Edition: DOI: 10.1002/ange.201501545

X-ray Crystallography in Open-Framework Materials

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coordination polymers · crystallization matrix · metal–organic frameworks · structure elucidation · X-ray crystallography

Open-framework materials, such as metal–organic frameworks (MOFs) and coordination polymers have been widely investigated for their gas adsorption and separation properties. However, recent studies have demonstrated that their highly crystalline structures can be used to periodically organize guest molecules and non-structural metal compounds either within their pore voids or by anchoring to their framework architecture. Accordingly, the open framework can act as a matrix for isolating and elucidating the structures of these moieties by X-ray diffraction. This concept has broad scope for development as an analytical tool where obtaining single crystals of a target molecule presents a significant challenge and it additionally offers potential for obtaining insights into chemically reactive species that can be stabilized within the pore network. However, the technique does have limitations and as yet a general experimental method has not been realized. Herein we focus on recent examples in which framework materials have been utilized as a scaffold for ordering molecules for analysis by diffraction methods and canvass areas for future exploration.

1. Introduction

Single crystal X-ray diffraction (SCXRD) is a ubiquitous structural characterization technique in the chemical sciences. From small molecules to solid-state materials SCXRD is employed to define the precise location of atoms in 3D space and thus afford insight into the intimate relationship between molecular structure and reactivity. For example, small-molecule SCXRD has played an important role in uncovering the details of many homogeneous catalytic mechanisms by elucidating the structures of reaction intermediates and products.[1] Furthermore, SCXRD has also been applied to delineating the non-covalent intermolecular interactions that form the basis of supramolecular chemistry.[2] Indeed, precisely determining the position of molecules in a crystal lattice has led to the development of the design principles that underpin the concept of crystal engineering.[3] The application of SCXRD to solid-state extended materials, such as coordination polymers and metal–organic frameworks (MOFs), is generally employed to delineate their network topologies and pore architectures and has been central to our understanding of how structural flexibility,[4] framework interpenetration,[5] and chemical functionality[6] relate to the physical properties of the material. By virtue of their open architectures, the pores of crystalline framework materials are replete with guest molecules in the "as-synthesized" form. These non-structural moieties are commonly omitted from the final structure solution, however, studies have demonstrated that identifying their location in the crystal lattice can afford a fundamental understanding of the material's physical properties.[7] A salient example is the application of SCXRD to establish preferential binding sites for gas molecules in "activated" materials.[8–10] Such experiments are of significant interest to chemists as they point to specific design features that may be modulated to afford enhanced adsorbate–adsorbent interactions.[9,10]

Using framework materials as a host matrix to facilitate structural analysis of guest molecules or non-structural atoms is a concept that is being increasingly explored. Indeed, recent work from Fujita and co-workers[11] demonstrated that the pores of coordination polymers can act as a "crystal-sponge"

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ordering guest molecules and allowing their structural characterization. This work complements previous studies[12] in which a highly reactive hemiaminal species, bound to molecular "cartridges" stacked and ordered within the layers of a 3D framework (Figure 1b), was stabilized and studied by X-ray diffraction. In addition, the chemistry of metal compounds bound to the structural architecture of framework materials has been examined by SCXRD. This work has shown that the products of molecular transformations induced chemically[13] or photochemically[14] can be precisely characterized. Together these examples highlight the various ways that framework materials can order non-structural molecules within the crystal lattice; within pore voids (Figure 1a), by intercalation (Figure 1b), or affixing to the network backbone (Figure 1c). Such versatility points towards the broad scope of using crystal lattices to order and structurally investigate molecular species that otherwise cannot be studied by SCXRD. It is noteworthy that, already, the crystalline-sponge strategy outlined by Fujita has advanced from proof-of-principle studies to being utilized as an analytical method.[15]

Herein we will explore the concept of using framework materials as a template for ordering non-structural atoms and guest molecules for SCXRD analysis by highlighting some recent salient examples. We note that there are many reports of clathrate compounds where the guest molecules have been structurally defined,[16] however, the focus of this Minireview is to consider examples where extended networks are employed with the intent of periodically arranging compounds for subsequent X-ray diffraction analysis. The growing interest in this strategy as a characterization tool coupled with the vast potential for designing new host frameworks of predetermined functionality and structure metrics means this area is poised for exciting new developments.

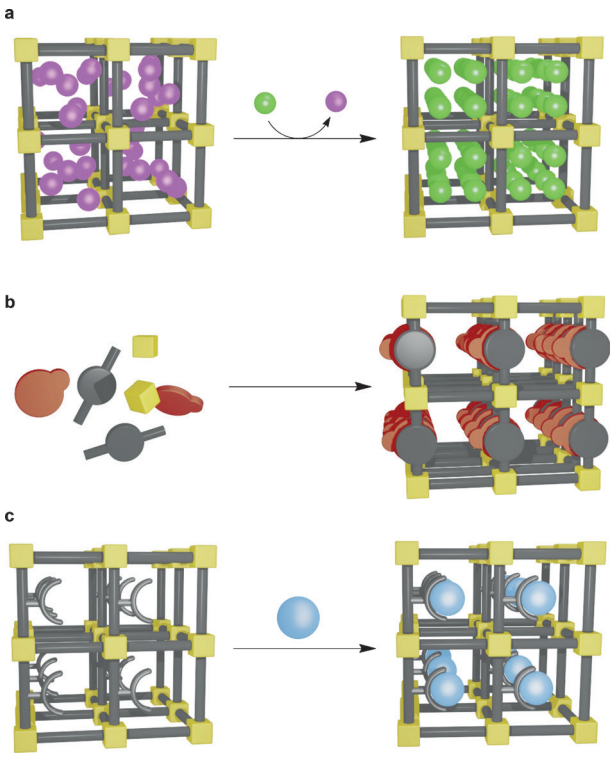

Figure 1. A schematic representation of the three approaches to order guest molecules within the pores of a MOF (yellow cubes and gray cylinders represent metal nodes and ligands respectively). a) Guest exchange resulting in ordering within the host framework (purple and green spheres represent different guest molecules); b) assembly of a framework in the presence of an intercalating cartridge molecule (cartridge molecule represented the by brick-red circular shape); c) affixing a guest molecule at a non-structural anchoring point pre- or post-synthetically (blue spheres represent affixed guest molecules).

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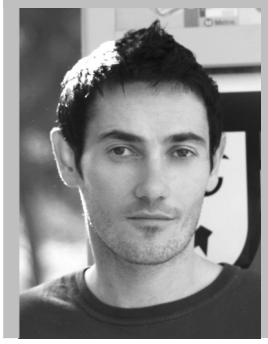

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1.1. Framework Pores as Host Matrices

One of the challenges presented by SCXRD is that crystals of sufficient quality are required to generate the requisite data for a successful structure solution. Although, over the past few decades, advances in X-ray detector technology and availability of synchrotron radiation sources for routine SCXRD experiments have facilitated studying smaller crystals, preparing diffraction-quality samples remains a potential limitation. Utilizing an extended network as a matrix for ordering guest molecules is one strategy that may remove the necessity of growing single crystals of a target compound. This was keenly observed by Fujita and co-

workers who recently reported that a coordination polymer termed a "crystal sponge" could be used to occlude guests in a periodic arrangement and facilitate their precise structural determination.[11] Indeed, the Fujita group has developed the idea of crystalline sponges over a number of years. Previously they suggested that the same host–guest interactions that have led to rich chemistry in discrete soluble systems could be translated to the solid state. This assumption was experimentally verified by demonstrating that the network pores showed a strong preference for sequestering C_{70} over C_{60}.[17] Their key finding from this work is that guest molecules could be exchanged in the solid state by a single-crystal-to-single-crystal (SC-to-SC) process and thus characterized by SCXRD.

Although it is not uncommon for guest molecules to be crystallographically "identified" within the pores of framework materials, this work delineated the potential for intentionally utilizing the framework's porous voids as a matrix for the periodic organization of guests. This elegant idea was realized recently[7b,11] when "crystalline sponges", $\{[(Co(NCS)_2)_3(2,4,6\text{-tris}(4\text{-pyridyl})\text{-}1,3,5\text{-triazine})_4]\cdot x(\text{solvent})\}_n$ and $\{[(ZnI_2)_3(2,4,6\text{-tris}(4\text{-pyridyl})\text{-}1,3,5\text{-triazine})_2]\cdot x(\text{solvent})\}_n$ (**1**) (**2**: 2,4,6-tris(4-pyridyl)-1,3,5-triazine), were employed to concentrate and order guest molecules within their pores thus facilitating their characterization by SCXRD (Figure 2). Notably, nanogram quantities of guest molecules could be exchanged into the framework by a SC-to-SC process and structurally elucidated by SCXRD without pre-crystallization. The advantages to using framework materials for the structural identification of unknown compounds compared to traditional approaches, including the small quantities of the unknown material required and no requirement for a single-crystal phase of that material, were expounded in this work.

However, the approach is not without its limitations and investigation of the literature in this area reveals that the "crystalline-sponge" strategy is not universally successful. The diffraction from the guest molecule is highly dependent upon the degree of ordering and in some instances unequivocal structural determination is not possible both in terms of accuracy and precision of the geometry of the guest molecule. Thus, for the approach to be successfully employed it is often important to exploit supramolecular interactions between host framework and guest to facilitate ordering. Of course this is not always possible. In addition, an intrinsic requirement of the technique is that the guest molecule is smaller than the pore cavity it resides within. This places practical limitations on the size and shape of molecules that can be studied. Accordingly, the "crystalline-sponge" approach should not be seen as a universal answer to structure-determination problems, rather a strategy that can be employed for selected examples.

Despite these reservations the unique environment provided by framework pores offers a broad scope for using the "crystal-sponge" strategy to analyze unstable moieties that otherwise would not be amenable to X-ray analysis. An example of this stabilizing effect has been reported by Ning et al.[18] who infiltrated and structurally characterized reactive acrylate esters within a framework material. In addition to post-synthetically encapsulating molecules within pore voids

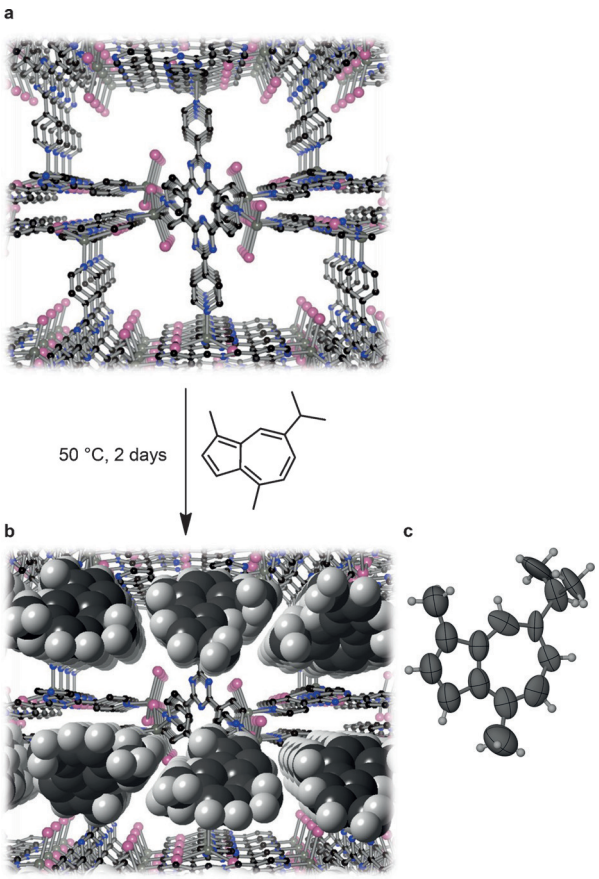

Figure 2. The ordering of guest molecules using the crystalline sponge **1**. a) as synthesized MOF (solvent molecules within pores are omitted for clarity); b) crystalline sponge **1** with guaiazulene guests ordered within the pores; c) guaiazulene as located within the pores of **1** represented as ellipsoids at 50% probability.

the molecular architecture of frameworks can be utilized to lock functionalized molecular cartridges between their walls. Indeed this strategy has been employed to structurally define an elusive hemiaminal group.[12] In this case a mixture of ZnI_2, **2** and 1-aminotriphenylene formed a 3D framework in which the electron-rich triphenylene cartridge resided between the electron-deficient layers formed by the organic scaffold of **2**. It is worth noting that such stacking of planar motifs in discrete species has been well studied by the Fujita group and undoubtedly guided the design of this system.[19] Structural characterization of this intercalated framework showed that the amine group of the triphenylene unit pointed into the pore channels and, as a result, its reactivity in the solid state could be accessed. A condensation reaction with acetaldehyde was carried out by a SC-to-SC process and the product was examined by SCXRD. Careful analysis of the diffraction data showed that at low temperature the hemiaminal intermediate of the Schiff-base reaction could be kinetically trapped and thus structurally defined (Figure 3). Accordingly, this study is a clear example of how frameworks can be used to isolate reactive species for structural characterization.

Employing an analogous approach, Fujita and co-workers used time-dependent X-ray crystallography to gain insight into the palladium-mediated bromination of a phenyl

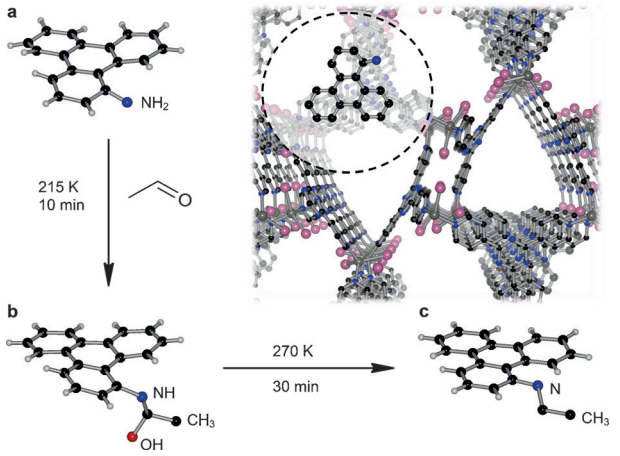

Figure 3. a) The 1-aminotriphenylene guest which is imbedded between ligand **2** in the framework of **1** (right); b) the transient hemiaminal intermediate, formed within the MOF pores by treating a crystal of **1** with acetaldehyde at 215 K for 10 min; c) the final imine product which was obtained by warming the hemiaminal intermediate in the MOF at 270 K.

group.[20] Electron-density maps indicated the presence of an Ar–Pd–Br intermediate and the subsequent elimination of the Pd atom to the brominated product Ar–Br. The observation of a Pd^{II} intermediate is a feature of this work as such compounds typically, and rapidly, convert into dinuclear $Pd_2(\mu\text{-}Br)_2$ species and are precipitated from solution. They noted that the insights garnered from this work must be considered in the context of the reaction medium, that is, that the geometric constraints imposed on the complex by the framework will affect potential reaction pathways. Nevertheless, this study represents the potential for using SCXRD to follow reactions within framework materials and highlights the significant structural insights provided by electron-density maps.

Utilizing framework materials as a molecular scaffold to facilitate the characterization of guests and non-structural atoms by SCXRD, largely a result of the pioneering work of the Fujita group, is beginning to realize its potential as an analytical tool. The origins of this concept may be traced to analogous host–guest chemistry at play in discrete systems in which supramolecular interactions have been shown to drive guest inclusion, and ultimately ordering within the host.[2] In combination with spectroscopic and purification techniques, framework-assisted crystallization of analytes will undoubtedly be a powerful method for unambiguously identifying unknown compounds. In addition, the potential to determine the structures of reactive or transient species within pore networks has been demonstrated.[7b,12] Given the vast library of similar chemistry that has been reported in discrete systems over the past decade[7b,21] the possibility for novel discoveries in this area is significant.

2. Framework Scaffolds for Molecular Organization

Whereas Fujita's approach has been to focus on the study of guest complexes it is also to possible to attach them to the framework itself (Figure 1c). The approach thus far employed exploits judiciously designed organic struts that not only bridge metal centers but also provide coordination sites to bind the metal complexes for subsequent investigation. Thus the target to be examined is anchored to the framework scaffold rather than being a vital structural component required for network propagation. Notably, this strategy allows modification of the chemical environment of the target complex without disrupting the framework structure.[22] In such cases, the rigid framework holds the target complex in its lattice position and, if single crystallinity is maintained, allows structural changes resulting from chemical (or photochemical) treatment of the crystals to be probed by X-ray diffraction studies.

An example of this strategy is to exploit the chemistry of a divergent multifunctional dicarboxylate ligand, commonly employed in MOF synthesis, which is also able to bind a metal complex, for example 2,2′-bipyridine-5,5′-dicarboxylate (**3**; Figure 4a,b). This approach has been successfully demonstrated by employing $\{M(\mathbf{3})(CO)_3X\}$ (M = Re, Mn, X = Cl, Br) as a ligand in the construction of MOFs, with the carboxylate donors of **3** binding either Mn^{II}[14a] or Cu^{II}.[14b]

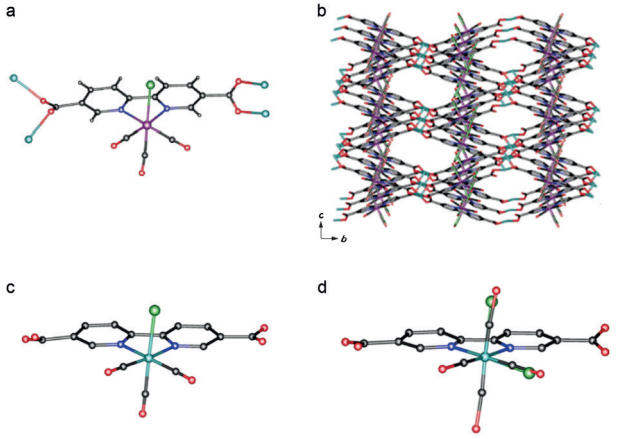

Figure 4. a) View of the $\{M(\mathbf{3})(CO)_3X\}$ ligand that is used to create a complex-bearing MOF (b) through reaction of the carboxylate groups with Mn^{II} salts. View of the photo-induced isomerization of the $\{Mn(\mathbf{3})(CO)_3Cl\}$ moiety from the *fac*-isomer (c) to the *mer*-isomer (d) within $\{Mn(DMF)_2[Mn(\mathbf{3})(CO)_3Cl]\}_n$. Single-crystal X-ray diffraction reveals approximately 25% conversion (*fac*- into *mer*-isomer) by detection of the chloride occupancy of the equatorial positions of the complex (shown in green in (d)). (Reproduced with permission from Ref. [14a]. Copyright Nature Publishing Group, 2010).C black, H gray, N blue, O red, Cl green, Re purple, Mn light blue.

Thus the $\{M(\mathbf{3})(CO)_3X\}$ unit is supported by the framework whilst not acting to propagate the MOF structure. The $\{M(\mathbf{3})(CO)_3X\}$ moiety has well understood photochemistry which can be probed by time-resolved spectroscopic studies, notably picosecond time-resolved IR (TRIR), to facilitate an understanding of the effect of the MOF on the properties of the framework-supported complex. Studies of the MOF-supported $\{Re(\mathbf{3})(CO)_3Cl\}$ moiety reveal the formation of both ^{3}MLCT and ^{3}IL (intraligand) π–π^* states. However, the metal-to-ligand charge transfer (MLCT) bands are not stable

and decay rapidly (ca. 20 ps) concurrent with further growth of the ^{3}IL band. Further, the TRIR spectra obtained 1 ns after laser excitation shows only the presence of ^{3}IL states. The ^{3}IL state of [Re(bpy)(CO)$_3$Cl] is not normally accessible in solution as it is higher in energy than the commonly observed ^{3}MLCT state. Thus it can be concluded that the MOF environment induces a change in the nature of the excited states of the framework-supported complex.

Further investigation of the tethered {M(**3**)(CO)$_3$X} complexes indicate that under suitable conditions it is possible to induce their isomerization. Thus, irradiation of {Mn(DMF)$_2$-[Re(**3**)(CO)$_3$X]}$_n$ for 22 h at 200 K leads to the observation of free CO in the MOF. Warming of these samples to above 250 K leads to the formation of the corresponding *mer*-isomer of the {M(**3**)(CO)$_3$X} species. For {Mn(DMF)$_2$[Re(**3**)-(CO)$_3$Cl]}$_n$, approximately 10% conversion into the *mer*-isomer is observed but the corresponding {Mn(**3**)(CO)$_3$Cl}-containing MOF, {Mn(DMF)$_2$[Mn(**3**)(CO)$_3$Cl]}$_n$, undergoes 25% conversion from the *fac*- into the *mer*-isomer. This higher level of isomerization allows direct characterization of the isomerization product by SCXRD experiments (Figure 4c, d).[14a] This study demonstrates that through suitable design it is possible to investigate photo-initiated structural transformations within MOF structures using SCXRD, particularly when sufficient conversion is achieved following photo-initiation.

A similar approach can be used to probe a more substantial structural transformation of a framework-supported metal complex by monitoring a chemical reaction. A recent study[13] has demonstrated that a Mn^{II} MOF ({Mn$_3$-(L)$_2$(L′)}$_n$) (L = bis(4-(4-carboxyphenyl)-1*H*-3,5-dimethylpyrazolyl)methane) can be prepared using a dicarboxylate ligand whose backbone incorporates a vacant binding site, in this case a bis(pyrazole) moiety (Figure 5). Instead of inserting the target complex in the initial synthesis, the bis(pyrazole) moiety is functionalized through a post-synthetic metalation step.[22,23] A post-synthetic strategy in principle allows insertion of a range of metal complexes into the same framework structure and has been employed successfully for a range of metal salts, $CoCl_2$, $CuCl_2$, $Zn(NO_3)_2$, $Cd(NO_3)_2$, for the bis(pyrazole)-decorated MOF.[13,24]

One of the transformations described utilized SCXRD to probe the reactivity of framework-supported cobalt complexes again using the {Mn$_3$(L)$_2$(L′)}$_n$ MOF. In this case post-synthetic metalation using $CoCl_2 \cdot 6H_2O$ facilitates the formation of {Mn$_3$(L)$_2$[(Co(L′)(H$_2$O)$_4$)]Cl$_2$}$_n$. Upon metalation of {Mn$_3$(L)$_2$(L′)}$_n$ the bis(pyrazole) unit of L′ switched from an *anti* to a *syn* conformation to chelate to the newly introduced metal center. Upon heating, these crystals change color from pink to blue. The process can be monitored by SCXRD as is shown to be due to substitution of water ligands on the [{bis(pyrazole)}Co(H$_2$O)$_4$]$^{2+}$ moiety for chloro ligands (formation of [{bis(pyrazole)}CoCl$_2$]) leading to a change in the cobalt coordination geometry from octahedral to tetrahedral. During this transformation a significant rotation of L′ is observed, highlighting the flexibility of the MOF system which likely aids in stabilizing secondary interactions of the extraneously introduced metal center and maintaining single crystallinity.

Of particular interest in this study was the introduction of [{Rh(CO)$_2$Cl}$_2$] into the ({Mn$_3$(L)$_2$(L′)}$_n$) MOF system, which proceeded in essentially quantitative yield to afford {Mn$_3$-(L)$_2$[Rh(L′)(CO)$_2$][RhCl$_2$(CO)$_2$]}$_n$ (where L = bis(4-(4-carboxyphenyl)-1*H*-3,5-dimethylpyrazolyl)methane). Two types of Rh^{I} centers are present in the framework: a [Rh(CO)$_2$] moiety bound by the bis(pyrazole) ligand and a [RhCl$_2$-(CO)$_2$]$^-$ anion which sits in the framework pores. Exposure of the framework to methyl iodide results in oxidative addition at the framework-supported [{bis(pyrazole)}Rh(CO)$_2$] center which can be characterized by SCXRD (Figure 6). The crystallographic studies unambiguously demonstrate oxidative addition reactions and show the formation of a [{bis-(pyrazole)}Rh(CO)(NCMe)(COMe)I]I center in which the Rh^{III} metal center adopts an octahedral geometry with the CO and MeCN ligands in the equatorial plane and the iodide ion and the C(=O)Me ligands occupying the axial positions.

The potential of using SCXRD for monitoring reactions through appropriately designed framework structures is further demonstrated by reactions at metallo-porphyrin containing MOFs.[25] PCN-224, a Zr-based MOF that is constructed using tetracarboxyphenylporphyrin bridging li-

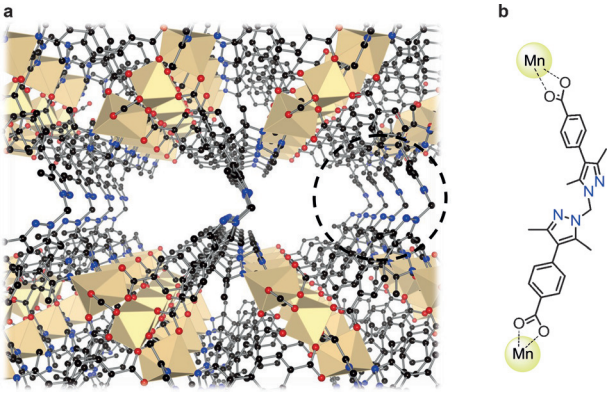

Figure 5. a) A perspective view of {Mn$_3$(L)$_2$(L′)}$_n$ along the *c* axis; b) the ligand L′ (highlighted in the broken circle in (a)) with vacant bis(pyrazole) donor centers. The difference between L and L′ is that L contains coordinated bis(pyrazole) donors which are part of the Mn$_3$ node.

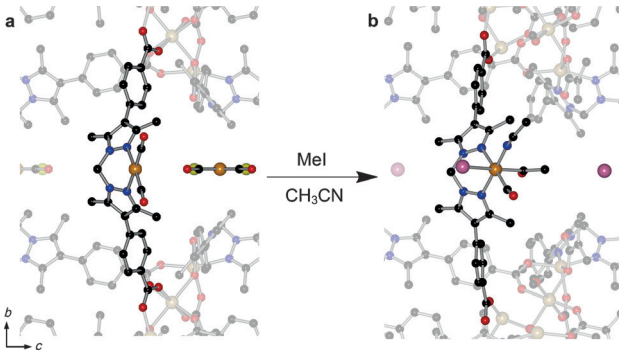

Figure 6. The oxidative addition of MeI to a [Rh(CO)$_2$]$^+$ complex within the pores of {Mn$_3$(L)$_2$(L′)}$_n$. X-ray structures of a) {Mn$_3$(L)$_2$[(Rh(L′)-(CO)$_2$][RhCl$_2$(CO)$_2$]}$_n$ and b) {Mn$_3$(L)$_2$[Rh(L′)(CO)(NCMe)(COMe)I]I}$_n$. C black, N blue, O red, Cl yellow, I pink, Rh gold.

gands, can be subsequently metalated to introduce Fe^{II} cations to the porphyrin binding site. The metalated MOF can be considered as a porous framework that is now decorated with heme-like groups along the walls of the cavities. The Fe-containing MOF was allowed to react with gaseous O_2 at −78 °C mimicking heme-like properties. The process can be monitored by SCXRD to unequivocally establish the structure of an Fe–porphyrin O_2 complex. The structure represents the first structurally characterized example of a five-coordinate, heme–O_2 adduct and which importantly does not have an additional base, such as imidazole, attached to the iron cation. In a similar vein to the studies described above the incorporation of the heme mimic into a MOF allows structural characterization of an unusual chemical species that is only observed transiently in its molecular form.

3. Challenges and Constraints

Herein we have highlighted some examples where framework materials have been employed as scaffolds to order molecules for SCRXD analysis. One of these, the "crystalline sponge" strategy shows promise as a complimentary tool to other analytical techniques for structure determination; however, there are several experimental constraints and challenges that need to be carefully considered. As highlighted by the Fujita group in a recent publication,[15] to occlude and order guest molecules the pore size and chemistry of the "crystalline sponge" must match that of the target compound. For example, a hydrophobic guest molecule requires a hydrophobic pore network. In instances where an insufficient ordering of the guest molecule is achieved, structural determination can prove difficult at best and impossible in the worst case. Poor diffraction from the guest molecules is perhaps the most limiting feature of the "crystalline-sponge" approach and even when the strategy is successful the quality of the diffraction data can severely limit precise and accurate determination of the guest's structure.

However, successful employment of the strategy has been demonstrated and in some instances the use of suitable supramolecular interactions between framework and guest, that facilitate ordering of guest molecules, are a potential tool to enhance the exploitation of framework structures as "crystalline sponges". The use of a cartridge approach by Fujita et al.[12,18] demonstrates the importance of such framework–guest interactions. Thus, to expand the application of this methodology, new frameworks will need to be synthesized that encompass a broader range of pore volumes and surface chemistries. However, given the expansive library of known framework materials[26] and a deep understanding of host–guest chemistry garnered from discrete systems, it can be anticipated that bespoke "crystalline sponges" can be synthesized that target guests of varied size and chemistry. We note that poor data quality can preclude precise assignment of molecular connectivity or stereochemistry of guests (particularly flexible molecules) in porous frameworks.[27] Thus, it can be anticipated that the use of traditional spectroscopic techniques may be necessary to unequivocally determine the structure of unknown compounds.

Monitoring inorganic transformations in the pores of extended networks also presents experimental-design considerations. For example, precise structural information requires high metal occupancies, which can be challenging for post-synthetic reactions.[22] In addition, a degree of structural flexibility is required to compensate for the geometric modifications that result upon chelating metal compounds and throughout chemical reactions. Indeed recent work by Long and co-workers has shown that post-synthetically chelating metals to an inflexible 2,2′-bipyridine-5,5′-dicarboxylate link introduces significant strain on the framework.[28] This introduces an interesting dichotomy as target frameworks require both enough flexibility to respond to guest molecules and also a suitable size match between host and guest. These potentially conflicting features demonstrate the challenge in designing suitable frameworks for the study of reactive guests.

Lastly, our experience indicates that crystal morphology is also important in facilitating guest inclusion. We found that crystal quality was best preserved for "plate" morphologies as they accommodate rapid guest diffusion and thus minimize potential damage through prolonged exposure to reactants. Accordingly, it seems likely that the qualities of the crystal, morphology, size, and crystallinity are all vital in such studies. Indeed poor crystallinity, or loss of crystallinity are perhaps the most significant barrier to the use of a given framework as a scaffold.

4. Future Prospects and Conclusions

Herein we have highlighted the broad scope for using open-framework materials as scaffolds that periodically organize moieties for precise structural elucidation by X-ray crystallography. Although, the application of this strategy is burgeoning its full potential as an analytical method is yet to be realized and some of its limitations remain to be overcome. For example, using porous crystals to probe dynamic processes could provide fundamental insight into molecular adsorption and catalysis. Indeed recent work from the Shionoya[29] and Fujita[20] groups clearly demonstrate the feasibility of such studies. In both cases meticulously planned and executed experiments were essential to capturing X-ray snapshots of transient species: a multi-step molecular adsorption in a crystalline nano-channel[29] and the observation of a palladium-mediated aromatic bromination.[20] The pore networks studied by Shionoya and co-workers were formed by the assembly of discrete macrocycles, however, in principle, the experimental approach applies to extended networks. Although MOFs are typically studied as hosts for guest molecules, experiments that unequivocally establish the routes taken by guest molecules through the framework structure would provide invaluable insight into how to design frameworks to enhance adsorption and trapping of target guests. Similarly the ability to probe the transport and organization of reagents around a target reactive site would provide fascinating information to both understand and enhance reaction pathways, either within frameworks or by analogy in solution-based processes.

A logical extension of such pursuits will be the design of bespoke frameworks for ordering and stabilizing guest molecules—a strategy that offers great promise for exploring novel chemistry by SCXRD. For example, oppositely charged guest–framework combinations have been utilized to introduce molecular catalysts into MOF pores by electrostatic attractions.[30] Examining analogous systems by SCXRD could provide further insight into the structure of active catalytic species or the first steps of bond-activation processes. Furthermore, designing functionally complex pore environments could, in principle, provide fundamental structural information with respect to selective adsorption by multivalent interactions in a solvent-free system.

In discrete cage systems, pore confinement effects can lead to the stabilization of highly reactive species[31] or enhancement of bimolecular reactions.[32] Hitherto, such chemistry remains largely unexplored in open-framework systems and is thus a rich area for future research. The observation and unequivocal characterization of a five-coordinate heme–O_2 adduct discussed in Section 2 demonstrates the power of using framework structures to periodically order and separate highly reactive or transient species. Such studies, and others discussed herein, illuminate a pathway to structural studies of highly illusive species.

There are many reactions and target molecules in many areas of chemistry that are just waiting to be observed and structurally characterized but until now SCXRD has not been a viable approach owing to the absence of single crystals. The approaches described herein illustrate that by using a framework to order your target, either by supporting on or trapping the target within a MOF, there are now clear opportunities to structurally characterize elusive species. Only glimpses of the power of this approach have been reported to date and significant challenges remain, however, it is clear that SCXRD of framework-hosted species has a highly promising future.

Acknowledgements

N.R.C. acknowledges the receipt of a Royal Society Wolfson Merit Award.

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 12860–12867
Angew. Chem. **2015**, *127*, 13052–13059

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Received: February 16, 2015
Revised: June 14, 2015
Published online: September 16, 2015

