CHEMICAL REVIEWS

REVIEW

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Postsynthetic Methods for the Functionalization of Metal−Organic Frameworks

Seth M. Cohen*

Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093-0358, United States

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1. INTRODUCTION

1.1. Background

Much of the initial interest and enthusiasm over the class of solids now known as metal−organic frameworks (MOFs) or porous coordination polymers (PCPs) came from their very high surface areas and hence an extremely high capacity to capture gases of interest in energy-related technologies (e.g., H_2, CH_4, CO_2).[1−4] Indeed, the majority of MOF studies are still focused on the gas capture/storage properties of these materials. Alongside this prominent interest in gas uptake, other potential applications of MOFs have begun to flourish in areas including catalysis,[5] luminescence,[6] and biotechnology.[7] Perhaps even more so than applications related to gas uptake, the development of MOFs for these other fields of interest is becoming increasingly reliant on the development of MOFs that possess complex chemical functionality that can impart sophisticated and nuanced chemical and physical properties to these materials.

In principle, the introduction of different functional groups into MOFs should be more straightforward when compared to that of other inorganic solids because MOFs possess an organic component (the ligand or linker) suitable for installing any number of chemical moieties. Indeed, some great success in this regard has been achieved by preparing MOFs with more than one organic component ("mixed component") to make MOF "copolymers",[8−10] some of which have been coined as multivariate MOFs (MTVMOFs).[11] However, the preparation of highly functionalized MOFs has been largely limited by the solvothermal synthetic methods used to prepare most MOFs. Under solvothermal conditions, ligands generally cannot contain functional groups that are thermally labile, result in problematic solubility, or can coordinate metal ions. In any of these cases, synthesis of the MOF will be complicated or altogether thwarted; unfortunately, many functional groups of interest fall into one or more of these categories. This limitation is probably best illustrated by examining the ligands that have been used to prepare the canonical isoreticular metal−organic framework (IRMOF) series of materials described by Yaghi and co-workers (Table 1).[11,12] As shown in Figure 1, IRMOFs have been prepared from a variety of 1,4-benzenedicarboxylate (BDC) and elongated, rigid dicarboxylate ligands. However, it is immediately apparent that the range of chemical functionality found within this family of ligands is rather limited. Functional groups such as alcohols (phenols), aldehydes, carboxylic acids, nitriles, azides, alkylamines, thiols (thiophenols), phosphines, and many others are absent from the list of ligands that have been used to prepare IRMOFs. In many cases, introduction of these functional groups onto the BDC scaffold would complicate or prevent MOF formation for the reasons stated above (e.g., ability to coordinate metal ions). At a very minimum, the introduction of such groups would likely necessitate identification of new reaction conditions (e.g., changes in temperature, time, solvent, metal salt) to obtain the desired IRMOF topology. Uncovering suitable reaction conditions for synthesizing a specific MOF topology with a modified ligand is often a very time-consuming and nontrivial endeavor.

Fortunately, there are alternative methods for introducing functional groups into MOFs. Postsynthetic methods have been used to achieve the chemical modification of many organic and

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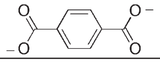
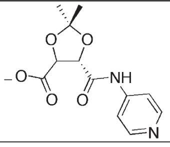
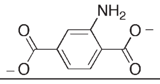
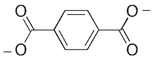
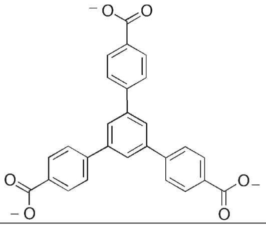
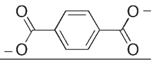
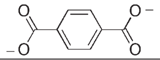
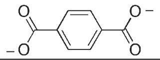
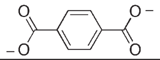
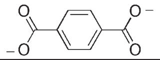
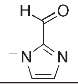
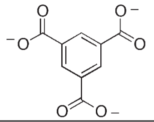
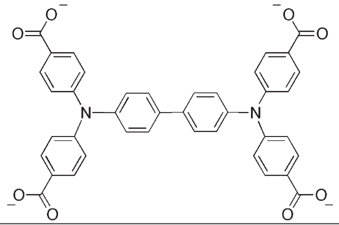
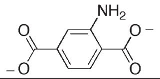
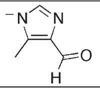
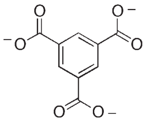
Table 1. List of Short (Acronyms) and Full Names of Some of the MOFs Discussed in This Review, Along with Their Empirical Formulas and the Ligands Used in Their Preparation

Acronym Name	Full MOF Name	Empirical Formula	Ligand (L1/L2)
IRMOF-1	Isoreticular MOF	Zn_4OL_3	
POST-1	Pohang University of Science and Technology	$Zn_3OL_3(H_2O)_3$	
MOF-LIC-1	MOF-Leiden Institute of Chemistry	$Gd_2O_{16}L_3(DMF)_4$	
DMOF-1	dabco MOF	$Zn_2(L1)_2(L2)$	 
UMCM-1	University of Michigan Crystalline Material	$Zn_4O(L1)_{4/3}(L2)$	
MIL-101	Material Institut Lavoisier	$Fe_3OL_3(H_2O)_2Cl$	
MIL-53	Material Institut Lavoisier	$Al(OH)L$	
MIL-68	Material Institut Lavoisier	$In(OH)L_2$	
UiO-66	University of Oslo	$Zr_6O_4(OH)_4L_6$	
ZIF-90	Zeolite-Imidazolate Framework	ZnL_2	
STAM-1	St. Andrews MOF	$Cu(H_2O)L$	
SNU-30	Seoul National University	$Zn_2L_2(H_2O)_2$	
CAU-1	Christian-Albrechts-University	$Al_4(OH)_2(OCH_3)_4L_3$	
SIM-1	Substituted Imidazolate Material	ZnL_2	
HKUST-1	Hong Kong University of Science and Technology	$Cu_3L_2(H_2O)_3$	

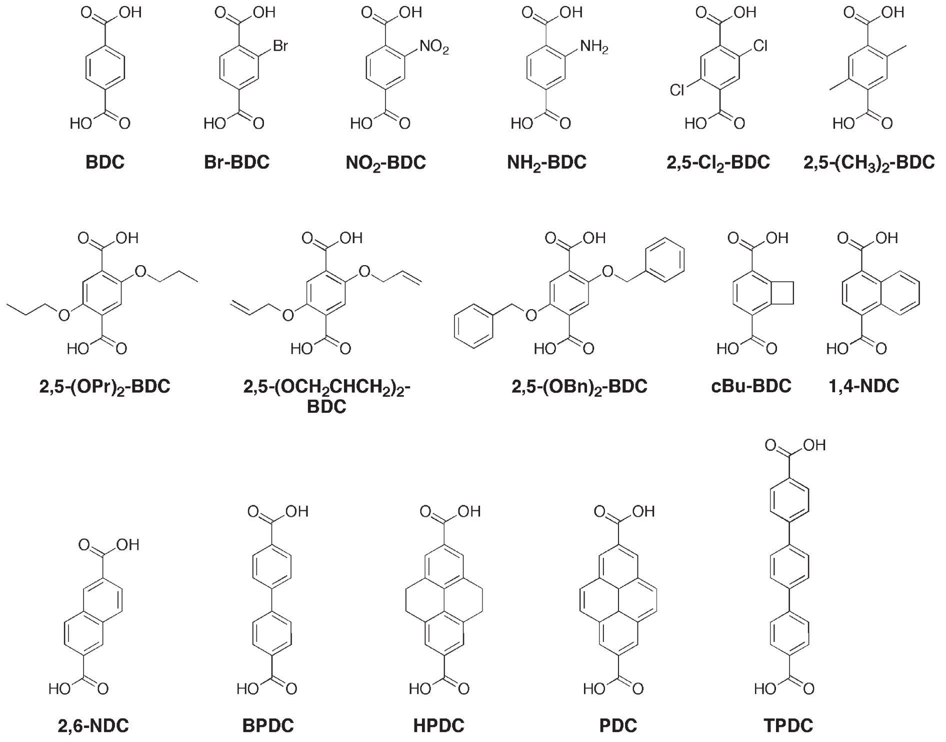


Figure 1. Partial list of dicarboxylate ligands (with abbreviations) that have been successfully utilized for the synthesis of IRMOFs.

inorganic materials. That is, chemical modification can be performed on the fabricated material, rather than on the molecule precursors (i.e., monomers). In this way, the newly introduced functional groups (and the reaction conditions required to introduce those groups) only need to be compatible with the final material, and any incompatibility with the synthetic methods required to obtain the material are circumvented. The chemical literature is abundant with this kind of late-stage or postsynthetic modification (PSM) approach with a wide variety of soft and hard materials. Within the realm of porous solids, there are several good examples, such as the postsynthetic modification of mesoporous silicates, among others.[13,14]

Postsynthetic methods are particularly attractive for use with MOFs for a variety of reasons. First, as already stated, the solvothermal reaction conditions that are used to prepare most MOFs greatly limit the types of functional groups that can be introduced presynthetically (i.e., as part of the ligand monomers). Second, MOFs contain an organic ligand component (unlike many other crystalline, inorganic solids) and hence open the possibility of employing the vast range of organic transformations developed by synthetic organic chemists. Finally, because MOFs are highly porous, the ability of reagents to access the interior of the solids suggests that functionalization can be achieved on both the interior and exterior of the material. This latter point is in contrast to many inorganic solids, such as quantum dots (QDs), gold nanoparticles (AuNPs), or microporous silicon, where only the surface of these materials is available for modification (e.g., by deposition of a chemical monolayer).[15]

The potential of postsynthetic approaches to the functionalization of MOFs has been recognized since the earliest reports of 3-dimensional (3-D) coordination solids. Indeed, in 1990 Robson described 3-D coordination solids based on metal cyanates.[16] In this early report, the authors speculate on what properties these new, crystalline materials might possess. Included in these speculations is the following prophetic statement: “Relatively unimpeded migration of species throughout the lattice may allow chemical functionalization of the rods subsequent to construction of the framework.”[16] This visionary quote captures the chemical discoveries that began to appear almost a decade later and will be the subject of this review.

This review will focus on the development of postsynthetic methods for the chemical modification and functionalization of MOFs and related coordination polymers. Although a relatively new area of research within the MOF field, PSM has become sufficiently mainstream that experiments for an inorganic undergraduate laboratory course have now been described.[17] In this review, an emphasis will be placed on chemical approaches that result in covalent modification of the organic linkers within the MOF framework. Some discussion of the modification of unsaturated metal sites located at the secondary building units (SBUs) of MOFs, as well as the addition of metal ions to “free” ligand sites in MOFs, will also be provided. A discussion of how these postsynthetic methods enable MOFs with new physical properties or chemical behaviors will also be discussed. Several reviews on PSM have recently appeared,[8,18−20] and herein we attempt to capture the complete history of PSM to date, as well as the most recent reports of PSM in the past few years. The first descriptions of PSM appeared in the literature in 1999 and underwent a significant rebirth in 2007; therefore, this review will cover reports in this subfield from 1999 until early 2011.

1.2. Defining Different Postsynthetic Methods

There are a variety of different ways by which a MOF can be modified in a postsynthetic manner, and each of these forms of modification has the capacity to alter the physical and chemical properties of the framework. At the most fundamental level, the desolvation of MOFs can be considered a form of PSM, as desolvation carries many of the hallmark characteristics of a "modified" material (when compared to the solvated material). Desolvated MOFs generally display poorer crystallinity (as evidenced by powder X-ray diffraction, PXRD), but produce materials with much higher gas sorption surface areas when compared to the solvated framework. Indeed, desolvated or "activated" MOFs are often given a distinct chemical designation to distinguish them from their solvated counterparts (sometimes designated "as" for as-synthesized). Drying with supercritical carbon dioxide has become a particularly useful method for activating MOFs.[21] Similarly, the exchange of guest molecules from MOFs, including anions and cations,[22−24] can dramatically alter the properties of these materials. Such noncovalent postsynthetic transformations have generated a number of interesting findings, but these types of ion-exchange reactions will not be reviewed here. Other very interesting inclusion phenomena that have been performed in a postsynthetic manner, such as micropatterning,[25] are also outside the scope of the present review as are postsynthetic schemes that involve the introduction of large guests[26,27] or the formation of metal nanoparticles.[28,29] Because even the most basic of procedures, such as MOF activation, could be categorized as forms of PSM, it is important that the definition of different types of PSM be provided here to distinguish these chemical reactions from the routine handling and guest inclusion phenomena of MOFs.

For the purposes of this review, postsynthetic modification of MOFs will be broadly divided into three areas: (a) covalent PSM, (b) dative PSM (previously referred to as coordinate covalent PSM),[19] and (c) postsynthetic deprotection (PSD). The type of chemical bond that is formed or broken during the postsynthetic approach distinguishes each of these methods. It is important to note that these different postsynthetic methods are not mutually exclusive, and this review will highlight several examples where more than one postsynthetic approach is used in combination with others. Perhaps the greatest utility of postsynthetic methods is the ability to utilize a combination of strategies (including standard presynthetic methods) to obtain materials of high complexity and functionality. In addition to achieving the desired chemical transformation, it is important that the MOF not be destroyed under the reaction conditions used. Therefore, we will generally only review transformations that clearly preserve the crystallinity of the MOF lattice. Indeed, postsynthetic methods are intended to produce novel materials that retain the characteristic features of MOFs, including high crystallinity, high surface areas, and a structure comprised of highly regular metal−ligand bonding. Postsynthetic approaches that result in degradation or collapse of the framework and do not preserve these features are regarded as less relevant within the context of producing new, porous MOF materials.

Covalent PSM is defined as the use of a reagent to modify a component of the MOF in a heterogeneous, postsynthetic manner to form a new covalent bond (Figure 2). The target of covalent PSM is generally the organic linker of the MOF, but examples of such modification to the SBUs have also been described on occasion. To date, covalent PSM is the most extensively investigated of the different postsynthetic methods. This was also the earliest of the postsynthetic methods to be described for MOFs. As will be described later, covalent PSM has proven a powerful and versatile method for introducing a broad range of chemical groups into MOFs.

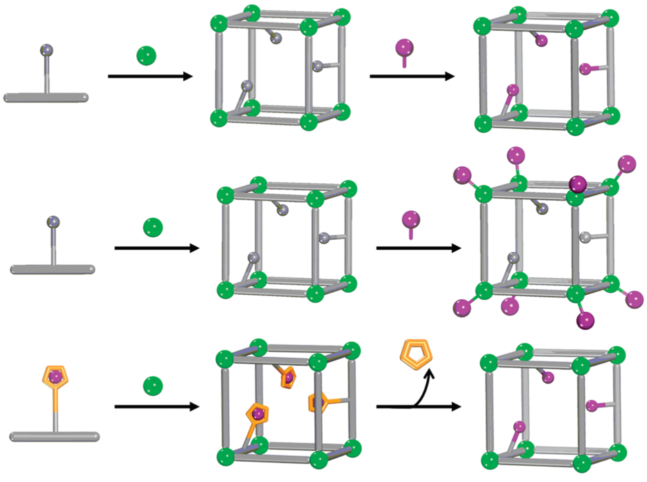


Figure 2. Generic schemes for (a) covalent PSM, (b) dative PSM, and (c) PSD.

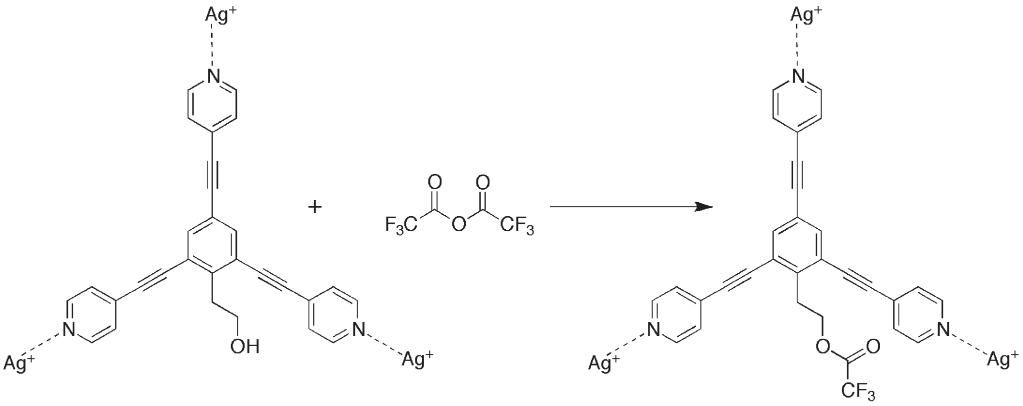
Dative PSM is defined as the use of a reagent that forms a dative (i.e., metal−ligand) bond with a component of the MOF in a heterogeneous, postsynthetic manner (Figure 2). In some examples of dative PSM, a ligand is added to the framework that coordinates to the SBU of the MOF. In other examples, a metal source is added to the MOF, which then becomes bound to the organic linker of the MOF via dative bonds. In either case, the modification of the MOF occurs through the formation of dative bonds.

Finally, in PSD a reaction is performed on the MOF in a postsynthetic manner that results in the cleavage of a chemical bond within an intact framework (Figure 2). In principle, any kind of chemical bond (e.g., covalent, dative, etc.) can be broken during a PSD reaction to reveal a chemical functionality and produce materials with different properties. As will be described herein, PSD has been less widely explored as a postsynthetic method when compared to conventional PSM; nevertheless, with just a few examples in hand, PSD has already been shown to be a distinct and useful approach for modifying MOFs.

1.3. Earliest Examples of PSM

It took nearly a decade after Robson initially described the concept of PSM[16] for the first reports of these methods to appear in the literature. These initial reports of covalent PSM predate the recent flurry of activity by more than seven years; therefore, these studies are discussed separately as standout examples of PSM that laid the foundation for the larger body of work that followed.

Starting around 1995, Lee and co-workers developed a class of MOF-like coordination solids constructed from Ag(I) ions and rigid nitrile-containing ligands.[30] It was on the basis of this broad class of MOFs, specifically a subgroup of materials based on the 3-fold-symmetric 1,3,5-tris(4-ethynylbenzonitrile)benzene,[31] that the first report of covalent PSM was described. Several 3-fold-symmetric nitrile ligands were assembled with silver triflate to obtain crystalline MOFs. Ligands with a variety of substituents in the 2-position of the central benzene ring were utilized, and the structures of the resulting materials were determined by single-crystal X-ray diffraction (XRD) or PXRD, which showed that they were isotypic (isoreticular) with previously reported materials that possess a 3-D (10,3) network topology with pseudohexagonal pores. Importantly, among the substituted ligands employed for this study, one contained a pendant alcohol group on the 2-position (Figure 3).[31] The installation of these pendant groups, sometimes referred to as



6·AgOTf

Figure 3. Symmetric 1,3,5-tris(4-ethynylbenzonitrile)benzene ligand used for the formation of a MOF upon complexation with silver triflate. The pendant alcohol group on this ligand served as a chemical handle for PSM with trifluoroacetic anhydride.

chemical “handles” or “tags”,[32,33] is an extremely important feature of this early PSM report, as the inclusion of these pendant functional groups is a hallmark feature of most ligands used for covalent PSM. As will be described in detail later, most ligands used for covalent PSM contain some sort of chemical functionality that does not interfere with MOF formation, but can be used as the site for modification in subsequent PSM reactions.

Upon assembly of a MOF from the alcohol-derivatized ligand, the MOF was exposed to vapors of trifluoroacetic anhydride, followed by quenching with benzyl alcohol to consume excess anhydride. Figure 3 shows the overall reaction on the ligand, which was proposed to occur in a heterogeneous fashion and with preservation of the crystalline structure. Figure 3 does not portray the MOF topology, but focuses rather on the postsynthetic chemical transformation; this format will be used throughout this review (structures of the MOFs can be found elsewhere[19] or in the references cited throughout). Retention of crystallinity was demonstrated by PXRD, and conversion of the alcohol to the trifluoromethyl ester was confirmed in situ by infrared (FTIR) spectroscopy. In addition, the MOF was dissolved in acetone-d_6 and analyzed by ^{1}H NMR, which unambiguously confirmed quantitative conversion of the alcohol to the ester. As stated by the authors, “We conclude that it is possible to chemically modify the **6**·AgOTf system with a covalent bond to an introduced guest molecule without destroying the overall crystalline topology.”[31] This first covalent PSM example beautifully highlights many key features that would become central to the recent renaissance in this area, including use of a ligand possessing a free functional group (e.g., tag, handle), chemical modification in a heterogeneous (i.e., solid−gas) manner, preservation of crystallinity after modification verified by X-ray diffraction methods, and dissolution of the solid after modification to permit use of solution ^{1}H NMR to characterize the reaction products. All of these principles and methods are now central features in the numerous reports of PSM that have appeared since 2007.

In a follow-up study by Lee and colleagues in 2000,[34] the same class of 1,3,5-tris(4-ethynylbenzonitrile)benzene ligands were appended with either pendant hydroxyl or silyl ether substituents and allowed to react with silyl triflates to form siloxanes. These reactions produced compounds with silyl ethers, but also products where two ligands were chemically “cross-linked” to form dimers of the ligands in the solid state.[34] Control reactions with other MOFs as well as quenching experiments were used to provide evidence that these PSM reactions were indeed occurring in a heterogeneous manner (e.g., on the intact MOF) and not through a ligand dissolution−reaction−recrystallization mechanism. Of even greater interest, some of the tris(nitrile) ligands used contained multiple hydroxy-terminated substituents, whereby chemical cross-linking with silyl triflates produced low molecular weight polymers (average MW ≈ 7×10^4 amu). Furthermore, these cross-linking reactions did not destroy the crystallinity or porosity of the material, but rather dramatically improved the chemical and thermal stability of the MOF.[34] Unlike the parent MOF, which was readily dissolved in polar solvents such as *t*-BuOH and water, the cross-linked MOF was found to remain crystalline and intact upon exposure to these solvents. Herein, this provides the first glimpse into the practical importance of PSM, whereby the modified MOF, which cannot be obtained by direct MOF synthesis, has improved chemical stability when compared to the parent MOF, without loss of crystallinity or porosity. Once again, the seminal work from Lee and co-workers was a harbinger of things to come.

In parallel with the work described above, Kim and colleagues also reported the successful PSM of a MOF in 2000.[35] This report described the ability of a chiral MOF (POST-1) to act as a heterogeneous, transesterification catalyst (Table 1); indeed, this report was more widely regarded as a seminal report on the use of MOFs as catalysts than for PSM. A base-mediated catalytic mechanism was proposed, where the catalytic sites in the MOF were purported to be basic pyridine nitrogen atoms from the organic linker, some of which, quite surprisingly, were not involved in coordination to the Zn(II)-derived SBUs. To verify that the pyridine nitrogen atoms were the catalytic sites, the authors performed alkylation of these atoms via PSM by using methyl and hexyl iodide (Figure 4). Alkylation of the sites proceeded with retention of crystallinity as confirmed by PXRD and suppressed catalytic activity of the framework. The PSM reaction converts POST-1 from a neutral (pyridyl) to a cationic (pyridinium) framework, which necessitates the presence of counterions. Evidence for I_3^- counterions was obtained by Raman spectroscopy.[35] The formation of the pyridinium groups was unambiguously verified by ^{1}H NMR obtained by dissolution of the MOF. Again, the work by Kim and co-workers illustrates many of the important features that are found in most PSM studies, including verification of crystallinity and the use of solution-phase ^{1}H NMR to characterize the products and

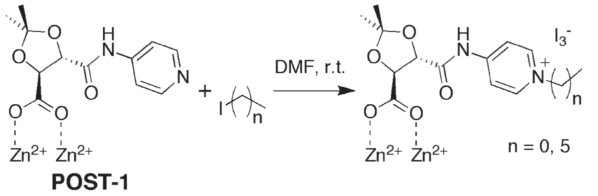


Figure 4. PSM of pyridine nitrogen atoms by alkyl halides in POST-1. Alkylation of these sites eliminates the catalytic activity of the framework, supporting a base-mediated mechanism for this catalytic MOF.

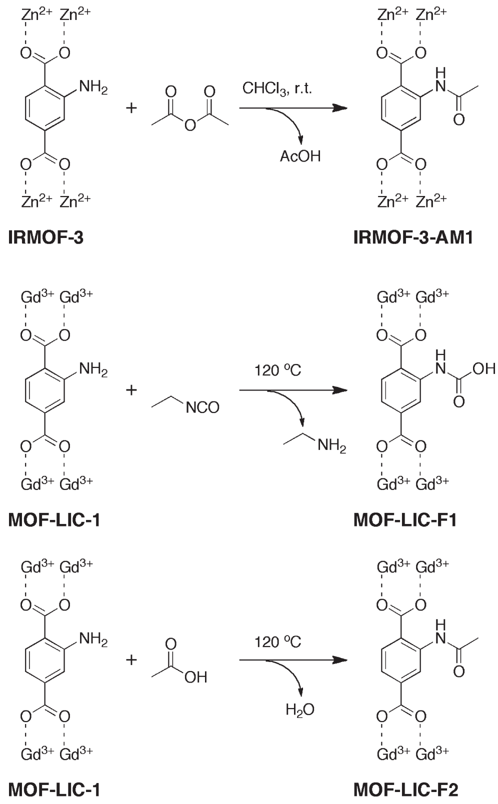


Figure 5. PSM of IRMOF-3 by acetic anhydride (top). PSM of MOF-LIC-1 by ethyl isocyanate (middle) and acetic acid (bottom).

determine the percent conversion. In addition, this study highlights the ability to control physical (charge) and chemical (catalytic) properties of the MOF by PSM.

Despite the groundbreaking findings provided by these studies, investigations on covalent PSM were essentially dormant for nearly seven years (some examples of dative modification appeared during this time, which will be described later). Not until 2007 did the re-emergence of covalent PSM become a prominent feature in the chemistry of MOFs. Indeed, the descriptor "postsynthetic modification" did not appear in the literature until 2007; however, since this time, there has been an explosion in activity that highlights the importance of this approach for the development of MOFs with complex functionality and function.

2. COVALENT PSM

2.1. First "Revival" Reports of PSM on MOFs

Starting in 2007, a number of reports describing the utility of PSM as a means to chemically alter MOFs began to appear. Many of these reports were focused on either amine- or aldehyde-tagged MOFs, the latter of which will be discussed in the next section. The term "postsynthetic modification" was coined by Wang and Cohen in 2007 to describe the reaction of IRMOF-3 (Figure 5) with acetic anhydride.[36] The term was derived by analogy to the process of post-translational modification, used to describe the chemical modification of protein amino acid residues after polypeptide synthesis.[37,38] IRMOF-3 is a derivative of the canonical IRMOF-1 (MOF-5), being comprised of 2-amino-1,4-benzenedicarboxylate (NH_2-BDC) and Zn(II) ions, the latter of which form Zn_4O SBUs.[12] The aromatic amines in IRMOF-3 do not engage in binding to the SBUs and thereby provide the chemical handle for performing PSM. Under mild conditions at room temperature, IRMOF-3 was acetylated in >90% yield with acetic anhydride to produce IRMOF-3-AM1 (AM = amide, Figure 5); subsequent studies showed that under optimized conditions quantitative conversion could be achieved.[39] The degree of conversion was confirmed by ^1H NMR upon digestion of IRMOF-3-AM1 in DMSO-d_6 and DCl (Figure 6).[36] The high degree of conversion highlights the fact that the reagent can access both the exterior and interior of the MOF, resulting in modification of all of the organic linkers.

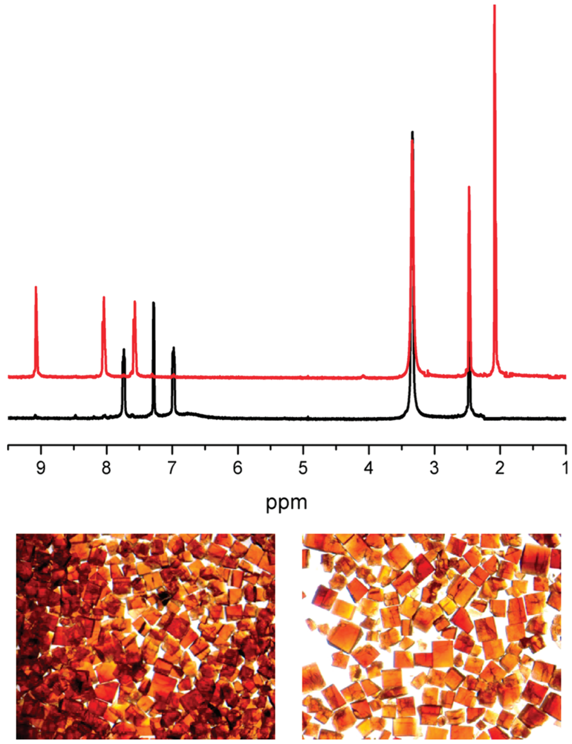


Figure 6. ^1H NMR spectrum (top) of IRMOF-3 (black) and IRMOF-3 after modification with acetic anhydride (IRMOF-3-AM1; red). ^1H NMR spectra were obtained after digestion of the materials in DMSO-d_6 and DCl. Photographs of IRMOF-3 before (bottom left) and after (bottom right) modification with acetic anhydride.

Photographs of the MOF crystals before (IRMOF-3) and after (IRMOF-3-AM1) modification with acetic anhydride give an indication of the clean single-crystal-to-single-crystal (SCSC) conversion that occurs during this reaction (Figure 6). The crystallinity and thermal stability of IRMOF-3-AM1 were verified by XRD, PXRD, and thermogravimetric analysis (TGA) studies. The porosity of IRMOF-3-AM1 was confirmed by volumetric gas uptake studies, which gave Brunauer−Emmett−Teller (BET)

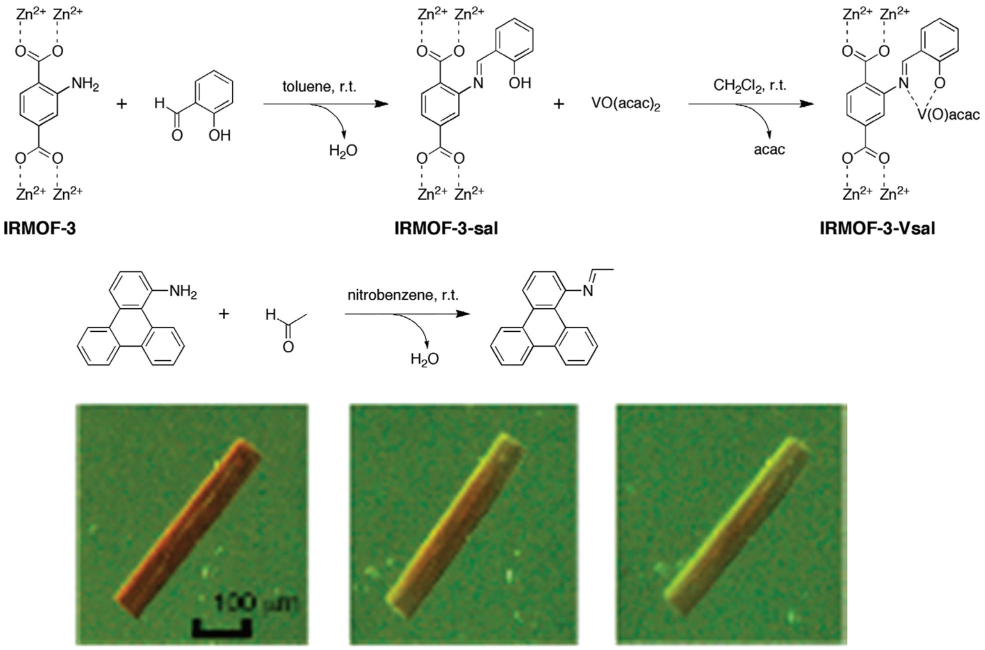


Figure 7. PSM of IRMOF-3 with salicylaldehyde (top) and subsequent metalation with VO(acac)$_2$·H$_2$O. This was the earliest example of combining covalent and dative PSM. PSM of an immobilized 1-aminotriphenylene guest with acetaldehyde inside a Zn(TPT) MOF (middle). Formation of the triphenylene Schiff base product could be observed by a change in color of the crystals from red to yellow (bottom). Reprinted from ref 42. Copyright 2008 American Chemical Society.

surface areas of ∼1400−1600 m^2/g. This value is substantially lower than that of unmodified IRMOF-3 (∼2400−2600 m^2/g),[39] but still characteristic of a highly porous solid. The observed drop in surface area has subsequently been shown in many studies to be typical of MOFs that undergo PSM.

Several other reports involving the PSM of amine-tagged MOFs appeared in early 2008. Gamez and co-workers reported the modification of a lanthanide-based MOF (MOF-LIC-1, LIC = Leiden Institute of Chemistry) that also employed NH$_2$-BDC as the organic linker (Table 1).[40] MOF-LIC-1 was treated with vaporized ethyl isocyanate or acetic acid (a gas solid heterogeneous reaction, unlike most other reported PSM reactions) at elevated temperatures (120 °C, 1 h) to afforded modified MOF-LIC-F1 and MOF-LIC-F2 that possess urethane and amide substituents (Figure 5). Importantly, both MOF-LIC-F1 and MOF-LIC-F2 were crystallographically characterized, and electron density associated with the modified substituents was observed (unlike the previous example with IRMOF-3). Indeed, the degree of PSM conversion could be estimated from the XRD structures at >90% and ∼50% for MOF-LIC-F1 and MOF-LIC-F2, respectively.[40] It was noted that the high temperature at which these transformations were performed did lead to some decomposition of the MOFs at longer reaction times, particularly when acetic acid was used.

Also in 2008, the group of Rosseinsky reported the condensation of salicylaldehyde with IRMOF-3 in toluene (room temperature (rt), 7 d).[41] This resulted in a modified MOF (IRMOF-3-sal) containing salicylidene (Schiff base) groups appended to the BDC linkers (Figure 7). Modification was characterized by solid-state ^{1}H MAS NMR, and combustion analysis suggested that ∼40% of the amine sites were converted to the salicylidene moiety. Noting that the salicylidene group is a good metal chelator, IRMOF-3-sal was metalated with VO(acac)$_2$·H$_2$O (acac = acetylacetonate) to produce IRMOF-3-Vsal.[41] This important finding demonstrated that installation of strong metal chelators onto the framework by PSM did not jeopardize the structural integrity of the material. Furthermore, these chelators are accessible for subsequent dative modification, thereby generating metal sites within the MOF suitable for additional reactivity. In this example, IRMOF-3-Vsal was examined as an oxidation catalyst for cyclohexene in the presence of *t*-BuOOH. IRMOF-3-Vsal did show activity (40% conversion in THF at 60 °C for 72 h), but the MOF degraded under the reaction conditions as gauged by PXRD.[41] Nonetheless, this report paved the way for many other investigations that combined covalent and dative PSM on a single MOF.

Finally, Fujita and co-workers reported another early example of PSM on an amine-tagged MOF.[42] As in the previous study, the condensation of an aldehyde with an amine group to produce an imine was described. However, unlike all the previous examples, PSM was not performed on the framework directly, but rather on an immobilized guest molecule within the framework. The molecular guest, 1-aminotriphenylene (Figure 7), is strongly bound to the MOF by stacking interactions with the tris(4-pyridyl)triazine (TPT) organic linker, which is connected into an extended structure via coordination to Zn(II) ions. Immersion of the MOF in a nitrobenzene solution of acetaldehyde resulted in a red to yellow color change in the crystals. This color change was due to a change in donor ability of the modified guest molecule and is indicative of the amine-to-imine conversion (Figure 7). XRD was used to unambiguously demonstrate conversion to the Schiff base product in an SCSC fashion. Subsequent studies showed that the same framework containing a 2-aminotriphenylene guest could undergo covalent PSM with anhydrides and isocyanates,[43] with single-crystal XRD evidence for formation of the PSM products. The ability to characterize the products of the covalent PSM reactions by single-crystal XRD has proven to be a major strength of this system and one only rarely duplicated by other PSM studies. Fujita went on to describe this chemistry as MOFs acting as “single-crystalline molecular flasks”, as the PSM reaction was occurring on guests within the pores of the MOF lattice. Despite this distinction, many comparisons between the chemistry of MOFs as single-crystalline molecular flasks and PSM have been drawn, so the other exciting results described by Fujita and co-workers in this area of research will be reviewed here as well.

2.2. Covalent PSM on Amine-Tagged MOFs

2.2.1. Zinc Carboxylate MOFs. All of the first revival reports on PSM, described in the previous section, involve the use of amine-tagged MOFs (or guests within the MOF). Indeed, within the current body of PSM research, amine-tagged MOFs have been used more extensively as chemical handles than any other functional group. This is probably due, in large part, to the commercial availability of NH_2-BDC and its relatively straightforward incorporation into a variety of MOFs.

The versatility of NH_2-BDC as a MOF building block was well illustrated by its ability to readily substitute for BDC in at least three different prototypical MOF topologies: IRMOF-1, DMOF-1 (D = 1,4-diazabicyclo[2.2.2]octane (dabco)), and UMCM-1 (UMCM = University of Michigan Crystalline Material).[44] Unlike IRMOF-1, DMOF-1 and UMCM-1 are MOF copolymers that utilize two organic linkers in their construction (Table 1). DMOF-1 uses BDC and dabco,[45] and UMCM-1 uses BDC and 4,4′,4″-benzene-1,3,5-triyl tribenzoate (BTB).[46] It was shown that, for both of these MOFs, with only slight modifications of the original reaction conditions, NH_2-BDC could be introduced in place of BDC.[44] In this way, two MOFs that are not readily amenable to PSM, DMOF-1 and UMCM-1, are readily reformulated as topologically identical materials (DMOF-1-NH_2 and UMCM-1-NH_2) that are “PSM-ready” with an amine tag. The topological fidelity of DMOF-1-NH_2 and UMCM-1-NH_2 was verified by a combination of XRD and PXRD studies.[44]

As anticipated, DMOF-1-NH_2 and UMCM-1-NH_2 readily undergo PSM with reagents such as anhydrides to form the corresponding amide-bearing materials (DMOF-1-AM*R* and UMCM-1-AM*R*, where *R* designates the remaining substituent, Figure 8).[44] By using a series of simple alkyl anhydrides of varying chain length, it was observed that the MOF topology/porosity could affect the yield of the PSM reaction. In general, PSM conversion drops with increasing length of the alkyl anhydride (ranging from >95% to as low as ∼1%), as might be expected on the basis of steric considerations.[39] In addition, when several zinc carboxylate MOFs are compared, the pore diameter decreases as UMCM (∼32 Å) > IRMOF (∼13 Å) > DMOF (∼7 Å) across this series of frameworks.[12,45,46] Consistent with this trend, it was observed that under identical reaction conditions linear alkyl anhydrides showed the highest degree of conversion with UMCM-1-NH_2, followed by IRMOF-3, and the lowest conversion with DMOF-1-NH_2.[44] The degree of conversion observed with branched alkyl anhydrides was more complex, with the *tert*-butyl analogue (pivalic anhydride) showing little modification with any of these MOFs. The poor reactivity of pivalic anhydride was later confirmed, as PSM of IRMOF-3 with the asymmetric butyric pivalic anhydride resulted only in the formation of IRMOF-3-AM3 (Figure 8).[47] Finally, it was shown that these MOFs will also react with isocyanates to produce MOFs with urea-linked substituents (e.g., IRMOF-3-UR*R*, UR = urea, Figure 8), although the yields of these reactions were generally lower than those of reactions with comparable anhydrides.[48]

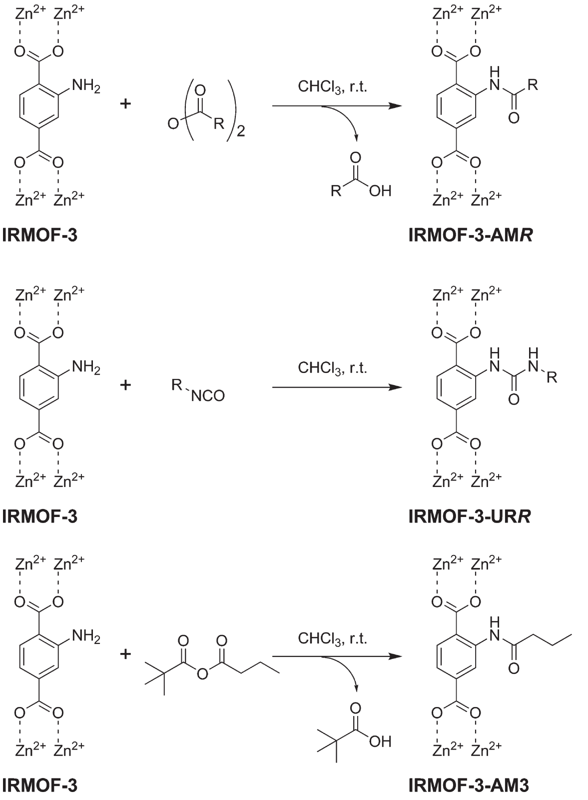


Figure 8. PSM of IRMOF-3 with anhydrides and isocyanates. Similar PSM reactions have been reported with several other amine-tagged MOFs, such as DMOF-1-NH_2, UMCM-1-NH_2, and others. The mixed asymmetric butyric pivalic anhydride only produces IRMOF-3-AM3 (bottom).

Amine-tagged MOFs were the first systems upon which so-called “tandem” covalent postsynthetic modification was performed, e.g., where more than one chemical reaction was performed in sequence on the same crystalline material. The initial report of tandem modification highlighted two types of tandem covalent PSM.[49] In the first approach, two different anhydrides, acetic anhydride and crotonic anhydride, were used to modify IRMOF-3 to produce a MOF with two different ligand substituents (IRMOF-3-AM1/Crot). By controlling the duration of the first reaction, the ratio of the two different substituents could be easily manipulated (as demonstrated by ^{1}H NMR upon digestion of the MOFs). In the second approach, the unsaturated crotonic anhydride was used to fully modify IRMOF-3, producing IRMOF-1-AMCrot, followed by treatment with bromine, resulting in bromination of the olefin-containing substituent (Figure 9).[49] In both approaches, the materials remained crystalline and porous as demonstrated by PXRD and gas sorption measurements. Both approaches highlight that two different covalent PSM reactions can be performed on a single framework to make highly functionalized materials. Indeed, in a follow-up study, it was shown that IRMOF-3 could be modified with up to four different anhydrides and/or isocyanates without loss of crystallinity.[47] These findings suggest that the combinations of functional MOF materials that can be produced by PSM are nearly limitless.

Ring-opening covalent PSM reactions with cyclic reagents have been performed on amine-tagged MOFs. Yaghi and co-workers reported the reaction of IRMOF-3 with two cyclic reagents, 1,3-propane sultone and 2-methylaziridine (Figure 10).[50] Modification

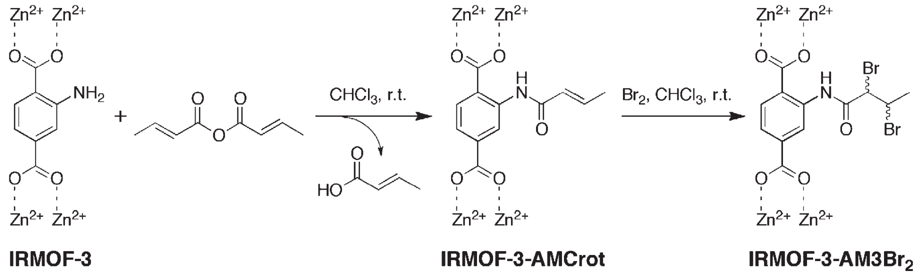


Figure 9. Tandem covalent PSM performed on IRMOF-3 to produce the brominated IRMOF-3-AM3Br_2.

by either reagent did not degrade the crystallinity of the MOF as gauged by PXRD analysis, and both remained porous after modification (modification with 2-methylaziridine resulted in a lower surface area than modification with 1,3-propane sultone). In the case of covalent PSM with 1,3-propane sultone, the resulting MOF displays free sulfonate groups within the framework pores (IRMOF-3b), while modification with 2-methylaziridine produces free alkylamine groups in the pores (IRMOF-3). Ring-opening covalent PSM reactions have also been reported with cyclic anhydrides (Figure 10);[47,51] a more detailed discussion of some of these systems is given later in this review.

Simple acylation of amine-tagged MOFs has been shown to be an effective method to modulate their physical properties. For example, introduction of aromatic groups to IRMOF-3 and UMCM-1-NH_2 via reaction with aryl anhydrides was shown to increase the hydrogen uptake capacity of these materials.[52] It is likely that a more exhaustive exploration of different amide substituents within MOFs could further improve the selectivity and isosteric heat of adsorption for hydrogen and other gases of interest. Indeed, modification of DMOF-1-NH_2 with simple alkyl anhydrides was shown to induce "breathing" (e.g., flexibility) into this MOF in the presence of several gases, most notably CO_2.[53] The ability to turn on and modulate this type of breathing behavior in a MOF via covalent PSM strongly suggests that the approach may be useful for generating materials with tunable and gated gas sorption properties.[1,2]

Perhaps a more significant modulation of physical properties obtained by simple acylation of an amine-tagged MOF was observed upon modification of IRMOF-3 with long-chain alkyl anhydrides. As mentioned earlier, the number of amine tags that are modified by covalent PSM in a MOF such as IRMOF-3 is reduced as the anhydride gets larger. Nevertheless, even low degrees of modification with long anhydrides can significantly improve the chemical stability of the frameworks. Many zinc carboxylate MOFs, most notably the IRMOFs, are very hygroscopic and show very limited stability with respect to protic solvents, including water.[54,55] This is a major impediment to the use of such materials in any practical application, where even atmospheric moisture can result in framework degradation. Within that context, it was found that modification of IRMOF-3 with long anhydrides (four or more methylene groups) could produce hydrophobic materials with dramatically improved stability with respect to water.[56] These modified IRMOF-3 samples (IRMOF-3-AM4, -AM5, -AM6, and -AM15) were shown to be hydrophobic on the basis of contact angle measurements with water. The materials were found to be extremely stable to moisture, even upon immersion in water, as evidenced by PXRD and scanning electron microscopy (SEM) measurements. It is important to note that, despite covalent PSM and their hydrophobic nature, these modified MOFs still showed extremely high accessible surface areas as gauged by nitrogen adsorption.[39] In addition, similar covalent PSM of a class of Al(III)-based MOFs (MILs, vide infra) resulted in an unusual class of superhydrophobic materials.[56]

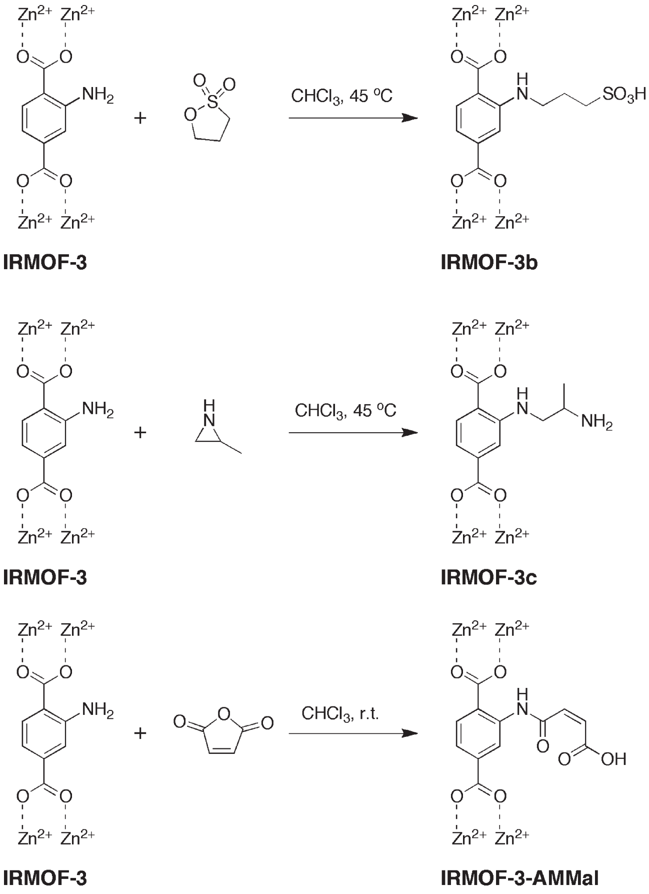


Figure 10. Covalent PSM ring-opening reactions on IRMOF-3.

Along these same lines, Jeong and co-workers showed that covalent PSM could be used to change the permeability of IRMOF membranes.[57] IRMOF-1 seed layers were grown on graphite-coated α-Al_2O_3 using a microwave synthetic procedure, followed by heteroepitaxial growth of IRMOF-3 membranes on the IRMOF-1 layer. Importantly, surfactants were used to prepared crack-free membranes. The IRMOF-3 membranes were found to possess gas permeability similar to that of IRMOF-1, with an unexpectedly high permeability for CO_2,[58] which was attributed to the amine tags of IRMOF-3. Treating the IRMOF-3 membranes with heptanoic anhydride produced

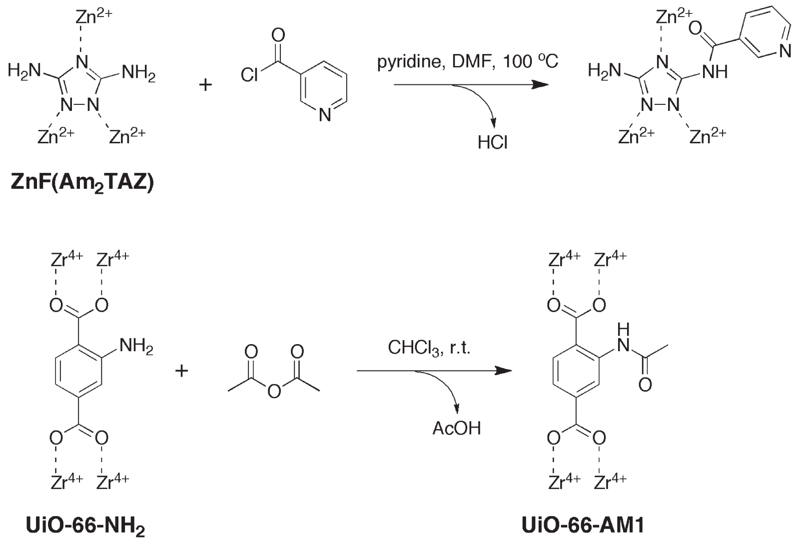


Figure 11. Covalent PSM on the amine-tagged MOFs ZnF(Am_2TAZ) and UiO-66-NH_2.

IRMOF-3-AM6 membranes with ∼91% conversion. Upon covalent PSM, the IRMOF-3-AM6 membranes displayed increased permeability to propane over CO_2, which was attributed to the addition of the hydrophobic substitutents.[57] Again, PSM is shown as a useful tool for tuning the physical properties of an MOF material that may prove useful for technology applications.

2.2.2. Chemically Robust MOFs. Subsequent studies by several laboratories have shown that the NH_2-BDC ligand is quite compatible with a number of BDC-derived MOFs, thereby providing PSM-ready derivatives of many known MOF materials. Other MOFs that have been shown to accommodate NH_2-BDC in place of BDC are MIL-53(Al) (MIL = Material Institut Lavoisier), MIL-101(Fe), MIL-101(Al),[59] CAU-1 (CAU = Christian-Albrechts-University),[60] and UiO-66 (UiO = University of Oslo) (Table 1).[61−63] Many of these MOFs are more chemically robust when compared with zinc carboxylate-based MOFs and hence open up the possibility of performing an even wider range of PSM reactions. The growing popularity of PSM is apparent as almost all studies on new amine-tagged MOFs either demonstrate or suggest the possibility of PSM on these materials.

The advantage of covalent PSM on more chemically stable MOFs has been suggested by comparing modification of IRMOF-3 with a MOF constructed of 3,5-diamino-1,2,4-triazole (Am_2TAZ) and Zn(II) ions.[64] Farrusseng and co-workers reported covalent PSM on the latter two MOFs using nicotinoyl chloride in DMF and pyridine at high temperature (Figure 11).[65] The high temperature and polar solvents used in these reaction conditions, combined with production of HCl as a byproduct, was found to degrade IRMOF-3 as evidenced by a substantial drop in accessible surface area (no PXRD data after PSM were provided, but the authors noted a loss in crystallinity). In contrast, PXRD data suggested that the triazole-based MOF remained crystalline under these conditions with up to 60% modification as estimated from elemental analysis. The MOFs produced in this study were tested as basic catalysts for the aza-Michael reaction and showed improved activity when compared with alkylamine-functionalized mesoporous silicas.[65]

The UiO class of materials described by Lillerud and co-workers are based on dicarboxylate ligands and the highly oxophilic Zr(IV) ion.[66] The oxophilicity and high nuclearity of the SBUs found in the UiO materials imparts these MOFs with quite good chemical stability. The UiO material is also highly tolerant of substitution on the dicarboxylate linker. As described in nearly simultaneous independent reports by Lillerud[62] and Cohen,[61] amino-, bromo-, and nitro-tagged analogues of UiO-66 (which uses BDC as the organic linker) were prepared. In general, the materials were found to possess good chemical and thermal stability, similar to that of the parent material. Access to UiO-66-NH_2 (derived from NH_2-BDC) provided a PSM-ready version of UiO-66, and not unexpectedly, UiO-66-NH_2 can be modified with anhydrides to make amide derivatives (Figure 11).[61,63] Quantitative conversion is observed with small anhydrides (e.g., acetic anhydride), and the quality of the resulting material (UiO-66-AM1) was confirmed with PXRD and gas sorption data. In one of these studies,[63] H/D exchange (by introduction of D_2O vapors) was cleverly used to assign bands in the FTIR spectra attributed to the amide substituents formed via covalent PSM. In addition to PSM chemistry, UiO-66-NH_2 was independently reported to act as a mixed acid—base catalyst for a cross-aldol condensation.[67] As will be described in other sections below, the chemical stability of the UiO-66 materials afforded other PSM opportunities.

Other chemically robust NH_2-BDC-containing MOFs have provided access to new PSM reactions, which would cause degradation of more chemically labile MOFs (e.g., IRMOFs). The MIL-53 class of materials have been extensively studied for their breathing behavior (i.e., framework flexibility). Férey and Stock reported the first synthesis and covalent PSM on MIL-53(Al)-NH_2 (MIL-53(Fe)-NH_2 had been previously reported by the same group).[68,69] They treated MIL-53(Al)-NH_2 with neat formic acid at elevated temperatures for several hours (Figure 12), producing the formylated MOF, which was characterized by a suite of methods including solid-state NMR and FTIR.[68] These reaction conditions would most certainly destroy more delicate MOFs and gave a clear indication that such robust MOFs would open up these types of materials to new chemistry.

The chemical stability of MIL-53(Al)-NH_2 made this material suitable for modification with anhydrides that produce pendant carboxylic acids, which at higher conversions degrade more chemically labile MOFs.[47] Treatment of MIL-53(Al)-NH_2 with

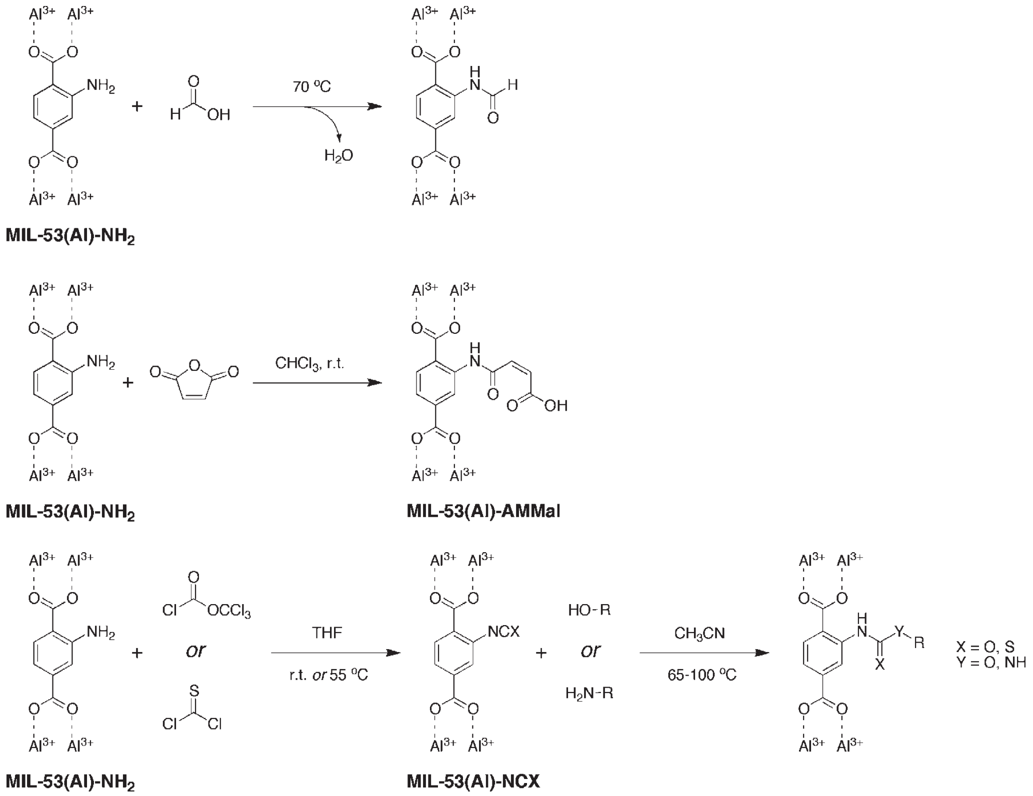


Figure 12. Covalent PSM of MIL-53(Al)-NH_2 with formic acid (top), maleic anhydride (middle), and with phosgene reagents (bottom). The greater chemical stability of MIL-53(Al)-NH_2 relative to many other MOFs allows for use of the harsh chemical treatments used in these PSM reactions.

succinic or maleic anhydride results in ~40% conversion of the amine sites to products containing pendant carboxylate groups within the pores of the MOF (MIL-53(Al)-AMSuc and MIL-53(Al)-AMMal, respectively, Figure 12).[51] The presence of these Brønsted acid sites within the MOFs was exploited as an opportunity to perform heterogeneous catalysis. Indeed, the more acidic MIL-53(Al)-AMMal was found to be a competent catalyst for the ring-opening reaction of epoxides with alcohols.[51]

Building upon these observations, it was found that MIL-53(Al)-NH_2 could undergo useful chemical transformations that were not accessible to other MOFs. Treatment of MIL-53(Al)-NH_2 with diphosgene or thiophosgene in THF resulted in ~90% conversion of the amine tags to isocyanate (MIL-53(Al)-NCO) or isothiocyanate (MIL-53(Al)-NCS) tags, respectively (Figure 12).[70] Conversion was readily monitored in the solid state by FTIR spectroscopy, which showed the emergence of characteristic iso(thio)cyanate stretches, and was verified by ^{1}H NMR spectroscopy upon digestion of the products in HF and DMSO-d_6. The MOFs remained highly crystalline under these harsh PSM conditions as evidenced by PXRD. PXRD data indicated that MIL-53(Al)-NCO and MIL-53(Al)-NCS were found to reside in a narrow pore (np) and large pore (lp) form, respectively, indicative of differences in the breathing behavior of the MILs bearing different functional groups. In addition, gas sorption data indicated that the uptake of gases was altered upon covalent PSM. For example, while MIL-53(Al)-NH_2 readily adsorbs both N_2 and CO_2, MIL-53(Al)-NCO was found to be selective for CO_2 adsorption under identical conditions. Finally, the presence of reactive functional groups in MIL-53(Al)-NCO and MIL-53(Al)-NCS allowed for additional (i.e., tandem) covalent PSM to be performed. Exposure of these materials to alcohols or amines resulted in conversion to the corresponding (thio)-carbamate- or (thio)urea-bearing MOFs (Figure 12).[70] These investigations clearly demonstrate that more robust amine-tagged MOFs provide access to more chemical reactions and hence a wider range of functionalized materials.

2.2.3. Imine Condensations and Alkylations. As already described, imine (Schiff base) condensations on amine-tagged MOFs have proved a highly fruitful area of study for covalent PSM. In addition to the aforementioned reports, an investigation of imine condensations on a MOF containing a 2-aminopyrazine ligand has also appeared in the literature.[71] Perhaps the most significant contribution of using the imine condensation on an amine-tagged MOF came from Fujita's crystalline molecular flasks.[72] By monitoring the reaction of acetaldehyde with the same 1-aminotriphenylene guest described earlier, the elusive hemiaminal intermediate of the condensation reaction could be trapped and crystallographically characterized. Covalent PSM of the MOF was performed in situ on a diffractometer at 215 K by flowing an ethyl acetate solution of acetaldehyde over the crystal; subsequent cooling to 90 K and collection of XRD data revealed the hemiaminal intermediate in ~36% yield.[72] These experiments show the power of PSM within the periodic structure of an MOF to allow for the detailed characterization of an otherwise elusive reactive intermediate.

The alkylation of an amine-tagged MOF has been reported in the context of using MOFs for biomedical applications.[7] An increasing number of studies are reporting on the use of MOFs for drug delivery, medical imaging, and other biotechnology applications; this subject has been reviewed elsewhere. Lin and co-workers have been at the forefront of such efforts, and in at least one study they have used covalent PSM to tailor MOF

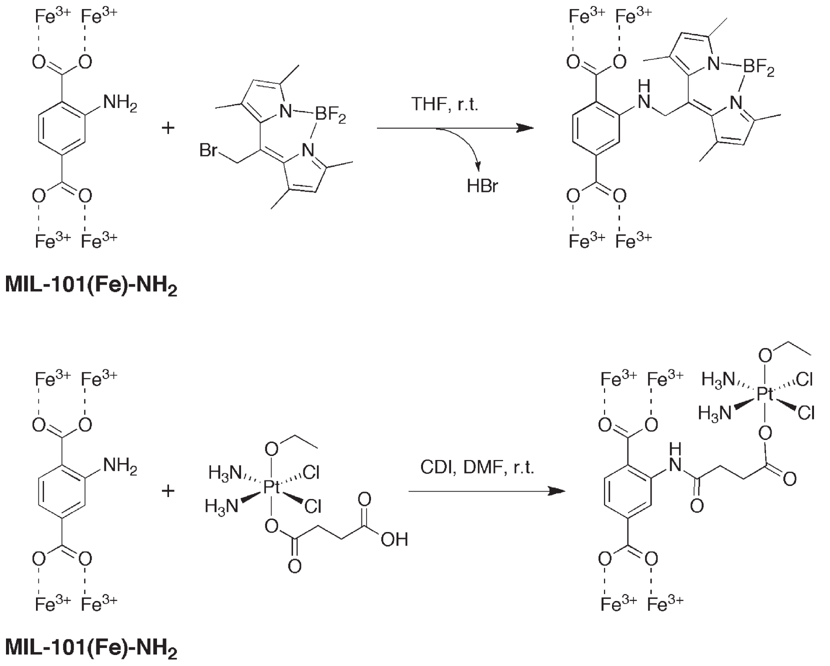


Figure 13. Covalent PSM of MIL-101(Fe)-NH_2 with reagents relevant to biomedical applications.

nanoparticles for such applications. A copolymer material with the MIL-101 topology was synthesized from $FeCl_3$, BDC, and NH_2-BDC under microwave heating conditions.[73] The resulting nanocrystals of MIL-101(Fe)-NH_2 could be prepared with up to ~17% NH_2-BDC content, providing an amine tag for covalent PSM. Although the Fe(III)-based framework is not as stable as the Cr(III) parent material, Fe(III) was viewed as advantageous for biocompatibility and possible use in magnetic resonance imaging (MRI). Acylation chemistry was performed with a Pt(IV) compound that can be released as a prodrug for the anticancer drug cisplatin (Figure 13). In addition, alkylation of the amine tags was achieved with 1,3,5,7-tetramethyl-4,4-difluoro-8-(bromomethyl)-4-bora-3a,4a-diaza-*s*-indacene (Br-BODIPY) in THF (Figure 13).[73] Covalent PSM of the BODIPY fluorophore to MIL-101(Fe)-NH_2 was used to monitor the stability of the nanoparticles in biological media and in cells. BODIPY grafted onto MIL-101(Fe)-NH_2 was nonfluorescent due to quenching from the Fe(III) SBUs, but upon degradation of the particles, the liberated BODIPY−NH_2-BDC conjugate was emissive.[73] This report demonstrates yet another covalent PSM reaction and the role that PSM may play in the future of advancing the application of MOFs to biotechnology.

2.3. Covalent PSM on Aldehyde-Tagged MOFs

Among the first examples of covalent PSM on an aldehyde-tagged MOF was that described by Burrows and co-workers.[32] Indeed, it was in this report that Burrows coined the use of the term "tag", describing it in the following way: "We define a 'tag' as a group or functionality that is stable and innocent (that is, non-structure-defining) during MOF formation, but that can be transformed by a post-synthetic modification." By combining Zn(II) and 2-formylbiphenyl-4,4′-dicarboxylic acid, an IRMOF-9 analogue (with a slightly modified SBU) was generated with aldehyde tags on the dicarboxylate ligand. Treatment of this MOF with a solution of 2,4-dinitrophenylhydrazine in DMF at room temperature resulted in covalent PSM with ~60% conversion to the hydrazone product that was apparent from a color change in the crystals from colorless to red.[32] Covalent PSM proceeds in an SCSC fashion, and an XRD structure determination of the hydrazone product was obtained. In addition, it was shown that the 2-formylbiphenyl-4,4′-dicarboxylic acid ligand could be combined with another biphenyl-4,4′-dicarboxylic acid ligand, thereby effectively "doping" the resulting MOF with a defined number of tagged ligands.[32]

The first covalent PSM described for a zeolite−imidazolate framework (ZIF) was performed with an aldehyde framework (Table 1). The ZIF series of materials are reported to be more stable than many other MOFs[74] and as such should prove robust under a greater range of PSM conditions. This was demonstrated with ZIF-90, which is prepared from imidazolate-2-carboxyaldehyde and Zn(II) and contains an aldehyde tag that proved amenable to PSM under reaction conditions that would not be suitable for a typical zinc(II) carboxylate-based MOF (e.g., IRMOF-3). In the first reaction, ZIF-90 was exposed to a solution of $NaBH_4$ in MeOH at 60 °C, resulting in reduction of the aldehyde to the corresponding alcohol (ZIF-91, Figure 14). The use of a strong reducing agent and a protic, polar solvent at elevated temperatures demonstrates the stability of the ZIF when compared to other systems such as an IRMOF, which would readily degrade under such reaction conditions. In a second reaction, ZIF-90 was combined with ethanolamine in MeOH at 60 °C to generate an imine substituent terminated with an alcohol group (ZIF-92, Figure 14). The crystallinity and composition of ZIF-91 and ZIF-92 were confirmed by PXRD and a variety of spectroscopic methods including FTIR and solid-state ^{13}C NMR. Gas sorption showed that the porosity of ZIF-91 was slightly lower when compared with that of ZIF-90, as is typically observed after covalent PSM. However, ZIF-92 was found to be essentially nonporous, which was expected on the basis of the presence of the larger ethanolamine substituents. The ZIF materials have a much smaller pore size when compared to IRMOFs, and hence, the pores can be more readily occluded by

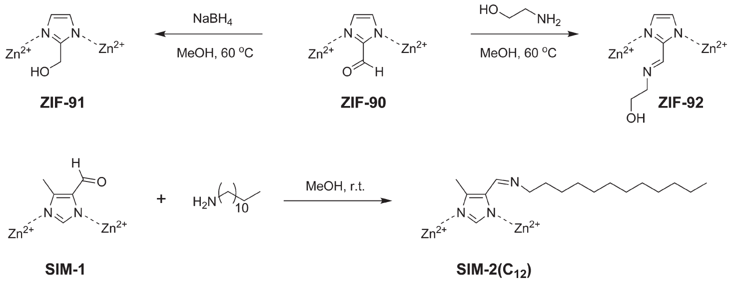


Figure 14. Covalent PSM on ZIF-90 with reducing agents or amines (top). The polar solvents used at elevated temperatures would not be tolerated by more chemically labile MOFs. Covalent PSM on SIM-1 with dodecylamine to produce the hydrophobic MOF SIM-2(C_{12}) (bottom).

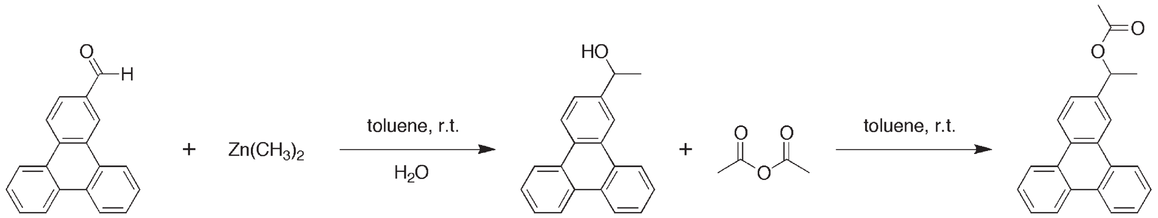


Figure 15. Tandem covalent PSM on an aldehyde-tagged triphenylene guest molecule with Lewis acidic organozinc reagents.

the introduction of substituents by PSM. The use of ZIFs highlights the importance of chemical stability in opening up the scope of chemical reactions that can be exploited by postsynthetic methods.

Caro and co-workers have exploited the imine condensation reaction between ZIF-90 and amines with great success to stabilize and modify ZIF membranes. In one study,[75] ZIF-90 was formed on an Al_2O_3 support that had been modified with (3-aminopropyl)triethoxysilane (APTES). The APTES molecules bound to the Al_2O_3 support presented primary amine groups that could react with the aldehyde group of ZIF-90 during MOF synthesis, creating a covalent linkage between the ZIF and the supporting substrate. The resulting ZIF films showed enhanced thermal and hydrothermal stability.[75] In a second study,[75] a ZIF-90 film was subjected to covalent PSM with ethanolamine (as discussed above) to produce a membrane with enhanced selectivity for H_2 transport over that of other gases such as CO_2. These studies by Caro show that covalent PSM can be performed on thin film formulations of MOFs with significant consequences for the stability of these films and their performance in chemical separations.

Covalent PSM on another ZIF-like MOF has been reported to enhance the catalytic activity of the framework. The group of Farrusseng synthesized SIM-1 (SIM = substituted imidazolate material) from Zn(II) ions and 4-methyl-5-imidazolecarboxaldehyde, which also contains an aldehyde tag on the framework (Table 1).[76] SIM-1 was treated with dodecylamine in anhydrous MeOH at room temperature to produce SIM-2(C_{12}), where ~22% of the aldehyde groups have been converted to imines possessing C_{12} alkyl chains (Figure 14).[77] SIM-1 and SIM-2(C_{12}) were then tested as a catalyst for the Knoevenagel condensation. These experiments showed that the more hydrophobic SIM-2(C_{12}) was a much better catalyst when compared to SIM-1. The increased catalytic activity was attributed to the greater substrate access to the catalytic (basic) sites by exclusion of water from the MOF. In this study, SIM-2(C_{12}) was used to prepare ethyl 2-cyano-3-methyl-5-phenylpent-2-enoate, a precursor of citronitrile, which is widely used in the cosmetic and fragrance industries.[77]

The single-crystalline molecular flask approach described by Fujita has also been applied to MOFs containing an aldehyde-tagged guest. Using the same MOF as described for their extensive studies with 1-aminotriphenylene guests, 2-formyltriphenylene was encapsulated.[43,78] The aldehyde-tagged guest could be converted to imine products by exposing the MOF to an ethyl acetate solution of amines. As with their other studies, XRD analysis was able to clearly demonstrate formation of the PSM product.[43] In a related study,[78] treatment of the same framework with organometallic zinc reagents (e.g., dimethylzinc) in toluene produced the secondary alcohol guest (Figure 15) in a PSM and SCSC fashion as clearly evidenced by XRD structure determination. The reaction within the framework was more rapid and selective than the same reaction in free solution, but expectedly was limited to smaller reagents that could fit within the pores of the framework (e.g., no reaction was observed with diphenylzinc). Furthermore, subsequent treatment of the crystals with acetic anhydride in a tandem PSM reaction resulted in quantitative conversion to the acetylated product (Figure 15), demonstrating the ability to perform tandem covalent PSM.[78] These studies show that even strongly Lewis acidic reagents can be used with some MOFs to perform covalent PSM.

2.4. Covalent PSM "Click" Chemistry

Click chemistry has become an important and popular chemical approach for the efficient conjugation of molecules ranging from proteins to polymers. Click chemistry generally (although not exclusively) refers to the 1,3-dipolar (Huisgen) cycloaddition reaction between an azide and an alkyne.[79] These couplings are often catalyzed by Cu(I), but catalyst-free forms of the reaction are also known.[80] Among the first examples of PSM click chemistry was a study by Goto et al. in 2008,[81] where a dicarboxylate ligand bearing two azide groups was combined with Zn(II) to obtain an IRMOF structure designated N3-MOF-16 (Figure 16). This MOF was then treated at elevated temperatures

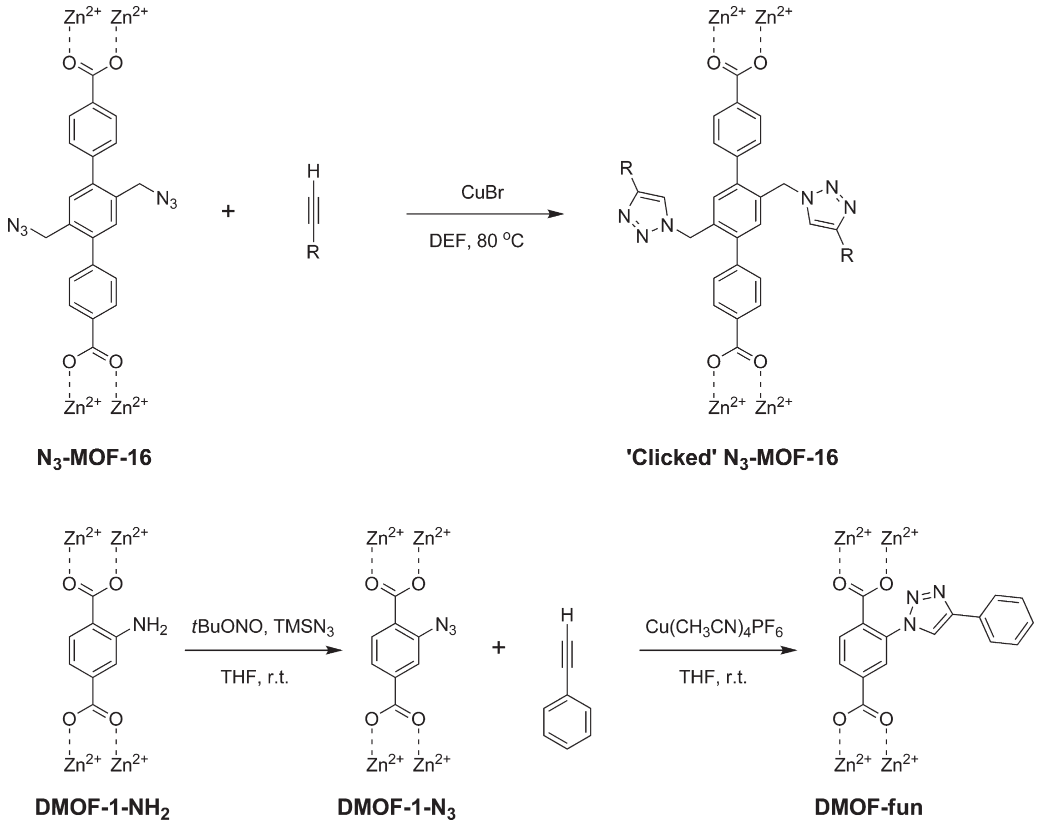


Figure 16. Click reaction performed on the azide-tagged N_3-MOF-16 (an isoreticular analogue of IRMOF-16, top). Tandem PSM of DMOF-1-NH_2 to DMOF-1-N_3 and finally to the triazole-bearing DMOF-fun (bottom).

(80 °C) in DEF with various alkynes and CuBr as the catalyst. The elevated temperatures used in these PSM experiments bring into question whether the reactions are entirely homogeneous, as the authors note that some dissolution of the crystals occurred and in the presence of certain alkynes (bearing free amines or carboxylic acids) that the crystals dissolved entirely. Nonetheless, with some alkynes the click reaction did proceed with essentially quantitative conversion to the expected triazole products (Figure 16) as gauged by solution ^{1}H NMR upon digestion of the crystals in DMSO-d_6 and DCl.[81] The stability of the modified MOFs was suggested by PXRD data, although no gas sorption data were provided. The authors suggest that click reactions, particularly if localized to the surface of the MOF, could be used to install gating groups or to encase the MOF in a polymer to make a hybrid particle.

More recently, Farrusseng and colleagues reported the formation of an azide-bearing MOF and subsequent click chemistry in an all-PSM approach.[82] Starting with DMOF-1-NH_2 or MIL-68(In)-NH_2 (both of which utilize NH_2-BDC as an organic linker), the amine group was transformed into an azide by treatment with *t*-BuONO and $TMSN_3$ (TMS = trimethylsilyl) in THF to produce the azide-bearing MOF. Formation of the azide group in DMOF-1-N_3 or MIL-68(In)-N_3 was confirmed by FTIR spectroscopy, which displayed a characteristic azide stretch at 2123 cm^{-1}. Combination of the azide-tagged MOFs with phenylacetylene and a Cu(I) source in THF produced the desired "clicked" MOF products in >90% conversion over both steps. A concomitant loss of the azide stretch is observed in the FTIR spectra upon completion of the click reaction. PXRD data of the PSM products suggest retention of overall long-range order, but the porosity of the resulting frameworks was reported to be extremely low, perhaps indicating some degree of framework degradation.[82] Nonetheless, direct conversion of amine-tagged to azide-tagged to triazole-modified MOFs is an impressive example of the power of PSM.

In the same year that Sada reported click chemistry on an azide-tagged MOF (vide supra),[81] Hupp and Nguyen reported on covalent PSM with alkyne-tagged MOFs.[83] A Zn(II)-based MOF was prepared from 2,6-naphthalenedicarboxylic acid and an acetylene-tagged bis(pyridyl) ligand. The alkyne tag was protected with a TMS group, which was removed postsynthetically using a fluoride source (TBAF = tetrabutylammonium fluoride) in THF. The large size of the TBA cation was purposefully chosen to selectively remove the TMS groups only from the surface of the MOFs.[83] After removal of the TMS group from the acetylene tags, these pendant groups were readily coupled to the fluorescent dye ethidium bromide monoazide (Figure 17). Microscopy experiments confirmed that the dye was successfully coupled to the MOF, in <1% yield, and only at the surface of the MOF as anticipated. Gas sorption measurements indicated that the MOF was still porous, with only a small loss in measured surface area. A poly(ethylene) glycol azide was also coupled to the MOF surface, which changed the wettability of the framework from hydrophobic to hydrophilic. Overall, this study not only was an important early example of covalent PSM using click chemistry, but also demonstrated many other important aspects of postsynthetic methods, including PSD (by fluoride removal of the TMS groups), surface-directed PSM, and the ability of PSM to significantly alter the physical properties (e.g., wettability) of

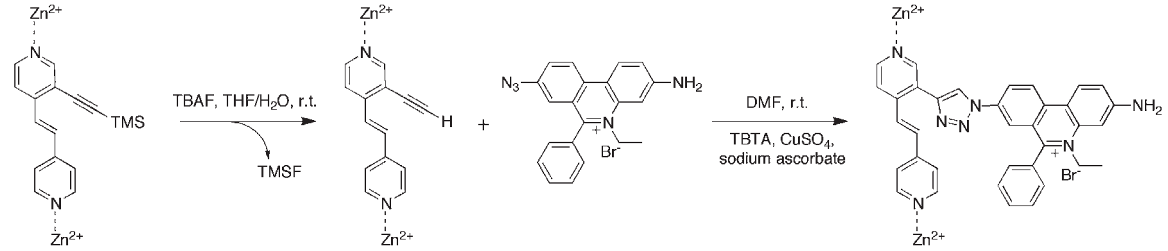


Figure 17. Covalent PSM via click chemistry on an alkyne-tagged MOF.

a MOF.[83] The former two topics will be discussed in more detail in other sections of this review.

Using Zn(II), the same alkyne-tagged bis(pyridyl) ligand, and a tetrakis(carboxylate) organic linker (instead of 2,6-naphthalenedicarboxylic acid), Hupp and Nguyen prepared a MOF upon which they were the first to demonstrate selective interior versus exterior PSM of a MOF crystal.[84] The alkyne-tagged MOF was impregnated with $CHCl_3$ and then treated with an aqueous KF solution. Taking advantage of the poor solubility of KF in organic solvents, only the surface TMS groups were removed due to the impermeability of KF into the $CHCl_3$ inside the crystal. The surface-deprotected MOF was then successfully coupled to ethidium bromide monoazide, followed by deprotection of the remaining (interior) alkyne tags with a dilute solution of tetraethylammonium fluoride (TEAF) in THF. The interior alkyne tags were then coupled to benzyl azide to produce a "core—shell"-modified MOF.[84] Using selective surface decomposition of the MOF with pyridine, MALDI-TOF-MS was used to confirm the core—shell distribution of the PSM process. This study is of particular importance for demonstrating the ability to control the physical localization of PSM on a MOF crystal. The synthesis of core—shell MOFs via solvothermal methods by other groups suggests alternative routes by which similar control over the spatial localization of PSM can be achieved.[10] The surface modification of MOFs is discussed later in this review (vide supra).

Fujita has also reported on covalent PSM click chemistry within his crystalline molecular flasks.[85] Using a triphenylene guest bearing an azide substituent, copper-free click reactions were realized by immersing the crystals in neat aceylene. Interestingly, it was found that these click reactions showed a strong regioselectivity, forming the 1,4-triazole preferentially over the 1,5-triazole. This regioselectivity was confirmed by XRD structure determination of the triazole guest within the framework. This regioselectivity is reversed when the same reactions are performed in free solution outside the restrictive pores of the MOF. Indeed, it was found that for a series of phenylacetylenes that the selectivity for forming the 1,4-triazole increased with the size of the para-substituent on the phenylacetylene substrate (H < F < Br < OMe).[85] This is yet another intriguing example of how chemical reactions within the confines of a MOF framework produce outcomes distinct from those of solution-phase chemistry.

2.5. Covalent PSM on MOFs with Alternative Handles

Scattered reports have described covalent PSM on MOFs that contain tags other than amines, aldehydes, alkynes, or azides. Burrows et al. described the use of two different thioether-tagged dicarboxylate ligands for covalent PSM. These biphenyldicarboxylate ligands were used to prepare IRMOF-9 analogues (with a slightly modified SBU) that were then oxidized by using dimethyldioxirane (DMDO) in acetone under ambient conditions (Figure 18).[33] PXRD analysis showed that the MOFs remained crystalline, and ^1H NMR spectroscopy on digested samples showed conversions ranging from 23% to quantitative for the two different ligand systems.

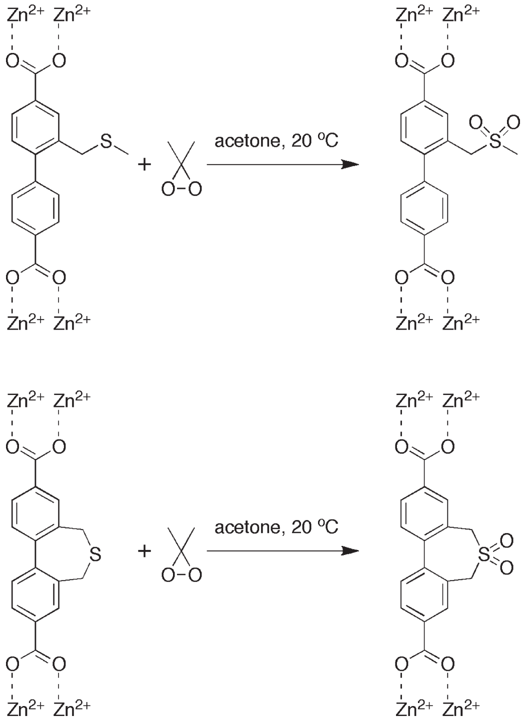


Figure 18. Covalent PSM on sulfur-tagged MOFs to produce sulfone-bearing MOFs.

Perhaps the most obviously incompatible functional group for PSM is a carboxylate group because the majority of MOFs use metal carboxylate MOFs as the linking motif. However, a serendipitous example of covalent PSM has been reported on a carboxylate-tagged MOF. Starting from benzene-1,3,5-tricarboxylate (BTC) and Cu(II), Morris and co-workers isolated a MOF where one of the carboxylate groups is esterified on each ligand (STAM-1; STAM = St. Andrews MOF) (Table 1).[86] Here the covalent PSM occurs in situ during MOF formation; hence, one might not define this example as strictly a case of PSM. Nonetheless, the authors show that this modification generates STAM-1, which has unique gas sorption properties due to its differential hydrophobic and hydrophilic surfaces. Of even greater interest, the monomethyl ester-modified ligand could be isolated in nearly quantitative yield by careful digestion of the MOF (Figure 19). This is significant as there are no high-yielding synthetic routes for this compound, and as such, this demonstrates the use of the

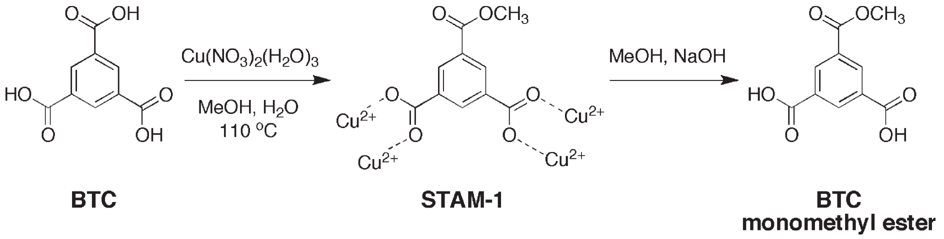


Figure 19. In situ covalent PSM of STAM-1, where the BTC ligand is esterified at only a single carboxylate group. The monomethyl ester product could be isolated in high yield by decomposition of STAM-1.

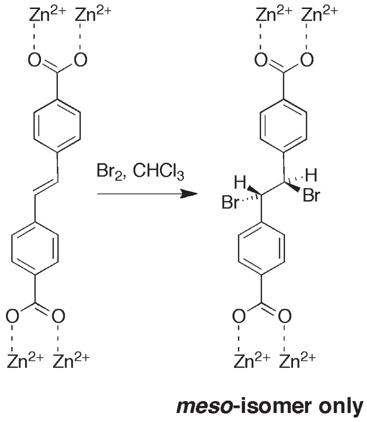


Figure 20. Covalent PSM of a stilbene-based IRMOF with Br_2. The *meso*-isomer of the bromination product is exclusively produced via PSM, while the same reaction on the free ligand produces both *meso*- and *rac*-isomers.

MOF as a "protecting group" in PSM.[86] As of yet, the results with STAM-1 are fairly unique as using a metal ion other than Cu(II) and alcohols other than MeOH does not produce analogues results. However, the authors suggest that similar reactions, wherein novel organic transformations can be performed on an MOF scaffold, may be possible and could open up entirely new avenues for the use of MOFs in chemical synthesis.

The influence of the MOF environment on a chemical reaction has been observed in other covalent PSM reactions. An interpenetrated IRMOF analogue was formed using *trans*-4,4′-stilbenedicarboxylate (SDC), which imparted the material with interesting luminescent properties.[87] Upon exposure to Br_2, the SDC ligands undergo covalent PSM to the dibromide adduct, forming only the *meso*-stereoisomer (as determined by ^{1}H NMR of the digested material, Figure 20).[88] When the same reaction is performed on the SDC ligand in solution (CH_2Cl_2), a 4:1 ratio of *meso*- to *rac*-isomers is formed. The stereoselectivity of the covalent PSM reaction was explained by hindered carbon—carbon bond rotation of the SDC when acting as a linker in the MOF, which only permits generation of the *meso*-product. These findings are yet another example of how covalent PSM can generate distinct reaction products (in this case with stereochemical control) when compared with homogeneous, solution-phase chemistry. Bromination of olefins in other MOFs has been reported as part of an investigation on tandem PSM (i.e., multiple, sequential modifications on a single framework),[49] but no information on any stereochemical preferences was described.

MOFs containing aryl halide ligands, such as 2-bromo-1,4-benzenedicarboxylate (Br-BDC), have been known for some time (e.g., IRMOF-2).[12] The numerous organic reactions that use aryl halides as a reactant suggest that MOFs containing these organic linkers should be good candidates for PSM. The first covalent PSM of a halide-tagged MOF was described using UiO-66-Br.[61] The UiO-66-Br derivative was selected over other Br-BDC MOFs, such as IRMOF-2, because of its good chemical stability. UiO-66-Br was treated with CuCN in *N*-methyl-2-pyrrolidone (NMP) under microwave irradiation (170 °C) for 10 min (Figure 21).[89] This PSM reaction yielded UiO-66-CN, which contains free nitrile groups within the pores of the framework, in ~90% yield as determined by ^{1}H NMR analysis of the MOF digested in HF in MeOD-d_4. The microwave heating conditions used were found to be superior to conventional heating, the latter of which gave a lower yield (~43%) and poorer crystallinity. The PSM-generated cyano group was characterized by NMR, FTIR, and ESI-MS methods. UiO-66-CN was confirmed to be robust and intact by PXRD analysis, gas sorption measurements, and SEM imaging. To compare covalent PSM with traditional solvothermal methods, the direct solvothermal synthesis of UiO-66-CN was performed with 2-cyano-1,4-benzenedicarboxylate (CN-BDC).[89] Although UiO-66-CN could be prepared by solvothermal methods, the synthesis required more steps and more time and was lower yielding than the PSM approach. In summary, the covalent PSM of UiO-66-Br to UiO-66-CN demonstrated the first PSM reaction on a halide-tagged MOF, as well as the first use of microwave irradiation to facilitate PSM.[89]

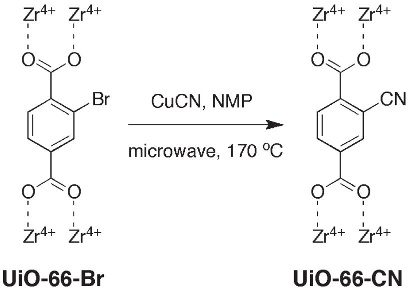
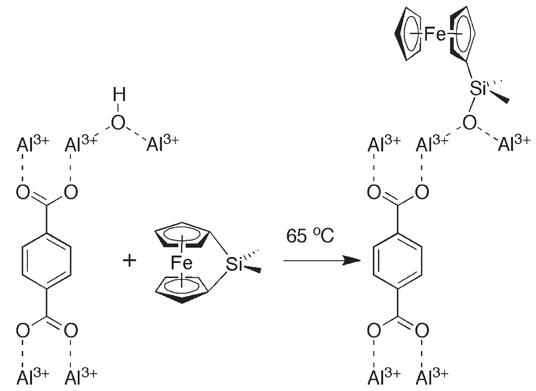


Figure 21. Covalent PSM of UiO-66-Br with CuCN.

2.6. Covalent PSM on SBUs and "Unfunctionalized" MOFs

MOFs without chemical tags are a particularly challenging target for PSM. Such materials require other features, as will be described below, to access various types of PSM. One intriguing report from Fischer and co-workers describes a rare covalent functionalization of the SBUs in a MOF.[90] Covalent PSM of a "tagless" MOF was obtained by treating MIL-53(Al) (prepard from BDC) with 1,10-ferrocenediyldimethylsilane. The ferrocene reagent undergoes a ring-opening reaction by making a covalent bond to bridging hydroxide groups that are found in the



MIL-53(Al)

Figure 22. Covalent PSM of the infinite SBU in MIL-53(Al).

infinite SBUs of MIL-53(Al) (Figure 22). Covalent PSM (~25% conversion) was supported by cyclic voltammetry, as well as ^1H and ^{13}C MAS NMR, which confirmed that the ferrocene units were bound to the MOF and not simply included as guest molecules. The modified MIL-53(Al) was found to act as a redox catalyst for benzene oxidation to phenol using H_2O_2 as an oxidant.[90]

Photochemical reactions have been recently reported as a means to initiate PSM in tagless MOFs. Using *trans*-1,2-bis(4-pyridyl)ethene (bpe), a ligand system widely investigated for photochemical [2 + 2] cycloadditions, Mir et al. showed that an SCSC light-driven covalent PSM reaction could be performed in a MOF.[91] Combination of Zn(II), bpe, and three different dicarboxylate ligands (including BDC) gave layered MOFs, with pairs of the bpe ligands in suitable proximity for undergoing photodimerization. Indeed, UV irradiation of the MOFs using a xenon lamp resulted in quantitative photodimerization of the bpe ligands. Two of the three MOFs prepared underwent photochemical covalent PSM in an SCSC fashion as evidenced by XRD structure determination, which revealed formation of the expected cyclobutane products (Figure 23). The change from a parallel to slightly canted arrangement of the pyridyl rings upon PSM results in a slight increase in the Zn−Zn distance and an overall small contraction in the overall cell volume (<5%).[91] In a similar study by Liu et al., photodimerization of the related ligand, 1,4-bis[2-(4-pyridyl)ethenyl]benzene (bpeb), was also reported within two MOFs in an SCSC fashion (Figure 23).[92] In one case, using a Cd(II)-derived MOF, both olefinic bonds within the bpeb ligand could be photodimerized within the framework; this dramatic postsynthetic change in the bpeb ligand causes a change in the coordination number of the Cd(II) ions within the SBU.

Beyond reactions at SBUs or photochemical cyclization reactions, a recent study has reported on the direct covalent PSM of a MOF that contains no chemical tag. In this case, the extraordinary chemical stability of MIL-101(Cr),[93] which is comprised of Cr(III) ions and BDC ligands, is exploited. Stock and co-workers were able to directly nitrate the aromatic ring of the BDC ligand with nitric acid to produce MIL-101(Cr)-NO_2 (Figure 24).[94] Nitration was confirmed by solution ^1H NMR of MIL-101(Cr)-NO_2 upon digestion in aqueous NaOH. MIL-101(Cr)-NO_2 was shown to be crystalline and porous by PXRD and gas sorption measurements. Importantly, MIL-101(Cr)-NO_2 could be cleanly and quantitatively reduced with $SnCl_2 \cdot 2H_2O$ to obtain MIL-101(Cr)-NH_2. With a conventional chemical handle in hand, MIL-101(Cr)-NH_2 could be treated with ethyl isocyanate to produce MIL-101(Cr)-UR2. It is necessary to highlight that although MIL-101(Cr)-NO_2 could be directly prepared from 2-nitro-1,4-benzenedicarboxylate (NO_2-BDC) under slightly modified reaction conditions, MIL-101(Cr)-NH_2 could not be prepared directly from NH_2-BDC.[94] This important report is a significant advancement in the field of PSM, showing that, with a suitable MOF and careful selection of reaction conditions, a truly tagless MOF can be made amenable to PSM. Furthermore, MOFs such as MIL-101(Cr) that have been difficult to functionalize (because of the high temperatures required for preparation of the material, which results in degradation of many functionalized ligands)[93] are now made accessible to PSM by this approach.

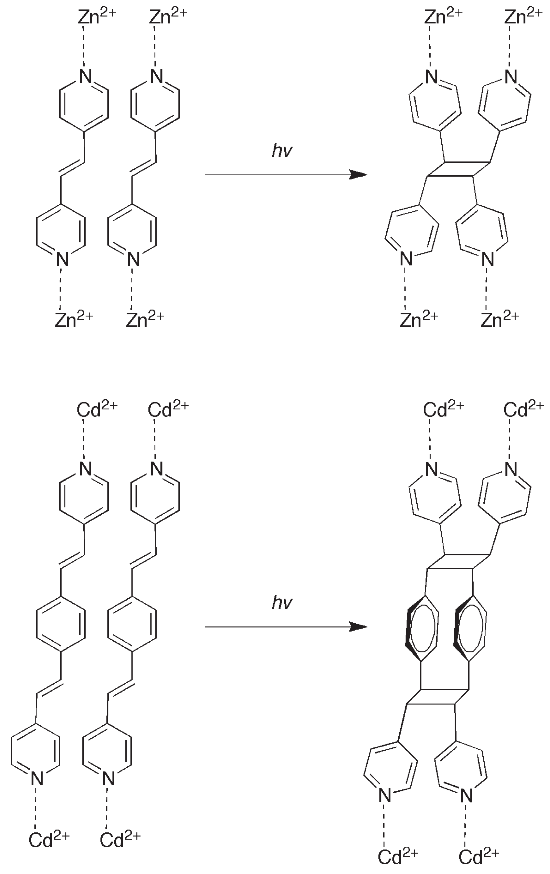


Figure 23. Photochemical covalent PSM on a tagless MOF containing either the bpe (top) or bpeb (bottom) ligand.

3. DATIVE PSM

3.1. Dative PSM on SBUs

Dative PSM at the SBUs of MOFs has become a mainstream approach for tuning the pore functionality of MOFs. Here we will highlight several examples that go beyond simple solvation/desolvation of a coordination site on an SBU, but rather focus on the modifications that resulted in new functionality or significant structural changes. Dative PSM was reported as far back as 1999,[95] with the original description of HKUST-1 (HKUST = Hong Kong University of Science and Technology) as a Cu(II) MOF with a paddlewheel SBU that has become among the most widely studied MOFs (Table 1). In this early report, the authors noted that the coordinated axial water molecules on the SBUs

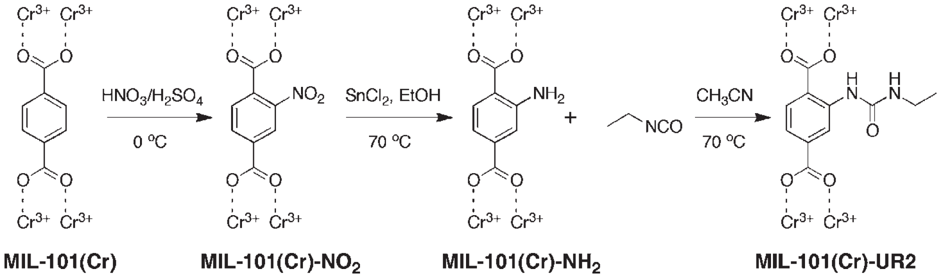


Figure 24. PSM of the tagless MIL-101(Cr) MOF.

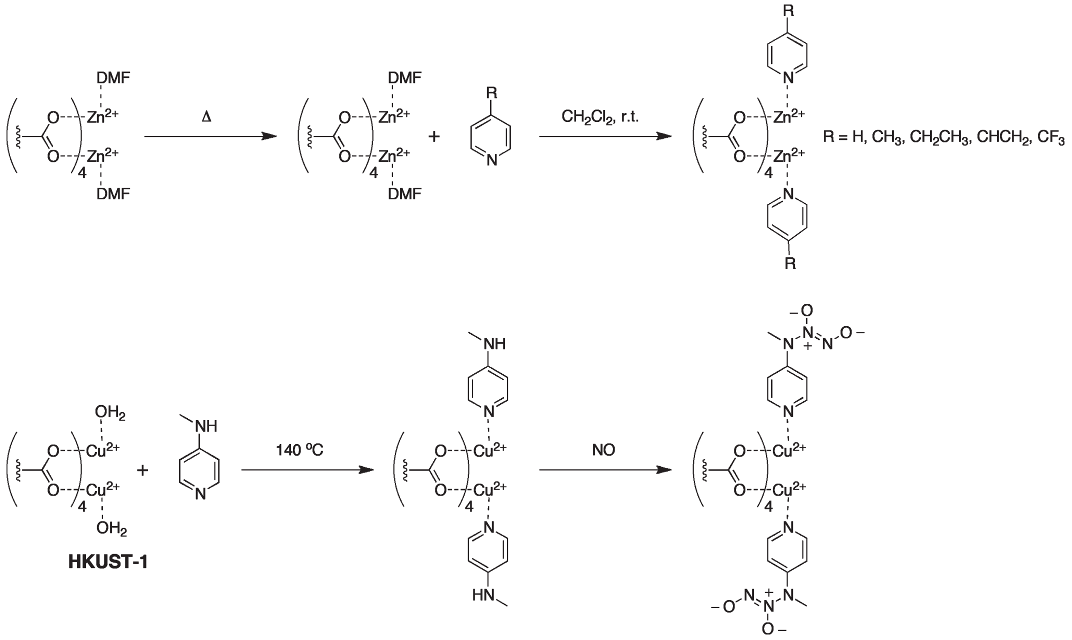


Figure 25. Dative PSM on the SBUs of several MOFs with pyridine derivatives.

could be removed by heating HKUST-1 in air to 100 °C. The resultant material could then be immersed in dry pyridine to obtain a material with pyridine molecules bound to the SBU. Importantly, the authors noted that the HKUST-1 derivative with pyridine bound to the SBUs could not be directly synthesized by solvothermal methods,[95] demonstrating early on the importance of dative PSM.

One of the first systematic studies on dative PSM at the SBUs was reported using a Zn(II) paddlewheel-derived MOF. Hupp and co-workers demonstrated that axially bound DMF solvent molecules could be removed from the paddlewheel SBUs under vacuum with heat.[96] The desolvated MOF could then be treated with pyridine derivatives in CH_2Cl_2 that bound to the axial sites left vacant on the SBUs by removal of DMF (Figure 25). Two particularly important observations were made in this study. First, several of the pyridine ligands introduced would decompose under standard solvothermal conditions, demonstrating how dative PSM could be used to introduce a thermally labile species into the MOF. Second, it was shown that H_2 uptake was dependent on the pyridine species coordinated to the SBUs, indicating that the MOF properties could be altered by dative PSM.[96]

Using a similar strategy, Rosseinsky and co-workers showed that dative PSM could be used to introduce a chemical tag suitable for capture of gases.[97] HKUST-1 was modified by vapors of 4-(methylamino)pyridine (4-map), which binds to coordination sites on the Cu(II) paddlewheel SBUs. It was noted that a 4-map derivative of HKUST-1 could not be directly synthesized by solvothermal methods. The modified HKUST-1 was then treated with NO, which formed a covalent NONOate (*N*-diazenium diolate) adduct and a proposed ammonium cation with the 4-methylamino groups of the 4-map ligands (Figure 25).[97] These materials were proposed as possible storage and release media for biological use of NO. The formation of NONOates by covalent PSM on amine-tagged MOFs has also been described.[98]

Two studies report on the coordination of simple amines to unsaturated metal sites within MOFs (Figure 26). In the first study, MIL-101(Cr) was desolvated under vacuum with heat to produce vacant coordination sites at the SBUs.[99] These sites were then modified with ethylenediamine, diethylenetriamine, or (3-aminopropyl)trialkoxysilane. Amine functionalization was characterized by FTIR and elemental analysis; PXRD and gas sorption measurements verified the crystallinity and porosity of the MOF after dative PSM. The amine-modified MOF was shown to exhibit enhanced catalytic activity for the Knoevenagel condensation of benzaldehyde and ethyl cyanoacetate. In addition, the amine-modified MOFs were used to help nucleate metal

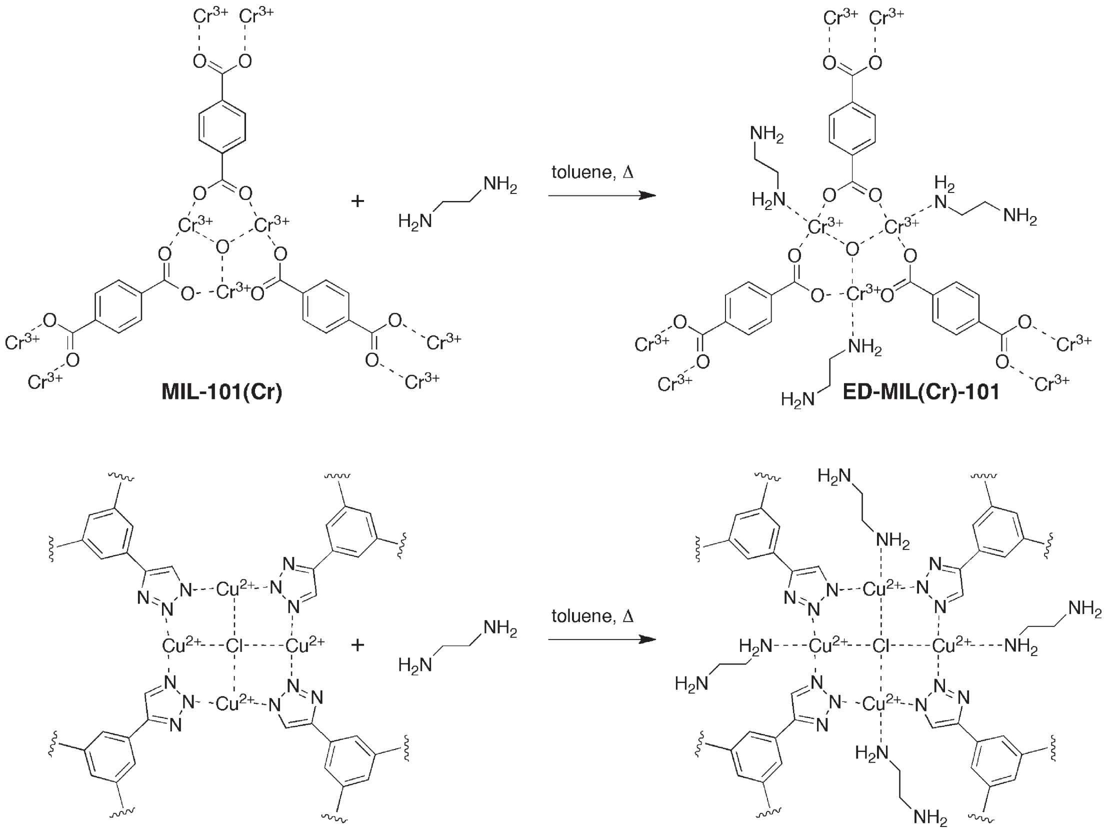


Figure 26. Dative PSM on the SBUs of several MOFs with simple alkylamines.

nanoparticles within the MOF. The nucleation of Pd nanoparticles resulted in a material that proved to be an active catalyst for the Heck reaction.[99] In the second study, ethylenediamine was used in the dative PSM of a copper(II) triazole MOF.[100] In this MOF, the SBUs are comprised of [Cu_4Cl] squares with each Cu(II) center possessing one solvent ligand. Upon activation of the MOF and removal of the bound solvent, dative PSM was achieved by exposing the MOF to a toluene solution of ethylenediamine. Binding of ethylenediamine was associated with a color change in the material from red to blue. Elemental analysis suggested only about one-quarter of the Cu(II) sites were modified by the procedure. In addition, a large drop in measurable surface area was noted (from 1770 to just 345 m^2/g), suggesting that the ethylenediamine ligands are sufficiently bulky to crowd the pores of this MOF. Despite this problematic crowding, the ethylenediamine-modified material did show improved selectivity for the sorption of CO_2 over N_2, as well as a much higher isosteric heat of adsorption at zero coverage for CO_2 when compared to the unmodified MOF (90 kJ/mol vs 21 kJ/mol).[100] The high isosteric heat of adsorption is consistent with chemisorption of CO_2 to the amine groups to form carbamates. Despite its lower overall capacity, the modified MOF showed good stability and an ability to cycle through multiple rounds of CO_2 sorption. These two related studies illustrate the ability of dative PSM to augment very different potential applications of MOFs (catalysis, CO_2 capture).

Dative PSM has been used to engender MOFs with new functional sites possessing catalytic activity. The Kim group modified vacant coordination sites on the SBUs of MIL-101(Cr) with either (*S*)-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide or (*S*)-*N*-(pyridin-4-yl)pyrrolidine-2-carboxamide.[101] These ligands coordinate to the SBUs via their pyridyl groups, leaving a pendant proline group free within the pores of the framework (Figure 27). The ligands were appended to the SBUs by treating MIL-101(Cr) with a solution of the ligand in $CHCl_3$ and heating to reflux for 1 d. The relatively harsh PSM conditions (high temperature) are a testament to the stability of the MIL-101(Cr) material,[93] which remains crystalline and porous after PSM as evidenced by PXRD and gas sorption measurements. The modified MOFs, designated CMIL-1 (pyridin-3-yl) and CMIL-2 (pyridin-4-yl; CMIL = chiral MIL) were examined for their capacity to act as catalysts for the asymmetric aldol reaction between aromatic aldehydes and ketones. Both CMIL-1 and CMIL-2 showed good yields (60−90%) and respectable ee values (55−80% for *R*-isomers). Importantly, control reactions with MIL-101(Cr) showed less than 10% conversion and 0% ee. In addition, the free ligands, when not immobilized in CMIL-1 or CMIL-2, also showed poorer ee values (29%).[101] Overall, this study showed that dative PSM could be used to easily engender MOFs with useful organocatalytic activity to produce an active, recyclable, and tunable catalyst.

Dative PSM with a ligand that serves to bridge two SBUs has been demonstrated in an SCSC manner. Suh and colleagues prepared the MOF SNU-30 (SNU = Seoul National University) from the tetracarboxylate linker *N*,*N*,*N*′,*N*′-tetrakis(4-carboxyphenyl)biphenyl-4,4′-diamine ($H_4TCPBDA$) and Zn(II) (Table 1).[102] SNU-30 contains dinuclear Zn(II) paddlewheel SBUs where water molecules are found at the axial positions of the Zn(II) centers. When crystals of SNU-30 are placed in a DMF solution of 3,6-bis(4-pyridyl)-1,2,4,5-tetrazine (bpta) at 80 °C

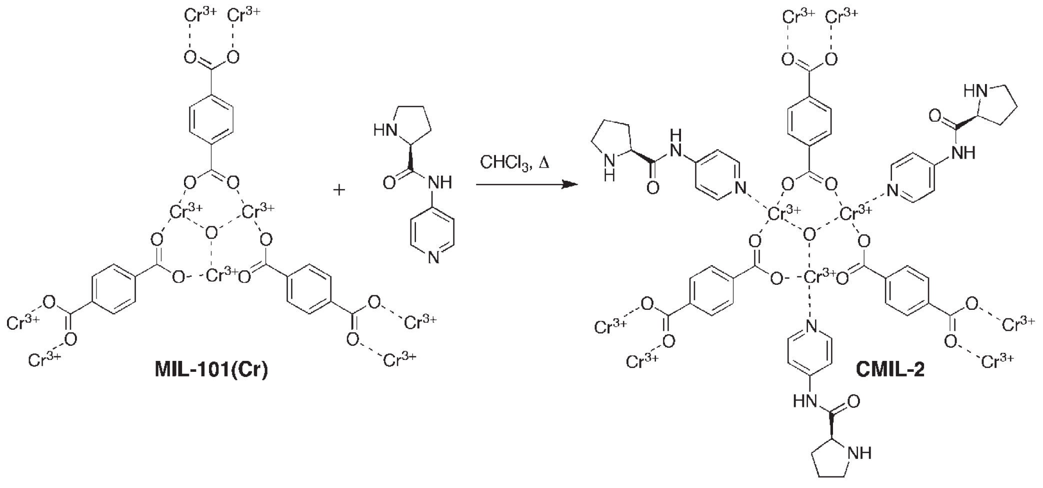


Figure 27. Dative PSM of MIL-101(Cr) to produce the organocatalytic framework CMIL-2.

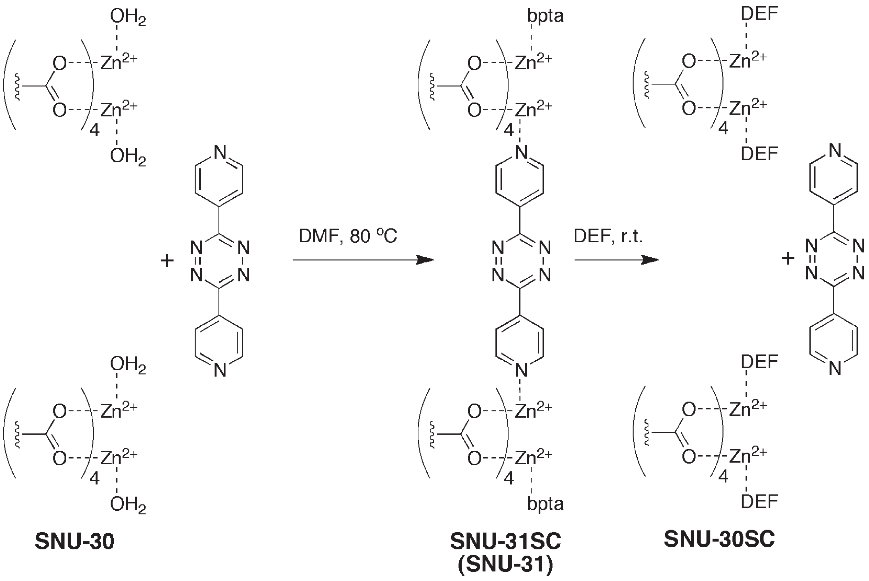


Figure 28. Dative PSM of SNU-30 with a bridging bpta ligand to generate SNU-31SC. Similarly, SNU-31 could be prepared directly under solvothermal conditions and treated with DEF to liberate the bpta ligands to produce SNU-30SC.

for 3 h, the crystals undergo a color change from yellow to red. Structural determination by XRD after the color change show that the bpta ligands bridge neighboring SBUs having displaced the axial water molecules on each Zn(II) center to form the new material SNU-31SC (Figure 28). This transformation occurs with complete retention of crystallinity in an SCSC manner. The addition of bpta in SNU-31SC generates a structure with a smaller pore aperture than SNU-30, hence demonstrating that dative PSM can be used to modulate the topological characteristics of MOFs. It was found that a nearly identical MOF could be prepared directly by solvothermal synthesis from Zn(II), bpta, and H_4TCPBDA, which crystallized in a different space group (SNU-31).[102] Immersion of crystals of SNU-31 in DEF for 7 d resulted in removal of the bpta ligands, producing the solvated MOF SNU-30SC (Figure 28). This study highlights that dative PSM can occur in a bridging binding mode between SBUs and in an SCSC reversible manner.

Perhaps the most dramatic example of dative PSM at SBUs does not involve coordination of a ligand to an SBU, but rather the postsynthetic replacement of the SBU metal ions (i.e., transmetalation). The Kim group prepared a cubic, sodalite-like MOF from Cd(II) (which formed Cd_4O SBUs) and a rigid, tricarboxylate ligand. Amazingly, when the Cd(II) MOF was soaked in an aqueous solution of $Pb(NO_3)_2$ for one week, complete exchange of the Cd(II) ions by Pb(II) ions was found to occur in an SCSC fashion (Figure 29).[103] The structural integrity of the MOF was sufficiently well maintained that the single-crystal XRD pattern of the transmetalated MOF was determined and the MOF found to be isostructural with the Cd(II)-based starting material. The process was found to be reversible, and the Pb(II) MOF could also be directly synthesized under solvothermal conditions. Perhaps even more intriguing, the Cd(II) ions could also be replaced with Dy(III) or Nd(III), which failed to produce MOFs from direct solvothermal methods. The higher charge of the lanthanides produces a cationic framework that was charge-balanced by the presence of nitrate anions.[103] This remarkable and rather surprising example of

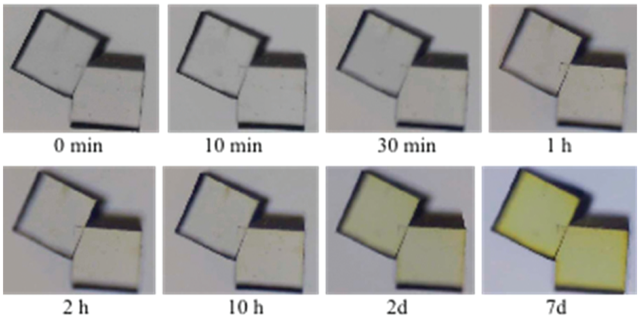


Figure 29. Photographs of dative PSM of a Cd(II)-based MOF. In this example, the Cd(II) ions of the SBUs are replaced by Pb(II) ions upon crystal soaking in an aqueous solution. Reprinted from ref 103. Copyright 2009 American Chemical Society.

dative PSM yet again shows the ability to obtain materials that are not readily realized by direct, conventional synthetic methods. In support of these findings, an independent report claimed the transmetalation of a Zn(II) MOF, derived from a tetracarboxylate ligand, with Cu(II).[104] In this case, the authors also stated that the Cu(II) MOF could not be directly synthesized via solvothermal methods and could only be prepared by dative PSM. The exchange of Zn(II) for Cu(II) could be monitored by a change in the color of the crystals (from colorless to blue-green) and quantified by elemental analysis. However, the crystallinity of the Cu(II)-containing transmetalated material was significantly reduced as gauged by PXRD analysis, and no porosity data were reported.[104]

3.2. Dative PSM on Organic Linkers

A few reports of dative PSM appeared during the dearth of studies on covalent PSM that occurred between 2001 and 2006. This was largely pioneered by Lin and co-workers, who intensely investigated the metalation of MOFs for use in heterogeneous, asymmetric catalysis.[5,105,106] In 2005, the Lin group described an MOF constructed from Cd(II) and (*R*)-6,6′-dichloro-2,2′-dihydroxy-1,1′-binaphthyl-4,4′-bipyridine, which contains pyridyl donors designed for assembly of the framework and an orthogonal, chiral 2,2′-binaphthol group suitable for dative PSM.[107] The MOF has large chiral channels and was stable to solvent removal as demonstrated by PXRD and gas sorption studies. More importantly, the MOF was treated with titanium isopropoxide ($Ti(O^iPr)_4$) to metalate the binaphthol sites and generate Lewis acidic metal centers (Figure 30). Being a relatively early study related to PSM, no detailed characterization of the metalated MOF was provided; however, later reports validated the proposed PSM strategy (vide infra). The metalated MOF was then used as a catalyst for the addition of $ZnEt_2$ to aromatic aldehydes to afford chiral secondary alcohols. The MOF proved to be a highly active catalyst that exhibited very high ee values.[107] The authors suggested that only one-third of the binaphthol sites were modified with $Ti(O^iPr)_4$, as two-thirds of the sites were likely inaccessible on the basis of the XRD structure of the MOF. Indeed, a related study by the same group showed that accessibility to the binaphthol sites and hence catalytic activity were highly dependent on the MOF topology.[108]

Subsequent studies with tetracarboxylate−binaphthol ligands allowed for the formation of a series of isoreticular, Cu(II) MOFs with paddlewheel SBUs.[109] The pore size in these MOFs could be tuned by the ligand structure (from 0.8 to 2.1 nm), and hence, upon dative PSM with $Ti(O^iPr)_4$, the catalytic behavior (i.e., enantioselectivity of the catalysts with respect to different substrates) could be modulated. Lin and co-workers did ultimately obtain XRD evidence for dative PSM in the binaphthol MOFs.[110] In a recent study, it was discovered that several Zn(II)-based, binaphthol-derived MOFs showed good catalytic activity, but poor ee values for the addition of $ZnEt_2$ to aromatic aldehydes when compared to their earlier findings. To determine the origin of this apparent discrepancy, an XRD structural analysis was undertaken that revealed that the Ti(IV) ions formed an intermolecular cross-link between two, independent binaphthol ligands within the MOF (Figure 30). Furthermore, the cross-linked binaphthol ligands originate from two independent frameworks, which are interpenetrated with each other in this MOF.[110] The low ee values observed with this catalyst were attributed to this inter- rather than intramolecular dative PSM metalation reaction.

Following an approach similar to that in the work of Lin, Hupp and co-workers reported the formation of metal alkoxides within a MOF using both Li(I) and Mg(II).[111] Dative PSM was performed on the diol ligand 1,2-di(pyridin-4-yl)ethane-1,2-diol. Detailed characterization of the metal coordination in the system was not possible, but upon activation, it was proposed that the metal ions were essentially free of solvent ligand. In support of this argument, it was found that lithiation of the MOF resulted in a modest improvement in H_2 uptake.[111]

Dative PSM has also been reported on tagless MOFs. The first of these studies was described by Long and colleagues, where IRMOF-1 was metalated with $Cr(CO)_6$ to form the piano stool Cr(0) arene complex.[112] IRMOF-1 was heated at high temperature (140 °C) in a sealed vessel with a solution of $Cr(CO)_6$ dissolved in dibutyl ether and THF. The material became red in color, indicative of formation of the piano stool complex. No single-crystal data were obtained, but the authors claimed that the PXRD pattern was unchanged from IRMOF-1. Furthermore, FTIR spectroscopy showed distinct stretches at 1990 and 1929 cm^{-1} that were indicative of the piano stool complex. Similar results with $Mo(CO)_6$ were obtained, but no details were provided. Photolysis of IRMOF-1-$Cr(CO)_3$ generated vacant coordination sites on the Cr(0) center, which was then available for binding by H_2 or N_2 gas.[112] A similar study, looking at the dative PSM of UiO-66 with $Cr(CO)_6$, has been described. In this later study, X-ray absorption near-edge structure (XANES) spectroscopy was used to provide evidence for formation of the arene complexes.[113]

A recent, very notable example of dative PSM was reported jointly from the laboratories of Yaghi and Long.[114] The ligand used in this study, 2,2′-bipyridine-5,5′-dicarboxylic acid (H_2bpydc), possesses the ubiquitous metal-binding 2,2′-bipyridine (bpy) core. The challenge with such a ligand is that the bpy core binds metal ions so avidly that it is likely to bind metal ions during solvothermal synthesis, either saturating such sites or hampering the preparation of any open framework structure. As stated by the authors, "The direct formation of frameworks bearing chelating ligand sites that are open to metal insertion is rare, since typically metal binding at these sites would occur during framework synthesis."[114] To overcome this limitation, Yaghi and Long devised a clever, but very simple solution to this problem by exploiting the hard−soft acid−base (HSAB) theory of coordination chemistry. The bpy chelator is generally classified as a soft ligand due to its strong π-accepting character, while carboxylates are considered hard donors, being primarily σ-donating ligands. Therefore, the selection of a hard, oxophilic metal ion to construct the framework, in this case Al(III), should

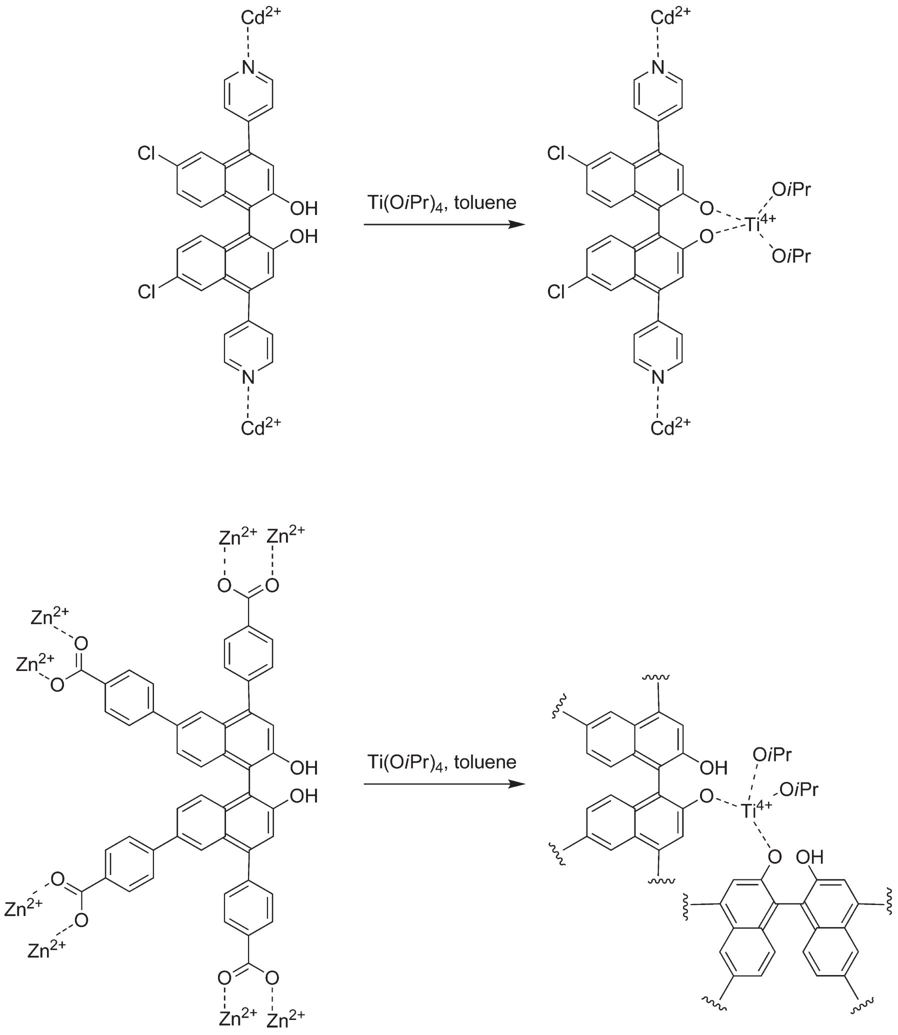


Figure 30. Dative PSM on various binaphthol-containing MOFs. The bottom structure was characterized by XRD and used to explain the lower stereoselective catalytic behavior of the MOF.

result in only coordination by the hard carboxylate donors during the solvothermal synthesis of the MOF. This is indeed the case, and combining H_2bpydc and $AlCl_3 \cdot 6H_2O$ in DMF at 120 °C produces the open framework MOF-253, which PXRD revealed to possess a topology isoreticular with MIL-53 (Figure 31). Importantly, MOF-253 is the first MOF to contain open bpy sites.

The accessibility of the bpy sites in MOF-253 was demonstrated by dative PSM (i.e., metalation) of the bpy unit with softer metal ions, including Cu(II) and Pd(II). Soaking of MOF-253 in acetonitrile solutions of $Cu(BF_4)_2$ or $PdCl_2$ could produce materials where >80% of the bpy ligands were metalated (as determined by elemental analysis, Figure 31).[114] PXRD confirmed that the framework structure remained intact upon metalation. Furthermore, the coordination environment of the framework-immobilized bpy complexes was elucidated by extended X-ray adsorption fine structure (EXAFS) spectroscopy. EXAFS showed that for the Pd(II)-modified material the coordination sphere of the Pd(II) center was best fit as with a square planar geometry containing two nitrogen donor atoms and two chloride donor atoms at distances of 2.038(3) and 2.296(1) Å, respectively.[114] This important example of dative PSM sits in striking contrast to related work from the Yaghi laboratory using a carbene-containing dicarboxylate ligand.[115] Although the same hard—soft orthogonal metalation strategy should work for a carboxylate—carbene ligand, it was found with Pd(II) that presynthetic (e.g., use of a metalloligand) rather than PSM was the better route for obtaining the metalated MOF (Figure 31). These contrasting results serve to demonstrate that, as with any chemical reaction, the optimal conditions for any given system or substrate will vary. Hence, having both pre- and postsynthetic methods for modifying MOFs is essential for developing a complete scope of functional MOF materials.

Although dative PSM has not yet succeeded with the carboxylate—carbene ligand described by Yaghi and co-workers, the general concept of introducing carbene-based organic linkers is an attractive approach for dative PSM. As with the examples above, a mixed carbene—carboxylate ligand has the potential to bind two different metal ions on the basis of HSAB theory; harder metals can coordinate the carboxylates to construct the framework, and soft metals can coordinate to the softer carbene sites. To date, there have been a number of mixed *N*-heterocyclic carbene (NHC)—carboxylate ligands described for the construction of coordination polymers or MOFs. Solids based on Zn(II),[116] Cu(II),[117] and Ce(III)[118] have been prepared from such ligands. Two reports have described dative PSM of the NHC

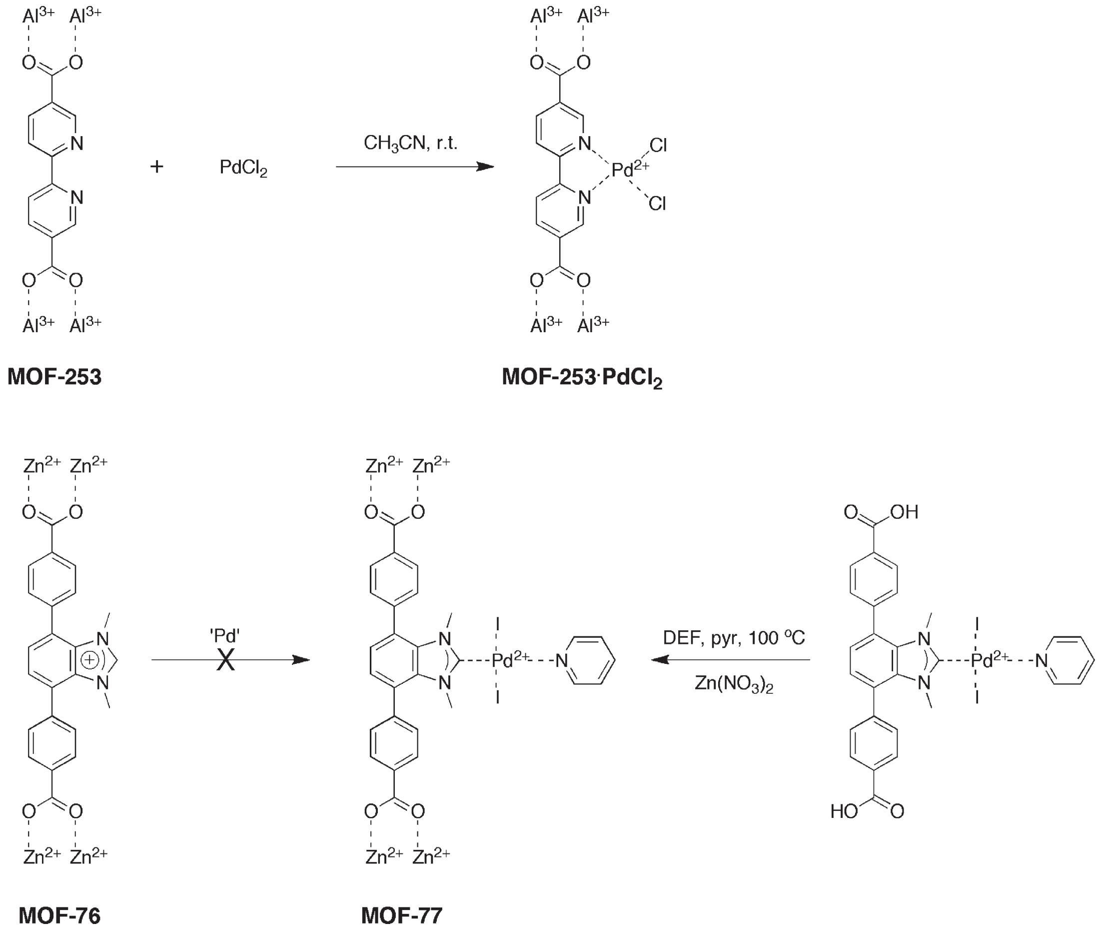


Figure 31. Dative PSM of the bpy-containing MOF-253 by $PdCl_2$ (top). In contrast, dative PSM was not effective with a related carbene ligand (bottom), and use of a metalloligand (i.e., presynthetic) approach was required to obtain the desired MOF.

ligand, but in both cases this process occurs in situ during MOF synthesis. In a series of studies by Son and co-workers, MOFs constructed from a mixed NHC−carboxylate ligand undergo dative PSM in situ. In the first example, an NHC−carboxylate ligand combined with a Cu(II) source led to a MOF linked by Cu(II) centers that also had Cu(I) coordinated to the NHC sites (Figure 32). It was proposed that in situ reduction of the Cu(II) to Cu(I) occurs during the solvothermal reaction to produce the Cu(I)−NHC complex.[117] In the second example, combination of the same NHC−carboxylate ligand with both Cu_2O and Ce(III) led to a MOF linked by Ce(III) centers and a Cu(I)−NHC complex at every other ligand site (Figure 32).[118] The observation that only half of the NHC sites are metalated in this system was explained by the stability of forming an overall neutral framework (metalation of all sites would result in a cationic framework). Interestingly, the latter example demonstrates discrimination of the carboxylate and carbene ligands based on HSAB theory; the harder Ce(III) ion binds exclusively to the carboxylate sites, and the softer Cu(I) ions bind to the carbene ligands. The aforementioned examples of dative PSM clearly do not originate from an isolable, metalated ligand (i.e., metalloligand). However, because modification occurs in situ, it is unclear from these studies whether this is a true dative PSM reaction. Nonetheless, NHC−carboxylate and other mixed carbene ligands hold great promise for obtaining PSM-ready MOFs that can support reactive, low-coordinate metal sites.

The idea of exploiting differences in HSAB properties to design ligands with orthogonal metal binding sites within MOFs has been explore with dicarboxylate ligands containing thioether moieties. 2,3,5,6-Tetrakis(methylthio)-1,4-benzenedicarboxylate was used to prepared a Pb(II)-based MOF that possessed free thiomethyl groups within the pores of the framework.[119] Although Pb(II) is generally considered a soft metal ion, in this particular case the Pb(II) ions formed infinite SBUs that did not engage in coordination with the thioether groups on the basis of the structure determined by XRD. Exposing the MOF to a benzene solution of $HgCl_2$ resulted in uptake of Hg(II) as evidenced by elemental analysis. An approximate 1:1 Pb:Hg ratio was obtained, but XRD was unable to unambiguously verify the location of the Hg(II) ions. However, control reactions with IRMOF-1 (which does not possess any pendant groups in the pores) showed little uptake of Hg(II), suggesting that the methylthio groups are required for sequestration of Hg(II) into the framework.[119] Other examples of PSM with MOFs possessing mixed carboxylate−thioether that takes advantage of the HSAB properties of these binding groups have been reported.[120]

Dative PSM has also been performed with a wholly intact coordination compound as the reactant. Bhattacharjee et al reported the modification of IRMOF-3 directly with $Mn(acac)_2$ (acac = acetylacetonate).[121] Imine formation between the free amine group of IRMOF-3 and an acac ligand of the $Mn(acac)_2$ complex effectively immobilized the Mn(II) complex onto the

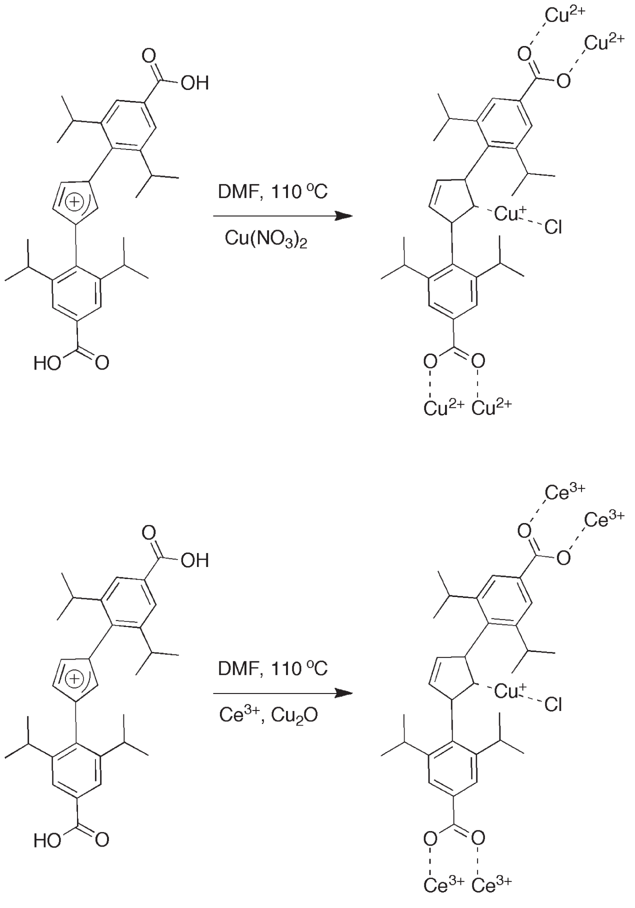


Figure 32. In situ dative PSM of a carbene-based MOF.

MOF to produce IRMOF-3[Mn] (Figure 33). PXRD and gas sorption measurements provide evidence that the IRMOF lattice is robust to the modification reaction. The primary evidence provided for PSM was elemental analysis, which suggested that the yield of this PSM reaction is rather low (~8%). The catalytic activity of IRMOF-3[Mn], when compared to IRMOF-3, also provided evidence for PSM. These MOFs were examined for the epoxidation of alkenes; while IRMOF-3 showed no activity, IRMOF-3[Mn] showed good activity against several alkene substrates. Indeed, IRMOF-3-[Mn] demonstrated better activity when compared to unsupported or alumina-supported Mn(acac)$_2$. In addition, IRMOF-3[Mn] proved to be a robust, recyclable catalyst with no loss in activity, product selectivity, or MOF stability over four catalytic cycles.[121]

3.3. Combined Covalent and Dative PSM

A number of reports have followed up on the original report of Rosseinsky,[41] who combined covalent and dative modification to generate engineered metal sites within MOFs. Corma and co-workers performed an identical covalent modification of IRMOF-3 with salicylaldehyde to produce a bidentate ligand within the MOF framework (Figure 7).[122] Approximately 3% of the amine sites were converted to salicylideneimine chelators. The modified MOF was subjected to dative PSM with NaAuCl$_4$ to obtain a material with ~2% by weight of immobilized Au(III). The material was shown to possess catalytic activity for both domino coupling and hydrogenation reactions.[122] A separate report described the use of the same material as a catalyst for the cyclopropanation of styrene with ethyl diazoacetate.[123]

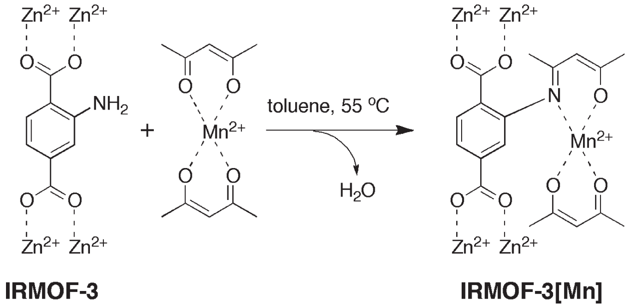


Figure 33. Dative PSM of IRMOF-3 with Mn(acac)$_2$. The resulting IRMOF-3[Mn] was an effective, recyclable, heterogeneous catalyst for alkene epoxidation.

Yaghi and co-workers also used imine condensation reactions to generate ligands for a combined covalent and dative PSM scheme.[124] UMCM-1-NH$_2$ was combined with 2-pyridinecarboxaldehyde in toluene for 5 d to undergo covalent PSM to produce a MOF that possessed pendant iminopyridine chelators within the pores. Formation of the Schiff base ligands could be observed by a color change from colorless to yellow during the reaction. This material then underwent dative modification (termed "isoreticular metalation" by the authors) with PdCl$_2$(CH$_3$CN)$_2$ in CH$_2$Cl$_2$ to give a framework with isolated Pd(II) sites (Figure 34). Again, a notable color change from yellow to purple was observed during the PSM reaction. Both PXRD and gas sorption experiments were used to confirm the crystallinity and porosity of the Pd(II)-loaded material. Using Pd K-edge EXAFS spectroscopy, evidence was provided that the included Pd(II) was not the PdCl$_2$(CH$_3$CN)$_2$ starting material, but rather a square planar complex with two Pd−Cl and two Pd−N donor atoms at distances of 2.276(2) and 1.993(2) Å, respectively.[124] The use of EXAFS to examine the metal complexes formed within the MOF was an important milestone for MOF chemistry and one that is likely to gain even more usage in future studies.[114]

Hupp and Nguyen also showed that covalent and dative PSM could be used to generate MOFs with specific metalation sites.[125] A layered-pillared MOF was constructed from Zn(II), a tetracarboxylate linker, and *meso*-1,2-bis(4-pyridyl)-1,2-ethanediol (DPG) organic "pillars" that linked the paddlewheel SBUs. The hydroxyl groups of the DPG ligands in this MOF are not engaged in metal coordination and hence were subjected to covalent PSM by treatment with succinic anhydride at elevated temperatures in DMF. This resulted in nearly quantitative conversion of the hydroxyl sites (as determined by solution ^{1}H NMR upon digestion of the MOF in NaOD and D$_2$O) and generation of free carboxylate sites within the framework. Crystallinity of the modified MOF was verified by PXRD; however, TGA and gas sorption analysis (with CO$_2$) indicated a substantial loss in accessible surface area upon covalent PSM. Exposure of the carboxylate-bearing MOF to a 75 ppm aqueous solution of CuCl$_2$ resulted in sufficient metal sequestration to reduce the Cu(II) concentration to 20 ppm after just 1 h. Longer exposure times (4 h) to the CuCl$_2$ solution resulted in a visible color change in the MOF from colorless to blue-green, clearly indicating binding of the Cu(II) to the MOF.[125] Although metal binding was evident by these experiments, no detailed information on the coordination mode to the Cu(II) ions was reported.

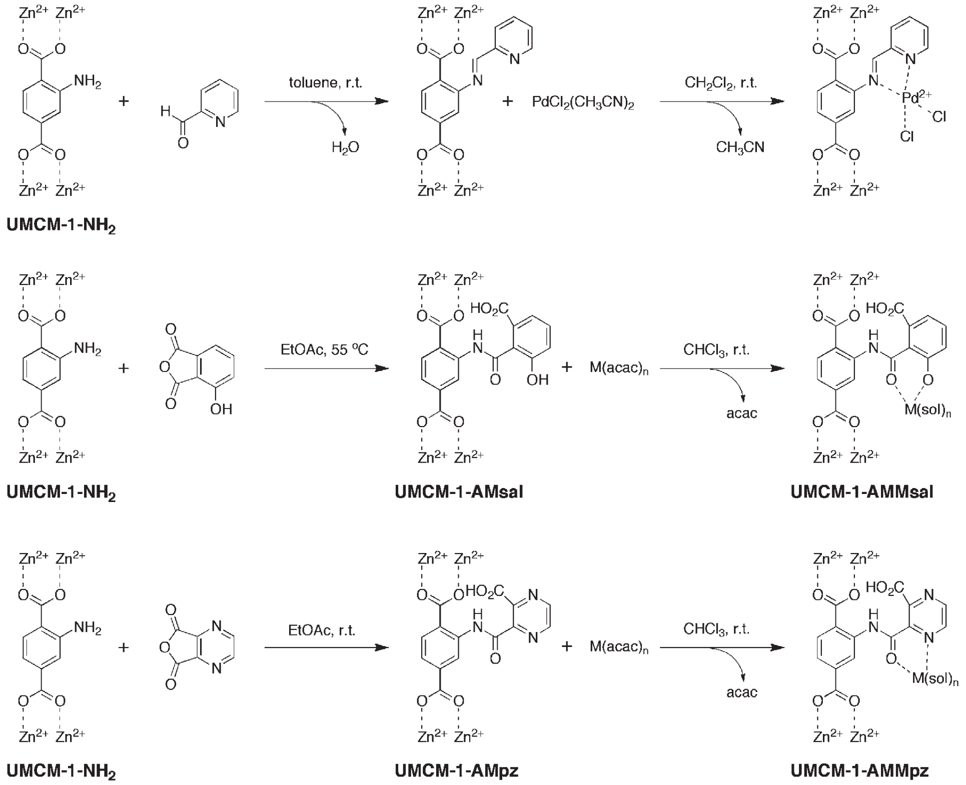


Figure 34. Examples of combined covalent and dative PSM.

A combination of covalent and dative PSM has been used to prepare MOFs possessing novel catalytic properties. Reaction of UMCM-1-NH$_2$ with either 3-hydroxyphthalic anhydride or 2,3-pyrazinedicarboxylic anhydride results in the formation of the modified MOFs UMCM-1-AMsal (sal = salicylate) and UMCM-1-AMpz (pz = carboxypyrazine) in 35% and 50% yield, respectively (Figure 34). As in the other examples described above, these two modified MOFs contain new metal binding sites as a result of PSM, which were shown to be readily metalated by several M(acac)$_n$ sources, including Fe(III), Cu(II), and In(III) (Figure 34).[126,127] PXRD and gas sorption studies definitively showed a preservation of crystallinity and porosity across both the covalent and dative modification steps. UV−vis reflectance spectroscopy confirmed binding of the Fe(III) and Cu(II) ions to the PSM-generated ligands;[126] however, a detailed study of the metal coordination environments in these materials is still lacking. The available spectroscopic evidence strongly suggests metal binding to the salicylate or carboxypyrazine ligands, but the details around the rest of the metal ion coordination sphere (e.g., coordination number and geometry, coordination by solvent vs residual acac ligands) are still unresolved.

The introduction of two different ligands (salicylate, carboxypyrazine) and three different metal ions prompted an investigation of whether these MOFs could demonstrate catalytic activity reminiscent of single-site catalysts, e.g., that catalytic activity would show a dependence on both the ligand and metal ion immobilized in the MOF. Such behavior would strongly suggest that the metals were bound at the PSM ligands and that these metal centers are essentially acting as immobilized molecular catalysts. To test this hypothesis, the metalated MOFs were examined in three Lewis acid-catalyzed reactions: the Mukaiyama aldol reaction, the ring-opening of epoxides with TMSN$_3$, and the ring-opening of epoxides with aniline. The Mukaiyama aldol reaction was best catalyzed by UMCM-1-AMFesal, while the ring-opening reactions were best catalyzed by UMCM-1-AMInpz when TMSN$_3$ was used as the nucleophile and by UMCM-1-AMInsal when aniline was used as the nucleophile.[126,127] The clear dependence on the nature of both the metal ion and ligand composition for obtaining optimal catalytic activity strongly supports the single-site nature of the catalysts. In all cases, the catalysts were shown to be stable and recyclable over at least three catalytic cycles. In addition, one of these reactions showed an interesting influence of the MOF structure on reactant selectivity. When different substrates were examined for the epoxide ring-opening with TMSN$_3$, it was observed that *cis*-stilbene epoxide was readily turned over, while *trans*-stilbene epoxide was not. Indeed, in the presence of both substrates, selective conversion of only *cis*-stilbene epoxide to the corresponding β-azido alcohol was observed.[127] Comparison with a soluble Cr(III) catalyst showed no significant preference for the two different stereoisomers, indicating that the origin of the selectivity resides in the containment of the catalyst within the MOF framework. Although the exact origin of this “MOF effect” has yet to be elucidated, the findings do suggest that the MOF cavity can impose novel stereochemical preferences on the behavior of a chemical system that cannot be readily achieved by simple solution-based catalysts.

4. SURFACE-DIRECTED FUNCTIONALIZATION AND PSM

The outer surface modification of MOFs has become a topic of increasing interest in the context of growing thin films, oriented

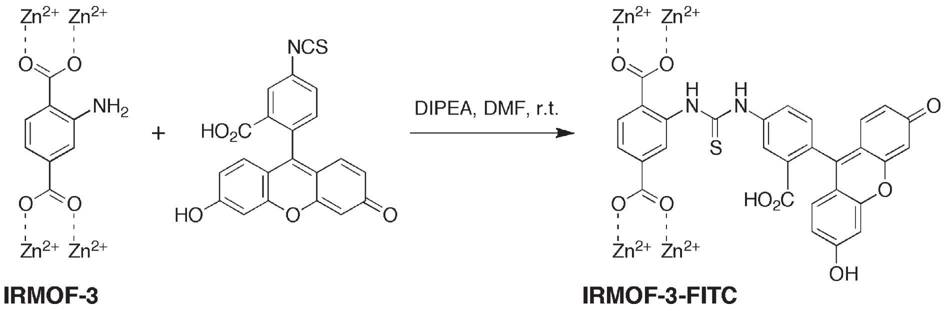


Figure 35. Covalent PSM of the surface of IRMOF-3 with the fluorophore FITC.

growth, and creating new material interfaces.[128] MOF-on-MOF growth studies and elegant examples of ligand exchange reactions have demonstrated the ability to modify MOF surfaces by growth of new material on an existing MOF substrate or replacement of surface ligands, respectively.[10,129−131] Several studies have been done on the encapsulation of MOF particles with other materials (e.g., silica, polymers),[132−136] but these are distinct from PSM approaches and will not be discussed here.

As discussed above, using solvent-exclusion effects, covalent PSM of a MOF surface has been achieved via click chemistry.[84] In this study, a dye molecule was appended to the MOF surface. Indeed, outer surface modification of MOFs with a fluorescent dye is distinguishable from encapsulation of a dye within the framework. Fischer and Metzler-Nolte examined different treatment protocols of organic fluorophores with both IRMOF-1 and IRMOF-3.[137] The MOFs were exposed to the dye in either a presynthetic (e.g., during solvothermal synthesis) or postsynthetic manner. IRMOF-1 crystals were exposed to fluorescein during or after solvothermal synthesis. Confocal laser scanning microscopy (CLSM) revealed a uniform distribution of fluorescein in IRMOF-1 microcrystals that were synthesized in the presence of the dye. IRMOF-1 exposed to fluorescein postsynthetically showed absorption of the dye only to the outer surfaces of the microcrystals, suggesting that the dye does not effectively penetrate deeply into the crystal under the reported conditions. In contrast, IRMOF-3, which differs only by the presence of an amino tag, did not take up fluorescein under identical pre- or postsynthetic methods. However, treatment of IRMOF-3 microcrystals with fluorescein isothiocyanate (FITC) revealed that outer surface functionalization of the MOF could be achieved via PSM (Figure 35).[137] Ultra-high-vacuum FTIR (UHV-FTIR), ESI-MS, and CLSM were all used to confirm the presence of trace amounts of FITC linked to the IRMOF-3 surface by thiourea linkages.

In a subsequent investigation, Fischer, Metzler-Nolte, and Wöll demonstrated a highly controlled approach to surface-directed PSM.[137] Crystals of a DMOF-1 analogue (which contained 1,4-naphthalene dicarboxylate as an organic linker) were grown on a gold substrate via liquid-phase epitaxy. The surface-bound MOF, which they termed a SURMOF (SURMOF = surface-attached crystalline and oriented metal−organic framework multilayers), was grown in a highly controlled fashion, and the layer-by-layer growth was detected as mass increases to the substrate as monitored by a quartz crystal microbalance. To create a PSM-ready surface, the SURMOF was exposed to copper acetate followed by NH_2-BDC, thereby installing the amine-tagged linker onto the surface of the SURMOF. As before, exposure of the material to FITC resulted in conjugation of the dye to the amine groups via formation of an isothiocyanate bond. The small amount of modification produced in this experiment makes traditional chemical methods of confirming the covalent, surface PSM difficult. However, quartz crystal microbalance measurements and fluorescence spectroscopy indicated that PSM had occurred and that it was specific to the amine-tagged SURMOF.[137] The authors highlighted the high level of control achieved by this liquid-phase epitaxy method of MOF growth and modification, which should allow for the preparation of material distinct interfaces and molecular “gates” at the external surfaces.

A recent report claims biomolecules to have been conjugated to the outer surface of MOFs via PSM.[138] The report describes the activation of pendant carboxylate groups from the organic linkers, which are displayed on the surface of the MOF crystal, and subsequent conjugation to two proteins—enhanced green fluorescent protein (EGFP) and *Candida antarctica* lipase B (CAL-B). Conjugation of these proteins was described for 1-D, 2-D, and 3-D MOFs comprised of different metal ions and dicarboxylate linkers; IRMOF-3 was used for the experiments with a 3-D MOF. Data were presented showing fluorescent emission from EGFP-modified MOFs. In addition, the authors claim that the CAL-B enzyme remains active for performing transesterification reactions after conjugation to the MOFs.[138] The coupling of biomolecules to MOFs represents an important frontier where PSM may play a substantial role; therefore, if the results of this study can be verified and further developed, many new applications of PSM and MOFs will become accessible.

5. POSTSYNTHETIC DEPROTECTION

PSD is a variety of PSM that is just beginning to gain attention as a postsynthetic functionalization method. The concept behind PSD is that a protected or “masked” functional group is introduced onto an organic linker, the linker is incorporated into a MOF under standard solvothermal conditions, and then the protecting group is removed in a postsynthetic fashion to reveal the desired functionality. To date, a handful of reports have appeared on PSD, but it is likely that many more studies will be published as the topic gains increasing attention.

Among the earliest examples of PSD was a serendipitous finding by Yamada and Kitagawa, where in situ deprotection of an organic linker was observed, resulting in a functionalized MOF.[139] Termed a “protection−complexation−deprotection” (PCD) process (Figure 36), the protection step involved the acetylation of 2,5-dihydroxyterephthalic acid (H_2dhybdc) with acetic anhydride to 2,5-diacetoxyterephthalic acid (H_2dacobdc).

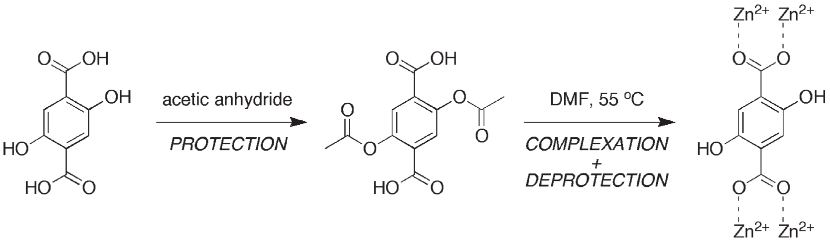


Figure 36. PCD process to generate a functionalized MOF. This experiment represents an early example of PSD.

In the complexation step, H_2dacobdc was combined with bipyridine and Zn(II) in DMF to obtain a MOF with a layered-pillared topology. As stated by the authors, "Unexpectedly and fortuitously, the acetoxyl groups were totally removed", producing the dhybdc ligand and a MOF with free hydroxyl groups within the pores.[139] Hence, in this scenario, the complexation and deprotection steps occur in tandem. The resulting free hydroxyl groups are involved in extensive intra- and intermolecular hydrogen bonding that is believed to help stabilize the MOF. NMR spectroscopy was used to examine the PCD process, which was observed to be slow, with some metal coordination clearly preceding removal of the acetyl groups. Although this PSD reaction was fortuitous in nature, the utility of this approach was well recognized by the authors, who noted that the strategy would be useful for preventing interpenetration, introducing functionality, and controlling pore diameter—all statements that would be verified in subsequent investigations.

Telfer and co-workers clearly demonstrated the utility of PSD in 2010 by validating the ability to prevent framework interpenetration.[140] The amine tag on the ligand 2-aminobiphenyl-4,4′-dicarboxylate was protected with a bulky *tert*-butylcarbamate (Boc) protecting group. Combination of this ligand with Zn(II) under solvothermal conditions gave an IRMOF-10 analogue showing a clear absence of framework interpenetration. The bulky *tert*-butyl groups prevent interpenetration, which is generally a difficult feature to control for MOFs produced from extended ligands. Thermolysis of the IRMOF at 150 °C in DMF resulted in removal of the Boc group (generating carbon dioxide and isobutylene) to generate an IRMOF with free amine tags within the pores (Figure 37). Crystallinity was preserved as determined by XRD and PXRD, although gas sorption measurements could not be obtained. Interestingly, attempts to produce IRMOF by directly employing 2-aminobiphenyl-4,4′-dicarboxylate have not been successful.[140] In 2011, Telfer produced a related result by using the thermolabile Boc group to introduce a proline substituent in an IRMOF.[141] The solvothermal synthetic conditions produced a noninterpenetrated IRMOF (IRMOF-Pro-Boc) with minimal racemization of the protected proline groups. As in the previous study, PSD was achieved with heat to liberate the Boc group from the proline subsitutent (under microwave irradiation conditions), generating an IRMOF (IRMOF-Pro) with free proline groups inside the pores of the framework (Figure 37). Importantly, it was shown that IRMOF-Pro could not be obtained from the ligand without the use of a Boc protecting group. IRMOF-Pro was shown to act as a heterogeneous, chiral organocatalyst, promoting an aldol reaction between acetone or cyclopentanone and 4-nitrobenzaldehyde with modest ee values.[141] These seminal papers highlight the value of PSD as an approach for realizing MOFs not readily obtained by solvothermal methods, while also providing a novel mechanism for controlling framework interpenetration.

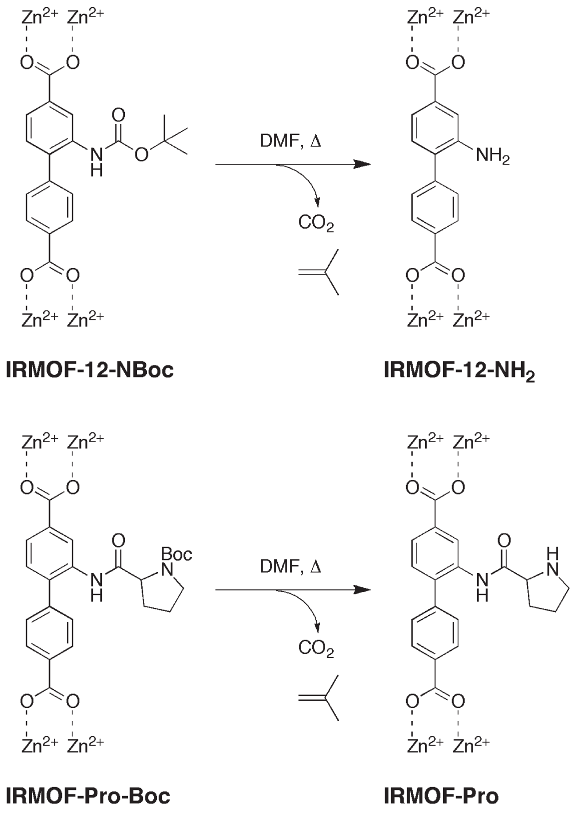


Figure 37. Thermally induced PSD on IRMOFs.

In addition to the thermal PSM already described,[91,92] photochemistry has also been employed to initiate PSD reactions. The first description of photochemical PSD was reported by Kitagawa and co-workers on the pillared material CID-N_3 (CID = coordination polymers with interdigitated structures), which contains Zn(II), bipyridine, and 5-azidoisophthalic acid that bears an azide tag.[142] Irradiation of CID-N_3 with a Hg lamp produced the reactive triplet nitrene as evidenced by FTIR and electron paramagnetic resonance (EPR) spectroscopy (Figure 38). A maximum of about 70% conversion to the nitrenes was achieved after 1 d of irradiation. Crystallographic evidence for conversion to the nitrene was also obtained, and the reactive nitrene was found to be disordered over three crystallographic positions. The ability to characterize the nitrene by XRD demonstrates the stabilization of this reactive species by immobilization on the framework structure. Exposure of the nitrene-bearing product to O_2 resulted in a mixture of nitroso- and nitro-bearing MOF products (Figure 38).[142] It was also reported that exposure of the nitrene MOF to CO resulted in formation of an isocyanate-tagged product. Hence, it was proposed that this photochemically

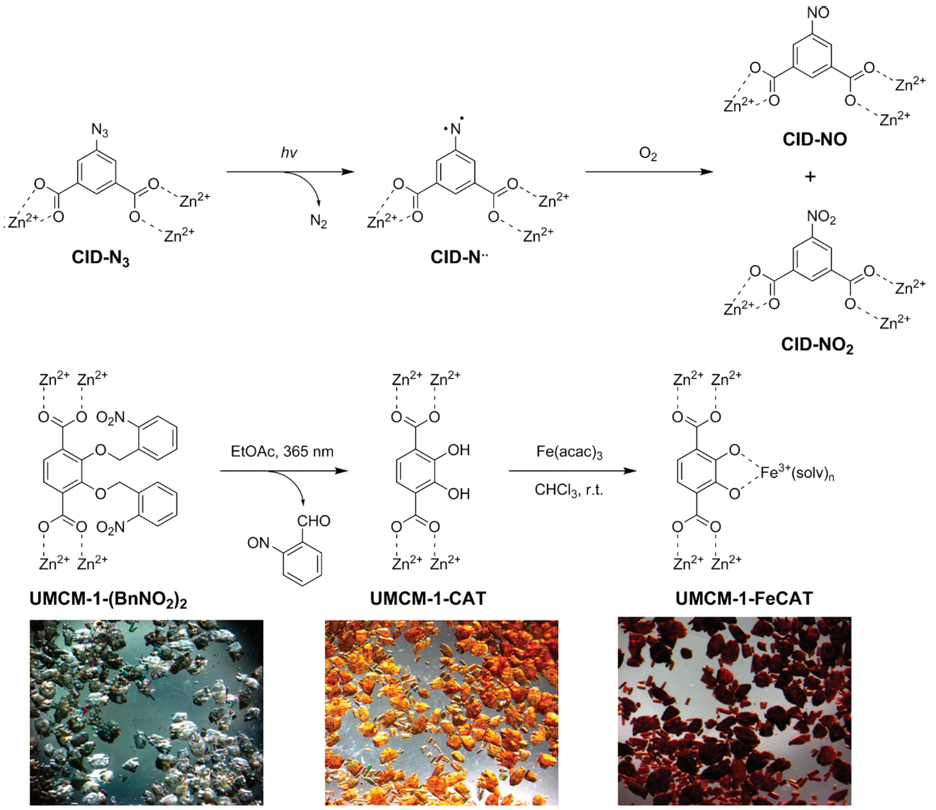


Figure 38. Reported examples of photochemical PSD. Photographs (bottom) of UMCM-1-$(BnNO_2)_2$ (left), UMCM-1-CAT (middle), and UMCM-1-FeCAT (right) showing the ability of the free catechol groups to bind Fe(III) within the framework. The orange color of UMCM-1-CAT has been attributed to trapped 2-nitrosobenzyaldehyde within the framework.

activated MOF could be used to trap certain guest species by generation of a reactive intermediate.

Photochemical PSD has also been used to reveal stable functional groups within a MOF that would be otherwise incompatible with solvothermal synthetic methods. A classic photochemical protecting group, 2-nitrobenzyl ether, was used to mask one or two hydroxyl groups on a BDC ligand. These ligands were then combined with BTB and Zn(II) to prepare crystalline solids that were shown by XRD to be identical to the UMCM-1 family of MOFs.[143] Moreover, the benzylic protecting groups could be located in the XRD data of UMCM-1-$(BnNO_2)_2$, confirming the stability of these protecting groups during the solvothermal synthetic procedure. Irradiation of either MOF with 365 nm light in ethyl acetate resulted in 75% to quantitative cleavage of the protecting groups, producing MOFs with free hydroxyl groups within the framework. The crystallinity of the photochemical PSD products was verified by XRD structure determination, which showed that the frameworks were completely intact. Importantly, gas sorption experiments confirmed an increase in the accessible surface area of the materials after PSD, consistent with liberation of the benzylic groups from the framework.[143] To demonstrate that the functional groups generated in these PSD reactions were intact and accessible, UMCM-1-CAT was treated with $Fe(acac)_3$. As expected, on the basis of the high affinity of the catechol group for a variety of transition-metal ions (including iron),[144,145] the crystals instantly became dark red upon exposure to Fe(III).[143] Amazingly, the production of an incredibly high-affinity metal binding site within the MOF does not disrupt the framework structure and remains completely accessible for metal binding. Photochemical approaches to initiating reactions in MOFs are likely to receive increasing attention on the basis of the increasing number of successful reports in this area.[146]

In addition to their work on conventional PSM described earlier,[83,84] Hupp and Nguyen have also been the first to describe a dative PSD reaction (e.g., selective demetalation).[147] The noninterpenetrated MnSO-MOF was prepared from dipyridyl Mn(salen)-derived and tetrakis(4-carboxyphenyl)benzene organic linkers in combination with Zn(II). Exposure of MnSO-MOF to H_2O_2 in a mixture of water and MeOH resulted in removal of Mn(III) from the salen linkers, as indicated by a color change from brown to yellow (Figure 39). Removal of the Mn(III) was confirmed by elemental analysis, which showed that as much as 90% of the Mn(III) ions could be removed without destruction of the framework. Applying the same solvent-exclusion strategy they employed for the click chemistry described above,[84] Mn(III) ions were selectively removed from the surface of MnSO-MOF by impregnating the MOF with chloroform prior to treatment with H_2O_2. Evidence for selective dative PSD at the surface of the MOFs was provided by examining the catalytic activity of the materials for olefin epoxidation with differentially sized substrates. At early reaction times, as-synthesized MnSO-MOF displayed little selectivity between small and large olefin substrates, while H_2O_2-treated MnSO-MOF showed a >16-fold preference for the smaller substrate. This suggests that, by removing the surface catalytic Mn(III) sites, only the smaller substrate, which can diffuse into

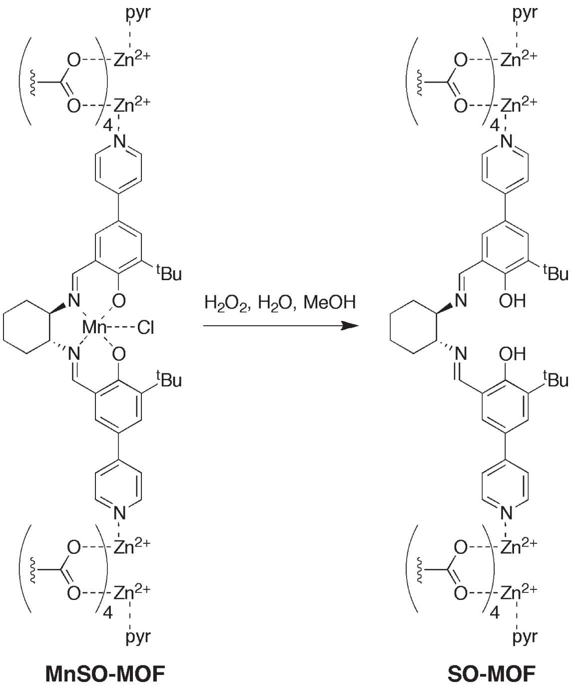


Figure 39. Dative PSD of Mn(III) from a salen-derived organic linker. Selective PSD was achieved on the exterior of the crystal by soaking the MOF in chloroform and limiting the exposure time to H_2O_2.

the interior of the framework, can undergo epoxidation.[147] This preliminary demonstration shows an important, complementary application of PSD, which is the removal of a chemical functionality from the MOF, in this case in a selective manner, to improve the overall characteristics of the material for a specific application.

6. CONCLUDING REMARKS

Postsynthetic approaches to the modification and functionalization of MOFs has become a vibrant area of chemical research, particularly within the past five years. Dozens of different chemical reactions have been reported on MOFs that include both organic transformations and inorganic reactions (ligand or metal addition/exchange). The resulting materials have been shown to engender MOFs with new properties relevant to gas sorption, catalysis, and biomedical applications. Despite their usefulness, these postsynthetic methods require a careful consideration of the reaction conditions, as well as exhaustive characterization of the solid-state products, to ensure that the reactions occur in a true SCSC fashion without degradation or collapse of the framework. Many advancements in postsynthetic methods are expected in the coming years that will further raise the importance of these methods in the chemistry of MOFs. Strategies to control the spatial distribution of modification are likely to become increasingly important to make materials with specific functional domains. The ability to perform multiple modification reactions to produce materials with functional groups in highly controlled relative orientations will be essential for creating sites for selective catalysis or guest trapping. Finally, the combination of prefunctionalization, with both PSM and PSD, will lead to MOFs of unprecedented complexity and function that are certain to be important for realizing the full potential of MOFs in a variety of technological applications.

AUTHOR INFORMATION

Corresponding Author

*E-mail: scohen@ucsd.edu.

BIOGRAPHY

Seth M. Cohen was born and raised in the San Fernando Valley suburbs of Los Angeles, California. He attended Stanford University and earned a B.S. degree in Chemistry and a B.A. degree in Political Science. He then attended graduate school at the University of California, Berkeley, and earned his Ph.D. under the guidance of Prof. Kenneth N. Raymond. After completing his Ph.D., he was an N.I.H. postdoctoral fellow in the laboratory of Prof. Stephen J. Lippard at the Massachusetts Institute of Technology. After his postdoctoral research, he began his independent career at the University of California, San Diego, where he is a Professor in the Department of Chemistry and Biochemistry. His research interests are primarily in the area of medicinal bioinorganic chemistry and metal−organic frameworks.

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