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Tandem Postsynthetic Modification of Metal–Organic Frameworks Using an Inverse-Electron-Demand Diels–Alder Reaction

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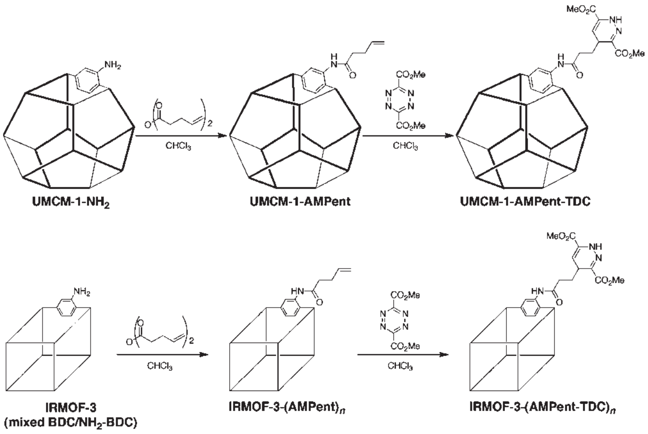
S Supporting Information

ABSTRACT: A postsynthetic modification (PSM) scheme for metal–organic frameworks (MOFs) has been developed using a tetrazine-based "Click" reaction. It was found that the efficacy of this modification procedure was dependent on the MOF topology and, in the case of an isoreticular MOF (IRMOF) system, required the formation of a mixed-ligand IRMOF with a suitable ratio of 1,4-benzenedicarboxylate (BDC) and an olefin-tagged BDC derivative. On the basis of the versatile use of tetrazine "Click" chemistry in bioconjugate chemistry, we expect that this scheme will prove to be a useful reaction for preparing functionalized materials, including MOFs.

Metal–organic frameworks (MOFs) are crystalline, porous solids constructed from inorganic metal-ion clusters and polytopic organic linkers.[1] Owing to their high surface areas, uniform pores, and chemical tunability, MOFs are of increasing interest for a variety of applications including gas adsorption,[2] catalysis,[3] and biomedicine,[4] among others.[5] Moreover, functionalization of MOFs is important in expanding the chemical diversity and potential applications of MOFs. Postsynthetic modification (PSM) has emerged as an important late-stage approach to functionalizing MOFs.[4,6–15] Generally, PSM requires that the organic ligand of the MOF contain a chemical "tag" or "handle", such as an amine, aldehyde, or alkyne, to provide a site for coupling to a soluble reagent. Among the chemical handles reported, MOFs bearing amine groups have been the most widely employed and investigated.[9,10,14,16–20] In order for PSM to achieve its full potential, it is essential that new chemical handles and new PSM reactions be developed for MOF functionalization.

Both alkyne and azide handles have been introduced into MOFs for use in "Click" chemistry for PSM.[21,22] This [3 + 2] cycloaddition generally requires a copper(I) catalyst to accelerate the reaction, which has the potential to be trapped in the pores of the MOF. Herein, we demonstrate that a "Click" Diels–Alder [4 + 2] cycloaddition reaction using tetrazines as the only reagent can be performed on MOFs in a PSM fashion.[23,24] As electron-deficient dienes, 1,2,4,5-tetrazines (also called *s*-tetrazines) and their derivatives rapidly react with electron-rich alkenes or alkynes by an inverse-electron-demand Diels–Alder reaction to yield dihydropyridazines or pyridazines (Scheme S1 in the Supporting Information, SI). These reactions are facile and reliable, can be used to prepare various substituted pyridazines, fused heterocycles, and have been employed in the labeling of biomolecules and as key steps in the total synthesis of complex organic molecules.[24–28] Recently, the use of this reaction was described for the functionalization of polymers.[29] In addition, these Click reactions do not require a catalyst or other coreagents and liberate dinitrogen as the only byproduct, making this transformation very attractive for use in the PSM of MOFs.

Scheme 1. Tandem Approach for PSM of UMCM-1-NH_2 (top) and Mixed IRMOFs (bottom) with a Tetrazine in an Inverse-Electron-Demand Diels–Alder Reaction



A stepwise, "tandem" approach was adopted for the PSM of MOFs by tetrazine reagents (Scheme 1).[19,30] UMCM-1-NH_2 (UMCM = University of Michigan Crystalline Material) was selected because of its large pore size and previous successes with PSM reactions.[8,20,31,32] UMCM-1-NH_2 was quantitatively modified with pentenoic anhydride to produce a functionalized MOF (UMCM-1-AMPent) with an olefin group appended to the 1,4-benzenedicarboxylate ligands [BDC; as confirmed by ^{1}H NMR spectroscopy upon digestion of the material in DCl/D_2O/dimethyl sulfoxide (DMSO)-d_6; Figure 1]. The olefin-bearing UMCM-1-AMPent was then treated with dimethyl-1,2,4,5-tetrazine-3,6-dicarboxylate (TDC)[33] at room temperature in $CHCl_3$ for 24 h. Digestion of the resulting material in DCl/D_2O/DMSO-d_6 followed by ^{1}H NMR analysis confirmed the formation of the expected Diels–Alder cycloaddition product (dihydropyridazine) with complete consumption of alkene (Figure 1). The new MOF, UMCM-1-AMPent-TDC, remained highly crystalline, stable, and microporous, as evidenced by single-crystal X-ray diffraction (XRD; Table S1 and Figure S1 in the SI), powder XRD (PXRD), thermal gravimetric analysis (Figure S2 in the SI), and gas sorption analysis. The Brunauer–Emmett–Teller (BET) surface area of UMCM-1-AMPent-TDC

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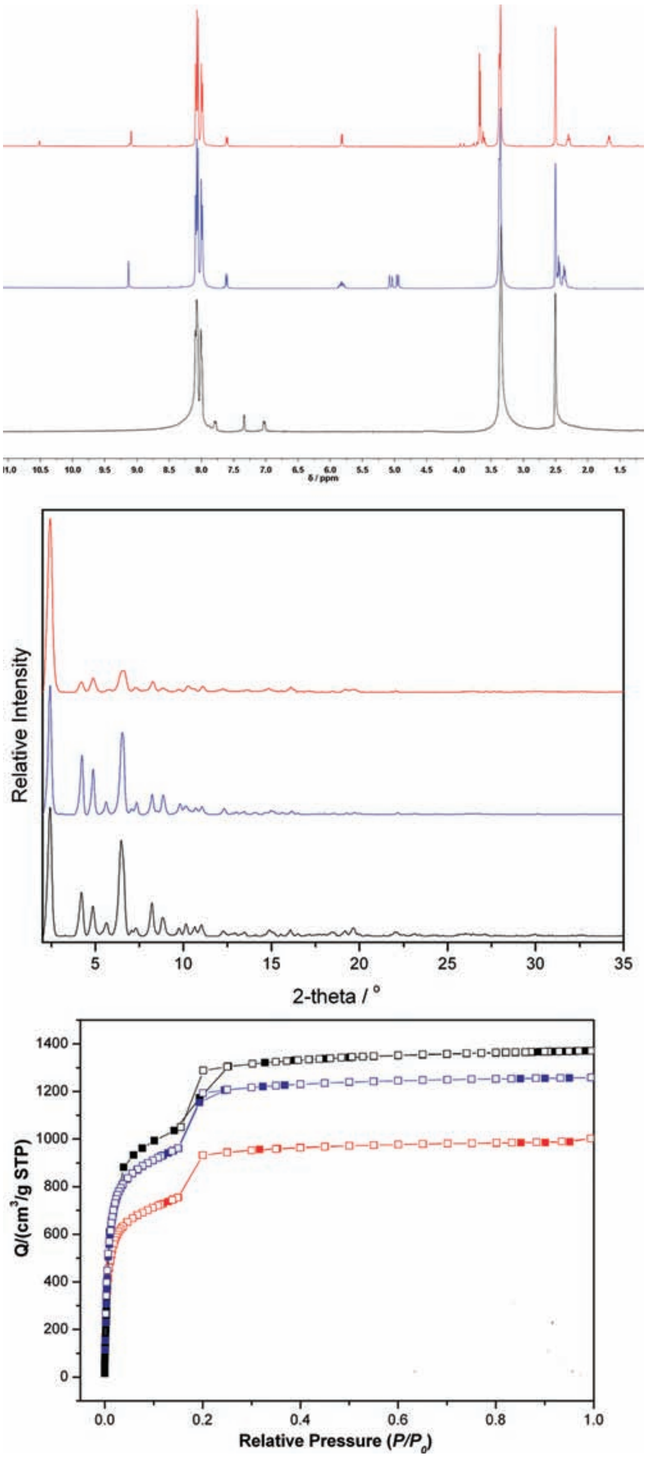

Figure 1. ^{1}H NMR spectra (top, samples digested in DCl/D$_2$O/DMSO-*d*$_6$), PXRD patterns (middle), and dinitrogen isotherms (bottom) of UMCM-1-NH$_2$ (black), UMCM-1-AMPent (blue), and UMCM-1-AMPent-TDC (red). The BET surface areas for the MOFs were ~4000, 3600, and 2800 m^2/g, respectively.

was determined to be ~2800 m^2/g (based on two independent experiments, Figure 1), which is lower than that of the parent UMCM-1-NH$_2$ but not unexpected based on the introduction of bulky substituents into the pores.

Other olefin groups were also found to be suitable for the tetrazine PSM reaction. Another tagged MOF, UMCM-1-URAl, which contains an olefin group attached to the BDC ligand via a urea linkage, was prepared (see the SI for details). UMCM-1-URAl was obtained by treating UMCM-1-NH$_2$ with allyl isocyanate (Scheme S2 in the SI), giving the olefin-bearing material in essentially complete conversion. UMCM-1-URAl was then treated with TDC, which underwent cycloaddition, quantitatively converting the olefin groups to the dihydropyridazine product (UMCM-1-URAl-TDC), as confirmed by ^{1}H NMR and electrospray ionization mass spectrometry (ESI-MS) analysis (Figure S3 in the SI). PXRD data showed that UMCM-1-URAl-TDC was highly crystalline as well (Figure S4 in the SI). In order to further generalize these findings for a different MOF topology, IRMOF-3 (IRMOF = isoreticular metal−organic framework) was prepared according to literature procedures and quantitatively modified with pentenoic anhydride. However, attempts to modify IRMOF-3-AMPent with TDC were incomplete, showing no more than ca. 20% conversion, even under reaction conditions utilizing elevated temperatures, longer reaction times, and excess TDC (Figure S5 in the SI).

The contrast between the facile reactivity of the UMCM system compared to the IRMOF suggested to us that the smaller pore size and steric crowding of the olefin groups in the latter might be hindering the progress of the PSM reaction with TDC. To test this hypothesis, a series of mixed-ligand MOFs,[34−40] comprised of both BDC and NH$_2$−BDC in different ratios, were prepared (Table S2 in the SI). As found in previous reports of mixed MOFs,[37,38] the mole fraction of NH$_2$−BDC in the IRMOF (obtained by ^{1}H NMR spectra of the digested products in DCl/D$_2$O/DMSO-*d*$_6$; Figure S6 in the SI) shows a linear relationship with the ratio of BDC and NH$_2$−BDC in the solvothermal reaction mixture. In this manner, IRMOFs were prepared containing from 44 to 100% NH$_2$−BDC in the framework (Table S2 in the SI). Treating any of the mixed-ligand IRMOFs with pentenoic anhydride resulted in a quantitative conversion to the mixed materials containing BDC and olefin-bearing BDC ligands [i.e., IRMOF-3-(AMPent)$_n$, where n = mole fraction of the functionalized ligand; Figure S7]. As expected, the BET surface areas of IRMOF-3-(AMPent)$_n$ materials show a linear increase as the proportion of modified ligand decreases (i.e., as n gets smaller; Table S3 in the SI). This finding is consistent with earlier studies on MOFs that had undergone different degrees of PSM.[20] The IRMOF-3-(AMPent)$_n$ materials were then further modified with TDC at 55 °C for 48 h. As shown in the ^{1}H NMR spectra of the digested products in Figure 2, when the mole fraction of olefin-functionalized BDC (i.e., AMPent-BDC) was ≤ 0.67, complete conversion to the cycloaddition product was obtained. The ^{1}H NMR data are supported by ESI-MS(−) analysis, which shows only product ions from the dihydropyridazine-containing BDC ligand (Figure S8 in the SI). PXRD (Figure S9 in the SI) and single-crystal XRD indicate that the final IRMOF-3-AMPent-TDC is highly crystalline (Figure S10 in the SI).

In conclusion, we successfully utilized an inverse-electron-demand Diels−Alder reaction for the PSM of two different MOF frameworks. It was discovered that for an IRMOF material modulating the ratio of tagged linker was essential for obtaining efficient functionalization, which highlights the importance of utilizing mixed-ligand MOFs. The applicability of this reaction should allow for PSM with MOFs bearing various dienophiles or heterodienophiles, such as electron-rich olefins, acetylenes, enol ethers, enamines, benzynes, and others. The ability to prepare diversely functionalized tetrazines should allow for the

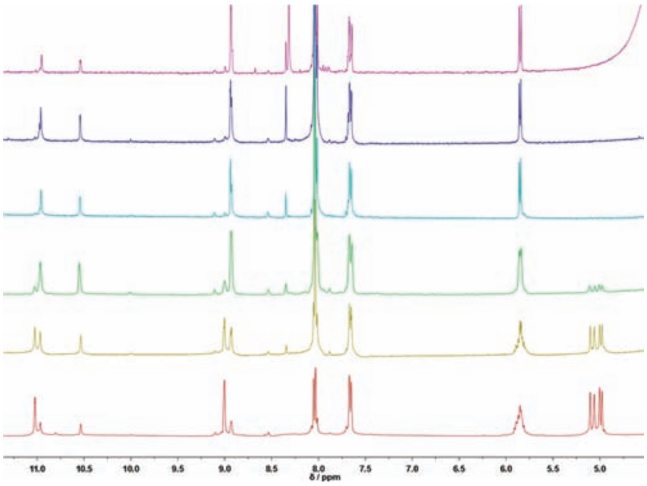

Figure 2. ^{1}H NMR spectra of IRMOF-3-(AMPent-TDC)$_n$ samples (digested in DCl/D_2O/DMSO-d_6). From top to bottom are shown IRMOF-3-(AMPent-TDC)$_{0.44}$, -(AMPent-TDC)$_{0.52}$, -(AMPent-TDC)$_{0.67}$, -(AMPent-TDC)$_{0.75}$, -(AMPent-TDC)$_{0.85}$, and -(AMPent-TDC)$_1$, respectively. Note the complete loss of the starting material olefin resonances at ~5 ppm in samples with ≤67% functionalized BDC ligand.

introduction of unprecedented, new functionality into MOFs. Indeed, our preliminary efforts demonstrate that different tetrazines and different olefin-tagged MOFs can undergo this chemistry, the results of which will be reported in due course.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Experimental details, Tables S1−S3, Schemes S1 and S2, and Figures S1−S10. This material is available free of charge via the Internet at http://pubs.acs.org.

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