Covalent surface modification of a metal–organic framework: selective surface engineering *via* Cu^I-catalyzed Huisgen cycloaddition†

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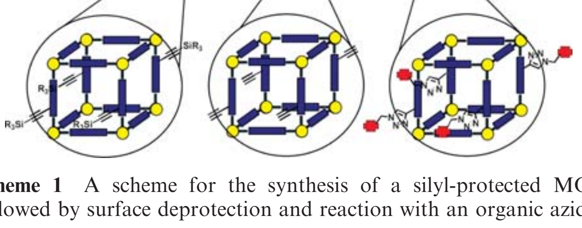
Received (in Berkeley, CA, USA) 26th March 2008, Accepted 15th August 2008
First published as an Advance Article on the web 8th October 2008
DOI: 10.1039/b805101a

A Zn-cornered, mixed-ligand, metal–organic framework (MOF) bearing TMS-protected acetylenes has been constructed and its surface decorated with organic molecules *via* 'click chemistry', in a demonstration of selective post-synthesis functionalization.

Within the last decade, metal–organic frameworks (MOFs) have established themselves as highly promising materials for a host of applications, including separations and catalysis,[1] as well as gas storage.[2] As the chemistry of MOFs advances, new applications continue to be added to an already impressive list, and in a symbiotic fashion, the emergence of novel applications often highlights the need for new types of materials. As an illustration, the Lin and Férey groups have recently introduced MOFs that have potential for *in vivo* application,[3] raising the question of how to tailor MOF nanocrystallites such that they present biocompatible, non-immunogenic surfaces and/or targeting groups. Herein, we demonstrate a modular, covalent strategy for the selective modification of MOF surfaces post-synthesis. The result is a new group of MOF materials with macroscopic surface characteristics that are completely different from those of the parent MOF.

The synthesis of new families of MOF materials that possess a wide range of chemical functionalities and/or steric environments while retaining framework crystallinity and porosity remains a labor-intensive endeavor. Incorporation of new functionalities into MOF synthesis, even with a ligand combination known to produce a given MOF structure, can lead to alternate topologies[4] or interfere with the framework building process, yielding amorphous materials. These challenges, together with the non-trivial task of solving MOF crystal structures, have made syntheses of functional MOFs unpredictable ventures. Recently, post-synthesis modification, the elaboration of a known MOF to give a series of new materials with the same structure but bearing different chemical functionalities, has been proposed as an efficient and rational route to new MOFs.[5] To extend this concept further into the realm of functional diversity, the post-synthesis reaction must satisfy a number of requirements: it should not undermine framework integrity, it must have exceptional coupling efficiency, and it should have a broad tolerance of functional groups. Sharpless' archetypal 'click' reaction, the Cu^I-catalyzed Huisgen cycloaddition of azides to terminal alkynes, satisfies all these conditions.[6] Hence we chose to employ this reaction for tailoring MOF surfaces, and set out to synthesize MOFs possessing silyl-protected $C{\equiv}C$ bonds that could be deprotected easily using conventional organic solution chemistry (Scheme 1). Such functionality would provide an extra level of control over the subsequent 'click' reaction: because Cu^I catalyzes addition to terminal alkynes exclusively, we can control where the cycloaddition occurs by selective deprotection (Scheme 1).

Given our extensive experience with zinc-cornered, mixed-ligand MOFs containing bis(pyridyl) struts,[7] we relied on the wide range of commercially available dicarboxylic acids to allow us to sample a vast ligand space with one bis(pyridyl) ligand. In this spirit, ligand **L1**, 3-[(trimethylsilyl)ethynyl]-4-[2-(4-pyridinyl)ethenyl]pyridine, was chosen for its synthetic ease of access (see ESI†). Upon combining 2,6-naphthalenedicarboxylic acid, **NDC**, with **L1**, pale-yellow single crystals of **1** can be obtained in good yield. X-Ray diffraction of a crystal of **1**‡ reveals a two-fold interwoven, paddle-wheel framework structure with the Si group residing in six positions with respect to the *ab* plane (Fig. 1). Both thermogravimetric analysis (TGA) and powder X-ray diffraction (PXRD) of a bulk sample of **1** indicate an irreversible change in the framework structure upon removal of solvent (ESI†, Fig. S4 and S5). Nevertheless, the Langmuir type-I N_2 adsorption isotherm at 77 K (ESI†, Fig. S6) clearly demonstrates that **1**



Scheme 1 A scheme for the synthesis of a silyl-protected MOF followed by surface deprotection and reaction with an organic azide.

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† Electronic supplementary information (ESI) available: Synthetic protocols and characterization data for compound **L1**; MALDI-TOF spectrum for dissolved $\mathbf{1}_{\mathbf{PEG}}$; TGA, PXRD, and N_2 absorption data for **1** and $\mathbf{1}_{\mathbf{E\text{-}click}}$. CCDC 682857. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b805101a

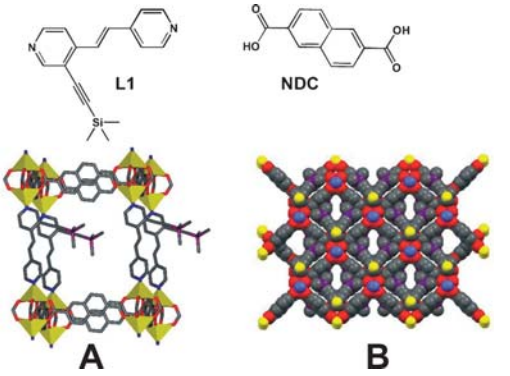

Fig. 1 (A) Schematic view of a single network unit for the doubly interweaving network **1**, formed between **L1** and **NDC**. (B) Crystal packing diagram of **1** showing network catenation and framework pores down the *c* axis.

remains permanently microporous after solvent removal, giving a BET surface area of $\sim 510\ \mathrm{m^2\ g^{-1}}$ and a pore width of 5.1 Å using the HK model.

To desilylate the surface of **1**, we employed tetrabutylammonium fluoride (TBAF) due to its ready availability as a solution in THF. In addition, the large size of the $\mathrm{NBu_4}^+$ counterion was expected to limit fluoride-based deprotection to the outermost layers of the MOF crystals.[8] The extent of deprotection can be evaluated by dissolving the outside of **1** with pyridine and analyzing the solution by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry (ESI†). The mass spectra of dissolved **1** and dissolved surface-deprotected **1** (**1**$_{\mathbf{deprot}}$) (Fig. 2) both showed evidence of **L1**$_{\mathbf{deprot}}$ ($[\mathrm{M} + \mathrm{H}]^+ = 207$). However, the peak for **L1** ($[\mathrm{M} + \mathrm{H}]^+ = 279$) dominated the spectrum for dissolved **1**; there was much less evidence of this protected ligand in the mass spectrum of **1**$_{\mathbf{deprot}}$. The evaluation of the Zn/Si ratio of an as-synthesized sample of **1** using inductively coupled plasma optical emission spectroscopy (ICP-OES) confirmed that a small amount of desilylation occurs in **1** (Zn/Si = 2.23 instead of 2 for a fully silylated MOF).

Ethidium bromide monoazide, **E**$_{\mathbf{azide}}$, was chosen as the azide to attach to the surface terminal alkynes because its fluorescence can be used to detect attachment. The 'click' reaction was carried out between **E**$_{\mathbf{azide}}$ and **1**$_{\mathbf{deprot}}$, with [**E**$_{\mathbf{azide}}$ + **1**] serving as a point of reference. In addition, we treated the non-alkynylated analog of **1**, $\mathrm{Zn_2(NDC)_2BPE}$ (**2**),[9] with **E**$_{\mathbf{azide}}$ as a control for potential non-specific interactions. Side-by-side comparison of the fluorescence microscopy images of the products obtained from these three reactions (Fig. 2, top right), suggested that no reaction occurred with **2** (Fig. 2(A)), as expected. While the reaction product from **1** (Fig. 2(B)) showed some fluorescence, its intensity was inconsistent and minor compared to that of the product derived from **1**$_{\mathbf{deprot}}$ (Fig. 2C), consistent with the low population of unprotected acetylenes for the former (*vide supra*). Confocal microscopy imaging/depth-profiling of the fluorescent intensity of microcrystals of **1**$_{\mathbf{deprot}}$ (Fig. 2(D)) confirms that elaboration with **E**$_{\mathbf{azide}}$ occurred exclusively on the surface: fluorescence from the inside of the crystals is negligible, and most intense from the outer surfaces. Dissolving the outer surface of the new material **1**$_{\mathbf{E\text{-}click}}$ with pyridine and analyzing the resulting solution using MALDI-TOF reveals a significant species with fragmentation peaks corresponding to the triazole product ($[\mathrm{M} - \mathrm{Br}]^+ = 546$, $[\mathrm{M} - \mathrm{Br} - \mathrm{CH_2CH_3} + \mathrm{H}]^+ = 518$ and $[\mathrm{M} - \mathrm{CH_2CH_3} + 2\mathrm{H}]^+ = 598$), establishing that **E**$_{\mathbf{azide}}$ is covalently attached to the deprotected MOF crystals (Fig. 2).

By comparing the UV-vis absorption spectra of the **E**$_{\mathbf{azide}}$ solution before and after the 'click' reaction, we determined that $<0.8\%$ of the dipyridyl ligands had been 'clicked' (see ESI,† Fig. S1)—a fraction that clearly will depend on crystal size. Importantly, **1**$_{\mathbf{E\text{-}click}}$ retained both its crystallinity and microporosity (see TGA and PXRD data in ESI†, Fig. S4 and S5). The $\mathrm{N_2}$ isotherm still has Langmuir type-I behavior, albeit with signs of capillary condensation. In addition, the BET surface area ($480\ \mathrm{m^2\ g^{-1}}$) and the HK method pore width (5.0 Å) are, within experimental error, the same as those for **1**. These results suggest no significant loss of integrity in framework **1** during the two modification reactions.

The ability to 'click' an organic azide to the surface of **1** non-destructively prompted us to explore its utility in changing the macroscopic surface properties of MOF **1**. We conjectured that covalently 'clicking' polyethylene glycol (PEG) chains to the surfaces of **1** would make them hydrophilic, and thus, wettable. To this end, we reacted **1**$_{\mathbf{deprot}}$ with *O*-(2-aminoethyl)-*O*′-(2-azidoethyl)nonethylene glycol, **PEG**$_{\mathbf{azide}}$. The MALDI-TOF mass spectrum of the dissolved MOF product (ESI†, Fig. S2) clearly showed peaks corresponding to the sodium salt of the PEGylated ligand, **L1**$_{\mathbf{PEG}}$, with the characteristic fragmentation pattern of PEG, verifying the PEGylation of **1** to form **1**$_{\mathbf{PEG}}$. The success of this reaction is clearly demonstrated in Fig. 3: a drop of colored water remains beaded on top of a layer of packed **1** while the same drop on a packed layer of **1**$_{\mathbf{PEG}}$ immediately permeates into the crevices of the material and spreads out. Clearly, modification of **1** with the hydrophilic PEG segment has rendered its surface hydrophilic. Contact angle measurements further contrast the wettability of **1** and **1**$_{\mathbf{PEG}}$ with water: the average angle was 126(2)° for **1**, while water wets the sample spontaneously in the case of **1**$_{\mathbf{PEG}}$. As a control, a sample of **1** was exposed to a solution of **1**$_{\mathbf{PEG}}$ for 24 h without the "click" catalyst (ESI†, Fig. S3). After rinsing, this sample still repels water.

In conclusion, we have successfully demonstrated the selective functionalization of MOF surfaces *via* covalent, post-synthesis modification. This strategy should allow chemists to decorate MOF surfaces with moieties that otherwise would be, due to size or chemical functionality, incompatible with MOF synthesis. The MOF retains its 'inner' characteristics, but attains new surface properties. One scenario where this ability may become important is in catalysis where surface functionalities have the potential to act as 'gates' for controlling access to MOF channels, affording selectivity based on hydrophobicity or electrostatics. Other applications where modulation of surface properties would be critical include the dispersion of MOFs in various media or as thin films on a substrate. Looking ahead, such modification of surface properties could play an important role in *in vivo* delivery applications where the known biocompatibility of the surface PEG chains may render the MOF non-immunogenic. Given the impressive tolerance and

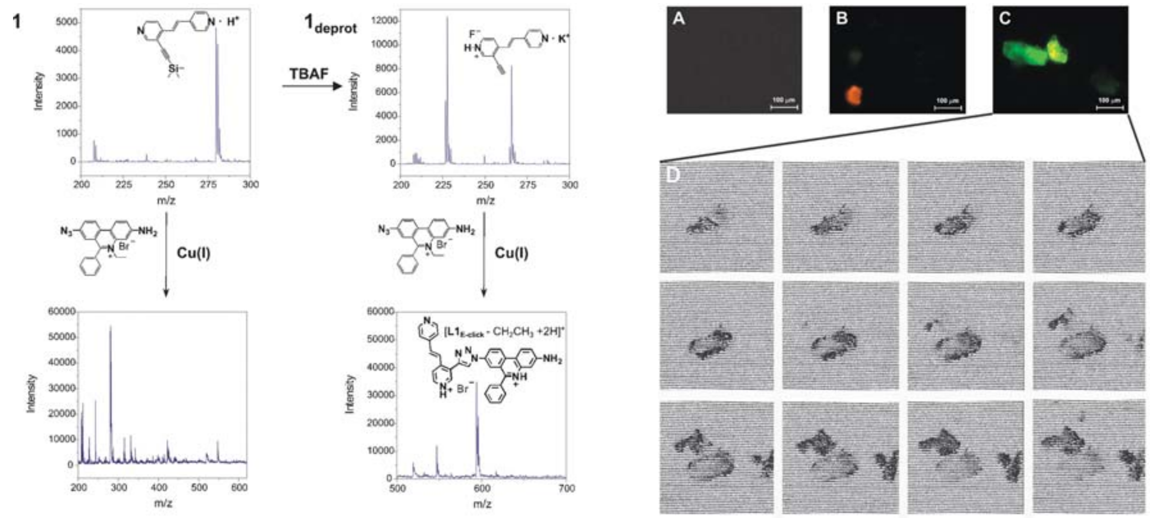

Fig. 2 Left: MALDI-TOF spectra confirming the deprotection and 'clicking' of **1**. Top right: Fluorescence microscopy images of: (A) **2**, (B) **1** and (C) $\mathbf{1_{deprot}}$ after the 'click' reaction. Bottom right: (D) A Z-axis series of confocal microscopic images of $\mathbf{1_{E\text{-}click}}$, represented as 2.5D topological plots (×63 magnification). From the top left panel, the fluorescence intensity of a modified MOF crystal can be viewed as horizontal slices as the focal point of the microscope traverses the height of the crystal, from top to bottom. The fluorescent area in the image started out as a dark sport in the middle of the panel, spread into a ring-shape, and then faded out as other modified crystals come into focus. This behavior is consistent with modification having occurred only at the surface of the crystal.

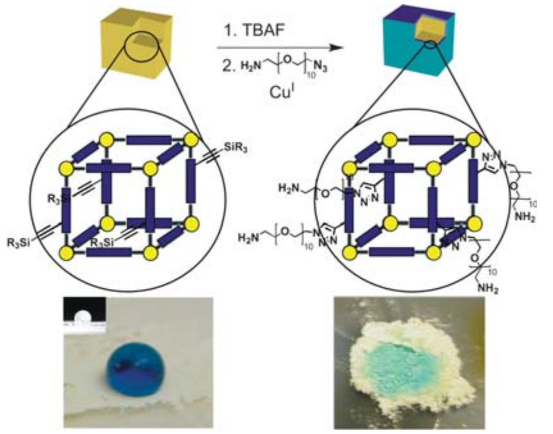

Fig. 3 Top: A schematic illustration of the transformation of hydrophobic **1** into hydrophilic $\mathbf{1_{PEG}}$. Bottom: The corresponding macroscopic materials show differences in wettability: A blue drop of water remains beaded of top of a packed powder sample of **1** (left image, inset shows side view of a drop), while spontaneously wetting a powder sample of $\mathbf{1_{PEG}}$ (right image).

versatility of the 'click' reaction, one can imagine altering MOFs to impart any desired property, bringing the elusive goal of rational design closer to realization.

Financial support for this work was provided by the US DOE, DTRA/ARO, AFOSR, and Institute of Catalysis in Energy Processes at Northwestern University (NU).

Notes and references

‡ *Crystal data*: Compound **1**: $C_{94}H_{88}N_8O_{20}Si_2Zn_4$, M = 1967.38, monoclinic, $C2/c$, a = 18.0511(8), b = 18.9764(8), c = 16.2258(6) Å, β = 98.90 (5)°, V = 5543.5(4) Å^3, Z = 2, D_c = 1.179 g cm^{-3}, μ = 0.938 mm^{-1}, $F(000)$ = 2032, GOF = 1.131; $R1$ and $wR2$ are 0.0552 and 0.1575, respectively, for 836 parameters and 13 792 reflections [$I > 2\sigma(I)$].

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