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# Post-synthetic modification of coordination networks

Guest Editors: Andy Burrows and Seth Cohen

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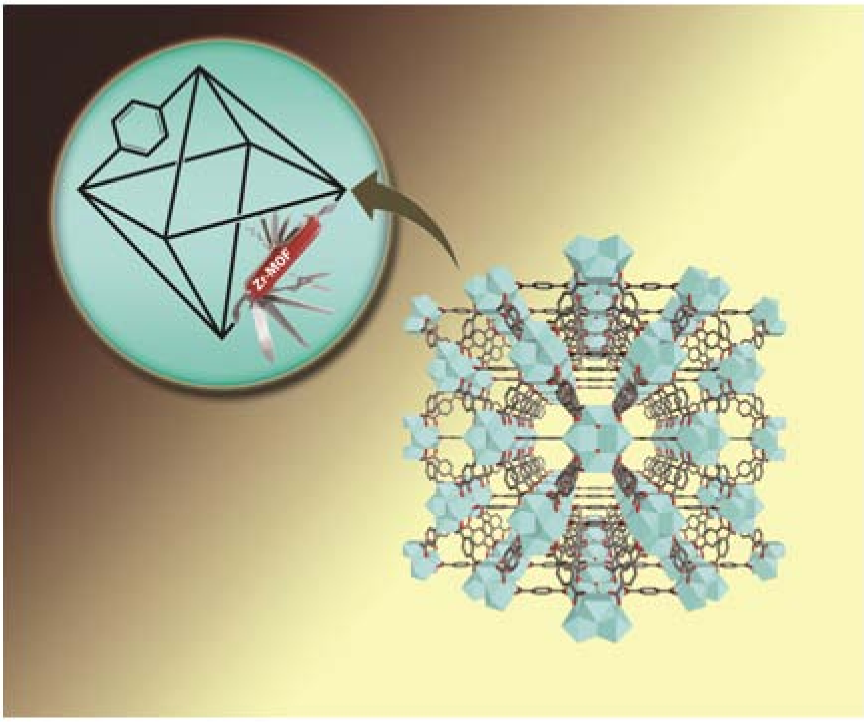

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**COMMUNICATION**

# Cu-mediated solid-state reaction in a post-functionalized metal–organic framework†

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**We serendipitously found that a functionalized MOF containing grafted copper species can react with itself without solvent in order to modify the chemical functions present on its walls. The use of EPR techniques allows new insight into the copper-mediated azide reduction.**

Reactions in the solid state are defined as chemical processes in which one or more solid reaction products are formed with diffusion of elementary particles within their interior, as comprehensively reviewed by Cohn.[1] The layer of reaction products increases by chemical reaction with the reactants adjacent to its boundaries. Solid-state reactions are known from thermal intracrystalline conversions (isomerizations or loss of volatile fragments), photoreactions, gas–solid reactions, and solid–solid reactions.[2]

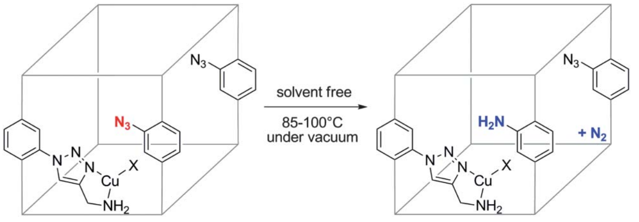
The reactivity in the solid state shows strict correlation with crystal packing because molecular migrations within the crystal are required for all reactions. Fujita extensively studied solid-state reactivity of compounds hosted in a robust crystalline porous structure, developing the concept of molecular flasks.[3–9] In this concept, organic guests are trapped in discrete porous nanocontainers, such as organometallic self-assembled cages, creating micro-environments and allowing specific reactions of the guest. Using this concept, Fujita and co-workers were able to get structural snapshots of chemical transformation intermediates thanks to *in situ* X-ray analyses.[10] They mounted a crystal of a porous coordination polymer containing a primary amine trapped into the framework on an X-ray diffractometer. With the amine-containing crystal being exposed to a flow of aldehyde solution, they were able to isolate the hemiaminal intermediate of the imine formation by regularly cooling the crystal at 90 K and collecting diffraction data.

Chemical reaction in the solid state without external reagents is rarely reported inside MOFs[11–14] even if it is generally acknowledged that well-defined isolated reactive single sites in MOFs will enable insight to be gained into reaction mechanisms.

Very recently, azide reductions have been reported using organometallic systems based on copper. The nature of the active centers and mechanism are unclear. Qiao *et al.* reported the Cu-catalyzed amination of halogenoarenes using sodium azide as amino source to give the corresponding *ortho*-functionalized aromatic amines.[15] The most efficient system was a combination of copper iodide with dimethyl ethylenediamine and caesium carbonate in ethanol. In the work of Sajiki *et al.*,[16] ethyl-4-azidobenzoate was reacted with $CuF_2$–$Et_3N$ in dimethylacetamide to give the corresponding aniline derivative in low yields. In a similar way, Ramana and Goriya reported the use of Cu(II) species combined with sodium ascorbate and proline to obtain the complete reduction of 4-azidonitrobenzene.[17] From these three studies, we can assume that the reduction can be performed in the presence of both copper and the nitrogen-based ligand. Nevertheless, the oxidation state and coordination of copper species are still unclear.

In this work, we report for the first time an intrareticular reaction in a MOF. The azido reduction which takes place in the microporous cavity is performed by copper-coordinated triazolyl moieties, introduced by postsynthetic click reaction into the MOF framework (Scheme 1).[18–21] The nature and oxidation state of heterogenized copper complex are characterized by cutting-edge EPR techniques.

In previous reports, we described an original functionalization method starting from amino-containing MOFs.[21] The first step consists of converting the amino groups on the framework walls into their analogous azido ($N_3$) groups. Without isolation or purification,



**Scheme 1** Copper-mediated intrareticular reduction of MOF azido functions to their amino analogues.

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the desired triazolyl-functionalized MOF materials are obtained by grafting the corresponding functionalized terminal alkyne using the copper-mediated Huisgen cycloaddition known as "click chemistry". To the best of our knowledge, we report here the first self-reaction of a metal–organic framework containing different functional groups introduced by postsynthetic modification.[22–28]

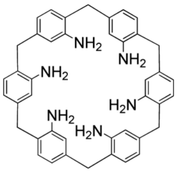
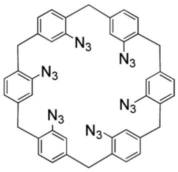
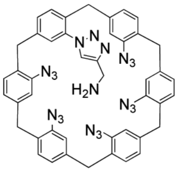
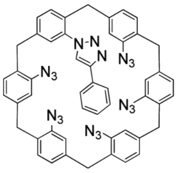
This study focuses on (In) MIL-68-$NH_2$ which is isostructural with MIL-68[29–32] and has a one-dimensional rod-shaped structure, formed by indium octahedra and 2-aminoterephthalates (BDC–$NH_2$) as bridging linkers. It is composed of hexahedral and triangular 1D-channels with apertures of 16 and 6 Å respectively. (In) MIL-68-$NH_2$ (**1**) was prepared according to the previously patented method.[33] It was obtained by precipitation reaction at room temperature. Afterwards the as-synthesized MOF was purified by multiple DMF treatments at 160 °C and soaked in $CH_2Cl_2$ for 24 h. According to our seminal work,[21] **1** was treated with *t*BuONO and $TMSN_3$ in THF overnight at room temperature to give the corresponding azido intermediate **2** (Table 1). The functionalized MOFs **3a** and **4a** were then obtained by adding an excess of propargylamine and phenylacetylene respectively, in the presence of $Cu(CH_3CN)_4PF_6$ in acetonitrile. All the obtained compounds **1** to **4** were analyzed by liquid $^1H$ NMR of the samples dissolved in a DCl–$D_2O$–DMSO-$d_6$ solution.

As shown in Fig. 1, the liquid $^1H$ NMR spectrum of the azido intermediate **2** reveals the full conversion of the amino moieties into the corresponding azido moieties according to the appearance of new aromatic broad signals at 7.7–7.8 ppm. This coincides with the disappearance of the three aromatic signals of **1** at 7.6, 7.8 and 7.9 ppm. The NMR spectrum of **3a** illustrates that the triazole with amino substituent was successfully formed following the above described method. It is noteworthy that the isolated single peak at 8.6 ppm is assigned to the proton of the triazolyl ring. The integrations of the signals show a grafting rate of 20%, similar to that found for **4a**. The assignment of new aromatic shifts for **4a** was previously described.[21] $N_2$ adsorption isotherms confirm that the porosity is maintained throughout the modification. However PXRD analyses show a slight decrease in crystallinity (see ESI†).

Elemental analysis shows that copper species from the Cu(I) salt used for the click reaction are present in both **3a** and **4a** samples. From these analyses, 1.3 wt% of copper remains in **3a**, corresponding to one copper atom for two triazolyl functions, whereas 3 wt% remains in **4a**. The higher amount of copper blocked in **4a** can be explained by the pore blocking due to phenyl substituents on the MOF framework.

In order to assess the nature of copper species confined in the frameworks of both **3a** and **4a**, continuous wave electron paramagnetic resonance spectroscopy (CW-EPR), pulsed EPR, and superconducting quantum interference device (SQUID) magnetometer measurements were performed on the samples. For **3a** and **4a**, susceptibility measurements showed the presence of $0.96 \times 10^{-7}$ mol of $S = 1/2$ spins per mg and $2.1 \times 10^{-7}$ mol of $S = 1/2$ spins per mg respectively (ESI†). Since Cu(II) is the only paramagnetic species which can be found in these systems, these experiments indicated 0.61 wt% and 1.32 wt% for **3a** and **4a** respectively. These results, combined with elemental analyses, allow us to establish that our solids contain both Cu(I) and Cu(II) species in approximately a 1 : 1

**Table 1** Functional composition of compounds **1** to **4**[a]

| | Structure | Amino (%) | Azido (%) | Triazolyl (%) |
|---|---|---|---|---|
| **1** |  | 100 | — | — |
| **2** |  | — | 100 | — |
| **3a** |  | — | 80 | 20 |
| **3b**[b] |  | 10 | 70 | 20 |
| **4a4b**[b] |  | — | 80 | 20 |

[a] According to $^1H$ NMR analysis. [b] After treatment at 100 °C under vacuum.

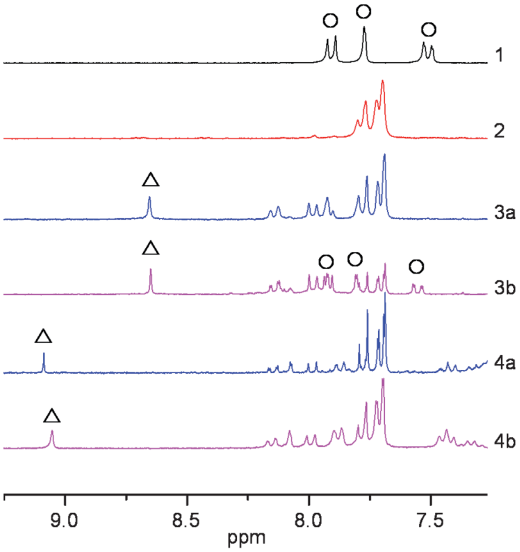


**Fig. 1** $^1H$ NMR spectra of compounds **1** to **4**. Typical peaks of BDC–$NH_2$ are marked by circles and triazolyl proton signals are indicated by triangles.

ratio. In order to further characterise these paramagnetic species, CW-EPR spectra were recorded (Fig. 2). The EPR spectrum of **3a** is characteristic of a Cu(II) ion in one site with a well-defined environment. In particular, copper hyperfine coupling is easily seen and spectral features are well pronounced.[34,35]

In sharp contrast with the previous result, the EPR spectrum of **4a** is broader and almost featureless with no visible copper hyperfine coupling. In addition to the central line, this spectrum exhibits a very broad feature which can be tentatively attributed to copper clusters. All these characteristics point to a non-specific Cu(II) species which can even be present in the framework as ill-defined aggregates.

These conclusions can be substantiated by an additional pulsed EPR experiment with a HYSCORE sequence. A HYSCORE sequence is used to observe hyperfine coupling in paramagnetic systems and is particularly suited for detecting nuclei with $I > 1/2$ spin, like $^{14}N$. It is able to sort three types of nuclei interacting with the Cu(II) ion: strongly and weakly coupled nuclei and "distant" nuclei, which are characterized by very low hyperfine constants. The latter correspond to peaks on the diagonal of the (+,+) quadrant, whereas the strongly and weakly coupled nuclei appear in the (−,+) and (+,+) quadrants, respectively.[36,37] The HYSCORE spectrum of **3a** is well defined and exhibits several features which can be unambiguously attributed to at least one strongly coupled $^{14}N$ and several weakly coupled $^{1}H$, some features probably belonging to a coordinating water molecule (Fig. 3).[34,35,38] It was impossible to repeat these pulsed EPR experiments for **4a** where no spin echo signal can be detected. One possible explanation is that Cu(II) ions are localized in non-specific sites and ill-defined aggregates have very short relaxation times.

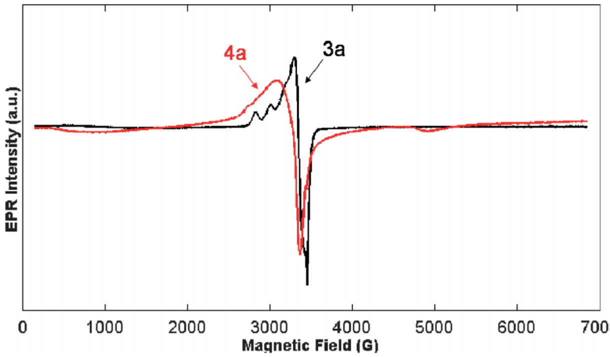


**Fig. 2** Comparison of CW-EPR spectra of **3a** (black) and **4a** (red).

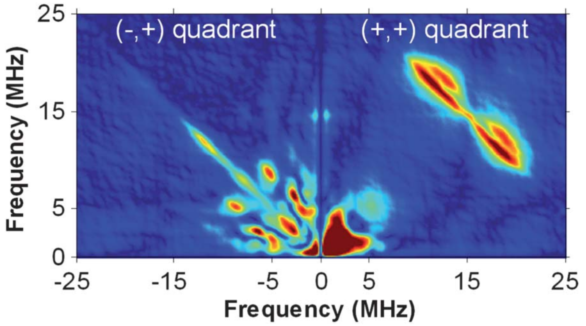


**Fig. 3** X-band HYSCORE spectrum of **3a**.

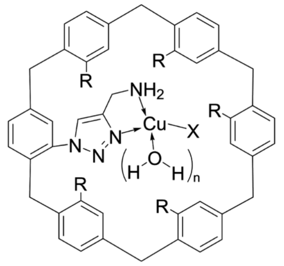
Indeed, the nitrogen atoms on the triazolyl ring and the free terminal amino group of **3a** provide a good environment for copper chelation as a *N*,*N*-donating group whereas only weakly coordinating triazolyl moieties are present in **4a**. We can thus postulate the existence of both copper(I) and (II) triazolylmethanamine complexes anchored into the MOF **3a**, as described in Scheme 2.

Compounds **3b** and **4b** were obtained by treating their parent compounds **3a** and **4a** under vacuum at 100 °C overnight (Table 1). Surprisingly, NMR spectra reveal that a partial reduction of the aromatic $-N_3$ moieties, to give the aromatic $-NH_2$ moieties, occurs during the treatment of **3a** and leads to the formation of **3b** (Fig. 1). Integration of signals shows that the new ratio between the functional groups in **3b** is azido : amino : triazolyl = 70 : 10 : 20, the percentage of triazolyl being, as expected, the same for both **3a** and **3b**. Nevertheless, the structural integrity and the porosity of **3b** are strongly affected by this intrareticular reaction (see ESI†). The same procedure was applied to **4a** to give **4b**. However, no sign of the azide reduction appeared in the NMR spectrum of **4b**. According to these results, the reduction of the azido occurs more easily in **3a**, which contains a well-defined copper complex (Scheme 2).

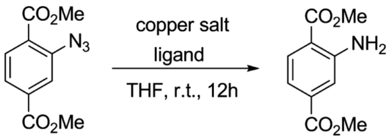
With copper-mediated reduction of azide into amines being already reported under homogeneous conditions,[15–17] we assumed that the solvent-free azide reduction proceeds *via* the involvement of the MOF-supported Cu complex described in Scheme 2.

In order to assess our hypothesis, we performed model reactions under homogeneous conditions. As a representative substrate, we used dimethyl azidoterephthalate, similar to the MOF building block, in the presence of copper salt and ligand in THF at room temperature (Scheme 3).

The results summarized in Table 2 show that copper(I) species combined with an excess of N-containing ligands allow the completion of the azide reduction (entries 2 and 5). Too low an amount of amino ligand leads to uncompleted reactions (entries 3 and 4), and copper(II) precursors show no activity (entries 7 and 8). It is noteworthy that neither copper(I) nor amine can alone promote the reduction (entries 5 and 6) and that reducing the



**Scheme 2** MOF-supported copper(I) triazolylmethanamine complex in **3a** (R = $NH_2$ or $N_3$).



**Scheme 3** Liquid-phase copper-mediated aryl azide reduction.

**Table 2** Liquid-phase Cu-mediated reduction of dimethyl azidoterephthalate[a]

| Entry | Cu source (eq.) | Ligand (eq.) | Yield (%)[b] |
|---|---|---|---|
| 1 | $Cu(ACN)_4PF_6$ (0.25) | Propylamine (5.5) | 50 |
| 2 | $Cu(ACN)_4PF_6$ (0.5) | Propylamine (5.5) | 100 |
| 3 | $Cu(ACN)_4PF_6$ (0.5) | Propylamine (2.75) | 10 |
| 4 | $Cu(ACN)_4PF_6$ (0.5) | Propylamine (1) | 5 |
| 5 | $Cu(ACN)_4PF_6$ (0.5) | None | <5 |
| 6 | None | Propylamine (5.5) | <1 |
| 7 | $Cu(acac)_2$ (0.5) | Propylamine (5.5) | <1 |
| 8 | CuO (0.5) | Propylamine (5.5) | <1 |

[a] Reaction conditions: dimethyl azidoterephthalate (0.09 mmol) in THF (3 mL) with copper and ligand stirred for 12 h at room temperature. Equivalents of copper and ligand are indicated in brackets. [b] Determined using $^1H$ NMR analysis.

amount of $Cu(ACN)_4PF_6$ from 5.5 to 2.75 equivalents reduces the yield from 100 to 50% (entry 1).

We thus determined that for this reaction to proceed, both copper(I) species and nitrogen-coordinating ligands are required, as found in the MOF **3a**.

Based on these findings, we can postulate that, in the MOF **3a**, the reduction of azido occurs *via* the oxidation of the copper(I) triazolylmethanamine complex in its vicinity, to give the corresponding amino and $N_2$. After $N_2$ removal, protons of Cu-coordinated water molecules (Scheme 2) are transferred to the remaining nitrogen to form the aryl amine. Indeed, Cu(II) dosing using a SQUID magnetometer shows an increase of the quantity of this ion under reaction conditions (100 °C under vacuum, see ESI†) since Cu(II) quantity increases from 0.61 wt% to 0.64 wt%.

In conclusion, we report here for the first time the self-reactivity of a MOF through the reaction between two of its functionalities anchored on its walls. A MOF-supported copper complex, introduced by click chemistry and characterized by EPR, was found to reduce some of the remaining azido functions in the MOF in the solid state by gentle heating under vacuum, the temperature used being much lower than that of the azide self-decomposition. Moreover, this case study could allow new insight into the mechanism of the copper-mediated azide reduction.

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