CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201101850

Palladium-Catalyzed C−H Bond Functionalization of a Metal–Organic Framework (MOF): Mild, Selective, and Efficient

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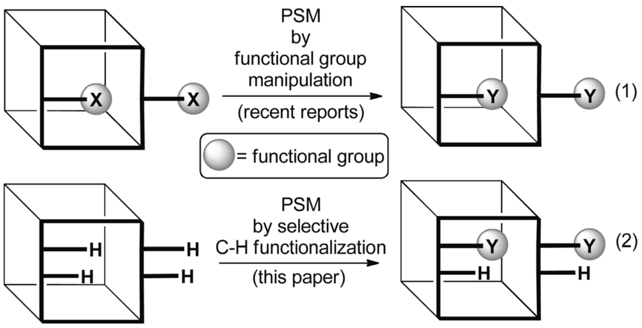
Dedicated to Professor David A. Evans on the occasion of his 70th birthday

Metal–organic frameworks (MOFs) are highly porous crystalline hybrid materials with applications in gas storage and separation, catalysis, drug delivery, and other fields.[1–6] The key features of MOFs lie in the structural diversity and adjustability of their framework topology based on simple variations in the metal ions and organic ligands. However, because the MOF formation process is based on self-organization, only certain topologies can be obtained. For a given set of metals and linkers, the structural variability is therefore limited. To allow fine tuning of the properties and to provide access to otherwise inaccessible MOFs, methods for the postsynthetic modification (PSM)[7,8] of known MOFs have emerged recently.[9] PSM allows the introduction of functionalities that are not tolerated under the conditions of MOF formation, and provides access to different topologies, incompatible with pre-existing structural motifs. In addition, PSM also represents an efficient and systematic approach for the rapid generation of a family of isoreticular MOFs.[9] However, the synthetic tools available for PSM are exceedingly restricted by the sensitivity of MOFs to heat, acids, and bases.[10] Furthermore, the small pore size and orderly structure of MOFs severely hinder the approach of the reacting molecules to the active site and thus limit the reagents available for PSM. So far, PSM of MOFs has relied on functional group interconversions, such as methylation of a pyridyl group,[11] deprotonation[12] or acylation of an alcohol or amine,[13] reduction of an aldehyde or formation of an imine,[14] "click" chemistry,[15] bromination of a double bond,[16] or photochemical deprotection.[17] Although functional group interconversion increases the versatility of MOFs, the requirement for an initial functionality greatly limits the synthetic potential of PSMs.

Functional groups are groups of atoms responsible for the characteristic chemical reactivity of a molecule. Nonacidic C−H bonds are ubiquitous in organic matter and are generally not classified as a functional group, because they are mostly unreactive under classical reaction conditions. In the past few years, however, transition-metal-based methods for C−H functionalization have made tremendous progress.[18,19] This chemistry seems to be optimal for the postsynthetic modification of MOFs, since it obviates the need for a pre-existing functional group. However, several challenges arise, once this powerful chemistry is applied to MOF modification. Although most C−H functionalization methods rely on rather forcing conditions, mild conditions[20–23] are crucial to preserve the MOF architecture. Furthermore, high levels of selectivity and excellent chemical yields are mandatory to maintain the uniformity of the material.



A method for the selective and efficient C−H bond functionalization of MOFs, with simultaneous preservation of the topology of the system, would significantly increase MOF structural diversity and could become a prototype for PSM of MOFs. Herein, we demonstrate the first step towards this goal: direct C−H phenylation of an indole-derived UMCM-1 (University of Michigan Crystalline Material-1)-type MOF through highly selective and efficient palladium catalysis.

MOF-5 and UMCM-1 represent two of the most well-known MOF structures. The structure of MOF-5 contains Zn_4O clusters and 1,4-benzenedicarboxylate (BDC),[24] whereas UMCM-1 consists of not only Zn_4O clusters and BDC, but also benzene-1,3,5-triyl-tribenzoate (BTB) linkers.[25] Thus, we commenced our study by assembling MOFs, utilizing 1-methylindole-4,7-dicarboxylic acid (**1**) as a BDC analogue. After extensive experimentation, the MOFs

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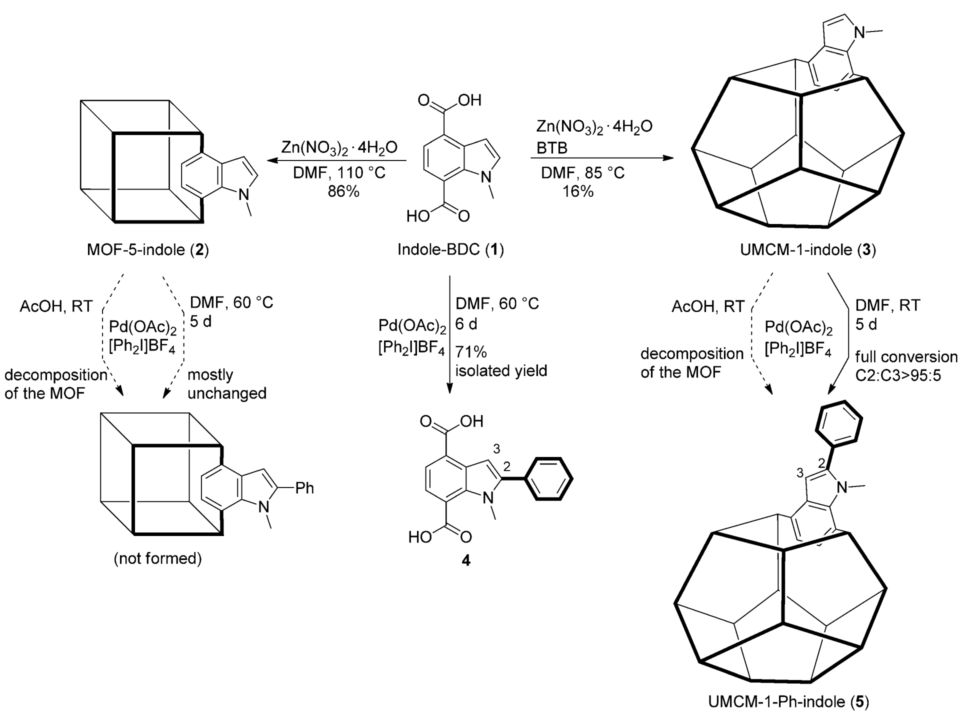
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201101850.



Scheme 1. Formation of indole–BDC-derived MOFs (**2** and **3**) (top) and (attempted) Pd-catalyzed phenylations (bottom).

MOF-5-indole (**2**) and UMCM-1-indole (**3**) were obtained as yellow needles in yields of 86 and 16%, respectively (Scheme 1, top).[26] These MOFs were fully characterized by powder X-ray diffraction (PXRD) and single-crystal structure analysis, which showed that their topologies were similar to those of MOF-5 and UMCM-1 (Figure 1). In addition, our PXRD measurements indicated that UMCM-1-indole (**3**) became amorphous upon drying. Consequently, gas adsorption measurement of **3** showed a maximum nitrogen uptake of only 155 cm^3 g^{-1}. The corresponding Brunauer–Emmett–Teller (BET) surface area is calculated to be (448 ± 5) m^2 g^{-1}, a factor of ten lower than what is reported for UMCM-1.[25,26] Such drastic difference could be attributed to the instability of the unmodified MOF, which collapsed upon drying. NMR spectroscopy and mass spectrometric analysis after acid hydrolysis further confirmed the structural integrity of the MOF linkers and, in the case of **3**, also determined the ratio of the linker molecules to be 1.33:1 (BTB/indole–BDC).

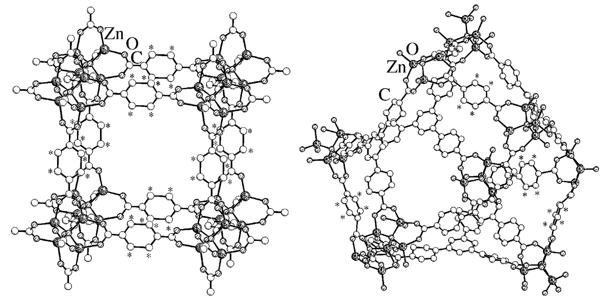


Figure 1. Single-crystal structures of MOF-5-indole (**2**) (left) and UMCM-1-indole (**3**) (right). The pyrrole ring of linker **1** (indicated by *) and the carbon and nitrogen atoms of the coordinated solvent molecules could not be found. Furthermore, no solvent molecules could be identified in the voids therefore the SQUEEZE routine was used.

We commenced our study on the selective functionalization of **2** and **3** by using [Ph$_2$I]BF$_4$ as the phenylating agent and AcOH as the solvent.[27–29] However, attempts to apply this previously developed condition[20c] for the PSM of the MOFs **2** and **3** proved to be ineffective due to the sensitivity of both MOF-5-indole and UMCM-1-indole to the highly acidic reaction conditions (Scheme 1).[26] Because we re-examined the reactivity of the indole linker **1** in homogeneous solution, the reaction medium was strategically chosen to preserve the integrity of the MOF. Pleasingly, the 2-phenylated indole **4** was obtained, when the solvent was changed from acetic acid to DMF. However, at room temperature, the reaction was not complete even after 13 days (44% yield). Full conversion was only achieved with 20 mol% of catalyst (Pd(OAc)$_2$), employed at 60 °C for six days, affording the desired product isolated in 71% yield.[26] Fortunately, an undesired Pd^{II}-catalyzed dimerization of the *N*-methylindole, which leads to the deactivation of the catalyst by forming Pd^0, is not possible within the rigid framework.[30]

With the optimal conditions established for the free organic linker, we began our effort to selectively functionalize the MOFs. Our initial attempt with MOF-5-indole (**2**) under the optimized conditions was unsuccessful, since only trace amounts of the phenylated indole were observed at either room temperature or 60 °C (Scheme 1). The lack of reactivity could be attributed to the small window size of the MOF, which restricts the entry of the reagents into the MOF. Based on this analysis, UMCM-1-type MOFs, which contain larger pores and windows, appear to be well suited for this transformation. Indeed, by treating UMCM-1-indole (**3**) under the optimized conditions in DMF, complete conversion to the phenylated UMCM-1-Ph-indole (**5**) was achieved within five days at room temperature with excellent regioselectivity (C2/C3 > 95:5; Scheme 1). The selective and quantitative 2-phenylation was determined by ^{1}H and ^{13}C NMR spectroscopy (Figure 2) and mass spectrometry of samples obtained after digesting the MOF under acidic conditions.[26] Moreover, both the crystallinity and the topology of the MOF were conserved, as revealed by PXRD (Figure S14 in the Supporting Information) and single-crystal structural

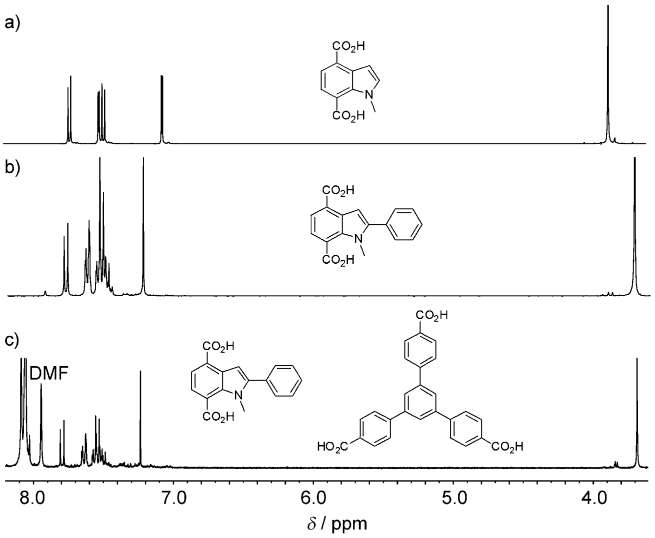


Figure 2. Comparison of ^{1}H NMR spectra: a) ^{1}H NMR spectra of the indole-linker **1**; b) ^{1}H NMR spectra of the phenylated indole-linker (**4**); c) ^{1}H NMR spectra of the mixture of the indole- and BTB-linker after digesting the modified UMCM-1-indole MOF (**5**).

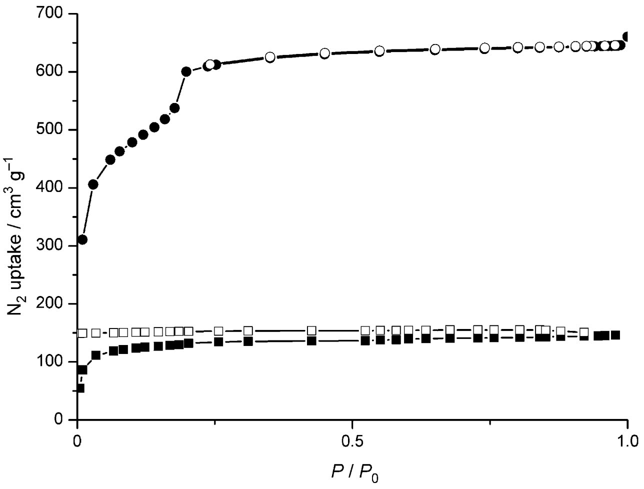


Figure 3. N_2 adsorption (● = UMCM-1-Ph-indole; ■ = UMCM-1-indole) and desorption (○ = UMCM-1-Ph-indole; □ = UMCM-1-indole) isotherms at 77 K of UMCM-1-indole (**3**) and UMCM-1-Ph-indole (**5**), respectively.

analysis. Importantly, mass spectrometry and ^{1}H NMR spectroscopy analysis of the supernatant solution after the completion of the reaction showed no trace of any free linker molecules. This result again indicates that the integrity of the MOF was preserved during the reaction and thus excludes any homogeneous reaction pathways. As expected, without the palladium catalyst, no desired functionalized MOF was observed even after prolonged reaction time. Intriguingly, trying to independently synthesize **5** from the 2-phenylated indole linker **4**, under the same conditions used to prepare UMCM-1-indole (**3**), resulted in the formation of crystals that had a different PXRD (Figure S15 in the Supporting Information).

The maximal N_2 uptake of UMCM-1-Ph-indole (**5**) was four times larger than the one observed for UMCM-1-indole (Figure 3; 645 vs. 154 cm^3g^{-1}; BET surface areas of (2085 ± 96) vs. (448 ± 5) m^2g^{-1}). Although the unmodified UMCM-1-indole turns amorphous and collapses upon drying, the modified UMCM-1-Ph-indole remains crystalline. However, after washing the modified UMCM-1-Ph-indole, 7.22 wt % of palladium remained. It represents one rare example for the application of C−H activation chemistry in the field of materials. Thus, transition-metal-catalyzed C−H functionalizations, with their ability to create functional groups from ubiquitous C−H bonds, should significantly expand the scope of MOFs and other materials.[31]

In conclusion, we have successfully achieved the postsynthetic modification of a MOF by C−H activation chemistry. The reaction proceeds quantitatively under mild conditions with remarkable chemo- and regioselectivity. During this process, the crystallinity of the MOF remains intact. This should inspire further investigation and development of other metal-catalyzed postsynthetic modifications of MOFs. The selective and efficient C−H functionalization of MOFs should dramatically expand the scope of accessible MOF structures and allow ample and facile variation of the properties of MOFs. Site-specific C−H functionalization should thus become an important tool for the preparation of materials with tailor-made and fine-tuned properties.

Experimental Section

UMCM-1-indole MOF (0.1 mmol according to the indole–BDC linker), $Pd(OAc)_2$ (0.02 mmol), and diphenyliodonium tetrafluoroborate (0.15 mmol) were placed into an oven-dried test tube vial with screw cap under air. The crystalline MOF material was taken out of a DMF-filled test tube vial with screw cap and placed on a glass plate. The majority of the residual DMF was removed with a pipette, and the wet crystals were transferred with a spatula into the reaction vial. Solvent was added by syringe and the flask was then closed and shaken at RT for the time indicated in the Supporting Information. A part of the crystalline material was taken out of the reaction mixture and the supernatant solution was decanted. The decanted solution was evaporated and analyzed by mass spectrometry and NMR spectroscopy, which showed no modified indole linker within the detectable range. The material was then washed three times with DMF, then three times with $CHCl_3$. Concentrated aqueous HCl was added to digest the MOF and afterwards removed under high vacuum. The residual solid material was taken up in MeOH, filtered through a Whatman filter, and subjected to HPLC-MS analysis.

Acknowledgements

We thank Prof. H. Eckert, Prof. M. Winter, and Prof. R. Pöttgen, and their co-workers for performing TGA, DSC, gas sorption, ICP-OES, and PXRD measurements. In addition, we thank Mohan Padmanaban and Fan Liu for helpful discussions. Generous financial support by the European Research Council (Starting Investigator Grant) and the Deutsche Forschungsgemeinschaft (SPP 1362) is gratefully acknowledged. The research of F.G. is supported by the Alfried Krupp Prize for Young University Teachers of the Alfried Krupp von Bohlen und Halbach Foundation.

Keywords: chemoselectivity · C–H activation · metal–organic frameworks · palladium · postsynthetic modification

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Received: June 16, 2011