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Micro-Cu$_4$I$_4$-MOF: reversible iodine adsorption and catalytic properties for tandem reaction of Friedel–Crafts alkylation of indoles with acetals†

Neng-Xiu Zhu,‡ Chao-Wei Zhao,‡ Jian-Cheng Wang, Yan-An Li and Yu-Bin Dong*

We report a convenient approach, the first of its kind, to construct a microscale non-metal@MOF composite catalytic host–guest system for an organic tandem reaction. The reported porous Cu$_4$I$_4$-MOF is able to reversibly adsorb molecular iodine at room temperature. The obtained I$_2$@Cu$_4$I$_4$-MOF host–guest system can be a highly heterogeneous catalyst to promote the Friedel–Crafts alkylation of indoles with acetals in a one-pot two-step fashion under solvent-free conditions at room temperature.

The design and fabrication of active catalytic species-loaded MOFs has become a very useful approach to access highly heterogeneous catalytic materials for sustainable organic reactions. In the context of catalyst support, MOFs are proven to be a promising class of carriers for stabilizing active catalytic species.[1] Thus far, the encapsulation of metals, especially precious nano metal species, such as Pt, Pd, Rh, Ru, Au, and Ag, in MOF hosts is the main theme in this field.[2] In contrast, the loading of other kinds of guest species, such as inorganic non-metal and organic species, with active catalytic properties has received considerably less attention.[3]

Very recently, the study of MOF-supported heterogeneous catalytic systems has tended to expand from single-step catalysed reactions to multistep catalysed tandem reactions due to the more and more serious sustainability and environmental issues. In principle, tandem reactions feature lower cost, fewer chemicals and lower energy consumption. Although significant progress in metal@MOF-catalysed cascade reactions has been made,[4] tandem reactions based on non-metal@MOF heterogeneous catalytic systems are, however, unprecedented.

As the counterpart of metal catalysts, metal-free catalysts have been well demonstrated to be very useful for a variety of organic transformations.[5] In principle, metal-free homogeneous catalytic species can also be incorporated into the MOFs and translate their heterogeneous counterparts. In this contribution, we report a Cu$_4$I$_4$-MOF which is able to reversibly upload molecular iodine. Furthermore, the resulting I$_2$@Cu$_4$I$_4$-MOF (**2**) can be a highly heterogeneous catalyst to promote acetal deprotection and Friedel–Crafts alkylation in tandem.

The desolvated Cu$_4$I$_4$-MOF (**1**) was prepared by a modified method previously reported by us (ESI†).[6] As shown in Fig. 1a, the CH$_3$CN solution of the tri-armed ligand **L** and CuI was refluxed for 1 h, and the obtained crystalline solid was further heated at 90 °C for an additional 1 h to generate light yellow micro-sized crystalline solids (Fig. 1b). The size of the Cu$_4$I$_4$-MOF particles is basically less than 20 μm based on the SEM image (Fig. 1b). The XRPD patterns of micro-sized **1** are identical to those of bulk crystals (Fig. S1, ESI†).

As described before, **1** possesses a 4-connected sra 2-fold interpenetrating framework containing 1D oval channels along the crystallographic *c* axis with a dimension of *ca.* 19 × 17 Å. Interestingly, when the crystalline solids of **1** were exposed to iodine vapour (p(I$_2$) is *ca.* 0.3 mm Hg) in a sealed vial, the colour of the sample changed rapidly from light yellow to dark brown with an elapse of time (Fig. 1b). The iodine adsorption process was monitored by thermogravimetric analysis (TGA), and the saturated iodine loading was reached in *ca.* 30 min to generate the I$_2$-loaded host–guest system of **2** ($\mathbf{0.75I_2 \subset Cu_4I_4L}$, an iodine content of up to 12.5%, Fig. 1c). Although we tried many times to get single crystals of **2**, it did not work. We believe that the I$_2$ species was stabilized in pores by the weak host–guest interactions, which is commonly observed in other I$_2$@MOF systems.[3] The encapsulated molecular iodine was unambiguously confirmed by the X-ray photoelectron spectroscopy (XPS) measurement (Fig. 1d). The XPS indicates that the valences of **2** included iodine species of 0 and −1, which further supports the existence of I$_2$ (guest) and I$^-$ (framework).[7] Notably, the above iodine loading is reversible. When **2** was heated at 120 °C for 3 h, the

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† Electronic supplementary information (ESI) available: Synthesis and characterization of **2**, detailed catalytic produce and additional figures and characterization data. See DOI: 10.1039/c6cc07027b

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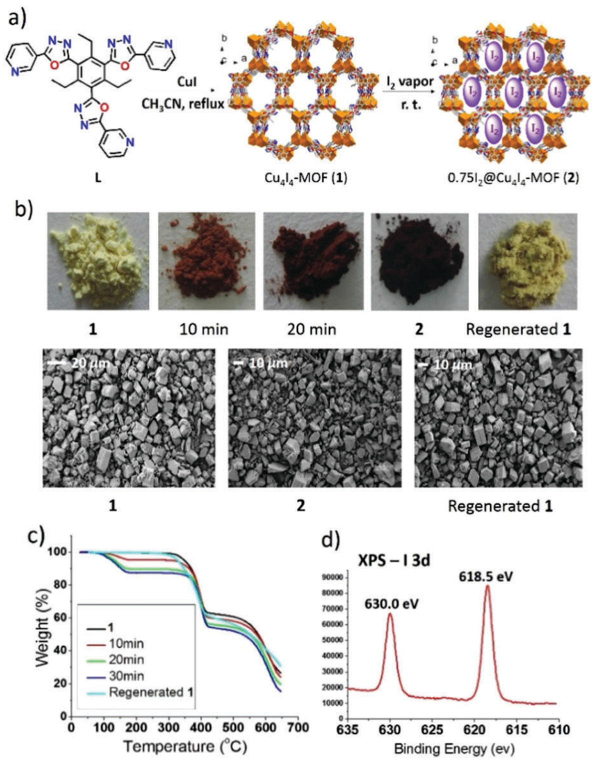


Fig. 1 (a) Synthesis of Cu$_4$I$_4$-MOF (**1**) and 0.75I$_2$@Cu$_4$I$_4$-MOF (**2**). (b) Photographs showing the iodine adsorption process of **1** and regenerated **1** by heating, and corresponding SEM images. (c) TGA traces of **1**, **1** in iodine vapour for 10 min and 20 min, and the regenerated **1**. (d) XPS spectrum of **2**.

encapsulated iodine was completely removed and **1** was regenerated, based on TGA analysis (Fig. 1c). XDPR patterns indicated that the crystallinity and structural integrity of **1** are maintained during this reversible I$_2$ loading process (Fig. S1, ESI†).

The porosity of iodine-loaded **2** was confirmed by a gas adsorption–desorption experiment. As shown in Fig. 2, the CO$_2$ adsorption capacity of **2** at 1 atm is 100.50 cm^3 g^{-1} (195 K) and the calculated Brunauer–Emmett–Teller (BET) surface area is 275.56 m^2 g^{-1}. Compared to **1** (the CO$_2$ adsorption capacity of **1** is 173.2 cm^3 g^{-1} (195 K) and the (BET) surface area of **1** is 641 m^2 g^{-1}),[6] the decrease in CO$_2$ adsorption capacity and corresponding surface area clearly resulted from the molecular iodine species loading. The pore size distribution curve, calculated from Barrett–Joyner–Halenda analysis, shows a narrow pore diameter distribution at *ca.* 1.30 nm for **2** (Fig. 2), which is slightly smaller than that of **1** (1.45 nm).[6]

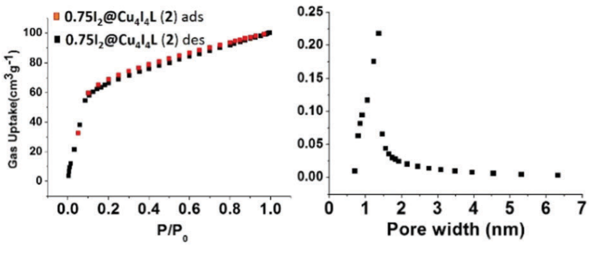


Fig. 2 Left: CO$_2$ adsorption isotherm for **2** at 195 K. Right: The pore width of **2** is centred at 1.3 nm.

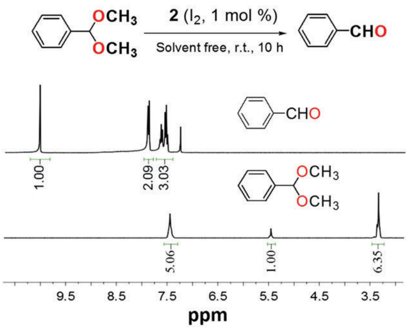


Fig. 3 **2** catalysed solvent-free benzaldehyde dimethyl acetal deprotection, and corresponding ^{1}H NMR spectrum for the product (300 MHz, 25 °C, CDCl$_3$).

Molecular I$_2$ is generally known to be a homogeneous catalyst and is widely applied to promote various organic transformations.[8] Iodine, however, is very scarce in the natural world. On the other hand, ^{129}I is an important radioisotope and very harmful to human health.[9] So the development of iodine-cycle-utilizing heterogeneous catalysts for eco-friendly demands is an urgent issue. Inspired by this, iodine-loaded compound **2** was firstly used to test the catalytic properties of benzaldehyde dimethyl acetal deprotection of benzaldehyde.

When benzaldehyde dimethyl acetal was treated by **2** (1 mol% I$_2$) under solvent-free conditions at room temperature, a quantitative yield (yield, >99%, ESI†) of benzaldehyde, based on a ^{1}H NMR spectrum, was obtained in 10 h (monitored by TLC). As shown in Fig. 3, no peaks relating to benzaldehyde dimethyl acetal can be detected in the ^{1}H NMR spectrum after the reaction, indicating that the **2**-catalysed benzaldehyde dimethyl acetal deprotection is clean and highly efficient.

In addition to that, **2** also exhibits highly active catalysis for the synthesis of bis(indolyl)methanes, which is an important class of compounds with a range of biological activities,[10] *via* indole Friedel–Crafts alkylation under solvent-free conditions (Fig. 4).

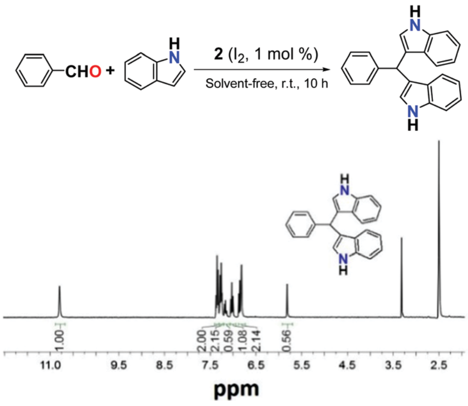


Fig. 4 **2**-catalysed solvent-free Friedel–Crafts alkylation of indole with benzaldehyde and corresponding ^{1}H NMR spectrum for the product (300 MHz, DMSO-d_6).

The treatment of benzaldehyde (1 mmol) with indole (2 mmol) in the presence of **2** (1.0 mol% I_2) at room temperature (10 h) afforded the corresponding Friedel–Crafts alkylation product in high yield (93%) after column chromatography purification (ESI†). In contrast, the synthesis of bis(indolyl)methane catalysed by **1** without iodine species resulted in a very low isolated yield (∼9%) under the same reaction conditions, suggesting that the encapsulated I_2 in the host framework is the main active catalytic species for this reaction. For the solid benzaldehyde substrates, the Friedel–Crafts alkylation can be carried out in xylene or by a solid-phase grinding method. For example, the alkylation of solid indole with solid 4-nitrobenzaldehyde can be performed in xylene (10 h) or by solid-phase grinding (ground for 10 min every other 2 h, 5 times) in the presence of **2** (I_2, 1 mol%) at room temperature. The corresponding yields are 90 and 89%, respectively (ESI†).

As shown above, I_2-loaded **2** herein is able to respectively facilitate benzaldehyde dimethyl acetal deprotection and indole Friedel–Crafts alkylation under solvent-free conditions at room temperature. So it is plausible to suppose that these two types of reactions could be integrated into a one-pot two-step reaction. Inspired by this, we performed the following experiment.

A mixture of benzaldehyde dimethyl acetal (1 mmol) and indole (2 mmol) in the presence of **2** (1 mol% I_2) was stirred at room temperature for 10 h (monitored by TLC), and the reaction residue was purified by column chromatography on silica gel using CH_2Cl_2/petroleum ether (1 : 3) as an eluent to afford the expected product as a white solid in 93% yield (Fig. 5, ESI†).

Notably, **2** herein exhibits typical heterogeneous catalytic behaviour under the reaction conditions. After each catalytic cycle, **2** could be easily recovered by centrifugation and filtration after adding ethyl acetate, and then directly reused in the next run. As a heterogeneous catalyst, **2** can be reused five times without significant loss in its catalytic activity (yields, 86–93%, Fig. 5a). The heterogeneity of **2** was further demonstrated by a leaching test. As shown in Fig. 5b, the reaction solution was removed quickly from **2** and transferred to another reaction vial under the same conditions after 4 h. No further increase in the product conversion was detected during the next 6 h without **2**. The I and Cu concentrations in the filtrate are 3.250 and 0.165 μg mL^{-1} (based on ICP), corresponding to 3.0% I and 0.2% Cu losses, respectively. The comparison of the XRPD patterns before and after the fifth catalytic cycle demonstrated that the crystallinity and structural integrity of Cu_4I_4-MOF were well maintained (Fig. 5c). TGA measurement (Fig. 5d) showed that the iodine amount in **2** after the five catalytic cycles of this tandem reaction is 11.5%, indicating that molecular iodine guest can be mostly stabilized in the MOF pores and only a tiny amount of iodine species leaching (*ca.* 8.0%) occurred during the reaction process. The small amount of I_2 leaching could be the reason for the slight decrease in catalysis efficiency of **2** during the recycling catalytic runs. The SEM image shows that the morphology of **2** was well preserved even after five catalytic runs (Fig. 5e).

To our knowledge, only two examples related to heterogeneous catalytic benzaldehyde dimethyl acetal deprotection and indole Friedel–Crafts alkylation tandem reaction have been reported.[11] The reported tandem reaction was catalysed by porous aluminosilicate (60 °C, CH_3CN)[11a] and triphenylphosphine-*m*-sulfonate/CBr_4 (r.t., CH_3CN)[11b] to generate the corresponding Friedel–Crafts alkylation product in 91 and 75% yields, respectively. In our case, the use of **2** has the experimental advantage of avoiding highly toxic CBr_4 species and that no higher temperature is needed. More importantly, the **2**-catalysed reaction needed no additional organic solvents except the reaction substrates. Thus as the reaction is easy to manipulate and avoids the use of toxic and volatile solvents, it could be considered a clean catalytic synthesis approach.

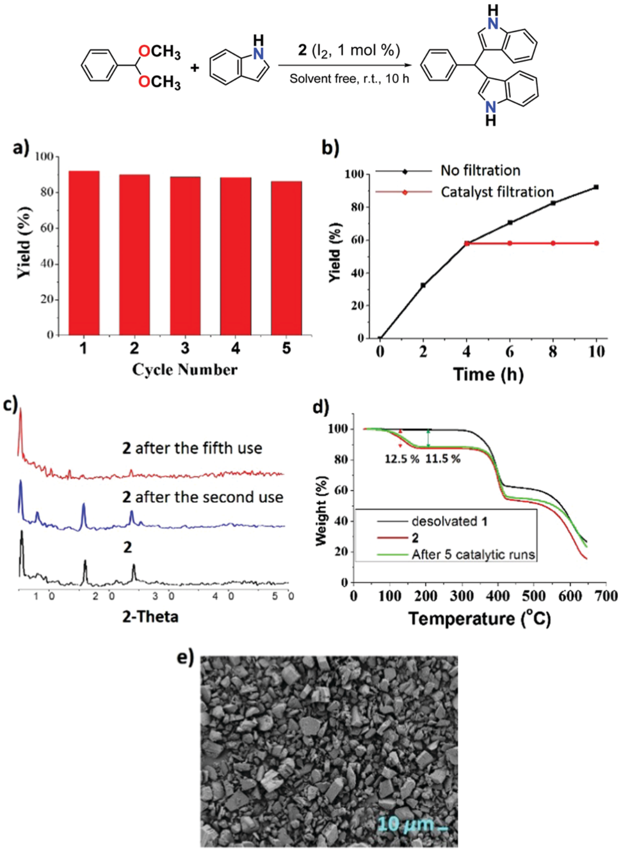
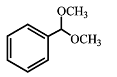
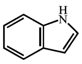
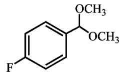
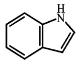
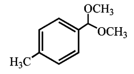
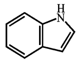
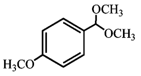
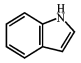
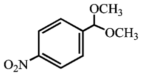
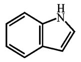
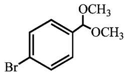
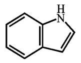
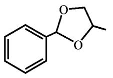
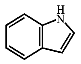
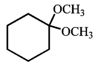
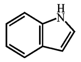
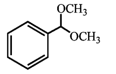
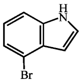


Fig. 5 (a) **2** can be reused for five catalytic cycles without loss of its catalytic activity. (b) Reaction time examination (black line) and leaching test (red line) for the tandem reaction. (c) XRPD patterns of **2**, **2** after the second catalytic run and **2** after the fifth catalytic run, respectively. (d) TGA traces of desolved **1**, **2** and **2** after five catalytic cycles, respectively. (e) SEM image of **2** after five catalytic runs.

The scope of this I_2-loaded host–guest catalytic system was explored by performing the acetal deprotection-Friedel–Crafts alkylation tandem reactions of various other substituted aromatic and aliphatic acetals with indoles. Table 1 summarizes the results of these reactions. We found that the substituted benzaldehyde acetals with either electron-donating or electron-withdrawing groups gave satisfactory overall isolated yields (87–90%), but are slightly lower than that of pristine benzaldehyde acetal. On the other hand, the combination of benzaldehyde acetal with bromo-substituted indole also resulted in a slightly lower isolated yield (86%, entry 9). In addition, reaction of aliphatic acetal (entry 8) proceeded efficiently, giving a good isolated yield (89%). Reaction of cyclic acetal (entry 7), however, gave a relatively lower

Table 1 Synthesis of bis(indolyl)methanes from substituted acetals and indoles catalysed by **2**[a]

Entry	Acetals	Indoles	Yield[b] (%)
1			93
2			90
3			88
4			87
5			89
6			90
7			85
8			89
9			86

[a] Conditions: solvent-free, **2** (1 mol% I_2), r.t., 10 h. [b] Isolated yield.

isolated yield (85%), which might be the result of the better stability of the reagent.[12]

In addition to that, larger sized 1-pyrenecarboxaldehyde acetal was also used as the substrate to perform the tandem reaction catalysed by **2** under the same reaction conditions (ESI†). The corresponding Friedel–Crafts alkylated product was obtained in a much lower isolated yield (*ca.* 28%), suggesting that the internal surface catalysis might be the predominant process, and the high catalytic activity exhibited by **2** should be a synergy effect of both the outside and internal surface catalytic processes.

In conclusion, we report a practical way to fabricate a non-metal@MOF catalytic host–guest system. The porous Cu_4I_4-MOF herein is able to incorporate with molecular iodine into an I_2@Cu_4I_4-MOF host–guest system which is a highly effective heterogeneous catalyst for an acetal deprotection-Friedel–Crafts alkylation tandem reaction under solvent-free conditions at room temperature.

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