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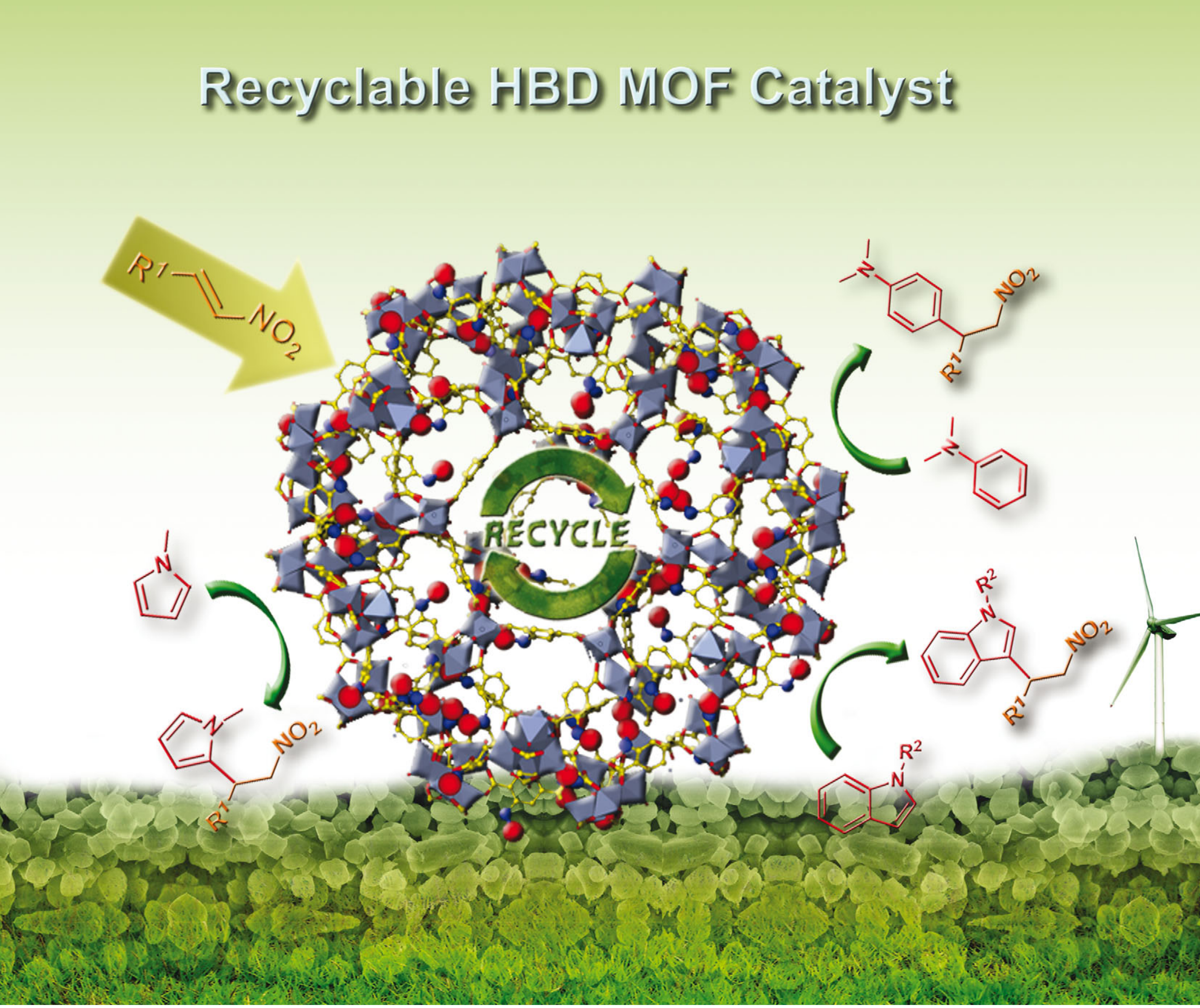

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Urea postmodified in a metal–organic framework as a catalytically active hydrogen-bond-donating heterogeneous catalyst†

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New functionally diverse urea-derived MOF hydrogen-bond-donating heterogeneous catalysts were achieved *via* postsynthetic modification, which exhibit excellent catalytic activity and very broad substrate scopes for the Friedel–Crafts alkylation reactions.

Metal–organic frameworks (MOFs) are some of the most newly emerging, widely studied porous materials, exhibiting potential applications in a wide range of areas including gas storage,[1a] separation,[1b] sensing[1c] and biomedicine.[1d] In particular, since the pioneering studies carried out by Kim *et al.*,[2a] Cohen *et al.*,[2b] Hupp *et al.*,[2c] Lin *et al.*[2d] and others, MOFs have increasingly gained popularity as some of the most prominent and powerful heterogeneous catalysts.[3] Despite the great success of the MOF heterogeneous catalysts, wide applications of these catalysts are impeded by drawbacks such as unsatisfactory yields, poor chemo- and/or stereoselectivities, and limited substrate scopes.[3] In this context, Farha, Hupp, and Scheidt *et al.* have recently reported seminal work[4] on the synthesis of a novel urea-containing MOF as a hydrogen-bond-donating (HBD) heterogeneous catalyst, which has shown an increased catalytic activity in comparison with similar HBD homogeneous catalysts. However, the incorporation of relatively large substrates for the catalytic Friedel–Crafts reaction in such a heterogeneous manner remains a significant challenge. Thus, from the perspective of developing a useful heterogeneous catalyst with high efficiency, the design of a novel and efficient MOF-derived HBD catalyst with large enough accessible pores/channels to tolerate differently sized substrates would still be particularly significant.

In recent years, postsynthetic modification (PSM) reactions have been proven to be a powerful tool for introducing functional groups into MOFs.[5] In this field, Cohen *et al.* reported seminal work on the use of MOFs bearing amino groups anchored with isocyanates to generate urea units within the structure.[6] Stock *et al.* elegantly demonstrated the only example of MIL-101 with ethyl isocyanate to produce the urea-derived MIL-101 in good yields.[7] Despite their great advantages, these reactions typically involved the introduction of only small groups into MOFs, whereas processes that facilitate the construction of urea-based MOFs with functionally diverse and reasonably large substituents in excellent yields remain largely unexplored. Moreover, no systematic study on the applications of such urea-based MOFs as the HBD heterogeneous catalysts has appeared in the literature to date. The attractive features of MIL-101, including thermal and chemical stability and broad apparent surface areas with large pores and windows,[8] render it a useful platform for the development of highly efficient heterogeneous catalysts.[9] We wondered about the possibility of the use of postsynthetic modification of MIL-101 with isocyanates providing highly porous and functionally diverse urea-derived MOFs, which might act as the key functional group capable of two-point hydrogen bonding through acidic N–H bonds as HBD catalysts.[10] Furthermore, such highly robust MOFs would not only possess spatially distinct hydrogen-bonding sites to prevent the oligomerization of the active catalyst,[11] but also possess accessible pores/windows large enough to admit reasonably large substrates and products to promise high catalytic activity. With these concerns, we herein report the preparation of the functionally diverse urea-containing MIL-101s in nearly quantitative conversions *via* postsynthetic modification. More significantly, they exhibit better catalytic activity and much broader substrate scopes bearing reasonable sizes and diverse functional groups than similar homogeneous[12] and known heterogeneous MOF HBD catalysts[4] for the Friedel–Crafts alkylation reactions, making them promising for advanced catalytic applications.

To determine the generality of this reaction for the synthesis of functionally diverse urea-containing MIL-101 heterogeneous catalysts, following a modified protocol described by Stock *et al.*,[7] three different isocyanates were treated with Cr-MIL-101-NH_2 in CH_3CN at 120 °C in a sealed tube for 12 h. Surprisingly, in all cases examined, isocyanates bearing various substituents, such as aliphatic and aryl groups with bulky, branched substituents, were successfully anchored onto the MIL-101 walls *via* covalent incorporation to afford Cr-MIL-101-UR**1–3**

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† Electronic supplementary information (ESI) available: Experimental procedures, product characterizations of new compounds and Fig. S1–S7. See DOI: 10.1039/c3cc42531b

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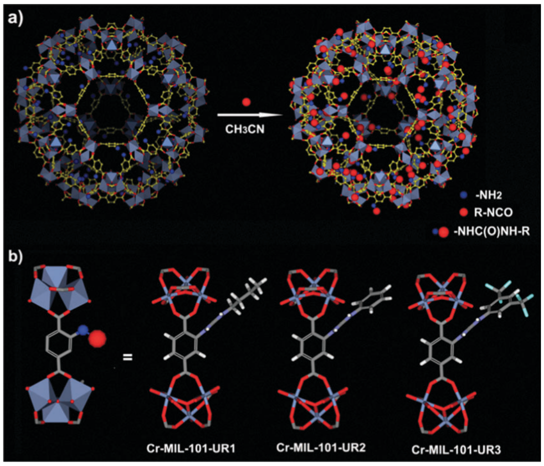


Scheme 1 Schematic representation of (a) postmodification of Cr-MIL-101-NH_2 with isocyanates to generate Cr-MIL-101-UR**1–3**; (b) the ligand structure and $[Cr_3O(CO_2)_6]$ cluster nodes.

in nearly quantitative conversion (Scheme 1). They were quantified using ^{1}H-NMR spectroscopy upon digestion of the modified MOFs in dilute base (Fig. 1a), together with various techniques including IR (Fig. S1, ESI†) and ESI-MS spectroscopy (Fig. S2, ESI†). This result was attributed to the larger accessible pores/windows of MIL-101 as compared to other MOFs,[6,13] thus rendering the introduction of functional groups more favorable. The catalyst loading of Cr-MIL-101-UR**1–3** is 2.61, 2.48 and 1.85 mmol g^{-1}, which was determined from elemental analysis data, respectively (ESI†). Powder X-ray diffraction (PXRD) data and scanning electron microscopy (SEM) images, similar to those of Cr-MIL-101, confirmed the retention of the parent framework structure with an octahedron-like morphology and the crystallinity of the resultant urea-derived MOFs (Fig. S3 and S4, ESI†). They also displayed chemical stability with good tolerance to different polar solvents, and thermal stability comparable to other MIL-101 derivatives, as determined by thermogravimetric analysis (TGA, Fig. S5, ESI†). Examination of the gas sorption behavior of these MOFs (Fig. 1b) indicated that all of the functionalized MOFs were still highly porous even after postmodification (BET surface area, 1409.9 m^2 g^{-1} for Cr-MIL-101-UR**1**, 1178.6 m^2 g^{-1} for Cr-MIL-101-UR**2**, 829.3 m^2 g^{-1} for Cr-MIL-101-UR**3**).

The catalytic activity of these urea-containing MIL-101 was first assessed by using Cr-MIL-101-UR**3** as the catalyst in the Friedel–Crafts alkylation between *trans*-β-nitrostyrene and *N*-methylpyrrole (Table 1).

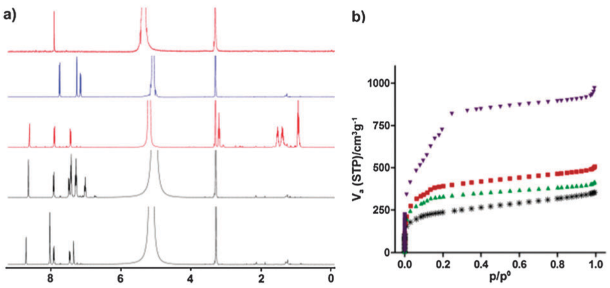
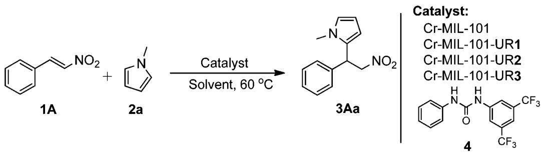


Fig. 1 (a) ^{1}H-NMR data of the linker molecules of the digested compounds (from top to bottom): Cr-MIL-101 (red), Cr-MIL-101-NH_2 (blue), Cr-MIL-101-UR**1** (orange) and Cr-MIL-101-UR**2** (purple), Cr-MIL-101-UR**3** (green). (b) N_2 sorption properties for MIL-101 (purple), MIL-101-UR**1** (red), MIL-101-UR**2** (green), MIL-101-UR**3** (black).

Table 1 Optimization of the urea-catalysed Friedel–Crafts reaction[a]



Entry	Catalyst	Solvent	Time (h)	Yield[b] (%)
1	Cr-MIL-101-UR**3**	DMF	36	Trace
2	Cr-MIL-101-UR**3**	THF	36	26
3	Cr-MIL-101-UR**3**	Acetone	36	27
4	Cr-MIL-101-UR**3**	CH_3CN	60	96
5[c]	Cr-MIL-101-UR**3**	CH_3CN	24	95
6[d]	Cr-MIL-101-UR**3**	CH_3CN	24	90
7[e]	Cr-MIL-101-UR**3**	CH_3CN	24	73
8[c]	Cr-MIL-101-UR**1**	CH_3CN	24	72
9[c]	Cr-MIL-101-UR**2**	CH_3CN	24	87
10	—[f]	CH_3CN	24	Trace
11	Cr-MIL-101	CH_3CN	48	22
12[c]	**4**	CH_3CN	24	79

[a] Reactions were conducted with **1A** (0.1 mmol), **2a** (0.2 mmol), and catalyst (15 mol%) in the solvent (0.15 mL). [b] Determined using ^{1}H NMR. [c] A 1 : 5 ratio (**1A** : **2a**) was used. [d] The loading of the catalyst was 10 mol%. [e] The loading of the catalyst was 5 mol%. [f] No catalyst.

No product was detected in DMF with 15 mol% of Cr-MIL-101-UR**3** at 60 °C for 36 h (Table 1, entry 1). Surprisingly, the screening of solvents revealed CH_3CN to be optimal to give the desired product **3Aa** in 96% yield (entries 1–4), suggesting that the solvent had a significant effect on the conversion of this reaction. Next, the molar ratio of **1A**/**2a** was screened, and the reaction time was remarkably reduced from 60 to 24 h by increasing the molar ratio from 1 : 2 to 1 : 5 (entries 4 and 5). We next studied this reaction under the optimal reaction conditions in the presence of Cr-MIL-101-UR**3** with different loadings, which could be reduced from 15 to 10 mol% without remarkably affecting the yield of **3Aa** (entries 5–7). All of the other modified urea-containing MOF heterogeneous catalysts were then examined, and Cr-MIL-101-UR**3** bearing proper steric bulkiness and electron-withdrawing substituents was noted to be beneficial for the reaction (entries 5, 8 and 9). A control experiment with 15 mol% of unmodified MIL-101 as the catalyst gave only 22% yield under the optimized reaction conditions (presumably catalysed by the Lewis acidic chromium center) (entry 11), demonstrating that the catalytic activity arises mainly due to the presence of urea groups. Notably, the removal of Cr-MIL-101-UR**3** by filtration after 12 h resulted in no further conversion, unambiguously revealing that the catalyst in this reaction is heterogeneous in nature. Most importantly, the same reaction performed with 1-(3,5-bis(trifluoromethyl)phenyl)-3-phenylurea **4**, which is prone to oligomerization as observed in the solid state,[11] as a catalyst under homogeneous conditions, resulted in a relatively lower yield (79%) in comparison with Cr-MIL-101-UR**3** (entry 12). The better reactivity in the case of the heterogeneous catalyst may partially originate from the catalyst spatial isolation achievable in such a confined porous MOF environment, which is also in agreement with the experimental findings with other results.[4]

With the optimized conditions in hand, we set out to explore the scope of this protocol with respect to other electron-rich nucleophiles. Changing the nucleophiles from *N*-methylpyrrole to reasonably larger substrates did not have a significant influence on the reactivity. For example, treating *N*,*N*-dimethylaniline (**2b**),

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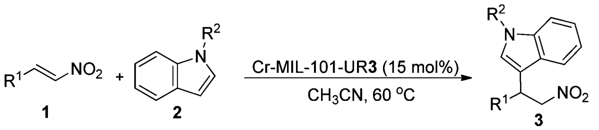
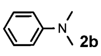
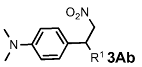
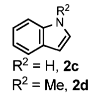
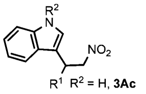
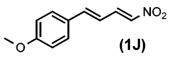
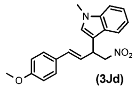
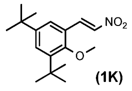
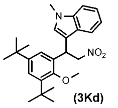
Table 2 Cr-MIL-101-UR**3**-catalysed Friedel–Crafts alkylation[a]



Entry	1	2	3	Yield[b] (%)
1	R^1 = Ph(**1A**)			95
2	R^1 = Ph(**1A**)			93
3	R^1 = Ph(**1A**)		**3Ad**	94
4	R^1 = 4-MeO-Ph (**1B**)	**2d**	**3Bd**	90
5	R^1 = 2-MeO-Ph (**1C**)	**2d**	**3Cd**	81
6	R^1 = 4-CF_3-Ph (**1D**)	**2d**	**3Dd**	90
7	R^1 = 4-Cl-Ph (**1E**)	**2d**	**3Ed**	88
8	R^1 = 2-naphthalene (**1F**)	**2d**	**3Fd**	91
9	R^1 = 2-furyl (**1G**)	**2d**	**3Gd**	92
10	R^1 = 2-thiophene (**1H**)	**2d**	**3Hd**	93
11	R^1 = propane (**1I**)	**2d**	**3Id**	65
12		**2d**		40 (80[c])
13		**2d**		17 (76[c])

[a] Reactions were carried out with **1** (0.1 mmol), **2** (0.12 mmol), Cr-MIL-101-UR3 (15 mol%), CH_3CN (0.15 mL). [b] The isolated yield is based on **1**. [c] The isolated yield in parentheses refers to the reaction catalyzed by **4**.

indole (**2c**), and 1-methylindole (**2d**) with **1A** even with a molar ratio of 1 : 1.2 gave the expected products **3Ab–Ad** in 93–95% yields, respectively, which is in sharp contrast to the result obtained for other MOF catalysts[4] (Table 2, entries 1–3). Next a variety of nitrostyrenes were further examined. Both electron-donating and -withdrawing groups on the phenyl ring were well tolerated affording the expected products (**3Bd–Ed**) in good yields (entries 4–7). (*E*)-1-(2-Nitrovinyl)naphthalene (**1F**) containing an extended conjugated system gave the corresponding product in 91% yield as well (entry 8). Heteroaromatic nitroalkenes were amenable to this protocol affording the expected products in excellent yields (entries 9 and 10). Aliphatic nitroalkene was also compatible with the reaction conditions, albeit displaying relatively sluggish reactivity (entry 11). Next, we turned our attention toward the longer-chained or larger nitroalkenes as substrates for this reaction. For **1J** and **1K**, the expected products **3Jd** and **3Kd** were obtained in only 40 and 17% yields, respectively (entries 12 and 13). However, the corresponding products were obtained in good yields (**3Jd** : 80%; **3Kd**: 76%) with **4** as the catalyst (Table 2, entries 12 and 13). The different sequences of catalytic activities corresponding to Cr-MIL-101-UR**3** in a heterogeneous manner and free urea **4** in a homogeneous manner demonstrated that catalysis in the case of the heterogeneous catalyst mainly took place within the pores of the MOF, thus exhibiting reagent size selectivity for such a heterogeneous catalyst. Finally, upon testing the recyclability of the urea-containing MOF heterogeneous catalyst, we found that the solids of Cr-MIL-101-UR**3** can be easily isolated from the reaction suspension by centrifugation and can be reused at least four times with little or no loss of activity (Fig. S6, ESI†) while retaining its crystallinity as verified by PXRD (Fig. S7, ESI†).

In summary, we have developed a simple and efficient method for the synthesis of new functionally diverse urea-derived MOF heterogeneous catalysts *via* postsynthetic modification. The resulting robust MOFs with large pores as HBD catalysts have shown remarkable catalytic activities in the Friedel–Crafts reactions, including much higher reaction activity *versus* the homogeneous catalyst, and much broader substrate scopes *versus* the known heterogeneous catalyst. Further studies toward the synthesis of chiral MOF HBD catalysts and their application to the asymmetric reactions are underway.

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