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Short Communication

One-pot synthesis of nitroalkenes via the Henry reaction over amino-functionalized MIL-101 catalysts

Huixian Yu, Jianwu Xie *, Yijun Zhong, Fumin Zhang, Weidong Zhu **

Key Laboratory of the Ministry of Education for Advanced Catalysis Materials, Institute of Physical Chemistry and Department of Chemistry and Life Sciences, Zhejiang Normal University, 321004 Jinhua, People's Republic of China

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ABSTRACT

Ethylenediamine moieties with different amounts were incorporated into the metal–organic framework MIL-101 to prepare the amino-functionalized MIL-101 materials, which were used as heterogeneous catalysts in the one-pot synthesis of nitroalkenes via the Henry reaction. Various reaction conditions were optimized. Under the optimized conditions, the selectivity towards nitroalkenes is extremely high in combination with nearly complete conversion of the reactant nitroalkanes. The amino-functionalized MIL-101 behaves as a true heterogeneous catalyst, can be easily recovered by filtration, and can be reused at least twice without significant loss of its catalytic performance.

1. Introduction

Nitroalkenes are of great synthetic potential in organic chemistry [1,2]. As the nitro group is a strong electron-withdrawing group, nitroalkenes are widespread used as versatile synthetic reagents in Michael addition [3], Friedel–Crafts alkylation [4,5], domino reaction [6,7], 1,3-dipolar cycloaddition [8,9], and Morita–Baylis–Hillman reaction [10,11]. In addition, the nitro group can be converted into various functional groups, such as carbonyl or amino derivatives [12–14]. Therefore, nitroalkenes have become important intermediates in organic synthesis. The classic method for the synthesis of nitroalkenes is to use the Henry reaction, i.e., the condensation of carbonyl compounds with nitroalkanes, followed by β-elimination of the resulting 2-nitro alcohols catalyzed by homogeneous catalysts [15–17]. In recent years, various heterogeneous catalysts such as amino-functionalized silicas (APS) [18,19], zeolite [20], and MCM-41 [21] have also been employed in the Henry reaction. However, most of the reported methods have one or more of the following drawbacks: use of expensive reagents, poor selectivity, complicated reaction assembly, and low yield of the desired products, etc.

Metal organic frameworks (MOFs) are nowadays at the front of materials research. In recent years, the combination of organic and inorganic subunits in fully crystalline porous materials has given rise to thousands of MOF structures with a vast topological richness [22,23]. Impressive progress has been made during the past decade, yielding promising results in the field of catalysis [24,25]. Although some MOF materials like MIL-101 have shown unusual thermal and chemical stability, the use of MOFs in applications like catalysis is still mainly limited by the lack of functional and selective sites in most ultra-stable MOFs [26]. Therefore, one of the current challenges is the development of stable MOFs including functional organic sites that could be used either directly or after post-synthetic modification.

Chromium(III) terephthalate MIL-101 is built up from super-tetrahedral (ST) building units, which are formed by rigid terephthalate ligands and Cr^{3+} octahedral clusters [26]. The resulting solid possesses two types of quasi-spherical mesoporous cages formed by 12 pentagonal and 16 faces, respectively. The so-called medium cavities are accessible through 1.2 nm pentagonal windows, while the large cavities are communicated through the same pentagonal windows and 1.6 nm hexagonal windows [27]. The presence of coordinatively unsaturated-metal sites (CUS) in MIL-101 allows its use as a mild Lewis acid and, more important, allows its post-functionalization via grafting of active species such as amines [28]. The zeotype cavities of two different sizes (extended MTN topology), the fully accessible porosity, together with a high thermal and chemical stability make MIL-101 an excellent candidate for catalytic purposes [28].

In this work an attempt was to incorporate amine moieties with different amounts into MIL-101 and then to use these amino-

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* Corresponding author. Tel./fax: +86 579 82282610.
** Corresponding author. Tel./fax: +86 579 82282932.
E-mail addresses: xiejw@zjnu.cn (J. Xie), weidongzhu@zjnu.cn (W. Zhu).

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functionalized MIL-101 materials as heterogeneous catalysts for the one-pot synthesis of various nitroalkenes, for the first time, to the best of our knowledge.

2. Experimental

MIL-101(Cr) was initially prepared from the hydrothermal reaction of terephthalic acid with $Cr(NO_3)_3 \cdot 9H_2O$, HF, and H_2O at 220 °C for 8 h. The as-synthesized MIL-101 was further purified by a three-step process using filtration, hot ethanol, and aqueous NH_4F solutions (see Supplementary data). The nomenclature used for the prepared amino-functionalized MIL-101 samples is GNM-1, GNM-2, GNM-3, and GNM-4 in abbreviation, corresponding to the different amounts of ethylenediamine (EDA in abbreviation) used during the preparation. For example, in a typical procedure for preparing GNM-3, the MIL-101 (0.5 g) dehydrated at 150 °C for 12 h was suspended in anhydrous toluene (30 mL). To this suspension, 2.25 mmol of EDA was added, and the mixture was stirred with heating to reflux for 12 h. For GNM-1, GNM-2, and GNM-4, 0.75, 1.5, and 3.0 mmol of EDA, respectively, were used, but the other preparation conditions were the same. The detailed methods for the characterization and the textural and physicochemical properties of the synthesized samples are presented in Supplementary data.

All catalytic measurements for the condensation of various aldehydes and nitromethane were carried out in a glass tube (20 mL) or flask (50 mL or 250 mL), depending on the total volume of the reaction medium, equipped with a reflux condenser and a magnetic stirrer. Before the reaction, the amino-functionalized MIL-101 catalysts were treated at 120 °C for 12 h in an oven to remove residual water in the samples. The reaction products were analyzed using a gas chromatograph (Agilent 6820) equipped with a capillary column (HP-5) and an FID detector. The detailed methods for catalytic measurements and analysis are described in Supplementary data.

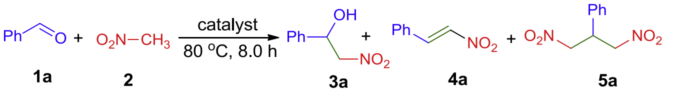
3. Results and discussion

We first decided to examine the reaction between benzaldehyde **1a** and nitromethane **2** in the presence of different catalysts, as shown in Table 1.

In an initial study, a series of organic solvents were screened for the reaction over GNM-3. It was found that GNM-3 exhibited a good catalytic activity for the condensation of benzaldehyde **1a** and nitromethane **2** in all the solvents and 2-nitrostyrene **4a** was obtained as a main product in almost all cases. As shown in Table 1, a type of solvent was found to have a significant effect on the conversion and selectivity under the same conditions. An excellent selectivity was obtained while the conversion was only moderate, when the reaction was carried out in cyclohexane (Table 1, entry 1), and using *n*-heptane as the solvent, the conversion was increased while the selectivity was almost the same as that using cyclohexane as the solvent (Table 1, entry 2). Using *n*-butanol as the solvent, differently, an excellent conversion was obtained but the selectivity was lowered, compared to those using cyclohexane and *n*-heptane as the solvents (Table 1, entry 4). In terms of the selectivity, toluene was revealed as the best medium, in which a moderate conversion was still obtained (Table 1, entry 3).

In order to get a higher conversion, various parameters, including the amount of EDA incorporated in MIL-101 and reaction temperature and time, were optimized using toluene as the solvent. By increasing the reaction temperature from 80 °C to 110 °C, the excellent conversion (100%) and selectivity (100%) were obtained in the presence of GNM-3 (Table 1, entry 5). However, the conversion was decreased, when the reaction time was shortened (Table 1, entries 6–8). The effects of the amount of EDA incorporated in MIL-101 on the catalytic activity and selectivity showed that under the same reaction conditions the selectivity was the same (100%) while the conversion was increased with increasing the amount of EDA incorporated in MIL-101 in the order of GNM-1, GNM-2, and GNM-3 (Table 1, entries 9, 10, and 5). However, GNM-4 having the highest amino loading in the MIL-101 supported catalysts investigated was less active than GNM-3 (Table 1, entry 11), probably ascribed to the overloaded EDA congregating near the entries of the cavities and the exterior surfaces of MIL-101, which would cause a strong diffusion resistance to the reactant molecules. In addition, the dehydrated MIL-101 as catalyst revealed a rather low activity (Table 1, entry 12), indicating that the support MIL-101 itself hardly catalyzed the Henry reaction. A homogeneous solution containing EDA in equivalent amount to that in GNM-3 was less active and selective than GNM-3 (Table 1, entry 13), which should be further clarified in our future work. In summary, it was found that GNM-3 was the best catalyst for the

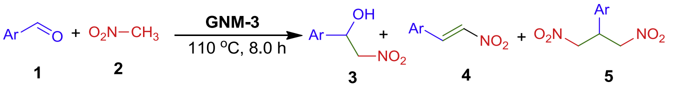
Table 1
Condensation of benzaldehyde 1a and nitromethane 2 over the amino-functionalized MIL-101 catalysts.[a]



Entry	Solvent	Catalyst[b]	*t* (h)	Conv. (%)[c]	Sel. (**4a**) (%)[d]
1	Cyclohexane	GNM-3	8.0	63	98 (2)[f]
2	*n*-Heptane	GNM-3	8.0	82	97 (3)[f]
3	Toluene	GNM-3	8.0	80	100
4	*n*-Butanol	GNM-3	8.0	98	60 (25)[f]
5[e]	Toluene	GNM-3	8.0	100	100
6[e]	Toluene	GNM-3	6.0	95	100
7[e]	Toluene	GNM-3	7.0	97	100
8[e]	Toluene	GNM-3	7.5	99	100
9[e]	Toluene	GNM-1	8.0	94	100
10[e]	Toluene	GNM-2	8.0	96	100
11[e]	Toluene	GNM-4	8.0	98	100
12[e]	Toluene	MIL-101	8.0	6	95 (5)[f]
13[e]	Toluene	EDA	8.0	98	94 (6)[f]

[a] Unless otherwise noted, the reactions were performed with 1 mmol of **1a**, 10 mmol of **2**, and 30 mg of catalyst in 2 mL of solvent at 80 °C.
[b] Amounts of EDA grafted in MIL-101, GNM-1: 1.67 mmol g^{-1}, GNM-2: 1.77 mmol g^{-1}, GNM-3: 1.97 mmol g^{-1}, and GNM-4: 2.06 mmol g^{-1}.
[c] Conversion of reactant **1a**.
[d] Selectivity for **4a**.
[e] At 110 °C.
[f] Selectivity for **3a**.

Table 2
Condensation of aldehyde 1 and nitromethane 2 over the amino-functionalized MIL-101 catalyst (GNM-3).[a]



Entry	Ar	Conv. (%)[b]	Sel. (**4**) (%)[c]	Sel. (**3**) (%)[d]	Sel. (**5**) (%)[e]
1	C_6H_5 (**1a**)	100	100 **4a**	–	–
2[f]	*p*-MeC_6H_4 (**1b**)	100	100 **4b**	–	–
3[f]	*p*-$MeOC_6H_4$ (**1c**)	100	100 **4c**	–	–
4	*p*-$NO_2C_6H_4$ (**1d**)	81	92 **4d**	8 **3d**	–
5	*m*-$NO_2C_6H_4$ (**1e**)	85	92 **4e**	8 **3e**	–
6	*p*-ClC_6H_4 (**1f**)	100	81 **4f**	19 **3f**	–
7	*m*-ClC_6H4 (**1g**)	83	93 **4g**	3 **3g**	4 **5g**
8	*o*-ClC_6H_4 (**1h**)	97	90 **4h**	10 **3h**	–
9	*p*-FC_6H_4 (**1i**)	93	90 **4i**	10 **3i**	–
10[f]	2-Naphthyl (**1j**)	100	88 **4j**	12 **3j**	–
11	2-Furanyl (**1k**)	100	93 **4k**	3 **3k**	4 **5k**
12	2-Thienyl (**1l**)	92	93 **4l**	7 **3l**	–
13[g]	C_6H_5 (**1a**)	98	99 **4a**	1 **3a**	–

[a] Unless otherwise noted, the reactions were performed with 1 mmol of **1**, 10 mmol of **2**, and 30 mg of catalyst GNM-3 in 2 mL of toluene at 110 °C for 8 h.
[b] Conversion of reactant **1**.
[c] Selectivity for **4**.
[d] Selectivity for **3**.
[e] Selectivity for **5**.
[f] 6 h.
[g] The reaction was performed with 45 mmol of **1**, 450 mmol of **2**, and 1.35 g of catalyst GNM-3 in 90 mL of toluene at 110 °C.

Henry reaction and the excellent conversion (100%) and selectivity (100%) were obtained after the reaction at 110 °C in toluene for 8.0 h (Table 1, entry 5).

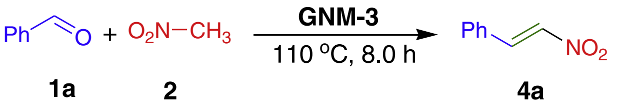
Having defined an efficiently catalytic system (GNM-3, toluene, 110 °C, and 8.0 h), the scope of the Henry reaction of aromatic aldehyde 1 and nitromethane **2** was explored. These results are summarized in Table 2. To assess the impact of the structural and functional motifs on the reaction, we tested a range of aromatic aldehydes. For all cases, aromatic aldehyde **1** reacted with nitromethane **2** led to the corresponding nitroalkene **4** in good to excellent conversion with high selectivity. Electron-donating groups in the *para*-position of benzaldehyde enhanced the reactivity of the aldehyde with nitromethane, and the corresponding nitroalkenes were formed in excellent conversion with high selectivity (Table 2, entries 2 and 3). Conversely, the slightly lower product selectivities were detected, when the reactant benzaldehydes with electron-withdrawing groups on the *ortho*, *meta* or *para* positions were used (Table 2, entries 4–9). The high conversion and selectivity were also obtained in the reactions of heteroaryl substituted aldehydes with nitromethane (Table 2, entries 10–12).

A reaction mechanism for the nitroalkanes catalyzed by the amino-functionalized MIL-101 catalysts is proposed, as illustrated in Scheme 1: (a) aldehyde **1** reacts with an amino group to form the intermediate of imine **I** and (b) the α-proton of nitromethane **2** is abstracted by another amino group, accompanied by the nucleophilic attack of the deprotonated nitromethane **III** on imine **I**, resulting in the product nitroalkane **4**.

In order to investigate the scalability of the synthesis of nitroalkenes via the Henry reaction over GNM-3, as an example, the condensation reaction of benzaldehyde and nitromethane was scaled up by 45 times in comparison with the reaction shown in Table 2, entry 1. The reaction was also proven effectively and conveniently to prepare the nitroalkene on a gram-scale (>5 g) with slightly inferior conversion and selectivity (Table 2, entry 13).

Being a heterogeneous catalyst in nature, the catalyst should be reusable. Therefore, the reusability of catalyst GNM-3 was investigated. The catalyst was indeed easily isolated from the reaction suspension after the reaction and was readily used in the next run. As shown in Table 3, in the second and third runs, the same selectivity as that in the first run for the desired product was reserved but the conversion was only slightly decreased in the second run and started to decrease significantly in the third run. The elemental analysis of the reused catalysts showed that the grafted EDA in GNM-3 extracted into the organic phase was the main cause for the reduced catalytic activity. The development of a stable amino-functionalized MIL-101 catalyst, therefore, remains a main challenge.

Table 3
Reusability of catalyst GNM-3 for the condensation of benzaldehyde and nitromethane.[a]



Run	N content in the catalyst (mmol g^{-1})	Conv. (%)[b]	Select. (**4a**)[c]
1	3.94 (1.97)[d]	100	100
2	3.64 (1.82)[d]	98	100
3	2.57 (1.29)[d]	76	100

[a] The reactions were performed with 15 mmol of **1**, 150 mmol of **2**, and 450 mg of catalyst GNM-3 in 30 mL of toluene at 110 °C and the catalyst was collected by filtration and used in the next runs.

[b] Conversion of reactant **1a**.

[c] Selectivity for **4a**.

[d] Numbers in parentheses denote the content of free amino groups available for the reaction.

4. Conclusions

The amino-functionalized MIL-101 catalyst worked well in the Henry reaction of various aldehydes and nitromethane with excellent selectivity and conversion for the synthesis of the corresponding nitroalkenes. There was an optimized amount of the amine grafted in MIL-101 for the catalytic performance. The solvent of the reaction medium that strongly affected the yield of nitroalkenes and toluene seemed to be the best solvent among the solvents screened. This heterogenized catalyst combined the advantages of both homogeneous and heterogeneous systems and therefore provided an easily recyclable and reusable solid catalyst that has uniform and precisely engineered active sites similar to those of its homogeneous counterpart.

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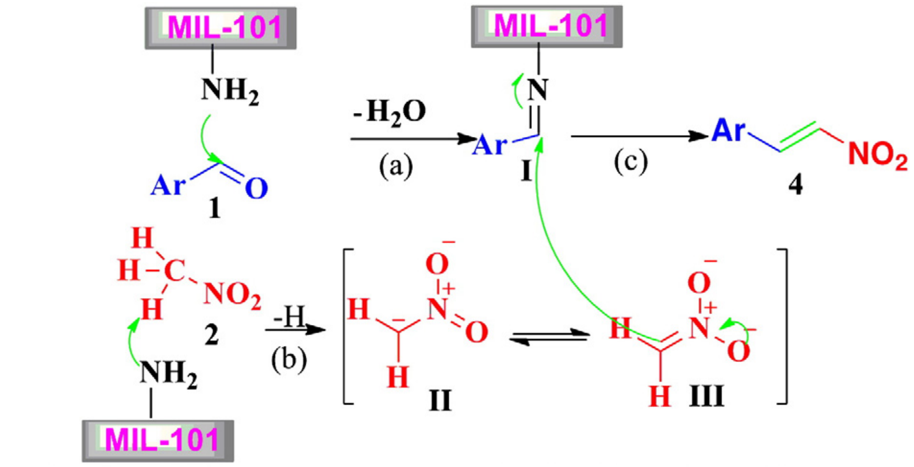

(a) formation of iminium; (b) deprotonation; (c) nucleophilic addition and hydrolysis

Scheme 1. Possible reaction mechanism.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.catcom.2012.09.032.

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