Chemoselective protection of hydroxyl and amine functional groups catalysed by MOFs

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Abstract

A simple and efficient solvent-free method was developed for the acetylation of alcohols and amines with acetic anhydride in excellent yields employing metal-organic framework $Cu_2(bdc)_2(dabco)$ catalyst under microwave irradiation. The salient features of this protocol are the short reaction time, ease of product isolation and reusability of the heterogeneous catalyst.

Keywords: $Cu_2(bdc)_2(dabco)$, acetylation, alcohols, amines, heterogeneous catalyst**.**

1. Introduction

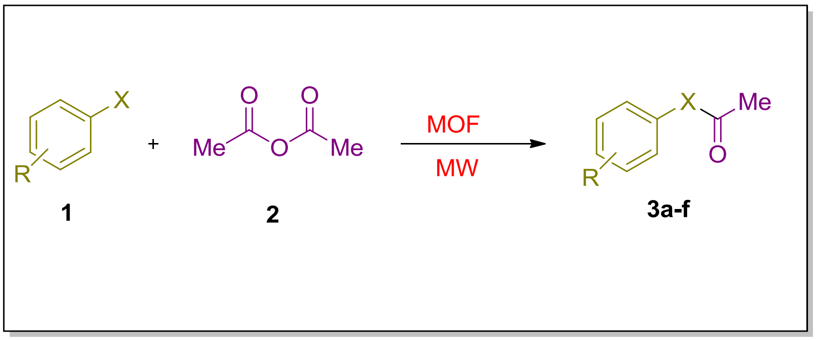
The protection of functional groups plays an important role in the synthesis of complex organic molecules. Protection of hydroxyl and amine group is one the most important transformation in organic synthesis. Protection of such functional groups is often necessary during the course of various transformations in multi-step synthesis, especially in the construction of polyfunctional molecules such as nucleosides, carbohydrates and natural products [1].

Among the various protecting groups used for the hydroxyl and amine groups, acetyl is one of the most common groups due to its stability in the acid reaction conditions and also easy deprotection using mild alkaline hydrolysis [2].

Various catalysts have been employed for this purpose, for example amine bases such as triethylamine and pyridine, 4-(N,N-dimethylamino) pyridine [3], P_2O_5/Al_2O_3 [4], zinc oxide [5], $RuCl_3$ [6], $Zn(OTf)_2$ [7] and Ni-nanoparticles [8].

Metal organic frameworks (MOFs) are nanoporous crystalline materials consisting of metal ions or metal clusters linked together by rigid organic bridging ligands [9]. MOFs are among the solids exhibiting the largest internal pore volume, largest surface area and lowest framework density. These features have been exploited for the use of these solids as gas adsorbents [10], hydrocarbon separator [11], energy storage [12], catalysis [13], drug delivery [14], sensor [15] and luminescence [16].

In continuation of our efforts towards exploring the applications of the MOFs as catalysts, here we report a simple and an efficient method for the acetylation of alcohols and amines with acetic anhydride using $Cu_2(bdc)_2(dabco)$ as a catalyst under microwave irradiation conditions in excellent yields (scheme 1).



Scheme 1. Acylation of alcohols/amines employing MOFs under microwave conditions

2. Experimental

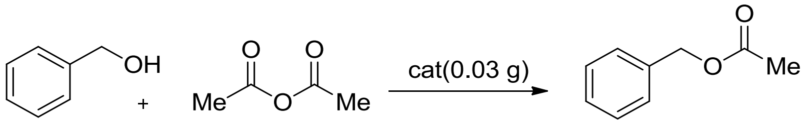
Protection of alcohols and amines with acetic anhydride under microwave irradiation; general procedure:

A flask was charged with acetic anhydride (2 mmol), alcohols/amines (1 mmol) and catalyst (0.03 g) and then it was carried under microwave irradiation. The progress of the reaction was monitored by TLC. After completion of the reaction, dichloromethane (3 × 5 mL) was added to the reaction mixture and the catalyst was separated by filtration. The organic phase was washed with saturated $KHCO_3$ solution (15 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure in a rotary evaporator to afford the crude product. The yields were isolated yields and calculated as mmol of purified product with respect to mmol of initial alcohol and amine.

3. Results and Discussion

Acetylation of benzyl alcohol (1 mmol) with acetic anhydride (2 mmol) in presence of 0.03 g MOF catalyst was studied under microwave irradiation as a model reaction. The reaction times, solvents, and reaction conditions were investigated (Table 1). In respect to the time and yield of the reaction, the best condition was chosen as in entry 6. The reaction was completed in just 6 min under microwave irradiation with 30 mg of $Cu_2(bdc)_2(dabco)$ as catalyst.

Table 1. Investigation of acetylation of benzyl alcohol with acetic anhydride[a]

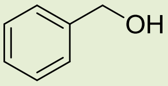
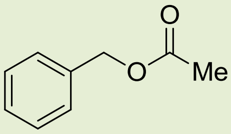


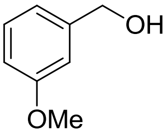
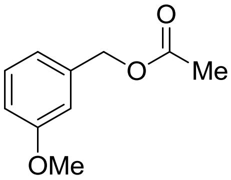
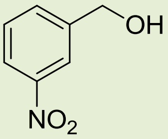
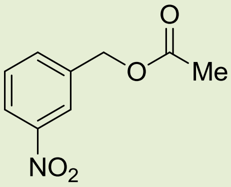
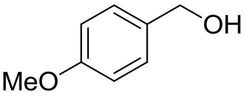
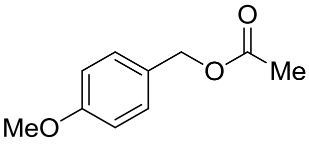
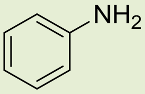
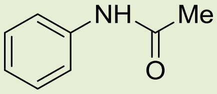
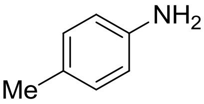
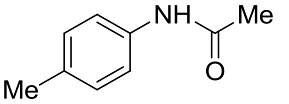
Entry	Solvent	Condition	Time (h)	Yield (%)[b]
1	EtOH	rt	15	100
2	EtOH	reflux	13	100
3	CH_2Cl_2	rt	11.5	100
4	CH_2Cl_2	reflux	9	100
5	-	ball-milling	5.5	100
6	-	MW	6 min	100

[a] benzyl alcohol (1.0 mmol), acetic anhydride (2.0 mmol), and $[Cu_2(bdc)_2(dabco)]$ (30 mg) as catalyst were used.
[b] The conversion was determined by GC analysis of the crude product.

Encouraged by our preliminary results, we subjected a series of alcohols and amines to acylation under the optimized conditions with the $Cu_2(bdc)_2(dabco)$ catalyst as summarized in Table 2.

Table 2. Acetylated derivatives of amines and alcohols in the presence of MOF.[a]

Entry	Substrate	Product	Time (min)	Yield(%)[b]
1			6	100

2			4	100
3			15	100
4			18	100
5			2	100
6			3	100

[a] Alcohol or amine (1.0 mmol), acetic anhydride (2.0 mmol), and $[Cu_2(bdc)_2(dabco)]$ (30 mg) as catalyst were used under microwave irradiation.

[b] The conversion yield was determined by GC analysis of the crude product.

4. Conclusions

In summary, we have described that MOF can be used as an available and environmentally friendly catalyst for acylation of alcohols and amines under microwave irradiation. The advantages of this procedure are solvent-free conditions, short reaction times, high yield, easy work up, recovery and reusability of the catalyst. The catalyst, heterogeneous by nature, showed excellent activity, affording high yields of desired products under solvent-free condition.

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