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Chemo Selective Protection of Aldehydes Functional Group Catalyzed by MOFs †

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Abstract: Metal-organic framework $Zn_2(BDC)_2(DABCO)$ was employed as a reusable heterogeneous acidic catalyst in the acylation reaction of various benzaldehydes with acetic anhydride under microwave irradiation. The outstanding features of this efficient solvent-free method are short reaction time, ease of product separation, greatest yields, and the ability to reuse the catalyst several times.

Keywords: Acetylation; aldehydes; heterogeneous catalyst; microwave

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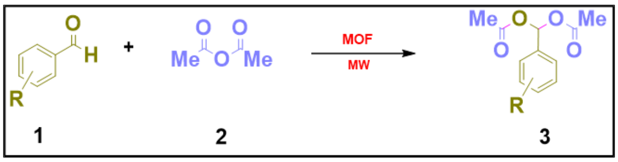
1. Introduction

In order to carry out the selective reactions in the desired position during multi-step procedures, it is necessary to protect parts of the molecules with various functional groups so they do not participate in the main reaction and also prevent the production of side products [1]. Compounds containing aldehydic carbonyl groups are commonly protected by transforming them into acetals, dithioacetal, oxathioacetals, and diacetate (acylal) [2]. The characteristic of stability in neutral environments, the comfort of preparation, and multiple applications, including as initiating materials for the Diels–Alder reaction, intermediates in industrial processes, geminal diacetates (acylals) have been highlighted among the various protection approaches of aldehydes [2,3]. Ethanethiol, acetic anhydride, alcohol are some of the reagents used to protect aldehydes [4]. The use of protic or Lewis acid catalysts such as AC-N-SO_4H [5], magnetic Fe_3O_4@C-600-SO_3H microspheres [6], SiO_2-$NaHSO_4$ [7], STO/Al-P [8], poly(p-hydroxybenzaldehyde-*co*-p-phenol sulfonate) [9], tungstosulfonic acid (TSA) [3], hexabromoacetone (HBA) [1], (MNPs-PSA) [2], 5,10,15,20-tetrakis(pentafluorphenylporphyrin) iron (III) chloride (Fe_5F) [10], plays an essential role in the better progress of the chemoselective reactions. Heterogeneous acid catalysts have advantages over their homogeneous type, such as simple separation via straightforward filtration, possible reuse, and convenient provision, which makes them an ideal choice for catalyzing synthesis reactions [4]. Metal-organic frameworks (MOFs) are a new type of hybrid material composed of metal nodes and organic ligands [11,12]. Since ligands and constituent metals are available in a wide variety, these versatile and adjust-able crystalline structures can be used for a variety of applications [13], including gas ab-sorption and storage [14,15], hydrocarbon separation [16], luminescence [17,18], sensors [19,20], drug delivery [21,22], energy storage [23], enzymes encapsulation [24,25], and catalysts [26]. In recent years, many studies have discussed the application of MOFs as heterogeneous catalysts in multi-step synthesis reactions, especially in the liquid phase. It has been found that the stability of the structure of MOFs in different chemical conditions, the presence of positive metal ions, high porosity, high surface-to-volume ratio, and the various preparation methods significantly contribute to the appropriate catalytic performance of the MOFs [27]. Continuing our efforts to investigate the catalytic performance of MOFs, we report a simple and efficient approach for protecting the carbonyl group in a range of benzaldehyde compounds using $M_2(BDC)_2(DABCO)$ as a Lewis acid catalyst under microwave irradiation conditions (Scheme 1). To investigate the catalytic performance of transition metals, such as Ni, Cu, Co, and Zn in $M_2(BDC)_2(DABCO)$ structures as Lewis acid catalysts, we investigated benzaldehyde acylation in the presence of $Ni_2(BDC)_2(DABCO)$, $Cu_2(BDC)_2(DABCO)$, $Co_2(BDC)_2(DABCO)$, and $Zn_2(BDC)_2(DABCO)$.



Scheme 1. Acylation of benzaldehyde employing MOFs under microwave conditions.

2. Materials & Methods

Protection of benzaldehydes with acetic anhydride under microwave irradiation; general procedure: Amount of 3 mmol acetic anhydrides, 1 mmol benzaldehyde, and 0.03 g $M_2(BDC)_2(DABCO)$ (M = Ni, Cu, Co, and Zn) catalyst was added in a flask and then exposed to microwave irradiation. The progress of the reaction was observed by GC. After the ending 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 and calculated as mmol of purified product with respect to mmol of initial benzaldehydes.

3. Results and Discussion

To determine which catalyst is the best for the acylation of benzaldehyde, 1 mmol benzaldehyde was examined with 3 mmol acetic anhydrides in the presence of 10 mg MOFs such as $Ni_2(BDC)_2(DABCO)$, $Cu_2(BDC)_2(DABCO)$, $Co_2(BDC)_2(DABCO)$, and $Zn_2(BDC)_2(DABCO)$, under both room temperature and microwave conditions (Table 1).

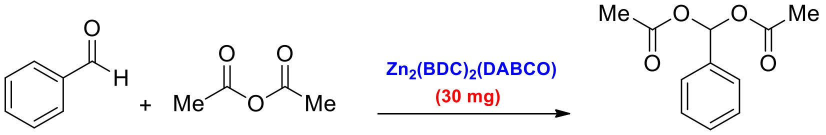
Table 1. Investigating the performance of the MOFs for the acylation reaction [a].

Entry	Catalyst	Room Temperature/Microwave	Time (h/min)	Yield (%) [b]
1	$Ni_2(BDC)_2(DABCO)$	R.T	24 h	100
		MW	19 min	93
2	$Cu_2(BDC)_2(DABCO)$	R.T	33 h	94
		MW	20 min	90
3	$Co_2(BDC)_2(DABCO)$	R.T	30 h	97
		MW	25 min	92
4	**$Zn_2(BDC)_2(DABCO)$**	**R.T**	**10 h**	**100**
		MW	**13 min**	**100**

[a] At room temperature and solvent-free condition. [b] Yields were determined by GC.

With respect to the time and reaction yield, $Zn_2(BDC)_2(DABCO)$ was the best among the others under microwave irradiation conditions. In addition, the reaction in solvent-free conditions and ambient temperature in the presence of different amounts of $Zn_2(BDC)_2(DABCO)$ catalyst, including 10, 20, 30, and 40 mg and various quantities of acetic anhydride including 1, 2, 3, and 4 mmol was investigated. The results indicated that the optimum amounts of catalyst and acetic anhydride are 30 mg and 3 mmol, respectively. To assess the solvent effect, acylation of benzaldehyde (1 mmol) with acetic anhydride (3 mmol) in presence of 30 mg of $Zn_2(BDC)_2(DABCO)$ catalyst was analyzed as a model reaction under different environmental conditions (Table 2).

Table 2. Investigation of acylation of benzaldehyde with acetic anhydride [a].

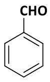
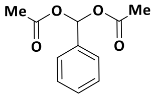
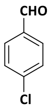
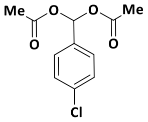
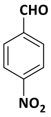
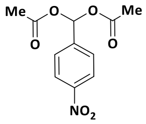
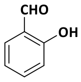
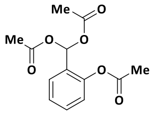
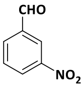
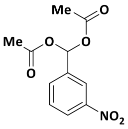
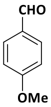
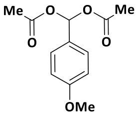
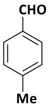
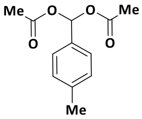


Entry	Solvent	Condition	Time (h)	Yield (%) [b]
1	EtOH	r.t	16.5	54
2	*n*-Hexane	r.t	22	73
3	EtOAc	r.t	20	57
4	CH3CN	r.t	18	52
5	Solvent-free	r.t	6	100
6	Solvent-free	ball-milling, r.t	3	93
7	**Solvent-free**	**MW**	**7 min**	**100**

[a] benzaldehyde (1.0 mmol), acetic anhydride (3.0 mmol), and $Zn_2(BDC)_2(DABCO)$ (30 mg) as catalyst were used. [b] The conversion was determined by GC analysis of the crude product.

In terms of time and reaction yield, the best conditions were found in entry 7. The reaction was completed in just 7 min under microwave irradiation and Solvent-free condition with 30 mg of $Zn_2(BDC)_2(DABCO)$ as the catalyst. Inspired by our introductory results, we subjected numerous of benzaldehydes to acylation under the optimized conditions with the $Zn_2(BDC)_2(DABCO)$ catalyst as summarized in Table 3.

Table 3. Acylated derivatives of benzaldehydes in the presence of MOF [a].

Entry	Substrate	Product	Time (min)	Yield (%) [b]
1			7	92
2			6	96
3			7	94
4			10	91
5			8	91
6			9	85
7			8	90

[a] benzaldehyde (1.0 mmol), acetic anhydride (3.0 mmol), and $Zn_2(BDC)_2(DABCO)$ (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, it was found that the catalytic activity of the organic metal framework $Zn_2(BDC)_2(DABCO)$ under solvent-free conditions and microwave irradiation is significant in the protection reactions of benzaldehydes. The unique advantages of this protocol include short reaction time, ability to recover and reuse the catalyst, solvent-free conditions, high efficiency, simple method.

Author Contributions: Conceptualization, S.M.; methodology, S.M. and L.P.; software, S.M. and L.P.; validation, L.P. and M.R.N.-J.; formal analysis, S.M.; investigation, S.M.; resources, S.M.; data curation, S.M. and L.P.; writing—original draft preparation, S.M.; writing—review and editing, S.M., L.P. and M.R.N.-J.; visualization, L.P.; supervision, M.R.N.-J.; project administration, M.R.N.-J.; funding acquisition, M.R.N.-J. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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