



Proceeding Paper Chemo-Selective Protection of Aldehydes Functional Group Catalyzed by MOFs [†]

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Abstract: A 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

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 that 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, and geminal diacetates (acylals), have been highlighted among the various protection approaches of aldehydes [2,3]. Ethanethiol, acetic anhydride, and alcohol are some of the reagents used to protect aldehydes [4]. The use of protic or Lewis acid catalysts such as AC-N-SO₄H [5], magnetic Fe₃O₄@C-600-SO₃H microspheres [6], SiO₂-NaHSO₄ [7], STO/Al-P [8], poly(p-hydroxybenzaldehyde-co-p-phenol sulfonate) [9], tungstosulfonic acid (TSA) [3], hexabromoacetone (HBA) [1], (MNPs-PSA) [2], and 5,10,15,20-tetrakis(pentafluorphenylporphyrin) iron (III) chloride (Fe₅F) [10] play an essential role in the better progress of the chemo-selective reactions. Heterogeneous acid catalysts have advantages over their homogeneous types, such as simple separation via straightforward filtration, possible reuse, and convenient provision, which make 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 adjustable crystalline structures can be used for a variety of applications [13], including gas absorption and storage [14,15], hydrocarbon separation [16], luminescence [17,18], sensors [19,20], drug delivery [21,22], energy storage [23], enzyme 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, and 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



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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). 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 such as Lewis acid catalysts, we investigated benzaldehyde acylation in the presence of Ni₂(BDC)₂(DABCO), Cu₂(BDC)₂(DABCO), Co₂(BDC)₂(DABCO), and Zn₂(BDC)₂(DABCO).



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

2. Materials and Methods

For the protection of benzaldehydes with acetic anhydride under microwave irradiation, the general procedure was as follows: 3 mmol acetic anhydrides, 1 mmol benzaldehyde, and 0.03 g M₂(BDC)₂(DABCO) (M = Ni, Cu, Co, and Zn) catalyst were added into 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 via filtration. The organic phase was washed with saturated KHCO₃ solution (15 mL), dried over anhydrous MgSO₄, 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).

Entry	Catalyst	Room Temperature/ Microwave	Time (h/min)	Yield (%) ^b
1	Ni ₂ (BDC) ₂ (DABCO)	R.T MW	24 h 19 min	100 93
2	Cu ₂ (BDC) ₂ (DABCO)	R.T MW	33 h 20 min	94 90
3	Co ₂ (BDC) ₂ (DABCO)	R.T MW	30 h 25 min	97 92
4	Zn ₂ (BDC) ₂ (DABCO)	R.T MW	10 h 13 min	100 100

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

^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 the presence of 30 mg of $Zn_2(BDC)_2(DABCO)$ catalyst was analyzed as a model reaction under different environmental conditions (Table 2).

		Zn ₂ (BDC) ₂ (DABC Me <u>(30 mg)</u>		O Me
Entry	Solvent	Condition	Time (h)	Yield (%) ^b
1	EtOH	r.t	16.5	54
2	<i>n</i> -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

Table 2. Investigation of acylation of benzaldehyde with acetic anhydrid	le ^a .
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^a Benzaldehyde (1.0 mmol), acetic anhydride (3.0 mmol), and Zn₂(BDC)₂(DABCO) (30 mg) were used as catalysts.
^b The conversion was determined via 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 in the solvent-free condition with 30 mg of $Zn_2(BDC)_2(DABCO)$ used as the catalyst. Inspired by our introductory results, we subjected numerous amounts 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	СНО	Me O Me O O O	7	92
2	CHO		6	96
3	CHO NO ₂		7	94
4	СНООН		10	91
5	CHO NO2		8	91
6	CHO		9	85
7	CHO		8	90

^a Benzaldehyde (1.0 mmol), acetic anhydride (3.0 mmol), and Zn₂(BDC)₂(DABCO) (30 mg) were used as catalysts under microwave irradiation. ^b The conversion yield was determined via 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, and simple method.

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