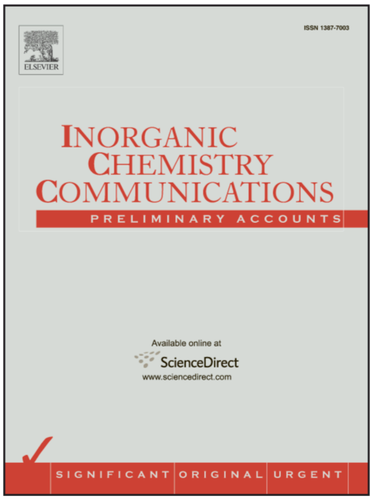

Short communication

A facile microwave-assisted Knoevenagel condensation of various aldehydes and ketones using amine-functionalized metal organic frameworks

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Graphical Abstract

A facile microwave-assisted Knoevenagel condensation of various aldehydes and ketones using amine-functionalized metal organic frameworks

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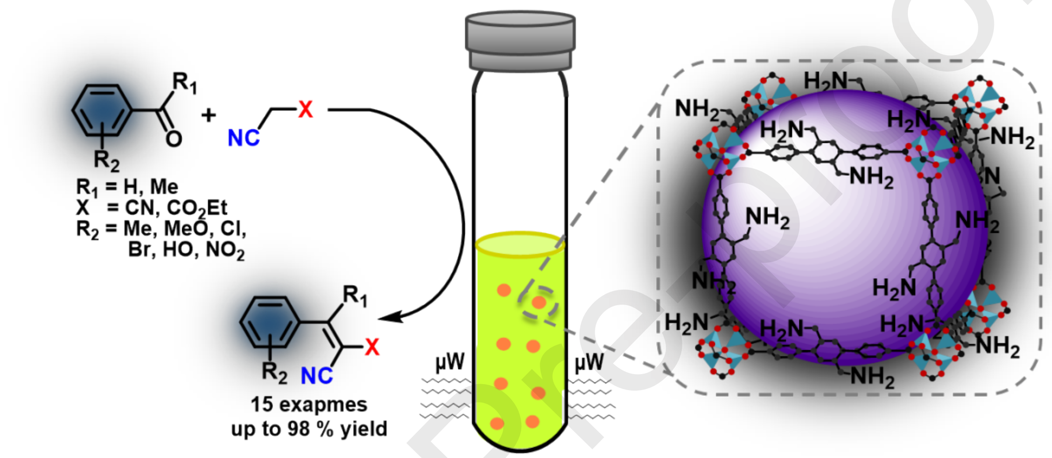

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Short Communication

A facile microwave-assisted Knoevenagel condensation of various aldehydes and ketones using amine-functionalized metal organic frameworks

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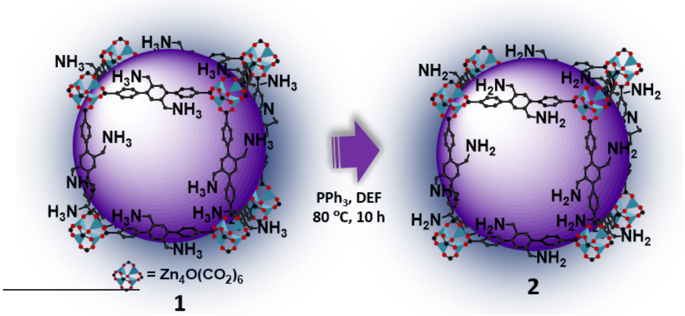
ABSTRACT

An amine-functionalized metal organic framework (MOF) was used as highly efficient and recyclable heterogeneous catalyst for Knoevenagel condensation of various aromatic aldehydes and ketones in ethanol. The catalytic efficiency was demonstrated by the high conversion of the reactants with 100 % selectivity under microwave (µW) irradiation, while dramatically reduced the reaction time as compared to the conventional heating method. Importantly, the MOF maintained its structural integrity after catalytic reactions and it could be reused several times without remarkable loss of activity.

Modern techniques are focused on the design of new methodologies able to make more efficient, simpler, faster, and cheaper chemical transformation processes [1]. Microwave (µW)-assisted organic synthesis has been recognized as one of the most powerful and sustainable tools in synthetic organic chemistry [2]. The application of µW energy is superior in comparison with conventional heating on accelerating chemical processes leading to radically reduce reaction times and increase yields and product purities by reducing unwanted side reactions [3]. The advantages of this enabling technology have subsequently also been exploited in the past such as medicinal chemistry [4], polymer synthesis [5], material sciences [6], nanoparticles research [7], and biochemical synthesis [8]. Importantly, the use of catalysts in conjunction with a µW may has significant advantages over traditional heating methods since the inverted temperature gradient under µW conditions may lead to an increased lifetime of catalyst through elimination of wall effects [9].



Metal organic frameworks (MOFs) have emerged as a newly developed materials with appreciable promise in growth of effective catalysts for synthetic organic chemistry [10]. Furthermore, MOFs are novel inorganic-organic hybrid materials that can be easily prepared from available precursors. The porous MOFs are promising new heterogeneous catalytic materials [11] due to well-ordered particle size, particle shape, pore size, pore shape, surface functionality and dynamic behavior in response to guest molecules. Importantly, MOFs-based catalysts can be readily recovered and reused after the catalytic reactions [12]. Therefore, MOFs are highly demanded catalytic materials to perform a variety of catalytic reactions in organic synthesis.

On the other hand, Knoevenagel condensation [13] is one of the most widely used methods for the formation of new carbon-carbon bonds [14]. Importantly, these carbon-carbon bond forming

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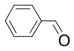
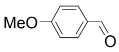
importance from the industrial point of view, a large number of various methods for the Knoevenagel condensation have been

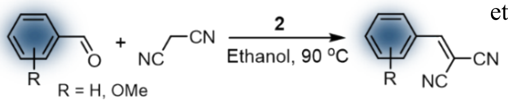
Table 1 Knoevenagel condensation of aldehydes catalyzed by **2** under μW irradiation and conventional heating method.[a]

Entry	Substrate	μwave irradiation		Conventional heating method	
		Time	Yield (%)[b]	Time	Yield (%)[b]
1		4 min	99	1.5 h	42
2		6 min	97	2.0 h	23

[a] Reaction conditions: substrate (1mmol), malononitrile (1 mmol), **2** (0.2 mmol of -NH_2 groups), ethanol (4 mL), μWave (200 W); [b] GC yield.

reported such as Lewis acids/bases [15], ultrasound irradiation [16], biotechnology [17], solid form [18], ionic material [19], and grindstone technique [20]. Unfortunately, these reactions often require harsh conditions such as extended reaction times, extra care, elevated temperatures and expensive catalysts. Therefore, the development of suitable energy saving synthetic method for the Knoevenagel condensation is highly desirable and a hot topic in current organic synthesis. Recently, amine-functionalized MOFs (**2**) (Scheme 1) were found to act as efficient catalysts in Knoevenagel condensation reactions [21]. The amine-functionalized MOFs were prepared from the azide functional group containing MOF (**1**) with triphenylphosphine (PPh_3) in diethylformamide (DEF) as described our earlier report and they can be used as a catalyst for Knoevenagel condensation reaction in organic synthesis [21]. Herein, we designed and developed very suitable μW-incorporated catalytic system using **2** for Knoevenagel condensation of various aromatic aldehydes and ketones (Table 2).

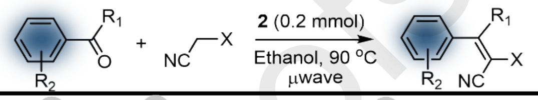
In the initial studies, we attempted the condensation of benzaldehyde with malononitrile under μW irradiation and conventional heating, respectively. The reactions were conducted in the presence of 0.2 mmol of **2** at 90 ℃ in ethanol. By employing μW irradiation, the reaction time was shortened from 1.5 h to 4 min in reaching full conversion (Table 1, entry 1). It is well-known that methoxy functional groups containing substrates are much more difficult to activate than other substrates. Remarkably, the condensation of 4-methoxybenzaldehyde with malononitrile proceeded faster and achieved high yield upon 6 min by μW irradiation, whereas the usual thermal heating gave very poor yield for 2 h (Table 1, entry 2). To our delight, the μW irradiation system showed good activity at very short reaction time for Knoevenagel condensation with 100% selectivity. With these encouraging result in hand, we next optimized the μwave conditions for the best performance of the catalyst. At first, the Knoevenagel condensation of benzaldehyde was performed with various amounts of **2** to screen the catalyst loading. As shown in Fig. 1a, the yield of the reaction gradually increased with increasing catalyst loading (0 to 0.2 mmol of –NH_2 groups). In addition, high catalytic activity was still observed with a very low catalyst loading. Although the reaction yield reached almost 100 % with 0.16 mmol of **2**, 0.2 mmol gave 100% yield for benzaldehyde at 90°C. Therefore, 0.2 mmol loading of **2** was determined to be the optimal loading. Furthermore, the effective solvent was screened to obtain higher efficiency under μW irradiation (Fig.1b). Water and toluene were poor solvents (14 to18% conversion) and the crystal structure of MOF material was deformed when water was used as a solvent. The Knoevenagel condensation of benzaldehyde was demonstrated only 45 to 58% conversion in acetonitrile, DMF and DME. The results showed that ethanol was the best solvent for the catalytic activity of the solvent used in condensations under μW irradiation. Having these optimized results in hand, the reactions of various aromatic substituted aldehydes with malononitrile or ethyl

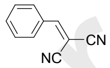
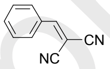
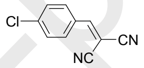
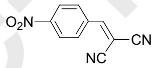
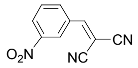
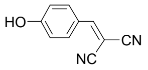
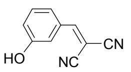
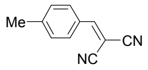
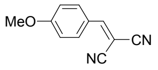
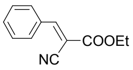
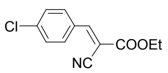
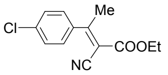
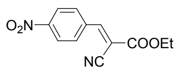
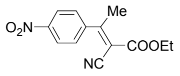
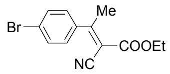
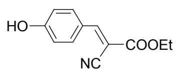


Scheme 1 Synthesis route of amine-functionalized MOFs (**2**).

the reactions are summarized in the following Table 2. Control experiment using compound **1** under exactly the same reaction conditions were carried out, showing that the **1** was less effective than compound **2** (Table 2, entry 1 and 2) that also confirmed by our conventional heating method [21]. However, **1** demonstrates catalytic activity would be due to coordinatively unsaturated zinc sites in the MOF networks [22]. Importantly, all

Table 2 Knoevenagel condensation of various aldehydes and ketones catalyzed by **2** under μW irradiation in ethanol.[a]



Entry	Product[a]	Time (min)	Yield (%)[b]	m.p. (^{o}C)	
				Found	Reported
[c] 1		4	36	84	84[17]
2		4	98	84	84[17]
3		4	95	159	162[17]
4		4	92	160	160[17]
5		4	84	107	107[18]
6		5	91	187	188[17]
7		5	87	164	164[18]
8		6	95	134	135[18]
9		6	94	133	113[18]
10		5	97	51	50[17]
11		6	92	88	88[17]
12		6	87	91	93[17]
13		5	94	130	131[17]
14		8	91	143	144[17]
15		8	82	83	84[17]
16		6	94	173	173[17]

[a] Reaction conditions: aldehyde/ketone (1mmol), malononitrile/ethyl cyanoacetate (1 mmol), **2** (0.2 mmol of -NH_2 groups), ethanol (4 mL), μWave (200 W); [b] isolated yield; [c] Calculated to have the same amount of Zn^{2+} (when comparing MOF-NH_3 and MOF-NH_2).

the products in high yield with 100 % selectivity under the defined μW irradiation conditions. The high catalytic activity of **2** for benzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, 3-nitrobenzaldehyde, 4-hydroxybenzaldehyde, 3-hydroxybenzaldehyde, 4-methylbenzaldehyde, and 4-methoxylbenzaldehyde with malononitrile was still maintained in ethanol (Table 2, entries 2-9). The electron withdrawing groups (EWG) somewhat reduced the reaction time (Table 2, entries 3-5) as compared to the electron donating groups (EDG) (Table 2, entries 6-9).

In further studies, extension of the scope of the Knoevenagel condensations catalyzed by **2** was explored to various aldehyde/ketone derivatives with ethyl cyanoacetate under μW-irradiation. Interestingly, the reaction of benzaldehyde with ethyl cyanoacetate proceeded smoothly to provide the corresponding product in high yield, 97% (Table 2, entry 10). The substrates with EWGs, such as 4-chlorobenzaldehyde, 1-(4-chlorophenyl)ethanone, 4-nitrobenzaldehyde, 1-(4-nitrophenyl)ethanone, 1-(4-bromophenyl)ethanone (Table 2, entries 11-15), along with the derivatives of EDGs, such as 4-hydroxybenzaldehyde (Table 2, entry 16) showed satisfactory yields up to 94% and EWGs gave the products in shorter time as compared to the EDGs. Furthermore, a variety of aromatic ketones also performed well to give the corresponding yields, affording up to 92% isolated yields by μW conditions (Table 2, entries 12, 14 and 15). These results were consistent with our hypothesis and suggested that the amine moieties together with structure of MOF can facilitate the formation of product for EWG/EDG substituents, thus enhancing the catalytic reactivity as depicted in Fig. S1. Moreover, EWGs along with EDGs promoted Knoevenagel condensation efficiently, whereas dramatically reduced the reaction time as compared to the conventional heating method [23]. Importantly, these results reveal that the use of μW irradiation into the catalysis leads to much higher rates within a very short reaction time than those which are achieved in conventional heating.

In order to further evaluate the catalyst's reactivity, we also compared catalyst **2** with some catalysts reported in the literature for the Knoevenagel condensation under μW irradiation. Interestingly, as shown in Table S1 (ESI), catalyst **2** (Table S1, entry 1) has many advantages over reported catalysts. Importantly, the high activity of catalyst **2** would be due to basicity, pore structure, thermal stability, surface functionality along with coordinatively unsaturated metal site of the MOF framework (Fig. 1c, and Fig. S2-S6; ESI) [21, 22].

We further turn our attention to reusability test of our catalyst **2** under μW irradiation. The recycling of the catalyst was examined by the coupling of benzaldehyde with malononitrile (Fig 1d). Interestingly, it was observed that very similar yields (100-98 %) with 100 % selectivity were obtained by carrying on five consecutive runs without any significant loss of catalytic activity. Significantly, the XRD patterns of catalyst **2** after 5th run was indistinguishable from those of the fresh one (Fig. 1c). It is suggested that no structural decomposition of the catalyst had occurred after the catalytic reaction and filtration.

In summary, catalyst **2** demonstrated remarkable activity for Knoevenagel condensation of various aromatic aldehydes and ketones under μWave irradiation conditions. Importantly, the reactions proceeded very quickly with high yields compared to conventional heating methods. Moreover, the catalyst **2** could be reused several times without further processing. More importantly, this method offers a very simple, fast, efficient, energy saving as well as easy way for the synthesis of a large number of important organic molecules. We believe that our present study will inspire the catalytic engineering in the field of organic synthesis.

This work is supported by Inha University Research Grant (2017)

Supplementary Material

Experimental details, TGA, XPS, pore volume vs diameter graphs, N_2 adsorption-desorption isotherms and comparison table. Electronic supplementary information (ESI) to this article can be found online at http://dx.doi.org/10.1016/j.inoche

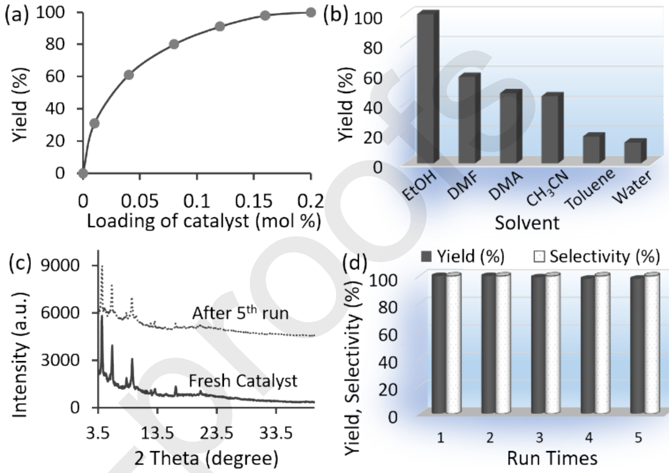


Fig. 1 Knoevenagel condensation of benzaldehyde with malononitrile catalysed by **2** (a) different catalyst loading, (b) in different solvents, and (d) recyclability test; in all cases the reaction conditions are same as Table 2 (entry 2); (c) XRD patterns of catalyst **2** (fresh & after 5th run).

References

[1] M. Leonardi, M. Villacampa, J. C. Menéndez, *Chem. Sci.*, **2018**, *9*, 2042-2064.

[2] G.-J. Ding, Y.-J. Zhu, C. Qi, B.-Q. Lu, F. Chen, J. Wu, *J. Mater. Chem. B*, **2015**, *3*, 1823–1830.

[3] Microwaves in Organic Synthesis, 3rd ed.; De La Hoz, A., Loupy, A., Eds.; Wiley-VCH: Weinheim, **2013**.

[4] M. Henary, C. Kananda, L. Rotolo, B. Savino, E. A. Owens, G. Cravotto, *RSC Adv.*, **2020**, *10*, 14170-14197.

[5] M. Adamski, T. J. G. Skalski, S. Xu, M. Killer, E. M. Schibli, B. J. Frisken, S. Holdcroft, *Polym. Chem.*, **2019**, *10*, 1668-1685.

[6] T. V. Medeiros, J. Manioudakis, F. Noun, J.-R. Macairan, F. Victoria, R. Naccache, *J. Mater. Chem. C*, **2019**, *7*, 7175-7195.

[7] M. Baghbanzadeh, L. Carbone, P. D. Cozzoli, C. O. Kappe, *Angew. Chem. Int. Ed.*, **2011**, *50*, 11312–11359.

[8] Y. Liu, Y. Nie, X. Lu, X. Zhang, H. He, F Pan, L. Zhou, X. Liu, X. J, S. Zhang, *Green Chem.*, **2019**, **21**, 3499-3535.

[9] Ü. Yılmaz, H. Küçükbay, S. Deniz, N. Şireci, *Molecules,* **2013**, *18*, 2501-2517.

[10] J. W. Liu, L. F. Chen, H. Cui, J. Y. Zhang, L. Zhang, C. Y. Su, *Chem. Soc. Rev.*, **2014**, *43*, 6011.

[11] Y. Hu, J. Zhang, H. Huo, Z. Wang, X. Xu, Y. Yang, K. Lin, R. Fan, *Catal. Sci. Technol.*, **2020**,*10*, 315-322.

[12] X. Feng, C. Xu, Z.-Q. Wang, S.-F. Tang, W.-J. Fu, B.-M. Ji, and L.-Y. Wang, *Inorg. Chem.*, **2015**, *54*, 2088.

[13] Knoevenage, E. *Berichte der Deutschen Chemischen Gesellschaft*, **1894**, *2*(27), 2345.

[14] Jones, G. *Organic Reactions*, **1967**, *15*, 204.

[15] Z. Wang, X. Yuan, Q. Cheng, T. Zhang, J. Luo, *New J. Chem.*, **2018**, *42*, 11610-11615.

[16] S. Zhao, X. Wang, L. Zhang, *RSC Adv.*, **2013**, *3*, 11691-11696.

[17] (a) U.R. Pratap, D.V. Jawale, R.A. Waghmare, D.L. Lingampalle, R.A. Mane, *New J. Chem*. **2011**, *35*(1), 49; (b) C. Wang, Z. Guan, Y. He, *Green Chem*. **2011**, *13*(8): 2048.

[18

Chem. **2003**, *5*(4), 408.

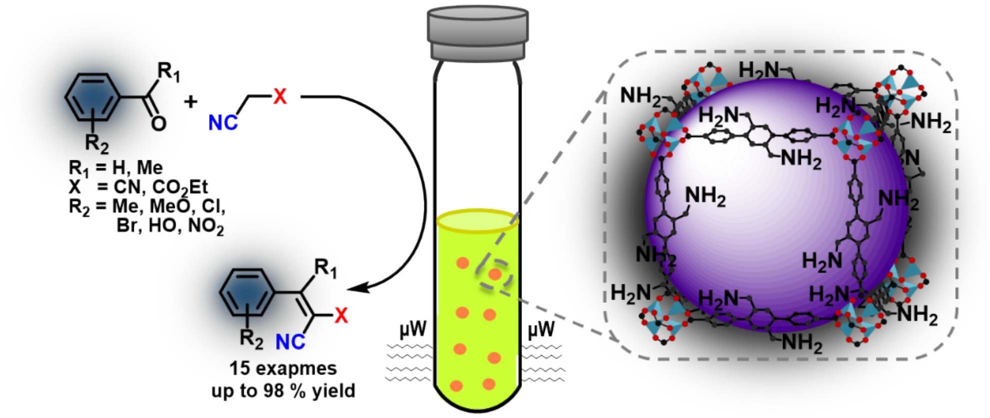
[19] D. Meng, Y. Qiao, X. Wang, W. Wen, S. Zhao, *RSC Adv.*, **2018**, *8*, 30180-30185.

[20] M.A. Pasha, K. Manjula, *J. Saudi Chem. Soc*. **2011**, *15*(3), 283.

[21] A. Taher, D.-J. Lee, B.-K. Lee, I.-M. Lee, *Synlett,* **2016***, 27,* 1433-1437.

[22] F.X.L. Xamena, F.G. Cirujano, A. Corma, *Microporous and Mesoporous Materials*, **2012**, *157*, 112.

Graphic


R1
O
R2
+
NC
X
R1 = H, Me
X = CN, CO2Et
R2 = Me, MeO, Cl, Br, HO, NO2
R1
R2
NC
X
15 exapmes
up to 98 % yield
μW
μW
NH2
H2N
NH2
H2N
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NH2
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H2N
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NH2

Hi

- A highly efficient and reusable amine-functionalized metal organic frameworks (MOFs) for the Knoevenagel condensation of various aldehydes and ketones in ethanol.

- The catalytic efficiency was demonstrated by the high conversion of the reactants with 100 % selectivity under microwave irradiation.

- The electron withdrawing groups along with electron donating groups promoted this Knoevenagel condensation efficiently and dramatically reduced the reaction time as compared to the conventional heating method

- This work provides a very simple, energy saving as well as easy way for organic synthesis

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☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

'Declarations of interest: none'

Au

Abu Taher: Conducted experimental work, analyzed the data, and Writing- Original draft preparation; **Ik-Mo Lee:** Supervision, reviewing and worked as project administrator; **Bilkis Jahan Lumbiny:** Initiated the project, designed experiments to develop this reaction, investigated the work.