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Function–Structure Relationship in Metal–Organic Frameworks for Mild, Green, and Fast Catalytic C-C Bond Formation

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S Supporting Information

ABSTRACT: Tunability in chemical functionality is a promising characteristic of metal-organic frameworks (MOFs), which plays an important role in developing and improving the practical applications of MOFs. Here, we applied this important feature of MOFs to be in line with sustainable development and green chemistry principles through the synthesis of MOF-based heterogeneous organocatalysts. According to our green functionalization strategy, some isostructural MOFs (azine decorated TMU-4 with the formula $[Zn(OBA)(BPDB)_{0.5}]_{n}$ 2DMF, azine-methyl functionalized TMU-5 with the formula $[Zn(OBA)(BPDH)_{0.5}]_n$ 1.5DMF, dihydro-tetrazine decorated TMU-34 with the formula $[Zn(OBA)(H_2DPT)_{0.5}]_n$ DMF, and tetrazine functionalized TMU-34(-2H) with the formula $[Zn(OBA)(DPT)_{0.5}]_n$ DMF, where $H_2OBA = 4,4'$ oxybis(benzoic acid), BPDB = 1,4-bis(4-pyridyl)-2,3-diaza-1,3-butadiene, BPDH = 2,5bis(4-pyridyl)-3,4-diaza-2,4-hexadiene, H₂DPT = 3,6-di(pyridin-4-yl)-1,4-dihydro-1,2,4,5-tetrazine, and DPT = 3,6-di(pyridin-4-yl)-1,2,4,5-tetrazine) have been applied for mild, green, and fast Knoevenagel condensation. These frameworks display different



Lewis basic catalytic activities owing to their different functionality and function accessibility. Contrary to extensive articles published about Knoevenagel condensation, this study involves the rare examples in Knoevenagel condensation with such mild conditions (room temperature and atmospheric pressure) and with a green solution (water as the solvent). Due to the combined synergic effects of the Lewis basicity of TMU-frameworks, the amphoteric and hydrogen bond-participating nature of water molecules, maximum conversion times are reached just after 30 min (for TMU-5) and 60 min (for TMU-34). Stability and recyclability tests show that TMU-5 and TMU-34 are completely stable in water at reaction conditions and can retain their crystallinity, porosity, and functionality even after five cycles without any specific reduction in their catalytic conversion. Since, in many cases, amine decorated MOFs are applied in Knoevenagel catalyzed condensation, this study is beneficial in providing information about the effects of azine and tetrazine functional groups in reactant activation and the acceleration of Knoevenagel condensation.

1. INTRODUCTION

Green chemistry is an area of chemistry that concerns the design of chemicals and processes that minimize or eliminate the application and generation of hazardous materials and their negative effects on the environment.¹ On the other hand, the scope of green chemistry is to make products that are effective and economical.² During recent years, green chemistry has been recognized as a culture and methodology to reach sustainable development. Green chemistry is based on 12 principles, in which two of them refer to the solvent and catalysis methods.³ Unlike conventional solvents that are not green, green solvents are generally derived from renewable resources and biodegrade to an innocuous, often naturally occurring product, and a green catalyst can be used in small quantities to repeat a reaction.⁴ Some kinds of catalysts such as enzymes, heterogeneous catalysts, and organocatalysts (in particular) are known to be at the center of green chemistry because they reduce the environmental impact of chemical processes.⁵ Therefore, simultaneous applications of green catalysts and solvents in a reaction for rate acceleration along with atom economic concerns are very promising according to green synthesis.

The term "organocatalysis" (combination of "organic" and "catalysis") is a key orientation in green synthetic chemistry. Organocatalysis is a type of catalysis where the catalyst is an organic (nonmetallic) compound. Organocatalysts predominantly consist of C, H, O, N, S, P, and other nonmetal elements found in organic compounds to accelerate chemical reactions. Organocatalysts accelerate the chemical reaction through formation of covalent bonds or noncovalent interactions.⁸ The advantages of organocatalysts include moisture and oxygen insensitivity, availability, low cost, and low toxicity, which confer a huge direct benefit in the production of pharmaceutical intermediates when compared with transition metal catalysts." Since there is no need for a metal-based catalyst when using an organocatalyst, organocatalysis serves as a contribution to green chemistry.

In recent years, the use of the term "heterogeneous organocatalyst" has been exclusively confined to a catalytic system that contains an organic molecule immobilized onto

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some sort of support material and is responsible for accelerating a chemical reaction.⁵ In this area, there is research on the use of organocatalysts on various inorganic supports, such as nanoparticle, silica, zeolitic, nanoporous, and hybrid inorganic– organic materials.⁵ Among these supports, metal–organic frameworks (MOFs) have been considered repeatedly.

MOFs are three-dimensional porous coordination polymers with special characteristics like high porosity, large surface area, high thermal and chemical stability, and high tunability in chemical functionality.^{9–11} MOFs are utilized in different types of applications such as gas adsorption and separation,¹² sensing and removal,^{13–17} electrochemistry,¹⁸ bio applications and drug delivery,¹⁹ photocatalysts and degradation,^{20,21} and other applications.²² Owing to the unique characteristics of MOFs they are being applied as heterogeneous organocatalysts in different reactions.^{23–25} Since MOFs are porous and have a controllable pore size, substrates with different dimensionality can diffuse into the pores, and since their pores can be functionalized with organic functional groups as organocatalytic sites, they can provide nano reactors for the acceleration of chemical reaction rates according to green chemistry principles.

Considering all these points (green chemistry principles in catalytic reactions, heterogeneity, and chemically tunable nature of MOFs by organic functional groups) we applied our TMU frameworks as heterogeneous organocatalysts in mild, green, and fast Knoevenagel condensation. In this way, we designed and synthesized some azine and tetrazine functionalized MOFs, which are completely stable and chemically active as heterogeneous organocatalysts in water as the greenest solvent. Then, we applied TMU-frameworks in very mild and effortless conditions (room temperature and atmospheric pressure) to catalyze Knoevenagel condensation. Our observations reveal that TMU-frameworks are completely effective for the activation of reactants in green and mild conditions and the promotion of very short reaction times.

2. EXPERIMENTAL SECTION

2.1. Materials and Instrumentation. *2.1.1. Materials.* All required chemicals, including H_2OBA (4,4'-oxybis(benzoic acid)) as an oxygen-donor ligand, 4-cyanopyridine, 4-pyridinecarbaldehyde, and 4-acetylpyridine for the synthesis of nitrogen-donor pillar spacers and solvents, were purchased from commercial suppliers and were used without further purification unless otherwise noted.

2.1.2. Instrumentation. Infrared spectra were recorded using a Thermo Nicolet IR 100 FT-IR. Ultrasonication was carried out in a SONICA-2200 EP ultrasonic bath (frequency of 40 kHz). X-ray powder diffraction (PXRD) measurements were performed using a Philips X'pert diffractometer with monochromated Cu K α radiation. Elemental analyses were carried out on a Thermo Scientific Flash 2000 CHNS elemental analyzer. Adsorption studies were performed using a TriStar II 3020 surface area analyzer from Micromeritics Instrument Corporation with N₂ at 77 K. Conversion percentages were calculated using gas chromatography coupled with a flame ionization detector (GC-FID (hp))

2.2. Synthesis of Pillar Spacers. All N-donor pillar spacers, including BPDB (1,4-bis(4-pyridyl)-2,3-diaza-1,3-butadiene), BPDH (2,5-bis(4-pyridyl)-3,4-diaza-2,4-hexadiene), H_2DPT (3,6-Di(pyridin-4-yl)-1,4-dihydro-1,2,4,5-tetrazine), and DPT (3,6-di(pyridin-4-yl)-1,2,4,5-tetrazine), were synthesized through the synthesis method reported previously.¹²

2.3. Synthesis of MOF Powders. In a general procedure for the synthesis of nanopowder of TMU-frameworks, 1 mmol (0.22 g) of $Zn(CH_3COO)_2$, 1 mmol of H_2OBA (0.26 g) as the oxygen donor ligand, and 1 mmol of the related N-donor ligand (0.21 g of BPDB for TMU-4, 0.24 g of BPDH for TMU-5, 0.24 g of H_2DPT for TMU-34, and 0.23 g of DPT for TMU-34(-2H)) were mixed together in the 30

mL of solvent (DMF, *N*,*N*'-dimethylformamide, for TMU-4, TMU-5, and TMU-34, but in the case of TMU-34, the solvent is a 1:1 volumetric mixture of DMF and acetonitrile) in an ultrasonic bath. The solution was sonicated for the required amount of time (30 min for TMU-4, 60 min for TMU-5 and TMU-34(-2H), and 160 min for TMU-34). Then, the solution was washed with DMF (3 × 5 mL) and dried at 80 °C in a preheated oven.

2.3.1. Data for TMU-4. Yield: 83% (80% based on H₂OBA). IR data (KBr pellet, ν/cm^{-1})-selected bands: 445(w), 523(w), 659(m), 692(m), 776(m), 875(m), 1021(w), 1089(m), 1159(s),1241(vs), 1389(vs), 1412(vs), 1500(s), 1568(s), 1608(vs), 1679(vs), 2926(w), and 3414(w-br). Elemental analysis (%) calculated for [Zn₂(C₁₄O₃H₈)₂(C₁₂H₁₀N₄)]·(C₃NOH₇)₂: C 55.3, H 4.0, N 8.4; found: C 55.8, H 4.2, N 8.5.

2.3.2. Data for TMU-5. Yield: 80% based on H₂OBA. IR data (KBr pellet, ν/cm^{-1})-selected bands: 652(s), 779(m), 873(m), 1021(m), 1092(m), 1162(s), 1233(vs), 1397(vs), 1499(m), 1631(vs), 1671(vs) and 3414(w-br). Elemental analysis (%) found for [Zn(C₁₄O₅H₈)-(C₁₄N₄H₁₄)_{0.5}]·(C₃ONH₇)_{1.5}: C 54.8, H 4.2, N, 8.8.

2.3.3. Data for TMU-34. Yield: 78% based on H_2OBA . IR (KBr pellet, cm⁻¹)-selected bands: 661(m), 778(m), 872(m), 1162(s), 1241(vs), 1407(vs), 1607(vs), 1674(s), 2928(m), 3273. Elemental analysis (%) calculated for $[Zn(C_{14}O_5H_8)(C_{12}N_6H_{10})_{0.5}] \cdot (C_3ONH_7)$: C 53.8, N 10.9, H 3.9; found: C 54.1, N 11.4, H 4.1.

2.3.4. Data for TMU-34(-2H). Yield: 85% based on H₂OBA. IR data (KBr pellet, ν/cm^{-1})-selected bands: 656(w), 780(w), 874(w), 1091(w), 1160(m), 1231(m), 1399(vs), 1500(s), 1629(s), 1672(s), 3429(m). Elemental analysis (%) found for $[Zn(C_{14}O_5H_8)-(C_{12}N_6H_8)_{0.5}]\cdot(C_{3}ONH_7)$: C 54.0, N 10.9, H 3.9.

2.4. General Procedure for the Knoevenagel Condensation. *2.4.1. Test Reaction.* In order to evaluate the catalytic activity of the azine and tetrazine functionalized TMU-MOFs in green conditions, we conducted Knoevenagel condensation of benzaldehyde (BA) with malononitrile (MN) in water as the green solvent and under solventless conditions. Prior to the many catalytic experiments, catalysts were activated at 120 °C for 48 h without any solvent exchange procedure, and after the catalytic tests, the stability of TMU-frameworks was evaluated in water.

A 6 mL screw cap glass vial with a magnetic stir bar was used to carry out the catalytic test reactions. First, 0.03 g of activated catalyst (corresponding to 0.034 mmol of azine and tetrazine groups and 1.7 mol % catalyst) was added to the glass vial followed by the addition of a 5 mL solution containing 2.5 mmol of malonitrile as the excess reagent and 2 mmol of benzaldehyde as the limited reagent. The reaction solution was stirred at room temperature and atmospheric pressure (without an inert atmosphere) in an aqueous medium. The progression of the reaction was easily monitored by GC analysis using an internal standard method (0.04 g of n-dodecane) at regular intervals of time after extraction in dichloromethane. GC peak characterizations were carried out using a prepared authentic solution of reactants and products in CH₂Cl₂. The analysis was carried out directly after sampling to avoid any additional conversion in the reaction mixture.

Echrom GC A90 gas chromatography with the flame ionization detector (China) was employed (Agilent HP-5 capillary column, 30 m \times 0.320 mm \times 0.25 μ m with temperature limits from 60 to 325 °C) for the reaction products.

2.4.2. Effects of Different Substrates. Different types of aldehydes (benzaldehyde, *p*-anisaldehyde, and 4-nitrobenzaldehyde) and malonitrile were applied in the catalytic reaction to evaluate the effects of the carbonyl C atom electrophilicity of the aldehydes in the reaction. In other reactions, different substrates with an active methylene group (malonitrile, acetyl acetone, and ethyl acetoacetate) along with benzaldehyde were applied in the catalytic reaction to evaluate the acidity of the active methylene group in the reaction. Some bulky aldehydes (1-naphthaldehyde and 9-anthracenecarbaldehyde) were applied to the catalytic reaction to evidence if the catalytic reaction had been conducted on the surface or in the pores of TMU-frameworks. The reaction conditions were similarly repeated for the test reaction.

2.4.3. Recyclability Test. After the catalytic reaction took place, the catalyst was recycled by centrifuging the reaction mixture followed by

Scheme 1. Structural Representation of Applied N- and O-Donor Ligands for the Construction of TMU-Frameworks







Figure 1. Green Knoevenagel condensation by TMU-frameworks. (a) Solvent-free conditions. (b) In the presence of water as a solvent.

filtration, washing with DMF (3 × 3 mL), and then dried overnight in a 80 °C preheated oven and reused five times for a recyclability test. The filtrated solution was subjected to GC analysis after any cycle.

3. RESULTS AND DISCUSSION

3.1. Synthesis and Structural Informations. The nanopowder of TMU-frameworks has been sonochemically synthesized using an O-donor H₂OBA ligand, Zn^{2+} metal ions, and related N-donor ligands, $[Zn(OBA)(BPDB)_{0.5}]_n \cdot 2DMF$ (TMU-4) by BPDB, $[Zn(OBA)(BPDH)_{0.5}]_n \cdot 1.5DMF$ (TMU-5) by BPDH, $[Zn(OBA)(H_2DPT)_{0.5}]_n \cdot DMF$ (TMU-34) by H₂DPT, and $[Zn(OBA)(DPT)_{0.5}]_n \cdot DMF$ (TMU-34(-2H)) by DPT (Scheme 1).¹²

TMU-4 and TMU-34 are developed on the basis of the deprotonation of H₂OBA oxygen-donor ligands and the coordination of Zn²⁺ metal centers in nonsymmetrical and distorted Zn#1–Zn#2 tetrahedral and square-planar geometries.^{12,26} The 2D sheets based on OBA²⁻ and Zn²⁺ building blocks are connected together using an azine functionalized N-donor BPDB ligand for TMU-4 and a dihydro-tetrazine functionalized N-donor H₂DPT ligand for TMU-34 to form 3D frameworks with a one-dimensional pore. On the basis of crystallographic data, the theoretical maximum open pore sizes (TMOPS)²⁷ of azine decorated pores of TMU-4 and dihydro-tetrazine pores of TMU-34 are 10.8 Å × 10.7 Å and 10.8 Å ×





10.5 Å (including van der Waals radius), respectively (Scheme 2).

The three-dimensional frameworks of TMU-5 and TMU-34(-2H) contain 3D interconnected pores, which are developed through the linking of paddle-wheel-based Zn-OBA 2D sheets by BPDH and DPT N-donor pillar spacers, respectively.^{26,28} The TMOPS of azine-methyl decorated TMU-5 and tetrazine decorated TMU-34(-2H) are 9.1 Å × 9.6 Å and 9.8 Å × 11.1 Å (including van der Waals radius), respectively (Scheme 2).

3.2. Knoevenagel Condensation. 3.2.1. Evaluation of Catalytic Activity of TMU-Frameworks. Applied TMU-frameworks are decorated with N-containing Lewis basic functions, so we applied them in a basic catalyzed Knoevenagel reaction to examine the effects of Lewis basicity and the function accessibility of azine and tetrazine functional groups. Since in many cases amine decorated MOFs are applied in catalyzed Knoevenagel reactions,²⁹ this study is beneficial in providing information about the effects of azine and tetrazine functional groups in Knoevenagel reactions. On the other hand, because of the stability of TMU-frameworks in water, green conditions (water as solvent or solvent-free conditions) were used. Therefore, in order to follow sustainable development and green chemistry principles, we applied TMU-4, TMU-5, TMU-34, and TMU-34(-2H) as heterogeneous basic organocatalysts in exclusively green catalysis conditions.

The results of test reactions with benzaldehyde and malonitrile in water and solvent-free conditions are illustrated in Figure 1. It is clear from Figure 1 that (I) the different functionality and Lewis basicity of TMU-frameworks lead to different conversions in an aqueous medium and solvent-free conditions and (II) the conversion data in water are much better for all four TMU-frameworks than for those conducted in solvent-free conditions. Therefore, it is necessary to clarify the synergic relationship between Lewis basic activity of TMU- frameworks and the reactivity of water molecules in the Knoevenagel reaction mechanism.

3.2.2. Proposed Catalytic Mechanism. Knoevenagel condensation is a basic catalyzed reaction between an aldehyde or ketone and a compound with an active methylene group such as malonitrile. Depending on the nature and strength of the basic catalyst, different mechanisms have been proposed.²⁹ Generally for a strong base, the catalytic mechanism progresses through the abstraction of acidic H atoms from active methylene compounds. In the case of moderately or weakly basic catalysis, the catalytic mechanism originates from the interaction of basic sites with benzaldehyde and activation of aldehyde or ketone followed by the addition of a methylene compound.³⁰

It is reported that in Knoevenagel condensation by amine decorated MOFs, benzaldehyde can be activated through the interaction with an amine group and the formation of imine through a new (amine)N=C(benzaldehyde) covalent bond that can be followed by the rearrangement and addition of malonitrile.

However, such a proposed mechanism is not useful in the case of benzaldehyde activation by TMU-frameworks because these frameworks contain azine and tetrazine functional groups, which lack $-NH_2$ groups. So, TMU-MOFs cannot activate benzaldehyde through the formation of imine. Instead of this, we propose that benzaldehyde can be activated through a noncovalent Lewis base—acid interaction between the azine and tetrazine groups of TMU-MOFs with the carbonyl C atom of benzaldehyde. Considering the Lewis basic strength of azine and tetrazine TMU-MOFs, the proposed catalytic mechanism is based on the activation of aldehyde and then on the addition of a methylene compound. Moreover, on the basis of Figure 1, it is clear that water molecules as a solvent have effective roles in accelerating the reaction rate and reactant activation.

In our proposed mechanism, the benzaldehyde carbonyl C atom is activated through a noncovalent Lewis base-acid interaction with the azine and tetrazine organocatalytic sites of

TMU-frameworks, and the benzaldehyde carbonyl O atom is activated through hydrogen bonding with the H atoms of water molecules (Scheme 3).

On the basis of Figure 1 it is clear that TMU-5 and TMU-34 frameworks display higher conversions in comparison to the related isostructure frameworks in water and solvent-free conditions. This phenomenon is acceptable through considering the different functionality and Lewis basicity of TMU-frameworks.

In two isostructural frameworks, TMU-5 and TMU-34-(-2H), with 3D interconnected pores, TMU-5 reaches maximum conversion (>99%) just after 30 min but TMU-34(-2H) reaches 60% conversion after 30 min. This significant difference in conversion yield and time is based on the different Lewis basicity of azine-methyl groups of TMU-5 and tetrazine groups of TMU-34(-2H). TMU-5 is functionalized with azine groups containing two adjacent N atoms with free nonbonding electrons (NBEs), which are not engaged with other parts of the framework through secondary interactions. These NBEs of the adjacent two N atoms improve the Lewis basic reactivity of azine groups inside the pores of TMU-5 through a lone pair-lone pair repulsion, which comes from an electrostatic interaction between NBEs in sp²-hybridized orbitals (filled-filled orbital interaction).^{31,32} Additionally, electron-donor methyl groups improve the basicity of azine groups.³³ However, in the case of TMU-34(-2H), each of the N atoms of s-tetrazine has one electron that directly participates in the aromatic π -system and another in the pair of NBEs. In the series of N-heterocyclic azines with an increasing number of electronegative N atoms, the electron density on N atoms is reduced, and N atoms are more electron-deficient.³⁴ Moreover, tetrazines are compounds having a deep color ranging from purple to orange to red because of the $n-\pi^*$ transition located in the visible spectrum. Therefore, due to the electron deficiency of s-tetrazine N atoms and the participation of N atoms' NBEs in the $n-\pi^*$ transition and the aromatic π -system, their basicity and therefore their coordination ability are poor.^{35,36} So, tetrazine functions of TMU-34(-2H) display lower Lewis basicity than the azinemethyl function of TMU-5. Therefore, TMU-5 is a stronger Lewis base in the Knoevenagel reaction.

In the case of the other isostructural MOFs with 1D pores, TMU-4 and TMU-34, the latter shows a higher conversion in water and solvent-free conditions (>99% conversion vs 57% conversion after 60 min). As a result, TMU-34 is a stronger base in the Knoevenagel reaction. In contradiction to TMU-34(-2H), the NBEs of the four N atoms of dihydro-tetrazine functions inside the pores of TMU-34 are not engaged in aromaticity, and they are localized. Also, the azine group of TMU-4 contains two sp²-hybridized nitrogen atoms, but the dihydro-tetrazine groups of TMU-34 contain two sp³hybridized nitrogen atoms (similar to amine) and two sp²hybridized nitrogen atoms (similar to azine). Therefore, owing to the simultaneous similarity between dihydro-tetrazine Lewis basic nitrogen atoms inside the pores of TMU-34 with azine and amine groups, it is possible that the dihydro-tetrazine functions inside the pores of TMU-34 are more effective in accelerating Knoevenagel condensation than the azine groups inside the pores of TMU-4.

Benzaldehyde activation by TMU-5 and TMU-34 is conducted through the noncovalent interactions between NBEs of nitrogen atoms related to azine and dihydro-tetrazine functions with a π^* -orbital related to the carbonyl C atom of benzaldehyde. In this condition, the benzaldehyde π -(CO) bond became ready for dissociation and the carbonyl C atom is highly electron deficient, which prepares it for nucelophilic addition by malonitrile and the formation of a new C–C bond (Scheme 3).

In the presence of water molecules, the solvent conversion (%) for all TMU-frameworks is higher than in the presence of solvent-free conditions (Figure 1). Obviously using water as a green, polar, and protic solvent has very important effects on the reaction mechanism. Repeatedly, it is reported that some 3d metals like Zn(II) and Cu(II) centers are effective in these kind of reactions by activation of the carbonyl group of an aldehyde through interactions with the oxygen atom of a carbonyl through a Lewis acid (3d metal)—base (benzaldehyde) interaction.^{37–40} However, in green and metal-free conditions, the H atom of water molecules can activate the aldehyde through aldehyde (C=O)…(H) water hydrogen bonding (Scheme 3).

Therefore, in the presence of TMU-5 and TMU-34 in water, the activation of an aldehyde can be done with two different methods: (I) through aldehyde (O=C)...(N) azine or dihydrotetrazine Lewis acid-base interactions and (II) through aldehyde (C=O)...(H) water molecule hydrogen bonding (Scheme 3). These two noncovalent interactions can activate benzaldehyde for the addition of malonitrile and subsequent product synthesis. The advantage of this mechanism is that it can be extended to a large variety of nitrogen-containing groups such as azine, azo, amide, and imidazole, not just the primary amines.

As a control experiment, we applied pristine azine-methyl functionalized BPDH and dihydro-tetrazine functionalized H₂DPT ligands to compare their Lewis basicity with TMU-5 and TMU-34. Equivalent molar quantities of BPDH and H_2DPT ligands (0.008 g) are applied to 5 cm³ of water at reaction conditions. BPDH and H₂DPT ligands are not soluble in water, and they act as a heterogeneous catalyst in water. The results show that after 60 min, conversion (%) reaches 55% and 40% for BPDH and H₂DPT, respectively, which reveals that TMU-5 and TMU-34 are more efficient catalysts than their pristine functional ligands. This is because TMU-frameworks and pristine ligands are heterogeneous, but TMU-frameworks contain Lewis basic functional pores that can act as Lewis basic nanoreactors. In these pores, the collision probability and interactions between reactants and catalytic sites increase resulting in maximum conversion and TON.

3.2.3. Further Investigation of the Reaction Mechanism. To prove the effects of functionality and Lewis basicity strength, we applied a linker exchange procedure. For each group of isostructural TMU-frameworks, the framework with weaker Lewis basicity transformed to the framework with stronger Lewis basicity by exchanging the functional pillar ligand. In this line, tetrazine decorated TMU-34(-2H) was transformed to azine-methyl functionalized TMU-5 through a linker exchange procedure (section 1, Supporting Information), and azine decorated TMU-4 was transformed to dihydro-tetrazine incorporated TMU-34. The results clearly show that as the ratio of azine-methyl and dihydro-tetrazine functional group increases, the reaction conversion (%) increases. These experiments can serve as an approval for our hypothesis that the Lewis basicity of a functional pillar is a determining factor in catalytic reaction progress.

3.2.4. More Details about Solvent Effects. The mechanism of Knoevenagel reactions is based on the formation of a charged transition-state intermediate,⁴¹ so water molecules, because of their amphoteric nature, hydrogen bond donor–acceptor properties, and high polarity, are effective in methylene group

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activation, carbonyl group activation, and stabilization of charged intermediates, respectively. In addition to these benefits and easy accessibility of water, using water as a solvent in catalytic reactions is completely in line with green chemistry principles. However, usually MOFs suffer from insufficient stability in water, and this is a challenging problem for using MOFs in green synthesis conditions. Fortunately, TMU-5 and TMU-34 are stable in catalytic conditions in water even after five cycles (section 3.2.6).

3.2.5. Catalyst Filtration Test. In order to gain direct observations, a filtration test was conducted between benzaldehyde and malonitrile in water at room temperature and atmospheric pressure. After the reaction progressed for 15 min, the catalysts, including TMU-5 and TMU-34, were separated by filtration. The filtrate was further stirred at the same conditions, and the composition was monitored at given time intervals (20, 25, 30, 45, and 60 min). The results for the reaction solution before and after catalyst filtration are displayed in Figure 2. There is no remarkable progress in the reaction after



Figure 2. Diagram related to the filtration tests of TMU-frameworks.

the catalyst filtration step, which indicates that no active functional ligands were leached into the liquid phase, and the presence of TMU-34 and TMU-5 as basic heterogeneous organocatalysts is essential for reaction progress.

3.2.6. Influence of Different Substrates on Knoevenagel Condensation. After observing the results of Knoevenagel condensation with TMU-34 and TMU-5, we extended our study to the use of different types of substituted aldehyde and methylene-containing compounds.

Substituted aldehydes, including p-anisaldehyde and 4nitrobenzaldehyde, were applied in a reaction with malonitrile to evaluate the roles of electron deficiency in the carbonyl C atom of aldehydes (Table 1). We had chosen these aldehyde substrates because they contain different types of substituents (the electron donating $(-OCH_3)$ substituent in *p*-anisaldehyde and the electron withdrawing $(-NO_2)$ substituent in 4nitrobenzaldehyde), which provide situations that help us investigate the effects of substitution on the electron deficiency of the carbonyl C atom of aldehyde and its activation by TMU-5 and TMU-34 basic catalysts. Table 1 shows that locating the electron withdrawing nitro group on benzaldehyde leads to maximum conversion (>99%) in shorter times. However, in the case of the electron donating methoxy group, maximum conversion is reached in longer times. This observation is apparent for both TMU-5 and TMU-34 frameworks, which clearly represent the positive and negative effects of electron withdrawing and donating groups in the Knoevenagel reaction in polar and amphoteric aqueous reaction media. The presence of electron withdrawing groups on the phenyl ring amplifies the electron deficiency and positive charge on the carbonyl C atom, which increases with interactions between the aldehyde C atom and the azine or tetrazine basic organocatalyst sites. Therefore, a better activation of aldehydes leads to maximum conversion in shorter times.

Benzaldehyde and different types of methylene-containing compounds, such as acetyl acetone, ethyl acetoacetate, and malonitrile, were applied to examine the effects of methylene group pK_a . Table 2 shows that a higher pK_a leads to a longer



Table 1. Effects of Aldehyde Substitution on Knoevenagel Condensation Conversion

TON means turnover number, mole numbers of limiting reagent per mole of catalytic azine and tetrazine sites.





*TON means turnover number, moles of benzaldehyde per mole of catalytic azine and tetrazine sites. $**pK_a$ in water.





^{*}TON means turnover number, moles of benzaldehyde per mole of catalytic azine and tetrazine sites.

maximum conversion time. So, on the basis of Table 2, we can determine that the acidity of the methylene group has positive effects on the catalyzed Knoevenagel reaction by TMU-5 and TMU-34. It seems that the higher acidity of methylene group makes the addition of a methylene compound to aldehyde (and molecular rearrangement through deprotonation of the methylene group to yield the product) easier after the activation of benzaldehyde by TMU-organocatalysts.

To understand whether the reaction is performed on the surface or inside the pores, some bulky aldehydes (1-naphthaldehyde (5.6 Å \times 7.5 Å), 9-anthracenecarbaldehyde

 $(9.6 \text{ Å} \times 6.4 \text{ Å}))$ substrates were used. It is clear that if the reaction was performed on the surface, an increase in size and dimensionality of the reactants will not have much of an effect on the reaction conversion. However, if the reaction was carried out inside the pores, an increase in the size and dimensionality of the reactants, due to greater difficulty in penetration to inside the cavities, will cause noticeable changes to the reaction conversion. Table 3 reveals that with an increase in the volume of the aldehyde substrate, the reaction conversion is noticeably reduced. Therefore, it can be concluded that the reaction is carried out in the pores and functionalized pores with azine-

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Figure 3. PXRD patterns of (a) TMU-5 and (b) TMU-34 frameworks in Knoevenagel condensation.



Figure 4. N₂ adsorption of (a) TMU-5 and (b) TMU-34 frameworks in Knoevenagel condensation.



Figure 5. FT-IR spectroscopy of (a) TMU-5 and (b) TMU-34 frameworks in Knoevenagel condensation.

methyl groups in TMU-5 and dihydro-tetrazine in TMU-34 act as Lewis basic nanoreactors in this reaction.

3.2.7. Stability and Reusability of TMU-Frameworks in Knoevenagel Condensation. One of the most important characteristics of MOFs as heterogeneous catalysts is their stability in reaction conditions. Although water is accessible and the greenest solvent for catalytic applications, many MOFs suffer from insufficient stability in water. Therefore, many MOFs are applied as catalysts in Knoevenagel condensation in conventional solvents, which are not in accordance with green synthesis roles.

For the evaluation of the stability of TMU-5 and TMU-34 after catalytic reaction, experiments have been conducted, and the results reveal that both frameworks retain their crystallinity on the basis of PXRD analysis (Figure 3), porosity on the basis of N₂ adsorption experiments (Figure 4), and functionality on the basis of FT-IR spectroscopy (Figure 5) after five cycles of catalytic tests.

The reusability test shows that there is not a significant change in the catalytic activity of TMU-5 and TMU-34 frameworks after five catalytic tests in Knoevenagel condensation (Figure 6). These results show that TMU-34 and especially TMU-5 are very



Figure 6. Reusability of (a) TMU-5 after 30 min and (b) TMU-34 after 60 min in Knoevenagel condensation.

Table 4. Comparison of Thio-5 and Thio-54 with Other MOT-Dased Catalysis in Denzauenyde and Matomutie Condens	Table 4. (Comparison of TM	MU-5 and TMU-34 with	Other MOF-Based Catal	ysts in Benzaldehy	de and Malonitrile Conde	nsation
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catalyst	function	solvent	temp (°C)*	time (min)	conversion (%)	ref.
TMU-5	azine-methyl	water	rt	30	>99	42
TMU-34	dihydro-tetrazine	water	rt	60	>99	this work
MIL-101(Cr)-ED	ethylene diamine	cyclohexane	80	30	90	43
NH ₂ -MIL-101(Al)	primary amine	toluene	80	30	61	30
NH ₂ -UiO-66	primary amine	toluene	23	120	5	44
ZIF-8	imidazolate	toluene	rt	360	91	45
Pb(cpna) ₂ ·2DMF·6H ₂ O	amide	acetonitrile	rt	1440	>99	46
Cu ₃ TATAT-3	triazine	acetonitrile	75	720	95	47
$Cd_2(Lglu)_2(bpe)_3(H_2O){\cdot}2H_2O$	amine	methanol	rt	360	>99	48
TMU-55	azine-methyl	water	rt	5	99	49
HTMU-55	azine	water	rt	5	87	49
*rt means room temperature.						

good candidates for real life use as heterogeneous basic catalysts in Knoevenagel condensation.

3.2.8. Comparison with Other MOF-Based Catalysts in Knoevenagel Condensation. Although there are large numbers of MOFs containing Lewis basic sites like amine, triazine, and amine as catalysts in Knoevenagel condensation, normally they are applied in conventional solvents that are not green. However, we compared the conversion percentage and time with other MOFs (Table 4) to show the basic capabilities of azine and tetrazine groups in green Knoevenagel condensation and the quite dispersible nature and stability of TMU-5 and TMU-34 in water.

Here, considering the aforementioned points such as (I) the polar/protic catalyzed nature of Knoevenagel reaction, (II) the stability of TMU-frameworks in aqueous solution, and (III) following the principles of green chemistry, we applied TMU-5 and TMU-34 as effective basic heterogeneous organocatalysts in green, mild, and fast Knoevenagel condensation.

4. CONCLUSION

In this work we synthesized some TMU-frameworks by a sonication method, and among them, TMU-5 and TMU-34 show good Lewis basicity as heterogeneous basic organocatalytic sites in the Knoevenagel reaction. We clarified that the improved basicity of an azine-methyl decorated TMU-5 and a dihydro-tetrazine decorated TMU-34 is useful for the activation of benzaldehyde. On the other hand, water molecules are effective in activating benzaldehyde through hydrogen bonding. After the activation of the carbonyl group of benzaldehyde by Lewis basic organocatalytic sites and water molecules, a methylene-containing substrate can be added to aldehyde to rearrange and yield the product under green (water as solvent) and mild (room temperature and atmospheric pressure) conditions. Maximum conversions are achieved in a very short amount of time while being subjected to green conditions, which is very rare in the literature. Recyclability and stability tests show that TMU-5 and TMU-34 can be applied to the Knoevenagel reaction for at least five cycles while retaining crystallinity, porosity, and functionality.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorg-chem.9b01819.

Tables for time-dependent exchange data and reaction conversion data for exchanged frameworks (PDF)

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REFERENCES

(1) Anastas, P.; Eghbali, N. Green chemistry: principles and practice. *Chem. Soc. Rev.* **2010**, *39*, 301–312.

(2) Anastas, P. T.; Kirchhoff, M. M. Origins, current status, and future challenges of green chemistry. *Acc. Chem. Res.* **2002**, *35*, 686–694.

(3) Li, C.-J.; Trost, B. M. Green chemistry for chemical synthesis. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 13197–13202.

(4) Byrne, F. P.; Jin, S.; Paggiola, G.; Petchey, T. H. M.; Clark, J. H.; Farmer, T. J.; Hunt, A. J.; Robert McElroy, C.; Sherwood, J. Tools and techniques for solvent selection: green solvent selection guides. *Sustainable Chem. Processes* **2016**, *4*, 7.

(5) Shaikh, I. R. Organocatalysis: Key Trends in Green Synthetic Chemistry, Challenges, Scope towards Heterogenization, and Importance from Research and Industrial Point of View. *J. Catal.* **2014**, 2014, 1.

(6) Dalko, P. I.; Moisan, L. In the golden age of organocatalysis. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138–5175.

(7) MacMillan, D. W. The advent and development of organocatalysis. *Nature* **2008**, 455, 304.

(8) List, B. Introduction: organocatalysis. *Chemical Reviews* **2007**, *107* (12), 5413–5415, DOI: 10.1021/cr078412e.

(9) James, S. L. Metal-organic frameworks. *Chem. Soc. Rev.* 2003, 32, 276–288.

(10) Masoomi, M. Y.; Morsali, A.; Dhakshinamoorthy, A.; García, H. Mixed-Metal MOFs: Unique Opportunities in Metal-organic Framework Functionality and Design. *Angew. Chem.* **2019**, *131* (43), 15330. (11) Ali Akbar Razavi, S.; Morsali, A. Linker functionalized metal-

organic frameworks. Coord. Chem. Rev. 2019, 399, 213023.

(12) Razavi, S. A. A.; Masoomi, M. Y.; Islamoglu, T.; Morsali, A.; Xu, Y.; Hupp, J. T.; Farha, O. K.; Wang, J.; Junk, P. C. Improvement of Methane–Framework Interaction by Controlling Pore Size and Functionality of Pillared MOFs. *Inorg. Chem.* **2017**, *56*, 2581–2588.

(13) Razavi, S. A. A.; Masoomi, M. Y.; Morsali, A. Double Solvent Sensing Method for Improving Sensitivity and Accuracy of Hg (II) Detection Based on Different Signal Transduction of a Tetrazine-Functionalized Pillared Metal–Organic Framework. *Inorg. Chem.* **2017**, *56*, 9646–9652.

(14) Razavi, S. A. A.; Masoomi, M. Y.; Morsali, A. Stimuli-Responsive MOF with Chemo-Switchable Properties for Colorimetric Detection of CHCl3. *Chem. - Eur. J.* **2017**, *23*, 12559–12564.

(15) Razavi, S. A. A.; Masoomi, M. Y.; Morsali, A. J. I. c. Host–Guest Interaction Optimization through Cavity Functionalization for Ultra-Fast and Efficient Water Purification by a Metal–Organic Framework. *Inorg. Chem.* **2018**, *57*, 11578–11587.

(16) Razavi, S. A. A.; Masoomi, M. Y.; Morsali, A. Ultrasonic assisted synthesis of a tetrazine functionalized MOF and its application in colorimetric detection of phenylhydrazine. *Ultrason. Sonochem.* **2017**, 37, 502–508.

(17) Razavi, S. A. A.; Masoomi, M. Y.; Morsali, A. Morphologydependent sensing performance of dihydro-tetrazine functionalized MOF toward Al (III). *Ultrason. Sonochem.* **2018**, *41*, 17–26.

(18) Morozan, A.; Jaouen, F. Metal organic frameworks for electrochemical applications. *Energy Environ. Sci.* **2012**, *5*, 9269–9290.

(19) Imaz, I.; Rubio-Martinez, M.; An, J.; Sole-Font, I.; Rosi, N. L.; Maspoch, D. Metal-biomolecule frameworks (MBioFs). *Chem. Commun.* **2011**, 47, 7287–7302.

(20) Li, Y.; Xu, H.; Ouyang, S.; Ye, J. Metal-organic frameworks for photocatalysis. *Phys. Chem. Chem. Phys.* **2016**, *18*, 7563–7572.

(21) Wang, C.-C.; Li, J.-R.; Lv, X.-L.; Zhang, Y.-Q.; Guo, G. Photocatalytic organic pollutants degradation in metal–organic frameworks. *Energy Environ. Sci.* **2014**, *7*, 2831–2867.

(22) Li, B.; Wen, H. M.; Cui, Y.; Zhou, W.; Qian, G.; Chen, B. Emerging multifunctional metal-organic framework materials. *Adv. Mater.* **2016**, *28*, 8819–8860.

(23) Liu, J.; Chen, L.; Cui, H.; Zhang, J.; Zhang, L.; Su, C.-Y. Applications of metal-organic frameworks in heterogeneous supramolecular catalysis. *Chem. Soc. Rev.* **2014**, *43*, 6011–6061. (24) Corma, A.; García, H.; Llabrés i Xamena, F. Engineering metal organic frameworks for heterogeneous catalysis. *Chem. Rev.* **2010**, *110*, 4606–4655.

(25) Huang, Y.-B.; Liang, J.; Wang, X.-S.; Cao, R. Multifunctional metal-organic framework catalysts: synergistic catalysis and tandem reactions. *Chem. Soc. Rev.* **2017**, *46*, 126–157.

(26) Masoomi, M. Y.; Stylianou, K. C.; Morsali, A.; Retailleau, P.; Maspoch, D. Selective CO2 capture in metal–organic frameworks with azine-functionalized pores generated by mechanosynthesis. *Cryst. Growth Des.* **2014**, *14*, 2092–2096.

(27) Cadiau, A.; Adil, K.; Bhatt, P.; Belmabkhout, Y.; Eddaoudi, M. A metal-organic framework–based splitter for separating propylene from propane. *Science* **2016**, 353, 137–140.

(28) Li, J.; Peng, Y.; Liang, H.; Yu, Y.; Xin, B.; Li, G.; Shi, Z.; Feng, S. Solvothermal Synthesis and Structural Characterisation of Metal-Organic Frameworks with Paddle-Wheel Zinc Carboxylate Clusters and Mixed Ligands. *Eur. J. Inorg. Chem.* **2011**, 2011, 2712–2719.

(29) Zhu, L.; Liu, X.-Q.; Jiang, H.-L.; Sun, L.-B. Metal-organic frameworks for heterogeneous basic catalysis. *Chem. Rev.* 2017, 117, 8129-8176.

(30) Hartmann, M.; Fischer, M. Amino-functionalized basic catalysts with MIL-101 structure. *Microporous Mesoporous Mater.* **2012**, *164*, 38–43.

(31) Fina, N. J.; Edwards, J. O. The alpha effect. Int. J. Chem. Kinet. 1973, 5, 1–26.

(32) Jencks, W. P.; Carriuolo, J. Reactivity of nucleophilic reagents toward esters. J. Am. Chem. Soc. **1960**, 82, 1778–1786.

(33) Carey, F. A.; Sundberg, R. J. Advanced Organic Chemistry, Part A: Structure and Mechanisms, 5th ed.; Springer Science & Business Media: 2007.

(34) Vogiatzis, K. D.; Mavrandonakis, A.; Klopper, W.; Froudakis, G. E. Ab initio study of the interactions between CO2 and N-containing organic heterocycles. *ChemPhysChem* **2009**, *10*, 374–383.

(35) Kaim, W. The coordination chemistry of 1, 2, 4, 5-tetrazines. *Coord. Chem. Rev.* **2002**, 230, 127–139.

(36) Clavier, G.; Audebert, P. s-Tetrazines as building blocks for new functional molecules and molecular materials. *Chem. Rev.* **2010**, *110*, 3299–3314.

(37) Zhang, G.; Yashima, E.; Woggon, W. D. Versatile Supramolecular Copper (II) Complexes for Henry and Aza-Henry Reactions. *Adv. Synth. Catal.* **2009**, *351*, 1255–1262.

(38) Paul, A.; Karmakar, A.; Guedes da Silva, M. F. C.; Pombeiro, A. J. L. Amide functionalized metal—organic frameworks for diastereoselective nitroaldol (Henry) reaction in aqueous medium. *RSC Adv.* **2015**, *5*, 87400–87410.

(39) Karmakar, A.; Oliver, C. L.; Roy, S.; Öhrström, L. The synthesis, structure, topology and catalytic application of a novel cubane-based copper (II) metal–organic framework derived from a flexible amido tripodal acid. *Dalton Trans.* **2015**, *44*, 10156–10165.

(40) Karmakar, A.; Guedes da Silva, M. F. C.; Pombeiro, A. J. L. Zinc metal–organic frameworks: efficient catalysts for the diastereoselective Henry reaction and transesterification. *Dalton Trans.* **2014**, *43*, 7795–7810.

(41) Jones, G. The K noevenagel Condensation. *Organic reactions* **2011**, *15*, 204–599.

(42) Masoomi, M. Y.; Beheshti, S.; Morsali, A. Mechanosynthesis of new azine-functionalized Zn (II) metal–organic frameworks for improved catalytic performance. *J. Mater. Chem. A* **2014**, *2*, 16863–16866.

(43) Hwang, Y. K.; Hong, D. Y.; Chang, J. S.; Jhung, S. H.; Seo, Y. K.; Kim, J.; Vimont, A.; Daturi, M.; Serre, C.; Férey, G. Amine grafting on coordinatively unsaturated metal centers of MOFs: consequences for catalysis and metal encapsulation. *Angew. Chem.* **2008**, *120*, 4212– 4216.

(44) Luan, Y.; Qi, Y.; Gao, H.; Andriamitantsoa, R. S.; Zheng, N.; Wang, G. A general post-synthetic modification approach of aminotagged metal–organic frameworks to access efficient catalysts for the Knoevenagel condensation reaction. *J. Mater. Chem. A* **2015**, *3*, 17320– 17331. (45) Tran, U. P.; Le, K. K.; Phan, N. T. Expanding applications of metal– organic frameworks: zeolite imidazolate framework ZIF-8 as an efficient heterogeneous catalyst for the knoevenagel reaction. *ACS Catal.* **2011**, *1*, 120–127.

(46) Lin, X.-M.; Li, T.-T.; Chen, L.-F.; Zhang, L.; Su, C.-Y. Two ligand-functionalized Pb (II) metal–organic frameworks: structures and catalytic performances. *Dalton Trans.* **2012**, *41*, 10422–10429.

(47) Miao, Z.; Luan, Y.; Qi, C.; Ramella, D. The synthesis of a bifunctional copper metal organic framework and its application in the aerobic oxidation/Knoevenagel condensation sequential reaction. *Dalton Trans.* **2016**, *45*, 13917–13924.

(48) Ugale, B.; Dhankhar, S. S.; Nagaraja, C. Construction of 3D homochiral metal-organic frameworks (MOFs) of Cd (ii): selective CO 2 adsorption and catalytic properties for the Knoevenagel and Henry reaction. *Inorg. Chem. Front.* **2017**, *4*, 348–359.

(49) Joharian, M.; Morsali, A.; Azhdari Tehrani, A.; Carlucci, L.; Proserpio, D. M. Water-stable fluorinated metal-organic frameworks (F-MOFs) with hydrophobic properties as efficient and highly active heterogeneous catalysts in aqueous solution. *Green Chem.* **2018**, *20*, 5336–5345.