Iran J Sci Technol Trans Sci (2018) 42:219–235
https://doi.org/10.1007/s40995-018-0495-y

RESEARCH PAPER

Copper Zirconium Phosphate as an Efficient Catalyst for Multi-component Reactions in Solvent-Free Conditions

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Received: 4 December 2015 / Accepted: 25 January 2016 / Published online: 29 January 2018
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Abstract
Copper zirconium phosphate nanoparticles were used as a convenient and efficient catalyst for multi-component reactions in solvent-free conditions. The catalyst is easy to prepare and shows interesting catalytic properties. The catalyst was characterized by some instrumental techniques such as ICP-OES, EDS, XRD, BET, NH_3-TPD, Py-FTIR, SEM, and TEM. These analyses revealed that the interlayer distance in the catalyst increased from 7.6 to 8.8 Å when Cu^{2+} was intercalated between the layers, whereas the crystallinity of the material was reduced. The steric and electronic properties of the different substrates had a significant influence on the reaction conditions. These protocols have the advantages of inexpensive materials, mild reaction conditions, excellent yields, short reaction times, and simple and clean work-up. This work introduces a new application of this catalyst, not described in the literature up to now. In addition, the catalyst can be recovered and reused for three times without a significant loss in its activity and selectivity.

Keywords Copper zirconium phosphate · Heterogeneous catalysis · Solvent-free · Nanoparticle and multi-component reactions

1 Introduction

Multi-component reactions (MCRs) are those reactions in which three or more reactants come together in a single reaction vessel to form a new product which contains portions of all the components. They have been known for over 150 years (Rotstein et al. 2014). In an MCR, there is a network of reaction equilibria, which all finally flow into an irreversible step yielding the product. MCRs have been proven to be extremely successful in producing molecular complexity in a single synthetic operation, and shown simple procedures, high atom economy, and high selectivity due to the formation of carbon–carbon and carbon–heteroatom bonds in one-pot. The challenge is to conduct an MCR in such a way that the network of pre-equilibrated reactions channel into the main product and do not yield side-products. The result is clearly dependent on the reaction conditions: solvent, temperature, catalyst, concentration, the kind of starting materials, and functional groups. Such considerations are of particular importance in connection with the design and discovery of novel MCRs (Rotstein et al. 2014; Slobbe et al. 2012).

Since heterocyclic compounds are commonly used in different fields of sciences and technology, the preparation of these compounds is an important part of synthetic organic chemistry. 3,4-dihydropyrimidin-2(1H)-ones (DHPMs) and their derivatives are one of the most important classes of MCRs products due to their wide range of biological and pharmacological properties such as antihypertensive, antiviral, antibacterial, anticancer, antitumor, anti-inflammatory agents, α_{1a}-antagonists, neuropeptide Y antagonists, and integral backbones of several calcium channel blockers (Gartner et al. 2005; Nasr-Esfahani et al. 2011; Niknam et al. 2007). The most straightforward procedure for the preparation of dihydropyrimidinones is the one-pot condensation of aldehydes with β-ketoester and urea under acidic conditions (Biginelli reaction). The great potential of DHPMs in pharmaceutical fields has accordingly triggered growing interest in their synthetic study. To improve the Biginelli

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Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40995-018-0495-y) contains supplementary material, which is available to authorized users.

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reaction conditions, various catalysts and reaction conditions have been studied such as $Fe_3O_4@SiO_2@Et\text{-}PhSO_3H$ (Mobaraki et al. 2014), $KAl(SO_4)_2{\cdot}12H_2O$ (Azizian et al. 2006), SBSSA (Tajbakhsh et al. 2012), $NH_4H_2PO_4/SiO_2$ (Tayebee et al. 2012), $Ce(SO_4)_2{\cdot}4H_2O$ (Davoodnia et al. 2014), $PhICl_2$ (Tale et al. 2013), sulfonated carbon (Moghaddas et al. 2012), $SnCl_2$/nano SiO_2 (Safaei Ghomi et al. 2013), Im-MNPs (Nazari et al. 2013), PFPAT (Khaksar et al. 2012), TSILs (Fang et al. 2010), $Cu(OAc)_2$ (Kathing et al. 2014), citric acid (Ghorbani-Choghamarani et al. 2013), SiO_2–$NaHSO_4$ (Chari and Syamasundar 2004), $NaHCO_3$/MW (Kefayati et al. 2015), $Cu(OTf)_2$ (Pasunooti et al. 2011), Nano-γ-$Fe_2O_3eSO_3H$ (Kolvari et al. 2014), ZBFBSB (Wang et al. 2015), β-cyclodextrin (Liberto et al. 2013), $Zn(OAc)_2$ (Karamat et al. 2010), ethylene glycol (Imtiaz et al. 2012), vitamin B_1 (Lei et al. 2010), SiO_2–$CuCl_2$ (Kour et al. 2014), SBNPSA (Jetti et al. 2014), PS-$PEGOSO_3H$ (Quan et al. 2011), $KHSO_4$ (Tu et al. 2004a, b), AMA (Sharghi and Jokar 2009), $H_5PW_{10}V_2O_{40}$/PipSBA-15 (Tayebee et al. 2013), SiO_2–$SnCl_4$, and SiO_2–$TiCl_4$ (Niknam et al. 2010).

As another important MCR, synthesis of 2-aminopyridine derivatives attracted enormous attention due to their wide applications. The N-heteroaromatic pyridine is prevalent in numerous natural products, pharmaceuticals, and functional materials, and is extremely important in the chemistry of biological systems. Among these compounds, 2-amino-3-cyanopyridine derivatives have been reported to possess remarkable pharmacological properties and activities such as antiviral, anticancer, antitubercular, antimicrobial, A_{2A} adenosine receptor antagonists, anticardiovascular, analgesic, kinase inhibitors, IKK-b inhibitors, carbonic anhydrase inhibitors, and fungicidal activities (Ayvaz et al. 2013; Movassaghi et al. 2007; Sarda et al. 2009). Moreover, 2-amino-3-cyanopyridines are highly reactive compounds. They are extensively utilized as reactant or reaction intermediates, because the cyanofunction of these compounds is suitably situated with common mono or bidentates to form a variety of heterocyclic compounds (Gouda et al. 2013). Therefore, the synthesis of these compounds continues to attract interest in organic chemistry. Various preparation methods for the synthesis of 2-amino-3-cyanopyridines have been reported such as $[EtNH_3]NO_3$ (Sarda et al. 2009), MWI (Gouda et al. 2013; Shi et al. 2005), $Yb(PFO)_3$ (Tang et al. 2011), $FePO_4$ (Zadpour and Behbahani 2015), TBBDA (Ghorbani-Vaghei et al. 2013), $Ti(dpm)(NMe_2)_2$ (Dissanayake et al. 2014), $[Bmim][BF_4]$ (Mansoor et al. 2012), cellulose–SO_3H (Mansoor et al. 2014), ultrasonic irradiation (Gupta et al. 2010; Safari et al. 2012), SBTETASA (Niknam et al. 2012), trifluoroethanol (Khaksar and Yaghoobi 2012), $[HO_3S(CH_2)_4MIM][HSO_4]$ (Davoodnia et al. 2011), PDTAS (Niknam et al. 2013), and also multiple step procedure using amino acid and refluxing (Girgis et al. 2004).

α-Zirconium phosphate (ZP) is one of the most important compounds in inorganic chemistry, and the layered structure of this material has been used in a variety of different fields (Gan et al. 2014; Sun et al. 2007). The layered structure of ZP consists of zirconium ions in a semiplanar arrangement, located slightly above and below the mean plane, while each Zr^{4+} ion is connected through the oxygen atoms of phosphate groups from above and below. Three of the four oxygen atoms in the phosphate groups are bonded to three different zirconium atoms. The fourth oxygen atom of the phosphate groups that bonds to a proton, the free –OH group, is pointing into the interlayer region (Chen et al. 2010; Sun et al. 2007). ZP behaves as a unique ion exchanger because of its exceptionally poor aqueous solubility, high thermal stability, resistance to radiation, and abrasive properties (Alhendawi 2014; Naik et al. 2010; Shi et al. 2011). The H^+ of the P–OH moiety in ZP can be exchanged for various other ions, which results in the enlargement of the interlayer distance (Cai et al. 2012; Dai et al. 2012; Yang et al. 2011). Several studies pertaining to the successful exchange of the H^+ of the P–OH group in ZP with various divalent and trivalent cations have been reported in the literature (Allulli et al. 1976; Clearfield and Kalnins 1976; Giannoccaro et al. 2005; Khare and Chokhare 2012). It has also been reported that ZP possesses excellent selectivity towards Pb^{2+}, Zn^{2+}, and Fe^{3+} as an ion exchanger (Dash et al. 2015; Zhang et al. 2015). Furthermore, ZP has been reported to exhibit antibacterial activity when it was loaded with Cu^{2+}, Zn^{2+}, or Ce^{3+} (Cai et al. 2012; Dai et al. 2012; Shi et al. 2011; Yang et al. 2011). Several reports have also appeared in the literature concerning the catalytic activities of ion exchanged materials of this type, including the use of zinc zirconium phosphate (ZPZn) as catalyst in the acetylation of alcohols and phenols and the use of zirconium phosphate–ferric chloride complex and potassium iron zirconium phosphate as catalyst in Friedel–Crafts reaction (1981; Alhendawi et al. 2014; Gawande et al. 2005; Karimi 2015a, b; Khare et al. 2015; Liu et al. 2015).

With growing environmental concerns, use of green and insoluble catalysts or of ecofriendly solvent-free conditions is more demanded. When an insoluble catalyst is used, it can be easily recovered from the reaction mixture by simple filtration and recycled and can be reused several times, making the process more economically and environmentally viable. Furthermore, the reported examples have demonstrated that heterogeneous catalysts typically require easier work-up procedures. With this in mind, and as part of ongoing work towards the development of efficient green catalysts for organic transformations, herein, the use of copper zirconium phosphate (ZPCu) as an efficient catalyst for the mild and convenient two MCRs is reported. This catalyst was characterized by ICP-OES, EDS, XRD, BET, NH_3-TPD, Py-FTIR, SEM, and TEM.

2 Experimental

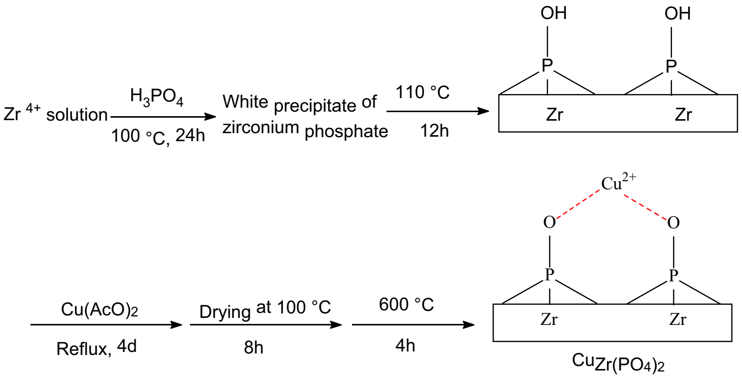
The chemical composition of the ZPCu catalyst was evaluated at different stages of the reaction (i.e., before and after the catalytic reaction) by ICP-OES using an Optima 7300 V ICP-OES spectrometer (PerkinElmer). The samples were ground into a fine powder and analyzed by XRD on a Philips X'pert X-ray diffractometer. The specific surface areas of the samples were determined from their N_2 adsorption–desorption isotherms using the Brunauer–Emmett–Teller (BET) method on a Quantachrome ChemBET 3000 instrument. Each sample was degassed at 400 °C for 2 h before being analyzed to remove any adsorbed species from their surfaces. Total acidity of the samples was determined by temperature-programmed desorption of ammonia (TPD-NH_3) with a Quantachrome ChemBET 3000. Before the adsorption of ammonia, the samples were pre-treated in He at 250 °C for 30 min and then, 1 h at 350 °C and cooled to 100 °C. Then ammonia was adsorbed on the samples for 1 h. The TPD-NH_3 was carried out between 150 and 550 °C, at 10 °C min^{-1}, and analyzed by a thermal conductivity detector (TCD) for continuous monitoring of the desorbed ammonia. Pyridine adsorption was used to determine the acidic sites using FTIR. Prior to the measurements, 20 mg of a catalyst was pressed in self-supporting disc and activated in the IR cell attached to a vacuum line at 350 °C for 4 h. The adsorption of pyridine was performed at 150 °C for 30 min. The excess of probe molecules was further evacuated at 150 °C for 0.5 h. The adsorption–evacuation was repeated several times until no changes in the spectra were observed. The surface morphologies of the α-ZP and ZPCu materials were studied by SEM on a Philips XL scabbing electron microscope (Philips). TEM images of ZPCu were obtained on CENTRA 100 TEM system (Zeiss). The FTIR spectroscopic measurements were carried out using a JASCO FT/IR (680 plus) spectrophotometer. The spectra were recorded in the range 400–4000 cm^{-1} using a KBr technique. The Melting points were measured on an Electrothermal IA9100 apparatus and are uncorrected. ^1H NMR spectra were recorded on Bruker-Avance 400 MHz spectrometers. The spectra were measured in $CDCl_3$ or DMSO-d_6, relative to TMS (0.00 ppm).

2.1 Catalyst Synthesis

The catalyst was prepared according to previously published procedures, with minor modifications (Allulli et al. 1976; Clearfield and Kalnins 1976; Khare and Chokhare 2012; Sun et al. 2007). ZP was prepared according to the following procedure. $ZrOCl_2{\bullet}8H_2O$ (5 g) was heated at reflux in a solution of H_3PO_4 (50 cm^3, 12 mol L^{-1}) for 24 h. The resulting mixture was cooled to ambient temperature to give a suspension, which was filtered, and the filter cake was then washed with a solution of H_3PO_4 (0.1 mol L^{-1}) until the filtrate was free of chloride ions. The filter cake was then washed several times with distilled water until the pH of the filtrate was neutral. The solid was then collected and dried in an oven at 110 °C for 12 h (Sun et al. 2007). ZPCu was prepared through an ion-exchange reaction (Allulli et al. 1976; Clearfield and Kalnins 1976; Khare and Chokhare 2012). Briefly, ZP (3 g) was dispersed in deionized water (50 cm^3) at 50 °C, and the resulting suspension was treated with a solution of $Cu(OAc)_2$ (100 cm^3, 0.1 mol L^{-1}) in water (excess amount of Cu^{2+}). This mixture was then heated at reflux for 4 days. It is noteworthy that the acetate ion performed effectively as a base to keep the hydrogen ion concentration in solution sufficiently low to achieve high loadings of the catalyst. A complete exchange between the cations and the hydrogen ions of the P–OH groups could not be achieved in less than 3 days or at temperatures below 80 °C (Yang et al. 2011). The resulting slurry was filtered hot to give a light white solid, which was washed with distilled water until no Cu^{2+} ions could be detected in the filtrate (i.e., until the filtrate was colorless). The solid product was then dried at 100 °C for 8 h before being calcined at 600 °C for 4 h to give the final product, ZPCu, as a pale green solid (Scheme 1).

2.2 General Procedure for the Preparation of DHPMs

A mixture of aldehydes (1 mmol), EAA (1 mmol,), urea or thiourea (1.1 mmol), and catalyst (1 mol%) was stirred at 80 °C in oil bath under solvent-free conditions for the specified time. The completion of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature, and then, cool water was added and stirred for 5 min. The crude product was collected by filtration and washed with ice-cold water. The residue was dissolved in a minimum amount of hot EtOH and then cooled to room temperature to afford the pure product. The catalyst was insoluble by filtration. All products are known compounds and were characterized by comparing their M.p, IR, and ^1H NMR spectra with those found in the literature (Kolvari et al. 2014; Liberto et al. 2013; Pasunooti et al. 2011; Wang et al. 2015).



Scheme 1 Summarized procedure for ZPCu preparation

2.3 General Procedure for the Preparation of 2-Amino-3-Cyanopyridines

A mixture of aldehyde (1 mmol), ketone (1 mmol), malononitrile (1 mmol), ammonium acetate (2 mmol), and catalyst (1.5 mol%) were stirred in one-pot at 60 °C for the appropriate time. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was washed with EtOH and the catalyst was removed. The corresponding pure solid product was obtained through recrystallized from hot EtOH affording the 2-amino-3-cyanopyridine derivatives. All products are known compounds and were characterized by comparing their M.p, IR, and ^{1}H NMR spectra with those found in the literature (Gupta et al. 2010; Mansoor et al. 2012, 2014; Niknam et al. 2012; Safari et al. 2012).

2.4 Recyclability Studies of Catalyst

To examine the recyclability of the catalyst, the used ZPCu was recovered from the reaction media and reused. For recycling, after the first use, the catalyst was separated from the reaction mixture by centrifugation, washed sequentially with ethanol and water before being dried at 110 °C for 2 h, and then activated at 450 °C for 2 h. The catalyst regeneration procedure in both mentioned MCRs is quite the same; hence, to shorten the manuscript, only the data of regenerated ZPCu in the synthesis of DHPMs are represented.

3 Results and Discussion

3.1 Characterization

The EDS and ICP-OES analyses of ZP and ZPCu are shown in Table 1 and Fig. 1. The results obtained in the current study for ZPCu were compared with those reported previously in the literature (Allulli et al. 1976; Clearfield and Kalnins 1976; Khare and Chokhare 2012). Our results revealed that there was a negligible leach of copper ions into the reaction media after the reaction (i.e., following the first use of the catalyst).

Figure 2 shows the powder XRD patterns of the ZP and ZPCu materials. The results show some characteristic reflections in the 2θ range of 5°–40°. The diffraction peak in ZP at $2\theta \sim 12°$ was assigned to a d002 basal spacing of 7.6 Å between the planes, which was consistent with the patterns previously reported for ZP and its derivatives with a hexagonal crystal system (Sun et al. 2007). It shows that the d-spacing of the (002) plane of ZPCu had increased, which indicated that the Cu^{2+} ions had intercalated into the interlayer of ZP and increased the d_{002} basal interlamellar spacing of ZP from 7.6 to 8.8 Å. It is well known that the ion radii of Cu^{2+} (0.72 Å) and hydrated Cu^{2+} (4.19 Å) are smaller than the basal spacing of ZP (7.5 Å) (Liu et al. 2009). These results, therefore, indicated that Cu^{2+} ions had inserted into the interlayer of ZP and increased the basal spacing of the modified ZP after the exchange (Allulli et al. 1976; Clearfield and Kalnins 1976; Khare and Chokhare 2012). Taken together, these data indicated that ZPCu had been formed successfully. The XRD pattern of the ZPCu catalyst after the seventh run showed that the basal spacing of ZP was about 8.5 Å, which was only a little larger than that of the fresh ZPCu catalyst. This increase may have occurred because of the presence of less Cu^{2+} on the surface of ZP, and an increase in the number of water molecules between the layers following the seventh run (i.e., Cu^{2+} ions may have been washed off during the regeneration of the catalyst, Table 1).

Figure 3 shows the N_2 adsorption–desorption isotherm of ZPCu, as a representative example, in the relative pressure range (p/p_0) of 0.01–1.0. The surface area of ZPCu was determined to be 121.6 m^2 g^{-1}. The isotherm

Table 1 Element contents of ZPCu (atm.%) and physical properties of the catalysts before and after reaction

Sample	Cu	O	Zr	P	BET ($m^2\ g^{-1}$)	Total acidity (mmol $NH_3\ g^{-1}$)
ZP	–	65.3	12.4	22.3	72.8	2.3
ZPCu[a]	12.7	54.4	11.8	21.1	–	–
ZPCu	12.5	54.1	12.1	21.3	121.6	1.9
ZPCu[b]	12.3	54.2	12.1	21.4	120.7	1.75
ZPCu[c]	4.2	63.8	12.2	19.8	72.3	0.71

[a] From EDS analysis

[b] After the first cycle

[c] After the seventh cycle

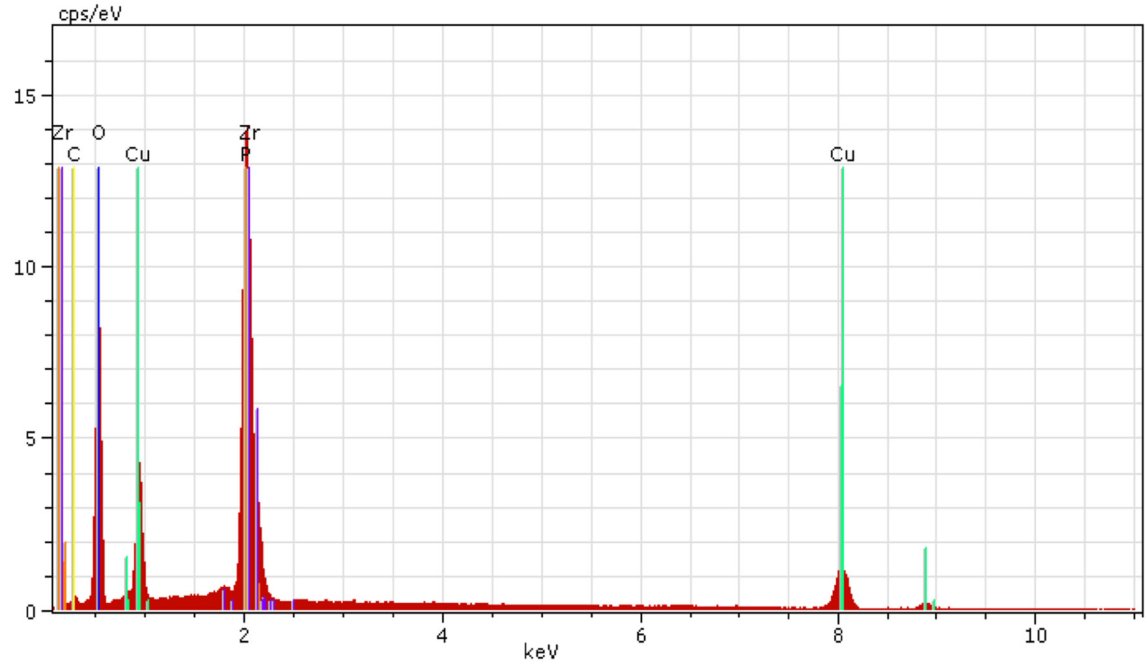


Fig. 1 EDS spectra of ZPCu

for ZPCu shows three adsorption stages. The first of these stages was observed at $p/p_0 < 0.44$, whereas the second stage was observed in the range of $0.37 < p/p_0 < 0.98$, and the third stage was observed at higher relative pressures ($p/p_0 > 0.98$). The N_2 adsorption–desorption isotherm of ZPCu exhibited a typical "type IV" isotherm shape with a distinct hysteresis loop, which is characteristic of a mesoporous material (Sing 1985). The hysteresis loop (type H3) is associated with the occurrence of capillary condensation in the mesopores, which indicates the presence of a mesoporous structure in the ZPCu catalyst. The observed increase in adsorption at the higher p/p_0 value indicated the presence of larger mesopores in the sample (Karimi 2015a). The surface area of ZPCu after the seventh run was found to be 72.3 $m^2\ g^{-1}$.

Pyridine adsorption was used to determine the acidic sites using FTIR. The main bands observed over the samples are assigned according to the literature data (Tyagi et al. 2006). Pyridine desorbed FTIR spectra of the ZPCu shows the strong bands at 1632 and 1541 cm^{-1}, indicating typical pyridinium ion. The band at 1488 cm^{-1} is a combination band between those at 1541 and 1444 cm^{-1}, corresponding to Brønsted and Lewis acid sites, respectively. Figure 3b shows the Py-FTIR spectra of the catalyst after the seventh run. It clearly represents that due to the replacement of Cu^{2+} on the surface of the catalyst with H^+ during the catalyst regeneration process, the Lewis acid sites are reduced (bant at 1444 cm^{-1} was reduced). On the other hand, the amount of Bronsted acid sites was increased (bant at 1632 cm^{-1} was reduced) (Fig. 4).

Total acidity of the samples was determined by temperature-programmed desorption of ammonia (TPD-NH_3) with a Quantachrome ChemBET 3000. TPD-NH_3 provides a quantitative estimation of the total number of acid sites

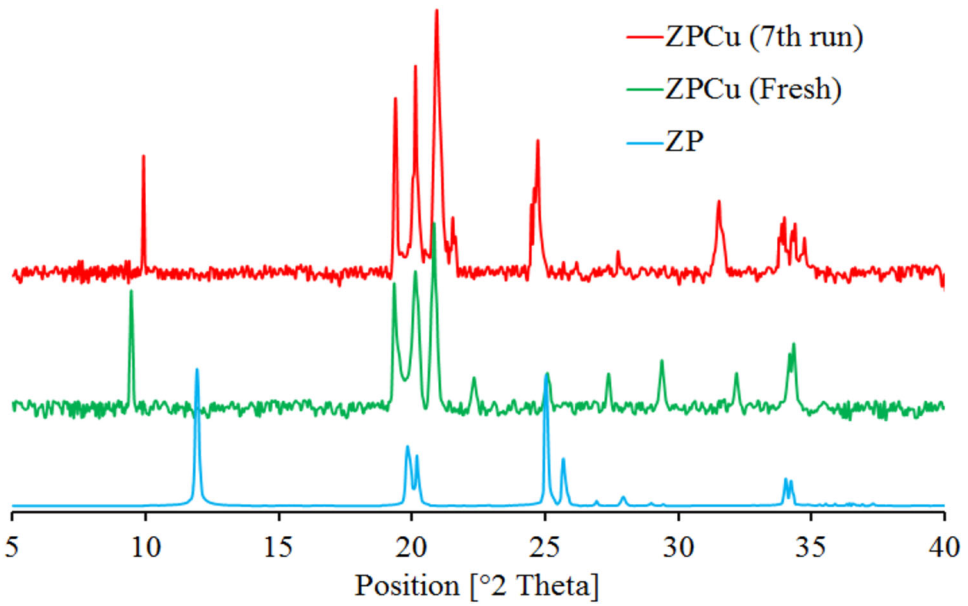


Fig. 2 XRD patterns of powder ZP (down), ZPCu fresh (middle), and ZPCu after the seventh run (up)

and the distribution of acid strengths. Because of the strong basicity of NH_3 gas, it was expected that all acid sites on the catalysts interact with NH_3. The total amount of NH_3 desorbed after saturation permits the quantification of the number of acid sites on the surface, while the position of the peak, desorption temperature, indicates the strength of the catalyst, i.e., the higher temperature of desorption, the stronger the acid strength (Karimi 2015a). The TPD-NH_3 curves of ZPCu are shown in Fig. 5. The ZPCu desorbed ammonia in a wide range of temperatures from 237 to 631 °C, which mostly corresponds to the medium and the strong acidic sites.

The NH_3 desorption peak at temperatures below 250 °C belongs to the physisorption/chemisorptions of NH_3

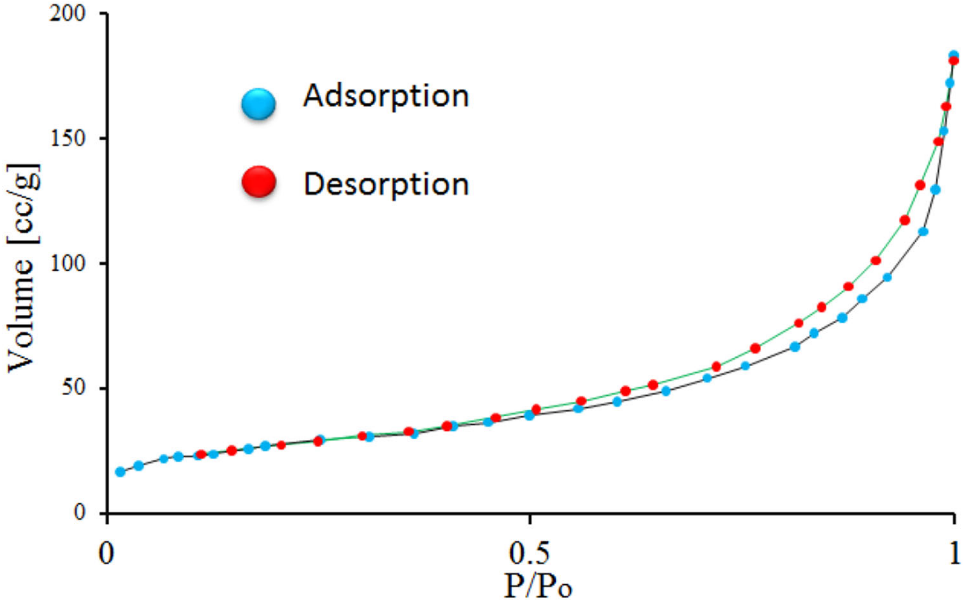


Fig. 3 N_2 adsorption–desorption isotherm of ZPCu

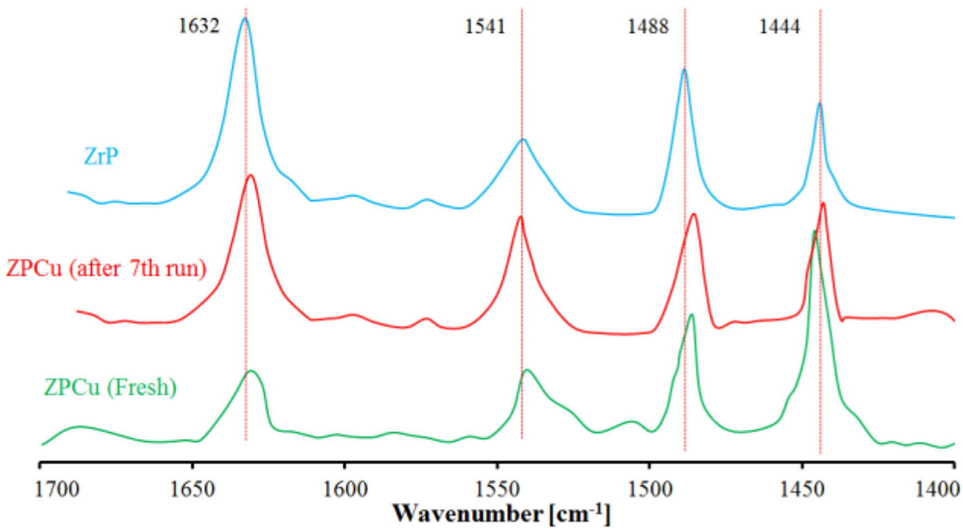


Fig. 4 Pyridine-desorbed FTIR spectra of ZP (up), ZPCu fresh (down), and ZPCu after the seventh run (middle)

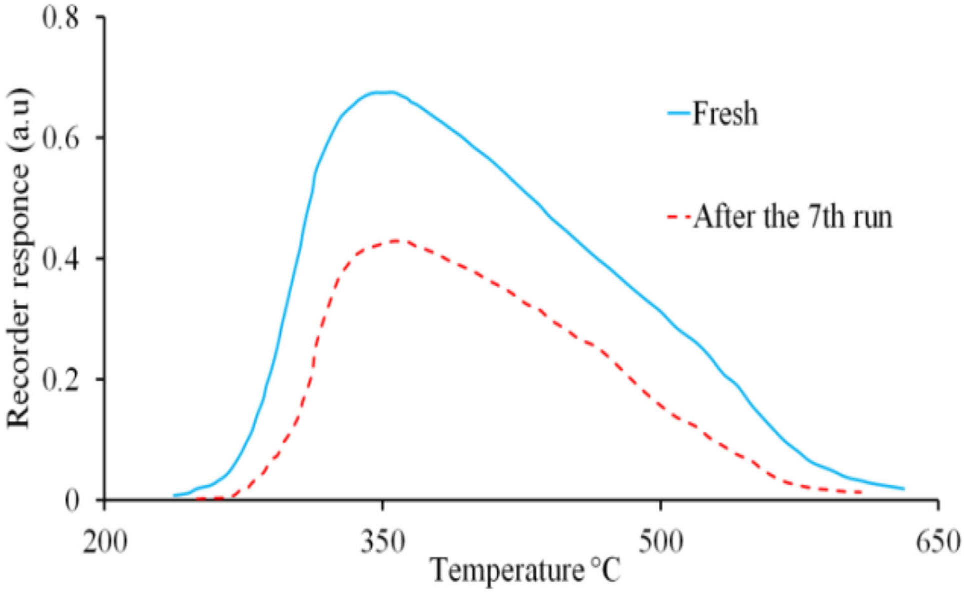


Fig. 5 NH_3-TPD profile of ZPCu

molecules on weak acidic sites. The peak at about 250–450 °C shows the existence of intermediate strength acidic sites, and finally, the peak at 450–538 °C demonstrates the presence of strong acidic sites on the surface of ZPCu. Figure 5 shows that the desorption of ammonia starts at almost 237 °C, centered at 350. The NH_3-TPD curves subsequently decreased with further increase in temperature and almost complete at 631 °C. This indicates that ZPCu contains a considerable number of acid sites which is attributed to the presence of Cu^{2+} groups on the surface of zirconium phosphate layers and make it suitable solid acid catalyst. The extent of desorptions is found to be ca. 1.9 mmol NH_3 g^{-1} of catalyst. A TPD experiment was carried out after the seventh cycle by recovering the catalyst, to magnify the difference from the fresh catalysts (Table 1).

The SEM image of ZP (Fig. 6a) revealed the presence of hexagonal plates with well-defined shapes and very smooth surfaces. Figure 6b, c shows the SEM images of ZPCu. These images revealed that the structure of ZPCu was much less ordered than that of ZP, and that the ZPCu

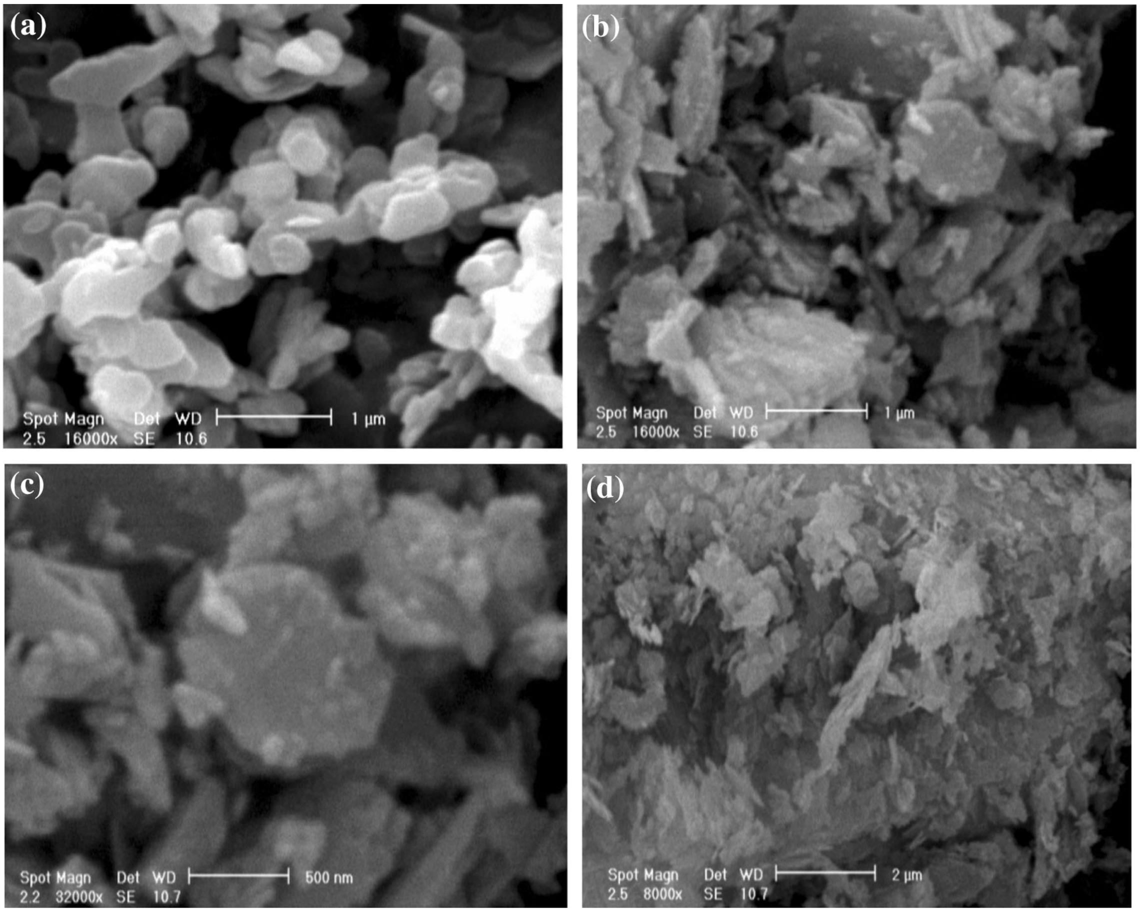


Fig. 6 SEM images of regular morphology of prepared **a** ZP, **b**, **c** ZPCu fresh, and **d** after the seventh run

particles had aggregated to form both sheets and spheres of different shapes and sizes.

Figure 7 shows the TEM images of ZPCu. It shows that ZPCu catalyst retained the original morphology of ZP (layered structure) and that the particles were approximately 150 nm in size. These images also showed nanoparticles of different sizes on the smooth surface of the ZP. The presence of metallic crystal nanoparticles on the surface of ZP indicated that the copper deposited on the surface of the ZP had agglomerated. Similar observations have also been reported for zinc and cerium with ZP (Cai et al. 2012; Dai et al. 2012).

Figures 6d and 7d show the SEM and TEM images of the catalyst following its seventh run, respectively. Both of these images showed that the sheets and particles had conglomerated to a much greater extent following the seventh run because of the process used to regenerate the catalyst.

3.2 Synthesis of DHPMs

To obtain the best reaction conditions, the reaction of benzaldehyde (1 mmol), ethyl acetoacetate (EAA) (1 mmol), and urea (1.1 mmol) was examined as a simple model under different conditions (Table 2). The reaction was carried out in various solvents as well as solvent-free conditions (Table 2, entries 1–8). As it is shown, under these conditions (Table 2, entries 1–7), the reactions were sluggish and low-to-moderate yields were obtained in the tested solvents. For this reaction, it proceeded most readily to give the highest yield of the product (**1a**) under solvent-free conditions (Table 2, entry 8). The yield and time were markedly influenced by the reaction temperature. Increasing the reaction temperature up to 80 °C enhanced the yield and reduced the required time, below 80 °C, the reaction proceeded slowly giving a relatively low yield, and no improvement was observed above 80 °C (Table 2, entries 9–13). The excess amount of the catalyst (Table 2, entries 14–16), or more reaction time (Table 2, entries 17–20) did not sharply influence the yield of the reaction, but decreasing them reduced the yield. In the absence of catalyst, the reaction failed to give the desired product even after prolonging reaction time (Table 2, entry 21). Hence, the best result was obtained when the reaction was carried

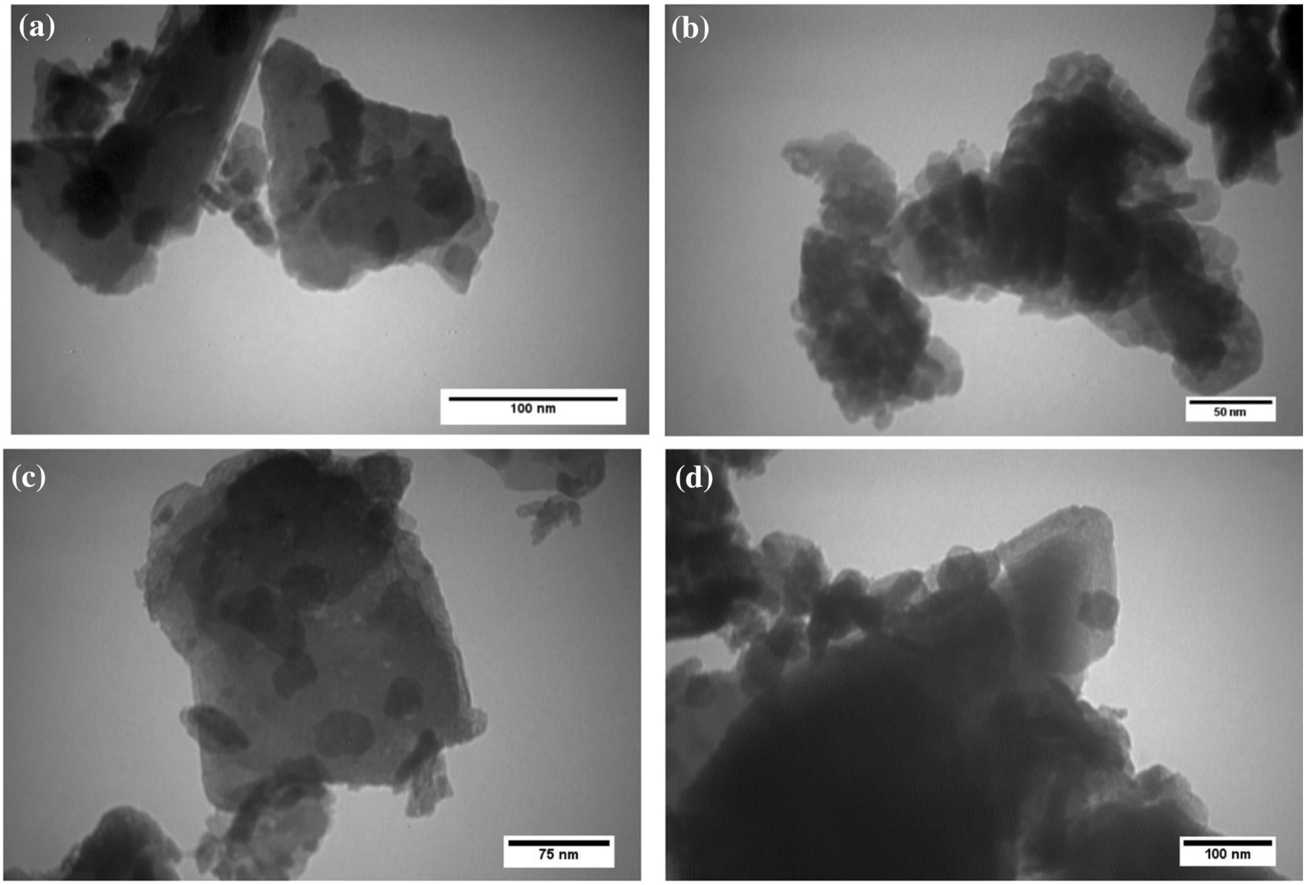


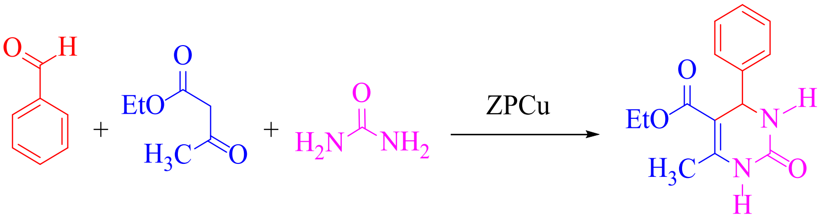
Fig. 7 TEM images of regular morphology of prepared **a**–**c** ZPCu fresh (different magnification) and **d** after the seventh run

out at 80 °C using 1 mol% of ZPCu under solvent-free conditions (Table 2, entry 8).

After optimization the reaction conditions, the generality of the procedure for the Biginelli adducts was investigated with various aldehydes, urea, or thiourea. A library of substituted DHPMs was obtained in good-to-excellent yields in appropriate reaction times under solvent-free conditions (Table 3). As demonstrated in Table 3, aromatic aldehydes bearing either electron-donating (ED) or electron-withdrawing (EW) groups were reacted easily to produce the corresponding DHPMs in good-to-excellent yields, and no undesirable side-products were observed. Interestingly, the condensation protocol was fairly general, and using this procedure, various functional groups survived during the course of the reaction. Furthermore, the conditions are mild enough to perform this reaction with acid-sensitive aldehydes such as furfuraldehyde and cinnamaldehyde (Table 3, entries 18 and 19) without the formation of any side-products, which are normally observed either in the presence of protic or Lewis acids. The aromatic aldehydes with EW substituents (Table 3, entries 6–17) were converted to the related DHPM derivatives in shorter reaction times than those with ED substituents (Table 3, entries 2–5). However, when aliphatic aldehydes (Table 3, entries 19–21) were used as the starting materials, the yield dropped significantly because of the lower activity of the carbonyl group in aliphatic aldehydes or due to decomposition or polymerization (Chari and Syamasundar 2004). In addition, the steric effects did show significant effect on the yields and reaction times. For example, ortho-substituted aromatic aldehydes (Table 3, entries 3, 6, 11, 15) with more steric hindrance gave lower yields in comparison to para-substituted (Table 3, entries 5, 8, 13, 17). It is noteworthy that the methodology was also successful when urea replaced with thiourea and the yields of the related products were fair (Table 3, entries 22–26).

Based on this results and previous reports (Moghaddas et al. 2012; Nasr-Esfahani et al. 2011; Safaei Ghomi et al. 2013; Tayebee et al. 2012), a plausible reaction mechanism for this synthesis is represented (Supplementary information, Scheme S1). To explore the advantages of this ZPCu-catalyzed reaction, the results of the present method under the optimized conditions were compared with those

Table 2 Reaction between urea, EAA, and benzaldehyde under different conditions



Entry	Solvent	Catalyst (mol%)	Temperature (°C)	Time (min)	Yield (%)[a]
1	CH_3CN	1	Reflux	90	61
2	*n*-Hexane	1	Reflux	90	28
3	Toluene	1	Reflux	90	35
4	THF	1	Reflux	90	55
5	CH_2Cl_2	1	Reflux	90	43
6	EtOH	1	Reflux	90	46
7	Et_2O	1	Reflux	90	16
8	Solvent-free	1	80	20	91
9	Solvent-free	1	50	60	34
10	Solvent-free	1	60	60	41
11	Solvent-free	1	70	40	67
12	Solvent-free	1	90	20	91
13	Solvent-free	1	100	20	92
14	Solvent-free	0.5	80	45	62
15	Solvent-free	3	80	20	92
16	Solvent-free	5	80	20	92
17	Solvent-free	1	80	5	32
18	Solvent-free	1	80	10	44
19	Solvent-free	1	80	15	71
20	Solvent-free	1	80	30	92
21[b]	Solvent-free	–	80	120	Trace

The reaction was carried out in 5 cm^3 of solvent

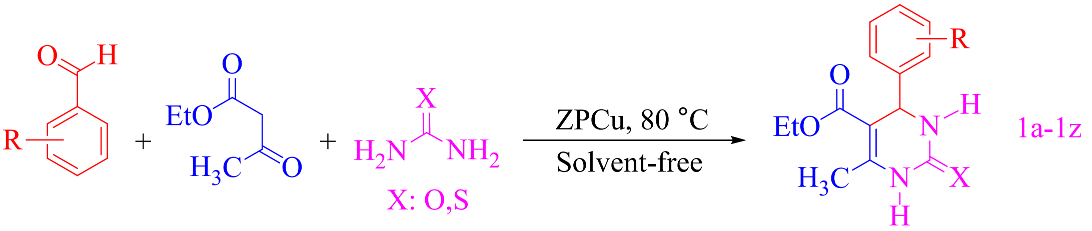
[a] The yields refer to the isolated pure products

[b] The reaction was carried out in the absence of ZPCu

reported in the literature for Biginelli reactions mediated by other catalysts (Table 4). Although some of the other catalysts gave marginally higher conversions, however, they required longer reaction time, higher temperature, and a higher amount of catalyst. The present method used a small amount (1 mol%) of an environmentally friendly catalyst under solvent-free conditions and required a relatively short reaction time. In addition, the ZPCu catalyst was easily separated from the reaction mixture after work-up and used several times.

The reusability of the catalyst was also investigated with the same model reaction under the optimized conditions. Upon completion of the reaction, the catalyst was recovered according to the procedure described in the experimental section and reused. As shown in Table 5, during the recycling experiment with fresh reactants, under the same reaction conditions, no considerable change in the activity of the catalyst was observed for at least six consecutive runs which clearly demonstrate the stability of the catalyst for these conditions in the Biginelli reaction.

Table 3 Synthesis of DHPMs using ZPCu under solvent-free conditions



Entry	Aldehyde	X	Product	Time (min)	Yield (%)	M.p^{a}	
						Found	Reported
1	C_6H_5CHO	O	1a	20	91	201–202	202–204
2	4-Me-C_6H_4CHO	O	1b	30	85	210–213	213–215
3	2-MeO-C_6H_4CHO	O	1c	40	84	257–259	259–260
4	3-MeO-C_6H_4CHO	O	1d	30	87	217–219	220–221
5	4-MeO-C_6H_4CHO	O	1e	40	83	203–205	202–204
6	2-Cl-C_6H_4CHO	O	1f	15	91	215–217	214–216
7	3-Cl-C_6H_4CHO	O	1g	10	93	192–194	190–193
8	4-Cl-C_6H_4CHO	O	1h	10	95	213–214	210–212
9	2,4-di-Cl-C_6H_4CHO	O	1i	20	90	249–251	248–250
10	2,6-di-Cl-C_6H_4CHO	O	1j	30	86	235–237	234–236
11	2-Br-C_6H_4CHO	O	1k	15	93	206–208	206–208
12	3-Br-C_6H_4CHO	O	1l	10	94	185–187	187–189
13	4-Br-C_6H_4CHO	O	1m	10	95	219–221	209–211
14	4-F-C_6H_4CHO	O	1n	10	95	185–187	184–186
15	2-NO_2-C_6H_4CHO	O	1o	20	91	221–223	223–224
16	3-NO_2-C_6H_4CHO	O	1p	10	93	226–228	270–272
17	4-NO_2-C_6H_4CHO	O	1q	10	95	207–209	205–206
18	2-Furyl	O	1r	30	82	201–202	201–202
19	$C_6H_5CH = CHCHO$	O	1s	30	88	230–231	228–230
20	$CH_3CH_2CH_2CHO$	O	1t	45	85	177–179	176–178
21	$(CH_3)_2CHCHO$	O	1u	45	81	190–192	191–193
22	C_6H_5CHO	S	1v	45	86	206–208	208–210
23	4-Me-C_6H_4CHO	S	1w	45	82	190–192	192–194
24	4-MeO-C_6H_4CHO	S	1x	45	80	148–150	150–152
25	4-Cl-C_6H_4CHO	S	1y	30	88	193–195	192–193
26	3-NO_2-C_6H_4CHO	S	1z	30	89	205–207	206–208

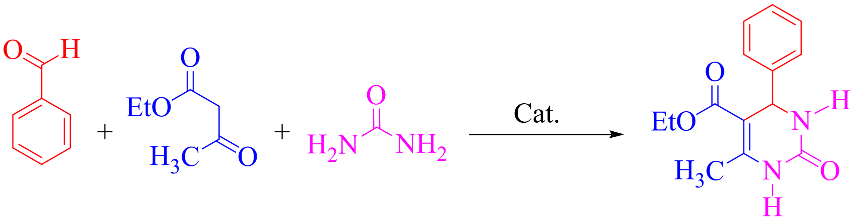
All products were characterized by M.p, IR, and ^{1}H NMR spectral data and comparison with those of authentic samples or reported data

[a] Isolated yield

3.3 Synthesis of 2-Amino-3-Cyanopyridines

To find out the suitable conditions for the reaction, a series of experiments were performed for the synthesis of 2-amino-4,6-diphenylnicotinonitrile (**2a**) as a model compound (Table 6). The reaction was performed in various solvents to identify the best solvent condition. Several classic solvents such as EtOH, MeOH, CH_3CN, H_2O, DMF, *n*-hexane, $CHCl_3$, THF, 1,4-dioxane, toluene, and also solvent-free conditions were examined. The experimental results showed that the yield of the product is higher under solvent-free conditions (Table 6, entry 11). To

Table 4 Comparison of efficiency of various catalysts in synthesis of (**1a**)



Entry	Catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]	References
1	$Ca(HSO_4)_2$	Solvent-free	90	30	80	Niknam et al. (2007)
2	$Zn(HSO_4)_2$	Solvent-free	90	150	74	Niknam et al. (2007)
3	Oxone	Solvent-free	90	30	75	Niknam et al. (2007)
4	Fe_3O_4-NPs	Solvent-free	80	16	90	Nasr-Esfahani et al. (2011)
5	SiO_2-$KAl(SO_4)_2$	Solvent-free	80	240	92	Azizian et al. (2006)
6	SBSSA	AcOH	110	60	81	Tajbakhsh et al. (2012)
7	$NH_4H_2PO_4$	Solvent-free	100	120	85	Tayebee et al. (2012)
8	$SnCl_2$/NPs-SiO_2	EtOH	Reflux	40	94	Safaei Ghomi et al. (2013)
9	Im-MNPs	Solvent-free	80	30	93	Nazari et al. (2013)
10	PFPAT	CH_3CN	R.T.	180	90	Khaksar et al. (2012)
11	$Cu(OAc)_2$	Solvent-free	100	5	94	Kathing et al. (2014)
12	Citric acid	EtOH	Reflux	180	90	Ghorbani et al. (2013)
13	$Cu(OTf)_2^b$	EtOH	100	60	95	Pasunooti et al. (2011)
14	$Fe_2O_3eSO_3H$ NPs[b]	Solvent-free	60	3	97	Kolvari et al. (2014)
15	ZBFBSB	Solvent-free	100	90	94	Wang et al. (2015)
16	β-Cyclodextrin	Solvent-free	100	180	85	Liberto et al. (2013)
17	α-ZrP	Solvent-free	80	60	75	This work
18	ZPCu	Solvent-free	80	20	91	This work

[a] The yields refer to the isolated pure products

[b] Microwave irradiation

Table 5 Catalyst reused for the synthesis of **1a**

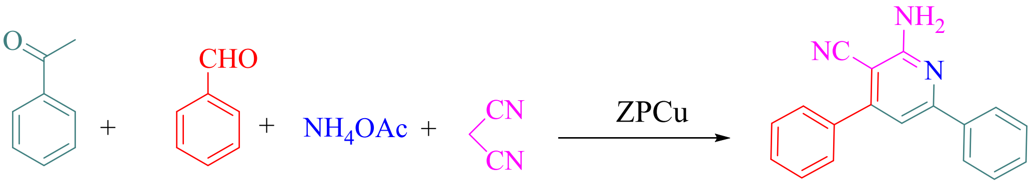
Reaction	Fress	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Run 7	Run 8
Bijinelli	91	89	89	89	88	85	83	68	41

Reaction conditions: benzaldehyde (1 mmol); EAA (1 mmol), urea (1.1 mmol); catalyst (1 mol%) at 80 °C and 20 min

further improvement of the reaction yield, five experiments in different temperatures were performed (Table 6, entries 11–15). It was observed that the application of a lower temperature gave the corresponding product in lower yield. The reaction provided little amounts of product without catalyst (Table 6, entry 20). The optimal conditions were determined as that the reaction was catalyzed by 1.5 mol% of ZPCu under solvent-free conditions at 60 °C in 60 min (Table 6, entry 11).

To delineate the scope and generality of our new protocol, this methodology was examined by the reaction of several substituted aldehydes and acetophenones (Table 7). The reaction succeeded well, providing the corresponding 2-amino-4,6-diphenylnicotinonitrile derivatives in fair-to-high yields, demonstrating the generality of the method and its well tolerance of both EW and ED substituents on the both aromatic rings. The electronic effect seemed to have a clear influence on the reaction, since the EW groups on the

Table 6 Synthesis of 2-amino-4,6-diphenylnicotinonitrile (**2a**) under different conditions



Entry	Solvent	Catalyst (mol%)	Temperature (°C)	Time (min)	Yield (%)[a]
1	EtOH	1.5	Reflux	120	71
2	H_2O	1.5	Reflux	120	Trace
3	MeOH	1.5	Reflux	120	66
4	$CHCl_3$	1.5	Reflux	120	41
5	CH_3CN	1.5	Reflux	120	45
6	THF	1.5	Reflux	120	53
7	DMF	1.5	100	120	61
8	*n*-Hexane	1.5	Reflux	120	16
9	1,4-Dioxane	1.5	Reflux	120	32
10	Toluene	1.5	Reflux	120	22
11	Solvent-free	1.5	60	60	88
12	Solvent-free	1.5	R.T.	120	Trace
13	Solvent-free	1.5	40	120	46
14	Solvent-free	1.5	80	60	88
15	Solvent-free	1.5	100	60	89
16	Solvent-free	0.5	60	90	35
17	Solvent-free	1	60	60	58
18	Solvent-free	3	60	60	72
19	Solvent-free	5	60	60	88
20[b]	Solvent-free	–	60	120	Trace

The reaction was carried out in 5 cm^3 of solvent

[a] The yields refer to the isolated pure products

[b] The reaction was carried out in the absence of ZPCu

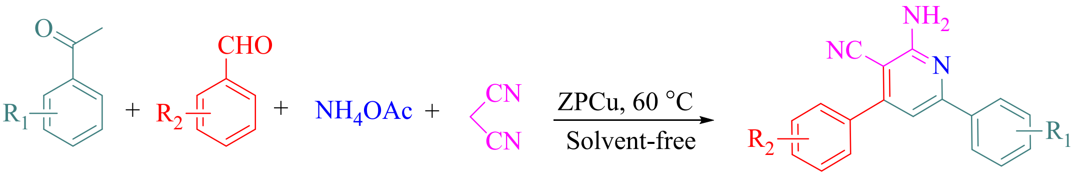
different aromatic rings resulted in better yields than ED groups. We also studied this condensation reaction with 2-substituted benzaldehyde, finding that the reaction time was longer and yields were somewhat lower than other aldehydes which were possibly attributed to the steric hindrance (Table 7, entries 4, 5). Surprisingly, the aliphatic aldehyde (hexanale) and the aliphatic ketone (acetone) gave no products. Obviously, the reactivity of aldehydes is the key factor for this one-pot transformation.

Based on this results and previous reports (Ghorbani-Vaghei et al. 2013; Khaksar and Yaghoobi 2012; Shi et al. 2005; Tang et al. 2011), a plausible reaction mechanism for this synthesis is represented (Supplementary information, Scheme S2). To show the value of the present work in comparison with reported results in the literature, the results of ZPCu catalyst for the synthesis of 2-amino-4,6-bis-(4-chlorophenyl)-nicotinonitrile (**2m**) was compared with results obtained by other groups (Table 8). As it can be seen from this table, ZPCu acts as an effective catalyst with respect to reaction temperature, time, and yield.

4 Conclusions

In summary, we have reported the catalytic performance of water-insoluble ZPCu in two MCRs. The catalyst was characterized by various methods and results showed good agreement with the literature. These conditions are compatible with some acid-sensitive functional groups. The attractive features of these procedures are short reaction times, mild reaction conditions, higher yields and no side reactions, ease of preparation and handling of the catalyst,

Table 7 Synthesis 2-amino-3-cyanopyridines using ZPCu under solvent-free conditions



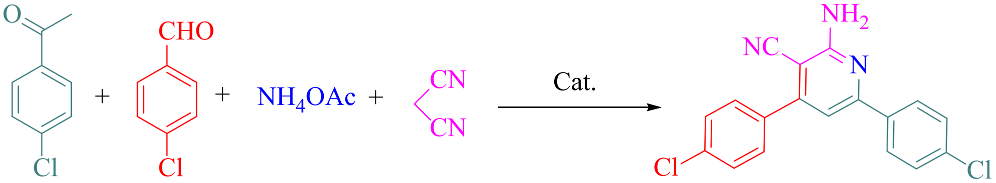
2a-2q

Entry	Ketone	Aldehyde	Product	Time (min)	Yield (%)	M.p[a]	
						Found	Reported
1	C_6H_5	C_6H_5	2a	60	88	185–187	184–186
2	C_6H_5	4-Me-C_6H_4	2b	75	83	177–179	176–178
3	C_6H_5	4-MeO-C_6H_4	2c	75	80	179–181	180–182
4	C_6H_5	2-Cl-C_6H_4	2d	45	90	191–193	193–195
5	C_6H_5	4-Cl-C_6H_4	2e	30	94	224–226	223–225
6	C_6H_5	4-Br-C_6H_4	2f	30	92	225–227	225–227
7	4-Me-C_6H_4	C_6H_5	2g	90	85	177–179	178
8	4-MeO-C_6H_4	C_6H_5	2h	90	82	179–181	177–179
9	4-Cl-C_6H_4	C_6H_5	2i	45	91	240–242	241–242
10	4-Br-C_6H_4	C_6H_5	2j	45	92	242–244	241–243
11	4-Cl-C_6H_4	4-Me-C_6H_4	2k	60	89	216–217	216–218
12	4-Cl-C_6H_4	4-MeO-C_6H_4	2l	60	86	203–203	204–205
13	4-Cl-C_6H_4	4-Cl-C_6H_4	2m	20	94	231–233	230–231
14	4-Me-C_6H_4	4-Cl-C_6H_4	2n	45	90	173–175	172–174
15	4-MeO-C_6H_4	4-Cl-C_6H_4	2o	45	88	195–197	195–196
16	4-F-C_6H_4	4-Cl-C_6H_4	2p	20	95	217–219	219–220
17	4-MeO-C6H4	4-MeO-C6H4	2q	90	82	160–162	160–162

All products were characterized by M.p, IR, and ^{1}H NMR spectral data and comparison with those of authentic samples or reported data

[b]Isolated yield

Table 8 Comparison of efficiency of various catalysts in synthesis of **2m**



Entry	Catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]	References
1	$[EtNH_3]NO_3$	Solvent-free	60	150	90	Sarda et al. (2009)
2	MWI[b]	Solvent-free	–	8	83	Shi et al. (2005)
3	$Yb(PFO)_3$	EtOH	Reflux	240	85	Tang et al. (2011)
4	$FePO_4$	EtOH	Reflux	240	93	Zadpour and Behbahani (2015)
5	TBBDA	Solvent-free	100	30	90	Ghorbani-Vaghei et al. (2013)
6	$[Bmim][BF_4]$	Solvent-free	60	300	88	Mansoor et al. (2012)
7	Cellulose–SO_3H	H_2O	60	150	94	Mansoor et al. (2014)
8	SBTETASA	Solvent-free	100	10	90	Niknam et al. (2012)
9	Trifluoroethanol	Solvent-free	Reflux	360	95	Khaksar and Yaghoobi (2012)
10	α-ZrP	Solvent-free	60	120	64	This work
11	ZPCu	Solvent-free	60	60	88	This work

[a]The yields refer to the isolated pure products

[b]Microwave irradiation

green aspects by avoiding toxic catalysts and solvents, the recyclability of the catalyst, and simple experimental procedure. This convenient technique is the most effective compared with the existing methods for the synthesis of coumarins and its derivatives. Further investigation on the new application of ZPCu as a Lewis acidic catalyst in other MCRs is extremely ongoing in our laboratory.

Acknowledgements I gratefully acknowledge the funding support received for this project from the Young Researchers and Elite Club, Shahreza, Isfahan, IR Iran.

References

Alhendawi H (2014) Synthesis and structural characterization of zirconium phosphate adipate dimethyl sulphoxide: a new lambda-type organic–inorganic layered material. J Chem Sci 126(4):975–979

Alhendawi H, Brunet E, Juanes O, Idhair S, Hammouda H, PayÁN E et al (2014) Functionalization of lambda-zirconium phosphate with ethylenediaminetetraacetic acid: synthesis, characterization and applications. J Chem Sci 126(6):1721–1727

Allulli S, Ferragina C, La Ginestra A, Massucci MA, Tomassini N, Tomlinson AAG (1976) Characterisation and electronic properties of some inorganic ion exchangers of the zirconium phosphate type containing transition-metal ions. J Chem Soc Dalton Trans 20:2115–2120

Ayvaz S, Çankaya M, Atasever A, Altuntas A (2013) 2-Amino-3-cyanopyridine derivatives as carbonic anhydrase inhibitors. J Enzym Inhib Med Chem 28(2):305–310

Azizian J, Mohammadi AA, Karimi AR, Mohammadizadeh MR (2006) $KAl(SO_4)_2{\cdot}12H_2O$ supported on silica gel as a novel heterogeneous system catalyzed Biginelli reaction: one-pot synthesis of di-hydropyrimidinones under solvent-free conditions. Appl Catal A 300(1):85–88

Cai X, Dai G-J, Tan S-Z, Ouyang Y, Ouyang Y-S, Shi Q-S (2012) Synergistic antibacterial zinc ions and cerium ions loaded α-zirconium phosphate. Mater Lett 67(1):199–201

Chari MA, Syamasundar K (2004) Silicagel supported sodium hydrogensulfate as a heterogenous catalyst for high yield synthesis of 3,4-dihydropyrimidin-2 (1H)-ones. J Mol Catal A Chem 221(1–2):137–139

Chen R-Y, Zhong J, Gu C-R, Chen C-L (2010) Computer simulation of *n*-butylamine-intercalated α-zirconium phosphate. J Chin Chem Soc 57(5A):1015–1021

Clearfield A, Kalnins JM (1976) On the mechanism of ion exchange in zirconium phosphates-XIII. Exchange of some divalent transition metal ions on α-zirconium phosphate. J Inorg Nucl Chem 38(4):849–852

Dai G, Yu A, Cai X, Shi Q, Ouyang Y, Tan S (2012) Synthesis, characterization and antimicrobial activity of zinc and cerium co-doped α-zirconium phosphate. J Rare Earth 30(8):820–825

Dash SS, Sahu MK, Sahu E, Patel RK (2015) Fluoride removal from aqueous solutions using cerium loaded mesoporous zirconium phosphate. New J Chem 39(9):7300–7308

Davoodnia A, Attar P, Morsali A, Eshghi H, Tavakoli-Hoseini N, Khadem S (2011) Experimental and theoretical studies on the tautomerism in 2-aminopyridines and 2 (1H)-pyridinones: synthesis of 2-amino-4-aryl-3-cyano-6-(3, 4-dimethoxyphenyl) pyridines and 4-aryl-3-cyano-6-(3, 4-dimethoxyphenyl)-2 (1H)-pyridinones. Bull Korean Chem Soc 32(6):1873–1878

Davoodnia A, Khashi M, Tavakoli-Hoseini N (2014) Cerium (IV) sulfate: a highly efficient reusable heterogeneous catalyst for the one-pot synthesis of 2, 3-dihydroquinazolin-4 (1H)-ones under solvent-free conditions. Chin J Catal 35(7):1054–1058

Dissanayake AA, Staples RJ, Odom AL (2014) Titanium-catalyzed, one-pot synthesis of 2-amino-3-cyano-pyridines. Adv Synth Catal 356(8):1811–1822

Fang D, Zhang D-Z, Liu Z-L (2010) One-pot three-component Biginelli-type reaction catalyzed by ionic liquids in aqueous media. Monatsh Chem 141(4):419–423

Gan H, Zhao X, Song B, Guo L, Zhang R, Chen C et al (2014) Gas phase dehydration of glycerol to acrolein catalyzed by zirconium phosphate. Chin J Catal 35(7):1148–1156

Gartner M, Sunder-Plassmann N, Seiler J, Utz M, Vernos I, Surrey T et al (2005) Development and biological evaluation of potent and specific inhibitors of mitotic kinesin Eg5. ChemBioChem 6(7):1173–1177

Gawande M, Deshpande S, Sonavane S, Jayaram R (2005) A novel sol–gel synthesized catalyst for Friedel-Crafts benzoylation reaction under solvent-free conditions. J Mol Catal A Chem 241(1):151–155

Ghorbani-Choghamarani A, Taghipour T, Azadi G (2013) One-pot, green and efficient synthesis of 3,4-dihydropyrimidin-2(1H)-ones or thiones catalyzed by citric acid. J Chin Chem Soc 60(10):1202–1206

Ghorbani-Vaghei R, Toghraei-Semiromi Z, Karimi-Nami R (2013) One-pot synthesis of 2-amino-3-cyanopyridine derivatives under solvent-free conditions. C R Chim 16(12):1111–1117

Giannoccaro P, Gargano M, Fanizzi A, Ferragina C, Aresta M (2005) Rh-ions and Rh-complexes intercalated in γ-titanium or γ-zirconium hydrogen phosphate as highly efficient catalysts for arene hydrogenation. Appl Catal A 284(1–2):77–83

Girgis AS, Kalmouch A, Hosni HM (2004) Synthesis of novel 3-pyridinecarbonitriles with amino acid function and their fluorescence properties. Amino Acids 26(2):139–146

Gouda MA, Berghot MA, Abd El Ghani GE, Khalil AE-GM (2013) Chemistry of 2-amino-3-cyanopyridines. Synth Commun 44(3):297–330

Gupta R, Jain A, Jain M, Joshi R (2010) "One-pot" synthesis of 2-amino-3-cyano-4, 6-diarylpyridines under ultrasonic irradiation and grindstone technology. Bull Korean Chem Soc 31(11):3180–3182

Imtiaz S, Khan MA, Sharif A, Ahmed E, Lin W-O, Munawar MA (2012) Alcohols promoted green protocol for Biginelli reaction. J Chin Chem Soc 59(11):1446–1448

Jetti SR, Bhatewara A, Kadre T, Jain S (2014) Silica-bonded *N*-propyl sulfamic acid as an efficient recyclable catalyst for the synthesis of 3,4-dihydropyrimidin-2-(1H)-ones/thiones under heterogeneous conditions. Chin Chem Lett 25(3):469–473

Karamat A, Khan MA, Sharif A (2010) Metal acetate mediated Biginelli one-pot synthesis. J Chin Chem Soc 57(5):1099–1101

Karimi H (2015a) An efficient selective oxidation of alcohols with zinc zirconium phosphate under solvent-free conditions. J Chin Chem Soc 62(7):604–613

Karimi H (2015b) Solvent-free chemoselective synthesis of 1,1-diacetates catalyzed by iron zirconium phosphate. J Chin Chem Soc 62(11):1000–1010

Kathing C, Rani JWS, Singh NG, Tumtin S, Nongrum R, Nongkhlaw R (2014) One-pot synthesis of 3,4-Dihydropyrimidin-2(1H)-ones catalysed by cupric acetate under solvent-free conditions. J Chin Chem Soc 61(11):1254–1258

Kefayati H, Mirfarhadi SM, Kazemi-Rad R (2015) Unexpected one-pot synthesis of novel 2-aminopyrimidine-4-ones under microwave irradiation. J Chin Chem Soc 62(2):107–111

Khaksar S, Yaghoobi M (2012) A concise and versatile synthesis of 2-amino-3-cyanopyridine derivatives in 2,2,2-trifluoroethanol. J Fluor Chem 142:41–44

Khaksar S, Vahdat S, Moghaddamnejad R (2012) Pentafluoropheny-lammonium triflate: an efficient, practical, and cost-effective organocatalyst for the Biginelli reaction. Monatsh Chem 143(12):1671–1674

Khare S, Chokhare R (2012) Oxidation of cyclohexene catalyzed by Cu(Salen) intercalated α-zirconium phosphate using dry tert-butylhydroperoxide. J Mol Catal A Chem 353–354:138–147

Khare S, Chokhare R, Shrivastava P, Kirar J (2015) Solvent-free liquid phase oxidation of styrene over iron zirconium phosphate using tert-butylhydroperoxide as an oxidant. Indian J Chem 54:1032–1038

Kolvari E, Koukabi N, Armandpour O (2014) A simple and efficient synthesis of 3,4-dihydropyrimidin-2-(1H)-ones via Biginelli reaction catalyzed by nanomagnetic-supported sulfonic acid. Tetrahedron 70(6):1383–1386

Kour G, Gupta M, Paul S, Rajnikant, Gupta VK (2014) SiO_2–$CuCl_2$: an efficient and recyclable heterogeneous catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones. J Mol Catal A Chem 392:260–269

Lei M, Ma L, Hu L (2010) An efficient and environmentally friendly procedure for synthesis of pyrimidinone derivatives by use of a Biginelli-type reaction. Monatsh Chem 141(9):1005–1008

Liberto NA, de Paiva Silva S, de Fátima Â, Fernandes SA (2013) β-Cyclodextrin-assisted synthesis of Biginelli adducts under solvent-free conditions. Tetrahedron 69(38):8245–8249

Liu CC, Wang MK, Chiou CS, Li YS, Yang CY, Lin YA (2009) Biosorption of chromium, copper and zinc by wine-processing waste sludge: single and multi-component system study. J Hazard Mater 171(1–3):386–392

Liu B, Ba C, Jin M, Zhang Z (2015) Effective conversion of carbohydrates into biofuel precursor 5-hydroxymethylfurfural (HMF) over Cr-incorporated mesoporous zirconium phosphate. Ind Crops Prod 76:781–786

Mansoor SS, Aswin K, Logaiya K, Sudhan SPN (2012) [Bmim]BF_4 ionic liquid: an efficient reaction medium for the one-pot multi-component synthesis of 2-amino-4,6-diphenylpyridine-3-carbonitrile derivatives. J Saudi Chem Soc. https://doi.org/10.1016/j.jscs.2012.07.011

Mansoor S, Aswin K, Logaiya K, Sudhan P, Malik S (2014) Aqueous media preparation of 2-amino-4,6-diphenylnicotinonitriles using cellulose sulfuric acid as an efficient catalyst. Res Chem Intermed 40(2):871–885

Mobaraki A, Movassagh B, Karimi B (2014) Hydrophobicity-enhanced magnetic solid sulfonic acid: a simple approach to improve the mass transfer of reaction partners on the surface of the heterogeneous catalyst in water-generating reactions. Appl Catal A 472:123–133

Moghaddas M, Davoodnia A, Heravi MM, Tavakoli-Hoseini N (2012) Sulfonated carbon catalyzed Biginelli reaction for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones and -thiones. Chin J Catal 33(4–6):706–710

Movassaghi M, Hill MD, Ahmad OK (2007) Direct synthesis of pyridine derivatives. J Am Chem Soc 129(33):10096–10097

Naik AH, Deb SB, Chalke AB, Saxena MK, Ramakumar KL, Venugopal V et al (2010) Microwave-assisted low temperature synthesis of sodium zirconium phosphate (NZP) and the leachability of some selected fission products incorporated in its structure—a case study of leachability of cesium. J Chem Sci 122(1):71–82

Nasr-Esfahani M, Hoseini SJ, Mohammadi F (2011) Fe_3O_4 nanoparticles as an efficient and magnetically recoverable catalyst for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones under solvent-free conditions. Chin J Catal 32(9–10):1484–1489

Nazari S, Saadat S, Fard P, Gorjizadeh M, Nezhad E, Afshari M (2013) Imidazole functionalized magnetic Fe_3O_4 nanoparticles as a novel heterogeneous and efficient catalyst for synthesis of dihydropyrimidinones by Biginelli reaction. Monatsh Chem 144(12):1877–1882

Niknam K, Zolfigol MA, Hossieninejad Z, Daneshvar N (2007) Efficient synthesis of 3,4-dihydropyrimidin-2(1H)-one using metal hydrogen sulfates $M(HSO_4)_n$ as catalyst under solvent-free conditions. Chin J Catal 28(7):591–595

Niknam K, Hasaninejad A, Arman M (2010) Synthesis of some new bis-3,4-dihydropyrimidin-2(1H)-ones by using silica-supported tin chloride and titanium tetrachloride. Chin Chem Lett 21(4):399–402

Niknam K, Jamali A, Tajaddod M, Deris A (2012) Synthesis of 2-amino-4,6-diarylnicotinonitriles using silica-bound *N*-propyl triethylenetetramine sulfamic acid as a recyclable solid acid catalyst. Chin J Catal 33(7–8):1312–1317

Niknam K, Rashidian R, Jamali A (2013) Synthesis of 2-amino-4,6-diarylnicotininitriles using 3-propyldiethylenetriamine-silica as a recyclable solid base catalyst. Sci Iran Trans C Chem Chem Eng 20(6):1863

Pasunooti KK, Chai H, Jensen CN, Gorityala BK, Wang S, Liu X-W (2011) A microwave-assisted, copper-catalyzed three-component synthesis of dihydropyrimidinones under mild conditions. Tetrahedron Lett 52(1):80–84

Quan Z-J, Ren R-G, Da Y-X, Zhang Z, Wang X-C (2011) Glycerol as an alternative green reaction medium for multicomponent reactions using PS-PEG-OSO_3H as catalyst. Synth Commun 41(20):3106–3116

Rotstein BH, Zaretsky S, Rai V, Yudin AK (2014) Small heterocycles in multicomponent reactions. Chem Rev 114(16):8323–8359

Safaei Ghomi J, Teymuri R, Ziarati A (2013) A green synthesis of 3,4-dihydropyrimidine-2(1H)-one/thione derivatives using nanosilica-supported tin(II) chloride as a heterogeneous nanocatalyst. Monatsh Chem 144(12):1865–1870

Safari J, Banitaba SH, Khalili SD (2012) Ultrasound-promoted an efficient method for one-pot synthesis of 2-amino-4,6-diphenylnicotinonitriles in water: a rapid procedure without catalyst. Ultrason Sonochem 19(5):1061–1069

Sarda S, Kale J, Wasmatkar S, Kadam V, Ingole P, Jadhav W et al (2009) An efficient protocol for the synthesis of 2-amino-4,6-diphenylpyridine-3-carbonitrile using ionic liquid ethylammonium nitrate. Mol Divers 13(4):545–549

Sharghi H, Jokar M (2009) Al_2O_3/$MeSO_3H$: a novel and recyclable catalyst for one-pot synthesis of 3,4-dihydropyrimidinones or their sulfur derivatives in Biginelli condensation. Synth Commun 39(6):958–979

Shi F, Tu S, Fang F, Li T (2005) One-pot synthesis of 2-amino-3-cyanopyridine derivatives under microwave irradiation without solvent. Arkivoc 2005(1):137–142

Shi QS, Tan SZ, Ouyang YS, Yang QH, Chen AM, Li WR et al (2011) Structure and antibacterial activity of copper-carried zirconium phosphates. Adv Mater Res 150:852–856

Sing KS (1985) Reporting physisorption data for gas/solid systems with special reference to the determination of surface area and porosity (Recommendations 1984). Pure Appl Chem 57(4):603–619

Slobbe P, Ruijter E, Orru RVA (2012) Recent applications of multicomponent reactions in medicinal chemistry. MedChemComm 3(10):1189–1218

Sun L, Boo WJ, Sue HJ, Clearfield A (2007) Preparation of α-zirconium phosphate nanoplatelets with wide variations in aspect ratios. New J Chem 31(1):39–43

Tajbakhsh M, Ranjbar Y, Masuodi A, Khaksar S (2012) A simple and environmentally benign protocol for Biginelli reactions catalyzed by silica-bonded S-sulfonic acid. Chin J Catal 33(9–10):1542–1545

Tale N, Shelke A, Bhong B, Karade N (2013) Regioselective chlorination at C-6 methyl position of 3,4-dihydropyrimidin-2(1H)-ones using (dichloroiodo)benzene. Monatsh Chem 144(7):981–986

Tang J, Wang L, Yao Y, Zhang L, Wang W (2011) One-pot synthesis of 2-amino-3-cyanopyridine derivatives catalyzed by ytterbium perfluorooctanoate [Yb(PFO)$_3$]. Tetrahedron Lett 52(4):509–511

Tayebee R, Maleki B, Ghadamgahi M (2012) Ammonium dihydrogen phosphate catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones. Chin J Catal 33(4–6):659–665

Tayebee R, Amini MM, Ghadamgahi M, Armaghan M (2013) H5PW10V2O40/Pip-SBA-15: a novel reusable organic–inorganic hybrid material as potent Lewis acid catalyst for one-pot solvent-free synthesis of 3,4-dihydropyrimidinones. J Mol Catal A Chem 366:266–274

Tu S, Fang F, Zhu S, Li T, Zhang X, Zhuang Q (2004a) A new biginelli reaction procedure using potassium hydrogen sulfate as the promoter for an efficient synthesis of 3,4-dihydropyrimidin-2(1H)-one. J Heterocycl Chem 41(2):253–257

Tu S, Fang F, Zhu S, Li T, Zhang X, Zhuang Q (2004b) A new Biginelli reaction procedure using potassium hydrogen sulfate as the promoter for an efficient synthesis of 3, 4-dihydropyrimidin-2 (1H)-one. Synlett 15(3):537–539

Tyagi B, Chudasama CD, Jasra RV (2006) Characterization of surface acidity of an acid montmorillonite activated with hydrothermal, ultrasonic and microwave techniques. Appl Clay Sci 31(1–2):16–28

Wang J, Li N, Qiu R, Zhang X, Xu X, Yin S-F (2015) Air-stable zirconocene bis(perfluorobutanesulfonate) as a highly efficient catalyst for synthesis of N-heterocyclic compounds. J Organomet Chem 785:61–67

Yang Y, Dai G, Tan S, Liu Y, Shi Q, Ouyang Y (2011) Structure and synergetic antibacterial effect of zinc and cerium carried sodium zirconium phosphates. J Rare Earths 29(4):308–312

Zadpour M, Behbahani F (2015) Iron(III) phosphate as a green and reusable catalyst for the synthesis of 4,6-disubstituted 2-aminopyridine-3-carbonitriles. Monatsh Chem 146(11):1865–1869

Zhang Q, Du X, Ma X, Hao X, Guan G, Wang Z et al (2015) Facile preparation of electroactive amorphous α-ZrP/PANI hybrid film for potential-triggered adsorption of Pb 2+ ions. J Hazard Mater 289:91–100