

A Novel Preparation of Zirconium Phosphate Nanoparticle and Its Application in Multi-Component Reactions

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ABSTRACT: A novel method for the preparation of α -zirconium phosphate (ZrP) nanoparticles as an eco-friendly and recyclable heterogeneous catalyst was studied. Polyethylene glycol (PEG) was used as the organic matrix which produced a better dispersion of ZrP nanoparticles. The catalyst was characterized by several physicochemical techniques such as ICP-OES, XRD, TPD-NH₃, pyridine-FTIR, BET, FTIR, TGA, SEM, and TEM. The acidic property of ZrP was studied in the synthesis of 2-amino-3-cyanopyridines. When the hexagonal ZrP nanoparticles were used as the catalyst, excellent yields were obtained. The catalyst was recovered and reused at least eight times without significant loss in its catalytic activity.

KEYWORDS: Hexagonal zirconium phosphate; Nanoparticles; Solvent-free; Solid acid catalyst; Multi-component reaction.

INTRODUCTION

Layered zirconium hydrogen phosphate with an α -type structure, $Zr(HPO_4)_2 \cdot H_2O$, is one of the most important inorganic materials as it shows several advantages such as extreme insolubility in water and organic solvents, high water tolerance ability, high thermal stability, and easy sedimentation. These properties made α -zirconium phosphate (ZrP) a suitable heterogeneous catalyst and catalyst support [1,2], excellent ion exchanger [3-5], an interesting intercalating agent [6], which also has been used in nanocomposite [7], proton conductor for fuel cells, drug delivery and immobilization of biological materials [8,9]. To satisfy the requirements for applications in different fields, it has been prepared by different methods in a wide variety of sizes from 2 nm to up to 2 μ m [10-12]. The crystal structure of ZrP is built up by covalent bonds between atoms in layers, hydrogen bonds, and van der Waals

forces between layers [12]. It consists of layers made of planes of zirconium atoms bonded, on both sides of each plane, to monohydrogen phosphate groups. Water molecules are placed in the interlayer region, forming a hydrogen-bonding network with the phosphate groups. The crystalline ZrP possesses weak and strong Brønsted and Lewis acid centers which are attributed to P-OH groups and the Zr^{4+} , respectively. Due to the presence of high hydroxyl group density on ZrP surface which can be assumed as hooks, various organic functional groups could adsorb on, allowing to control both the reactivity and selectivity of the reaction (Fig. 1). In the past few years, increasing attention has been attracted to the development of new approaches for the preparation of various ZrP nano compounds such as nanoparticles [13,14], nanoplates [15] and nanocomposites [16,17]. Polyethylene glycol (PEG) is a flexible, biocompatible, water-soluble, liquid or

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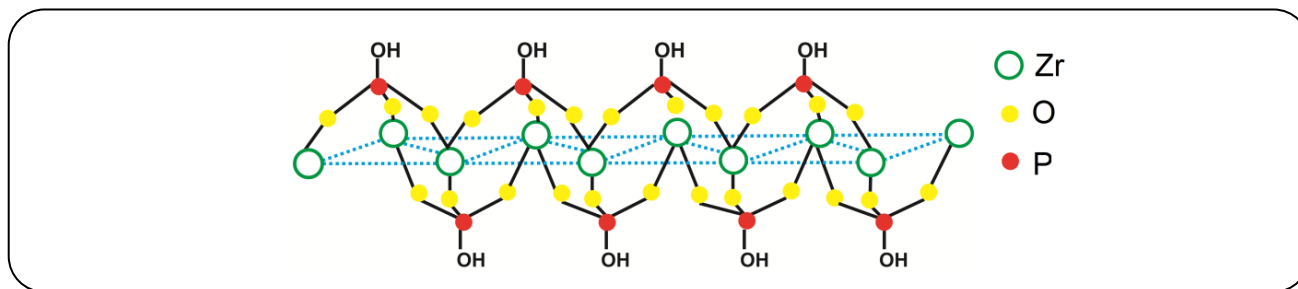


Fig. 1: Schematic structure of hexagonal α -zirconium phosphate.

low-melting solids, depending on its molecular weight. There are some new polymer-based precursor methods to produce nanocomposites and nanoparticles [18,19].

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 [20]. In a MCR, there is a network of reaction equilibria, which all finally flow into an irreversible step yielding the product. 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. As an important MCR, synthesis of N-heteroaromatic pyridines attracted enormous attention due to their wide applications. Among these compounds, 2-amino-3-cyanopyridine derivatives have been reported to possess remarkable pharmacological properties and activities such as antiviral, anticancer, antitubercular, antimicrobial, and fungicidal activities [21-23]. 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 $[\text{EtNH}_3]\text{NO}_3$ [22], MWI [24,25], $\text{Yb}(\text{PFO})_3$ [26], FePO_4 [27], TBBDA [28] $\text{Ti}(\text{dpm})(\text{NMe}_2)_2$ [29] and also multiple steps procedure using amino acid and refluxing [30].

An aim of this research is to introduce an eco-efficient methodology that allows decreasing the amount of waste and less use of hazardous materials. With these in mind, and as part of ongoing work towards the development of efficient and green catalysts based on zirconium phosphate [14] and some of its ion exchanged derivatives [3], for organic transformations, herein a novel synthesis of zirconium phosphate using PEG as dispersing agents is reported. There is no report available in the literature for using hexagonal ZrP nanoparticles as a catalyst for the synthesis of 2-amino-3-cyanopyridines. It is very

important to note that for the reactions in which water participates as a by-product, only a few solid acids show acceptable performance and stability [31]. Also, we investigated this synthesis over $[\text{Hmim}]\text{HSO}_4$, $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$, $\text{P}_2\text{O}_5/\text{SiO}_2$ and α -ZrP (prepared in the absence of the polymer). The obtained results were compared with those reported before in the literature.

EXPERIMENTAL SECTION

Catalyst synthesis

Typically, a 2% solution of PEG-200 ($M_w = 190\text{-}210$) was prepared by dissolving PEG in deionized water. By adding HCl, the pH value was adjusted about 3. 50 mL of a 1 M solution of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ added dropwise to precursor solution and heated at the 50 °C for 1 h with constant stirring using a magnetic stirrer. To the resulting homogeneous solution, under ultrasonication, 50 mL of a 2 M H_3PO_4 solution was added dropwise at 50-60 °C for 1 h. The resulted mixture was allowed to age for 30 min, then the precipitate was filtered, washed several times with distilled water and then dried in an oven at 80 °C overnight. The obtained white colored fluffy precursor was ground and calcined at 600 °C for 3 h to decompose the organic matrix. The final product, the desired pure hexagonal α -zirconium phosphate ($\text{Zr}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$) nanocrystals, was identified as ZrP.

The detailed procedure for the preparation of the α -ZrP can be found in the literature [12]. 1-H-3-methylimidazolium bisulfate $[\text{Hmim}]\text{HSO}_4$ [32], $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ and $\text{P}_2\text{O}_5/\text{SiO}_2$ [33] were prepared according to previously reported procedures (supplementary information, Pages S6-S8).

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 (15 mg) was 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. Also, different reactions, as described above, were performed over P_2O_5/Al_2O_3 and P_2O_5/SiO_2 (pre-activated at 120 °C for 2 h) (10 mol%), and $[Hmim]HSO_4$ (7 mol%). The results were compared with those obtained from ZrP (Table 3). All the products are known and were characterized by M.p, IR and 1H NMR spectral data and comparison with those of authentic samples or reported data (supplementary information, Pages S12-S16).

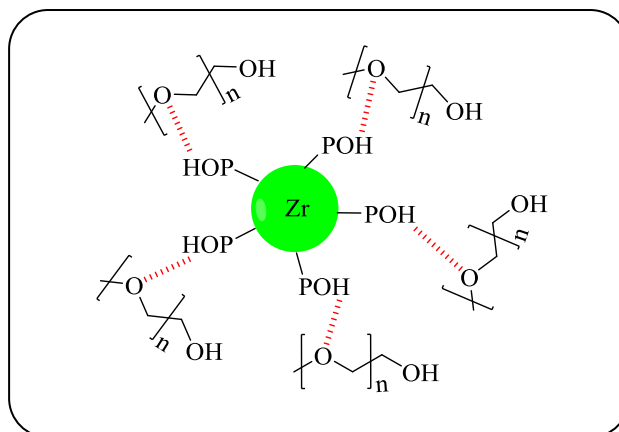
Catalyst regeneration

For recycling, after the first use, the catalyst was separated from the reaction mixture by centrifuge, washed with ethanol successively, and refluxed with 10% (w/v) H_2O_2 for 1 h. It was then washed with water, dried at 110 °C for 1 h and finally activated at 400 °C for 2 h [1]. The regenerated catalyst was used under the optimum reaction conditions to study the performance of the recovered catalyst. After every reaction cycle, the catalyst was recovered, washed, and activated as described above.

RESULTS AND DISCUSSION

We have previously reported the preparation of ZrP nanoparticles using Polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA) [14]. In order to achieve a better dispersion and better-qualified nanoparticles, PEG was used and some modification was made to the method. The PEG shell encapsulates the nanoparticles and weakens interactions between neighboring nanoparticles, thereby hindering unwanted precipitation of the zirconium phosphates used in this work (Scheme 1). This prevents particles aggregation and controls their average size and shape. On addition of phosphate ions into the PEG/Zr^{4+} solution, the formation of ZrP began immediately. The PEG was used as the dispersing agent, an organic matrix which also acted as a template for the nanoparticles.

The interactions between polar parts of PEG and the P-OH groups of ZrP play an important role in the better distribution of ZrP. After calcination of PEG/ZrP at 600 °C



Scheme 1: Interactions between polymers and the P-OH groups of ZrP.

for 3 h and decomposition of the organic matrix, pure ZrP nanoparticles with hexagonal shape were obtained.

Characterization of the catalysts

Table 1 represents the ICP data, in where the P/Zr ratio was found to be 1.91 and 1.74 for ZrP and α -ZrP, respectively [1,10].

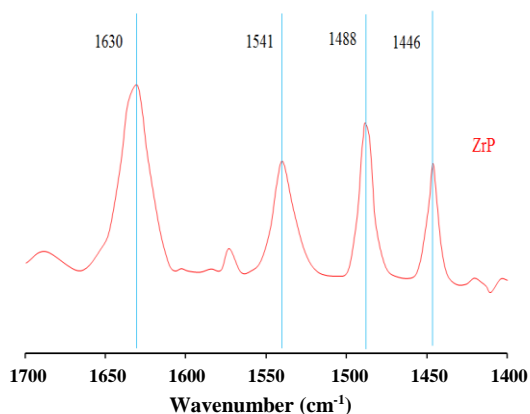
Pyridine has been verified to be an excellent FT-IR spectroscopy probe to characterize the nature of the acid sites of catalyst and the resulting IR spectrum is shown in Fig. 2. The main bands observed over the samples are assigned according to the literature data [2]. The origin of Brønsted acidity of the samples is due to the presence of P-OH groups. The pyridine-desorbed FT-IR spectra of ZrP showed characteristic strong bands about 1446 cm^{-1} which are assigned to the coordinated pyridine in Lewis acid sites. The pyridinium ions are formed by the transfer of protons from the P-OH groups in the ZrP to the organic base. The absorption peak about 1630 and 1541 cm^{-1} are caused by pyridine adsorbed on Brønsted acid sites [1,2]. Additionally, the band at 1488 cm^{-1} indicates the combination band between those adjacent Lewis and Brønsted acid sites at 1541 and 1446 cm^{-1} respectively [1]. It is obvious from the figure that the prepared ZrP shows a higher number of Brønsted acid sites accompanied by low amounts of Lewis acid sites.

The morphology of the ZrP nanoparticles was characterized by SEM [1,10,12] and TEM [12,13,15]. Typically, the SEM micrograph of ZrPs shows the hexagonal plates in which the disks had well-defined shapes with the very smooth surface, solid layers are placed parallel,

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

Sample	O	P	Zr	BET (m ² /g)	Total acidity (mmol NH ₃ /g)
ZrP	62.8	24.4	12.8	144.6	3.1
ZrP ^[a]	63.1	24.2	12.7	143.1	3.02
ZrP ^[b]	67.8	21.5	10.7	81.7	1.5
α -ZrP	70.4	18.8	10.8	73.5	0.81

a) After the first cycle. b) After the 8th cycle.

**Fig. 2: Pyridine-desorbed FTIR spectra of the calcined ZrP.**

showing good crystallinity (Fig. 3 a and b). However, there are some incomplete plates which are ellipse.

The TEM images (Fig. 4 a and b) show that the ZrP particles are hexagonal with smooth surfaces. Because of the condensation reactions between hydroxyl groups of adjacent particles during aging or calculation, particles in some cases are attached together which cause more agglomeration. The average diameter of ZrP nanoparticles is about 40-55 nm. SEM and TEM results of all the calcined ZrPs samples show similar uniform morphology and are in fair congruence with the earlier reports [12,13].

The weight loss curve of ZrP is shown in Fig. 5. The TG pattern was obtained from 50 to 1100 °C. Dehydration led to a weight loss of ZrP due to water removal from the catalyst. The thermal decomposition of ZrP takes place in two main steps; the first step, centered around 100 °C can be attributed to the loss of adsorbed and/or intercalated molecules, such as water (crystallization water) [11]. The crystallinity is associated with fairly distinct thermal behaviors: with increasing crystal size, the loss of crystallization water is progressively shifted toward high temperature and hence

less separated from the loss of condensation water [10,11]. The second step is due to the subsequent POH condensation, leading to the formation of layered ZrP₂O₇. It is known that heating zirconium phosphonates in the presence of oxygen or air leads to the formation of cubic zirconium pyrophosphate, ZrP₂O₇ [34,35]. The step between 210 and 600 °C is attributed to the loss of water due to the condensation of the HPO₄ groups, leading to the formation of cubic zirconium pyrophosphate.

A detailed discussion about XRD, FT-IR, BET, and TPD-NH₃ of the catalyst is represented in the supplementary information (Pages S2-S5).

Synthesis of 2-amino-3-cyanopyridines

Initially, the conversion of malonitrile, ammonium acetate, benzaldehyde and acetophenone to 2-amino-4,6-diphenylnicotinonitrile (**1a**) was selected as the model reaction to determine the optimal conditions. The results are summarized in Table S2. The best result was obtained when the reaction was carried out under solvent-free conditions at 60 °C in 60 min. To delineate the scope and generality of our new protocol, this methodology was examined by the reaction of several substituted aldehydes and acetophenones (Table 2).

The reaction succeeded well, providing the corresponding 2-amino-4,6-diphenylnicotinonitrile derivatives in fair to excellent yields, demonstrating the generality of the method and its well tolerance of both EW and ED substituents on both aromatic rings. The electronic effect seemed to have a clear influence on the reaction, since the EW groups on the 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 2, entry 4). Surprisingly, the aliphatic aldehyde

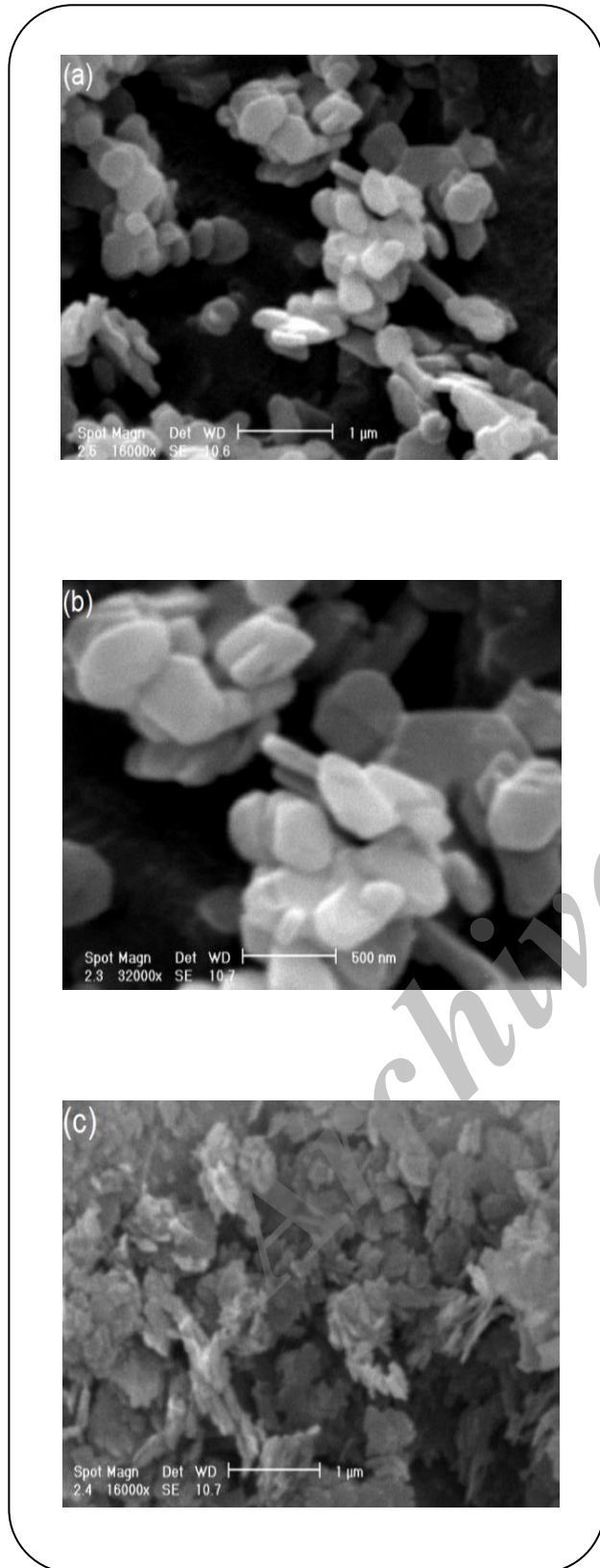


Fig. 3: SEM images of ZrP(a,b) fresh and (c) after the 8th run.

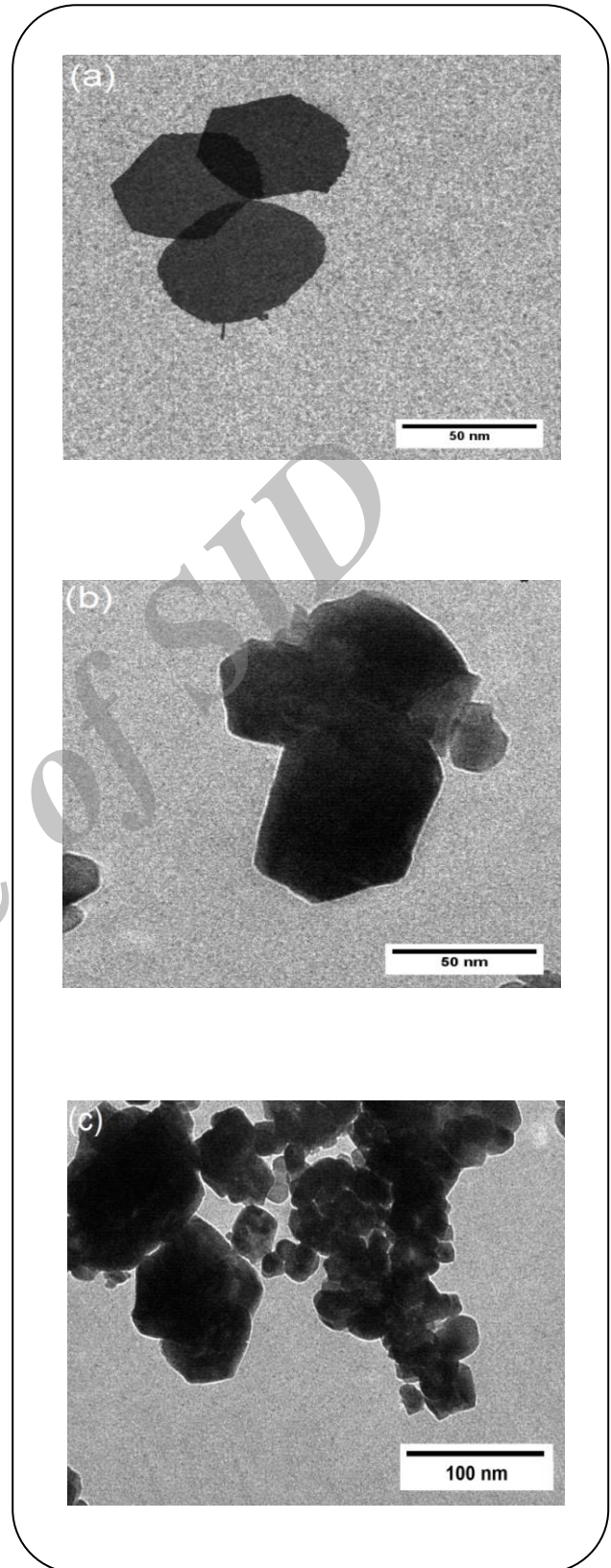


Fig. 4: TEM images of ZrP (a,b) fresh and after the 8th run (c).

Table 2. Synthesis 2-amino-3-cyanopyridines using ZrP under solvent-free conditions.^a

Entry	R ₁	R ₂	Product	Time (min)	Yield (%)	M.p. ^b		Ref.
						Found	Reported	
1	H	H	1a	60	88	185-187	184-186	[25-28]
2	H	4-Me	1b	75	83	177-179	176-178	[25-28]
3	H	4-MeO	1c	75	80	179-181	180-182	[25-28]
4	H	2-Cl	1d	45	90	191-193	193-195	[25-28]
5	H	4-Cl	1e	30	94	224-226	223-225	[25-28]
6	H	4-Br	1f	30	92	225-227	225-227	[25-28]
7	4-Me	H	1g	90	85	177-179	178	[25-28]
8	4-MeO	H	1h	90	82	179-181	177-179	[25-28]
9	4-Cl	H	1i	45	91	240-242	241-242	[25-28]
10	4-Br	H	1j	45	92	242-244	241-243	[25-28]
11	4-Cl ₄	4-Me	1k	60	89	216-217	216-218	[25-28]
12	4-Cl	4-MeO	1l	60	86	203-203	204-205	[25-28]
13	4-Cl	4-Cl	1m	20	94	231-233	230-231	[25-28]
14	4-Me	4-Cl	1n	45	90	173-175	172-174	[25-28]
15	4-MeO	4-Cl	1o	45	88	195-197	195-196	[25-28]
16	4-F	4-Cl	1p	20	95	217-219	219-220	[25-28]
17	4-MeO ₄	4-MeO	1q	90	82	160-162	160-162	[25-28]

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

b) Isolated yield.

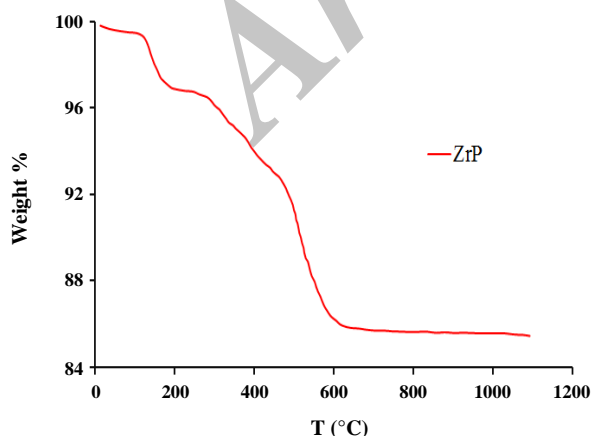
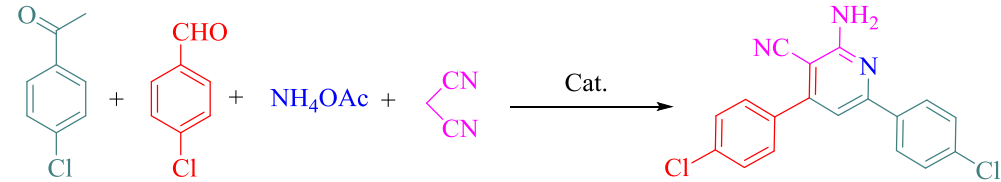


Fig. 5: The weight loss curves of ZrP sample.

(hexanal) and the aliphatic ketone (acetone) gave no products. Obviously, the reactivity of aldehydes is the key factor for this one-pot transformation. On the basis of literature studies, a plausible mechanism is proposed (Scheme S1). It seems due to the presence of acidic P-OH groups on the ZrP surface, it acts as a Brønsted acid catalyst which can activate the carbonyl group. To compare the efficiency of our catalyst with the reported catalysts, we have tabulated the results of these catalysts for the synthesis of 1m in Table 3. It is clear from this Table that our method is superior to some of the previously reported catalysts in terms of reaction conditions, and yield (Table 3).

Table 3: Comparison of efficiency of various catalysts in the synthesis of **1m**.


Entry	Catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%) ^a	Ref.
1	FePO ₄	EtOH	Reflux	240	93	[27]
2	Trifluoroethanol	Solvent-free	Reflux	360	95	[36]
3	[EtNH ₃] ⁺ NO ₃ ⁻	Solvent-free	60	150	90	[22]
4	Yb(PFO) ₃	EtOH	Reflux	240	85	[26]
5	MW ^b	Solvent-free	-	8	83	[25]
6	[Bmim][BF ₄]	Solvent-free	60	300	88	[37]
7	Cellulose-SO ₃ H	H ₂ O	60	150	94	[38]
8	SBTETASA	Solvent-free	100	10	90	[39]
9	TBBDA	Solvent-free	100	30	90	[28]
10	[Hmim]HSO ₄	Solvent-free	60	120	38	This Work
11	P ₂ O ₅ /SiO ₂	Solvent-free	60	120	43	This Work
12	P ₂ O ₅ /Al ₂ O ₃	Solvent-free	60	120	51	This Work
13	α-ZrP	Solvent-free	60	120	64	This Work
14	ZrP	Solvent-free	60	60	88	This Work

^a The yields refer to the isolated pure products.

^b Microwave irradiation.

To show the value of the present work in comparison with reported results in the literature, we compared the results of ZrP catalyst for the synthesis of 2-amino-4,6-bis(4-chlorophenyl)nicotinonitrile (**1m**) with results obtained by other groups (Table 3). As it can be seen from this Table, ZrP acts as an effective catalyst with respect to reaction temperature, time, and yield.

CONCLUSIONS

A novel method for the preparation of hexagonal zirconium phosphate nanoparticles has declared. The ZrP was characterized by various methods and showed great agreement with previous reports. We have demonstrated that ZrP is an efficient and recyclable catalyst for the MCRs. It seems that the surface of ZrP with hydroxyl groups (P-OH) plays an important role in the acidity of the catalyst. Recovery of the inexpensive catalyst, easy purification, high yields, wide substrate scope,

solvent-free conditions, shorter reaction times and temperatures over the previously reported methods are some of our important advantages.

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