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Nano-$NiZr_4(PO_4)_6$ as a superior catalyst for the synthesis of propargylamines under ultrasound irradiation

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Abstract: An easy and rapid method for the synthesis of propargylamines has been achieved through a three-component reaction of phenylacetylene, aromatic aldehydes, and morpholine or piperidine using nano-$NiZr_4(PO_4)_6$ under ultrasound irradiation. Atom economy, a wide range of products, excellent yields in short times, reusability of the catalyst, and low catalyst loading are some of the important features of this protocol.

Keywords: nanocatalyst; one-pot synthesis; phenylacetylene; propargylamine; ultrasonic conditions.

1 Introduction

Propargylamines exhibit significant biological properties such as anti-Parkinson [1] and anti-Alzheimer's disease [2], anti-apoptotic potential [3], and monoamine oxidase inhibition [4]. Propargylamines have been used as important substrates and intermediates for the preparation of different nitrogen compounds such as oxazoles [5], pyrroles [6], tetrahydrofuran [7], 1,2-dihydroquinoline [8], and 3-aminoindoles [9]. Recently, reports have appeared on the preparation of chiral allenes from chiral propargylamines using ZnI_2 [10], $AgNO_3$ [11], $KAuCl_4$ [12], and $ZnBr_2$ [13]. Finding effective methods for the synthesis of propargylamines is of great interest. The synthesis of propargylamines has been achieved using such catalysts as copper(I) bromide [14], PbS-Au [15], copper impregnated on magnetite [16], zinc acetate [17], copper(I) salts in $[bmim]PF_6$ [18], bis(imine)/copper(I) complexes [19], Cu(I)-modified zeolites [20], Ag-NaY zeolite [21], and two-dimensional mesoporous copper silicate [22]. However, some of the reported methods suffer from drawbacks such as long reaction times, harsh reaction conditions, and the use of toxic and non-reusable catalysts. Recently, several nanocatalysts have been utilized for the preparation of organic compounds under ultrasonic irradiation [23, 24]. Compared to conventional heating, which creates thermal energy in the macro system, ultrasound irradiation is able to activate numerous reactions by providing the activation energy in the micro environment [25–29]. $MZr_4(PO_4)_6$ ceramics as heterogeneous catalysts are interesting because of their unique properties and potential applications in diverse fields [30, 31]. In the present study, we investigated an easy and rapid method for the synthesis of propargylamines through a three-component reaction of phenylacetylene, aromatic aldehydes, and morpholine or piperidine using nano-$NiZr_4(PO_4)_6$ under ultrasound irradiation (Scheme 1).

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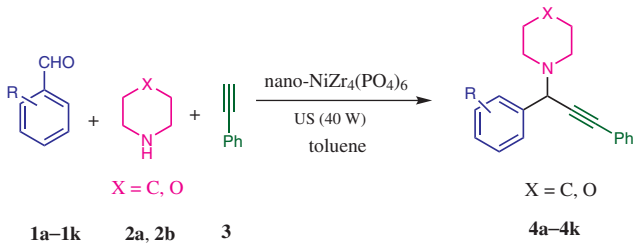
2 Results and discussion

2.1 Structural analysis of nano-$NiZr_4(PO_4)_6$

$ZrOCl_2$ and $Ni(NO_3)_2 \cdot 2H_2O$ were used as the starting materials for the synthesis of nano-$NiZr_4(PO_4)_6$. Ultrasonic irradiation was carried out before and after the solvothermal step to speed up dissolution and to break the interactions between particles. At the beginning of the reaction, the reactant particles and the methylamines are dispersed randomly in the glycol solution under ultrasound irradiation. $NiZr_4(PO_4)_6$ forms gradually around the methylamine molecule. After calcination at high temperature, methylamine decomposes into carbon dioxide, carbon monoxide, and nitrogen oxide to yield nano-$NiZr_4(PO_4)_6$.

The X-ray diffraction (XRD) patterns of nano-$NiZr_4(PO_4)_6$ are shown in Fig. S1 (Supporting Information available online). The pattern agrees well with the reported data (JCPDS No. 45-0013) (Supporting Information). The morphology and particle size of nano-$NiZr_4(PO_4)_6$ were investigated by scanning electron microscopy (SEM),



Scheme 1: Synthesis of propargylamines under ultrasound irradiation.

as shown in Fig. S2 (Supporting Information). The SEM images show particles with diameters in the range of nanometers.

The elemental compositions of the nanocatalyst were analyzed by energy-dispersive spectroscopy (EDS), which confirmed the presence of Ni, Zr, P, and O in the compound (Fig. S3, Supporting Information).

The magnetic properties of nano-$NiZr_4(PO_4)_6$ were evaluated with the help of a vibrating sample magnetometer (VSM) (Fig. S4, Supporting Information). The saturation magnetization for nano-$NiZr_4(PO_4)_6$ is ~0.03 emu g^{-1}.

In order to investigate the size distribution of the nanoparticles, dynamic light scattering (DLS) was carried out, as presented in Fig. S5 (Supporting Information). The size distribution is centered around 138.3 nm.

Thermogravimetric analysis (TGA) was used to monitor the thermal stability of nano-$NiZr_4(PO_4)_6$. A 1.9% decrease in weight between 50 and 300°C is due to the loss of absorbed solvent on the external surface and molecules trapped among the nanoparticles (Fig. S6, Supporting Information).

Figure S7 (Supporting Information) shows a Fourier transform infrared (FT-IR) spectrum of nano-$NiZr_4(PO_4)_6$. The bands at 1012, 1096, and 1165 cm^{-1} correspond to the asymmetric stretching vibrations of P–O in the PO_4 tetrahedron (ν_3), and the band at 965 cm^{-1} is due to the symmetric stretching vibrations (ν_1). Three bands of the asymmetric bending vibrations (ν_4) occur at 562, 589, and 625 cm^{-1}. The symmetric bending vibration (ν_2) is responsible for the absorption band at ~445 cm^{-1} [30, 31].

2.2 Catalytic behavior of the nanocatalyst in the synthesis of propargylamines

We commenced our investigation by testing the reaction of phenylacetylene (**3**), morpholine (**2b**), and benzaldehyde (**1a**) as a model reaction for the synthesis of propargylamines. To obtain the ideal reaction conditions for the synthesis of compound **4a**, we studied diverse catalysts and solvents, which are shown in Table 1. Screening of the different catalysts such as $CuCl_2$, $ZrOCl_2$, $Ni(OAC)_2$, nano-ZrO_2, nano-Fe_3O_4, and nano-$NiZr_4(PO_4)_6$ revealed nano-$NiZr_4(PO_4)_6$ (3 mol%) as the most effective catalyst to perform this reaction under ultrasonic irradiation (40 W) (Table 1). In this study, ultrasound irradiation was used as

Table 1: Optimization of reaction conditions using different catalysts under different conditions.[a]

Entry	Solvent (conditions)	Catalyst (quantity in mol%)	Time (min)	Yield (%)[b]
1	Toluene (reflux)	No catalyst	500	Trace
2	DMF (reflux)	$CuCl_2$ (7 mol%)	500	39
3	THF (reflux)	$ZrOCl_2$ (5 mol%)	600	34
4	Toluene (reflux)	$Ni(OAC)_2$ (4 mol%)	400	48
5	Toluene (reflux)	Nano-ZrO_2 (4 mol%)	450	40
6	Toluene (reflux)	Nano-Fe_3O_4 (4 mol%)	450	17
7	CH_3CN (reflux)	Nano-$NiZr_4(PO_4)_6$ (5 mol%)	120	42
8	THF (reflux)	Nano-$NiZr_4(PO_4)_6$ (5 mol%)	120	53
9	DMF (reflux)	Nano-$NiZr_4(PO_4)_6$ (5 mol%)	120	59
10	Toluene (reflux)	Nano-$NiZr_4(PO_4)_6$ (5 mol%)	120	75
11	CH_3CN (US: 40 W)[c]	Nano-$NiZr_4(PO_4)_6$ (4 mol%)	15	60
12	THF (US: 40 W)	Nano-$NiZr_4(PO_4)_6$ (4 mol%)	15	71
13	DMF (US: 40 W)	Nano-$NiZr_4(PO_4)_6$ (4 mol%)	15	74
14	Toluene (US: 30 W)	Nano-$NiZr_4(PO_4)_6$ (3 mol%)	10	82
15	Toluene (US: 40 W)	Nano-$NiZr_4(PO_4)_6$ (3 mol%)	10	92
16	Toluene (US: 50 W)	Nano-$NiZr_4(PO_4)_6$ (3 mol%)	10	92
17	Toluene (US: 40 W)	Nano-$NiZr_4(PO_4)_6$ (2 mol%)	10	87
18	Toluene (US: 40 W)	Nano-$NiZr_4(PO_4)_6$ (4 mol%)	10	92

[a]Phenylacetylene (1.2 mmol), morpholine (1.2 mmol), and benzaldehyde (1 mmol). [b]Isolated yield. [c]Ultrasonic irradiation.

Table 2: Synthesis of propargylamines.[a]

Entry	Amine	R	Product	Time (min)	Yield (%)[b]
1	Morpholine	H	**4a**	10	92
2	Morpholine	4-Cl	**4b**	10	95
3	Morpholine	2-Me	**4c**	15	88
4	Morpholine	4-Me	**4d**	15	87
5	Morpholine	2-Cl	**4e**	10	93
6	Morpholine	4-NO_2	**4f**	10	96
7	Morpholine	4-OMe	**4g**	15	87
8	Piperidine	3-Me	**4h**	15	90
9	Piperidine	4-Br	**4i**	10	96
10	Piperidine	H	**4j**	10	94
11	Piperidine	4-Cl	**4k**	10	96

[a]Phenylacetylene (1.2 mmol), morpholine or piperidine (1.2 mmol), arylaldehydes (1 mmol), and nano-$NiZr_4(PO_4)_6$ (3 mol%) in toluene under ultrasonic irradiation (40 W). [b]Isolated yield.

a green and complementary technique for the preparation of propargylamines. When the catalysis was performed under ultrasound irradiations, the reaction rate increased considerably, whereas longer reaction times were required under conventional heating. Also, ultrasound irradiation improved the yields of the reactions and shortened the reaction times. A possible explanation for the positive result is that ultrasonic irradiation increases the number of active bubble cavities and the size of these bubbles, resulting in higher maximum collapse temperatures. We explored the feasibility of the reaction by choosing some representative substrates (Table 2). Better yields were achieved with substrates having electron-withdrawing groups.

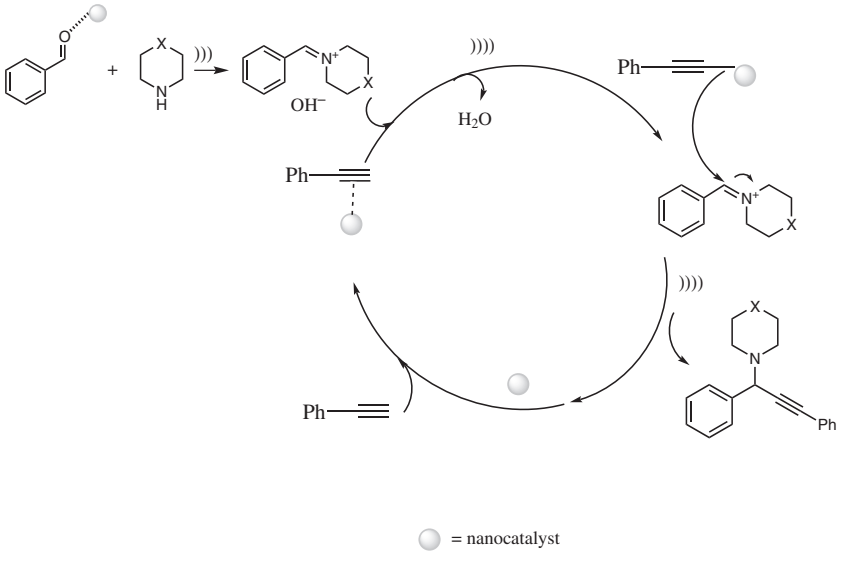
The reusability of the nano-$NiZr_4(PO_4)_6$ catalyst was examined for the synthesis of product **4a**, and it was found that product yields decreased only by small amounts on each reuse (run 1, 92%; run 2, 92%; run 3, 92%; run 4, 91%; run 5, 90%). In the recycling procedure of nano-$NiZr_4(PO_4)_6$, ethyl acetate was added to dilute the reaction mixture after terminating the reaction. The catalyst was insoluble in the solvent and was separated by centrifuging. The catalyst was washed with ethanol 4–5 times to ensure the complete removal of any organic residuals; the catalyst was reused for further catalytic reaction cycles.

2.3 Proposed reaction mechanism

A proposed mechanism for the synthesis of propargylamines using nanocatalysts under ultrasound irradiation is shown in Scheme 2. In the beginning, the aldehyde activated by the nanocatalyst is condensed with the secondary amine to give an iminium ion, while the nanocatalyst activates the C–H bond of the terminal alkyne to generate a nickel(II) acetylide intermediate. The nickel(II) acetylide intermediate then starts a nucleophilic attack on the iminium ion to give propargylamines [32–34].

3 Conclusions

In conclusion, we demonstrated an efficient method for the synthesis of propargylamines through a three-component reaction of phenylacetylene, aromatic aldehydes,



Scheme 2: Possible mechanism for the synthesis of propargylamines in the presence of nano-$NiZr_4(PO_4)_6$.

and morpholine or piperidine using a nano-$NiZr_4(PO_4)_6$ catalyst under ultrasound irradiation. The remarkable advantages of this methodology are short reaction times, high to excellent product yields, operational simplicity, low catalyst loading, and the use of ultrasound as a powerful source of energy.

4 Experimental section

4.1 Materials and apparatus

All organic materials were purchased from Sigma-Aldrich and Merck and were used without further purification. A multiwave ultrasonic generator (Sonicator 3200; Bandelin, MS 73, Germany), equipped with a converter/transducer and titanium oscillator (horn), 12.5 mm in diameter, operating at 20 kHz with a maximum power output of 200 W, was used for ultrasonic irradiation. The ultrasonic generator automatically adjusted the power level. TGA curves are recorded using a V5.1A DUPONT 2000 instrument. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer. Powder XRD was carried out on a Philips X'pert diffractometer with monochromatized ZrK_α radiation ($\lambda = 1.5406$ Å). In order to study the particle size and the morphology of the nano-$NiZr_4(PO_4)_6$, field-emission (FE)-SEM images of the products were recorded using a HITACHI S4160 FE-SEM instrument. The magnetic measurements of the samples were carried out using a VSM (Meghnatis Daghigh Kavir Co., Kashan Kavir, Iran) at room temperature with an applied magnetic field sweeping between ±10 kOe (1 kOe = 7.96×10^4 A m^{-1}).

4.2 Preparation of nano-$NiZr_4(PO_4)_6$

$ZrOCl_2$ was used as the zirconium source. First, 1 mmol of $ZrOCl_2 \cdot 8H_2O$ and 1 mmol of $Ni(NO_3)_2 \cdot 2H_2O$ were added to 15 mL of $HO(CH_2)_2OH$ and sonicated at 30 W power to complete dissolution. Afterward, 0.8 mL H_3PO_4 (85%), 4 mmol of NH_4Cl, and 1.4 mL of an aqueous solution of CH_3NH_2 (25.0–30.0%) were added consecutively, and the mixture was sonicated for 30 min. Then, the reaction mixture was transferred into a Teflon-lined autoclave under autogenous pressure at 200°C for 5 days. When the reaction was completed, a dispersed precipitate was obtained. The solid was filtered and washed with distilled water and ethanol several times. Subsequently, the product was dried at 50°C for 5 h and calcinated at 700°C for 2 h. Afterward, the solid was added to 20 mL of DMF and sonicated at 95 W power for 2 h. Finally, the resulting product was filtered, washed with distilled water and absolute ethanol, and dried at 150°C for 2 h in vacuum to afford pure nano-$NiZr_4(PO_4)_6$ particles.

4.3 General procedure for the synthesis of propargylamines

A mixture of morpholine or piperidine (1.2 mmol), benzaldehydes (1 mmol), phenylacetylene (1.2 mmol), and 3 mol% of nano-$NiZr_4(PO_4)_6$ in toluene (15 mL) was sonicated at 40 W power for the appropriate time [monitored by thin-layer chromatography (TLC)]. After completion of the reaction (TLC), ethyl acetate was added. The catalyst was insoluble in ethyl acetate, and it could therefore be recycled by a simple filtration. The crude product obtained was purified by column chromatography using ethyl acetate-*n*-hexane.

5 Supporting information

Some characteristics of the nano-$NiZr_4(PO_4)_6$ particles as well as spectral data and copies of the ^{1}H NMR spectra of compounds **4a**–**4k** are given in the Supporting Information available online (https://doi.org/10.1515/znb-2017-0178).

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Graphical abstract

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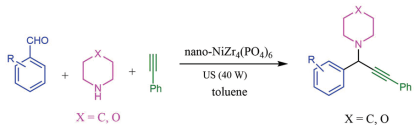

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