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ARTICLE

Nano magnetic sulfated zirconia ($\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$): an efficient solid acid catalyst for green synthesis of α - aminonitriles and imines

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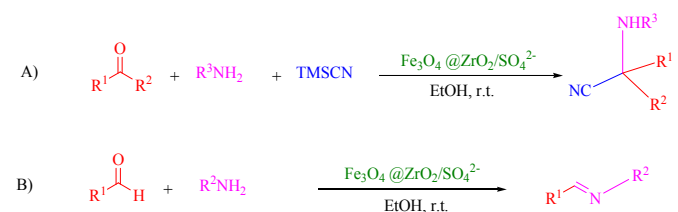
Abstract In this research, nano magnetic sulfated zirconia was prepared and characterized by Fourier transforms infrared spectroscopy (FT-IR) spectra, Scanning electron microscopy (SEM) images, Transmission electron microscopy (TEM), energy dispersive X-ray spectroscopy (EDX), X-ray diffraction (XRD) measurements and vibrational sample magnetometry (VSM). Its catalytic activity was investigated in one-pot three component green synthesis of α -aminonitriles using various aldehydes and ketones at room temperature in ethanol. This protocol has various advantages such as: simple work-up, short reaction time, high product yields and easy recovery and reusability of the catalyst.

Keywords: Nano magnetic sulfated zirconia, Fe_3O_4 , imines, strecker reaction, α -aminonitriles, and green synthesis.

Introduction

Over 90% chemical processes employ catalysts. Among these processes, acid catalysts are playing an important role in organic synthesis and transformations. The use of conventional liquid acids, and Lewis acids such as H_2SO_4 , HCl , HF , AlCl_3 , BF_3 , ZnCl_2 and SbF_5 pose significant risks in handling, containment, disposal and regeneration due to their toxic and corrosive nature¹. There is a necessary need to eliminate the aggressive and ecologically harmful mineral acids to carry out a large number of acid-catalyzed industrial processes. This can be achieved by the development of strong solid acid catalysts that are stable and active at moderate temperatures². Sulfated zirconia is one of the most important solid super acid catalysts³ that have gained much attention for isomerization reactions for their high strength of acidity, non-toxicity and high activity at low temperatures⁴⁻⁶. It has also been used for other different acid catalyzed reactions such as: cracking⁷, alkylation, acylation, esterification, nitration, oligomerization^{8,9}. Strecker reaction, which was described primarily in 1850, is the first multi component reaction (MCR) and the most straightforward methods for the synthesis of α -aminonitriles¹⁰. α -aminonitriles are valuable intermediates for the synthesis of α -amino acids, 1,2-diamines, and various nitrogen-containing heterocyclic such as imidazoles and thiadiazoles¹¹, and other pharmacologically useful molecules such as Saframycin A¹², Ecteinascidin 743¹³. The typical strecker reaction employed HCN , KCN or NaCN as cyanide sources^{10,14,15}. But these sources are hazardous, toxic and involve harsh reaction conditions, several modifications of the strecker reaction have been reported using a variety of cyanide agents, such as Bu_3SnCN ¹⁶, $\text{K}_2[\text{Fe}(\text{CN})_6]$ ¹⁷, $\text{CH}_3(\text{OH})(\text{CN})\text{CH}_3$ ¹⁸, and TMSCN ¹⁹ under various conditions. Among these cyanide sources for the synthesis of α -aminonitriles, trimethylsilyl cyanide (TMSCN) is a promising alternative, safe, easy

to handle and more effective cyanide ion sources for the nucleophilic addition reactions. Protocols based on TMSCN often require Bronsted or Lewis acid catalytic system. Therefore many homogeneous catalysts, such as $\text{Pr}(\text{OTf})_3$ ²⁰, RuCl_3 ²¹, $\text{Sc}(\text{OTf})_3$ ²², RhI_3 ²³, iodine²⁰ and $\text{Fe}(\text{Cp})_2\text{PF}_6$ ²⁴, have been developed in recent years. In order to overcome problems associated with homogeneous catalyst, some heterogeneous catalysts including polymer-supported scandium triflate²⁵, MCM-41 anchored sulfonic acid²⁶, K_2PdCl_4 ²⁷, poly(4-vinyl pyridine)- SO_2 complex²⁸, guanidine HCl ²⁹ have also been introduced. But most of these methods have some drawbacks such as expensive reagents, long reaction times, low yields and tedious work-up procedures. Therefore we introduce $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ as a nano magnetic acid catalyst which can promote the one-pot three component strecker reaction of aldehydes/ ketones and amines with TMSCN to afford α -aminonitriles (scheme 1, A). In order to overcome the problems arising during separation of the catalyst from the reaction mixture, $\text{ZrO}_2/\text{SO}_4^{2-}$ is mounted on magnetic nanoparticles. In this research we also investigated formation the corresponding imines as the strecker reaction intermediates (scheme 1, B).



Scheme 1: The strecker reaction of carbonyl compounds and amines with TMSCN catalyzed by $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (A), synthesis of imines by $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (B)

Results and discussion

Catalyst characterizations

Fig. 1 shows the XRD patterns of the prepared Fe_3O_4 and $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$. As can be seen in Fig. 1, six characteristic peaks of Fe_3O_4 ($2\theta = 30.1, 35.4, 43.0, 53.5, 57.0$ and 62.5) are observed³⁰. Also the peaks of the Fe_3O_4 could be seen for the synthesized $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (XRD pattern of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$). The peak position of Fe_3O_4 are unchanged during the production of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$, indicating that the crystalline structure of the magnetite is essentially maintained. Additional diffraction peaks around $30.6, 51.1,$ and 60.1 are attributed to ZrO_2 .

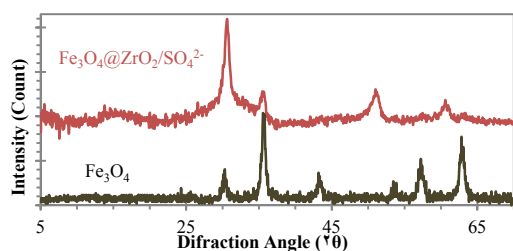


Fig. 1: The X-ray diffraction patterns of Fe_3O_4 and $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$

The X-ray powder diffraction (XRD) pattern in the $30.6, 51.1$ and 60.1 2θ range for $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ showed that after calcination the tetragonal phase is the major form present. Crystalite size of Fe_3O_4 was calculated to be 16 nm by applying the Scherrer equation. The IR spectra of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ is shown in Fig. 2. A broad peak about 3400 cm^{-1} was observed which is attributed to $\sigma_{\text{O-H}}$ stretching mode of water that adsorbed from air on the surface of catalyst. Hydrogen bonding causes the broadness of this peak. A peak about 1630 cm^{-1} attributed to δ O-H bending mode of water associated with the sulfate group. A strong band assigned to the stretching vibration of S=O observed at 1126 cm^{-1} and a middle peak at approximately 1400 cm^{-1} observed in the spectra assigned to asymmetric of covalent σ S=O band. The peak at around 600 cm^{-1} attributed to Zr=O band and the vibration peak of Fe-O band at about 500 cm^{-1} . The TEM and SEM micrographs that provide accurate information on the particle size and morphology of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ depicted in (Fig. 3). The homogeneous structure of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ with Fe_3O_4 Core and average particles size of about 30 and 25 nm respectively was showed. The results of the VSM measurement of the catalyst were depicted in Fig. 4, with confined field from -1000 to 1000 Oe. Bare nanoparticles of Fe_3O_4 possessed high saturation magnetization 53.8 emu/g at room temperature and decrease to 12.7 emu/g for $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$. It is due to the formation of the magnetite core and $\text{ZrO}_2/\text{SO}_4^{2-}$ coating.

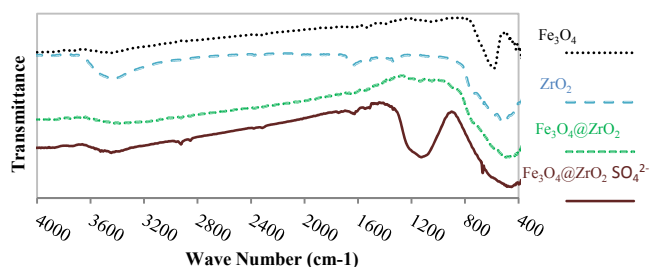


Fig. 2: FT-IR spectra of the $\text{Fe}_3\text{O}_4, \text{ZrO}_2, \text{Fe}_3\text{O}_4@\text{ZrO}_2$ and $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$

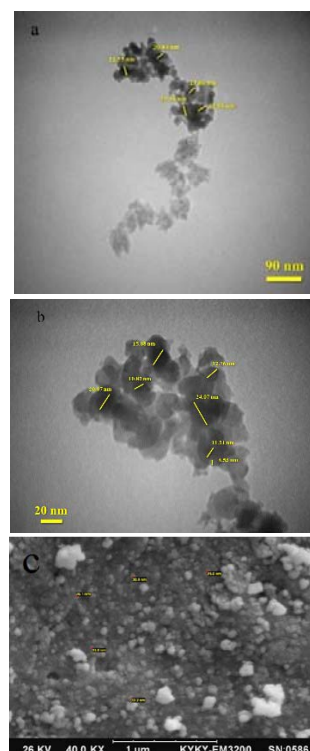


Fig. 3: TEM (a and b) and SEM (c) micrographs of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$

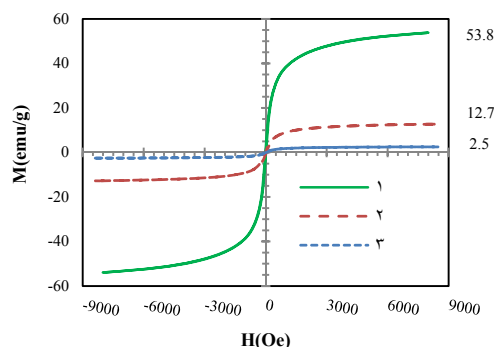


Fig. 4: Saturation magnetization curve of the Pure Fe_3O_4 (1), $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ calcinated at N_2 atmosphere (2) and calcinated at air atmosphere.

According to saturation magnetization curve that depicted in (Fig 4) it is obvious that there is no hysteresis, in the magnetization sweep. Therefore, magnetic coercivity of nanostructures is zero, suggest that the Fe_3O_4 contained samples are superparamagnetic. we have obtained EDX spectrum of the $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$, indicated that there were only Fe, O, Zr and S elements in the structure of the catalyst and the amount of iron in catalyst was 21%. All the results suggest that $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ has been successfully synthesized.

Catalytic properties

To assess the catalytic activity of the $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$, it was applied in the first multicomponent reaction for synthesis of α -aminonitriles. In order to optimize reaction conditions, the reaction of 4-chlorobenzaldehyde, aniline, and TMSCN (mole ratio 1:1:1.2) as model reaction was chosen and the effects of the solvent and various catalysts were investigated (Table 1). It seems noteworthy to mention that the reaction was not successful in the absence of the catalyst (entry 1-3, Table 1). Metal oxide nanoparticles such as nano- Fe_3O_4 and ZrO_2 rendered higher yields in CH_3CN than water and EtOH (entries 4-9, Table 1). Also, we evaluated the effects of $\text{ZrO}_2/\text{SO}_4^{2-}$ and $\text{Fe}_3\text{O}_4@\text{ZrO}_2$ in this model reaction, but much to our surprise, when $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (60 mg) was used as the catalyst, the reaction went to completion in 10 minutes and 97% of product was isolated (entry 16, Table 1). It was observed that addition of Fe_3O_4 to sulfated zirconia dramatically affected catalytic activity in the synthesis of α -aminonitriles (entries 12, 16, 17, Table 1), it was found that iron oxide (Fe_3O_4) modifies the sulfated zirconia surface by generating acidic sites of medium strength. Doping sufficiently the sulfated zirconia with iron, can be increased the total number of acidic sites with lower strength. These changes, especially the simultaneous presence of two acidic type sites with different strengths, are interesting for catalytic activity³¹. The ionic nature of S=O imparts the Bronsted acid site to the catalyst which enhance the acidity of material and thereby reinforcing catalytic activity (entries 13, 16, Table 1). As shown in Table 1 it was found that EtOH is suitable solvent to give the desired products in high yields and relatively short reaction time in comparison with other solvents.

Table 1. Optimization of the $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ catalyzed model reaction for synthesis of aminonitriles^(a).

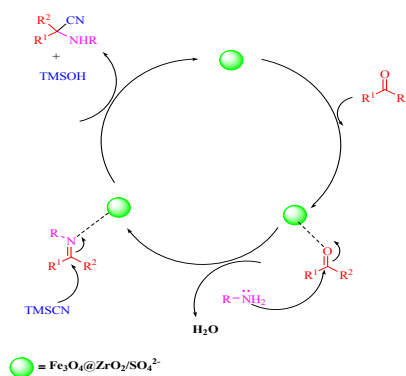
Entry	Catalyst	Solvent	Time (min)	Yield (%) ^b
1	-	EtOH	120	Trace
2	-	H ₂ O	240	18
3	-	CH ₂ Cl ₂	240	Trace
4	Nano- Fe_3O_4 (10 mol %)	CH ₃ CN	90	75
5	Nano- Fe_3O_4 (10 mol %)	H ₂ O	90	68
6	Nano- Fe_3O_4 (10 mol %)	EtOH	60	68
7	Nano- ZrO_2 (10 mol %)	CH ₃ CN	45	85
8	Nano- ZrO_2 (10 mol %)	H ₂ O	120	58
9	Nano- ZrO_2 (10 mol %)	EtOH	60	60
10	$\text{ZrO}_2/\text{SO}_4^{2-}$ 100 mg	CH ₃ CN	90	90
11	$\text{ZrO}_2/\text{SO}_4^{2-}$ 100 mg	H ₂ O	90	Trace
12	$\text{ZrO}_2/\text{SO}_4^{2-}$ 100 mg	EtOH	90	85
13	$\text{Fe}_3\text{O}_4@\text{ZrO}_2$ 60 mg	EtOH	180	85
14	$\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ 50 mg	CH ₃ CN	40	80
15	$\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ 50 mg	EtOH	40	90
16	$\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ 60 mg	EtOH	10	97
17	$\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ 100 mg	EtOH	25	93

^aReaction conditions: 4-chlorobenzaldehyde (1.0 mmol), aniline (1.0mmol), trimethylsilyl cyanide (1.2 eq), catalyst, solvent (2.0 ml), room temperature. ^b Isolated yields.

After optimization of the reaction conditions, to show the general applicability of this protocol, a series of α -aminonitriles were synthesized by reacting various aldehydes, ketones and amines with TMSCN in presence of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ in EtOH at room temperature. The obtained results are summarized in Table 2. Separation and purification were very simple in these reactions. $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ is not soluble in boiling EtOH and the catalyst was separated by external magnet from the desired products during their recrystallization from EtOH. Irrespective of the carbonyl compound used, the reaction proceeded to give the corresponding product with varying degrees of success (Table 2). Acid sensitive aldehydes such as furfural worked well without the formation of any side products and afforded the α -aminonitrile derivatives in 85% yield (Table 2, entry 13), also unsaturated aldehyde such as Cinnamaldehyde, produced excellent yields, without any decomposition or polymerization (Table 2, entry 12). Aliphatic amines such as benzylamine as well as aromatic amines afforded good yields. Since imines are known as the strecker reaction intermediates, we investigated the imine formation from aldehydes and aniline in presence of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ under the same condition. To the best of our knowledge, only a few researches on the strecker reaction with ketones have been reported^{24, 32, 33}.

Regarding the fact that ketones react hardly due to their steric hindrance, our catalyst was effective because we carried out strecker reaction with ketone derivatives easily. The results for synthesis of the imines have been summarized in Table 3. For the new products (Table 2, entry 23, 24) the structure was determined by ¹H NMR and ¹³C NMR. For the known compounds, which are all the other products in Table 2 and 3, their physical and spectroscopic data were compared with those of authentic samples and found to be identical.

In general, substituted aromatic amines with electron-withdrawing groups require shorter reaction time in comparison to those with electron-donating groups. Aromatic aldehyde substituted electron-withdrawing groups increased reaction rate. Aromatic amines with electron-donating groups in decreased nucleophilicity of the nitrogen reagent and increase reaction time because of substituted electron-donating increased basicity nitrogen and the result with absorb H⁺ is deactivated. Efficiency comparison of the catalytic activity of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ with several previous methods is presented in Table 4. The results show that this method is superior to some of the earlier methods in terms of yields and reaction times. The suggested mechanism for the formation of α -aminonitriles is shown in Scheme 3. According to this mechanism, $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ catalyze the *in situ* formation of the imine intermediate through activation the oxygen atom of the carbonyl group. In the presence of the catalyst, the imine carbon is attacked by cyanide to give the product.



Scheme 2: The plausible mechanism for synthesis of α -aminonitriles catalysed by $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$.

Reusability of the catalyst was also evaluated in the model reaction. After completing the reaction, the catalyst was removed by an external magnet, washed with ethanol and dried at room temperature and used directly for the next reaction. A slight decrease of conversion (85%) was observed in fourth and fifth cycles; this could be due to loss of catalyst around during the reaction recycling. These results indicate that the $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ could be recovered and reused five times without any considerable loss of catalytic activity (Fig. 5).

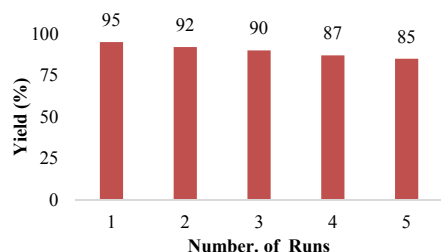


Fig. 5: Recycling of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ for the synthesis of α -aminonitriles

After completing the reaction the catalyst was separated and washed several times and have not seen any change in its structure, with FT-IR spectra of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ was confirmed the presence of sulfate ion on the catalyst (Fig. 6).

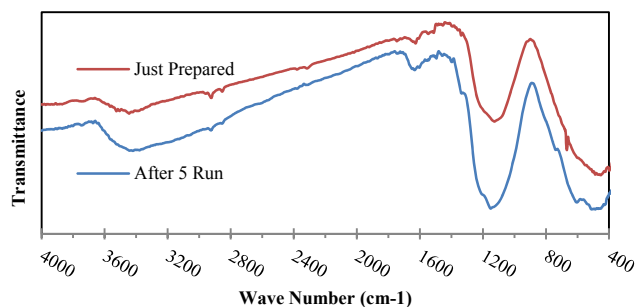
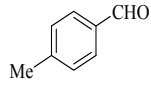
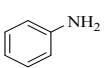
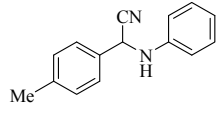
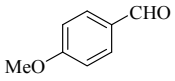
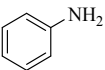
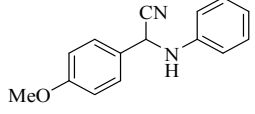
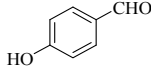
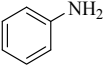
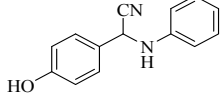
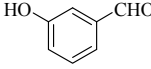
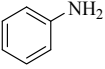
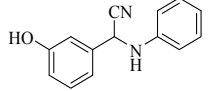
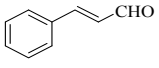
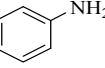
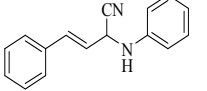
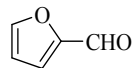
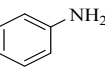
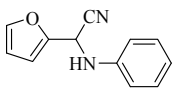
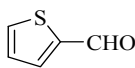
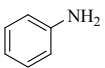
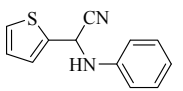
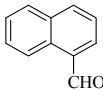
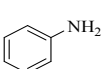
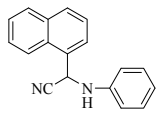
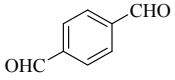
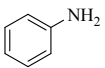
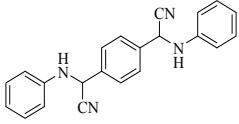
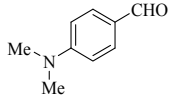
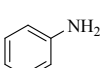
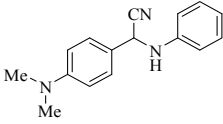
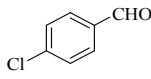
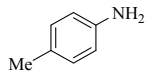
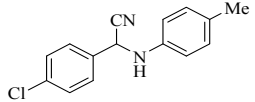
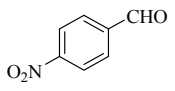
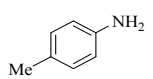
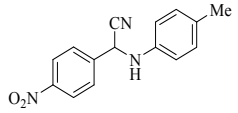
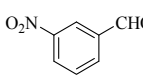
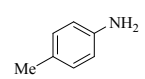
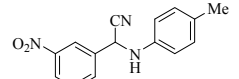
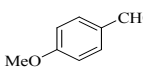
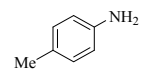
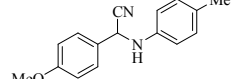
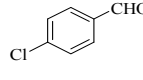
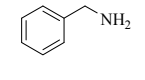
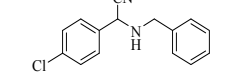
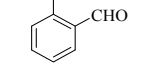
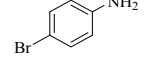
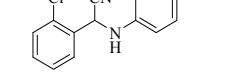
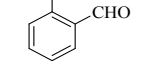
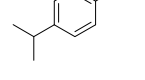
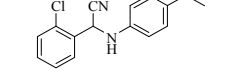
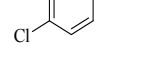
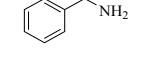
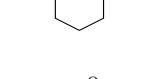
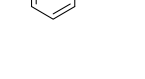
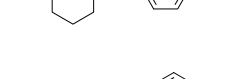
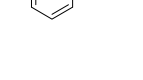
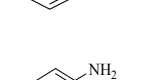
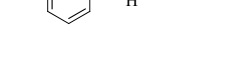
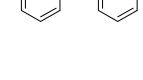



Fig. 6: The FT-IR spectra of the $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ just prepared and after 5 runs

Table 2. Strecker reaction of various aldehydes or ketones and amines in the presence of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ as the catalyst ^a

Entry	Aldehyde/ketone	Amine	Product	Time (min)	Yield (%) ^b	Mp (ref)
1				10	97	113-115 26
2				30	95	80-82 ³⁵
3				25	93	67-70 ³⁵
4				30	90	115-117 ³⁶
5				90	92	75-78 ³⁷
6				15	90	114-116 ³⁸
7				20	93	84-86 26


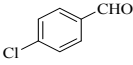
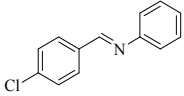
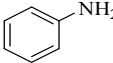

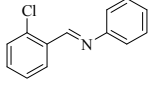
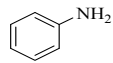
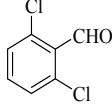
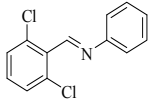
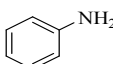
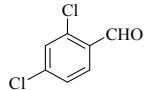
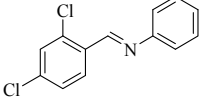
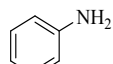
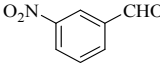
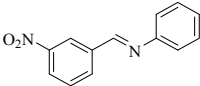
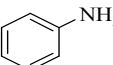
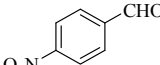
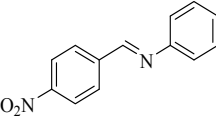
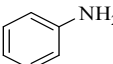
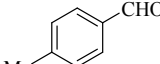
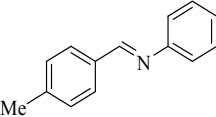
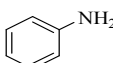
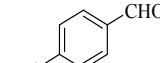
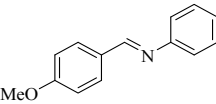
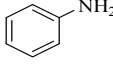
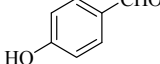
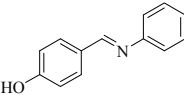
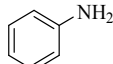
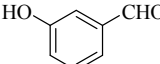
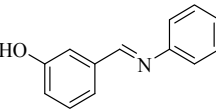
Entry	Aldehyde/ketone	Amine	Product	Time (min)	Yield (%) ^b	Mp (ref)
8				35	95	78-80 ³⁵
9				35	93	91-92 ³⁹
10				20	95	120-122 ²⁷
11				70	93	Oil ⁴⁰
12				50	96	117-119 ³⁹
13				60	85	72-74 ⁴¹
14				40	90	97-99 ³⁵
15				40	87	93-95 ⁴²
16 ^c				120	90	154-157 ³⁷
17				70	90	107-110 ⁴³
18				25	95	87-90 ³⁶
19				40	96	83-85 ³²

Entry	Aldehyde/ketone	Amine	Product	Time (min)	Yield (%) ^b	Mp (ref)
20				25	93	Oil ²⁶
21				30	89	102-105 ²⁶
22				50	90	Oil ¹⁷
23				120	95	112-116 This work
24				40	95	69-70 This work
25			-	No reaction	-	-
26				50	95	69-71 ²⁶
27				70	90	150-151 ⁴⁴
28			-	No reaction	-	-

^a Reaction conditions: aldehyde or ketone (1.0 mmol), amine (1.0 mmol), TMSCN (1.2 eq), catalyst (60 mg), in EtOH (2.0 ml) at room temperature,

^b Isolated yield, ^c Reaction condition: aldehyde (1.0 mmol), amine (2.0 mmol), TMSCN (2.4 eq), catalyst (100 mg) in EtOH (3.0 ml).

Table 3. Preparation of Imines through reaction of aldehydes and aniline catalyzed by $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (a).

Entry	Amine	Aldehyde	Product	Time (min)	Yield (%) ^b	Mp (Ref)
1				1	90	57-59 ⁴⁵
2				3	93	35-36 ⁴⁶
3				10	87	58-60 ⁴⁷
4				2	90	88-89 ⁴⁸
5				2	90	62-64 ⁴⁹
6				2	95	88-90 ⁴⁹
7				3	96	42-45 ⁴⁹
8				1	85	63-64 ⁴⁹
9				5	90	193-195 ⁴⁹
10				7	70	105-107 ⁴⁹

^a Reaction conditions: 1.0 mmol aldehyde, 1.0 mmol aniline and 60 mg catalyst in 2.0 ml EtOH at room temperature. ^b Isolated yields.

Table 4. A comparison of the efficiency of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ with other catalysts on the condensation of 4-chlorobenzaldehyde, aniline and TMSCN.

Entry	Catalyst	Solvent	Time (min)	Yield (%) ^a	Ref
1	$\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (60 mg)	EtOH	10	97	This work
2	MCM-41- SO_3H (5 mg)	EtOH	30	98	26
3	B-MCM-41 (50 mg)	EtOH	90	98	32
4	PVP- SO_2 (100 mg)	CH_2Cl_2	6 h	89	28
5	Cellulose sulfuric acid (50 mg)	CH_3CN	80	90	34
6	$\text{Fe}(\text{Cp})_2\text{PF}_6$ (5 mol %)	-	20	91	24
7	K_2PdCl_4 (10 mol %)	H_2O	30	91	27

Experimental

Chemicals and Instruments

All solvents and chemicals were purchased from Merck or Fluka chemical companies. FT-IR spectra were obtained over the region 400-4000 cm^{-1} with a Nicolet IR 100 FT-IR with spectroscopic grade KBr. The powder X-ray diffraction pattern was recorded using a X-PERT-PRO diffractometer with $\text{Cu K}\alpha$, ($\lambda = 1.54 \text{ \AA}$) irradiation, in the range of 5 to 80 (2θ) with a scan Step of 0.026. The morphology of catalyst was studied with scanning electron microscopy using SEM (KYKY, EM 3200) on gold coated samples. The magnetic properties of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ nanoparticles were measured with a vibrating magnetometer/ Alternating Gradient Force Magnetometer (VSM/, MDKFD)

Preparation of the magnetic Fe_3O_4 nanoparticles (MNPs)

Ferric acid and ferrous salts were employed as precursors for the synthesis of Fe_3O_4 nano particles. Briefly, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (12.2 g, 0.04 mol) and $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (4.7 g, 0.02 mol) were dissolved in 100 ml distilled water under vigorous stirring. After 10 minutes, the solution was heated at 50 $^\circ\text{C}$ under nitrogen atmosphere. Consequently, the ammonium hydroxide solution (25%) was added dropwise to the reaction mixture to maintain the reaction pH about 9. Afterward, the reaction mixture was cooled at room temperature and black precipitate which was separated by external magnet from the reaction mixture, repeatedly washed with de-ionized water for several times to remove the remaining impurities. At the final step nanoparticles was dried at 60 $^\circ\text{C}$ in vacuo.

Synthesis of $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$

Initially 30g ZrCl_4 were dissolved in 1000 ml EtOH: H_2O (1:1) to form a colorless solution and aqueous ammonia (10%) was added dropwise under vigorous stirring until the pH of the solution reached 2. Then 3g $\text{Fe}_3\text{O}_4\text{NPs}$ was added to the mixture, after that aqueous ammonia (10%) was added dropwise again under sonication up to pH 9. The precipitate was filtered, thoroughly washed with distilled water, the absence of chloride ion was confirmed by AgNO_3 test. Subsequently the obtained solid was dipped in $(\text{NH}_4)_2\text{SO}_4$ (3 mol.L⁻¹) aqueous solution at room temperature for 24 h. Then the solid was filtered, dried without washing overnight at 100 $^\circ\text{C}$ and calcined at 600 $^\circ\text{C}$, for 6 h in the N_2 atmosphere.

General procedure for the synthesis of α -aminonitriles

A mixture of aldehyde (or ketone) (1.0 mmol), amine (1.0 mmol), trimethylsilylcyanide (TMSCN) (1.2 eq, 0.15 ml) and $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (60 mg) in EtOH 96% (2.0 ml) was stirred at room temperature for an optimized time (Table 2). After completion of the reaction, as indicated by thin-layer chromatography (TLC), the catalyst was separated by an external magnet and reused for five times in other fresh reactions without a considerable loss of activity. Then the products were crystallized by EtOH 96% (5 ml) to give pure desired α -aminonitriles.

General procedure for the synthesis of imines as the strecker reaction intermediates

A mixture of aldehyde (or ketone) (1.0 mmol), amine (1.0 mmol) and $\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$ (60 mg) in EtOH 96% (2.0 ml) was stirred at room temperature for an optimized time (Table 3). After completion of the reaction, as indicated by thin-layer chromatography (TLC), the catalyst was separated by an external magnet and reused for five times in other fresh reactions without a considerable loss of activity. Then the products was crystalized by EtOH 96% (5 ml) to give pure desired imines.

Back titration in aqueous media catalyst ($\text{Fe}_3\text{O}_4@\text{ZrO}_2/\text{SO}_4^{2-}$)

The amount of released $[\text{H}^+]$ by catalyst was determined by back titration. In a container which contained 35 ml of distilled water, 0.5 g of NaCl, 0.5 g catalyst and 10 ml NaOH (0.1 M) were added and stirred for 24 h on a magnetic stirrer until neutralized $[\text{H}^+]$ which produced from catalyst hydrolysis. Then three drops of phenolphthalein were added to the container and the solution titrated with 0.1 M solution of hydrochloric acid. The end point was reached when the colour changed from pink to colourless⁵⁰.

Spectral data for the representative compounds:

3.3.1: 2-(4-chlorophenyl)-2-(phenylamino)acetonitrile (Table 2, entry 1): Mp: 113-115 $^\circ\text{C}$, IR(KBr): ν 3305, 2232, 1602, 1494, 790 cm^{-1} . ¹H-NMR (500 MHz, CDCl_3) δ 8.0, (d, 2H), 7.8(d, 2H), 7.3(t, 2H), 6.9(t, 1H), 6.76 (d, 2H), 5.33 (d, 1H), 3.74 (br s, 1H). ¹³C NMR (125 MHz, CDCl_3): δ 142.3, 135.5, 133.3, 131.6, 130.5, 122.6, 119.7, 116.3, 50ppm.

3.3.2: 2-(2, 4-dichlorophenyl)-2-(phenylamino) acetonitrile (Table 2, entry 4): Mp: 115-117 $^\circ\text{C}$, IR (KBr): ν 3323, 2241, 1622, 1469, 748 cm^{-1} . ¹H- NMR (500 MHz, CDCl_3) δ 5.23 (d, 1H), 6.29 (d, 1H), 6.86 (d, 2H), 6.92 (t, 1H), 7.27-7.34 (m, 3H), 7.41 (d, 2H) ppm.

3.3.3: 2-(4-phenyl)-2-(phenylamino) but-3- acetonitrile (Table 2, entry 12): Mp: 117-119 $^\circ\text{C}$, IR (KBr): ν 3344, 2223, 1602, 1504, 1442 cm^{-1} . ¹H- NMR (500 MHz, CDCl_3) δ 4.08 (br, 1H), 5.37 (d, 1H), 6.73 (d, 2H), 6.86 (t, 1H), 7.23 (m, 2H), 7.39-7.42 (m, 3H), 7.53-7.56 (m, 2H).

3.3.4: 2-(2-thienyl)-2-(phenylamino) acetonitrile (Table 2, entry 14): Mp: 97-99 $^\circ\text{C}$, IR (KBr): 3378, 2243 cm^{-1} ; ¹H NMR (CDCl_3 , 500 MHz) δ 3.92 (d, 1H), 5.58 (d, 1H), 6.93 (d, 2H), 7.29 (t, 1H), 7.38 (q, 1H), 7.41-7.53 (m, 4H) ppm.

3.3.5: 2-(4-isopropylphenylamino)-2-(2-chlorophenyl) acetonitrile (Table 2, entry 25), Mp: 69-70, IR (KBr): ν 3334, 2233, 1612, 1515 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 7.71 (t, 1H), 7.20-7.70 (m, 6H), 6.7 (d, 2H), 5.7 (s, 1H), 2.8 (septet 1H), 1.2 (d, 6H) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 142.8, 141.5, 133.6, 132.3 (d), 131.4, 130.8, 129.5, 128.2, 127.6, 118.3, 115 ppm.

3.3.6: 2-(4-bromophenylamino)-2-(2-chlorophenyl) acetonitrile (Table 2, entry 24), Mp: 112-116, IR (KBr): ν 3342, 2314, 1593, 1496 cm^{-1} . ^1H -NMR (500 MHz, CDCl_3): δ = 7.75 (t, 1H), 7.34-7.51 (m, 6H), 6.54 (d, 2H), 5.58 (s, 1H), 4(s, br, 1H) ppm. ^{13}C -NMR (125 MHz, CDCl_3): δ = 144.4, 133.6, 132.6, 131.7(d), 130, 129.4, 128.3, 117.8, 119.3, 112.9 ppm.

Conclusion

In conclusion, we have demonstrated that sulfated zirconia supported on magnetic nanoparticles can act as a novel, heterogeneous, efficient nano catalyst for the one-pot three component synthesis of α -aminonitrile derivatives through a green and facile method. This method offers several advantages including high yields, short reaction times, easy work up procedure, reusability of catalyst and environmentally benign reaction conditions.

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Notes and references

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