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Spinel-type zinc aluminate ($ZnAl_2O_4$) nanoparticles prepared by the co-precipitation method: A novel, green and recyclable heterogeneous catalyst for the acetylation of amines, alcohols and phenols under solvent-free conditions

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ABSTRACT

Zinc aluminate ($ZnAl_2O_4$) nanoparticles with an average particle size of about 8 nm were easily prepared by the co-precipitation method using aqueous ammonia solution as the precipitating agent. This nanosized spinel-type oxide was characterized by TGA, XRD, FT-IR, TEM, and surface area measurement and used as the heterogeneous catalyst for the acetylation reaction. Efficient acetylation of various amines, alcohols and phenols was carried out over $ZnAl_2O_4$ nanoparticles using acetic anhydride and/or acetyl chloride as the acetylating agents at room temperature without the use of a solvent. The method is highly selective, allowing the alcoholic hydroxyl group to be protected while the phenolic hydroxyl group remains intact, and the amine group can be acetylated in the presence of the hydroxyl group. This method is fast and has a high yield. It is also clean, safe, cost effective, compatible with substrates that have other functional groups and very suitable for practical organic synthesis. In addition, the catalyst can be reused without significant loss of activity. Indeed, the catalytic activity of the $ZnAl_2O_4$ nanoparticles is higher than that of bulk $ZnAl_2O_4$.

The protection of –OH and $–NH_2$ functional groups is one of the most important transformations in organic chemistry, both for fundamental research and industrial manufacturing [1,2]. This transformation is usually performed with acetic anhydride and/or acetyl chloride in the presence of either basic or acidic catalysts. Numerous catalytic systems are available for this transformation [3–26], but most of them are homogeneous and non-recoverable, and they often have disadvantages, such as prolonged reaction times, low yields, harsh conditions, use of harmful organic solvents, tedious work-up procedures, the requirement for excess reagents/catalysts, and the use of explosive, moisture-sensitive, or expensive catalysts.

Heterogeneous catalytic materials play a very important role in the selective protection of functional groups in ways that are economically advantageous and environmentally friendly [27,28]. They can be recovered easily from the reaction mixture by simple filtration, and reused several times, making the process more economically and environmentally viable. Heterogeneous catalysts such as yttria–zirconia based catalysts [29], simple metal oxides [30–32], montmorillonite K10 and KSF [33–35], $HClO_4$-SiO_2 [36], H_2SO_4-SiO_2 [37], $AlPW_{12}O_{40}$ [38], zeolites [39,40], Nafion-H [41], HBF_4-SiO_2 [42], KF-Al_2O_3 [43], silica embedded-triflate catalysts [44], MoO_3-Al_2O_3 [45], $NaHSO_4$-SiO_2 [46], sulfated zirconia [47], $(NH_4)_{2.5}H_{0.5}PW_{12}O_{40}$ [48], [TMBSA][HSO_4] ionic liquid [49], silica-bonded cobalt(II) salen [50], and silica-bonded N-propyl sulfamic acid and S-propyl sulfuric acid [51,52] have been reported for the acetylation of alcohols, phenols, thiols, and amines. From a practical viewpoint, the development of simple, inexpensive, widely applicable and environmentally benign catalysts/procedures is still an active area of research.

Among various inorganic solids, spinel-type mixed oxides (AB_2O_4) are well known for their rich catalytic action. These oxides are non-toxic, inexpensive, very stable materials with strong resistance to acids and alkalis, and they have high melting points and relatively high surface areas. These properties make them suitable for use as solid heterogeneous catalysts for organic transformations. Among them, zinc aluminate ($ZnAl_2O_4$) has been used extensively as a heterogeneous catalyst in many reactions, such as cracking, dehydration, hydrogenation, dehydrogenation, dehydrogenative condensation of normal alcohols, methylation of phenolic compounds and N-alkylation of 2-hydroxypyridine with methanol [53,54]. These catalytic applications prompted us to test this spinel-type mixed oxide as a heterogeneous catalyst for the acetylation reaction.

In this work, which is a continuation of our studies of the catalytic acetylation reaction using inorganic solids as heterogeneous catalysts [55,56], we wish to describe the preparation of spinel-type zinc aluminate ($ZnAl_2O_4$) nanoparticles by the co-precipitation

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method and its application as a heterogeneous catalyst for the efficient acetylation of alcohols, phenols and amines under mild conditions (solvent-free, atmospheric pressure, room temperature). This article demonstrates that spinel-based catalysts have great potential for use "green" organic transformations. To the best of our knowledge, this is the first report of catalytic acetylation using a spinel-type AB_2O_4 mixed oxide.

1. Experimental

All chemicals and solvents were purchased from either Merck or Fluka and used as received. ^1H NMR spectra were recorded on a Bruker 500-MHz instrument. GC–MS analysis was carried out on a Shimadzu QP 5050 GC–MS instrument. Melting points were obtained using an Electrothermal-9200 instrument.

1.1. Catalyst preparation

Zinc aluminate nanoparticles were prepared in aqueous solution from metal nitrates by co-precipitation method using ammonia as a precipitating agent as follows. $Zn(NO_3)_2{\cdot}6H_2O$ (20 mmol) dissolved in 10 mL of distilled water was added to a solution of $Al(NO_3)_3{\cdot}9H_2O$ (40 mmol) in 10 mL of distilled water. Then, the appropriate amount of aqueous ammonia solution (25 wt%) was added to the above solution, and the mixture was stirred until complete precipitation occurred at a pH between 8 and 9. The precipitate was filtered, washed with distilled water, and dried. The dry precipitate was calcined at 600 °C for 4 h to obtain the $ZnAl_2O_4$ nanoparticles.

For a comparison, commercial $ZnAl_2O_4$ (S.D. Fine Chemicals, India; 99.5%) with surface area of 4.2 m^2/g, and average particle size of 65 μm) and four nanosized $ZnAl_2O_4$ samples prepared according to the reported methods in the literature [57–60] have also been studied as the heterogeneous catalysts in the acetylation reaction.

1.2. Catalyst characterization

The X-ray diffraction studies were performed on a Bruker D8 Advance X-ray diffractometer using Cu Kα radiation (λ = 0.15418 nm). Infrared spectra were recorded on a Shimadzu system FT-IR 8400 spectrophotometer using the KBr pellet method. The particle size and morphology of the $ZnAl_2O_4$ nanoparticles were investigated by using a LEO-906E transmission electron microscope (TEM) with an accelerating voltage of 80 kV. In the process of preparing the TEM specimen, a small amount of the powder was dispersed in ethanol in an ultrasonic bath for 30 min, and few drops of the resulting suspension were placed onto a carbon-coated copper grid. Specific surface area was calculated by the BET method using N_2 adsorption–desorption experiments carried out at −196 °C on a Micromeritics ASAP 2010. Before each measurement, the sample was outgassed at 200 °C for 3 h. The specific surface area of the $ZnAl_2O_4$ nanoparticles was 86 m^2/g.

1.3. Catalytic tests

Amine, alcohol and/or phenol (10 mmol) were added to a mixture of $ZnAl_2O_4$ nanoparticles (0.1 g) and acetic anhydride (10 mmol) or acetyl chloride (15 mmol). The mixture was stirred for an appropriate time at room temperature. The progress of the reaction was monitored by TLC or GC–MS. When the reaction was completed, 10 mL of ethyl acetate were added, and the mixture was filtered to separate the $ZnAl_2O_4$ catalyst. The solid catalyst was washed twice with 5 mL of ethyl acetate. The combined organic phases were washed with a 10% solution of sodium hydrogen carbonate, and then the organic phases were dried over Na_2SO_4. The solvent was removed to obtain the product. If further purification of the product was needed, it was dissolved in ethyl acetate and passed through a short column of silica gel using carbon tetrachloride-ethyl acetate as an eluent. All products were characterized on the basis of GC–MS, FT-IR and ^1H NMR spectral data and by comparing the spectra to those of authentic samples or reported data. The results are summarized in Tables 1–5.

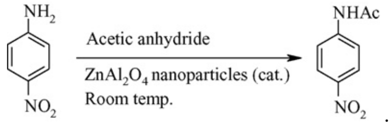
In a similar manner, the acetylation reaction of some substrates was also carried out in the presence of commercial bulk-$ZnAl_2O_4$ and nano-$ZnAl_2O_4$ samples prepared by other methods. The results are compared in Tables 6 and 7.

2. Results and discussion

2.1. Characterization of $ZnAl_2O_4$ nanoparticles

Inorganic nanoparticles have been receiving increased attention because they exhibit unusual physical and chemical properties that are significantly different from those of relatively larger particles of the same materials. These unusual properties have been attributed to the extremely small sizes and the high specific surface areas of the nanoparticles. It is well known that the catalytic activity of inorganic materials depends strongly on particle size, morphology, and microstructure. Therefore, the preparation and characteriza-

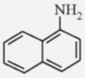
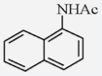
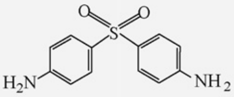
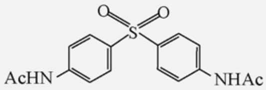
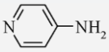
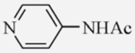
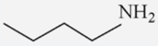
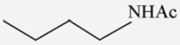
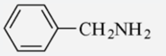
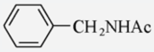
Table 1
Acetylation of 4-nitroaniline with acetic anhydride over $ZnAl_2O_4$ nanoparticles under different conditions.[a,b]



Entry	Amount of catalyst (g)	Solvent	Time (min)	Conversion[c] (%)	Yield[d] (%)
1	–	–	30	20	17
2	0.01	–	30	58	52
3	0.05	–	30	65	61
4	0.1	–	8	100	92
5	0.2	–	8	99	93
6	0.3	–	8	99	92
7	0.1	Acetonitrile	120	65	60
8	0.1	Toluene	90	50	44
9	0.1	Acetone	80	61	55
10	0.1	Dichloromethane	90	58	52

[a] Reaction conditions: 4-nitroaniline (10 mmol), acetic anhydride (10 mmol), with or without solvent at rt.
[b] In all cases, selectivity was over 99% determined by GC–MS analysis of the crude product mixture.
[c] Conversions were determined by GC–MS analysis of the crude product mixture.
[d] Yields are for isolated pure product.

Table 2
Acetylation of amines with acetic anhydride over nano-$ZnAl_2O_4$.[a,b]

Entry	Amine	Product	Time (min)	Conversion[c] (%)	Yield[d] (%)
					
1	G = H		5, (5, 5, 5)[e]	98, (98, 97, 98))[e]	94, (93, 91, 90)[e]
2	4-Me		3	100	96
3	2-Me		3	100	95
4	4-Et		5	100	96
5	4-Pr^i		3	100	96
6	4-MeO		3	100	96
7	4-Cl		5	99	93
8	2-Cl		4	99	93
9	2,4-Cl_2		8	98	92
10	4-Br		6	99	92
11	4-I		4	97	90
12	3-NO_2		6	97	91
13	4-CN		8	95	88
14	4-CHO		8	96	86
15	3-MeCO		10	96	88
16			8	96	90
17			5	98	92
18			8	98	90
19			10	97	87
20			7	98	92

[a] Reaction conditions: amine (10 mmol), acetic anhydride (1 equiv. per NH_2 group), catalyst (0.1 g), without solvent at rt.

[b] In all cases, selectivity was ≥99% determined by GC–MS analysis of the crude product mixture.

[c] Conversions were determined by GC–MS analysis of the crude product mixture.

[d] Yields are for isolated pure product.

[e] The reactions was carried out with the recovered catalyst in three consecutive runs.

tion of nanoparticles with well-controlled size, shape and chemical homogeneity are interesting and important for catalytic purposes.

Co-precipitation is one of the simplest techniques for preparing nanoparticles of numerous inorganic materials. In this simple and inexpensive method, salts of the required metals are dissolved in water and co-precipitated by adding a precipitating agent. In fact, the precipitates obtained are solid solutions that contain the cations mixed together, essentially on an atomic scale. Because of the high degree of homogenization, much lower temperatures are sufficient for the reaction to occur. For these reasons, the co-precipitation method was selected for the preparation of $ZnAl_2O_4$ nanoparticles in this work. The overall process for the preparation of $ZnAl_2O_4$ from Al^{3+} and Zn^{2+} nitrates and ammonium hydroxide as the precipitating agent can be written as follows:

$$\begin{tikzcd} Zn(NO_3)_2 + 2Al(NO_3)_3 \arrow[r, "NH_3{\cdot}H_2O"] & Zn(OH)_2.2Al(OH)_3 \arrow[d, "\Delta"] \\ & ZnAl_2O_4 + 4H_2O \end{tikzcd}$$

First, thermal gravimetric analysis (TGA) of the co-precipitated $Zn(OH)_2{\cdot}2Al(OH)_3$ precursor was conducted, as shown in Fig. 1. In the TGA curve, there are two distinct weight loss steps. The first weight loss that occurred between 50 and 110 °C is attributed to the evaporation of physically adsorbed water molecules. The second weight loss step that occurred between 200 and 550 °C is due to the decomposition of anhydrous $Zn(OH)_2{\cdot}2Al(OH)_3$ to $ZnAl_2O_4$. This finding confirms that the decomposition reaction of the double hydroxide precursor is completed at about 550 °C. Therefore, we selected 600 °C as the calcination temperature for preparing the $ZnAl_2O_4$ nanoparticles.

The purity and crystallinity of the $ZnAl_2O_4$ nanoparticles were examined by using powder X-ray diffraction (XRD), as shown in Fig. 2. It can be seen in Fig. 2 that the diffraction peaks are broadened markedly due to the small size effect of the particles. The peaks appearing at $2\theta = 31.32°$, 36.90°, 44.88°, 49.10°, 55.65°, 59.45°, 65.25°, 74.07°, and 77.35° can be indexed as (2 2 0), (3 1 1), (4 0 0), (3 3 1), (4 2 2), (5 1 1), (4 4 0), (6 2 0), and (5 3 3) crystal planes of

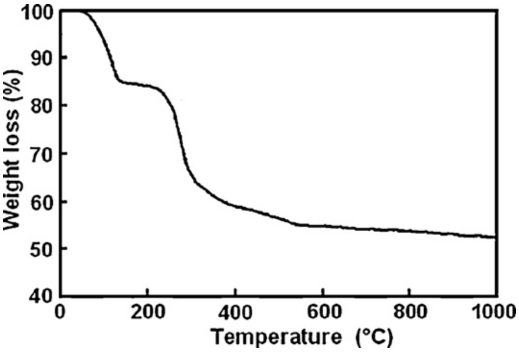
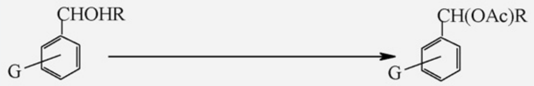
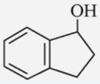
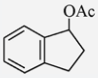
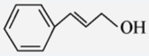
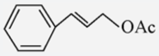
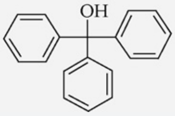
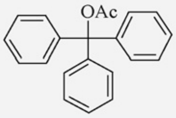
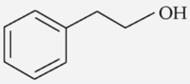
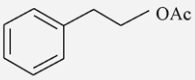
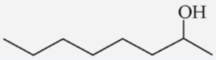
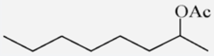
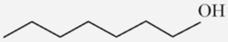
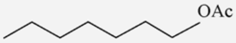
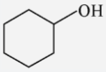
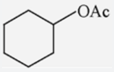
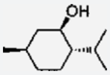
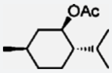
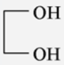
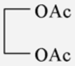
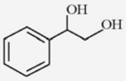
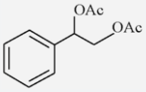
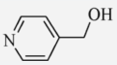
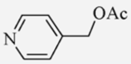


Fig. 1. TGA curve of $ZnAl_2O_4$ precursor.

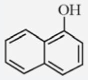
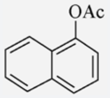
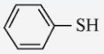
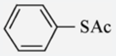
Table 3
Acetylation of alcohols with acetyl chloride over nano-$ZnAl_2O_4$.[a,b]

Entry	Alcohol	Product	Time (min)	Conversion[c] (%)	Yield[d] (%)
					
1	R = H; G = H		18, (18, 20, 20)[e], 20[f]	100, (99, 98, 99)[e], 0[f]	90, (90, 88, 88)[e], 0[f]
2	R = H; G = 4-Me		15	100	95
3	R = H; G = 4-tert-Bu		16	100	94
4	R = H; G = 4-MeO		15	100	94
5	R = H; G = 2,4-$(MeO)_2$		16	98	94
6	R = H; G = CN		23	92	87
7	R = H; G = 3-NO_2		15	95	90
8	R = H; G = 2-NO_2		20	93	88
9	R = H; G = 4-CF_3		35	91	85
10	R = H; G = 4-F		20	94	88
11	R = H; G = 4-Cl		16	98	92
12	R = H; G = 4-Br		15	96	90
13	R = CH_3; G = H		20, (22, 22, 24)[e]	99, (99, 98, 98)[e]	94, (92, 90, 89)[e]
14	R = C_2H_5; G = H		20	98	92
15	R = C_6H_5; G = H		15	97	90
16	R = 4-Cl-C_6H_4; G = H		14	98	91
17	R = 4-$MeOC_6H_4$; G = 4-MeO		12	98	92
18			30	94	86
19			30	93	88
20			48	82	72
21			20	98	92
22			32	94	86
23			26	96	88
24			25	96	88
25			30	98	89
26			28	98	90
27			26	98	91
28			30	90	85

[a] Reaction conditions: alcohol (10 mmol), acetyl chloride (1.5 equiv. per OH group), catalyst (0.1 g), without solvent at rt.
[b] In all cases, selectivity is ≥99% determined by GC–MS analysis of the crude product mixture.
[c] Conversions were determined by GC–MS analysis of the crude product mixture.
[d] Yields are for isolated pure product.
[e] The reaction was carried out with the recovered catalyst in three consecutive runs.
[f] Control experiment in the absence of catalyst.

the cubic crystalline structure of $ZnAl_2O_4$, respectively, in accordance with the standard JCPDS card of cubic spinel-type $ZnAl_2O_4$ (JCPDS File No. 05-0669). The XRD pattern shows that the product is single-phase and that the only peaks detected were the characteristic peaks of the cubic phase $ZnAl_2O_4$. This result confirms that the $ZnAl_2O_4$ nanoparticles obtained in this work are of very high purity. The average particle size was calculated by X-ray diffraction line broadening using the Debye–Scherrer equation [61], $d = (0.9\lambda)/(h_{1/2}\cos\theta)$, where d is the grain size; λ is the wavelength of the X-ray (Cu K_α, 0.15418 nm); θ is the diffraction angle of the peak; and $h_{1/2}$ is the full-width at half-height of the peaks. The average particle size calculated using the most intense peak

Table 4
Acetylation of phenols with acetyl chloride over nano-$ZnAl_2O_4$.[a,b].

Entry	Phenol	Product	Time (min)	Conversion[c] (%)	Yield[d] (%)
					
1	G = H		36, (36, 37, 37)[e], 36[f]	99, (98, 98, 99)[e], 0[f]	95, (95, 94, 94)[e], 0[f]
2	4-Me		34	98	93
3	4-Cl		35	99	96
4	4-MeO		30	100	93
5	4-Br		38	100	95
6	2,4-$(Cl)_2$		42	98	94
7	4-NO_2		46, (46, 48, 47)[e]	93, (93, 90, 92)[e]	85, (85, 83, 84)[e]
8	2,4-$(NO_2)_2$		53	90	82
9			40	95	86
10			40	94	86

[a] Reaction conditions: phenol (10 mmol), acetyl chloride (15 mmol), catalyst (0.1 g), without solvent at rt.
[b] In all cases, selectivity is ≥99% determined by GC–MS analysis of the crude product mixture.
[c] Conversions were determined by GC–MS analysis of the crude product mixture.
[d] Yields are for isolated pure product.
[e] The reaction was carried out with the recovered catalyst in three consecutive runs.
[f] Control experiment in the absence of catalyst.

(3 1 1) at $2\theta = 36.90^\circ$ was 7.6 nm. This value is in accordance with TEM observations (see Fig. 4).

Fig. 3 shows the FT-IR spectrum of the $ZnAl_2O_4$ nanoparticles obtained by calcining the precursor at 600 °C for 4 h. Below 1000 cm^{-1}, two strong bands around 670 and 560 cm^{-1} were observed, which are related to Al–O stretching and O–Al–O bending vibrations of AlO_6 groups in the spinel-type $ZnAl_2O_4$ structure, respectively [62]. This result is in agreement with the result obtained from the XRD analysis. It is noted that the number and shape of FT-IR bands of $ZnAl_2O_4$ is dependent to its preparation method. It shows two or three bands in range of 450–700 cm^{-1}. In some reported methods, $ZnAl_2O_4$ was formed as a mixture of the normal spinel (Al^{3+} ions in octahedral sites of AlO_6 groups) and the inverse spinel (Al^{3+} ions in octahedral AlO_6 and tetrahedral AlO_4 sites) [63,64]. In these cases, the number of bands below 700 cm^{-1} increases. However, in most published papers, $ZnAl_2O_4$ showed two main bands with or without shoulder in range 450–700 cm^{-1}. In present work, two bands were appeared in the FT-IR spectrum, confirming that the pure spinel-type $ZnAl_2O_4$ was formed.

It is well known that the catalytic activity of AB_2O_4 spinels is strongly dependent on the shape, size, and size distribution of the particles. The size and shape of the $ZnAl_2O_4$ particles were investigated by TEM, as shown in Fig. 4. The TEM image reveals that the powder is composed of loosely aggregated extremely fine particles. From this image, it is evident that the particles have a semi-spherical morphology, a narrow size distribution, and homogeneous shape.

From the data obtained by TEM micrograph, a particle-size histogram can be drawn, and the mean size of the particles can be determined. Fig. 5 shows the particle-size distribution of the $ZnAl_2O_4$ nanoparticles. It can be seen that the particle sizes possess a narrow size distribution in a range from 4 to 12 nm, and the mean particle diameter is about 8 nm. Actually, the mean particle size determined by TEM is very close to the average particle size calculated by the Debye–Scherrer formula from the XRD pattern.

The specific surface area of the $ZnAl_2O_4$ nanoparticles measured by the BET method, was 86 m^2/g. This relatively high specific surface area of $ZnAl_2O_4$ is beneficial to its catalytic activity.

2.2. *The acetylation reaction over $ZnAl_2O_4$ nanoparticles*

In order to investigate the activity of spinel-type $ZnAl_2O_4$ nanoparticles as a heterogeneous catalyst, the acetylation of 4-nitroaniline (10 mmol) with acetic anhydride (10 mmol) was chosen as the model reaction at room temperature. In the absence of the $ZnAl_2O_4$ catalyst about 17% of 4-nitroacetanilide was obtained after 30 min (Table 1, entry 1). Then, we examined

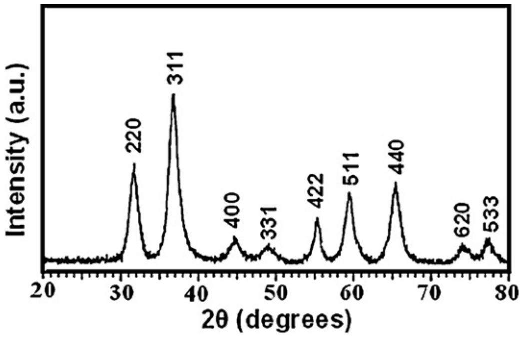


Fig. 2. XRD pattern of $ZnAl_2O_4$ nanoparticles.

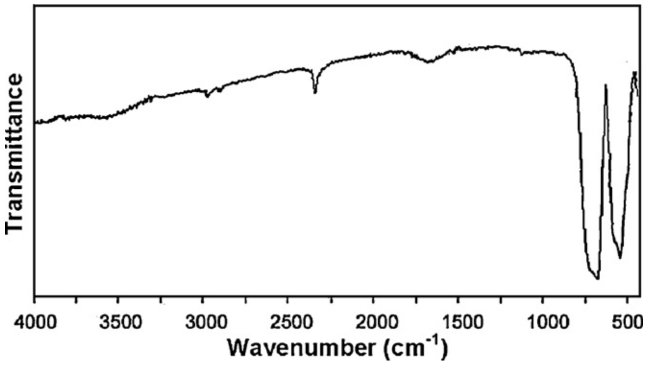
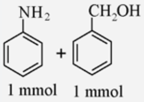
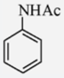
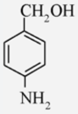
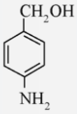
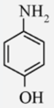
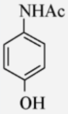
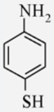
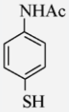
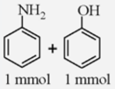
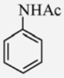
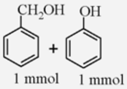
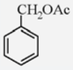
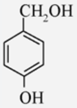
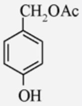
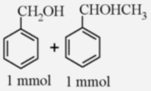
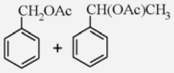


Fig. 3. FT-IR spectrum of $ZnAl_2O_4$ nanoparticles.

Table 5
Inter- and intramolecular competitive acetylation over nano-$ZnAl_2O_4$.[a].

Entry	Substrate	Product	Time (min)	Yield[b] (%)
1			5	93[c]
2			5	90
3			6	94
4			4	91
5			5	95[c]
6			20	92[c]
7			16	90
8			20	(45 + 43)[c]

[a] Reaction conditions: substrate (10 mmol), catalyst (0.1 g), acetic anhydride (10 mmol for entries 1–5) and acetyl chloride (15 mmol for entries 6–8), without solvent at rt.
[b] Yields are for isolated pure products.
[c] GC–MS yields.

this reaction in the presence of different loadings of $ZnAl_2O_4$ catalyst (Table 1, entries 2–6). As shown in Table 1, the conversion of 4-nitroaniline and the yield of 4-nitroacetanilide were increased with the increase of the amount of nanocatalyst from 0.01 to 0.1 g/10 mmol of 4-nitroaniline (Table 1, entries 2–4). However, amounts greater than 0.1 g of catalyst produced no significant increase in the conversion and yield of product (Table 1, entries 5 and 6). The optimal amount of $ZnAl_2O_4$ was 0.1 g/10 mmol of 4-nitroaniline which resulted in a 92% isolated yield of 4-nitroacetanilide after 8 min at room temperature under solvent-free conditions. This reaction was also studied using some organic solvents such as acetonitrile, toluene, acetone, and dichloromethane (Table 1, entries 7–10). However, the best result in terms of reaction time, substrate conversion, and product yield was achieved when the reaction was carried out without solvent. Therefore, the acetylation reactions were carried out hereafter under solvent-free conditions.

To evaluate the scope of this method, the acetylation of primary aromatic amines containing both electron-donating as well as electron-withdrawing groups and primary aliphatic amines with acetic anhydride over $ZnAl_2O_4$ nanoparticles was investigated at room temperature under solvent-free conditions (Table 2). All of

Table 6
Comparison of the acetylation over nano-$ZnAl_2O_4$ and commercial bulk-$ZnAl_2O_4$.[a].

Entry	Substrate	Nano-$ZnAl_2O_4$		Bulk-$ZnAl_2O_4$	
		Time (min)	Yield[b] (%)	Time (min)	Yield[b] (%)
1	3-Nitroaniline	6	91	45	80
2	Benzyl alcohol	18	90	65	78
3	1-Phenylethanol	20	94	60	76
4	Phenol	36	95	90	70
5	4-Nitrophenol	50	85	120	61

[a] Reaction conditions: substrate (10 mmol), acetic anhydride (10 mmol for entry 1) and acetyl chloride (15 mmol for entries 2–5), catalyst (0.1 g), without solvent at rt.
[b] Yields are for isolated pure products.

Table 7
Comparison of the catalytic activity of $ZnAl_2O_4$ nanoparticles prepared by five different methods in acetylation of 4-nitroaniline and benzyl alcohol as the model substrates.[a,b]

Entry	Preparation method [Ref.]	S_{BET} ($m^2\,g^{-1}$)/particle size (nm)	4-Nitroaniline		Benzyl alcohol	
			Time (min)	Conversion[c] (%)/yield[d] (%)	Time (min)	Conversion[c] (%)/yield[d] (%)
1	Co-precipitation method[e]	86/8	8	100/92	18	100/90
2	Sol–gel technique [57]	58/20	13	97/88	28	97/86
3	Alkoxide route [58]	126/28	6	100/94	14	100/95
4	Citrate technique [59]	230/5–20	4	100/97	11	100/96
5	Hydrothermal method [60]	99/10	7	99/93	16	99/92

[a] Reaction conditions: substrate (10 mmol), acetic anhydride (10 mmol for 4-nitroaniline) or acetyl chloride (15 mmol for benzyl alcohol), $ZnAl_2O_4$ nanoparticles as the catalyst (0.1 g), without solvent at rt.

[b] In all cases, selectivity is ≥99% determined by GC–MS analysis of the crude product mixture.

[c] Conversions were determined by GC–MS analysis of the crude product mixture.

[d] Yields are for isolated pure product.

[e] This work.

the amines that we studied were acetylated at selectivity greater than 99% and conversions exceeding 95% with reaction times of less than 10 min. In each case, the excellent yields of the corresponding acetylated derivative were obtained (88–96%). The high activity of $ZnAl_2O_4$ nanoparticles was demonstrated by high conversions and isolated yields obtained for anilines having electron-withdrawing groups (Table 2, entries 12–15). Other primary aromatic amines and aliphatic amines gave the corresponding acetamides in high yield under the present reaction conditions (Table 2, entries 16–20). As can be seen in Table 2, functional groups such as –Ome, –CHO, –COMe, –CN, and $–NO_2$ remained unchanged under the reaction conditions. The conversion of aniline to acetanilide on a 100-mmol scale proceeded just as well as the 10 mmol reaction (14 min, 95% isolated yield).

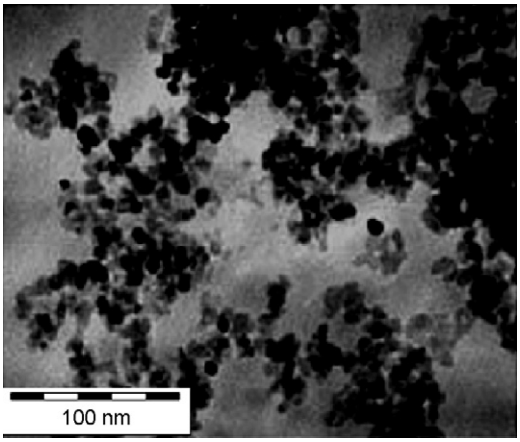


Fig. 4. TEM image of $ZnAl_2O_4$ nanoparticles.

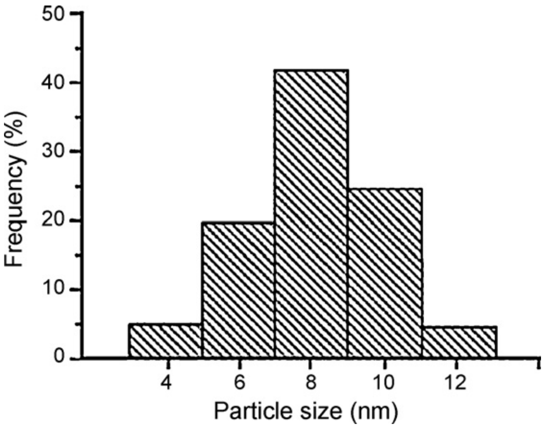


Fig. 5. Particle-size distribution of $ZnAl_2O_4$ nanoparticles.

To explore the potential of this catalytic system, we studied the acetylation of alcohols under solvent-free conditions. The reaction with acetic anhydride was too sluggish for practical application. In order to overcome this drawback, acetyl chloride was used as an acetylating agent. In a short reaction time, the desired esters were obtained in excellent yields from the reaction of a variety of benzylic, primary, secondary, and hindered tertiary alcohols (10 mmol) with acetyl chloride (15 mmol) in the presence of an optimal amount of $ZnAl_2O_4$ (0.1 g). The conversions of the alcohols and isolated yields of products are given in Table 3. As can be seen in Table 3, all primary benzylic alcohols were selectively converted to the corresponding acetates in quantitative yields without any evidence of the formation of side products (Table 3, entries 1–12). In all cases, electron-rich benzylic substrates as well as electron-deficient substrates were converted to the acetate derivatives with high yields. Various secondary alcohols were converted to the corresponding acetates as well (Table 3, entries 13–18). In a controlled-blank experiment, the acetylation of benzyl alcohol with acetyl chloride under similar reaction conditions did not proceed in the absence of catalyst (Table 3, entry 1).

This acetylation protocol is also efficient for allylic systems. For example, cinnamyl alcohol was selectively converted to the corresponding acetate and the double bond remained intact under the reaction conditions (Table 3, entry 19). It is very interesting to note that a sterically hindered tertiary alcohol such as triphenylmethanol can also be acetylated with moderate yield, albeit with longer reaction time (Table 3, entry 20). Aliphatic alcohols were also converted into the corresponding acetate compounds with high yields under the same reaction conditions (Table 3, entries 21–24). It is noteworthy that in the case of an optically active alcohol, the reaction proceeded well with retention of configuration (Table 3, entry 25). The efficiency of the catalyst can be seen clearly in the acetylation of di-hydroxy compounds under similar conditions (Table 3, entries 26 and 27). Furthermore, the heteroaromatic alcohol 4-pyridine methanol was converted to the corresponding acetate with high yield (Table 3, entry 28). Among the various alcohols studied, primary benzylic alcohols were found to be most reactive, giving the corresponding acetylated products with shorter reaction times. In each case, no by-products were found by GC–MS analysis.

The scope of this reaction was further extended for the acetylation of phenols. As shown in Table 4, phenol and differently substituted phenols were acetylated with excellent conversions (≥93%) and high yields (82–96%), albeit after longer reaction times in comparison with alcohols. In all cases, selectivity for the acetylated products was greater than 99%. The excellent activity of

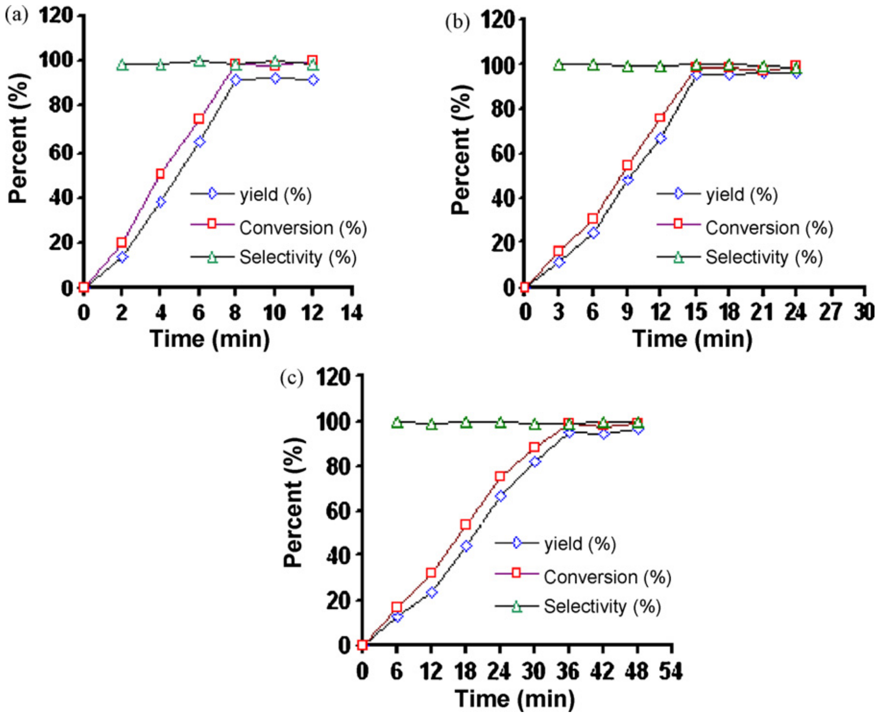


Fig. 6. The variation of conversion, selectivity and yield of product versus reaction time for (a) 4-nitroaniline, (b) 4-methylbenzyl alcohol and (c) phenol. Reaction conditions: substrate (10 mmol), acetic anhydride (10 mmol for 4-nitroaniline) or acetyl chloride (15 mmol for 4-methyl benzyl alcohol and phenol), $ZnAl_2O_4$ nanoparticles as the catalyst (0.1 g), without solvent at rt.

$ZnAl_2O_4$ nanoparticles was demonstrated by the high conversions and yields obtained for phenols that have electron-withdrawing groups (Table 4, entries 7 and 8).

In order to examine the chemoselectivity of the present method, inter- and intramolecular competitive acetylations of substrates containing $-NH_2$ and –OH groups were studied. Selective acetylation of $-NH_2$ groups in the presence of –OH groups was observed at room temperature with one equivalent of acetic anhydride (Table 5, entries 1–5). This might be due to the fact that the $-NH_2$ group has greater nucleophilicity than the –OH group. This selective acetylation of a primary $-NH_2$ group over a primary –OH group by this process is of considerable synthetic importance and is difficult to achieve with many other reagents. Also, an alcoholic –OH group was selectively acetylated in the presence of a phenolic –OH group (Table 5, entries 6 and 7). No selectivity was observed between primary and secondary alcohols, such as benzyl alcohol and 1-phenylethanol (Table 5, entry 8).

The effect of reaction time on the conversion of substrate, isolated yield and selectivity of acetylated product was also studied in the acetylation of 4-nitroaniline, 4-methylbenzyl alcohol and phenol as the model substrates (Fig. 6). It is evident from the graphs that conversions and yields increased with time and that the highest conversions, as well as the highest yields of products, for 4-nitroaniline, 4-methybenzyl alcohol, and phenol were obtained after 8, 15, and 36 min, respectively. Selectivity to acetylated product is more than 99% and remained almost constant with time.

The reusability of the catalyst was investigated in the acetylation of aniline, benzyl alcohol, 1-phenylethanol, and phenol under optimized conditions. After reaction with each of these substrates, ethyl acetate was added, and the mixture was filtered to separate the catalyst. The recovered catalyst was washed with acetone, dried, and activated at 200 °C for 1 h. It was reused as the catalyst in the next run under the same conditions. The catalytic results indicate that there is no appreciable difference in either activity or selectivity even after three runs (Table 2, entry 1; Table 3, entries 1 and 13; Table 4, entries 1 and 7). As shown in Fig. 7, XRD and FT-IR spectra of the recycled $ZnAl_2O_4$ catalyst did not show significant change after the third run in comparison with the fresh catalyst (Figs. 2 and 3). This observation confirmed that the structure of the nanoparticles was stable under the reaction conditions and was not affected by the reactants.

For a comparison and to investigate the small size effect of $ZnAl_2O_4$ nanoparticles on the reaction, the acetylation of several substrates was also investigated on a commercial bulk $ZnAl_2O_4$ with surface area of $4.2\,m^2/g$ and average particle size of 65 μm under the optimized conditions. The results obtained are compared in Table 6. Although acetylated products were obtained through both conditions, the isolated yields were improved and the reaction times were shortened when the $ZnAl_2O_4$ nanoparticles were used. Clearly, the reaction times using the bulk $ZnAl_2O_4$ were eight times longer than the times required when the $ZnAl_2O_4$ nanoparticles were used. For complete comparison, the XRD, FT-IR, and SEM of this conventional catalyst are shown in Fig. 8. As can be seen in Fig. 8, the XRD and FT-IR spectra of the conventional catalyst are different mainly due to its large particle sizes.

To evaluate the effect of preparation method on the catalytic activity, we prepared nanosized $ZnAl_2O_4$ powders using four different methods that have been reported in the literature [57–60]. The activity of these nano-$ZnAl_2O_4$ catalysts was compared with $ZnAl_2O_4$ prepared in the present study via the acetylation of 4-nitroaniline and benzyl alcohol under the optimized reaction conditions. The results are summarized in Table 7. Although the differences in the activities of various nanosized $ZnAl_2O_4$ catalysts in terms of conversion and product yield are not remarkable, the reaction time was shortened in the case of catalysts with higher surface area (Table 7, entries 3 and 4). It is obvious from Table 7 that the surface area and activity of nano-$ZnAl_2O_4$ catalysts depend on the preparation method. Further work in this area with various substrates is under the way.

Although the exact mechanism for this reaction over $ZnAl_2O_4$ nanoparticles is not very clear, we think that it is similar to that of other catalysts as proposed in the literature [32]. As shown in

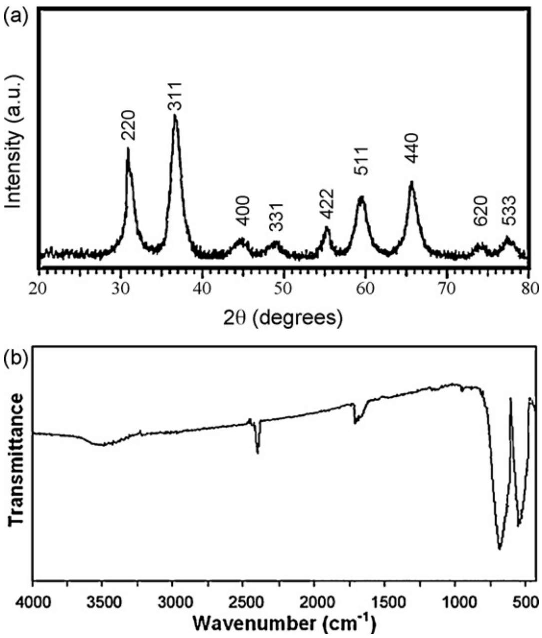


Fig. 7. (a) XRD pattern and (b) FT-IR spectrum of the recovered $ZnAl_2O_4$ catalyst after the third cycle.

Scheme 1, catalytic acetylation is initiated by coordinating carbonyl group of acetic anhydride/acetic chloride to unsaturated aluminum and zinc ions on the surface of the nanoparticles as Lewis acidic sites. This coordination of carbonyl groups to the acidic sites on the surface of the catalyst changes its character from being a low-reactive electrophile into a moderately or reactive electrophile. This activated carbonyl group is attacked by heteroatom (N or O) of substrate, which is a reactive nucleophile, to produce the corresponding acetate. The reaction steps are evident without comment.

From the results of Tables 6 and 7, we conducted that the chemisorption of the carbonyl group of acetylating agents upon the surface of the $ZnAl_2O_4$ catalyst is very important to the outcome of the reaction. In a manner that is similar to other heterogeneous catalytic reactions, this reaction was takes place mainly on the surface of the particles of the catalyst, and surface atoms make a distinct contribution to its catalytic activity. In fact, the surface atoms behave as Lewis acid centers where the chemical reaction can be activated catalytically. On the other hand, the number of surface atoms in the nanoparticles is a larger fraction of the total, and they provide more contact area for reactants and catalyst, mainly due to their high surface-to-volume ratio and high surface area compared to bulk particles. Therefore, the greater catalytic activity of $ZnAl_2O_4$ nanoparticles compared to the activity of bulk $ZnAl_2O_4$ can be attributed to the better coordination of the carbonyl group to nano-$ZnAl_2O_4$ due to the participation of more surface Lewis acidic sites in the reaction. This statement is also confirmed by the results that are presented in Table 7.

3. Conclusions

In this research, $ZnAl_2O_4$ nanoparticles prepared by the co-precipitation method were successfully used as a novel, efficient, and recyclable heterogeneous catalyst for the acetylation of alcohols, phenols, and amines with acetic anhydride and/or acetyl chloride under solvent-free conditions. Among the various substrates, the acetylation of anilines and primary aliphatic amines proceeded the most rapidly. Selective acetylation of –NH_2 groups in the presence of –OH groups and alcoholic –OH in the presence of phenolic –OH was observed. The $ZnAl_2O_4$ catalyst was easily pre-

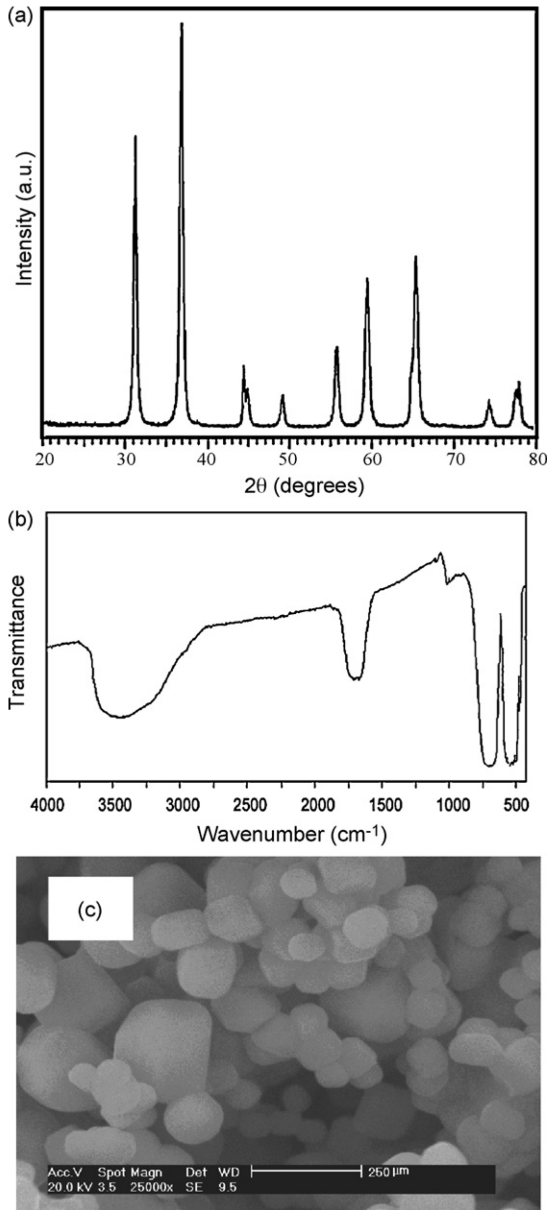
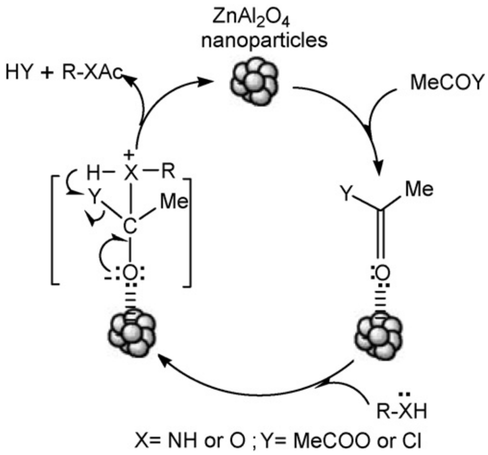


Fig. 8. (a) XRD pattern, (b) FT-IR spectrum and (c) SEM of the commercial bulk-$ZnAl_2O_4$ used as a catalyst.



Scheme 1. The proposed catalytic cycle for the acetylation reaction over $ZnAl_2O_4$ nanoparticles.

pared and reusable without loss of activity. XRD and FT-IR analyses confirmed that the structure of the catalyst did not change after reaction. In this paper, we have provided the first description of the acetylation of amines, alcohols, and phenols with acetic anhydride or acetyl chloride over a nano-$ZnAl_2O_4$ catalyst.

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