Research Article

Synthesis of Triarylpyridine derivatives using Nano ZnO

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Abstract

Nano Zinc Oxide was found to be highly convenient, green and recyclable heterogeneous catalyst for the synthesis of 2,4,6-triarylpyridines through one-pot three component reaction of substituted chalcones, Acetophenone and Ammonium acetate at 80 ^{o}C using ethyl alcohol as solvent.

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Introduction

In the fast decades, Multi component reactions [MCRs] have an important role in organic synthesis. These are one step reactions, where the reactants are subjected into a single reactor to form a desired product with good yields, without any intermediate formation. Its importance is mainly in the synthesis, such as medicine, bio degradable plastics and natural products. So that having great advantage over convergent and conventional synthesis [2-5]. The formation of Carbon-Carbon bond in organic molecules is crucial and a great deal of research has been focused on this area now a days. Improving the effectiveness of these MCRs with other strategies such as improving yield, short reaction time and magnetically separable catalysts is the key component in the proposed method [6-9]. In recent, this strategy became important development in the drug discovery in the context of synthesis of biologically active compounds. This method increase the efficiency of the reaction and decrease the number of laboratory operations along with solvents and chemicals used, also reduce the reaction time and facilitate the yield of products than the normal multistep methods.

Pyridine ring systems represent an important class of compounds [10,11] not only for their theoretical interest but also because they constitute the skeleton of some alkaloids, [12-16] antitumor, antibiotics[17].Due to their stacking ability, some pyridines are used in supra molecular chemistry [18]. These compounds have also attracted considerable attention in recent years because of their wide range of pharmaceutical activities such as anti-malerial, vasodilator, anticonvulsant, anesthetic, antiepileptic and agrochemicals such as fungicidal, pesticide and herbicidal. [19-22] Therefore, the discovery of novel MCRs is an interesting topic for synthetic chemistry researchers. Hence in continuation of our work to develop eco-friendly technique for synthesis of heterocyclic compounds an attempt has been made to synthesize chalcone derivatives by Claisen-Schmidt condensation [23] and now another attempt has been made to synthesize 2,4,6-Triarylpyridines (**Figure 1**).

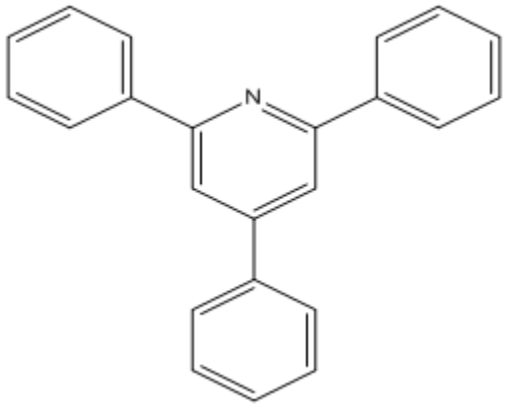


Figure 1 : 2,4,6-Triarylpyridine

Experimental methods

Materials and Reagents

All chemicals used in this process are of AR grade fine chemicals, without any further purification. The synthesized products were characterized by ^{1}H- NMR(400MHz)spectra were obtained using Bruker-Advance spectrophotometer in $CDCl_3$. FTIR spectra were recorded on Bruker Alpha FT-IR with Opus 6.1 version, Mass spectra were determined on Perkin- Elmer PESCIEX-API 2000, equipped with ESI source used online with a HPLC system after the UV detector. XRD spectra were recorded on PANanalytical-Xpertpro diffractometer and the average crystallite size was determined from the corresponding XRD data. The micro structural morphology was studied with a scanning electron microscope(SEM) JEOL-JSM 6610 LV. Magnetization measurements were made using a commercial vibrating sample magnetometer (VSM) model BHU-50 of Riken Denshi Co. Ltd. Japan.

General procedure for the Synthesis of Catalyst

For the preparation of Nano Zinc Oxide catalyst by wet chemical method, 0.2 M solution of $Zn(NO_3)_2$ and 0.4M NaOH were used. Zinc nitrate was dissolved in water to which sodium hydroxide was added drop-wise with continuous stirring at room temperature leading to generation of metal hydroxides. The stirring was continued for 6 hrs at 85 ^{o}C. The reaction mixture was then filtered and dried in oven at 60 ^{o}C. The as-synthesized powder, thus obtained was calcined in a Muffle furnace at 600 ^{o}C for 2 hours and furnace cooled. The product was characterised by SEM, EDAX and XRD.

Characterizations of catalyst

Characterization of nano ZnO was done based on *JCPDS* values. For all doped and un-doped ZnO samples the absorption peaks in the range of 600 - 700 cm^{-1} could be attributed to the ZnO stretching modes [24, 25]. In our FT-IR spectra the main peaks observed were: absorption peaks in the range of 1100 - 1600 cm^{-1} corresponding to the Zn-OH bending mode [25] and this band could be normally reduced by calcinations process at higher temperature [26, 27], a broad band in the 2900 - 3700 cm^{-1} region which can be explained as overlapping O-H stretching modes and C-H stretching modes (**Figure 2**).

X-ray diffraction pattern of ZnO nanoparticles show sharp and well defined peaks. It indicates. the good crystallinity of synthesized material. The observed 2θ values are consistent with the standard JCPDS values(JCPDS No.80-0075) which specify the wurtzite structure of ZnO nano particles d-values were compared with standard JCPDS files and showed presence of pure oxides(**Figure 3**). SEM image shows the surface morphology of the oxide nano particles. Zinc oxide nano particles are fine with spherical shape and average grain size is below 70 nm (**Figure 4**). EDAX confirms the presence of metals Zn and Oxygen in expected atomic percentage (**Figure 5**).

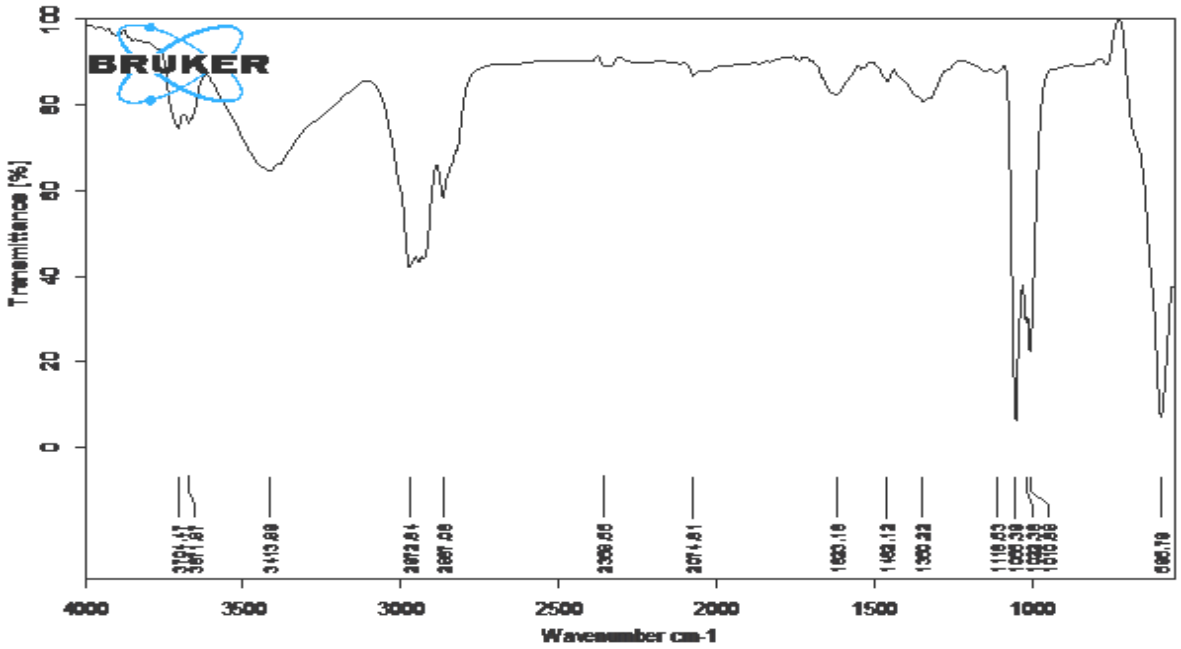


Figure 2 FT-IR of nano ZnO

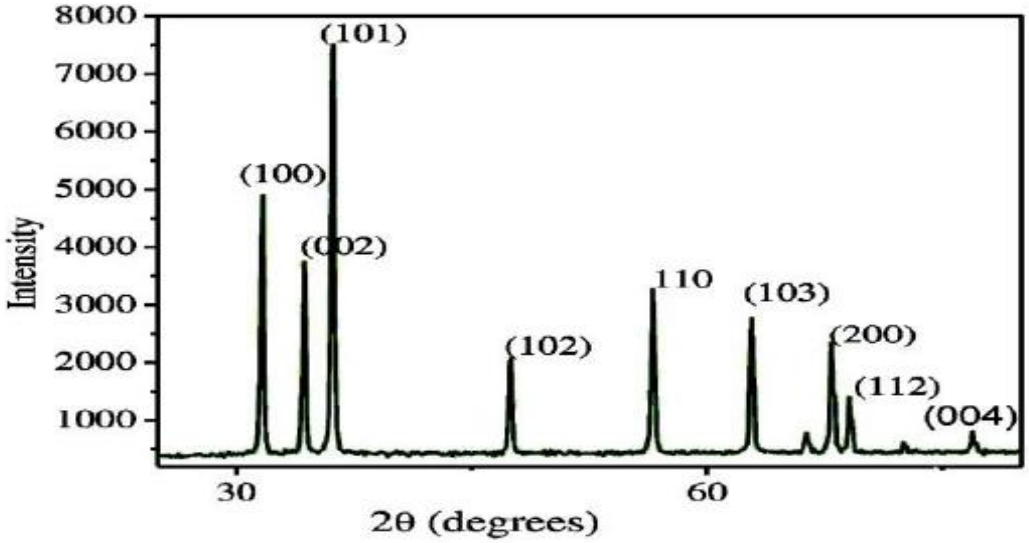


Figure 3 XRD of nano ZnO

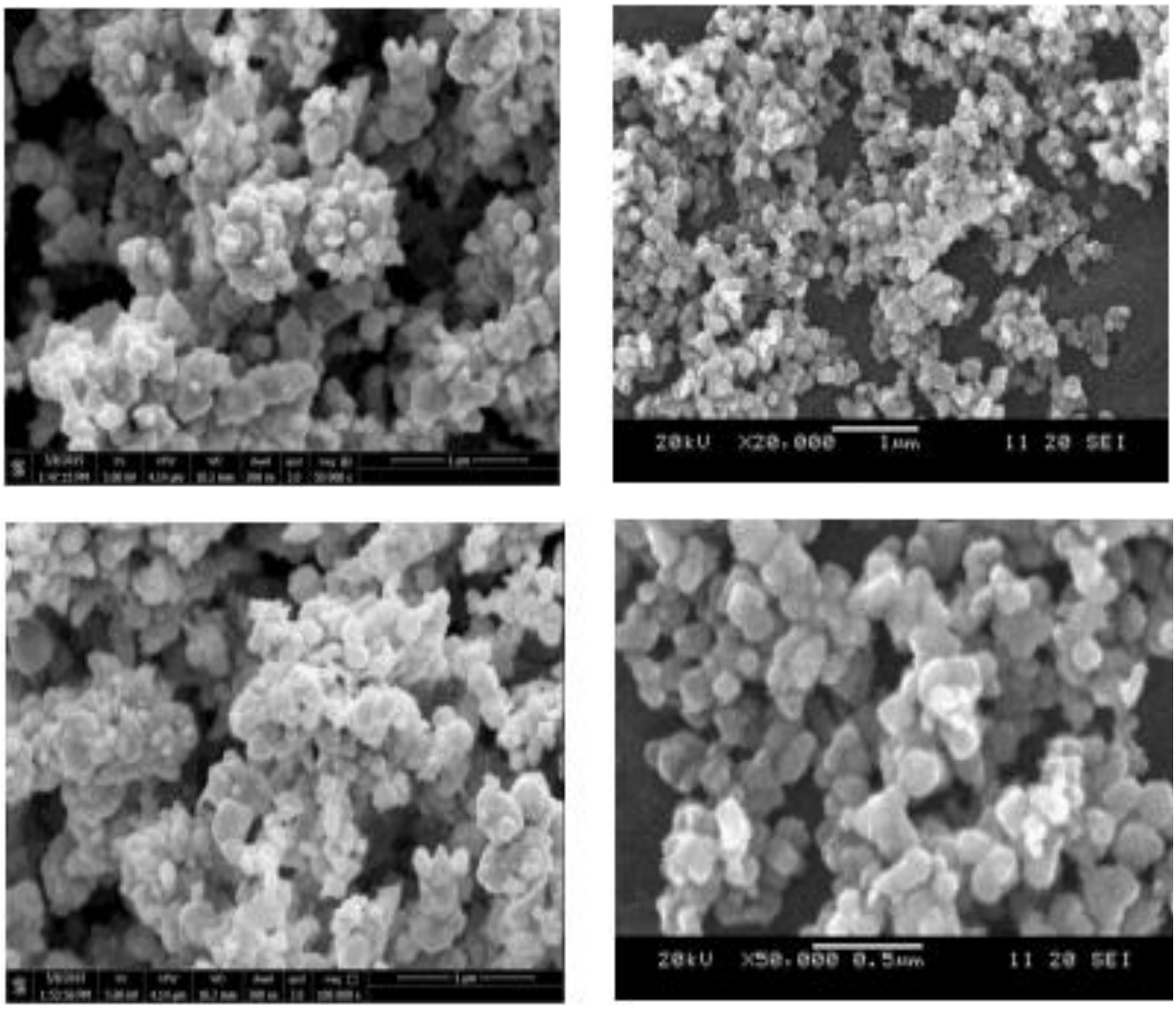


Figure 4 SEM of nano ZnO

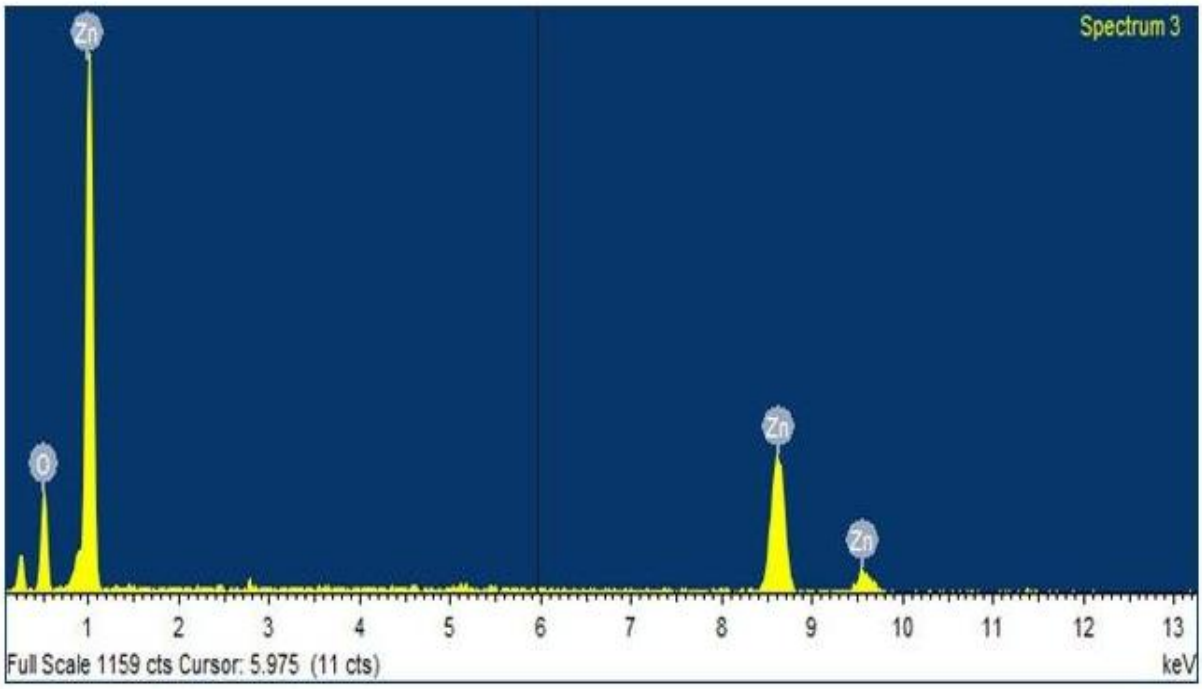


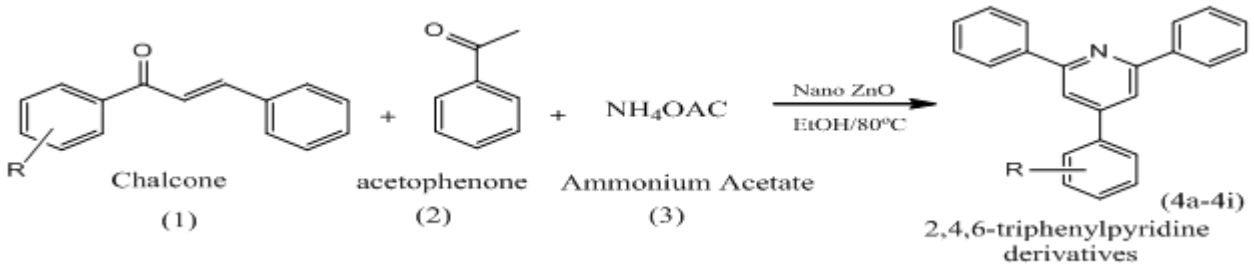
Figure 5 ***EDAX of nano ZnO***

General procedure for synthesis of 2,4,6-Triarylpyridines

A mixture of Chalcone (i.e. 1,3-diphenyl prop-2-ene-1-one prepared by well known Claisen-Schmidt condensation which was our previous published paper ref. No.[23]) (10 mmol), Acetophenone (10 mmol) and Ammonium acetate(10 mmol) and nano Zinc Oxide catalyst (500mg) (which is activated previously in microwave oven for 2 minutes) were taken in a 50 ml round bottomed flask and 5ml of Ethanol was added as solvent. Then the reaction mixture was refluxed at 80 ^{o}C for 1hr. The progress of the reaction was monitored by thin layer chromatography(n-Hexane, Ethyl acetate 3:1). The catalyst was simply recovered by filtration and washed by dichloromethane. Then the reaction mixture was concentrated under rotary evaporator and then the solid product was re-crystallised from hot ethanol for several times to get pure product. The corresponding products were confirmed by FT-IR, ^{1}H-NMR, MASS spectral analysis (**Table 1**).

Table 1 synthesis of 2,4,6-triphenylpyridine derivatives

S.No.	Chalcone	R	Compound	Time(min)	Yield(%)
1	1,3-diphenylprop-2-en-1-One(4a)	H	2,4,6-triphenylpyridine	60	90
2	1-phenyl-3-(p-tolyl)prop-2-en-1-one(4b)	4-CH3	2,6-diphenyl-4-(p-tolyl)pyridine	70	88
3	3-(4-chlorophenyl)-1-phenylprop-2-en-1-one(4c)	4-Cl	4-(4-chlorophenyl)-2,6-diphenylpyridine	65	90
4	3-(4-hydroxyphenyl)-1-phenylprop-2-en-1-one(4d)	4-OH	4-(2,6-diphenylpyridin-4-yl)phenol	65	85
5	3-(4-nitrophenyl)-1-phenylprop-2-en-1-one(4e)	4-NO2	4-(4-nitrophenyl)-2,6-diphenylpyridine	75	85
6	3-(4-bromophenyl)-1-phenylprop-2-en-1-one(4f)	4-Br	4-(4-bromophenyl)-2,6-diphenylpyridine	70	90
7	3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one(4g)	2-OH	2-(2,6-diphenylpyridin-4-yl)phenol	75	85
8	3-(2-nitrophenyl)-1-phenylprop-2-en-1-one(4h)	2-NO2	4-(2-nitrophenyl)-2,6-diphenylpyridine	70	85
9	3-(2-chlorophenyl)-1-phenylprop-2-en-1-one(4i)	2-Cl	4-(2-chlorophenyl)-2,6-diphenylpyridine	65	90



Scheme 1 Synthesis of 2,4,6-Triarylpyridines derivatives catalyzed by nano ZnO

Plausible mechanism

It is assume that initially intermolecular condensation of the 1,3-diphenyl prop-2-ene-1-one with Acetophenone occurs to result in 1,5-diketone, then undergoes ring closure in the presence of ammonium acetate which acts as the nitrogen source as well as the cyclisation agent to afford 2,4,6-triphenylpyridines.

Spectral data of Triarylpyridine derivatives

2,4,6-triarylpyridine(4a)

IR (KBr)cm^{-1}: 3011(Aromatic C=N Str), 1484, 1430(Aromatic C=C Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.18- 8.34(m, 6H,Ar-H), 7.52-7.76(m,8H,Ar-H),7.22-7.43(m, 3H,Ar-H). ESI-MS m/z(%): 307 ($[M+H]^+$ 100).

1-phenyl-3-(p-tolyl)prop-2-en-1-one(4b)

IR (KBr)cm^{-1}: 3032(Aromatic C=N Str), 1479(Aromatic C=C Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.11- 8.26(m, 6H,Ar-H), 7.56-7.72(m,8H,Ar-H). 7.36-7.41(m, 2H,Ar-H), 2.36(m,3H,-CH_3). ESI-MS m/z(%): 321 ($[M+H]^+$ 100).

3-(4-chlorophenyl)-1-phenylprop-2-en-1-one(4c)

IR (KBr)cm^{-1}: 3023(Aromatic C=N Str), 1426(Aromatic C=C Str),726(-Cl Str). ^{1}H NMR (400 mHz, $CDCl_3$): δ 8.25-8.32(m, 6H,Ar-H), 7.51-7.62(m,8H,Ar-H)7.23-7.33(m, 2H,Ar-H). ESI-MS m/z(%): 341 ($[M+H]^+$ 100).

3-(4-hydroxyphenyl)-1-phenylprop-2-en-1-one(4d)

IR (KBr)cm^{-1}: 3226(-OH Str), 3011(Aromatic C=N Str), 1462, 1434(Aromatic C=C Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.12- 8.35(m, 6H,Ar-H), 7.52-7.73(m,8H,Ar-H), 7.24-7.46(m, 2H,Ar-H), 5.32(m, 1H,-OH). ESI-MS m/z(%):323 ($[M+H]^+$ 100).

3-(4-nitrophenyl)-1-phenylprop-2-en-1-one(4e)

IR (KBr)cm^{-1}: 3011(Aromatic C=N Str), 1492, 1425(Aromatic C=C Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.21- 8.45(m, 6H,Ar-H), 7.52-7.76(m,8H,Ar-H),7.17-7.33(m, 2H,Ar-H). ESI-MS m/z(%): 352 ($[M+H]^+$ 100).

3-(4-bromophenyl)-1-phenylprop-2-en-1-one(4f)

IR (KBr)cm^{-1}: 3019(Aromatic C=N Str), 1435, (Aromatic C=C Str),571(-Br Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.25-8.35(m, 6H,Ar-H), 7.55-7.73(m,8H,Ar-H),7.22-7.35(m, 2H,Ar-H). ESI-MS m/z(%): 385 ($[M+H]^+$ 100).

3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one(4g)

IR (KBr)cm^{-1}: 3227(-OH Str),3026(Aromatic C=N Str), 1492, 1422(Aromatic C=C Str). ^{1}H NMR (400 mHz, $CDCl_3$): δ 8.12- 8.34(m, 6H,Ar-H), 7.56-7.73(m,7H,Ar-H),7.22-7.42(m, 3H,Ar-H), 5.34(m, 1H,-OH). ESI-MS m/z(%): 323 ($[M+H]^+$ 100).

3-(2-nitrophenyl)-1-phenylprop-2-en-1-one(4h)

IR (KBr)cm^{-1}: 3013(Aromatic C=N Str), 1492, 1426(Aromatic C=C Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.21- 8.35(m, 6H,Ar-H), 7.42-7.54(m,7H,Ar-H),7.21-7.37(m, 3H,Ar-H). ESI-MS m/z(%):352 ($[M+H]^+$ 100).

3-(2-chlorophenyl)-1-phenylprop-2-en-1-one(4i)

IR (KBr)cm^{-1}: 3017(Aromatic C=N Str), 1492, 1426(Aromatic C=C Str), 725(-Cl Str).^{1}H NMR (400 mHz, $CDCl_3$): δ 8.17- 8.36(m, 6H,Ar-H), 7.42-7.64(m,7H,Ar-H).7.24-7.33 (m, 3H,Ar-H). ESI-MS m/z(%): 341 ($[M+H]^+$ 100).

Results and Discussion

Effect of loading of catalyst on the synthesis of 2,4,6-Triarylpyridines derivatives

The present reaction observed under different amounts of catalyst. The result reveals that 500mg of catalyst is enough to get the good yield of product. On further increment of catalyst quantity will not lead appreciable change in the yield of product. Hence 500mg of catalyst was taken to perform the reaction. The results are as tabulated in **Table 2**.

Effect of solvent on synthesis of 2,4,6-Triarylpyridines derivatives

Investigation of reaction medium for the process revealed that solvents playing a major role in the reaction. The results are summarized in **Table 3**. It was found that polar solvents such as acetic acid, CH_3CN and C_2H_5OH were much better than non-polar solvents. Trace amount of yield observed when H_2O was used as solvent, presumably due to the aggregation of the hydrophobic catalyst. Although CH_3COOH is effective, low yield was obtained when the catalyst was reused, therefore we selected C_2H_5OH as solvent.

Table 2 Effect of catalyst loading on the formation of 2,4,6-Triarylpyridines derivatives

S.No.	Catalyst loading in (mg)	Time (min)	Yield (%)
1.	200	50	30
2.	300	50	50
3.	400	50	80
4.	500	50	90
5.	600	50	90

Effect of Temperature on Synthesis of 2,4,6-Triarylpyridines derivatives

The reaction temperature for the formation of 2,4,6-Triarylpyridines derivatives with nano Zinc Oxide catalyst is 80 ^oC is presented in table 4. It is observed that at below 80 ^oC temperature yield of the product is low and reaction time is high. So we have confirmed 80 ^oC is suitable temperature for this reaction (**Table 4**).

Table 3 Effect of solvent on synthesis of 2,4,6-Triarylpyridines derivatives

S. No.	Catalyst	Solvent	Time	Yield (%)
1	ZnO	H_2O	6 hrs	traces
2	ZnO	CH_2Cl_2	5 hrs	35
3	ZnO	CH_3COOH	4 hrs	50
4	ZnO	CH_3CN	1.5 hrs	60
5	ZnO	C_2H_5OH	1 hr	90

Table 4 Effect of Temperature on the formation of 2,4,6-Triarylpyridines derivatives

S.No.	Catalyst	Temperature(^oC)	Time	Yield (%)
1	ZnO	R.T.	9h	20
2	ZnO	40	5h	50
3	ZnO	50	1.5h	60
4	ZnO	80	1 hr	90

Recycling of the Catalyst

Catalyst reusability is of major task in heterogeneous catalysis. Catalyst recycling was achieved by filtration of reaction mixture the catalyst washed thrice with ethyl acetate, dried and the fresh reactants dissolved in ethyl alcohol was introduced into the round bottom flask, followed by refluxing, allowing the reaction to proceed for the next run. The catalyst was consecutively reused for five times without any noticeable loss of its catalytic activity (**Table 5**).

Table 5 Recyclability of the catalyst in synthesis of 2,4,6-Triarylpyridines derivatives

Run no.	Yield (%)
1	90
2	88
3	85
4	83
5	80

Conclusion

In conclusion, we have developed a convenient approach for the synthesis of 2,4,6-Triarylpyridine derivatives by using chalcones, Acetophenone and Ammonium Acetate n as substrates and nano ZnO is as an effective catalyst, Furthermore, present procedure resulting in the formation of substituted 2,4,6-Triarylpyridines in high yields. The catalyst can be recovered, and reused at least up to five cycles for the synthesis of 2,4,6-Triarylpyridines derivatives with much loss in the yield.

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