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# ZnO nanoparticles catalyzed C–N bond-forming reactions: A highly efficient protocol to convert electron-deficient anilines to formanilides

Tulan Chandra Saikia, Saddam Iraqui & Md. Harunar Rashid*
Department of Chemistry, Rajiv Gandhi University, Rono Hills, Doimukh 791 112, Arunachal Pradesh, India
E-mail: harunar.rashid@rgu.ac.in

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Herein, we report a protocol for the conversion of electron-deficient anilines to formanilides at room temperature using ZnO nanoparticles (NPs). The ZnO NPs of different shapes have been synthesized by conventional co-precipitation techniques and are characterized fully using different microscopic, diffractometric and spectroscopic techniques. The developed protocol is simple, green, inexpensive, and highly efficient. The products can be conveniently separated from the reaction mixture without using the conventional tedious and expensive chromatographic techniques. The protocol is effective for a wide range of substituted anilines, aliphatic amines and heterocycles with moderate to excellent yield. The catalyst is highly stable and is reusable up to the 5th cycle without loss of catalytic activity.

**Keywords:** Formanilides, heterogeneous catalyst, C–N bond formation, nanoparticles, zinc oxide

The construction of the C–N bond in a greener way has been a great deal of research interest for decades to academic and industrial researchers due to the versatile application of nitrogen-containing organic compounds including formanilides[1,2]. Formanilides are important intermediates to synthesize valuable organic compounds such as N, N-diaryl ureas,[3] nitrogen-bridged heterocycles,[4,5] cancer chemotherapeutic agents,[6] quinolone antibiotics,[7] N-aryl imidazoles,[8] 1,2-dihydroquinolines,[9] aryl isocyanides,[10-13] formamidines,[14-16] etc. Formanilides are found to be an important constituent in pharmaceutically important drugs and bioactive molecules[17,5,6]. They are also useful reagents in Vilsmeier formylation reactions[18]. Furthermore, formanilides are Lewis bases, which are known to catalyze many organic transformations[19-21]. Besides, the formyl group is also an important amino protecting group in peptide synthesis since N-formyl de-protection can easily be achieved without affecting the peptide bond[22,23]. Several methods have been reported on the synthesis of formanilides. Some of the prominent formylating methods use formic acid-dicyclohexyl carbodiimide,[24] chloral,[25] formic acid esters,[26] chlorodimethoxytriazine,[27] ammonium formate,[28] formic acids in polyethylene glycol,[29] formic acids in sodium formate,[19] and so on[30]. However, most of these methods suffer from various drawbacks such as harsh reaction conditions, low yield, high reaction temperature, long reaction time, use of expensive and toxic formylating agents and catalysts, and the removal of by-products. Very recently few researchers have reported the N-formylation of anilines to synthesize formanilides using metal oxide nanoparticles (NPs). For instance, Mamani et al. reported the use of sulfonic acid supported on hydroxyapatite-encapsulated-$\gamma$-$Fe_2O_3$ as a heterogeneous, reusable, and highly efficient catalyst for N-formylation of amines under solvent-free conditions at room temperature[31]. However, there are difficulties in the preparation of the catalyst and the availability of reagents. Furthermore, HCl evolution occurs during the preparation of the catalyst. An eco-friendly N-formylation of amines was reported by Sajadi et al. using nano $CeO_2$ as a reusable catalyst under solvent-free ultrasonic irradiation conditions at room temperature.[32] Das et al. reported an expeditious, simple, highly efficient, and green protocol for the N-formylation of amines using $Al_2O_3$ nanorods as catalysts under solvent-free conditions.[33] Further, Hosseini-Sarvari et al. reported the use of commercial ZnO as catalysts for the N-formylation of amines under solvent-free conditions at 70 °C.[34]

Although a handful of advancement has been made in recent times for the improvement of the reaction conditions, most of these reported protocols fail to furnish an excellent yield of formanilides from electron-deficient anilines at room temperature within a short reaction time. Hence, it is highly desirable to develop a simple but effective protocol for the synthesis of formanilides under a base-free and ligand-free condition using the less expensive and environmentally friendly catalyst. ZnO NPs are one of such low cost and low toxicity materials which gained popularity in the field of catalysis due to their well-defined size and shape, large surface area, high abundance in the earth, and excellent activities towards different organic reactions.[35-38] The above properties of ZnO and our continuous effort in designing a green, effective, and convenient protocol for various organic reactions has prompted us to use nanosized ZnO catalyst in the synthesis of formanilides under ambient conditions. Subsequently, we report herein the synthesis of ZnO NPs by precipitation technique which has been characterized fully using various sophisticated instrumental techniques. The synthesized ZnO NPs has been used as an efficient catalyst in the N-formylation of amines in a simple, mild and convenient way. The effect of the morphology of ZnO NPs has also been studied.

## Experimental Section

### Materials and methods

Zinc acetate dihydrate [$Zn(CH_3COO)_2 \cdot 2H_2O$], methanol ($CH_3OH$; EMPARTA), sodium hydroxide pellet [NaOH], potassium hydroxide pellet [KOH], aniline, and formic acid were purchased from Merck, India. Commercial ZnO (99% purity) was purchased from Fisher Scientific, India. All the substituted anilines were purchased from Sigma-Aldrich. The reagent and chemicals were used without further purification. In a bath of freshly prepared aqua–regia solution (HCl: $HNO_3$ = 3:1, v/v); all the glassware was cleaned and then rinsed thoroughly with double distilled water and dried in an air oven. All the solutions were prepared either in methanol or water as per the requirement.

## Synthesis of ZnO nanoparticles

Spherical ZnO NPs were synthesized by the co-precipitation method following a previously reported method with some modification[39]. In a typical synthesis, 5 mL of zinc acetate solution (0.5 M in methanol) was added to 237.5 mL methanol taken in a round bottom flask of volume 500 mL fitted with a reflux condenser and placed in an oil bath preheated to 60 ºC. To the stirring zinc acetate solution was added 7.5 mL potassium hydroxide solution (1.0 M in methanol) dropwise and the reaction mixture was further heated at the same temperature for 5 h. After that, the reaction mixture was allowed to cool down to room temperature followed by removal of the solvent in a rotary evaporator to reduce the volume to 25 mL. The solid product was then isolated from the reaction mixture by centrifugation at 12000 rpm for 20 min. The product was purified from any trace of impurity by repeated washing with methanol and centrifugation. Finally, the isolated solid was dried in an oven at 60 ºC under vacuum for 12 h. This sample was designated as ZnO-1. Further to synthesize rod-shaped ZnO, another set of reaction was performed following the same procedure. But in this case, the reduced reaction mixture was subjected to reflux under constant stirring at 60 ºC for 10 h. After that, the product was isolated by centrifugation as performed in the previous set of reactions. The sample was designated as ZnO-2. Additionally, another sample (sample ZnO-3) was prepared in an aqueous medium using NaOH as a precipitating agent at 60 °C for 2 h maintaining all other reaction conditions identical.

## Formylation of anilines

In a 10 mL round bottom flask 4-nitroaniline (1 mmol) was mixed with a powder sample of ZnO NPs (10 mol%) by magnetic stirring for 10 min under aerobic conditions. Formic acid (3 mmol) was added dropwise to this mixture and the progress of the reaction was monitored by thin-layer chromatography (TLC). After completion, the reaction was quenched with 5 ml of ethyl acetate and extracted with an additional 30 mL of ethyl acetate and 15 ml of water. The organic layer was washed with saturated $NaHCO_3$ solution followed by brine solution and then dried in $Na_2SO_4$. The solvent was then removed in a rotary evaporator (Buchi) at 40 ºC until a high viscous liquid was obtained. Into the high viscous liquid, 20 mL *n*-hexane was poured and hand-shaken for 1 min. As the product is insoluble in *n*-hexane, the formation of two distinct layers was observed. The upper layer containing the possible impurity of the remaining reactant was discarded and the process was repeated five times to completely remove the reactant impurities. Interestingly there was no indication of reactant left in the lower organic layer as monitored by TLC. The product was further dried in vacuum for 30 min and kept at 4 ºC in a running refrigerator for further use. The product was characterized by $^1H$ NMR and $^{13}C$ NMR.

## Characterization

X-ray diffraction (XRD) study of dried ZnO powder was carried out in a Phillips X'pert Pro multipurpose diffractometer at an accelerating voltage of 40 kV using Cu $k_\alpha$ radiation ($\lambda$=1.54 Å) as X-ray source. The scanning electron microscopy study of the powder sample was carried out in a JEOL (JSM 7600F) electron microscope at an accelerating voltage of 5 kV. For transmission electron microscopic (TEM) studies, a drop of methanolic suspension of ZnO was cast on a carbon-coated copper grid. The excess liquid was soaked with tissue paper followed by drying in the air. The micrographs were then recorded in a high-resolution JEOL electron microscope (JEM 2100EM) at an accelerating voltage of 200 kV. ImageJ software (National Institute of Health) was used to measure the size and interplane spacing values of the NPs. For UV–vis spectroscopic analysis, a small quantity of dried ZnO powder was dispersed in methanol under ultrasonic vibration and the requisite volume of the colloidal ZnO suspension was transferred into a quartz cuvette of path length 1.0 cm and the spectrum was recorded in an Agilent Cary60 spectrophotometer in the wavelength region of 300–800 nm against methanol as blank. The photoluminescence (PL) spectra of the same suspension of ZnO NPs were recorded in a Cary Eclipse fluorescence spectrophotometer at an excitation wavelength of 340 nm.

## Results and Discussion

Powder X-ray diffraction was used to check the purity and the phase structures of the synthesized ZnO nanostructures. Figure 1 shows the XRD patterns of the products prepared under different reaction conditions. The diffractograms show the presence of diffraction peaks at 2θ = 31.6, 34.4, 36.1, 47.3, 56.5, 62.7, 67.8, 69.2, 72.3, and 76.7° with *d*-spacing values of 0.282, 0.26, 0.248, 0.191, 0.0162, 0.148, 0.138, 0.135, 0.13, and 0.124 nm. These peaks correspond to the reflection from planes (100), (002), (101), (102), (110), (103), (200), (112), (201) and (202) respectively[40]. The diffraction data matches well with the reported values for the hexagonal phase ZnO (JCPDF No. 36-1451)[40,36]. The absence of peaks due to impurities indicates the formation of pure and crystalline ZnO.

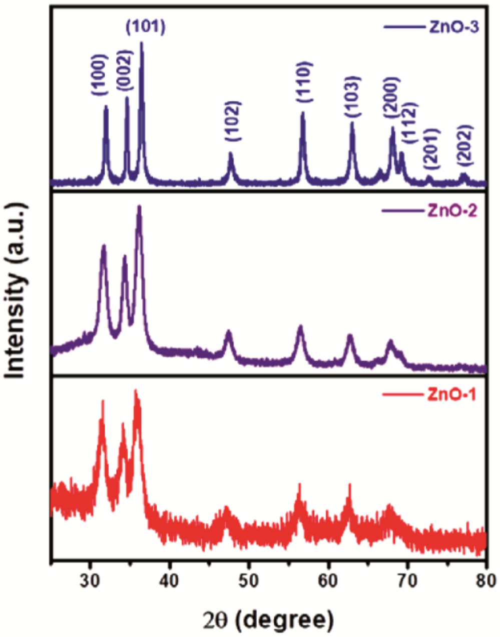


Fig. 1 — XRD pattern of different samples of ZnO NPs: ZnO-1 was prepared using KOH in methanol at 60 °C; ZnO-2 was prepared by ageing concentrated suspension of sample ZnO-1 at 60 °C under reflux condition and ZnO-3 is prepared using NaOH in water at 60 °C

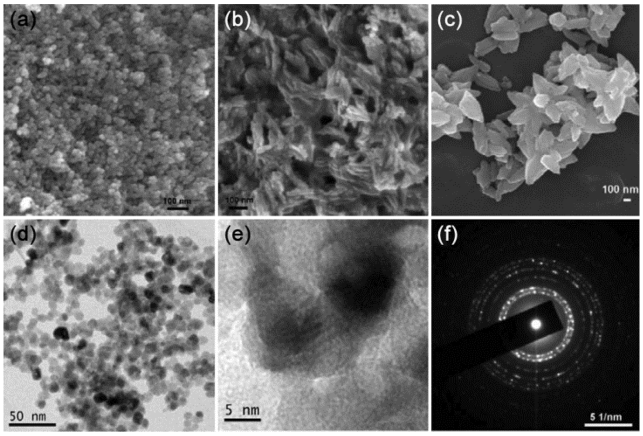


Fig. 2 — SEM images of different samples of ZnO NPs: (a) ZnO-1, (b) ZnO-2 and (c) ZnO-3. (d) Low-resolution and (e) high-resolution TEM images of sample ZnO-1. (f) SAED pattern recorded from sample ZnO-1

To study the topography of the synthesized ZnO NPs, a scanning electron microscopy (SEM) study was carried out. Figure 2a shows the formation of highly dispersed spherical ZnO NPs in sample ZnO-1. The sizes of such ZnO NPs are below 15 nm. The SEM image of sample ZnO-2 (Figure 2b) obtained after ageing the concentrated sample ZnO-1 at 60 °C for 10 h under reflux conditions shows the presence of rod-like structures. It seems that these rod-like structures are formed by the attachment of the spherical ZnO NPs. These microscopic results match well with the report claimed by Pacholski et al[39]. Figure 2c shows the SEM image of sample ZnO-3 prepared using NaOH in water which clearly shows the formation of assembled structures with no defined morphology. Further, the transmission electron microscopy (TEM) image of ZnO NPs (sample ZnO-1) was recorded to confirm the size and morphology of ZnO NPs. Figure 2d shows the formation of well-defined nearly uniform spherical NPs in sample ZnO-1. The diameters of these ZnO NPs are varied from 8 to 12 nm. The high-resolution TEM (HRTEM) micrograph recorded from such ZnO NPs (Figure 2e) shows the presence of perfectly aligned lattice fringes with an interplane spacing of 0.28 nm which corresponds to the (100) crystal planes in ZnO. The SAED pattern (Figure 2f) recorded from such ZnO NPs consisted of bright spots superimposed on a circular ring pattern which might be due to the overlapping of the particles on the TEM grid.

The UV-vis absorption spectra of the methanolic suspension of powder samples were recorded to study the optical properties of the formed ZnO nanostructures (Figure 3a). All the samples exhibited a strong absorption peak centred at 357 nm which is attributed to the near band edge (NBE) absorption of wurtzite hexagonal ZnO[41,42]. This peak is blue-shifted relative to its bulk value of 380 nm which represents the decrease in the size of the particle[43,44]. Figure 3b shows the room temperature photoluminescence (PL) spectra of ZnO NPs recorded from their methanolic suspension at an excitation wavelength of 340 nm. Due to intrinsic defects, ZnO usually exhibits several emission bands in the UV and visible spectral region[45]. The PL spectra shown in Figure 3b exhibited four emission bands in regions 416, 460, 486, and broadband at 530 nm. The ultraviolet-blue emission at 416 nm is attributed to a zinc vacancy ($V_{Zn}$) as reported by Zhao et al[46]. The blue emission centred at 460 nm is attributed to the oxygen vacancies ($V_O$) as reported earlier[47]. The emission at 486 nm might originate due to the electron transition between the level of the ionized oxygen vacancies ($V_O$) and the interstitial oxygen[48]. The green emission at 530 nm is attributed to the recombination of the electrons with a photogenerated hole trapped in a highly ionized oxygen vacancy[49].

ZnO NPs are known to exhibit catalytic activities towards organic transformation[35-38]. Inspired by the recent report on the bulk ZnOcatalyzed N-formylation of aniline with formic acid, we chose this reaction to assess the catalytic activity of the synthesized ZnO NPs under a mild environment with the expectation that ZnO NPs would provide better results. For the initial investigation, we chose 4-nitroaniline (1 mmol) as the model substrates to react with formic acid (3 mmol) in the absence of any solvent at room temperature. In the absence of catalyst, no product formation was observed even after six hours. When 10 mol% of ZnOnanocatalyst (sample ZnO-1) was used 4-nitroformanilide formation was spotted on TLC plate within 5 min. Inspired by this satisfactory result, we optimized the reaction condition for the amount of formic acid and catalyst loading in the

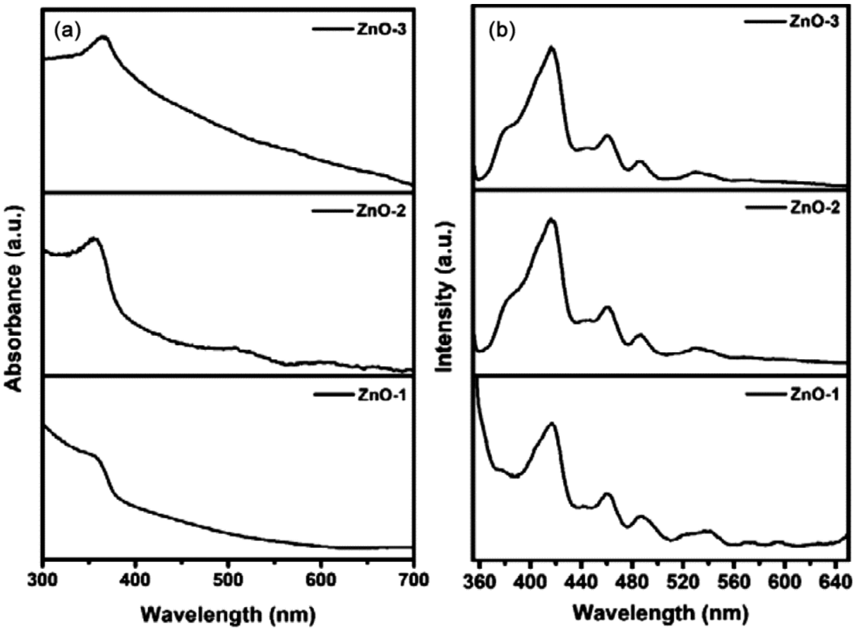
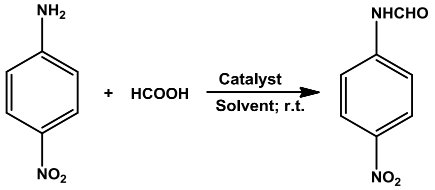


Fig. 3 — (a) UV-vis absorption and (b) room temperature photoluminescence spectra of different samples of ZnO NPs recorded from their methanolic suspension

absence and presence of solvents like water, methanol, ethanol, and their mixtures (Table I) at room temperature to follow the principles of green chemistry as far as possible. First, we fixed formic acid at 3 mmol and the amount of catalyst at 10 mol% and varied the solvent (Table I; entry 3-7). We observed that the highest yield was obtained in 20 min when a mixture of water and ethanol (1: 1) was used as the solvent. So, in the next assessment, we fixed the solvent system and varied the amount of catalyst from 10 mol% to 5 mol% (Table I; entry 7-10) to optimize the catalyst loading. We observed that 7 and 10 mol% are equally efficient to produce a yield of 96% in 20 min. So, in the next step, we fixed the catalyst amount at 7 mol% and varied the concentration of formic acid from 3 mmol to 2.3 mmol (Table I; entries 8, 11, and 12). We observed that 2.5 mmol of formic acid with respect to 1 mmol 4-nitroaniline gave the best result with 96% of yield in 20 min (Table I; entry 11). So, 2.5 mmol of formic acid was considered for the remaining study. When the same reaction was repeated with the remaining two ZnO samples, we observed that the performance of these samples was not satisfactory compared to sample ZnO-1 (Table I; entries 11, 13, and 14). So, we chose sample ZnO-1 as the catalyst in the synthesis of other substituted formanilides. It may be mentioned that the purpose of synthesizing ZnO-3 is to compare and assess the effect of the morphology of ZnO nanostructures on catalytic activity.

The generality of the developed protocol was expanded to synthesize other substituted formanilides with the optimized reaction condition from a wide range of substituted anilines with electron-withdrawing and electron-donating groups at the *ortho*, *meta*, and *para* positions to heterocyclic amine, cyclic aliphatic amines and straight-chain aliphatic amines. It is interesting to note that the substituted anilines possessing either electron-withdrawing or electron-donating groups do not differ much in reactivity in this reaction protocol (Table II; entry 2-10). The electron-withdrawing group, when attached to the ortho position of aniline, (Table II; entries 2 &10) does hinder the reactivity of this reaction. This can be attributed to the negative inductive effect of electron-withdrawing groups as well as the steric effect of the already substituted groups of aniline. The hindrance effect is dominant in the case of diphenylamine (Table II; entry 18); which does not undergo reaction because of two bulky phenyl groups attached to the amine. Further, we have performed a formylation reaction with heterocyclic aliphatic and cyclic aliphatic compounds. It was observed that the

Table I — Optimization of the reaction condition for the synthesis of 4-nitroformanilide[a]

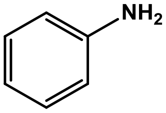
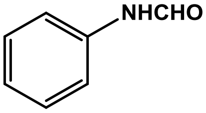
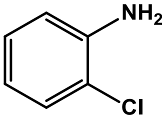
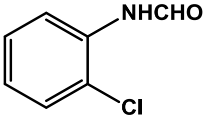
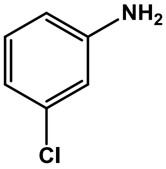
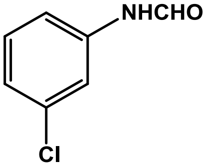
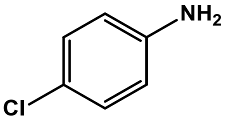
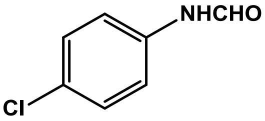
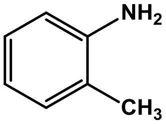
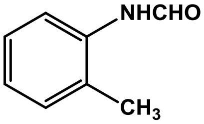
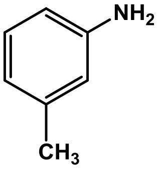
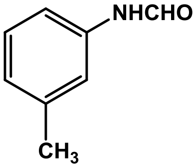
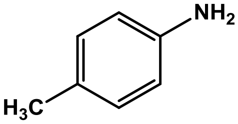
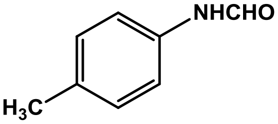
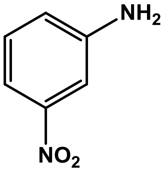
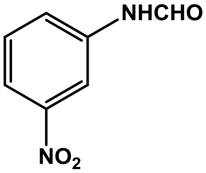
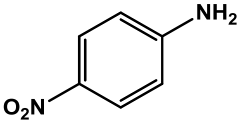
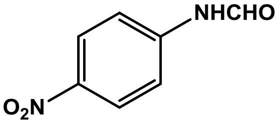
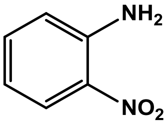
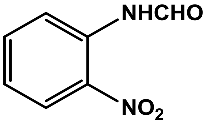
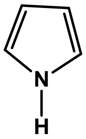
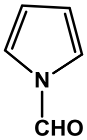


| Entry | Formic acid (mmol) | Catalyst | Catalyst amount (mol%) | Solvent (vol : vol) | Time (min) | Yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | 3 | - | - | - | 360 | 0 |
| 2 | 3 | ZnO-1 | 10 | - | 80 | 70 |
| 3 | 3 | ZnO-1 | 10 | $H_2O$ | 60 | 75 |
| 4 | 3 | ZnO-1 | 10 | $CH_3OH$ | 60 | 72 |
| 5 | 3 | ZnO-1 | 10 | $C_2H_5OH$ | 60 | 75 |
| 6 | 3 | ZnO-1 | 10 | $H_2O + CH_3OH$ (1: 1) | 60 | 75 |
| 7 | 3 | ZnO-1 | 10 | $H_2O + C_2H_5OH$ (1:1) | 20 | 96 |
| 8 | 3 | ZnO-1 | 7 | $H_2O + C_2H_5OH$ (1: 1) | 20 | 96 |
| 9 | 3 | ZnO-1 | 6 | $H_2O + C_2H_5OH$ (1: 1) | 40 | 80 |
| 10 | 3 | ZnO-1 | 5 | $H_2O + C_2H_5OH$ (1: 1) | 40 | 80 |
| 11 | 2.5 | ZnO-1 | 7 | $H_2O + C_2H_5OH$ (1: 1) | 20 | 96 |
| 12 | 2.3 | ZnO-1 | 7 | $H_2O + C_2H_5OH$ (1: 1) | 40 | 70 |
| 13 | 2.5 | ZnO-2 | 7 | $H_2O + C_2H_5OH$ (1: 1) | 60 | 86 |
| 14 | 2.5 | ZnO-3 | 7 | $H_2O + C_2H_5OH$ (1: 1) | 60 | 60 |

[a] Reaction condition: nitroaniline (1.0 mmol); solvent (1 mL)

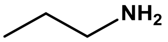
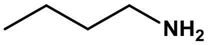
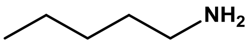
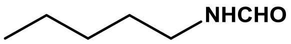
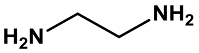
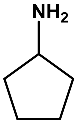
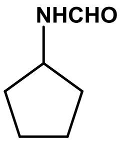
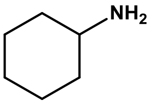
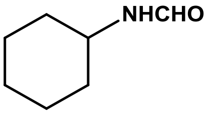
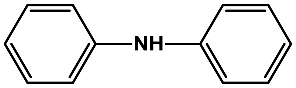
[b] Isolated yield

Table II — The substrate scope of N-formylation of various amines with formic acid under optimize conditions[a]

| Entry | Substrate | Product | Time (min) | Yield[b](%) |
|---|---|---|---|---|
| 1 |  |  | 20 | 96 |
| 2 |  |  | 40 | 92 |
| 3 |  |  | 20 | 97 |
| 4 |  |  | 20 | 96 |
| 5 |  |  | 30 | 95 |
| 6 |  |  | 20 | 98 |
| 7 |  |  | 20 | 98 |
| 8 |  |  | 20 | 96 |
| 9 |  |  | 20 | 96 |
| 10 |  |  | 30 | 80 |
| 11 |  |  | 50 | 70 |

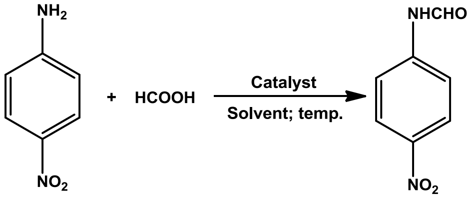
(*Contd*.)

Table II — The substrate scope of N-formylation of various amines with formic acid under optimize conditions[a] (*Contd.*)

| Entry | Substrate | Product | Time (min) | Yield[b](%) |
|---|---|---|---|---|
| 12 |  | No reaction | 60 | - |
| 13 |  | No reaction | 60 | - |
| 14 |  |  | 60 | Trace |
| 15 |  | No reaction | 60 | - |
| 16 |  |  | 60 | Trace |
| 17 |  |  | 60 | 52 |
| 18 |  | No reaction | 60 | - |

[a]Reaction conditions: amines (1 mmol); formic acid (2.5 mmol); solvent (water-ethanol / 1: 1 volume ratio, 1 mL); catalyst (12 mg / 7 mol%)
[b]Isolated yield

Table III — Comparison of the developed protocol of synthesizing 4-nitroformanilide to some earlier reports



| Entry | Catalyst | Solvent | Time | Temperature (ºC ) | Yield (%) | Reference |
|---|---|---|---|---|---|---|
| 1 | - | - | 210 m | r.t./ ultrasound | 95 | 54 |
| 2 | - | PEG-400 | 4-6 h | r.t | 86 | 29 |
| 3 | HCOONa | - | 3.5 h | r.t | 92 | 19 |
| 4 | $CoFe_2O_4@SiO_2$-PTA | - | 60 m | r.t | 89 | 55 |
| 5 | Protic ionic liquid | - | 4 h | 70 | 79 | 56 |
| 6 | Silica sulphuric acid | - | 46 m | 50-60 | 65 | 57 |
| 7 | Bulk ZnO | - | 12 h | 70 | 77 | 34 |
| 8 | ZnO NPs | Water-ethanol (1: 1; 1 mL) | 20 m | r.t | 96 | This work |
| 9 | Commercial ZnO* | Water-ethanol (1: 1; 1 mL) | 1 h | r.t | - | This work |

*No significant conversion was observed after 1 h of reaction.

current protocol is not suitable for simple alkyl amines. Whereas the heterocyclic compounds took a long time and also the product yield is low. Pyrrole produced 70% yield while cyclohexyl and cyclopentyl amines yielded 50% trace amount of product (Table II; entry 11, 16-17). It is reported that N-formylation of primary and secondary aliphatic amines with formic acid required a comparably high reaction temperature (60-80 °C) and a long reaction time under mostly harsh conditions[50-52]. In the current protocol mild reaction condition is maintained to comply with the Green Chemistry perspective and so the required activation energy could not be acquired by the aliphatic amines to undergo an N-formylation reaction with formic acid.Also keeping in mind, the cost and energy effectiveness, we did not perform the reaction beyond room temperature. Further, the result of the current study is compared with some other systems (Table III) that revealed the effectiveness of the current protocol in the formylation of aromatic amines

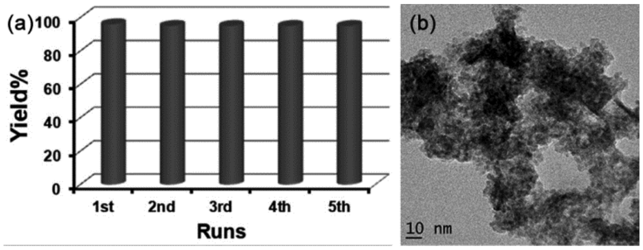
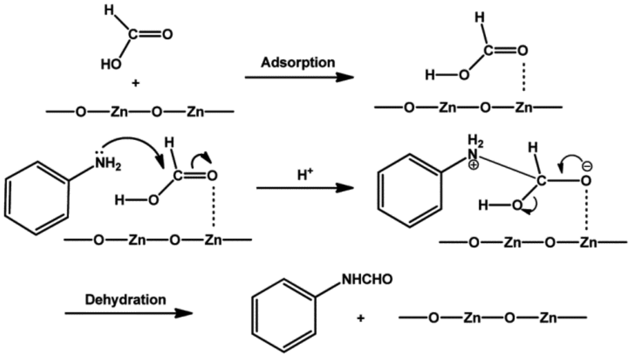


Fig. 4 — (a) Histogram showing the reusability performance of ZnOnanocatalyst in the synthesis of 4-nitroformanilide from aniline and (b) TEM image of reused ZnO NPs (sample ZnO-1)

at room temperature. It is observed that the current protocol is not only efficient at room temperature but also takes a much shorter time than other similar reaction systems. We believe that this is the most advantageous feature of this protocol. To the best of our knowledge, only Bose et al. reported microwave promoted N-formylation reaction with formic acid within such a shorter time. This signifies the importance of the current protocol[53].

One of the most attractive properties of heterogeneous catalysts is the reusability of the catalyst from green chemistry and industrial perspective. To test the reusability of ZnOnanocatalyst under the current reaction conditions, we chose 4-nitroaniline (6 mmol), formic acid (15 mmol), and 42 mol% ZnOnanocatalyst in 6 ml of the solvent system (1: 1 ethanol-water mixture). We carried out the reaction taking six times the scale of the model reaction for easy recovery of the catalyst. The nanocatalyst was isolated by centrifugation after thecompletion of the first run of the reaction washed with ethyl acetate followed by water and then dried the isolated catalyst in a vacuum oven overnight at 60 °C. The dried catalyst was used for further reaction of formic acid and 4-nitroaniline. We observed that the catalyst remained efficient up to the fifth cycle delivering excellent yields (Figure 4a). The morphology of the reused catalyst was investigated by microscopy analysis (Figure 4b) and we observed that after catalyst, the morphology of ZnO NPs nearly remains same.



Scheme 1 — The proposed reaction mechanism of ZnO NPs catalyzed N-formylation of amines

The mechanism of the reaction between aniline or substituted aniline with formic acid is assumed to be a nucleophilic addition to the carbonyl group followed by dehydration.[32] However, in the absence of sufficient activation energy and/or a suitable environment for the substrates required to go for completion of the reaction is not achievable. In contrast, the basic amine substrate prefers to interact with formic acid in a typical way of Lewis acid-base type reaction. This happens most of the time when the two substrates aniline and formic acid are mixed at low temperatures and hence product formation is not observed for several hours. However, in the presence of ZnO NPs, activation of the carbonyl group of formic acid take place via adsorption on the catalyst surface and thereby increases the electrophilic character of formic acid (Scheme 1). This was followed by the nucleophilic attack of the amine group. The resulting intermediate undergoes dehydration to give the final product formanilides. The presence of ethanol in the reaction mixture does not interfere with the desired product formation but increased the solubility of the amines. Sajadi et al. reported a similar mechanism for the formylation of amines using $CeO_2$ catalysts[32]. The main advantages of using ZnO NPs in the formylation of aromatic amines are-(i) the reaction can be carried out at room temperature within a short period, (ii) no toxic solvent is needed, (iii) the use of toxic formylating agent can be avoided, (iv) excellent reusability of the catalyst without loss of further catalytic activity and (v) electron-deficient anilines can easily be converted to formanilides which is not observed in most of the reports (vi) recrystallization and column chromatography is not needed to purify the product.

## Conclusion

A facile and efficient protocol has been developed for the formanilides synthesis at room temperature using spherical ZnO NPs as the catalyst. The protocol is simple, economical, and environment-friendly. The simple separation of the product from the reaction mixture without using expensive and tedious column chromatography techniques makes the process more beneficial for practical purposes. The protocol can be extended to a wide array of substituted anilines with electron-withdrawing and electron-donating groups at the *ortho*, *meta*, and *para* positions, aliphatic amines and heterocycles to get the desired formanilides with moderate to excellent yield. The excellent reusability and the scope for diverse substrate compatibility further enhance the versatility of the protocol.

## Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/58776

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## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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