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PIPES-ZnO NPs coupled catalyst for the synthesis of 2-((1H-indol-3-yl)(phenyl)methyl)-5,5-dimethylcyclohexane-1,3-diones

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ABSTRACT

Synthesis, characterization and catalytic application of Zinc Oxide nanoparticles (ZnO NPs) with 1,4-Piperazinediethanesulfonic acid (PIPES) have been explored as a coupled catalyst for the condensation reaction of Dimedone (1), Benzaldehyde and (2) Indole (3) in stipulated period of time to give 2-((1H-indol-3-yl)(phenyl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4) under ultrasound irradiation technique at 60 °C temperature. Pharmacological importance of targeted products along with surface properties of ZnO NPs and Bronsted acidity of PIPES together became promising advantages for this protocol to establish.

Introduction

As far as the current ecological scenario is concerned, chemistry people have to think not only on promising catalytic activities while developing methodology but also have to believe about the budding spectrum of bio-activity of targeted products and green chemistry aspects as well. As an element of this environment let's ask a question to ourselves about how to make earth liveable? Yes, chemists can play a little role in this while working in the laboratory that may be from an academy or industry or research institute. Herein, our attempts are on the same way to contribute as much as possible.

One pot multicomponent reactions (MCRs) are reliable, time saving routes and can cover high insight of green chemistry. MCRs produces heterocyclic scaffolds by means of cyclization and coupling reactions [1]. One can also inculcate desired functionality by choosing proper reactant. Nano catalysis is indeed a smart approach because of it possess extraordinary catalytic assets towards organic MCRs [2]. Alongside organocatalyst offers needful belongings including less affection towards oxygen and humidity and user friendliness with economical and ecological benefits [3]. Besides ultrasound irradiation techniques have been proved as alternative non-traditional energy source to accelerate rate of organic reactions [4].

Keeping these features in mind we have chosen one pot MCR driven by nanocatalysts (ZnO NPs) coupled with organocatalysts (PIPES) under ultrasound irradiation techniques for the synthesis of targeted moiety. This combination offers bunch of benefits as different mode of activities possess by proposed product due to presence of nitrogen containing heterocyclic ring structure in the molecule [5]. The broad spectrum of bioactivities revealed by substituted indole moiety such as antimicrobial activities [6], anti-hepatitis, anti-oxidant, anti-cancer, anti-malarial, anti-diabetic, anti-tubercular, anti-leishmanial, anti-convulsant, ccnanti-histaminic, anti-hypertensive, tubulin polymerization and enzyme inhibition [7]. It has been observed that the molecule with indole ring having varieties of applicability such as a precursor, reagent, an intermediate, an active pharmaceutical ingredient (API) and targeted drug molecule [8]. Synthetic methodologies biochemical studies, molecular docking [9], structure activity relationship (SAR) study [10], isolation of natural product like Azepine-Indole Alkaloids from Psychotria nemorosa [11], drug discovery and analysis have also been reported in the literature.

Because of versatility of indole moiety different synthetic routes have been established in the literature [8,12–20].

Results and discussion

Initially, efforts have been made to perform one pot multicomponent

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reaction of Dimedone 1, Benzaldehyde 2, Indole 3 and alcohol as a solvent in the presence of PIPES (3 mol %) under an ultrasound irradiation technique (Scheme 1). We observed that within half an hour reaction mixture turns to blood red colour, we thought reaction is completed but actually it was not. After monitoring the reaction by thin layer chromatography we found that reaction is just begun to form product. Afterword reaction is continually irradiated in sonicator bath for 24 h nevertheless very less yield of the product (22 %) was isolated by column chromatography (85% n-hexane: 15% ethyl acetate) (Table 1, entry 1). Alongside we performed the same model reaction in the presence of ZnO nanoparticles catalyst somehow yield of the product increased up to 33 % within 24 h (Table 1, entry 2). Still results were not satisfactory for us because product formed was in less % yield and for isolation of products it needs column chromatography which is not expected in green chemistry practices.

For the betterment of results consistently we took efforts by optimizing the catalyst concentration in the same solvent that is ethanol (Table 1, entry 3–9). In continuation of our work in search of better catalysts [21–25] we attempted to combine PIPES (Bronsted acid) with ZnO NPs and interestingly we got better results for the same reaction. We encouraged with these results consciously herein, equimolar quantity of reactants viz Dimedone 1, Benzaldehyde 2 and Indole 3 in alcohol was mixed in the presence of ZnO NPs-PIPES we got significant yield of the product (Table 1, entry 9). Later on we tried to set the same reaction in various solvents in the presence of optimized catalyst concentration we did not found better percent yield of the product (Table 1, entry 10–15). While ultrasound irradiation one thing we noticed that after one hour irradiation reaction temperature was increased up to 54 °C that is due to acoustic cavitations occurred in the reaction vessel. Continuous ultrasound irradiations and catalytic role of ZnO NPs-PIPES accelerated organic reactions in proper way to form higher yield of the products at milder conditions (Scheme 2).

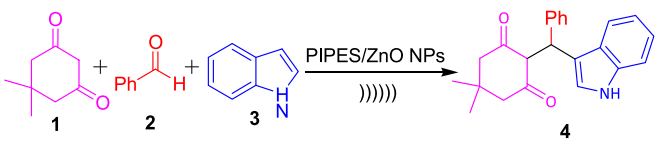
Therefore, the optimized reaction condition (Table 1, entry 9) further we applied for the synthesis of 2-((1H-indol-3-yl)(phenyl) methyl)-5,5-dimethylcyclohexane-1,3-dione derivatives by using various aliphatic, aromatic as well as heteroaromatic aldehydes. (Table 2).

After derivatization it has been perceived that this protocol is employable for different precursors with activating and deactivating substitutions. Also very less difference in the yield of the product has been detected though the aldehydes are of different types. Hence, in contemplation of generalization we propose this protocol in academic as well as industrial research laboratories.

Experimental

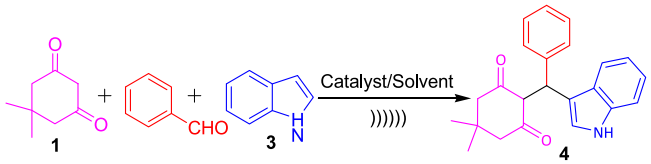
Procedure for the synthesis of 2-((1H-indol-3-yl)(phenyl)methyl)-5,5-dimethylcyclohexane-1,3-diones (4a): In a 20 mL hard glass test tube a mixture of Benzaldehyde (0.212 g, 0.002 mol), dimedone (0.280 g, 0.002 mol) were mixed in the presence of ZnO NPs-PIPES coupled catalyst (Table 1 entry 9) in ethanol and subjected for ultrasonic irradiation for one and half an hour. After that indole (0.234 g, 0.002 mol) was added portion wise at same reaction condition. The progress of reaction was monitored by TLC (ethyl acetate:n-hexane). After completion of reaction the product was poured on crushed ice, thus obtained product was filtered, dried and recrystallized by using ethanol to get pure product.

Synthesis of ZnO Nanoparticles: ZnO nanoparticles were



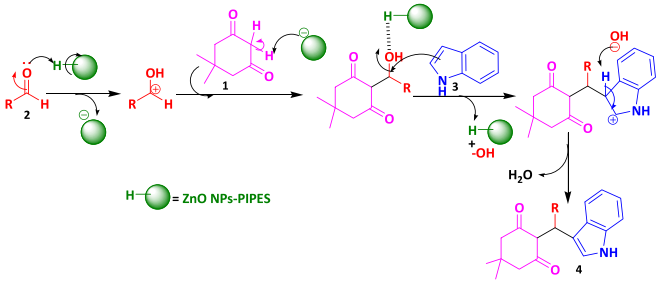
Scheme 1. Model reaction.

Table 1
Optimization of reaction conditions using PIPES/ZnO NPs catalyst.[a]



Sr. No.	Catalyst(mol) PIPES	ZnO NPs	Solvent	Time (hr)[b]	Yield (%)[c]
1	3	0	Ethanol	24	22
2	0	3	Ethanol	24	33
3	3	3	Ethanol	24	38
4	6	0	Ethanol	24	28
5	0	6	Ethanol	24	45
6	6	6	Ethanol	24	55
7	9	0	Ethanol	24	35
8	0	9	Ethanol	24	50
9	**9**	**9**	**Ethanol**	**04**	**82**
10	9	9	Ethanol + Water (60:40)	08	64
11	9	9	Isopropyl alcohol	08	68
12	9	9	Dichloro Methane	06	56
13	9	9	Ethyl Acetate	06	55
14	9	9	Acetone	06	70
15	9	9	Acetonitrile	06	70

[a] Reaction conditions: Dimedone **1** (0.280 g), Benzaldehyde **2** (0.212 g), and Indole **3** (0.234 g) in solvent (25 mL) were irradiated in ultrasonic bath at ambient temperature.
[b] Reaction time.
[c] Isolated yield.



Scheme 2. Mechanistic pathway of proposed reaction.

Table 2
Substrate scope for the synthesis of targeted products (4a-4n).[a]

Entry	R/Aldehydes	Time (Hrs)	Isolated yield (%)	M.P. (°C)
4a	C_6H_5	4	82	140–142
4b	2-ClC_6H_4	4	82	137–139
4c	3-ClC_6H_4	4	79	131–133
4d	4-ClC_6H_4	4	84	134–136
4e	2,4-ClC_6H_3	4	80	148–150
4f	3-$NO_2C_6H_4$	4.5	76	139–141
4 g	4-$NO_2C_6H_4$	4.5	78	129–131
4 h	4-$OCH_3C_6H_4$	4	84	154–156
4i	2-Furyl	4.5	80	162–164
4j	2-Thienyl	4.5	80	176–178
4 k	$CH_3CH=CH$	4	85	128–130
4 l	$C_6H_5CH=CH$	4	84	190–192
4 *m*	$CH_3CH_2CH_2$	3.5	90	121–124
4*n*	CH_3	3.5	85	134–136

[a] Reaction conditions: Dimedone 1 (0.280 g), Benzaldehyde 2 (0.212 g), and Indole 3 (0.234 g) in alcohol (25 mL), ultrasonic irradiation, ambient temperature.

synthesized by the modified chemical successive ionic layer adsorption and resorption techniques using the chemical ingredients as $ZnCl_2$ (0.2 M) and deionized H_2O. The cationic and anionic sources were mixed in a beaker at constant room temperature in an equi-proportion, the reaction was carried out for 6 h to results in formation of precipitate which is settled at the bottom of the reaction bath. Thus obtained precipitate was continuously washed in distilled water for 30 min to remove excess unwanted chemical ingredients and dried in air tied dark desiccator for about 3 h, as obtained powder is then crushed at manual ball mill for 30 min till we get fine powder.

Spectral analysis for synthesized Compounds

2-((1H-indol-3-yl)(phenyl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4a); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.12 (s, 6H, CH_3), 2.28 (s, 4H, CH_2), 3.69 (s, 1H, CH), 4.49 (s, 1H, CH), 6.68 (s, 1H, Ar-H), 6.75 (m, 5H, Ar-H), 7.10 (dd, J1 = 8.5 and J2 = 7.29, 1H, Ar-H), 7.3 (dd, J1 = 7.29 and J2 = 6.80, 1H, Ar-H), 7.6 (d, J = 7.10, 1H, Ar-H), 7.72 (d, J = 10.0, 1H, Ar-H), 9.72 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.00, 24.01, 36.80,58.50, 67.90, 107.30, 110.03, 114.93, 115.96, 116.80, 118.09, 118.5, 120.00, 122.35, 124.14, 129.03, 130.91, 145.05, 170.07; HRMS (ESI); $[M + H]^+$ for $C_{23}H_{23}NO_2$: 345.68. IR ν max/cm^{-1} (KBr): 3692 (N–H), 3065 (C-H), 1699 (C-O), 1550 (C-C), 1315 (C-N).

2-((2-chlorophenyl)(1H-indol-3-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4b); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.45 (s, 6H, CH_3), 2.24 (s, 4H, CH_2), 3.57 (s, 1H, CH), 4.31 (s, 1H, CH), 6.56 (s, 1H, Ar-H), 6.90 (d, J = 7.8, 2H, Ar-H), 7.10 (dd, J1 = 8.2 and J2 = 7.8, 1H, Ar-H), 7.21 (dd, J1 = 7.4 and J2 = 7.08, 1H, Ar-H), 7.35 (d, J = 4.0, 2H, Ar-H), 7.56 (d, J = 6.8, 1H, Ar-H), 7.70 (d, J = 9.94, 1H, Ar-H), 9.66 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.00, 24.09, 37.19, 59.18, 69.17, 110.03, 112.03, 116.03, 117.06, 118.28, 117.64, 119.08, 208.13; HRMS (ESI); $[M + H]^+$ for $C_{23}H_{24}ClNO_2$: 381.25; IR ν max/cm^{-1} (KBr): 3664 (N–H), 3023 (C-H), 1705 (C-O), 1566 (C-C), 1322 (C–N), 818 (C–Cl).

2-((3-chlorophenyl)(1H-indol-3-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4c); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.15 (s, 6H, CH_3), 2.40 (s, 4H, CH_2), 3.97 (s, 1H, CH), 4.51 (s, 1H, CH), 6.66 (s, 1H, Ar-H), 7.09 – 7.18 (m, 8H, Ar-H), 9.66 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 25.60, 30.09, 59.19, 70.17, 111.03, 112.57, 116.45, 117.26, 118.48, 117.00, 119.00, 208.02; HRMS (ESI); $[M + H]^+$ for $C_{23}H_{24}ClNO_2$: 383.15; IR ν max/cm^{-1} (KBr): 3740 (N-H), 2999 (C-H), 1999 (C-O), 1628 (C-C), 1385 (C-N), 830 (C-Cl).

2-((4-chlorophenyl)(1H-indol-3-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4d); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.15 (s, 6H, CH_3), 2.40 (s, 4H, CH_2), 3.97 (s, 1H, CH), 4.51 (s, 1H, CH), 6.66 (s, 1H, Ar-H), 7.18 (d, J = 8.0, 2H, Ar-H), 7.00 – 7.40 (m, 6H, Ar-H), 10.06 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 25.60, 30.09, 59.19, 70.17, 111.03, 112.57, 116.45, 117.26, 128.48, 117.00, 119.00, 208.20;. HRMS (ESI); $[M + H]^+$ for $C_{23}H_{24}ClNO_2$: 383.15; IR ν max/cm^{-1} (KBr): 3740 (N-H), 2999 (C-H), 1999 (C-O), 1628 (C-C), 1385 (C-N), 830 (C-Cl).

2-((2,4-dichlorophenyl)(1H-indol-3-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4e); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.11 (s, 6H, CH_3), 2.32 (s, 4H, CH_2), 3.98 (s, 1H, CH), 4.50 (s, 1H, CH), 6.70 (s, 1H, Ar-H), 7.00 – 7.40 (m, 8H, Ar-H), 9.99 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 25.60, 30.09, 59.19, 70.17, 111.03, 112.57, 116.45, 117.26, 118.48, 117.00, 119.00, 208.11;. HRMS (ESI); $[M + H]^+$ for $C_{23}H_{21}Cl_2NO_2$: 383.15; IR ν max/cm^{-1} (KBr): 3780 (N-H), 2080 (C-H), 2018 (C-O), 1725 (C-C), 1405 (C-N), 905 (C-Cl).

2-((1H-indol-3-yl)(3-nitrophenyl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4f); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.12 (s, 6H, CH_3), 2.32 (s, 4H, CH_2), 3.88 (s, 1H, CH), 4.59 (s, 1H, CH), 6.75 (s, 1H, Ar-H), 7.0 (dd, J1 = 8.2 and J2 = 7.8 Hz, 1H, Ar-H), 7.51 (dd, J1 = 7.4 and J2 = 6.8, 1H, Ar-H), 7.8 (d, J = 5.0, 1H, Ar-H), 7.6 (d, J = 8.0, 1H, Ar-H), 7.9 (d, J = 7.0, 1H, Ar-H), 8.01 (d, J = 10.02, 1H, Ar-H), 8.20 (d, J = 4.13, 1H, Ar-H), 8.25 (d, J = 7.6 2H, Ar-H), 10.10 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm):18.5, 26.1, 35.3, 59.0, 67.9, 107.7, 110.8, 114.7, 116.9, 117.1, 117.4, 117.8, 118.5, 130.8, 131, 132.1, 148.4, 149.5, 145.7, 208.7;. HRMS (ESI); $[M + H]^+$ for $C_{23}H_{22}N_2O_4$: 390.16. IR ν max/cm^{-1} (KBr): 3730 (N-H), 3068 (C-H), 1717 (C-O), 1526 (C-C), 1382 (N-O), 1333 (C-N).

2-((1H-indol-3-yl)(4-nitrophenyl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4 g); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.12 (s, 6H, CH_3), 2.32 (s, 4H, CH_2), 3.88 (s, 1H, CH), 4.59 (s, 1H, CH), 6.75 (s, 1H, Ar-H), 7.0 (dd, J1 = 8.2 and J2 = 7.4 Hz, 1H, Ar-H), 7.51 (dd, J1 = 7.4 and J2 = 6.8, 1H, Ar-H), 7.6 (d, J = 5.0, 1H, Ar-H), 7.8 (d, J = 8.0, 1H, Ar-H), 7.8 (d, J = 7.0, 1H, Ar-H), 8.00 (d, J = 10.02, 1H, Ar-H), 8.01 (d, J = 4.13, 1H, Ar-H), 8.20 (d, J = 7.6 2H, Ar-H), 10.10 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm):18.5, 26.6, 35.3, 59.0, 67.9, 107.7, 110.8, 114.7, 116.9, 116.9, 117.1, 117.4, 117.8, 118.5, 130.8, 131, 132.1, 148.4, 149.5, 145.7, 208.7;. HRMS (ESI); $[M + H]^+$ for $C_{23}H_{22}N_2O_4$: 390.16. IR ν max/cm^{-1} (KBr): 3730 (N-H), 3068 (C-H), 1717 (C-O), 1608 (C-C), 1382 (N-O), 1333 (C-N).

2-((1H-indol-3-yl)(4-methoxyphenyl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4 h); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.60 (s, 6H, CH_3), 3.51 (s, 3H, CH_3), 2.42 (s, 4H, CH_2), 3.86 (s, 1H, CH), 4.51 (s, 1H, CH), 6.66 (s, 1H, Ar-H), 7.05 (d, J = 8.0, 2H, Ar-H), 7.01 – 7.39 (m, 6H, Ar-H), 10.01 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 26.50, 30.90, 56.0, 59.99, 70.17, 111.03, 112.57, 116.45, 117.26, 128.48, 117.00, 119.00, 208.01;. HRMS (ESI); $[M + H]^+$ for $C_{24}H_{25}NO_3$: 376.09; IR ν max/cm^{-1} (KBr): 3792 (N-H), 3014 (C-H), 2022 (C-O), 1702 (C-C), 1401 (C-N).

2-((furan-2-yl)(1H-indol-3-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4i); ^{1}H NMR (400 MHz,$CDCl_3$, TMS, δ ppm): 1.10 (s, 6H, CH_3), 2.47 (s, 4H, CH_2), 3.81 (s, 1H, CH), 4.71 (s, 1H, CH), 6.86 (s, 1H, Ar-H), 5.89–7.10 (m 3H, Ar-H), 7.15 – 7.25 (m, 4H, Ar-H), 10.00 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 26.50, 30.90, 56.0, 59.99, 70.17, 105.9, 110.0, 115.42, 127.45, 122.13, 141.06, 208.30;. HRMS (ESI); $[M + H]^+$ for $C_{21}H_{21}NO_3$: 336.60; IR ν max/cm^{-1} (KBr): 3612 (N-H), 3070 (C-H), 2212 (C-O), 1685 (C-C), 1501 (C-N).

2-((1H-indol-3-yl)(thiophen-2-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (4j); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.11 (s, 6H, CH_3), 2.38 (s, 4H, CH_2), 3.91 (s, 1H, CH), 4.59 (s, 1H, CH), 6.80 (s, 1H, Ar-H), 6.60–6.92 (m 3H, Ar-H), 7.18 – 7.37 (m, 4H, Ar-H), 9.98 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 25.99, 30.40, 31.30, 59.09, 74.87, 111.0, 115.07, 122.42, 122.95, 123.13, 127.16, 144.6, 208.30; HRMS (ESI); $[M + H]^+$ for $C_{21}H_{21}NO_2S$: 352.30; IR ν max/cm^{-1} (KBr): 3612 (N-H), 3070 (C-H), 2212 (C-O), 1685 (C-C), 1501 (C-N), 834 (C-S).

2-((E)-1-(1H-indol-3-yl)but-2-enyl)-5,5-dimethylcyclohexane-1,3-dione (4 k); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 1.20 (s, 6H, CH_3), 1.82 (s, 3H, CH_3), 2.29 (s, 4H, CH_2), 3.61 (s, 1H, CH), 3.95 (s, 1H, CH), 5.46 (s, 2H, CH), 6.79 (s, 1H, Ar-H), 7.18 – 7.25 (m, 4H, Ar-H), 9.99 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 19.90, 26.93, 30.30, 31.10, 59.40, 72.60, 111.11, 111.87, 119.01, 120.23, 122.22, 125.90, 127.16, 135.31, 208.00; HRMS (ESI); $[M + H]^+$ for $C_{20}H_{23}NO_2$: 310.20; IR ν max/cm^{-1} (KBr): 3567 (N-H), 3103 (C-H), 2242 (C-O), 1681 (C = C), 1557 (C-N).

2-((E)-1-(1H-indol-3-yl)-3-phenylallyl)-5,5-dimethylcyclohexane-1,3-dione (4 l); ^{1}H NMR (400 MHz,$CDCl_3$, TMS, δ ppm): 1.12 (s, 6H, CH_3), 2.34 (s, 4H, CH_2), 3.66 (s, 1H, CH), 3.92 (s, 1H, CH), 6.06 (s, 1H, CH), 6.44 (s, 1H, CH), 6.80 (s, 1H, Ar-H), 7.18 – 7.21 (m, 4H, Ar-H), 7.22–7.30 (m, 5H, Ar-H), 10.13 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 26.63, 30.40, 33.55, 59.40, 72.56, 111.13, 111.17, 119.00, 120.12, 122.20, 126.30, 126.41, 127.56, 128.0, 128.70, 135.20, 208.00;. HRMS (ESI); $[M + H]^+$ for $C_{20}H_{25}NO_2$: 312.20; IR ν max/cm^{-1} (KBr): 3597 (N-H), 3009 (C-H), 1750 (C-O), 1621 (C = C).

2-(1-(1H-indol-3-yl)butyl)-5,5-dimethylcyclohexane-1,3-dione (4 m); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ ppm): 0.98 (t, 3H, CH_3), 1.12 (s, 6H, CH_3), 1.62 (q, 2H, CH_2), 1.50 (t, 2H, CH_2), 2.40 (s, 4H, CH_2), 3.29 (s, 1H, CH), 3.45 (s, 1H, CH), 6.80 (s, 1H, Ar-H), 7.18 – 7.25 (m, 4H, Ar-H), 9.99 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.40, 19.90,

26.30, 30.34, 36.10, 43.90, 59.30, 72.60, 111.11, 119.01, 120.23, 125.90, 127.16, 136.51, 208.00;. HRMS (ESI); $[M + H]^+$ for $C_{20}H_{23}NO_2$: 310.20; IR ν max/cm^{-1} (KBr): 3642 (N-H), 3129 (C-H), 1742 (C-O), 1701 (C = C), 1580 (C-N).

2-(1-(1H-indol-3-yl)ethyl)-5,5-dimethylcyclohexane-1,3-dione (4n); ^{1}H NMR (400 MHz,$CDCl_3$, TMS, δ ppm): 1.13 (s, 3H, CH_3), 1.33 (d, 3H, J = 4.5, CH3), 2.41 (s, 4H, CH_2), 3.40 (q, 1H, CH), 3.60 (d, 1H, J = 5.3, CH), 6.80 (s, 1H, Ar-H), 7.18 – 7.25 (m, 4H, Ar-H), 10.09 (s, 1H, NH); 13C NMR (100 MHz, $CDCl_3$, δ ppm): 19.10, 24.19, 26.59, 30.39, 59.30, 111.10, 113.01, 120.23, 122.10, 127.50, 136.41, 208.00; HRMS (ESI); $[M + H]^+$ for $C_{18}H_{21}NO_2$: 284.10; IR ν max/cm^{-1} (KBr): 3511 (N-H), 3043 (C-H), 1675 (C-O), 1701 (C = C), 1580 (C-N).

Characterizations of Synthesized ZnO NPs: The ZnO NPs are characterized for structural properties using X-ray diffraction (XRD) pattern obtained on Panalytic X-Pert Pro using Cu Kα radiation (λ = 1.5405 Å) in the range of 20°-60°. Transmission electron microscopy (TEM) image obtained using JEM 2000 EXII. The surface morphology of the thin films probed by atomic force microscope (AFM) images obtained on Bruker AXS multimode scanning probe microscope. The optical characterization performed using spectrophotometer Perkin Elmer LAMBDA 750 in absorbance mode.

X-ray diffraction pattern (XRD)

Fig. 1 represents the X-ray diffraction pattern (XRD) obtained from ZnO NPs, peaks corresponding to (1 0 0), (1 0 1) and (1 1 0) planes are observed at 31.71°, 36.27and 56.29° respectively confirms ZnO (JCPDS data card 36–1451) along preferred C axis orientation possessing Hexagonal Wrutzite structure [26–28]. The inter-planner spacing (d) is found to be ≈ 2.8 to 3.83 Å for the preferred (1 0 0) orientation and the lattice parameters are found to be matching well with standard JCPDS data card [29]. The average crystallite size calculated using the Debye-Scherer formula is found to be 12 nm.

Transmission electron microscopy (TEM)

Transmission electron microscopy analysis was used to study the structural aspects of ZnO nanoparticles. The presence of fine grains can be seen from the surface morphology observed in the planar micrograph as shown in Fig. 2. And the presence of diffused rings pattern in the selective area electron diffraction (SAED) confirms the nanostructure of ZnO (inset of Fig. 2) [30].

Compositional analysis

Fig. 3 shows the energy dispersive X-ray spectrum (EDAX) obtained from ZnO nanoparticles. From figure it can be seen that the peaks corresponding to Zinc (Zn) and Oxygen (O) are obtained which confirms the expected elemental tresses with nearly equal proportionate of elemental compositions.

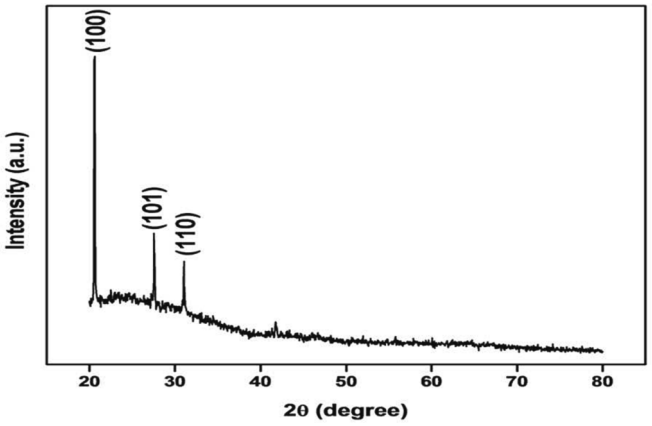


Fig. 1. XRD Pattern of ZnO nanoparticles prepared by chemical method at room temperature.

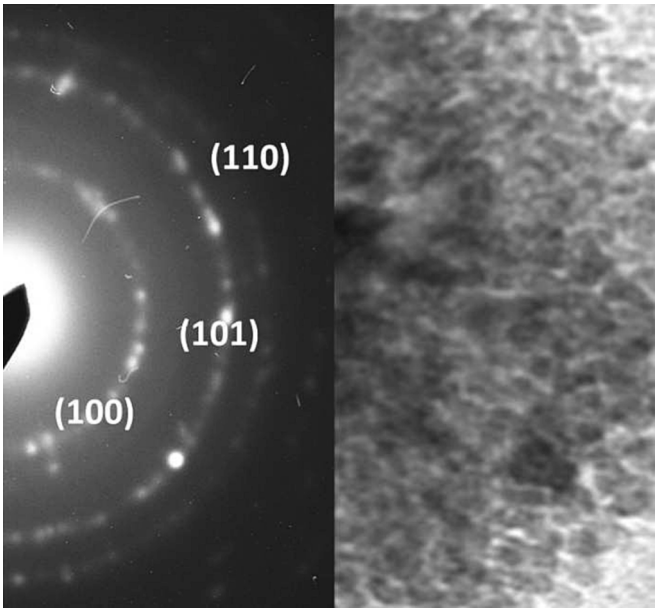


Fig. 2. Transmission electron microscopy image of ZnO nanoparticles.

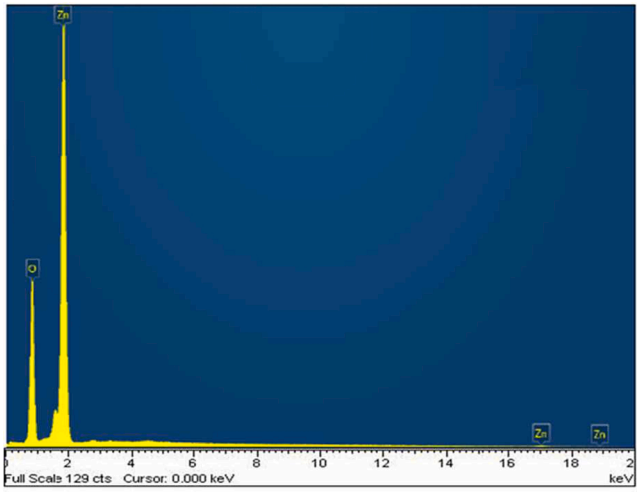


Fig. 3. EDAX Spectra obtained from ZnO nanoparticles used for elemental analysis and compositional confirmation.

Surface morphology

Surface morphology being one of the major contenders for deciding the nature of material, hence it is studied using atomic force microscopy (AFM) as shown in Fig. 4. The homogenous granular distribution of grains can be seen which also supports the claim of it being nanostructure in nature, the obtained average particle size is 15 nm [31].

Conclusions

In conclusions, we have established an ultrasound assisted strategic protocol which is having bunch of promising advantages of ZnO NPs-PIPES coupled catalyst and non conventional route. As size of nanoparticles we obtained is 12 to 15 nm which shows magnificent surface

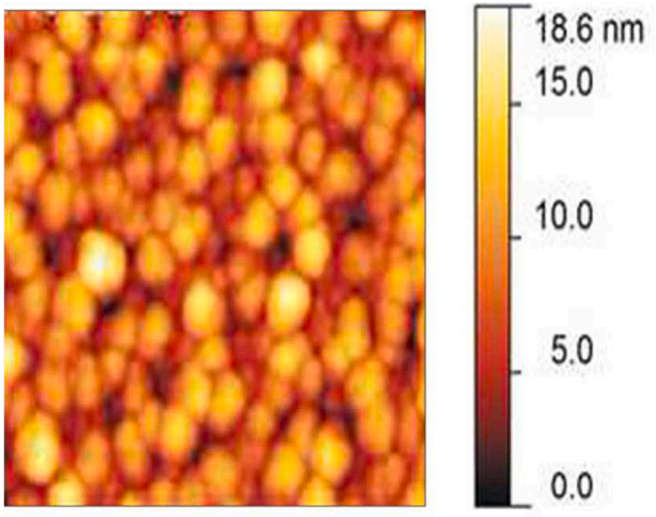


Fig. 4. AFM Images obtained from ZnO nanoparticles used for morphological nature understanding.

catalytic properties in congruent with mild Bronsted acidity of PIPES. Reaction rate and yield of the product were increased in remarkable amount which has been proved by mechanistic role of coupled catalyst. Herein, catalytic role can be extended for all other condensation reactions.

CRediT statement

Ms. Suchita S. Gadekar optimized synthetic protocols for the synthesis of targeted moiety using ZnO NPs by conventional as well as non-conventional methods. Dr. Rajesh Joshi Synthesized ZnO NPs and characterized it. Dr. Balaji Madje described the catalytic role of PIPES-ZnO NPs. Dr. Suryakant Sapkal performed synthesis of molecules by using Organocatalysts. Dr. Suryakant Sapkal performed synthesis of derivatives by using coupled catalysts. Writing- Reviewing and editing have been done by all authors. Dr. S. T. Salunke Made some technical and contextual addition in the manuscript. Overall methodology is developed by all authors. Validation of results and analysis of compound is done by Suchita and Suryakant.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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