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RESEARCH ARTICLE

Nanosized ZnO Under Solvent Free Condition: A Smart and Ecofriendly Catalyst to Microwave Assisted Synthesis of 3, 4-dihydropyrimidin-2(1H)-ones/Thiones

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Abstract: ***Background***: Heterogeneous synthesis of nitrogen containing heterocyclic compounds such as dihydropyrimidin-2(1H)-one/thione derivatives is an important research. Use of nanocrystalline ZnO has demonstrated for heterocyclic compounds which are routinely used in medicinal chemistry due to their therapeutic and pharmacological properties. In this context the solvent free synthesis of pyrimidine derivatives are reported.

Methods: Synthesis of ZnO nanomaterials is carried out by precipitation method, which is further used for synthesis of dihydropyrimidin-2(1H)-ones/thiones derivatives. Stoichiometric amount of aromatic aldehydes (1), urea (2) and ethyl acetoacetate (3) were taken in beaker. Then, 10 mmol percent nanocrystalline ZnO powder was added as a catalyst in the reaction mixture which was subjected to heated at 55°C in microwave oven.

Results: Microwave assisted synthesis of 3,4-Dihydropyrimidin-2(1H)-ones/thiones has been successfully carried out using eco-friendly ZnO nanoparticles as catalysts. Nanocrystalline ZnO of particle size in the range 60-80nm was prepared by decomposing the Zinc Oxalate intermediate at 500°C XRD analysis indicates the formation of highly crystalline hexagonal phase of ZnO. Solvent free synthesis using reported method have confer 95% yield which is greater than organic solvents such as DMF, Dioxane, THF, Toluene for heterogeneous synthesis.

Conclusion: Successfully accomplished 'green' synthesis of dihydropyrimidone/thiones derivatives was demonstrated. Use of nanocrystalline ZnO is found to be an efficient catalyst for heterogeneous Biginelli reaction. Solvent free reactions gave the better yield compared to the use of organic solvents.

Keywords: Biginelli reaction, green synthesis, heterogeneous catalysis, nanocrystalline ZnO.

1. INTRODUCTION

Dihydropyrimidin-2(1H)-ones/thiones derivatives form an important class of heterocyclic compounds due to their therapeutic and pharmacological properties [1]. Dihydropyrimidinones (DHPMs Fig. **1A**) moiety occurs in many drugs and synthetic products. DHPMs and their derivatives are very important; since, they behave as a calcium channel blocker, such as antihypertensive agents (R-SQ 32 926) [2], α_{1a}-adrenrgic antagonists, inhibitors of fatty acid transporters, and in mitotic kinesin inhibition [3-6] (Monastrol, Fig. **1B**). Batzelladine (Fig. **1C 1D 1E**) alkaloids contain a dihydropyrimidine core, which has been found to possess anti-HIV activity [7, 8]. DHPMs moiety exhibits antiviral [9], antibacterial and antifungal [10], anticancer [11, 12] (S-Monastrol) activity. They are also used as starting material for the synthesis of Rosuvastatin (Fig. **2**), selective and competitive inhibitor of HMG-CoA reductase [13], the enzyme responsi-

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2. EXPERIMENTAL

2.1. Synthesis of ZnO Catalyst

For the synthesis of nanostructured ZnO, zinc sulphate (99.9%, sd-fine chemicals) and oxalic acid (99%, sd-fine chemicals) have been used as precursor material. The intermediate zinc oxalate was obtained by adding oxalic acid (0.1N) solution drop wise into zinc sulphate (0.1N) with constant stirring. The precipitate of intermediate zinc oxalate complex was washed with distilled water (~1 lit) and dried at 80 °C in heating oven. Further, intermediate powder material was decomposed at 500°C in order to obtain nanostructured zinc oxide.

2.2. Characterization of Powdered ZnO Catalyst

The thermal study of as-synthesized zinc oxalate was carried out using Thermo Gravimetric Analyzer (TGA-DTA, Metler-Toledo Star System) up to 1000°C in air at the heating rate of 10°C/min. Powder X-ray Diffractograms (XRD) were recorded on X-ray diffractometer (Rigaku-D8/MaX-2200V) using CuKα-radiation with Ni filter. The surface morphology and particle size were determined using a field emission scanning electron microscope (FESEM HITACHI S-4800).

2.3. Measurement of Catalytic Activity to Biginelli Reaction

Stoichiometric amount of aromatic aldehydes (**1**) (0.5g, 4.71mmol), urea (**2**) (0.28g, 4.71 mmol) and ethyl acetoacetate (**3**) (0.61g, 4.71mmol) were taken in beaker (Scheme **1**). Then, 10 mmol percent nanocrystalline ZnO powder was added as a catalyst in the reaction mixture which was subjected to heating at 55°C in microwave oven. Reaction was monitored by TLC technique. After completion of the reaction, the resultant mixture was allowed to cool and then 10ml of ethyl acetate was added to it in order to separate the product. The catalyst was recovered by filtration using whatman-42 filter paper. Subsequently, catalyst was dried in an oven and recycled. Meanwhile, the filtrate was washed first with sodium bicarbonate followed by water, concentrated to get solidified compound and then recrystallized to get pure product. The structural purity of compounds was confirmed by ^{1}H-NMR & ^{13}C-NMR spectral techniques.

3. RESULTS AND DISCUSSION

Biginelli reaction is well known homogenous acid catalyzed reaction. It is also found that Lewis acids are superior over Brønsted acids due to better selectivity and higher yields having less reaction time require for completion [46]. Various Lewis acids, LiBr [34], $AlCl_3$ [35], $InBr_3$ [37], $BF_3.OEt_2$ [47], $FeCl_3$ and $LaCl_3$ [48] were reported for the synthesis of dihydropyrimidin-2(1H)-ones/thiones.

In view of this, the synthesis of dihydropyrimidin-2(1H)-ones/thiones was carried out using nano sized ZnO catalyst. The synthesis of ZnO catalyst was carried out by solution based precipitation technique in accordance with the protocol of our earlier report [49]. We also reported that effect of morphology of catalyst is further useful for altering the photo-catalytic activity [44]. Hence, the synthesis of proposed catalyst is carried out using precipitation technique as described in the experimental section.

3.1. Thermal Study of Zinc Oxalate

The intermediate sample prepared was dried at 120°C for 8 hours before they were subjected to thermo gravimetric analysis (TGA). Figure **2** depicts the TGA/DTA curves for decomposition of zinc oxalate synthesized in aqueous solvent. TGA showed a weight loss in two steps at 140°C and 380°C and DTA displayed two endothermic peaks corresponding to these temperatures.

Hence the decompositions of intermediate were carried out at 500°C to obtain nanocrystalline ZnO catalyst. The phase purity of ZnO catalyst was checked by using XRD and nano scale micro structure was as certained with FE-SEM.

3.2. Structural Study by XRD

Figure **3** shows the typical X-ray diffraction pattern of as-synthesized nanocrystalline ZnO material. XRD pattern reveals formation of highly phase-pure wurtzite structure. The lattice constant values obtained from the XRD patterns were

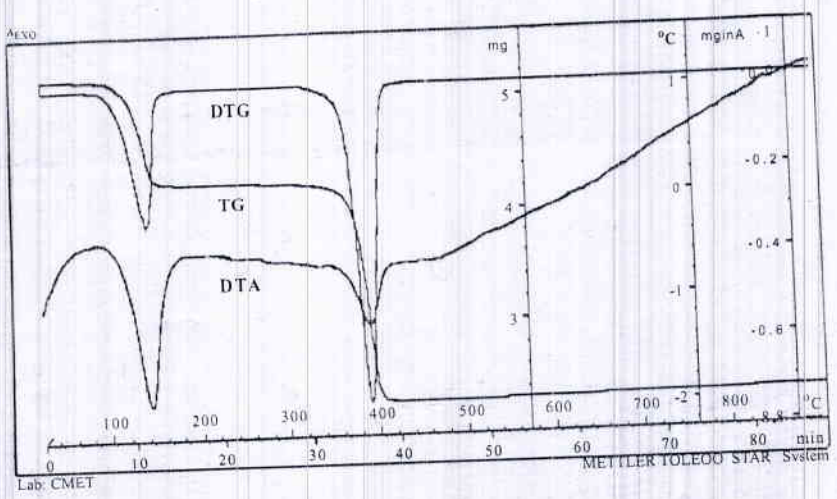


Fig. (2). TGA/DTA/DTG of intermediate zinc oxalate

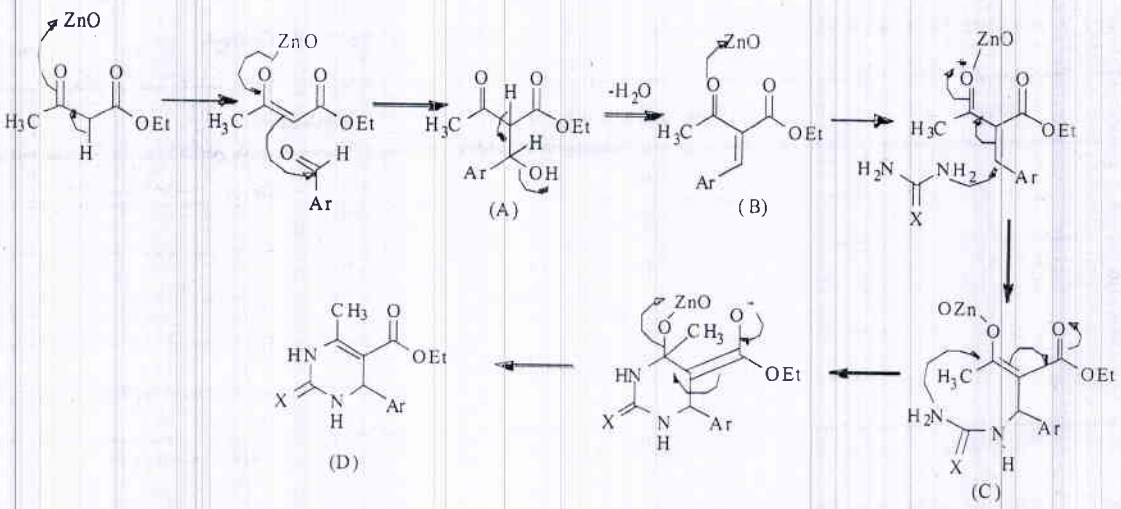
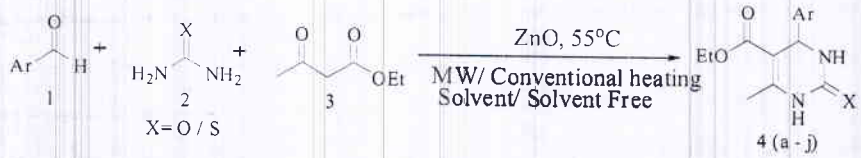


Fig. (5). Proposed mechanism of Synthesis of 3, 4-Dihydropyrimidin-2(1H)-ones/thiones



Reaction Scheme (1)

In the proposed work, as synthesized nano ZnO catalyst is used for synthesis of dihydropyrimidin-2(1H)-ones as per Scheme 1.

Before using the ZnO catalyst for this reaction, we have checked the feasibility of reaction without catalyst and found trace amount of product (Table 1, entry 1). This clearly indicates that this reaction requires catalyst. Hence for optimization of the catalyst amount, we performed the reaction using different mole % of ZnO and results are summarized in Table 1.

With increase in the amount of catalyst, yield is progressively enhanced up to certain value. Above 10 mol% of the catalyst amount, the reaction yield remained constant (92-94% entry 4-6). Among the chosen amount of catalyst concentration range for this study, 10 mol% catalyst exhibits maximum 92% yield (Table 1, Entry 4). Hence, for further study, we have used 10 mol% catalysts.

For the effect of solvent on product yield, we performed this reaction in different solvents such as DMF, Toluene, THF and 1,4-dioxane. The results obtained are tabulated in Table 2. However, we observed that for solvent free conditions product yield was 92% (entry5), which is far better as compared to that of reported solvents (Table 2, entries 1-4). The solvent free synthesis is green approach it will become, an alternative to overcome the environmental issue. Hence, synthesis of proposed further reaction is carried out for solvent free condition and also various substitutions.

Depending on this optimized results; we performed this reaction using various substituted aromatic aldehydes as given below are shown in Table 3.

Table 3 shows in the proposed Biginelli reaction for the plane benzaldehyde gives almost 90-92% yield (entries 4a and 4g) due to aromatic substitution. Also, the reaction carried out in presence of any electron donating or electron withdrawing group on aromatic aldehyde affects the rate and yield of reaction due to resonance and inductive effect. Presence of OH and OMe group on aromatic aldehyde gives less than 90% yield, (entries 4d, 4e and 4i) due to electron donating effect. While, presence of electron withdrawing groups, chlorine, fluorine and nitro group on aromatic aldehyde gives almost 90 to 95% yield (entries 4b, 4c, 4f, 4h and 4j). Electron withdrawing group on benzaldehyde increases the rate and yield due to carbonyl carbon of aldehydes which are more electron deficient and attack of nucleophile takes place more easily.

Above spectroscopic data of all proposed organic materials synthesized by Biginelli reactions are well matched with desired product material. Nanocrystalline ZnO catalyst is separated using Whatman no. 42 at the end of reactions. For recycling, catalyst is activated at 120°C for two hours. Yield of desired product for recirculation of catalyst is almost same. Our overall methodology showed recycling of catalyst is feasible, economical, environmental friendly than the routine homogenous Biginelli reaction.

In nutshell, we have performed the facile and environmental friendly Biginelli reaction using nanocrystalline ZnO catalyst. The catalyst used can be recycled while the same reaction yield is still retained. We believe our methodology is alternative to homogenous Biginelli reaction and easy to scale up from the end application point of view.

4b:-Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 2): Mp 218 °C (lit. [52] mp217-218 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (s, 1H, NH), 7.26~7.32 (m, 4H, H-2', H-3', H-5'& H-6'), 5.71 (s, 1H, NH), 5.40 (d, J = 4.0 Hz, 1H, H-4), 4.10 (q, J =8.0 Hz, 2H, $\underline{CH_2}$-CH_3), 2.37 (s, 3H,CH_3), 1.20 (t, J = 8.0 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR. (DMSO-d_6, 100 MHz): δ 164.46 (EtO$\underline{C}$=O), 151.75 (C-2', 147.20 (C-6), 142.4 (C-4'), 131.4 (C-1'), 127.18 (C-3' & C-5'), 127.08 (C-2' & C-6'), 98.46 (C-5), 58.37 ($\underline{CH_2}$-CH_3), 52.99 (C-4), 17.08 (CH_3), 13.09 (CH_2-$\underline{CH_3}$).

4c:-Ethyl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table 3, entry 3): Mp 204°C (lit. [52] mp201-202 °C); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 9.38 (bs, 1H,NH), 8.19 (d, J = 7.6 Hz, 2H, H-3'& H-5'), 7.89 (bs, 1H, NH), 7.48 (d, J = 7.6 Hz, 2H, H-2', & H-6'), 5.44 (s, 1H, H-4), 3.96 (q, J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_3), 2.48 (s, 3H, CH_3), 1.07 (t, J = 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.56 (EtO$\underline{C}$=O), 159.86(C-2), 151.89(C-6),149.28(C-1'), 146.64 (C-3'& C-5'), 127.56(C-4'), 123.75(C-2' & C-6'), 98.10(C-5), 59.30($\underline{CH_2}$-CH_3), 53.58(C-4), 17.77(CH_3), 13.96(CH_2-$\underline{CH_3}$).

4d:-Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 4): Mp 246°C (lit. [52] mp245-247 °C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.62 (br s, 1H, NH), 7.15(d, J = 8Hz, 2H, H-2' & 6-H'), 6.8 (d, J = 8Hz 2H, H-3' & H-5'), 6.60 (s, 1H, NH) 5.15 (s, 1H, H-4), 4.20 (br s, 1H, OH), 4.02 (q, J = 7.2 Hz, 2H, $\underline{CH_2}$-CH_3), 2.20 (s, 3H, CH_3), 1. 0 (t, J = 7.2 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 167.3(EtO$\underline{C}$=O), 158.1(C-2), 154.9(C-6), 146.1(C-4'), 136.8(C-1'), 127.3(C-2' & C-6'), 114.9(C-3 & C-5'), 100.7(C-5), 59.3($\underline{CH_2}$-CH_3), 54.4(C-4), 18.1(CH_3), 13.9 (CH_2-$\underline{CH_3}$).

4e:-Ethyl 4-(3, 4-dimethoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 5): Mp174°C (lit. [52] mp 174-176 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.81 (s,1H, NH), 6.83 (d, J = 8 Hz, 2H, H-5' & H-6'), 6.78(s, 1H, H-2'), 6.42 (s, 1H, NH), 5.34 (s, 1H, H-4), 4.05 (q, J = 8.0 Hz, 2H, $\underline{CH_2}$-CH_3), 2.31 (s, 3H, CH_3), 1.16 (t, J = 8.0 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.84(EtO$\underline{C}$=O), 154.11(C-2), 149.00 (C-6), 148.69(C-3'), 146.34(C-4'), 136.54(C-1'), 118.67(C-6'), 111.19(C-5'), 109.98(C-2'), 101.43(C-5), 60.05($\underline{CH_2}$-CH_3), 55.19(C-4), 18.55(CH_3), 14.28(CH_2-$\underline{CH_3}$).

4f:-Ethyl (4-fluorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 6): Mp 182°C (lit. [52] mp 182-184 °C); H NMR ($CDCl_3$, 400 MHz) : δ 8.5 (s, 1H, NH), 7.18 (t, J = 8.0 Hz & 4.0 Hz 2H, H-2' & H-6'), 6.88(t, J = 12 Hz & 8.0 Hz 2H, H-3' & H-5'), 6.17 (s, 1H, NH), 5.29 (s, 1H, H-4), 3.99 (q, J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_3), 2.25 (s, 3H, CH_3), 1.07 (t, J= 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 165.7(EtO$\underline{C}$=O), 163.7(C-4'), 161.21(C-2), 153.82(C-6), 146.56(C-1'), 139.78(C-6'), 128.46(C-3'), 128.38(C-5'), 115.75(C-2'), 101.39(C-5), 60.21($\underline{CH_2}$-CH_3), 55.08(C-4), 18.7(CH_3), 14.3(CH_2-$\underline{CH_3}$).

4g:-Ethyl 6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 7): Mp 206°C (lit. [52] mp208-210 °C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ10.58 (bs, 1H, NH), 9.90 (bs, 1H, NH), 7.40-7.50 (m, 5H, H-2', H-3', H-4', H-5'& H-6'), 5.40 (s, 1H, H-4), 4.20 (q, J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_3), 2.40 (s, 3H, CH_3), 1.32 (t, J = 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 176.2(EtO$\underline{C}$=O), 165.2(C-2), 143.0(C-6), 141.90(C-1'), 129.2(C-3' & C-5'), 128.3(C-2' & C-6'), 126.4(C-4'), 100.8(C-5), 60.0($\underline{CH_2}$-CH_3), 54.3(C-4), 28.0(CH_3), 14.2(CH_2-$\underline{CH_3}$).

4h:-Ethyl4-(4-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5carboxylate

(Table **3**, entry 8): Mp 190°C (lit. [52] mp192-194 °C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.62 (s, 1H, NH), 9.95 (s, 1H, NH), 7.70 (d, J = 8.0 Hz, 2H, H-3'& H-5'), 7.50 (d, J = 8.0 Hz, 2H, H-2' & H-6'), 5.40 (s, 1H, H-4), 4.25 (q, J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_3), 2.80 (s, 3H, CH_3), 1.25 (t, J = 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 174.1 (EtO$\underline{C}$=O), 165.20(C-2), 145.20(C-4'), 143.29(C-6), 132.00 (C-1'), 128.50(C-3' & C-5'), 128.20(C-2' & C-6'), 100.10 (C-5), 60.00($\underline{CH_2}$-CH_3), 53.40(C-4), 17.10(CH_3), 13.9(CH_2-$\underline{CH_3}$).

4i:-Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-thioxo -1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry 9): Mp 202°C (lit. [52] mp202-203 °C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.10 (br s, 1H, NH), 9.00 (br s, 1H, NH), 7.50 (br s, 1H, OH), 7.20 (d, J = 7.9 Hz, 2H, H-2' & H-6'), 6.75 (d, J = 7.9 Hz, 2H, H-3' & H-5'), 5.20 (s, 1H, H-4), 4.10 (q, J = 6.7 Hz, 2H, $\underline{CH_2}$-CH_3), 2.30 (s, 3H, CH_3), 1.10 (t, J = 6.7 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 166.8(EtO$\underline{C}$=O), 154.6(C-2), 147.0(C-6), 146.5(C-4'), 146.0(C-1'), 138.7(C-2'), 120.7(C-6'), 109.3(C-3'), 108.0(C-5'), 101.0(C-5), 59.6($\underline{CH_2}$-CH_3), 55.3(C-4), 17.1(CH_3), 13.1(CH_2-$\underline{CH_3}$).

4j:-Ethyl4-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

(Table **3**, entry **10**): Mp 182°C (lit. [52] mp 182-184 °C); ^{1}H NMR (DMSO-d_6, 300 MHz) : δ 10.60 (s, 1H, NH), 9.90 (s, 1H, NH), 7.40 (m, 4H, H-2', H-3', H-5' & H-6'), 5.20 (s, 1H, H-4), 4.20 (q, J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_3), 2.55 (s, 3H, CH_3), 1.25 (t, J = 7.1 Hz, 3H, CH_2-$\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz) : δ 174.2(EtO$\underline{C}$=O), 165.0(C-2), 163.1 (C-4'), 160.0(C-6), 139.77(C-2'), 139.73(C-6'), 128.49(C-3'), 128.38(C-5'), 115.4(C-1'), 100.6(C-5), 59.6($\underline{CH_2}$-CH_3), 53.39(C-4), 17.14(CH_3), 13.92(CH_2-$\underline{CH_3}$).

Above spectroscopic data of all proposed organic materials synthesized by Biginelli reactions are well matched with desired product material. Nanocrystalline ZnO catalyst is separated using Whatman no. 42 at the end of reactions. For recycling, catalyst is activated at 120°C for two hours. Yield of desired product for recirculation of catalyst is almost

reaction between ketene silylacetals and aldimines. *Tetra. Lett.*, **2007**, *48*, 6449-6452.

[31] Yan, H.P.; Yang, Y.; Tong, D.M.; Xiang, X.; Hu, C.W. Catalytic conversion of glucose to 5-hydroxymethylfurfural over SO_4^{2-}/ZrO_2 and SO_4^{2-}/ZrO_2-Al_2O_3 solid acid catalysts. *Catal. Comm.*, **2009**, *10*, 1558-1563.

[32] Reddy, B.M.; Patil, M.K.; Rao, K.N.; Reddy, G.K. An easy-to-use heterogeneous promoted zirconia catalyst for Knoevenagel condensation in liquid phase under solvent-free conditions. *J. Mol. Catal. A. Chem.*, **2006**, *258*, 302-307.

[33] Fazaeli, R.; Tangestaninejad, S.; Aliyan, H.; Moghadam, M. One-pot synthesis of dihydropyrimidinones using facile and reusable polyoxometalate catalysts for the Biginelli reaction. *Appl. Catal. A.*, **2006**, *309*, 44-51.

[34] Maiti, G.; Kundu, P.; Guin, C. One-pot synthesis of dihydropyrimidinones catalyzed by lithium bromide: An improved procedure for the Biginelli reaction. *Tetra. Lett.*, **2003**, *44-13*, 2757-2758.

[35] Shaikh, S.S. Synthesis and characterization of derivative derived from 1,4- Dihydropyrimidine. *Res. J. Chem. Sci.*, **2014**, *4*(11), 18-21.

[36] Mithun, A.; Bantwal, S.H.; Nalilu, S.K. Convenient one pot synthesis of some novel derivatives of thiazolo [2,3-b] dihydropyrimidinone possessing 4-methylthiophenyl moiety and evaluation of their antibacterial and antifungal activities. *Eur. J. Med. Chem.*, **2007**, *42*(3), 380-385.

[37] Nan, Y.F.; Yao, F.Y.; Zhong, C.; Shan, W.W.; Ji, T.W.; Clovis, P. Indium(III) bromide-catalyzed preparation of dihydropyrimidinones: Improved protocol conditions for the Biginelli reaction. *Tetrahedron*, **2002**, *58*, 4801-4807.

[38] Javad, S.; Zohre, Z. Biginelli reaction on Fe_3O_4-MWCNT nanocomposite: Excellent reactivity and facile recyclability of the catalyst combined with ultrasound irradiation. *RSC. Adv.*, **2013**, *3*, 17962-17967.

[39] Pourshamsian, K. ZnO-NPs as an efficient reusable heterogeneous catalyst for synthesis of 1,4-Dihydropyrimidine derivatives in solvent-free conditions. *Int. J. Nano. Dimens.*, **2015**, *6*(1), 99-104.

[40] Prakash, N.H.R.; Bhojya, N.H.S.; Aravinda, T. Nano-Titanium dioxide (TiO_2) mediated simple and efficient modification to Biginelli reaction. *Afri. J. Pure. App. Chem.*, **2009**, *3*(9), 202-207.

[41] John, M.; Tapas, S.; Asim, B. Fe_3O_4@mesoporous SBA-15: A robust and magnetically recoverable catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones via the Biginelli reaction. *Dalton Trans.*, **2012**, *41*, 6173-6181.

[42] Anqi, W.; Xiang, L.; Zhongxing, S.; Huanwang, J. New magnetic nanocomposites of ZrO_2-Al_2O_3-Fe_3O_4 as green solid acid catalysts in organic reactions. *Cat. Sci. Tech.*, **2014**, *4*, 71-80.

[43] Fatemeh, G.; Rashid, B.; Alireza, K. Performing Biginelli Reaction using catalytic system of melamine sulfonic acid and ZnO nanotube. *Life Sci. J.*, **2012**, *9*(4), 5699-5704.

[44] Kanade, K.G.; Kale, B.B.; Baeg, J.O.; Lee, S.M.; Lee, C.W.; Moon, S.J.; Chang, H. Self-assembled aligned Cu doped ZnO nanoparticles for photocatalytic hydrogen production under visible light irradiation. *Mat. Chem. Phy.*, **2007**, *102*, 98-104.

[45] Prashanth, G.K.; Prashanth, P.A.; Utpal, B.; Manoj, G.; Nagabhushana, B.M.; Ananda, S.; Krishnaiah, G.M.; Sathyananda, H.M. *In vitro* antibacterial and cytotoxicity studies of ZnO nanopowders prepared by combustion assisted facile green synthesis. *Int. J. Modern Sci.*, **2015**, *1*, 67-77.

[46] Francesco, F.; Ferdinando, P.; Luigi, V. $AlCl_3$ as an efficient Lewis acid catalyst in water. *Tet. Lett.*, **2001**, *42*, 1131-1133.

[47] Essa, H.H.; Daniel, R.S.; Ulf, H.D. Unprecedented catalytic three component one-pot condensation reaction: An efficient synthesis of 5-Alkoxycarbonyl-4-aryl-3,4-dihydropyrimidin-2(1H)-ones. *J. Org. Chem.*, **1998**, *63*(10), 3454-3457.

[48] Lu, J.; Bai, Y.; Wang, Z.; Yang, B.; Ma, H. One-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones using lanthanum chloride as a catalyst. *Tetra. Lett.*, **2000**, *41*, 9075-9078.

[49] Kanade, K.G.; Kale, B.B.; Aiyer, R.C.; Das, B.K. Effect of solvents on the synthesis of nano-size zinc oxide and its properties. *Mat. Res. Bull.*, **2006**, *41*, 590-60.

[50] JCPDS card No. 36-1451.

[51] Cullity, B.D. *Elements of X-Ray Diffraction*; Addison-Wesley: Reading, MA, **1977**, 102.

[52] Karade, H.N.; Sathe, M.; Kaushik, M.P. Synthesis of 4-Aryl Substituted 3,4-Dihydropyrimidinones using silica-chloride under solvent free conditions. *Molecule*, **2007**, *12*, 1341-1351.