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SiO_2-$CuCl_2$: An efficient and recyclable heterogeneous catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones

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Abstract

Silica supported copper (II) chloride is prepared as a green heterogeneous catalyst for the synthesis of biologically and pharmaceutically important 3,4-dihydropyrimidin-2(1*H*)-ones under microwave and thermal conditions. The catalyst has been characterized by various instrumental techniques such as FTIR, SEM, TEM, TGA and AAS. In addition, products are characterized by ^{1}HNMR, IR, ^{13}CNMR and mass spectral data. The reaction of *m*-nitrobenzaldehyde, ethylacetoacetate and urea produced 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2-(1*H*)-one and its structure has been determined using X-ray crystallography which also showed the inter-molecular H-bonding packing arrangement of molecules.

Keywords

Dihydropyrimidinones; diphenic acid; silica; copper (II) chloride; microwave; thermal; acetonitrile

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1. Introduction

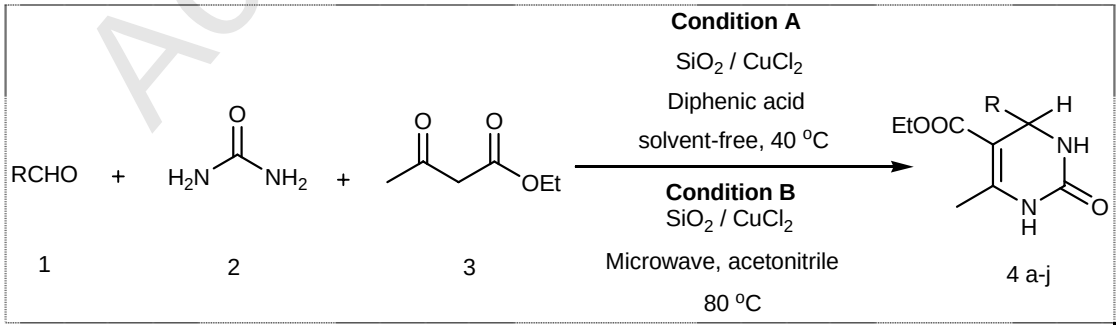
What makes researchers looking into the field of catalysis with continuous discovering every newer aspect of it is enfolded in its applicability in industry. Catalysis comprises a new way to meet the demands of energy and sustainability for the synthesis of organic compounds in the most economical way along with ecological concern **[1, 2]**. Supporting transition metals onto the solid supports provide a large surface area for reactants to get adsorbed, come closer and get able to react faster followed by desorption of reactants leaving the catalyst to be regenerable. Among transition metals, copper as a choice to explore comes from its mild nature, easy availability and less toxic nature.

Synthesizing heterocyclic bioactive molecules by replacing the old classical methods with new eco-friendly techniques like as with heterogeneous catalysts represents one of the most vibrant research areas in organic chemistry. Dihydropyrimidinones (Bignelli compounds) and their derivatives belong to an important class of heterocyclic compounds that have attracted attention due to their interesting pharmacological and biological profiles**[3]**. Their applications in the field of drug research have stimulated the development of a wide range of synthetic methods for their preparation and chemical transformations. Aryl-substituted 3,4-dihydropyrimidin--2(1*H*)-one and their derivatives are an important class of substances in organic and medicinal chemistry. These derivatives have remarkable pharmacological properties such as calcium channel blockers, α-1a-antagonists, HIV inhibitors of gp-120-CD4, anti-hypertensive, anti-viral, anti-tumor, anti-bacterial, anti-fungal, anti-cancer, anti-inflammatory agents**[4,5]**, melanin-concentrating hormone receptor antagonist**[6]** and neuropeptide Y (NPY) antagonist**[7].** These can be used as therapeutics in cardiovascular diseases, angina pectoris, or benign prostatic hyperplasia**[8]**. Moreover, its derivatives are found in a large family of natural products with broad biological activities. Various marine

alkaloids containing the dihydropyrimidinone moiety have interesting biological properties, such as batzelladine alkaloids that are potent HIV gp-120- CD4 inhibitors**[9]**.

Many nucleosides that have 5-substituted pyrimidine moiety have been shown to inhibit the growth of murine mammary carcinoma virus. Pyrimidine cores with extended π-systems possess interested fluorescent properties, and similar compounds are useful in the development of advanced electronic and photonic materials**[10,11,12]**.

In history, the Biginelli reaction represents a classical approach for the preparation of 3,4-dihydropyrimidin-2(1*H*)-ones by the one-pot condensation of an aromatic aldehyde, *β*-ketoester and urea in the presence of a mineral acid catalyst and alcohol solvent. Various reagents have been used for the synthesis of dihydropyrimidin-2-(1*H*)-ones such as chloroacetic acid**[13]**, $InBr_3$**[14]**; BF_3OEt_2 in combination with transition metal salts**[15]**, amberlyst 15**[16]**, $ZnCl_2$**[17]**, $SnCl_2$/ChCl**[18]**, SiO_2-Cl**[19]** and copper triflates**[20]**. But the reported reagents are associated with certain drawbacks such as larger reaction times, tedious work-up procedures and even handling of catalyst. In order to overcome these drawbacks, copper(II) chloride in combination with silica has been used as heterogeneous catalyst under thermal and microwave conditions for one-pot synthesis of Biginelli compounds as shown in **Scheme 1.**

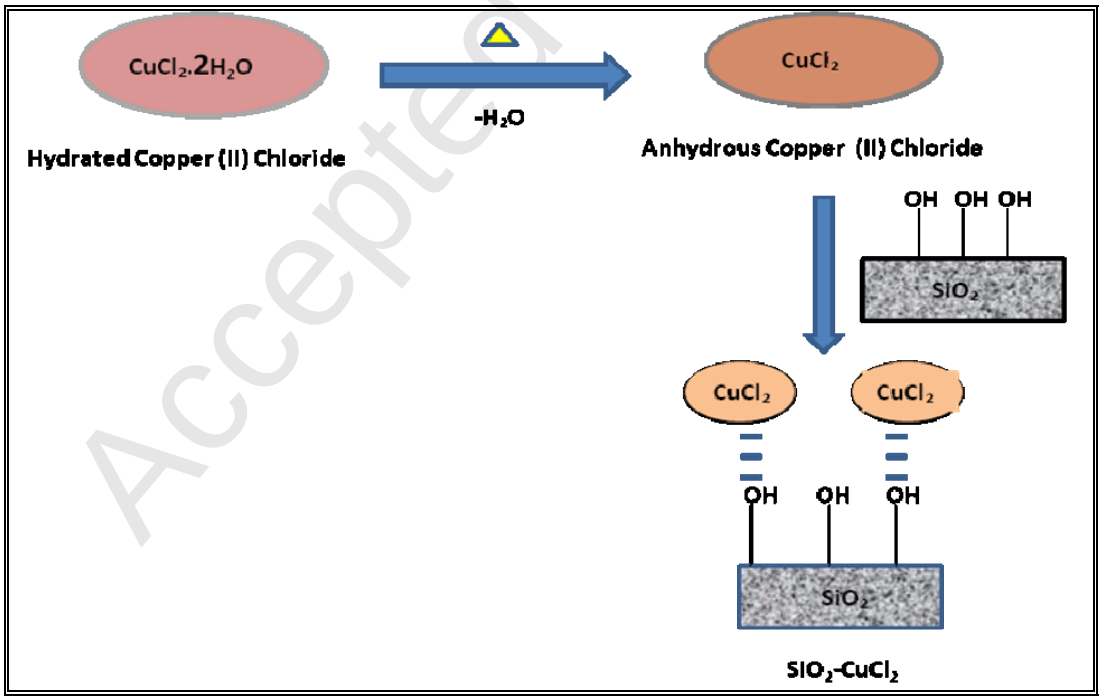


Scheme 1

2. Experimental

2.1 *Preparation of catalyst- silica supported copper (II) chloride [SiO_2 - $CuCl_2$]*

In order to support copper(II) chloride onto silica, the silica gel (15 g, K 100) was activated by adding silica gel (15g, K 100) to a solution of HCl : H_2O (1:1, 300 mL) in a round-bottom flask (500 mL) and the reaction mixture was stirred at 120 ^oC for 12 h. The activated silica was filtered at pump, washed with water till washings were neutral and dried in an oven at 110 ^oC for 5 h. The yield obtained was 13.8g. Then the activated silica (10 g, K 100) was stirred with anhydrous $CuCl_2$ (0.2 g) in dry ether (50 ml) at room temperature for 4 h. The catalyst was filtered, washed with water till washings were colourless and dried in an oven at 90-100 ^oC for 5 h. The yield obtained was 8.6g.



Scheme 1: A schematic approach for the synthesis of silica supported copper(II)chloride

2.2 *Characterization of Catalyst*

To conform the support of metal onto silica, the catalyst was thoroughly characterized by various instrumental techniques like FTIR, TGA, SEM, TEM and AAS and the results has been given as under:

FTIR

The FTIR spectrum of catalyst showed strong absorption peaks at 473 cm^{-1} (Si-O-Si bending vibration), 805 cm^{-1} (symmetric stretching) & 1098 cm^{-1} (anti-symmetric stretching of Si-O), 1631 cm^{-1} (bending vibration of physically adsorbed water and 3433 cm^{-1} due to Si-OH stretching vibration). For SiO_2-$CuCl_2$, an additional peak was observed at 669 cm^{-1} which corresponds to Cu-Cl stretching vibrations **(Fig. 1)**.

TGA

To check the thermal stability of the catalyst (SiO_2-$CuCl_2$), a thermo-gravimetric analysis (TGA) was done which showed a slight weight loss upto 225 ^oC followed by continuous weight loss upto 718.3 ^oC. The analysis indicated the stability of catalyst up to a range of 0-249.1 ^oC and hence is safe to be used in carrying out the reaction under chosen conditions (room temperature, 40 ^oC and 80 ^oC) **(Fig. 2)**.

Scanning Electron Microscope (SEM)

Further to study the microstructure and morphology of the catalyst (SiO_2-$CuCl_2$), a study of Scanning Electron Microscope (SEM) has been performed. The SEM images of the catalyst showed that the surface of SiO_2-$CuCl_2$ was found to be a fine powder with porous structure and it was observed that copper chloride particles are adsorbed onto the surface of silica **(Fig. 3).**

Transmission Electron Microscope (TEM)

A TEM has also been performed to see the morphology of metal particles. The TEM micrographs indicated that Cu is uniformly distributed onto the surface of silica **(Fig. 4)**. The mean diameter was found to be 2 nm which confirms the nano-size nature of the catalyst. It was found that no bulk aggregation of the metal occurred indicating that the Cu was finally dispersed onto the surface of silica. The TEM micrograph (**a**) infers formation of nano copper (average size 2 nm) and from (**b**) it is inferred that SiO_2-$CuCl_2$ shows the formation of molecular sieves which offers entrapment of metal particles inside these sieves of silica and thus displaying a host-guest relationship.

Atomic Absorption Spectrophotometric Analysis (AAS)

The amount of copper loaded onto the surface of silica was determined by AAS analysis. The catalyst was stirred in dil. HNO_3 and then subjected to AAS analysis. SiO_2-$CuCl_2$ contained 0.015 g of Cu per gram of catalyst.

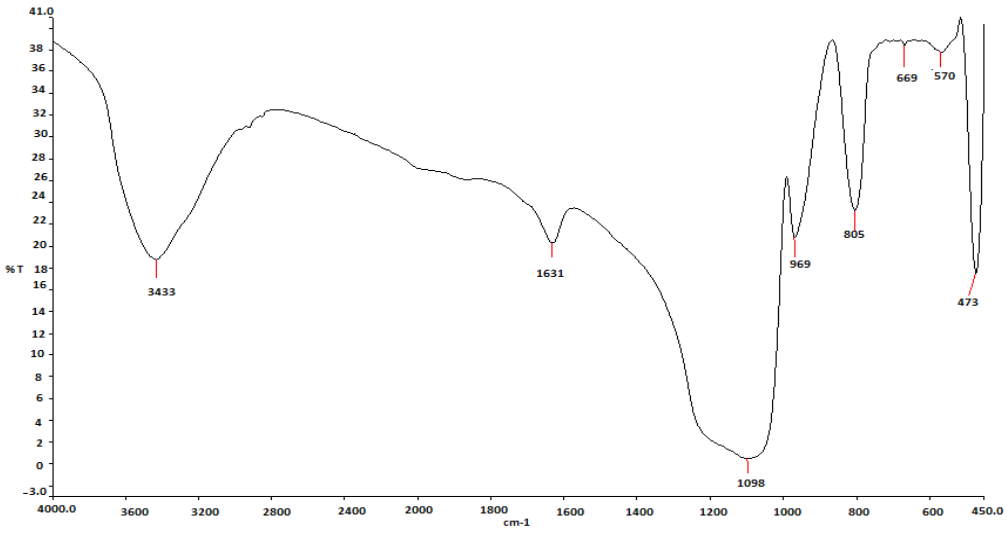


Fig. 1 FTIR of SiO_2-$CuCl_2$

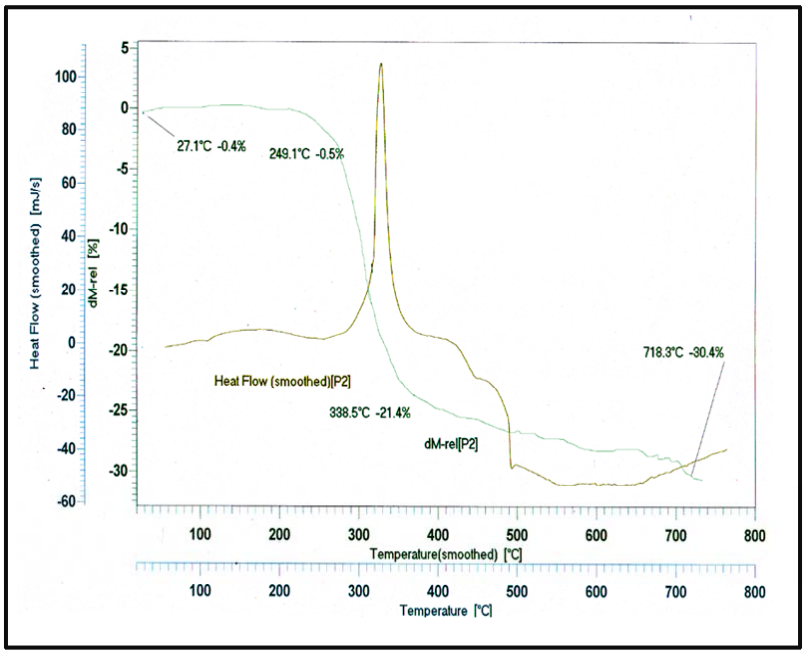
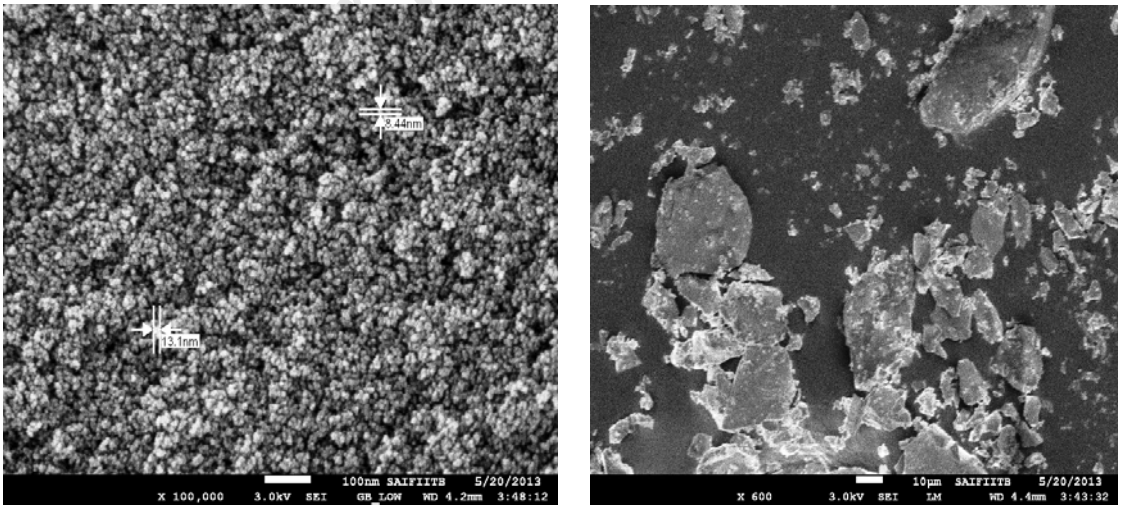
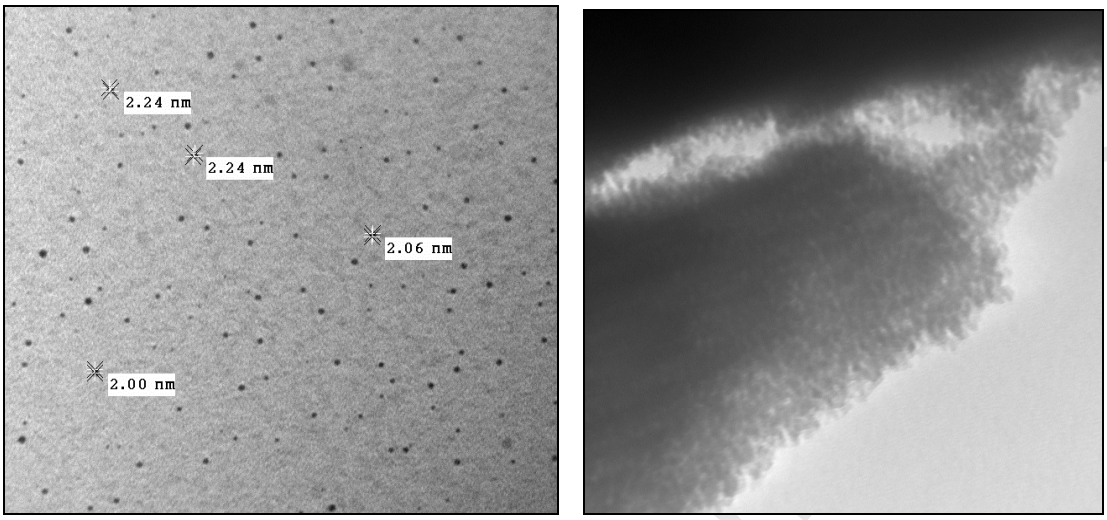


Fig. 2 TGA of SiO_2-$CuCl_2$



(a) **(b)**

Fig. 3 SEM images of SiO_2-$CuCl_2$ (a) 100, 000 X (b) 600 X



(a) An average size of 2nm **(b)** Molecular sieve formation

Fig. 4 TEM micrographs of SiO_2-$CuCl_2$

2.3 *Instrumentation*

All melting points were taken on Perfit melting point apparatus and are uncorrected. IR spectra were recorded using KBr disc on Perkin Elmer FTIR spectrophotometer. The mass spectra were recorded on Esquire 3000 Bruker Daltonics spectrometer (ESI). ^{1}H NMR spectra were recorded in DMSO-d_6 on Bruker Avance III (400 MHz) spectrometer using TMS as an internal standard. TGA was recorded on Linseis STA PT-1000 (Germany) Thermal Analyser with heating rate of 10 ^oC/ min. FTIR was recorded on Perkin Elmer-Spectrum RX-IFTIR spectrophotometer. X-ray diffractograms were recorded in 2θ range of 10-80 ^oC on a Panalytical's X'Pert Pro X-ray diffraction spectrometer using CuKα radiation.The atomic absorption spectrometric analysis (AAS) was done on Avanta-M atomic absorption spectrometric manufactured by GBC scientific agencies. SEM images were recorded on JEOL JSM-6400 Scanning Electron Microscope. TEM images were recorded on Technai G2 20 S Twin (FEI Netherland) Transmission Electron Microscope. Microwave reactions were carried out in microwave of CEM Discover of MaTHews. NC made in USA with model:

Discover System and model no.: 908010 having volts: 180/264 VAC, max. current: 6.3 A, freq: 50/60 Hz and max. power: 700 w.

2.4 *General procedure for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by SiO_2 / $CuCl_2$*

Condition A (under thermal conditions)

All starting materials were purchased from Aldrich and were used without any further purification. In a typical experiment, a mixture of aldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol), urea (0.5 mmol), diphenic acid (0.02g) were taken in a round-bottom flask (100 mL) and SiO_2/ $CuCl_2$ (0.05g) was added to it and stirred at 40^o C in solvent-free conditions for appropriate time (**Table 3**). To this reaction mixture, 25-30 ml of ethylacetate was added and heated on a water bath. This reaction mixture was filtered while hot under vacuum using a sintered glass crucible. Washings of hot water were given to remove the water soluble diphenic acid and impurities. To the resultant, anhydrous sodium sulphate was added and kept for an overnight. Then, resultant was filtered to remove hydrated sodium sulphate and the filterate was concentrated to get the crude product. The product thus obtained was purified through crystallization using ethylacetate. The reaction was monitored through TLC in 15% ethyl acetate and petroleum ether. The structures of the products were confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data and comparison with authentic samples available commercially or prepared according to the literature methods.

Condition B (under microwave conditions, temp: 80 ^{o}C, pressure: 250, power: 200, stirring: high)

In a microwave tube, aldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol), urea (0.5 mmol) and SiO_2/ $CuCl_2$ (0.05g) were taken and stirred at 80^o C in acetonitrile for appropriate time in a microwave **(Table 3)**. To this reaction mixture, 25-30 ml of ethylacetate was added and heated on a water bath. This reaction mixture was filtered while hot under vacuum using a sintered glass crucible. Washings of distilled water were given to remove the water soluble

impurities. The resultant was dried over anhydrous sodium sulphate and was filtered to remove hydrated sodium sulphate. The filterate was concentrated to get the crude product which was purified by crystallization using ethylacetate. The reaction was monitored through TLC in 15% ethyl acetate and petroleum ether. The structures of the products were confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data and comparison with authentic samples available commercially or prepared according to the literature methods.

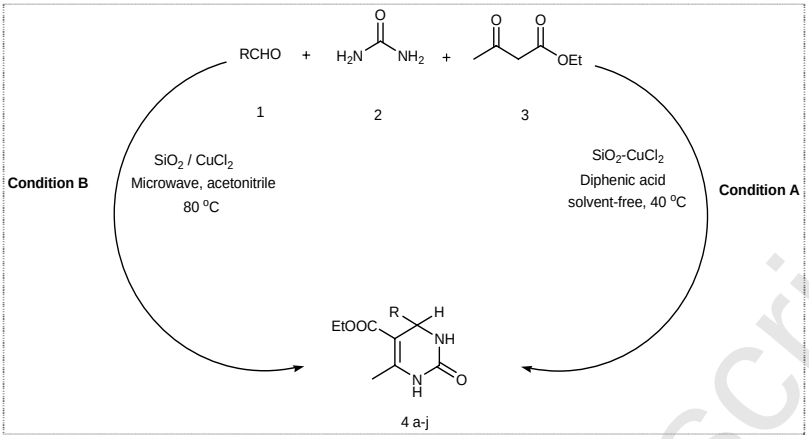
3. Results and Discussion

3.1 *Optimization*

To study the catalytic activity of silica supported copper (II) chloride, the synthesis of 3,4-dihydropyrimidin-2(1*H)*-ones *via* one-pot condensation of aldehydes, ethyl acetoacetate and urea was carried out under two set of conditions such as Condition A (Thermal): at 40 ^{o}C using 0.02 g of diphenic acid in solvent-free conditions on an oil-bath and Condition B (Microwave): without diphenic acid in acetonitrile at 80 ^{o}C. To select the appropriate conditions for the catalytic activity of SiO_2/ $CuCl_2$, benzaldehyde (0.5 mmol) was selected as the test substrate and the reaction was carried out in different conditions as shown in **Table 1** among which the studied conditions gave the best results. To test the generality of the newly developed protocol for the synthesis of 3,4-dihydropyrimidin-2(1*H)*-ones various substituted aromatic aldehydes, hetero-aromatic aldehydes and aliphatic aldehydes were taken. Aromatic aldehydes, hetero-aromatic aldehydes gave good to excellent yields **(Table 3)** but with aliphatic aldehydes the yields were very low with exception of formaldehyde as substrate which gave an exceptionally good result**.** In order to make comparative study, microwave conditions were also tried for the reaction using SiO_2/ $CuCl_2$ in acetonitrile at 40 ^{o}C but the product formed was impossible to separate from the catalyst so the reaction was carried out in acetonitrile at 80 ^{o}C in a microwave oven which gave good results in few minutes. For optimization of reaction conditions under microwave, a test reaction was carried out using

benzaldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol) and urea (0.5 mmol) using SiO_2/ $CuCl_2$ (0.05 g) in acetonitrile (2 ml) at 80 ^oC, it was found that reaction under microwave irradiation produced good results. So a series of reactions have been carried out and found that good to excellent yields were obtained. Comparative studies between solvent-free condition at 40 ^oC using diphenic acid and under microwave condition at 80 ^oC in acetonitrile without diphenic acid have been carried out as shown in (Table 2) and found that reaction under microwave irradiation are fast, clean, economic and proceeds with good to excellent yields. The structure-activity relationship has also been drawn under solvent-free conditions at 40 ^oC and in acetonitrile (microwave) at 80 ^oC and found that in case of aromatic aldehydes substituted with electron-donating groups gave 85-88% yields while aromatic aldehydes substituted with electron-withdrawing groups gave 80-95% yields and hetero-aromatic aldehydes gave 82-92% yields. In case of aliphatic aldehydes, formaldehyde gave an yield of 92%, with acetaldehyde and butanal the yields obtained were in traces. Similar methodology was applied for the synthesis of 3,4-dihydropyrimidin-2(1*H)*-thiones from aldehyde, thiourea and ethyl acetoacetate but we found multiple product formation and reaction was not completed even after prolonged reaction times under the chosen conditions.

In order to study the importance of catalyst in the studied reaction, different control experi-
-ments was run using *m*-nitrobenzaldehyde as the substrate. First, the reaction was run using only silica at 40 ^oC thermally (**entry 1**, **Table 2**) and the reaction was run for a period of 16hrs. The result obtained were in traces. Second, another experiment with only diphenic acid at 40 ^oC thermally was carried out and it was observed that reaction stops at an intermediate stage in even after 8hrs of total run (**entry 2**, **Table 2**). Third, microwave conditions were shifted to thermal (i.e. 80 ^oC, acetonitrile without diphenic acid, thermally) and an yield of 60% product was obtained in 4hrs (**entry 3**, **Table 3**) in comparison to microwave where it is 88% in 30 mins (**entry 4f**, **Table 3**).



Scheme 3: SiO_2-$CuCl_2$ catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones.

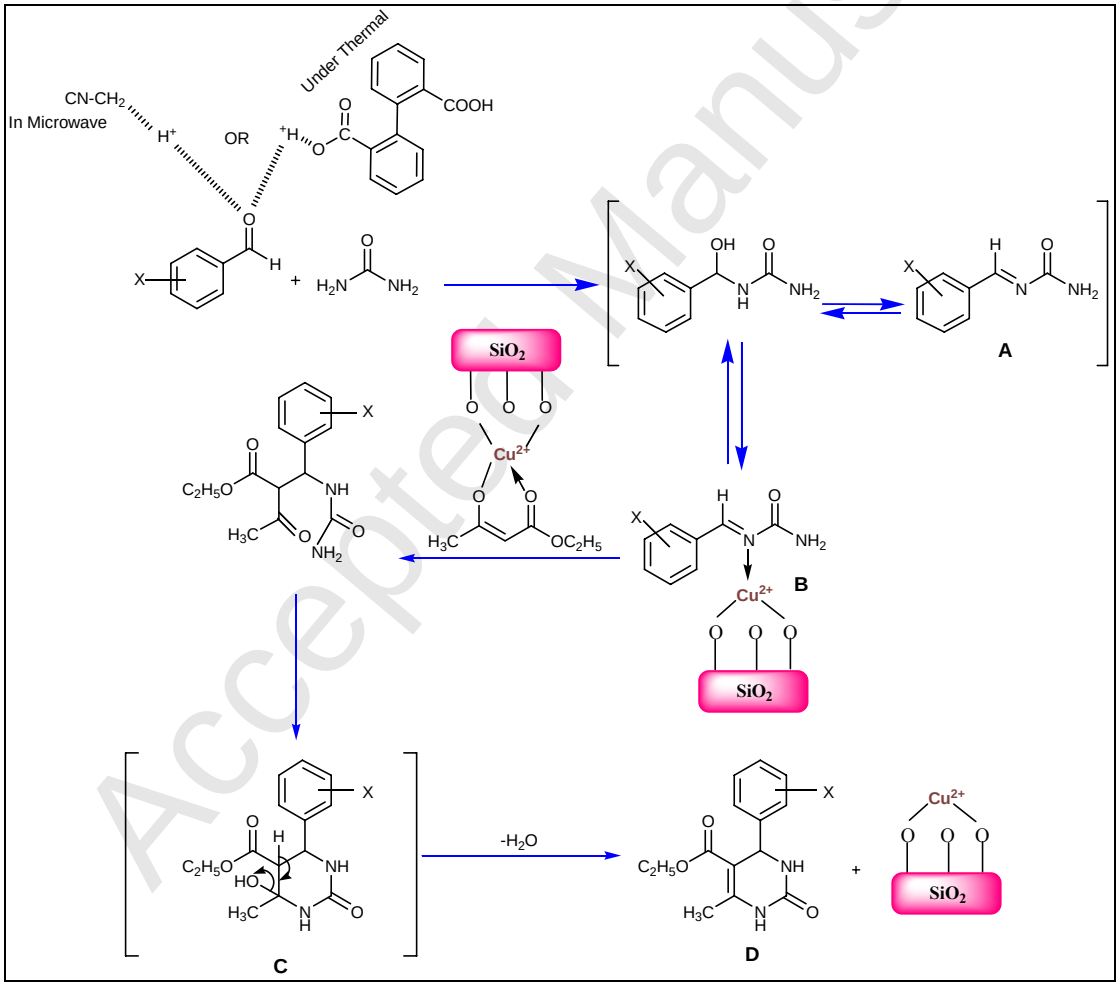
3.2 *Proposed Mechanism*

In the proposed mechanism, the initial step involves the formation of imine (A). Cu^{2+} coordinate with the nitrogen atom of imine to give an intermediate (B), which activates the C=N bond towards the nucleophilic attack. Further, complexation of *β*-ketoester with Cu^{2+} increases the nucleophilicity of *α*-carbon of enolate, facilitating the attack on imine carbon and attack of free amidic group to *β*-carbonyl carbon results in the formation of six-membered heterocyclic intermediate (C), which on dehydration gives the desired DHPMs (D) as shown in **Scheme 4**.

Role of Diphenic acid

Diphenic acid is a bronsted acid and is a weak acid which shows weak acidic nature in aqueous solution. Here, in thermal conditions, we assume the acid is needed to provide polar conditions for reaction to occur and to polarize the carbonyl group of aldehyde to make nucleophilic-electrophilic attack more fascile. For the purpose of generosity, a control experiment with only diphenic acid, *m*-nitrobenzaldehyde as substrate moiety at 40 °C thermally was run and it was found that reaction never moved ahead of intermediate stage. This intermediate has been trapped and confirmed through ^{1}H NMR and m.pt of 190 °C which

doesn't match to the product and any of reactants used. Also, the diphenic acid can be thought of acting as co-catalyst but assumption of providing polarity is connected to acetonitrile providing polar conditions in microwave and no requirement of diphenic acid. So, we propose diphenic acid to act as a source of providing polar conditions to the reaction occurring thermally at 40 °C.



Scheme 4: Proposed mechanism for the one-pot synthesis of 3,4-dihydropyrimidin-2(*1H)*-ones.

Table 1: Effect of different set of conditions for silica supported copper (II) chloride catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones using solvent-free conditions and microwave irradiation.

Entry	Reaction Conditions[a]	Amounts	Yield (%)
1	Catalyst	-	
	Diphenic acid	-	-
	(Solvent-free)	-	
2	Catalyst	0.05 g	42[b]
	Diphenic acid	-	
	(Solvent-free)	-	
3	Catalyst	0.05 g	70[b]
	Diphenic acid	0.01 g	
	(Solvent-free)	-	
4	**Catalyst**	**0.05 g**	**94[b]**
	Diphenic acid	**0.02 g**	
	(Solvent-free)	**-**	
5	Catalyst	0.01g	50[c]
	Diphenic acid	-	
	(Acetonitrile)	2 ml	
6	Catalyst	0.02 g	65[c]
	Diphenic	-	
	(Acetonitrile)	2 ml	
7	**Catalayst**	**0.05 g**	**90[c]**
	Diphenic acid	**-**	
	(Acetonitrile)	**2 ml**	

[a]**Reaction conditions:** Aldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol), urea (0.5 mmol).

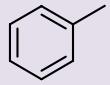
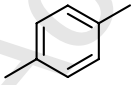
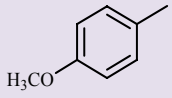
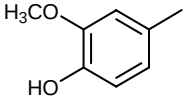
[b]**Isolated yields** under thermal condition.

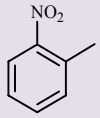
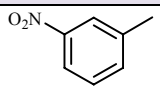
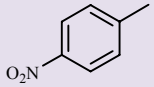
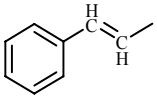
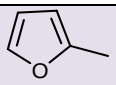
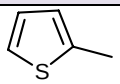
[c]**Isolated yields** under microwave condition.

Table 2:Different control experiments with *m*-nitobenzaldehyde as substrate

Entry	Control Experiments	Time (h)	Results
1	siliica	16	trace
2	Diphenic acid	8	Intermediate stage
3	MW to Thermal	4	60% yield

Table 3: Comparitive studies for the synthesis of 3, 4-Dihydropyrimidin-2-(*1H)*-ones using solvent-free condition at 40 ^{o}C (thermal) and in acetonitrile at 80 ^{o}C (microwave)

Entry	R	Thermal[a]		Microwave[b]		M.P./ Lit. M.P. (^{o}C)
		Time (h)	Yield(%)[c]	Time (min)	Yield(%)[d]	
4a		2	94	15	90	200-202/ 206-208**[16]**
4b		2.20	88	18	87	214-216/ 215-216**[15]**
4c		2.45	86	22	80	200-202/ 201-202**[16]**
4d		4.5	84	28	72	232-234/ 233-235**[21]**

4e		3.5	80	15	82	208-210/ 208-210**[16]**
4f		1.20	85	30	88	226-229/ 227-229**[16]**
4g		2	95	40	82	210-212/ 211-213**[16]**
4h		2.5	90	55	85	230-232/ 230-232**[16]**
4i		1.5	92	50	83	198-200/ 200-201**[22]**
4j		1.45	82	45	90	204-206/ 206-208**[22]**
4k	H	1.30	92	-	-	242/242-244 **[14]**
4l	CH_3	2.00	trace	-	-	
4m	*n*-Bu	6.30	trace	-	-	

[a]**Reaction conditions:** Aldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol), urea (0.5 mmol), SiO_2/ $CuCl_2$ (0.05g) and diphenic acid (0.02g) at 40° C in solvent-free conditions.

[b]**Reaction conditions:** Aldehyde (0.5 mmol), ethyl acetoacetate (0.5 mmol), urea (0.5 mmol), SiO_2/ $CuCl_2$ (0.05g) in microwave at 80 °C in acetonitrile (2 ml) without diphenic acid.

[c]**Isolated yields** refer to the yields obtained by crystallization from ethylacetate : petroleum ether under thermal condition.

[d]**Isolated yields** refer to the yields obtained by crystallization from ethylacetate : petroleum ether under microwave condition.

3.3 *Recyclability of SiO_2 / $CuCl_2$*

To test the recyclability of SiO_2/ $CuCl_2$ under thermal and microwave conditions for one-pot synthesis of 3,4-dihydropyrimidin-2(1*H)*-ones, a series of five consecutive runs in case of benzaldehyde (**entry 4a, Table 3**) were carried out and the results are represented in **(Fig. 5)**.

These results demonstrated that SiO_2/ $CuCl_2$ was recyclable upto fifth run without any significant loss of activity and after fifth run little drop in activity of catalyst was observed. To recycle the catalyst, the used catalyst is given two washings of warm ethylacetate and water each and finally the catalyst is dried under oven at 90- 100 ^oC for 3 hrs.

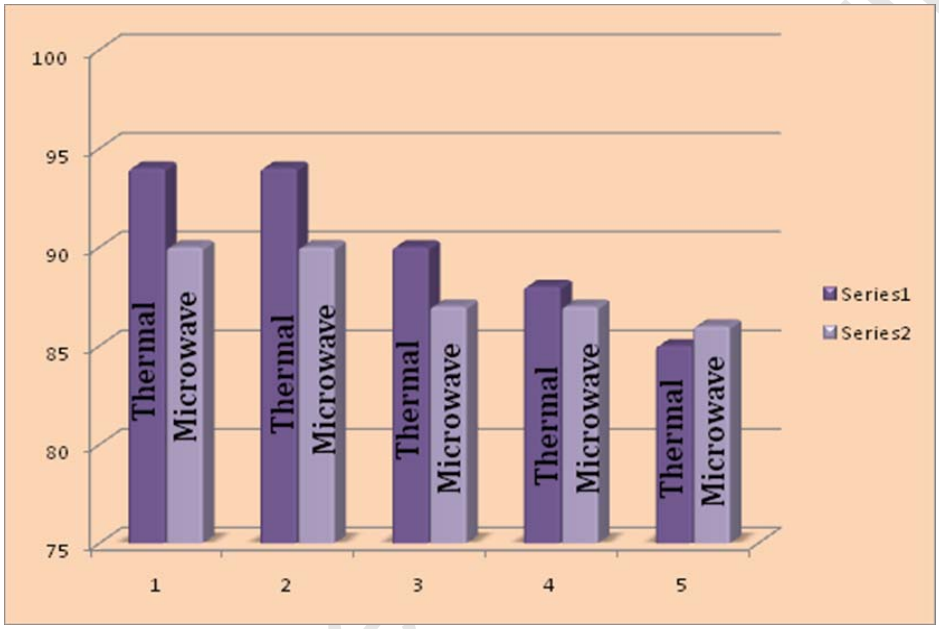


Fig. 5 Recyclability of SiO_2-$CuCl_2$ in case of benzaldehyde (**entry 4a, Table 3**) under thermal conditions and microwave conditions.

4. *XRD of 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2-(1H)-one (4f)*

X-ray intensity data of 28767 reflections were collected on *X'calibur* CCD area-detector diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å). **(Table 4)** depicted the unit cell parameters and other crystallographic details. The crystal used for data collection was of dimensions 0.30 x 0.20 x 0.20 mm. The cell dimensions were determined by least-squares methods. The data was corrected for Lorentz, polarisation and absorption factors. The structure was solved by direct methods using SHELXS97**[23]**. All non-hydrogen atoms of the molecule were located in the best E-map. During an anisotropic refinement of all

the non-hydrogen atoms, atoms C19 and C20 were found to be thermally disordered and their occupancies were refined to two equally occupied orientations here labeled (C19A and C19B) and (C20A and C20B), respectively [occupancies 0.60 (1) and 0.40 (1)]. All the hydrogen atoms (except N1 and N3 H atoms) were geometrically fixed and allowed to ride on the corresponding non-hydrogen atoms with C-H= 0.93-0.98 Å, with $U_{iso}(H) = 1.2U_{eq}(C)$, except for the methyl groups where $U_{iso}(H) = 1.5U_{eq}(C)$. Full-matrix least-squares refinement was carried out using SHELXL97. The geometry of the molecule was calculated using the PLATON**[24]** and PARST**[25]** softwares. Atomic scattering factors were taken from International Tables for X-ray Crystallography (**1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4**). The crystallographic data are summarized in **(Table 4)**. CCDC- 940361 has been given to the compound **(4f)**. **Fig. 4** shows the ORTEP diagram of **(4f)[26]** and it comprises of a pyrimidine ring and a phenyl ring **(Fig. 4)**. Bond lengths and angles of the **(4f)** are within normal ranges**[27]**. The dihedral angle between the pyrimidine and phenyl ring is 82.42 (6)^{o}. Packing view of the molecules in the unit cell viewed down the (a and b) axis is shown in **(Fig. 5)**. In the crystal, molecules are stabilized and held together by strong N-H…O and C-H…O intermolecular interactions **(Table 5)**.

Table 4: Crystal and experimental data of 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3, 4-dihydropyrimidin-2(*1H*)-one (4f)

CCDC No	940361
Crystal description	Block-shaped
Crystal colour	white
Crystal size	0.3 x 0.2 x 0.2 mm
Empirical formula	$C_{14}\ H_{15}\ N_3\ O_5$
Formula weight	305.29
Radiation, Wavelength	Mo *Kα*, 0.71073 Å

Unit cell dimensions	a =8.6831(3), b =11.8302(3), c = 13.7550(4) Å, β= 93.399(3) º
Crystal system	Monoclinic
Space group	P 21/n
Unit cell volume	1410.47(7)
No. of molecules per unit cell, Z	4
Temperature	293(2)
Absorption coefficient	0.111 mm^{-1}
F(000)	640
Scan mode	ω scan
θ range for entire data collection	3.43 <θ<26.00 º
Range of indices	h= -10 to 10, k= -14 to 14, l= -16 to 16
Reflections collected / unique	28767 / 2764
Reflections observed (I > 2σ(I))	1786
R_{int}	0.0751
R_{sigma}	0.0465
Structure determination	Direct methods
Refinement	Full-matrix least-squares on F^2
No. of parameters refined	215
Final R	0.0535
wR(F^2)	0.1203
Weight	$1/[\sigma^2(F_o^2)+(0.0499 P)^2+ 0.4217 P]$ where $P=[F_o^2 +2F_c^2] / 3$
Goodness-of-fit	1.055
$(\Delta/ \sigma)_{max}$	0.001 (for tors H16A)
Final residual electron density	- 0.277 <Δρ < 0.234 $Å^{-3}$
Measurement	*X'calibur system – Oxford diffraction make, U.K.*
Software for structure solution	SHELXS97 (Sheldrick, 2008)
Software for refinement	SHELXL97 (Sheldrick, 2008)
Software for molecular plotting	ORTEP-3 (Farrugia, 2012) PLATON (Spek, 2009)
Software for geometrical calculation	PLATON (Spek, 2009) PARST (Nardelli, 1995)

Table 5: Hydrogen–bonding geometry (e.s.d.`s in parentheses)

D–H…A	D–H(Å)	H…A(Å)	D…A(Å)	D–H…A(°)
N1-H1…O2[i]	0.93(2)	1.88(2)	2.811(3)	174(2)
C16-H16B…O2[i]	0.96	2.58	3.428(3)	148
N3-H3…O17 [ii]	0.86(3)	2.25(2)	3.051(3)	155(2)

Symmetry: (i) -x,-y+1,-z+2 (ii) -x+1/2,+y-1/2,-z+1/2+1

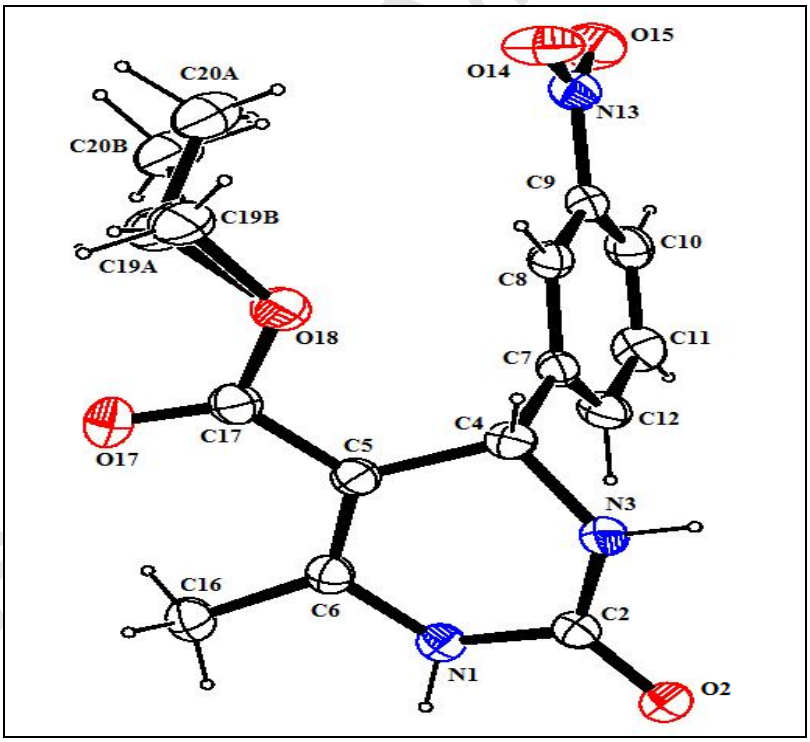
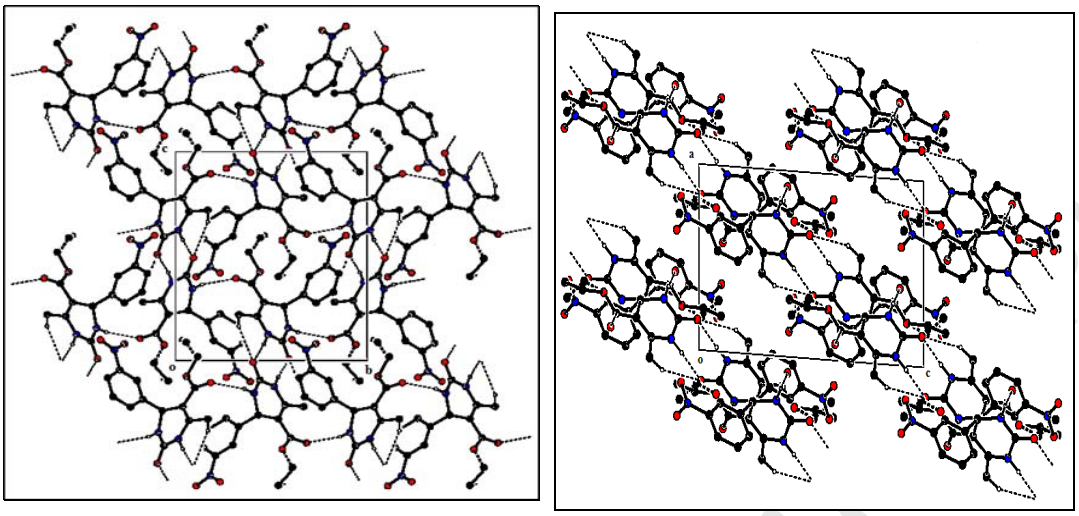


Fig. 6 ORTEP diagram representation of 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one **(4f)**



(a) **(b)**

Fig. 7 The packing arrangement of molecules **(a)** viewed down the a-axis **(b)** viewed down the b-axis

5. Conclusion

In conclusion, we have developed methodologies for one-pot synthesis of 3,4-dihydropyrimidin-2(1*H)*-ones using silica supported copper (II) chloride as solid heterogeneous catalyst under thermal and microwave conditions. The benefits of the new protocol include greener reaction conditions such as less toxicity of metal, economical nature of copper, easy work-up of reaction, less reaction times with greater yields and tolerance for various functional groups. Moreover, recyclability of catalyst using solvent-free conditions and in acetonitrile makes process economic and cost-effective that lies in the area of "**Green Chemistry**".

6. Spectral Data of 3,4-dihydropyrimidin-2(1*H*)-ones

(4a-j)

5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (4a)

IR (KBr, υ_{max} in cm^{-1}): 3243, 1726, 1649.

^{1}H-NMR (DMSO-d_6): δ 1.07 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.25 (s, 3H, -CH_3), 3.95 (q, 2H, J= 7.2Hz, -OCH_2CH_3), 5.14 (d, 1H, J= 3.2Hz, -CH), 7.23 (m, 5H, Ar-H), 7.74 (bs, 1H, -NH), 9.19 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.52, 18.22, 54.42, 59.68, 99.77, 126.70, 127.75, 128.86, 145.28, 148.79, 152.62, 165.82.

MS (ESI): 261 (M+1).

5-(Ethoxycarbonyl)-6-methyl-4-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (4b)

IR (KBr, υ_{max} in cm^{-1}): 3158, 1715, 1632.

^{1}H-NMR (DMSO-d_6): δ 1.08 (t, 3H, J= 7.1Hz, -OCH_2CH_3), 2.18 (s, 3H, -CH_3), 2.76 (s, 3H, -CH_3), 3.96 (q, 2H, J= 7.1Hz, -OCH_2CH_3), 5.09 (d, 1H, J= 2.7Hz, -CH), 7.18 (s, 4H, Ar-H), 7.82 (bs, 1H, -NH), 9.18 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.51, 18.26, 34.26, 53.65, 60.61, 101.02, 123.26, 125.65, 134.78, 148.39, 151.92, 156.42, 165.56.

MS (ESI): 275 (M+1).

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4c)

IR (KBr, υ_{max} in cm^{-1}): 3243, 1725, 1651.

^{1}H-NMR (DMSO-d_6): δ 1.08 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.24 (s, 3H, -CH_3), 3.37 (s, 3H, -OCH_3), 3.97 (q, 2H, J= 7.2Hz, -OCH_2CH_3), 5.08 (d, 1H, J= 3.2Hz, -CH), 6.86 (d, 2H, J= 8.4Hz, Ar-H), 7.13 (d, 2H, J= 8.4Hz, Ar-H), 7.67 (bs, 1H, -NH), 9.15 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.57, 18.21, 53.79, 55.52, 59.61, 100.04, 114.17, 127.85, 137.51, 148.46, 152.61, 158.91, 165.84.

MS (ESI): 291 (M+1).

5-(Ethoxycarbonyl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4d)

IR (KBr, υ_{max} in cm^{-1}): 3374, 3239, 1721, 1655.

^{1}H-NMR (DMSO-d_6): δ 1.09 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.12 (s, 3H, -CH_3), 3.42 (s, 3H, -OCH_3), 3.82 (q, 2H, 6.9Hz, -OCH_2CH_3), 5.41 (d, 1H, J= 2.8HZ, -CH), 5.68 (s, 1H, -OH) 7.62 (m, 3H, Ar-H), 7.94 (bs, 1H, -NH), 9.31 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.54, 18.21, 50.18, 56.41, 59.64, 101.02, 112.32, 117.72, 121.24, 139.18, 142.67, 146.24, 151.55, 158.69, 167.42.

MS (ESI): 307 (M+1).

5-(Ethoxycarbonyl)-4-(2-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4e)

IR (KBr, υ_{max} in cm^{-1}): 3237, 1730, 1618.

^{1}H-NMR (DMSO-d_6): δ 1.07 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.26 (s, 3H, -CH_3), 3.96 (q, 2H, J= 6.8Hz, -OCH_2CH_3), 5.27 (d, 1H, J= 3.2Hz, -CH), 7.40 (m, 4H, Ar-H), 7.90 (bs, 1H, -NH), 9.36 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.52, 18.33, 54.08, 60.03, 98.66, 124.32, 128.08, 128.13, 133.53, 138.08, 149.05, 150.17, 152.74, 165.16.

MS (ESI): 306 (M+1).

5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4f)

IR (KBr, υ_{max} in cm^{-1}): 3229, 1724, 1630.

^{1}H-NMR (DMSO-d_6): δ 1.08 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.28 (s, 3H, -CH_3), 3.96 (q, 2H, J= 7.0Hz, -OCH_2CH_3), 5.30 (d, 1H, J= 3.2Hz, -CH), 7.64 (m, 4H, Ar-H), 8.13 (bs, 1H, -NH), 9.36 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.47, 18.31, 54.00, 59.88, 98.81, 121.46, 122.84, 130.71, 133.46, 147.44, 148.20, 149.89, 152.25, 165.54.

MS (ESI): 306 (M+1).

5-(Ethoxycarbonyl)-4-(4-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4g)

IR (KBr, υ_{max} in cm^{-1}): 3235, 1740, 1631.

^{1}H-NMR (DMSO-d_6): δ 1.07 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.08 (s, 3H, -CH_3), 3.97 (q, 2H, J= 7.2Hz, -OCH_2CH_3), 5.27 (d, 1H, J= 2.28Hz, -CH), 7.49 (d, 2H, J= 9.18Hz, Ar-H), 7.90 (bs, 1H, -NH), 8.21 (d, 2H, J= 9.16Hz, Ar-H), 9.37 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.49, 18.32, 31.15, 54.11, 59.91, 98.64, 124.31, 128.13, 147.16, 149.86, 152.23, 165.54.

MS (ESI): 306 (M+1).

5-(Ethoxycarbonyl)-6-methyl-4-styryl-3,4-dihydropyrimidin-2(1*H*)-one (4h)

IR (KBr, υ_{max} in cm^{-1}): 3242, 1702, 1652.

^{1}H-NMR (DMSO-d_6): δ 1.18 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.08 (s, 3H, -CH_3), 4.09 (q, 4H, J= 7.2Hz, -OCH_2CH_3), 4.73 (d, 1H, J= 2.8Hz, -CH), 6.16 (dd,1H, J= 16Hz, 6.4Hz, -CH=C–H), 6.33 (d,1H, J= 15.6Hz, H-C=CH) 7.23 (m, 5H, Ar-H), 7.55 (bs, 1H, -NH), 9.14 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.71, 18.21, 52.33, 59.71, 98.27, 126.79, 128.06, 128.59, 129.15, 130.40, 136.69, 149.00, 153.08, 165.69.

MS (ESI): 287 (M+1).

5-(Ethoxycarbonyl)-4-(2-furfuryl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4i)

IR (KBr, υ_{max} in cm^{-1}): 3225, 1695, 1640.

^{1}H-NMR (DMSO-d_6): δ 1.12 (t, 3H, J= 7.1Hz, -OCH_2CH_3), 2.26 (s, 3H, -CH_3) 4.01 (q, 2H, J=7.1Hz, -OCH_2CH_3), 5.19 (s, 1H, -CH), 6.08 (m, 3H, Ar-CH), 7.75 (bs, 1H, -NH), 9.24 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.18, 18.25, 48.93, 59.76, 100.12, 121.14, 126.04, 131.18, 149.23, 152.16, 155.94, 165.62.

MS (ESI): 251 (M+1).

5-(Ethoxycarbonyl)-6-methyl-4-(2-thienyl)-3,4-dihydropyrimidin-2(1*H*)-one (4j)

IR (KBr, υ_{max} in cm^{-1}): 3215, 1734, 1668**.**

^{1}H-NMR (DMSO-d_6): δ 1.15 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.22 (s, 3H, -CH_3), 4.05 (q, 2H, J= 7.2Hz, -OCH_2CH_3) 5.41 (1H, s, -CH), 6.89 (m, 3H, Ar-CH), 7.91 (bs, 1H, -NH), 9.31 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.61, 18.13, 49.79, 59.85, 100.27, 123.99, 125.10, 127.15, 149.11, 149.21, 152.72, 165.51.

MS (ESI): 267 (M+1).

5-(Ethoxycarbonyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4k)

^{1}H-NMR (DMSO-d_6): δ 1.16 (t, 3H, J= 7.2Hz, -OCH_2CH_3), 2.14 (s, 3H, -CH_3), 3.88 (1H, s, -CH), 4.02 (q, 2H, J= 7.2Hz, -OCH_2CH_3), 7.02 (bs, 1H, -NH), 8.86 (bs, 1H, -NH).

^{13}C-NMR (DMSO-d_6): δ 14.73, 17.89, 59.60, 94.83, 149.20, 153.22, 165.83.

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Highlights:

- We have prepared a novel recyclable heterogeneous catalyst: SiO_2-$CuCl_2$.
- The catalyst has been fully characterized by FTIR, SEM, TEM, TGA AND AAS studies.
- 3,4-dihydropyrimidinones have been synthesized under thermal and microwave condition.
- Products of the reaction have been characterized using ^{1}HNMR, ^{13}CNMR, mass and IR.
- X-ray : 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(*1H*)-one.