Hydrotalcite: A novel and reusable solid catalyst for one-pot synthesis of 3,4-dihydropyrimidinones and mechanistic study under solvent free conditions

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ABSTRACT

Synthesis of 3,4-dihydropyrimidinones/thiones, a multicomponent synthesis using ethyl acetoacetate, substituted aromatic aldehydes, and urea/thiourea has been carried out in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcite as a reusable solid catalyst. The work has been carried out under thermal solvent-free conditions without microwave irradiations, and under microwave irradiation. In this method excellent yield of 3,4-dihydropyrimidinones/thiones is reported in shorter duration. Hydrotalcites are non-toxic, easy to separate and recyclable catalyst hence making this process environment friendly. Mechanistic study of the reaction using hydrotalcites as catalyst has been studied under thermal conditions without microwave irradiations.

1. Introduction

Dihydropyrimidinones (DHPMs) exhibit various types of pharmacological activities such as antibacterial and antifungal [1], antiviral [2], antioxidative [3], as well as anti-inflammatory [4]. In addition, being potent calcium channel modulators, they display coronary dilation and antihypertensive effects [5]. DHPMs also have been reported to be anticancer agents [6,7] and anti-HIV agent [8,9]. Recently, several synthetic procedures for the preparations of dihydropyrimidinones have been reported using different Lewis acids [10–30]. Apart from this ceric ammonium nitrate under ultrasound irradiations [31], Ziegler–Natta catalyst [32], Baker's yeast [33], Nefion-H, KSF clay with dry acetic acid under microwave irradiations [34], heteropoly acids [35], etc. have been found to be effective. Study of literature processes using Ph$_3$P, P$_2$O$_5$/SiO$_2$, P$_2$O$_5$, and silica shows that lower yield is obtained at higher temperature and long reaction duration. Zeolites have potential of recycling needs high temperature and long reaction time. Ammonium carbonate and tributyl borate has disadvantage of long reaction time and are not recyclable. Hydrotalcites (HTs) are synthetic or natural layered materials made of positively charged two-dimensional sheets of mixed

hydroxides with water and exchangeable charge-compensating anions [36]. Hydrotalcites are increasingly regarded as a good alternative to the traditional homogenous base catalysts such as NaOH and KOH for several base-catalyzed reactions that are important for the pharmaceutical and fragrance industries [37,38]. A well-documented example is the isomerization of eugenol and safrole [39]. As far as green chemistry is concerned, hydrotalcites offer several advantages over these corrosive, dissolved catalysts, easy separation from the reaction mixture, recycling possibilities, decreased corrosion of the reactor, so forth [40]. The range of applications of hydrotalcite base materials is virtually unlimited. Hydrotalcites can be involved in the preparation of catalysts dedicated to the production of H$_2$ [41], wide range of organic compounds [42], and production of biodiesel by trans-esterification of triglycerides with methanol [43]. In addition to the above numerous experimental investigations have been published on the use of hydrotalcites for catalytic applications [44]. There is a need to evaluate environmentally benign catalytic system and hydrotalcite meets the needs. It is reusable, non-toxic, does not use organic solvent and reaction is completed in 35 min. Thus it is a rapid process. The scale-up process when we used 100 mmol of ethyl acetoacetate **1**, aromatic substituted aldehyde **2** and urea/thiourea **3** in presence of 0.4 g of hydrotalcite as catalyst under solvent free conditions (Scheme 1) resulted in good yield. After the reaction the catalyst can be recycled. Thus hydrotalcites has been evaluated as a recyclable, easily separable and robust catalyst.

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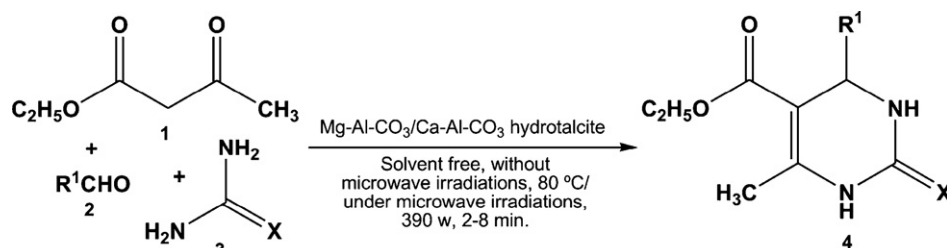
Scheme 1. Synthesis of dihydropyrimidinones. X = O, S.

2. Experimental

The ethyl acetoacetate, substituted aromatic aldehydes, urea/thiourea, and metal salts used were purchased from Himedia and Rankem. The synthesized compounds were characterized by comparing the observed spectral data and physical properties with those of authentic samples [15,18]. Melting points were determined on electrical melting point apparatus in an open capillary and were uncorrected. UV–vis spectra were recorded on Chemito Spectrascan 2600 double beam in acetonitrile, IR spectra were recorded on Schimadzu Prestize 21 spectrometer using KBr pellate, ^{1}H NMR spectra were recorded on BRUKER AVANCE II 400 NMR Spectrometer using $CDCl_3$ as an internal standard and Mass spectra were recorded on Agilent ION TRAP 6310 instrument.

2.1. Catalyst preparation

Mg–Al–CO_3 was prepared by one pot hydrothermal reaction at 175 °C for 6 h and autogenous pressure in aqueous media to obtain small and high surface area particles [44]. In a typical reaction, Mg and Al hydroxides (metallic ratio 3:1) were taken and corresponding ratio of sodium bicarbonate was added and pH was maintained at 8.5. After aging the slurry for 12 h, white precipitate was filtered, washed and dried [45].

Ca–Al–CO_3 was prepared by mixing salt solutions containing Ca^{2+} and Al^{3+} in Ca/Al molar ratio of 3:1. The solution P^H was raised to 8.0 using 25% NH_4OH. The thick white slurry was heated at 175 °C and in autogenous pressure in an autoclave. After completion the precipitate was aged for 12 h and filtered, washed with deionized water and dried [45].

2.2. Synthesis of 5-(ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one under solvent free conditions

Ethyl acetoacetate (5 mmol, 0.46 cm³), benzaldehyde (5 mmol, 0.51 cm³), urea (6 mmol, 0.36 g) and 0.02 g Mg–Al–CO_3 hydrotalcite, as catalyst were taken in a round bottom flask and contents heated on oil bath at 80 °C for about 35 min. The reaction was monitored by TLC using ethyl acetate/hexane (4:6) as eluent. After completion, the reaction mixture was cooled to room temperature. The product formed was separated by dissolving in ethanol or dichloromethane. The solid catalyst was recovered by filtration. The removal of solvent resulted in the recovery of product which was recrystallized using ethyl acetate or ethanol.

2.3. Synthesis of 5-(ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one under microwave irradiations

Ethyl acetoacetate (5 mmol, 0.46 cm³), benzaldehyde (5 mmol, 0.51 cm³), urea (6 mmol, 0.36 g) and 0.02 g hydrotalcite (Ca–Al–CO_3) as catalyst were taken in round bottom flask and irradiated in microwave oven for about 8 min. The reaction was

monitored by TLC using ethyl acetate/hexane (4:6) as eluent. After completion, the reaction mixture was cooled to room temperature. The product was dissolved using ethanol or dichloromethane. The solid catalyst was recovered by filtration. The removal of solvent gave product which was recrystallized using ethyl acetate or ethanol.

Substituted aromatic benzaldehydes having substituents viz. 4-methoxybenzaldehyde, 4-methylbenzaldehyde, 4-chlorobenzaldehyde, 4-dimethylaminobenzaldehyde, 4-nitrobenzalde-hyde, 4-hydroxybenzaldehyde and salicylaldehyde were used to synthesize various substituted dihydropyrim-idinones. Thiourea analogues were also synthesized by using benzaldehyde and 4-methoxybenzaldehyde. Similar method as reported above for urea was used to synthesize dihydropyrimidi-nones/thiones using hydrotalcites as catalyst.

3. Results

Mg:Al atomic ratio was measured using X-ray microanalysis and found 3.16, which is in good agreement with the metallic ratio (3) taken in solution. The value of x [$x = M^{III}/M^{II} + M^{III}$] was found to 0.24, which suggest the purity of hydrotalcite [46]. The PXRD patterns (Fig. 1) for hydrotalcite Mg–Al–CO_3 shows a $c/3$ value 7.76 Å. This indicates a gallery height of 2.96 Å (assuming a thickness of 4.8 Å for the cationic sheets). The material is reasonably crystalline and suggests a relatively well ordered sheet arrangement [47]. The crystalline size of this sample was found 24.87 nm as calculated using Scherrer formula [48]. Typical SEM images (Fig. 2) of Mg–Al–CO_3 hydrotalcite indicates the existence of lamellar particles which looks like rounded hexagonal shape and typical of hydrotalcites like material. The material was found mesoporous with the surface area 90 m²/g.

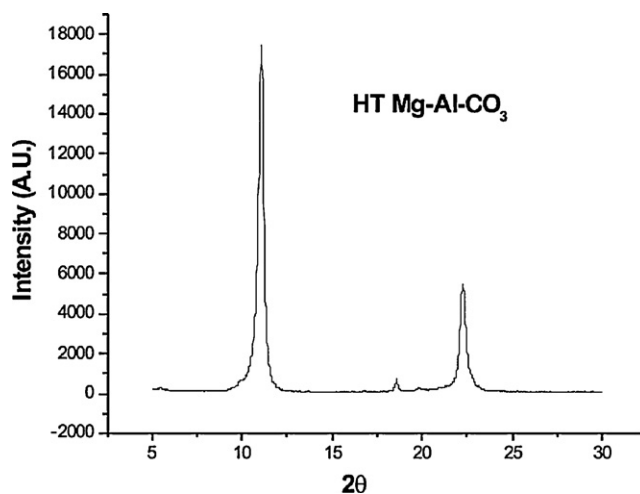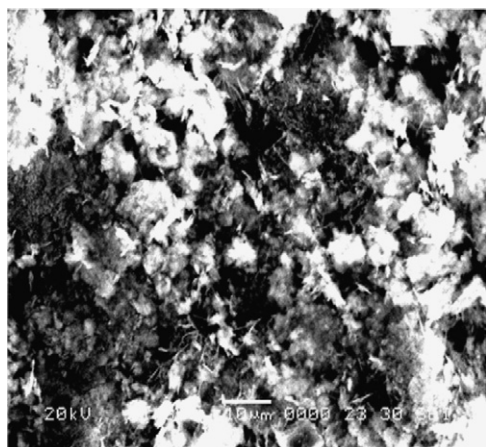**Fig. 1.** PXRD pattern of Mg–Al–CO_3 hydrotalcite.

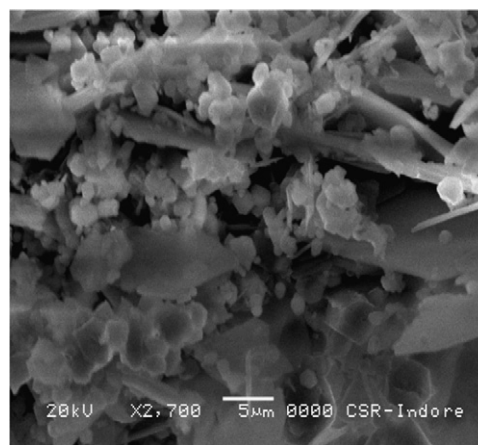**Fig. 2.** SEM-image of Mg–Al–CO₃ hydrotalcite.

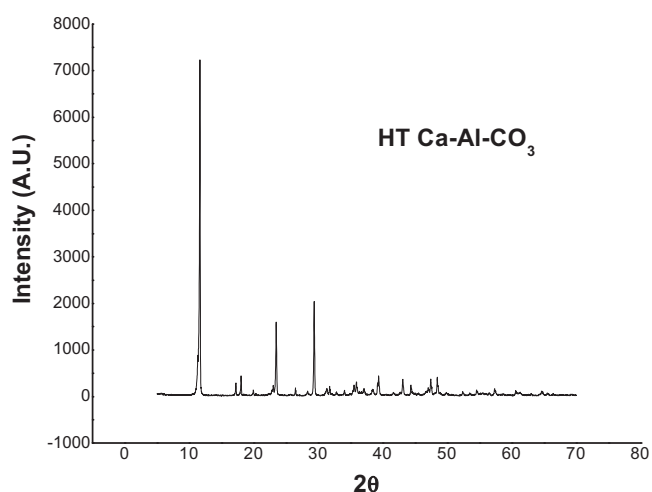
Fig. 4. SEM-image of Ca–Al–CO₃ hydrotalcite.

Fig. 3. PXRD pattern of Ca–Al–CO₃ hydrotalcite.

Metallic ratios of hydrotalcite were analyzed using EDX. The Ca:Al metal ratio was found in good agreement with the initially taken metallic ratio. The observed value for Ca–Al–CO₃ was 3.2:1. The PXRD patterns (Fig. 3) for the hydrotalcite Ca–Al–CO₃ exhibits features commonly shown by layered materials. There are narrow, symmetric, strong lines at low 2θ values and weaker, less symmetric lines, at high 2θ value [49]. Scherrer equation was used to estimate the crystalline size of the material [48]. The PXRD pattern shows a c value 22.767 Å, a value 3.83 Å and crystalline size 47.035 nm (L). The crystallographic parameter a equals the average cation–cation distance in the brucite like layers, while parameter c is three times the distance from the centre of one layers to the next and is controlled mostly by size (and orientation) of the inter layer anion and electrostatic forces operating between the inter layer anion and layers. The particles of hydrotalcite Ca–Al–CO₃ clearly exhibit the hexagonal shape (Fig. 4); however, big needle shape particles are also visible [49].

3.1. Catalytic activity

The catalytic activity of Mg–Al–CO₃ and Ca–Al–CO₃ has been explored for the synthesis of 3,4-dihydropyrimidinones/thiones under solvent free conditions and under microwave irradiations, results are incorporated in Tables 1 and 2.

The change in ethyl acetoacetate concentration shows that optimum yield is obtained when ethyl acetoacetate and benzaldehyde ratio is 1:1. An increase in ethyl acetoacetate concentration leads to decrease in yield. Similarly increase in urea concentration leads to decrease in yield. For optimization of reaction temperature reaction was carried out at different temperatures and concluded that better results were obtained at 80 °C (Table 3).

For optimization of the above reaction system, a number of sets of reaction were carried out. In the first step individual metal hydroxides (participated in the formation of Mg–Al–CO₃ and Ca–Al–CO₃ hydrotalcite) such as Mg(OH)₂, Al(OH)₃, Ca(OH)₂ and NaHCO₃ were used to catalyze the reaction and it was observed that the yield of the desired product was low (Table 4). In second

Table 1
Hydrotalcite catalyzed synthesis of 3,4-dihydropyrimidinones in solvent free conditions.[a]

Entry	R¹	X	Mp. (°C)[b]	Mg–Al–CO₃ hydrotalcite		Ca–Al–CO₃ hydrotalcite	
				Time (min)	Yield[c] (%)	Time (min)	Yield[c] (%)
1	C₆H₅	O	204–206	35	84	35	69
2	4-(CH₃O)-C₆H₄	O	202–203	30	82	45	61
3	4-(CH₃)-C₆H₄	O	216–217	60	75	60	57
4	4-(Cl)-C₆H₄	O	214–215	45	74	45	59
5	4(Nme₂)-C₆H₄	O	255–257	60	79	60	62
6	4-(NO₂)-C₆H₄	O	211–213	60	81	60	64
7	4-(OH)-C₆H₄	O	121–122	55	76	50	65
8	2-(OH)-C₆H₄	O	201–201	60	72	60	65
9	C₆H₅	S	207–208	60	78	60	62
10	4-CH₃O-C₆H₄	S	152–154	60	71	60	59

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C, solvent free thermal conditions without microwave irradiations, 30–60 min.
[b] Melting points were uncorrected.
[c] Isolated yield.

Table 2
Hydrotalcite catalyzed synthesis of 3,4-dihydropyrimidinones under microwave irradiations.[a]

Entry	R^1	X	Mp. (°C)[b]	Mg–Al–CO_3 hydrotalcite		Ca–Al–CO_3 hydrotalcite	
				Time (min)	Yield[c] (%)	Time (min)	Yield[c] (%)
1	C_6H_5	O	204–205	2	86	6	67
2	4-(CH_3O)-C_6H_4	O	201–203	6	82	8	63
3	4-(CH_3)-C_6H_4	O	216–218	8	71	6	59
4	4-(Cl)-C_6H_4	O	214–215	6	79	8	62
5	4(Nme_2)-C_6H_4	O	255–257	8	80	8	66
6	4-(NO_2)-C_6H_4	O	210–212	6	83	8	67
7	4-(OH)-C_6H_4	O	121–122	8	72	8	61
8	2-(OH)-C_6H_4	O	201–201	8	76	6	63
9	C_6H_5	S	208–209	6	78	6	66
10	4-CH_3O-C_6H_4	S	153–154	6	76	6	62

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), under microwave irradiations, 6–8 min.
[b] Melting points were uncorrected.
[c] Isolated yield.

Table 3
Effect of temperature on the yield of 3,4-dihydropyrimidin-2($1H$)-ones synthesis in solvent free conditions without microwave irradiations.[a]

Entry	Temperature (°C)	Yield[b] (%)	
		Mg–Al–CO_3 hydrotalcite	Ca–Al–CO_3 hydrotalcite
1	60	52	49
2	70	79	62
3	80	84	69
4	85	80	64
5	90	78	61
6	100	64	58

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C, solvent free thermal conditions without microwave irradiations, 35 min.
[b] Isolated yield.

Table 4
Optimization of reaction condition for the synthesis of 3,4-dihydropyrimidinones.

Entry	Catalyst	Time (min)	Basicity[d]	Yield[e] (%)
1	Mg–Al–CO_3 hydrotalcite[a]	35	0.095	84
2	Ca–Al–CO_3 hydrotalcite[a]	35	0.112	69
3	Calcined Mg–Al hydrotalcite[a]	35	0.098	69
4	Calcined Ca–Al hydrotalcite[a]	35	0.119	52
5	Rehydrated Mg–Al hydrotalcite[a]	35	0.091	82
6	Rehydrated Ca–Al hydrotalcite[a]	35	0.109	66
7	$Mg(OH)_2$ [a]	55	0.121	36
8	$Al(OH)_3$ [a]	55	0.102	52
9	$Ca(OH)_2$ [a]	45	0.101	39
10	MgO[a]	55	0.033	56
11	Al_2O_3 [a]	65	0.022	52
12	CaO[a]	55	0.007	42
13	$NaHCO_3$ [c]	300	0.120	-
14	KOH[b]	300	0.121	62
15	Alumina supported KOH[b]	300	0.199	65
16	Alumina supported NaOH[b]	300	0.188	68
17	No catalyst	300	-	10

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C solvent free thermal conditions, 35 min.
[b] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 90 °C solvent free thermal conditions, 300 min.
[c] Sticky product i.e. not easy to work up.
[d] Basicity was measured in mmol/g.
[e] Isolated yield.

step individual metal oxides such as Al_2O_3, MgO and CaO was used to catalyze the above reaction. It was observed that the yield of the desired product is low. In the third step hydrotalcites (Mg–Al–CO_3 and Ca–Al–CO_3) used in the experiment were heated at 773 K in muffle furnace for 6 h to get calcined hydrotalcites. On calcinations at a high temperature, the Lewis basicity of hydrotalcites increases, while the Brönsted basicity decreases. The Brönsted basicity is required for the reaction. It is essentially due to hydroxyl groups in

the brucite layer which are eliminated as water upon calcinations. It is reported that calcined hydrotalcites contain surface basicity due to hydroxyl groups. The catalytic activity of calcined hydrotalcites was lower than that of the corresponding uncalcined hydrotalcites. The basicity of hydrotalcite is sensitive to Mg/Al and Ca/Al ratio. The total basicity of hydrotalcites increases gradually with the Mg/Al or Ca/Al molar ratio and comes to maximum value at the Mg/Al or Ca/Al ratio of 3.0. Further increases the Mg/Al or Ca/Al molar ratio decreases the basicity. These calcined hydrotalcites were used to catalyze the above reaction and found that the yield of the desired product is low. In the last step calcined hydrotalcites were rehydrated by adding distilled water to recover hydrotalcites, dried the recovered hydrotalcites at about 200 °C for 2 h, and then used to catalyze the above reaction and concluded that there is no increment in the yield of the desired product. In another experiment alkali-treated alumina (NaOH and KOH) was also tried to catalyze the reaction and concluded that the yield of the desired product was not high as observed with hydrotalcites used in the experiment (Table 4, entries 15 and 16). The yield of the product was very poor in the absence of hydrotalcites.

3.2. Analytical data of synthesized product

5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (Table 1, entry 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.07 (t, 3H, $J = 7.2$ Hz, OCH_2CH_3), 2.24 (s, 3H, CH_3), 3.95 (q, 2H, $J = 7.1$ Hz, OCH_2CH_3), 5.23 (d, 1H, $J = 2.24$ Hz, CH), 7.23 (m, 5H, C_6H_5), 7.55 (s, 1H, NH), 8.97 (s, 1H, NH); IR (ν_{max}/cm^{-1}) 3244, 1726, 1651; λ_{max}(CH_3CN)/nm 332, 206; ESI-MS: m/z 261.1 (M+H), Anal. Calcd. for $C_{14}H_{16}N_2O_3$: 260.2914, found 260.1231; Mp.: 204–206 °C.

3.3. Basicity of the hydrotalcites

In order to check the effect of basicity of hydrotalcites catalyst on the yield of the synthesized dihydropyrimidinones, hydrotalcites with different metallic ratio of Mg–Al–CO_3 and Ca–Al–CO_3 was tried under solvent free conditions without microwave irradiations and concluded that (3:1) Mg–Al–CO_3, Ca–Al–CO_3 were more suitable hydrotalcites to catalyze the above reaction under solvent free without microwave irradiations (Table 5).

The basic strength of the hydrotalcites (Mg–Al and Ca–Al) was determined by phenol adsorption method as earlier reported [52]. In this procedure standard solutions of phenol in cyclohexane were prepared at room temperature. After plotting calibration curve, 20 ml of 100 ppm solution was taken in separate conical flasks to which 0.2 g of the HTs (Mg–Al/Cal–Al) catalyst was added and the mixture was kept in a shaker for 3 h. After equilibrium was reached, the catalyst was removed by filtration. The procedure was repeated

Table 5
Effect of basicity of hydrotalcite on yield of 3,4-dihydropyrimidinones.[a]

Entry	Type of hydrotalcite	Time (min)	Basicity[b]	Yield[c] (%)
1	(2:1) Mg–Al–CO$_3$	50	0.087	72
2	(3:1) Mg–Al–CO$_3$	35	0.095	84
3	(4:1) Mg–Al–CO$_3$	50	0.117	79
4	(2:1) Ca–Al–CO$_3$	50	0.061	64
5	(3:1) Ca–Al–CO$_3$	35	0.071	69
6	(4:1) Ca–Al–CO$_3$	50	0.079	62

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C, solvent free thermal conditions, 35 min.
[b] Basicity was measured in mmol/g.
[c] Isolated yield.

for other catalyst. The amount of phenol absorb by the catalyst was determined using following formula:

$$q_e = \frac{(C_o - C_e)V}{W}$$

where

q_e = quantity of phenol adsorb,
C_o = initial conc. of phenol,
C_e = conc. of phenol at equilibrium,
W = wt. of the catalyst (g).

3.4. Mechanistic study

In the synthesis of 3,4-dihydropyrimidinones, theoretically three routes are possible viz. Knoevenagel mechanism, iminium mechanism and enamine mechanism. In order to find out exact route for the synthesis of Biginelli type dihydropyrimidinones in presence of hydrotalcites, we carried out three sets of reactions. Firstly, ethyl acetoacetate was treated with benzaldehyde as a result of which Knoevenagel condensate was obtained which was further treated with urea under solvent free conditions in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcite catalyst, desired product was not formed. Secondly, benzaldehyde was treated with urea yielded Schiff base/iminium ion which was then treated with ethyl acetoacetate under solvent free conditions in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcite to give 3,4-dihydropyrimidinones. Finally ethyl acetoacetate was treated with urea, enamine product was formed, which was then treated with benzaldehyde in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcite, desired product was not formed. Hence, it may be concluded that the second route using iminium route is the most possible for the synthesis of 3,4-dihydropyrimidinone in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcites, which supports the iminium ion mechanism given by Kappe (Scheme 2). In the present paper, in support of reaction mechanism condensation of urea and benzaldehyde under solvent free traditional heating in presence and absence of catalyst was studied and observed that with catalyst, yield of the product is higher than in absence of catalyst because in presence of catalyst reaction goes in forward direction resulted high yield of the product whereas in absence of catalyst some amount of the benzaldehyde got oxidized into benzoic acid which was isolated and confirmed by melting point (Mp. 123 °C).

Polar surface hydroxyl groups are proposed as the active catalytic species of HTs involved in the title reaction. It is confirmed by performing the same reaction with calcined HTs (Mg–Al/Ca–Al mixed oxides) where the conversion is low.

3.5. Recyclability of catalyst

Hydrotalcites act as a solid heterogeneous catalyst; hence recyclability of the catalyst was investigated. After reaction the catalyst

Table 6
Reusability of catalyst by using Mg–Al–CO$_3$ hydrotalcite.

Entry	Reaction conditions	Reaction reuse cycles				
		I	II	III	IV	V
1	Solvent-free conditions[a]	80	80	79	78	78
2	Microwave irradiations[b]	86	85	85	84	83

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C, solvent free thermal conditions, 35 min.
[b] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), solvent free under microwave irradiations, 2 min.
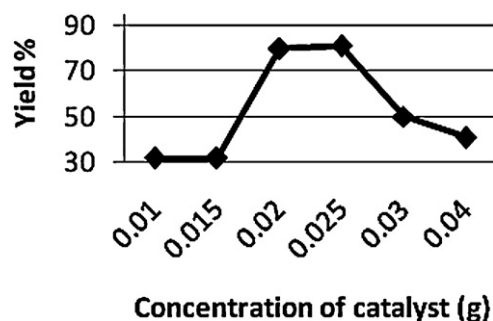

Fig. 5. Effect of catalyst concentration on product yield.

can be easily recovered, washing with distilled water and drying in a vacuum oven at about 70 °C for 4 h. The recovered catalyst can be reused for model reaction at least four additional times in subsequent reaction without significant decrease in product yields (Table 6).

4. Discussion

During the present synthesis 0.02 g hydrotalcites was used as catalyst. The effect of catalyst concentration on yield and reaction time was evaluated. The change in catalyst quantity shows that when catalyst amount was changed from 0.01 to 0.015 g there was no change in yield but when catalyst was increased to 0.02 g the yield was 84% (Fig. 5). If concentration of catalyst was doubled the yield decreased.

The catalytic activities of hydrotalcites Mg–Al–CO$_3$ and Ca–Al–CO$_3$ as reported in Tables 1 and 2 (entries 1–10) show that both hydrotalcites acts as heterogeneous catalyst. The yield obtained from Mg–Al–CO$_3$ is higher than obtained using Ca–Al–CO$_3$ in solvent free thermal conditions and under microwave irradiations. The yield using different substituted aromatic aldehydes ranges from 71 to 86%. The hydrotalcites catalyst is recyclable, which is essential for designing truly "green" synthesis protocol.

The results (Tables 1 and 2) show that substituted aromatic aldehydes containing both electron donating and electron withdrawing groups afforded high yields of the desired product with high purity this shows that electronic effects are not playing role on the yield of the synthesized product. Thiourea also gave similar results for the generation of 3,4-dihydropyrimidinones. This also suggests that replacement of oxygen by sulfur in urea has no significant effect on the yield of the synthesized product. The reaction under microwave irradiation was extremely fast and got completed in 2–8 min (Table 2). Moreover, better results were obtained as compared to reported catalysts (Table 7).

5. Conclusions

The synthesized hydrotalcites Mg–Al–CO$_3$, Ca–Al–CO$_3$ act as an efficient catalyst for the synthesis of 3,4-dihydropyrimidinones in solvent free without microwave irradiations and under microwave
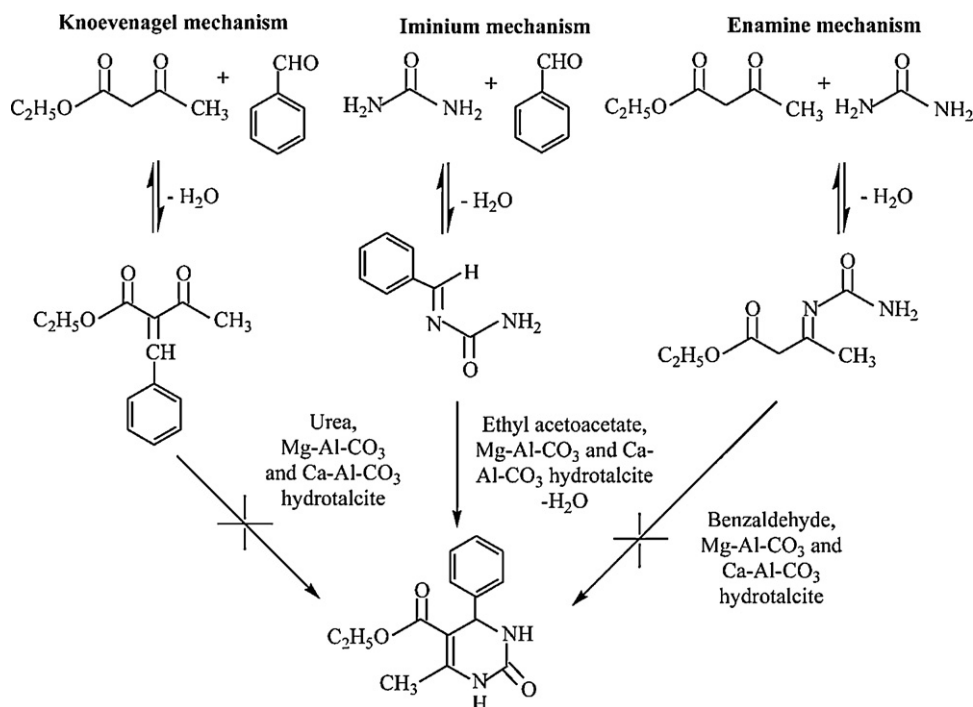
Scheme 2. Possible mechanistic route of 3,4-dihydropyrimidin-2(1H)-one synthesis in presence of Mg–Al–CO$_3$ and Ca–Al–CO$_3$ hydrotalcite.

Table 7
Comparison of the yield of the synthesis of 3,4-dihydropyrimidinones in presence of various systems.

Entry	Catalyst	Time (min)	Temperature (°C)	Yield[b] (%)	Reference
1	PPh$_3$	600	100	54	[28b]
2	(NH$_4$)$_2$CO$_3$	240	55–60	92	[28c]
3	Tributyl borate	300	RT[c]	80	[28d]
4	P$_2$O$_5$/SiO$_2$	240	85	47	[50]
5	P$_2$O$_5$	240	85	61	[50]
6	SiO$_2$	420	85	65	[50]
7	Zeolite	720	80	80	[51]
8	Natural HEU type zeolite	240	100	75	[29]
9	Mg–Al–CO$_3$ hydrotalcite[a]	35	80	84	Present work
10	Ca–Al–CO$_3$ hydrotalcite[a]	35	80	69	Present work

[a] *Reaction conditions*: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1 mmol), 80 °C, solvent free thermal conditions, 35 min.
[b] Isolated yield.
[c] Room temperature.

irradiations. In the present procedure metal hydroxides, metal oxides, alkali treated alumina, calcined hydrotalcites, rehydrated hydrotalcites was also used to catalyze the above reaction and concluded that Mg–Al–CO$_3$, Ca–Al–CO$_3$ were best to catalyze the reaction. The present procedure is fast and the yield of the product is excellent. The hydrotalcites solid catalyst may be reused without an appreciable loss of catalytic activity. This makes present method easy to work and environmentally friendly. Other catalysts used in the experiment were non-recyclable, non-environmentally friendly or not easy to work up.

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