

Rice husk SiO₂ (NPs) supported-BO₃H₃: a highly active, solvent-free and recyclable catalyst to dihydropyrimidin-2(1*H*)ones(thiones) and coumarin-3-carboxylic acid synthesis

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3,4-Dihydropyrimidin-2(1*H*)ones(thiones) (DHPM) and coumarin-3-carboxylic acid are obtained in excellent to good yield by employing green catalyst under solvent-free condition. The condensation of substituted arylaldehyde, 1,3-diketoester and urea/thiourea in the presence of green catalyst after 1 h of stirring at 50°C resulted in DHPM. The reaction of substituted *o*-hydroxybenzaldehyde with Meldrum's acid in the presence of catalyst under sonication for a few minutes gave coumarin-3-carboxylic acid. Here, we have used Lewis acid catalyst RHA-SiO₂(NPs)-BO₃H₃ derived from the agro-waste of rice husk, a heterogeneous catalyst for important organic scaffold synthesis. The reaction required low catalyst loading (1.2 mg) to achieve a target product under solvent-free condition. A series of other derivatives of heterogeneous catalysts synthesized are RHA-SiO₂, RHA-SiO₂(NPs), RHA-SiO₂-BO₃H₃. We examined their catalytic activity in the synthesis of DHPM and coumarin-3-carboxylic acid. Only the reaction catalysed by RHA-SiO₂(NPs)-BO₃H₃ gave excellent yield of the product. The final isolated pure product has been fully characterized by various spectroscopic methods and confirmed.

Keywords: Agro-waste, coumarin-3-carboxylic acid, dihydropyrimidin-2(1*H*)ones(thiones), heterogeneous catalyst, rice husk.

GREEN chemistry, a process to reduce or eliminate the use of hazardous solvents or catalysts for the generation of active ingredients of chemical products, is applicable to all branches of chemistry¹⁻³. Green chemistry is actively seeking ways to make products considering the safety of the environment and human health². The use of organic solvents is undesirable in green chemistry, since they are one of the major sources of emission of hazardous

volatile organic compounds³. In green chemistry, the solvent should not be toxic⁴, flammable or hazardous or corrosive, and it should not harm the environment⁵. Hence, the need for solvent-free and recyclable catalysts has encouraged both the fine chemicals and pharmaceutical industries to search for alternative methods⁶. Recently, the development of reusable catalyst in the chemical industry to synthesize fine chemicals and bioactive molecules has become a major scope for the production of bulk quantities to meet the demands⁷. The majority of these novel heterogeneous catalysts are derived from the family of silicates⁸, since silica displays many favourable properties, such as excellent stability (chemical and thermal)^{9,10}, high surface area¹¹, good accessibility, and surface modification to provide catalytic centres¹¹. The silicon atoms are tetrahedrally coordinated and the system has neutral charge with high surface area of silica (Figure 1 *a*). In silica nanoparticles (NPs), the terminal surface with silanol group (Figure 1 *b*) hydrogen positive charge density is very small and it can be considered as a very weak Bronsted acid site^{12,13}. In this case, the tetrahedrally coordinated boron generates a strong O-H polarization when a substitution of boron by silica occurs (Figure 1 *c*)¹³. These Bronsted acid sites are clearly stronger than the silanol group and we believe that they exist in well-prepared structured silica borate¹⁴. The literature survey revealed that silica-based catalyst shows diversified applications in the modern chemical synthetic procedure¹⁵. So here we explore the agriculture feedstock waste rice husk as a silica source, and its surface modification

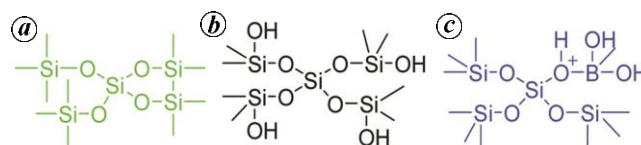


Figure 1. Structure of silicate variants.

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by other reagents that gave strong Lewis acid property was employed for the Biginelli reaction^{16,17}. The extensive use of silica nanoparticles (SNPs) and their composites in various chemical industries has resulted in the derived from natural waste products^{18,19}. Rice husk is an agricultural waste material with 90–94% silica²⁰. Rice husks are abundantly available in all rice-producing countries, and the annual production amounts to 80 million tonnes²¹. It is reported that for every tonne of rice produced, nearly 0.23 tonne of husk is formed as an agricultural waste. The major rice-producing countries are India, China, Malaysia, Egypt and Nepal²². The utility of rice husk is less explored. Presently, it is used in fuel extraction in small portions²³. A major amount is burnt, leading to the emission of choking smoke, which causes the black cloud phenomenon and affects human health and global climate by emitting particulate matter and other gaseous pollutants²⁴. Hence, its efficient utilization is necessary to prevent environment pollution²⁵. Here, we explore agro-waste-derived silica as a source for the development of inexpensive and reusable modified heterogeneous catalyst for the synthesis of important bioactive molecules.

3,4-Dihydropyrimidin-2(1*H*)ones/(thiones) (DHPM)

The natural product with specific scaffold plays important role in biological functions²⁶. To fulfil the bulk requirement, synthetic methods are developed to synthesize natural products as well as their mimetics. Although a variety of methods have been reported to synthesize heterocyclic compounds with different core structures^{27,28}, poly-substituted and poly-functionalized heterocyclic derivative synthesis remains a challenge to the scientific community²⁹. The sequences are widespread, but preparation of some of the substitution patterns and functional groups is a difficult challenge till date²⁹. The synthetic variables that have to be optimized are time, cost, overall yield, and simple reaction set-up, safety and environmental acceptability³⁰. Thus, multicomponent reactions (MCRs) are one-pot reaction procedures, which are easier to perform in a single step to isolate the product, compared to multi-step synthesis³¹. Thus MCR strategy is a highly desirable approach in drug discovery for the generation of several scaffold products³². The importance of the multi-component reactions in the early stage was contributed by eminent scientists such as Passerini³³, Strecker³⁴, Hantzsch's³⁵, Biginelli³⁶, Robinson³⁷, and more MCRs reported in the literature³⁸. In 1893, the Italian chemist Pietro Biginelli discovered MCRs that allow the synthesis of dihydropyrimidin-2(1*H*)ones(thiones) (DHPM)³⁹. For this, he carried out a one-pot, three-component reaction through cyclocondensation reaction of 1,3-dicarbonyl compounds, aldehyde and urea/thiourea in the presence of a catalytic amount of mineral acid HCl in ethanol solvent. Many Biginelli products have demon-

strated applications in biological systems⁴⁰, because they closely resemble the chemically used nifedipine (Figure 2 *a*), nitedipine (Figure 2 *b*) and felodipine (Figure 2 *c*) scaffold structures⁴¹. Other marine natural alkaloids and batzelladine B also resemble the Biginelli product scaffold⁴². Furthermore, the modified Biginelli products showed antiproliferative⁴³, antiviral, antifungal and antitubercular activities^{44,45}. Overwhelming demand for the Biginelli products, resulted in challenges for the chemists to develop a simple and efficient synthetic method for their synthesis⁴⁶. To overcome the limitations of harsh condition, long reaction time and low yield of the original Biginelli reaction method, several faster synthetic methodologies such as microwave irradiation⁴⁷, ultrasound irradiation⁴⁸, ionic liquids^{49–51} and different types of acidic⁵², basic⁵³, metal oxide⁵⁴, NP⁵⁵ and enzyme catalyst⁵⁶ methods have been reported. The chemical reagent catalysed Biginelli reactions include bio-waste⁵⁷, inorganic^{58–82}, organic^{83–85} and many more catalysts are reported in the literature. In spite of the vast number of reported methods available, one-pot synthesis suffers from drawbacks such as the use of expensive catalyst⁸⁶, strong acidic condition⁸⁷, organic solvent and long reaction time⁸⁸. Therefore, to overcome some of these limitations, a milder reaction condition, eco-friendly and solvent-free protocol is required. In recent times, ionic liquids-assisted Biginelli reactions are demonstrated to be an environmentally acceptable protocol, and a more advantageous method. Aiming to develop greener and inexpensive protocol, we have demonstrated the synthesis of DHPM employing agro-waste-derived silica functionalized boric acid as a heterogeneous catalyst under solvent-free condition.

Coumarin-3-carboxylic acid

Coumarins are well-known naturally occurring oxygen-heterocyclic compounds isolated from various plants as

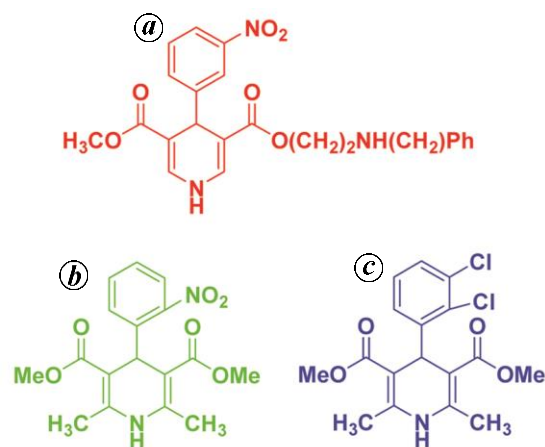


Figure 2. Structure of (a) nifedipine, (b) nitedipine and (c) felodipine.

well as using synthetic methods⁸⁹. The potential pharmacological activities of coumarin and its derivatives, including antifungal⁹⁰, antioxidant⁹¹, anticancer⁹², antibacterial⁹³, analgesic⁹³, anti-inflammatory⁹⁴, antibiotic, antitumour and more inhibiting activities have been reported⁹⁵. Coumarin derivatives are also extensively employed in agrochemicals, insecticides, perfumes, fragrances and additives in cosmetics and food⁹⁶. As a result, coumarins are important scaffolds for chemists to explore various synthetic strategies. Among different methods available, Knoevenagel condensation is widely employed for the synthesis of coumarin-3-carboxylic acid from the reaction of substituted salicylaldehyde with cyanoacetates or malonates in the presence of a catalyst such as ammonium acetate^{97,98}, piperdinium acetate and piperidine⁹⁸. At present, Meldrums' acid is preferred for the Knoevenagel condensation because of advantages in terms of yield, reaction time and isolation of final products. There are several catalysts reported in the literature for the condensation of salicylaldehyde and Meldrum's acid like SnCl₂ (ref. 99), FeCl₃ (ref. 97), Clay¹⁰⁰, ammonium acetate⁹⁸, potassium dihydrogen phosphate¹⁰¹ and potassium phosphate¹⁰², Yb(OTf)₃ (ref. 103) and silica sulphuric acid¹⁰⁴. In spite of some merits of these protocols, the demerits include low yield, harsh reaction condition, tedious work-up, side reactions, use of toxic organic solvents, and expensive catalysts, and requirement of final product purification. Thus, there is need for novel methodologies, which provide greener catalyst for the synthesis of pharmacologically potent coumarin-3-carboxylic acids¹⁰⁵.

As far as green chemistry practice is concerned, the reactions are performed under solvent-free or water condition¹⁰⁶. Alternatively, the catalyst derived from natural agro-waste can be used to explore novel inexpensive catalysts^{107,108}. In continuation of our efforts to explore greener synthetic methods and demonstration of organic transformations, we have recently reported one-pot mechanochemical coumarin-3-carboxylic acid synthesis in the presence of WEPBA¹⁰⁵. In the present study, we consider another agro-waste (rice husk)-derived silica as solid support and its surface-modified boric acid demonstrates synthesis of DHPM and coumarin-3-carboxylic acid under solvent-free and recyclable catalyst. The method is not only cost-effective and environmentally benign, but also experimentally simple, easy to work-up, reusable, eliminates the use of toxic organic solvents and gives the final product in good to excellent yields.

Results and discussion

Rice husk is an agricultural waste with high amorphous silica content. Several silica extraction procedures from rice husk have been reported in the literature. We have employed an environment-friendly method under con-

trolled calcination condition in an electric muffle furnace at 700°C (Figure 3).

The resulting white ash product was subjected to ²⁹Si magic angle spinning-nuclear magnetic resonance, X-ray diffraction (XRD) (Supplementary Figure 4), energy dispersive X-ray and Fourier transform infrared spectroscopy, elementary analysis by EDX (Supplementary Figure 2), and also compared with commercially available column and TLC silica. The scanning electron microscope image of RHA-SiO₂ showed uniform surface morphology (Supplementary Figure 1), and RHA-SiO₂(NPs)-BO₃H₃ showed roughening of the surface because of the BO₃H₃ on RHA-SiO₂(NPs) (Supplementary Figure 3). The particle size of the catalyst was observed to be 164.7 nm. Comparison of FT-IR spectra of other silica sources and RHA-SiO₂(NPs)-BO₃H₃ showed strong absorption of -OH group at 3550–3200 cm⁻¹. The XRD pattern also revealed that, both RHA-SiO₂ and RHA-SiO₂(NPs) are amorphous in nature (Supplementary Figures 4 and 5). The ²⁹Si NMR and XRD data revealed that silica derived from RHA is similar to commercial silica (Figure 4). Further to create more active surface area on the silica derived from RHA for better catalytic activity, we adopted the procedure of Farshid *et al.*^{67,68} to synthesize silica NPs. First, we examined the catalytic activity of RHA-SiO₂ alone in the model reaction benzaldehyde **1** (1 mmol), ethylacetoacetate **2** (1 mmol) and urea **3** (1 mmol) or thiourea (1 mmol) under thermal stirring condition at 50°C (Scheme 1 and Table 1), and observed incomplete reaction with low yield product isolation. To improve the catalytic activity of RHA-SiO₂, we synthesized RHA-SiO₂(NPs) and examined its catalytic activity in a model reaction and found improvement of the product isolation, as expected for the NP activity (Table 1). Further, we extended to synthesize RHA-SiO₂-supported BO₃H₃ as a strong Lewis acid heterogeneous catalyst and succeeded in the preparation of both RHA-SiO₂-BO₃H₃

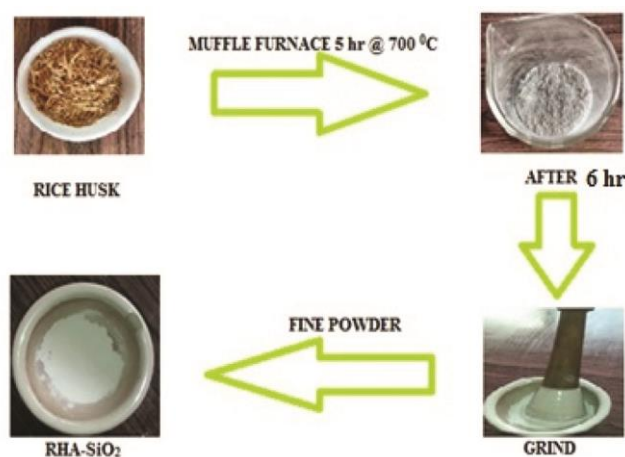


Figure 3. Synthesis of SiO₂ from rice husk.

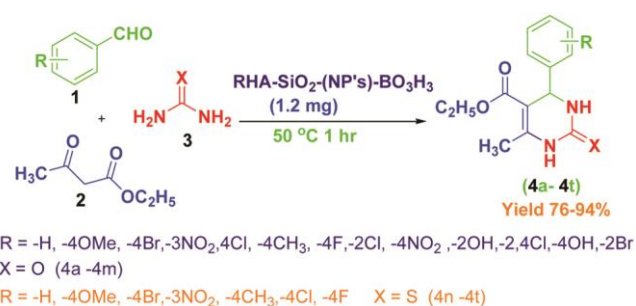
and RHA-SiO₂(NPs)-BO₃H₃. The resulting heterogeneous catalysts were examined for their activity in a model reaction under thermal stirring condition (Table 1). Surprisingly, we found that the reaction catalysed by RHA-SiO₂(NPs)-BO₃H₃ gave the excellent product isolation with clean reaction compared to any of the other RHA-SiO₂-derived catalysts (Table 1). To better optimize the reaction method catalysed by RHA-SiO₂(NPs)-BO₃H₃, we examined the synthesis of DHPM using one-pot condensation of substituted aryl aldehyde, ethylacetoacetate and urea or thiourea under three different reaction conditions, viz. (i) grinding; (ii) microwave irradiation at 300 W and (iii) thermal stirring at 50°C for 1 h under solvent-free condition (Table 2). No product was obtained for the aliphatic aldehydes like formaldehyde and acetaldehyde. The above three comparative method studies revealed that thermal method @ 50°C in 1 h stirring method found clean reaction with good to excellent target production isolation (Table 2). Extension of the same reaction condition for the synthesis of DHPM from substituted arylaldehyde, ethylacetoacetate and thiourea showed similar isolation of the product in excellent yield (Table 3). All isolated final products were examined for purity and homogeneity using various spectroscopic methods. To check the substituted electronic factor compatibility of the present method, we performed reactions with electron-withdrawing group substituted on aromatic aldehyde that gave 81–83% yield, and electron-donating group on aromatic aldehyde that gave 83–89% yield (Table 3).

We also examined this method for aliphatic aldehydes such as formaldehyde that gave 42% and acetaldehyde which gave trace amount of product isolation. In the case of aliphatic aldehyde, formaldehyde gave a yield of 42% and acetaldehyde gave products trace amounts. In order to study the minimal amount of heterogeneous catalyst RHA-SiO₂(NPs)-BO₃H₃ required for the 1 mmol reactions, reactions using different amounts of catalyst were carried. Initially the reaction started with 0.2 mg of RHA-SiO₂ (NPs)-BO₃H₃ @ 50°C while stirring (Table 4) and it continued for a period of 1 h. The isolated product was found in trace amount. The amount of catalyst in the second and successive experiment reactions was increased by 0.2 mg interval in each reaction up to 2.2 mg in a model reaction. In all these experiments product isolation increased with increase in the amount of catalyst up to 1.2 mg. The optimized amount of catalyst required for the 1 m mol scale in a model reaction was 1.2 mg, which gave Biginelli product isolation in good to excellent yield. Further increase in the amount of catalyst up to 2.2 mg showed no change in product yield (Table 3). So a series of 0.2 mg interval increase in catalyst in a model reaction was carried out and it was found that 1.2 mg of RHA-SiO₂(NPs)-BO₃H₃ gave isolation of product in excellent yield.

To test the recyclability of RHA-SiO₂(NPs)-BO₃H₃ catalyst for one-pot synthesis of DHPM, a series of five consecutive runs in a model reaction were carried out (Table 4). Figure 5 shows the isolated product in each cycle. The results demonstrated that, RHA-SiO₂(NPs)-BO₃H₃ was recyclable up to the fourth run without much significant loss of catalytic activity, and after the fifth run there was a decrease in catalytic activity. To recycle the catalyst, the first-cycle catalyst after reaction was treated with two times methanol and water wash, and finally dried in an oven @ 100°C for 3 h and used for the next cycle reaction.

The plausible mechanism for the formation of product dihydropyrimidine through agro-waste derived silica functionlized-boric acid is presented in Scheme 2. The mechanism clearly revealed that, the formation of a complex of 1,3-diketone with the catalyst followed by substitution of active methylene aldehyde-urea adduct leads to cyclization.

Further we also compared the agro-waste-derived catalyst with those reported in the literature for the synthesis of DHPM (Table 5). The literature reported methods have



Scheme 1. General reaction of dihydropyrimidin-2(1H)ones(thiones) synthesis.

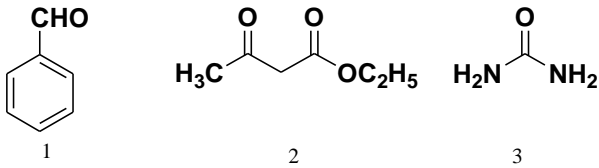
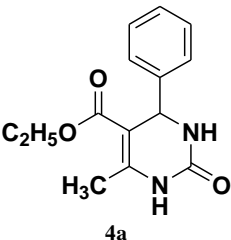
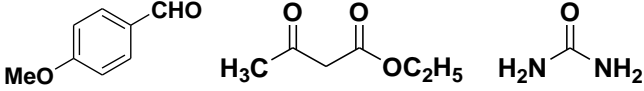
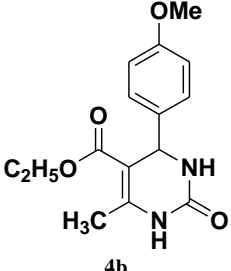
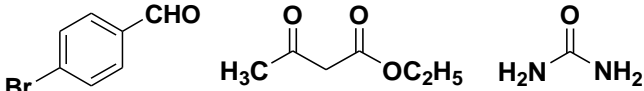
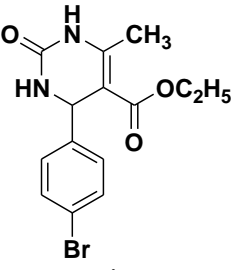
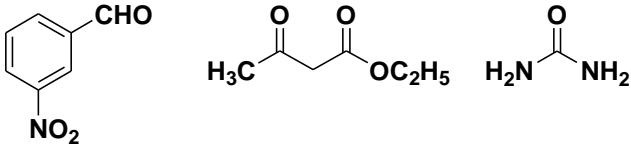
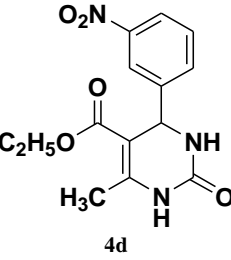
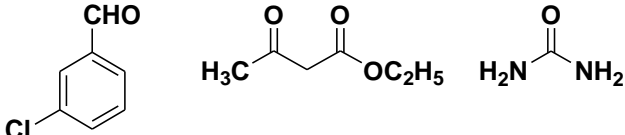
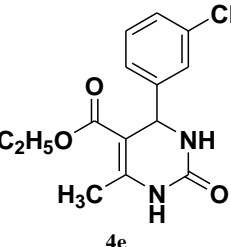
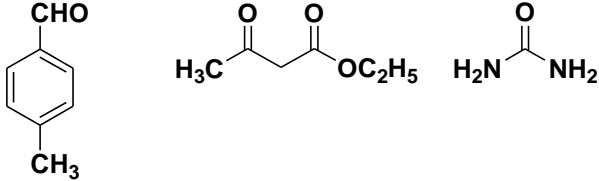
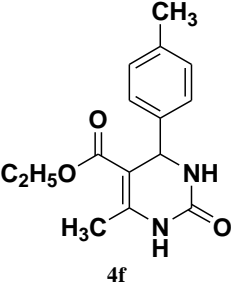
Table 1. Comparison of different RHA-SiO₂-derived catalysts for the synthesis of dihydropyrimidin-2(1H)ones (thiones)

Catalyst	Yield (%)
RHA-SiO ₂	60
RHA-SiO ₂ (NPs)	70
RHA-SiO ₂ -BO ₃ H ₃	79
RHA-SiO ₂ (NPs)-BO ₃ H ₃	94

Table 2. Different method experiment catalysed by RHA-SiO₂(NPs)-BO₃H₃

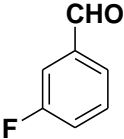
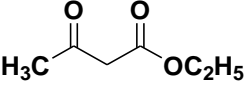
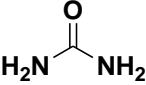
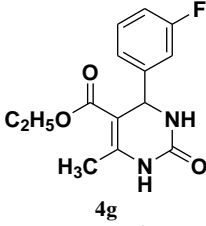
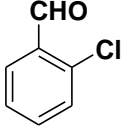
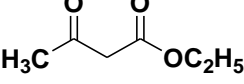
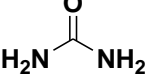
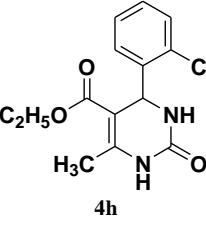
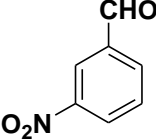
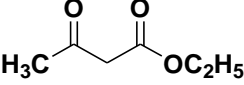
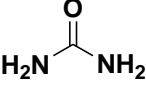
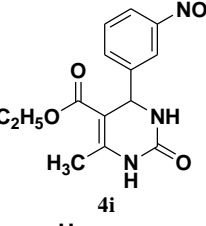
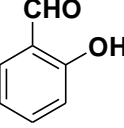
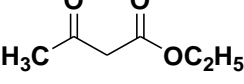
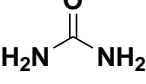
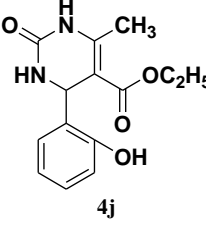
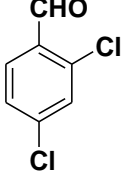
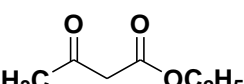
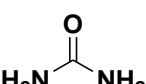
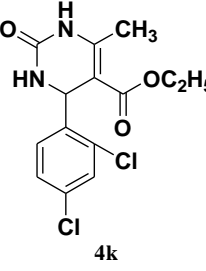
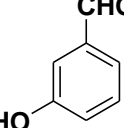
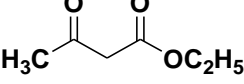
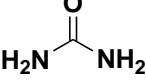
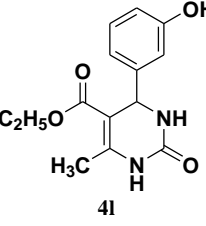
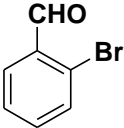
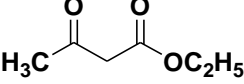
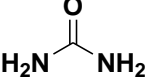
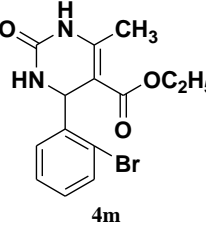
Method	Time (h)	Yield (%)
Grinding	1	Nil
Microwave	1	43
Thermal stirring	1	94

Table 3. Structure of Biginelli products and reactants with physical data

Entry	Reactant	Product	Yield (%)	Melting point (°C)
1	 <p>1</p> <p>2</p> <p>3</p>	 <p>4a</p>	92	202–204
2	 <p>1</p> <p>2</p> <p>3</p>	 <p>4b</p>	83	204–206
3	 <p>1</p> <p>2</p> <p>3</p>	 <p>4c</p>	85	–
4	 <p>1</p> <p>2</p> <p>3</p>	 <p>4d</p>	81	225–227
5	 <p>1</p> <p>2</p> <p>3</p>	 <p>4e</p>	83	212–214
6	 <p>1</p> <p>2</p> <p>3</p>	 <p>4f</p>	85	210–212

(Contd)

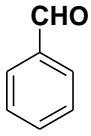
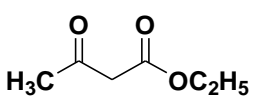
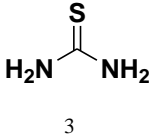
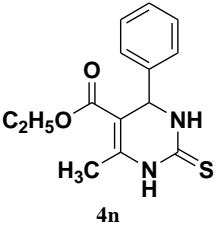
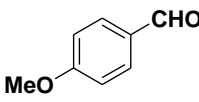
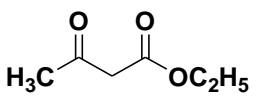
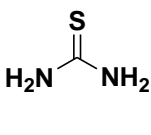
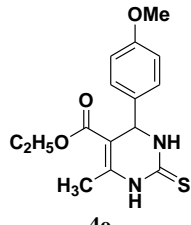
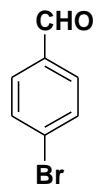
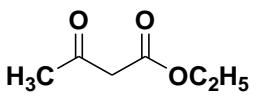
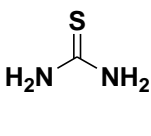
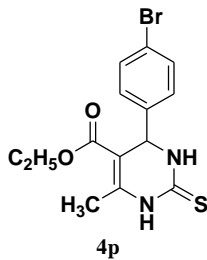
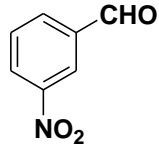
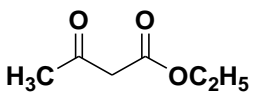
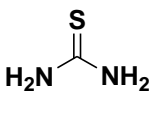
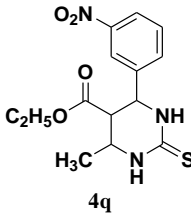
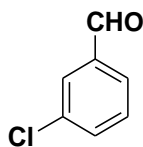
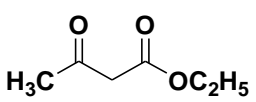
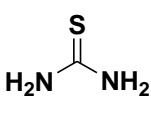
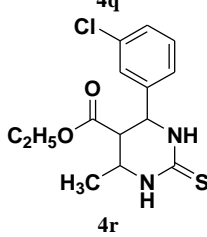
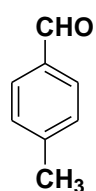
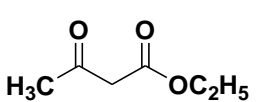
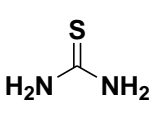
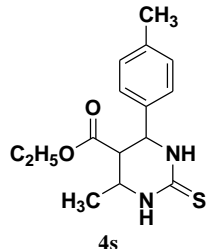
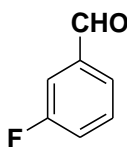
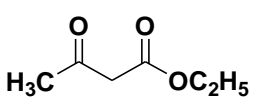
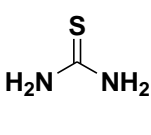
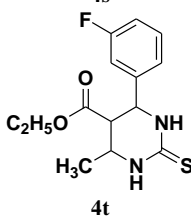
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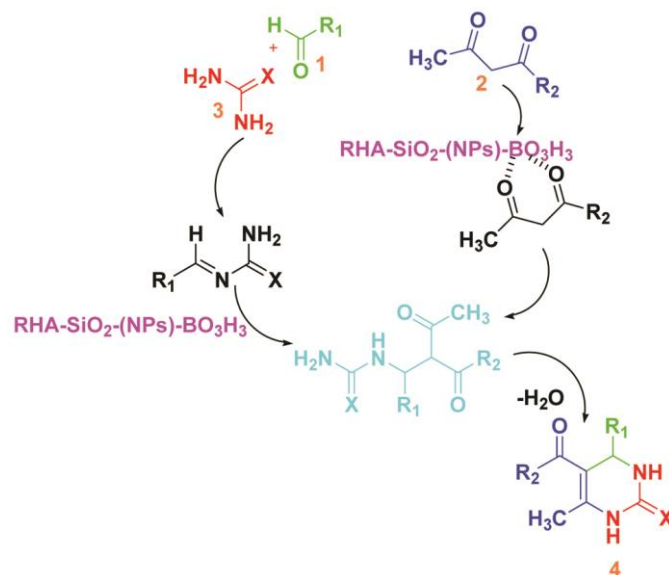
Entry	Reactant	Product	Yield (%)	Melting point (°C)		
7	 <chem>O=Cc1ccc(F)cc1</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)C1=CC=C(F)C=C1</chem> 4g	89	183–185
8	 <chem>O=Cc1ccccc1Cl</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1cc(Cl)cccc1</chem> 4h	92	215–217
9	 <chem>O=Cc1ccc([N+](=O)[O-])cc1</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1ccc([N+](=O)[O-])cc1</chem> 4i	87	208–210
10	 <chem>O=Cc1ccccc1O</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1cc(O)cccc1</chem> 4j	79	202–204
11	 <chem>O=Cc1cc(Cl)cc(Cl)c1</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1cc(Cl)c(Cl)cc1</chem> 4k	83	250–252
12	 <chem>O=Cc1ccc(O)cc1</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1ccc(O)cc1</chem> 4l	84	230–232
13	 <chem>O=Cc1ccccc1Br</chem>	 <chem>CC(=O)CC(=O)OCC</chem>	 <chem>NC(=O)N</chem>	 <chem>CC(=O)N(C(=O)OCC)C(=O)c1cc(Br)cccc1</chem> 4m	–	–

(Contd)

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Table 3. (Contd)

Entry	Reactant	Product	Yield (%)	Melting point (°C)	
14		 		85	206–208
15		 		84	192–194
16		 		81	–
17		 		78	210–212
18		 		79	180–182
19		 		80	–
20		 		87	214–218



Scheme 2. Plausible mechanism of RHA-SiO₂(NPs)-BO₃H₃-catalysed Biginelli reaction⁶⁰.

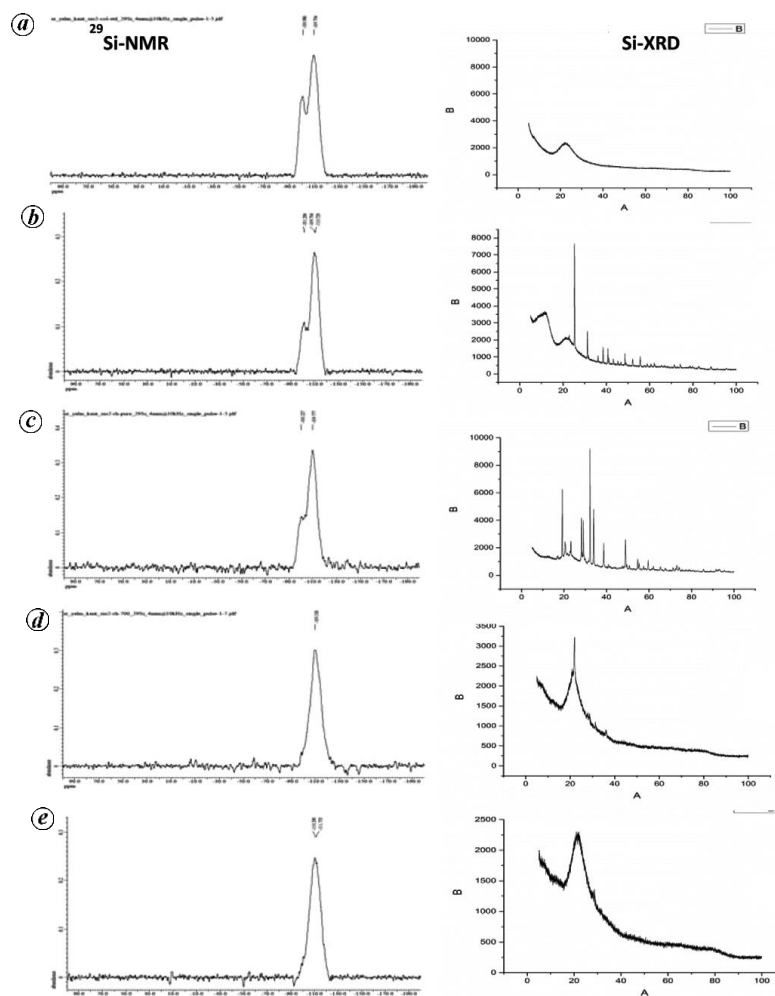


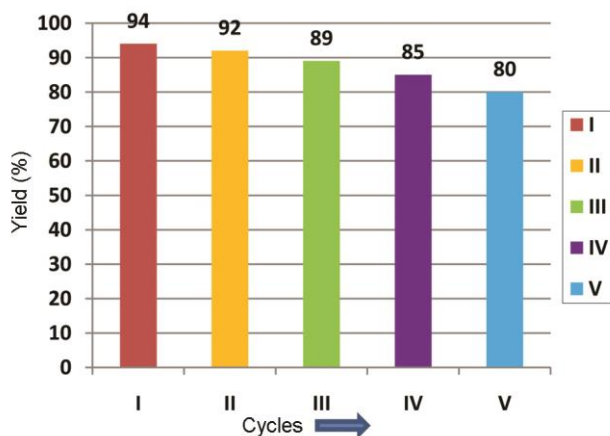
Figure 4. ²⁹Si-NMR and XRD data of different forms of silica. *a*, ²⁹Si-NMR and XRD of column silica commercial; *b*, ²⁹Si-NMR and XRD of TLC silica commercial; *c*, ²⁹Si-NMR XRD of pure silica from RHA; *d*, ²⁹Si-NMR and XRD of RHA-SiO₂ in the absence of air at 700°C in a muffle furnace; *e*, ²⁹Si-NMR and XRD of RHA-SiO₂ in an electrical furnace.

Table 4. Optimization of RHA-SiO₂(NPs)-BO₃H₃ required for the reaction

Catalyst	Amount (mg)	Time (h)	Yield (%)
RHA-SiO ₂ (NPs)-BO ₃ H ₃	0.2	1	-
	0.4	1	10
	0.6	1	29
	0.8	1	55
	1.0	1	89
	1.2	1	94
	1.4	1	94
	1.8	1	94
	2.0	1	94
	2.2	1	94

Table 5. Comparison of the present method with others available in the literature

Catalyst and quantity	Time (h)	Yield (%)	Reference
SbCl ₃ /20 mol%	20	77	55
H ₂ SO ₄ /0.5 mol%	12	55	55
Nafion-H/100 wt%	10	70	55
HOCl ₃ /15 mol%	2-3	85	56
Aq. Zn(BF ₄) ₂ /0.6 mol%	3-7	80	59
Ca(NO ₃) ₂ ·4H ₂ O/10 mol%	2-18	42-82	60
InCl ₃ /10 mol%	6-9	95	62
GaCl ₃ /0.15 mmol	6	95	63
Nano-γ-Fe ₂ O ₃ -SO ₃ H/0.15 (g)	3	95	64
RHA-SiO ₂ (NPs)-BO ₃ H ₃	0.5-1	76-94	Present method

**Scheme 3.** Synthesis of coumarin-3-carboxylic acid.**Figure 5.** Recyclability and activity of RHA-SiO₂(NPs)-BO₃H₃ under thermal condition @ 50°C for 1 h stirring.

their own advantages, but some of the disadvantages include longer reaction time, poor yield, use of organic solvent and expensive catalyst. So the present method employed is a greener reaction medium, is solvent-free, with shorter reaction time and requires small amount of green catalyst. Also, it is readily available in sufficient quantity naturally to get the product as agro-waste inexpensive catalyst employed for multi-component reactions, giving excellent product isolation with reusability of catalyst up to four times without loss of its activity.

We also extended the catalytic activity of RHA-SiO₂(NPs)-BO₃H₃ for one-pot synthesis of substituted coumarin-3-carboxylic acid (**6a-6j**, Table 6) as a heterogeneous recyclable catalyst assisted by ultrasonication (Scheme 3). In the literature coumarin-3-carboxylic acid synthesis employed organic base or acid catalysed in the

Table 6. Physical data and reaction condition of coumarin-3-carboxylic acid

Entry	Aldehyde	Product	Time (min)	Yield (%)	Melting point (°C)
1	2-OHC ₆ H ₄ 5	6a	46	85	188–190
2	2-OH,3-BrC ₆ H ₃	6b	37	91	194–196
3	2-OH,3-ClC ₆ H ₃	6c	29	90	116–118
4	2,3-OHC ₆ H ₃	6d	38	89	202–204
5	2-OH,4-N(C ₂ H ₅) ₂ C ₆ H ₃	6e	49	81	209–211
6	2-OH,3-C(CH ₃) ₂ ,6-CH ₃ -C ₆ H ₂	6f	34	91	212–214
7	2,3,4-OHC ₆ H ₂	6g	32	92	204–206
8	2-OH,3-OMeC ₆ H ₃	6h	35	86	193–195
9	2-OH,5-NO ₂ C ₆ H ₃	6i	29	73	232–234
10	2-OH,5-ClC ₆ H ₃	6j	31	88	120–122

presence of organic solvent¹⁰⁹. Also the reported methods have longer reaction time, use expensive catalysts and without reusability of catalysts. Due to the present environment concerns and safe reaction conditions in synthetic chemistry, it is recommended to adopt reusable catalyst and solvent-free condition methods. In this regard, only few of the methods reported meet this criterion of green chemistry^{105,107}. In connection with greener synthetic protocol for organic reactions, we have demonstrated agro-waste derived as a catalytic medium for the synthesis of several bio-active molecules¹⁰⁷. We further explored the developed silica functionalized-boric acid for another important reaction, Knoevenagel condensation of substituted salicylaldehyde with Meldrum's acid in 1 mmol scale as a model reaction. To check reaction compatibility, we performed condensation in three different methods in a model reaction in presence of a catalyst: conventional stirring at 50°C for 1–2 h, ultra sonication for 45 min and microwave irradiation. The reaction assisted by ultrasonication gave excellent isolation of product compared to the other two methods. Table 6 provides details of the reaction condition and physical data of coumarin synthesized.

Overall, we have demonstrated that agro-waste derived silica functionalized-boric acid is a active catalyst with recyclable catalyst for DHPMs and coumarin-3-carboxylic acid synthesis. The method has advantages such as being a green protocol, inexpensive, environmentally benign, solvent-free and simple work-up giving good to excellent yield isolation of the products in pure form.

Conclusion

In summary, we have demonstrated one-pot synthesis of DHPM and coumarin-3-carboxylic acid derivatives using agricultural waste rice husk-derived silica-supported BO_3H_3 as a heterogeneous catalyst @ 50°C with 1 h stirring and ultrasonication conditions respectively. The present method is greener, solvent-free, economical, easy work-up, mild reaction condition, with good to excellent yield isolation. The method is suitable for various electron-donating and electron-withdrawing substituents present on the aryl aldehyde substrate. Additional advantage of this method is recyclability of the catalyst and the process is also cost-effective as silica is derived from natural agro-waste that falls in the area of 'green chemistry'.

Supporting information summary: Materials and methods, general synthetic procedure and characterization data are available in the supporting information.

Conflict of interest: The authors declare no conflicts of interest.

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