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# Silica supported sodium hydrogen sulfate ($NaHSO_4$–$SiO_2$): A novel, green catalyst for synthesis of pyrazole and pyranyl pyridine derivatives under solvent-free condition via heterocyclic β-enaminones

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ABSTRACT

$NaHSO_4$–$SiO_2$ is used as an efficient, mild and reusable catalyst for the synthesis of novel heterocyclic pyrazole (**5a**–**h**) and pyranyl pyridine (**7a**–**h**) derivatives via heterocyclic β-enaminones (**3a**–**d**) under thermal solvent-free conditions. The remarkable features of this green, new methodology are high conversions, cleaner reaction profile, simple experimental and work-up procedures. Structures of the newly synthesized compounds have been elucidated on the basis of elemental analysis and spectral data (IR, $^1$H NMR, $^{13}$C NMR and mass spectrometry). The catalyst is characterized for the first time by using scanning electron microscopy–energy dispersive X-ray (SEM–EDX) and powder XRD. The catalyst can be reused several times without significant loss of its catalytic activity.

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## 1. Introduction

Development of new solid-phase (solvent-free) reactions and transferring solution phase reactions to solid-phase are subjects of recent interest in the context of generating libraries of molecules for the discovery of biologically active leads and also for the optimization of drug candidates [1]. Hence, the challenges facing chemist this century is to develop new transformations that are not only efficient, selective and high yielding but also environmentally benign. A solvent-free organic reaction is an important synthetic strategy from the viewpoint of green and sustainable chemistry. Researchers have demonstrated that the solvent-free organic syntheses are generally faster, selective, higher yielding with cleaner products, environmentally benign and involve simple operational procedure as compared to the classical reaction [2].

Heterogeneous catalysts have gained much importance in recent years due to economic and environmental considerations. These catalysts are advantageous over homogeneous catalysts as they can be easily recovered from the reaction mixture by simple filtration and can be reused after activation, thereby making the process economically viable. A tremendous interest has sparked in various chemical transformations promoted by catalysts under heterogeneous conditions [3,4]. Silica supported sodium bisulfate ($NaHSO_4$–$SiO_2$) has been found to be an efficient, inexpensive, non toxic, recyclable and ecofriendly heterogeneous catalyst in various useful chemical transformations such as protection and deprotection [5], Knovenagel condensation [6], and Biginelli reaction [7]. It is also used in the synthesis of dihydropyridines [8], xanthenes [9], homoallylic amines [10], pyrazolines [11], amides [12], quinazolinones [13], and imidazoles [14].

Pyrazole ring is an important structural motif present in numerous pharmacological and agrochemically important compounds, including inhibitors of HIV-I reverse transcriptase [15] and celecoxib derivatives as anti inflammatory agent [16]. Pyrazoles can be synthesized by 1,3-dipolar cycloadditions of diazo compounds [17], reaction of chalcones and hydrazines [18], a four-component coupling of terminal alkynes, hydrazine, carbon monoxide and aryl iodides [19] and the direct condensation of 1,3-diketones and hydrazines in fluoroalcohol [20]. A variety of other catalysts such as $H_2SO_4$ [21], polystyrene supported sulfonic acid [22], zirconium sulfophenyl phosphonate [23], Sc $(OTf)_3$ [24], Y-zeolite [25], Mg $(ClO_4)$ [26] have been also employed to affect this transformation.

On the other hand, pyridine is one of the most prevalent heterocycle being the core fragment of different natural products and pharmaceutical active agents [27]. In addition to classical pyridine syntheses such as the Kröhnke reaction, many new approaches have been also reported in the literature including condensation of amines and carbonyl compounds, cycloaddition reactions, multicomponent reaction [28–31] etc. Despite the wide range of conceptually different syntheses of pyrazole and pyridine

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derivatives only few approaches toward these heterocyclic structure employing β-enaminones, active methylene compounds and hydrazine derivative have been disclosed in the literature [32]. However, in spite of their potential utility, some of the reported methods suffer from certain drawbacks such as long reaction time, expensive reagents, harsh reaction conditions, low product yields and high temperature. Therefore, improvements in these reaction conditions required the development of efficient, cost effective, safe, mild and environmentally benign procedures. Thus, based on the above findings and in continuation of our interest in the development of new methodologies [33], we report herein, the use of silica supported sodium bisulfate ($NaHSO_4$–$SiO_2$) as a mild, highly efficient, and recyclable heterogeneous catalyst for the synthesis of pyrazole and pyranyl pyridine derivatives by the reaction of β-enaminone with different hydrazines and active methylene compounds respectively under thermal solvent-free condition in excellent yields. The catalyst was recyclable up to four cycles. The structure and morphology of the catalyst was established for the first time with the help of powder XRD, scanning electron microscopy (SEM) and energy dispersion analytical X-ray (EDX).

## 2. Experimental

### 2.1. General

Melting points of all synthesized compounds were taken in a Riechert Thermover instrument and are uncorrected. The IR spectra (KBr) were recorded on Perkin Elmer RXI spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DRX-300 and Bruker Avance II 400 spectrometer using tetramethylsilane (TMS) as an internal standard and DMSO-$d_6$/$CDCl_3$ as solvent. DART-MS were recorded on a JEOL-Accu TOF JMS-T100LC mass spectrometer having a DART source. Elemental analyses (C, H and N) were conducted using the Elemental vario EL III elemental analyzer and their results were found to be in agreement with the calculated values. 5-Acetyl-barbituric acid, 5-acetyl-1,3-dimethylbarbituric acid and 3-acetyl-4-hydroxycoumarin were synthesized by reported procedures [34]. Other chemicals were of commercial grade and used without further purification. The homogeneity of the compounds was checked by thin layer chromatography (TLC) on glass plates coated with silica gel G254 (E. Merck) using chloroform–methanol (3:1) mixture as mobile phase and visualized using iodine vapors. X-ray diffractograms (XRD) of the catalyst were recorded in the $2\theta$ range of 10–70° with scan rate of 4°/min on a Rigaku Minifax X-ray diffractometer with Ni-filtered Cu Kα radiation at a wavelength of 1.54060 °A. The SEM–EDX characterization of the catalyst was performed on a JEOL JSM-6510 scanning electron microscope equipped with energy dispersive X-ray spectrometer operating at 20 kV.

### 2.2. Preparation of catalyst

The catalyst silica-supported sodium hydrogen sulfate ($NaHSO_4$–$SiO_2$) was prepared by reported procedure [35].

### 2.3. General procedure for the synthesis of heterocyclic β-enaminones under thermal solvent-free condition

A mixture of dehydroacetic acid/3-acetyl-4-hydroxycoumarin/5- acetylbarbituric acid/5-acetyl-1,3-dimethylbarbituric acid (**1a**–**d**) (1.00 mmol) and DMF-DMA (**2**) (1.00 mmol) was added into a round bottom flask. The resulting mixture was heated at 70 °C in an oil bath for specified time (Table 1). The progress of reaction was monitored by TLC. The reaction mixture (after being cooled to room temperature) was poured into ice cold water (20 mL) and stirred for 5–10 min. The bright yellow solid, thus, obtained was filtered, washed with water, dried and recrystallized from ethanol to afford pure products **3a**–**d**.

**Table 1**
Synthesis of β-enaminones[a] (**3a**–**d**) and their derived pyrazoles[b] (**5a**–**h**).

| Entry | Product | R | Time[c] (min) | Yield[d] (%) |
|---|---|---|---|---|
| 1 | **3a** | – | 5 | 93 |
| 2 | **3b** | – | 5 | 92 |
| 3 | **3c** | – | 10 | 89 |
| 4 | **3d** | – | 10 | 92 |
| 5 | **5a** | H | 5 | 94 |
| 6 | **5b** | Ph | 5 | 90 |
| 7 | **5c** | H | 5 | 92 |
| 8 | **5d** | Ph | 5 | 92 |
| 9 | **5e** | H | 10 | 87 |
| 10 | **5f** | Ph | 10 | 85 |
| 11 | **5g** | H | 10 | 90 |
| 12 | **5h** | Ph | 10 | 89 |

[a] Reaction conditions: heterocyclic methyl ketones (**1a**–**d**, 1.00 mmol) and DMF-DMA (**2**, 1.00 mmol) heated under thermal solvent-free condition.
[b] Reaction conditions: β-enaminones (**3a**–**d**, 1.00 mmol), hydrazines (**4a**–**b**,1.00 mmol), and $NaHSO_4$–$SiO_2$ (100 mg) heated under solvent-free condition.
[c] Reaction progress monitored by TLC.
[d] Isolated yields.

### 2.4. General procedure for the synthesis of pyrazoles under thermal solvent-free condition

To a mixture of **3a**–**d** (1.00 mmol) and hydrazine hydrate **(4a)**/phenyl hydrazine (**4b)** (1.00 mmol), $NaHSO_4$–$SiO_2$ (100 mg) was added. The reaction mixture was heated at 70 °C for specified time (Table 1). After completion of the reaction (checked by TLC), the reaction mixture was cooled to room temperature and mixed thoroughly with 10 mL of ethyl acetate. The solid inorganic material was filtered off. After separation of solid, the solvent was evaporated under reduced pressure. The white solid, thus, obtained was washed with water and dried. Further purification was made by recrystallization from ethanol to afford pure products **5a**–**h**.

### 2.5. General procedure for the synthesis of pyranyl pyridine derivatives under solvent-free condition

To a mixture of β-enaminone **3a** (1.00 mmol), active methylene compounds **6a**–**h** (1.00 mmol), ammonium acetate (3.00 mmol), $NaHSO_4$–$SiO_2$ (100 mg) was added. The reaction mixture was heated at 70 °C over a heating mantle for specified time. After completion of the reaction (monitored by TLC) the contents were cooled to room temperature and mixed thoroughly with (10 mL) of ethyl acetate. The catalyst was removed by filtration and reused. After separation of catalyst, the solvent was evaporated under reduced pressure. The resulting solid residue was washed with cold water to remove any unreacted ammonium acetate, filtered and dried to afford the crude products. The pure product was obtained by recrystallization from ethyl alcohol.

## 3. Results and discussion

### 3.1. Characterization of the catalyst

#### 3.1.1. Powder X-ray diffraction (XRD) analysis of the catalyst

The structure of the prepared catalyst ($NaHSO_4$–$SiO_2$) was identified by powder XRD. X-ray patterns of the catalyst was recorded at $2\theta$ = 10–70° range (Fig. 1). A broad peak centered at $2\theta$ angle in the range 18–30° confirmed the formation of amorphous silica–$NaHSO_4$ matrix [36].

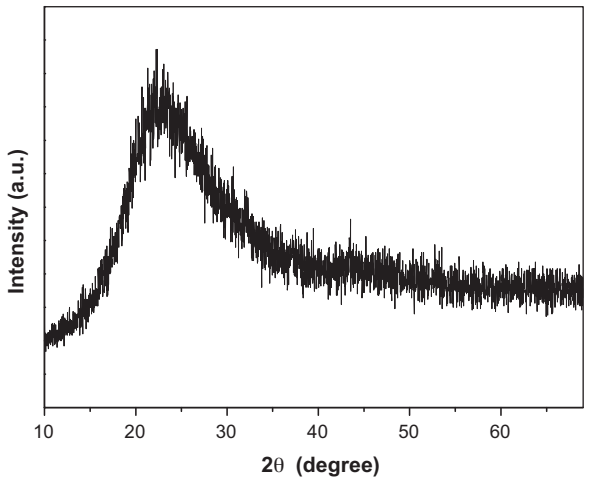



**Fig. 1.** The powder XRD pattern of fresh catalyst.

### 3.1.2. SEM–EDX analysis of the catalyst

To study the surface morphology of the catalyst, SEM micrographs of the catalyst was employed. The SEM images of the catalyst (Fig. 2) showed an even distribution of $NaHSO_4$ on the surface of the silica gel. No conglomeration or layering of $NaHSO_4$ was observed on the surface of silica gel.

Further, EDX analysis (Fig. 3) of the catalyst showed the presence of Na, S, O and Si elements suggesting the formation of expected catalytic system.

The increased reactivity of $NaHSO_4$ supported on silica material may be due to the catalyst and support interactions resulting in the changes in surface properties of reactive sites. To the best of our knowledge there is no report on the characterization of the catalyst ($NaHSO_4$–$SiO_2$) using SEM–EDX study.

### 3.2. Synthesis of heterocyclic β-enaminones

β-Enaminones have been used as valuable intermediates for the synthesis of a vast variety of pharmacologically active compounds [37]. Various method for the synthesis of β-enaminones have been reported including condensation of active methyl and active methylene compounds with N,N-dimethylformamide dimethylacetal under reflux condition or by using microwave irradiation [38]. These methods suffer from drawbacks such as higher temperature and longer reaction time to achieve moderate to high yields of the products. Martins et al. reported an efficient ionic liquid catalyzed synthesis of β-enaminones using [Bmim].$BF_4$ and [Omim].$BF_4$ as catalysts under solvent-free conditions [39]. However, ionic liquids especially imidazolium based systems containing $BF_4$ anions are toxic in nature as they liberate hazardous HF and their high cost and disposability make their utility limited [40]. Taking into consideration of all these limitations we have developed a simpler and clean protocol for the synthesis of β-enaminones at lower temperature. As a preliminary study, we first investigated the synthesis of heterocyclic β-enaminones **3a**–**d** by condensation of heterocyclic methyl ketones **1a**–**d** with N,N-dimethylformamide dimethylacetal (DMF-DMA) (**2**) by thermal heating under solvent- and catalyst-free condition at 70 °C for 5–10 min. The corresponding enaminones **(3a–d)** were obtained in excellent yields (89–93%) (Table 1).

The structure of isolated β-enaminones **3a**–**d** (Scheme 1) was verified by elemental analyses and spectroscopic data (IR, $^1$H NMR, $^{13}$C NMR and MS). The infrared (IR) spectrum of **3a** exhibited the broad band for OH group at 3429 $cm^{-1}$ and a sharp strong band at 1712 $cm^{-1}$ for lactone carbonyl group. Another absorption band at 1609 $cm^{-1}$ along with a shoulder at 1649 $cm^{-1}$ was due to C=C and C=O of α,β-unsaturated system. The $^1$H NMR spectrum displayed two doublets at $\delta$ 6.65 and 8.05 with coupling constant $J$ = 12.3 Hz assignable to the two olefinic protons Ha and Hb respectively. The coupling constant value indicates that the **3a** existed predominantly in the *E*-configuration (Scheme 1). The remaining methyl and heterocyclic moiety protons were present at their normal values. The $^{13}$C NMR spectrum showed signal at $\delta$ 185.9 for α,β-unsaturated carbonyl group whereas olefinic carbons C-2′ and C-3′ were present at $\delta$ 91.5 and 156.8 respectively and other carbon signals appeared at their appropriate positions. Further, evidence for the formation of **3a** was obtained by mass spectrum which showed molecular ion peak at (*m/z*) 223.

### 3.3. Catalytic reaction

In order to study the generality of our methodology toward heterocyclic compounds, the synthesis of pyrazole and pyridine derivatives was explored. In our initial investigations for optimization of appropriate reaction conditions, at first the synthesis of compound **5a** was selected as a model reaction. Thus, an equimolar mixture of β-enaminone (**3a**) and hydrazine hydrate (**4a**) was heated at 70 °C under solvent-free neat condition. The reaction proceeded very slowly and product was obtained in lower yield even after prolong heating (Table 2, entry 1) demonstrating the need of a catalyst. A comparative study was also carried out using different catalysts such as $P_2O_5$–$SiO_2$, $Zn(CH_3COO)_2$, $Zn(NO_3)_2$, $ZnCl_2$ $AlCl_3$, $FeCl_3$, Zn(L-proline)$_2$, PTS, and L-proline and it was observed that either reactions were not successful or products were obtained in poor yields. When the model reaction was performed in the presence of $NaHSO_4$–$SiO_2$ (100 mg) under solvent-free condition, product **5a** was obtained in excellent yield (94%) within shorter time (5 min) (Table 2, entry 2).

### 3.3.1. Effect of different supports

To establish the use of silica as the best support for $NaHSO_4$, other supports were also investigated (Table 2). The model

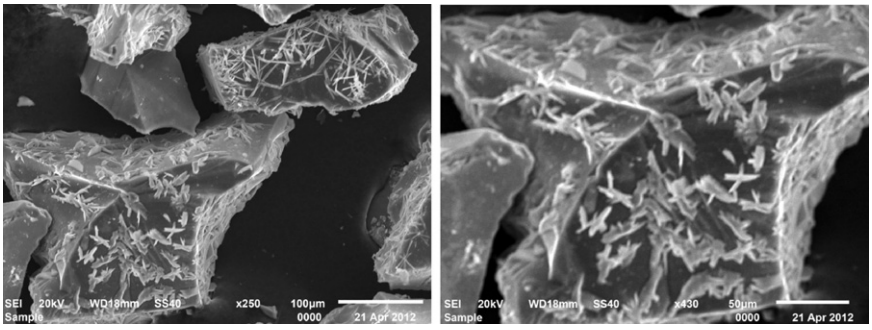



**Fig. 2.** SEM images of the catalyst ($NaHSO_4$–$SiO_2$) at different magnifications.

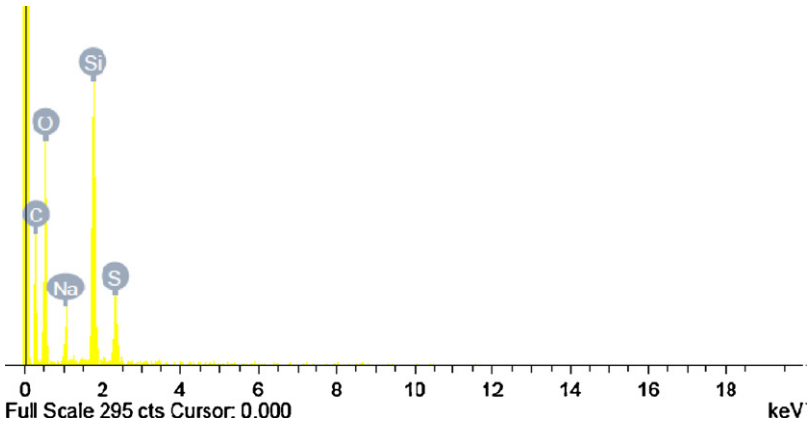
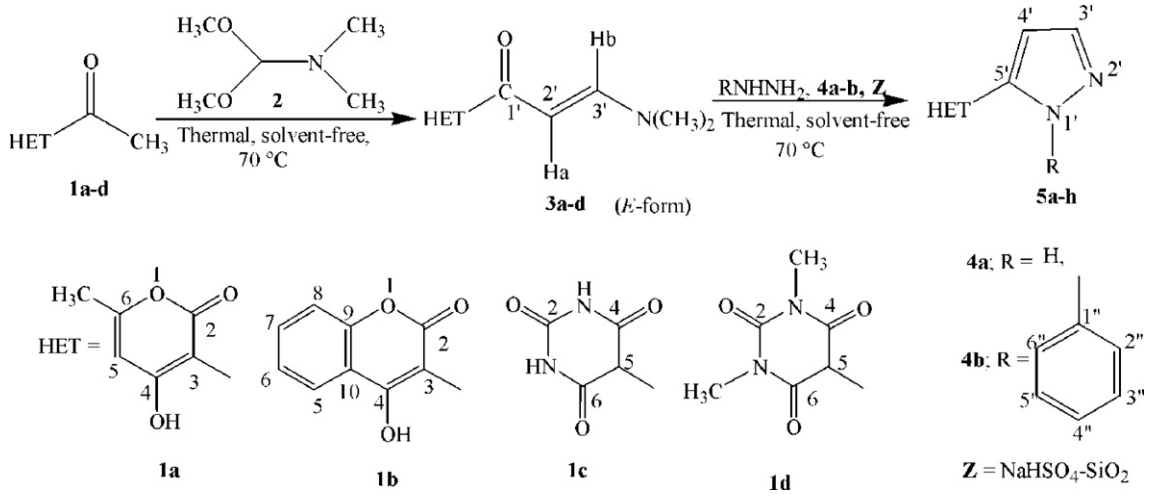
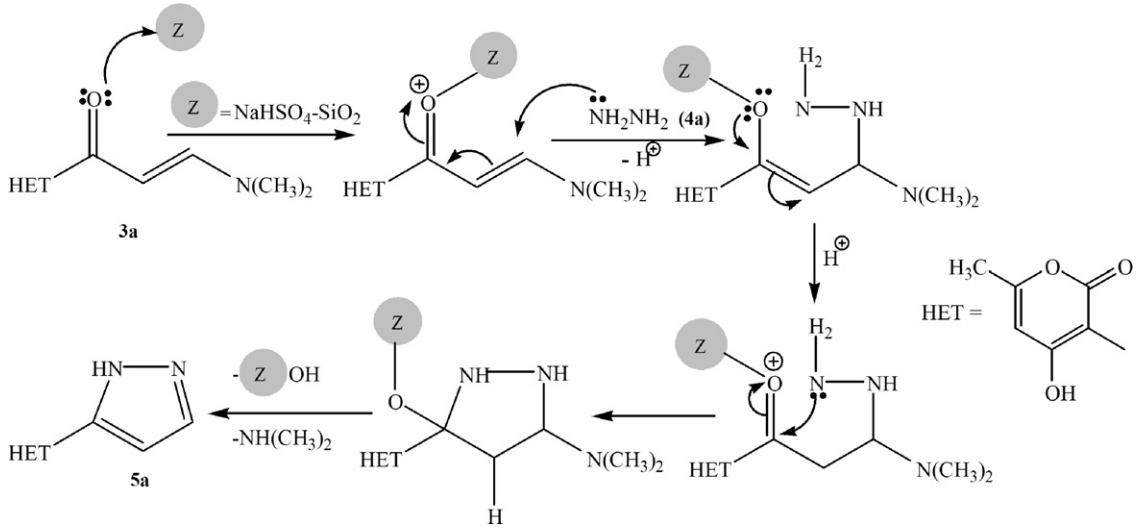



**Fig. 3.** EDX analysis of the catalyst ($NaHSO_4$–$SiO_2$).

reaction, thus, when carried out with $NaHSO_4$–alumina (acidic, basic, neutral), the TLC showed formation of product but the reaction did not complete even after longer reaction time (Table 2, entries 3,4,5). Further, when the silica gel alone was employed in lieu of $NaHSO_4$–$SiO_2$, no measurable product was obtained (Table 2, entry 6) while with $NaHSO_4$ in pure form the reaction was again not successful (Table 2, entry 7). Among the examined supports, for $NaHSO_4$, silica gel showed the best results. Therefore, silica-supported $NaHSO_4$ was used as catalyst for all reactions. The increase in rate of reaction employing $NaHSO_4$–$SiO_2$ may be due




**Scheme 1.** Synthesis of heterocyclic β-enaminons (**3a–d**) and pyrazoles (**5a–h**).




**Scheme 2.** Proposed mechanism for the formation of **5a**.

**Table 2**
The screening of different supports on the model reaction.[a]

| Entry | Support | Time[b] | Yield[c] (%) |
|---|---|---|---|
| 1 | No catalyst | 4 h | 43 |
| 2 | $NaHSO_4$–$SiO_2$ | 5 min | 94 |
| 3 | $NaHSO_4$–alumina (acidic) | – | Incomplete |
| 4 | $NaHSO_4$–alumina (basic) | – | Incomplete |
| 5 | $NaHSO_4$–alumina (neutral) | – | Incomplete |
| 6 | $SiO_2$ | 3.5 h | Trace |
| 7 | $NaHSO_4$ | 3 h | 52 |

[a] Reaction conditions: β-enaminone (**3a**, 1.00 mmol), hydrazine hydrate (**4a**, 1.00 mmol), and $NaHSO_4$–$SiO_2$ (100 mg) heated under thermal solvent-free condition.
[b] Reaction progress monitored by TLC.
[c] Isolated yields.

**Table 3**
Comparative study of compound **5a** using solution conditions versus the solvent-free method.

| Entry[a] | Solvent | Temperature | Time[b] | Yield[c] (%) |
|---|---|---|---|---|
| 1 | Solvent-free | 70 °C | 5 min | 94 |
| 2 | Acetic acid | Reflux | 7 h | 76 |
| 3 | EtOH | Reflux | 3 h | 68 |
| 4 | MeOH | Reflux | 6 h | 64 |
| 5 | Isopropanol | Reflux | 8 h | 58 |
| 6 | $CH_2Cl_2$ | Reflux | 48 h | 35 |
| 7 | $CH_3CN$ | Reflux | 48 h | 38 |

[a] Reaction conditions: β-enaminone (**3a**, 1.00 mmol), hydrazine hydrate (**4a**, 1.00 mmol), and $NaHSO_4$–$SiO_2$ (100 mg).
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

to increased surface area of the catalyst. A plausible mechanism for the formation of **5a** in the presence of $NaHSO_4$–$SiO_2$ has been shown in Scheme 2.

### 3.3.2. Effect of solvents

In order to study the solvent effect, the model reaction was carried out in different solvents such as acetic acid, dichloromethane ($CH_2Cl_2$), acetonitrile ($CH_3CN$), methanol (MeOH), ethanol (EtOH) and isopropanol. When the reaction was performed in EtOH, MeOH, isopropanol lower yield of the product (**5a**) was obtained after longer time period (Table 3, entries 3, 4, 5) whereas in $CH_2Cl_2$ and $CH_3CN$, only trace amounts of the product was obtained (Table 3, entries 6, 7). Using acetic acid relatively high yield of the product was obtained (Table 3, entry 2) but reaction took longer time period for completion. When the reaction was carried out under solvent-free condition, both the yield and reaction time were significantly improved (Table 3, entry 1).

### 3.3.3. Loading of the catalyst

In order to optimize the amount of catalyst used for the catalysis of the reaction to form the desired product **5a**, we analyzed the reaction by varying the loading amount to 40, 60, 80, 100 and 120 mg of $NaHSO_4$–$SiO_2$. Generally, the rate of reaction and yield increases over the amount of catalyst. It was found that the optimum amount of catalyst turned out to be 100 mg in order to obtain the best result. No such significant improvement in the yield was observed on increasing the loading to 120 mg, whereas, decreasing the amount of catalyst to 40 mg resulted in lowering of the yield (Table 4).

### 3.3.4. Recycling study of the catalyst

We also investigated the reusability of the catalyst under solvent-free condition using model reaction of β-enaminone (**3a)** with hydrazine hydrate (**4a)** in the presence of $NaHSO_4$–$SiO_2$ (100 mg) (Table 5). After completion of the reaction, the mixture was cooled to room temperature, and the organic part was

**Table 4**
Effect of catalyst loading on the synthesis of **5a**.[a]

| Entry | Catalyst (mg) | Time[b] (min) | Yield[c] (%) |
|---|---|---|---|
| 1 | 40 | 45 | 58 |
| 2 | 60 | 35 | 74 |
| 3 | 80 | 10 | 89 |
| 4 | 100 | 5 | 94 |
| 5 | 120 | 5 | 94 |

[a] Reaction conditions: β-enaminone (**3a**, 1.00 mmol), hydrazine hydrate (**4a**, 1.00 mmol), heated under thermal solvent-free condition.
[b] Reaction progress monitored by TLC.
[c] Isolated yields.

**Table 5**
Recycling data of the catalyst for the model reaction.[a]

| Catalyst recycles | Time[b] | Yield[c] (%) |
|---|---|---|
| I | 5 min | 94 |
| II | 5 min | 94 |
| III | 5 min | 94 |
| IV | 5 min | 94 |
| V | 10 min | 89 |

[a] Reaction conditions: β-enaminone (**3a**, 1.00 mmol), hydrazine hydrate (**4a**, 1.00 mmol), and $NaHSO_4$–$SiO_2$ (100 mg) heated under thermal solvent-free condition.
[b] Reaction progress monitored by TLC.
[c] Isolated yields.

dissolved in ethyl acetate (10 mL). The mixture was filtered for separation of the catalyst. The recovered catalyst was washed with ethyl acetate (3× 10 mL), dried in oven at 100 °C for 3 h and used for the subsequent catalytic runs. The results (Table 5) showed that the catalyst was active up to four cycles.

The identity of the recovered catalyst was checked by powder XRD and SEM analysis. It was observed that peaks remained the same (Fig. 4), and also there was no change in the morphology of the catalyst (Fig. 5) as compared to the fresh catalyst.

Under these optimized reaction conditions the scope and generality of the present method was further demonstrated by reaction of different heterocyclic β-enaminones (**3a**–**d**) with various hydrazine derivatives **(4a**–**b**) under solvent-free condition. All the reactions proceeded smoothly and the reaction was completed within 5–10 min to afford the products (**5a**–**h**) in excellent yields (85–94%) (Table 1). The structure of products **5a**–**h** (Scheme 1) was deduced from their elemental analysis and spectral data (IR, $^1$H NMR, $^{13}$C-NMR and MS). The IR spectrum of **5a** showed two broad absorption bands at 3171 $cm^{-1}$ and 3045 $cm^{-1}$ due to the presence of OH group of lactone and NH group of pyrazole moieties

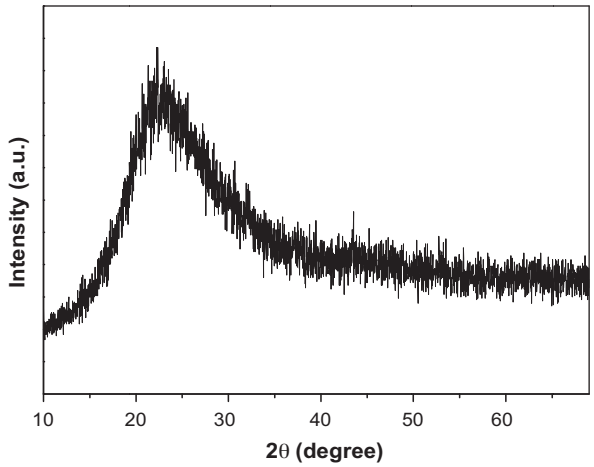



**Fig. 4.** The powder XRD pattern of recovered catalyst after four runs.

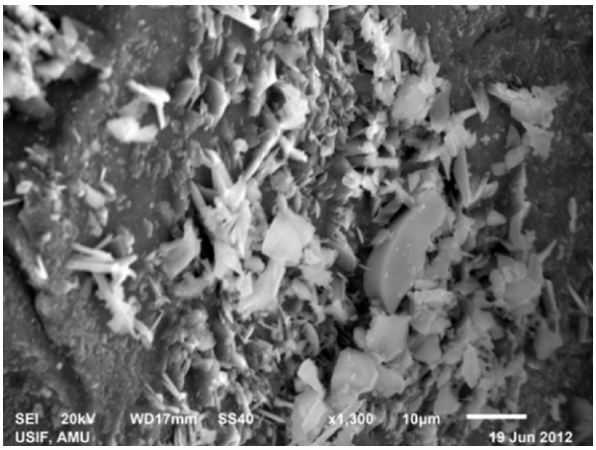


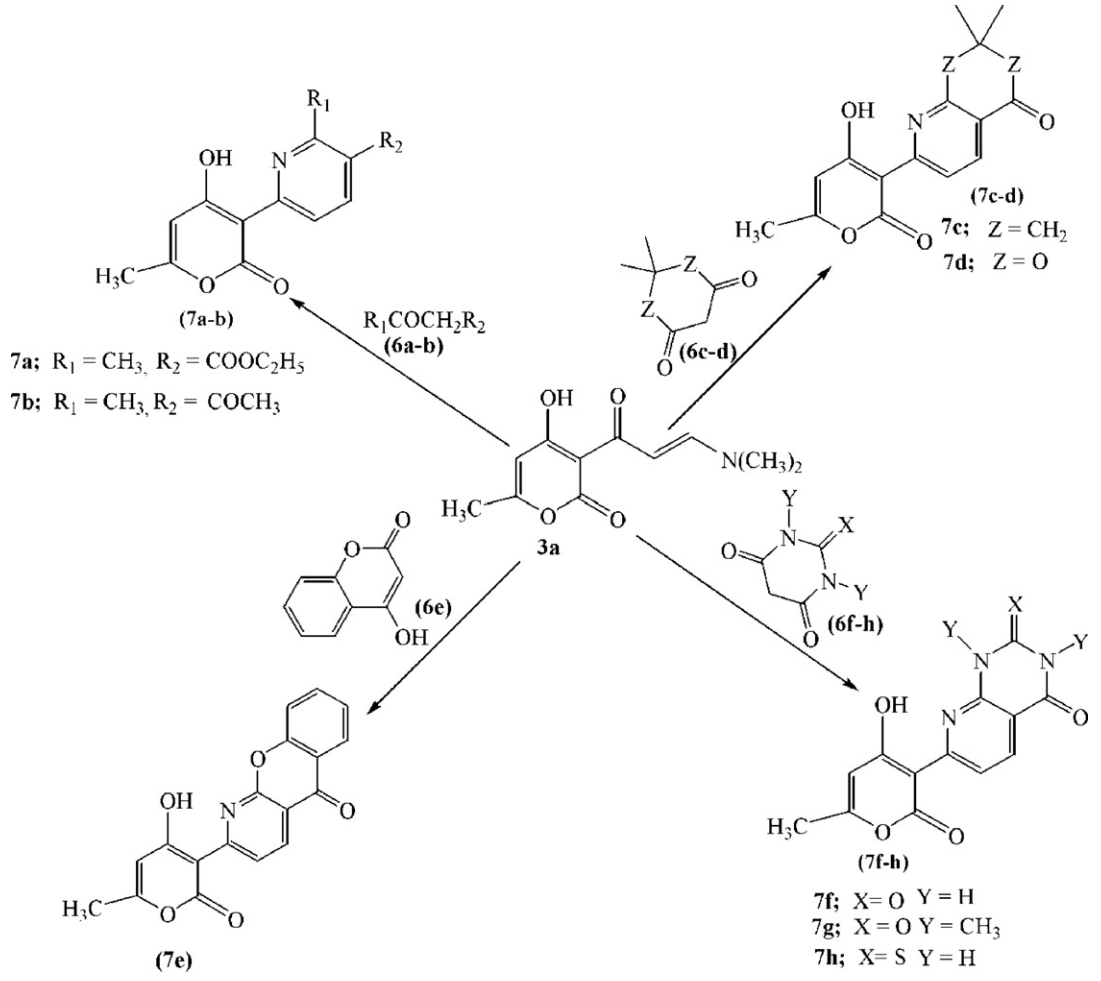

**Fig. 5.** The SEM image of recovered catalyst after four runs.

respectively. A sharp and strong absorption band for the lactone carbonyl group was discernible at 1696 $cm^{-1}$. In the $^1H$ NMR spectrum the presence of pyrazole moiety was inferred by two doublets at $\delta$ 6.91 ($J$ = 3 Hz) and $\delta$ 7.89 ($J$ = 3 Hz) for C-4′, C-3′ protons respectively and a broad singlet for NH proton at $\delta$ 13.36. The $^{13}C$ NMR spectrum showed signal at $\delta$ 145.6, 100.6, and 130.1 for C-3′, C-4′, and C-5′ carbons of pyrazole moiety. The other peaks were present at their normal values and are mentioned in the experimental section. The structure of compound **5a** was further confirmed by mass spectrum which showed $M^+$ at ($m/z$) 192.

### 3.4. Synthesis of pyranyl pyridine derivatives

Efforts were made to synthesize pyranyl pyridine derivatives (**7a–h**) employing (**3a**) (1.00 mmol), different cyclic/acyclic active methylene compounds (**6a–h**) (1.00 mmol) and ammonium acetate (3.00 mmol) as an ammonia source in the presence of $NaHSO_4$–$SiO_2$ under same reaction conditions (Scheme 3).

All reactions proceeded efficiently and the desired products were obtained in excellent yields (81–93%) in short reaction times (5–25 min) (Table 6). The structure of compounds **(7a–h)** was deduced on the basis of IR, $^1H$ NMR, $^{13}C$ NMR and mass spectrometry. The IR spectrum of the newly synthesized compound (**7a**) exhibited characteristic absorption bands at 3065, 1717 and 1697 $cm^{-1}$ due to the presence of OH, ester, and lactone carbonyl groups respectively. $^1H$ NMR exhibited two doublets at $\delta$ 8.85 and 8.44 for $H_4$ and $H_5$ proton of pyridine moiety. Presence of ester group was inferred by quartet at $\delta$ 4.44 ($J$ = 7.2 Hz) and triplet at $\delta$ 1.42 ($J$ = 6.9 Hz) for $OCH_2$ and $CH_3$ protons respectively. The $^{13}C$ NMR spectrum showed characteristic signals at $\delta$ 142.2 and 119.7 for C4 and C5 carbons of pyridine moiety respectively. Other peaks were at their normal values and discussed in the experimental section. Further confirmation for the structure **7a** was provided by mass spectrometry which showed $M^+$ at 289.15 as base peak.




**Scheme 3.** General scheme for the products formed by the reaction of (**3a**) with different active methylene compounds (**6a–h**), ammonium acetate catalyzed by $NaHSO_4$–$SiO_2$ at 70 °C.

**Table 6**
Synthesis of compounds **7a**–**h**.[a]

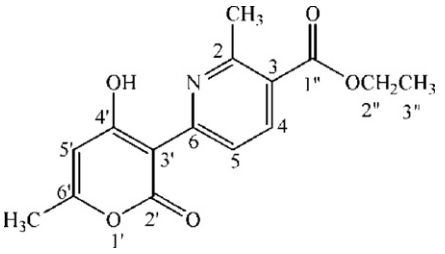
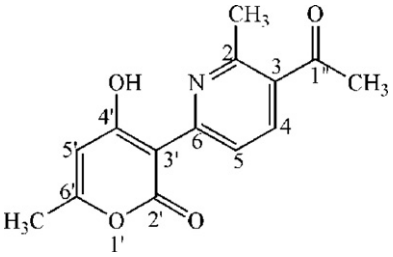
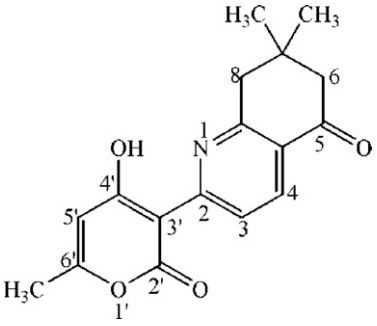
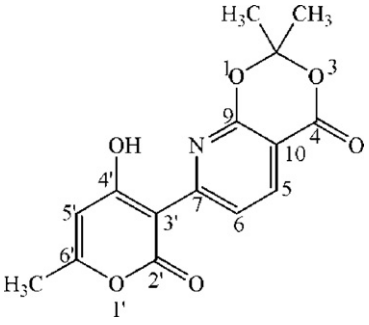
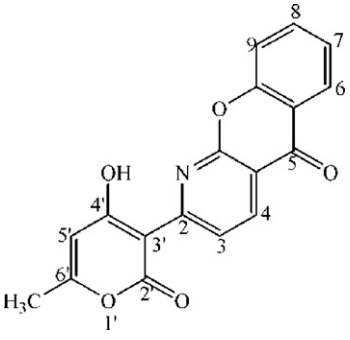
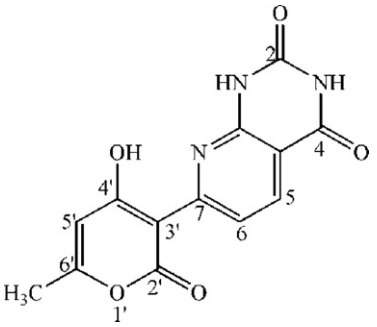
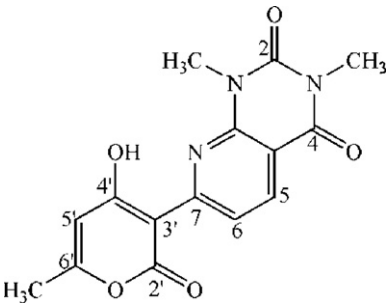
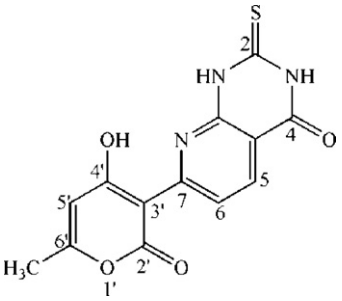
| Entry | Product | Time[b] (min) | Yield[c] (%) | M.P. (°C) |
|---|---|---|---|---|
| **7a** |  | 5 | 93 | 129–131 |
| **7b** |  | 5 | 88 | 201–205 |
| **7c** |  | 10 | 89 | >300 |
| **7d** |  | 10 | 84 | >300 |
| **7e** |  | 15 | 81 | >300 |

Table 6 (*Continued*)

| Entry | Product | Time[b] (min) | Yield[c] (%) | M.P. (°C) |
|---|---|---|---|---|
| **7f** |  | 25 | 89 | >300 |
| **7g** |  | 15 | 93 | 239–241 |
| **7h** |  | 20 | 90 | >300 |

[a] Reaction conditions: β-enaminone (**3a**, 1.00 mmol), active methylene compounds (**6a**–**h**, 1.00 mmol), ammonium acetate (3.00 mmol), and $NaHSO_4$–$SiO_2$ (100 mg) heated under solvent-free condition.
[b] Reaction progress monitored by TLC.
[c] Isolated yields.

## 4. Conclusion

In summary, this paper describes a convenient and efficient process for the synthesis of novel pyrazole and pyranyl pyridine derivatives under thermal solvent-free conditions using $NaHSO_4$–$SiO_2$ as an efficient catalyst. Present methodology offers very attractive features as excellent yields of the product in shorter reaction time, simple work-up procedure, economic viability and reusability of the catalyst and first time synthesis of hitherto unknown heterocyclic β-enaminones at lower temperature. We believe that this method has provided a better scope for the synthesis of pyrazole and pyridine derivatives and will be a more practical alternative to the other existing methods.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molcata.2012.07.024.

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