

Nano-SiO₂/Taurine as a new natural based catalyst for synthesis of hexahydroquinolines derivative

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ABSTRACT

In this research work, Nano-SiO₂/Taurine was synthesized and characterized by FT-IR, energy dispersive X-ray analysis (EDX), scanning electron microscopy (SEM), X-ray diffraction patterns (XRD), Thermogravimetric analysis (TGA) and MAP analysis. Nano-SiO₂/Taurine has considerable benefits such as simple preparation protocol, simple handling, high acidic property, reusability and high stability. Nano-SiO₂/Taurine was used as a catalyst for the synthesis of hexahydroquinolines by the reaction of ethyl acetoacetate, dimedone and ammonium acetate with various aldehydes. These reactions were carried out under solvent-free conditions at 85 °C. The present protocol is simple, eco-friendly and efficient. The hexahydroquinolines were produced at high yields and short reaction times.

Keywords: Nano-SiO₂/Taurine, hexahydroquinoline, dimedone, ethyl acetoacetate

1. Introduction

Hexahydroquinolines [1, 2] from *N*-heterocyclic compounds family [3-5], have a wide range of biological and pharmaceutical application such as anti-tumour, anti-diabetic and also modulation of calcium channels [6-11]. A classical protocol for the synthesis of these compounds is three-component condensation reaction of aldehyde with ethyl acetoacetate, 1,3-diketone and ammonia in acetic acid or alcohol [12-14]. Recently, certain protocols for the synthesis of hexahydroquinolines have been reported by using catalysts such as [pyridine-SO₃H]Cl [15], threo-(1S, 2S)-2-amino-1-(4-nitrophenyl)-1,3-propanediol [16], Iron (III) trifluoroacetate [17], ionic liquid [18], cerium (IV) ammonium nitrate [19], Sc(OTf)₃ [20], γ-Fe₂O₃ [21], SBA-15/SO₃H nanoreactor [22], KH₂PO₄ [23], sulfamic acid-functionalized nano-titanium dioxide [24], nano-CoAl₂O₄ [25], nano-ZrO₂-SO₃H [26], ZrOCl₂·8H₂O [27], silica-bonded imidazolium-sulfonic acid chloride [28], nano-Fe₃O₄-TiO₂-SO₃H [29], 1,3-

disulfonic acid imidazolium hydrogen sulfate [30], amino alcohol [31,32], (IRMOF-3) [33], SBA-SO₃H [34], [MPIIm][HSO₄]₂@SBA-15 [35], SBA-15/NHSO₃H [36] and graphene oxide supported ionic liquid [37], eggshell-based nano-magnetic solid acid [38].

Taurine, (2-aminoethanesulfonic acid), which is found in meat, fish and egg exists as a zwitterion with pK_a=1.5 ensuring that it is fully ionized to the sulfonate [39, 40]. Previously, Taurine was used as a catalyst for preparation of barbituric and thiobarbituric acid derivatives in water [41]. In this work, we have supported the taurine on nano-silicagel, prepared Nano-SiO₂/Taurine, and applied it for the synthesis of polyhydroquinolines as catalyst.

2. Experimental

2.1. General

FT-IR, Bruker, Equinox 55 spectrometer, and NMR [Bruker (DRX-400 Avance)], were used for recording FTIR and NMR spectra, respectively. Buchi melting point B-540 B.V.CHI apparatus was used for determination of melting points. X-ray Diffraction (XRD) spectrum was recorded by a Philips Xpert MPD diffractometer. Field Emission Scanning Electron

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Microscopy (FESEM) was obtained on a TESCAN, Mira III. The EDX-MAP analysis was done with FESEM instrument from TESCAN company (France), model MIRA II with SAMX detector. Thermal gravimetric analysis (TGA) was done by the “STA 50” from Bahr company (German).

2.2. Preparation of Nano-Silica chloride

Firstly, in a 250 ml round bottomed flask, 10 g of Nano silicagel and 40 ml of thionyl chloride (toxic and should be used under ventilator) were refluxed for 48 hours. Then, the reaction mixture was cooled and filtered and washed several times with dichloromethane. Then the resulting nano-silica chloride particles were dried at ambient temperature.

2.3. Preparation of Nano-SiO₂/Taurine

In a 100 ml round bottomed flask, 1 mmol of Taurine (2-aminoethanesulfonic acid), 1 g of nano-silica chloride and 20 ml of ethanol were refluxed for 15 hours. The reaction mixture was filtered, cooled, washed with ethanol and dried. The resulting catalyst is as white powder and does not require special maintenance.

2.4. Preparation of hexahydroquinoline derivatives (general protocol)

A mixture of the dimedone (1.0 mmol), ammonium acetate (1.0 mmol), aldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol) and Nano-SiO₂/Taurine (0.05 g) was stirred at 80 °C in absence of any solvent. The progress of reaction was scanned by TLC (ethyl acetate: n-hexane, 1:4). At the end of reaction, 20 ml of hot ethanol was added to the reaction mixture. Then, the Nano-SiO₂/Taurine catalyst was filtered. The solid

product was generated by adding water to the filtrate and then crystallized in ethanol.

3. Results and Discussion

In this research, Nano-SiO₂/Taurine as a new catalyst was prepared and characterized (**Scheme 1**). At first, for the synthesis of nano-silica chloride, a mixture of thionyl chloride and nano-silica gel was refluxed for 48 h, filtered, washed with CH₂Cl₂ and dried. In this protocol, OH groups of silica gel were substituted by Cl of thionyl chloride. Then, a mixture of nano-silica chloride, taurine and ethanol was refluxed to replace Cl atom of silica chloride with NH₂ group of taurine. The characterization of Nano-SiO₂/Taurine, was done by FT-IR, XRD, FESEM, EDS and TGA.

3.1. Characterization of Nano-SiO₂/Taurine

3.1.1. FT-IR analysis

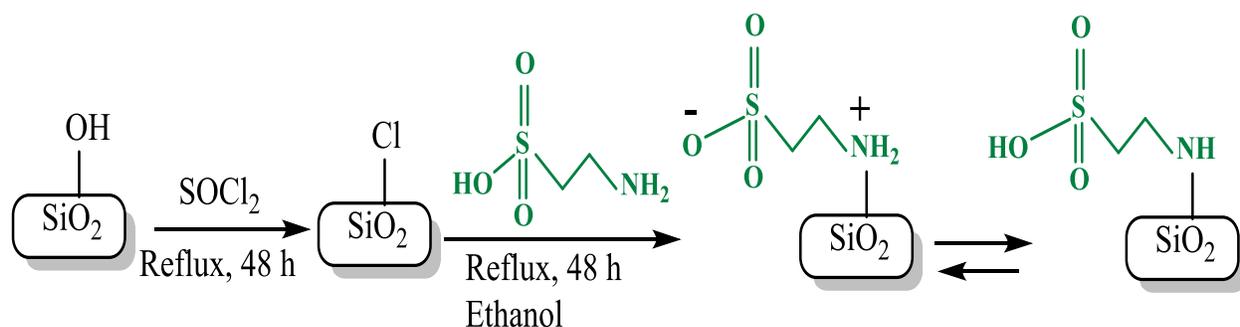
Fig. 1 shows the FT-IR spectra of Taurine, Nano-Silica chloride, Nano-SiO₂/Taurine and reused Nano-SiO₂/Taurine. **Fig. 1c** shows the bands at 1613 and 1508 cm⁻¹ which are attributed to the S=O, 1174 cm⁻¹ to S-O and 1034 cm⁻¹ to Si-O stretching vibration and 796 cm⁻¹ is attributed to the Si-O-Si bending vibration. Meanwhile, the signals between 1700-2000 cm⁻¹ show the ammonium salt form (R₂NH₂)⁺ in the catalyst.

3.1.2. Morphology analysis

Fig. 2 presents the FESEM image of Nano-SiO₂/Taurine to investigate its particle size and surface morphology. According to this result, the particles of Nano-SiO₂/Taurine have a quasi-spherical shape of 23 nm size.

3.1.3. EDX analysis

EDX spectrum of Nano-SiO₂/Taurine (**Fig. 3**) shows its the elemental compositions including 6.92, 63.68, 28.57 and 0.55% for N, O, Si and S, respectively.



Scheme 1. Preparation of Nano-SiO₂/Taurine

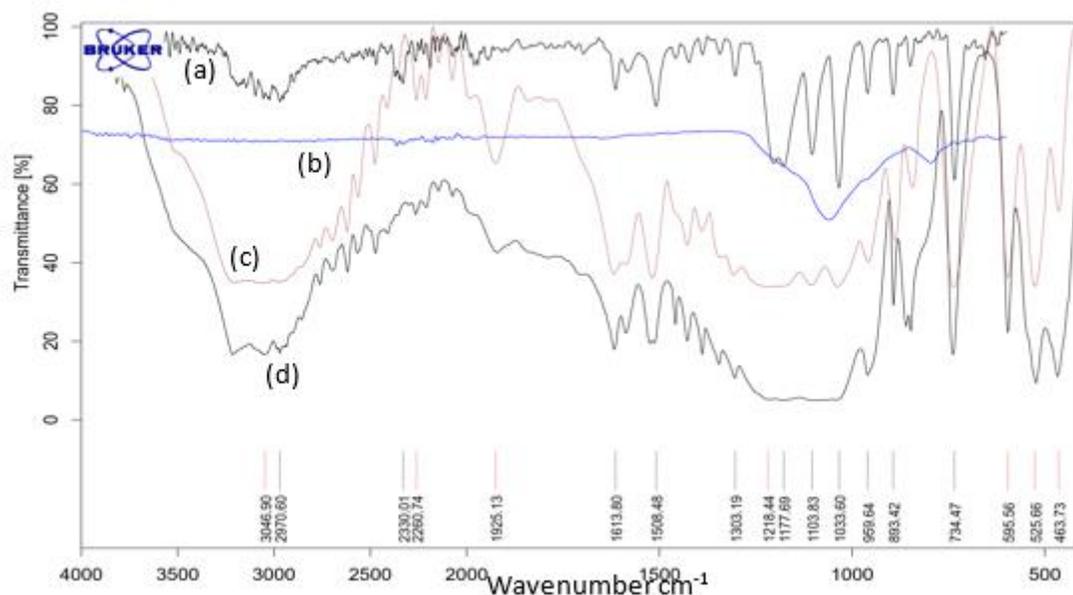


Fig. 1 FT-IR spectra of (a) Taurine, (b) Nano-Silica chloride, (c) Nano-SiO₂/Taurine and (d) reused Nano-SiO₂/Taurine

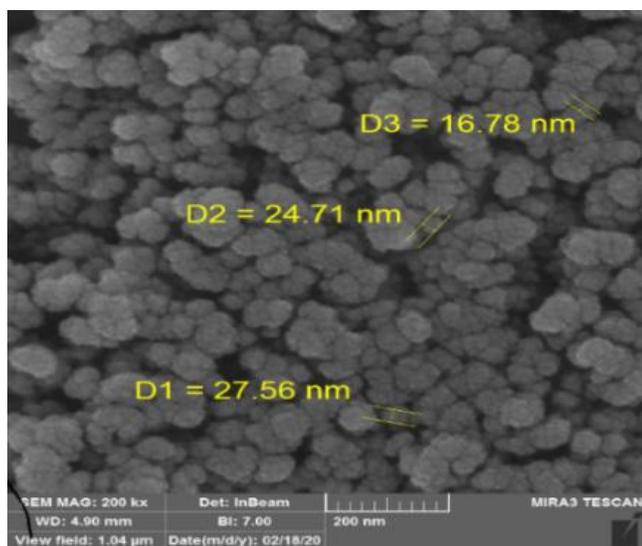


Fig. 2. FESEM image of Nano-SiO₂/Taurine

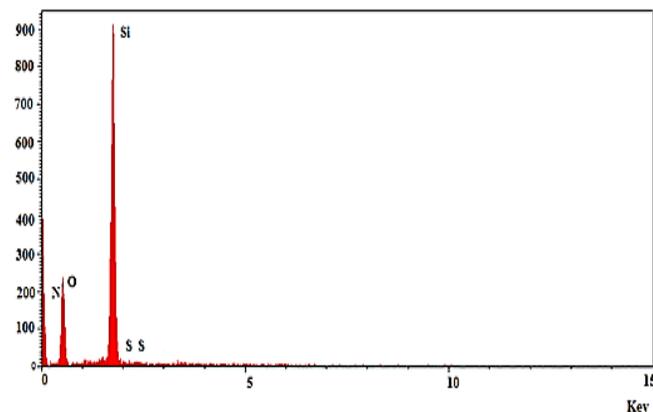


Fig. 3 EDS of Nano-SiO₂/Taurine

3.1.4. Mapping analysis

The elemental maps of Nano-SiO₂/Taurine show homogenous distribution of elements in its structure (**Fig. 4**).

3.1.5. TGA-DTA analysis

Fig. 5 shows the TGA-DTA analysis thermogram of Nano-SiO₂/Taurine in the range of 50–820 °C. The first decrease of weight (1 %) was assigned to the catalyst moisture removal (endothermic effect at 50–100 °C). The main weight loss stage in 100–300 °C (3%) is due to Nano-SiO₂/Taurine decomposition. At 820 °C, the char yield of the catalyst is 8%.

3.1.6. XRD analysis

According to the XRD patterns of Nano-SiO₂/Taurine (**Fig 6**, 2θ=10–80 °), a wide peak at 2θ = 23.525 °C with FWHM = 2.3616 shows the presence of nano silica gel in the catalyst. According to Scherrer equation, the particle size of catalyst is 3.4 nm.

3.2. Study of Nano-SiO₂/Taurine catalytic activity hexahydroquinoline

We have investigated the efficacy of various solvents and also solvent-free conditions on the condensation reaction of dimedone, ammonium acetate, 4-nitrobenzaldehyde and ethyl acetoacetate as a model reaction under various conditions (**Table 1**). According to obtained data, the best conditions were obtained by using 0.0^o g of Nano-SiO₂/Taurine under solvent free conditions at 80 °C (**Table 1**). We have examined the reaction of ethyl acetoacetate, ammonium acetate and dimedone with various aldehydes under optimized conditions (**Table 2**).

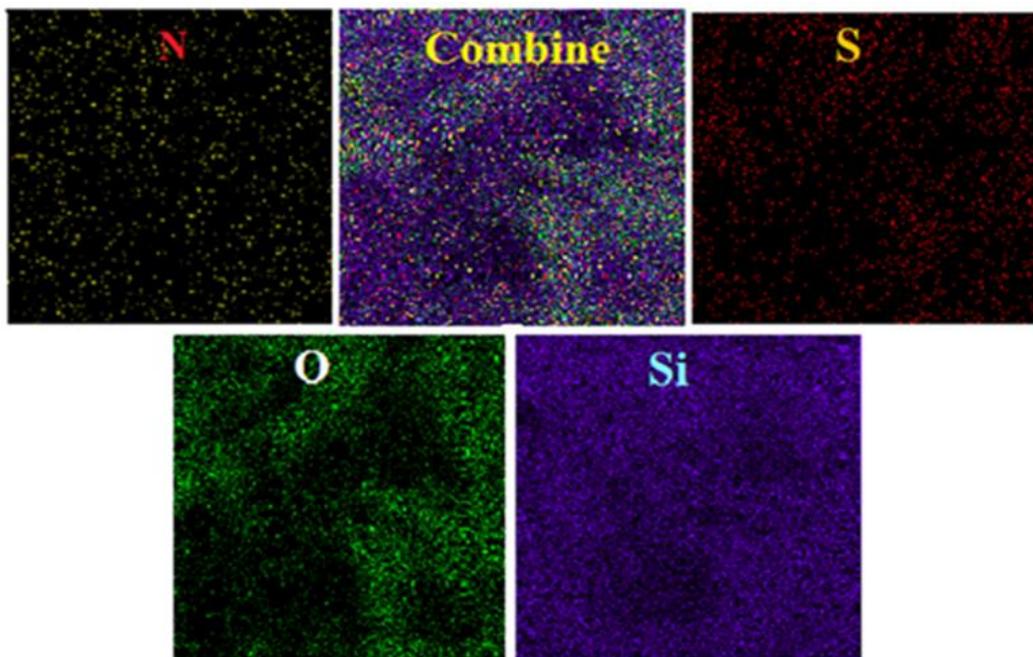


Fig. 4 Maps of Nano-SiO₂/Taurine

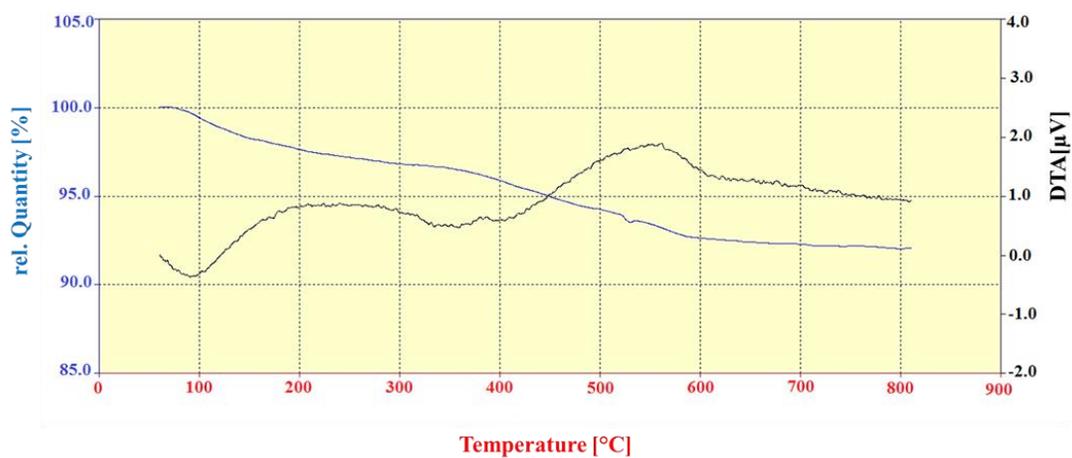


Fig. 5 TGA of Nano-SiO₂/Taurine

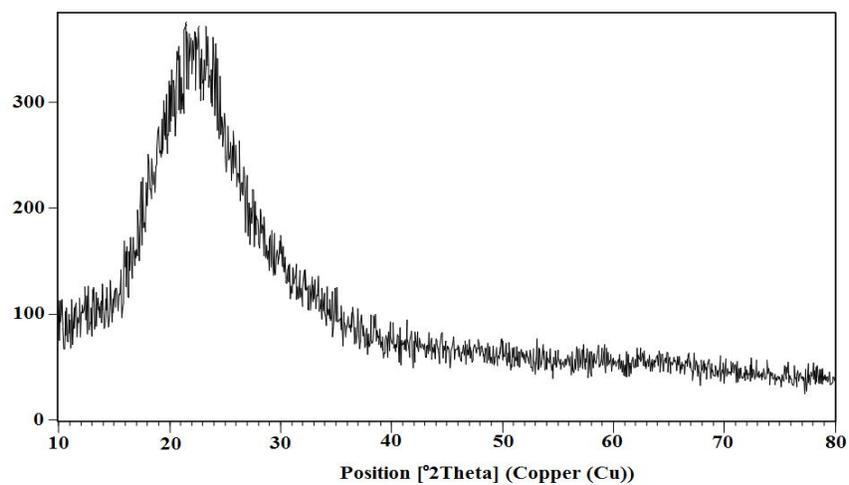
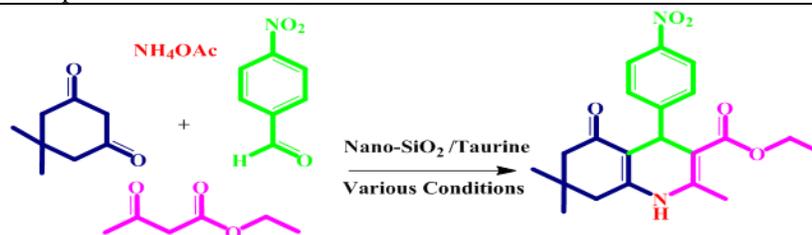
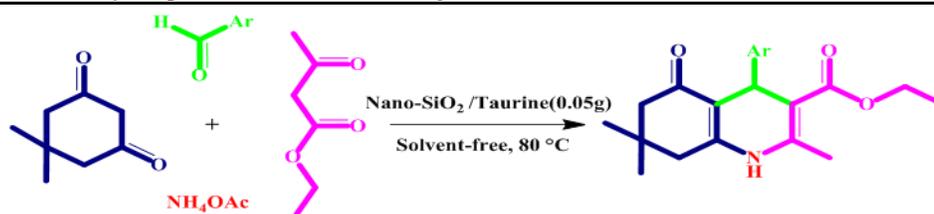


Fig. 6 XRD of Nano-SiO₂/Taurine

Table 1. The condensation reaction of dimedone (1 mmol), ammonium acetate (1 mmol), 4-nitrobenzaldehyde (1 mmol), ethyl acetoacetate (1 mmol) in the presence of Nano-SiO₂/Taurine under various conditions.

Row	Nano-SiO ₂ /Taurine (g)	Solv.	Cond.	Time (min)	Yield (%) ^a
1	0.0075	S.F.	80 °C	60	71
2	0.01	S.F.	80 °C	45	83
3	0.02	S.F.	80 °C	30	89
4	0.05	S.F.	80 °C	10	95
5	0.07	S.F.	80 °C	10	96
6	-	S.F.	80 °C	130	23
7	0.05	S.F.	R.T.	60	53
8	0.05	CH ₂ Cl ₂	Reflux	60	50
9	0.05	CH ₃ CN	Reflux	120	38
10	0.05	EtOH	Reflux	120	50
11	0.05	H ₂ O	Reflux	120	40
12	0.05	S.F.	70 °C	40	86
13	0.05	S.F.	90 °C	40	90

^aIsolated yields**Table 2.** Synthesis of hexahydroquinoline derivatives using Nano-SiO₂/Taurine at 80 °C under solvent-free condition^a

Row	Ar	Time (min)	Yield ^b (%)	M.P. (°C) Obs.	M.P. (°C) Rep. [Ref.]
1	4-NO ₂ -C ₆ H ₄	10	95	204-206	203-205 ^[42]
2	2-NO ₂ -C ₆ H ₄	15	93	207-209	208-210 ^[43]
3	4-Cl-C ₆ H ₄	20	89	245-247	245-246 ^[44]
4	4-Br-C ₆ H ₄	25	90	256-258	255-257 ^[45]
5	2-OMe-C ₆ H ₄	32	89	243-245	244-246 ^[46]
6	4-N(CH ₃) ₂ -C ₆ H ₄	35	88	222-225	224-227 ^[43]
7	2,4-(Cl) ₂ -C ₆ H ₃	25	89	244-246	243-245 ^[43]
8	2-OEt-C ₆ H ₄	15	90	218-220	217-220 ^[47]
9	C ₆ H ₅	25	90	200-203	203-205 ^[45]
10	2-Cl-C ₆ H ₄	25	91	202-205	207 ^[48]
11	2,6-(Cl) ₂ -C ₆ H ₃	32	87	243-245	244-245 ^[30]
12	2,4-(OMe) ₂ -C ₆ H ₃	25	86	234-236	235-238 ^[46]

^aThe amount ratio of dimedone (1 mmol), ammonium acetate (1 mmol), benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol).^bIsolated yields

A proposed mechanism for synthesis of hexahydroquinoline in presence of Nano-SiO₂/Taurine

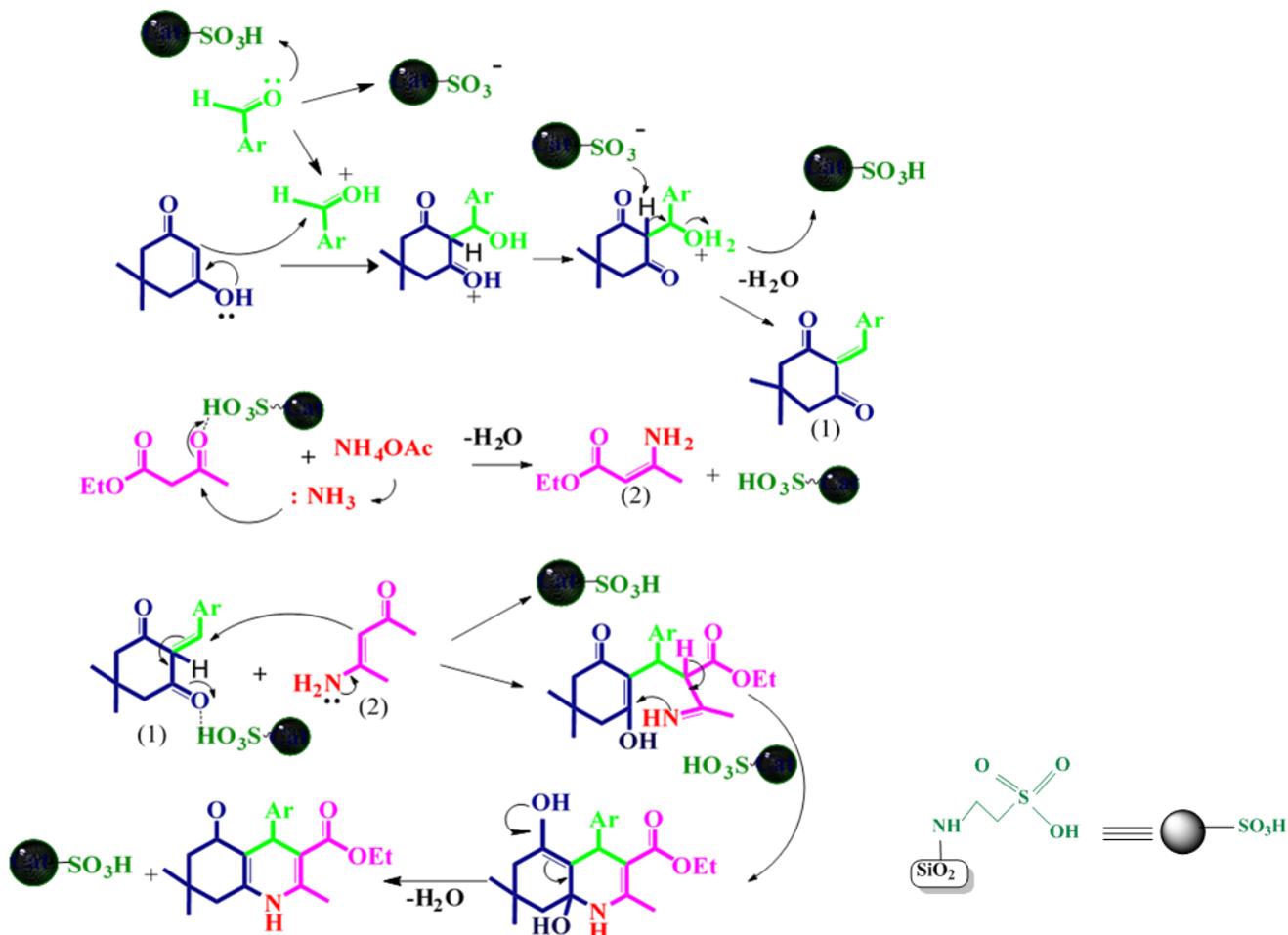
is shown in **Scheme 2**. First, the enol form of the dimedone reacts with the catalyst activated aldehyde

and forms enone **1**. NH_4OAc elaborates NH_3 which attacks to the ketone group of ethyl acetoacetate to form enamine **2**. Hexahydroquinoline derivatives are formed *via* conjugate addition of the enamine **2** to the enone **1** followed by cyclization.

The reusability of the catalyst is important for commercial applications. To examine the reusability of the catalyst, the condensation reaction of 4-nitrobenzaldehyde, ammonium acetate, ethyl acetoacetate and dimedone was studied. In the final step

of reaction, the catalyst was separated by simple filtration, washed with CH_2Cl_2 , dried at 50°C and reused for the same reaction (**Fig. 7**).

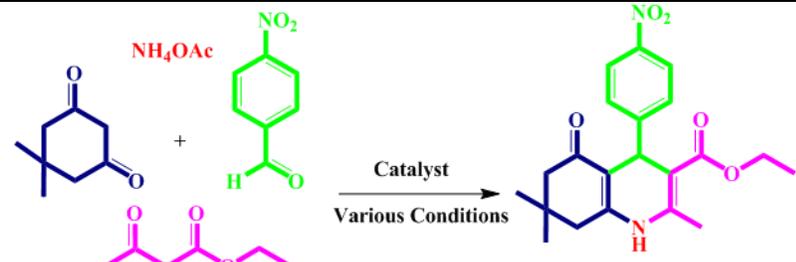
According to **Table 3**, the efficacy of the Nano- $\text{SiO}_2/\text{Taurine}$ was compared with some reported catalysts for the synthesis of hexahydroquinoline derivatives. Nano- $\text{SiO}_2/\text{Taurine}$ is comparable with the most of reported catalysts in yields and time of reaction.



Scheme 2. Mechanism for preparation of hexahydroquinoline in the presence of Nano- $\text{SiO}_2/\text{Taurine}$



Fig 7. Catalyst recycling experiment

Table 3. Synthesis of hexahydroquinoline derivatives in the presence of previously reported catalysts.


Row	Catalyst	Solvent	Conditions	Time (h)/ Yield ^a (%)
1	Yb(OTf) ₃	EtOH	R.T.	5/90[49]
2	p-TSA	EtOH	R.T.	2/93[50]
3	Organocatalysts	EtOH	R.T.	2/85[51]
4	Scolecite	EtOH	Reflux	0.75/93[52]
5	Hf(NPf ₂) ₄	C ₁₀ H ₁₈	60 °C	3/95[53]
6	SSA	S.F.	60 °C	0.75/92[54]
7	CSc(OTf) ₃	EtOH	R.T.	4/93[55]
8	DBH	S.F.	130 °C	0.5/90[56]
9	DCH	S.F.	130 °C	0.5/90[56]
10	Cs _{2.5} P _{0.5} W ₁₂ O ₄₀	S.F.	110 °C	6/92[57]
11	Nano-SiO ₂ /Taurine	S.F.	85 °C	0.15/95[this work]
12	Taurine	S.F.	85 °C	0.08/95[this work]

^aIsolated Yield

4. Conclusions

Finally, we successfully show the catalytic activity of Nano-SiO₂/Taurine in the hexahydroquinolines synthesis by Hantzsch reaction of dimedone, aldehydes, ethyl acetoacetate and ammonium acetate in the absence of any solvent. The present protocol is simple, eco-friendly and efficient. The hexahydroquinolines were produced in short times and good yields. Also Nano-SiO₂/Taurine has considerable benefits such as reusability and stability.

Acknowledgments

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