ORIGINAL PAPER



# Nano-sawdust-OSO<sub>3</sub>H as a new, cheap and effective nanocatalyst for one-pot synthesis of pyrano[2,3-*d*]pyrimidines

B. Sadeghi<sup>1</sup> · M. Bouslik<sup>1</sup> · M. R. Shishehbore<sup>1</sup>

Received: 22 November 2014 / Accepted: 29 April 2015 © Iranian Chemical Society 2015

Abstract An atom-efficient, three-component synthetic methodology has been developed for the preparation of biologically important pyrano[2,3-d]pyrimidines using nano-sawdust-OSO<sub>3</sub>H as a new catalyst. The reaction involves the use of barbituric acid or thiobarbituric acid, malononitrile and aldehydes. A wide range of aldehydes is compatible in this reaction, producing excellent yields in short time. The morphology of nanocatalyst (nanosawdust-OSO<sub>3</sub>H) was observed using a scanning electron microscopy (SEM). The decomposition steps and thermal stability of the catalyst were investigated by thermal analysis techniques (TGA/DTG). The sawdust-OSO<sub>3</sub>H surface was studied by energy dispersive X-ray spectroscopy (EDX) method to find out the chemical composition. Also, the vibrational spectrum analysis (FT-IR) of the catalyst has been performed.

**Keywords** Pyranopyrimidines  $\cdot$  Thiobarbituric acid  $\cdot$  Malononitrile  $\cdot$  Green chemistry  $\cdot$  Nano-sawdust-OSO<sub>3</sub>H

### Introduction

Recently, multi-component, one-pot synthesis have become one of the most attractive reactions due to their vast applications such as high selectivity, mild reaction condition and construction of several bonds in a single operation. These reactions are widely applied in pharmaceutical chemistry for producing different structures and combinatorial

B. Sadeghi sadeghi@iauyazd.ac.ir libraries for drug discovery [1]. Pyrano[2,3-*d*]pyrimidines are some examples of multi-component reactions. Pyrimidine derivatives are attractive, because they generally show biological properties such as antibacterial, antitumor and analgesic activities [2–4].

In recent years, there has been growing interest in finding inexpensive and effective solid acid nanocatalyst such as nanocrystalline  $\text{TiO}_2\text{-}\text{HCIO}_4$  [5], nano- $\text{TiCl}_4\text{·}\text{SiO}_2$  [6–9] nano- $\text{SnCl}_4\text{·}\text{SiO}_2$  [10, 11] nano- $\text{BF}_3\text{·}\text{SiO}_2$  [12–15]  $\text{HCIO}_4$ -SiO<sub>2</sub> nanoparticles [16] and nano silica sulfuric acid [17– 23]. Sawdust is one of the most common materials that used for various chemical industries such as removing pollutants from water [24], the color removal from textile industry [25], the removing cationic, anionic and disperse dyes from aqueous solution [26] and the  $\text{CuFe}_2\text{O}_4$ /sawdust composite was used for removal of cyanine acid blue from aqueous solution [27].

The sawdust consists of cellulose, lignin and hemicelluloses that cellulose is composed of a long chain of glucose molecules, lignin is a complex polymer composed of phenylpropane units, and hemicelluloses are branched polymers composed of xylose, arabinose, galactose, mannose, and glucose [28–31]. The lignocellulosic material of sawdust includes a wide variety of hydroxyl groups that can be used as active sites for the preparation of solid acid catalysts.

In this study, the sawdust has been used as adsorbent for the preparation of nano-sawdust- $OSO_3H$  whose average size is small and is well distributed. The presence of new functional groups on the surface of sawdust- $OSO_3H$ resulted in a dramatic increase of surface polarity and acidity, thereby improving the catalytic efficiency of the nano-sawdust- $OSO_3H$ .

Recently some conditions and catalysts such as microwave irradiation [32], ionic liquids [33], ultrasonic

<sup>&</sup>lt;sup>1</sup> Department of Chemistry, Yazd Branch, Islamic Azad University, P.O. Box 89195-155, Yazd, Iran

irradiation [34], diammonium hydrogen phosphate [35], L-proline [36],  $H_{14}[NaP_5W_{30}O_{110}]$  [37], sulfonic acid nanoporous silica (SBA-Pr-SO<sub>3</sub>H) [38] and choline chloride·ZnCl<sub>2</sub> [39] have been applied for the pyrano[2,3-*d*]pyrimidine synthesis. Although many of the reported methods are effective, but, some of them suffer from disadvantages such as harsh reaction conditions, use of hazardous solvents, long reaction times, complex working and purification procedures, long volume of catalyst loading and moderate yields. Therefore, the development of a simple, mild and efficient method is still needed. In continuation of our previous research on the use of solid acids in organic synthesis [14–21], the nanosawdust-OSO<sub>3</sub>H as a new catalyst has been applied for the synthesis of pyrano[2,3-*d*]pyrimidine derivatives.

# Experimental

Melting points were determined with an Electrothermal 9100 apparatus. IR spectra were recorded on a Shimadzu IR-470 spectrometer. <sup>1</sup>H NMR spectra were obtained using Bruker Avance 300. The morphologies of the nanoparticles were observed using FESEM of a MIRA3 TESCAN microscope with an accelerating voltage of 15 kV. Thermogravimetric



analysis was performed using a TG 209 F1 (Netzsch Germany). The IR spectrum of the catalyst was recorded using a model Bruker Tensor 27 FT-IR operating in the range 400–4000 cm<sup>-1</sup>. The EDX analysis was done using a SAMx analyser. The chemicals for this work were purchased from Fluka and were used without further purification.

### Synthesis of nano-sawdust-OSO3H

The sawdust was collected from sawmill in Farrokhi city, Iran. Sawdust was washed several times to remove adhering dirt and then dried at 60 °C for 24 h. The dried sawdust was ground to pass through a 1 mm sieve and labeled as sawdust [27]. The nano-sawdust-OSO<sub>3</sub>H was prepared by combination of chlorosulfonic acid (2.33 g) drop by drop over 10 min via a syringe to sawdust powder (6 g) in a 50 ml flask at 0 °C. The reaction mixture was then stirred and then after 30 min, the ashy powder was separated and washed with diethyl ether. The obtained solid was dried in an oven at 60 °C for 4 h and then pulverized at the mortar. The size of particles was obtained below 100 nm using SEM.

# General procedure for the preparation of compounds 4a-l

Nano-sawdust-OSO<sub>3</sub>H (0.02 g) was added to a stirred mixture of the aromatic aldehyde (1 mmol), malononitrile (1 mmol) and barbituric acid or thiobarbituric acid (1 mmol) in EtOH (5 mL). The materials were mixed and refluxed for the appropriate time. The progress of the reaction was followed by TLC (*n*-hexane:ethyl acetate 3:1). After completion of the reaction, the mixture was filtered to remove the catalyst. After evaporation of the solvent, the crude product was re-crystallized from hot ethanol to obtain the pure compound.

## **Results and discussion**

In continuation of our investigation into the application of solid acids in organic synthesis, we studied the application of sawdust as a green, inexpensive and available surface to synthesis of solid acid nanocatalyst. In this study,





sawdust-OSO<sub>3</sub>H nanoparticles were prepared and characterized (Fig 1). The catalytic activity of nanoparticles was investigated for synthesis of pyrano[2,3-d]pyrimidines derivatives, by the condensation of a aldehyde **1a-1**, malononitrile **2** and barbituric acid or thiobarbituric acid (**3a,b**) (Scheme 1).

The morphology and size of sawdust and sawdust- $OSO_3H$  were observed by SEM images. As shown in Fig. 2, the size of nano-sawdust- $OSO_3H$  is below 100 nm.



Fig. 2 SEM micrograph of nano-sawdust-OSO<sub>3</sub>H

Table 1 Chemical analysis of sawdust and sawdust-OSO3H

	Sawdust		Sawdust-OSO <sub>3</sub> H		
Element	W %	A %	W %	A %	
С	56.85	65.35	42.98	52.68	
0	39.89	34.42	45.85	42.19	
S	-	-	11.17	5.13	

Fig. 3 EDX of sawdust

The results of EDX analyses of the sawdust and sawdust-OSO<sub>3</sub>H are given in Table 1.

Chemical analysis of sawdust gave carbon and oxygen as the major elements with small amounts of gold (Fig. 3). The elemental analysis by EDX identified the high peak of sulfur and carbon in the nano-sawdust-OSO<sub>3</sub>H (Fig. 4). Presence of sulfur in the EDX indicates the chemical interaction of chlorosulfonic acid with the surface of sawdust. Sawdust-OSO<sub>3</sub>H nanoparticles were prepared according to procedure as shown in Scheme 2.

Sawdust-OH + ClSO<sub>3</sub>H  $\rightarrow$  Sawdust-OSO<sub>3</sub>H + HCl

The thermal decomposition of the sawdust and nanosawdust-OSO<sub>3</sub>H has been studied using a combination of thermogravimetry (TGA) and derivative thermogravimetry (DTG) methods up to 800 °C under nitrogen atmosphere. The structural transformation is observed by TG curves which are supported by DTG studies. Thermal analysis has proved to be useful in determining the structure of nanosawdust-OSO<sub>3</sub>H and the thermal stability as well as the decomposition mode under controlled heating rate. Three thermal decomposition mass loss steps are observed for the nano-sawdust-OSO<sub>3</sub>H (a) 14.02 % mass loss at 142 °C related to the loss of the moisture, (b) 12.34 % mass loss at 190 °C related to the further loss of the moisture and (c) 37.45 % mass loss at 440 °C related to the decomposition of cellulose and lignin (Fig. 5).

Figure 6 is the TG and derivative TG (DTG) profiles showing the thermal degradation characteristics of sawdust at a heating rate of 30 ml/min. The initial step of degradation at 66 °C corresponds to 4.24 % mass loss, perhaps due to the removal of moisture. The second step of decomposition in DTG curve shows mass losses at 343 °C and 61.11 % perhaps due to the degradation hemicellulose units. This degradation indicates that the hemicellulose







 $Sawdust-OH + ClSO_{3}H \rightarrow Sawdust-OSO_{3}H + HCl$ 

#### Scheme 2 Preparation of nano-sawdust-OSO<sub>3</sub>H

units reacted with the chlorosulfonic acid in the nanosawdust-OSO<sub>3</sub>H. The major mass loss of nearly 82 % is due to the devolatilization of the hemicelluloses, cellulose and lignin as shown in Fig. 6. The mass loss of 19.38 % at the third step associated with  $T_{DTG}$  peak at 443 °C corresponds to the mass loss of the decomposition of cellulose. The lignin degradation is observed as a shoulder of the final peak at 495 °C.

Also, the acid capacity of nano-sawdust- $OSO_3H$  as a criterion of H<sup>+</sup> sites was determined using acid–base titration. The value of 0.78 was obtained.

In FT-IR spectrum of nano-sawdust- $OSO_3H$  (Fig. 7), the hydroxyl bands of sawdust and sulfonic acid appeared at

3428 cm<sup>-1</sup>. The C–H stretching vibrations of the aliphatic systems for cellulose and hemicelluloses units observed at 2932 cm<sup>-1</sup>. The C=C stretching vibrations of the phenyl rings in the lignin unit observed at 1645 cm<sup>-1</sup>. The symmetric and asymmetric O=S=O stretching vibrations appeared at 1066 and 1232 cm<sup>-1</sup>. The S–O stretching vibrations observed at 850 cm<sup>-1</sup>.

In order to determine the optimum quantity of nanosawdust-OSO<sub>3</sub>H, the reaction of barbituric acid, malononitrile and benzaldehyde was carried out under reflux in ethanol using different quantities of nano-sawdust-OSO<sub>3</sub>H. As shown in Table 2, 0.02 g of nano-sawdust-OSO<sub>3</sub>H gives an excellent yield in 15 min.

To study the scope of the reaction, a series of aldehydes with barbituric acid or thiobarbituric acid and malononitrile were examined by nano-sawdust- $OSO_3H$  as catalyst. The results are shown in Table 3. In all cases, aromatic aldehyde substituted with either electron-donating









Fig. 7 FT-IR spectrum of nano-sawdust-OSO $_3$ H

Table 2	Optimization of the
reaction	conditions for synthesis
of <b>4a</b>	

Entry	Catalyst (amount) Solvent/cond	ition Time (min)	Yield
1	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) CH <sub>2</sub> Cl <sub>2</sub> /reflux	x 15	Trace
2	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) EtOH/reflux	15	94
3	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) CH <sub>3</sub> CN/reflu	x 15	Trace
4	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) DMF/reflux	15	47
5	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) H <sub>2</sub> O/reflux	15	83
6	Nano-Sawdust-OSO <sub>3</sub> H (0.01 g) EtOH/reflux	15	73
7	Nano-Sawdust-OSO3H (0.03 g) EtOH/reflux	15	95
8	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) EtOH/reflux 2nd run	15	92
9	Nano-Sawdust-OSO <sub>3</sub> H (0.02 g) EtOH/reflux 3rd run	15	87

**Table 3** Synthesis ofpyrano[2,3-d]pyrimidines

Entry	Ar	X	Product	Time (min)	Yield <sup>a</sup>	M.P. (°C) Ref. <sup>b</sup>
1	C <sub>6</sub> H <sub>5</sub>	0	4a	15	94	206–208 (208–210) [32]
2	4-ClC <sub>6</sub> H <sub>4</sub>	0	4b	8	91	232–234 (231–232) [39]
3	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	0	4c	10	86	225–227 (226–227) [38]
4	2-ClC <sub>6</sub> H <sub>4</sub>	0	4d	20	87	212–214 (213–215) [32]
5	$3-NO_2C_6H_4$	0	4e	8	93	259–261 (262–263) [34]
6	$4-NO_2C_6H_4$	0	4f	10	92	230–232 (237–238) [34]
7	4-BrC <sub>6</sub> H <sub>4</sub>	0	4g	12	85	228–230 (230–231) [35]
8	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	0	4h	12	87	272–274 (279–280) [39]
9	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	S	4i	22	83	120–122 (116–118) [39]
10	$3-NO_2C_6H_4$	S	4j	20	72	230–232 (230–233) [39]
11	3-ClC <sub>6</sub> H <sub>4</sub>	S	4k	25	69	236–237 (234–237) [39]
12	$4-NO_2C_6H_4$	S	41	20	75	236–238 (232–235) [39]

Ratio of aldehyde (mmol): barbituric acid or thiobarbituric acid (mmol): malononitrile (mmol): catalyst (g) is 1:1:1:0.02

<sup>a</sup> Isolated yield

<sup>b</sup> All products are known and were identified by their melting points, IR and <sup>1</sup>H NMR spectra





or electron-withdrawing groups underwent the reaction smoothly and formed products in approving yields.

With the above-mentioned results in hand, a plausible mechanism of this reaction was proposed in Scheme 3. The initiation step of this chain process was begun with the interaction of aldehyde 1 and nano-sawdust-OSO<sub>3</sub>H as a

solid acid catalyst. The subsequent step was Knoevenagel condensation between the activated aldehyde and malononitrile **2** to form intermediate **5**. Then the Michael addition of barbituric acid or thiobarbituric acid (**3a,b**) to intermediate **5** would furnish intermediate **6**. Finally, the product **4** was obtained by an intramolecular cyclization and tautomerism. **Table 4** Comparison of nano-sawdust-OSO<sub>3</sub>H and various catalyst in the synthesis of pyrano[2,3-*d*]pyrimidine derivatives

Entry	Catalyst	Solvent	Condition	Time	Yield	Ref.
1	_	H <sub>2</sub> O	MW	3–5 min	86–94	[32]
2	[BMIm]BF <sub>4</sub>	[BMIm]BF <sub>4</sub>	90 °C	3–5 h	82–95	[33]
3	_	$H_2O$	US	1–3 h	62–78	[34]
4	DAHP <sup>a</sup>	EtOH	r.t	2 h	71-81	[35]
5	L-proline	EtOH	r.t	30-150 min	68-88	[36]
6	H <sub>14</sub> [NaP <sub>5</sub> W <sub>30</sub> O <sub>110</sub> ]	EtOH	Reflux	3060 min	85–90	[37]
7	SBA-Pr-SO <sub>3</sub> H	_	140 °C	5–45 min	30–90	[38]
8	Choline chloride·ZnCl <sub>2</sub>	EtOH	US	30–240 s	42–98	[ <mark>39</mark> ]
9	Nano-sawdust-OSO3H	EtOH	Reflux	8–25 min	69–94	This work

<sup>a</sup> 3-Deoxy-D-arabino-heptulosonate-7-phosphate

In order to establish better catalytic activity of nanosawdust-OSO<sub>3</sub>H, the synthesis of pyrano[2,3-d]pyrimidine derivatives was compared with other catalysts reported in literature [32-39]. As shown in Table 4, synthesis of these compounds catalyzed by nano-sawdust-OSO<sub>3</sub>H in EtOH offers production of the corresponding products in shorter time, much efficient yield and milder condition is done, while other methods require more amount of catalyst and longer reaction time for synthesis of pyrano[2,3-d]pyrimidines.

### Conclusion

The present investigation shows that nano-sawdust-OSO<sub>3</sub>H a capable nanocatalyst to be used for pyrano[2,3-*d*]pyrimidine synthesis via one-pot reaction of aldehydes, malononitrile and barbituric acid or thiobarbituric acid. Nano-sawdust-OSO<sub>3</sub>H was successfully prepared and characterized using TGA/DTG, EDX, FT-IR and SEM. Prominent among the advantages of this method are such as shorter reaction times, simple work-up, affords excellent yield, and re-usable for a number of times without appreciable loss of activity. The present method does not involve any hazardous organic solvent. Therefore, this procedure could be classified as green chemistry.

**Acknowledgments** The research Council of the Islamic Azad University of Yazd is gratefully acknowledged for the financial support for this work.

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