Iranian Journal of Organic Chemistry Vol. 11, No. 4 (2019) 2719-2724

Nano-sawdust-$OSnCl_3$: An efficient,versatile and novel reagent for the one-pot synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives

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Received: August 2019; Revised: September 2019; Accepted: October 2019

Abstract: Sawdust contains a high level of phenolic and cellulose compounds; it can be used as a substrate for the preparation of solid acid catalysts. In this work, the novel nano-sawdust-$OSnCl_3$ catalyst was synthesized via preparing Sawdust, produced inYazd, as a support followed by treatment with tintetrachloride ($SnCl_4$) in the research laboratory of the faculty of Chemistry, islamicazad university, Yazd branch and identified by fourier transform infrared spectroscopy (FT-IR), field emission scanning electron microscopy (FE-SEM) and X-ray diffraction spectroscopy (EDX). The size of the nano-sawdust-$OSnCl_3$nanocatalystisbelow 100 nm whichwas shown by a scanning electron microscope. The catalytic activity of the solid acid catalyst has been successfully examined in a one-pot, three-component condensation reaction of an aldehyde, malononitrileand kojic acid in refluxing ethanol to furnish 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives. Consequently, pyran annulated heterocycles were obtained. The proposed approach has some advantagessuch as excellent yields, mild reaction conditions, short reaction times and eco-friendly.

Keywords: Nano-sawdust-$OSnCl_3$, Pyran derivatives, Kojic acid, Green biosynthesis, Solid acid.

Introduction

One of the most significant researches, nanoscience and nanotechnology are improvement frontiers in modern science. Due to the unique dimensions and size, physical properties, easy recyclabilityand large specific surface area of nanostructures [1], significantattentionis given tothe nanoparticles in a wide variety ofapplicationsincluding catalysis, biomedical use, energy storage, enzyme encapsulation, photonics, and drug delivery [2-5]. During the past years, the use of recyclable heterogeneous catalyst (prepared by supporting solid support via homogenous precursors) has received significant importance in organic chemistry [6].

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The sawdust is an agricultural by-product and would be an excellent bio-resource for preparing solid acids because of its high absorption ability, low cost, and easy sustainability [7]. Much like other agricultural lignocellulolysic biomass, such as coconut shell [8], sawdust [9], peanut shell [10] sawdust ismainly composed of lignin, cellulose and hemicelluloses. Consequently, the main active sites of sawdust are a wide variety of hydroxyl groups that can be used for the preparation of solid acid catalysts [9]. The multi-component (three reactant or more) reactions (MCRs) have been developed in organic chemistry and modern drug discovery owing to the generation of biologically active products [11]. In addition, high atom-economy, cost-effectively, energy saving, lower reaction time and raw materials, structural complexity and environmentally benign synthesis of chemically and biologically important organic frameworks are the most

advantageous features encountered in MCRs [12-14]. 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives are some examples of multi-component synthesis thatcompose of three starting materials reacting in a single flask. Functionalized oxygen-heterocycles are of interest due to their potential medicinal and biological activity. Polyfunctionalized pyranderivatives are oxygen-containing heterocycles that are common structural subunits ina variety of important biological effects such as antimicrobial, antifungal, anticancer, antioxidant, anti-tumor and anti-HIV [15-19]. Considering the importance of biologically active pyrantemplates, an efficient and environmentally benign approach was developed for the synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives *via* one-pot three-component condensation of an aldehydes, 5-hydroxy-2-hydroxymethyl-4*H*-pyran-4-one (kojic acid) and malononitrile in the presenceofnano-sawdust-$OSnCl_3$ as a readily available, highly efficient, recyclable and versatile catalyst in EtOH as an inexpensive and non-toxic medium.

Result and Discussion

In association with our recent achievement on the design of innovative recyclable heterogeneous nanocatalystsfor the production of heterocycles [8-10, 22], herein the synthesis of nano-sawdust-$OSnCl_3$as highly efficient novel heterogeneous nano-catalyst for the preparation of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives was studied. The novel nano-sawdust-$OSnCl_3$ catalyst was simply prepared as presented in Scheme 1.

Sawdust-OH + $SnCl_4$ → Sawdust-$OSnCl_3$ + HCl

Scheme 1. Preparation of nano-sawdust-$OSnCl_3$

As presented in Figure **1**, the average particle size of nano-sawdust-$OSnCl_3$ and its distribution were analyzed by FE-SEM. As shown in FE-SEM, the sizes of nano-sawdust-$OSnCl_3$ are below100 nm.On the other hand,the spots on the sawdust surface can be attributed to tin tetrachloride groups (Figure **1b**). The spot EDX results indicates these observations.

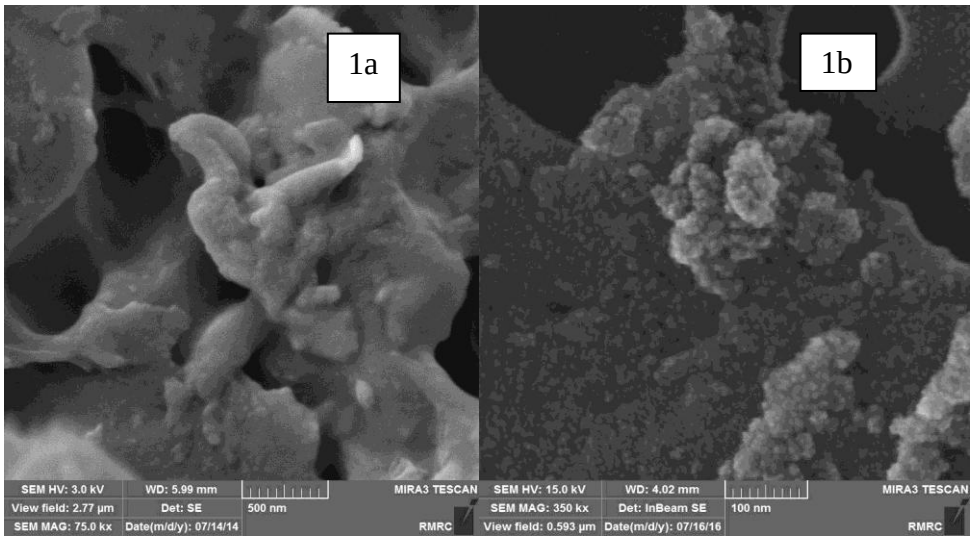


Figure 1: (**a**)SEM micrograph of sawdust (**b**) SEMmicrograph of nano-sawdust-$OSnCl_3$

As could be seen in Figure **2**, elemental composition of the sawdust and nano-sawdust-$OSnCl_3$ was investigated by EDX analysis which is shown in Table 1. Sawdust is composed of C and O (Figure **2a**) while nano-sawdust-$OSnCl_3$ (Figure **2b**) is composed of C, O, Cl and Sn. Presence of tin and chlorine in the EDX indicates the chemical interaction of tin tetrachloride with the surface of sawdust.

Table 1: Chemical analysis of Sawdust and nano-sawdust-$OSnCl_3$

Element	Sawdust (W%)	nano-sawdust-$OSnCl_3$ (W%)
C	56.85	40.27
O	39.89	26.46
Cl	-	18.20
Sn	-	15.07

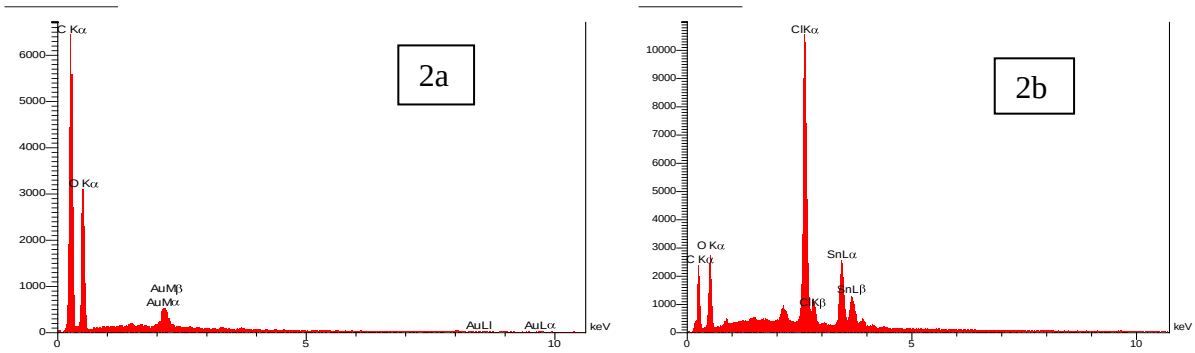


Figure 2: (**a**) EDX of Sawdust and (**b**) EDX of nano-sawdust-$OSnCl_3$

A broad peak for the hydroxyl bands of cellulose units at 3422 cm^{-1} is exhibited in FT-IR spectrum of nano-sawdust-$OSnCl_3$ (Figure **3**). The C-H stretching vibrations of the aliphatic systems for cellulose and hemicelluloses unitsare observed at 2925 cm^{-1}. The absorption bands at nearly 1450 and 1643 cm^{-1} indicate the C═C bonds in phenyl rings of lignin unit. The Sn-O and Sn-Cl stretching vibrationsare observed at 1543 and 1044 cm^{-1}. The FTIR data and the presence of these elements in the EDX vividly confrim the actual event of chemical interaction of tintetrachloride with the surface area of saw dust.

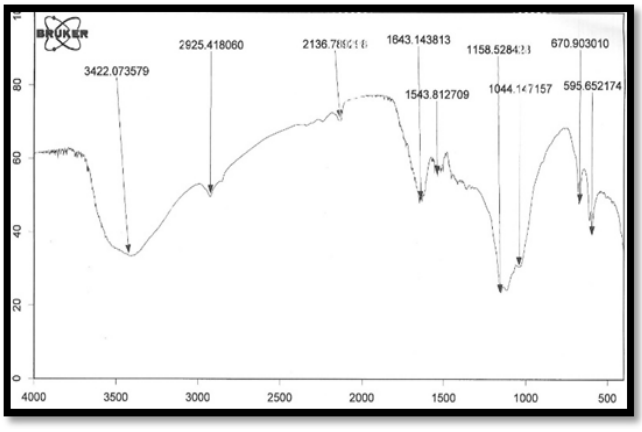
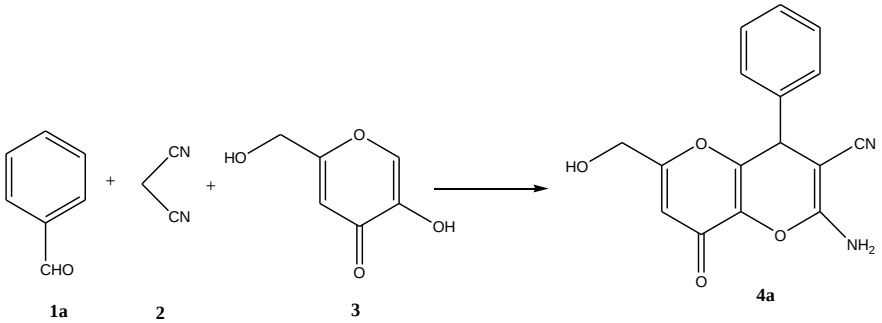


Figure 3: FT IR spectrum of nano-sawdust-$OSnCl_3$ catalyst

After synthesis and characterization of the nano-sawdust-$OSnCl_3$ as a novel, stable and eco-friendly nano catalyst, the performance of nano-sawdust-$OSnCl_3$ in the synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrilederivativesis investigated. First, a test model reaction is done with 1 mmol benzaldehyde, 1 mmol kojic acid and 1 mmol malononitrile in the existence of various amounts of nano-sawdust-$OSnCl_3$ using different solvents. The results of these experiments are reported in Table **2**. In the absence of nano-sawdust-$OSnCl_3$, desired product is not formed (Table **2**, entry 1). The favorable result is found with 4mg nano-sawdust-$OSnCl_3$ in refluxing ethanol (Table **2**, entry 2). To regenerate the nano-sawdust-$OSnCl_3$, after completion of the reaction, the mixture is filtered and recrystallized from hot ethanol; catalyst is separated and washed with ethanol and then dried to obtain the solid remainder. This procedureis repeated for two cycles and the yield of product **4a**does not change significantly (Table **2**, entries 9, 10). A remarkable advantage of this technique is that the catalyst can be recovered at the end of the reaction and can be used several times without losing its activity. To regenerate the nano-sawdust-$OSnCl_3$, after completion of the reaction, the mixture was filtered and recrystallized from hot ethanol; catalyst was separated and washed with *n*-hexane and then dried to obtain the solid remainder. This procedure repeated for two cycles

and the yield of product **4a** did not change significantly (Table **2**, entries 11, 12).

Table 2. Optimization of the reaction conditions for synthesis of **4a**



Entry	Catalyst (mg)	Solvent	Time (min)	Yield[b] (%)
1	nano-sawdust-OSnCl$_3$ (0)	EtOH	120	0
2	nano-sawdust-OSnCl$_3$ (4)	EtOH	20	94
3	nano-sawdust-OSnCl$_3$ (4)	*n*-Hexane	20	Trace
4	nano-sawdust-OSnCl$_3$ (4)	H_2O	20	52
5	nano-sawdust-OSnCl$_3$ (4)	CH_3CN	20	45
6	nano-sawdust-OSnCl$_3$ (2)	EtOH	20	79
7	nano-sawdust-OSnCl$_3$ (3)	EtOH	20	82
8	nano-sawdust-OSnCl$_3$ (5)	EtOH	20	95
9	nano-sawdust-OSnCl$_3$ (4) 2nd run	EtOH	20	92
10	nano-sawdust-OSnCl$_3$ (4) 3rd run	EtOH	20	89

[a] Reaction condition: benzaldehyde (1 mmol), malononitrile (1 mmol) and kojic acid (1 mmol) under reflux in various solvents.
[b] Isolated yields.

After optimizing tests, thereaction of kojic acid and malononitrile with a variety of substituted aldehydesis conducted under the optimized condition for the synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives (Scheme **2**). Results have been displayed in Table 3 indicating that different aromatic aldehydeswhich are substituted by either electron-donating or electron-withdrawing groups could react with kojic acid and malononitrile smoothly and give products in excellent yield. A detailed reaction mechanism for the synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrilederivatives **(4)** using nano-sawdust-OSnCl$_3$, which act as a solid acid catalysis in all steps is outlined in Scheme 3. Initially, nano-sawdust-OSnCl$_3$ activates the malononitrile and aldehyde to form the olefin **(5)**. Then, the Michael addition of kojic acid **(3)** with olefin **(5)** in the presence of nano-sawdust-OSnCl$_3$gives intermediate **(7)**, which then makes the inner molecular ring **(8)** to be formed after a tautomeric proton shift in the existence of catalyst to produce the corresponding product **(4)**

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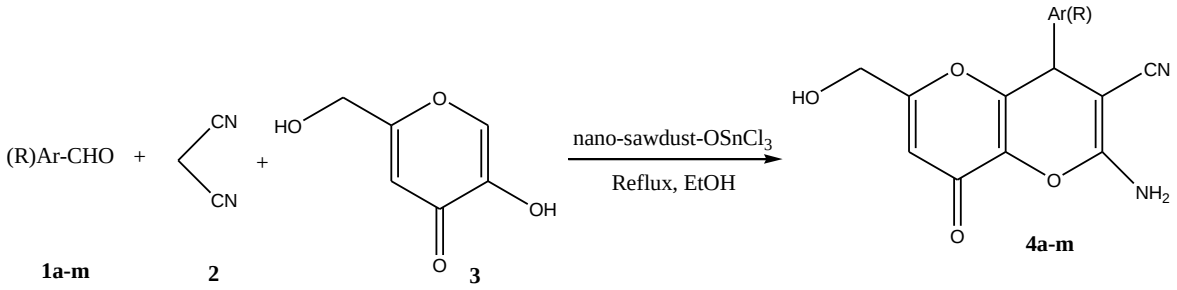


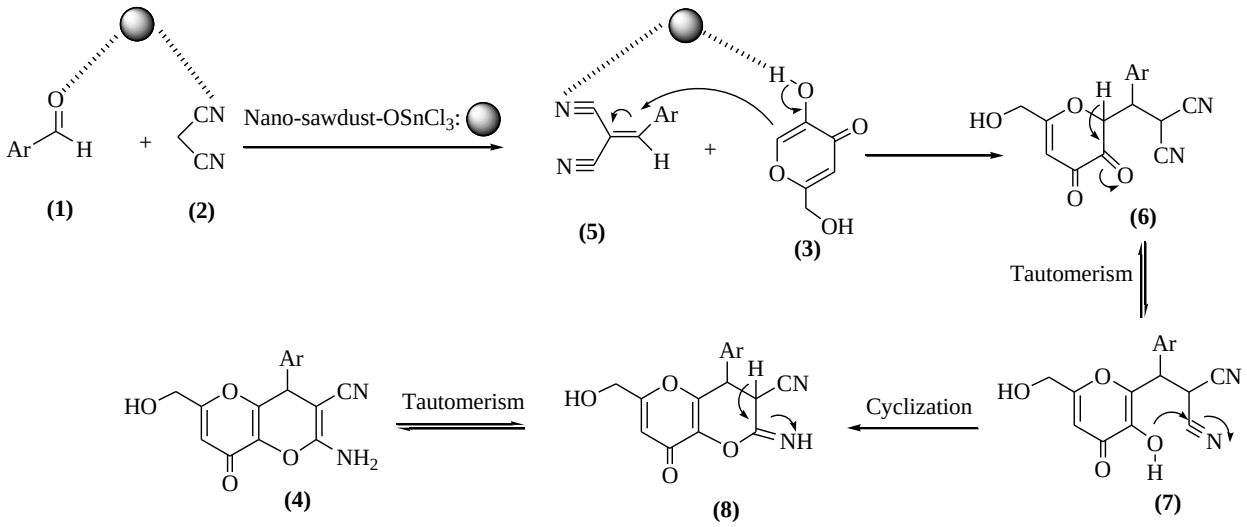
1a-m **2** **3** **4a-m**

Scheme 2. Synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives in the presence of nano-sawdust-$OSnCl_3$ as a catalyst

Table 3. Synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives [a]

Entry	Ar	Product[b]	Time(min)	Yield[c]	M.P.(ºC)[Ref.]
1	C_6H_5	4a	20	94	220-222 [20]
2	2-Cl-C_6H_4	4b	20	93	211-213 [21]
3	4-F-C_6H_4	4c	20	92	248-250 [20]
4	3-Br-C_6H_4	4d	20	91	243-245 [21]
5	3-CH_3-C_6H_4	4e	25	90	220-222 [21]
6	3-NO_2-C_6H_4	4f	15	95	258-260 [21]
7	4-CN-C_6H_4	4g	15	96	240-242[21]
8	2,4-Cl_2-C_6H_3	4h	20	90	239-241 [21]
9	2-OH-3-CH_3O-C_6H_3	4i	25	92	249-251[21]
10	4-Cl-3-NO_2-C_6H_3	4j	15	97	246-248[21]
11	3,5-$(CH_3O)_2$-C_6H_3	4k	30	87	271-273 [21]
12	4-Pyridyl	4l	30	89	233-235[20]
13	n-Butyr	4m	30	90	184-186 [21]

[a] Reaction condition: aldehyde (1 mmol), malononitrile (1 mmol),kojic acid (1 mmol) and nano-sawdust-$OSnCl_3$ (4 mg) in ethanol (5 mL) under reflux condition.
[b] Isolated yields.



Scheme 3: Suggested mechanism for the synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitriles in the presences of nano-sawdust-$OSnCl_3$ as a catalyst

Conclusion

To conclude, a well-organized, eco-friendly, and simple procedureis introducedfor the efficient synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives in high to excellent yields *via*a one-pot three-component reaction by using nano-sawdust-$OSnCl_3$ as a mild, effective, non-toxic and inexpensive solid acid catalyst in ethanol without the addition of organic co-solvent. The promising points for the presented methodology can be summarized environmental acceptability, economic viability, easy work-up, short reaction time, high atom economy, and compliance with the green chemistry protocols. Meanwhile, solid phase acidic catalyst could be reused for a number of times without appreciable loss of activity. Moreover, thepresent work is expected to show interesting pharmacology activities and may act as potential drug candidates, since pyran and chromene motifs have a vast range of biological activities.

Experimental

The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were determined with an Electrothermal 9100 apparatus. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-400 Avance spectrometer at solution in DMSO using TMS as internal standard. The morphologies of the nanoparticles were observed using FE-SEM of a MIRA3 TESCAN microscope with an accelerating voltage of 15 kV. The IR spectra of the catalyst were recorded using a model Bruker Tensor 27 FT-IR. The EDX analysis was done using a SAMx-analyzer.

Preparation of nano-sawdust-$OSnCl_3$

First, the sawdust was collected from sawmill in Farokhi city of Iran and washed several times with deionized water to remove adhering.Then, it was dried at 60 °C for 24h. The dried sawdust was pulverized at the mortar and sieved using a 20-mesh sieve and labeled as sawdust. To prepare nano-sawdust-$OSnCl_3$, $SnCl_4$ (0.7 ml) was added dropwise over 10 min via a syringe to sawdust powder (1 g) in 5 ml of chloroform at 0 ℃. The reaction mixture was stirred and, after 60 min, the ashy powder was separated and washed with chloroform (15 ml) and *n*-hexane (15 ml), respectively. Subsequently, for obtaining a fine and homogenized nano-sawdust-$OSnCl_3$powder, the obtained solid was dried in an oven at 60 °C for 4h and then pulverized at the mortar.

General procedure for preparation of compounds 4a-m

Nano-sawdust-$OSnCl_3$ (4 mg) were added to a stirred mixture of aldehyde **1** (1 mmol), malononitrile **2** (1 mmol) and kojic acid **3** (1 mmol). The materials

were mixed and heated under reflux in EtOH (5 mL) for the appropriate time as mentioned in Table 3. The progress of the reaction was followed by TLC (*n*-hexane: ethyl acetate 3:1). After completion of the reaction,the reaction mixture was filtered to remove the catalyst and thenthe crude product was recrystallized from hot ethanol to obtain the pure compound by evaporation of the solvent.

Acknowledgements

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

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