



Original Research Article

Synthesis of 2-amino-4H-pyran derivatives in aqueous media with nano-SnO₂ as recyclable catalyst

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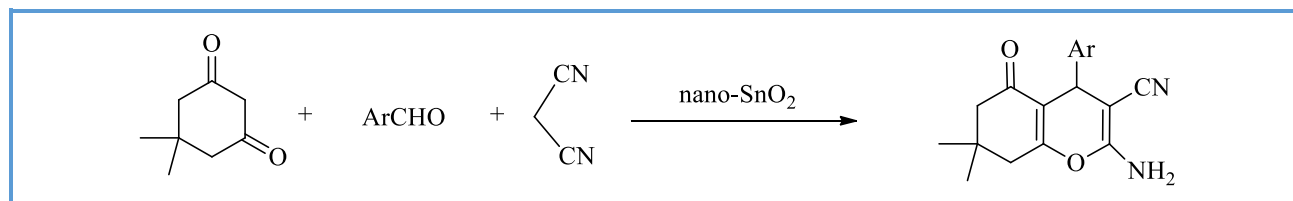
KEYWORDS

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ABSTRACT

A nano-SnO₂ catalyzed environmentally benign strategy for the synthesis of 2-amino-4H-pyran derivatives via the multi-component reaction between aryl aldehydes, β-dicarbonyl compounds and malononitrile in aqueous media under reflux conditions in excellent yields is established. The structures of the synthesized compounds were confirmed using IR, ¹H-NMR. The elemental analysis and morphology of the catalyst was characterized using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). This one-pot three component protocol provides an efficient improved pathway for the synthesis of pyrans in the terms of short reaction times, simple working up procedure and recyclability of catalyst.

Graphical Abstract



Introduction

Tetrahydrobenzo [b] pyran derivatives have been widely utilized industrially as agrochemicals, cosmetics and pigments and are reported to exert broad spectrum biological and pharmacological activities, these include anticoagulant, spasmolytic, diuretic, anticancer, antianaphylactin and cognitive enhancement properties [1–4].

The multicomponent reactions (MCRs) have been considered in synthesis of organic [5–16], combinatorial, bioactive medicinal and heterocyclic compounds, because of the compact reactions, easy and simply procedures and good yields. Advantages of MCRs are wide are including simple and uncomplicated protocols, inexpensive reactants and green considerations. The additional benefits of MCRs are shorter reaction times and application of green solvent and in generally cost-effective approach and environmental friendly [17].

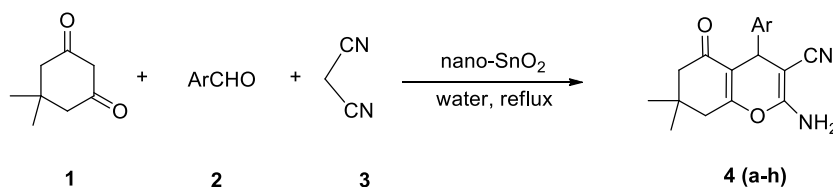
Tetrahydrobenzo [b] pyrans have been synthesized by various methods from MCRs approaches [18]. The simplest procedure is a one-pot, three-component condensation between malononitrile, dimedone and an appropriate aldehyde utilizing variety of conditions, solvents and catalysts [19].

Environmental impact of chemical synthesis, particularly on an industrial scale, has always been a source of great concern due to nature and amount of waste generated. Utilization of benign solvents, such as water, and use of highly efficient reactions and/or catalysts should aid in reduction of waste and thus, minimizing environmental pollution. Furthermore,

materials or catalysts that can be used in several different applications should garner special consideration. Tin dioxide is one such candidate. It is generally used in various optical and electronic devices and solid-state gas sensors [20, 21]. However, presence of reactive surface functionalities, tunable composition and formation of defects in its lattice structure should render catalytic activity to this material.

The specific surface area, due to particle size and pore size distribution, and ratio of surface/volume increase considerably as the size of a material decreases. The nano-sized materials usually do not satisfy the thermodynamic equilibrium, are structurally heterogeneous, and may have significantly different properties than bulk material. Their surface contains large numbers of readily accessible active sites that can serve as domains for adsorption and catalysis. SnO₂ nanostructures have been successfully synthesized by variety of methods including molten-salt synthesis [22] sol-gel [23], microwave [24, 25], carbothermal reduction [26], chemical precipitation [27], laser-ablation [28], hydrothermal method [29, 30], and sonochemical [31], techniques.

As a part of our work on multicomponent reactions (MCRs) and developing new selective and environmental friendly methodologies for the synthesis of various heterocyclic compounds, and in continuation of our research on the use of water as solvent, we are going to introduce nano-SnO₂ as a mild and highly efficient catalyst for the synthesis of 2-amino-4H-pyrans at ambient conditions (Scheme 1).



Scheme 1. Synthesis of substituted 2-amino-4H-pyran

Experimental

Material and methods

Chemicals were purchased from the Merck (Darmstadt, Germany) and Sigma-Aldrich chemical Co. All products were characterized using spectra and physical data. Characterizations were carried out using the Melting points (Electrothermal 9100), ^1H NMR (Bruker 500 MHz), TEM (HRTEM, TF 20 Tecnai G2 200 kV FEI), Fourier transform infrared (model Nexus-870, Nicolet Instrument), thin layer chromatography (TLC) on commercial aluminum-backed plates of silica gel.

Preparation of catalyst Nano-SnO₂

The catalyst preparation procedure involved a facile and low-cost solid-state reaction method [32]. Mixture solid powders of SnCl₂·2H₂O (10 mmol, 2.26 g) and sodium hydroxide (20 mmol, 0.08 g) in an agate mortar were well mixed, and then ground at room temperature (r.t.) for 15 min. and mixed together with NaCl (AR grade) in a molar ratio of 1:2, respectively, and then this mixture was ground for another 30 min. The precursors were oxidized and grown into SnO₂ nanorods by annealing for 2 h at 400 °C. The mixture was washed with a large quantity of distilled water to remove chlorine ion, then dried for 2 h at 60 °C. The yield of SnO₂ nanorods is over 98%.

Typical procedure for preparation of 2-amino-4H-pyran derivatives

A mixture of a ring substituted benzaldehyde (1 mmol), malononitrile (66 mg, 1 mmol), dimedone (140 mg, 1 mmol) and nano-SnO₂ (30 mg) in 10 mL of water were stirred and refluxed for appropriate time. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the mixture was cooled to room

temperature; the precipitate was filtered and washed with ethanol. The crude products were purified by re-crystallization from ethanol to give **4**. The structure of the compounds was confirmed from spectroscopic data. The characterization data are summarized below.

2-amino-5,6,7,8-tetrahydro-5-oxo-4-phenyl-7,7-dimethyl-4H-Benzo-[b]-pyran-3-carbonitrile (**4a**)

IR (KBr) (ν_{max} / cm⁻¹): 3390, 3290, 2935, 2200, 1685, and 1600. ^1H NMR (CDCl₃, 500 MHz): δ 0.98 (3H, singlet), 1.05 (3H, singlet), 2.1 (1H, AB quartet of doublets), 2.25 (1H, AB quartet of doublets), 2.51 (2H, broad singlet), 3.37 (singlet, NH₂), 4.32 (1H, s), 7.15 (3H, multiplet), 7.2 (2H, multiplet).

2-amino-5,6,7,8-tetrahydro-5-oxo-4-(4-chloro-phenyl)-7,7-dimethyl-4H-Benzo-[b]-pyran-3-carbonitrile (**4b**)

IR (KBr) (ν_{max} / cm⁻¹): 3410, 3310, 3005, 2200, 1695, and 1605. ^1H NMR (CDCl₃, 500 MHz): δ 0.95 (3H, singlet), 1.04 (3H, singlet), 2.08 (1H, AB quartet of doublets), 2.26 (1H, AB quartet of doublets), 2.51 (2H, singlet), 3.34 (Singlet, NH₂), 4.20 (1H, s), 7.17 (2H, doublet), 7.35 (2H, doublet).

Results and Discussion

Based on previous studies to develop new and heterogeneous catalyst systems for fine chemical preparation, we have established a one-pot, three-component tandem Knoevenagel cyclocondensation reaction of various aldehydes with malononitrile and dimedone in water in the presence of nano-SnO₂ as available, green and inexpensive catalyst in good yields for synthesizing of 2-amino-4H-pyrans.

The dimensions of utilized SnO₂ nanoparticles were determined with TEM

(Figure 1). The SnO₂ nanoparticles utilized in the following investigation were between 20 and 50 nm in diameter.

The malononitrile was condensed with the aldehyde activated by catalyst via the

Knoevenagel type coupling to produce the cyanocinnamionitrile derivatives. Michael addition of these derivatives with dimedone followed by rearrangement and cyclization give rise to desired products (Scheme 2).

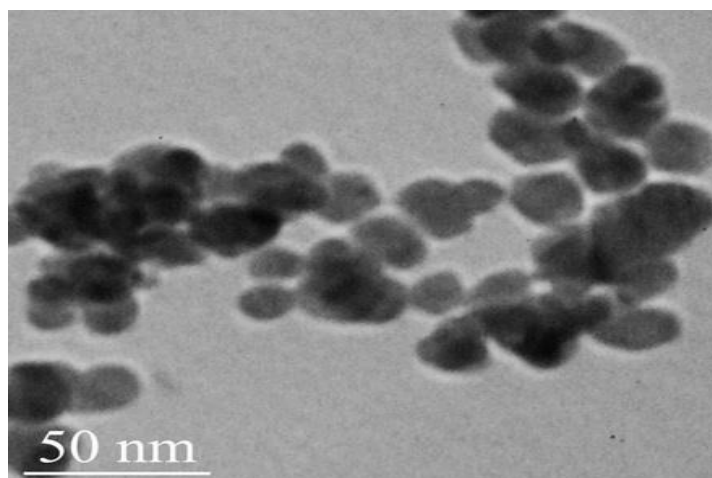
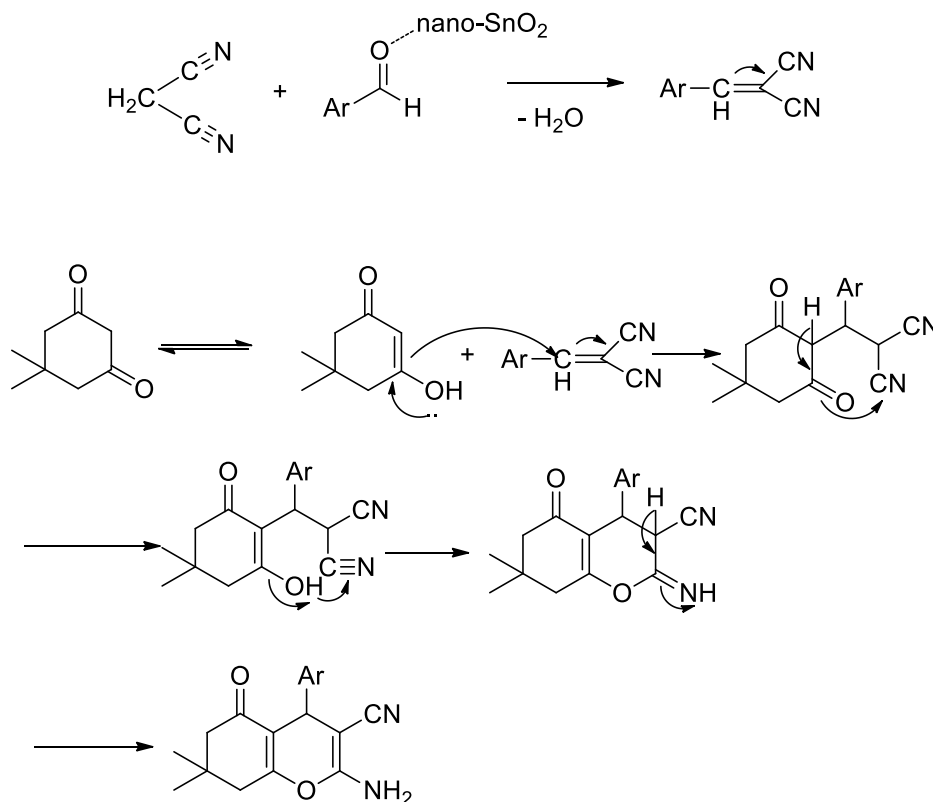


Figure 1. TEM image of nano-SnO₂



Scheme 2. A plausible mechanism for the one-pot three-component Synthesis of 2-amino-4H-Pyran Derivatives

It is noteworthy to mention that, the nature of substituents on the aromatic ring showed little to no apparent effect on this conversion, because they were obtained in high yields in relatively short reaction times. The results are demonstrated in Table 1.

The effect of various solvents on the synthesis of **4a** was also assessed. This reaction was carried out in several solvents; however, the best results in terms of yield and reaction time/efficiency were obtained in water (Table 2).

Table 1. Synthesis of substituted 2-amino-4H-Pyran catalyzed by nano-SnO₂ complex

Entry	Ar	Product	Yield (%) ^a	m.p. (°C)	
				Found	Reported [33]
1	C ₆ H ₅	4a	90	228-229	227-229
2	4-ClC ₆ H ₅	4b	95	216-218	214-216
3	4-NO ₂ C ₆ H ₅	4c	97	178-180	181-183
4	3-NO ₂ C ₆ H ₅	4d	97	213-215	215-216
5	4-CH ₃ C ₆ H ₅	4e	93	219-220	219-221
6	4-OCH ₃ C ₆ H ₅	4f	91	200-202	197-199
7	4-OHC ₆ H ₅	4g	89	206-207	208-210
8	2-ClC ₆ H ₅	4h	95	209-211	208-210

^aYields refer to isolated products

^b benzaldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and nano-SnO₂ (30 mg) in 10 mL of water under reflux condition

Table 2. Synthesis of **4a** in the presence of different solvents using nano-SnO₂ as a catalyst

Entry	Solvent	Yield (%) ^a
1	THF	68
2	C ₂ H ₅ OH	87
3	CH ₃ CN	85
4	CHCl ₃	71
5	water	90

^aYields were analyzed by GC

The best yields for all reactions were obtained after 1 h. The reactions proceeded well with 5 mol% of catalyst. Higher amounts catalyst did not produce higher yields. At the end of each reaction, the catalyst was recovered by a simple filtration. The recycled catalyst was

washed with methanol and reused in subsequent reactions. The efficiency of new vs. recycled was investigated. The results indicate that the catalyst affords similar yields when reused for up to five trials, however, subsequent uses result in lower yields (Table 3).

Table 3. Comparison of efficiency of recycled nano-SnO₂ in synthesis of **4a**

Entry	Time (hour)	Yield (%)
1	1.5	98
2	2	95
3	3	92
4	4	85
5	4.5	83

To understand the catalytic merit of nano-SnO₂, the results of this investigation with those reported in literature with various catalysts

were compared (Table 4). Nano-SnO₂ catalyst results in better or comparable yields under shorter reaction times.

Table 4. Comparison of various catalysts for the synthesis of 2-amino-4H-Pyran derivatives

Entry	Catalyst	Solvent	Yield (%)	Time	Reference
1	NaBr	free	60-95	10-15 min	[34]
2	(S)-Proline	H ₂ O/EtOH	78-98	30 min	[35]
3	HDMBAB	H ₂ O	84-93	7-8 h	[36]
5	Na ₂ SeO ₄	EtOH/H ₂ O	80-98	0.75-3 h	[37]
6	TMAH	H ₂ O	79-93	0.5-2 h	[38]
7	TBAF	H ₂ O	73-98	30-300 min	[39]
8	MgO	EtOH/H ₂ O	90-96	22-33 min	[40]
9	nano-SnO ₂	H ₂ O	89-97	8-20 min	Present study

Conclusion

In this work, we discussed a highly efficient green procedure for preparing 2-amino-4H-pyrans via a condensation reaction of various aldehydes, malononitrile and dimedone in the presence of nano-SnO₂ as a catalyst in water. The procedure offers several advantages including high yields, operational simplicity, environmental-friendly solvent, recoverable/reusable catalyst, and low cost; rendering it a useful and attractive industrial process for the synthesis of these compounds. In this research study nano-SnO₂ as an efficient catalyst was synthesized and characterized by SEM and TEM analysis. According to the data presented in this study, the 2-amino-4H-pyrans have been synthesized in the presence of nano-SnO₂ catalyst compared to other articles with high efficiency and in a shorter time.

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