

# A Facile and Highly Efficient Three Component Synthesis of Pyran and Chromene Derivatives in the Presence of Nano SnO<sub>2</sub> as a catalyst

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## Abstract

Nano tin dioxide was employed as a catalyst for efficient and facile preparation of pyran derivatives via the one-pot three component condensation reaction of various aldehydes with malononitrile and dimedone. Chromene derivatives via the one-pot three component condensation reaction of various aldehyde with malononitrile and 4-hydroxycoumarin were also synthesized by this novel catalyst. The described novel synthesis method proposes several advantages of mild condition, safety, high yields, short reaction times compared to the traditional method of synthesis.

**Keywords:** Nano tin dioxide, Pyran, Chromene.

## 1. Introduction

Coumarins and their derivatives are used in the fields of biology, medicine and polymer science. They are similarly existent or used in cigarettes [1-4], perfumes and cosmetics [1-5], alcoholic beverages [6] and laser dyes [7]. Coumarins have been found to be related with a number of cases of homicide and suicide in Korea [8]. In recent years, 4H-benzo[b] pyran have attracted strong attention due to

their useful biological and pharmacological properties, such as spasmolytic, anticoagulant, anticancer, diuretic, antianaphylactin characteristics [9-11]. Some pyrans can be employed as photoactive materials [12]. Also, the 4H-pyran group is a basic of the structures of a series of natural products [13, 14]. In continuation of our investigations on the development of new synthetic methodology [15,16], we herein report an innovative, convenient, mild and efficient

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procedure for the synthesis of pyrans and chromene derivatives. One-pot three component condensations of aldehyde derivatives with malononitrile and dimedone (pyran synthesis) or 4-hydroxycoumarin (chromene synthesis) were utilized for synthesizing of pyrans and chromene derivatives, respectively. The experiments carried out using the nano tin dioxide ( $\text{SnO}_2$ ) under ambient temperature.

## 2. Material and methods

NMR spectra were determined on a Fourier-transform (FT)- NMR Bruker AV-400 spectrometer in dimethyl sulfoxide  $\text{DMSO}-d_6$  and are expressed in  $\delta$  values relative to tetramethylsilane; coupling constants ( $J$ ) are measured in Hz. Melting points were determined on a ELECTR THERMAL9100. Infrared spectra were recorded on a RAYLEIGH WQF-510 Fourier transform instrument. Commercially available reagents were used throughout without further purification.

### 2.1. General procedure for the synthesis of pyran and chromene derivatives

A mixture of aldehyde derivatives (1.0 mmol), malononitrile (1.0 mmol), dimedone (pyran synthesis) or 4-hydroxycoumarin (chromene synthesis) (1.0 mmol) and  $\text{SnO}_2$  as a nano catalyst (1 mol%) in ethanol (2 mL) was stirred at room temperature for an appropriate time. The progress of the reaction was monitored by TLC (*n*-hexan/ethyl acetate 4:1). After completion of the reaction, the resulting solid (crude product) was filtered and then recrystallized with ethanol–water to obtain pure product. The physical data (mp, NMR, IR) of these known compounds were found to be identical with those reported in the literature.

### 2.2. Spectral data for the synthesis of coumarin derivatives

*2-amino-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile* (Table 1, entry 9): M.p: 178-180 °C; IR (KBr):  $\nu$  3110, 3041, 1706, 1606, 1519, 1309, 1201, 1103, 941;  $^1\text{H-NMR}$  (400 MHz;  $\text{DMSO}-d_6$ ; TMS):  $\delta$  H = 0.91 (s, 3H), 1.04 (s, 3H), 2.13 (d,

$J = 8.3$  Hz, 2H), 2.28 (d,  $J = 8.4$  Hz, 2H), 4.37 (s, 1H), 7.19 (s, 2H, NH), 7.46 (d,  $J = 8.5$  Hz, 2H), 8.18 (d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO}-d_6$ ; TMS):  $\delta$  C = 19.0, 27.4, 28.7, 32.3, 36.1, 50.3, 57.4, 112.2, 119.8, 124.1, 129.1, 146.7, 152.8, 159.0, 163.6, 196.2.

*2-amino-4-(4-nitrophenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile* (Table 1, entry 23): M.p: 258-260; IR (KBr):  $\nu$  3367, 1608, 1552, 1342, 1240, 761;  $^1\text{H-NMR}$  (400 MHz;  $\text{DMSO}-d_6$ ; TMS):  $\delta$  H = 4.67 (s, 1H), 7.48 (d,  $J = 8.1$  Hz, 2H), 7.75 (t, 2H), 7.92 (d,  $J = 8.3$  Hz, 1H), 8.14 (t, 1H), 8.15 (d,  $J = 8.3$  Hz, 1H), 8.43 (d,  $J = 8.2$  Hz, 1H), 8.70 (s, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO}-d_6$ ; TMS):  $\delta$  C = 37.2, 57.2, 103.2, 113.3, 114.1, 116.8, 117.1, 123.1, 123.6, 124.2, 124.4, 124.8, 133.2, 133.6, 147.1, 154.4, 158.4, 159.7, 160.1.

## 3. Results and Discussion

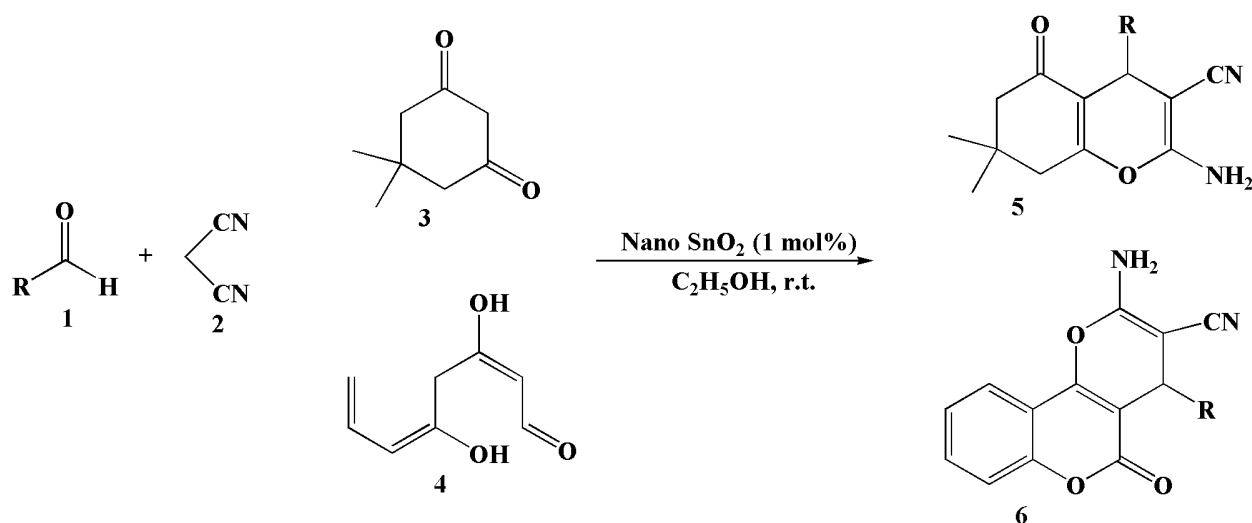
Herein, we report an efficient and facile process for the preparation of pyran and chromene derivatives in the presence of  $\text{SnO}_2$  as a nano catalyst. According to Scheme 1, the synthesis was done through a mixture of aldehyde derivatives with malononitrile and dimedone (synthesis of pyran derivatives) or 4-hydroxycoumarin (synthesis of chromene derivatives) in ethanol solvent at room temperature.

Afterward conclusion the improved reaction conditions, additional experimentations were preceded by execution the reaction between a series of aromatic aldehyde derivatives with malononitrile and dimedone (in the synthesis of pyran) or 4-hydroxycoumarin (in the synthesis of chromene). To show the general applicability of this technique, various aldehydes were proficiently reacted with one equivalents of malononitrile and dimedone or 4-hydroxycoumarin in the similar conditions. These results refreshed us to inspect the possibility and the generalization of this new procedure for various aldehyde derivatives under improved conditions. As shown in Table 1, a series of aldehyde derivatives underwent electrophilic substitution reaction with malononitrile and dimedone or 4-hydroxycoumarin to give a varied series of substituted

pyran and chromene derivatives in good to excellent yields without any side products. The nature and electronic properties of the substituents on the aromatic ring effect the conversion rate, and aromatic aldehyde having electron-withdrawing groups on the aromatic ring (Table 1, entries 9 and 23) react faster than electron-donating groups (Table 1, entries 12 and 28). Though meta and para-substituted aromatic aldehyde provided good results and ortho-substituted aromatic aldehyde gave lower yields because of the steric effects. As well, the work-up of present method was easy. It contains the pouring of reaction mixture on

ethanol-water to precipitate the solid, which could be composed by separation to give the corresponding pyran and chromene product with better yield.

The influence of solvent on the yield of pyran (5) and chromene (6) is given in Table 2. The reaction of 4-nitrobenzaldehyde (1) with malononitrile (2) and dimedone (3) (in the synthesis of pyran) or 4-hydroxycoumarin (4) (in the synthesis of chromene) was selected as a typical reaction to study the effect of solvent. The experimentation results showed that ethanol was the most effective solvent.



Scheme 1. Synthesis of pyran and chromene derivatives using SnO<sub>2</sub> as a nanocatalyst.

Table 1. Synthesis of pyran and chromene derivatives employing of 1 mol% nano SnO<sub>2</sub> catalyst.

Entry	Dimedone or 4-hydroxycoumarin	R	Time (min)	Yield (%)	M.p (°C)
1	Dimedone	Ph	10	93	267-269
2	Dimedone	2-Cl	9	94	215-217
3	Dimedone	3-Cl	7	95	234-236
4	Dimedone	4-Cl	6	96	210-212
5	Dimedone	3-Br	8	95	226-228
6	Dimedone	4-F	7	95	178-180
7	Dimedone	2-NO <sub>2</sub>	7	96	209-211
8	Dimedone	3-NO <sub>2</sub>	5	97	216-218
9	Dimedone	4-NO <sub>2</sub>	3	98	178-180
10	Dimedone	4-Me	8	96	215-217
11	Dimedone	4-NMe <sub>2</sub>	4	98	199-201
12	Dimedone	4-OMe	8	96	198-200

13	Dimedone	3,4-(OMe) <sub>2</sub>	10	95	157-159
14	Dimedone	PhCH=CH	12	93	204-206
15	Dimedone	Furfuryl	12	92	216-218
16	4-hydroxycoumarin	Ph	15	94	257-260
17	4-hydroxycoumarin	3-Cl	11	95	240-242
18	4-hydroxycoumarin	4-Cl	10	96	258-260
19	4-hydroxycoumarin	4-F	11	95	261-263
20	4-hydroxycoumarin	4-Br	11	95	253-255
21	4-hydroxycoumarin	2-NO <sub>2</sub>	10	97	255-257
22	4-hydroxycoumarin	3-NO <sub>2</sub>	8	97	267-269
23	4-hydroxycoumarin	4-NO <sub>2</sub>	7	98	258-260
24	4-hydroxycoumarin	2-Me	12	95	263-265
25	4-hydroxycoumarin	4-Me	10	96	254-255
26	4-hydroxycoumarin	3-OH	13	95	268-270
27	4-hydroxycoumarin	4-OH	11	96	265-267
	4-hydroxycoumarin	4-OMe	10	96	231-233
	4-hydroxycoumarin	3,4-(OMe) <sub>2</sub>	13	94	229-231
	4-hydroxycoumarin	4-NMe <sub>2</sub>	7	97	267-269

**Table 2.** Solvent effect in the synthesis of pyran (Table 1- entry 9) and chromene (Table 1- entry 23)<sup>a</sup>

Entry	Solvent	Reaction time/min		Yield <sup>b</sup> /%	
		Pyran	Cheromene	Pyran	Cheromene
1	Solvent-free	15	18	87	85
2	H <sub>2</sub> O	25	30	71	67
3	C <sub>2</sub> H <sub>5</sub> OH	3	7	98	98
4	CHCl <sub>3</sub>	15	20	91	90
5	THF	10	14	93	93
6	CH <sub>3</sub> CN	8	10	97	96
7	CH <sub>3</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	12	15	92	91
8	Toluene	30	33	81	78
9	Benzene	45	51	80	75

Reaction condition: <sup>a</sup> 4-Nitrobenzaldehyde (1 mmol), malononitrile (1 mmol), dimedone or 4-hydroxycoumarin (1 mmol), SnO<sub>2</sub> (1 mol%), solvent (2 mL); <sup>b</sup> Isolated yield.

The reusability of the catalysts was tested using the reaction of 4-nitrobenzaldehyde with malononitrile and dimedone or 4-hydroxycoumarin as a perfect substrate. At the end of the reaction, CH<sub>2</sub>Cl<sub>2</sub> was added to the mixture. The aqueous layer was separated and used without further purification. In this media, as exposed in Table 3, the

improved catalyst can be recycled at least four added times in consequent reactions without considerable loss in the catalytic activity.

The morphology, crystal structure and sizes of the SnO<sub>2</sub> nano-catalyst in different synthetic stage are characterized by X-Ray diffraction. The powder X-ray

diffraction pattern of reaction media (SnO<sub>2</sub> nano-catalyst in pure form) (Figure 1) was recorded on a Rigaku D/Max-2200 model diffractometer equipped with horizontal goniometer in  $\theta/2\theta$  geometry. The Copper K $\alpha$  ( $\lambda = 1.5418$  Å) radiation was used and the sample was scanned between 3–80 degrees  $2\theta$ . The sharp peaks in the diffractogram indicate that the reaction media (SnO<sub>2</sub> nano-catalyst in pure form) containing crystalline species. There are several major peaks with  $2\theta$  values of 26.6, 33.9, 37.9, 42.6, 51.8, 54.7 and 57.8, corresponding to SnO<sub>2</sub> crystal planes of (1 0 1), (1 1 0), (1 1 1), (2 1 0), (2 1 1), (2 2 0), (0 0 2), respectively. All reflections of SnO<sub>2</sub> NPs are in excellent accordance with a tetragonal rutile structure (JCPDS 41-1445).

The field emission scanning electron microscopy (FE-SEM) micrographs of nanoparticles obtained from the different stage of the reaction were shown in Figure 2. It can be concluded that due to the existence of hydroxyl functional units on the structure of nanoparticles, the interaction of SnO<sub>2</sub> nanoparticles and starting materials for

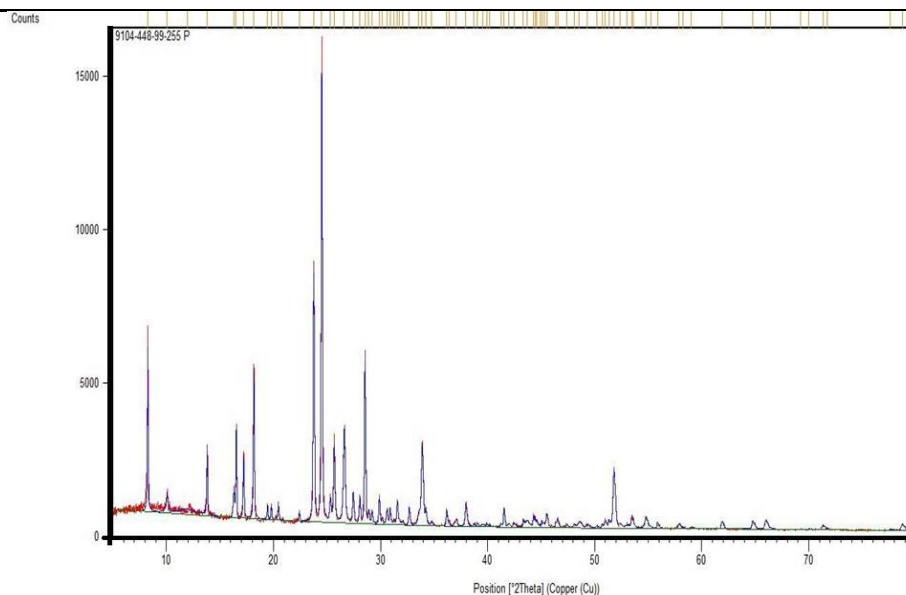
synthesis of pyran and chromene derivatives were in very strong states, which cause acceleration in synthesis of these derivatives.

#### 4. Conclusions

The self-determining of this paper is to describe simple, facile and efficient SnO<sub>2</sub> to catalyze one-pot three component condensation for the synthesis of pyran and chromene derivatives. The experimental process for this reaction is extra ordinarily superficial and involves no toxic organic solvents. The catalyst suggestions numerous advantages counting cleaner reactions, mild reaction conditions, high yield of the products, shorter reaction times, lower catalytic loading as well as simple experimental and isolation procedures. In addition, the catalyst was talented to be recycled simply for four-time tests with a significant decrease in the catalytic activity of the recovered catalyst.

**Table 3.** Reusability studies of the catalyst for synthesis of pyran (Table 1- entry 9) and chromene (Table 1- entry 23).

Number of experiments		Fresh	1	2	3
Isolated yield (%)	Pyran	98	97	95	94
	Chromene	98	96	93	90



**Figure 1.** XRD diffraction patterns of reaction media (SnO<sub>2</sub> nano-catalyst).

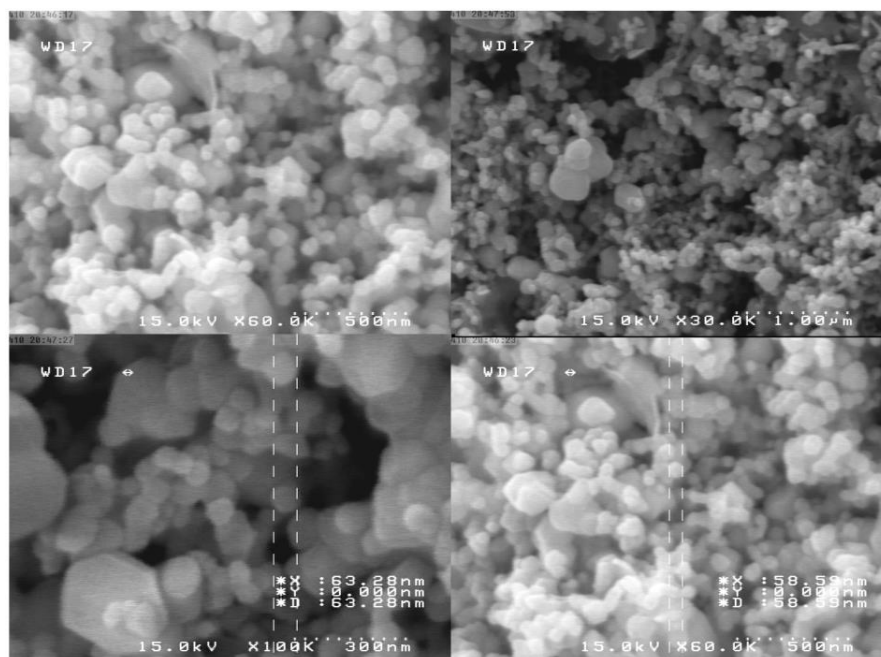


Figure 2. FESEM micrographs of SnO<sub>2</sub> nanoparticles

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