

## Efficient synthesis of tetrahydrobenzo[*b*]pyran derivatives catalyzed by poly(4-vinylpyridine) as a green and heterogeneous recyclable basic catalyst under solvent-free conditions

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**Abstract:** A green and highly efficient procedure is reported for the one pot synthesis of tetrahydrobenzo[*b*]pyran derivatives catalyzed by poly(4-vinylpyridine) as a heterogenous and recyclable basic catalyst under solvent-free conditions. This procedure provides many advantages such as recyclability of the catalyst, simple work-up, clean procedure, short reaction times and high yields of the products.

**Keywords:** Poly(4-vinylpyridine), Tetrahydrobenzo[*b*]pyran, Solvent-free conditions, Basic catalyst.

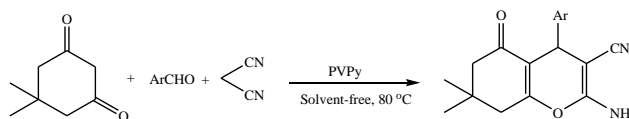
### Introduction

The synthesis of tetrahydrobenzo[*b*]pyran derivatives has attracted considerable attention because of their noteworthy anticoagulant, spasmolytic, diuretic, anticancer, and antianaphylactic properties [1]. Moreover, these compounds can be employed as pigments, photoactive materials [2], and they constitute the structural unit of a series of natural products [3]. Furthermore, The pyran pharmacophore is an important core structure of many natural products [4]. In view of the importance, many procedures have been reported for the synthesis of tetrahydrobenzo[*b*]pyran derivatives. The conventional synthesis involves the condensation of 5,5-dimethylcyclohexane-1,3-dione (dimedone) with aromatic aldehyde and malononitrile in different conditions. For the synthesis of tetrahydrobenzo[*b*]pyrans various catalysts such as Ce<sub>1</sub>Mg<sub>x</sub>Zr<sub>1-x</sub>O<sub>2</sub> [5], Trisodium citrate [6], MgO [7], PMA.SiO<sub>2</sub> [8], TEAA [9], LiBr [10], K<sub>3</sub>PO<sub>4</sub> [11], IRA-400 (OH<sup>-</sup>) [12], CA-SiO<sub>2</sub> [13], ZnO-beta zeolite [14], TBAB [15], Ph(BOH)<sub>2</sub> [16], acidic ionic liquids [17],

and basic ionic liquids [18], [TETA]TFA [19], Aliquat<sup>®</sup>336 [20], have been reported. However, some of these methods require prolonged reaction time, use of expensive catalyst, low yields of products and toxic solvents. Therefore, introduction of new methods and catalysts for the synthesis of tetrahydrobenzo[*b*]pyran derivatives in terms of potential simplicity, high activity, low cost, high yields and short reaction times is still in demand. In recent years, practical applications of solid catalysts in organic synthesis have increased owing to the advantages of heterogeneous catalysis such as high catalytic activity, simple work-up, easy recovery, catalyst reuse and mild reaction conditions. In particular, solid basic catalysts have proved to be valuable in organic reactions due to the good catalytic activity and reaction rate improvement, easier work-up, recyclability and the eco-friendly reaction conditions. It has found that poly(4-vinylpyridine) was a cheap and commercially available reagent and its structure assured us that this reagent can be used as a green and basic catalyst in organic synthesis reactions. In comparison with other commercially available catalyst, poly(4-vinylpyridine) is safe, easy to handle and

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environmentally benign. Recently, we have reported that poly(4-vinylpyridine) (PVPy), as a green and basic catalyst, can catalyze the synthesis of chromene derivatives [21]. Also, in the previous research, application of poly(4-vinylpyridine) for the protection of different types of functional groups have been reported [22]. In continuation of these studies and our research program to develop the efficient and green catalysts in the organic synthesis [23-29], herein, we wish to report the applicability of poly(4-vinylpyridine) (PVPy) as a green, commercially available and recyclable basic catalyst for the synthesis of tetrahydrobenzo[*b*]pyran derivatives under solvent-free conditions (Scheme 1).



**Scheme 1.** Synthesis of tetrahydrobenzo[*b*]pyrans catalyzed by PVPy.

## Results and discussion

In order to optimize the reaction conditions, the reaction of benzaldehyde, malononitrile and dimedone was studied under a variety of conditions. The best result was achieved by running the reaction of each substrate (with 1mmol) in the presence of 0.1 g of PVPy at 80 °C under solvent-free conditions (Table 1, entry 1). Using these optimized conditions, the reaction of various aromatic aldehydes was studied (Table 1).

**Table 1.** Synthesis of tetrahydrobenzo[*b*]pyrans catalyzed by PVPy.

Entry	Aldehyde	Time(min)	Yield (%) <sup>a</sup>	M. P. (°C)	
				Found	Reported
1	C <sub>6</sub> H <sub>5</sub> CHO	15	93	230-232	236-238[16]
2	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CHO	10	91	181-1183	180-182[16]
3	3-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CHO	15	91	210-212	210-212[16]
4	3-ClC <sub>6</sub> H <sub>4</sub> CHO	18	92	227-229	228-229[16]
5	4-ClC <sub>6</sub> H <sub>4</sub> CHO	12	93	208-210	207-209[16]
6	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	10	91	115-117	114-116[19]
7	4-Me <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CHO	45	89	213-215	214-215[19]
8	4-BrC <sub>6</sub> H <sub>4</sub> CHO	15	92	201-203	199-200[16]
9	4-MeOC <sub>6</sub> H <sub>4</sub> CHO	30	90	205-207	204-205[16]
10	2-MeOC <sub>6</sub> H <sub>4</sub> CHO	22	88	195-197	194-196[16]
11	4-MeC <sub>6</sub> H <sub>3</sub> CHO	20	92	213-215	215-218[16]
12	4-HOC <sub>6</sub> H <sub>4</sub> CHO	45	90	212-214	216-218[16]
13	3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> CHO	60	89	155-157	155-158[20]
14	4-Cl-3-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	12	91	202-203	-

<sup>a</sup> Isolated pure products.

Various aromatic aldehydes with either electron-donating or electron-withdrawing groups, efficiently reacted to afford the desired products in good to high yields. The evaluation showed that the electron-withdrawing groups such as nitro on aromatic ring increase the time of reactions, whereas electron-releasing groups such as methoxy and methyl decrease the time of reactions. Aliphatic aldehydes remain intact under the same reaction conditions. Therefore, this method can be useful for the chemoselective synthesis of tetrahydrobenzo[*b*]pyran derivatives from aromatic aldehydes in the presence of aliphatic ones. The experimental procedure with poly(4-vinylpyridine) is very simple and the catalyst can be removed easily by filtration. Very low amount of the catalyst is needed

and the desired products were easily recrystallized from hot ethanol and obtained in good to high yields during short reaction times.

The recyclability of the catalyst is one of the most important advantages and makes it useful for commercial applications. Therefore the recyclability of poly(4-vinylpyridine) was investigated. To explore these properties, the reaction of benzaldehyde, dimedone and malononitrile were selected again as a model (Table 2). After completion of the reaction, the recovered catalyst was washed with hot ethanol and after dryness was reused in the next similar run. This process was repeated for 6 consecutive runs and the desired product was obtained in high yields after 1-6 runs.

**Table 2.** Recyclability study of PVPy.

Run	1	2	3	4	5	6
Time(min)	15	15	18	18	20	25
Yield (%) <sup>a</sup>	93	92	92	92	90	90

<sup>a</sup> Isolated pure product.

In order to demonstrate the competence of this method, Table 3 compares the results from the synthesis of tetrahydrobenzo[b]pyrans in the presence

**Table 3.** Comparison of the efficiency of PVPy in the synthesis of tetrahydrobenzo[b]pyrans from benzaldehyde with other reported methods.

Entry	Reagent	Conditions	Time (min)	Yield (%) <sup>a</sup>	Reference
1	Ce <sub>1</sub> Mg <sub>x</sub> Zr <sub>1-x</sub> O <sub>2</sub>	EtOH/reflux	35	91	5
2	MgO	H <sub>2</sub> O-EtOH/reflux	27	94	7
3	K <sub>3</sub> PO <sub>4</sub>	H <sub>2</sub> O-EtOH/r.t	45	94	11
4	TBAB	H <sub>2</sub> O /reflux	40	90	15
5	PVPy	Solvent-free	15	93	This work

<sup>a</sup> Isolated pure products.

## Conclusion

In conclusion, we have developed a simple, mild and efficient method for the multi-component synthesis of tetrahydrobenzo[b]pyrans catalyzed by poly(4-vinylpyridine) as a commercially available and solid basic recyclable catalyst under solvent-free conditions. Poly(4-vinylpyridine) can promote the yields and reaction times over 6 runs without significant loss in its activity and efficiency. Furthermore, high yields of products, short reaction times, simplicity of work-up and clean procedure, will make this procedure a useful addition to the available methods.

## Experimental

### General:

Chemicals were purchased from Fluka and Merck chemical companies. The IR spectra were recorded on a Perkin Elmer 781 Spectrophotometer. All the NMR spectra were recorded on a Bruker Advance 400 MHz. Yields refer to isolated pure products. Yields refer to isolated pure products.

### General procedure for the synthesis of tetrahydrobenzo[b]pyran derivatives:

A mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and PVPy (0.1 g) was heated in an oil bath (80 °C) for the appropriate times according to Table 1. After

of PVPy and some of the other catalysts. In comparison with previously reported procedures, PVPy promoted the reaction very effectively and gave the desired products in very short times at high yields. Very low amount of the catalyst was needed. This catalyst is cheap, easy to handle and commercially available. It can be recovered simply by filtration and can be reused in the next runs without major yield decrease of the products. Moreover, our procedure is environmentally friendly as it does not use any toxic auxiliary or solvent.

completion of the reaction (monitored by TLC, n-Hexane/Ethyl acetate, 3:1), the mixture reactions was cooled to room temperature, acetone was added and the catalyst was recovered by filtration to be reused subsequently. The filtrate was evaporated to dryness and the solid residue recrystallized from hot ethanol to give pure products in high yields. The structure of the products was confirmed by IR, <sup>1</sup>H NMR and melting points and compared with authentic samples prepared by reported methods. The spectral and analytical data for the new compound are as follows:

Table 1, entry 14. Yellow solid, mp: 202-203 °C; IR (KBr) cm<sup>-1</sup>: 3410, 3300, 3210, 2900, 2200, 1660, 1600, 1540, 1360, 1210, 1140, 1040. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz): 1.04 (3H, s), 1.15 (3H, s), 2.12 (2H, dd), 2.23 (2H, s), 4.38 (1H, s), 7.22 (2H, s), 7.53-7.56 (1H, m), 7.70 (1H, d, *J* = 8.4 Hz), 7.88 (1H, s). <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 100 MHz): 27.50, 28.59, 32.29, 35.49, 50.33, 56.52, 57.22, 111.78, 119.80, 123.42, 124.59, 131.99, 133.28, 146.46, 148.02, 159.05, 163.75, 196.29. Elem. Anal. Found: C, 57.89%; H, 4.19% N, 11.37% (calculated for C<sub>18</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>Cl: C, 57.84%; H, 4.13%; N, 11.24 %).

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