



Nano-rice bran /TiCl₄ a highly efficient catalyst for the one-pot synthesis of pyrano[3,2-b]pyrans

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Abstract

Nano-rice bran/TiCl₄ has been prepared from rice bran and TiCl₄ in *n*-hexane as solvent. Then nano-rice bran/TiCl₄ has been introduced as a novel catalyst for the three component synthesis of pyrano [3,2-*b*] pyrans from the simple one-pot reaction between aryl aldehydes, cyano acetamide and kojic acid. Cleanliness, an eco-friendly catalyst, simple methodology, short time, and excellent yields of products are some advantages of this method.

Keywords: *Nano-rice bran/TiCl₄, Pyrano [3,2-*b*] pyrans, Cyanoacetamide, Kojic acid, Aryl aldehydes.*

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Introduction

In recent times, multicomponent reactions (MCRs) have attracted much attention in combinatorial and medicinal chemistry [1, 2]. MCRs involve three or more starting materials reacting in a single flask to form a new product, where basically all the atoms contribute to the newly formed product[3]. It is well known that pyran structural units occur in various molecules exhibiting diverse biological activities[4]. Such as miticidal activity,[5]antiviral activity,[6] stimulant activity,[7]and insecticidal activity[8]. Few reports have been described for the synthesis of substituted pyrano[3,2-b] pyrans. Sheik Mansoor et al. [1] reported the synthesis of a series of 2-amino-4-aryl-4H,8H-6-methyl-8-oxopyrano[3,2-b]pyrans by three component reaction of an aromatic aldehyde, malononitrile or a cyano acetate, and 5-hydroxy-2-methyl-4H-pyran-4-one catalyzed by silica-bonded N-propylpiperazine sodium n-propionate (SBPPSP) in aqueous ethanol. Rahmati et al. [9] developed a 1,4-diazabicyclo[2,2,2]octane (DABCO) catalyzed efficient synthesis of 2'-amino-6'-(hydroxymethyl)-8'H-spiro[indoline-3,4'-pyrano[3,2-b]pyran-2,8'-diones by one-pot, three-component reaction of isatin, kojic acid, and an active methylene compound, in methanol. Li et al. [10] synthesized a series of 2-amino-4-aryl-4H,8H-6-methyl-8-oxo-pyrano[3,2-b]pyrans from an aromatic aldehyde, malononitrile or a cyano acetate, and allomaltol via a one-pot three-component reaction in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄), with a catalytic amount Et₃N. Although these methods are useful, there is still a need to develop methods with numerous advantages such as environmentally benign, easy workup, cost-effectiveness, and good stability for the synthesis of pyrano[3,2-b]pyrans of prime importance. Rice is the most important cultured crop in Asia, and the countries including China, Indonesia, Bangladesh, Thailand, Vietnam, Japan and Philippine that has been used as a staple food for more than half of the population in the world [11, 12]. Rice bran is one of the abundant agricultural by-products in Asia. Several studies have been reported that rice bran is a good source of protein, vitamins, micronutrients, and anti oxidants [13]. We have investigated the preparation of nano-rice bran/TiCl₄ from rice bran and TiCl₄ in *n*-hexane as solvent. Then we have reported the new and mild procedure for one pot synthesis of pyrano[3,2-b]pyrans by the reaction of aryl aldehydes, cyano acetamide and kojic acid in the presence nano-rice bran/TiCl₄ as a new, inexpensive and eco-friendly bio-based catalyst in water as solvent at room temperature.

Experimental

All chemicals for this work were purchased from Merck, Aldrich and Fluka chemical companies and used without any additional purification. Melting points were measured with an Electrothermal

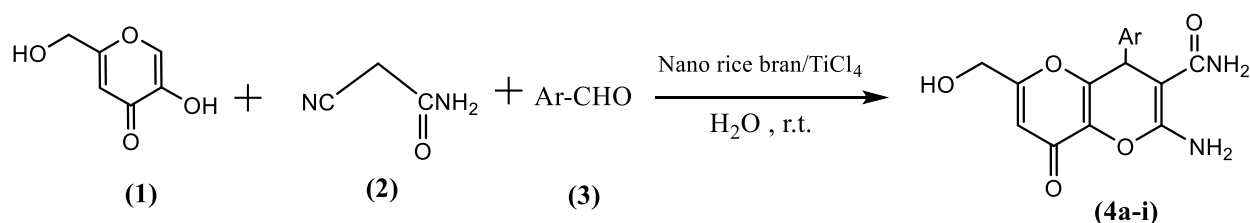
9100 apparatus. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Spectrospin Advance 400 spectrometer using TMS as an internal standard. Elemental analyses were recorded using a Thermo Finnigan Flash EA-1112. The morphologies of the nanoparticles were observed using FESEM of a Mira 3 TESCAN microscope with an accelerating voltage of 15 kV and The EDX analysis was done using a SAMx analyser.

Preparation of nano-rice bran /TiCl₄

To a round-bottomed flask containing rice bran (0.5 g) and *n*-hexane(10 ml), TiCl₄ (1.2 ml) was added dropwise and mixture was stirred well at 0°C for 10 min, the flask was sealed at room temperature for 24 h. Then the reaction mixture was filtered and dried at room temperature.

General procedure for synthesis of pyrano[3,2-*b*]pyrans

In a typical experiment, a round-bottomed flask fitted with magnetic stirring bar was charged with water (15 mL), nano-rice bran /TiCl₄ (0.03 g), kojic acid (1 mmol), cyano acetamide (1.2 mmol) and aryl aldehyde (1 mmol). The flask was stirred at room temperature. After completion of the reaction (monitored by TLC), the mixture was filtered to remove the catalyst. After evaporation of the solvent, the crude product was re-crystallized to obtain the pure compound. So we have reported the new procedure for synthesis of pyrano[3,2-*b*]pyrans (**4a-i**), by the condensation of, kojic acid (**1**), cyano acetamide(**2**) and aryl aldehyde (**3**)in the presence nano-rice bran/TiCl₄(Scheme 1, table 1).The synthesis of pyrano[3,2-*b*]pyrans by nano-rice bran /TiCl₄was compared with other catalysts reported in literature [9–11] (Table 2). Synthesis of pyrano[3,2-*b*]pyrans catalyzed by nano-rice bran/TiCl₄offers production of the corresponding products in shorter time and milder condition is done, while other methods require more amount of catalyst and longer reaction time for synthesis of pyrano[3,2-*b*]pyrans.



Scheme 1. Synthesis of pyrano[3,2-*b*]pyrans.

Table 1. Synthesis of some pyrano[3,2-b]pyran derivatives.

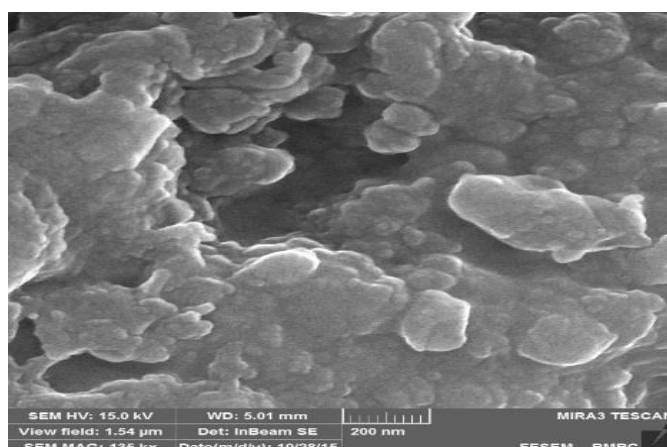
Entry	Product	Ar	Yield %	m.p. (°C)
1	4a	2-OHC ₆ H ₄	88	202-208
2	4b	5-Br,2-OHC ₆ H ₃	90	240-242
3	4c	4-CNC ₆ H ₄	85	108-112
4	4d	3-OCH ₃ C ₆ H ₄	96	183-186
5	4e	Pyridin-2-yl	86	235-240
6	4f	2-OH,5-NO ₂ C ₆ H ₃	90	159-163
7	4g	4-FC ₆ H ₄	92	152-156
8	4h	2-NO ₂ C ₆ H ₄	89	128-132
9	4i	4-NO ₂ C ₆ H ₄	87	142-146

Table 2. Comparison of nano-rice bran /TiCl₄ and various catalyst in the synthesis of pyrano[3,2-b]pyrans.

Entry	Catalyst	Solvent	Condition	Time	Yield	Ref.
1	SBPPSP	EtOH/H ₂ O	Reflux	12-35 min	84-95	1
2	DABCO	MeOH	Reflux	12 h	74-95	9
3	Et ₃ N	[Bmim]BF ₄	r.t	8-180 min	69-99	10
4	Nano-rice bran /TiCl ₄	H ₂ O	r.t.	15-20 min	85-96	Present work

Results and discussion

Nano-rice bran /TiCl₄ was prepared and characterized. Morphology and structural of the rice bran and nano-rice bran/TiCl₄ were observed by SEM images as shown in Figure 1 and figure 2 respectively. The results of EDX analyses of the rice bran and nano-rice bran /TiCl₄ are given in figures 3 and 4.

**Figure 1.** SEM image of rice bran.

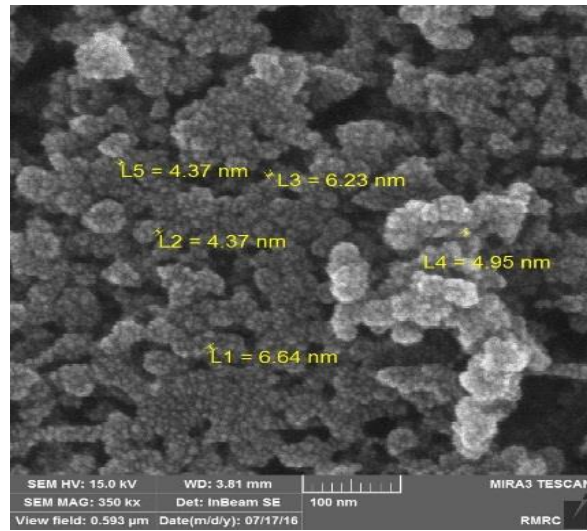


Figure 2. SEM image of nano-rice bran /TiCl₄.

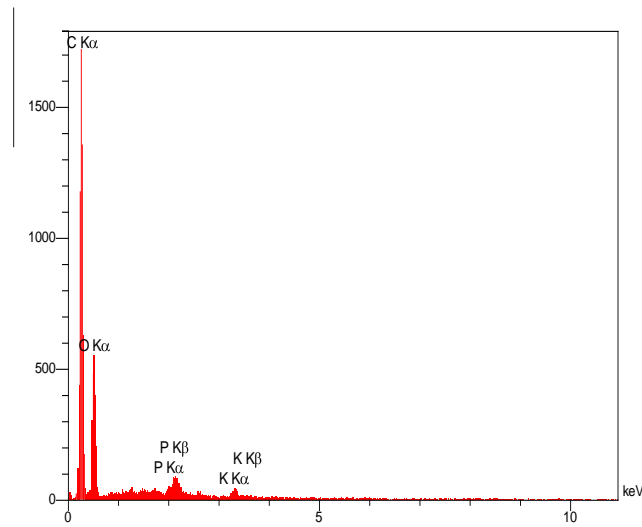


Figure 3. EDX of rice bran.

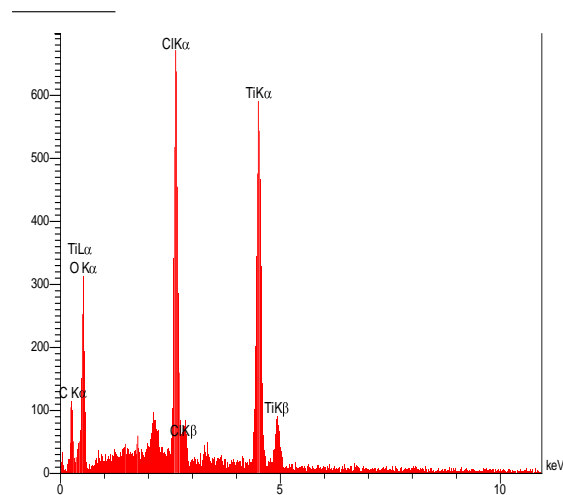
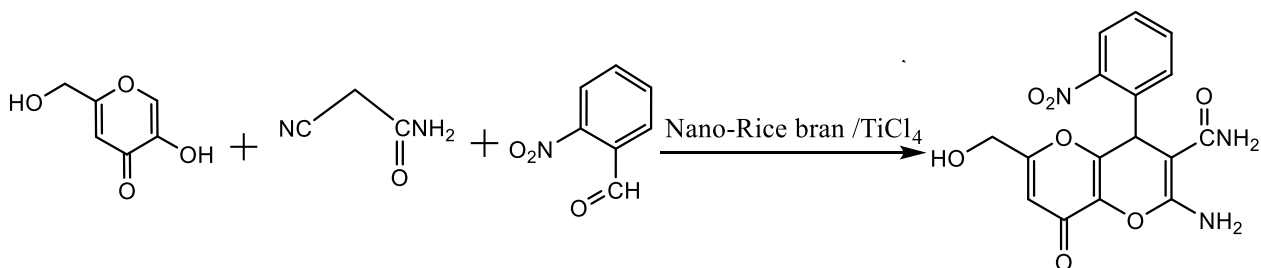


Figure.4. EDX of nano-rice bran /TiCl₄.*Reaction condition in the synthesis pyrano[3,2-b]pyrans*

Reaction of cyanoacetamide, kojic acid and 2-nitrobenzaldehyde was considered as a model reaction (scheme 2). Several solvents such as, EtOH/H₂O, EtOH, CH₃CN and H₂O were tested as media. Among the solvents, the best yield was obtained using H₂O. In order to determine the optimum quantity of nano-rice bran /TiCl₄, model reaction was carried out stirred at room temperature in water using different quantities of nano-rice bran /TiCl₄. Among the different quantities of nano-rice bran /TiCl₄, 0.03 g of nano-rice bran /TiCl₄ gives an excellent yield in 15 minute. The highest yield was obtained when 1.2mmolcyanoacetamide were reacted with 1.0 mmol of kojic acid and 1.0 mmol 2-nitrobenzaldehyde in H₂O at room temperature. When cold media or refluxing H₂O was used, decrease of yield was observed. Also we have found in the absence of the catalyst, in the presence of rice bran, and in the presence of TiCl₄ the product formation was unsuccessful.

**Scheme 2.** Model reaction to optimize the reaction conditions.*Characterization data of the compounds**2-amino-6-(hydroxymethyl)-4-(2-hydroxyphenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4a)*

White powder; IR (KBr, cm⁻¹): 3600(OH), 3420 (NH₂), 3115(NH₂), 1648 (C=O), 1617(C=O); ¹HNMR (400 MHz, DMSO) δ: 7.93 (s, 2H, NH₂), 7.42 (m, 1H, Ar-H), 7.05 (m, 1H, Ar-H) 6.97 (s, 2H, NH₂), 6.59 (m, 1H, Ar-H), 6.21 (s, 1H, CH), 6.09 (m, 1H, Ar-H), 5.43 (s, 1H, CH), 5.22 (s, 1H, OH), 4.22 (m, 2H, CH₂) ppm; Anal. Calcd. for C₁₆H₁₄N₂O₆ (%): C, 58.18; H, 4.27; N, 8.48. Found: C, 58.16; H, 4.32; N, 8.46.

2-amino-4-(5-bromo-2-hydroxyphenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4b)

White powder; IR (KBr, cm⁻¹): 3550(OH), 3385(NH₂), 3195(NH₂), 1643(C=O), 1614(C=O); ¹HNMR(400 MHz, DMSO) δ: 7.74 (s, 2H, NH₂), 7.43(d, 1H, J=3.2 Hz, Ar-H), 7.15(s, 2H, NH₂), 7.02-7.05(m, 2H, Ar-H), 6.49(s, 1H, CH), 6.15(s, 1H, CH), 6.12 (s, 1H, OH), 4.99(s, 1H, OH), 3.91-

4.17(dd,2H, $J=15.6$ Hz, $J=4.6$ Hz,CH₂) ppm; Anal. Calcd.for C₁₆H₁₃BrN₂O₆ (%): C,46.96; H, 3.20; N, 6.85. Found: C, 46.90; H, 3.28; N, 6.83.

2-amino-4-(4-cyanophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4c)

White powder; IR (KBr, cm⁻¹): 3550(OH),3300(NH₂), 2200 (CN),1644(C=O), 1612(C=O);¹HNMR (400 MHz, DMSO) δ : 9.38(s, 2H, NH₂), 7.57-7.38 (dd, 4H, $J=8$ Hz, Ar-H), 6.44(s, 2H, NH₂), 6.33(s, 1H, CH), 6.07(s,1H, CH), 5.64(s, 1H, OH), 4.14-4.27(dd, 2H, $J=15.6$ Hz, $J=4.5$ Hz, CH₂) ppm;Anal. Calcd.for C₁₇H₁₃N₃O₅ (%): C, 60.18; H, 3.86; N, 12.38. Found: C, 60.10; H, 3.81; N, 12.33.

2-amino-6-(hydroxymethyl)-4-(3-methoxyphenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4d)

White powder; IR (KBr, cm⁻¹): 3365(NH₂), 1700(C=O), 1651(C=O);¹HNMR (400 MHz, DMSO) δ : 8.28 (s, 2H, NH₂), 7.59-8.15 (m, 4H, Ar-H), 6.36 (s, 2H, NH₂), 6.15 (s, 1H, CH), 5.23 (s, 1H, CH), 5.05 (t, 1H, OH),4.37 (s, 3H, CH₃), 4.15-4.29(dd, 2H, $J=9.2$ Hz, $J=4$ Hz, CH₂) ppm;Anal. Calcd.for C₁₇H₁₆N₂O₆ (%): C, 59.30; H, 4.68; N, 8.14. Found: C, 59.28; H, 4.70; N, 8.18.

2-amino-6-(hydroxymethyl)-8-oxo-4-(pyridin-2-yl)-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4e)

Yellow powder; IR (KBr, cm⁻¹): 3375 (NH₂), 3270 (NH₂), 1695(C=O), 1622(C=O);¹HNMR (400 MHz, DMSO) δ : 8.78(s, 2H, NH₂), 7.94(d, 1H, Ar-H), 6.38(s, 2H, NH₂), 6.17(s, 1H, CH), 6.14(s, 1H, CH), 5.69(s, 1H, OH), 4.31(s, 2H, CH₂)ppm;Anal. Calcd.for C₁₅H₁₃N₃O₅ (%): C, 57.14; H, 4.16; N, 13.33. Found: C, 57.10; H, 4.20; N, 13.38.

2-amino-4-(2-hydroxy-5-nitrophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4f)

White powder; IR (KBr, cm⁻¹): 3300(NH₂), 3250(NH₂), 1665(C=O), 1624(C=O);¹HNMR (400 MHz, DMSO), δ : 7.81 (s,2H, NH₂),6.82-6.91 (m, 3H, Ar-H),6.50 (s, 2H,NH₂), 6.33 (s, 1H, OH),5.74 (t, 1H, $J=6$ Hz,OH),4.12-4.35 (dd, 2H, $J=15.6$ Hz, $J=5.6$ Hz), ppm;Anal. Calcd.for C₁₆H₁₃N₃O₈ (%): C, 51.21; H, 3.49; N, 11.20. Found: C, 51.18; H, 3.52; N, 11.28.

2-amino-4-(4-fluorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4g)

Whitepowder; IR (KBr, cm^{-1}): 3340(NH_2), 3285(NH_2), 1644($\text{C}=\text{O}$), 1610($\text{C}=\text{O}$); ^1H NMR(400 MHz, DMSO) δ : 9.98(s, 2H, NH_2), 7.42-7.47 (t, 1H, $J=8.8\text{Hz}$, Ar-H), 7.35-7.38(m, 1H, Ar-H), 7.14-7.18(m, 2H, Ar-H), 6.55(s, 2H, NH_2), 6.30 (s, 1H, CH), 5.71 (t, 1H, $J=10\text{Hz}$, OH), 5.02 (s, 1H, CH), 4.17-4.28 (dd, 2H, $J=15.6\text{Hz}$, $J=4.5\text{Hz}$, CH_2) ppm; Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{FN}_2\text{O}_5$ (%): C, 57.83; H, 3.94; N, 8.43. Found: C, 57.88; H, 3.89; N, 8.50.

2-amino-6-(hydroxymethyl)-4-(2-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4h)

Whitepowder; IR (KBr, cm^{-1}): 3425(NH_2), 3250(NH_2), 1706($\text{C}=\text{O}$), 1632($\text{C}=\text{O}$); ^1H NMR(400 MHz, DMSO) δ : 9.21(s, 2H, NH_2), 7.52-8.28 (m, 4H, Ar-H), 6.41(s, 1H, CH), 6.30(s, 1H, CH), 6.29(s, 2H, NH_2), 5.53(s, 1H, OH), 4.09-4.21(dd, 2H, $J=15.6\text{Hz}$, $J=4.4\text{Hz}$, CH_2) ppm; Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_7$ (%): C, 53.49; H, 3.65; N, 11.70. Found: C, 53.48; H, 3.70; N, 11.76.

2-amino-6-(hydroxymethyl)-4-(4-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carboxamide (4i)

Whitepowder; IR (KBr, cm^{-1}): 3455(NH_2), 3310(NH_2), 1643($\text{C}=\text{O}$), 1613($\text{C}=\text{O}$); ^1H NMR (400 MHz, DMSO) δ : 9.37(s, 2H, NH_2), 7.65-8.24 (dd, 4H, $J=8.8\text{Hz}$, Ar-H), 6.52(s, 2H, NH_2), 6.30(s, 1H, CH), 6.12(s, 1H, CH), 5.63(s, 1H, OH), 4.14-4.25(dd, 2H, $J=15.6\text{Hz}$, $J=4.5\text{Hz}$, CH_2) ppm; Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_7$ (%): C, 53.49; H, 3.65; N, 11.70. Found: C, 53.47; H, 3.68; N, 11.68.

Conclusion

The present investigation shows that nano-rice bran/ TiCl_4 a capable nanocatalyst to be used for pyrano[3,2-b]pyrans synthesis via one-pot reaction of kojic acid, aromatic aldehydes and cyanoacetamide. Nano-rice bran/ TiCl_4 was successfully prepared and characterized using SEM and EDX analysis. The presence of new functional groups on the surface of rice bran/ TiCl_4 resulted in a dramatic increase of surface polarity and acidity, thereby improving the catalytic efficiency of the nano-rice bran/ TiCl_4 . Prominent among the advantages of this method are such as shorter reaction times, simple work-up and excellent yield.

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