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Electrospun KF-PVA composite nano-fibers: an efficient water soluble catalyst for the multi-component, preparation of pyrano[3,2-c]chromene derivatives

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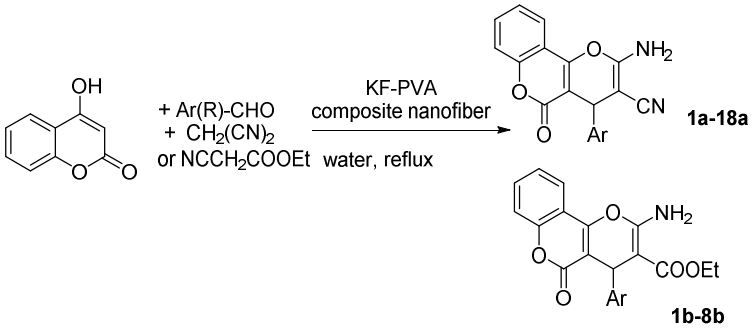
ABSTRACT
A nanofiber type catalyst of electrospun KF-Polyvinyl alcohol composite nanofibers was used for the synthesis of pyrano[3,2-c]chromene derivatives *via* multi-component reaction of aromatic aldehydes, malononitrile/ethyl cyanoacetate and 4-hydroxycoumarin in aqueous media.
Keywords*: multicomponent reaction; pyrano[3,2-c]chromene; KF-Polyvinyl alcohol composite nanofibers; 4-hydroxycoumarin*.

1. INTRODUCTION

During the years pyrano[3,2-c]chromene derivatives have gained considerable interest as they are showed a great variety of biological and pharmaceutical activities such as spasmolytic, diuretic, anticoagulant, anti-cancer, and anti-anaphylactic activity. Interestingly some diseases such as Alzheimer's, Huntington's and Parkinson's can be enhanced by fused structures of pyrano[3,2-c]chromenes [1-4]. The general procedure for the preparation of pyrano[3,2-c]chromene-3-carbonitrile derivatives includes the multi-component condensation reaction of *via* multi-component reaction of aromatic aldehydes, malononitrile, and 4-hydroxycoumarin. Many different basic or acidic materials such as DBU, [bmim]OH, TBAB, titanium dioxide, sodium tungstate, $ZnAl_2O_4$–Bi_2O_3 composite nano-powder, ZnO, CuO, MgO, Bi_2O_3 and spinel zinc ferrite were proved viable catalysts for this reaction [5-16].

There are no few reports regarding the application of KF-Polyvinyl alcohol composite nanofibers in the preparation of organic compounds. However, the discovery of new synthetic methodologies that facilitate the development of organic compounds is of great interest. One approach to address this challenge involves the development of new synthesized environmentally friendly catalysts to catalyze the reaction [17-30]. Therefore, the scope of the present work was extended for the multi-component condensation reaction of aromatic aldehydes, malononitrile/ethyl cyanoacetate and 4-hydroxycoumarin in aqueous media to afford pyrano[3,2-c]chromene derivatives using KF-PVA composite nanofibers as a green, environmentally friendly catalyst (Scheme 1).



Scheme 1. Preparation of pyrano[3,2-c]chromene derivatives using KF-Polyvinyl alcohol composite nanofibers.

2. EXPERIMENTAL SECTION

All reagents were purchased from Merck and Aldrich and used without further purification. Field emission scanning electron microscope (FE-SEM) image was obtained on HITACHI S-4160. Transmission electron microscopy (TEM) image was taken using a Philips EM-430 microscope operated at 80 kV. The NMR spectra were recorded on a Bruker Avance DPX 400 MHz instrument. The spectra were measured in DMSO-d_6 relative to TMS (0.00 ppm). Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel Polygram SIL G/UV 254 plates.

2.1. Preparation of KF-Polyvinyl alcohol composite nanofibers. A 1M solution of KF in water was performed. The solution was combined with a solution of PVA. The ratio of KF to the PVA is 40/60 Wt.%. Thus, a viscous gel of KF/PVA composite was obtained. The above gel was put in a syringe. The positive terminal of a high voltage power supply was connected to the metallic syringe tip (a needle with a diameter of 0.6 mm) while the negative terminal was connected to a conductive drum covered with aluminum foil as a collector of fibers. A voltage of 20 kV and a speed of 0.5 mlh^{-1} were applied to the solution, and a dense web of fibers was collected on the aluminum foil.

2.2. General procedure. A mixture of aldehydes (1 mmol), 4-hydroxycoumarin (1 mmol), malononitrile/ethyl cyanoacetate (1 mmol), and KF-Polyvinyl alcohol composite nanofibers (40 mol%) was refluxed in water (10 mL) for the appropriate time. TLC monitored the progress of the reaction. After completion of the reaction, the solvent was concentrated, and crystallization from EtOH purified the crude products. The spectral data of selected compounds is given below:

2-amino-5-oxo-4-phenyl-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile **(Table 2, Product 1a):** ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 4.17 (s, 1H, CH), 6.41 (s, 2H, NH_2), 7.34-7.70 (m, 9H)

ppm; Elemental analysis: Found: C, 72.06; H, 3.75; N, 8.77% $C_{19}H_{12}N_2O_3$; requires: C, 72.15; H, 3.82; N, 8.86%.

2-amino-5-oxo-4-(p-tolyl)-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile **(Table 2, Product 2a):** ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 2.29 (s, 3H, CH_3), 4.77 (s, 1H, CH), 6.38 (s, 2H, NH_2), 7.07 (d, 2H, *J* = 8.0 Hz), 7.22 (d, 2H, *J* = 8.0 Hz), 7.57-7.73 (m, 4H) ppm; Elemental analysis: Found: C, 72.63; H, 4.18; N, 8.40% $C_{20}H_{14}N_2O_3$; requires: C, 72.72; H, 4.27; N, 8.48%.

2-amino-4-(4-methoxyphenyl)-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile **(Table 2, Product 3a):** ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 3.78 (s, 3H, OCH_3), 4.80 (s, 1H, CH), 6.44 (s, 2H, NH_2), 6.94 (d, 2H, *J* = 7.9 Hz), 7.44 (d, 2H, *J* = 8.0 Hz), 7.57-7.73 (m, 4H) ppm; Elemental analysis: Found: C, 69.27; H, 3.96; N, 7.99% $C_{20}H_{14}N_2O_4$; requires: C, 69.36; H, 4.07; N, 8.09%.

2-amino-4-(4-nitrophenyl)-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile **(Table 2, Product 10a):** ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 5.17 (s, 1H, CH), 6.97 (s, 2H, NH_2), 7.44 (d, 2H, *J* = 7.8 Hz), 7.58-7.73 (m, 4H), 8.12 (d, 2H, *J* = 7.8 Hz) ppm; Elemental analysis: Found: C, 63.11; H, 2.96; N, 11.53% $C_{19}H_{11}N_3O_5$; requires: C, 63.16; H, 3.07; N, 11.63%.

3. RESULTS SECTION

The morphology of KF/PVA composite nanofibers were investigated using SEM and TEM images and the results are revealed in Figures 1,2. Figure 1 shows that the randomly oriented nanofibers have uniform shapes and sizes. The composite nanofibers diameter is different from <100 nm to a few micrometers. The increase in the fiber diameter is due to several points of agglomeration.

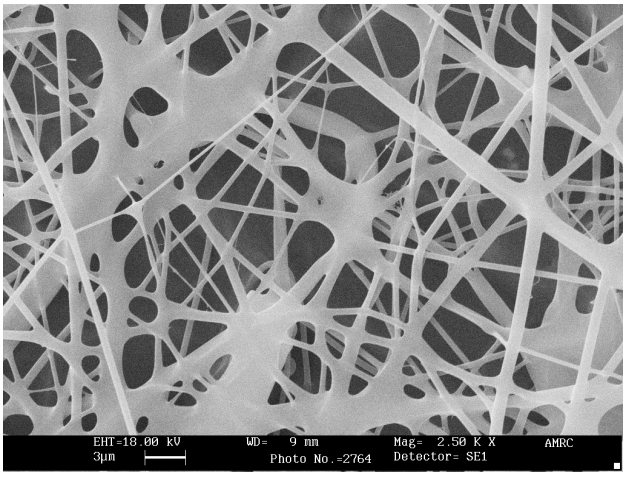


Figure 1. FE-SEM micrograph of KF-PVA composite nano-fibers.

The TEM image shows that the particles of KF are well dispersed within the nanofibers and confirm that the fibers have nanoscale diameters (Figure 2).

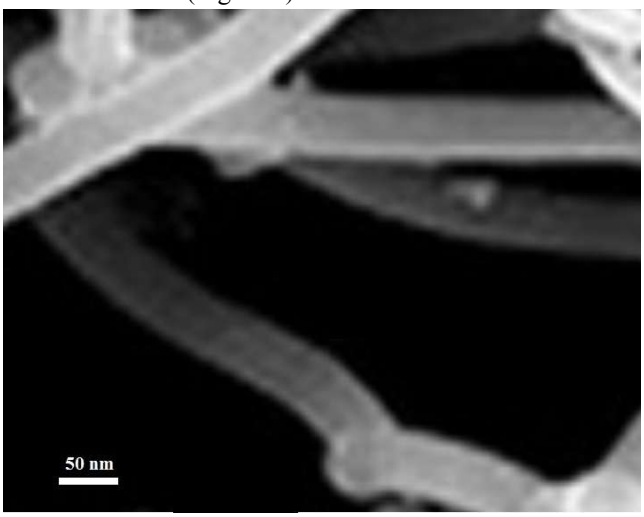


Figure 2. TEM image of KF-PVA composite nano-fibers.

Figure 3 shows UV–Vis spectrum of the KF/PVA composite nanofibers. It is clearly observable from the figure that there is no absorption in the visible for PVA. While a KF/PVA composite nanofiber has a strong absorption in the UV range (259 nm).

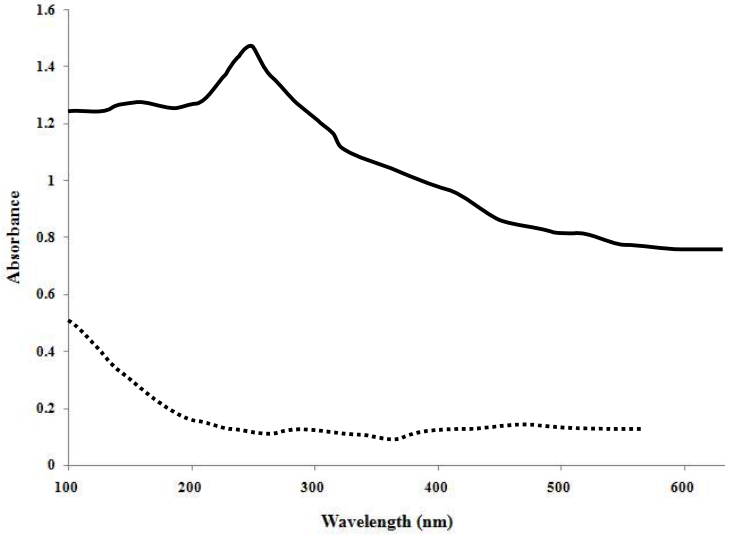


Figure 3. UV–Vis absorption spectra of PVA (dashed line) and KF-PVA composite nano-fibers.

The catalytic activity of the as-prepared KF/PVA nanofibers was examined by the condensation reaction of aromatic aldehydes, malononitrile/ethyl cyanoacetate, and 4-hydroxycoumarin.

Table 1. Optimization of the reaction conditions

Entry	Catalyst amount (mol%)	Solvent (5 mL)	Temperature (°C)	Time (h)/ Yield (%)[a]
1	40	-	r.t.	2/-
2	40	Hexane	Reflux	2/-
3	40	EtOAc	Reflux	2/55
4	40	EtOH	Reflux	2/69
5	40	Et_2O	Reflux	2/-
6	40	CH_2Cl_2	Reflux	2/-
7	40	CH_3CN	Reflux	2/45
8	40	H_2O	Reflux	2/93
9	-	H_2O	Reflux	2/0
10	20	H_2O	Reflux	3/49
11	60	H_2O	Reflux	2/86
12	80	H_2O	Reflux	1/87

[a]Isolated yield

First, to optimize the reaction conditions, the condensation of benzaldehyde, malononitrile and 4-hydroxycoumarin was examined in different polar and non-polar solvents at reflux temperatures (Table 1). The reaction affords substantially no

product at room temperature, in the absence of a catalyst and non-polar solvents e.g. hexane, CH_2Cl_2, and Et_2O. The main reason for these results is that the temperature has an essential role in the progress of the reaction. Using polar solvents such as EtOH, EtOAc and CH_3CN a poor to moderate yield was obtained. Finally, it was observed that water is the best choice to have an excellent yield (93%) of product in 2h. Increasing of the catalyst amounts did not improve the product yield.

Encouraged by this result, The catalytic activity of the as-prepared KF/PVA nanofibers was examined by the condensation reaction of different aromatic aldehydes, malononitrile/ethyl cyanoacetate and 4-hydroxycoumarin to afford a series of pyrano[3,2-c]chromene derivatives in high yields (Table 2). The reactions worked well with almost all the aldehydes. However, aromatic aldehydes bearing electron withdrawing groups (such as nitro and halide), showed better reactivity and the reactions were completed in shorter time.

Table 2. Preparation of pyrano[3,2-c]chromene-3-carbonitrile derivatives using KF-Polyvinyl alcohol composite nanofibers (40 mol%).

Product	Aldehyde	Time (h)	Yield (%)[a]	M.p.[°C]
1a	Benzaldehyde	2	93	256-258
2a	4-Methylbenzaldehyde	3	84	253-255
3a	4-Methoxybenzaldehyde	4	80	249-251
4a	3,4,5-tri Methoxybenzaldehyde	4	86	224-226
5a	4-Chlorobenzaldehyde	1.5	90	263-265
6a	3-Chlorobenzaldehyde	1.5	94	244-246
7a	2,4-diChlorobenzaldehyde	2	87	256–258
8a	2,6-diChlorobenzaldehyde	3	92	274-277
9a	2,3-diChlorobenzaldehyde	3	82	273-276
10a	4-Nitrobenzaldehyde	1.5	90	259–261
11a	3-Nitrobenzaldehyde	1.4	87	264-266
12a	4-Bromobenzaldehyde	1.5	86	255-257
13a	4-Fluorobenzaldehyde	2	89	262-264
14a	4-Hydroxybenzaldehyde	4	79	267-269
15a	2-Thiophene carboxaldehyde	3	74	253-255
16a	Furfural	3	70	230-232
17a	2-Chlorobenzaldehyde	3	77	274-276
18a	4-*N,N'*-Dimethylamino benzaldehyde	4	72	225-227
1b	Benzaldehyde	2	76	201-203
2b	4-Methylbenzaldehyde	3	83	190-192
3b	4-Methoxybenzaldehyde	5	89	164-166
4b	4-Chlorobenzaldehyde	1.6	88	192-194
5b	2,4-diChlorobenzaldehyde	2	85	202-204
6b	4-Nitrobenzaldehyde	1.5	90	241-243
7b	3-Nitrobenzaldehyde	1.5	94	249-251
8b	4-Hydroxybenzaldehyde	4	81	260-262

[a]Isolated yield; All product were characterized by their NMR analysis.

4. CONCLUSIONS

In this study, KF/PVA nanofibers were used to synthesize a series of pyrano[3,2-c]chromene derivatives *via* multi-component condensation reaction of aromatic aldehydes, malononitrile/ethyl cyanoacetate and 4-hydroxycoumarin in high yields.

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6. ACKNOWLEDGEMENTS

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