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## Short Communication

# Ionic liquid immobilized onto fibrous nano-silica: A highly active and reusable catalyst for the synthesis of quinazoline-2,4(1 H,3 H)-diones



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#### ARTICLE INFO

#### ABSTRACT

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Keywords: KCC-1 Quinazoline-2,4(1 H,3 H)-dione Nanoparticle One-pot synthesis Green chemistry Fibrous nano-silica In this study, a novel fibrous nano-silica (KCC-1) supported ionic liquid (KCC-1/IL) with high surface area and easy accessibility of active sites was successfully developed by a facile approach. The synthesized KCC-1/IL nanocatalyst exhibited excellent catalytic activity for the synthesis of quinazoline-2,4(1 H,3 H)-diones from CO<sub>2</sub> and 2-aminobenzonitriles under mild conditions to the easy accessibility of the active sites. A high catalytic activity and ease of recovery from the reaction mixture by using filtration and several reuses without any significant loss in performance are additional eco-friendly attributes of this catalytic system.

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#### 1. Introduction

Quinazoline-2,4(1 H,3 H)-diones are an important class of pharmaceutical intermediates. Synthesis of quinazoline-2,4(1 H,3 H)-diones using CO<sub>2</sub> and 2-aminobenzonitriles as raw materials has attracted considerable interest, and various kinds of catalysts have been used to promote the reactions, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [1], Cs<sub>2</sub>CO<sub>3</sub> [2], 1-butyl-3-methylimidazolium hydroxide ([Bmim]OH) [3], MgO/ZrO<sub>2</sub> [4], 1,1,3,3-tetramethylguanidine (TMG) [5], ZnCl<sub>2</sub> [6], [Bmim]Ac [7], and so on. However, these reaction systems are more or less subjected to some drawbacks, such as long reaction time, high pressure of CO<sub>2</sub>, use of organic solvents, and difficulty in recycling the catalysts.

Recently, the use of nanocatalysts has increased rapidly and has resulted in the development of several active and efficient nanocatalysts for various protocols [8–18]. These systems have several advantages over conventional catalysts, such as superior activity and improved stability. Combining metal nanoparticles with a support of choice provides a large field for the discovery of new, highly active nanocatalysts for important and challenging reactions, which also offer the additional advantage of recyclability. Surface functionalized mesoporous materials have emerged as one of the most important research areas in the field of advanced functional materials. Fibrous nano-silica (KCC-1), which features a high surface area and easy accessibility through its fibers (as opposed to the traditional use of pores), is reported by Polshettiwar et al. [19] This would be an ideal catalyst support candidate for the fabrication of noble metal-based catalysts that exhibit high accessibility of active sites and excellent catalytic activity. In this article, we designed and synthesized ionic liquid functionalized KCC-1. Then the strength was tested for the synthesis of quinazoline-2,4(1 H, 3 H)-diones.

#### 2. Experimental

#### 2.1. Materials and methods

Chemical materials were purchased from Fluka and Merck in high purity. Melting points were determined in open capillaries using an Electrothermal 9100 apparatus are uncorrected. FTIR spectra were recorded on a VERTEX 70 spectrometer (Bruker) in the transmission mode in spectroscopic grade KBr pellets for all the powders. The particle size and structure were observed by using a Philips CM10 transmission electron microscope operating at 100 KV. Powder X-ray diffraction data was obtained using Bruker D8 Advance model with Cu ka radiation. The thermogravimetric analysis (TGA) was carried out on a NETZSCH STA449F3 at a heating rate of 10 °C min<sup>-1</sup> under nitrogen. The magnetic measurement was carried out in a vibrating sample magnetometer (VSM) (4 in., Daghigh Meghnatis Kashan Co., Kashan, Iran) at room temperature. NMR spectra were recorded in CDCl<sub>3</sub> on a Bruker Avance



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#### Table 1

Physicochemical properties of the silica-supported ionic liquid nanocatalysts and of the precursor materials.

Entry	Material	Surface area [m <sup>2</sup> g <sup>-1</sup> ]	BJH PV [cm <sup>3</sup> g <sup>-1</sup> ]	BJH PS [nm]	IL loading [wt.%]	
1	KCC-1/IL	281	0.50	6.8	22.2	

DRX-400 MHz instrument spectrometer using TMS as internal standard. The purity determination of the products and reaction monitoring was accomplished by TLC on silica gel polygram SILG/UV 254 plates.

#### 2.2. General procedure for the preparation of KCC-1 NPs

In this study, KCC-1 was successfully synthesized by a traditional hydrothermal method [20]. TEOS (2.5 g) was dissolved in a solution of cyclohexane (30 mL) and 1-pentanol (1.5 mL). A stirred solution of cetylpyridinium bromide (CPB 1 g) and urea (0.6 g) in water (30 mL) was then added. The resulting mixture was continually stirred for 45 min at room temperature and then placed in a teflon-sealed hydrothermal reactor and heated at 120 °C for 5 h. The silica formed was isolated by centrifugation, washed with deionized water and acetone, and dried in a drying oven. This material was then calcined at 550 °C for 5 h in air.

# 2.3. General procedure for the preparation of KCC-1/3-chloropropylsilane $\ensuremath{\mathsf{NPs}}$

KCC-1 (2 mmol) and THF (20 mL) were mixed together in a beaker, and then NaH (20 mmol) was dispersed in to the mixture by ultrasonication. 3-chloropropyltriethoxysilane (22 mmol) was added drop-wise at room temperature and stirred for another 16 h at 60 °C. The resultant products were collected and washed with ethanol and deionized water in sequence, and then dried under vacuum at 60 °C for 2 h for further use.

#### 2.4. General procedure for the preparation of KCC-1/IL NPs

First, hexamethylenetetramine (100 mmol) and KCC-1/3-chloropropylsilane (5 mmol) were dissolved in dry ethanol (50 mL) under stirring. The resulting mixture was refluxed for 24 h under nitrogen protection. After removal of ethanol in vacuum, the solid residue was dissolved in water. The obtained solution was concentrated under vacuum and then extracted with ethanol-tetrahydrofuran. Subsequently, ion exchange with sodium tetrafluoroborate (110 mmol) in ethanol/ water was performed for 48 h at ambient temperature. After the solvent



Fig. 2. FTIR spectra of (a) KCC-1 NPs, and (b) KCC-1/IL NPs.

was removed, the resulting mixture was filtered, after which the filtrate was dried under vacuum at 100 °C.

#### 2.5. General procedures for preparation of quinazoline-2,4(1 H,3 H)-diones

2-aminobenzonitrile (1 mmol), and KCC-1/IL NPs (0.0007 g) were added. The autoclave was closed, purged twice with CO<sub>2</sub> gas, pressurized with 0.8 MPa of CO<sub>2</sub> and then heated at 70 °C for 60 min. Then the reactor was cooled to ambient temperature, and the resulting mixture was transferred to a 50 mL round bottom flask. Upon completion, the progress of the reaction was monitored by TLC when the reaction was completed, EtOH was added to the reaction mixture and the KCC-1/IL NPs were separated by distillation under vacuum. Then the solvent was removed from solution under reduced pressure and the resulting product purified by recrystallization using n-hexane/ethyl acetate.

#### 3. Results and discussion

This procedure was adapted to functionalize KCC-1 thus affording silica-supported ionic liquid catalysts: KCC-1/IL nanocatalysts involved several steps (Scheme 2). The fibers of silica support have many Si-OH groups on the surfaces; thus, it was expected that the silica support could be easily functionalized with 3-chloropropyltriethoxysilane to form KCC-1/3-chloropropylsilane NPs. Then, fibrous nano-silica supported ionic liquid (silica support/IL), which is featured with easy accessibility of active sites and high catalytic activity, was synthesized by a simple, cost-effective procedure.

A study of the physicochemical properties (specific surface area, cumulative pore volume, and pore size) of KCC-1/IL is reported in Table 1. High ionic liquid loading (22.2 wt.%, Table 1) could be obtained under identical preparation conditions for all support.



Fig. 1. SEM image of the fresh KCC-1/IL NPs (a), TEM images of the fresh KCC-1/IL NPs (b), and TEM images of KCC-1/IL NPs after ten reuses (c).



Fig. 3. (a) XRD pattern of KCC-1/IL NPs; (b) TGA diagram of KCC-1/IL NPs; and (c) Adsorption–desorption isotherms of KCC-1 and KCC-1/IL NPs.

The TEM and SEM images of the KCC-1/IL catalysts were shown in Fig. 1. As can be seen from Fig. 1a and b, the KCC-1/IL NPs had a consistent particle size range of 150–170 nm. Subsequently, ionic liquid was coated on the KCC-1 to form KCC-1/IL (Fig. 1b). The recyclability test was stopped after ten runs. Comparison of TEM images of used catalyst (Fig. 1c) with those of the fresh catalyst (Fig. 1b) showed that the morphology and structure of KCC-1/IL NPs remained intact after ten recoveries. Low agglomeration of KCC-1/IL NPs can be seen.

The reactions were monitored by FTIR, as shown in Fig. 2. For unmodified KCC-1, the band at 1100 cm<sup>-1</sup> was assigned to the vibration of the Si–O bonds (Fig. 2a). After the supported ionic liquid on the surface of KCC-1, two bands at 2931 and 2890 cm<sup>-1</sup> associated with C–H stretching significantly enhanced. Meanwhile, two new bands at 1486

Table 2	
Textural parameters of prepared compounds. <sup>a</sup>	

Entry	Catalyst/cycle reusability	Specific surface area (m²/g)	Pore volume (cm <sup>3</sup> /g)	Average pore radius (nm)
1	KCC-1	593	0.802	2.09
2	KCC-1/IL	510	0.682	1.27

<sup>a</sup> Calculated by the BJH method.

Application of the silica support/ILs for the catalytic synthesis of quinazoline-2,4(1 H,3 H)-dione.<sup>a</sup>

Entry	Catalyst	Yield (%) <sup>b</sup>
1	KCC-1/IL/Cl	67
2	KCC-1/IL/FeCl <sub>4</sub>	78
3	KCC-1/IL/HSO <sub>4</sub>	42
4	KCC-1/IL/H2PW12O40	86
5	KCC-1/IL/BF <sub>4</sub>	97

<sup>a</sup> Reaction conditions: 2-aminobenzonitrile (1 mmol), silica support/ILs NPs (0.001 g), and CO<sub>2</sub> 1.5 MPa, at 120  $^\circ$ C under solvent-free conditions after 2 h.

<sup>o</sup> Isolated yields.

and 1568 cm<sup>-1</sup> associated with C–H and C–C stretching appeared, respectively (Fig. 2b).

X-ray diffraction patterns and the infrared spectra of KCC-1/IL NPs have been measured in order to obtain more information about their crystallographic features and molecule structures. The XRD patterns of KCC-1 NPs, and as-prepared KCC-1/IL NPs catalyst were shown in Fig. 3a. The broad peak between 20 and 30° corresponds to amorphous silica.

TGA experiments were carried out by heating samples under air up to 800 °C in order to check the amount of the encapsulated fibrous nano-silica, and ionic liquid, and obtain information on their thermal stability. As seen in Fig. 3b, two weight loss stages were observed in flow air. About 9.7 wt.% weight loss was observed in the first stage (40–250 °C) corresponding to the loss of small molecules such as physically absorbed water. In the second stage (400–600 °C), weight loss is about 19.2 wt.%, which can be attributed to the pyrolysis of cross-linking organic group derivatives.

The N<sub>2</sub> adsorption–desorption isotherms of all samples (Fig. 3c) exhibit type-IV isotherms with an obvious H1-type hysteresis loop, revealing strong evidence of mesoporous cylindrical or rod-like pores. These results indicate that the mesoporous texture of the materials was preserved during the surface modification, which was due to the loading of the functional group in KCC-1 and KCC-1/IL NPs. A considerable decrease in height of the capillary condensation step about the final product is observed with respect to decrease in average pore diameter, pore volume and surface area (Table 2).

Five separated reactions were examined in the presence of KCC-1/IL/ Cl, KCC-1/IL/BF<sub>4</sub>, KCC-1/IL/FeCl<sub>4</sub>, KCC-1/IL/HSO<sub>4</sub>, and KCC-1/IL/ H<sub>2</sub>PW<sub>12</sub>O<sub>40</sub>. The results of these studies showed that KCC-1/IL/Cl, KCC-1/IL/FeCl<sub>4</sub>, KCC-1/IL/HSO<sub>4</sub>, and KCC-1/IL/H<sub>2</sub>PW<sub>12</sub>O<sub>40</sub> as catalysts gave the desired product in average to good yield (42–86%) (Table 3, entries 1–4). A similar reaction in the presence of KCC-1/IL/BF<sub>4</sub> as a non-

Table 4			
Synthesis of guinazoline-2,4(	1 H,3 H)-dione b	v KCC-1/IL NPs in	different solvents. <sup>a</sup>

Entry	Solvent	Yield (%) <sup>b</sup>
1	EtOH	73
2	H <sub>2</sub> O	85
3	CH <sub>3</sub> CN	-
4	THF	32
5	CH <sub>2</sub> Cl <sub>2</sub>	48
6	EtOAc	72
7	DMF	60
8	Toluene	64
9	<i>n</i> -Hexane	-
10	CHCl <sub>3</sub>	51
11	DMSO	83
12	MeOH	46
13	Dioxane	-
14	Solvent-free	97

<sup>a</sup> Reaction conditions: 2-aminobenzonitrile (1 mmol), KCC-1/IL NPs (0.001 g), and CO<sub>2</sub>
 1.5 MPa, at 120 °C of solvents after 2 h.
 <sup>b</sup> Isolated yields.

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Fig. 4. (a) Effect of the amount of the catalyst on yield of quinazoline-2,4(1 H,3 H)-dione; (b) Effect of temperature on yield of quinazoline-2,4(1 H,3 H)-dione; (c) Effect of CO<sub>2</sub> pressure dependence with KCC-1/IL NPs catalyst system; and (d) Effect of time on yield of quinazoline-2,4(1 H,3 H)-dione.

supported catalyst gave the desired product in excellent yield (97%) due to the formation of by-products (Table 3, entry 5). Comparison of KCC- $1/IL/BF_4$  with other ionic liquid, demonstrates the advantage of  $BF_4$  as anion obtained the highest efficiency.

Having proved correct and complete synthesis of the catalysts, the catalysts performance and stability with the synthesis of quinazoline-2,4(1 H,3 H)-dione tested. In order to optimize the reaction conditions and obtain the best catalytic activity, the reaction of CO<sub>2</sub> and 2-aminobenzonitrile was used as a model, and was conducted under different reaction parameters such as amount of the catalyst, temperature, time, and solvent. Initially, the model reaction was carried out in several solvents to investigate the efficiency of the catalyst. In this study, it was found that conventional heating at 70 °C under solvent-free (Table 4) in 60 min at 0.8 bar CO<sub>2</sub> pressure in the presence 0.0007 g of KCC-1/IL is more efficient, with respect to reaction time and yield of the desired quinazoline-2,4(1 H,3 H)-dione (Fig. 4).

Since KCC-1/IL NPs were the most active of the one-component catalysts, they were tested in the conversion of six other terminal 2aminobenzonitriles (1a-f) into the synthesis of quinazoline-2,4(1 H,3 H)-diones (2a-f) (Scheme 1), results being shown in Table 5. In each case, the quinazoline-2,4(1 H,3 H)-diones were obtained with good to excellent isolated yield after 1 h using 0.0007 g of catalyst under solvent-free conditions at 70 °C under a constant pressure of carbon dioxide.



Scheme 1. Synthesis of quinazoline-2,4(1 H,3 H)-diones from CO<sub>2</sub> and 2-aminobenzonitriles.

We compared the catalytic performance of our catalyst with literature reported catalysts for the synthesis of quinazoline-2,4(1 H,3 H)-dione (Table 6). Table 6 clearly demonstrates that lower temperature, the minimum amount of catalyst, lower pressure of carbon dioxide and shorter reaction time were required for the synthesis of quinazoline-2,4(1 H,3 H)-dione, using KCC-1/IL NPs, while an appropriate, highly perfect, performance of the present catalyst was observed for this reaction.

These observations indicated that the catalysts were stable and could tolerate the present reaction conditions. The recyclability of catalysts was examined using the model reaction under identical conditions. After the required time, the catalysts were recovered from the reaction mixture by filtration, washed with ethyl acetate, and subsequently dried at 100 °C then reused. After ten consecutive reuses, KCC-1/IL NPs exhibited almost identical catalytic activity (Fig. 5a). The recyclability test was stopped after ten runs. Comparison of TEM images and FT-IR spectra (Figs. 1c and 5b) of used catalyst with those of the fresh catalyst (Figs. 1a,b and 2b) showed that the morphology and structure of KCC-1/IL NPs remained intact after ten recoveries. In order to know whether the reaction takes place at the surface of KCC-1/IL NPs or any IL species, ICP analysis of the remaining mixture after catalyst and product separation was investigated upon reaction completion. The amount of ionic liquid leaching after the ten repeated recycling was 4.2%. These

Table 5	
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Synthesis of quinazoline-2,4(1 H,3 H)-dione derivatives catalyzed by KCC-1/IL NPs.<sup>a</sup>

Entry	R	Product	Yield (%) <sup>b</sup>
1	Н	2a	97
2	Br	2b	91
3	F	2c	94
4	Cl	2d	92
5	Me	2e	88
6	NO <sub>2</sub>	2f	96

 $^{\rm a}\,$  Reaction condition: 2-aminobenzonitrile derivatives (1 mmol), KCC-1/IL NPs (0.0007 g), CO\_2 0.8 MPa, 1 h.

<sup>b</sup> Yield refers to isolated product.



Scheme 2. Schematic illustration of the synthesis for KCC-1/IL NPs.

observations indicated that the catalyst was stable and could tolerate the present reaction conditions.

#### 4. Conclusions

We developed a novel kind of robust catalytic hybrids based on the ionic liquid functionalized KCC-1 and used it as a nanocatalyst support for the first time. The ionic liquid was directly grafted from the KCC-1. These catalysts as an efficient, nontoxic, green, economical and recyclable catalytic protocol for the reaction of  $CO_2$  with 2-aminobenzonitriles to produce quinazoline-2,4(1 *H*,3 *H*)-diones in good to excellent yield under mild reaction condition have been developed. This synthetic method provides a green way to effectively prepare low-cost ionic liquid based catalysts and is promising for the development of other useful materials.

Table 6		
Comparison of the catalytic efficiency	of KCC-1/IL NPs with various ca	atalysts.

Entry	Catalyst	MPa (CO <sub>2</sub> )	Solvent	Temperature (°C)	Amount catalyst	Time (h)	Yield (%) <sup>a</sup>
1		2		120	-	10	[3]
1 2	-	2	-	120	- 5 mol (%)	10	10[3]
2	t_BuOK	3		120	$5 \mod (\%)$	18	_[3]
1	<i>L</i> -DUOK	2	_	120	5 mol (%)	10	5[3]
-4 5	Et N	2	-	120	5 mol (%)	10	20[3]
5	[Pmim]PE	2	-	120	5 mol (%)	10	[3]
7	[Bmim]HSO	2	_	120	5 11101 (%)	10	[3]
8	[Bmim]OH	3		120	$\frac{10}{10}$ mol (%)	18	01[3]
9	TMC	10		120	5  mol(%)	4	80 <sup>[5]</sup>
10	$M_{\sigma}O/7rO_{o}$	37	DMF	130	10  mol(%)	12	92 <sup>[4]</sup>
11	CuCla	5	DMF	200	1 equiv	5	20[6]
12	HgCla	5	DMF	200	1 equiv	5	15 <sup>[6]</sup>
12	FeCla	5	DMF	200	1 equiv	5	_[6]
14	AlCla	5	DMF	200	1 equiv	5	_[6]
15	SnCla	5	DMF	200	1 equiv	5	_[6]
16	TiCl	5	DMF	200	1 equiv	5	2[6]
17	ZnCl <sub>2</sub>	5	DMF	200	5 equiv	5	90 <sup>[6]</sup>
18	K <sub>2</sub> CO <sub>2</sub>	13	DMF	100	0.25 equiv	4	35 <sup>[2]</sup>
19	NacOs	1.3	DMF	100	0.25 equiv	4	0 <sup>[2]</sup>
20	KF	1.3	DMF	100	0.25 equiv	4	40 <sup>[2]</sup>
21	КОН	1.3	DMF	100	0.25 equiv	4	55 <sup>[2]</sup>
22	Cs <sub>2</sub> CO <sub>3</sub>	1.3	DMF	100	0.25 equiv	4	94 <sup>[2]</sup>
23	DBU	10	_	80	0.1 equiv	4	91 <sup>[1]</sup>
24	[Bmim]Ac	0.1	-	90	0.1 mol (%)	10	92 <sup>[7]</sup>
25	KCC-1/IL NPs	0.8	-	70	0.4 mol (%)	1	97

<sup>a</sup> Reaction conditions: 2-aminobenzonitrile (1 mmol), and CO<sub>2</sub> in different solvents and in different amounts of catalyst, temperature, and time.



Fig. 5. (a) Reuses performance of the catalysts; and (b) FT-IR spectrum of recovered KCC-1/IL NPs.

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