

RESEARCH PAPER

Synthesis and Characterization of a Novel Nanosilica Supported Bipyridinium Chloride Nanocomposite and its Application as a Basic Catalyst in the One-pot Preparation of Tetrahydrobenzo[b]pyran, Dihydropyrano[3,2-c]chromene and Dihydropyrano[4,3-b]pyran Derivatives

Ali Reza Kiasat^{1*}, Sheida Hamid¹ and Seyyed Jafar Saghanezhad²

¹ Chemistry Department, Faculty of Sciences, Shahid Chamran University of Ahvaz, Ahvaz, Iran

² ACECR-Production Technology Research Institute, Ahvaz, Iran

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ABSTRACT

A novel rice-husk-silica supported n-propyl bipyridinium chloride (RHPrBPCI) has been prepared. Due to the basicity of RHPrBPCI, it was decided to evaluate its catalytic activity in the one-pot preparation of tetrahydrobenzo[b]pyran, dihydropyrano[3,2-c]chromene and dihydropyrano[4,3-b]pyran derivatives. The catalyst was characterized by FT-IR, SEM and TGA analyses. This methodology offers several advantages including easy work-up procedure, high yields of the products, short reaction times, recyclable catalyst and green reaction medium.

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INTRODUCTION

Multi-component reactions (MCRs) are defined as one-pot processes which three or more substrates combine either simultaneously, or through a sequential addition procedure that does not require any change of solvent. Quite recently MCRs have gained importance especially in the total synthesis of natural products, and medicinal heterocyclic compounds, because of their simplicity, higher yield of the products, and lower reaction times [1,2].

4*H*-pyran derivatives as an important class of heterocycles, have attracted strong attention to their useful biological and pharmacological properties

* Corresponding Author Email: akiasat@scu.ac.ir

such as anticoagulant, spasmolytic, diuretic, anticancer and antianaphylactin characteristics [3]. 4*H*-Pyrans also occur in various natural products [4]. It has also reported that some of benzopyran derivatives have photochemical activities [5]. Development of 4*H*-pyrans synthesis has been of considerable interest in organic synthesis, because of their wide biological and pharmaceutical activities. Consequently numerous methods have been reported for the synthesis of 4*H*-pyrans [6].

Dihydropyrano[3,2-c]chromenes derivatives are also a class of important heterocycles with a wide range of biological properties such as spasmolytic, diuretic, anticoagulant, anti-cancer and anti-

anaphylactic activity [7]. Despite their importance from pharmacological, industrial and synthetic point of views, comparatively few methods have been reported for the preparation of pyrano[3,2-*c*]chromene derivatives [8].

Some of the reported procedures require long reaction times, multi-step reactions and complex synthetic pathways, afford products with only modest yields, and non-reusability of the catalyst. Therefore, the development of more effective methods for their preparation is still necessary.

It is well known that fused pyran derivatives possess a variety of pharmacological and biological properties, such as fungicidal, insecticidal, acaricidal [9], antiviral, antileishmanial [10] and anticonvulsant activity [11]. Moreover, they have been introduced as non-peptide human immunodeficiency virus (HIV) protease inhibitors [12]. Despite their wide range of pharmacological, industrial and synthetic applications, the synthesis of pyrano[4,3-*b*]pyrans has received little attention [13].

In continuation of our interest to introduce organic units into the skeleton framework of the ordered mesoporous silica [14-18], herein we would like to introduce a novel nanocomposite, rice-husk-silica supported *n*-propyl bipyridinium chloride (RHPPrBPCl), for the one-pot preparation of tetrahydrobenzo[*b*]pyran, dihydropyrano[3,2-*c*]chromene and dihydropyrano[4,3-*b*]pyran derivatives (Scheme 1).

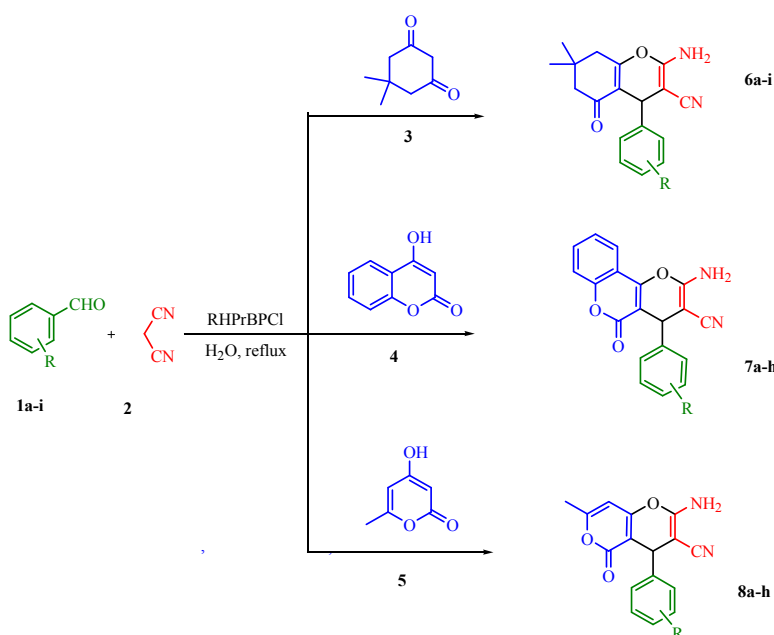
EXPERIMENTAL

General

All commercially available chemicals were purchased from Fluka and Merck companies and used without further purification. Products were characterized by their physical constant and comparison with authentic samples. Reaction monitoring was accomplished by TLC on silica gel polygram SILG/UV 254 plates. The IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectro-photometer using KBr pellets for the samples and catalyst in the range of 4000-400 cm^{-1} . ^1H and ^{13}C NMR spectra were recorded in CDCl_3 and $\text{DMSO-}d_6$ on a Bruker Advanced DPX 400 MHz spectrometer using TMS as internal standard. The SEM analyses were carried out using a LEO 1455VP Scanning Electron Microscope, operating at 1-30 KV. Thermal stability of the supported catalyst was examined by BÄHR, SPA 503 Thermogravimetric Analyzer (TGA) at heating rate of 10 $^\circ\text{C min}^{-1}$ over the temperature range of 40-700 $^\circ\text{C}$.

General Procedure for the Preparation of (*n*-Prpyl-trimethoxy silane)-4,4'-bipyridinium Chloride (PTBPCl)

PTBPCl was prepared according to Arenas *et al.* [21] with some modification. In a 50 ml RBF, 1.24 g (8 mmol) 4,4'-bipyridine was dissolved in 5 ml of DMF, afterwards 8 mmol 3-chloropropyl trimethoxy silane was added dropwise. The mixture



Scheme 1. Preparation of tetrahydrobenzo[*b*]pyrans (6a-i), dihydropyrano[3,2-*c*]chromenes (7a-h) and dihydropyrano[4,3-*b*]pyrans (8a-h) in the presence of RHPPrBPCl

was stirred at 90 °C under Argon atmosphere for 72 h. Finally, the precipitate was filtered and washed with methanol and dried at 90 °C for 2 h.

General Procedure for the Preparation of RHPPrBPCI

In a 500 ml RBF, 3 g of rice-husk nanosilica, was dissolved in 350 ml of 1 M NaOH for 24 h. Afterwards the mixture was filtered to remove any residue. Then 2 g of PTBPCI was added to the filtrate. The pH of this solution was adjusted to pH = 5.0 by addition of 3.0 M HNO₃ solution. In this case, the solution was aged for 24 h. Subsequently the precipitate was filtered and washed repeatedly with water and at last with acetone. The obtained silica was dried at 60 °C for 24 h.

General Procedure for the Preparation of Benzopyran Derivatives in the Presence of RHPPrBPCI in Water

A 50 ml RBF was charged with aromatic aldehydes (1 mmol), malononitrile (1.2 mmol), 1,3-dicarbonyl compound, (dimedone, 4-hydroxy coumarine and 4-hydroxy-6-methyl-2-pyrone) (1 mmol), RHPPrBPCI (0.01 g) and 10 ml deionized water. The mixture was in an oil-bath for specific time (7-45 min). Completion of the reaction was indicated by TLC [TLC n-hexane/ethyl acetate (7:3)]. After completion of the reaction (as indicated in Table

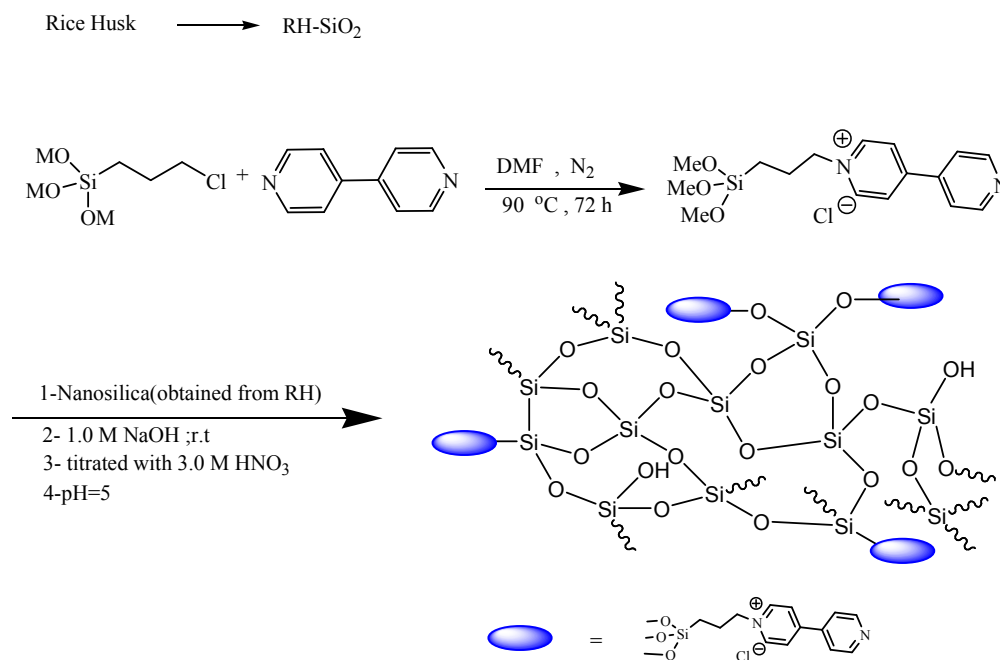
2), the mixture was filtered. The solid was washed with 15 ml hot ethanol to dissolve the product. The products were recrystallized in ethanol again.

General Procedure for the Recovery of RHPPrBPCI

A 50 ml RBF was charged with 4-methyl benzaldehyde (1 mmol), malononitrile (1.2 mmol), dimedone (1 mmol), RHPPrBPCI (0.01 g) and 10 ml deionized water. The mixture was placed in an oil-bath for specific time. Completion of the reaction was indicated by TLC [TLC n-hexane/ethyl acetate (7:3)]. After completion of the reaction, the mixture was filtered. The solid was washed with 15 ml hot ethanol to dissolve the product (the yield was calculated). The residue (RHPPrBPCI) was washed with hot ethanol twice, dried at 60 °C for 2 h and used for the next run (Fig. 6).

RESULTS AND DISCUSSION

In the first step, nanosilica was extracted from rice husk according to Adam *et al.* [19]. In the second step, n-propyl trimethoxy silane-4,4'-bipyridinium chloride (SiBP) was prepared *via* nucleophilic substitution of 4,4'-bipyridine and (n-propyl)trimethoxy silane. In the last step, nanosilica was converted to sodium silicate in NaOH solution, and subsequently SiBP was added to prepare RHPPrBPCI in acidic medium *via* sol-gel process (Scheme 2).



Scheme 2. General procedure for the preparation of RHPPrBPCI

The obtained nanocomposite was characterized *via* FT-IR, SEM and TGA techniques. The FT-IR spectra of rice husk silica (Fig. 1) and the nanocomposite (RHPrBPCL) were recorded. A broad peak in 3200-3600 cm^{-1} is related to stretching vibration of OH groups of silica surface and absorbed water molecules in silica. The presence of water in silica is further confirmed by characteristic bending vibration at 1640 cm^{-1} . The strong stretching vibration of Si-O-Si is observed at 1099 cm^{-1} . Further peaks at 446 and 800 cm^{-1} are due to Si-O vibrations.

In FT-IR spectrum of RHPrBPCL, other than RH-SiO₂ peaks, characteristic peaks of propyl bipyridinium chloride moiety is observed at 1400, 1480 and 1545 cm^{-1} (Fig. 2).

Qualification of a catalyst for promoting a specific reaction needs further analyses, including inspection of surface morphology and thermal stability. Accordingly after initial confirmation of nanocomposite with FT-IR, it was decided to inspect the surface morphology *via* SEM and thermal stability *via* TGA.

In SEM images of the nanocomposite, the agglomerated nanoparticles are observed which with further dispersion can efficiently spread throughout the reaction vessel (Fig. 3).

Inspection of the thermal stability of the RHPrBPCL nanocomposite *via* TGA indicated that there are two weight reduction steps in thermogram. The first weight reduction (20%) is occurred up to 190 °C which is related to the

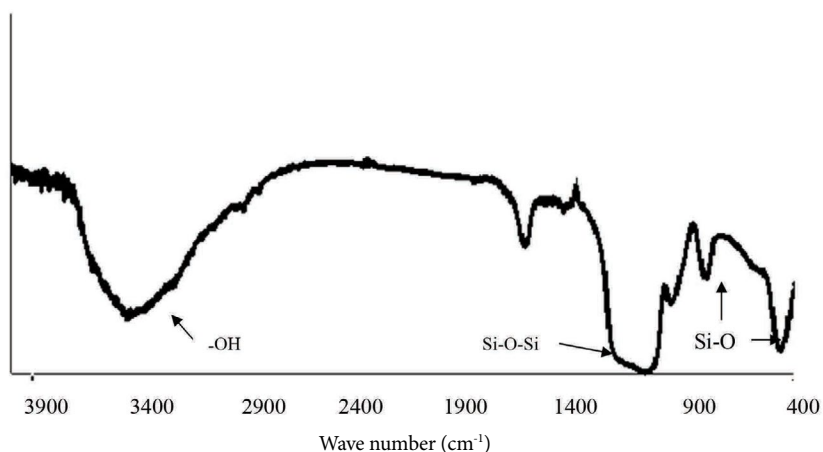


Fig. 1. FT-IR spectrum of RH-SiO₂

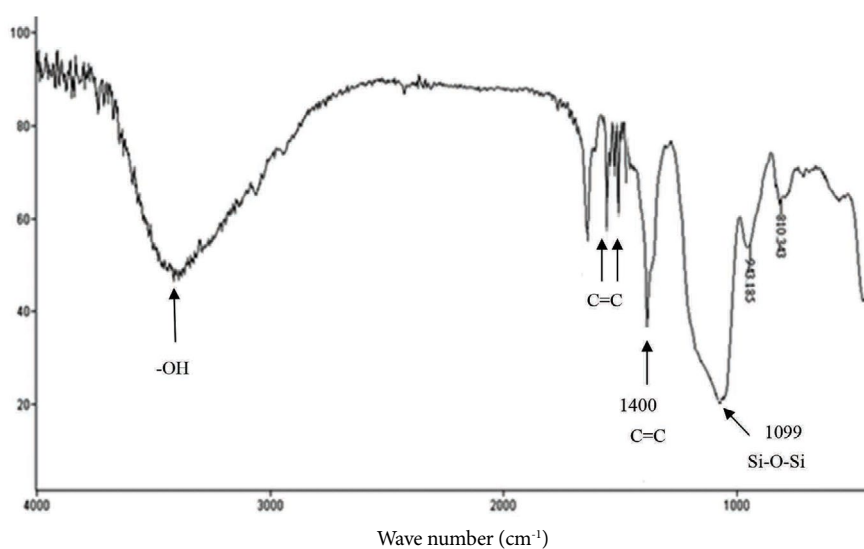


Fig. 2. FT-IR spectrum of RHPrBPCL

evaporation of absorbed water molecules from silica. The second weight reduction (40%) is occurred in the range of 280-450 °C, which can be attributed to the decomposition of organic moiety of the composite. According to this analysis, we can say that 40% of the composite is organic and 40% is inorganic which is stable up to 700 °C in this thermogram (Fig. 4).

After qualification of catalyst with FT-IR, SEM and TGA analyses, it was decided to explore the catalytic activity of this catalyst in the one-pot preparation of benzopyran derivatives in aqueous medium. In this regard, the three-component reaction of aromatic aldehydes, malononitrile and 1,3-dicarbonyl compounds (dimedone, 4-hydroxy coumarine and 4-hydroxy-6-methyl-2-pyrone) in the presence of RHPPrBPCI as the catalyst was investigated (Scheme 1).

In the first step, the reaction conditions, including temperature, solvent and amount of catalyst were optimized for the reaction of 4-methyl benzaldehyde, malononitrile and dimedone (Scheme 2, Table 1). With optimized conditions in hand, the MCRs were performed in water at reflux conditions and in the presence of 0.01 g of the catalyst.

Delighted with these results, we decided to synthesize a library of benzopyran derivatives *via* the three-component reaction of aromatic

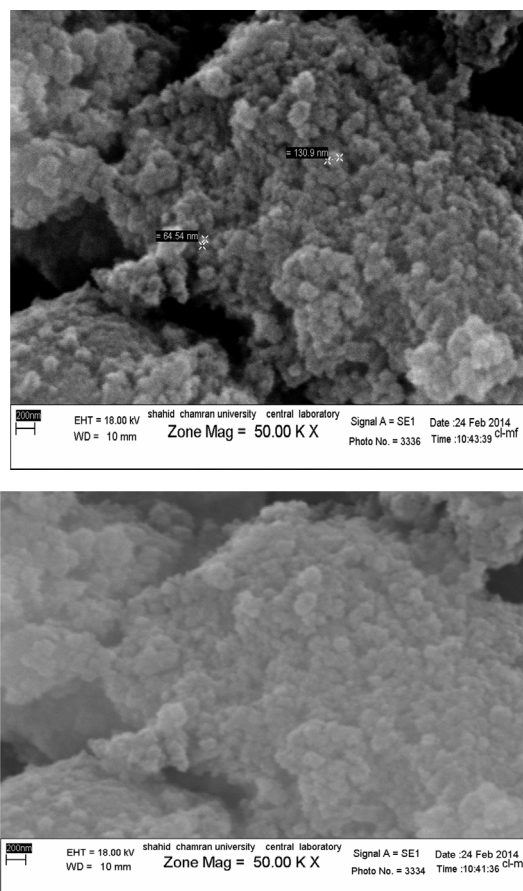


Fig. 3. SEM images of RHPPrBPCI nanocomposite

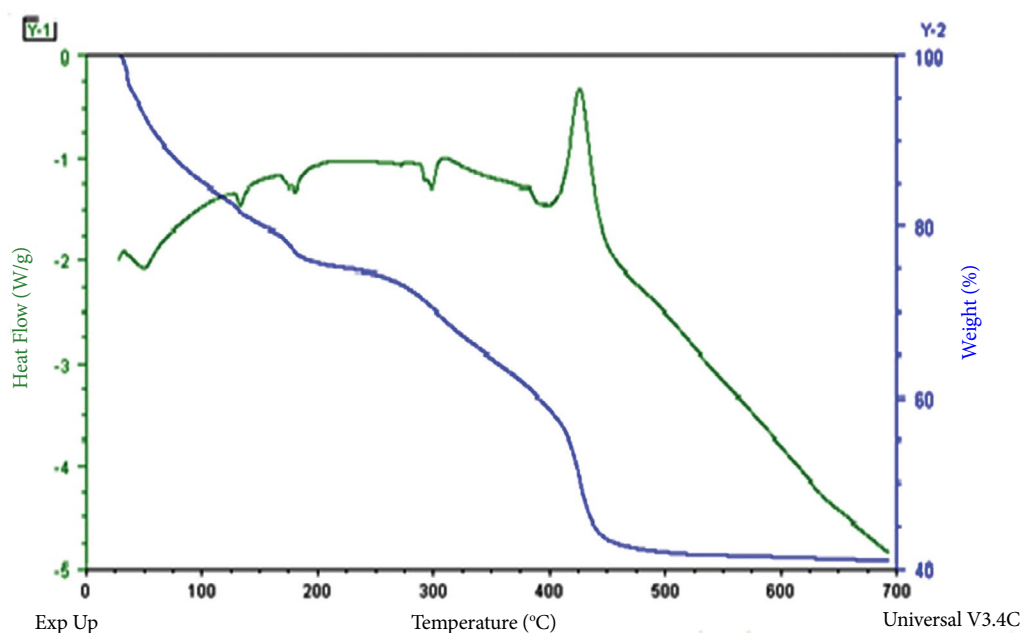


Fig. 4. TGA diagram of RHPPrBPCI nanocomposite

Table 1. Optimization of the Reaction of 4-Methyl Benzaldehyde, Malononitrile and Dimedone

Entry	Catalyst (g)	Temp. (°C)	Solvent	Time (min)	Yield (%)																																														
1	0.01	r.t.	Water	180	55																																														
2	0.01	60	Water	120	75																																														
3	0.01	80	Water	60	83																																														
4	-	80	Water	480	15																																														
5	0.03	80	Water	55	85																																														
6	0.05	80	Water </tr <tr><td>7</td><td>0.07</td><td>80</td><td>Water</td><td>45</td><td>87</td></tr> <tr><td>8</td><td>0.10</td><td>80</td><td>Water</td><td>40</td><td>85</td></tr> <tr><td>9</td><td>0.01</td><td>100</td><td>-</td><td>30</td><td>25</td></tr> <tr><td>10</td><td>0.01</td><td>Reflux</td><td>Water</td><td>30</td><td>94</td></tr> <tr><td>11</td><td>0.01</td><td>Reflux</td><td>Ethanol</td><td>30</td><td>75</td></tr> <tr><td>12</td><td>0.01</td><td>Reflux</td><td>Water/ethanol</td><td>30</td><td>75</td></tr> <tr><td>13</td><td>0.01</td><td>Reflux</td><td>DCM</td><td>30</td><td>35</td></tr> <tr><td>14</td><td>0.01</td><td>Reflux</td><td>Acetonitrile</td><td>30</td><td>75</td></tr>	7	0.07	80	Water	45	87	8	0.10	80	Water	40	85	9	0.01	100	-	30	25	10	0.01	Reflux	Water	30	94	11	0.01	Reflux	Ethanol	30	75	12	0.01	Reflux	Water/ethanol	30	75	13	0.01	Reflux	DCM	30	35	14	0.01	Reflux	Acetonitrile	30	75
7	0.07	80	Water	45	87																																														
8	0.10	80	Water	40	85																																														
9	0.01	100	-	30	25																																														
10	0.01	Reflux	Water	30	94																																														
11	0.01	Reflux	Ethanol	30	75																																														
12	0.01	Reflux	Water/ethanol	30	75																																														
13	0.01	Reflux	DCM	30	35																																														
14	0.01	Reflux	Acetonitrile	30	75																																														

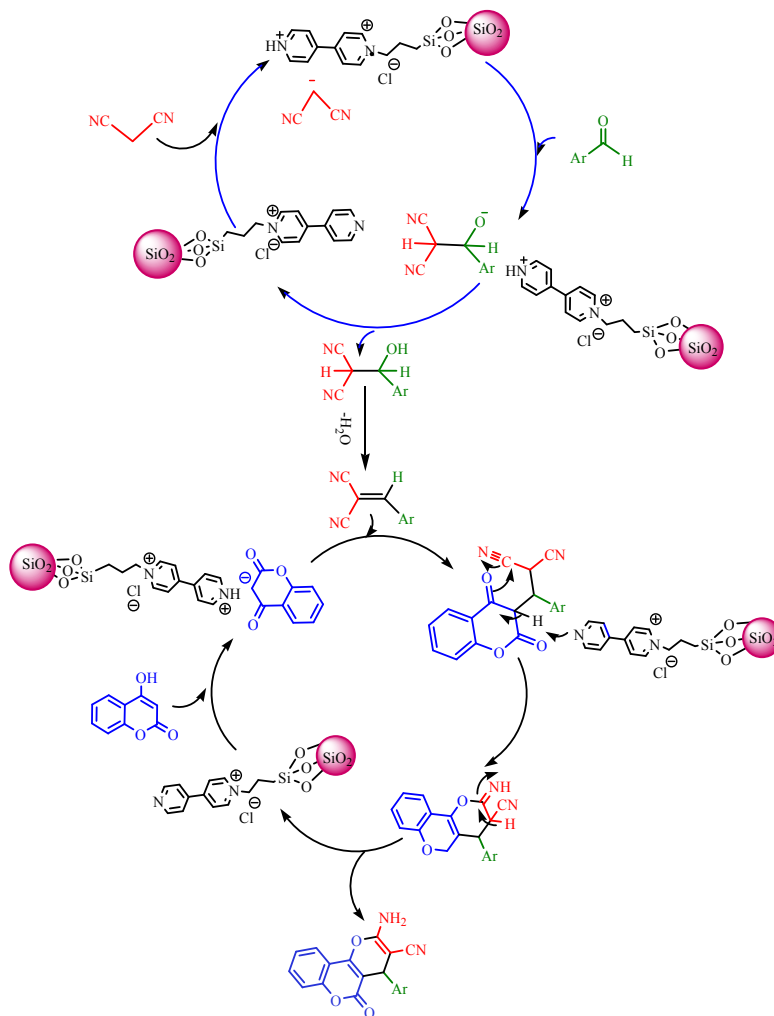


Fig. 5. Postulated mechanism for the synthesis of dihydro pyrano chromenes

aldehydes, malononitrile and 1,3-dicarbonyl compounds (dimedone, 4-hydroxy coumarine and 4-hydroxy-6-methyl-2-pyrone) in the presence of RHPPrBPCL as a dual ionic liquid-basic catalyst.

According to the obtained results (Table 2),

RHPPrBPCL has efficiently catalyzed the reaction as a phase transfer catalyst and the corresponding products were obtained with good to excellent yield. Furthermore electron-donating or electron-withdrawing groups did not have any significant

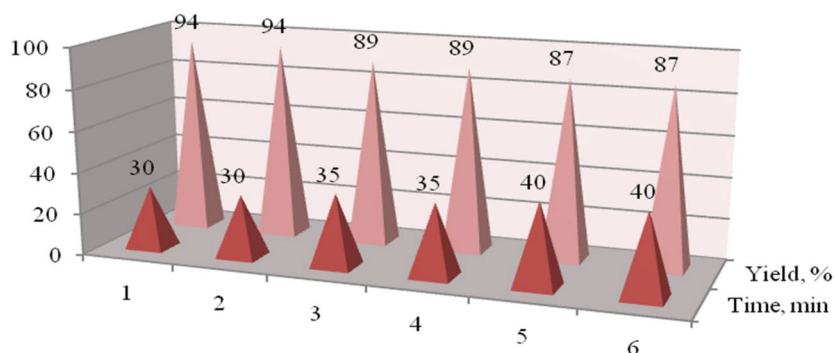


Fig. 6. Recyclability of RHPPrBPCL in the reaction of 4-methyl benzaldehyde, malononitrile and dimedone

Table 2. One-pot preparation of Tetrahydrobenzo[b]pyran (6a-i), Dihydropyrano[3,2-c]chromenes (7a-h), and Dihydropyrano[4,3-b]pyranes (8a-h) in the Presence of RHPPrBPCL

Entry	R	1,3-Dicarbonyl compound	Product	Time (min)	Yield (%)
1	H	Dimedone	6a	10	90
2	4-NO ₂	"	6b	7	96
3	3-NO ₂	"	6c	10	90
4	2-NO ₂	"	6d	20	88
5	4-Cl	"	6e	20	89
6	2-Cl	"	6f	25	86
7	4-Me	"	6g	30	94
8	4-OMe	"	6h	30	92
9	4-N(Me) ₂	"	6i	45	86
10	H	4-Hydroxy coumarine	7a	15	90
11	4-NO ₂	"	7b	10	97
12	3-NO ₂	"	7c	15	88
13	2-NO ₂	"	7d	20	85
14	4-Cl	"	7e	20	89
15	2-Cl	"	7f	25	85
16	4-Me	"	7g	25	88
17	4-N(Me) ₂	"	7h	45	84
18	4-OMe	"	7i	40	87
19	H	4-Hydroxy-6-methyl-2-pyrone	8a	15	92
20	4-NO ₂	"	8b	10	96
21	3-NO ₂	"	8c	15	87
22	2-NO ₂	"	8d	20	85
23	4-Cl	"	8e	20	89
24	2-Cl	"	8f	25	88
25	4-Me	"	8g	35	91
27	4-OMe	"	8h	40	90

effect on the reaction yield, albeit electron-withdrawing groups lower the reaction time. The postulated mechanism has been shown (Fig. 5) [20].

To validate the structure of the desired products, FT-IR, ¹H NMR and ¹³C NMR of these products were obtained. In the FT-IR spectra, a sharp characteristic peak at about 2200 cm⁻¹ is due to stretching vibration of the CN group. Also, a sharp peak at 1715 cm⁻¹ corresponds to 1,3-dicarbonyl moiety. Moreover, two bands in the region of 3200-3450 cm⁻¹ are related to NH₂ group. It is noteworthy that the presence of CN group in the products is confirmed by a peak at 110-120 ppm in ¹³C NMR.

Due to importance of green chemistry and recycling the solvents and catalysts, the recyclability of nanocomposite was assessed in the reaction of 4-methyl benzaldehyde, malononitrile, and dimedone. The result is shown in Fig. 6. The activity of nanocomposite is slightly decreased after 6 times of reuse.

CONCLUSIONS

A novel rice-husk-silica supported n-propyl bipyridinium chloride (RHPPrBPCl) with dual feature of being ionic liquid and basic catalyst, was prepared and utilized in the one-pot preparation of tetrahydrobenzo[*b*] pyran, dihydropyran[3,2-*c*] chromene and dihydropyran[4, 3-*b*]pyran derivatives. The catalyst was characterized by FT-IR, SEM and TGA analyses. This methodology offers several advantages including easy work-up procedure, high yields of the products, short reaction times, recyclable catalyst, and green reaction medium.

ACKNOWLEDGMENTS

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