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## Introduction

Ionic liquids are essential and efficient catalysts for the production of industrially important chemicals. Millions of tons of ionic liquids are annually consumed as catalysts, which require costly and inefficient separation of the catalysts from homogeneous reaction mixtures. Moreover, ionic liquids have received considerable interest as eco-friendly solvents, catalysts and reagents in organic synthesis because of their unique properties such as low volatility, non-flammability, high thermal stability, negligible vapor pressure and ability to dissolve a wide range of materials.<sup>1,2</sup> Though ILs possess promising advantages, their widespread practical application are still prevented by several disadvantages such as high viscosity, which results in ILs taking only a minor part in the catalyzed reactions for chemical production; homogeneous reactions are difficult to conduct due to the separation and reuse procedures, which consequently result in high cost due to the use of relatively large amounts of ILs as opposed to economic criteria. To address these disadvantages, supported IL materials have become more interesting and have found desirable applications as solid organocatalysts. This class of advanced materials possesses the properties of ILs and behaves as bulk ILs. The supported ionic liquid has a better performance in numerous fields with the merits of both a homogeneous ionic liquid and heterogeneous solid material. The use of

# A heteropolyacid-based ionic liquid immobilized onto magnetic fibrous nano-silica as robust and recyclable heterogeneous catalysts for the synthesis of tetrahydrodipyrazolopyridines in water<sup>†</sup>

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The application of a heteropolyacid containing an ionic liquid based organosilica (Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW) catalyst for the synthesis of tetrahydrodipyrazolopyridines is demonstrated. Because of the amplification effect of the IL, high loading capacities of the heteropolyacid were achieved. The catalyst system could be successfully recovered and reused several times without any significant decrease in activity and selectivity. The synthesized Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW nanocatalyst exhibited excellent catalytic activity in multicomponent reactions under mild conditions due to the easy accessibility of the active sites.

a recyclable strong ionic liquid in organic reactions is often considered to follow the principles of green chemistry, i.e., these catalyzed processes consume a minimum amount of energy and reagents or auxiliaries and minimize waste. Therefore, in order to reduce these problems, a supported IL catalyst as a novel solid catalyst combining the advantageous characteristics of ILs has been designed for catalyzed reactions. In recent years, the use of solid ionic liquid catalysts has offered important advantages in organic synthesis, for example, operational simplicity, environmental compatibility, non-toxicity, reusability, low cost, and ease of isolation. In this regard, a solid ionic liquid, a product that is easily synthesized from ionic liquids on ordered and non-ordered silica gel, has shown immense potential as an efficient and easily retrievable solid support/catalyst in various important organic syntheses.3-7 Mesoporous poly(ionic liquid)s (MPILs) simultaneous combine the features of mesoporous materials, polymers and ionic liquids (ILs), providing numerous new functionalities that can be applied in the fields of adsorption, separation, and catalysis. The practical performances of MPILs are closely related to their pore structures, which motivates the development of various pore formation strategies.8-11 Mesoporous silica materials are known as good supports for fluorescence probes, which is due to their unique characteristics such as excellent solvent dispersibility, good optical transparency in the visible region, favorable biocompatibility, large surface area and open pore structure, and abundant functionalization sites in the silica network.<sup>12-14</sup> Some silica-based mesoporous materials, such as SBA-15, MCM-41, MCM-48, and HMS, have been reported as inorganic carriers of chemosensors.15-21 However, most of these optical nanoprobes have some limitations, which include the requirement of using organic or aqueous-organic solvent

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Scheme 1 Synthesis of tetrahydrodipyrazolopyridines in the presence of  $Fe_3O_4/KCC-1/IL/HPW$  MNPs.

mixtures, poor performance for removal of metal ions, and poor accessibility of analytes to sensing sites inside the pores. Recently, Vivek Polshettiwar reported the synthesis of a new fibrous silica nanosphere (KCC-1) with a high surface area, large open pore structure, and high thermal and hydrothermal stabilities.<sup>22</sup> KCC-1 has a unique fibrous morphology, and the high surface area is attributed to its fibrous morphology and not to pores, which can be valuable in the design of silica-supported catalysts, hydrogen storage, drug delivery, as a chromatography support, and in versatile composite materials.<sup>23-27</sup>

Pyrazoles exist in some compounds that are used as pharmaceuticals and agrochemicals. A number of pyrazole containing compounds such as Celebrex, Viagra and Acomplia have been successfully commercialized.<sup>28,29</sup> Pyrazoles have also found applications in the agrochemical industry as ultraviolet stabilizers and energetic materials and in the field of photoprotectors.<sup>30–33</sup> Numerous methods have been employed for the synthesis of pyrazole derivatives, *e.g.*, the use of microwave irradiation,<sup>34,35</sup> ionic liquids,<sup>36</sup> TMSCl–NaI,<sup>37</sup> metal triflates,<sup>38,39</sup> molecular iodine,<sup>40,41</sup> SiO<sub>2</sub>–NaHSO<sub>4</sub>,<sup>42</sup> SiO<sub>2</sub>–HClO<sub>4</sub>,<sup>43</sup> ceric ammonium nitrate,<sup>44</sup> phenylboronic acid,<sup>45</sup> PTSA–SDS,<sup>46</sup> and organocatalysts.<sup>47</sup>

In our previous research, we prepared a novel ILfunctionalized ordered mesofibers organosilica (KCC-1/IL) material using ionic liquid and tetramethoxysilane as silica precursors. The KCC-1/IL material was then used as an efficient support for the immobilization of heteropolyacid (KCC-1/IL/ HPW) and as a catalyst.48 However, isolation and recovery of these tiny nanocatalysts from the reaction mixture is not easy. Conventional techniques (such as filtration) are not efficient because of the nano size of the catalyst particles. This limitation hampers the economics and sustainability of this nanocatalyst. To overcome this issue, the use of magnetic nanoparticles has emerged as a viable solution; their insoluble and paramagnetic nature enables easy and efficient separation of the catalysts from the reaction mixture with an external magnet. In continuation of our studies in this field, we reported the use of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/ HPW nanocatalysts as an efficient catalyst for the synthesis of tetrahydrodipyrazolopyridine derivatives (Scheme 1).

### Experimental

#### 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 and are uncorrected. FTIR spectra were obtained on a VERTEX 70 spectrometer (Bruker) in the transmission mode in spectroscopic grade KBr pellets for all the powders. The particle size and structure of the nanoparticles were observed using a Philips CM10 transmission electron microscope operating at 100 kV. Powder X-ray diffraction data were obtained using a Bruker D8 Advance model with Cu ka radiation. Thermogravimetric analysis (TGA) was carried out on a NETZSCH STA449F3 at a heating rate of 10  $^{\circ}$ C min<sup>-1</sup> under nitrogen. <sup>1</sup>H and <sup>13</sup>C NMR spectra were observed on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.46 MHz, BRUKER DRX-400 AVANCE spectrometer at 400.22 and 100.63 MHz, respectively. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates. Mass spectra were acquired on a Shimadzu GCMS-**OP5050** Mass Spectrometer.

#### General procedure for the preparation of Fe<sub>3</sub>O<sub>4</sub> nanoparticles

The synthesis procedure is illustrated as follows: (1) 0.01 mol  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  and 0.03 mol  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  were dissolved in 200 mL of distilled water, followed by the addition of polyethylene glycol (PEG) (1.0 g, MW 6000). (2) Sodium hydroxide (NaOH) was added to the solution and the pH value was controlled in the range  $12 \leq \text{pH} \leq 13$ . (3) Different amounts of hydrazine hydrate (N<sub>2</sub>H<sub>4</sub>·H<sub>2</sub>O, 80% concentration) were added to the abovementioned suspension. The reaction was continued for about 24 h at room temperature. During this period, the pH value was adjusted by NaOH and kept in the range  $12 \leq \text{pH} \leq 13$ . The black Fe<sub>3</sub>O<sub>4</sub> NPs were then rinsed several times with deionized water.

#### General procedure for the preparation of Fe<sub>3</sub>O<sub>4</sub>/KCC-1 MNPs

The Fe<sub>3</sub>O<sub>4</sub>/KCC-1 core-shell microspheres were synthesized according to the previously reported method.49 0.02 mol of Fe<sub>3</sub>O<sub>4</sub> MNPs was dispersed in a mixture of 80 mL of ethanol, 20 mL of deionized water and 2.0 mL of a 28 wt% concentrated ammonia aqueous solution ( $NH_3 \cdot H_2O$ ), followed by the addition of 0.20 g of tetraethyl orthosilicate (TEOS). After vigorous stirring for 24 h, the final suspension was repeatedly washed, filtered several times and dried at 60 °C in air. Fe<sub>3</sub>O<sub>4</sub>/SiO<sub>2</sub> (0.25 g) was dispersed in an aqueous solution (30 mL) containing urea (0.3 g) to form solution A under ultrasonication for 1 h. Cetylpyridinium bromide (CPB) (0.5 g) was added to 0.75 mL of n-pentanol and 30 mL cyclohexane to form solution B. Solution A was added to solution B under stirring at room temperature. Then, 1.25 g TEOS was added dropwise to the abovementioned solution. The resulting mixture was continually stirred for 1 h at room temperature and then maintained at 120 °C for 5 h, thus inciting the reaction. After the reaction was completed, the mixture was allowed to cool to room temperature, and the Fe<sub>3</sub>O<sub>4</sub>/KCC-1 core-shell microspheres were isolated by strong magnetic suction, then washed with deionized water and acetone, and dried overnight in a drying oven at 40 °C. This material was then calcined at 550 °C for 5 h in air.

#### General procedure for the preparation of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/3chloropropylsilane MNPs

 $\rm Fe_3O_4/KCC$ -1 NPs (2 mmol) and THF (20 mL) were mixed together in a beaker, and then NaH (20 mmol) was dispersed into the mixture by ultrasonication. 3-Chloropropyltriethoxysilane (22 mmol) was added dropwise at room temperature and stirred for another 16 h at 60 °C. The resultant product was collected and washed with ethanol and deionized water, and then dried under vacuum at 60 °C for 2 h for further use.

# General procedure for the preparation of $Fe_3O_4/KCC-1/IL/HPW$ MNPs

First, 1-methylimidazole (100 mmol) and Fe<sub>3</sub>O<sub>4</sub>/KCC-1/3chloropropyltriethoxysilane (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  $H_3PW_{12}O_{40}$  (110 mmol) in ethanol/water was performed for 72 h at ambient temperature. After the solvent was removed, the resulting mixture was filtered, after which the filtrate was dried under vacuum at 100 °C.<sup>48</sup>

# General procedure for the preparation of tetrahydrodipyrazolo pyridine

A 50 mL conical flask was charged with a mixture of hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), and Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs (0.1 mg) in H<sub>2</sub>O (15 mL). The mixture was stirred for 2 min at room temperature followed by the addition of aldehyde (1.0 mmol) and ammonium acetate (3.0 mmol). The reaction mixture was stirred at room temperature for 30 min. After completion of the reaction and monitored by TLC, the catalyst Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs were separated by an external magnet. The precipitate was washed with EtOH to afford the pure product and then dried well under vacuum pump.

## **Results and discussion**

The synthesis of  $Fe_3O_4/KCC-1/IL/HPW$  nanocatalysts involved several steps (Scheme 2). The fibers of the magnetic KCC-1 have numerous Si–OH groups on the surface; thus, it was expected

CPB and TEOS

(KCC-1)

Scheme 2 Schematic for the synthesis of  $Fe_3O_4/KCC-1/IL/HPW$ .



Fig. 1 TEM image of the fresh  $Fe_3O_4/KCC-1/IL/HPW$  MNPs (a) and  $Fe_3O_4/KCC-1/IL/HPW$  MNPs after ten reuses (b).

that KCC-1 could be easily functionalized with 3-chloropropyltriethoxysilane to form  $Fe_3O_4/KCC-1/3$ -chloropropylsilane MNPs. Then, a magnetic fibrous nano-silica supported heteropolyacid-based ionic liquid ( $Fe_3O_4/KCC-1/IL/HPW$ ) was realized.

The size and structure of the  $Fe_3O_4/KCC-1/IL/HPW$  MNPs were evaluated using transmission electron microscopy (TEM) (Fig. 1). The average size of the  $Fe_3O_4$  MNPs is about 30–40 nm. Uniform and monodisperse  $Fe_3O_4/KCC-1/IL/HPW$  materials with radial-like channels were synthesized successfully. The length of the silica fibres coming out of the centre of the  $Fe_3O_4/$ KCC-1/IL/HPW and distributed in all directions was estimated to be 220–250 nm (Fig. 1a). Comparison of TEM images of the used catalyst (Fig. 1b) with those of the fresh catalyst (Fig. 1a) showed that the morphology and structure of  $Fe_3O_4/KCC-1/IL/$ HPW MNPs remained intact after ten recoveries. Very low agglomeration of  $Fe_3O_4/KCC-1/IL/HPW$  MNPs can be observed.

The FT-IR spectra of KCC-1 and Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW are presented in Fig. 2. For KCC-1, the broad absorption bands at 1089 cm<sup>-1</sup> and 3654 cm<sup>-1</sup> are attributed to Si-O-Si unsymmetrical stretching and OH, respectively. The two peaks at 799 cm<sup>-1</sup> and 467 cm<sup>-1</sup> are from the Si-O-Si symmetrical stretching and bending, respectively (Fig. 2a). Compared to the spectrum of KCC-1, three new peaks at approximately 1642, 3024, and 3219 cm<sup>-1</sup> appeared in the spectrum of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW, corresponding to the ring vibration of imidazole and stretching vibrations of the saturated and unsaturated C-H bonds on the imidazole ring, respectively (Fig. 2b). These results indicated that the imidazolium IL had been successfully introduced onto the surface of KCC-1. The characteristic IR bands of  $H_2PW_{12}O_{40}^{-}$  at 963, 657, 590, and 467 cm<sup>-1</sup> were clearly observed in the IR spectrum of the as-prepared Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/ HPW MNPs catalyst (Fig. 2b). These facts are consistent with the synthesis design and confirm that the H<sub>2</sub>PW<sub>12</sub>O<sub>40</sub><sup>-</sup> units are highly dispersed or were taken up on the net cross-linking chitosan in the single molecule form.

The powder X-ray diffraction patterns of KCC-1,  $Fe_3O_4/KCC$ -1, and  $Fe_3O_4/KCC$ -1/IL/HPW are shown in Fig. 3. As can be observed, all samples possess the typical diffraction peaks at (220), (311), (400), (422), (511) and (440), which are in good agreement with the data for a standard  $Fe_3O_4$  sample, as



Fig. 2 FTIR spectra of Fe $_3O_4$ /KCC-1NPs (a) and Fe $_3O_4$ /KCC-1/IL/HPW NPs (b).



Fig. 3 XRD analysis of (a)  $Fe_3O_4$ , (b)  $Fe_3O_4/KCC$ -1, and (c)  $Fe_3O_4/KCC$ -1/IL/HPW MNPs.

reported in the JCPDS card (no. 19-0629) (Fig. 3a). In addition to the peaks of iron oxide, the XRD pattern of  $Fe_3O_4/SiO_2/KCC-1$ core–shell nanoparticles presented a broad featureless XRD peak at low diffraction angles, which corresponded to the amorphous silica (Fig. 3b). Fig. 3c shows a typical XRD pattern for the  $Fe_3O_4/KCC-1/IL/HPW$  MNPs. There was no change in it. Furthermore, the diffraction peaks ascribed to crystalline tungstophosphoric acid were observed in the XRD pattern of the as-prepared  $Fe_3O_4/KCC-1/IL/HPW$  MNPs. By contrast with the XRD pattern of  $Fe_3O_4/KCC-1/IL/HPW$  MNPs (Fig. 3b), it was found that an envelope peak centered at  $20.4^{\circ}$  in the XRD pattern of  $Fe_3O_4/$ KCC-1/IL/HPW MNPs (Fig. 3c) was the peculiar diffraction peak of the amorphous chitosan.

TGA experiments were carried out by heating the samples under air up to 800  $\,^\circ\mathrm{C}$  in order to check the amount of





encapsulated fibrous nano-silica, ionic liquid, heteropolyacid, and obtain information on their thermal stability. As seen in Fig. 4, three weight loss stages were observed in flow air. About 2.0 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 (250–550 °C), the weight loss is about 10.5 wt% and can be attributed to the pyrolysis of cross-linking organic group derivatives. The weight loss in the third stage (550–610 °C) is about 14.0 wt%, which should be assigned to the further decomposition of chitosan residues and the release of H<sub>2</sub>O from the thermal decomposition of HPW or its relevant ammonium salts formed by the electrostatic interaction between the amino group cations in chitosan and H<sub>2</sub>PW<sub>12</sub>O<sub>40</sub><sup>-</sup> anions.

The magnetic properties of the nanoparticles were characterized using a vibrating sample magnetometer (VSM). The magnetization curves of the obtained nanocomposite, registered at 300 K, showed that nearly no residual magnetism was detected (Fig. 5), which means that the nanocomposite exhibited paramagnetic characteristics. Magnetic measurements show that pure Fe<sub>3</sub>O<sub>4</sub> and Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW have saturation magnetization values of 55.4 and 23.1 emu g<sup>-1</sup>, respectively. These nanocomposites with paramagnetic characteristics and high magnetization values can quickly respond to the external



Fig. 5 Room-temperature magnetization curves of the nano catalysis.

Table 1The effect of heteropoly acid on the synthesis of tetrahy-<br/>drodipyrazolo pyridine

Entry	Heteropoly acid	Yield <sup><math>a,b</math></sup> (%)	
1	$H_{3}PW_{12}O_{40}$	96	
2	H <sub>3</sub> SiW <sub>12</sub> O <sub>40</sub>	87	
3	$H_3PMo_{12}O_{40}$	81	

 $^a$  Reaction conditions: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), benzaldehyde (1.0 mmol) and ammonium acetate (3.0 mmol), water (3 mL), catalyst (0.5 mg), heating under reflux, 1 h.  $^b$  GC yields [%].

magnetic field and quickly redisperse once the external magnetic field is removed. These results reveal that the nanocomposites exhibit a good magnetic response, which suggests potential applications for targeting and separation.

Preliminary investigations involved screening for three different heteropoly acids in the catalyst structure, namely, tungstophosphoric acid  $(H_3PW_{12}O_{40})$ , silicotungstic acid  $(H_3SiW_{12}O_{40})$  and molybdophosphoric acid  $(H_3PMo_{12}O_{40})$ , for the synthesis of tetrahydrodipyrazolo pyridine. The experiments were carried out at room temperature. Analysis of the reaction mixture on TLC showed complete conversion of the starting material. According to the results, we chose  $H_3PW_{12}O_{40}$  for the synthesis of tetrahydrodipyrazolo pyridine (Table 1).

We examined the effect of solvent on the synthesis of tetrahydrodipyrazolo pyridine using the Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs by heating under reflux (Table 2). The solvent does affect the performance of the catalyst. n-Hexane, benzene, CCl<sub>4</sub>, and cyclohexane, which are non-polar solvents, gave tetrahydrodipyrazolo pyridine in a lower yield than that obtained under solvent-free conditions (Table 2, entry 12-15). CH<sub>3</sub>CN, THF, CH<sub>2</sub>Cl<sub>2</sub>, DMF, toluene, dioxane, CHCl<sub>3</sub>, EtOAc, and DMSO, all aprotic polar solvents, also gave tetrahydrodipyrazolo pyridine in low yields. The reaction did better in protic solvents. i-PrOH and ethanol gave tetrahydrodipyrazolo pyridine in average yields (Table 2, entries 1 and 20). In contrast, the use of methanol resulted in an increased yield of 70%, whereas the yield was remarkably increased up to 96% when H<sub>2</sub>O was used as the solvent in the presence of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs. In this study, it was found that water was more efficient (Table 2, entry 2) over other organic solvents. A solvent that stabilizes one of the two competing transition states and controls the selectivity should enhance the selectivity of the product obtained via the stabilized transition state. For example, in multicomponent reactions, higher reaction rates and selectivities are often obtained in polar solvents compared to non-polar solvents, which has been attributed to enhanced hydrogen bonding between the solvent and the transition state, as well as enforced hydrophobic interactions when conducted in water, which facilitates alignment of the substrates.<sup>50</sup> The ability to use water as the reaction medium greatly increases the green credentials of the method. We also investigated the crucial role of temperature in the synthesis of tetrahydrodipyrazolo pyridine in the presence of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs as the catalyst. Results clearly indicated that the catalytic activity is not sensitive to reaction

Table 2The effect of solvent and temperature for synthesis of tet-<br/>rahydrodipyrazolo pyridine<sup>a</sup>

Entry	Solvent	Temp. (°C)	$\operatorname{Yield}^{b}(\%)$
1	EtOH	r.t.	61
2	H <sub>2</sub> O	r.t.	96
3	H <sub>2</sub> O	60	96
1	H <sub>2</sub> O	80	96
5	H <sub>2</sub> O	100	96
5	CH <sub>3</sub> CN	r.t.	33
7	THF	r.t.	24
3	$CH_2Cl_2$	r.t.	29
Ð	EtOAc	r.t.	45
10	DMF	r.t.	22
11	Toluene	r.t.	25
12	<i>n</i> -Hexane	r.t.	16
13	Benzene	r.t.	10
14	$CCl_4$	r.t.	16
15	Cyclohexane	r.t.	9
16	CHCl <sub>3</sub>	r.t.	40
17	DMSO	r.t.	34
18	MeOH	r.t.	63
19	Dioxane	r.t.	20
20	i-PrOH	r.t.	53
21	Solvent-free	r.t.	20

<sup>*a*</sup> Reaction conditions: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), benzaldehyde (1.0 mmol) and ammonium acetate (3.0 mmol), catalyst (0.1 mg), 30 min. <sup>*b*</sup> GC yields [%].

temperature. The best temperature for this reaction was at room temperature. Temperatures greater than room temperature do not cause changes in the efficiency of the reaction (Table 2, entry 2–5).

Then, the amount of catalyst necessary to promote the reaction efficiently was examined. It was observed that the variation in the  $Fe_3O_4/KCC-1/IL/HPW$  MNP amount had an effective influence. The best amount of  $Fe_3O_4/KCC-1/IL/HPW$  MNP was 0.1 mg, which afforded the desired product in 96% yields (Fig. 6). Under the optimal conditions, the reaction



**Fig. 6** Optimization of the conditions for synthesis of tetrahydrodipyrazolo pyridines: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), benzaldehyde (1.0 mmol) and ammonium acetate (3.0 mmol), water (3 mL), at room temperature, 1 h.



Fig. 7 Effect of time on yield of tetrahydrodipyrazolo pyridines: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), benzaldehyde (1.0 mmol) and ammonium acetate (3.0 mmol), catalyst (0.1 mg), water (3 mL), at room temperature.

progress in the presence of 0.1 mg of Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs was monitored by GC. Using this catalyst system, excellent yields of tetrahydrodipyrazolo pyridine can be achieved in 30 min (Fig. 7). No apparent by-products were observed by GC in all the experiments and tetrahydrodipyrazolo pyridine was obtained in a 96% yield.

To further evaluate the efficiency of the catalyst, different control experiments were performed and the obtained data are shown in Table 3. Initially, a standard reaction was carried out using Fe<sub>3</sub>O<sub>4</sub> and Fe<sub>3</sub>O<sub>4</sub>/KCC-1; no product formation was observed after a reaction time of 1 h. The result of this study showed that the desired product was not formed in any amount (Table 3, entries 1 and 2). When Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL was used as the catalyst, a reaction was observed, although the yield of the desired product was average (Table 3, entries 3). The ILs could not give satisfactory catalytic activity under mild reactions. Based on these results, we continued the research to improve the yield of the product by adding HPW to the catalyst. Notably, there was not much difference in the reaction yields when the reaction was carried out using Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW and IL/ HPW catalyst (Table 3, entries 4 and 5). The nano-sized particles increased the exposed surface area of the active site of the catalyst, thereby enhancing the contact between reactants and

 
 Table 3
 Influence of different catalysts for the synthesis of tetrahydrodipyrazolo pyridine<sup>a</sup>

Entry	Catalyst	$\operatorname{Yield}^{b}(\%)$	
1	Fe <sub>3</sub> O <sub>4</sub>	_	
2	Fe <sub>3</sub> O <sub>4</sub> /KCC-1	_	
3	Fe <sub>3</sub> O <sub>4</sub> /KCC-1/IL	58	
4	Fe <sub>3</sub> O <sub>4</sub> /KCC-1/IL/HPW	96	
5	IL/HPW	96	
4 5	Fe <sub>3</sub> O <sub>4</sub> /KCC-1/IL/HPW IL/HPW	96 96	

<sup>*a*</sup> Reaction conditions: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), benzaldehyde (1.0 mmol) and ammonium acetate (3.0 mmol), water (3 mL), at room temperature, 30 min. <sup>*b*</sup> Isolated yield.

Table 4 The loading amount of HPW in Fe\_3O\_4/KCC-1/IL/HPW and Fe\_3O\_4/SiO\_2/IL/HPW

Entry	Catalyst	wt%
1	Fe <sub>3</sub> O <sub>4</sub> /SiO <sub>2</sub> /IL/HPW	3.1
2	Fe <sub>3</sub> O <sub>4</sub> /KCC-1/IL/HPW	6.9
3	Fe <sub>3</sub> O <sub>4</sub> /SiO <sub>2</sub> /IL/HPW after ten reuses	1.7
4	$Fe_3O_4/KCC-1/IL/HPW$ after ten reuses	6.8

catalyst dramatically, mimicking homogeneous catalysts. Moreover, the activity and selectivity of the nano-catalyst can be manipulated by tailoring the chemical and physical properties such as size, shape, composition and morphology. As a result,  $Fe_3O_4/KCC-1/IL/HPW$  was used in the subsequent investigations because of its high reactivity, high selectivity and easy separation.

To assess the exact impact of the presence of KCC-1 in the catalyst,  $Fe_3O_4/KCC-1/IL/HPW$  was compared with  $Fe_3O_4/SiO_2/IL/HPW$ . The loading amount of HPW in  $Fe_3O_4/KCC-1/IL/HPW$  and  $Fe_3O_4/SiO_2/IL/HPW$  were determined by inductively coupled plasma mass spectrometry (ICP-MS). The amount of HPW in  $Fe_3O_4/KCC-1/IL/HPW$  was more than double that of the  $Fe_3O_4/SiO_2/IL/HPW$ . It is interesting that the amount of HPW after reuse of the catalyst for ten consecutive cycles was more than quadruple in the  $Fe_3O_4/KCC-1/IL/HPW$  compared to the  $Fe_3O_4/SiO_2/IL/HPW$ . This remarkable ability of the  $Fe_3O_4/KCC-1/IL/HPW$  mesostructure may be attributed to KCC-1 units that effectively manage the reaction through preventing HPW agglomeration and releasing and recapturing HPW during the reaction process (Table 4).

We compared the catalytic performance of our catalyst with literature reported catalysts for synthesis of tetrahydrodipyrazolo pyridine (Table S1†). Table S1† clearly demonstrates that the highest efficiency for the synthesis of tetrahydrodipyrazolo pyridine was found using Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs, whereas an appropriate, highly perfect performance of the present catalyst was observed for this reaction. Table S1† clearly demonstrates that lower temperature, minimum catalyst amount, shorter reaction time and the use of water as a solvent, *i.e.*, the requirements for the green synthesis of tetrahydrodipyrazolo pyridine, were met using our catalyst, whereas an appropriate, highly perfect performance of the present catalyst was observed for this reaction.

After optimization of the reaction conditions, to delineate this approach, particularly in regard to library construction, this methodology was evaluated using hydrazine hydrate, ethyl acetoacetate, and ammonium acetate, and a variety of different substituted aldehydes in the presence of  $Fe_3O_4/KCC-1/IL/HPW$ MNPs under similar conditions. As can be seen from Table 5, electronic effects and the nature of substituents on the aromatic ring did not show strongly obvious effects in terms of yields under the reaction conditions. Aromatic aldehydes containing electron-withdrawing groups or electron-donating were employed and reacted well to afford the desired products in excellent yields with high purity.

Table 5Synthesis of tetrahydrodipyrazolo pyridines in the presence of<br/>the Fe $_3O_4$ /KCC-1/IL/HPW catalyst in water<sup>a</sup>

Entry	R	$\operatorname{Yield}^{b}(\%)$	MP (°C)
1	н	96	237-239 (ref. 51)
2	Cl	95	257 255 (ref. 51) 251–253 (ref. 52)
3	F	97	258-260 (ref. 51)
4	$NO_2$	98	>300 (ref. 51)
5	MeO	92	181-183 (ref. 51)
6	Me	93	245-247 (ref. 52)
7	НО	90	269-271 (ref. 51)
8	NC	95	287-240 (ref. 51)
9	$Me_2N$	91	238–240 (ref. 51)

<sup>*a*</sup> Reaction conditions: hydrazine hydrate (2.0 mmol), ethyl acetoacetate (2.0 mmol), aldehydes (1.0 mmol) and ammonium acetate (3.0 mmol), catalyst (0.1 mg), water (15 mL), at room temperature, 30 min. <sup>*b*</sup> Isolated yields (%).

The recovery and reuse of a catalyst are highly preferable for a catalytic process. In this regard, the recyclability of the Fe<sub>3</sub>O<sub>4</sub>/ KCC-1/IL/HPW MNPs was investigated in a model reaction of hydrazine hydrate, ethyl acetoacetate, benzaldehyde, and ammonium acetate under optimized reaction conditions. The recovered catalyst was washed with ethylacetate, dried at room temperature and reused for a similar reaction. It is worth noting that the heterogeneous property of the Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW MNPs facilitates the efficient recovery of the catalyst from the reaction mixture during the work-up procedure so that the catalyst could be recycled and reused for ten consecutive trials without loss of its catalytic activity (Fig. 8). No significant loss of efficiency of the catalyst was observed even after 10 more reaction cycles. Moreover, in order to know whether the reaction takes place at the surface of the Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW or with free HPW species, ICP-MS analysis of the remaining mixture after catalysis and product separation was investigated upon reaction completion. The amount of HPW after the ten repeated recycling was 6.8% and the amount of HPW leached into the reaction mixture was very low. These observations indicated that the catalyst was stable and could tolerate the present reaction conditions.



Fig. 8 Reuses performance of the catalysts.

## Conclusions

In summary, the design and preparation of a novel HPW containing an IL-based ordered mesofibers magnetic organosilica (Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW) and its catalytic application for the synthesis of tetrahydrodipyrazolo pyridines have been described. The catalyst could be recovered and reused at least ten times with no decrease in its activity and selectivity. Based on these results, we conclude that although the Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL nanostructure acts as cobweb for the soluble HPW species, it can also operate as a nanoscaffold to retake the HPW into the mesofibers, thereby avoiding wide agglomeration of the HPW. This superior effectiveness of the Fe<sub>3</sub>O<sub>4</sub>/KCC-1/IL/HPW nanocatalyst may be ascribed to the isolated IL units incorporated in the mesofibers, which could control the reaction mechanism by preventing the formation of agglomerated HPW as well as stabilizing the active catalytic HPW species.

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