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Functionalized superparamagnetic Fe_3O_4 as an efficient quasi-homogeneous catalyst for multi-component reactions

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Tetrabutylammonium valinate ionic liquid $[NBu_4][Val]$ supported on 3-chloropropyltriethoxysilane grafted superparamagnetic Fe_3O_4 NPs (VSF) was synthesized and characterized by fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), transmission electronic microscopy (TEM), scanning electronic microscopy (SEM), thermal gravimetric analysis (TGA), and vibrating sample magnetometer (VSM). The VSF catalyst was used as an efficient "quasi-homogeneous" catalyst for multi-component synthesis of 1,4-dihydropyridines and 2-amino-4-(indol-3-yl)-4*H*-chromenes at room temperature. VSF catalyst was recovered by using an external magnet and recycled for six times without significant loss in catalytic activity. Moreover, VSF is a "quasi-homogeneous" catalyst can bridge the gap between homogeneous and heterogeneous catalysis.

Introduction

Superparamagnetic nanoparticles (MNPs) play a pivotal role in modern science and technologies due to their wide range of applications in various fields such as biotechnology/biomedicine, data storage, magnetic fluids, magnetic resonance imaging and heterogeneous catalysis.[1] The MNPs have been found as sustainable catalysts or catalyst supports in organic synthesis due to their unique properties including huge surface area, non-toxic, recoverable with an external magnet, and avoids the work up/filtration of the catalyst.[2] The functionalized MNPs have been increasingly exploited in the area of biomedicine and catalysis.[3] Several metal NPs or metal complexes including palladium,[4] gold,[5] ruthenium,[6] copper,[7] osmium,[8] platinum and nickel,[9] iridium/rhodium,[10] vanadium,[11] and manganese[12] have been supported on the MNPs to explore catalytic potential for various organic conversions. The ionic liquid functionalized ferrite materials were used as support for stabilization of various metal NPs.[13] However, limited reports available on metal free, ionic liquid functionalized MNPs as recyclable catalysts for multicomponent reactions.[14]

Ionic liquids have been subject of intense study for last few decades due to their applications in various fields including homogeneous catalysis.[15] Amino acid based ionic liquids (AAIL) have found interesting applications in catalysis,[16] but their uses as immobilization or supporting on solid materials were found to be very limited.[17] AAILs were either solids or liquids of extremely high viscosity have limitations in efficiencies of heat and mass transfer processes. The physico-chemical properties of AAIL may be tuned by changing either cations or anions derived from amino or carboxylic acid functional groups of amino acid to overcome these limitations.[18] Recently, tetraalkylammonium-based amino-acid ionic liquids $[NBu_4][AA]$ ILs with lower viscosities were reported as an efficient medium for absorption of CO_2,[19] and also as ligands or catalysts for few organic conversions.[20]

The field of "Quasi-homogeneous" catalysis is the frontier between homogeneous and heterogeneous catalysis. This has the advantages offered by both the heterogeneous catalysis, with the characteristic of recovery and recyclability of the catalyst, and the homogeneous catalysis, with the characteristic of low catalyst loading and selectivity of the required product.[21] In 1996, Bonnemann *et al.* demonstrated the quasi-homogeneous catalytic nature of platinum colloids for enantioselective hydrogenation of ethylpyruvate to (R)-ethyllactate.[22] Schuth *et al.* reported the efficient use of aluminum-stabilized copper colloids as a quasi-homogeneous catalyst for methanol synthesis.[23] Recently, Luo *et al.* reported the ionic liquid supported MNPs as "quasi-homogeneous" catalyst for synthesis of benzoxanthenes.[24] In this context, we presumed that the immobilization or supporting of highly charged low viscous $[NBu_4][AA]$ ILs on solid Fe_3O_4 NPs can show the properties of quasi-homogeneous catalyst to bridge the gap between heterogeneous and homogeneous catalysis.

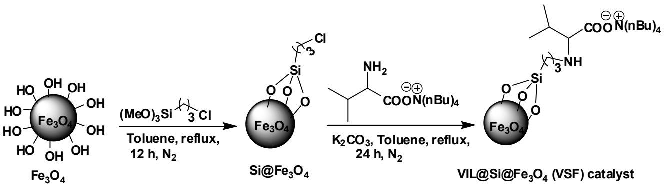
It is apparent to study the catalytic potential of such quasi-homogeneous catalyst in multi-component reactions for the construction of biologically relevant scaffold in a single step. 1,4-Dihydropyridines (1,4-DHPs) are such privileged pharmacological scaffolds which exhibit significant biological activities in the treatment of cardiovascular disease as calcium channel blockers.[25] Chromenes and indoles are another class of compounds found in a number of natural products with wide range of biological activities.[26,27] 2-Amino-4-(indol-3-yl)-4*H*-chromenes are hybrid molecules, which comprises the incorporation of two pharmacophores such as chromenes and indoles with the intention to exert dual biological activities.

In view of developing efficient green approach for the synthesis of 1,4-dihydropyridines, very few MNPs such as nano-γ-Fe_2O_3,[28] γ-Fe_2O_3-SO_3H,[29] Fe_3O_4–CeO_2[30] and ZrO_2–Al_2O_3–Fe_3O_4[31] have been reported as recyclable catalysts. To the best of our knowledge, there is no report exists for the one-pot synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromenes *via* Knoevenagel/Pinner/Friedel-Crafts reaction using MNPs as recyclable catalysts. As a part of our ongoing work towards the development of efficient recyclable catalysts for the synthesis of biologically important molecules,[32] we report herein, the VSF as a quasi-homogeneous catalyst for the synthesis of 1,4-dihydropyridines and 2-amino-4-(indol-3-yl)-4*H*-chromenes.

Results and Discussions

Synthesis and Characterization of VSF catalyst

VSF nano material was synthesized by the grafting of the tetrabutylammonium valinate [NBu_4][Val] ionic liquid (VIL) on 3-chloropropyltriethoxysilane coated Fe_3O_4 NPs using a simple conventional heating protocol (Scheme 1) and characterized by fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), transmission electronic microscopy (TEM), scanning electronic microscopy (SEM), thermal gravimetric analysis (TGA), and vibrating sample magnetometer (VSM).



Scheme 1: Synthesis of N_{4444}VIL@Si@Fe_3O_4 (VSF) catalyst

The XRD pattern of Fe_3O_4 clearly conforms the formation of cubic spinel structure with the diffraction peaks at 2*θ* are 30.16°, 35.53°, 43.33°, 53.64°, 57.39° and 62.76° which correspond to the phases (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1), and (4 4 0) respectively (Figure 1). The XRD pattern is in well agreement with the reported data (JCPDS no. 65-3107).[33] The mean crystallite size and the mean particle size was determined using the Scherrer formula and found to be 11.6 nm.

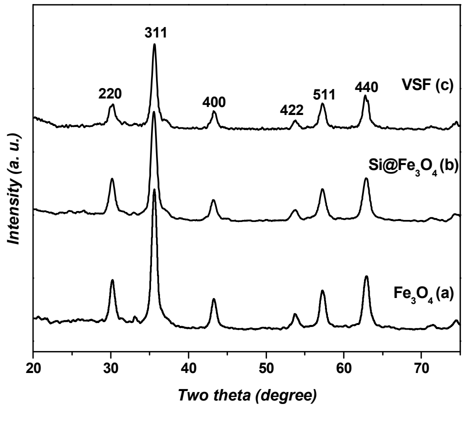


Figure 1: X-ray diffraction patterns of (a) Fe_3O_4 NPs; (b) Si@Fe_3O_4; (c) VSF

The calculated mean crystallite size is consistent with the result measured from the TEM images. There were no considerable changes observed in the x-ray diffraction pattern and crystallite size of silica coated ferrite and VSF (Figure **1b** and **1c**). However, the intensity of the related peaks of silica-coated and VSF are slightly reduced (Figure 1).

The functional groups of as synthesized VSF material and its precursors were characterized from FT-IR technique as shown in Figure 2**.** Three characteristic bands correspond to Fe-O vibration and surface hydroxyl groups of Fe_3O_4 appeared at 581, 1622 and 3426 cm^{-1} respectively (Figure 2a). The characteristic bands of chloropropyl silane coated ferrite appeared at 1039, 1129 cm^{-1} and 2940, 1415 cm^{-1} which correspond to Si-O-Si stretching and C-H stretch, bend respectively (Figure 2b). The characteristic bands at 1666 cm^{-1} corresponds to the carbonyl functional group of VIL (Figure 2c). Moreover, the presence of functional groups in VSF such as Fe-O, Si-O-Si, C-H, carbonyl were conformed from the bands at 581, 1129 and 1039, 1415, 1657 cm^{-1} respectively (Figure 2d).

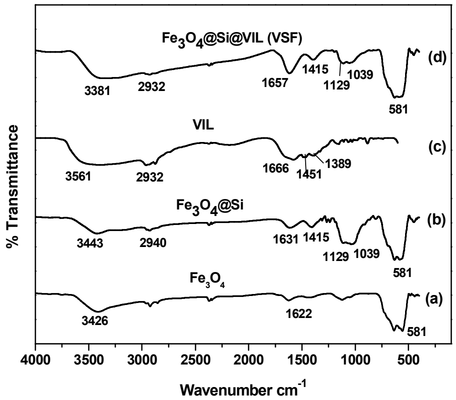


Figure 2: FT-IR of (a) Fe_3O_4 NPs; (b) Si@Fe_3O_4; (c) VIL; (d) VSF

The surface morphology of Fe_3O_4 NPs and VSF were characterized from scanning electronic microscopy technique (SEM) as shown in Figure 3. The results clearly showed that there was a change in the morphology of VSF (3c, 3d) as compared with Fe_3O_4 NPs (3a, 3b). Furthermore, the internal morphology and size of VSF NPs were characterized from transmission electronic microscopy (TEM) as shown in Figure 4.

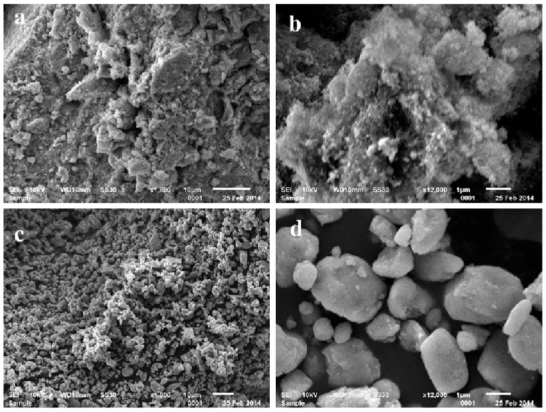


Figure 3: Low to high magnified SEM images of (a), (b) Fe_3O_4 NPs and (c), (d) VSF

The particle size of nano particles was calculated from TEM and found to be varied from 7.35 nm to 12.5 nm which is consistent with the result calculated from PXRD data using the Scherrer formula.

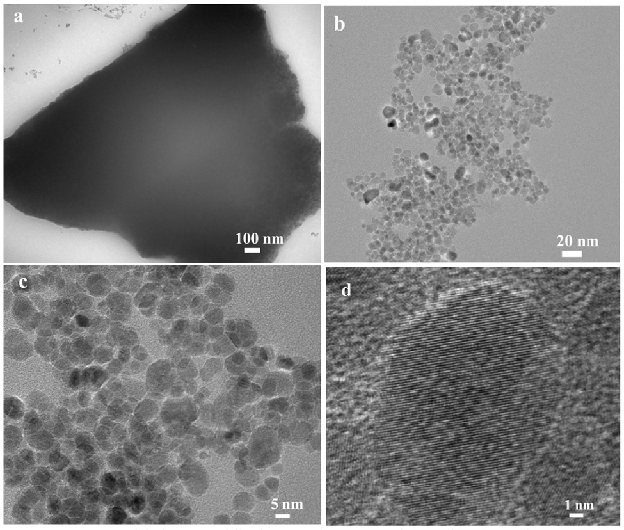


Figure 4: Low to high magnified TEM images of (a), (b), (c), (d) VSF

The thermal stability and percentage of organic functional groups chemisorbed/grafted on Fe_3O_4 NPs were determined by TGA analyses (Figure 5). The weight loss at temperature 150 ºC can be attributed to the water desorption from surface of MNPs (Figure 5). The curve (b) shows a weight loss of 4.4% at temperature range 150-550 ºC corresponds to the decomposition of 3-chloropropyltriethoxysilane on Fe_3O_4. The curve (c) shows weight loss of 6.1% corresponds to decomposition of VIL. Moreover, the weight loss above 600 ^oC corresponds to decomposition of Fe_3O_4 to 3FeO. The TGA calculations reveal that 6.1% of ionic liquid was grafted on Fe_3O_4 NPs.

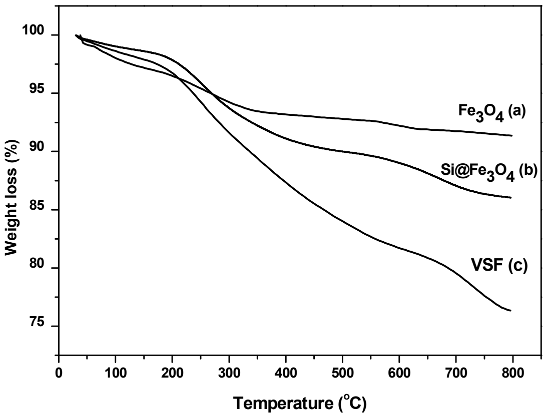


Figure 5: TGA curves of (a) Fe_3O_4 NPs; (b) $Si@Fe_3O_4$; (c) VSF

The magnetic properties of the VSF, $Si@Fe_3O_4$, and Fe_3O_4 NPs were measured by vibrating sample magnetometer (Figure 6). The saturation magnetization of bare Fe_3O_4 was found to be 44.8 emu/g. There was slight decrease in magnetization of $Si@Fe_3O_4$ and VSF, such as 36.1 and 37.3 emu/g respectively. The slight decrease in saturation magnetization was due to the successful supporting of chloropropyl triethoxysilane and ionic liquid on Fe_3O_4 NPs respectively. Moreover, the results indicates that these materials showed a typical superparamagnetic behavior with negligible remanence, Mr (emu/g) and coercivity, Hc (Oe) as shown in inset (Figure 6). The superparamagnetic behavior and high saturation magnetization of these materials are very beneficial in heterogeneous catalysis as it can be easily recoverable by external magnetic field.

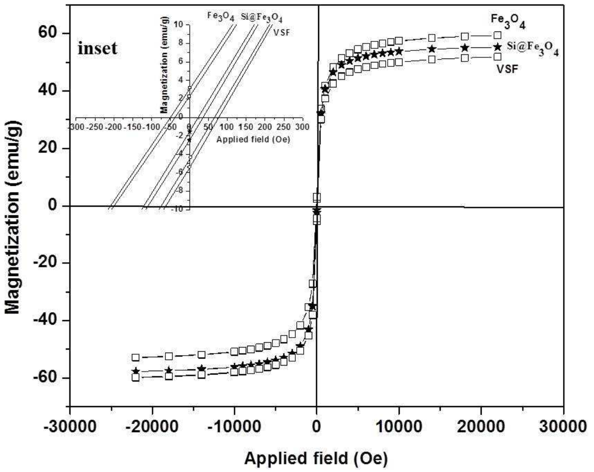
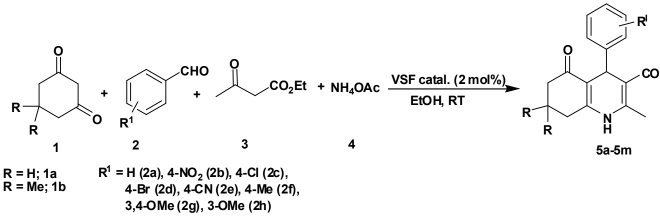


Figure 6: Magnetization curves of Fe_3O_4 NPs; $Si@Fe_3O_4$; and VSF

VSF as a quasi-homogeneous catalyst for multi-component reactions

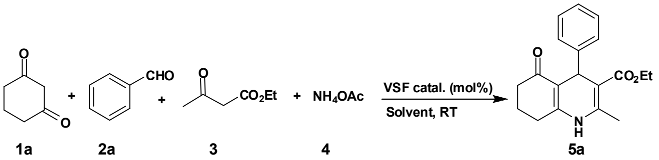
Initially, the catalytic potential of VSF NPs were investigated for the synthesis of 1,4-dihydropyridines *via* Hantzsch reaction as shown in Scheme 2. The optimization of reaction conditions were studied for the model reaction between 1,3-cyclohexanedione, benzaldehyde, ethyl acetoacetate and ammonium acetate for the synthesis of 1,4-dihydropyridine **5a**.



Scheme 2: VSF catalyzed one-pot synthesis of 1,4-dihydropyridines.

The reaction was performed in the presence of different VSF catalyst loading under benign solvents such as water, EtOH and without solvent at room temperature (Table 1, Entry 1-6). The results showed that 2 mol% of catalyst and ethanol as a solvent was the best condition to afford product **5a** in excellent yield in short reaction time (Table 1, Entry 5). When the reactions were performed in the presence of Fe_3O_4 and $Si@Fe_3O_4$ NPs under optimized conditions, the product **5a** was formed in moderate yields (Entries, 7 and 8). In the presence of VIL as a catalyst the product **5a** was formed in 60% yield (Entry 9). Next, we studied the model reaction in the absence of catalyst under optimized conditions, a trace amount of product formation was observed even after prolonged reaction time (Table 1, Entry 10). However, the catalytic activity of either Fe_3O_4 (heterogeneous) or VIL (homogeneous) alone was found to be sluggish with moderate yields of **5a**. The combined properties of VSF, a quasi-homogeneous catalyst, gave the best result to afford the DHP **5a** in 90% yield at room temperature (Table 1, Entry 5).

Table 1: Optimization study for VSF catalyzed one-pot synthesis of 1,4-dihydropyridine **5a**.[a]

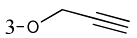


Entry	Catal. (mol%)	Solvent	Time (min)	Yield (%)[b]
1	VSF (10)	Water	60	70
2	VSF (10)	EtOH	40	84
3	VSF (10)	No solvent	80	65
4	VSF (5)	EtOH	30	84
5	**VSF (2)**	**EtOH**	**30**	**90**
6	VSF (1)	EtOH	30	80
7	Fe_3O_4 (2)	EtOH	120	50
8	Si@Fe_3O_4 (2)	EtOH	120	40
9	VIL (2)	EtOH	30	60
10	No catalyst	EtOH	240	Trace

[a]1,3-cyclohexanedione (1 mmol), aldehyde (1mmol), ethylacetoacetate (1 mmol), NH_4OAc (1.5 mmol), catalyst (mol%) and solvent (4 mL) at room temperature; [b]Isolated yield.

With these interesting results, we investigated the generality of VSF catalyst for several substituted aryl aldehydes, 1,3-cyclohexanedione/dimedone and ammonium acetate under optimized conditions as shown in Table 2. The aryl aldehydes having electron withdrawing groups such as NO_2, Cl, Br and CN at *para* position showed less reactivity as compared with simple benzaldehyde (Table 2, Entries 2-5). Moreover, the aldehydes bearing electron donating groups such as OMe, Me at *para* and *meta* positions gave excellent yields in short reaction time (Table 2, Entries 6-9).

Table 2: VSF catalyzed one-pot synthesis of 1,4-dihydropyridines.[a]

Entry	R	R[1]	Product **5**	Time (min)	Yield (%)
1	H	H	**5a**	25	94
2	H	4-NO_2	**5b**	40	87
3	H	4-Cl	**5c**	40	95
4	H	4-Br	**5d**	35	91
5	H	4-CN	**5e**	45	93
6	H	4-Me	**5f**	30	89
7	H	4-OMe	**5g**	20	93
8	H	3,4-OMe	**5h**	20	92
9	H	3-OMe	**5i**	20	93
10	Me	H	**5j**	25	94
11	H	4-OBn	**5k**	40	91
12	H		**5l**	40	85
13	EAA	H	**5m**	35	85

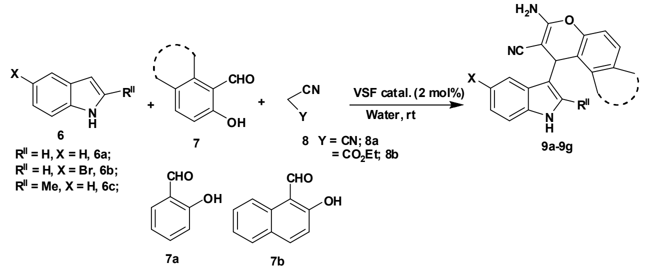
[a]1,3-cyclohexanedione (1 mmol), aldehyde (1mmol), ethylacetoacetate (1 mmol), NH_4OAc (1.5 mmol), VSF catalyst (2 mol%) and EtOH (4 mL) at room temperature; [b]isolated yield.

A comparative study on catalytic performance of VSF with other MNPs catalysts for the synthesis of 1,4-dihydropyridines **5a, 5m** and **5j** are shown in Table 3. To our delight, VSF is a best quasi-homogeneous catalyst to afford the products **5a** and **5m** in high yields at room temperature with turn over number values 39.66 and 35.86 respectively. In contrast, other MNPs such as nano-γ-Fe_2O_3, γ-Fe_2O_3-SO_3H, Fe_3O_4–CeO_2 and ZrO_2–Al_2O_3–Fe_3O_4 are either required high temperature condition (80-90 °C) to yield the products or obtained the low TON values (Table 3).

Table 3: Comparative study of MNPs catalysts for the synthesis of 1,4-dihydropyridines **5a** and **5m**.

5	Catalyst	Time (min)	Temp. (°C)	Yield (%)	TON	Ref
5m	γ-Fe_2O_3	25	90	95	6.53	28
5m	γ-Fe_2O_3-SO_3H	60	90	98	9.44	29
5j	Fe_3O_4–CeO_2	33	RT	93	3.75	30
5m	ZrO_2–Al_2O_3–Fe_3O_4	90	80	94	43.34	31
5a	**VSF**	**25**	**RT**	**94**	**39.66**	**-**
5m	**VSF**	**35**	**RT**	**85**	**35.86**	**-**

We further extended the scope of VSF catalyst for the synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromenes *via* Knoevenagel/Pinner/ Friedel-Crafts reaction as shown in Scheme 3.



Scheme 3: VSF catalyzed one-pot synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromenes.

In order to find the optimize reaction conditions, a model reaction between salicylaldehydes, indole and malononitrile using 2 mol% VSF catalyst in the presence of various polar and non-polar solvents was studied. Interestingly, when water was used a solvent the reaction proceeded smoothly to afford the product **9a** in excellent yield 93% (Table 3, Entry 6). Whereas the organic solvents such as EtOH, DMSO, CH_3CN, THF and CH_2Cl_2 gave the product **9a** in poor to moderate yield 40-60% (Entries 1-5). The reason for high catalytic activity of VSF catalyst in water as a solvent is may be the tendency of water to enhance the rate of organic reactions due to the interactions such as hydrogen bonding and the “Breslow effect” wherein the hydrophobic aggregation of organic molecules decreases the area of the non-polar surface and, in turn, reduces the activation energies.[34]

Table 3: Effect of solvent on VSF catalyzed one-pot synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromene **9a.**

Entry	Solvent	Time (min)	Yield (%)[b]
1	EtOH	90	60
2	DMSO	90	55
3	CH_3CN	90	50
4	THF	90	43
5	CH_2Cl_2	90	40
6	**Water**	**30**	**93**

[a]Reaction condition: Indoles (1 mmol), salicylaldehydes (1 mmol), and malononitrile (1 mmol), VSF catalyst (2 mol%), Solvent (1.5 mL) were stirred at room temperature. [b]Isolated yield.

Next, we examined the generality of VSF catalyst for the synthesis of substituted 2-amino-4-(indol-3-yl)-*4H*-chromenes **9a-9g** from the various substrates such as indoles (**6a-6c**), 2-hydroxy aromatic aldehydes (**7a**, **7b)** and active methylene compounds (**8a**, **8b)** as shown in Table 4. Interestingly, almost all the substrates afforded the desired products selectively in good to excellent yield 80-94% in short reaction time (Table 4, Entry 1-7).

The plausible mechanism of VSF catalyzed one-pot synthesis of 2-amino-4-(indol-3-yl)-4*H*-chromene **9a** is depicted in Figure 7. Probably, the high catalytic activity of VSF catalyst is due to the presence of active sites such as low-coordinated sites, and surface vacancies of nano Fe_3O_4, and carboxylate anion and ammonium ion from ionic liquids can act as conjugate base and acid respectively. Moreover, the combination of both the properties makes VSF as an efficient quasi-homogeneous catalyst. The basic sites of VSF can promote the Knoevenagel condensation between salicylaldehyde **7a** and malononitrile **8a** to afford the olefinic product **10,** followed by a Pinner reaction to yield the iminochromene intermediate **B**. Furthermore, Friedel-Crafts alkylation of indole **6a** with iminochromene **B** results the formation of 2-amino-4-(indol-3-yl)-4*H*-chromene **9a**.

Table 4: VSF catalyzed one-pot synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromenes.[a]

Entry	Indole 6	Aldehyde 7	Comp. 8	Product 9	Time (min)	Yield (%)[b]
1	**6a**	**7a**	**8a**	**9a**	15, 60[c]	94, 55[c]
2	**6a**	**7a**	**8b**	**9b**	30	85
3	**6b**	**7a**	**8a**	**9c**	20	87
4	**6b**	**7a**	**8b**	**9d**	35	82
5	**6c**	**7a**	**8a**	**9e**	15	90
6	**6c**	**7a**	**8b**	**9f**	30	83
7	**6a**	**7b**	**8a**	**9g**	35	87

[a]Reaction condition: Indoles (1 mmol), salicylaldehydes (1 mmol), and malononitrile (1 mmol), VSF catalyst (2 mol%), Water (1.5 mL) were stirred at room temperature. [b]Isolated yield.[c] Fe_3O_4 used as catalyst.

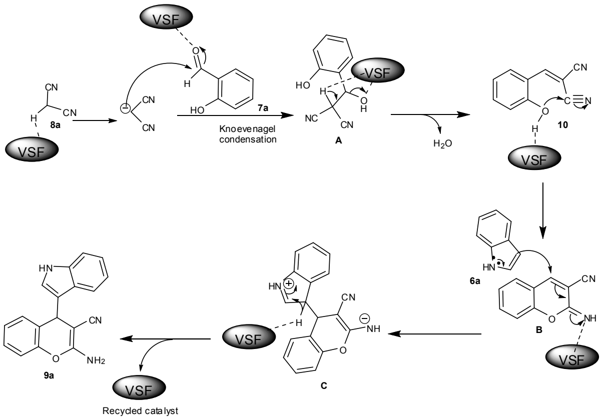


Figure 7: Plausible mechanism of VSF catalyzed one-pot synthesis of 2-amino-4-(indol-3-yl)-*4H*-chromene **9a**.

The recyclability of VSF catalyst was investigated for the reaction between 1,3-cyclohexanedione, benzaldehyde, ethyl acetoacetate and ammonium acetate in the synthesis of 1,4-dihydropyridine **5a** as shown in Figure 8.

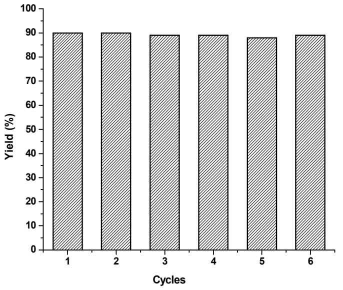


Figure 8: Recycling study of VSF catalyst for the synthesis of 1,4-dihydropyridine **5a**.

After the completion of reaction, the catalyst was separated from the reaction mixture magnetically by using external magnet. The catalyst was washed with ethanol for 3-4 times to remove the residual product, dried at 70 °C and used for the next cycle. The procedure was repeated for six times, there was no significant loss in catalytic activity of VSF catalyst was observed (Figure 8).

Concluions

We have doveloped VSF as a superparamagnetic quasi-homogeneous catalyst to bridge the gap between homogeneous and heterogeneous catalysis for the multi-component synthesis of 1,4-dihydropyridines and 2-amino-4-(indol-3-yl)-4*H*-chromenes. The present protocol can provide a superior alternative to the existing methods with advantages such as catalyst is non-toxic, superparamagnetic and easily recoverable with an external magnet, avoids the work up/filtration and high activity/selectivity with excellent yileds. The high catalytic activity of VSF catalyst is due to the presence of active sites such as low-coordinated sites, and surface vacancies of nano Fe_3O_4, and carboxylate anion and ammonium ion from VIL.

Experimental

Powder X-ray diffraction (PXRD) patterns were recorded in a Siemens D500 instrument, using Cu-Ka radiation (l~1.54050 AÊ) and equipped with AT Diffract software. Identification of the crystalline phases were by comparison with the JCPDS ®les.10. TGA analysis (Perkin Elmer, Pyris Diamond) with a heating rate of 10 °C/min in nitrogen atmosphere was used to study the thermal decomposition behavior of samples with respect to α-Al_2O_3 as the reference. Fourier transform infrared (FT-IR) spectra were recorded on Perkin Elmer and the samples were prepared by mixing the samples with KBr. Scanning electron microscopy (SEM) measurement was performed on a JEOL JSM-6610LV electron microscope. The superparamagnetic properties of the samples were studied by using a superconducting quantum interference device (SQUID) magnetometer. Transmission electron microscopy (TEM) measurement was performed on a JEOL 2100F transmission electron microscope. The samples were supported on carbon-coated copper grids for the TEM experiment. Melting points were measured with a Buchi B-540 melting-point apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were measured on a BruckerAC-200 instrument.

Procedure for the preparation of Fe_3O_4 MNPs

The Fe_3O_4 nanoparticles were prepared according to Massart's method. The aqueous solution of 2 eq. $FeCl_3\cdot6H_2O$ (5.8 g in 50 mL water) was mixed with the aqueous solution of 1 eq. $FeCl_2\cdot4H_2O$ (2.2 g in 50 mL water). The mixture was stirred vigorously at 85 °C for 30 min, and then 10 mL of ammonia (28% aqueous solution) was added quickly. The reaction was further stirred for another 30 min at 85 °C to afford the Fe_3O_4 nanoparticles as black precipitate. The obtained Fe_3O_4 NPs was collected by using external magnet, washed with water followed by ethanol and dried at 80 °C in oven.

General procedure for the synthesis of $[NBu_4][Val]$ ionic liquid:

$[NBu_4][Val]$ ionic liquid was prepared by modified literature method.[35] Tetrabutylammonium hydroxide solution (40%, 10 mmol) was added to an aqueous suspension of valine (10 mmol). The resultant reaction mixture was stirred at room temperature for 12 h. The water was removed in vacuo at 80 °C and the resultant residue was dissolved in CH_3CN (40 mL) and filtered to remove the unreacted valine. The filtrate was dried over Na_2SO_4, filtered and excess of solvent was removed in vacuo to afford the desired tetrabutylammonium valinate ionic liquid as low viscous colourless oil.

Procedure for the Preparation of Fe_3O_4@Si$(CH_2)_3$-NVIL (VSF): The supporting of $[NBu_4][Val]$ ionic liquid on silica grafted ferrite is illustrated in Scheme 1. In a typical procedure, 3 g of Fe_3O_4 and 3-chloropropyltriethoxysilane (6 mmol) in 40 mL of dry toluene was refluxed under nitrogen for 12 h. The obtained grafted Fe_3O_4@Si$(CH_2)_3$-Cl was filtered out, washed twice with dry toluene and once with anhydrous diethyl ether, and dried at 75 °C for 6 h in vacuum. Then $[NBu_4][Val]$ ionic liquid (10 mmol) was added to the round bottom flask containing Fe_3O_4@Si$(CH_2)_3$-Cl (1 mmol) in 50 mL of dry toluene and the mixture was refluxed for 24 h. The resulting solid was filtered out, washed and dried in a similar manner to give the Fe_3O_4@Si$(CH_2)_3$-NVIL (VSF). After usual workup and washings, the material was dried at 75 °C for 5 h in vacuum oven.

General procedure for the synthesis of 1,4-dihydropyridines (5a-5m) :
A mixture of 1,3-cyclohexanedione **1** (1 mmol), aldehyde **2** (1 mmol), ethyl-acetoacetate **3** (1 mmol), ammonium acetate **4** (1.5 mmol), and VSF nanoparticles (10 wt%) in ethanol (4 mL) were stirred at room temperature. After completion of the reaction (monitored by TLC), the superparamagnetic VSF catalyst was separated from the reaction mixture using an external magnet. The obtained crude products (5a-5m) were purified by recrystallization from hot ethanol. The purified compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, HRMS, elemental analysis.

Ethyl4-(4-(benzyloxy)phenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5k): Off white solid; mp 250-253 °C; IR (KBr) 3294, 3215, 3081, 2938, 1697, 1607, 1490, 1384, 1224, 1176, 1080 cm^{-1}; ^{1}H NMR (400 MHz; DMSO; Me_4Si) δ = 9.08 (brs, 1H), 7.40-7.29 (m, 5H), 7.02 (d, J = 7.9 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 4.99 (s, 2H), 4.81 (s, 1H), 3.96 (q, J = 7.3 Hz, 2H), 2.46-2.45 (m, 2H), 2.25 (s, 3H), 2.19-2.16 (m, 2H), 1.90-1.68 (m, 4H), 1.11 (t, J = 7.3 Hz, 3H) ppm. ^{13}C NMR (100 MHz; DMSO; Me_4Si) δ = 194.62, 167.04, 156.30, 151.11, 144.56, 140.35, 137.28, 128.36, 127.47, 114.00, 111.24, 103.64, 69.00, 58.98, 36.70, 34.64, 26.07, 20.76, 18.19, 14.14 ppm. HRMS (ES): Calcd 417.1940, found 417.1937; Anal. Calcd for $C_{26}H_{27}NO_4$: C, 74.80; H, 6.52; N, 3.35; Found: C, 74.79; H, 6.51; N, 3.36.

Ethyl2-methyl-5-oxo-4-(3-(prop-2-yn-1-yloxy)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5l): White solid; mp 260-263 °C; IR (KBr) 3279, 3243, 3077, 2941, 1701, 1607, 1488, 1381, 1221, 1037 cm^{-1}; ^{1}H NMR (400 MHz; DMSO; Me_4Si) δ = 9.14 (brs, 1H), 7.09 (t, J = 7.3 Hz, 1H), 6.75 (d, J = 7.3 Hz, 1H), 6.72-6.69 (m, 2H), 4.87 (s, 1H), 4.67 (s, 2H), 3.98 (q, J = 7.3 Hz, 2H), 3.53 (s, 1H), 2.26 (s, 3H), 2.18 (s, 3H), 1.87-1.74 (m, 3H), 1.12 (t, J = 7.3 Hz, 3H) ppm. ^{13}C NMR (100 MHz; DMSO; Me_4Si) δ = 194.52, 166.71, 156.93, 151.51, 149.29, 145.00, 128.64, 120.41, 114.25, 111.37, 110.87, 103.31, 79.31, 77.93, 59.06, 55.07, 36.67, 35.34, 26.11, 20.74, 18.21, 14.14 ppm. HRMS (ES): Calcd 365.1627, found 365.1630; Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83; Found: C, 72.30; H, 6.36; N, 3.82.

General procedure for the synthesis of 2-amino-4-(indol-3-yl)-4*H*-chromene derivatives (9a-9f): A mixture of indoles **6** (1 mmol), 2-hydroxy aromatic aldehydes **7** (1mmol), active methylene compounds **8** (1 mmol), and 10 wt% VSF nanoparticles in 1.5 mL of water were stirred at room temperature. After completion of the reaction (monitored by TLC), the superparamagnetic VSF catalyst was separated from the reaction mixture using an external magnet. The obtained crude products were recrystallized from ethanol to get pure compounds (9a-9f).

2-Amino-4-(5-bromo-1*H*-indol-3-yl)chroman-3-carbonitrile (9c): Yellow solid; mp 180-182 °C; IR (KBr) 3449, 3382, 3320, 3241, 3206, 3083, 2852, 2346, 2372, 2195, 1661, 1612, 1583, 1491, 1449, 1456, 1422, 1405, 1332, 1273, 1259, 1227, 1076, 1098, 1042, 845, 882, 794, 752, 580, 521 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.20 (br s, 1H), 7.39 (br s, 1H), 7.22-7.16 (m, 4H), 7.05-6.95 (m, 3H), 5.02 (s, 1H), 4.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.59, 148.75, 135.86, 129.66, 128.55, 127.54, 125.43, 124.13, 122.60, 121.81, 120.42, 118.84, 116.58, 113.12, 60.49, 32.70; HRMS (ES): Calcd 367.0320, found 367.0322; Anal. Calcd for $C_{18}H_{14}BrN_3O$: C, 58.71; H, 3.83; N, 11.41; Found: C, 58.72; H, 3.82; N, 11.41.

Ethyl2-amino-4-(5-bromo-1H-indol-3-yl)-4*H*-chromene-3-carboxylate (9d): Yellow solid; mp 145-147 °C; IR (KBr) 3412, 3318, 2958, 2926, 1731, 1666, 1607, 1518, 1483, 1455, 1399, 1297, 1227, 1185, 1043, 883, 750, 654 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (br s, 1H), 7.74 (s, 1H), 7.21-7.13 (m, 4H), 7.04-6.96 (m, 2H), 6.28 (s, 1H), 5.24 (s, 1H), 4.12-4.04 (m, 2H), 1.16 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.43, 160.24, 148.98, 134.76, 127.69, 126.37, 124.71, 124.18, 123.30, 122.96, 122.72, 121.83, 115.60, 112.60, 112.18, 59.44, 31.02, 14.30; HRMS (ES): Calcd 412.0423, found 412.0421; Anal. Calcd for $C_{20}H_{17}BrN_2O_3$: C, 58.13; H, 4.15; N, 6.78; Found: C, 58.12; H, 4.13; N, 6.79.

2-Amino-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile (9e): Yellow solid; mp 202-204 °C; IR (KBr) 3331, 2961, 2933, 2185, 1646, 1604, 1576, 1486, 1457, 1394, 1224, 1040, 744, 593, 562 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.86 (br s, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.16-7.14 (m, 1H), 7.08-7.00 (m, 3H), 6.96-6.95 (m, 2H), 6.92-6.88 (t, J = 7.3 Hz), 5.10 (s, 1H), 4.52 (s, 2H), 2.47 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.84, 148.70, 135.43, 131.97, 129.49, 127.90, 126.93, 124.94, 122.67, 121.06, 120.16, 119.34, 118.15, 115.94, 113.87, 60.56, 31.23, 11.57; HRMS (ES): Calcd 367.0320, found 367.0322; Anal. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94; Found: C, 75.72; H, 5.04; N, 14.01.

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Notes and references

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Graphical Abstract

Functionalized superparamagnetic Fe_3O_4 as an efficient quasi-homogeneous catalyst for multi-component reactions

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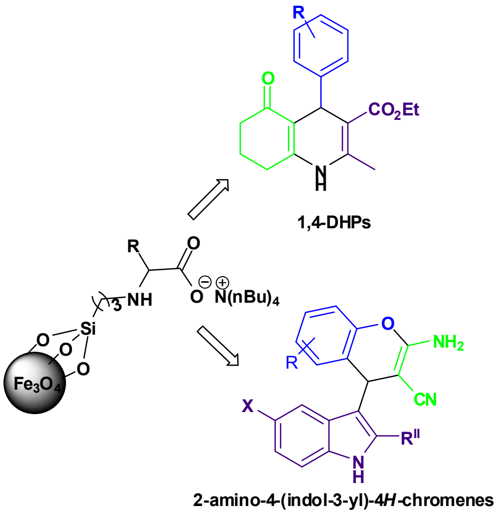

Tetrabutylammonium valinate ionic liquid [NBu_4][Val] supported on 3-chloropropyltriethoxysilane grafted superparamagnetic Fe_3O_4 NPs (VSF) was synthesized and characterized by fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), transmission electronic microscopy (TEM), scanning electronic microscopy (SEM), thermal gravimetric analysis (TGA), and vibrating sample magnetometer (VSM). The VSF catalyst was used as an efficient "quasi-homogeneous" catalyst for multi-component synthesis of 1,4-dihydropyridines and 2-amino-4-(indol-3-yl)-4*H*-chromenes at room temperature. VSF catalyst was recovered by using an external magnet and recycled for six times without significant loss in catalytic activity. Moreover, VSF is a "quasi-homogeneous" catalyst can bridge the gap between homogeneous and heterogeneous catalysis.