© Indian Academy of Sciences

REGULAR ARTICLE

[Fesipmim]Cl as highly efficient and reusable catalyst for solventless synthesis of dihydropyridine derivatives through Hantzsch reaction

AKANSHA AGRWAL[a],[*] ⓘ and VIRENDRA KASANA[b]

[a]Department of Chemistry, KIET Group of Institutions, Delhi-NCR, Meerut Road (NH-58), Ghaziabad 201 206, India
[b]Department of Chemistry, G. B. Pant University of Agriculture and Technology, Pantnagar, India
E-mail: akansha.agrwal90@gmail.com

Abstract. In the present investigation, magnetic ferrite nanoparticles (ferrite NPs) were synthesized and coated with silica (ferrite@SiO_2NPs) by using the sol-gel method. After that, silica propylmethylimidazolium chloride ionic liquid [Sipmim]Cl was prepared and linked with the above-prepared ferrite@SiO_2NPs to synthesize ferrite silica propylmethylimidazolium chloride [Fesipmim]Cl catalyst. The formation of [Fesipmim]Cl catalyst was confirmed by Fourier-transform infrared (FT-IR) spectroscopy analysis. X-ray diffraction (XRD) analysis confirmed the structure of ferrite NPs and ferrite@SiO_2 NPs. Transmission electron microscopy (TEM) evidenced the successful formation of ferrite NPs and ferrite@SiO_2 NPs. Scanning electron microscopy (SEM) results revealed the change in morphology of ferrite NPs, ferrite@SiO_2NPs and [Fesipmim]Cl. The magnetic properties of [Fesipmim]Cl catalyst were measured by vibrating sample magnetometer (VSM). The efficiency of the [Fesipmim]Cl catalyst was checked by using it for the synthesis of different derivatives of dihydropyridine through Hantzsch reaction *via* a three-component coupling reaction of substituted benzaldehydes, ethyl/ methyl acetoacetate and ammonium acetate. The formation and structures of all the synthesized compounds were confirmed by FT-IR, ^{1}HNMR, ^{13}C NMR spectral analyses. The reusability of the catalyst [Fesipmim]Cl was checked up to seven cycles and found to have excellent activity up to five cycles.

Keywords. 1, 4-Dihydropyridine; Hantzsch reaction; ferrite nanoparticles (NPs); [Sipmim]Cl, [Fesipmim]Cl.

1. Introduction

Catalysts accelerate the rate of chemical reactions, increase yield and reduce activation energy but the serious problem with catalytic reactions is the separation of catalyst from the reaction mixture so that it can be reused. To overcome this problem, a heterogeneous catalyst can be used in organic synthesis.[1] In the present time, heterogeneous catalysts are being prepared by using various substances in a simple whole ratio.[2] Heterogeneous catalysts can be efficiently prepared by modifying the support by using the nanosystem and joining it with catalysts.[3] Magnetic nanoparticles (NPs) are an important class of nanomaterials which are the best solution to support the preparation of heterogeneous catalysts.[4] To make the catalytic system heterogeneous, the catalyst can be bonded with magnetic NPs which allow the catalyst to remain immiscible in the reaction mixture, and after completion of reaction makes its separation easier for further use, thus reducing the waste and making the catalytic system greener. To protect the magnetic properties of magnetic NPs, their core can be coated with some inert, inorganic, non-magnetic material like silica which can be easily bonded with most of the catalytic species. A number of heterogeneous catalytic systems such as ionic liquid supported on silica,[5] nano nickel-cobalt ferrite,[6] HMMS,[7] nano ZSM-5,[8] and cucurbit (6) uril-OSO_3H[9] with good recovery and efficient activity have been reported. Ionic liquids

have a major application in synthetic organic chemistry.[10] Ionic liquids can be used as immobilized catalysts[11] which gain efficient activity and selectivity. Moreover, they can also be used as solvents[12] which promote and provide a medium to various chemical, biochemical, enzymatic and industrial reactions.

Multicomponent reactions (MCRs)[13–15] are gaining importance in modern organic chemistry for the synthesis of multifunctional biologically active molecules from readily available starting materials without isolation of intermediates. Hantzsch reaction affords 1, 4-dihydropyridines (DHPs) in a single step. DHP nucleus is an essential component of biologically important molecules possessing important pharmacological properties. DHP drugs such as nifedipine, nicardipin, felodipine, etc., are used for the treatment of hypertension as an effective calcium channel blocker.[16] DHPs exhibit antitumor,[17] anti-inflammatory[18] and analgesic[19] activities. More than twelve medicinally important compounds having DHP nucleus are manufactured and used all over the world.[20–22] A large number of methods for the synthesis of DHPs have been developed including microwave-assisted reaction,[23–29] ultrasound irradiation,[30] solar thermal energy,[31] ionic liquids and water-ethanol green solvents,[32–37] solid support[38,39] and visible light.[40] Various catalytic systems have been developed to improve Hantzsch reaction by using nano ZnO,[41] PPh$_3$,[42] phenylboronic acid,[43] I$_2$,[44] CAN,[45] tetrabutylammonium hydrogen sulphate,[46] Baker's Yeast,[47] organocatalysts[48] and metal triflates.[49] All these methods are associated with one or more drawbacks like long reaction time, harsh reaction conditions, toxic catalysts and tedious workup. We herein report, for the first time, the use of [Fesipmim]Cl as an efficient, reusable and green catalyst for the synthesis of 1, 4-DHP derivatives.

2.   Materials and methods

2.1   General details

All the reagents and chemicals were purchased from Himedia, India and were used without further purification. IR spectra were recorded on Brucker FT-IR spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded on Brucker AVANCE II 400 MHz and Brucker AVANCE II 500 MHz instruments using CDCl$_3$. Melting points were recorded using Decibel digital melting point apparatus. The purity of products and reaction progress was checked by TLC on silica gel plates using hexane: ethyl acetate solvent system and visualized using iodine vapors and UV light. TEM measurements were performed on a JSM- 1011

transmission electron microscope. SEM was recorded on JEOL (JSM-6610 LV) using a primary beam voltage of 5 kV. XRD spectra of powdered samples were recorded at room temperature over Rigaku-Geigerflex X-Ray diffractometer using Cu-Kα radiation (λ = 0.154 nm) in the range of 10°–70° at 30 kV and 15 mA with step size 0.05 and step time of 19.2 sec. VSM was performed on instrument PAR Model 155.
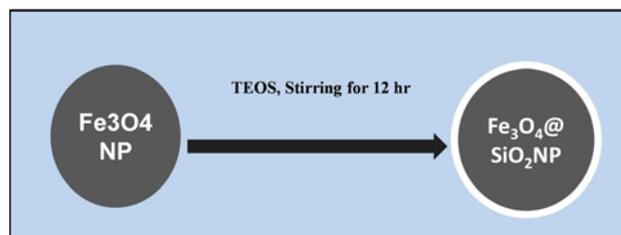
2.2   Synthesis of ferrite nano particles (Fe$_3$O$_4$ NPs)

Ferrite magnetic NPs were prepared by modifying the method reported in the literature.[50] FeCl$_2$·4H$_2$O (0.01 mol) and FeCl$_3$·6H$_2$O (0.02 mol) were dissolved in 200 mL of distilled water. After that, under the fast mechanical stirring, 25 mL (30%) NH$_3$ solution was added to the solution. The reaction was continued for 24 h at room temperature. The prepared black ferrite NPs were then washed several times with distilled water and dried at 80 °C under vacuum.

2.3   Coating of silica on ferrite NPs (Fe$_3$O$_4$@SiO$_2$NPs)

The silica-coated magnetic nanoparticles (ferrite@SiO$_2$-NPs) were prepared using a sol-gel method.[51] In the whole process, ferrite NPs were discrete in a combination of ethanol, distilled water and concentrated ammonia water. After slow addition of 1.2 mL TEOS, the solution was constantly stirred for 12 h. The prepared ferrite@SiO$_2$ NPs were washed and re-dispersed in deionized water for further use (Scheme 1).

2.4   Synthesis of [Sipmim]Cl ionic liquid

1-Methylimidazole (4.8 mL, 0.06 mol) and (3-chloropropyl) triethoxysilane (14.5 mL, 0.07 mol) were refluxed at 80 °C for 24 h (Scheme 2). The unreacted volatile material was distilled off under reduced pressure. The crude product was washed with diethyl ether (5×5 mL). The remaining diethyl ether was removed under vacuum at room temperature, to give a yellowish viscous liquid.

Scheme 1.   Coating of silica on ferrite nano particles.

2.5 Synthesis of [Fesipmim]Cl catalyst

Ferrite@SiO$_2$ NPs (2 g) and 25 mL of dry toluene were mixed in a beaker and then dispersed into the mixture by ultrasonication. 1-Methyl-3-(3-trimethoxysilylpropyl)-1H-imidazol-3-ium chloride (1 gm, 2.7 mmol) was added dropwise at room temperature and stirred for 16 h at 80 °C (Scheme 3). 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.

2.6 Synthesis of dihydropyridine derivatives using [Fesipmim]Cl catalyst

Substituted benzaldehyde (1 m mole), ethyl/methyl acetoacetate (2 m mole) and ammonium acetate (1.2 m mole) were taken in a round bottom flask, [Fesipmim]Cl (100 mg) was added and heated on a water bath at 80 °C (Scheme 4). Progress of the reaction was checked over silica gel TLC plates using hexane and ethyl acetate (80:20) solvent system. After completion of the reaction, the catalyst was separated from the reaction mixture using an external magnet. The catalyst was washed with ethanol 4-5 times and used for the next cycle. The process was repeated for five times. The solid crude product was collected and dissolved in hot EtOH. The filtrate was concentrated and the solid crude product was purified by recrystallization in aqueous EtOH.
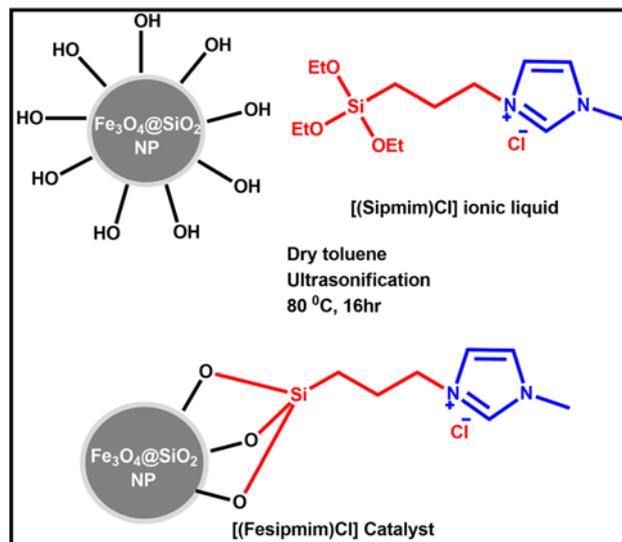
3. Results and Discussion

3.1 FT-IR analysis of [Fesipmim]Cl

The functional groups of the synthesized [Fesipmim]Cl catalyst and its precursors were characterized
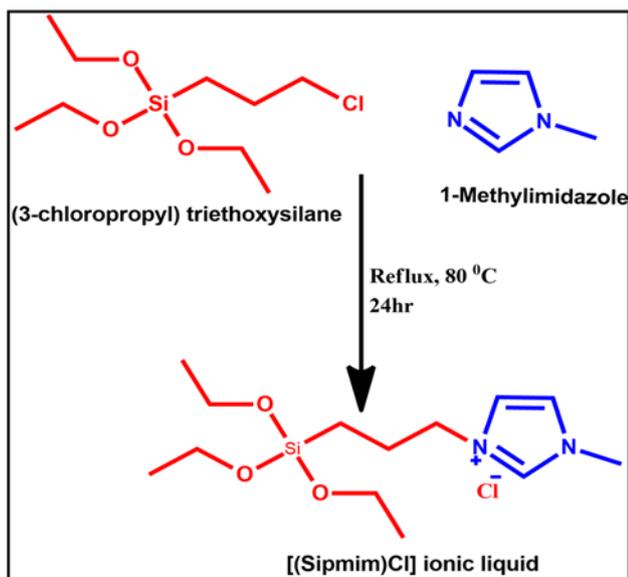
Scheme 2. Synthesis of silica propyl methyl imidazoliumchloride[(Sipmim)Cl] ionic liquid.

Scheme 3. Synthesis of ferrite silica propyl methyl imidazolium chloride ([Fesipmim]Cl) catalyst.

by FT-IR technique (Figure 1). FTIR analysis was carried out to differentiate the chemical structure of ferrite and modified ferrite NPs. In ferrite NPs, two characteristic peaks were at 560 and 3472 cm^{-1} due to Fe-O and Fe-OH (Figure 1a), while in silica-coated NPs the peaks were observed at 568, 963 and 1089 cm^{-1} due to Fe-O, Si-O and Si-O-Si group respectively, and at 798 cm^{-1} the peak is due to Si-O-Si bending and at 3422 cm^{-1} due to Fe-OH and Si-OH stretching (Figure 1b). In the spectra of [Fesipmim]Cl catalyst two new bands were seen at 1536 cm^{-1} and 2851 cm^{-1} which were due to the bending vibration of -NH and –CH stretching vibration (Figure 1c).

3.2 TEM analysis of Ferrite and Silica-coated ferrite NPs

The internal morphology and size of ferrite NPs (-Figure 2a) and silica-coated ferrite NPs (Figure 2b) were characterized by TEM analysis. The morphological and size changes were observed in Silica coated ferrite MNPs. In TEM analysis size of Ferrite NPs were 7-11 nm which increased in silica-coated ferrite NPs.

3.3 SEM analysis of [Fesipmim]Cl catalyst

The surface morphology of Fe$_3$O$_4$MNPs, silica-coated nanoparticles and [Fesipmim]Cl catalyst were characterized by using SEM technique (Figure 3). The results clearly showed that there was a change in morphology.
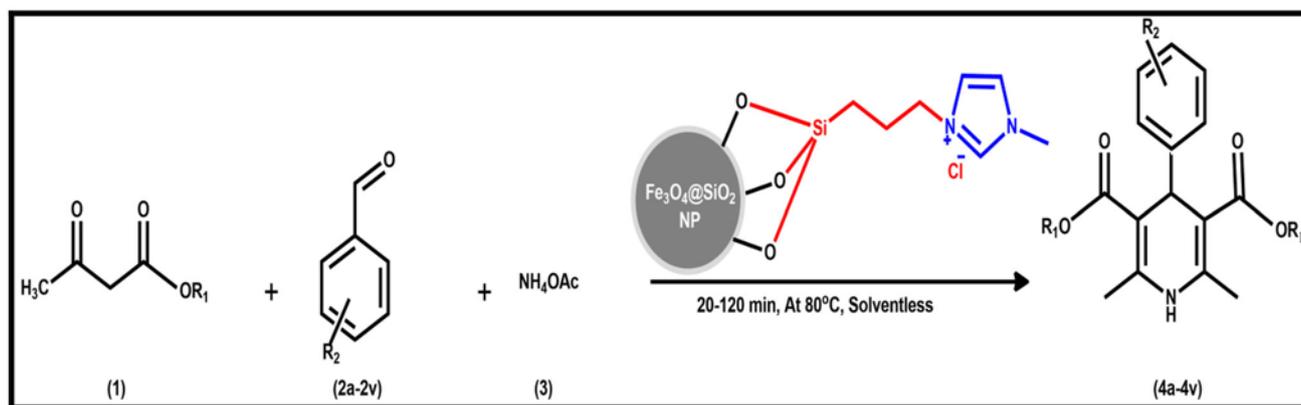
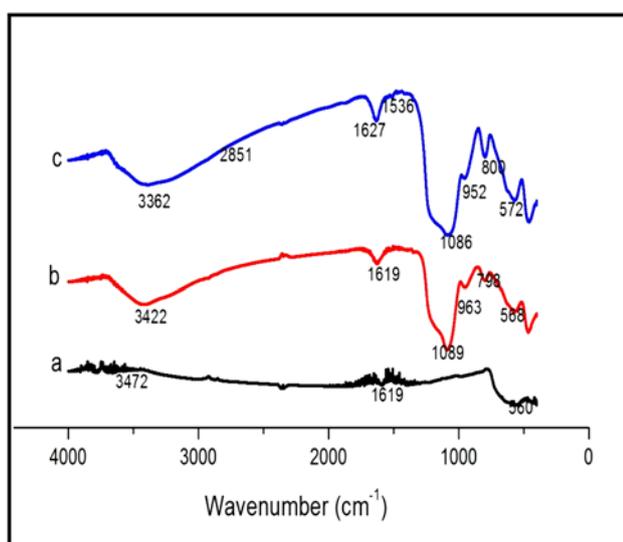**Scheme 4.** Synthesis of dihydropyridine derivatives catalyzed by ([Fesipmim]Cl).

Figure 1. FTIR of Fe$_3$O$_4$ NPs (b) Fe$_3$O$_4$@SiO$_2$ NPs (c) ([Fesipmim]Cl) catalyst.

3.4 *VSM analysis of [Fesipmim]Cl catalyst*

The magnetic properties of [Fesipmim]Cl catalyst, silica-coated ferrite NPs and ferrite NPs were measured by VSM (Figure 4). The saturation magnetization of ferrite NPs (Figure 4a) was found to be 44.4 emu g^{-1}. There was a decrease in the magnetization of silica-coated ferrite NPs (Figure 4b) to 22 emu g^{-1}. This decrease was because of the coating of silica on ferrite NPs. There was again a decrease in the magnetization of IL supported on silica-coated ferrite NPs (Figure 4c) catalyst to 13 emu g^{-1}. Due to this magnetic behavior of the [Fesipmim]Cl catalyst, it is easily separable from the reaction mixture by using an external magnetic field.

3.5 *XRD analysis of ferrite NPs and [Fesipmim]Cl catalyst*

The XRD pattern of Fe$_3$O$_4$ clearly conforms to the formation of a cubic spinel structure with the diffraction peaks (2θ) at 30.24°, 35.51°, 43.05°, 52.88°,
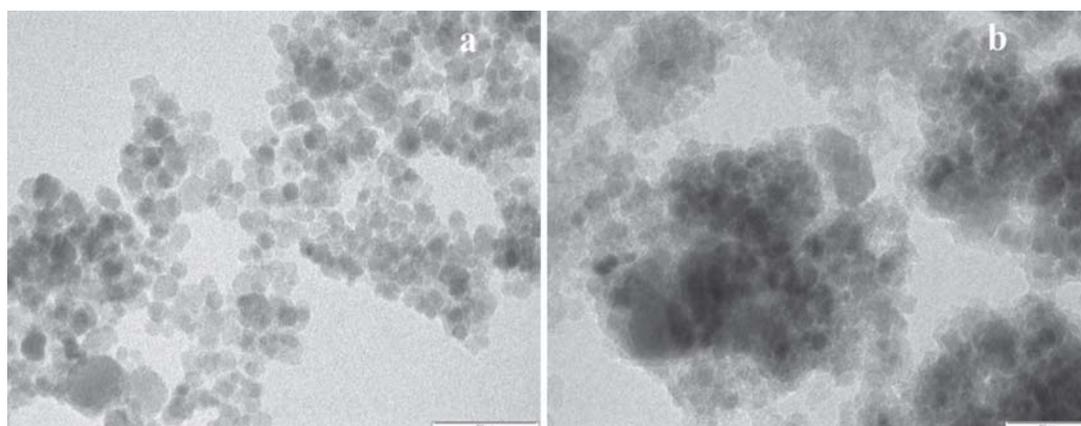

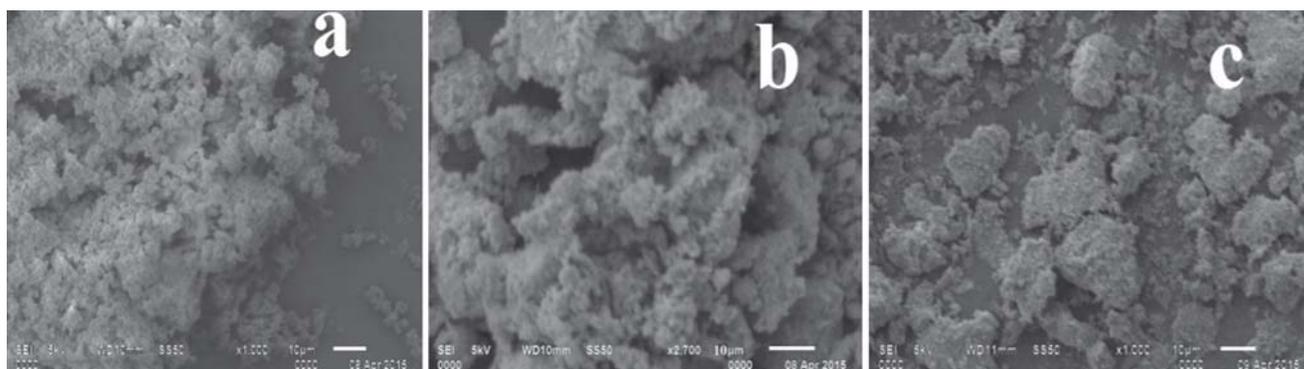**Figure 2.** TEM images of (a) Ferrite NPs (b) Silica-coated Ferrite NPs.

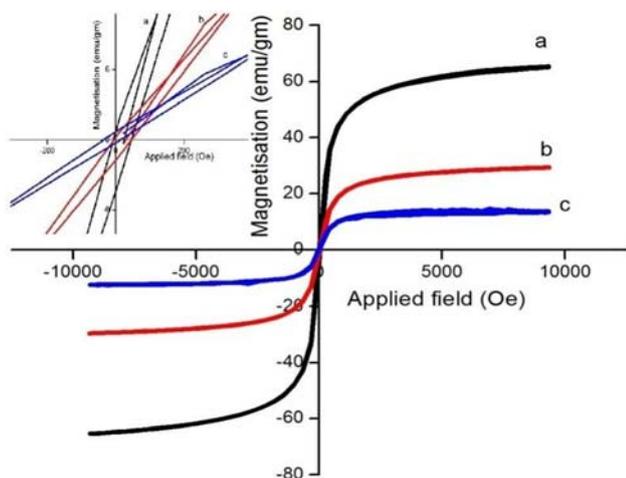**Figure 3.** SEM images of (a) Ferrite NPs (b) Silica-coated Ferrite NPs (c) ([Fesipmim]Cl) catalyst.

Figure 4. VSM of (a) Ferrite NPs (b) Silica-coated Ferrite NPs (c) ([Fesipmim]Cl) catalyst.

Figure 5. (a) XRD pattern of Ferrite NPs (b) XRD pattern of ([Fesipmim]Cl) catalyst.

57.19° and 62.11°, which correspond to (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1), and (4 4 0) phases, respectively (Figure 5a). A broad peak in the spectrum of [Fesipmim]Cl at $2\theta = 23.25°$ is due to the coating of silica which is amorphous in nature (Figure 5b). The XRD pattern is in good agreement with the reported data (JCPDS card no. 85-1436).[52]

3.6 *Plausible mechanism*

Based on the results and the previous works reported, the plausible mechanism of the Hantzsch reaction catalyzed by [Fesipmim]Cl is proposed (Scheme 5). The catalyst increases the electrophilic character of the carbon of aldehyde group. The product formation completes by cyclisation followed by dehydration.

3.7 *Reaction optimization*

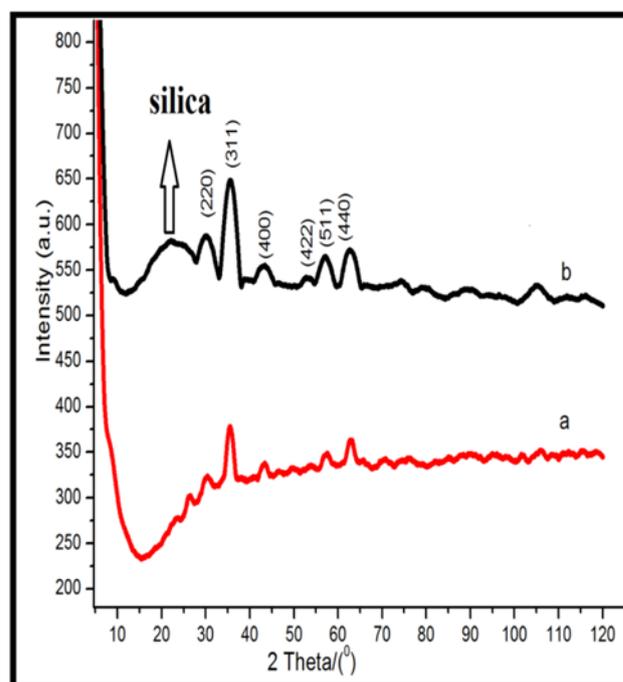A representative reaction taking ethylacetoacetate, benzaldehyde and ammonium acetate as reactants using [Fesipmim]Cl as catalyst under solventless condition were carried out, first, to optimize the temperature. The reaction mixture was stirred at room temperature. The reaction did not take place even up to 12 h. Then, the reaction was tried at temperatures 40 °C, 50 °C, 60 °C, 70 °C, 80 °C, 90 °C and 100 °C. With an increase in temperature, the yield increased steadily and time of reaction decreased. After 80 °C the yield did not increase and time did not decrease. So, the 80 °C temperature was taken as optimum.

To establish the necessary role of catalyst, we tried the representative reaction in the absence of catalyst at 80 °C under solventless condition, and in solvents water and ethyl alcohol. No reaction was observed even after 12 h
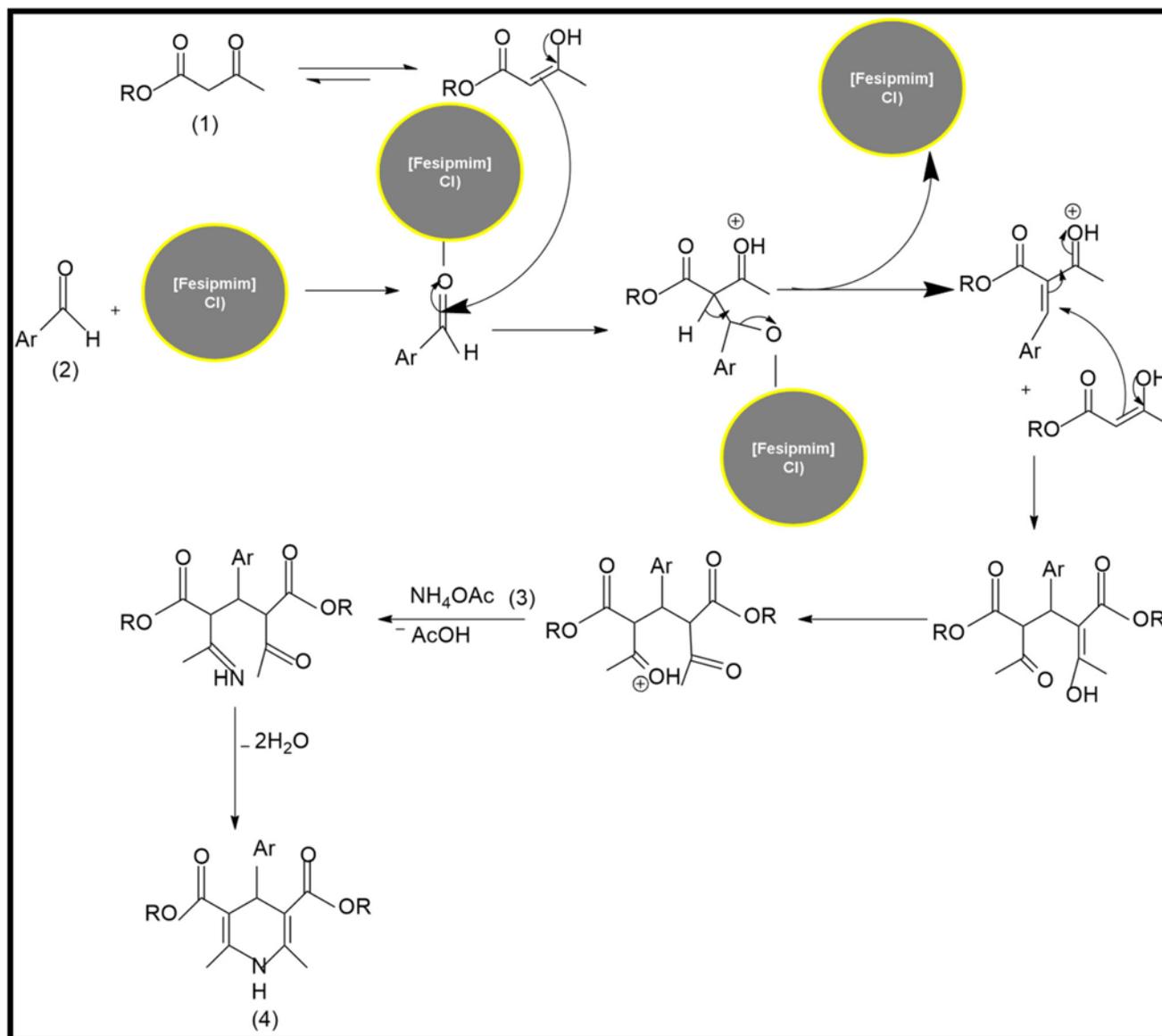
Scheme 5. Plausible Mechanism of the Hantzsch Reaction catalyzed by ([Fesipmim]Cl).

Table 1. Optimal conditions for the synthesis of 4k catalyzed by [Fesipmim]Cl at 80 °C.

Entry	Catalyst	Solvent	Time (hour)	Yield (%)
1	–	–	12	–
2	–	Water	12	–
3	–	Ethanol	12	–
4	1-Methylimidazole	–	4	40
5	(3-chloropropyl) triethoxysilane	–	5	20
6	Ferrite NPs	–	12	–
7	Ferrite@SiO$_2$ NPs	–	12	–
8	[(Sipmim)Cl] ionic liquid	–	0.33	95
9	([Fesipmim]Cl) catalyst	–	0.33	95

Table 2. Synthesis of 1, 4-dihydropyridines catalyzed by [Fesipmim]Cl.
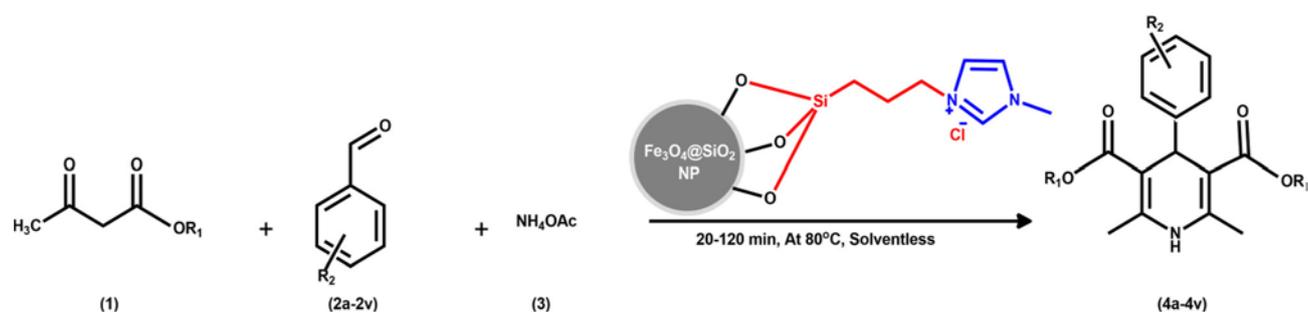
Code	-R_1	-R_2	Yield (%)	M.P. (°C)	Time (min)
4a	- C_2H_5	4-furyl	90	155–157	20
4b	- C_2H_5	4-CH_3	85	117–119	80
4c	- C_2H_5	3,4(OCH_3)$_2$	90	142–144	120
4d	- C_2H_5	3-OH	95	170–172	80
4e	- C_2H_5	4-OH	90	210–215	80
4f	- C_2H_5	4-Cl	90	145–148	50
4g	- C_2H_5	4-OCH_3	90	150–152	40
4h	- C_2H_5	3-OCH_3	85	138–140	100
4i	- C_2H_5	4-NO_2	70	125–128	80
4j	- C_2H_5	3-NO_2	80	162–164	40
4k	- C_2H_5	-H	95	150–152	20
4l	- CH_3	-H	90	170–172	20
4m	- CH_3	3-NO_2	90	154–160	50
4n	- CH_3	4-NO_2	90	120–125	30
4o	- CH_3	3-OCH_3	95	125–130	80
4p	- CH_3	4-OCH_3	85	138–140	30
4q	- CH_3	4-Cl	90	154–156	40
4r	- CH_3	4-OH	95	210–212	40
4s	- CH_3	3-OH	85	165–170	120
4t	- CH_3	3,4(OCH_3)$_2$	90	155–157	80
4u	- CH_3	4-CH_3	90	117–122	80
4v	- CH_3	4-furyl	85	180–185	20

stirring. To prove the catalytic action of [Fesipmim]Cl catalyst *vis-à-vis* its initial reactants i.e., 1-Methylimidazole, (3-chloropropyl) triethoxysilane, [Sipmim]Cl ionic liquid, ferrite NPs and ferrite@SiO2NPs, we carried out a reaction in the presence of individual initial reactants. In the presence of ferrite NPs and ferrite@SiO$_2$NPs reaction did not take place. In the presence

of 1-Methylimidazole the yield was 40% and it took 4 h to complete the reaction. In the presence of (3-chloropropyl) triethoxysilane, it took 5 h to complete the reaction affording only 20% yield. [Sipmim]Cl ionic liquid catalyzed the reaction and afforded 70% yield and it took 4 h to complete the reaction while at 80 °C the reaction completed within 0.33 h affording 95% yield. [Fesipmim]Cl catalyst gave the same results. It may be concluded that [Sipmim]Cl ionic liquid also works as an efficient catalyst. The advantage of supporting it on nanoparticles provides it reusability (Table 1).

Table 3. Optimization of the amount of [Fesipmim]Cl catalyst for the formation of 4k.

Entry	Catalyst (mg)	Time (hour)	Yield (%)
1	20	7	50
2	40	5	65
3	60	4	75
4	80	3	85
5	100	0.33	95
6	120	0.33	95

3.8 *Substrate scope*

To investigate the substrate scope of the reaction, various benzaldehyde derivatives were tried. The products were obtained in excellent yield. The reaction took 20 to 120 min to complete. The reaction was found
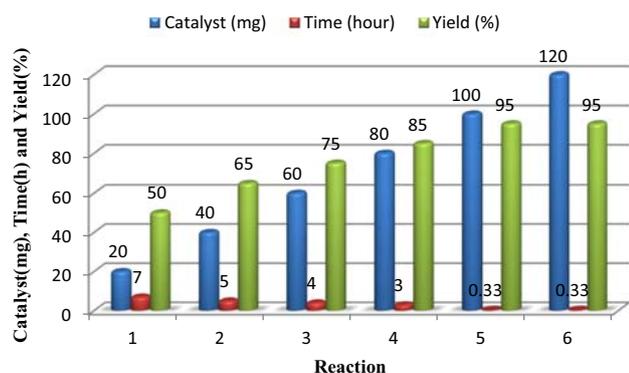
Figure 6. Optimization of catalyst amount on reaction against compound 4k.
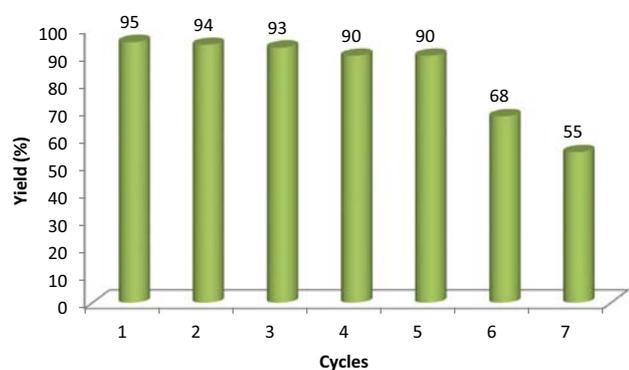

Figure 7. Recycling study of ([Fesipmim]Cl) catalyst against compound 4k.

feasible for electron-withdrawing as well as electron-donating groups on the benzene ring of benzaldehyde derivatives, and ethyl as well as methyl esters of acetoacetate ester, clearly proving wide substrate scope of the reaction catalyzed by [Fesipmim]Cl (Table 2).

3.9 *Catalyst loading*

To optimize the catalyst loading, the reaction was tried under optimum conditions of temperature for different

amounts of catalyst (Table 3, Figure 6). The results indicate that with an increase in the amount of catalyst from 20 mg to 100 mg, there is an increase in the yield from 50-95% with a decrease in time. No significant improvement in the yield of the product was observed with further increase in the catalyst amount from 100 mg to 120 mg. Hence, 100 mg of [Fesipmim]Cl catalyst was found to be the optimum amount for the representative reaction.

3.10 *Recycling study of the catalyst*

To show the reusability of [Fesipmim]Cl catalyst, the catalyst was recovered from the reaction mixture, washed with alcohol, dried at 100–110 °C for 3 h and reused up to seven cycles. There was not a significant decrease in yield up to five cycles. In the sixth cycle, the yield decreased to 68% and in the seventh cycle, the yield decreased to 55% (Figure 7). The results clearly indicate that the activity of the catalyst remains intact up to five cycles, and in subsequent cycles, the catalyst degrades and consequently loses its activity. It can be concluded that catalyst may be used efficiently up to five cycles.[7]

3.11 *Comparison of the efficiency of [Fesipmim]Cl catalyst with other reported catalysts*

To illustrate the superiority of [Fesipmim]Cl catalyst, we compared our results with the catalysts reported in the literature (Table 4). A perusal of the table reveals that time taken for the reaction carried out using catalyst [Fesipmim]Cl is least (20 min) in comparison to the methods reported in the literature. Moreover, the catalyst works well under solventless conditions and is reusable indicating the superiority of our method.

Table 4. Comparison of the efficiency of [Fesipmim]Cl catalyst with other reported catalysts.

Entry	Catalyst	Condition	Time (min)	Yield (%)	Reference
1	PPh$_3$	EtOH /Reflux	300	72	[42]
2	TMSCL/NaI	CH$_3$CN	360–480	80	[53]
3	Silica gel/NaHSO$_4$	CH$_3$CN	360	85	[38]
4	3,4,5-TrifluoroBenzene boronic Acid	ionic liquid	240	90	[54]
5	[(Fesipmim)Cl]	Solvent less	20	95	Our work

4. Conclusions

A magnetic nanoparticle supported ionic liquid catalytic system [Fesipmim]Cl has been successfully prepared. The formation of the catalyst was confirmed by FT-IR, TEM, SEM, XRD and VSM analysis. The efficiency of the [Fesipmim]Cl catalyst was validated by its successful applicability for the synthesis of different derivatives of dihydropyridine derivatives through Hantzsch reaction *via* a three-component coupling reaction of different benzaldehydes, ethyl/methyl acetoacetate and ammonium acetate. The reusability of the catalyst [Fesipmim]Cl was found intact up to five cycles. In conclusion, [Fesipmim]Cl has been developed as a green, reusable and highly efficient catalyst for the three-component synthesis of dihydropyridine derivatives affording excellent yields. The key advantages of the present environmentally benign process are reusability of catalyst, solventless condition, easy work-up and excellent yields.

Supplementary Information (SI)

Experimental and spectroscopic data are available at www. ias.ac.in/chemsci.

Acknowledgements

Compliance with ethical standards

Conflict of interest There is no conflict of interest from the authors.

References

1. Bagheri S, Muhd J N and Bee A H S 2014 Titanium dioxide as a catalyst support in heterogeneous catalysis *Sci. World J.* **2014** 727496
2. Liu R, Jin R, An J, Zhao Q, Cheng T and Liu G 2014 Hollow-shell-structured nanospheres: A recoverable heterogeneous catalyst for rhodium-catalyzed tandem reduction/lactonization of ethyl 2-acylarylcarboxylates to chiral phthalides *Chem. - An Asian J.* **9** 1388
3. Singh S B and Tandon P K 2016 Catalysis: A brief review on Nano-Catalyst *J. Energy Chem. Eng.* **2** 106
4. Chaturvedi S, Dave P and Shah N 2012 Applications of nano-catalyst in new era *J. Saudi Chem. Soc.* **16** 307
5. Nejadshafiee V and Naeimi H 2018 Molecular Ionic Liquid Supported on Mesoporous Silica Nanoparticles-Imprinted Iron Metal: A Recyclable Heterogeneous Catalyst for One-Pot, Three-Component Synthesis of a Library of Benzodiazepines *Curr. Org. Synth.* **16** 136
6. Korupolu R B, Maripi S, Madasu S B, Majji R K, Ganta R K and Chilla P N 2017 Nano nickel-cobalt ferrite catalyzed one pot synthesis of 14-Aryl-14H-dibenzo[a, j]xanthenes and 12-Aryl-8, 9, 10, 12-tetrahydrobenzo[a]xanthene-11-one derivatives *Orient. J. Chem.* **33** 122
7. Safaei-Ghomi J, Enayat-Mehri N and Eshteghal F 2018 4-(4′-Diamino-di-phenyl)-sulfone supported on hollow magnetic mesoporous Fe3O4@SiO2 NPs: As a reusable and efficient catalyst for the synthesis of ethyl 2-amino-5,10-dihydro-5,10-dioxo-4-phenyl-4H benzo[g]chromene-3-carboxylates *J. Saudi Chem. Soc.* **22** 485
8. Kumari A, Kaur B, Srivastava R and Sangwan R S 2015 Isolation and immobilization of alkaline protease on mesoporous silica and mesoporous ZSM-5 zeolite materials for improved catalytic properties *Biochem. Biophys. Rep.* **2** 108
9. Saghanezhad S J, Nazari Y and Davod F 2016 Cucurbit[6]uril-OSO3H: A novel acidic nanocatalyst for the one-pot preparation of 14-aryl-14H-dibenzo[a,j]xanthenes and 1,8-dioxo-octahydro-xanthenes *RSC Adv.* **6** 25525
10. Ferlin N, Courty M, Van Nhien A N, Gatard S, Pour M, Quilty B, Ghavre M, Haib A, Kummerer K, Gathergoog N and Bouquillon S 2013 Tetrabutylammonium prolinate-based ionic liquids: A combined asymmetric catalysis, antimicrobial toxicity and biodegradation assessment *RSC Adv.* **3** 26241
11. Litschauer M and Neouze M A 2008 Nanoparticles connected through an ionic liquid-like network *J. Mater. Chem.* **18** 640
12. Heravi M M, Zakeri M, Karimi N, Saeedi M, Oskooie H A and Tavakoli-Hosieni N 2010 Acidic ionic liquid [(CH2)4SO3HMIM] [HSO4]: A green media for the simple and straightforward synthesis of 2,4,5-trisubstituted imidazoles *Synth. Commun.* **40** 1998
13. Bonne D, Coquerel Y, Constantieux T and Rodriguez J 2010 1,3-Dicarbonyl compounds in stereoselective domino and multicomponent reactions *Tetrahedron Asymm.* **21** 1085
14. Choudhury L H and Parvin T 2011 Recent advances in the chemistry of imine-based multicomponent reactions (MCRs) *Tetrahedron* **67** 8213
15. Biggs-Houck J E, Younai A and Shaw J T 2010 Recent advances in multicomponent reactions for diversity-oriented synthesis *Curr. Opin. Chem. Biol.* **14** 371
16. Triggle D J 2007 Calcium channel antagonists: Clinical uses-Past, present and future *Biochem. Pharmacol.* **74** 1
17. Gekeler R 1995 Chemosensitizers in tumor therapy: new compounds promise better efficacy *Drugs Future* **20** 499
18. Shinde S 2002 Synthesis and anti-inflammatory activity of 1,4-dihydropyridines *Acta Pharm.* **52** 281
19. Gullapalli S and Ramarao P 2002 L-type Ca2+ channel modulation by dihydropyridines potentiates κ-opioid receptor agonist induced acute analgesia and inhibits development of tolerance in rats *Neuropharmacology* **42** 467

20. Bossert F, Meyer H and Wehinger E 1981 4-Aryldihydropyridines, a New Class of Highly Active Calcium Antagonists *Angew. Chemie Int. Ed. English* **20** 762

21. Gilpin R K and Pachla L A 1999 Pharmaceuticals and Related Drugs *Anal. Chem.* **71** 217

22. Cosconati S, Marinelli L, Lavecchia A and Novellino E 2007 Characterizing the 1,4-dihydropyridines binding interactions in the L-type Ca^{2+} channel: Model construction and docking calculations *J. Med. Chem.* **50** 1504

23. Kidwai M, Saxena S, Mohan R and Venkataramanan R 2002 A novel one pot synthesis of nitrogen containing heterocycles: An alternate methodology to the Biginelli and Hantzsch reactions *J. Chem. Soc. Perkin 1* **2** 1845

24. Anniyappan M, Muralidharan D and Perumal P T 2002 Synthesis of hantzsch 1,4-dihydropyridines under microwave irradiation *Synth. Commun.* **32** 659

25. Öhberg L and Westman J 2001 An Efficient and Fast Procedure for the Hantzsch Dihydropyridine Synthesis under Microwave Conditions *Synlett* **2001** 1296

26. Lee Y A and Kim S C 2011 Synthesis of 1,4-dihydropyridine using microwave-assisted aza-Diels-Alder reaction and its application to Amlodipine *J. Ind. Eng. Chem.* **17** 401

27. Khadilkar B M, Gaikar V G and Chitnavis A A 1995 Aqueous hydrotrope solution as a safer medium for microwave enhanced hantzsch dihydropyridine ester synthesis *Tetrahedron Lett.* **36** 8083

28. Vanden Eynde J and Mayence A 2003 Synthesis and aromatization of Hantzsch 1,4-dihydropyridines under microwave irradiation. An overview *Molecules* **8** 381

29. Yadav J S, Subba Reddy, B V and Reddy P T 2001 Unprecedented synthesis of hantzsch 1,4-dihydropyridines under biginelli reaction conditions *Synth. Commun.* **31** 425

30. Shaabani A, Rezayan A H, Rahmati A and Sharifi M 2006 Ultrasound-accelerated synthesis of 1,4-dihydropyridines in an ionic liquid *Monatsh. Chem.* **137** 77

31. Mekheimer R A, Hameed A A and Sadek K U 2008 Solar thermochemical reactions: Four-component synthesis of polyhydroquinoline derivatives induced by solar thermal energy *Green Chem.* **10** 592

32. Legeay J C, Vanden Eynde J J and Bazureau J P 2005 Ionic liquid phase technology supported the three component synthesis of Hantzsch 1,4-dihydropyridines and Biginelli 3,4-dihydropyrimidin-2(1H)-ones under microwave dielectric heating *Tetrahedron* **61** 12386

33. Yadav J S, Reddy B V S, Basak A K and Narsaiah A V 2003 Three-component coupling reactions in ionic liquids: An improved protocol for the synthesis of 1,4-dihydropyridines *Green Chem.* **5** 60

34. Jin T S, Zhang J S, Xiao J C, Wang A Q and Li T S 2004 Clean Synthesis of 1,8-Dioxo-octahydroxanthene Derivatives Catalyzed by *p*-Dodecylbenezenesulfonic Acid in Aqueous Media *Synlett.* **2004** 0866

35. Zonouz, A M and Sahranavard N 2010 Synthesis of 1,4-Dihydropyridine Derivatives Under Aqueous Media *E-Journal Chem.* **7** 372

36. Tamaddon F, Razmi Z and Jafari A A 2010 Synthesis of 3,4-dihydropyrimidin-2(1H)-ones and 1,4-dihydropyridines using ammonium carbonate in water *Tetrahedron Lett.* **51** 1187

37. Evdokimov N M, Magedov I V, Kireev A S and Kornienko A 2006 One-Step, Three-Component Synthesis of Pyridines and 1,4-Dihydropyridines with Manifold Medicinal Utility *Org. Lett.* **8** 899

38. Adharvana C M and Syamasundar K 2005 Silica gel/$NaHSO_4$ catalyzed one-pot synthesis of Hantzsch 1,4-dihydropyridines at ambient temperature *Catal. Commun.* **6** 624

39. Gordeev M F, Patel D V and Gordon E M 1996 Approaches to combinatorial synthesis of heterocycles: A solid-phase synthesis of 1,4-dihydropyridines *J. Org. Chem.* **61** 924

40. Ghosh S, Saikh F, Das J and Pramanik A K 2013 Hantzsch 1,4-dihydropyridine synthesis in aqueous ethanol by visible light *Tetrahedron Lett.* **54** 58

41. Tamaddon F and Moradi S 2013 Controllable selectivity in Biginelli and Hantzsch reactions using nanoZnO as a structure base catalyst *J. Mol. Catal. A Chem.* **370** 117

42. Debache A, Ghalem W, Boulcina R, Belfaitah A, Rhouati S and Carboni B 2009 An efficient one-step synthesis of 1,4-dihydropyridines via a triphenylphosphine-catalyzed three-component Hantzsch reaction under mild conditions *Tetrahedron Lett.* **50** 5248

43. Debache A, Boulcina R, Belfaitah A, Rhouati S and Carboni B 2008 One-pot synthesis of 1,4-dihydropyridines via a phenylboronic acid catalyzed Hantzsch three-component reaction *Synlett.* **2008** 509

44. Ko S, Sastry M N V, Lin C and Yao C F 2005 Molecular iodine-catalyzed one-pot synthesis of 4-substituted-1,4- dihydropyridine derivatives via Hantzsch reaction *Tetrahedron Lett.* **46** 5771

45. Ko S and Yao C F 2006 Ceric Ammonium Nitrate (CAN) catalyzes the one-pot synthesis of polyhydroquinoline via the Hantzsch reaction *Tetrahedron* **62** 7292

46. Tewari N, Dwivedi N and Tripathi R P 2004 Tetrabutylammonium hydrogen sulfate catalyzed eco-friendly and efficient synthesis of glycosyl 1,4-dihydropyridines *Tetrahedron Lett.* **45** 9011

47. Lee J H 2005 Synthesis of Hantsch 1,4-dihydropyridines by fermenting bakers' yeast *Tetrahedron Lett.* **46** 7329

48. Kumar A and Maurya R A 2007 Synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction using organocatalysts *Tetrahedron* **63** 1946

49. Wang L M, Sheng J, Zhang L, Han J W, Fan Z Y, Tian H and Chan T Q 2005 Facile $Yb(OTf)_3$ promoted one-pot synthesis of polyhydroquinoline derivatives through Hantzsch reaction *Tetrahedron* **61** 1539

50. Azgomi N and Mokhtary M 2015 Nano-$Fe_3O_4@SiO_2$ supported ionic liquid as an efficient catalyst for the synthesis of 1,3-thiazolidin-4-ones under solvent-free conditions *J. Mol. Catal. A Chem.* **398** 58

51. Deng M, Zhao H, Zhang S, Tian C, Zhang D, Du P, Liu C, Cao H and Li H 1970 High catalytic activity of immobilized laccase on core–shell magnetic nanoparticles by dopamine self-polymerization *J. Mol. Catal. B Enzym.* **112** 15

52. Wang Y, Zhu Q and Tao L 2011 Fabrication and growth mechanism of hierarchical porous Fe3O4 hollow submicrospheres and their magnetic properties *CrystEngComm* **13** 4652

53. Sabitha G, Reddy G S K K, Reddy C S and Yadav J S 2003 A novel TMSI-mediated synthesis of Hantzsch

1,4-dihydropyridines at ambient temperature *Tetrahedron Lett.* **44** 4129

54. Sridhar R and Perumal P T 2005 A new protocol to synthesize 1,4-dihydropyridines by using 3,4,5-trifluorobenzeneboronic acid as a catalyst in ionic liquid: Synthesis of novel 4-(3-carboxyl-1H-pyrazol-4-yl)-1,4-dihydropyridines *Tetrahedron* **61** 2465