

Efficient one-pot four-component synthesis of 1,4-dihydropyridines promoted by magnetite/chitosan as a magnetically recyclable heterogeneous nanocatalyst

Ali Maleki · Maryam Kamalzare · Morteza Aghaei

Received: 6 October 2014 / Accepted: 28 November 2014 / Published online: 10 December 2014
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Abstract 1,4-Dihydropyridines are synthesized from various aromatic aldehyde, dimedone or 1,3-cyclohexandione, ethyl acetoacetate or methyl acetoacetate and ammonium acetate catalyzed by magnetite/chitosan at room temperature under mild reaction conditions. This process offers an easy and efficient synthesis of 1,4-dihydropyridine derivatives in high yields. The benefits of this protocol are simplicity, nontoxicity, low cost, simple work-up, and an environmentally benign nature. The catalyst is recovered by filtration and reused at least five times without significant loss in catalytic activity.

Keywords Nanocatalyst · Multicomponent reactions · Chitosan · Fe₃O₄ · 1,4-dihydropyridine · Heterogeneous

Introduction

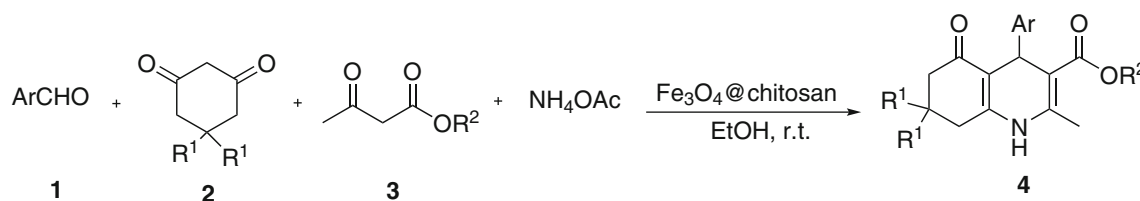
In recent years, applying heterogeneous catalysts in organic synthesis is become popular because they are removable from the reaction media by simple filtration and reusable. In addition, to achieve high activity in heterogeneous catalysts, composite nanoparticles are the logical strategy because of a large surface to volume ratio, thus increasing catalytic activity. Furthermore, magnetic nanoparticles, especially supported magnetic nanocatalysts, have attracted considerable interest in both academic and industrial researches because they are viable alternatives to conventional materials, readily available, simple separation by an

external magnet and high degree of chemical stability in various organic and inorganic solvents [1–10].

Dihydropyridines are privileged heterocyclic ring systems because of their broad and significant pharmacological properties and they are also analogues of NADH coenzymes. 1,4-Dihydropyridine derivatives have applications as calcium channel blockers for the treatment of cardiovascular diseases including hypertension. They are also used as antidiabetic agents, anti-tumor, geroprotective, anti-therosclerotic, and bronchodilator [11–14]. The first molecules of 1,4-dihydropyridines were reported by Hantzsch in 1882. It is a one-pot four component synthesis of 1,4-dihydropyridine by two molecules of ethyl acetoacetate, aldehyde and ammonia. This procedure does not need any additives and the reaction was done either at reflux in alcohol or in acetic acid; furthermore, the reaction suffer from long reaction times and low-yields of products [15]. Due to significance of dihydropyridine derivatives in the synthesis of various class of drugs several synthesis procedures have been presented such as use of microwaves [16, 17], high temperature at reflux [18–22], ionic liquid [23], SiO₂/HClO₄ [24], SiO₂/NaHSO₄ [25], I₂ [26], Bakers' yeast [27], metal triflates [28], tetrabutylammonium hydrogen sulfate [29], organocatalysts [30], PTSA [31], iron trifluoroacetate [32], TMSCl [33] and Ni nanoparticles [34].

Some of the above-mentioned methods for the synthesis of 1,4-dihydropyridine derivatives have one or more negative points such as expensive reagents, tedious work-up, moisture sensitive, toxic and harsh reaction conditions, thus developing an efficient protocol with a powerful catalyst for the synthesis of 1,4-dihydropyridine is still of prime importance. On the other hand, catalysis is a key part of green chemistry, and one of the fundamental needed challenges facing chemists now is to design and apply of

A. Maleki (✉) · M. Kamalzare · M. Aghaei
Catalysts and Organic Synthesis Research Laboratory,
Department of Chemistry, Iran University of Science and
Technology, 16846-13114 Tehran, Iran
e-mail: maleki@iust.ac.ir



Scheme 1 One-pot four-component reaction synthesis of 1,4-dihydropyridine derivatives **4a–4ai**

eco-friendly catalysts [35–38]. A stable and green catalyst is defined as low preparation cost, high activity, great selectivity, high stability, efficient recovery, and good recyclability [39].

In continuation of our recent works to applying heterogeneous nanocatalysts in organic synthesis [40–44], herein, we wish to report Fe_3O_4 @chitosan as a green heterogeneous catalyst for the synthesis of 1,4-dihydropyridine derivatives **4a–4ai** via a one-pot four-component Hantzsch condensation reaction using various aromatic aldehyde (1) 5,5-dimethyl-1,3-cyclohexanedione (dimedone) or 1,3-cyclohexanedione (2) ethyl acetoacetate or methyl acetoacetate (3) and ammonium acetate in ethanol in good to excellent yields at room temperature (Scheme 1). The main advantages of this protocol are using ethanol as a green solvent, inexpensive catalyst and easy preparation, mild reaction conditions, high yields, easy work-up, simple filtration and ability of reusing catalyst.

Experimental

General

All solvents, chemicals and reagents were purchased from Merck, Fluka and Aldrich. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. The scanning electron microscopy (SEM) images were obtained on a Seron AIS 2100. Fourier transform infrared (FT-IR) spectra were recorded using Perkin-Elmer spectrometer; using pellets of the nanomaterials diluted with KBr. The ^1H NMR spectra were recorded on Bruker DRX-300 Avance spectrometer at 300.13 MHz. The elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL.

Preparation of Fe_3O_4 @chitosan nanocomposite

First, 1 g of chitosan powder was added into a 100 mL of 0.1 M acetic acid and the mixture was stirred to form a 1 % (w/v) clear chitosan solution. Then, the homogeneous solution was filtered through a synthetic cloth to remove any undissolved materials and degassed by keeping the

solution into vacuum oven for 3 h to remove the trapped air bubbles. After that, 2 mL of glycolic acid and calculated amount of Fe_3O_4 nanoparticles [black powder, average particle size 30 nm (TEM), purity 99 % and specific surface area 55 m^2/g] were dispersed in the chitosan solution by stirring at room temperature and then it was sonicated for 1 h. The resulting solution was stirred overnight at room temperature. After that, the resulted gel separated from the reaction mixture by a permanent magnet, washed several times with EtOH, and dried on a ceramic plate at room temperature during 48 h to obtain the chitosan-supported magnetite nanoparticles.

Synthesis of dihydropyridine derivatives

A mixture of an aldehyde (1.0 mmol), dimedone or 1,3-cyclohexanedione (1.0 mmol), ethyl acetoacetate or methyl acetoacetate (1.0 mmol) and ammonium acetate (1.0 mmol) in 5 mL of EtOH was stirred at room temperature in the presence of a catalytic amount of Fe_3O_4 @chitosan (0.03 g) for the appropriate times to obtain dihydropyridines derivatives. After completion of the reaction, as indicated by thin layer chromatography (TLC)

Table 1 Optimization of the reaction conditions in the model reaction

Entry	Catalyst	Amount of catalyst (g)	Solvent	Time (min)	Yield ^a (%)
1	Fe_3O_4 @chitosan	0.01	EtOH	180	Trace
2	Fe_3O_4 @chitosan	0.02	EtOH	120	51
3	Fe_3O_4 @chitosan	0.03	EtOH	70	90
4	Fe_3O_4 @chitosan	0.04	EtOH	70	90
5	Fe_3O_4 @chitosan	0.03	MeOH	70	74
6	Fe_3O_4 @chitosan	0.03	EtOAc	75	79
7	Fe_3O_4 @chitosan	0.03	CH_2Cl_2	70	82
8	Fe_3O_4 @chitosan	0.03	CH_3CN	70	87
9	Fe_3O_4 @chitosan	0.03	<i>n</i> -hexane	140	Trace
10	Fe_3O_4	0.03	EtOH	120	Trace
11	chitosan	0.03	EtOH	120	Trace
12	–	–	EtOH	150	Trace

^a Isolated yield

Table 2 Synthesis of dihydropyridine derivatives **4a–4ai** in the presence of Fe₃O₄@chitosan

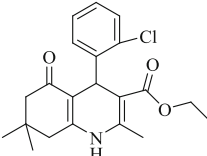
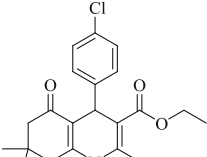
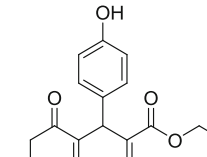
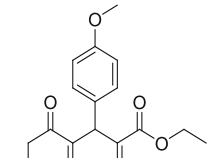
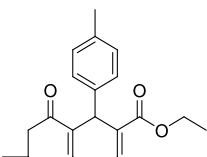
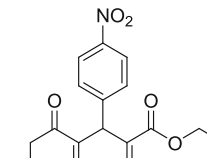
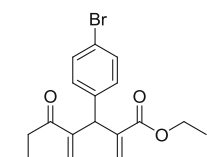
Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
1	 4a	60	95	207–209	207–209 [45]
2	 4b	70	90	242–244	243–245 [46]
3	 4c	75	88	235–236	234–236 [47]
4	 4d	80	92	258–260	258–260 [48]
5	 4e	85	93.5	257–259	258–259 [49]
6	 4f	40	93	255	247–249 [47]
7	 4g	50	87	257–258	255–257 [46]

Table 2 continued

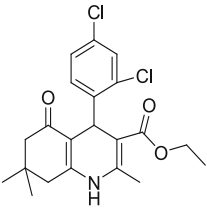
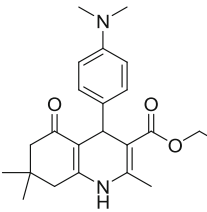
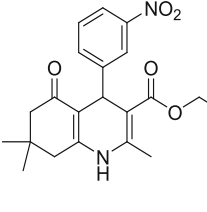
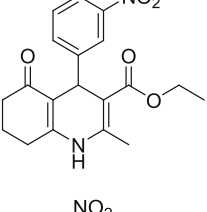
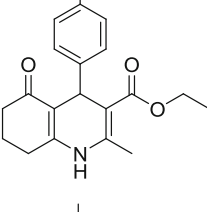
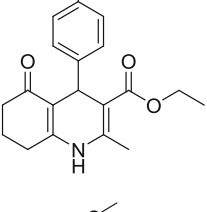
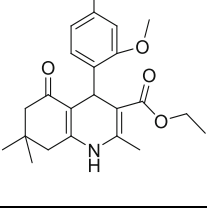
Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
8	 4h	30	90	245–246	243–245 [50]
9	 4i	130	93	233–235	233–235 [45]
10	 4j	50	92.5	175–176	174–176 [34]
11	 4k	60	95	212–214	204–206 [51]
12	 4l	55	89	196–198	201–203 [49]
13	 4m	90	91	245–248	244–246 [52]
14	 4n	54	90.5	235–237	237–238 [23]



Table 2 continued

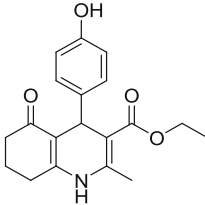
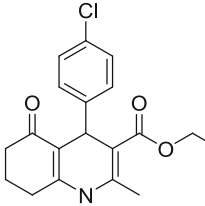
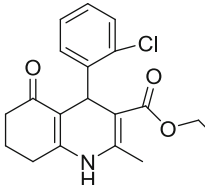
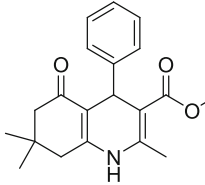
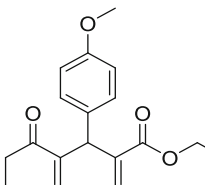
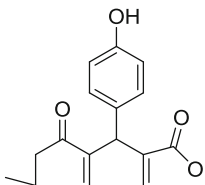
Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
15	 4o	90	92	249–250	252 [53]
16	 4p	75	95	236	235–237 [54]
17	 4q	70	90	236–237	236.6–237 [55]
18	 4r	140	84	186–188	188–189 [56]
19	 4s	90	92	189–191	193–195 [26]
20	 4t	78	96	293	288–290 [53]

Table 2 continued

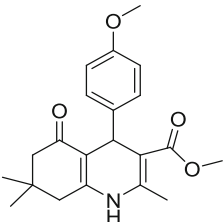
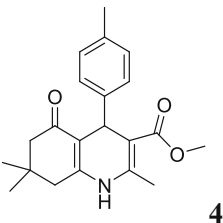
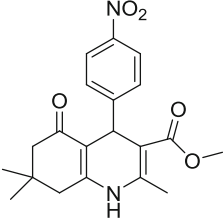
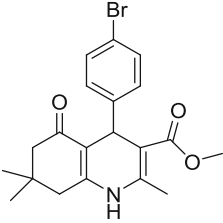
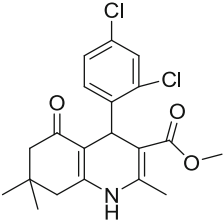
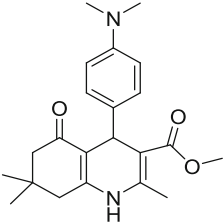
Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
21	 4u	82	96	256–258	257–259 [47]
22	 4v	87	97	272–273	271–273 [56]
23	 4w	43	87	254–256	252–254 [57]
24	 4x	76	89	263–265	263–264 [58]
25	 4y	33	91	248–250	250–252 [57]
26	 4z	135	86	256–258	258 [59]



Table 2 continued

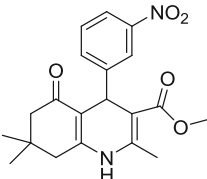
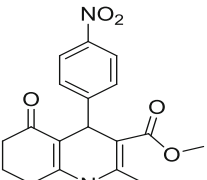
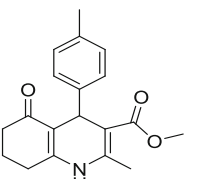
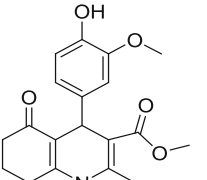
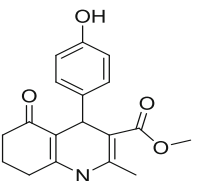
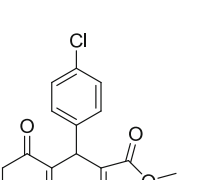
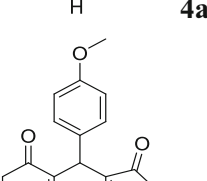
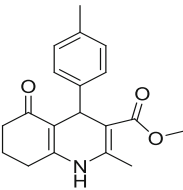
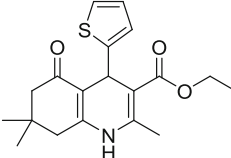
Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
27	 4aa	55	91	221–223	223–224 [57]
28	 4ab	58	87	215–217	219–221 [55]
29	 4ac	89	97	233–234	238–240 [57]
30	 4ad	85	98	250–252	248–251 [53]
31	 4ae	80	96	250–252	256–257 [53]
32	 4af	73	91	216	221–223 [52]
33	 4ag	85	86	208–211	208–211 [52]

Table 2 continued

Entry	Product	Time (min)	Yield (%) ^a	Mp (°C)	
				Observed	Reported
34		91	97	237–239	238–240 [57]
35		85	93	222–224	223–225 [45]

^a Isolated yield

(*n*-hexane/ethyl acetate 3/1), the catalyst was separated magnetically from the reaction mixture, washed with ethanol, and used for subsequent reactions after drying. Pure dihydropyridines **4a–4ai** was afforded by evaporation of the solvent, followed by recrystallization from EtOH.

Spectral data of the product **4ai**

IR (KBr) (ν_{\max} cm^{-1}) = 3,274, 3,207, 2,960, 1,701, 1,647, 1,604, 1,492, 1,379, 1,215, 1,072. ¹H NMR (300 MHz, CDCl₃): δ_{H} (ppm) = 1.04 (s, 3H, CH₃), 1.10 (s, 3H, CH₃), 1.27 (t, 3H, *J* = 7.1 Hz, CH₃), 2.22–2.34 (m, 4H, 2CH₂), 2.38 (s, 3H, CH₃), 4.16 (q, 2H, *J* = 7.1 Hz, OCH₂), 5.42 (s, 1H, CH), 6.19 (br s, 1H, NH), 6.84 (d, 2H, *J* = 1.8 Hz, H-Ar), 7.03 (t, 1H, *J* = 2.1 Hz, H-Ar). Anal. Calcd for C₁₉H₂₃NO₃S: C, 66.06; H, 6.71; N, 4.05. Found: C, 67.11; H, 6.63; N, 3.94.

Results and discussion

The Fe₃O₄@chitosan nanocatalyst was first prepared by a sol–gel method modified in our previous reports [42]. Then, it was characterized by SEM analysis. The particle size was studied by SEM and the identification of Fe₃O₄@chitosan morphology was based on the analysis of SEM images. The obtained SEM images of nanoparticles clearly showed that Fe₃O₄ nanoparticles were properly supported on chitosan.

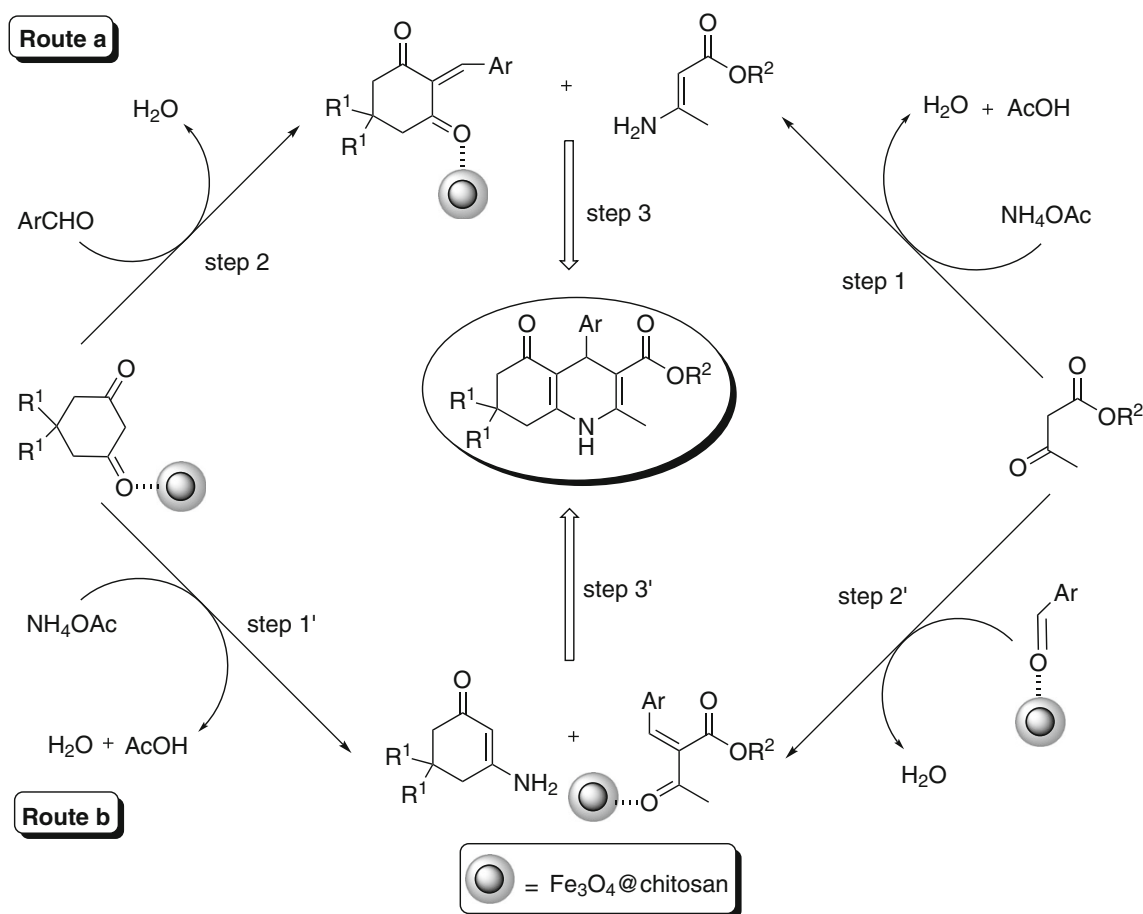
To optimize the reaction conditions, we checked the four-component condensation reaction of dimedone (1 mmol), ethyl acetoacetate (1 mmol), 4-chlorobenzaldehyde (1 mmol) and ammonium acetate (1 mmol) in the presence of different catalytic amounts of Fe₃O₄@chitosan

at room temperature in 5 mL of EtOH, as a model reaction. It was found that 0.03 g of catalyst was enough to catalyze the reaction to produce high yields of dihydropyridines derivatives. As shown in Table 1 (Entries 1–4), using 0.03 g of the catalyst was enough to progress the reaction and an increment of the catalyst amount did not improve the yields. In the second stage the effect of solvent was studied. As can be seen from Table 1 (Entries 5–9), it was found that EtOH is the best solvent for this reaction to produce high yields in short reaction time in comparison with other polar, non-polar, protic and aprotic solvents.

To study the generality of this method, different types of starting material were reacted in the synthesis of 1,4-dihydropyridines. As illustrated in Table 2, aromatic aldehyde with both electron withdrawing groups and electron donating groups react well to give the products in good to excellent yields. As it predicted starting from aldehyde with electron withdrawing groups (such as nitro group) the condensation reaction occurs in the lower time in comparison with electron donating groups (such as alkoxy group).

As shown in Scheme 2, the proposed mechanism of this reaction could be in two forms. In step 2 and 2' which are Knoevenagel reaction involves coupling of aldehyde with active methylene compound. Furthermore, in step 3 and 3' a Michael addition of intermediates gives the target products.

In addition, the reusability of this heterogeneous nanocatalyst is one of its important plus point and also this potency leads us to use it in commercial and industrial applications. One of the natural ability of this heterogeneous catalyst that makes it special is easy separation from the reaction media by an external magnetic bar. By washing with acetone or ethanol and drying it at room



Scheme 2 Two proposed mechanistic routes of the reaction

Table 3 Reusability studies of the nanocatalyst on the model reaction

Run	Fresh	1	2	3	4	5
Isolated yield (%)	90	90	90	89	89	87

temperature it can be reused several times. As indicated in Table 3, the reusability of the present composite nanocatalyst is examined in the model reaction.

Conclusion

In summary, Fe₃O₄@chitosan was prepared and used as a green, magnetically recyclable and efficient composite nanocatalyst for the synthesis of chemically and biologically important dihydropyridine derivatives by a simple, clean, eco-friendly and inexpensive method. This protocol can be applied in large-scale and industrial synthesis of heterocyclic compounds, because it can be simple recovered and reused several times without significant decreasing in its catalytic activity.

Acknowledgments The authors gratefully acknowledge the partial support from the Research Council of the Iran University of Science and Technology.

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References

- Gawande, M.B., Luque, R., Zboril, R.: The rise of magnetically recyclable nanocatalysts. *Chem. Soc. Rev.* **42**, 3371–3393 (2013)
- Gawande, M.B., Branco, P.S., Varma, R.S.: Nano-magnetite (Fe₃O₄) as a support for recyclable catalysts in the development of sustainable methodologies. *Chem. Soc. Rev.* **42**, 3371–3393 (2013)
- Wang, D., Astruc, D.: Fast-growing field of magnetically recyclable nanocatalysts. *Chem. Rev.* **114**, 6949–6985 (2014)
- Kainz, Q.M., Linhardt, R., Grass, R.N.: Palladium nanoparticles supported on magnetic carbon-coated cobalt nanobeads: highly active and recyclable catalysts for alkene hydrogenation. *Adv. Funct. Mater.* **24**, 2020–2027 (2014)
- Shelke, S.N., Bankar, S.R., Mhaske, G.R., Kadam, S.S., Murade, D.K.: Iron oxide-supported copper oxide nanoparticles (Nanocat-Fe-CuO): magnetically recyclable catalysts for the synthesis of



- pyrazole derivatives, 4-methoxyaniline, and Ullmann-type condensation reactions. *ACS Sustain. Catal. Eng.* **2**, 1699–1706 (2014)
- Sá, S., Gawande, M.B., Velhinho, A., Veiga, J.P., Bundaleski, N.: Magnetically recyclable magnetite–palladium (Nanocat-Fe–Pd) nanocatalyst for the Buchwald–Hartwig reaction. *Green Chem.* **16**, 3494–3500 (2014)
 - Gawande, M.B., Rathi, I., Nogueira, D.: Magnetite-supported sulfonic acid: a retrievable nanocatalyst for the Ritter reaction and multicomponent reactions. *Green Chem.* **15**, 1895–1899 (2013)
 - Shokouhimehr, M., Piao, Y., Kim, J., Jang, Y., Hyeon, T.: A magnetically recyclable nanocomposite catalyst for olefin epoxidation. *Angew. Chem. Int. Ed.* **46**, 7039–7043 (2007)
 - Shirini, F., Abedini, M.: Application of nanocatalysts in multicomponent reactions. *J. Nanosci. Nanotechnol.* **13**, 4838–4860 (2013)
 - Montazeri, H., Amani, A., Shahverdi, H.R., Haratifar, E., Shahverdi, A.R.: Separation of the defect-free Fe₃O₄–Au core/shell fraction from magnetite-gold composite nanoparticles by an acid wash treatment. *J. Nanostruct Chem.* **3**, 25–28 (2013)
 - Sausins, A., Duburs, G.: Synthesis of 1,4-dihydropyridines by cyclocondensation reactions. *Heterocycles* **27**, 269–289 (1988)
 - Gaudio, A.C., Korokovas, A., Takahata, Y.: Quantitative structure-activity relationships for 1,4-dihydropyridine calcium channel antagonists (nifedipine analogues): a quantum chemical/classical approach. *J. Pharm. Sci.* **83**, 1110–1115 (1994)
 - Mager, P.P., Coburn, R.A., Solo, A.J., Triggler, D.J., Rothe, H.: QSAR, diagnostic statistics and molecular modelling of 1,4-dihydropyridine calcium antagonists: a difficult road ahead. *Drug Des. Disc.* **8**, 273–289 (1992)
 - Gordeev, M.F., Patel, D.V., Gordon, E.M.: Approaches to combinatorial synthesis of heterocycles: a solid-phase synthesis of 1,4-dihydropyridines. *J. Org. Chem.* **61**, 924–982 (1996)
 - Hantzsch, A.: Ueber die synthese pyridinartiger verbindungen aus acetessigäther und aldehyd ammoniak. *Justus Liebigs Ann. Chem.* **215**, 1–82 (1882)
 - Agarwal, A., Chauhan, P.M.S.: Solid supported synthesis of structurally diverse dihydropyrido[2,3-d]pyrimidines using microwave irradiation. *Tetrahedron Lett.* **46**, 1345–1348 (2005)
 - Ohberg, L., Westman, J.: An efficient and fast procedure for the Hantzsch dihydropyridine synthesis under microwave conditions. *Synlett* **8**, 1296–1298 (2001)
 - Breitenbucher, J.G., Figliozzi, G.: Solid-phase synthesis of 4-aryl-1,4-dihydropyridines via the Hantzsch three component condensation. *Tetrahedron Lett.* **41**, 4311–4315 (2000)
 - Liang, J.C., Yeh, J.L., Wang, C.S., Liou, S.F., Tasi, C.H., Chen, I.: Heterocyclic bibenzimidazole derivatives as topoisomerase I inhibitors. *J. Bioorg. Med. Chem. Lett.* **10**, 719–723 (2002)
 - Miri, R., Niknahad, H., Vesal, G., Shafiee, A.: Synthesis and calcium channel antagonist activities of 3-nitrooxyalkyl, 5-alkyl 1,4-dihydro-2,6-dimethyl-4-(1-methyl-5-nitro-2-imidazolyl)-3,5-pyridinedicarboxylates. *IL Farmaco* **57**, 123–128 (2002)
 - Dondoni, A., Massi, A., Minghini, E., Sabbatini, S., Bertoasi, V.: Model studies toward the synthesis of dihydropyrimidinyl and pyridyl α -amino acids via three-component biginelli and Hantzsch cyclocondensations. *J. Org. Chem.* **68**, 6172–6183 (2003)
 - Dondoni, A., Massi, A., Minghini, E., Bertoasi, V.: Multicomponent Hantzsch cyclocondensation as a route to highly functionalized 2- and 4-dihydropyridylalanines, 2- and 4-pyridylalanines, and their n-oxides: preparation via a polymer-assisted solution-phase approach. *Tetrahedron* **60**, 2311–2326 (2004)
 - Ji, S.J., Jiang, Z.Q., Lu, J., Loh, T.P.: Facile ionic liquids-promoted one-pot synthesis of polyhydroquinoline derivatives under solvent free conditions. *Synlett* **5**, 831–832 (2004)
 - Maheswara, M., Siddaiah, V., Damu, G.L., VenkataRao, C.: An efficient one-pot synthesis of polyhydroquinoline derivatives via Hantzsch condensation using heterogeneous catalyst under solvent-free conditions. *Arkivoc* **2**, 201–206 (2006)
 - Chari, M.A., Syamasundar, K.: Silica gel/NaHSO₄ catalyzed one-pot synthesis of Hantzsch 1,4-dihydropyridines at ambient temperature. *Catal. Commun.* **6**, 624–626 (2005)
 - Ko, S., Sastry, M.N.V., Lin, C., Yao, C.F.: Molecular iodine-catalyzed one-pot synthesis of 4-substituted-1,4-dihydropyridine derivatives via Hantzsch reaction. *Tetrahedron Lett.* **46**, 5771 (2005)
 - Kumar, A., Maurya, R.A.: Bakers’ yeast catalyzed synthesis of polyhydroquinoline derivatives via an unsymmetrical Hantzsch reaction. *Tetrahedron Lett.* **48**, 3887–3890 (2007)
 - Wang, L.M., Sheng, J., Zhang, L., Han, J.W., Fan, Z., Tian, H., Qian, C.T.: Facile Yb(OTf)₃ promoted one-pot synthesis of polyhydroquinoline derivatives through Hantzsch reaction. *Tetrahedron* **61**, 1539–1543 (2005)
 - Tewari, N., Dwivedi, N., Tripathi, R.P.: Tetrabutylammonium hydrogen sulfate catalyzed eco-friendly and efficient synthesis of glycosyl 1,4-dihydropyridines. *Tetrahedron Lett.* **45**, 9011–9014 (2004)
 - Kumar, A., Maurya, R.A.: Synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction using organocatalysts. *Tetrahedron* **63**, 1946–1952 (2007)
 - Cherkupally, S.R., Mekalan, R.: PTSA catalyzed facile and efficient synthesis of polyhydroquinoline derivatives through Hantzsch multi-component condensation. *Chem. Pharm. Bull.* **56**, 1002–1004 (2008)
 - Adibi, H., Samimi, H.A., Beygzadeh, M.: Iron(III) trifluoroacetate and trifluoromethanesulfonate: recyclable Lewis acid catalysts for one-pot synthesis of 3,4-dihydropyrimidinones or their sulfur analogues and 1,4-dihydropyridines via solvent-free Biginelli and Hantzsch condensation protocols. *Catal. Commun.* **8**, 2119–2124 (2007)
 - Sabitha, G., Reddy, G.S.K., Reddy, C.S., Yadav, J.S.: A novel TMSI-mediated synthesis of Hantzsch 1,4-dihydropyridines at ambient temperature. *Tetrahedron Lett.* **44**, 4129–4131 (2003)
 - Sapkal, S.B., Shelke, K.F., Shingate, B.B., Shingare, M.S.: Nickel nanoparticle-catalyzed facile and efficient one-pot synthesis of polyhydroquinoline derivatives via Hantzsch condensation under solvent-free conditions. *Tetrahedron Lett.* **50**, 1754–1756 (2009)
 - Sheldon, R.A.: Fundamentals of green chemistry: efficiency in reaction design. *Chem. Soc. Rev.* **41**, 1437–1451 (2012)
 - Walsh, P.T., Li, H., De Parrodi, C.A.: A green chemistry approach to asymmetric catalysis: solvent-free and highly concentrated reactions. *Chem. Rev.* **107**, 2503–2545 (2007)
 - NasirBaig, R.B., Varma, R.S.: Stereo- and regio-selective one-pot synthesis of triazole-based unnatural amino acids and β -amino triazoles. *Chem. Commun.* **48**, 5853–5855 (2012)
 - NasirBaig, R.B., Varma, R.S.: Alternative energy input: mechanochemical, microwave and ultrasound-assisted organic synthesis. *Chem. Soc. Rev.* **41**, 1559–1584 (2012)
 - Gawande, S.B., Branco, P.S., Varma, R.S.: Nanocatalysis and prospects of green chemistry. *Chem. Sus. Chem.* **5**, 65–68 (2012)
 - Maleki, A.: Fe₃O₄/SiO₂ nanoparticles: an efficient and magnetically recoverable nanocatalyst for the one-pot multicomponent synthesis of diazepines. *Tetrahedron* **68**, 7827–7829 (2012)
 - Maleki, A.: One-pot multicomponent synthesis of diazepine derivatives using terminal alkynes in the presence of silica-supported superparamagnetic iron oxide nanoparticles. *Tetrahedron Lett.* **54**, 2055–2059 (2013)
 - Maleki, A., Ghamari, N., Kamalzare, M.: Chitosan-supported Fe₃O₄ nanoparticles: a magnetically recyclable heterogeneous nanocatalyst for the syntheses of multifunctional benzimidazoles and benzodiazepines. *RSC Adv.* **4**, 9416–9423 (2014)

43. Maleki, A., Kamalzare, M.: Fe₃O₄@cellulose composite nano-catalyst: preparation, characterization and application in the synthesis of benzodiazepines. *Catal. Commun.* **53**, 67–71 (2014)
44. Maleki, A., Rahimi, R., Maleki, S., Hamidi, N.: Synthesis and characterization of magnetic bromochromate hybrid nanomaterials with triphenylphosphine surface-modified iron oxide nanoparticles and their catalytic application in multicomponent reactions. *RSC Adv.* **4**, 29765–29771 (2014)
45. Tajbakhsh, M., Alinezhad, H., Norouzi, M., Akbari, M., Bagheri, S.: Proticpyridinium ionic liquid as a green and highly efficient catalyst for the synthesis of polyhydroquinoline derivatives via Hantzsch condensation in water. *J. Mol. Liq.* **177**, 44–48 (2013)
46. Song, S.J.J., Shan, Z.X., Jin, Y.: One-pot synthesis of hexahydroquinolines via Hantzsch four-component reaction catalyzed by a cheap amino alcohol. *Synth. Commun.* **40**, 3067–3077 (2010)
47. Zare, A., Abi, F., Moosavi-Zare, A.R., Beyzavi, M.H., Zolfigol, M.A.: Synthesis, characterization and application of ionic liquid 1,3-disulfonic acid imidazolium hydrogen sulfate as an efficient catalyst for the preparation of hexahydroquinolines. *J. Mol. Liq.* **178**, 113–121 (2013)
48. Safari, J., Banitaba, S.H., Khalili, S.H.: Cobalt nanoparticles promoted highly efficient one pot four-component synthesis of 1,4-dihydropyridines under solvent-free conditions. *Chin. J. Catal.* **32**, 1850–1855 (2011)
49. Heravi, M., Saeedi, M., Karimi, N., Zakeri, M., Beheshtiha, Y.S., Davoodnia, A.: Brønsted acid ionic liquid [(CH₂)₄SO₃HMIM][HSO₄] as novel catalyst for one-pot synthesis of Hantzsch polyhydroquinoline derivatives. *Synth. Commun.* **40**, 523–529 (2010)
50. Singh, S.K., Singh, K.N.: Glycine-catalyzed easy and efficient one-pot synthesis of polyhydroquinolines through Hantzsch multicomponent condensation under controlled microwave. *J. Heterocycl. Chem.* **47**, 194–198 (2010)
51. Surasani, R., Kalita, D., Rao, A.V.D., Yarbagi, K., Chandrasekhar, K.B.: FeF₃ as a novel catalyst for the synthesis of polyhydroquinoline derivatives via unsymmetrical Hantzsch reaction. *J. Fluor. Chem.* **135**, 91–96 (2012)
52. Peng, H.N., Zheng, D.G., Peng, X.M.: *p*-Toluene sulfonic acid catalyzed one-pot synthesis of unsymmetrical 1,4-dihydropyridines derivatives via Hantzsch reaction. *Asian J. Chem.* **23**, 1833–1837 (2011)
53. Yang, X.H., Zhou, Y.H., Liu, C.H.G., Lin, X.Y., Cui, J.F., Zhang, P.H.: Synthesis and antioxidant evaluation of novel 4-aryl-hexahydroquinolines from lignin. *Arkivoc* **10**, 327–329 (2011)
54. Hong, M., Cai, C.H., Yi, W.B.: Hafnium (IV) bis(perfluorooctanesulfonyl)imide complex catalyzed synthesis of polyhydroquinoline derivatives via unsymmetrical Hantzsch reaction in fluorosulfuric acid medium. *J. Fluorine Chem.* **131**, 111–114 (2010)
55. Li, J., He, P., Yu, Ch.: DPTA-catalyzed one-pot regioselective synthesis of polysubstituted pyridines and 1,4-dihydropyridines. *Tetrahedron* **68**, 4138–4144 (2012)
56. Mohammadi, A., Hadadzahmatkesh, A., Asghariganjeh, M.R.: FeNH₄(SO₄)₂·12H₂O (alum)-catalyzed preparation of 1,4-dihydropyridines: improved conditions for the Hantzsch reaction. *Monatsh. Chem.* **143**, 931–933 (2012)
57. Qin, X.Y., Jin, T.S., Zhou, Z.X., Li, T.S.H.: Silica sulfuric acid: an efficient and versatile catalyst for one-pot synthesis of substituted 5-oxo-1,4,5,6,7,8-hexahydroquinoline derivatives. *Asian J. Chem.* **22**, 1179–1182 (2010)
58. Nasr-Esfahani, M., Abdizadeh, T.: Vanadatesulfuric acid-catalyzed novel and eco-benign one-pot synthesis of polyhydroquinoline derivatives under solvent-free conditions. *Orient. J. Chem.* **28**, 1249–1258 (2012)
59. Sainani, J.B., Shah, A.C., Arya, V.P.: Synthesis of 4-aryl-1,4,5,6,7,8-hexahydro-5-oxo-2,7,7-trimethyl-quinoline-3-carboxylates and amides. *Indian J. Chem. Sect. B* **33**, 526–531 (1994)

