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ORIGINAL PAPER

A Nano-sized Nd–Ag@polyoxometalate Catalyst for Catalyzing the Multicomponent Hantzsch and Biginelli Reactions

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Abstract

For the first time the catalytic activity of $AgNdSiW_{11}$, was examined in two named reactions, namely Hantzsch and Biginelli reactions. A simple, eco-friendly and highly efficient one-pot synthesis of polyhydroquinoline derivatives via Hantzsch multicomponent reactions (MCRs) involving cyclocondensation of differently-substituted aldehydes, β-ketoesters or dimedone, active methylene compounds, and ammonium acetate as a source of nitrogen, in the presence of $AgNdSiW_{11}$ as a catalyst in $EtOH/H_2O$ under reflux conditions in high yields was successfully achieved. Furthermore, the catalytic performance of $AgNdSiW_{11}$ was also successfully tested in the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones via Biginelli MCR involving cyclocondensation of differently-substituted aldehydes, ethyl acetoacetate and urea as source of nitrogen in the presence of $AgNdSiW_{11}$ under reflux conditions in $EtOH/H_2O$. This prolific combination of Ln and POMs inaugurates a powerful class of catalysts for the different chemical transformations, which overcomes key limitations of previously established salts and Lewis acidic metals-based catalysts under low catalyst loading, the use of water scavengers, dry solvents and additives for facilitating the specialized experimental setups commonly employed to the organic reactions.

Keywords Mono-lacunary Keggin · Multicomponent reaction · One-pot manner · Polyhydroquinolines · Hantzsch reaction · Dihydropyrimidones · Biginelli reaction

Introduction

The application of efficient, easy to recover, reusable and eco-friendly catalysts to comply with the principles of green chemistry is a key priority for synthetic organic chemists [1]. Polyoxometalates (POMs), as anionic early-transition-metal oxide clusters, are a well-known and efficient class of catalysts with a unique set of characteristics such as high redox potential, high thermal stability, strong acid–base properties, high proton mobility and good solubility in polar solvents [2–7]. Owing to their numerous surface oxygen atoms, POMs have been viewed as inorganic multidentate ligands which can coordinate to metals [8]. One strategy to improve the catalytic activity of POMs is using them as inorganic ligands via their combinations with d- and f-metal ions. Lacunary POMs are good candidates for the construction of d–f heterometallic compounds, since they have a large number of different potential and versatile coordination sites and modes. The incorporation of lanthanoid (Ln) ions into the lacunary site of the POM framework enhances the catalytic properties [9]. However, examples of POM-based d–f heterometallic compounds are relatively rare [10, 11], and the synthesis of new POM-based d–f heterometallic compounds is still a challenge. On the other hand, Ag^+ ions have flexible coordination modes and high affinity to O donors, which may easily form covalent links between Ag^+ and POMs.

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Thus, Ag^+ is a suitable synthon as metal ion for the construction of POM-based d–f heterometallic compounds. Recently, Zhang et al. [12] successfully synthesized and characterized a two-dimensional (2D) purely inorganic 4d–4f heterometallic compound $[La(H_2O)_8][Ag\{La(H_2O)_6\}_2\{SiW_{11}La(H_2O)_4O_{39}\}_2]\cdot 13H_2O$, based on mono-lacunary Keggin-type $\{\alpha\text{-}SiW_{11}O_{39}\}$, and used it as an efficient photocatalyst for the photodecomposition of RhB dye.

In continuation of our interest in exploring POMs catalysis in organic transformations leading to the heterocyclic systems [13–15], the purely inorganic 4d–4f heterometallic compound attracted our attention. In our latest papers, we clearly demonstrated the role of lanthanoid ions and silver ions in improving the catalytic activity of POMs [16–18]. In this study, the combination of POM catalysts with the lanthanoid and silver ions, is expected to be more promising due to synergism effect.

Herein, we wish to report the preparation and characterization of purely inorganic Nd–Ag heterometallic compound $[Nd(H_2O)_8][Ag\{Nd(H_2O)_6\}_2\{SiW_{11}Nd(H_2O)_4O_{39}\}_2]\cdot 6H_2O$ ($AgNdSiW_{11}$) based on mono-lacunary Keggin-type $\{\alpha\text{-}SiW_{11}O_{39}\}$and reveal its activity as a heterogeneous catalyst in important named reactions in organic chemistry, namely Hantzsch and Biginelli reactions.

A multicomponent reaction (MCR), which is occasionally referred to as a "Multi component Assembly Process" (MCAP), is a chemical reaction in which three or more compounds react in a sequential and one vessel manner to afford highly selective products in which the majority of the atoms of the starting materials are included in a single product [19, 20]. Their atom economy, efficacy, mild reaction conditions, high convergence and associated step economy along with their general compatibility with green solvents validate and justify their places in the toolbox of sustainable synthetic methodologies [15].

1,4-Dihydropyridines (DHPs) are an important class of biologically and pharmacological potential compounds, which are derived from a pyridine structure. These compounds exhibit intriguing biological properties and are commonly employed as L-type calcium channel blockers [21], as in the prescribed drug nifedipine and some other some commercially available drugs with a 1,4-dihydropyridine core (Fig. 1) [22]. The synthesis of DHPs was introduced by Arthur Hantzsch in 1882, is the efficient, environmentally benign, less time consuming and cost-effective method [23, 24]. Accordingly, DHPs are frequently synthesized via Hantzsch MCR, involving various aldehydes, beta ketoesters and a source of nitrogen such as ammonium acetate (Scheme 1) [25]. One of the main disadvantages of the Hantzsch DHP synthesis is the long reaction times needed for full conversion. However, this problem has been circumvented by performing the reaction under microwave irradiation (MWI) [26, 27].

In addition, several methods have been reported for the synthesis of polyhydroquinolines (PHQs) by using dimedone instead of ketoesters [28] (Scheme 1). This methodology was developed by conducting the reaction under ultrasound irradiation [29], MWI [30], the support of solar thermal energy [31], infrared irradiation [32], grinding [33], ionic liquids [34], and metal halides or triflates [35]. Furthermore, several solid materials as supports have widely been employed for the synthesis of polyhydroquinolines such as V-TiO_2 NPs [36], Ni(II)-Vanillin-MCM-41 [37], Mn@PMO-IL [38], Co_3O_4-CNTs [39], glucosulfonic acid immobilized on Fe_3O_4 (GSA@MNPs) [40] and SBA-15/SO_3H nanoreactor [41, 42].

The Biginelli reaction is a multicomponent chemical reaction that form 3,4-dihydropyrimidin-2(1*H*)-ones from ethyl acetoacetate, differently-substituted benzaldehydes and urea [43]. It was first reported in 1893 by Pietro Biginelli [44, 45], as a very sophisticated strategy to straightforward synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (DHPMs) in a one-pot fashion [46]. DHPMs frequently exhibit biological potentiality, and compounds such as piperastrol [47] enastron [48], monastrol [49], (and analogues), and other derivatives [50] (Fig. 2) are well-established as calcium channel modulators as reviewed extensively, elsewhere [51, 52].

We are interested in heterocyclic chemistry [53–59], especially in the synthesis of heterocyclic systems via MCR [60–63] being conducted under heterogeneous catalysis in aqueous media [64]. In the last few decades, our group has been engaged in heteropolyacids and their polyoxymetalate-catalyzed reactions. The results of these efforts along with other activities have been included in several review articles [13]. Based on the points mentioned above and in continuation of our interest in exploring green heterogeneous catalysts for organic transformations leading to the heterocyclic systems, herein we report our successful attempt to apply $AgNdSiW_{11}$ as an efficient and reusable catalyst in the synthesis of polyhydroquinoline derivatives via the Hantzsch reaction (Scheme **1**) and dihydropyrimidones via the Biginelli reaction (Scheme 2).

Results and Discussion

In continuation of our above-mentioned interest in the catalyzed synthesis of heterocyclic compounds [64] via MCR [60] using HPAs and their polyoxometalates as efficient catalysts [65] under green conditions [66], in this research, we tried to extend our research activities, focusing our attention to examine the catalytic activity of a virgin heteropoly acid, $AgNdSiW_{11}$ in the synthesis of a

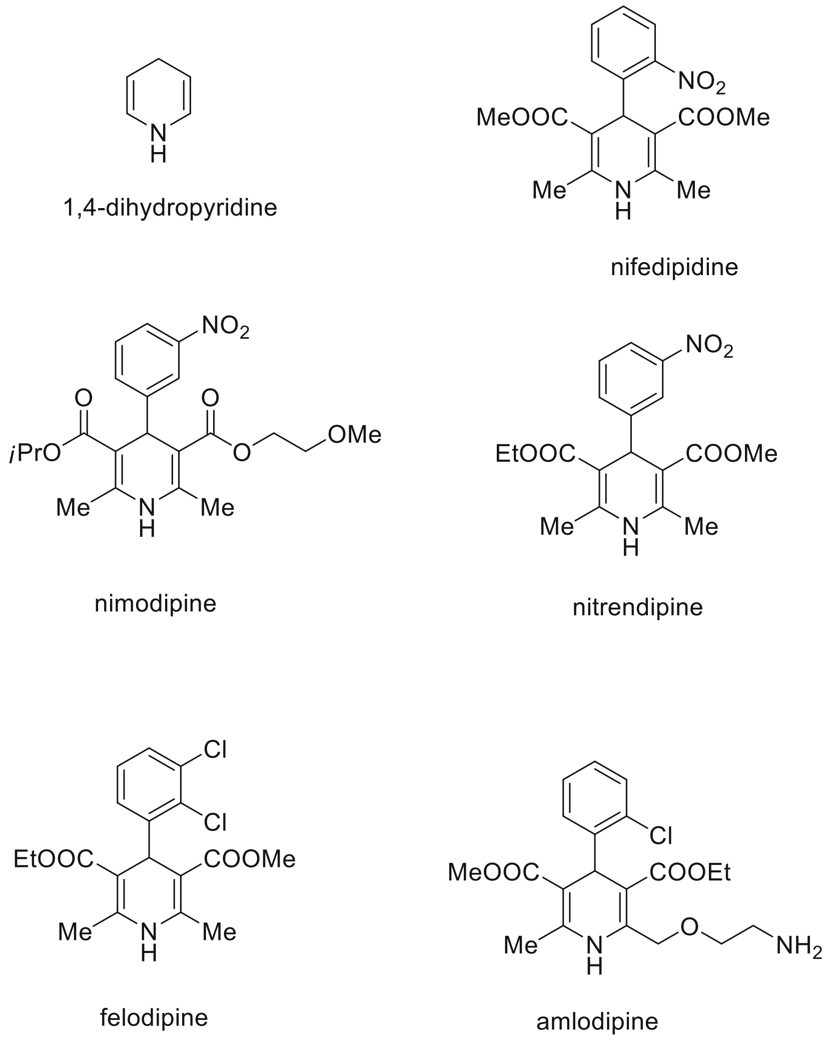
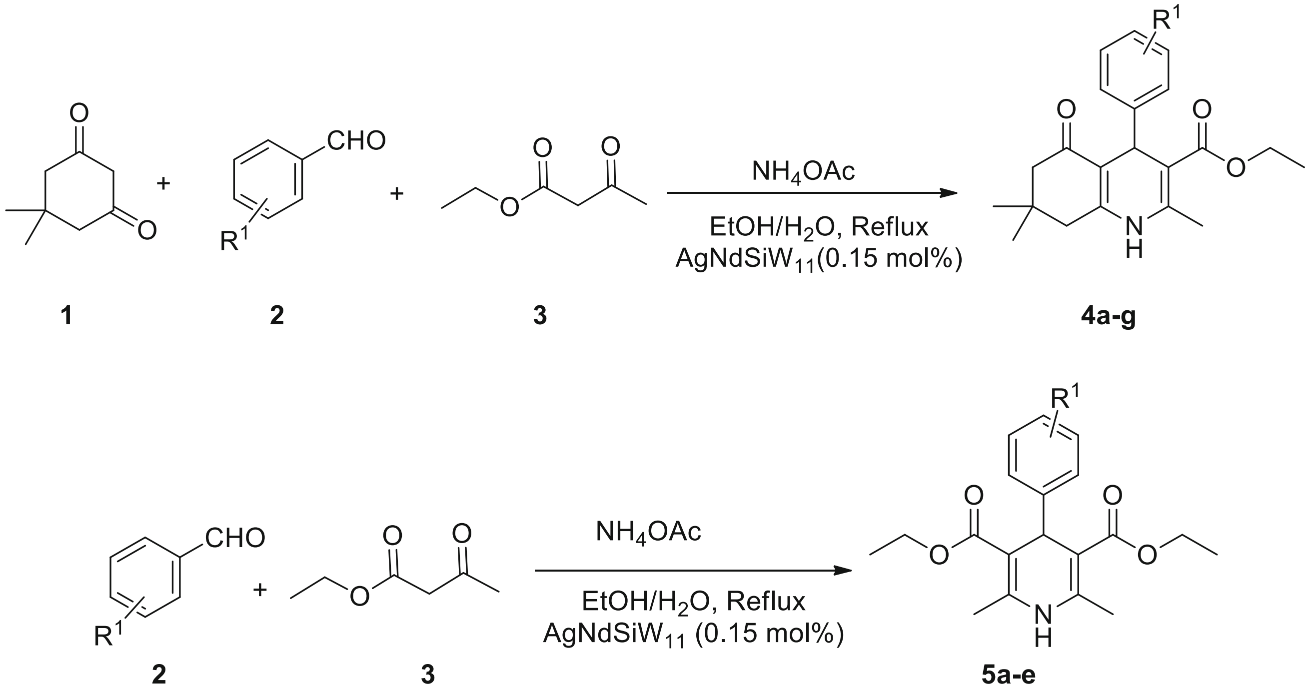


Fig. 1 Some commercially available drugs with a 1,4-dihydropyridine core

heterocyclic system via MCRs. Initially, we prepared α-$K_8SiW_{11}O_{39}\cdot 13H_2O$ by modification of previously reported method [67]. $AgNdSiW_{11}$ was prepared according the procedure described in (Ref. [12]), but $Nd(NO_3)_3\cdot 6H_2O$ was used instead of $La(NO_3)_3\cdot 6H_2O$. Infrared spectroscopy, ICP, and elemental analysis results show that this catalyst is isostructural with the compound reported in (Ref. [12]) (Fig. 3). In this compound, two mono-substituted $\{SiW_{11}Nd(H_2O)_4O_{39}\}_2$ clusters (abbreviated to $SiW_{11}Nd$) polymerize together to form a dimer and also the dimers are linked by Ag^+ and Nd^{3+} heterometallic cations displaying a 2D network. Presence of the Ag^+ and Nd^{3+} heterometallic cations and the mono-substituted $(SiW_{11}Nd)_2$ dimer with the high charge density and big volume compared with the SiW_{12} polyanions exert considerable influence on the catalytic activity of this compound.

Therefore, we used this inorganic catalyst in the Hantzsch MCR involving 4-chlorobenzaldehyde, dimedone, ethyl acetoacetate, and ammonium acetate as model reaction expecting to give the corresponding ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-*oxo*-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate **4a**. First, we conducted the reaction in water/ethanol under reflux condition but in the absence of any catalyst. This un-catalyzed reaction, proceeded sluggishly (monitored by TLC, using 7:3 *n*-hexane/ethyl acetate as eluent) and only trace amount of the desired expected product was detected in a long reaction time. This attempt showed the necessity of the presence of the catalyst in the above mentioned Hantzsch MCR. It is worthwhile mentioning that the effects of other polar and non-polar solvents such as H_2O, EtOH, EtOH/H_2O, EtOAc, CH_3CN and CH_2Cl_2, as well as solvent-free conditions were examined in the model reaction (Table 1). Having the prepared $AgNdSiW_{11}$ in hand, we conducted the model reaction in the presence of catalytic amounts of aforementioned HPA in H_2O/EtOH under reflux condition. The progress of the reaction was monitored by TLC (using 7:3 *n*-hexane/ethyl acetate as eluent), showing the model



Scheme 1 Synthesis of polyhydroquinoline **4a–g** and 1,4-dihydropyridines **5a–f** via the Hantzsch reaction

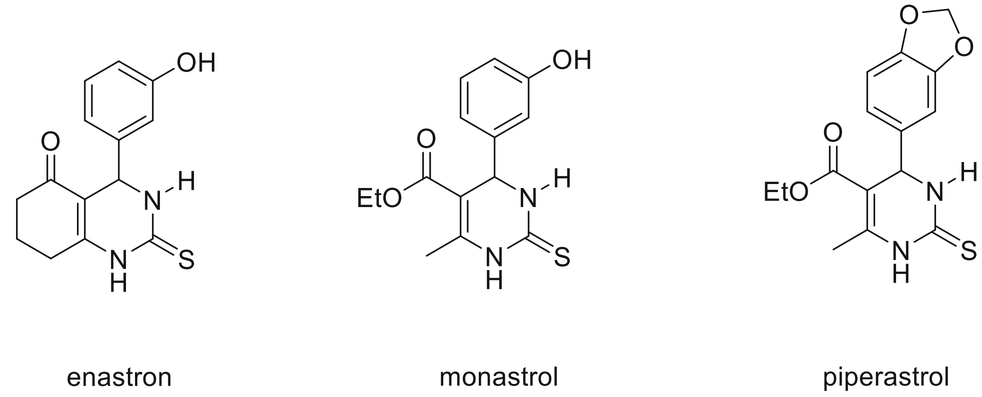
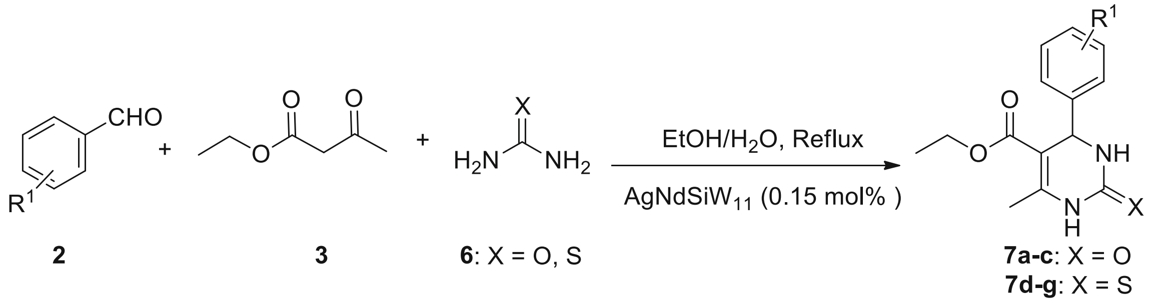


Fig. 2 Some selected biologically active DHPMs



Scheme 2 Synthesis of dihydropyrimidones via the Biginelli reaction

reaction proceeded smoothly and cleanly, consuming the starting materials and producing the expected product. The best result was obtained when the reaction was conducted using 0.15 mol% of catalyst in refluxing EtOH/H$_2$O, in which the corresponding ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-*oxo*-1,4,5,6,7,8-hexahydroquinoline-3-carboxylates were formed in 90% yield in 30 min (Table 1, entry 6). Thus, this secured optimal reaction conditions,

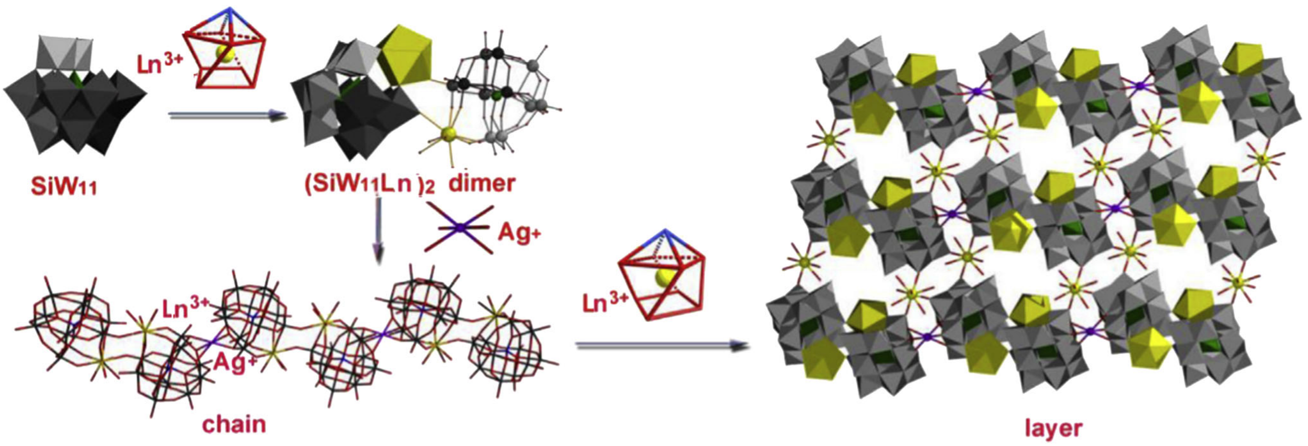


Fig. 3 View of the structural composition of the 2D layers in the catalyst [12]

Table 1 Optimization of reaction conditions for the synthesis of ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-*oxo*-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate

Entry	Solvent	Temperature	Time	Catalyst amount (mol%)	Yield (%)
1	EtOH	Reflux	30	0.15	75
2	H_2O	Reflux	30	0.15	50
3	EtOAc	Reflux	30	0.15	60
4	CH_2Cl_2	Reflux	30	0.15	60
5	CH_3CN	Reflux	30	0.15	75
6	EtOH/H_2O	Reflux	30	0.15	90
7	EtOH/H_2O	RT	2 h	0.15	10
8	EtOH/H_2O	Reflux	2 h	No catalyst	20
9	EtOH/H_2O	Reflux	30	0.08	40
10	EtOH/H_2O	Reflux	30	0.2	90

were applied in Hantzsch MCR involving differently-substituted benzaldehydes, dimedone, ethyl acetoacetate/methyl acetoacetate and ammonium to provide the corresponding hexahydroquinoline-3-carboxylates in 50–98% yields. The results are illustrated in Table 1.

Under secured optimal reaction conditions, the scope, limitations and generality of this strategy was tested for the synthesis of ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-*oxo*-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate. The generality of method was established by using differently-substituted benzaldehydes bearing either electron-releasing or electron-withdrawing moieties in the *ortho*, *meta*, and *para* positions (Scheme 1). In all cases the corresponding polyhydroquinoline derivatives were obtained in good to excellent yields in relatively short times without the formation of any detectable by-products. The results are shown in Table 2.

Encouraged by these results, we examined the role of AgNdSiW$_{11}$ in the Biginelli reaction, which is another important MCR named reaction. The reaction of 4-chlorobenzaldehyde, ethyl acetoacetate and urea in the presence of AgNdSiW$_{11}$ was chosen as the model reaction. The progress of the reaction was monitored by TLC (using 7:3 *n*-hexane/ethylacetate as the mobile phase and silicagel as the stationary phase). The best result was obtained when the above reaction was performed in EtOH/H_2O under reflux conditions to give 3,4-dihydropyrimidin-2(1*H*)-one **7a** in 67% yields.

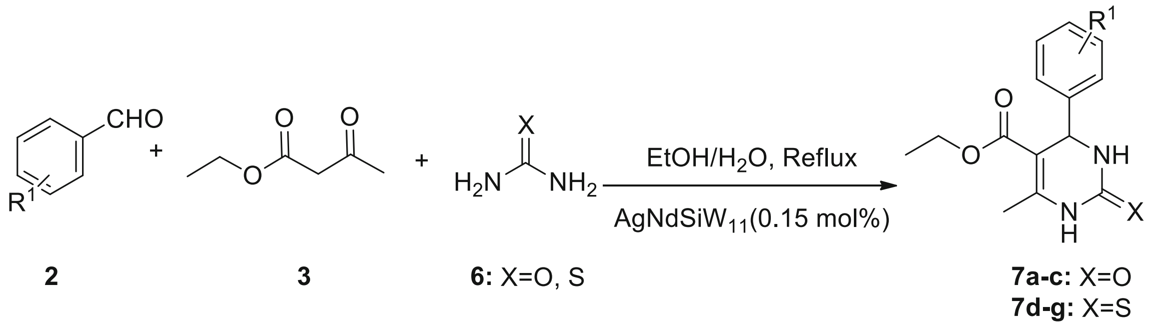
The substrate scope of this reaction was also tested. We used differently-substituted benzaldehydes bearing either electron-releasing or electron-withdrawing substituents in the *ortho*, *meta*, and *para* positions with ethyl acetoacetate and urea or thiourea under already established optimized reaction conditions (Scheme 1). In all cases, the corresponding 3,4-dihydropyrimidin-2(1*H*)-one derivatives **7a**–**g** were obtained in good to excellent yields in relatively short times without the formation of any detectable by-products. The results are summarised in Table 3.

A proposed mechanism for the catalytic activity of AgNdSiW$_{11}$ in the Hantzsch reaction is illustrated in Scheme 3. Initially, the bonding complex was generated by catalyst. Then, a Knoevenagel condensation of the 1,3-dicarbonyl compound with the aldehyde affords an α,β-unsaturated carbonyl compound **8** while the reaction of ammonia with another equivalent of the 1,3-dicarbonyl compound generates an enamine **9**. We believe that the rate

Table 2 Synthesis of polyhydroquinoline **4a–g** and 1,4-dihydropyridines **5a–f** in the presence of AgNdSiW$_{11}$ in H$_2$O/EtOH under reflux condition

Entry	R^1	Time	Product	Yield	mp (°C)	
					Found	Reported
1	4-Cl	30 min	**4a**	90	235–238	235–238 [64]
2	4-NO$_2$	1.5 h	**4b**	97	233–235	236–239 [68]
3	3-NO$_2$	1 h	**4c**	90	179–181	178–179 [69]
4	4-Me	5 h	**4d**	94	253–255	255–257 [68]
5	4-OMe	2 h	**4e**	61	259–261	257–259 [70]
6	2-OH-3-OMe	10 min	**4f**	60	237–239	238–240 [71]
7	2-OMe	30 min	**4g**	98	240–242	240–242 [72]
8	4-Cl	1 h	**5a**	63	136–139	129–135 [73]
9	4-NO$_2$	1.15 h	**5b**	83	120–122	118–127 [74]
10	3-NO$_2$	30 min	**5c**	55	153	144–154 [73]
11	4-Me	3 h	**5d**	50	129–131	131–134 [68]
12	4-OMe	1.45 h	**5e**	53	127–131	132–140 [73]
13	2-OMe	1 h	**5f**	70	136–139	135–137 [68]

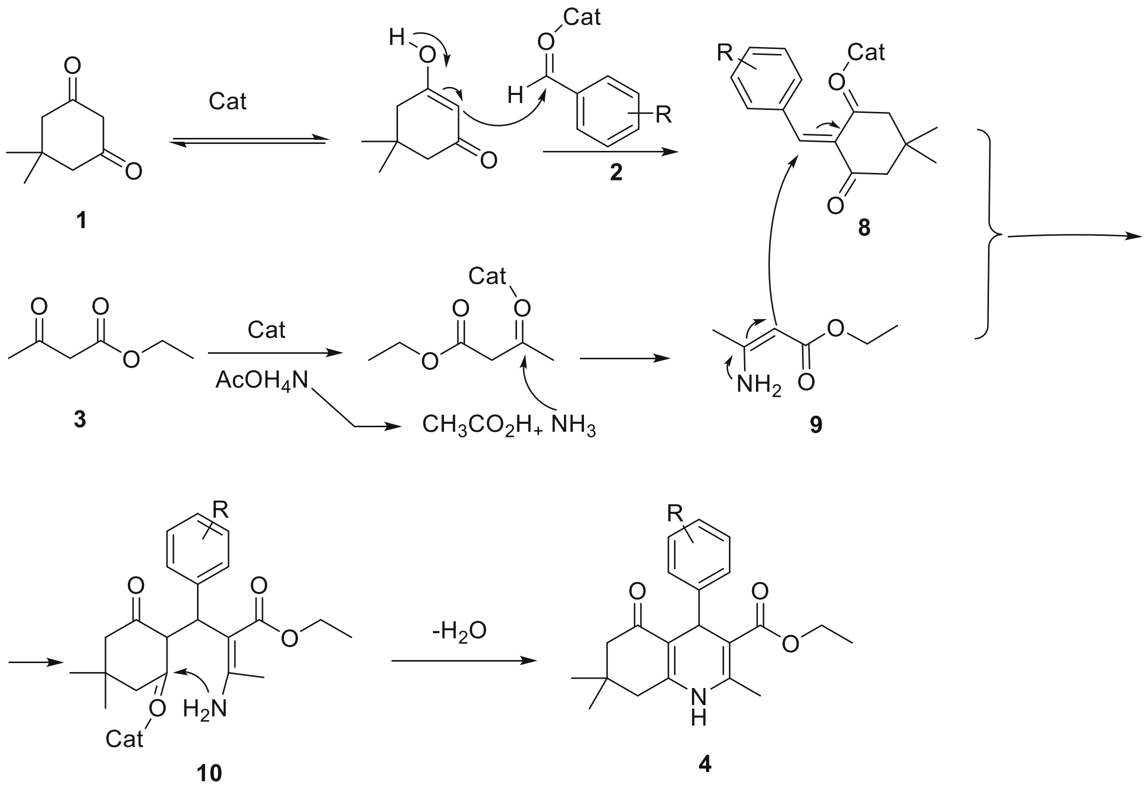
Table 3 Synthesis of 3,4-dihydropyrimidin-2(1*H*)-one derivatives **7a–g** in the presence of AgNdSiW$_{11}$



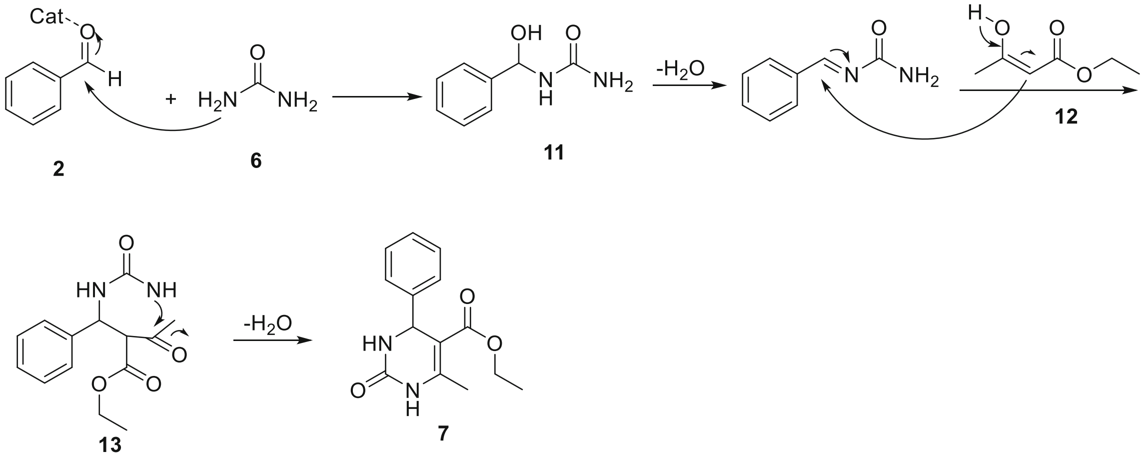
Entry	R^1	Time	Product	Yield	mp (°C)	
					Found	Reported
1	4-Cl	3 h	**7a**	67	205–207	207–210 [75]
2	3-NO$_2$	5 h	**7b**	63	194	192 [76]
3	4-Me	1 h	**7c**	65	203–204	203–204 [77]
4	4-Cl	30 min	**7d**	90	176–180	179–180 [77]
5	3-NO$_2$	20 min	**7e**	80	173–175	172 [78]
6	4-Me	15 min	**7f**	93	178–180	180–184 [79]
7	4-OMe	10 min	**7g**	92	168–170	172 [80]

determining step is the Michael addition of the enamine to the α,*β*-unsaturated carbonyl compound. Nevertheless, unlike the already recognized mechanism for the Hantzsch reaction, the enamine intermediate prefers to attack the carbon atom of the C=O double bond (carbon *β* of **8**) instead of the carbon atom of the C=C double bond (carbon α of **8**). Consequently, the intermediate **10** is subjected into an intramolecular addition of the amino to the carbon–carbon double bond to give the 1,2-dihydropyridine, which upon further oxidation gives the desired polyhydroquinoline **4** [81].

A proposed mechanism for the formation of dihydropyrimidines **7** is shown in scheme 4. Here, also initially, the bonding complex was formed by catalyst. Subsequently, the acylimine intermediate **11** is generated by the reaction between an aldehyde and urea. On the other hand, condensation of enol **12** with the acylimine generates an intermediate which is subjected into cyclization followed



Scheme 3 Suggested mechanism for Hantszch reaction



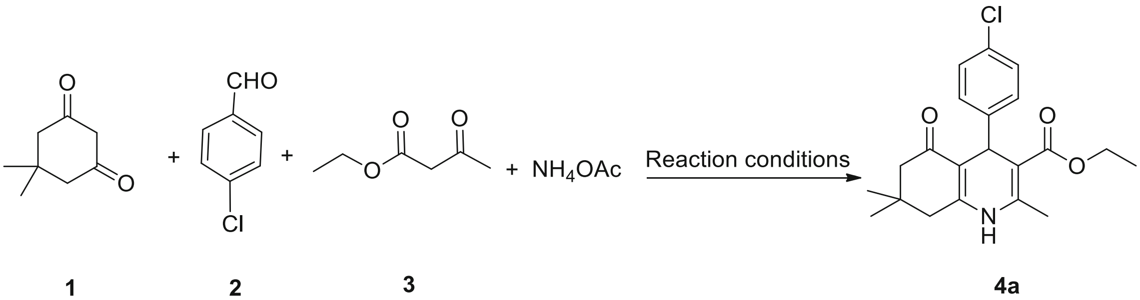
Scheme 4 Suggested mechanism for Biginelli reaction

by dehydration to give the corresponding dihydropyrimidines **7** [82].

To show the merits of this catalyst, its catalytic activity in the model reaction involving 4-Cl-benzaldehyde, dimedone and ethyl acetoacetate was compared with those reported, previously (Table 4). As shown in Table 4, the catalytic activity of $AgNdSiW_{11}$ was compared with already reported catalysts such as Mn@PMO-IL [38], I_2 [83], ascorbic acid [84], V–TiO_2 NPs [36], $K_7[PW_{11}CoO_{40}]$ [85], ED/MIL-101(Cr) [43], ZnO NPs [86], *p*-TSA [87], FeF_3 [88] cellulose sulfuric acid [80], nicotinic acid [89], TEDETA@BNPs [90], and TrzMOP [81].

The comparison showed that our designed and selected catalyst is very effective according to several criteria: it gives the desired products in a shorter reaction time; the catalyst is reusable; and the EtOH/H_2O reaction medium is a benign one. Curiously, the persistence of this work, which is introducing a catalyst with potential application for improving organic transformations and specifically in the synthesis of two distinct and important

Table 4 The comparison of the catalytic activity of $AgNdSiW_{11}$ with formerly reported catalysts



Entry	Solvent	Catalyst	Catalyst amount	Temperature/°C	Time	Yield	Refs.
1	Solvent-free	Mn@PMO-IL	1 mol%	80	20 min	87	[38]
2	Solvent-free	I_2	30 mol%	r.t.	6 h	99	[83]
3	Solvent-free	Ascorbic acid	5 mol%	80	3 h	89	[84]
4	Solvent-free	V–TiO_2 NPs	2 mol%	80	14 min	82	[36]
5	CH_3CN	$K_7[PW_{11}CoO_{40}]$	1 mol%	Reflux	30 min	80	[85]
6	EtOH	ED/MIL-101(Cr)	4 mol%	80	2 h	90	[43]
7	Solvent-free	ZnO NPs	10 mol%	R.T	20 min	98	[86]
8	EtOH	*p*-TSA	10 mol%	R.T	2 h	90	[87]
9	EtOH	FeF_3	5 mol%	75–80	1 h	92	[88]
10	Solvent-free	Cellulose sulfuric acid	10 mol%	100	2–5 h	78	[80]
11	Solvent-free	nicotinic acid	100 mg	80	5 min	95	[89]
12	EtOH	TEDETA@BNPs	24 mg	80	1 h	95	[90]
13	EtOH	TrzMOP	1 mg	120	10 min	57	[81]
14	EtOH	TrzMOP	1 mg	120, MW	10 min	98	[81]
15	$EtOH/H_2O$	$AgNdSiW_{11}$	0.15 mol%	Reflux	30	80	This work

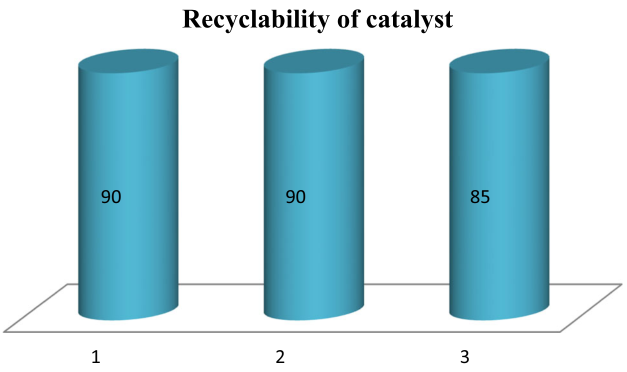


Fig. 4 Recyclability of catalyst for the synthesis of **4a**

heterocyclic systems dihydropyridines (DHPs) and dihydropyrimidin-2(1*H*)-ones were provided via two well-established and recognized MCR Hantzsch, and Biginelli reactions, respectively.

Catalyst Reusability

To clarify whether $AgNdSiW_{11}$ could act as a heterogeneous catalyst and in view of the distinction of the reusability especially in large-scale production, the reusability of $AgNdSiW_{11}$ was studied. To resolve, the model reaction in Hantzsch reaction, it was conducted in the presence of the freshly prepared catalyst. Upon completion of the reaction (indicated by TLC), it was separated by centrifuging, washed, dried and used the second reaction run. The reusability of the catalyst was examined for three successive reaction runs. This observation showed that the catalyst could be recovered and recycled up to three reaction runs without significant loss in its catalytic activity (Fig. 4).

Experimental Section

Materials and Physical Methods

All chemical used in this research were purchased from Merck Company and used as received. Melting points were measured by an Electro thermal 9200 apparatus. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. All obtained products are known compounds and were identified by comparison of their melting points and FTIR spectra with those of authentic samples and found being identical. The α-$K_8SiW_{11}O_{39}\cdot 13H_2O$ precursor was synthesized and characterized by IR spectroscopy in accordance to the literature [67].

Synthesis of $[Nd(H_2O)_8][Ag\{Nd(H_2O)_6\}_2\{SiW_{11}Nd(H_2O)_4O_{39}\}_2]\cdot 6H_2O$ ($AgNdSiW_{11}$)

In a typical experiment, α-$K_8SiW_{11}O_{39}\cdot 13H_2O$ (752 mg, 0.25 mmol) was dissolved in water (8 mL). To it was added a solution of $Nd(NO_3)_3.6H_2O$ (230.5 mg, 0.50 mmol) in water (5 mL) was added, dropwise slowly at 60 °C, followed by addition solution of $AgNO_3$ (849.4 mg, 0.50 mmol, 5 mL). The pH value of resulting solution was adjusted to about 3.6 by addition of HNO_3 solution and then stirred for 10 min at 60 °C. The solution was left to stand in air at room temperature (and the final pH of obtained solution is ca. 4.1). A white precipitate was formed in 2 days. After removal of the initially precipitated solid, the clear solution was again leftover to in air at room temperature, and cooled down to obtain a solid which was filtered off to give the title product. (Yield 47% based on Nd). Elemental analysis for $AgH_{68}Nd_5O_{114}Si_2W_{22}$: Anal. Calc.: Ag, 1.59; H, 1.00; Nd, 10.61; W, 59.51 (%). Found: Ag, 1.64; H, 0.98; Nd, 10.30; W, 59.22 (%).

Infrared Spectroscopy

In the FT-IR spectrum of Nd–Ag–SiW_{11}, four characteristic vibration bands of the Keggin-type structures corresponding to ν(Si–Oa), ν(W–Od), ν(W–Ob–W), and ν(W–Oc–W) are observed at 952, 887, 770 and 721 cm^{-1}, respectively [80, 81]. Relative to the saturated Keggin cluster $[\alpha\text{-}SiW_{12}O_{40}]^{4-}$ [59], the vibration bands are red-shifted. The ν(W–Ob–W) vibration is split into three bands due to the insertion of neodymium (Nd) atom with the corresponding reduction in symmetry. Additionally, the band centered at 3411 cm^{-1} is attributed to the ν(OH) vibration of water molecules (Fig. 5).

The morphology of catalyst was studied by scanning electron microscope (SEM) analyses. As shown in Fig. 6, the presence of nano size particles is confirmed.

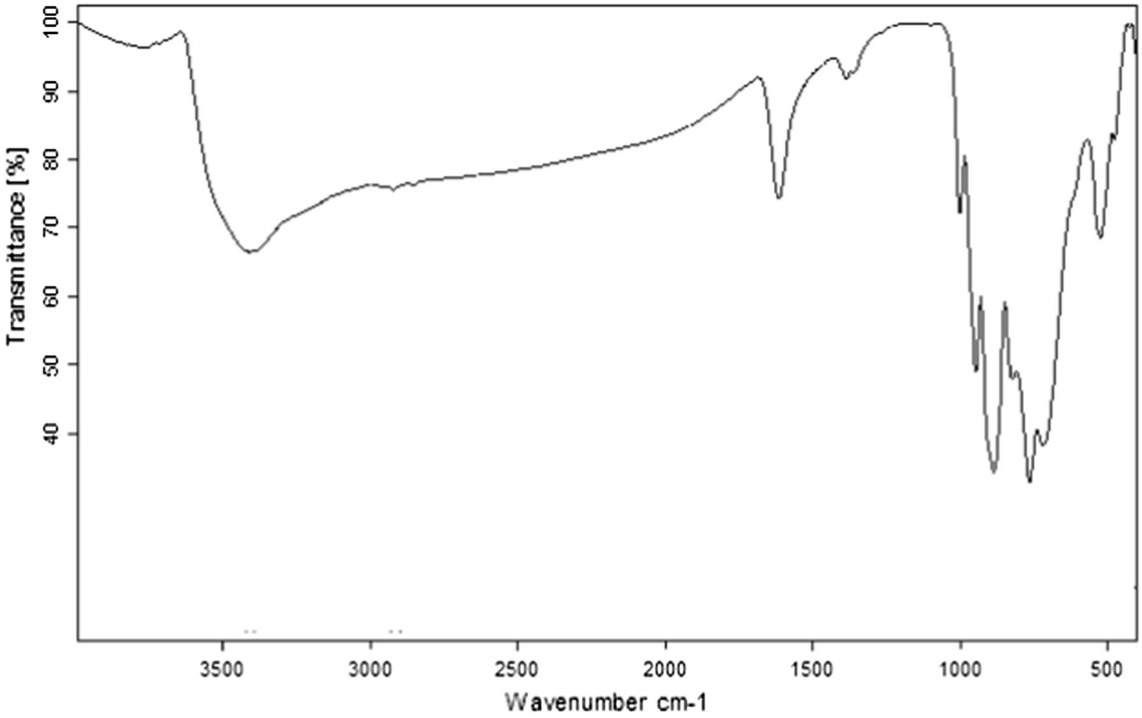


Fig. 5 FT-IR spectrum of the catalyst $AgNdSiW_{11}$

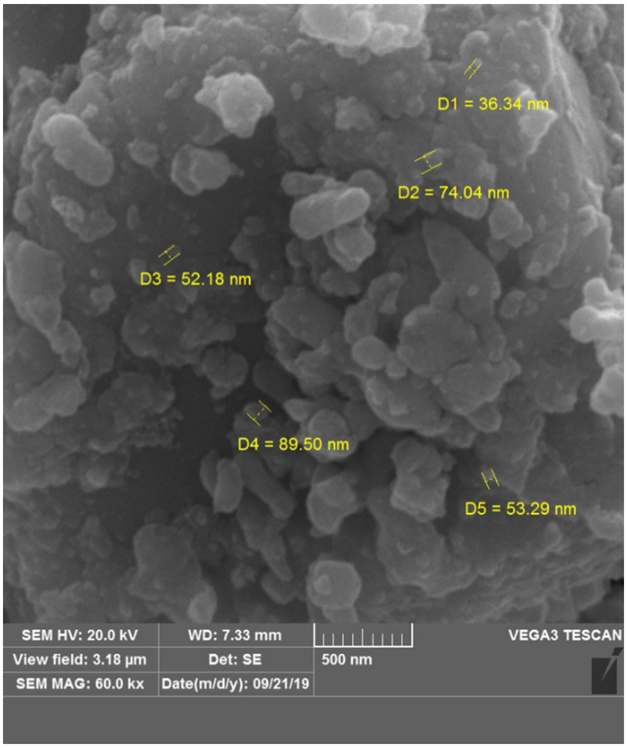


Fig. 6 SEM analyses of the catalyst $AgNdSiW_{11}$

Synthesis of Polyhydroquinoline: General Procedure

A mixture of the differently-substituted benzaldehydes (0.5 mmol), dimedone (0.5 mmol), ethyl acetoacetate (0.5 mmol) and ammonium acetate (1 mmol) was stirred in the presence of freshly made $AgNdSiW_{11}$ (0.15 mol%) in $EtOH/H_2O$ (4 mL) under reflux conditions. Upon completion of the reaction (monitored by thin layer chromatography (TLC), the reaction mixture was cooled to room temperature. The, catalyst was separated by centrifugation and washed with a mixture of hexane and petroleum ether and dried at room temperature to obtain the corresponding products **4a–g**.

Synthesis of 1,4-Dihydropyridines (DHPs): General Procedure

A mixture of substituted benzaldehydes (0.5 mmol), ethyl acetoacetate (1 mmol) and ammonium acetate (1 mmol) was stirred in the presence of $AgNdSiW_{11}$ (0.15 mol%) in $EtOH/H_2O$ (4 mL) under reflux conditions. Upon, completion of the reaction (monitored by TLC) the reaction mixture was cooled to room temperature. The catalyst was separated by centrifugation, washed with hexane and petroleum ether and dried at room temperature to give the corresponding products **5a–f**.

Synthesis of 3,4-Dihydropyrimidin-2(*1H*)-ones: General Procedure

A mixture of the differently benzaldehydes (0.5 mmol), ethyl acetoacetate (1 mmol), urea or thiourea (0.5 mmol) in the presence of $AgNdSiW_{11}$ (0.15 mol%) was stirred in $EtOH/H_2O$ (4 mL) under reflux condition. Upon completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Then, the catalyst was separated by centrifugation and washed with hexane and petroleum ether at ambient temperature. The corresponding products **7a–g** were identified by comparison of their melting points as well as their FTIR spectra.

Conclusion

In summary, we have presented a highly efficient and green protocol for MCR synthesis of polyhydroquinolines, 1,4-dihydropyridines and 3,4-dihydropyrimidin-2(1*H*)-ones as biologically potent compounds employing $AgNdSiW_{11}$ as a green, heterogeneous and recyclable catalyst in $EtOH/H_2O$ in a one-pot fashion. This strategy offers substantial improvements in the reaction rates and yields. Herein, it was demonstrated the catalytic activity of $AgNdSiW_{11}$ for the first time. It can be reused for several times with high efficiency. This catalyst was effectively employed in two MCR named reactions, namely the Hantzsch and Bignelli reactions, to give different polyhydroquinolines and pyrimidones. This strategy benefits from using water/ethanol as solvent and that the catalyst which can be reused several times giving high yields within a relatively short reaction time. Our protocol benefits from the merits of heterogeneous catalysis as well as being doubly green through using water/EtOH as solvent. Thus, this protocol can be well applicable in industry as well as academia.

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References

1. N. Lotfian, M. M. Heravi, M. Mirzaei, and B. Heidari (2019). *Appl. Organometal. Chem.* **33**, e4808. https://doi.org/10.1002/aoc.4808.
2. F. de Azambuja and T. N. Parac-Vogt (2019). *ACS Catal.* **9**, 10245–10252. https://doi.org/10.1021/acscatal.9b03415.
3. M. M. Heravi, M. Mirzaei, S. Y. Shirazi Beheshtiha, V. Zadsirjan, F. Mashayekh Ameli, and M. Bazarga (2018). *Appl. Organometal. Chem.* **32**, e4479. https://doi.org/10.1002/aoc.4479.

4. S. Derakhshanrad, M. Mirzaei, and J. T. Mague (2019). *Inorg. Chem. Res.* **2**, 40–49. https://doi.org/10.22036/icr.2019.194182.1052.
5. M. Arefian, M. Mirzaei, and H. Eshtiagh-Hosseini (2016). *Inorg. Chem. Res.* **1**, 183–190. https://doi.org/10.22036/icr.2017.93979.1038.
6. M. Samaniyan, M. Mirzaei, R. Khajavian, H. Eshtiagh-Hosseini, and C. Streb (2019). *ACS Catal.* **9**, 10174–10191. https://doi.org/10.1021/acscatal.9b03439.
7. S. Taleghani, M. Mirzaei, H. Eshtiagh-Hosseini, and A. Frontera (2016). *Coord. Chem. Rev.* **309**, 84–106.
8. M. Mirzaei, H. Eshtiagh-Hosseini, M. Alipour, and A. Frontera (2014). *Coord. Chem. Rev.* **275**, 1–8. https://doi.org/10.1016/j.ccr.2014.03.012.
9. M. Arab Fashapoyeh, M. Mirzaei, H. Eshtiagh-Hosseini, A. Rajagopal, M. Lechner, R. Liu, and C. Streb (2018). *Chem. Commun.* **54**, 10427–10430. https://doi.org/10.1039/c8cc06334f.
10. H. Pang, C. J. Gómez-García, J. Peng, H. Ma, C. Zhangd, and Q. Wu (2013). *Dalton Trans.* **42**, 16596–16601. https://doi.org/10.1039/C3DT51899J.
11. J. W. Zhao, Y. Z. Li, L. J. Chen, and G. Y. Yang (2016). *Chem. Commun.* **52**, 4418–4445. https://doi.org/10.1039/C5CC10447E.
12. C. Zhang, X. Fu, H. Ma, H. Pang, and B. Zhou (2017). *Solid State Sci.* **73**, 36–40. https://doi.org/10.1016/j.solidstatesciences.2017.09.005.
13. M. M. Heravi and Z. Faghihi (2014). *J. Iran. Chem. Soc.* **11**, 209–224.
14. F. F. Bamoharram, M. Roshani, M. M. Heravi, and S. Safaie (2006). *Phosphorus Sulfur Silicon Relat. Elem.* **181**, 2833–2843. https://doi.org/10.1080/10426500600865004.
15. S. Sadjadi, M. M. Heravi, and N. Nazari (2016). *RSC Adv.* **6**, 53203–53272. https://doi.org/10.1039/C6RA02143C.
16. M. Tamimi, M. M. Heravi, M. Mirzaei, V. Zadsirjan, and N. Lotfian (2019). *Appl. Organometal. Chem.* **33**, e5043. https://doi.org/10.1002/aoc.5043.
17. M. Daraie, M. M. Heravi, M. Mirzaei, and N. Lotfian (2019). *Appl. Organometal. Chem.* **33**, e5058. https://doi.org/10.1002/aoc.5058.
18. N. Lotfian, M. M. Heravi, M. Mirzaei, and M. Daraie (2020). *J. Mol. Struct.* **1199**, 126953.
19. S. Brauch, S. S. Van Berkel, and B. Westermann (2013). *Chem. Soc. Rev.* **42**, 4948–4962. https://doi.org/10.1039/c3cs35505e.
20. J. Zhu and H. Bienaymé *Multicomponent Reactions* (Wiley-VCH, Weinheim, 2005).
21. N. Edraki, A. R. Mehdipour, M. Khoshneviszadeh, and R. Miri (2009). *Drug Discov. Today.* **14**, 1058–1066. https://doi.org/10.1016/j.drudis.2009.08.004.
22. D. A. Horton, G. T. Bourne, and M. L. Smythe (2003). *Chem. Rev.* **103**, 893–930. https://doi.org/10.1021/cr020033s.
23. S. S. Mansoor, K. Aswin, K. Logaiya, and S. P. N. Sudhan (2017). *Arab. J. Chem.* **10**, S546–S553. https://doi.org/10.1016/j.arabjc.2012.10.017.
24. R. M. Maurya, N. Sainia, and F. Avecilla (2016). *RSC Adv.* **6**, 2671–2680. https://doi.org/10.2174/13852728226661811091245 47.
25. L. Kurti and B. Czako *Strategic Applications of Named Reactions in Organic Synthesis* (Elsevier, Amsterdam, 2005).
26. V. Eynde, J. Jacqes, and A. Mayence (2003). *Molecules* **8**, 381–391. https://doi.org/10.3390/80400381.
27. P. T. Baraldi, T. Noël, Q. Wang, and V. Hessel (2014). *Tetrahedron Lett.* **55**, 2090–2092. https://doi.org/10.1016/j.tetlet.2014.02.041.
28. M. Nasr-Esfahani, M. Montazerozohori, and R. Raeatikia (2014). *Maejo. Int. J. Sci. Technol.* **8**, 32–40.
29. J. Y. He, H. Z. Jia, Q. G. Yao, S. J. Liu, H. K. Yue, H. W. Yu, and R. S. Hu (2015). *Ultrason. Sonochem.* **22**, 144–148. https://doi.org/10.1016/j.ultsonch.2014.05.026.
30. S. J. Tu, J. F. Zhou, X. Deng, P. J. Cai, H. Wang, and J. C. Feng (2001). *Chin. J. Org. Chem.* **21**, 313–316.
31. R. A. Mekheimer, A. A. Hameed, and K. U. Sadek (2008). *Green Chem.* **10**, 592–593. https://doi.org/10.1039/B715126H.
32. R. Gómez-Pliego, R. Osnaya, I. Zamora, B. Velasco-Bejarano, G. Arroyo, R. S. Juan, J. Trujillo, F. Delgado, and R. Miranda (2007). *J. Mex. Chem. Soc.* **51**, 181–184.
33. S. Kumar, P. Sharma, K. K. Kapoor, and M. S. Hundal (2008). *Tetrahedron* **64**, 536–542. https://doi.org/10.1016/j.tet.2007.11.008.
34. X. Y. Zhang, Y. Z. Li, X. S. Fan, G. R. Qu, X. Y. Hu, and J. J. Wang (2006). *Chin. Chem. Lett.* **17**, 150–152.
35. L. M. Wang, J. Sheng, L. Zhang, J. W. Han, Z. Y. Fan, H. Tian, and C. T. Qian (2005). *Tetrahedron* **61**, 1539–1543. https://doi.org/10.1016/j.tet.2004.11.079.
36. G. B. Dharma Rao, S. Nagakalyan, and G. K. Prasad (2017). *RSC Adv.* **7**, 3611. https://doi.org/10.1039/c6ra26664a.
37. M. Nikoorazm, A. Ghorbani-Choghamarani, and M. Khanmoradi (2016). *RSC Adv.* **6**, 56549–56561. https://doi.org/10.1039/C6RA09371J.
38. M. Nasr-Esfahani, D. Elhamifar, T. Amadeh, and B. Karimi (2015). *RSC Adv.* **5**, 13087–13094. https://doi.org/10.1039/C4RA12673D.
39. Z. Zarnegar, J. Safari, and Z. M. Kafroudi (2015). *New J. Chem.* **39**, 1445–1451. https://doi.org/10.1039/C4NJ01588F.
40. M. Hajjami and B. Tahmasbi (2015). *RSC Adv.* **5**, 59194–59203. https://doi.org/10.1039/c5ra08952b.
41. S. Rostamnia and F. Pourhassan (2013). *Chin. Chem. Lett.* **24**, 401–403. https://doi.org/10.1016/j.cclet.2013.03.020.
42. S. Rostamnia, H. Alamgholiloo, and M. Jafari (2018). *Appl. Organometal. Chem.* **32**, e4370. https://doi.org/10.1002/aoc.4370.
43. A. C. Boukis, B. Monney, and M. A. Meier (2017). *Beilstein J. Org. Chem.* **13**, 54–62.
44. C. O. Kappe (2000). *Acc. Chem. Res.* **33**, 879–888. https://doi.org/10.1021/ar000048h.
45. G. C. Tron, A. Minassi, and G. Appendino (2011). *Eur. J. Org. Chem.* **28**, 5541–5550. https://doi.org/10.1002/ejoc.201100661.
46. S. Panda, P. Khanna, and L. Khanna (2012). *Curr. Org. Chem.* **16**, 507–520. https://doi.org/10.2174/138527212799499859.
47. R. F. Canto, A. Bernardi, A. M. O. Battastini, D. Russowsky, and V. L. Eifler-Lima (2011). *J. Brazil. Chem. Soc.* **22**, 1379–1388. https://doi.org/10.1590/S0103-50532011000700025.
48. H. Y. K. Kaan, V. Ulaganathan, O. Rath, H. Prokopcová, D. Dallinger, C. O. Kappe, and F. Kozielski (2010). *J. Med. Chem.* **53**, 5676–5683. https://doi.org/10.1021/jm100421n.
49. M. A. Blasco, S. Thumann, J. Wittmann, A. Giannis, and H. Gröger (2010). *Bioorg. Med. Chem. Lett.* **20**, 4679–4682. https://doi.org/10.1016/j.bmcl.2010.05.063.
50. H. L. Luo, W. Yang, Y. Li, and S. F. Yin (2010). *Chem. Nat. Compd.* **46**, 412–416. https://doi.org/10.1007/s10600-010-9630-5.
51. C. O. Kappe (2000). *Eur. J. Med. Chem.* **35**, 1043–1052. https://doi.org/10.1016/S0223-5234(00)01189-2.
52. L. M. Ramos, Y. Ponce de Leon, A. Y. Tobio, M. R. dos Santos, H. C. de Oliveira, A. F. Gomes, F. C. Gozzo, A. L. de Oliveira, and B. A. Neto (2012). *J. Org. Chem.* **77**, 10184–10193. https://doi.org/10.1021/jo301806n.
53. M. M. Heravi and B. Talaei *Advances in Heterocyclic Chemistry*, vol. 114 (Elsevier, Amsterdam, 2015), pp. 147–225. https://doi.org/10.1016/bs.aihch.2015.02.001.

54. M. M. Heravi and T. Alishiri *Advances in Heterocyclic Chemistry*, vol. 113 (Elsevier, Amsterdam, 2014), pp. 1–66. https://doi.org/10.1016/B978-0-12-800170-7.00001-8.
55. M. M. Heravi and V. Zadsirjan *Advances in Heterocyclic Chemistry*, vol. 117 (Elsevier, Amsterdam, 2015), pp. 261–376. https://doi.org/10.1016/bs.aihch.2015.08.003.
56. M. M. Heravi and B. Talaei *Advances in Heterocyclic Chemistry*, vol. 122 (Elsevier, Amsterdam, 2017), pp. 43–114. https://doi.org/10.1016/bs.aihch.2016.10.003.
57. M. M. Heravi, N. Nami, N. Seifi, H. A. Oskooie, and R. Hekmatshoar (2006). *Phosphorus Sulfur Silicon Relat. Elem.* **181**, 591–599. https://doi.org/10.1080/10426500500269646.
58. M. M. Heravi and B. Talaei *Advances in Heterocyclic Chemistry*, vol. 113 (Elsevier, Amsterdam, 2014), pp. 143–244. https://doi.org/10.1016/B978-0-12-800170-7.00004-3.
59. M. M. Heravi and V. F. Vavsari *Advances in Heterocyclic Chemistry*, vol. 114 (Elsevier, Amsterdam, 2015), pp. 77–145. https://doi.org/10.1016/bs.aihch.2015.02.002.
60. M. M. Heravi, S. Khaghaninejad, and N. Nazari *Advances in Heterocyclic Chemistry*, vol. 112 (Elsevier, Amsterdam, 2014), pp. 183–234. https://doi.org/10.1016/B978-0-12-800171-4.00005-6.
61. M. M. Heravi, E. Hashemi, Y. S. Beheshtiha, S. Ahmadi, and T. Hosseinnejad (2014). *J. Mol. Catal. A Chem.* **394**, 74–82. https://doi.org/10.1016/j.molcata.2014.07.001.
62. S. Sadjadi, M. M. Heravi, and M. Malmir (2018). *Appl. Organometal. Chem.* **32**, e4029. https://doi.org/10.1002/aoc.4029.
63. R. Mirsafaei, M. M. Heravi, T. Hosseinnejad, and S. Ahmadi (2016). *Appl. Organometal. Chem.* **30**, e823–830. https://doi.org/10.1002/aoc.3509.
64. R. Mirsafaei, M. M. Heravi, S. Ahmadi, M. H. Moslemin, and T. Hosseinnejad (2015). *J. Mol. Catal. A Chem.* **402**, 100–108. https://doi.org/10.1016/j.molcata.2015.03.006.
65. S. Sadjadi and M. M. Heravi (2016). *Curr. Org. Chem.* **20**, 1404–1444.
66. M. M. Heravi, M. Vazin Fard, and Z. Faghihi (2013). *Green Chem. Lett. Rev.* **6**, 282–300. https://doi.org/10.1080/17518253.2013.846415.
67. A. Tézé and G. Hervé (1990). *Inorg. Synth.* **27**, 93.
68. N. Mizuno and M. Misono (1998). *Chem. Rev.* **98**, 199–218.
69. M. M. Heravi and S. Sadjadi (2009). *J. Iran. Chem. Soc.* **6**, 1–54. https://doi.org/10.1007/BF03246501.
70. S. S. Wang and G. Y. Yang (2015). *Chem. Rev.* **115**, 4893–4962. https://doi.org/10.1021/cr500390v.
71. S. R. Bhusare, S. C. Jadhvar, H. M. Kasraliker, S. V. Goswami, and A. V. Chakrawar (2017). *Res. Chem. Intermed.* **43**, 7211–7221. https://doi.org/10.1007/s11164-017-3069-2.
72. R. Ghorbani-Vaghei, S. M. Malaekehpoor, P. Hasanein, R. Karamyan, and M. Asadbegy (2016). *Res. Chem. Intermed.* **42**, 4715–4731. https://doi.org/10.1007/s11164-015-2310-0.
73. Y. Murthy, A. Rajack, M. T. Ramji, C. Praveen, and K. A. Lakshmi (2012). *Bioorg. Med. Chem. Lett.* **22**, 6016–6023. https://doi.org/10.1016/j.bmcl.2012.05.003.
74. R. F. Affeldt, E. V. Benvenutti, and D. Russowsky (2012). *New J. Chem.* **36**, 1502–1511. https://doi.org/10.1039/c2nj40060j.
75. M. Tajbakhsh, B. Mohajerani, M. M. Heravi, and A. N. Ahmadi (2005). *J. Mol. Catal. A Chem.* **236**, 216–219. https://doi.org/10.1016/j.molcata.2005.04.033.
76. H. Firdous, A. M. Zafar, M. N. Khan, N. Parveen, M. A. Munawar, and M. A. Khan (2015). *Asian J. Chem.* **27**, 455. https://doi.org/10.14233/ajchem.2015.16953.
77. J. Javidi, M. Esmaeilpour, and F. N. Dodeji (2015). *RSC Adv.* **5**, 308–315. https://doi.org/10.1039/c4ra09929j.
78. A. Mobinikhaledi, N. Foroughifar, and A. Ghorbani (2005). *Phosphorus Sulfur Silicon Relat. Elem.* **180**, 1713–1719. https://doi.org/10.1080/104265090885174.
79. M. Hajjami and E. Ghiasbeygi (2016). *Russ. J. Org. Chem.* **52**, 429–432. https://doi.org/10.1134/S1070428016030222.
80. N. S. Begum and D. Vasundhara (2009). *J. Chem. Res.* **2009**, 201–204. https://doi.org/10.3184/030823409X425064.
81. S. K. Das, S. Mondal, S. Chatterjee, and A. Bhaumik (2018). *ChemCatChem.* **10**, 2488–2495. https://doi.org/10.1002/cctc.201702013.
82. S. S. Mansoor, S. S. Shafi, and S. Z. Ahmed (2016). *Arab. J. Chem.* **9**, S846–S851. https://doi.org/10.1016/j.arabjc.2011.09.018.
83. S. Ko, M. Sastry, C. Lin, and C. F. Yao (2005). *Tetrahedron Lett.* **46**, 5771–5774. https://doi.org/10.1016/j.tetlet.2005.05.148.
84. I. Sehout, R. Boulcina, B. Boumoud, T. Boumoud, and A. Debache (2017). *Synth. Commun.* **47**, 1185–1191. https://doi.org/10.1080/00397911.2017.1316406.
85. M. M. Heravi, K. Bakhtiari, N. M. Alamgholiloo, F. F. Bamoharram, M. Saeedi, and H. A. Oskooie (2007). *J. Mol. Catal. A Chem.* **264**, 50–52. https://doi.org/10.1016/j.molcata.2006.09.004.
86. M. Kassaee, H. Masrouri, and F. Movahedi (2010). *Monat. Chem. Chem. Mon.* **141**, 317–322. https://doi.org/10.1007/s00706-010-0252-1.
87. S. R. Cherkupally and R. Mekala (2008). *Chem. Pharm. Bull.* **56**, 1002–1004. https://doi.org/10.1248/cpb.56.1002.
88. R. Surasani, D. Kalita, A. D. Rao, K. Yarbagi, and K. Chandrasekhar (2012). *J. Fluorine Chem.* **135**, 91–96. https://doi.org/10.1016/j.jfluchem.2011.09.005.
89. J. Davarpanah, M. Ghahremani, and O. Najafi (2019). *J. Mol. Struct.* **1177**, 525–535. https://doi.org/10.1016/j.molstruc.2018.10.002.
90. A. Ghorbani-Choghamarani, Z. Heidarnezhad, B. Tahmasbi, and G. Azadi (2018). *J. Iran. Chem. Soc.* **15**, 2281–2293. https://doi.org/10.1007/s13738-018-1417-9.