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SYNTHESIS OF 1,4-DIHYDROPYRIDINE DERIVATIVES USING NANO-ZIRCONIA SULFURIC ACID AS HIGHLY EFFICIENT RECYCLABLE CATALYST

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ABSTRACT
The catalytic effect of zirconia Sulfuric Acid (ZrSA) nanoparticle which is synthesized from the reaction of ZrO_2 with chlorosulforic acidhas been investigated in the synthesis of 1,4-dihydropyridines by one-pot three-component reaction of aliphatic\aromatic aldehydes, ammonium acetate, and ethyl acetoacetate *via*Hantzsch reaction. Different reaction conditions were studied in the presence of ZrSA nanoparticle as catalyst. The results showed that this catalyst acts as effective heterogeneous catalyst than others reported catalysts in previously published literatures and the reaction proceeded more easily and gave the highest yields of the products in shorter reaction times under thermal solvent-free conditions. Simple isolation of the products, and usage of eco-friendly catalysts are other features of this procedure. In addition, the catalyst was easily recovered and used in multiple catalytic cycles.

KEYWORDS: Solid acid nano-catalyst, Reusability, Zirconia sulfuric acid (ZrSA), 1,4-Dihydropyridines, Solvent-free.

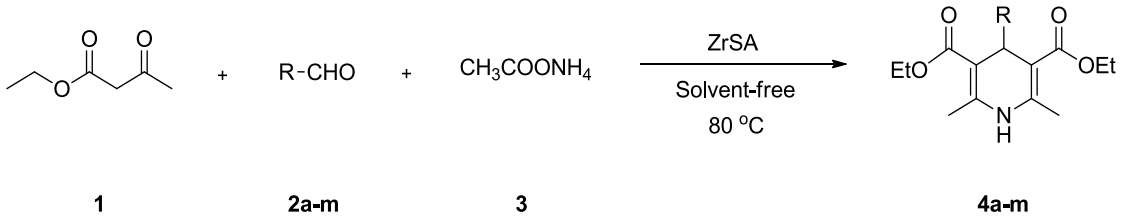
INTRODUCTION
Acid-catalysts areone of the most frequently applied processes in chemical industry, which has been a major area of research interest[i-iii]. Commonly, liquid inorganic acids includingH_2SO_4, HCl and H_3PO_4 are part of the homogeneous acidcatalysts. Despite their application in the wide productionof industrial chemicals, many disadvantagessuch as high toxicity, corrosive nature, hazards inhandling and difficult separation from the products make them not so useful. Furthermore, the synthesis using homogeneous catalysts have major problem of catalyst recovery and reuse. Thesedifficultiesare not in the range of green chemistry.According to these disadvantages, in order to improvedrawbacks of these catalysts, replacement of them bynovel, nontoxic, eco-friendly, recyclable heterogeneouscatalysts with improved efficiency has been the important topicofresearchers during the last decades. Heterogeneouscatalysts showimportant role in many aspects of environmentaland economic in many industrial processes.Theypresented someexcellence including great reactivity, operationalsimplicity, low toxicity, non-corrosive nature and thepotential of the

recyclability[iv-viii]. Furthermore,most of the heterogeneous catalysts show better product selectivity, so that by-product can be easily separated[ix-x].One of the important routes for developing novel heterogeneous catalysts is immobilizing of homogenous precursors on a solidsupport[xi-xiii].The metal oxide nanoparticles such as TiO_2, MgO, Al_2O_3, and ZnO are reported as useful heterogeneous catalyst agents in thesynthesis of organic compounds[xiv-xvi]. Nano zirconia (ZrO_2) is one of the most important metal oxide nanoparticles with high surface area, mechanical strength and thermal stability which has widely application in chemical industry especially as catalyst[xvii-xix].

1,4-Dihydropyridines (DHPs) are an important class oforganic compounds which were synthesized *via*Hantzsch reaction includes the condensation of aldehydes, ammonium acetate, and ethyl acetoacetate, as primary reagents[xx].Some literatures demonstrated therapeutic effects of 1,4-DHPs such as calcium channel antagonism[xxi], geroprotection[xxii], and neuroprotection[xxiii]. 1,4-DHPs are excellent starting synthons for antidyslipidemic[xxiv], antiarrhythmic[xxv], antitumor[xxvi], antibacterial and antitubercular[xxvii], antidiabetic[xxviii], anti-HIV[xxix], anticonvulsant[xxx], andantithrombotic[xxxi] effects.

Many synthetic protocols were developed to accelerate the rate of 1,4-DHPs synthesis and to improve the yield. Various Lewis and Brønsted acid catalyst have been utilized in the construction of the 1,4-DHPsskeleton[xxxii-xlvi]. Major drawbacks of these procedures include expensive reagents, use of large amounts of toxic organic solvents, prolonged heating and side reactions. All of these disadvantages make further improvement of the synthesis of such molecules essential. Therefore, the development of a new greener and more convenient method using a new catalyst with high catalytic activity for the synthesis of 1,4-DHPsis highly desirable.

Prompted by these facts and as part of our research program on the development of convenient methods using reusable catalysts for the synthesis of organic compounds[xlvii-lii],we report here the results of our investigation on the application of ZrO_2-SO_3H (ZrSA) nanoparticle as heterogeneous catalyst inthe synthesis of 1,4-DHPs (Scheme 1).



1 **2a-m** **3** **4a-m**

Scheme 1. ZrSA catalyzed synthesis of 1,4-DHPs.

RESULTS AND DISCUSSION

Characterization of the catalyst

For our investigations, the catalyst ZrO_2–SO_3H (ZrSA) was prepared according to the previously published literature procedure[lv]. The ZrSA catalyst was characterized by FT-IR, and pH analysis. The FT-IR spectrum of the nano-ZrO_2 and ZrSAare shown in Fig. 1(1) and (2), respectively. In Fig. 1(1), the characteristic vibrational bands of the Zr–O bond at 576 and 752 cm^{-1}, as well as band belonging to the Zr–OH group at 1627 cm^{-1}. The FT-IR spectrum of the catalyst also contained absorbance band at 3421 cm^{-1}, which indicated the presence of water. These observations confirm the structure of nano-ZrO_2 and areconsistent with the previously reported evidence[lv]. The FT-IR spectrum of the ZrSA catalyst prepared in the current study (Fig. 1(2)) revealed new bonds at 820-890 and 1060–1180 cm^{-1} which are related to the O=S=O asymmetric and symmetric stretching vibration and S–O stretching vibration of the sulfonic groups (-SO_3H), respectively. The appeared broad band around

2700–3600 cm^{-1} related to the OH stretching absorption of the SO_3H group. All these specifications acknowledge nano-ZrO_2 structurethat has functionalized with sulfonic acid groups. The density of the SO_3H groups was measured using NaOH (0.1 N) as titrant by acid-base potentiometric titration. The amount of SO_3H in the catalyst was 2.46 mmol/g.

Evaluation of catalytic activity of ZrSA in the synthesis of 1,4-DHPs

In the effort to develop an efficient and environmentally benign method for synthesis of 1,4-DHPs we initiated our studies by adding a catalytic amount of ZrSAto a mixture of ethyl acetoacetate (2 mmol), 4-chlorobenzaldehyde (1 mmol), and ammonium acetate (1 mmol), as model reaction in different solvents such as EtOH, H_2O, MeOH, CH_3CN, CH_2Cl_2, CH_3CO_2Et, and also under solvent-free conditions (Table 1). We were pleased to see that the reaction was efficiently catalyzed by ZrSA under solvent-free conditions at elevated temperature leading to a high yield of product **4d**. The reaction conditions were then optimized by conducting the reaction at different temperatures and using different amounts of catalyst. Low yield of the product was obtained in the absence of the catalyst at 80 °C after 120 min (entry 1) indicating that the catalyst is necessary for the reaction. The best result was obtained when the reaction was run at 80 °C in the presence of 0.1 g ZrSAunder solvent-free conditions (entry 15).

Table 1. Synthesis of compound **4d** in the presence of the ZrSA nanoparticle as catalyst under different reaction conditions

Entry	Catalyst amount (g)	Solvent	T (°C)	Time (min)	Yield (%)
1	-----	-----	80	120	17
2	0.02	-----	60	80	42
3	0.02	-----	80	75	49
4	0.02	-----	100	75	48
5	0.04	-----	60	70	50
6	0.04	-----	80	68	54
7	0.04	-----	100	70	54
8	0.06	-----	60	56	61
9	0.06	-----	80	45	70
10	0.06	-----	100	55	69
11	0.08	-----	60	37	78
12	0.08	-----	80	32	86
13	0.08	-----	100	35	84
14	0.10	-----	60	20	89
15	0.10	-----	80	15	96
16	0.10	-----	100	18	94
17	0.12	-----	60	15	90
18	0.12	-----	80	15	95
19	0.12	-----	100	17	92
20	0.10	EtOH	Reflux	120	55
21	0.10	MeOH	Reflux	120	50
22	0.10	CH_2Cl_2	Reflux	120	41
23	0.10	CH_3CN	Reflux	120	49
24	0.10	H_2O	Reflux	120	63
25	0.10	CH_3CO_2Et	Reflux	120	60

Reaction conditions: ethyl acetoacetate**1** (2 mmol), 4-chlorobenzaldehyde **2d** (1 mmol), and ammonium acetate **3** (1 mmol).

*Isolated yields.

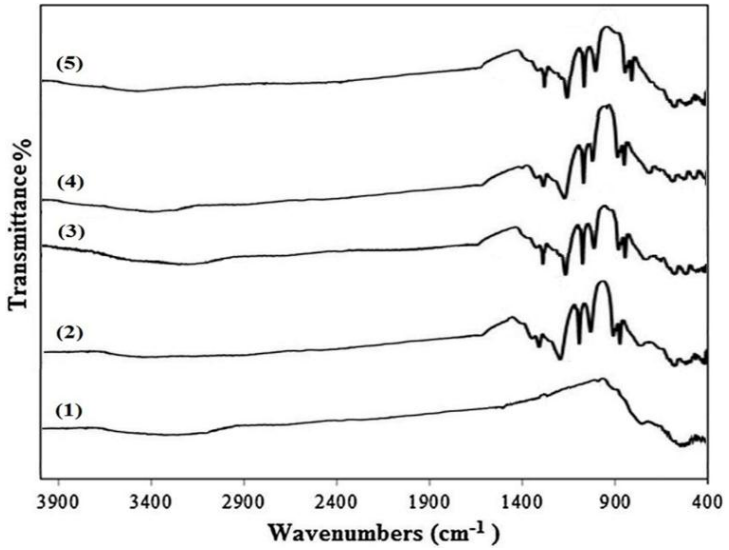


Fig. 1.FT-IR spectra of ZrO_2 (1), fresh catalyst ZrSA ((2), first run), and recovered catalysts (3-5)

Thereafter, the applicability of the method was evaluated for the synthesis of other 1,4-DHPs using a wide range of substituted aliphatic/aromatic aldehydes (Table 2). ZrSA nanoparticle efficiently catalyzed the reactions, giving the desired products **4a-m** in high yields over relatively short reaction times. Easy separation of obtained products from the catalyst makes this method useful for the synthesis of 1,4-DHPs. Purity checks with melting points, TLC, and the ^{1}H NMR spectroscopic data reveal that only one product is formed in all cases and no undesirable side-products are observed. The structures of all products were characterized by IR spectroscopy and a comparison of their melting points with those of the authentic samples. The structures of all known products **4a-4m** were deduced from their ^{1}H NMR and FT-IR spectral data and a comparison of their melting points with those of authentic samples. For example, as shown in Fig. 2, the ^{1}H NMR spectrum of **4e** in $CDCl_3$ showed sharp singlet at δ 1.24 ppm related to two methyl groups, a multiplet at δ 4.05–4.20 ppm for diastereotopic protons in two methylene groups, a singlet signal at δ 4.99 ppm for methine group as well as the signals in the aromatic region due to 4 aromatic protons, indicating the formation of the compound **4e**.

Table 2. ZrSA nanoparticle catalyzed synthesis of 1,4-DHPs [a].

Entry	R	Product[b]	Time /min	Isolated Yield/ %	m.p. (°C)	
					Found	Reported
1	Ph	**4a**	12	94	156-158	156-158[xxxv]
2	4-MeC_6H_4	**4b**	16	95	135-137	136-138[xl]
3	4-$MeOC_6H_4$	**4c**	13	96	160-161	159-160[xxxv]
4	4-ClC_6H_4	**4d**	15	96	147-149	148-150[xxxv]
5	4-FC_6H_4	**4e**	13	97	147-149	147-149[xxxvii]
6	4-BrC_6H_4	**4f**	14	95	160-162	162-164[xl]
7	3-BrC_6H_4	**4g**	13	91	164-166	162-164[lvi]
8	4-$O_2NC_6H_4$	**4h**	12	93	133-135	130-132[xxxviii]
9	3-$O_2NC_6H_4$	**4i**	15	94	163-165	162-164[xxxvi]
10	4-HOC_6H_4	**4j**	19	92	229-231	228-231[xxix]
11	2-thienyl	**4k**	12	97	171-172	172-174[xxix]
12	n-propyl	**4l**	16	91	110-112	110-112[lvii]
13	Et	**4m**	16	90	109-111	110-112[lvii]

[a]**Reaction conditions:** ethyl acetoacetate **1** (2 mmol), an aliphatic\aromatic aldehyde **2a-2m**(1 mmol), ammonium acetate 3 (1 mmol),) andZrSA(0.1 g) at 80 °C under solvent-free conditions..
[b]All the products were characterized according to their FT-IR and ^{1}H NMR spectral data and comparison of their melting points with those of authentic samples.

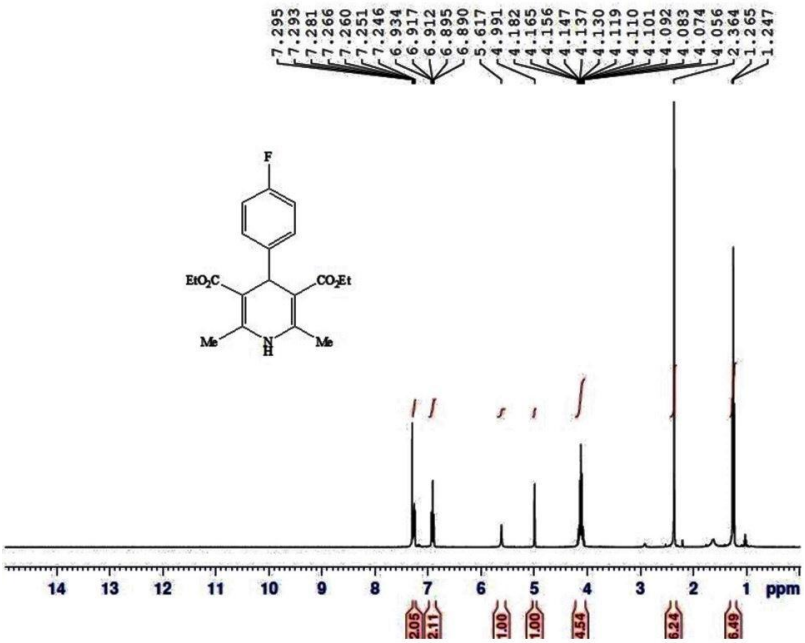


Fig. 2. The ^{1}H NMR spectrum of compound **4e** in $CDCl_3$ solvent.

We compared the results obtained using ZrSA as catalyst with previously reported for results for the synthesis of 1,4-DHPs in the presence of various catalysts (Table 3). Our reaction conditions showed shorter reaction times than all the other conditions and gave high yields of the desired products.

Table 3. Comparison of the efficiencies of different catalysts for the synthesis of 1,4-DHPs

Catalyst	Conditions			Time (min)	Yield (%)	Ref.
	Solvent	T/°C	Other			
TMSCL-NaI	CH_3CN	r.t	-----	360-480	73-80	xxvii
VB_1	-----	r.t	-----	40	80-94	xxviii
SiO_2 -$NaHSO_4$	-----	r.t	-----	300-480	75-90	xxix
PEG-400	-----	90	-----	240-420	75-95	xxx
silica sulfuric acid	-----	r.t	-----	15-45	90-97	xxxi
$CeCl_3$_7H2O	CH_3CN	r.t	-----	180-360	61-94	xxxii
Salicylic Acid	-----	80	-----	120	64-89	xxxiii
Iodine (I_2)	-----	40	-----	45-300	64-89	xxxiv
PPh_3	EtOH	reflux	-----	120-300	72-95	xxxv
t-BuOK	-----	60	-----	120-600	23-84	xxxvi
Cellulose sulfuric acid	-----	100	-----	120-300	78-92	xxxvii
PDAG-Co	-----	80	-----	360-480	75-99	xxxviii
SiO2 -NaHSO4	-----	r.t	-----	300-480	75-90	xxxix
TBAHS	-----	80	-----	30-90	90-98	xl
[PS-IM(CH2)4SO3H][HSO4]	EtOH	reflux	-----	120-210	80-95	xli
ZrSA	-----	r.t	-----	12-19	90-97	This work

We also used the model reaction to evaluate the reusability of the ZrSA catalyst. After completion of the reaction, the catalyst was recovered as described in the experimental section. The separated catalyst was washed with hot ethanol and subsequently dried at 50 °C

under vacuum for 1 h before being reused in a similar reaction. We found that the catalyst could be used at least four times with only a slight reduction in activity (Fig. 3). Furthermore, the FT-IR spectra of the recovered catalysts (Fig. 1(3–5)) were almost identical to the spectrum of the fresh catalyst (Fig. 1(2)), indicating that the structure of the catalyst was unchanged by the reaction.

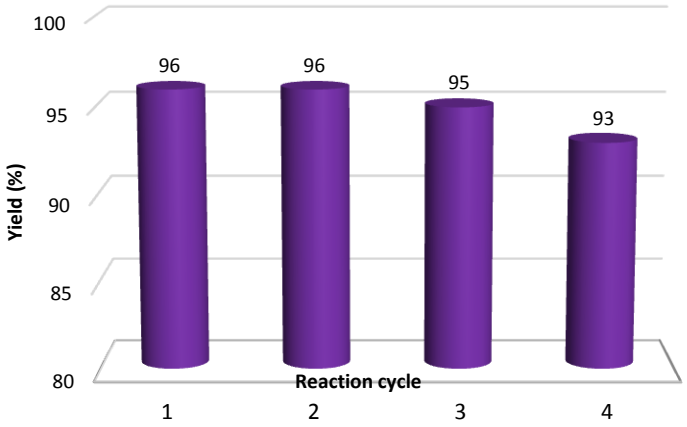
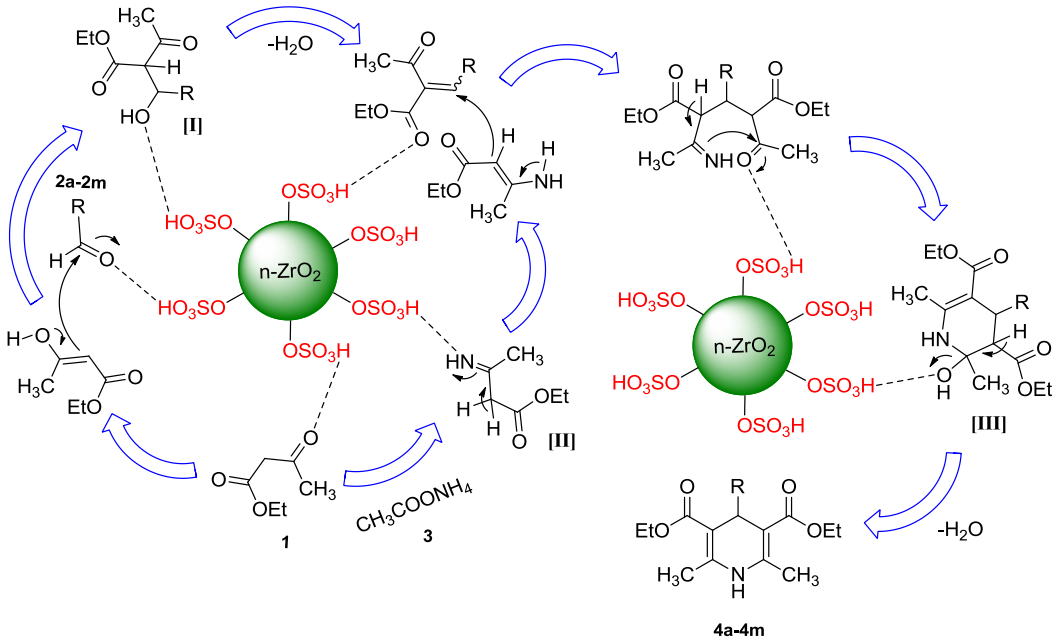


Fig. 3. Effect of recycling on catalytic performance of ZrSA in the synthesis of **4d** in model reaction

Plausible mechanism for this reaction may proceed as depicted in Scheme 2. ZrSA could act as Brönsted acid and therefore promote the necessary reactions. The catalyst would play a significant role in increasing the electrophilic character of the electrophiles in the reaction. According to this mechanism, the ZrSA catalyst facilitates the formation of intermediates I, II, and III. Under these conditions, however, attempts to isolate the proposed intermediates failed even after careful monitoring of the reactions.



Scheme 2. Plausible mechanism for the ZrSA-catalyzed formation of 1,4-DHPs.

EXPERIMENTAL

All chemicals were available commercially and used without additional purification. Zirconium oxide (ZrO_2) was purchased from Aldrich. Melting points were recorded using a Stuart SMP3 melting point apparatus. The FT-IR spectra of the products were obtained with KBr disks, using a Tensor 27 Bruker spectrophotometer. The ^{1}H NMR spectra were recorded using Bruker 400 and 500 spectrometers.

General experimental procedure for the synthesis of 1,4-DHPs 4a-4m catalyzed by ZrSA

A mixture of ethyl acetoacetate **1** (2 mmol), an aldehyde **2a-2m** (1 mmol), ammonium acetate **3** (1 mmol), and ZrSA (0.1 g) as catalyst was heated in the oil bath at 80 °C for 12–19 min. The reaction was monitored by TLC. Upon completion of the transformation, hot ethanol was added and the catalyst removed by filtration under hot conditions. The catalyst was washed with a small portion of hot ethanol. After cooling, the combined filtrate was allowed to stand at room temperature. The precipitated solid was collected by filtration, and recrystallized from ethanol to give compounds **4a-4m** in high yields.

FT-IR and ^{1}H NMR data

Diethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (4a) FT-IR (ν, cm^{-1} KBr disc): 3343, 3059, 2980, 1683, 1649, 1491, 1375, 1215, 1161, 827; ^{1}H NMR (500 MHz, $CDCl_3$): δ1.24 (t, *J* = 7.2 Hz, 6H,2CH_3), 2.36 (s, 6H, 2CH_3), 4.06-4.19 (m, 4H, 2CH_2, diastereotopic protons), 5.03 (s, 1H, CH), 5.57 (s br., 1H, NH), 7.10-7.35 (m, 5H, aromatic CH).

Diethyl 2,6-dimethyl-4-(*p*-tolyl)-1,4-dihydropyridine-3,5-dicarboxylate (4b) FT-IR (ν, cm^{-1}KBr disc):3336, 3069, 2959, 1651, 1606, 1492, 1398, 1366, 1222, 1146; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.26 (t, *J* = 7.1 Hz, 6H,2CH_3), 2.31 (s, 3H, CH_3), 2.36 (s, 6H, 2CH_3), 4.05-4.18 (m, 4H, 2CH_2, diastereotopic protons), 4.99 (s, 1H, CH), 5.60 (s br., 1H, NH), 7.04 (d, *J* = 7.8 Hz, 2H, aromaticCH), 7.20 (d, *J* = 7.8 Hz, 2H, aromatic CH).

Diethyl 4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4c) FT-IR (ν, cm^{-1}KBr disc):3342, 3089, 2984, 1689, 1650, 1509, 1490, 1372, 1338, 1210, 1140, 1031, 834; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.26 (t, *J* = 7.1 Hz, 6H,2CH_3), 2.36 (s, 6H, 2CH_3), 3.79 (s, 3H, OCH_3), 4.05-4.20 (m, 4H, 2CH_2, diastereotopic protons), 4.96 (s, 1H, CH), 5.58 (s br., 1H, NH), 6.78 (d, *J* = 8.6 Hz, 2H, aromatic CH), 7.23 (d, 2H, *J* = 8.6 Hz, aromatic CH).

Diethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4d) FT-IR (ν, cm^{-1}KBr disc): 3358, 3094, 2987, 1696, 1651, 1487, 1334, 1213, 1118, 1094, 843; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.25 (t, *J* = 7.1 Hz, 6H,2CH_3), 2.36 (s, 6H, 2CH_3), 4.05-4.18 (m, 4H, 2CH_2, diastereotopic protons), 4.99 (s, 1H, CH), 5.66 (s br., 1H, NH), 7.20 (d, *J* = 8.3 Hz, 2H, aromatic CH), 7.24 (d, *J* = 8.3 Hz, 2H, aromatic CH).

Diethyl 4-(4-fluorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4e) FT-IR (ν, cm^{-1}KBr disc): 3343, 3067, 2985, 1687, 1652, 1489, 1334, 1211, 1123, 1091, 866; ^{1}H NMR (400 MHz, $CDCl_3$):δ1.24 (t, *J* = 7.2 Hz, 6H,2CH_3), 2.36 (s, 6H, 2CH_3), 4.05-4.20 (m, 4H, 2CH_2, diastereotopic protons), 4.99 (s, 1H, CH), 5.68 (s br., 1H, NH), 6.91 (t, *J* = 8.4 Hz, 2H, aromatic CH), 7.26 (dd, *J*= 8.2, 6.0 Hz, 2H, aromatic CH).

Diethyl 4-(4-bromophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4f) FT-IR (ν, cm^{-1}KBr disc): 3359, 3097, 2985, 1691, 1657, 1484, 1369, 1333, 1212, 1169, 1118, 1012, 845; ^{1}H NMR (500 MHz, $CDCl_3$): δ1.25 (t, *J* = 7.1 Hz, 6H, 2CH_3), 2.36 (s, 6H, 2CH_3), 4.05-4.18 (m, 4H, 2CH_2, diastereotopic protons), 4.98 (s, 1H, CH), 5.61 (s br., 1H, NH), 7.19 (d, *J* = 8.4 Hz, 2H, aromatic CH), 7.35 (d, *J* = 8.4 Hz, 2H, aromatic CH).

Diethyl 4-(3-bromophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4g) FT-IR (ν, cm^{-1}KBr disc): 3325, 3084, 2979, 1707, 1663, 1490, 1378, 1337, 1219, 1091, 1054,

1027, 852; ^{1}H NMR (400 MHz, $CDCl_3$): δ1.26 (t, *J* = 7.1 Hz, 6H, $2CH_3$), 2.35 (s, 6H, $2CH_3$), 4.07-4.22 (m, 4H, $2CH_2$, diastereotopic protons), 4.95 (s, 1H, CH), 5.69 (s br., 1H, NH), 7.10 (t, *J* = 7.8 Hz, 1H, aromatic CH), 7.20-7.26 (m, 2H, aromatic CH), 7.44 (t, *J* = 1.8 Hz, 1H, aromatic CH).

Diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (4h)FT-IR (ν, cm^{-1}KBr disc):3345, 3090, 2991, 1706, 1645, 1525, 1487, 1347, 1213, 1118, 1051, 879; ^{1}H NMR (500 MHz, $CDCl_3$, ppm):δ1.25 (t, *J* = 7.1 Hz, 6H,$2CH_3$), 2.39 (s, 6H, $2CH_3$), 4.05-4.18 (m, 4H, $2CH_2$, diastereotopic protons), 5.13 (s, 1H, CH), 5.72 (s br., 1H, NH), 7.48 (d, *J* = 8.7 Hz, 2H, aromatic CH), 8.11 (d, *J* = 8.7 Hz, 2H, aromatic CH).

Diethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (4i)FT-IR (ν, cm^{-1}KBr disc):3346, 3091, 2991, 1706, 1646, 1525, 1488, 1446, 1371, 1348, 1301, 1214, 1119, 1052, 879; ^{1}H NMR (400 MHz, $CDCl_3$):δ1.25 (t, *J* = 7.1 Hz, 6H,$2CH_3$), 2.40 (s, 6H, $2CH_3$), 4.05-4.20 (m, 4H, $2CH_2$, diastereotopic protons), 5.13 (s, 1H, CH), 5.75 (s br., 1H, NH), 7.40 (t, *J* = 7.9 Hz, 1H, aromatic CH), 7.67 (dt, *J* = 7.7, 1.3 Hz, 1H, aromatic CH), 8.03 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H, aromatic CH), 8.16 (t, *J* = 1.9 Hz, 1H, aromatic CH).

Diethyl 4-(4-hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4j)FT-IR (ν, cm^{-1}KBr disc):3417, 3343, 3067, 2985, 1687, 1651, 1489, 1454, 1372, 1245, 1211, 1143, 1091, 883; ^{1}H NMR (400 MHz, $CDCl_3$):δ 1.14 (t, *J* = 7.1 Hz, 6H, $2CH_3$), 2.25 (s, 6H, $2CH_3$), 3.90-4.06 (m, 4H, $2CH_2$, diastereotopic protons), 4.75 (s, 1H, CH), 6.58 (d, J = 8.4 Hz, 2H, aromatic CH), 6.93 (d, *J*= 8.4 Hz, 2H, aromaticCH), 8.73 (s br., 1H, NH or OH), 9.10 (s br., 1H, NH or OH).

Diethyl 2,6-dimethyl-4-(thiophen-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate (4k)FT-IR (ν, cm^{-1}KBr disc): 3344, 3110, 2979, 1692, 1655, 1486, 1369, 1329, 1210, 1129, 1093, 853; ^{1}H NMR (400 MHz, $CDCl_3$):δ1.30 (t, *J* = 7.1 Hz, 6H, $2CH_3$), 2.36 (s, 6H, $2CH_3$), 4.17-4.27 (m, 4H, $2CH_2$, diastereotopic protons), 5.37 (s, 1H, CH), 5.95 (s br., 1H, NH), 6.82 (dt, *J*= 3.2, 0.8 Hz,1H,arom-H), 6.87 (dd, *J*= 5.2, 3.6 Hz,1H,arom-H), 7.08 (dd, *J*= 5.0, 1.2 Hz, 1H, arom-H).

Diethyl 2,6-dimethyl-4-propyl-1,4-dihydropyridine-3,5-dicarboxylate (4l)FT-IR (ν, cm^{-1}KBr disc): 3351, 2956, 1699, 1645, 1491, 1300, 1211, 1160, 1082, 794; ^{1}H NMR (400 MHz, $CDCl_3$, δppm): 0.86 (t, 3H, *J*= 7.1 Hz, CH_3), 1.19-1.34 (m, 4H, $2CH_2$), 1.31 (t, 6H, *J*= 7.2 Hz, $2CH_3$), 2.30 (s, 6H, $2CH_3$), 3.94 (t, 1H, *J*= 5.2 Hz, CH), 4.12-4.29 (m, 4H, $2CH_2$, diastereotopic protons), 5.65 (s br., 1H, NH).

Diethyl 4-ethyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4m)FT-IR (ν, cm^{-1}KBr disc): 3316, 2968, 1699, 1652, 1499, 1369, 1303, 1134, 1073, 882; ^{1}H NMR (400 MHz, $CDCl_3$):δ0.78 (t, *J*= 7.4 Hz, 3H, CH_3), 1.32 (t, *J*= 7.0 Hz, 6H, $2CH_3$), 1.35-1.41 (m, 2H, CH_2), 2.32 (s, 6H, $2CH_3$), 3.94 (t, *J*= 5.2 Hz, 1H,CH), 4.12-4.29 (m, 4H, $2CH_2$, diastereotopic protons), 5.48 (s br., 1H, NH).

CONCLUSION

In summary, we showed thatZrSA catalyzed the synthesis of 1,4-DHPs by one-pot,three-component reaction of aliphatic\aromatic aldehydes, ethyl acetoacetate, and ammonium acetate, at 80 °C under solvent-free conditions. The method was relatively fast and high yielding, and the work-up was easy. The catalyst can be recycled after simple handling, and used at least four times without any substantial reduction in its catalytic activity. The procedure is also advantageous in the sense that it is a fast reaction under solvent-free conditions and therefore operates under environmentally friendly conditions.

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